

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



Plate 8. Some eye colors in *Drosophila melanogaster*. © 1997 C. M. Wallace. An Art Institute of Chicago. In: *Evolution and Ecology*, (1997)

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

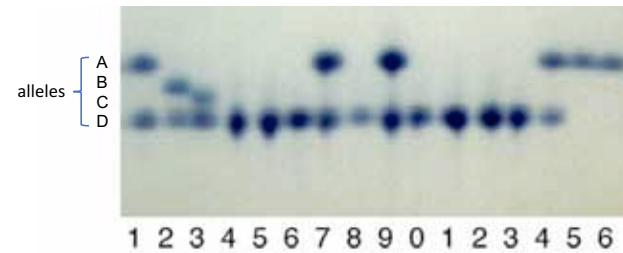
Interaction of Technology and Discovery: gel electrophoresis.

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!

Phosphoglucumutase population variation visualized on a gel



One locus, 4 alleles, 12 homozygotes, 6 heterozygotes

Lewontin & Hubby 1966

TABLE 3
Proportion of loci, out of 11, 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				
<i>Drosophila</i>	28	24	0.529	0.150
Others	4	18	0.531	0.151
Haplodiploid wasps*	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*	4	40	0.233	0.037
Plants†	8	8	0.464	0.170

(After Selander 1976)

*Females are diploid, males haploid

†Human, chimpanzee, pigtailed macaque, and Southern elephant seal

*Predominantly 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?

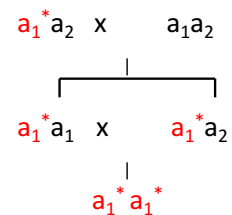
Small population size? and Non-Random Mating?
(inbreeding and/or drift)

Which processes create variation, which
processes destroy variation?

Erosion of Genetic Variability by Two Processes

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

Inbreeding- Mating of relatives



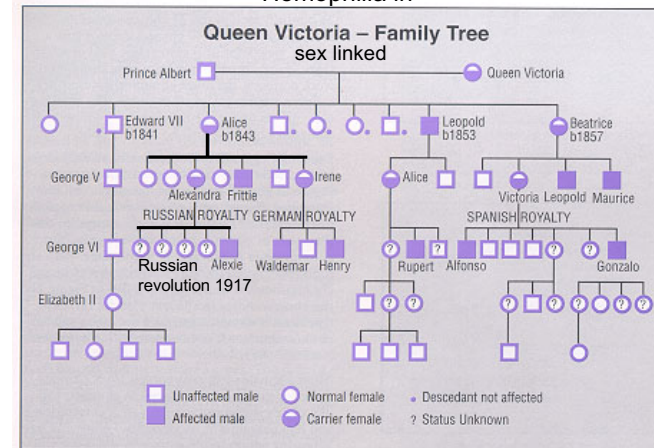
alleles identical by
descent



Inbreeding Depression

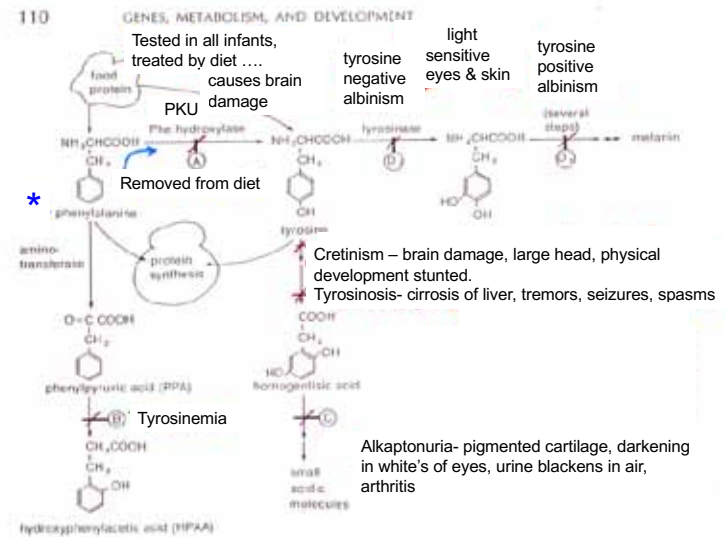
- Decrease in fitness associated with inbreeding.
- F = inbreeding coefficient
- Or the probability that an individual has two alleles that are identical by descent.
- Inbreeding can happen in large or small populations.

Hemophilia in



Inbreeding (cont.)

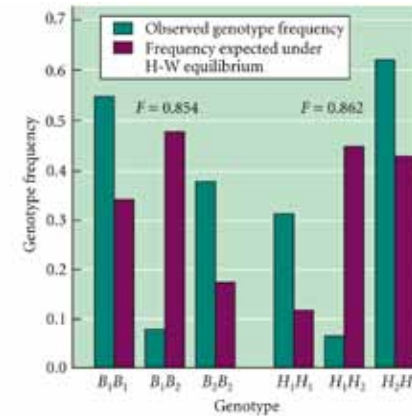
- Positive assortative mating & mating of relatives increases the probability that recessive alleles will become homozygous & be expressed
- although possible in large populations, more common in small populations.
- Example, metabolic disorders of the melanin pathway



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

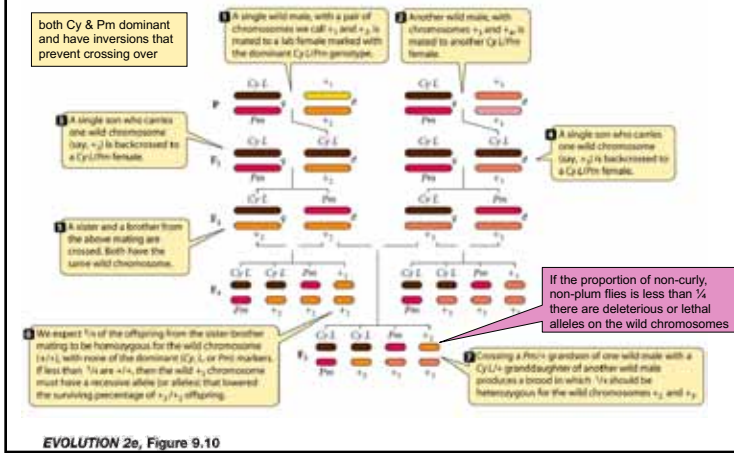
- Inbreeding affects all loci equally
- Common in plants
- aa individuals ---> all aa offspring
- bb individuals --> all bb offspring
- ab individuals --> 1/4 aa, 1/2 ab, 1/4 bb
- Each generation % heterozygotes in the population decreases.
- This is the ultimate form of positive assortative mating!

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



EVOLUTION 2e, Figure 9.9

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



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

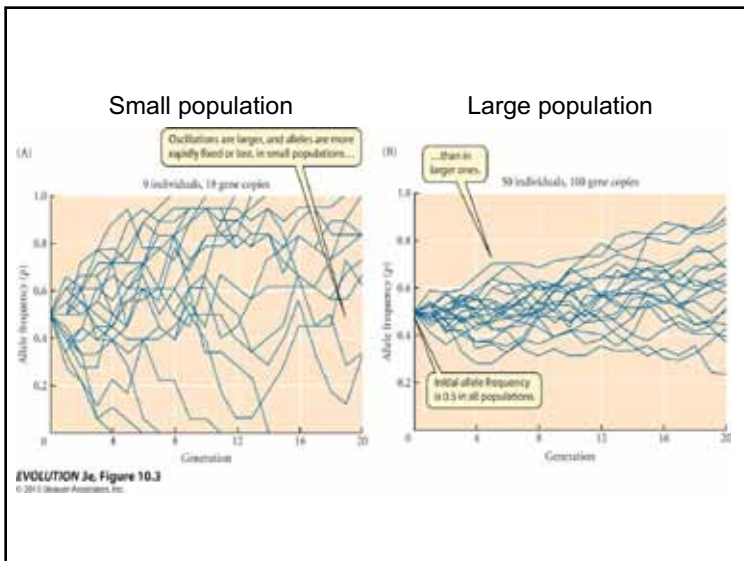
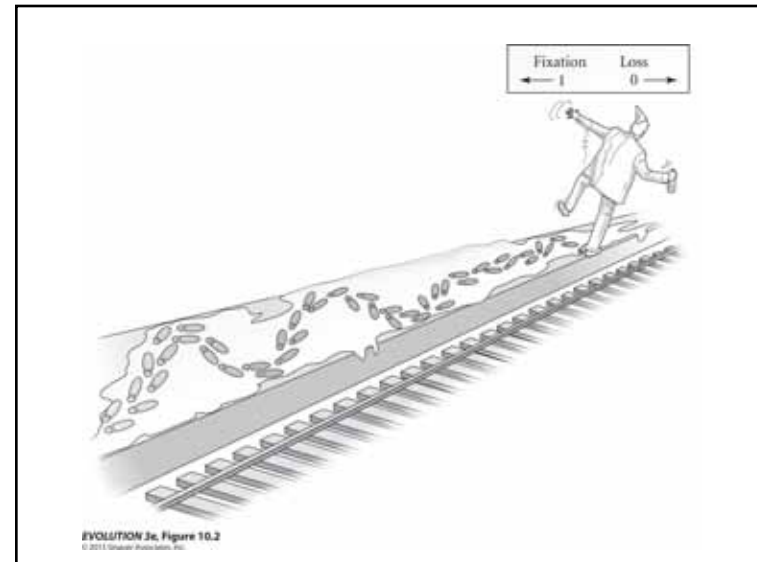
Compared plants with long histories on inbreeding to those free of inbreeding

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

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

Assumptions of Hardy Weinberg

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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):

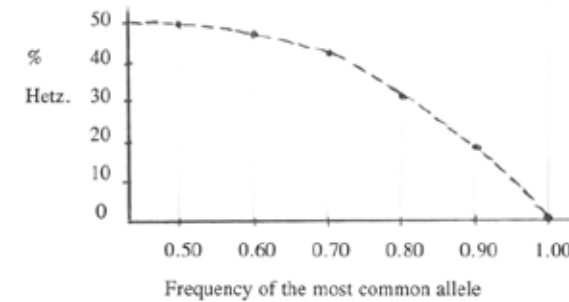
aa = 0.25 0.36 0.49 0.64 0.81

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

Effective Population Size, N_e

Reasons for N_e not equal to census size

1) Some males or females don't mate.

- a) Dominant males, harems (or sex ratio not 1:1)
- b) Sneaky males may achieve secret matings
- c) Observed matings may be thwarted.

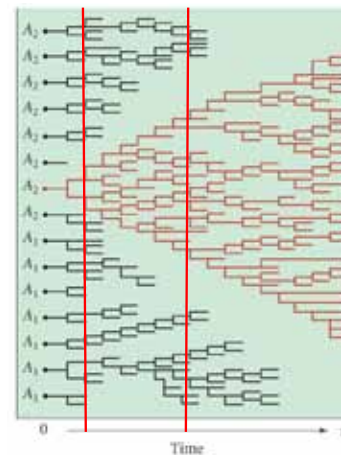
Consequence: Some individuals leave fewer progeny than others (increases inbreeding)

Video clips: Hedge sparrow from BBC, David Attenborough's "Life of Birds" series, "Finding Partners" <http://www.bbc.co.uk/programmes/p007tx02>

Elephant seal territoriality <https://www.youtube.com/watch?v=JrzenOfcmBo>

See also: Sea lion territoriality <https://www.youtube.com/watch?v=pzrj0Gye4Ws>

Coalescence & inbreeding



Initially 15 copies. Most go extinct by chance.
Average relatedness increases

At time "t" all copies "descend from" or "coalesce to" a single ancestor

Smaller poplins, faster coalescence

Time to coalescence is $2N$ generations, where N = popln size

Additional Reasons for N_e not equal to census size—

- 2) Sex ratio different from 1 : 1
- 3) Natural selection causing progeny number to vary among genotypes
- 4) Given overlapping generations, offspring may mate with parental generation
- 5) Fluctuations in population size over time

Drift generally depletes genetic variation

However, in certain circumstances drift can actually enhance genetic variation.

Applications of genetic drift to conservation Biology

Conservation Problem:

You are a population biologist and you are called upon to help save an endangered species that if left alone will soon be eliminated in the wild by an introduced predator. The only hope is captive breeding.



Hypothetical organism

Facts: Populations are small; genetically isolated-- widely scattered. You can only afford to maintain and breed 100 individuals.

Goal: Maintain as much genetic variability as possible; Keep costs manageable

Question: Is it best to collect 100 individuals from one population or 10 individuals from each of ten populations?

<http://www.futuretimeline.net/blog/2014/06/1-2.htm#V9lQuYVWuQIE>

Genetic bottlenecks

- Causes:
- natural environmental fluctuations (gradual or catastrophic)
- Human intervention- hunting or habitat conversion
- Founder events

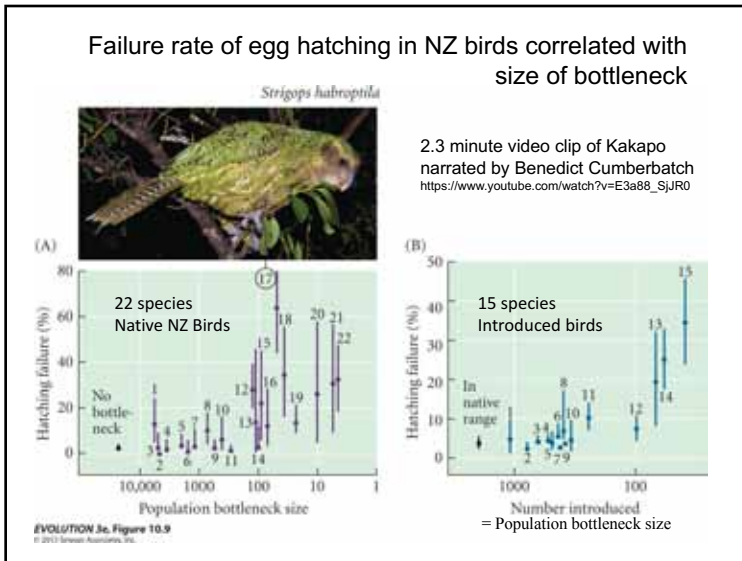


<http://animals.nationalgeographic.com/animals/mammals/cheetah/>

Elephant Seal

- Reduced by hunting
- 20 animals in 1890's.
- Harems- Avg. only 20% of males mate
- 1970's recovered to 30,000
- 1974 Survey: 24 allozymes
- All loci monomorphic (one allele)





Finnish People

Genetic Drift in Small Populations (original colonists)

Bottleneck- separated for centuries (4,000 yr)

Different set of genetic diseases

Pääbo et al. 1996. PNAS

DNA- Y-chromosome & mtDNA

54 Finns

28 Saami (resident Laplanders)

100 Europeans

Finns least variable

<http://1140.photobucket.com/albums/r4/swamimuktananda/finland.jpg>

Saami People

<http://virtual.finland.fi/finfo/images/people/saami2.jpg>; <http://www.saminuorat.se/media/38957.jpg>; <http://www.arcticpeoples.org/wp-content/uploads/2008/02/ome-photo.jpg>; http://upload.wikimedia.org/wikipedia/commons/thumb/8/87/Saami_Family_1900.jpg/800px-Saami_Family_1900.jpg

Founder events: one or a few individuals colonize an isolated area

Are oceanic islands deserts of genetic diversity?

Founder events and bottlenecks

- Two parents (or a pregnant female) founding a new population carry at most four different alleles at a given locus.
- At most loci, one, two or three alleles tend to predominate; founders will most likely carry the most common allele.
- Thus, many alleles will be lost in a bottleneck no matter how long it is
- Extended bottlenecks will tend to reduce variability further due to genetic drift in the small population
- Short bottlenecks will not reduce variability substantially as demonstrated next...

Effects of founder population size on population heterozygosity:

- H_0 = Source population proportion of heterozygotes
- N = # of colonists
- H_f = Heterozygosity of the founder

• Then $H_f = (1 - 1/(2N)) H_0$

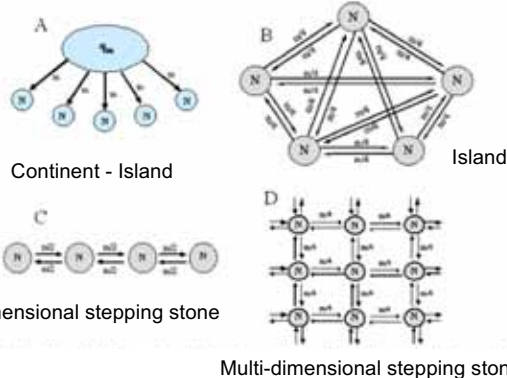
With $N =$ two colonists

$$H_f = (1 - 1/(2N)) H_0 \text{ or}$$

$$H_f = (1 - 1/4) H_0 \text{ or}$$

$$H_f = 3/4 H_0$$

Models of Gene Flow



Isolation by distance. Subpopulations or individuals on landscape surrounded by a series of concentric circles depicting probability of gene flow.

Which model seems most realistic: isolation by distance or perfect panmixia (island model)?

Does migration always = gene flow?

What is the effect of gene flow on among population variation?

Studies of gene flow in species of high versus low vagility



<http://www.eyefetch.com/image.aspx?ID=452439>



<http://www.encyclopediainalabama.org/face/Multimedia.jsp?id=m-3167>



Flighted & flightless NZ stoneflies



Zelandoperla decorata

Flighted lineage: *Z. decorata*
Flightless lineage: *Z. fenestrata*

McCulloch, Wallis, and Waters. 2009. Mol. Ecol.



mtDNA phylogeographic analysis used to survey population structure

Structure definition: populations form geographic groups that differ genetically from each other.

No structure = no variation or variation with no geographic pattern

Flighted & flightless NZ stoneflies



McCulloch, Wallis, and Waters. 2009. Mol. Ecol.

Flighted lineage: *Zelandoperla decorata*

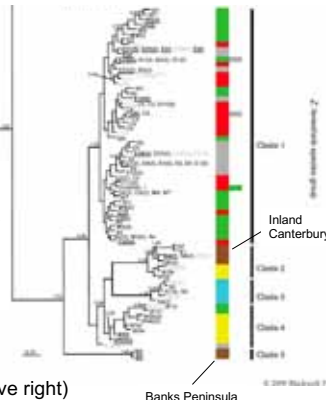


Numerous haplotypes are found at multiple localities in flighted lineage

Bayesian COI phylogeny (continued above right)

Colored bars = geographic origin of the specimen.

Flightless lineage: *Z. fenestrata*
Geographic clusters of related haplotypes



Small poplns. + low gene flow + genetic drift = increased differentiation among populations

Selection, Drift, Gene flow balance

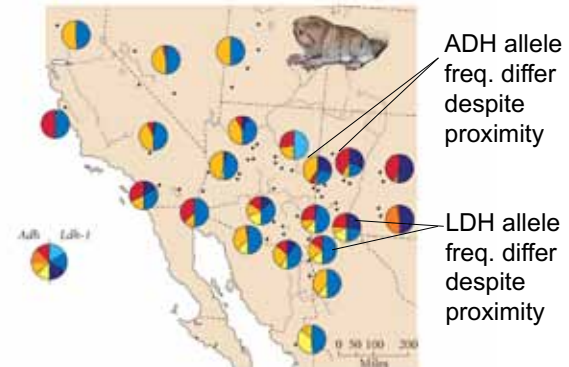
Balance btw selection, drift and geneflow can maintain variability if environment changes



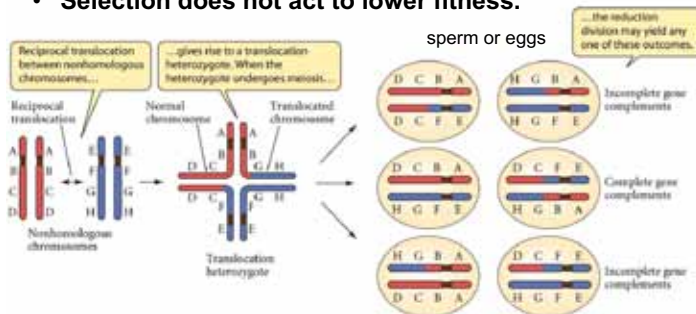
Lake Erie, Banded water snake

Pocket gopher, *Thomomys bottae*

- High among population genetic differences = low gene flow, small population sizes
- Strong selection unlikely in this case

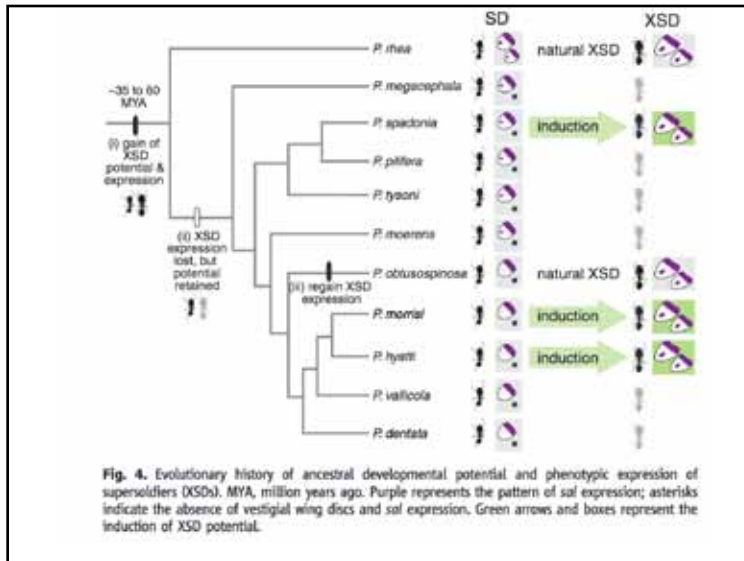


- Pocket Gophers have different chromosomal translocations fixed across species/subspecies.
- Reciprocal translocations lower fitness.
- They can only be fixed by genetic drift.
- **Selection does not act to lower fitness.**



Futuyma 3e, Fig 8.25

The end



Albino mutations

Lamar, 1997, World Publications; <http://www.marinecreatures.com/Albino-1-plastron.gif>;
<http://www.migaloo whale.org/images/whiteturtle.jpg>; http://farm4.static.flickr.com/3197/2434385205_7f113d1d8e.jpg