

Lecture 16. Genetic Variation (cont.)

EEB 2245, C. Simon, 23 March 2017

Last time...

- Importance of variation, polymorphisms
- Mendel's laws
- Deviations from Mendelian ratios (genetic and non genetic causes)
- Heritability, plasticity, selection, common garden, genetic assimilation, canalization
- Epigenetic inheritance
- H-W equation, assumptions, terminology, usefulness

This Time..

- Usefulness of Hardy Weinberg
- Early 20th century perception of variation in natural populations
- Importance of Lewontin & Hubby 1966
- Inbreeding
- Gene Flow
- Genetic Drift

Assumptions of Hardy Weinberg

- Diploid population
- No New Mutations
- Random Mating (no inbreeding)
- **“infinite” population size (no drift)**
- **No Migration of alleles**
- No Natural selection (or tight linkage w another gene under selection)
- Only one population has been sampled.

If the H-W equilibrium is temporarily perturbed, and that perturbation is removed, how long will it take the population to return to an equilibrium?

What do we mean by equilibrium?

So why do we care about the H-W equilibrium?

Classical geneticists

- T.H. Morgan and his students (Columbia University, early 1900's) found *Drosophila* variants only rarely.
- Wild type was the common type,
- Variants viewed as rare and deleterious
- Segregation of deleterious recessives would limit numbers of variable loci



History of Evolutionary Biology

- 1900-1920's- Chromosomal basis of inheritance, nature of mutations T.H. Morgan, A. Sturtevant, C. Bridges, and H.J. Muller, *The Mechanism of Mendelian Heredity*. 1915. Nobel 1933.
- 1930's and 40's- The Modern Synthesis
- 1953- Watson, Crick and Franklin. Structure of DNA. Followed by deeper understanding of nature of mutation and inheritance.
- 1960's- Debate on the relative amount of variation in natural populations. Protein gel electrophoresis.
- **Lewontin and Hubby. 1966.**
- 1970's- Debate on the relative importance of selection versus drift. Sanger DNA sequencing
- 1985- PCR- rapid advances in gene sequencing

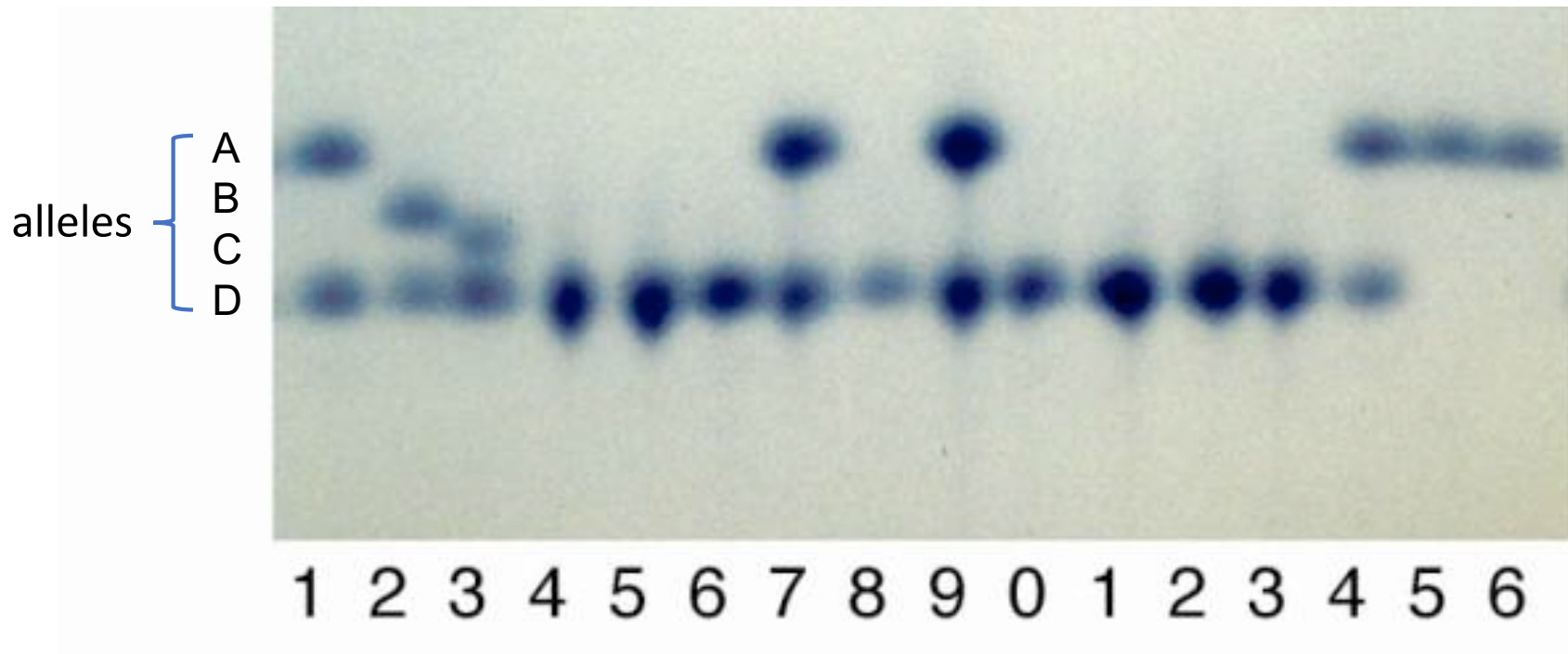
Interaction of Technology and Discovery: gel electrophoresis.

Hubby, J.L. and R.C. Lewontin. 1966. a Molecular approach to the Study of Genic Heterozygosity in Natural Populations. I. the Number of alleles at Different Loci in *Drosophila pseudoobscura*. Genetics 54(2):577-594.

Lewontin, R.C. and J.L. Hubby. 1966a. a Molecular approach to the Study of Genic Heterozygosity in Natural Populations. II. amount of Variation and Degree of Heterozygosity in Natural Populations of *Drosophila pseudoobscura*. Genetics 54(2):595-609.

- allozyme polymorphisms inherited in Mendelian fashion
- Used as “typical of the genome as a whole”
- Could be used to sample variation in natural populations, quickly and efficiently, heterozygotes visible!

Phosphoglucomutase population variation visualized on a gel



One locus, 4 alleles, 12 homozygotes, 6 heterozygotes

Lewontin & Hubby 1966

TABLE 3

Proportion of loci, out of 18, polymorphic and proportion of the genome estimated to be heterozygous in an average individual for each population studied


Population	No. of loci polymorphic	Proportion of loci polymorphic	Proportion of genome heterozygous per individual	Maximum proportion of genome heterozygous
Strawberry Canyon	6	.33	.148	.173
Wildrose	5	.28	.106	.156
Cimarron	5	.28	.099	.153
Mather	6	.33	.143	.173
Flagstaff	5	.28	.081	.120
Average		.30	.115	.155

- 18 protein (enzyme) loci, five populations
- avg. 30% polymorphic (2-6 alleles)
- average fly was heterozygous at 12% of loci
- Population biologists (~1967-1987) population biologists sampled variation in many species

by the mid 1970's...

“Heterozygosity”

Genetic variation at allozyme loci in animals and plants



	Number of species examined	Average number of loci per species	Average proportion of loci	
			Polymorphic per population	Heterozygous per individual
Insects				
Drosophila	28	24	0.529	0.150
Others	4	18	0.531	0.151
Haplodiploid wasps^a	6	15	0.243	0.062
Marine invertebrates	9	26	0.587	0.147
Marine snails	5	17	0.175	0.083
Land snails	5	18	0.437	0.150
Fish	14	21	0.306	0.078
Amphibians	11	22	0.336	0.082
Reptiles	9	21	0.231	0.047
Birds	4	19	0.145	0.042
Rodents	26	26	0.202	0.054
Large mammals^b	4	40	0.233	0.037
Plants^c	8	8	0.464	0.170

(After Selander 1976)

^aFemales are diploid, males haploid

^bHuman, chimpanzee, pigtailed macaque, and Southern elephant seal

^cPredominantly outcrossing species

Heterozygosity

H = 1 minus the proportion of homozygotes

where

p^2 = the frequency of allele “a”

q^2 = the frequency of allele “b”

$$H = 1 - \sum p^2 + q^2$$

For more than two alleles...

$$H \text{ of the population} = 1 - \sum_i p_i^2$$

Where i = all alleles 1 through i

What processes affect variation in natural populations?

Mutations?

Natural selection?

(or tight linkage w another gene under selection)

Gene flow?

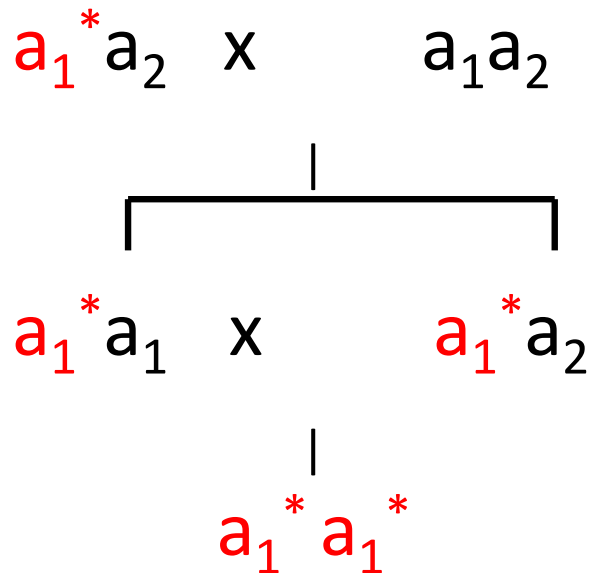
Small population size? and Non-Random Mating?
(inbreeding and/or drift)

Which processes create variation, which
processes destroy variation?

Erosion of Genetic Variability by Two Processes

1. **Inbreeding**- Positive assortative mating leads (makes mating with relatives more likely) → heterozygote deficiency
2. **Drift**- by chance, some individuals will not leave offspring (not mate or offspring will die).

Inbreeding- Mating of relatives



alleles identical by
descent



Inbreeding Depression

- Decrease in fitness associated with inbreeding.
- F = inbreeding coefficient
- Or the probability that an individual has two alleles that are identical by descent.
- Inbreeding can happen in large or small populations.

Hemophilia in

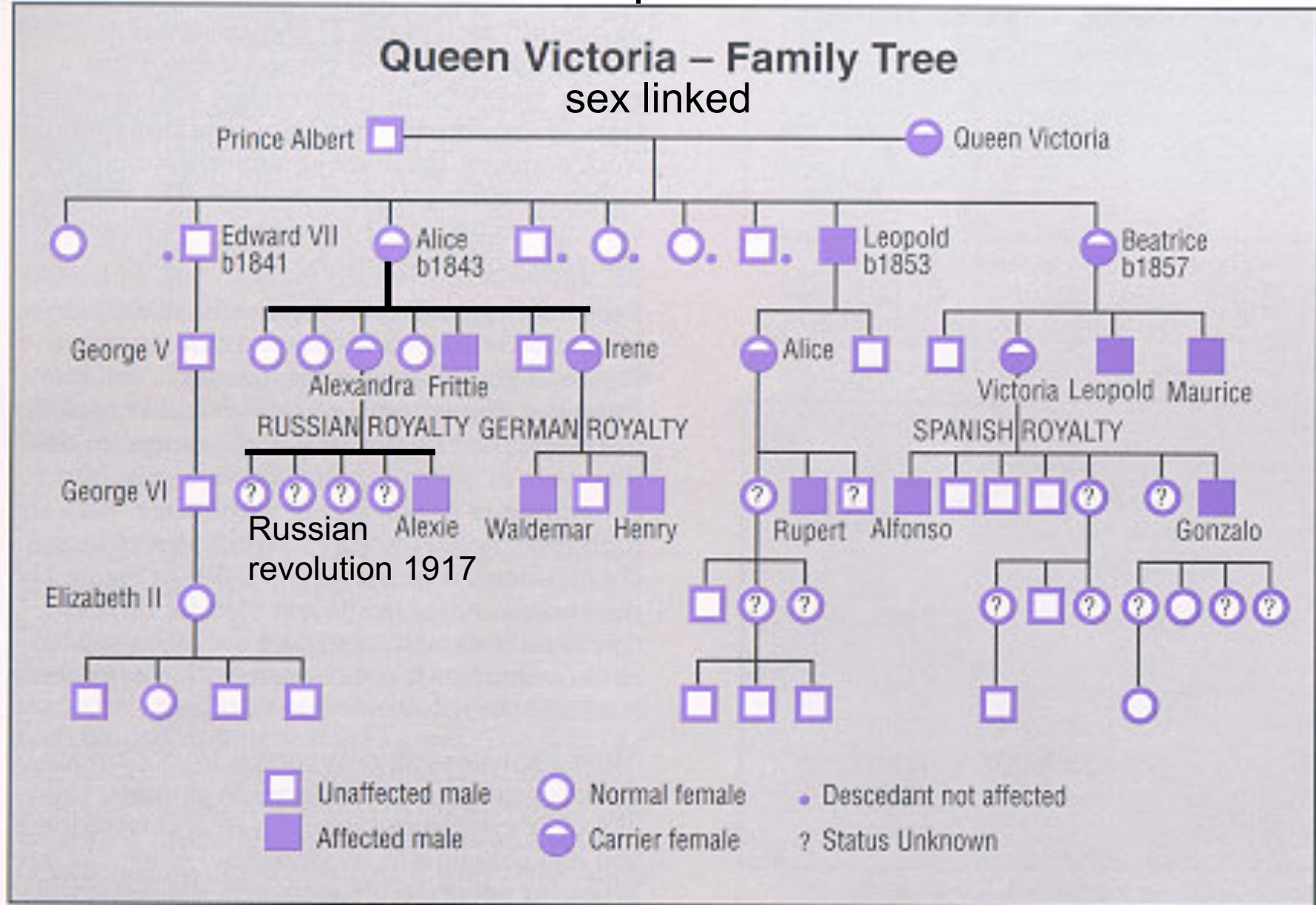
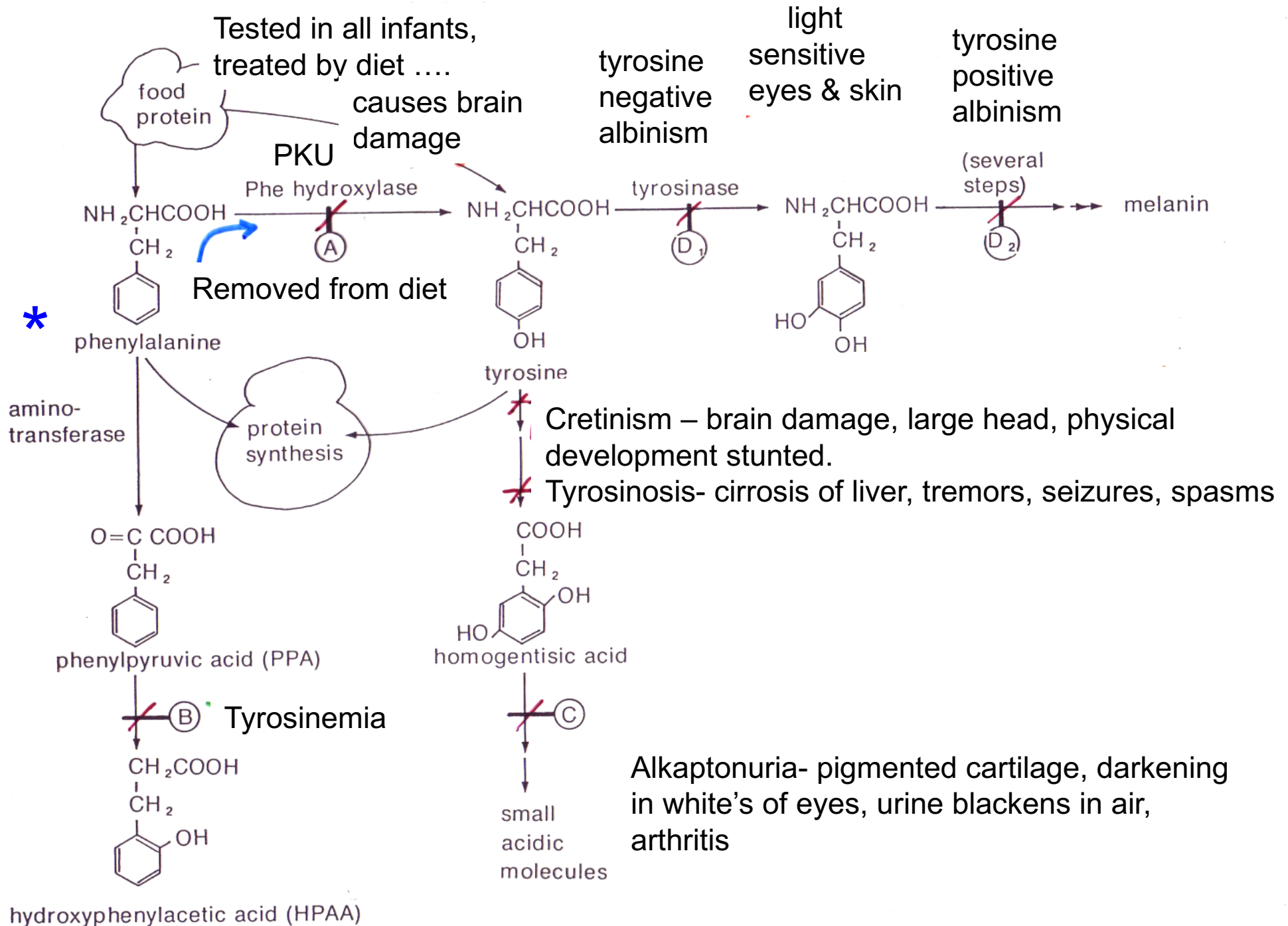


Figure 1. Queen Victoria's family tree.

Inbreeding (cont.)

- Positive assortative mating & mating of relatives increases the probability that recessive alleles will become homozygous & be expressed
- although possible in large populations, more common in small populations.
- Example, metabolic disorders of the melanin pathway



Self Fertilization: the most extreme inbreeding; mating is not random!

- Inbreeding affects all loci equally
- Common in plants
- aa individuals ---> all aa offspring
- bb individuals --> all bb offspring
- ab individuals --> $\frac{1}{4}$ aa, $\frac{1}{2}$ ab, $\frac{1}{4}$ bb
- Each generation % heterozygotes in the population decreases.
- This is the ultimate form of positive assortative mating!

Figure 9.9 Inbreeding. Genotype frequencies observed at 2 loci (B locus and H locus) in a population of selfing *Avena fatua* (oats) compared with those expected under Hardy-Weinberg equilibrium

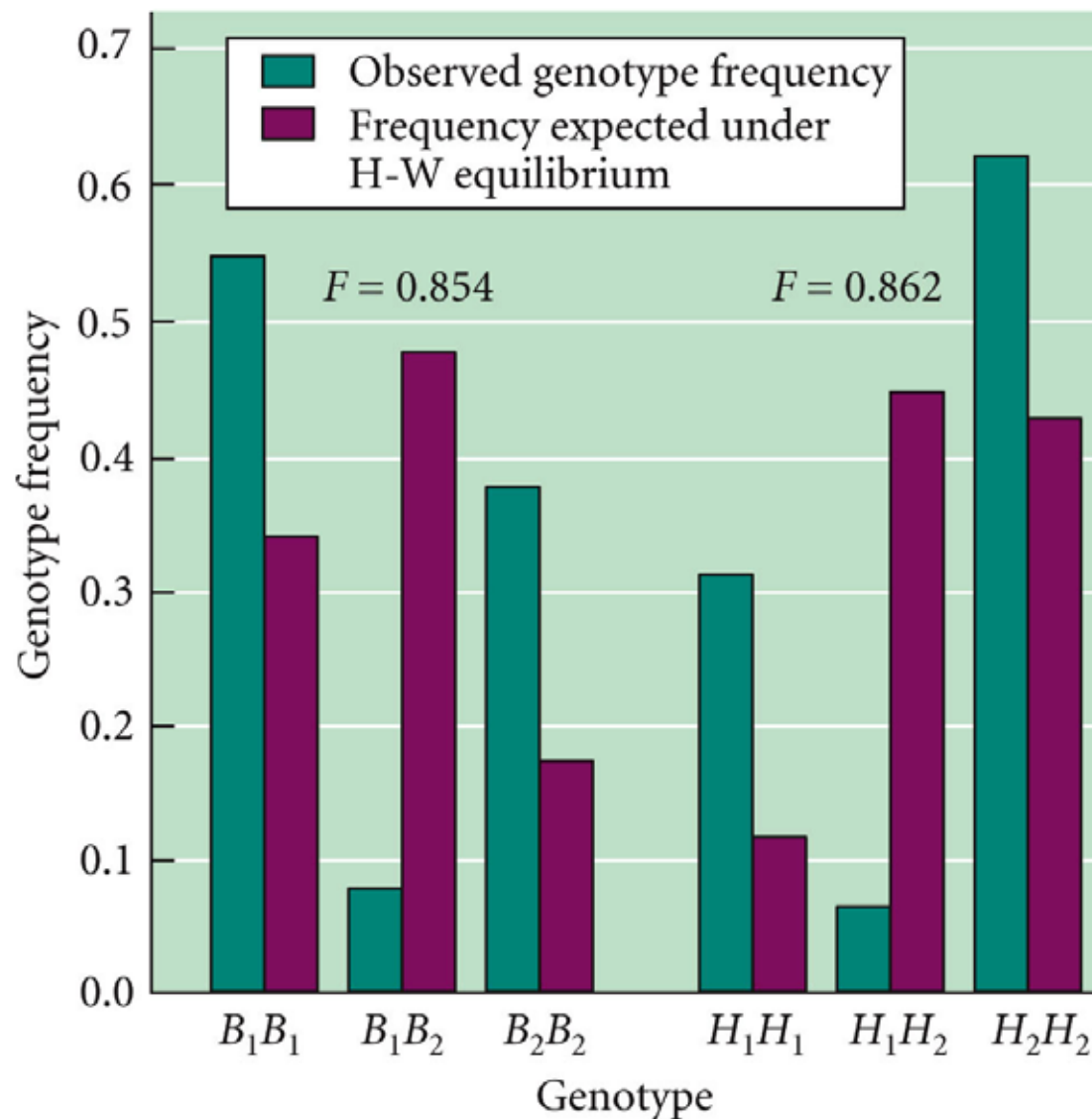
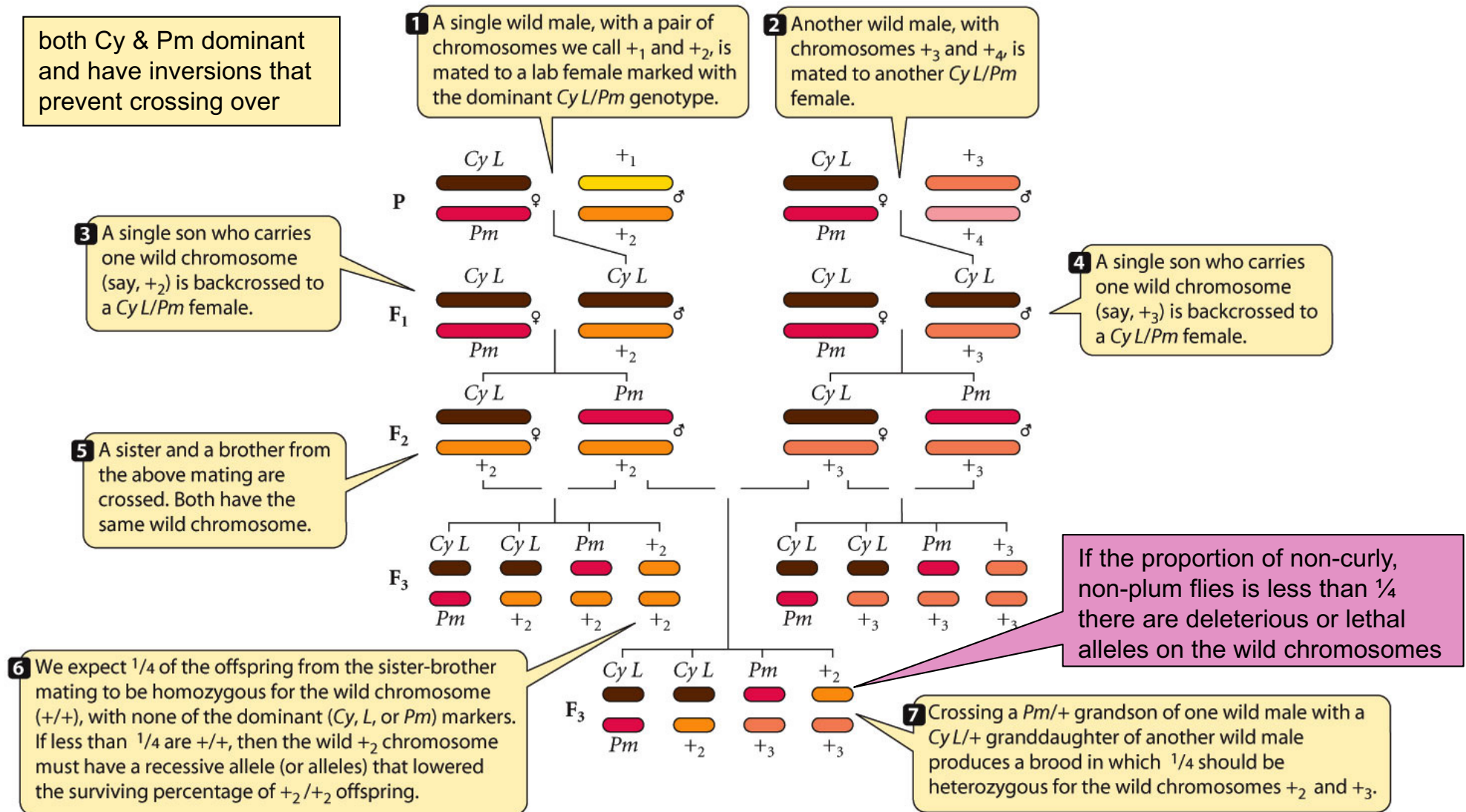


Fig 9.10 Crossing technique for making a chromosome homozygous; to detect recessive deleterious alleles



Lethal & Deleterious alleles are Common

Classic Studies.

- Dobzhansky: Laboratory crosses of *Drosophila pseudoobscura* --> nearly every fly in a population carries a chromosome that if homozygous would substantially reduce prob. survival &/or fertility
- Morton, Crow, Mueller: studies of human marriages btw relatives; average person carries 3-5 recessive lethals (acting between late fetal & adult stages).

Relevance of inbreeding & drift to
conservation biology debated

Glanville Fritillary. Saccheri et al. 1998. Nature 329: 441-442



http://farm1.static.flickr.com/62/178414666_916d0eaa2a.jpg?v=0

42 poplns surveyed in 1,600 dry meadows

Extinction & recolonization common

Metapopln (weak gene flow)

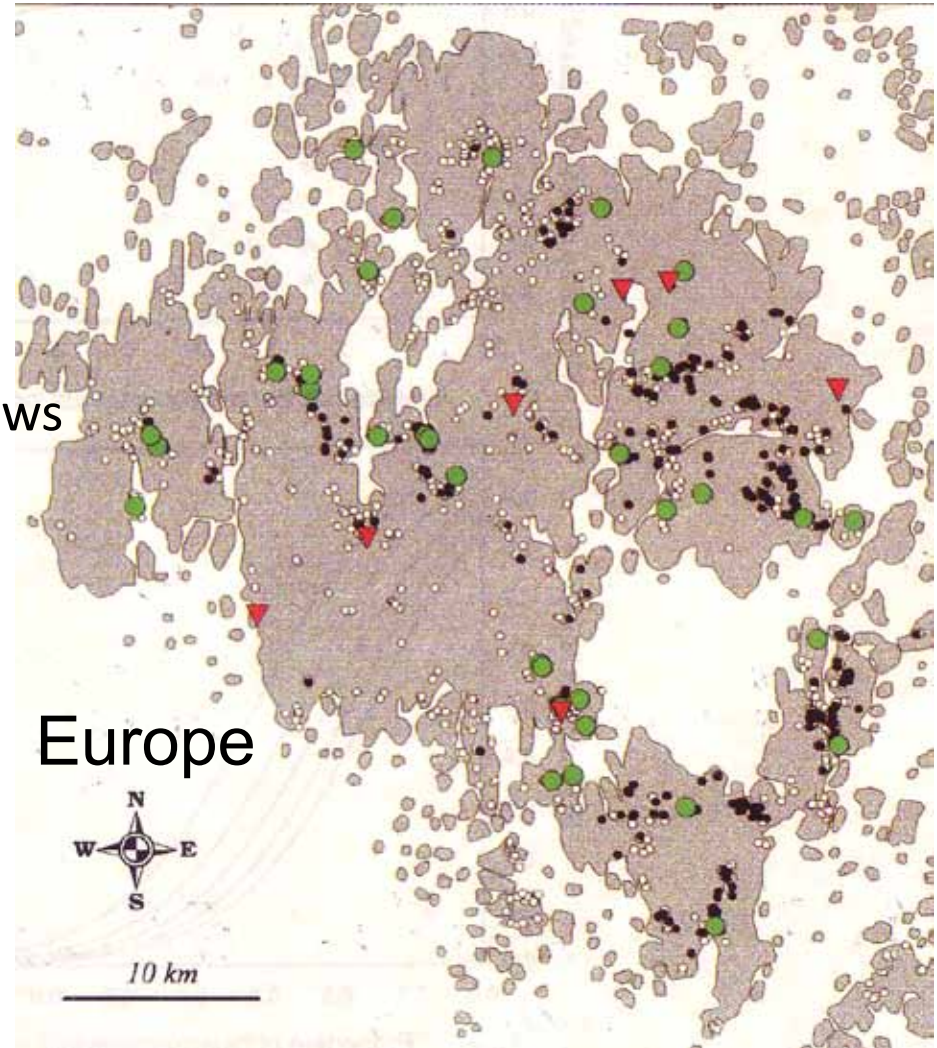
Scored 8 polymorphic allozyme loci

White = all known suitable meadows

black = butterfly larvae present

Green = 35 populations surviving summer

Red = seven poplns. went extinct



Populations w/ less allozyme variability went extinct more often; also measured life history consequences

Spielman et al (2004)

- Analysis of a large literature sample of genetic variability in critically endangered, endangered, and vulnerable species.
- 170 threatened taxa with either allozyme, microsatellite, or minisatellite data available.
- Compared heterozygosity of the 'threatened' species vs heterozygosity of the nearest related non-threatened species.
- Showed threatened species w statistically significantly lower heterozygosity

.

Conservation biological consequences of small populations

- 1) Island populations have lower genetic diversity
- 2) Captive populations show increased risk of extinction via inbreeding
- 3) Wild plants with low and high genetic variability planted in experimental fields showed that more deaths occurred in lower variability plants.
- 4) Sparrows living on an island off the coast of Vancouver have been monitored since 1959. Inbred females showed a significant decrease in reproductive success. After a population crash, immigration from the mainland was shown to restore genetic variability.

Recovery from Inbreeding

Inbred Small Population: Speke's Gazelle rescued from extinction (Templeton & Read, 1984): The promise of purging

<https://www.youtube.com/watch?v=L7L2HfenJK8>



http://image20.weashots.com/21/8/1/81/218080181ayRXml_ph.jpg

D. L. Byers, D. M. Waller. (1999) Do plant populations purge their genetic load? Effects of population size and mating history on inbreeding depression. *annual Review of Ecology and Systematics* 30:479-513



Darwin- grew self-fertilizing morning glories → fewer seeds, stunted seedlings; But-- recovered after several generations inbreeding; no explanation. Line named Hero

Reviewed 52 plant studies

Compared plants with long histories on inbreeding to those free of inbreeding

Only 38% showed purging (selfing-reduced inbreeding depression)

Conclusion: Purging doesn't always work; can be dangerous

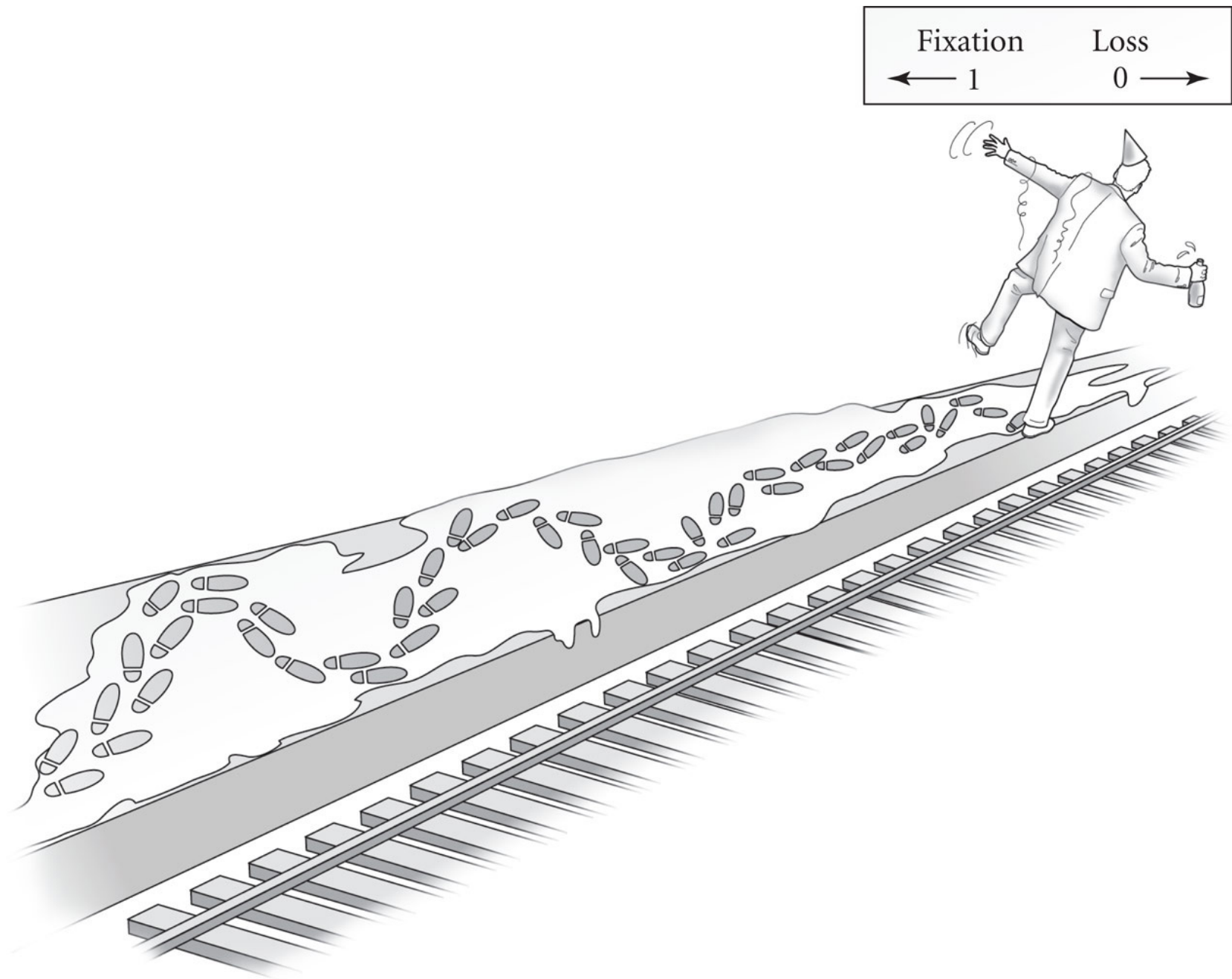
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Genetic Drift



<http://www.geograph.org.uk/photo/3135083>



EVOLUTION 3e, Figure 10.2

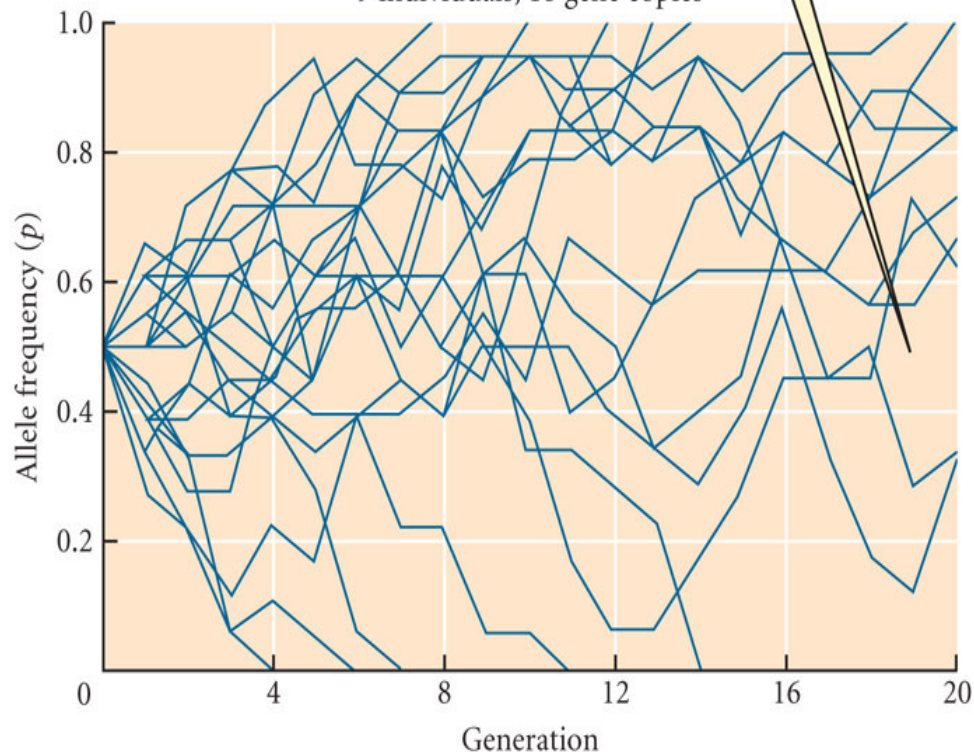
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Small population

(A)

Oscillations are larger, and alleles are more rapidly fixed or lost, in small populations...

9 individuals, 18 gene copies

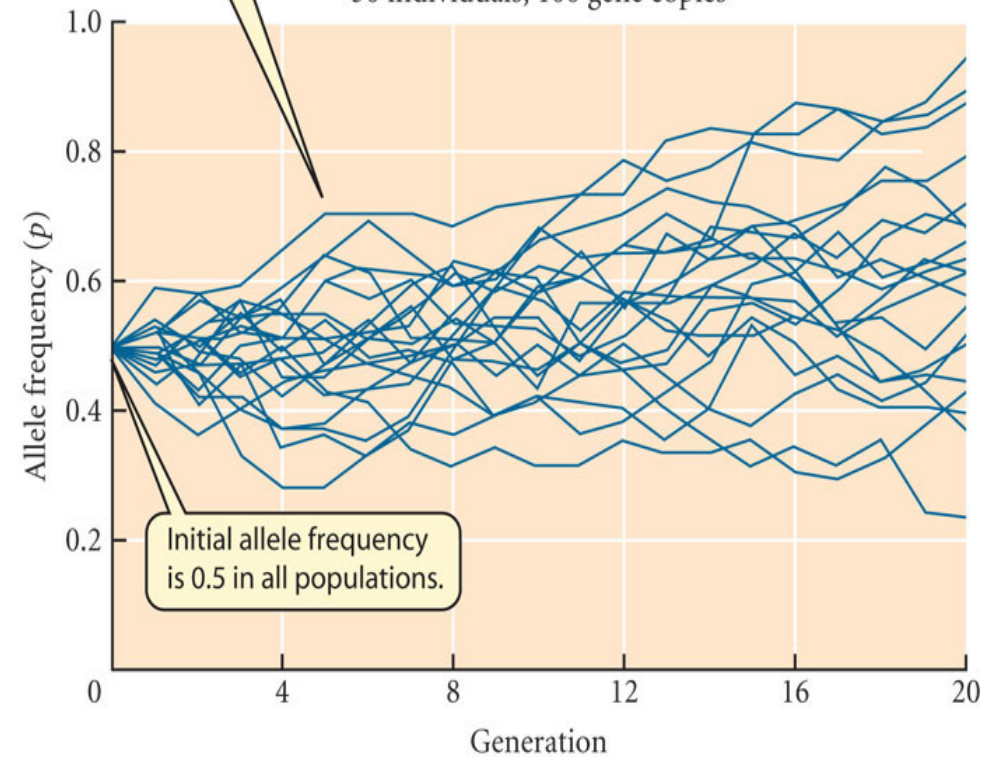


Large population

(B)

...than in larger ones.

50 individuals, 100 gene copies



Initial allele frequency is 0.5 in all populations.

Random genetic drift can result in non-adaptive evolution because one allele is replaced by another (fixed) by chance.

Genetic Drift

The effect of recessive allele freq. on heterozygosity:

allele freq.:

a = 0.5 0.6 0.7 0.8 0.9 “a” fixed

b = 0.5 0.4 0.3 0.2 0.1 “b” lost

Genotype freq. (at H-W equilibrium):

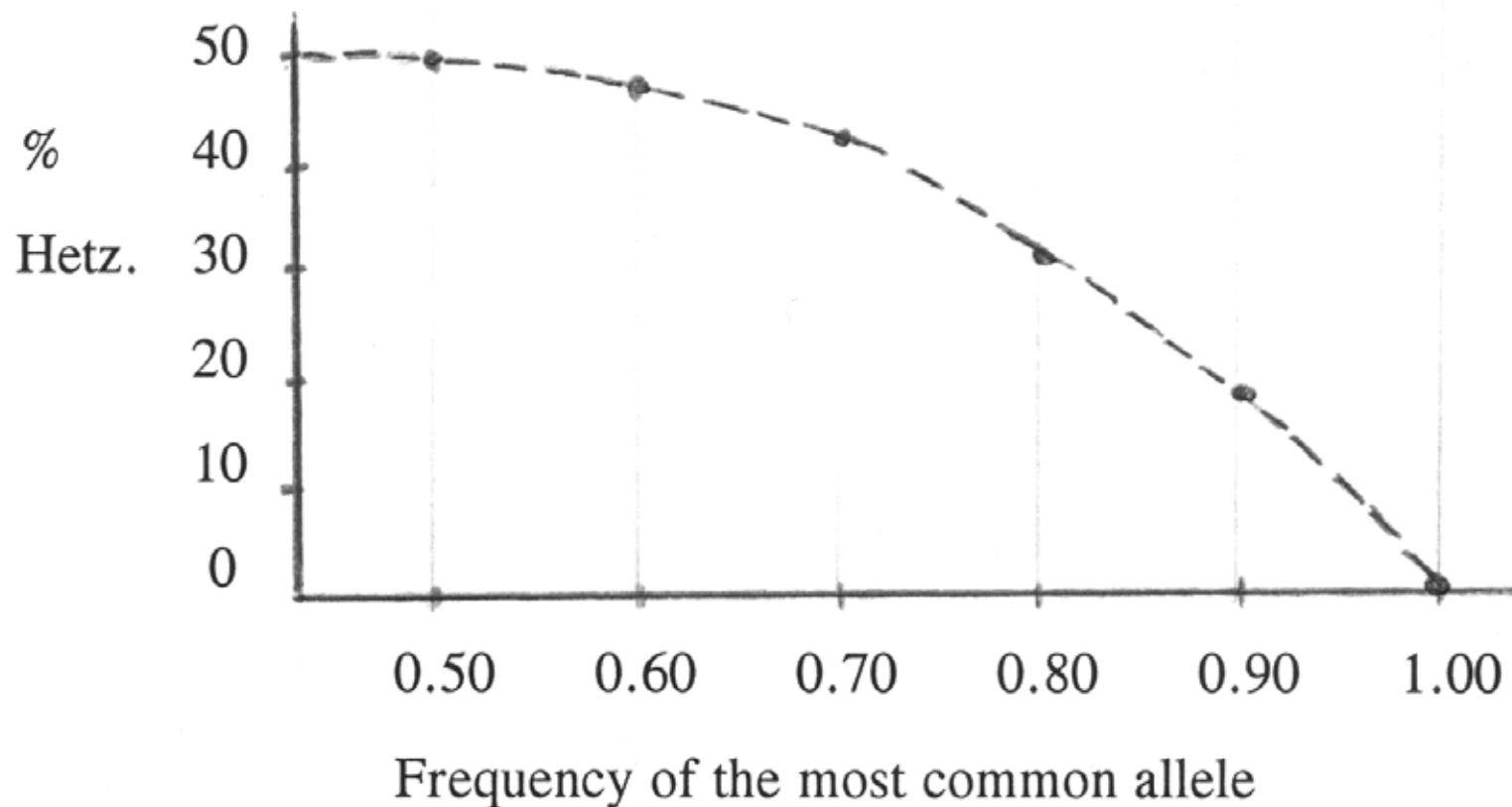
aa = 0.25 0.36 0.49 0.64 0.81

ab = 0.50 0.48 0.42 0.32 0.18

bb = 0.25 0.16 0.09 0.04 0.01

Genetic Drift

Note that as one allele becomes rare, the proportion of heterozygotes (the heterozygosity of the population) declines as a direct consequence



End lecture, 23 March 2017