

## 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 20<sup>th</sup> century perception of variation in natural populations
- Importance of Lewontin & Hubby 1966

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?

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

Classical geneticists ....

- T.H. Morgan and his students 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

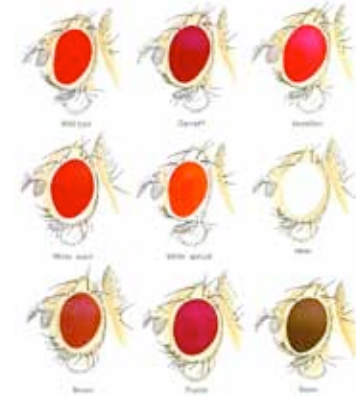


FIGURE 6. Some eye colors in *Drosophila melanogaster*. (After Z. M. Hall, in the laboratory of Genetics by Hartman and Austin, University, 1981.)

History of Evolutionary Biology ....

- 1900-1920's- Chromosomal basis of inheritance, nature of mutations
- 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

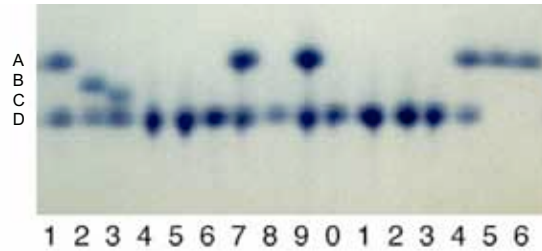
### Interaction of Technology and Discovery: gel electrophoresis.

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) sampled variation in many species

by the mid 1970's...

### Genetic variation at allozyme loci in animals and plants

"Heterozygosity"

	Number of species examined	Average number of loci per species	Average proportion of loci	
			Polymorphic per population	Heterozygous per individual
<b>Insects</b>				
Drosophila	28	24	0.529	0.150
Others	4	18	0.531	0.151
Haplodiploid wasps*	6	15	0.243	0.062
<b>Marine</b>				
Invertebrates				
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 <sup>b</sup>	4	40	0.233	0.037
Plants <sup>c</sup>	8	8	0.464	0.170

(After Selander 1976)

\*Females are diploid, males haploid

<sup>b</sup>Human, chimpanzee, pigtailed macaque, and Southern elephant seal

<sup>c</sup>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"

$$H = 1 - \sum_i p_i^2 + q_i^2$$

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

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?

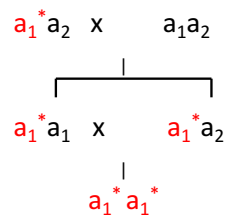
Small population size? and Non-Random Mating?  
(inbreeding and/or drift)

Which processes create variation, which processes destroy variation?

### Erosion of Genetic Variability by Two Processes

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

### Inbreeding- Mating of relatives

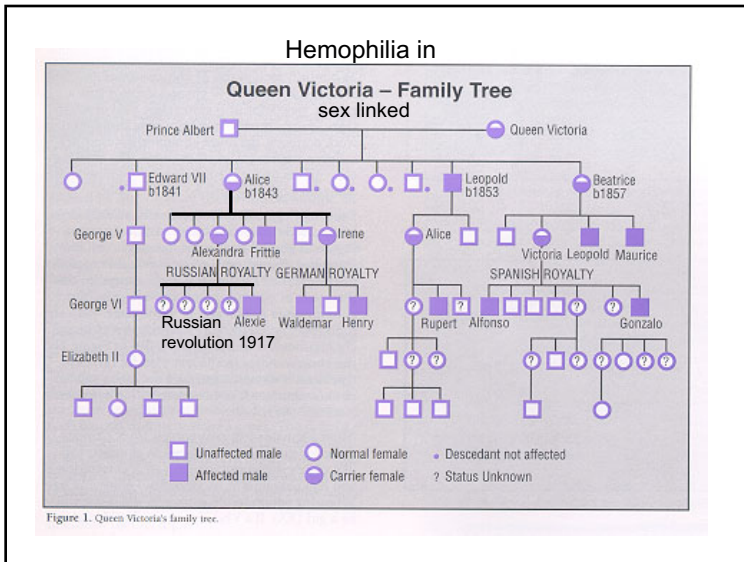


alleles identical by descent



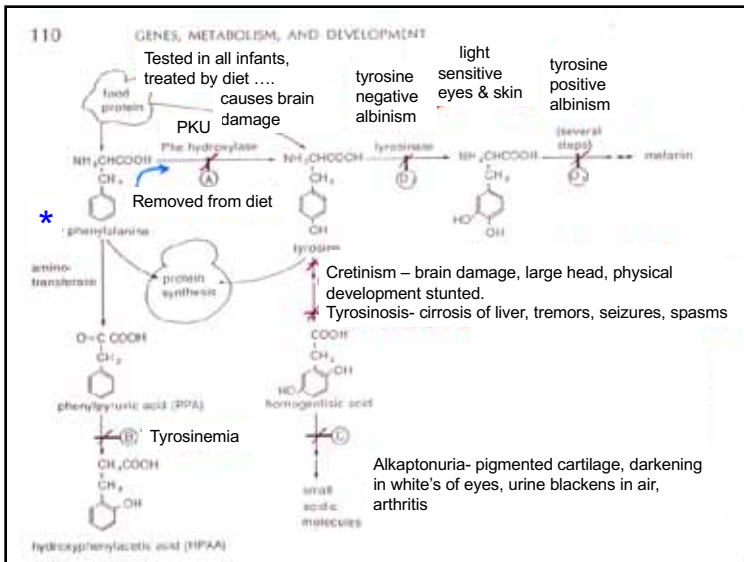
### Inbreeding Depression

- 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.



Inbreeding (cont.)

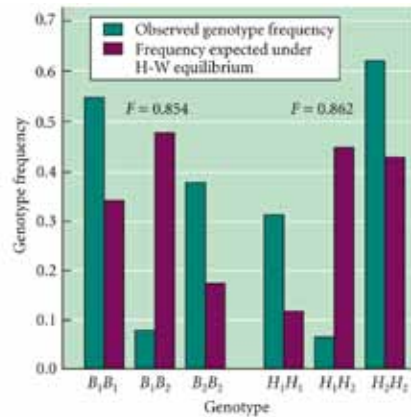
- Positive assortative mating & mating of relatives increases the probability that recessive alleles will become homozygous & be expressed
- although possible in large populations, more common in small populations.
- Example, metabolic disorders of the melanin pathway



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

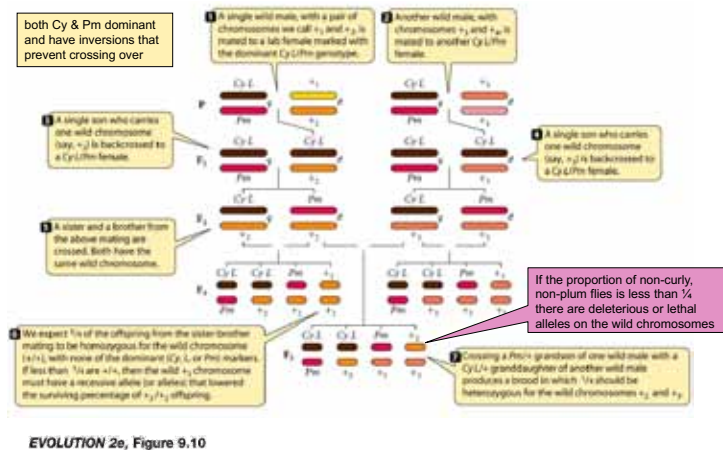
- Inbreeding affects all loci equally
- Common in plants
- aa individuals --> all aa offspring
- bb individuals --> all bb offspring
- ab individuals --> 1/4 aa, 1/2 ab, 1/4 bb
- Each generation % heterozygotes in the population decreases.
- This is the ultimate form of positive assortative mating!

Figure 9.9 Inbreeding. Genotype frequencies observed at 2 loci 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



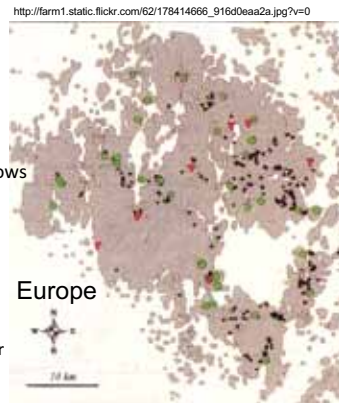
EVOLUTION 2e, Figure 9.10

### Lethal & Deleterious alleles are Common

- 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](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

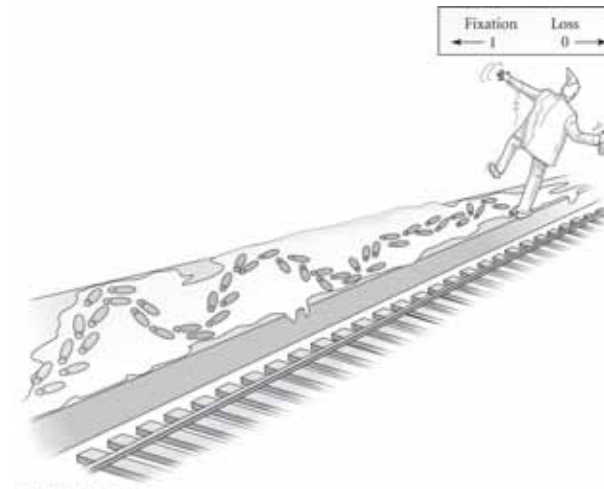
Only 38% showed purging (selfing-reduced inbreeding depression)

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

## Genetic Drift

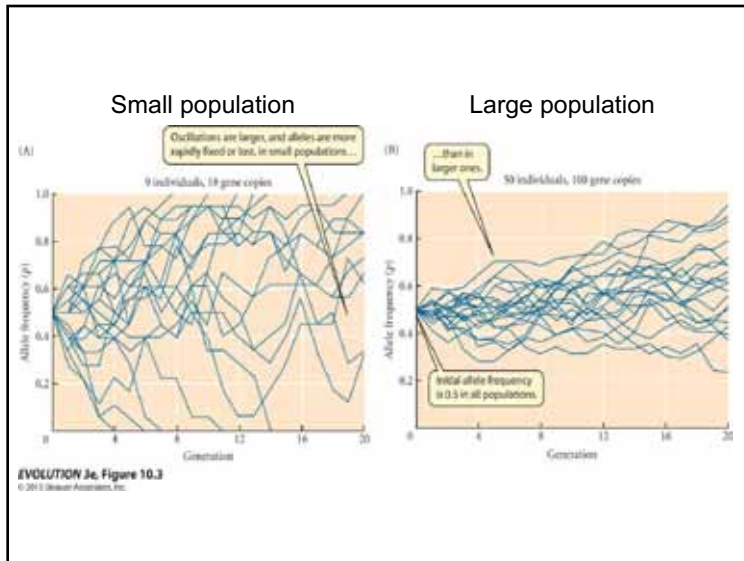


<http://www.geograph.org.uk/photo/3135083>



EVOLUTION 3e, Figure 10.2  
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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

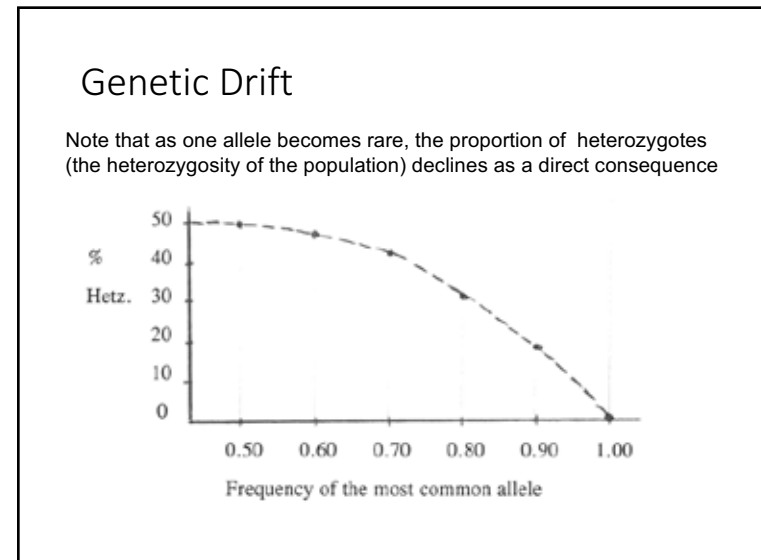
The effect of recessive allele freq. on heterozygosity:

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



## 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.

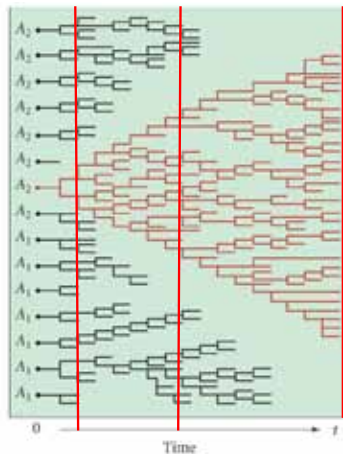
Consequence: Some individuals leave fewer progeny than others (increases inbreeding)

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

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

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 poplns, 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.

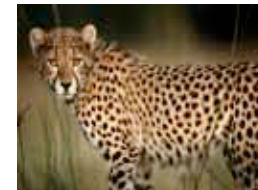
**Goal:** Maintain as much genetic variability as possible; Keep costs manageable

**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#.V9lQuYWuQjE>

#### Genetic bottlenecks

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



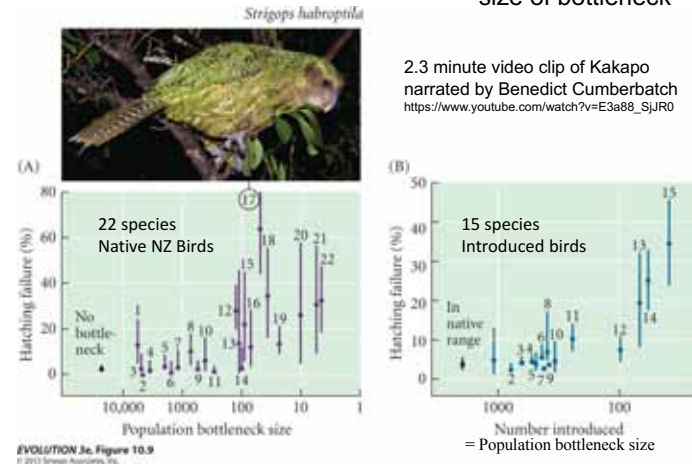
<http://animals.nationalgeographic.com/animals/mammals/cheetah/>

## 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)



## Failure rate of egg hatching in NZ birds correlated with size of bottleneck



## 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://i140.photobucket.com/albums/r4/swamimuktananda/finland.jpg>

## Saami People



<http://virtual.finland.fi/info/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](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  $H_f = (1 - 1/(2N)) H_0$

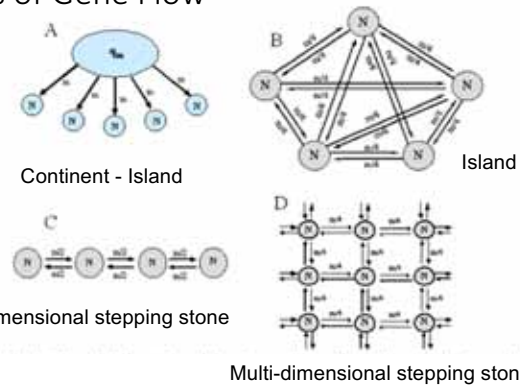
With  $N =$  two colonists

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

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

$$H_f = 3/4 H_0$$

### 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.encyclopediaofalabama.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

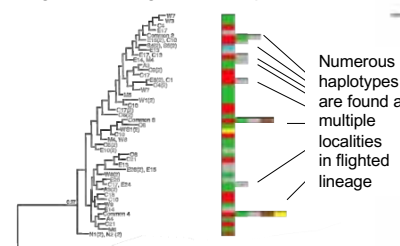


McCulloch, Wallis, and Waters. 2009. Mol. Ecol.

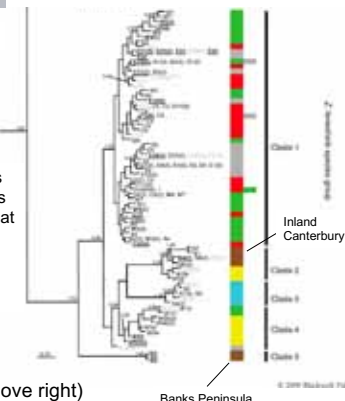
Colored bars = geographic origin of the specimen.

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

Flighted lineage: *Zelandoperla decorata*



Bayesian COI phylogeny (continued above right)



Banks Peninsula



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

Selection, Drift, Gene flow balance

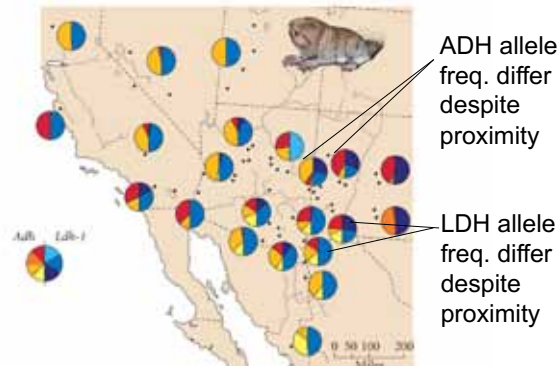
Balance btw selection, drift and geneflow can maintain variability if environment changes



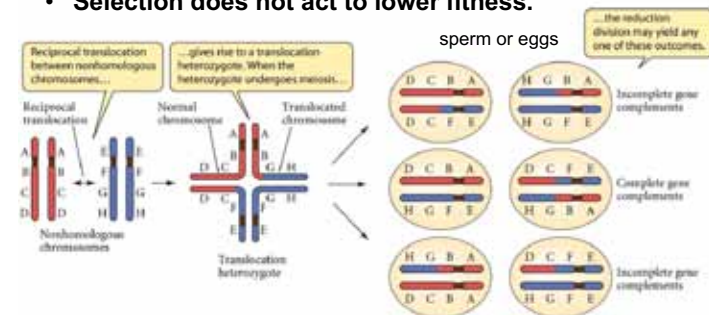
Lake Erie, Banded water snake

Pocket gopher, *Thomomys bottae*

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

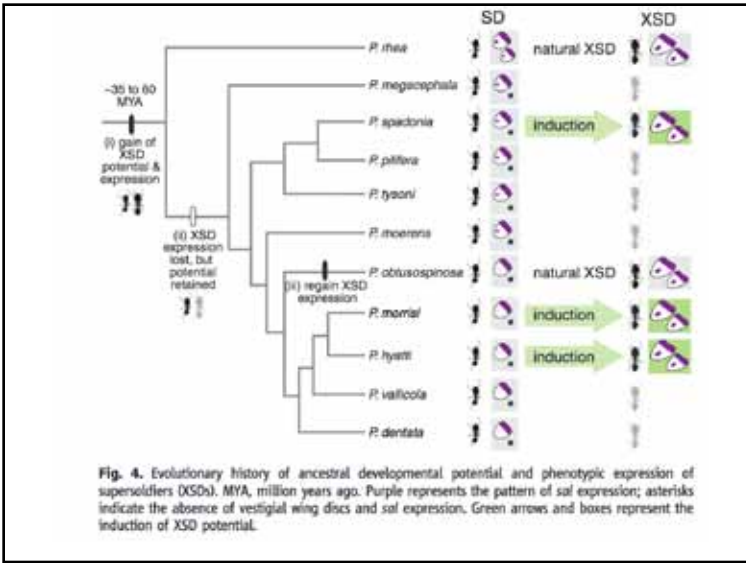
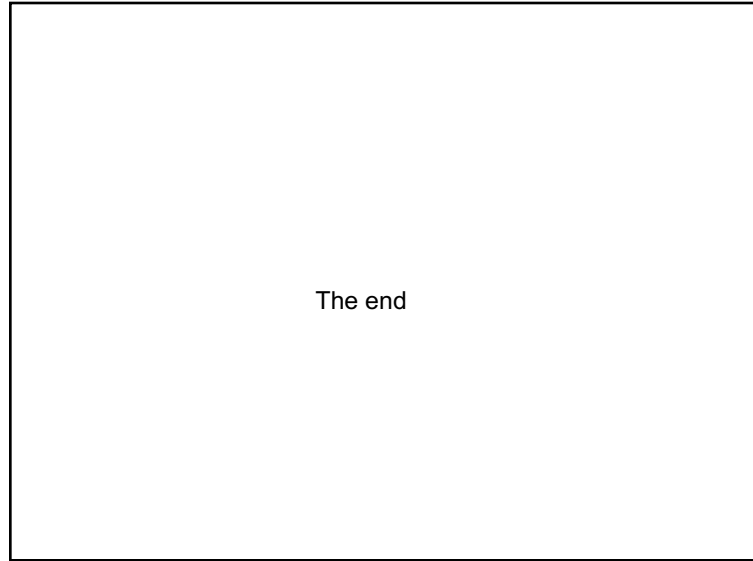


- Pocket Gophers have different chromosomal translocations fixed across species/subspecies.
- Reciprocal translocations lower fitness.
- They can only be fixed by genetic drift.
- **Selection does not act to lower fitness.**



Futuyma 3e, Fig 8.25





### 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](http://farm4.static.flickr.com/3197/2434385205_7f113d1d8e.jpg)