Lecture 15. Genetic Variation

EEB 2245, C. Simon, 21 March 2017

Last time…

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

This time…

- H-W equation, assumptions, terminology, usefulness
- Epigenetic inheritance
- Importance of Lewontin & Hubby 1966
- Understanding deviations from H-W ratios

This 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

Genetic Variation

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

- Systematists work with “type specimens”
- Also study with-in and among-population trait variability
- 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/g/l/lg3734+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)
- Multilocus traits w many alleles such as hair and skin color
- Swallowtail butterfly, *Papilio dardanus,* males non-mimetic, females mimic three very different species

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

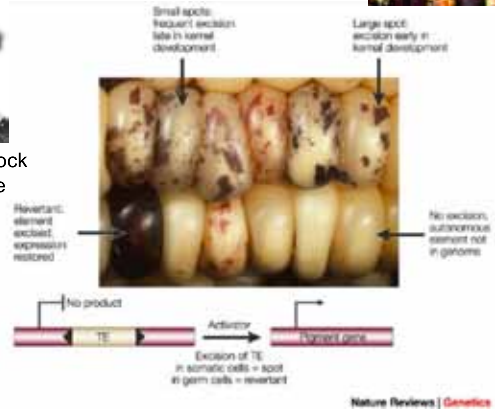
•**Independent assortment-** segregation of one pair of alleles is unrelated to the segregation of any other pair of alleles (we now know about linkage)

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

Transposable elements

Barbara McClintock
1983 Nobel Prize



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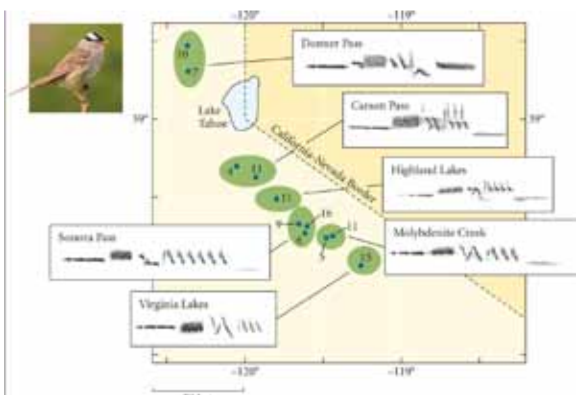
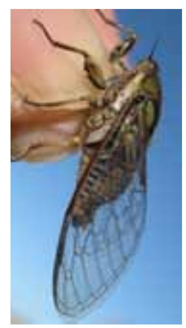
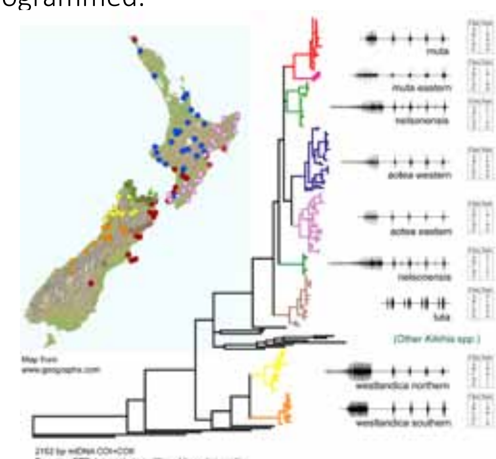
Cultural inheritance (not Mendelian)- songs are learned in birds. Dialects are common.



White-crowned sparrow, *Zonotrichia leucophrys*

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.

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

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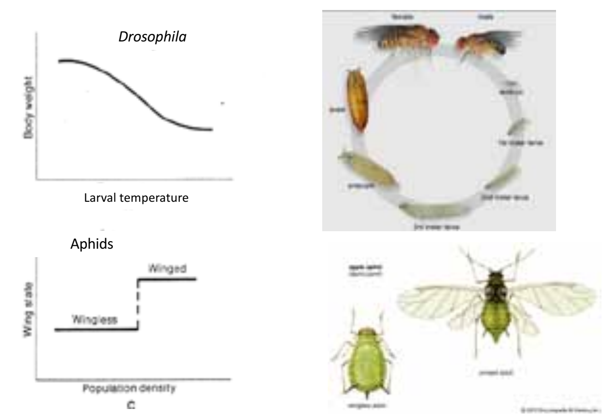
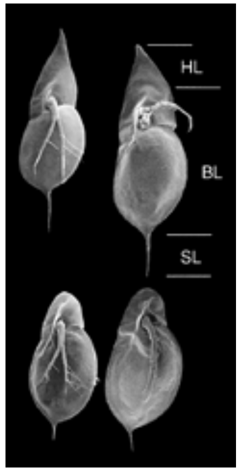


Plastic response, e.g., to presence of predators

- 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

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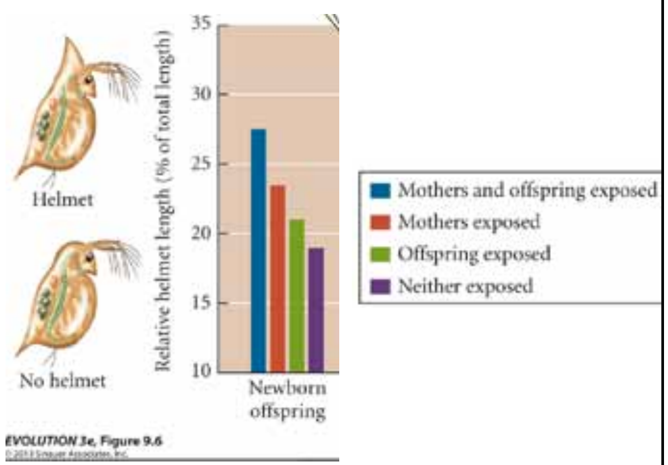
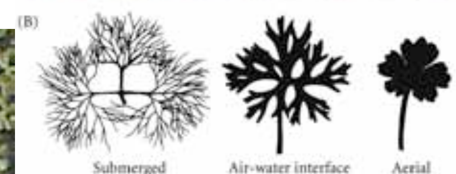
Plasticity can be amplified by Maternal Effects



Plastic response to the environment

Spring vs Fall geometrid caterpillars, *Nemoria arizonaria*

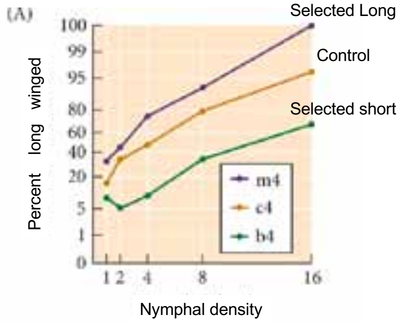
Water-crowfoot leaves, *Ranunculus aquitilis*



Evolution 2e Futuyma, ©Sinauer Press.

Genetic selection on a phenotype and plasticity affecting a phenotype can both be present

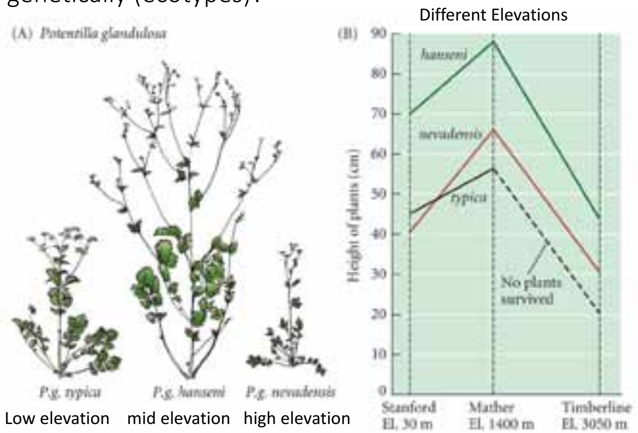
Long vs short wing planthoppers- 3 lines



c = control lines
m = lines selected for long wings
B = lines selected for short wings

The trait "wing length"…..
- can be selected in the lab
- has a genetic basis
- is variable
- responds to density environment (plastic)

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

High temperature morph

Manduca sexta: Tobacco Hornworm
Green at all temperatures.

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 ay environment, aging, maternal & paternal condition.

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

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

Methylation- location varies across lineages

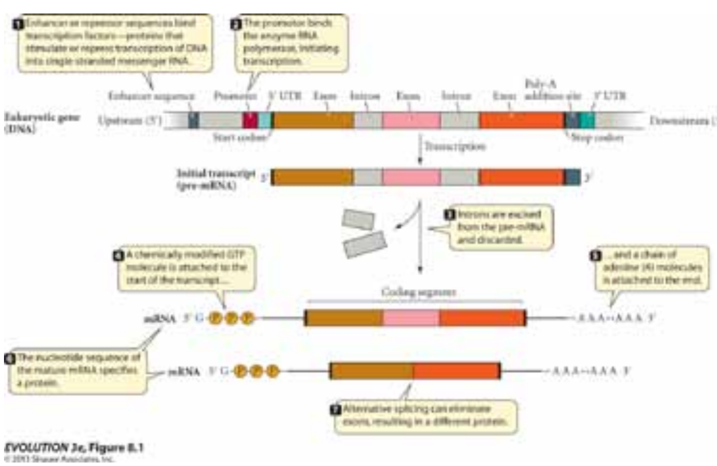
Table 1 Evolutionary overview of DNA methylation

Species	Common name	CG methylation (%)[a]	Methylation status: Gene body	Promoter	Transposons	Reference(s)
Homo sapiens	Human	70–80	Yes	Yes	Yes	10
Mus musculus	House mouse	74	Yes	Yes	Yes	38
Apis mellifera	Honey bee	<1	Yes	No	No	38, 88
Harpegnathos saltator	Jerdon's jumping ant	<0.2	Yes	No	No	17
Camponotus floridanus	Florida carpenter ant	<0.2	Yes	No	No	17
Nasonia vitripennis	Jewel wasp	1–2	Yes	No	No	132
Arabidopsis thaliana	Thale cress	22–24	Yes	Yes	Yes	25, 38

[a]CG methylation levels listed here in insects (*A. mellifera, H. saltator, C. floridanus, N. vitripennis*) 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 (85, 88, 123).

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

Futuyma 3e chapter 8. Reviews basic genetics.



Epigenetic inheritance

- E.g., DNA methylation, juvenile hormone, nutrition, involved in castes of social insects

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

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- Population Processes (violations of HW assumptions)

Mendel's laws

- Worked out for simple traits affected by one locus with a small number of alleles
- Populations as a whole can deviate from Mendelian ratios as can be discovered using the HW equation.

What does the H-W equation state?

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

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- Genotype frequencies of the offspring can be predicted by the equation: $p^2 + 2pq + q^2 = 1$

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 x aa → F_1

All the F_1 will be Aa (phenotype A) Aa x Aa → F_2

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

¼ AA, ½ Aa, ¼ 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: A	a	Frequency of each genotype
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

Two ways to calculate allele frequencies….

Terminology

Number indiv. each genotype | Number of each allele A a | Frequency of each genotype

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

p = freq of "A" allele = #A alleles / total # alleles = 100/200 = 0.50

p = (D + ½ H) = 0.25 + ½ (0.50) = 0.50

q = freq of "a" allele = # a alleles / total # alleles = 100/200 = 0.50

q = (R + ½ H) = 0.25 + ½ (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?

Population processes that cause deviation from Mendelian ratios in natural populations and can be predicted by the H-W equation.

These processes are 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.

More on polymorphisms…

- at any given locus, each individual carries max. two alleles
- Populations may harbor many alleles at each locus

Examples:

- ABO blood groups- 3 alleles, 6 genotypes
- MHC (cell surface immune proteins, multigene family, genes very polymorphic, hundreds of alleles,
- General proteins (enzymes- allozymes)- typically two or three common alleles in a population, some loci may have dozens to hundreds of alleles).

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 ay 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

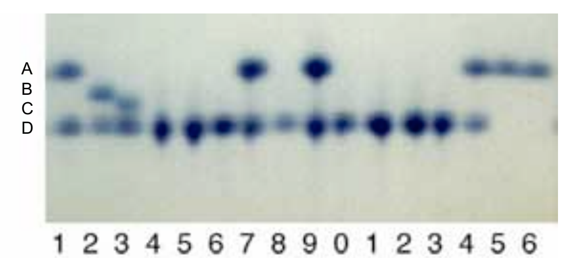
Interaction of Technology and Discovery: gel electrophoresis.

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. Huaay. 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 pseudooascura*. 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

ay 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	Average proportion of loci: Heterozygous per individua
Insects				
Drosophilia	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 Selander1976)

[a]Females are diploid, males haploid

[b]Human, chimpanzee, pigtailed macaque, and Southern elephant seal

[c]Predominantly outcrossing species

Heterozygosity

H = 1 minus the proportion of homozygotes

p^2 = the frequency of allele "a"

q^2 = the frequency of allele "b"

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

H 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 <u>chance</u>, 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

$a_1^* a_2$ x $a_1 a_2$

$a_1^* a_1$ x $a_1^* a_2$

$a_1^* a_1^*$

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

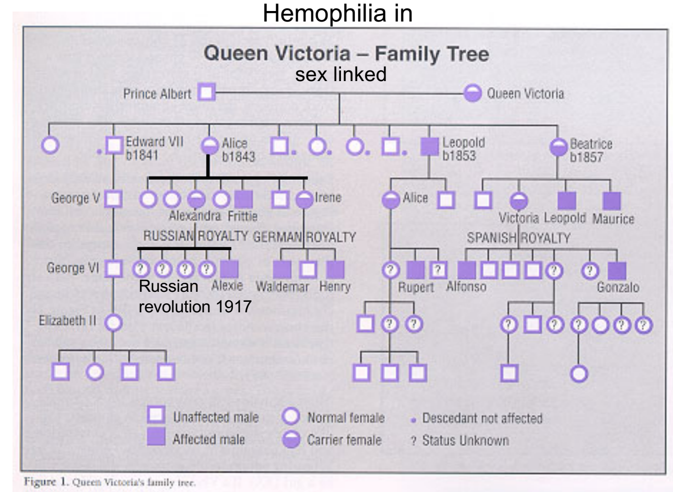
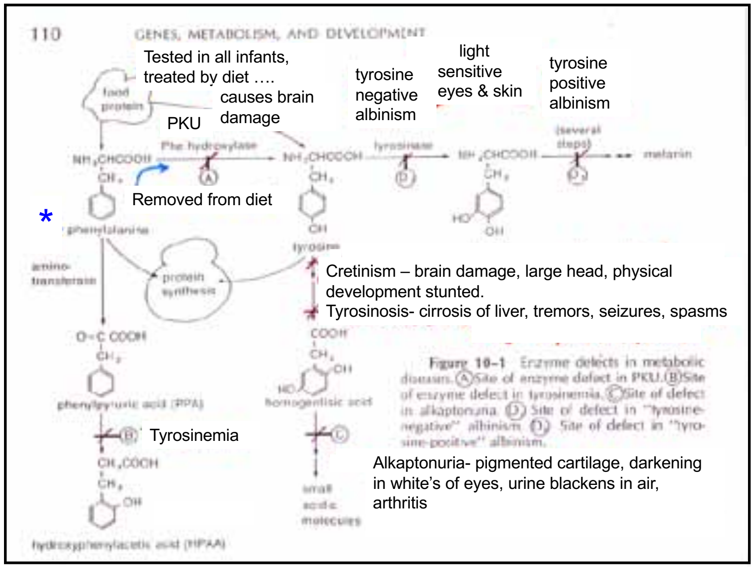


Figure 1. Queen Victoria's family tree.

Inareeding (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

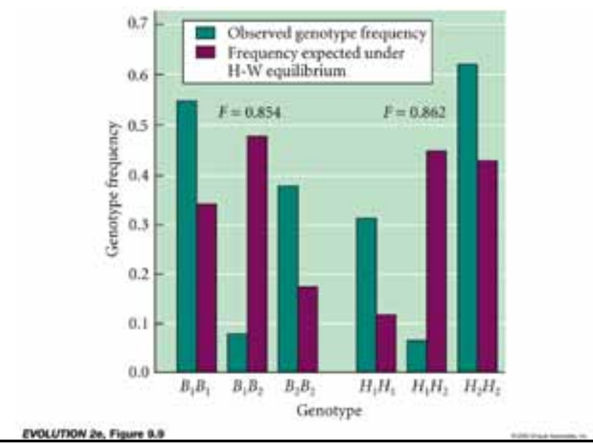
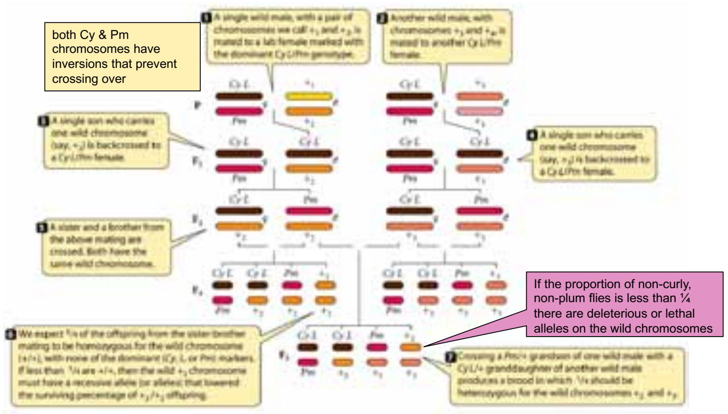


Fig 9.10 Crossing technique for making a chromosome homozygous; to detect recessive deleterious alleles



EVOLUTION 2e, **Figure 9.10**

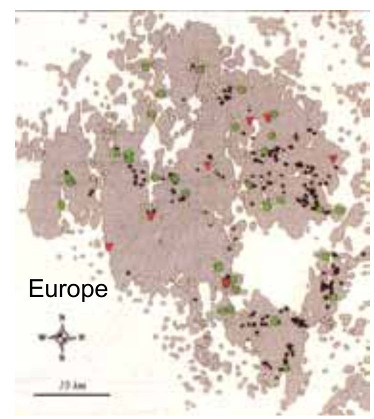
Lethal & Deleterious alleles are Common

- 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

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)

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 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, microsattelite, or minisattelite 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

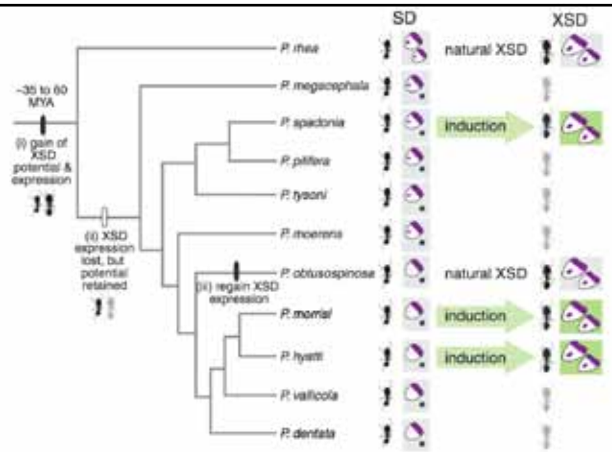
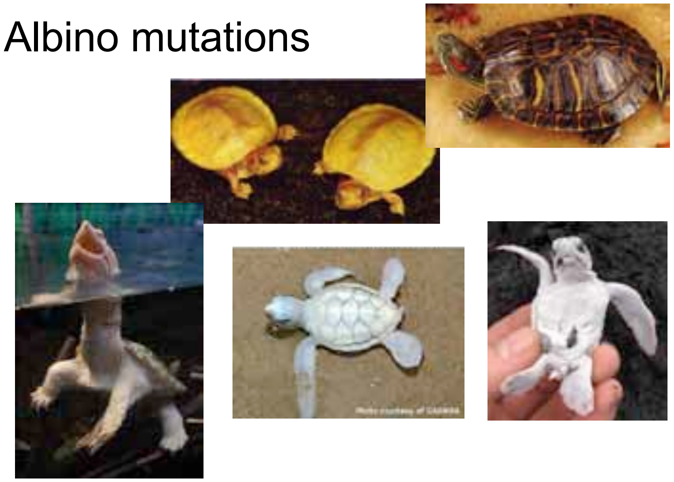


Fig. 4. Evolutionary history of ancestral developmental potential and phenotypic expression of supersoldiers (XSDs). MYA, million years ago. Purple represents the pattern of sal expression; asterisks indicate the absence of vestigial wing discs and sal expression. Green arrows and boxes represent the induction of XSD potential.

Albino mutations



Lamar, 1997, World Publications; http://www.marinecreatures.com/Albino-1-plastron.gif; http://www.migaloowhale.org/images/whiteturtle.jpg; http://farm4.static.flickr.com/3197/2434385205_7f113d1dbe.jpg