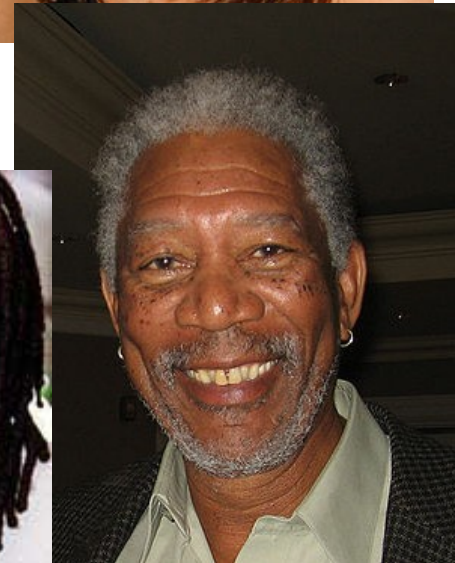
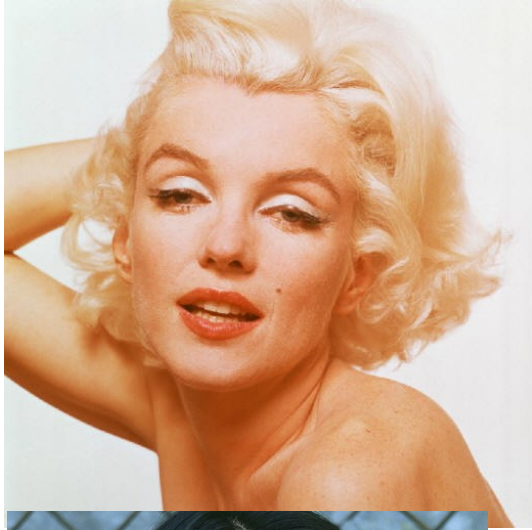


# GENETIC AND PHENOTYPIC VARIATION

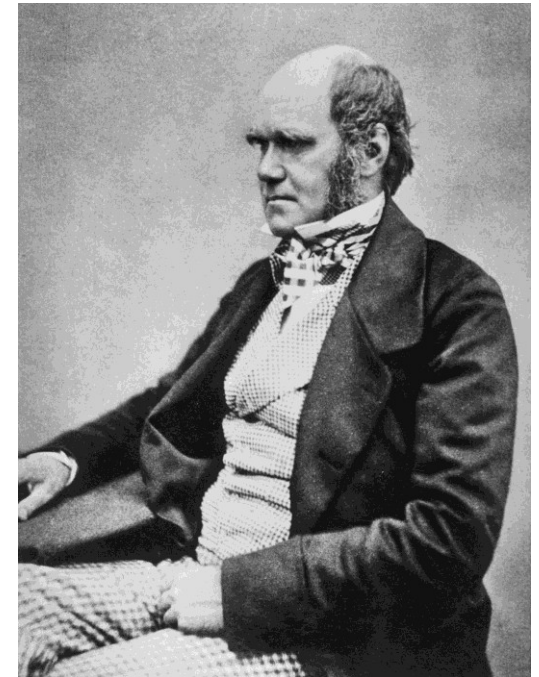


## Evolution as a two-stage process:

1. variation among individuals in a population
2. changes in the proportion of variants from generation to generation

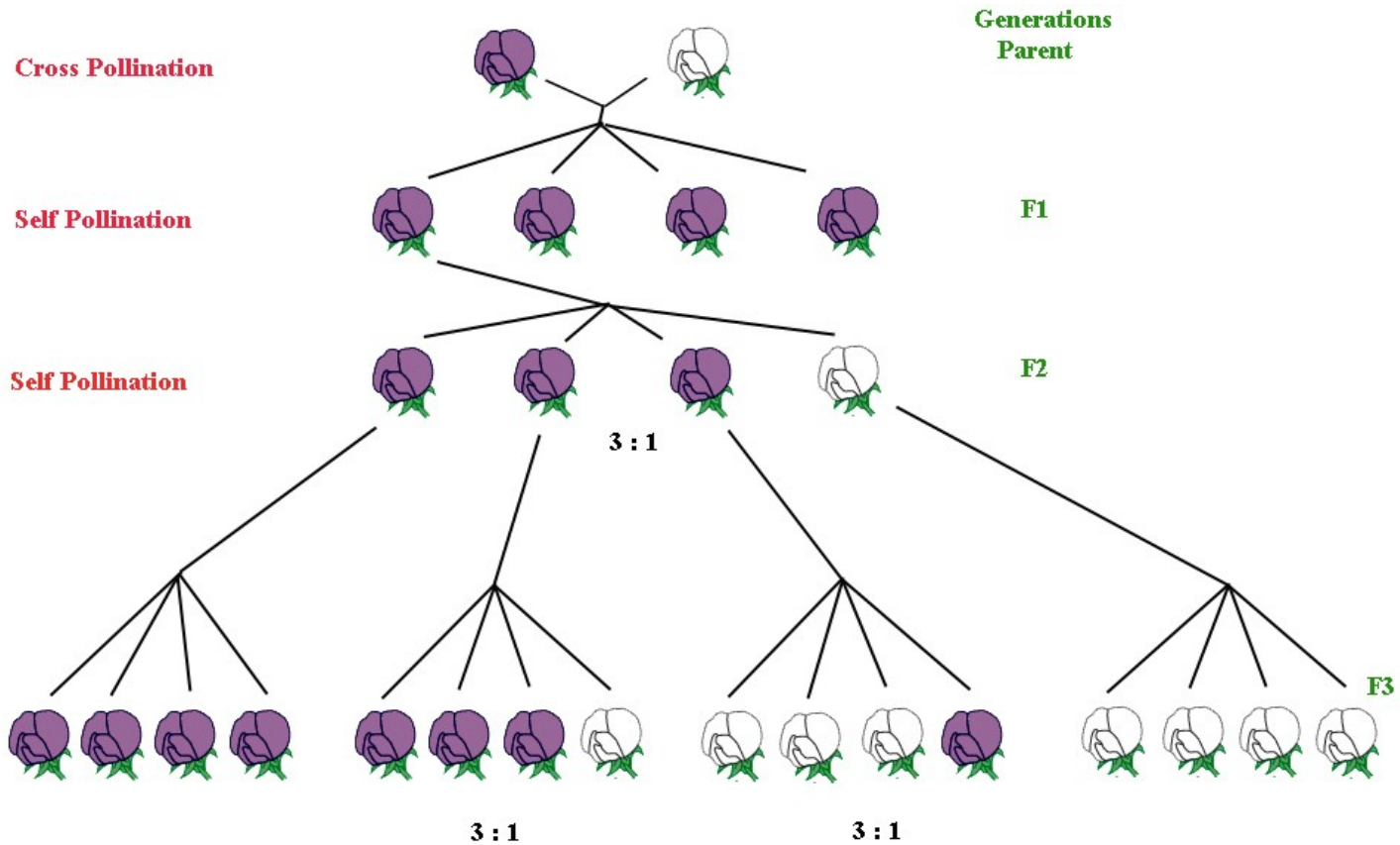
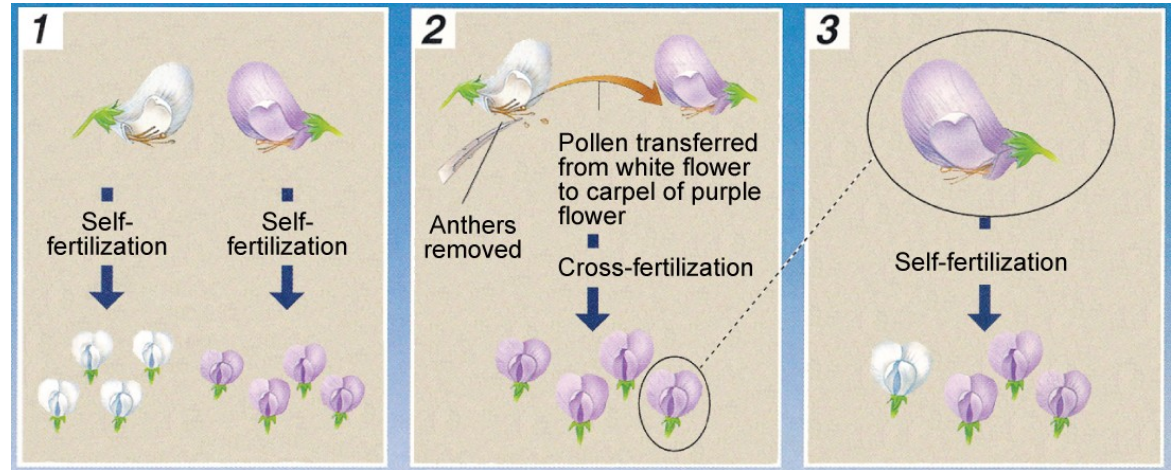


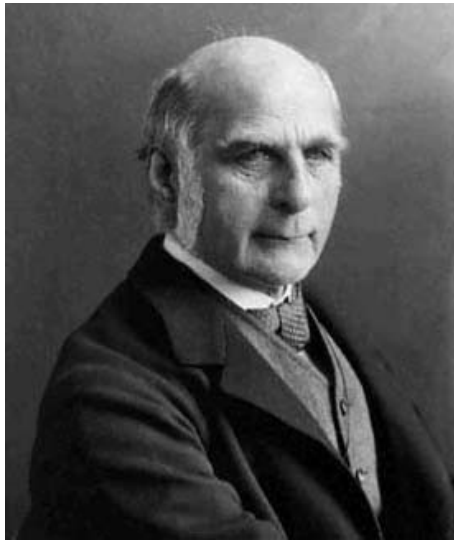
R.A. Fisher



The increase in mean fitness due to natural selection is proportional to the additive genetic variance in fitness.

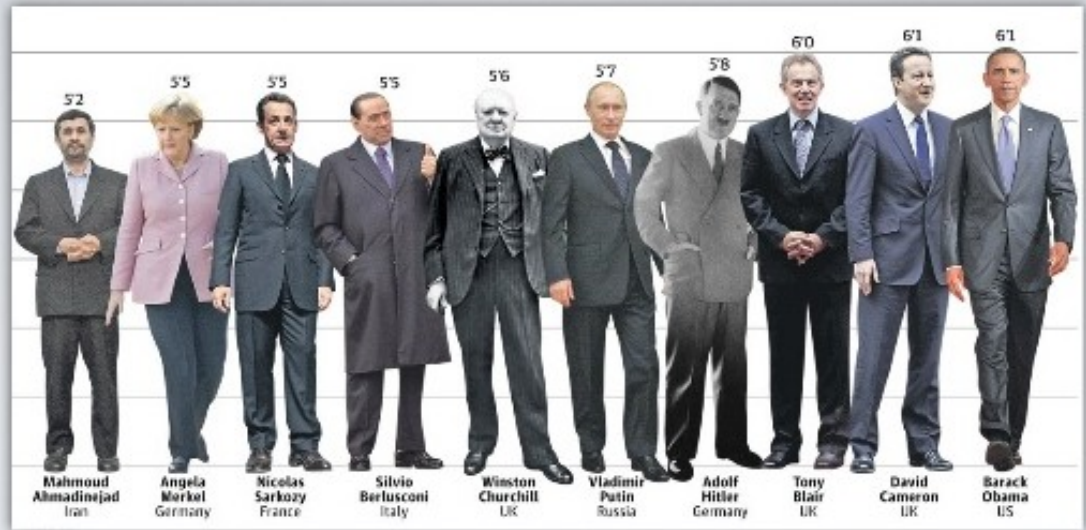






F. Galton

## Continuous And Discontinuous Variation



CVHS GCSE POWERPOINT SHARE

### Biometricians: continual variation

many genes

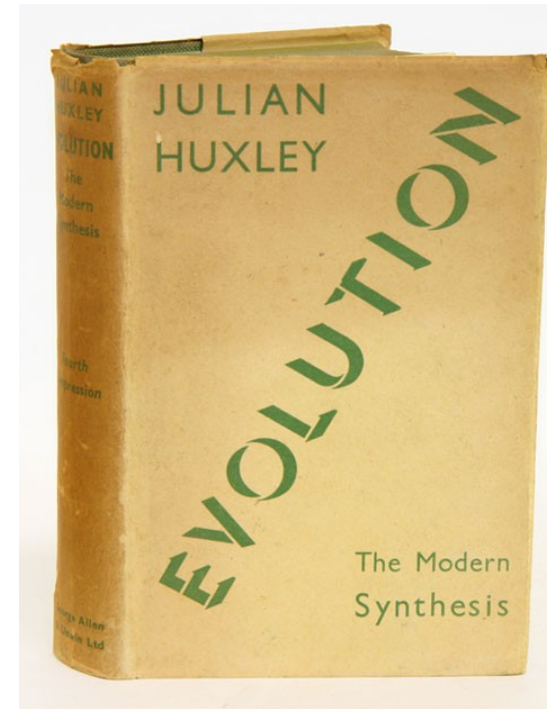
often strong influence of environment

## Sources of phenotypic variation:

differences in genotype

differences in environmental conditions

maternal influences (paternal influences)



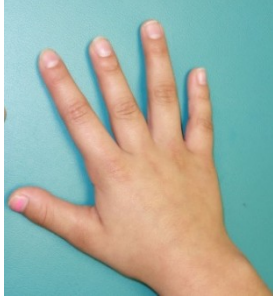

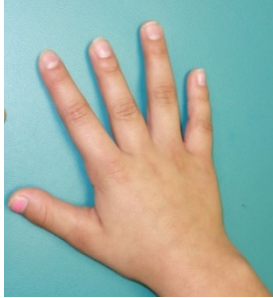

## Paradox:

for evolutionary biologists important to study phenotypes

for geneticists easier to directly study molecules



Reginald C. Punnett: brachydactyly

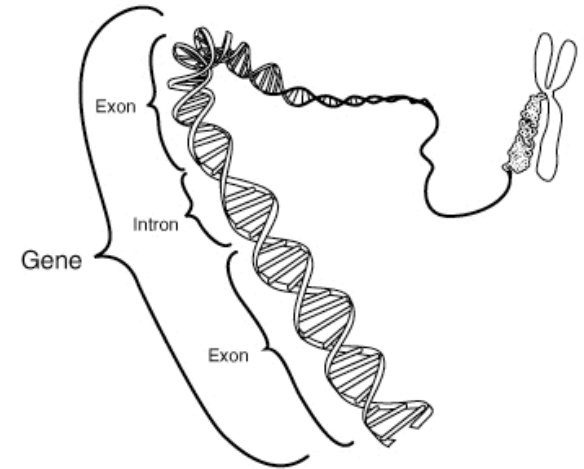
	$B$	$b$
$B$	 $BB$	 $Bb$
$b$	 $Bb$	 $bb$



George Udny Yule

Why don't we observe the 3:1 ratio in *populations*?





**gene** ... till now difficult to define/delimit

**locus** ... here = gene

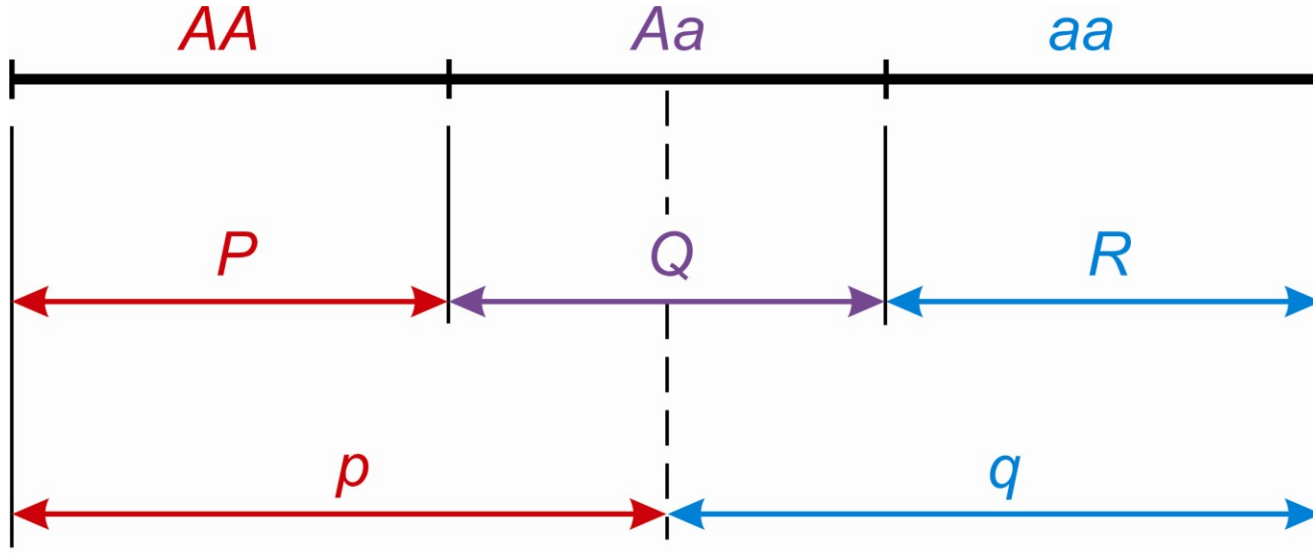
**alleles** = alternative forms of genes (now broader meaning – segment of DNA)

**genome** = set of all genes of an individual (nuclear, mitochondrial...)

**genotype** = set of alleles of one or more genes of an individual

**haplotype** (**haploid genotype**) = combination of alleles inherited together

# Genotype and allele frequencies



Frequencies: genotype:  $P$  ( $f_{AA}$ ),  $Q$  ( $f_{Aa}$ ),  $R$  ( $f_{aa}$ )

allele (gene):  $p$  ( $A$ ),  $q$  ( $a$ )

$$P + Q + R = 1$$

$$p + q = 1$$



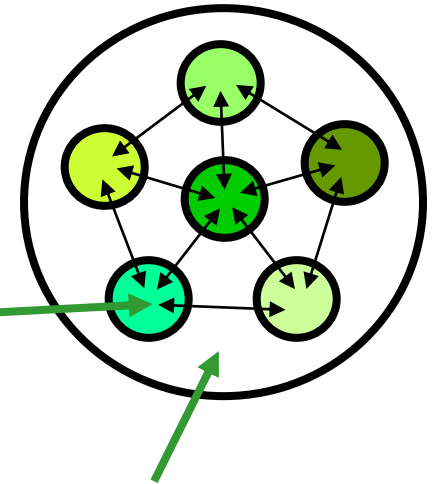
# Evolution takes place in populations...

T. Dobzhansky, E. Mayr:

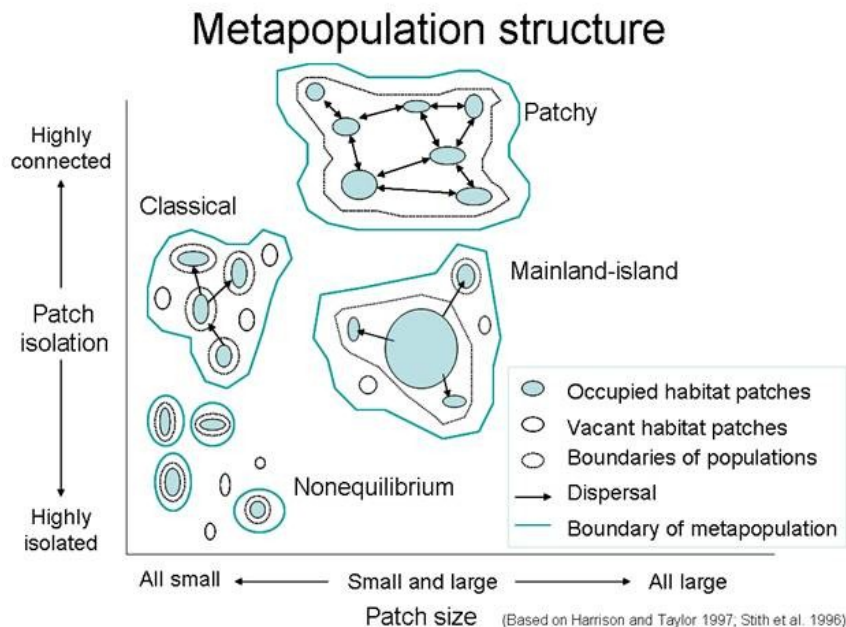
population as a shared **gene pool**

≈ set of shared alleles or gametes

local populations (subpopulations, demes)



global population, metapopulation



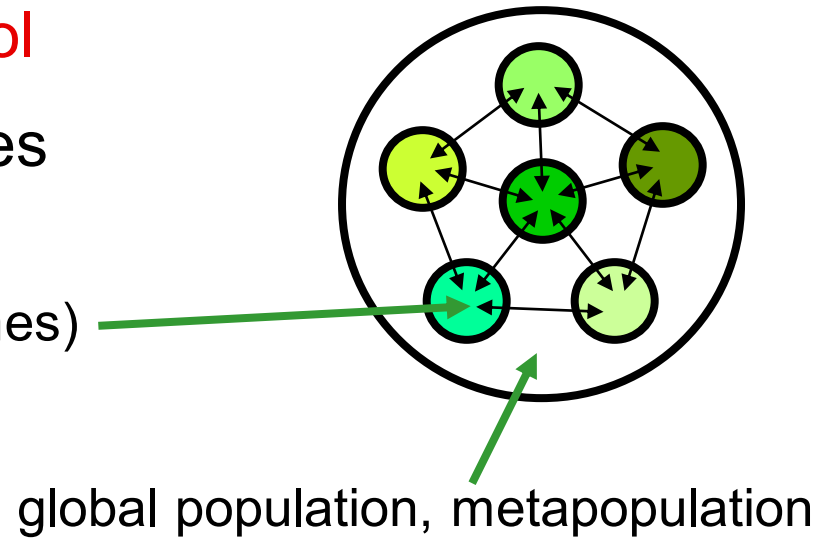
# Evolution takes place in populations...

T. Dobzhansky, E. Mayr:

population as a shared **gene pool**

≈ set of shared alleles or gametes

local populations (subpopulations, demes)



Local populations also share a **system of mating**

populations natural, experimental, agricultural, model

# Model populations – Hardy-Weinberg population

## Characteristics:

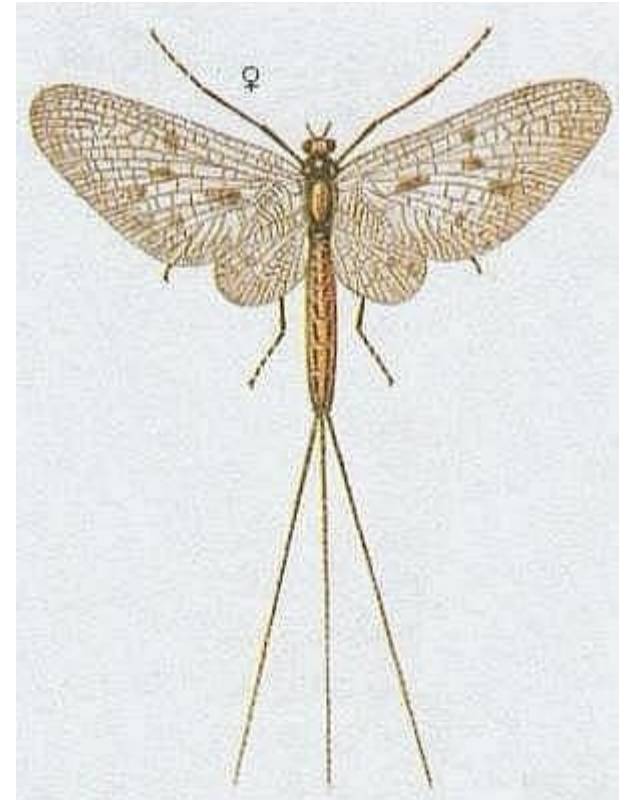
diploid

sexual reproduction

discrete generations

2 alleles, „fair“ segregation 1:1

same frequencies of alleles in both sexes



# Model populations – Hardy-Weinberg population

## Characteristics:

random mating (panmixis)

non-random: assortative mating, inbreeding

very large (effectively infinite) size

no gene flow

no mutation

no selection



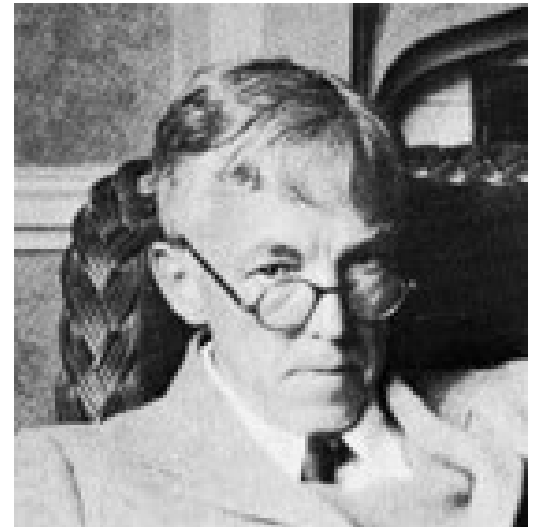
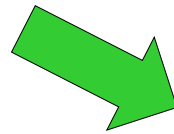
# Why don't we observe the Mendelian ratios in nature?



R. C. Punnett



1908



Godfrey Harold Hardy

# HARDY-WEINBERG PRINCIPLE

		Father's gametes	
		Alela: A	a
Mother's gametes	A p	AA $p \times p = p^2$	Aa pq
	a q	Aa $q \times p = qp$	aa $q^2$

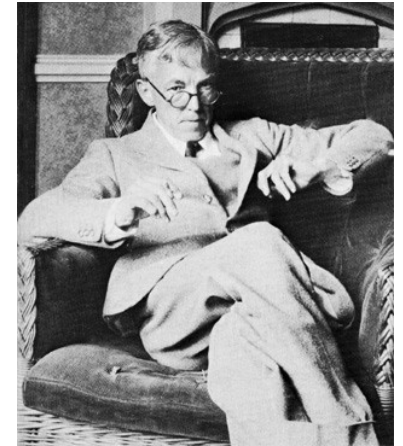
Genotype frequencies in zygotes:

$$f_{AA} = p^2$$

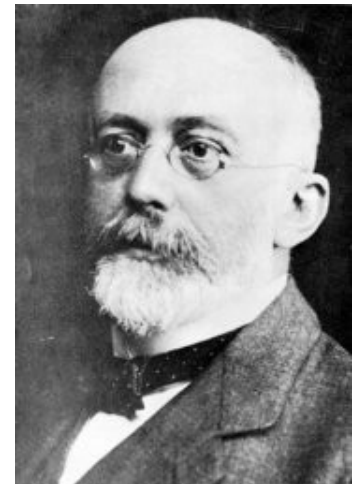
$$f_{Aa} = pq + qp = 2pq$$

$$f_{aa} = q^2$$

$$p^2 + 2pq + q^2 = 1$$



Godfrey Harold Hardy  
(1877-1947)



Wilhelm Weinberg  
(1862-1937)

# HARDY-WEINBERG PRINCIPLE

1. Allele frequencies stable across generations  
= Hardy-Weinberg equilibrium (HWE)
2. HWE achieved within a single generation of random mating

## Generalization:

X-linked genes:

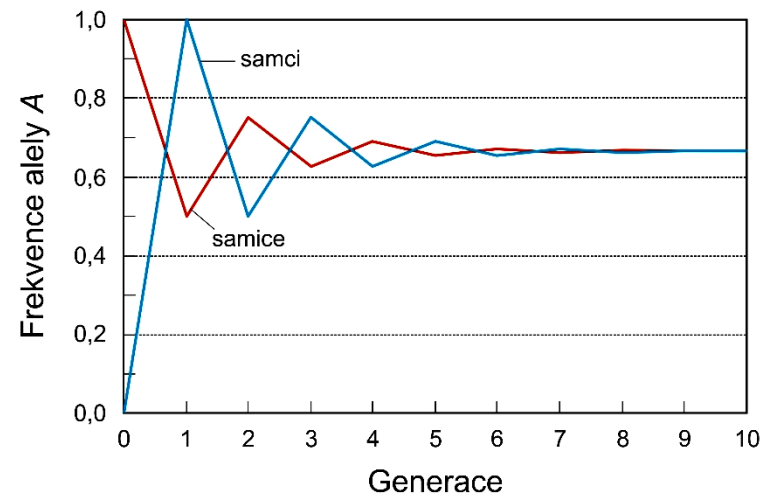
$$\text{females: } p^2 + 2pq + q^2$$

$$\text{males: } p + q$$

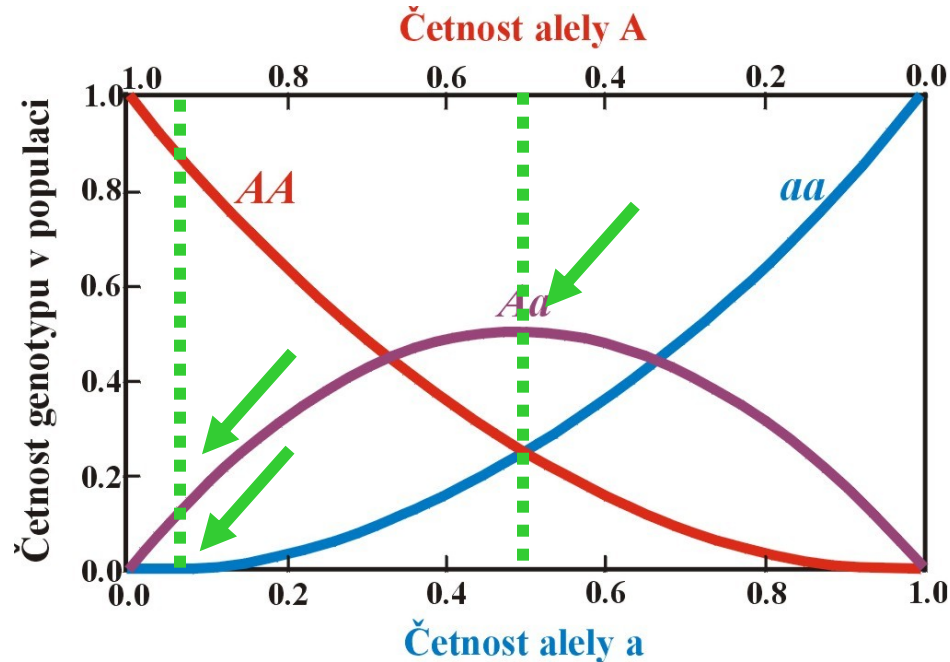
more than 2 alleles:

$$3 \text{ alleles: } p^2 + q^2 + r^2 + 2pq + 2pr + 2qr$$

$$\text{in general } p_i^2 + 2p_{ij}$$



# Frekvencies of rare alleles



heterozygotes most frequent when  $p = q = 0,5$

$f_{Aa}$  decreases with  $2pq$

$f_{aa}$  decreases with  $q^2 \Rightarrow f_{Aa} / f_{aa}$  increases  $\rightarrow$  rare allele „hidden“ for selection in heterozygous state



# Possible causes of HWE violation:

## Methodic causes:

null alleles, allelic dropout

## Violation of some of the assumptions of the H-W population:

### Heterozygote deficiency:

selection against heterozygotes

nonrandom mating (inbreeding, assortative mating)

structured populations (different allele frequencies, cf. Wahlund effect)

### Heterozygote excess:

selection in favour of heterozygotes

nonrandom mating (outbreeding, negative assortative mating)

migration

mutation

# GENETIC VARIATION IN POPULATIONS

## Methods of the study of genetic variation:

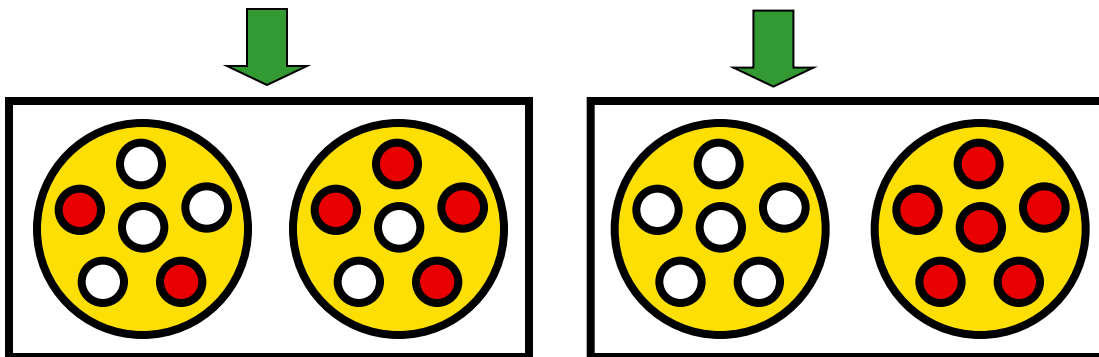
protein electrophoresis

analysis of restriction fragments  
(Southern blotting, RFLP, DNA fingerprinting)

PCR, sequencing, NGS, microsatellites ...



## Polymorphism and polytypy



## Polymorphism:

proportion of polymorphic loci ( $P$ )

sample size usually finite  $\Rightarrow$

limit 5% ( $P_{0.05}$ ) or 1% ( $P_{0.01}$ )

number of alleles per locus ( $A$ ; allele diversity, allele richness)

mean observed heterozygosity ( $H_o$ )

mean expected heterozygosity ( $H_e$ ) = gene diversity

nucleotide polymorphism ( $\theta$ )

nucleotide diversity ( $\pi$ )

# GENETIC VARIATION IN NATURAL POPULATIONS

Issue of the extent of variation in natural populations:



T.H. Morgan, H. Muller:  
„classical“ model  
limited variability



A. Sturtevant, T. Dobzhansky:  
„equilibrium“ model  
variation widespread

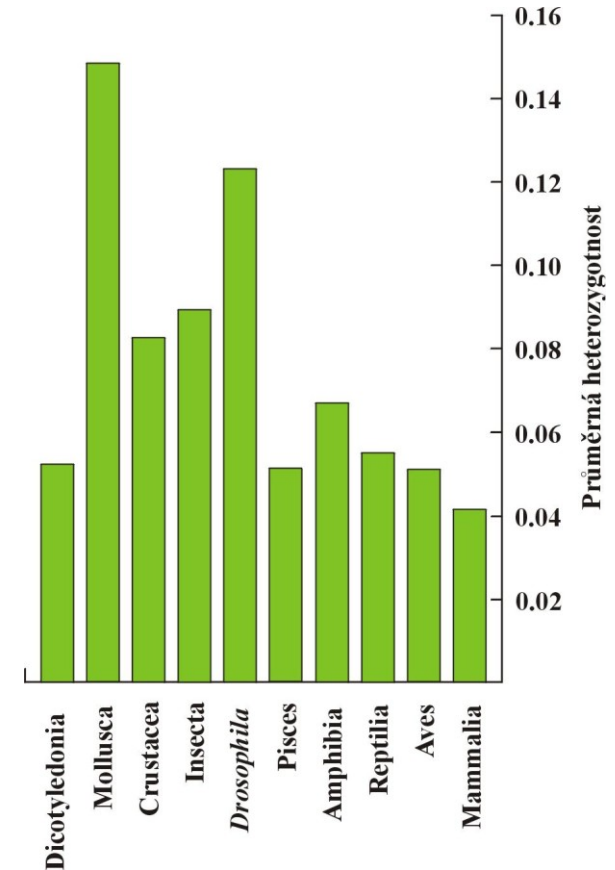




# GENETIC VARIATION IN NATURAL POPULATIONS

1966: Harry Harris – humans; Richard Lewontin, John Hubby – *D. pseudoobscura*

Taxon	Počet zkoumaných druhů	Podíl lokusů polymorfních	Průměrná heterozygotnost
<b>Bezobratlí</b>			
mořští plži	5	0.175	0.083
suchozemští plži	5	0.457	0.150
ostatní mořští bezobratlí	9	0.587	0.147
haplodiplovní blanokřídlí	6	0.243	0.062
<i>Drosophila</i>	43	0.431	0.140
ostatní hmyz	23	0.329	0.074
bezobratlí celkem	93	0.397	0.112
<b>Obratlovcí</b>			
ryby	51	0.152	0.051
obojživelníci	13	0.269	0.079
plazi	17	0.219	0.047
přasi	7	0.150	0.047
hrochovi	26	0.202	0.054
savci	46	0.147	0.036
obratlovci celkem	135	0.173	0.049
<b>Rostliny celkem</b>	473	0.505	–



microsatellites, minisatellites → high mutation rate, high variability  
question to what extent protein electrophoresis representative?

# VARIATION AT MORE LOCI

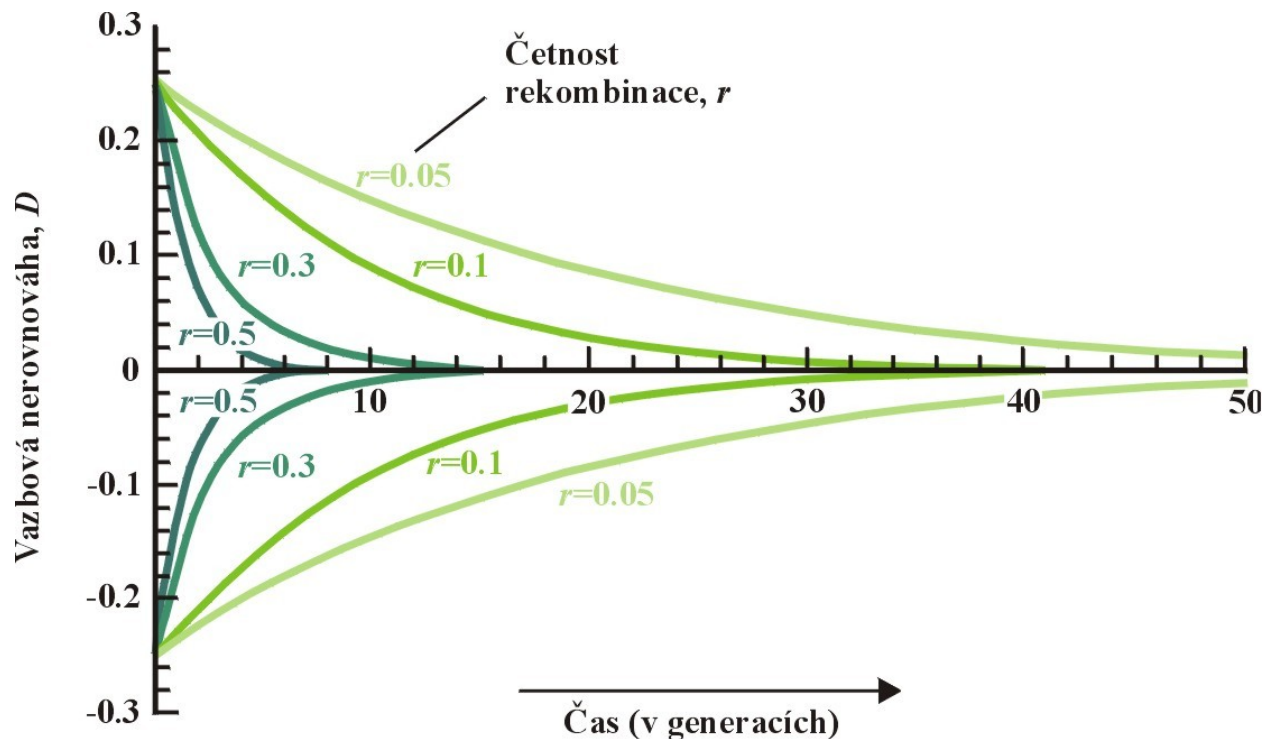
proximity of loci = **linkage**

valid H-W assumptions  $\Rightarrow$  formation of linkage equilibrium

this proces can be slow  $\Rightarrow$  **linkage disequilibrium (LD)**

coefficient of LD:  $D$

relation of  $D$  to recombination  $r$  :



## Causes of linkage disequilibrium:

absence of recombination (eg. inversion)

nonrandom mating

selection

recent mutation

sample is a mixture of 2 species with different allele frequencies

recent merging of 2 populations

random genetic drift

LD needn't exist only  
between loci on the same  
chromosome!

# INBREEDING

= mating between relatives

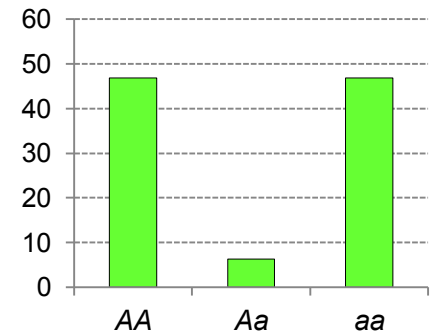
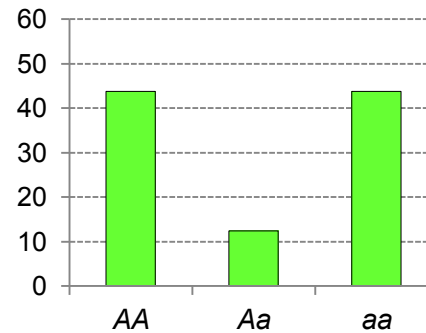
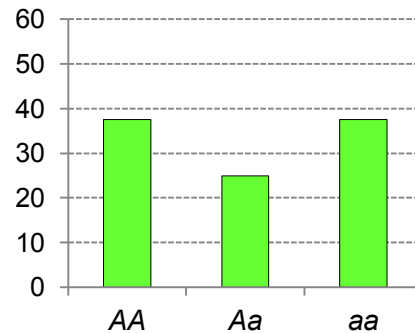
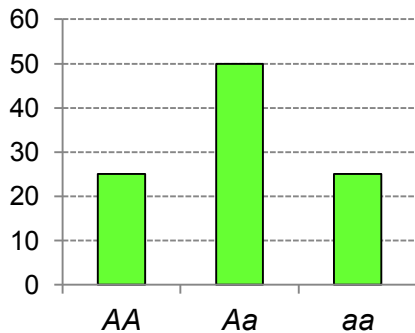
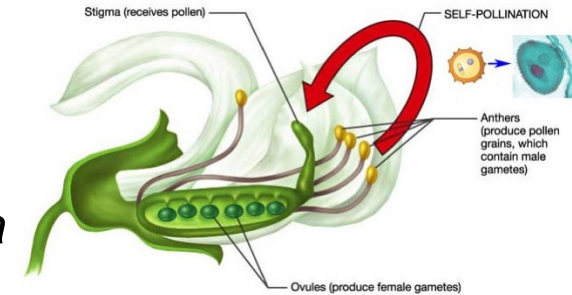
eg. repeated autogamy (self-fertilization, self-pollination):

initial generation (HWE):  $1/4 AA$ ,  $2/4 Aa$ ,  $1/4 aa$

1. gen. of selfing:  $3/8 AA$ ,  $2/8 Aa$ ,  $3/8 aa$

2. gen. of selfing:  $7/16 AA$ ,  $2/16 Aa$ ,  $7/16 aa$

3. gen. of selfing:  $15/16 AA$ ,  $2/32 Aa$ ,  $15/16 aa$

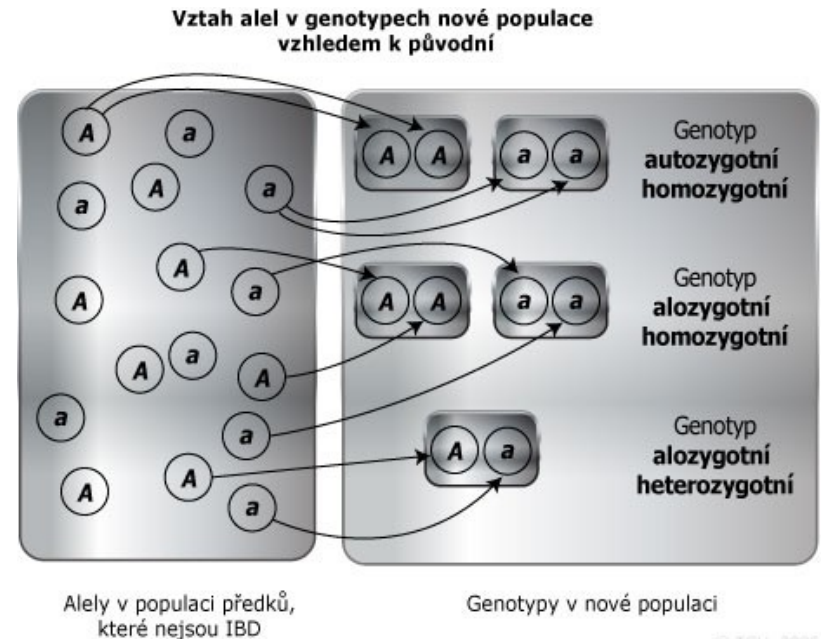




# INBREEDING COEFFICIENTS

## 1. Pedigree inbreeding, $F$ :

= probability of autozygosity



**autozygosity:**

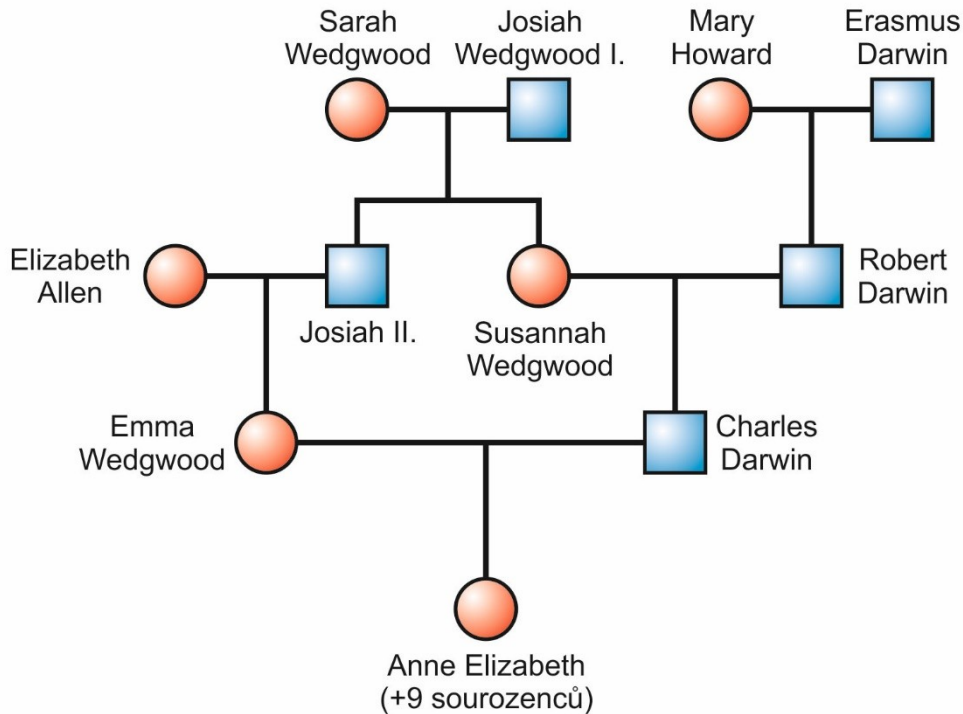
alleles identical by descent (IBD), always homozygous

**allozygosity:**

either heterozygote or homozygote (alleles identical by state, IBS)

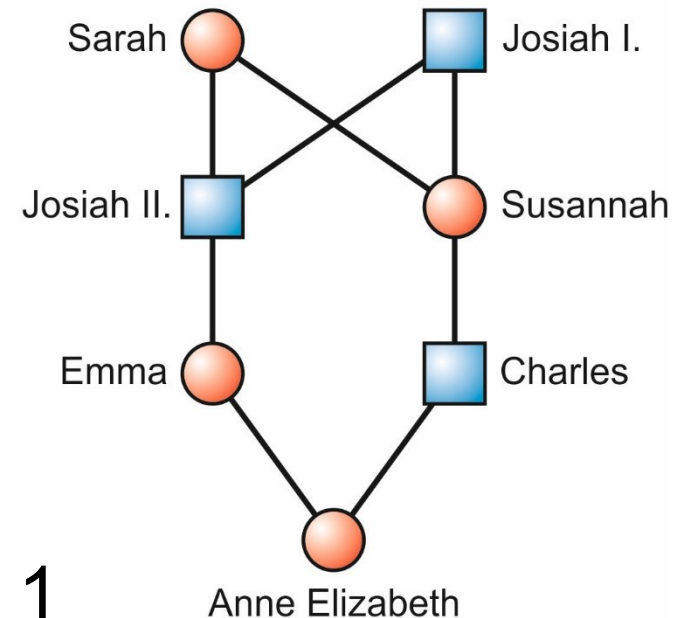
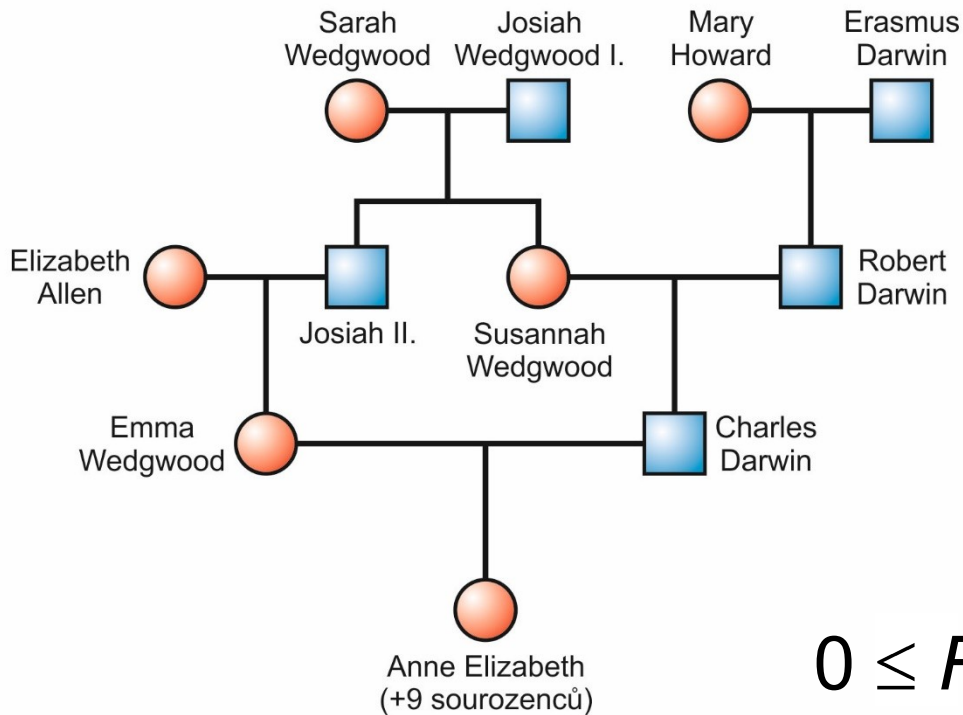
**Inbred population** = pop. in which the probability of autozygosity due to inbreeding  $>$  in panmictic population

$F$  = probability that an individual inherited both alleles at a locus from the same ancestor (both alleles are IBD)



**Inbred population** = pop. in which the probability of autozygosity due to inbreeding  $>$  in panmictic population

$F$  = probability that an individual inherited both alleles at a locus from the same ancestor (both alleles are IBD)



$$0 \leq F \leq 1$$



## 2. System-of-mating inbreeding, $F_{IS}$ :

= deviation from HWE

$$F_{IS} = (H_e - H_o) / H_e \quad -1 \leq F_{IS} \leq +1$$

$H_o$  = observed

$H_e$  = expected heterozygosity



$F$  and  $F_{IS}$  don't measure the same thing!

$F$  is the individual measure,  $F_{IS}$  is the group measure

Pr.: hutterites (anabaptists) of the Great Plains in USA and Canada

in spite of respecting the incest taboo this is one of the most inbred human groups known ( $F = 0,0255$ )

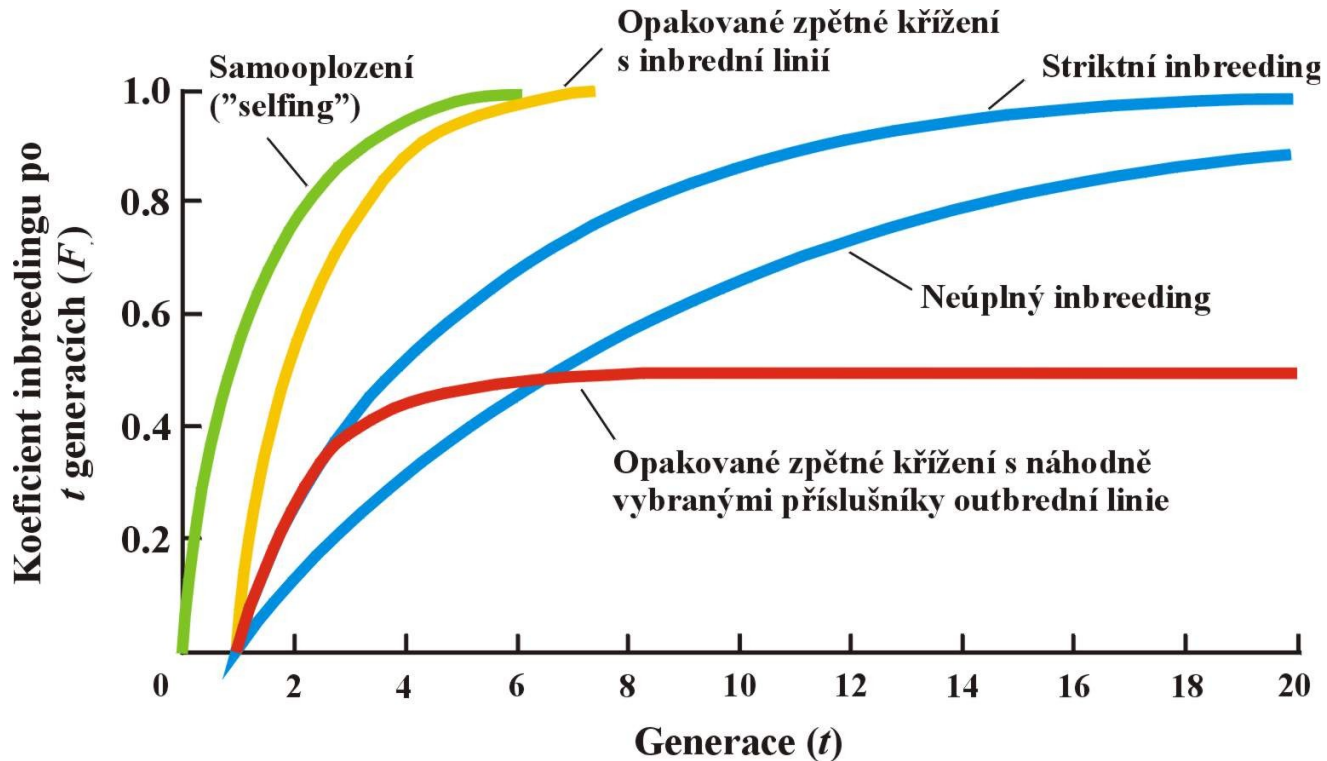
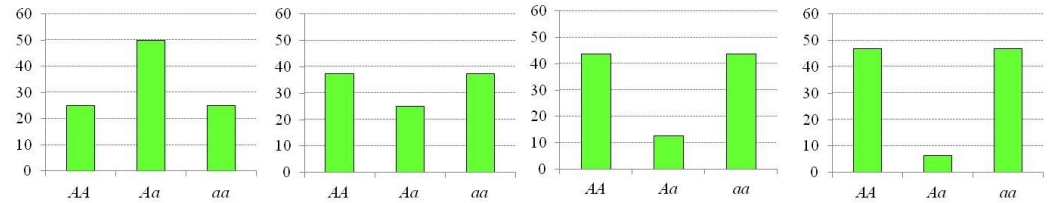
caused by a small number of founders (Protestants from Tyrol and Carinthia, 16th century)

# Genetic effects of inbreeding:

inbreeding changes genotype frequencies (increase of homozygote freq.)

× allele freqs. don't change

affects all loci





# Phenotypic effects of inbreeding:

## inbreeding depression

diseases, reduced fertility  
and/or viability



*Leavenworthia alabamica*



**BUT!** Not always must inbreeding be deleterious (eg. many species of embryophyte (land) plants are self-fertilising). Moreover, the inbreeding effects can differ within a single species depending on environment.

## Inbreeding depression in humans:

the Amish: haemophilia B, anemia, myotonic dystrophy, Ellis-van Creveld syndrome (dwarfism, polydactyly), defects in nail development, dental defects



Vadoma tribe, Zimbabwe (tzv. „Ostrich people“): ectrodactyly

Mormons of Hilldale (Utah) and Colorado City (Arizona)

Amazonia Indians

aristocratic dynasties



## Human inbreeding depression:

Charles II of Spain:

unnaturally big head, deformed mandible, weak body, difficulties with walking and other defects, mental and psychical defects, impotence, sterility



Francis II:

in some children mental retardation, hydrocephaly, seizures, some unable of living without assistance







Maria Theresa



Francis I of Lorraine

hybrid vigour  
(heterosis)

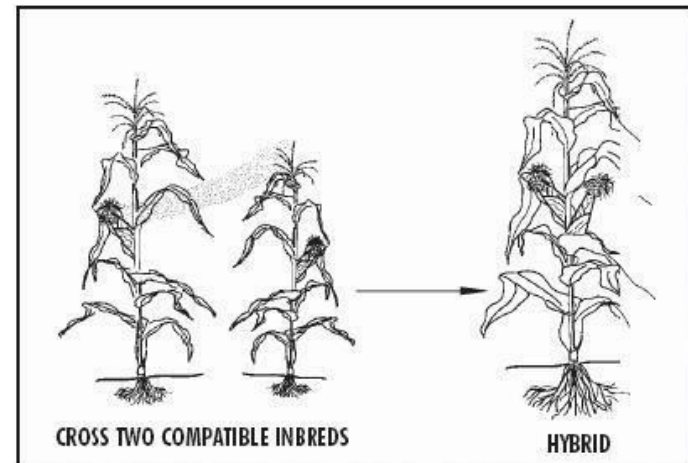


Figure 6. Cross pollination of two inbreds to produce a vigorous hybrid.

# ASSORTATIVE MATING

= higher probability of mating between individuals with the same phenotype

can be caused by active mating preference but another causes can exist as well

eg.: phytophagous insects – individuals living at different host species can mature in different times  $\Rightarrow$  more frequent mating between individuals of the same phenotype (confinement to the host) without active mating preference

$\Rightarrow$  this is only a positive phenotypic correlation

assortative mating causes deficit of heterozygotes

assortative mating causes linkage disequilibrium (LD)

## Differences between inbreeding and assortative mating:

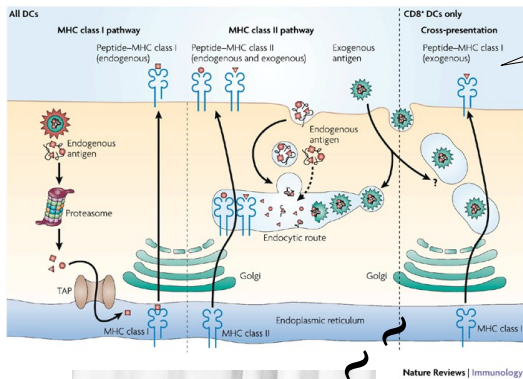
affects only locus (loci) connected with preferred phenotype    inbreeding  
affects all loci

ass. mating is a powerful evolutionary force (strong LD at more loci)  
× inbreeding only strengthens existing LD, and only in the case of selfing, in other cases recombination „more successful“ → reduction of LD



# NEGATIVE ASSORTATIVE (DISASSORTATIVE) MATING

= preference of mates with different phenotypes  
results in intermediary allele frequencies, reduces LD  
eg. preference of males with different MHC (mouse, man)



MHC



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