

Lecture 15. Genetic Variation

EEB 2245, C. Simon, 21 March 2017

Last time...

- Uses of Evolutionary Biology (continued)
- Evolution vs Creationism

This time...

- Importance of variation, polymorphisms
- Mendel's laws
- Deviations from Mendelian ratios (genetic and non genetic causes)

This Time..

- Heritability, plasticity, selection, common garden, genetic assimilation, canalization
- Epigenetic inheritance
- H-W equation, assumptions, terminology, usefulness
- Importance of Lewontin & Hubby 1966

Genetic Variation

Variation in traits results in multiple phenotypes within a population or “polymorphism”

- Systematists work with “type specimens”
- But in nature, species are not unvarying types
- Traits vary with-in and among-populations
- Thousands of examples of polymorphic traits,
 - Examples: color or color pattern
 - Albino, melanistic, green vs. yellow, brown (or pink)
 - Mimicry pattern polymorphism

Albino mutations



<http://www.popartuk.com/q/1g3734+brothers-albino-tiger-and-bengal-tiger-poster.jpg>; <http://www.hedgehogs.org/albino-hedgehog.jpg>
<http://media.ebaumsworld.com/picture/DamianRules/albino1.jpg>; <http://rebel5ive.lbbhost.com/AlbinoFawn/AlbinoSquirrel.jpg>

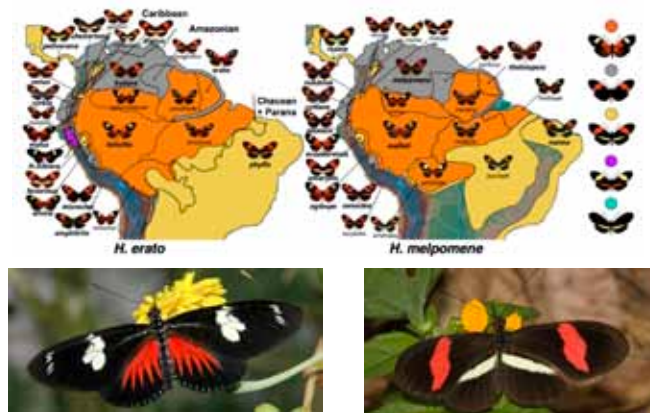
Green/Brown Color Polymorphism *Kikihia peninsularis* cicadas from NZ



Orange and purple morphs, *Pisaster ochraceus* starfish Pacific NW

http://resweb.llu.edu/sdunbar/students/Perumal_clip_image002_0002.jpg

Heliconius butterflies- color pattern polymorphisms controlled by one large region of the genome less than one megabase long containing ~ 20 genes differing in expression among the different forms.



Polymorphism Examples in Futuyma:

- Blue geese vs snow geese (2 alleles, 1 locus)
- Swallowtail butterfly, *Papilio dardanus*, males non-mimetic, females mimic three very different species
- Multilocus traits w many alleles such as hair and skin color

Simple Mendelian Inheritance

Given the following mating (one trait).. $AA \times aa \rightarrow F_1$
 A - dominant, a - recessive

All F_1 genotype Aa (phenotype A) $Aa \times Aa \rightarrow F_2$

In F_2 , recessive alleles segregate out
 but minority (25%)

$\frac{1}{4} AA, \frac{1}{2} Aa, \frac{1}{4} aa$

	A	a
A	AA	Aa
a	aA	aa

Review from basic biology....

Mendel's laws

Dominance- two alleles, one from each parent. recessive alleles will segregate out in the next generation (hidden variation). Dominance can also be incomplete.

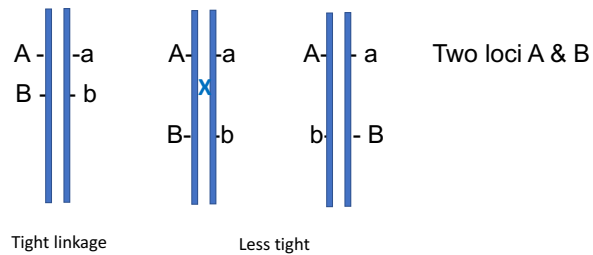
•**Segregation**- paired alleles segregate at random into gametes

•**Independent assortment**- segregation of one pair of alleles is unrelated to the segregation of any other pair of alleles

Non-Mendelian Inheritance

Many factors can cause deviations from Mendelian ratios

e.g., tight linkage- alleles close together on the same chromosome.



Non-Mendelian Inheritance

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e.g., tight linkage- alleles close together on the same chromosome.

Violates Independent assortment

segregation of one pair of alleles **will be** related to the segregation of other pairs of alleles

The farther apart two loci on a chromosome, the more likely they are to assort independently

Crossing over.

Genes on same chromosome can assort independently

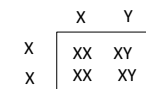
Causes of deviation from Mendelian ratios of offspring allele frequencies in crosses

- Tight Linkage (genetic hitch-hiking)
- Meiotic drive (segregation distortion)
- Lethal alleles
- Epistasis (many genes affecting one trait)
- Transposable elements
- New mutations (rare)
- Non-genetic variation- Cultural inheritance
- Plastic response to the environment
- Non-genetic variation- Maternal effects
- Epigenetic inheritance

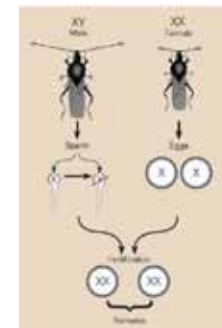
Violation of Mendel's laws

- **Independent assortment-** segregation of one pair of alleles unrelated to the segregation of any other
- Violated by Meiotic Drive = Segregation distortion
- x-linked genes.
- increases the proportion of x-bearing sperm (producing females).

Normal genotypes



Distorted genotypes



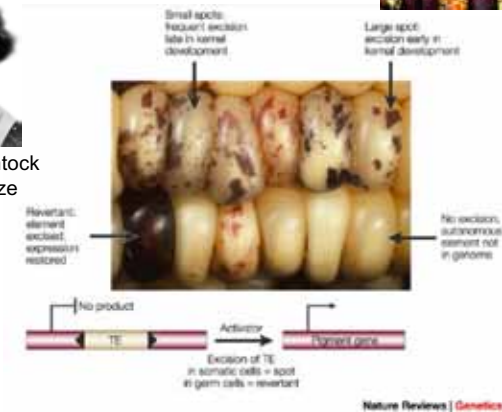
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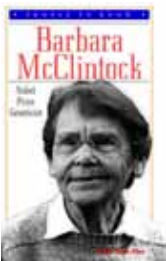
Transposable elements



Barbara McClintock
1983 Nobel Prize



Barbara McClintock (1902-1992)

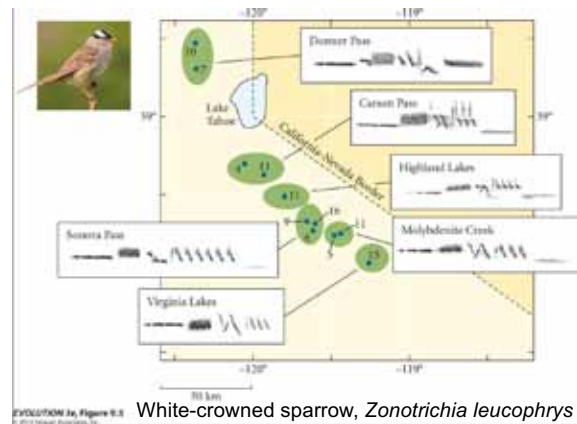


- PhD, Cornell, 1927- maize genetics
- First genetic map for maize
- Role of telomere and centromere
- Cornell –Missouri (1936) -- Cold Spring Harbor (1941)
- 1940's-50's discovered transposition in maize
- National Academy of Sciences 1944
- 1953 –Due to harsh skepticism--- stopped publishing on transposition
- 1983 – awarded Nobel Prize for this work

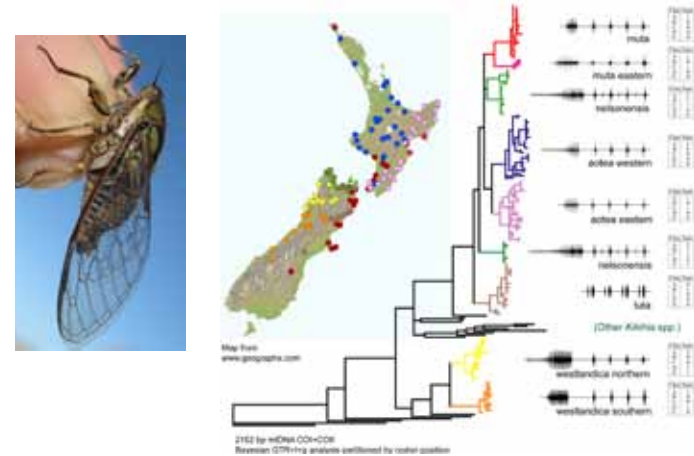
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Cultural inheritance (not Mendelian)- songs are learned in birds. Dialects are common.



In contrast songs of insects and frogs are innate – genetically programmed.



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Phenotypic plasticity

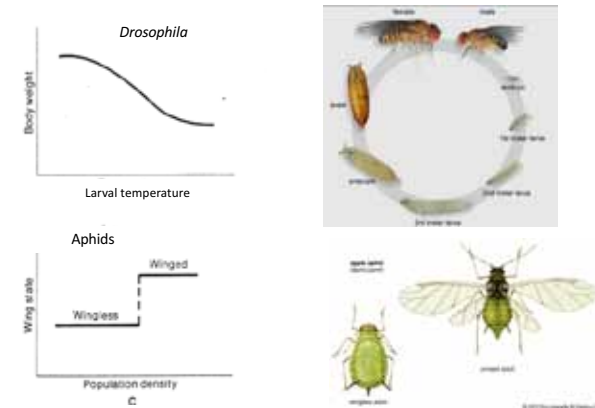
- The capacity of an organism, of a given genotype, to express different phenotypes under different environmental conditions.

Not all variation is heritable.

Some variation comes solely from a plastic response to environmental stimuli.

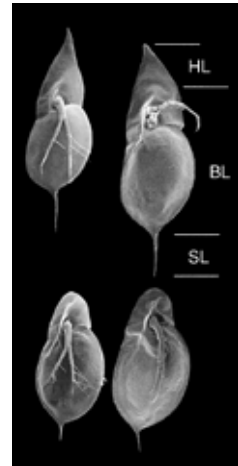
$$V_{\text{total}} = V_{\text{genetic}} + V_{\text{environment}}$$

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Plastic response, e.g., to presence of predators

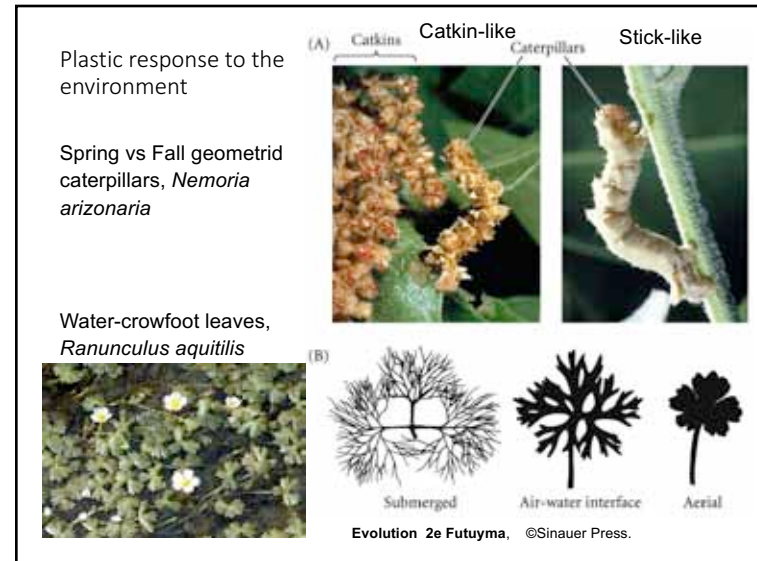
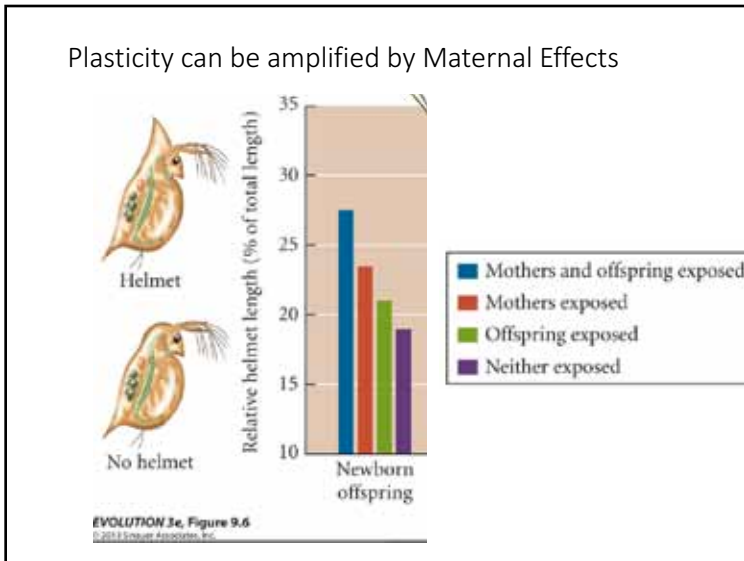
- Water containing chemical cues from predators (kairomones) ...
- induces changes in exoskeleton over life of *Daphnia cucullata*, water fleas
- Helmet length,
- body length,
- tail spine length



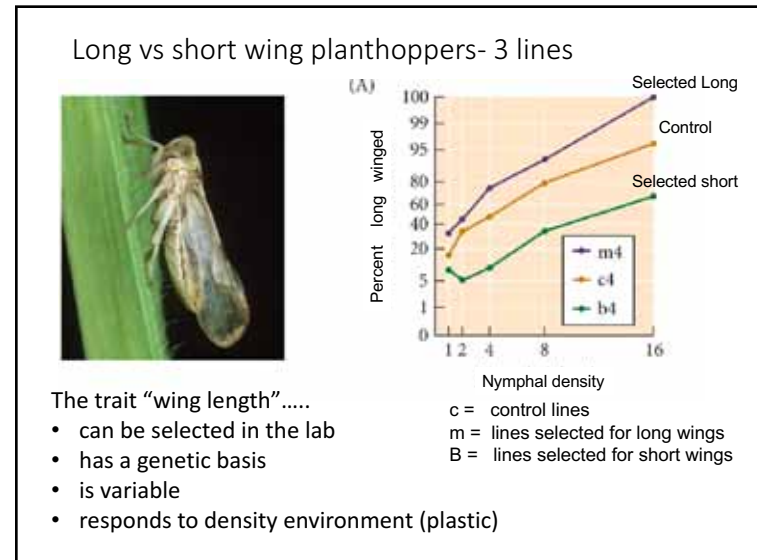
Daphnia cucullata

Causes of deviation from Mendelian ratios of offspring allele frequencies in crosses

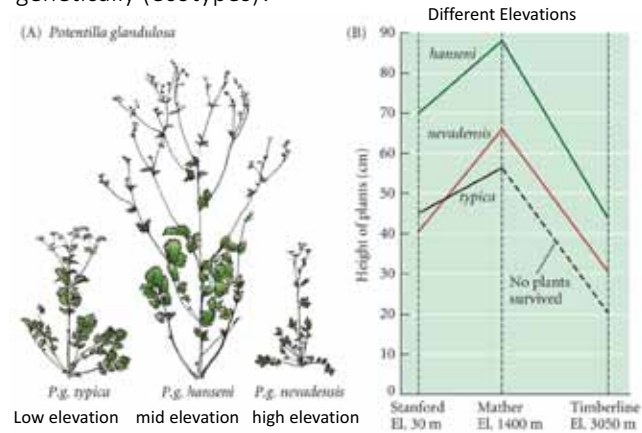
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Both genetics and plasticity can affect a phenotype simultaneously



Clausen, Keck, & Hiesey. 1940. Common garden experiments. Are these plastic varieties or different genetically (ecotypes)?



Two theories for the effect of phenotypic plasticity on evolution...

- Plasticity will allow optimal phenotypic response to a wide variety of environments and therefore shield the genotype from selection.
- Phenotypic change induced by a new environment may prove adaptive and become genetically assimilated (Mary Jane West-Eberhard).

Genetic Assimilation- Waddington 1953

- *Drosophila* cross-vein sometimes fails to appear if pupa given a heat shock.
- Waddington artificially selected individuals that responded to the heat shock over many generations.
- Eventually, a large proportion of the population was cross-veinless even without heat shock.
- The trait was genetically assimilated (no longer plastic).

Does plasticity become genetically assimilated?



Manduca quinquemaculata
Tomato hornworm

Low temperature morph



Manduca sexta: Tobacco Hornworm
Green at all temperatures.



High temperature morph

Definition: canalization

- Environmentally canalized- insensitive to alteration by environmental changes.
- Genetically canalized- a phenotype with a low sensitivity to the effects of mutation

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Epigenetic signals

- DNA methylation,
- Histone modifications (acetylation)
- Noncoding RNAs
- Transcription factors (TFs)

Control heritable cell memory and maintain cell identity. Effects behavior and lifespan.

Yan et al. 2015. ann. Rev. Entomol.

Epigenetic inheritance

- E.g., DNA methylation
 - Methyl group joined to C-G couplet during replication
 - Can prevent or lower gene expression
 - Can be influenced by environment, aging, maternal & paternal condition.



Futuyma Example- mutant toadflax, caused by extensive methylation of floral symmetry gene.

Methylation is lost in some lineages, e.g., *Drosophila* and *Nematodes*.

Methylation- location in gene varies across lineages

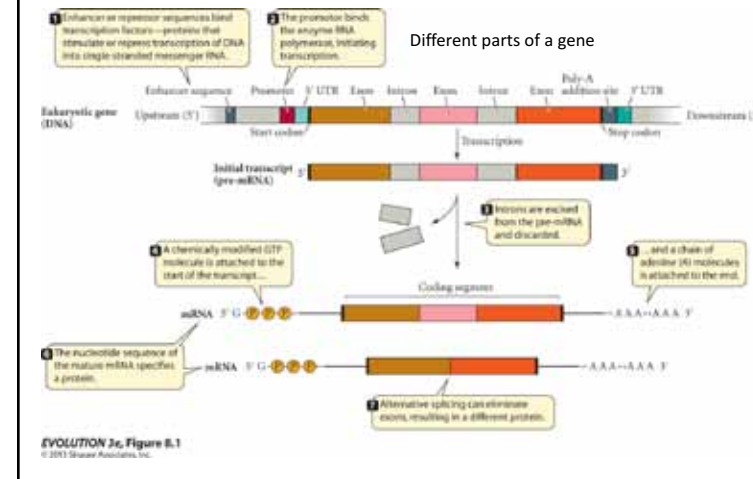
Table 1 Evolutionary overview of DNA methylation

Species	Common name	CG methylation (%) ^a	Methylation status			Reference(s)
			Gene body	Promoter	Transposons	
<i>Homo sapiens</i>	Human	70-80	Yes	Yes	Yes	10
<i>Mus musculus</i>	House mouse	74	Yes	Yes	Yes	38
<i>Apis mellifera</i>	Honey bee	<1	Yes	No	No	88, 88
<i>Harpegnathus saltator</i>	Jordan's jumping ant	<0.2	Yes	No	No	17
<i>Camponotus floridanus</i>	Florida carpenter ant	<0.2	Yes	No	No	17
<i>Nasutia termitaria</i>	Jewel wasp	1-2	Yes	No	No	132
<i>Arabidopsis thaliana</i>	Thale cress	22-24	Yes	Yes	Yes	25, 33

^aCG methylation levels listed here in insects (*A. mellifera*, *H. saltator*, *C. floridanus*, *N. termitaria*) have been measured by bisulfite conversion followed by genome-wide sequencing (BS-seq). Another approach, amplified fragment length polymorphism (AFLP), is likely to overestimate DNA methylation (37, 88, 132).

Yan et al. 2015. Ann. Rev. Entomol.

Futuyma 3e chapter 8. Reviews basic genetics.



Epigenetic inheritance

- All ants in a colony share the same genes regardless of caste
- DNA methylation, juvenile hormone, nutrition → castes of social insects



Queens, males, workers (minors, majors, super majors)

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A knowledge of Mendelian genetics led population geneticists Hardy and Weinberg to independently come up with the same equation to predict genotype frequencies in a population.

These processes equivalent to the assumptions necessary for the HW equation to work

- Diploid population
- No Natural selection (or tight linkage w another gene under selection)
- No Migration of alleles
- No New Mutations
- Random Mating
- Only one population has been sampled.

What does the H-W equation state?

Given that the assumptions of H-W are not violated then...

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What does the H-W equation state?

Given that the assumptions of H-W are not violated then...

- Allele frequencies will not change from one generation to the next, and
- Genotype frequencies of the offspring can be predicted by the equation: $p^2 + 2pq + q^2 = 1$
- Where p = freq of allele A
 q = freq of allele a, and
 $p + q = 1$

A Naïve geneticist asked...

Given the following mating (one trait).. $AA \times aa \rightarrow F_1$

All the F_1 will be Aa (phenotype A) $Aa \times Aa \rightarrow F_2$

In the F_2 , recessive alleles will segregate out but will be in the minority (25%)

$\frac{1}{4} AA, \frac{1}{2} Aa, \frac{1}{4} aa$

	A	a
A	AA	Aa
a	aA	aa

In future generations, will "a" disappear?

No, Allele frequencies will not change from one generation to the next.

Calculations (but first some terminology...)

Terminology

Number indiv. each genotype	Number of each allele		Frequency of each genotype
	A	a	
25 AA	50		.25 = D
50 Aa	50	50	.50 = H
25 aa		50	.25 = R
Total number of indiv. = 100	Total number of alleles = 200		

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Two ways to calculate allele frequencies....

$$p = \text{freq of "A" allele} = \#A \text{ alleles} / \text{total \# alleles} = 100/200 = 0.50$$

$$p = (D + \frac{1}{2} H) = 0.25 + \frac{1}{2} (0.50) = 0.50$$

$$q = \text{freq of "a" allele} = \#a \text{ alleles} / \text{total \# alleles} = 100/200 = 0.50$$

$$q = (R + \frac{1}{2} H) = 0.25 + \frac{1}{2} (0.50) = 0.50$$

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?

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.
- 1970's- Debate on the relative importance of selection versus drift. DNA sequencing
- 1985- PCR- rapid advances in gene sequencing

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 8. Some eye colors in *Drosophila melanogaster*. (After Z. M. Williams on the inheritance of Genes by Bateson and Ruddle, 1939.)

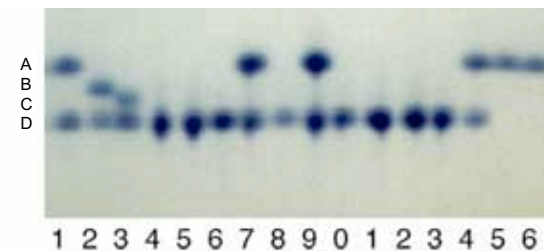
Interaction of Technology and Discovery: gel electrophoresis.

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!

Phosphoglucosmutase 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*	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	0.356	0.082
Reptiles	9	9	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

p² = the frequency of allele "a"q² = the frequency of allele "b"

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

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

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

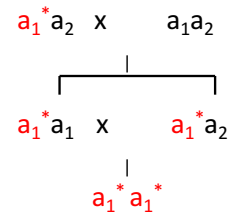
Small population size; Non-Random Mating (inbreeding and/or drift)

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.

Hemophilia in

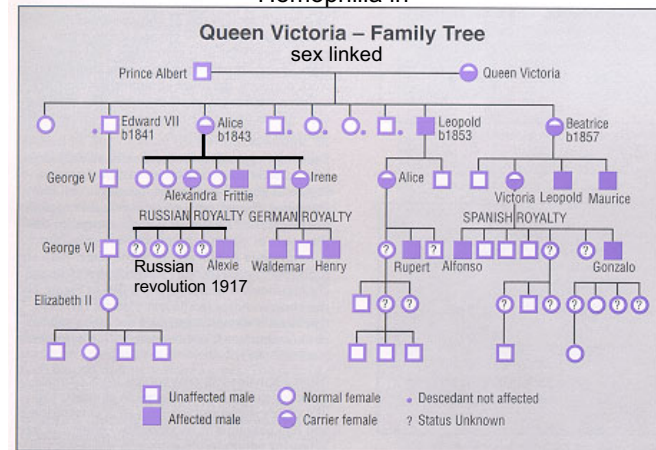
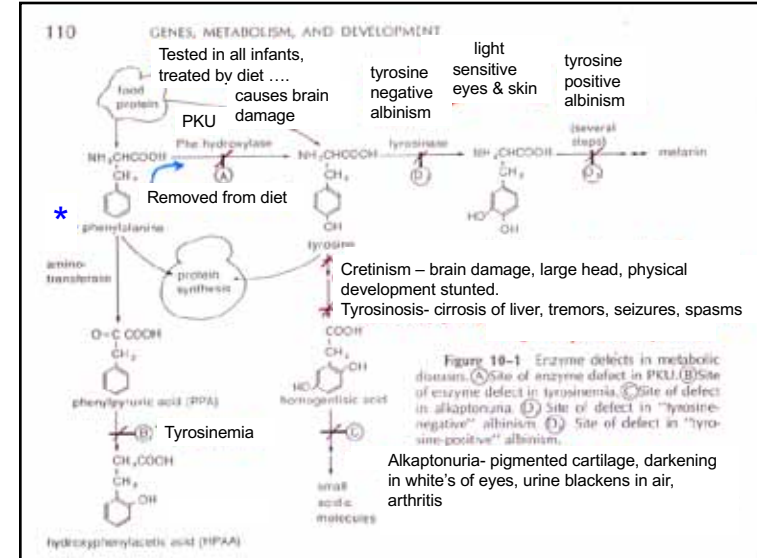


Figure 1. Queen Victoria's family tree.

Inbreeding (cont.)

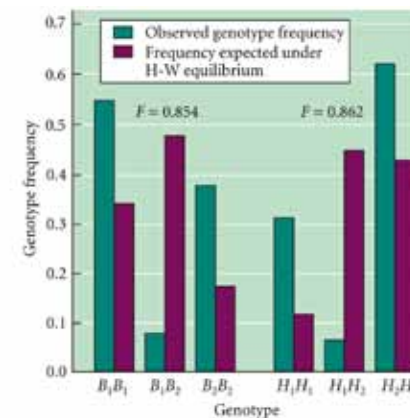
- Positive assortative mating & mating of relatives increases the probability that recessive alleles will become homozygous & be expressed
- although possible in large populations, more common in small populations.
- Example, metabolic disorders of the melanin pathway



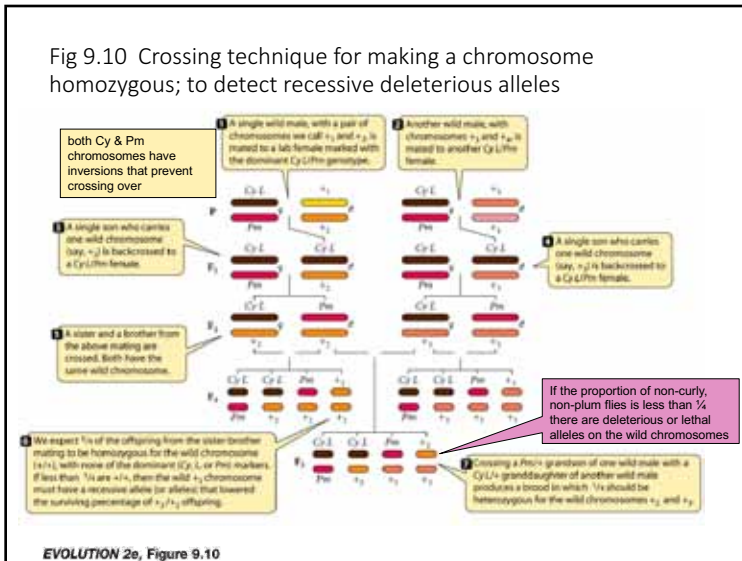
Self Fertilization: the most extreme inbreeding; mating is not random!

- Inbreeding affects all loci equally
- Common in plants
- aa individuals ---> all aa offspring
- bb individuals --> all bb offspring
- ab individuals --> 1/4 aa, 1/2 ab, 1/4 bb
- Each generation % heterozygotes in the population decreases.

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



Lethal & Deleterious alleles are Common

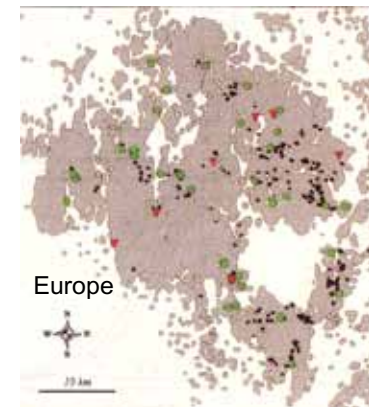
- Dobzhansky: Laboratory crosses of *Drosophila pseudoobscura* --> nearly every fly in a population carries a chromosome that if homozygous would substantially reduce prob. survival &/or fertility
- Morton, Crow, Mueller: studies of human marriages btw relatives; average person carries 3-5 recessive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



http://farm1.static.flickr.com/62/178414666_916d0ea2a.jpg?v=0



42 poplins surveyed in 1,600 dry meadows
 Extinction & recolonization common
 Metapoplin (weak gene flow)
 8 polymorphic allozyme loci

White = all known suitable meadows
 black = butterfly larvae present
 Green = 35 populations surviving summer
 Red = seven poplins. went extinct

Populations w/ less 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

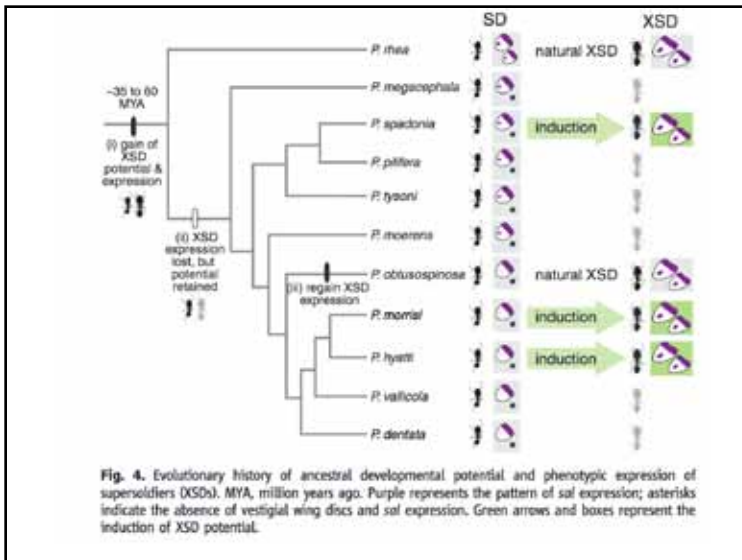
Reviewed 52 plant studies

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

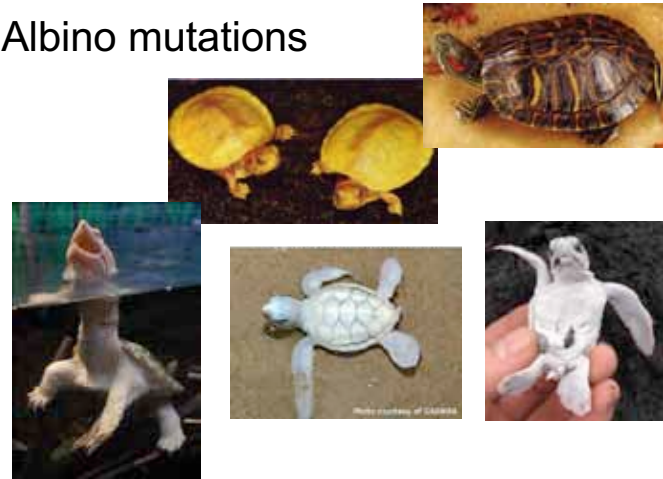
Only 38% showed purging (selfing-reduced inbreeding depression)

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

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