Week 9

Joe Felsenstein

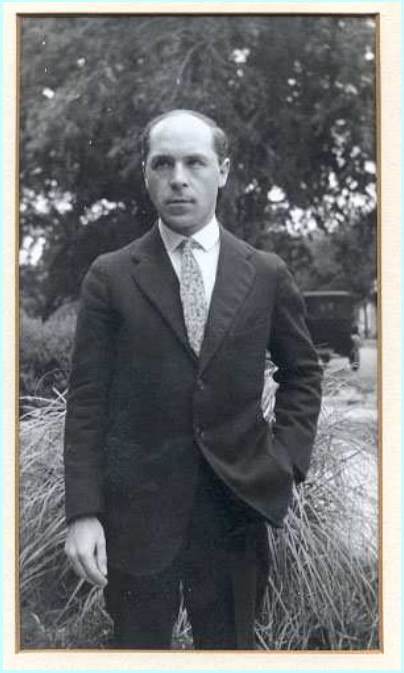
Genome 562, 2017

Effect of a bottleck on effective number

Number of generations at:		Effective pop ulation number	
$N_i = 10$	$N_i = 1000$	N_e (approximate)	N_e (exact)
1	99	502.51	496.25
5	95	168.07	164.74
10	90	91.74	89.86
25	75	38.83	38.13
50	50	19.80	19.56
75	25	13.29	13.21
90	10	11.10	11.07
99	1	10.10	10.10

Views of genetic variation before 1966

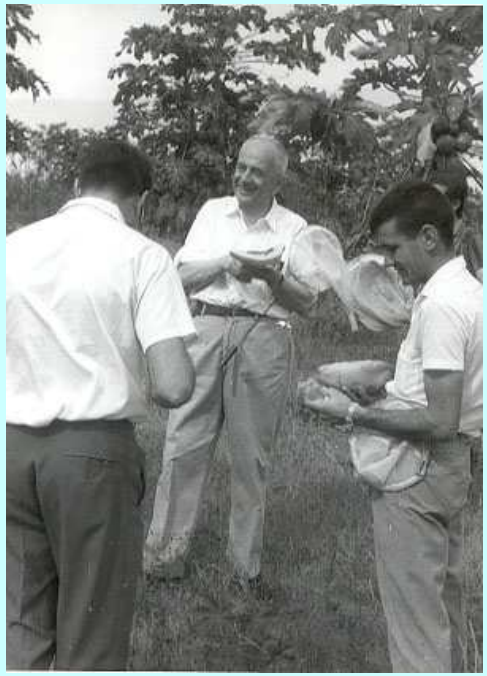
The Classical view



Hermann Joseph Muller

Most loci will be homozygous
for the “wild-type allele"
but a few mutants will exist

The Balancing Selection view



Theodosius Dobzhansky

Most loci will be polymorphic
due to balancing selection
with strong selection

Polymorphism on a gel

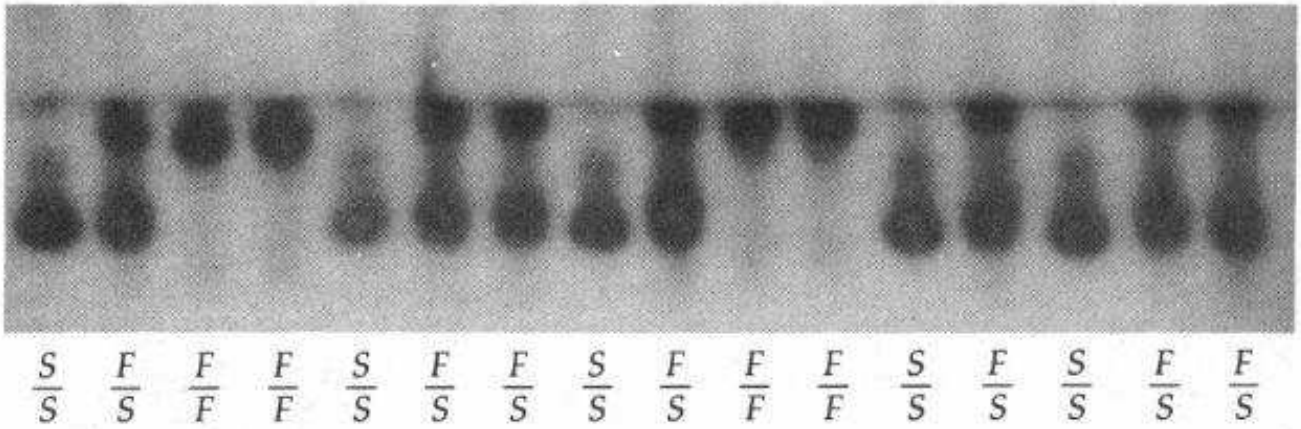


Figure 4. Results of electrophoresis of the enzyme glucose phosphate isomerase-1 from 16 cultured cell lines originating from individuals of the mouse, *Mus musculus*. The gene that codes for the enzyme is *Gpi-1*. In this sample, some individuals are homozygous for an allele (*S*) corresponding to a slow-migrating enzyme, some are homozygous for an allele (*F*) corresponding to a fast-migrating enzyme, and the rest are heterozygous (*F*/*S*). The inferred genotypes of the cell lines are indicated beneath the enzyme bands. This enzyme is a monomer, so the heterozygotes exhibit two enzyme bands of differing mobility. (Courtesy of S. E. Lewis and F. M. Johnson.)

Lewontin and Hubby's 1966 work

Richard Lewontin, about 1980

Lewontin, R. C. and J. L. Hubby. 1966. 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:** 595-609.

Neutral mutation theory

James F. Crow and Motoo Kimura, 1972

Tomoko Ohta, recently

Kimura, M., and J. F. Crow. 1964. The number of alleles that can be maintained in a finite population. *Genetics* **49:** 725-738.

Kimura, M. 1968. Evolutionary rate at the molecular level. *Nature* **217:** 624-626.

Kimura, M., and T. Ohta. 1971. Protein polymorphism as a phase of molecular e8volution. *Nature* **229:** 467-469.

DNA sequencing reveals a similar picture

Marty Kreitman

Kreitman, M. 1983. Nucleotide polymorphism at the alcohol-dehydrogenase Locus of *Drosophila melanogaster*. *Nature* **304:** 412-417.

Kreitman's sample of 11 ADH gene sequences, front end

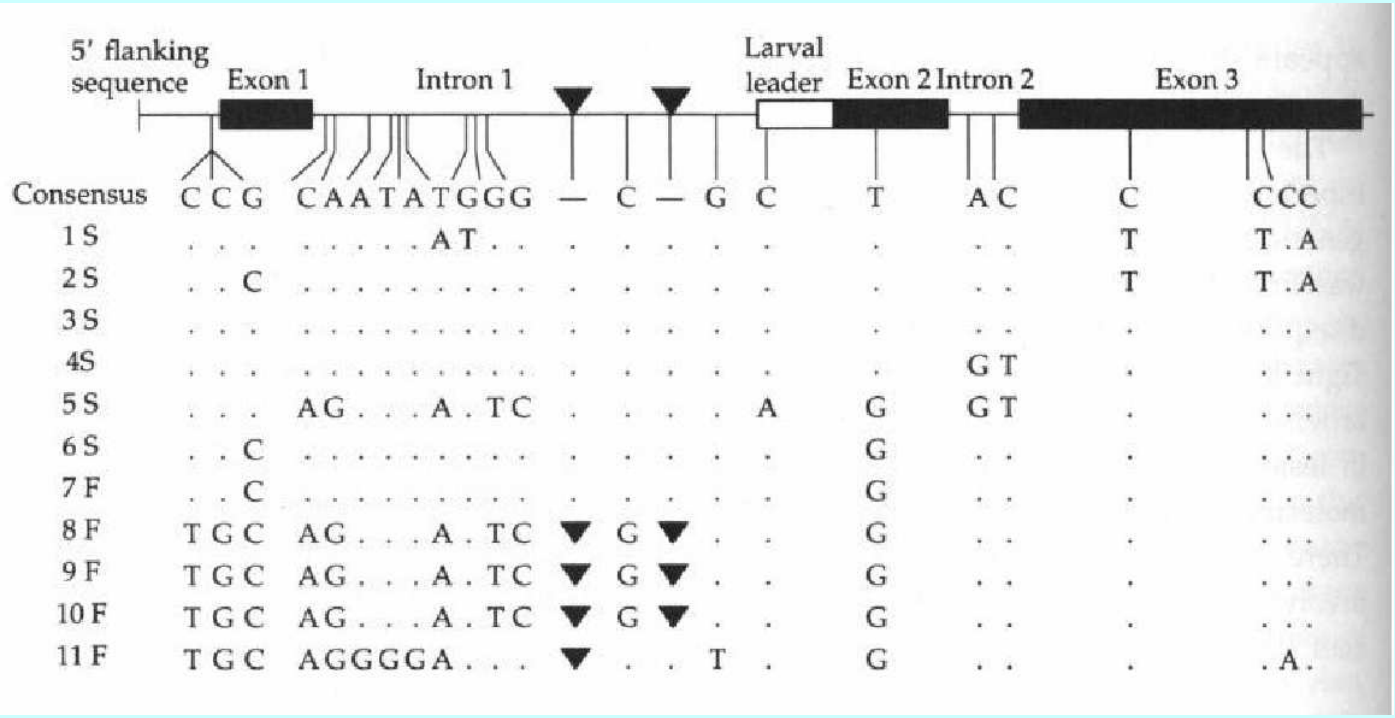
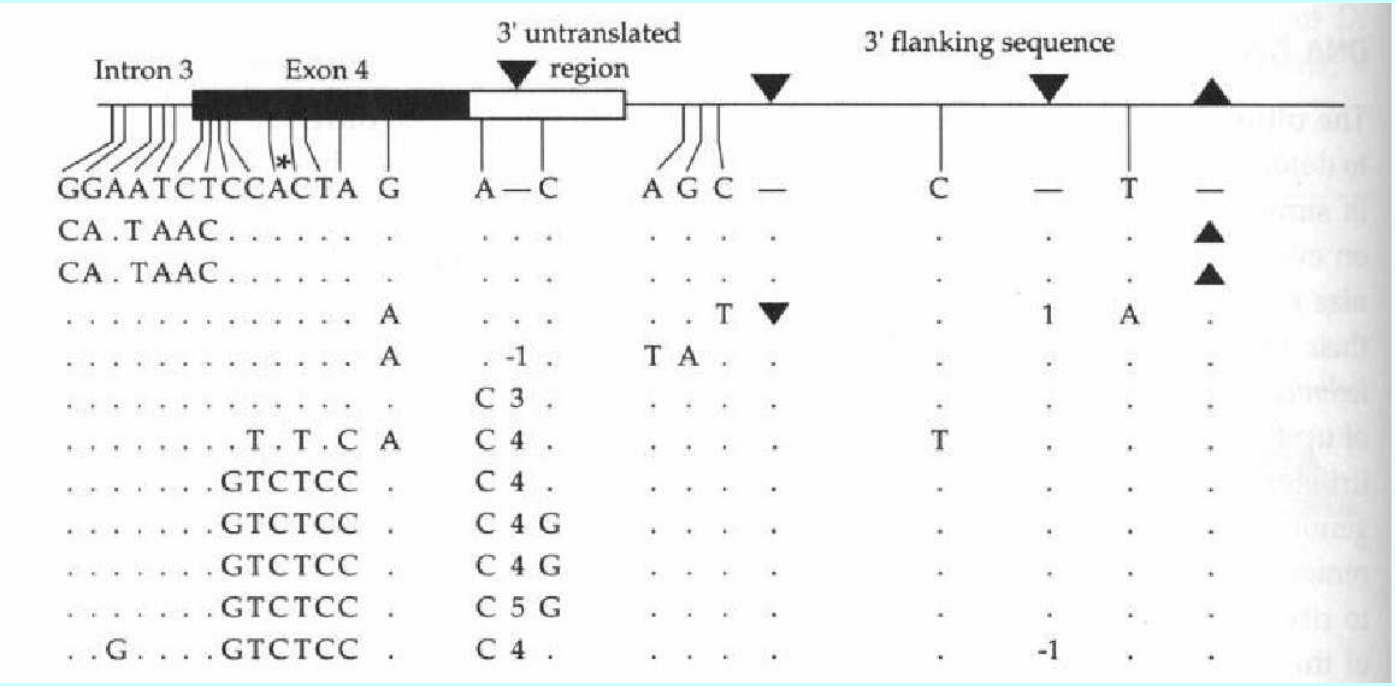


Figure 4. Polymorphic nucleotide sites among 11 alleles of the alcohol dehydrogenase gene of *Drosophila melanogaster*. The first line gives a consensus sequence for *Adh* at sites that vary; subsequent lines give the nucleotides from each copy for the polymorphic sites. A dot indicates that the site is identical to the consensus sequence. The triangles indicate sites of insertion or deletion relative to the consensus sequence. The star in exon 4 indicates the site of the amino acid replacement (lysine for threonine) responsible for the *fast-slow* mobility difference in the *Adh* protein. (After Kreitman 1983.)

Kreitman's sample of 11 ADH gene sequences, tail end



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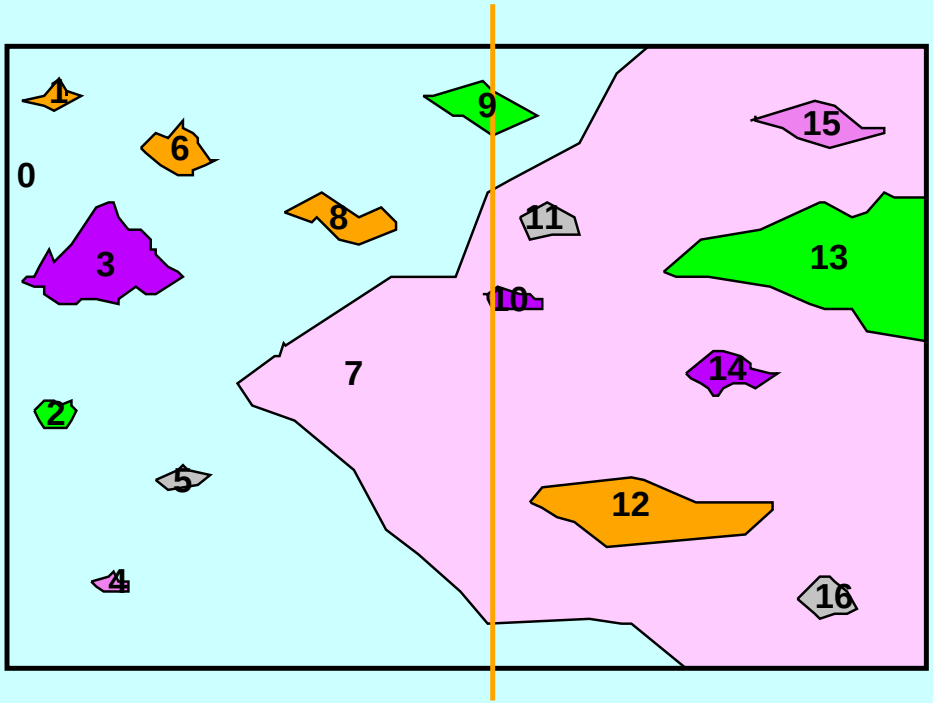
Individual alleles do not stay at an equilibrium

Crow and Kimura, 1964; Lewontin and Hubby, 1966;
Kimura, 1968; King and Jukes, 1969; Kimura and Ohta, 1971

assume: population size N, rate u of neutral mutations, all different



Heterozygosity at any point is expected to be

$$\frac{4Nu}{4Nu + 1}$$