Fisher's Fundamental Theorem of Natural Selection

Sir Ronald Fisher
1890-1962

"The rate of increase in fitness of a population at any time is equal to its genetic variance in fitness at that time"

1

How do we know if a gene exists if it's not variable?

2

Lecture 7

The maintenance & measurement of genetic variation

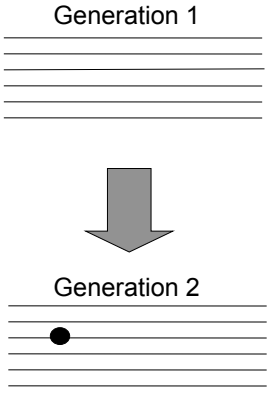
1. What processes influence the maintenance of genetic variation in populations?

2. How do we measure genetic variation and how much exists in populations?

3

What processes influence patterns of genetic diversity?

i) Mutation



Population of 3 diploid individuals

- ultimate source of genetic variation
- caused by random errors during replication

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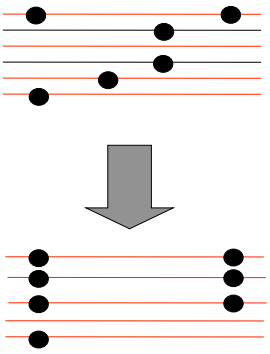
What processes influence patterns of genetic diversity?

iii) Random genetic drift



Population of 3 diploid individuals

- random sampling effects every generation
- drift important when populations become small

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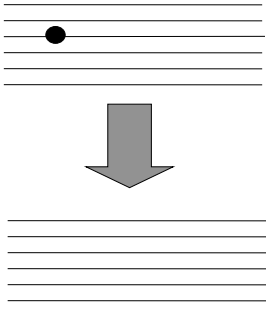
What processes influence patterns of genetic diversity?

iv) Natural selection:

a) purifying (negative) selection



Population of 3 diploid individuals

- mutations that reduce fitness removed by selection

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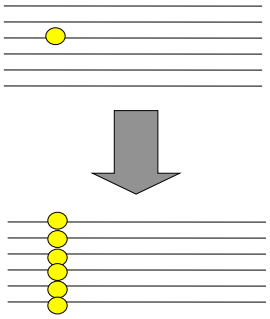
What processes influence patterns of genetic diversity?

iv) Natural selection:
b) positive selection (adaptation)



Population of 3 diploid individuals

• mutations that increase fitness become fixed

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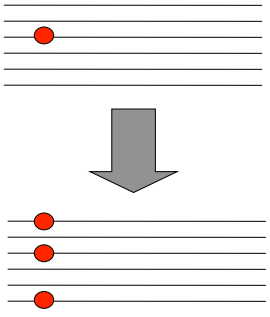
What processes influence patterns of genetic diversity?

iv) Natural selection
c) balancing selection



Population of 3 diploid individuals

• natural selection maintains diversity
e.g. heterozygote advantage

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Different processes can increase or decrease genetic diversity within populations

i) Mutation
ii) Recombination
iii) Genetic drift
iv) Natural selection

Many controversies in evolutionary biology concern the relative importance of these forces in evolution

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What are the important parameters used to measure patterns of genetic variation?

Polymorphism (*P*)

- Proportion of gene loci that are polymorphic

Heterozygosity (*H*)

- Average frequency of heterozygous individuals per gene locus*

*A site on a chromosome that is usually a gene

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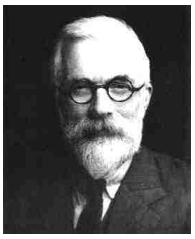
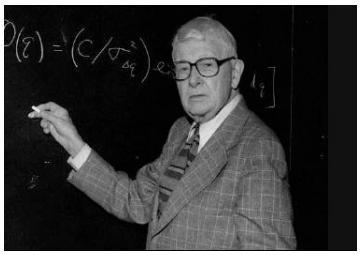
Foundations of population genetics



R.A. Fisher
1890 -1960

J.B.S. Haldane
1882 -1964



S. Wright
1889 -1988

- 1930-50 theoretical population genetics was initiated by Fisher, Haldane & Wright and provided the foundations for "Neo-Darwinism" and the "New Synthesis"
- they showed that continuous variation and Darwinian natural selection were entirely consistent with Mendel's Laws
- they also demonstrated the evolutionary significance of genetic variation leading to several key questions and development of the field of ecological & evolutionary genetics

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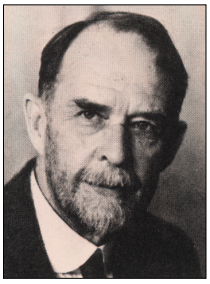
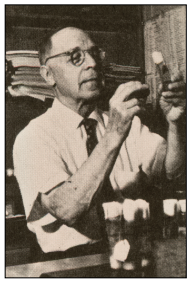
Classical school *Balance school*

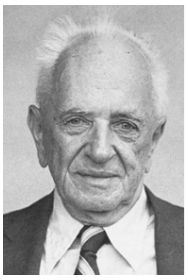


T. H. Morgan
(1866-1945)



H. J. Muller
(1890-1967)

E.B. Ford*
(1901-1988)



T. Dobzhansky
(1900-1975)

The two schools differed in their predictions on how much genetic variation occurs in natural populations

* Founder of Oxford school of ecological genetics

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Two models of population genetic structure

Classical

- Morgan, Muller
- Wild type is best genotype
- most mutations are deleterious/lethal... → negative (purifying) selection
- ...but the occasional mutation is beneficial → positive selection (adaptation)

↓

Predict: high homozygosity, low polymorphism

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Two models of population genetic structure

Balance

- Ford, Dobzhansky
- No best or ideal genotype; different genotypes are adapted to different conditions

balancing selection ←

↓

Predict: low homozygosity, high polymorphism

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Early evidence for the existence of genetic variation

- Selection experiments on quantitative traits in different groups of organisms
- Involves controlled breeding and selection of individuals for many generations

→ **Artificial selection**

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Phenotypic variation

The organism as observed – used when discussing a trait or a feature of an organism that varies

Environmental effects

Genetic variation

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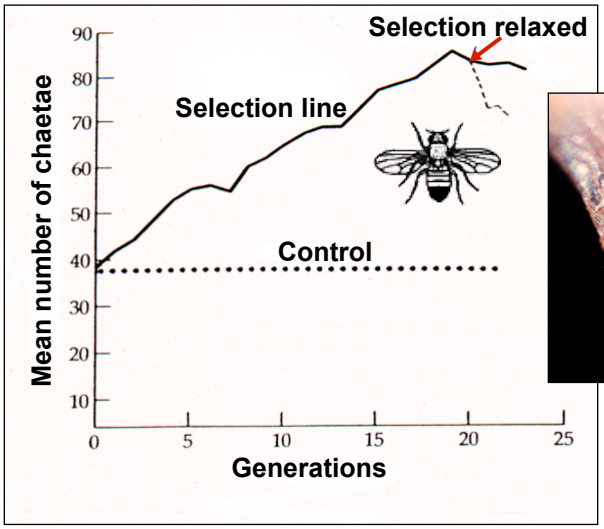
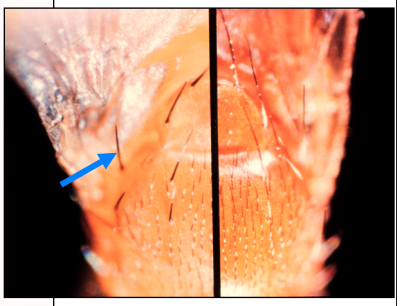
Selection response for bristle number in fruit flies - Drosophila melanogaster





Control involves random mating

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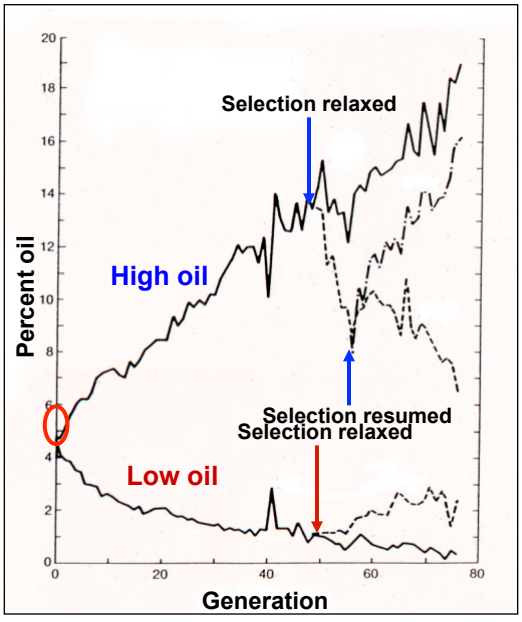
Selection response in maize



This type of artificial selection is the basis of plant breeding and is used to improve crop varieties

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Results of artificial selection experiments on quantitative traits

• Selection responses demonstrate that abundant genetic variation exists for polygenic (quantitative) traits

• But no information on key population genetic parameters (*P* & *H*) also comparative studies difficult as traits studied often group specific

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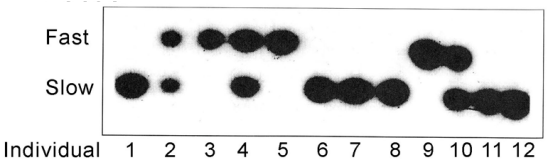
R.C. Lewontin - Harvard

Richard Lewontin and the electrophoresis revolution



- Allozyme* gel electrophoresis provided a way to ask - "what proportion of genes are variable (polymorphic)?"- a fundamental dispute between the classical and balance schools

- Initiated large scale surveys of electrophoretic variation in enzymes & proteins in diverse organisms and provided the first empirical evidence supporting the balance school

Allozymes = different forms of the same protein

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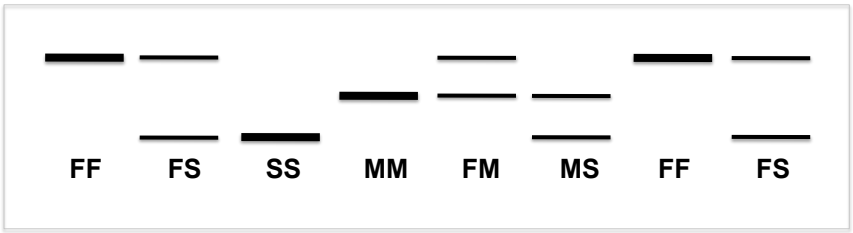
Protein electrophoresis – measuring diversity at genes controlling enzymes & proteins

Monomorphic gene

Polymorphic gene



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Advantages of studies of enzyme polymorphism

- Many loci can be examined
- Can be used in nearly any organism
- Loci co-dominant, heterozygotes can be identified
- Variation examined close to DNA level
- Provides genetic marker loci for other studies

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TABLE 3 Lewontin & Hubby 1966

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
Strawberry Canyon	California	6	.33	.148
Wildrose	California	5	.28	.106
Cimarron	Colorado	5	.28	.099
Mather	California	6	.33	.143
Flagstaff	Arizona	5	.28	.081
Average			.30	.115

Drosophila subobscura (18 loci in 5 populations)
Polymorphism (*P*) = 0.3 (30%)
Heterozygosity (*H*) = 0.11 (11%)

See Lab Chapter 4!

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Table 4-2. Genetic variation in natural populations of groups of animals and plants (Ayala 1984).

Organisms	No. of species surveyed	Average no. of loci surveyed per species	Average Polymorphism	Average Heterozygosity
Invertebrates				
Drosophila	28	24	0.529	0.150
Wasps	6	15	0.243	0.062
Other insects	4	18	0.531	0.151
Marine invert.	14	23	0.439	0.124
Land snails	5	18	0.437	0.150
Vertebrates				
Fishes	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
Mammals	30	28	0.206	0.051
Plants				
Self-pollinating	33	14	0.179	0.058
Outcrossing	36	11	0.511	0.185
Overall averages				
Invertebrates	57	22	0.469	0.134
Vertebrates	68	24	0.247	0.060
Plants	69	13	0.345	0.121

Do these results support the predictions of the Classic School or the Balance School (or neither!)?

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What maintains genetic variation?

1. **Balancing selection**
   - heterozygote advantage, frequency-dependent selection
2. **Mutation-selection balance**
   - less fit types maintained by mutation
3. **Variation is selectively neutral**
   - different types do not differ in their fitness hence none eliminated by selection

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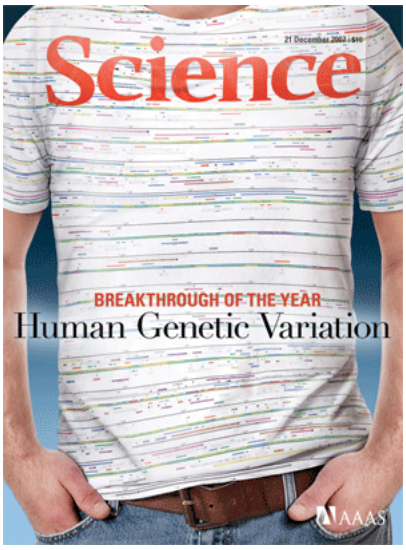
Studying genetic variation at the DNA level



DNA sequencer

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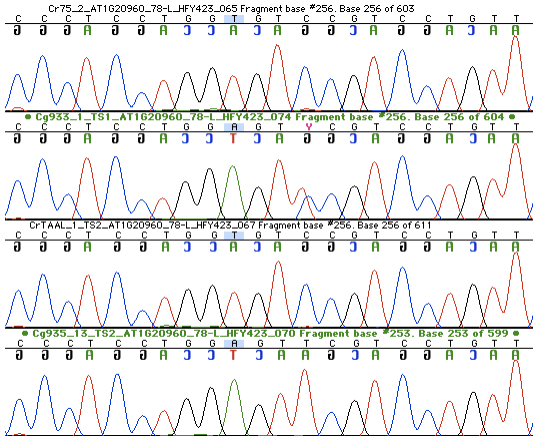
DNA sequencing allows differences between individuals in single nucleotides to be identified



SNP's = single nucleotide polymorphisms can be measured for thousand of genes

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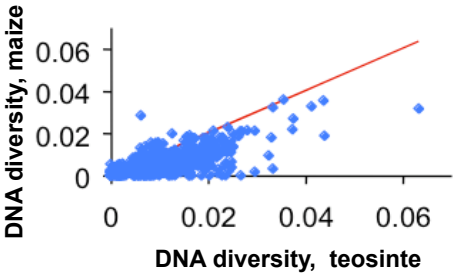
DNA variation in maize vs. teosinte



Stephen Wright (EEB) and colleagues found that domestication of maize from its progenitor teosinte caused a 57% reduction in variation at SNP's; they estimate that 1200 genes have been affected by artificial selection

Science (2005)

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