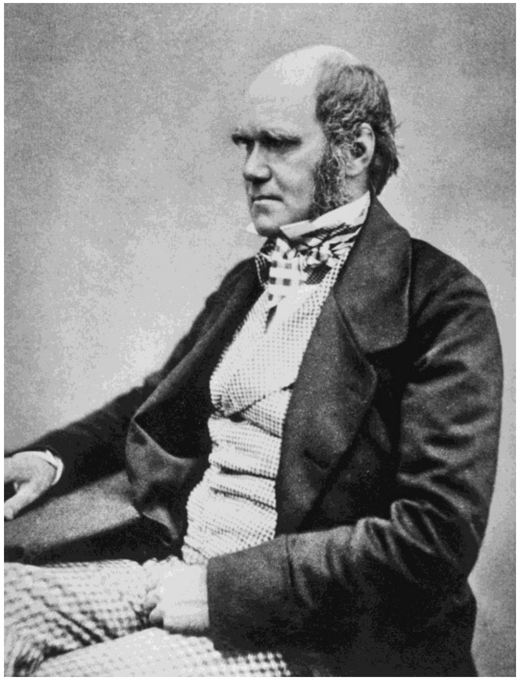
GENETIC AND PHENOTYPIC VARIATION

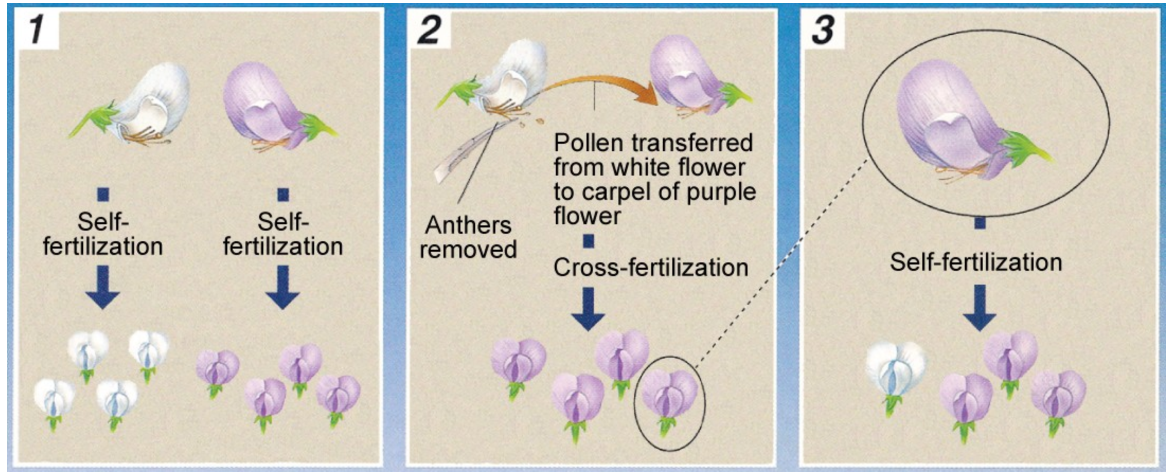
Evolution as a two-stage process:

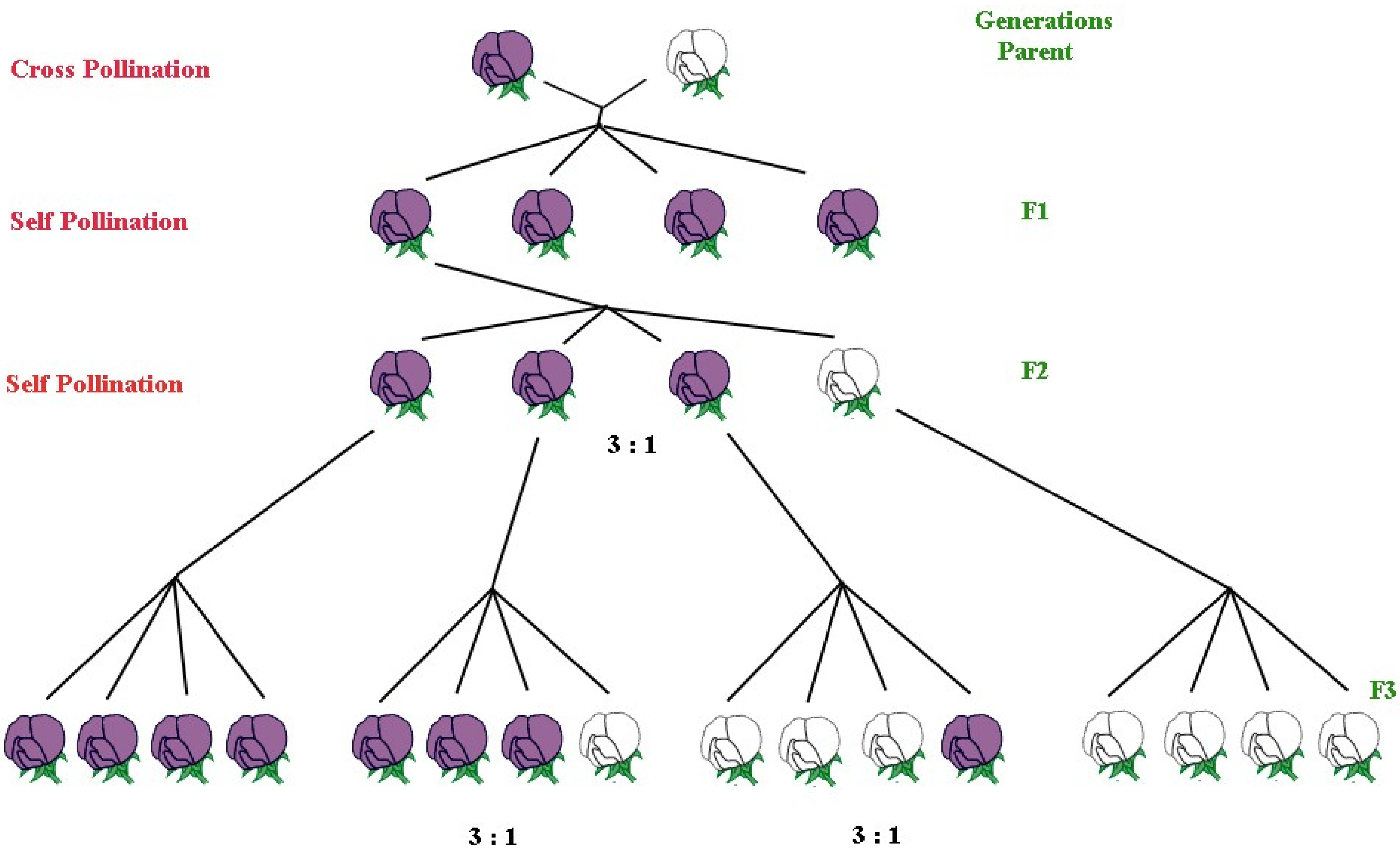
1. variation among individuals in a population
2. changes in the proportion of variants from generation to generation

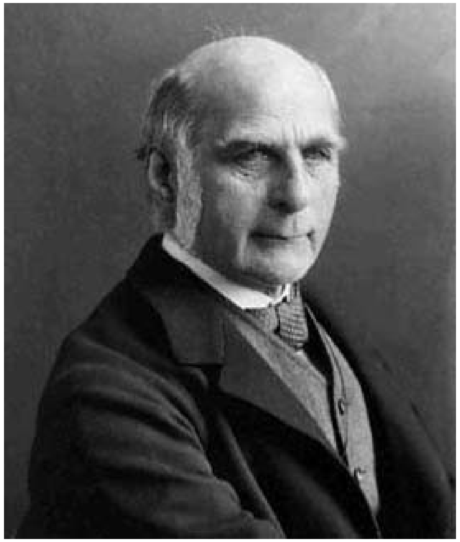


R.A. Fisher

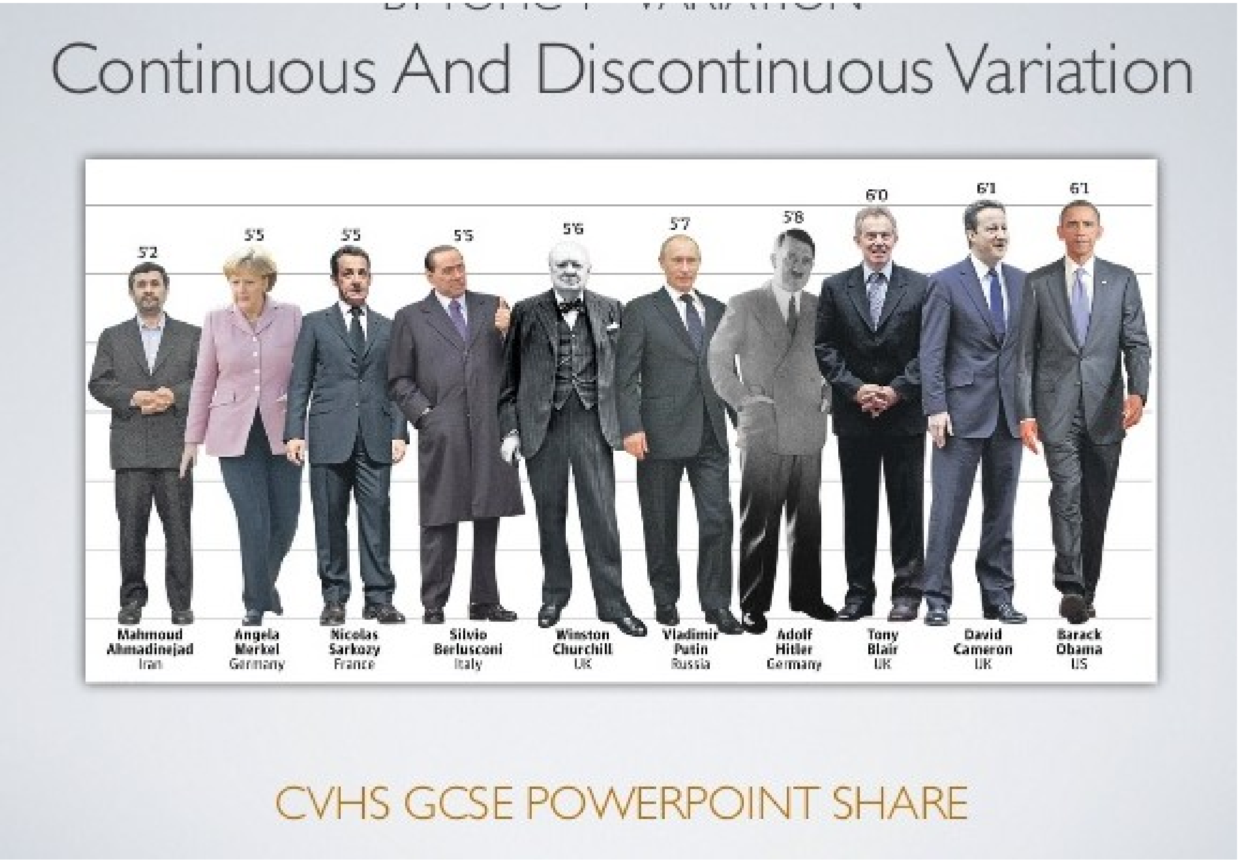
The increase in mean fitness due to natural selection is proportional to the additive genetic variance in fitness.


1
Self-fertilization
Self-fertilization
2
Anthers removed
Pollen transferred from white flower to carpel of purple flower
Cross-fertilization
3
Self-fertilization


Generations
Parent
Cross Pollination
Self Pollination
F1
Self Pollination
F2
3 : 1
F3
3 : 1
3 : 1



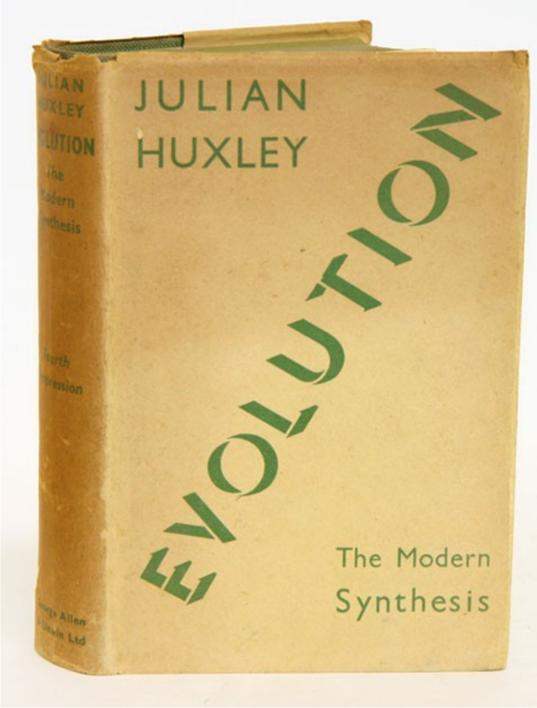
F. Galton



Biometricians: continual variation

- many genes
- often strong influence of environment

Sources of phenotypic variation:



differences in genotype

differences in environmental conditions

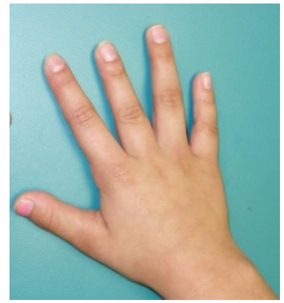
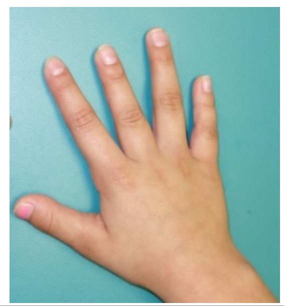
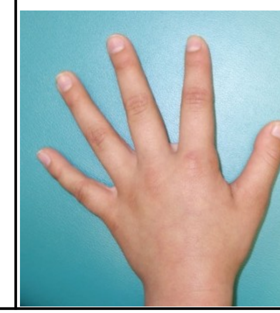
maternal influences (paternal influences)

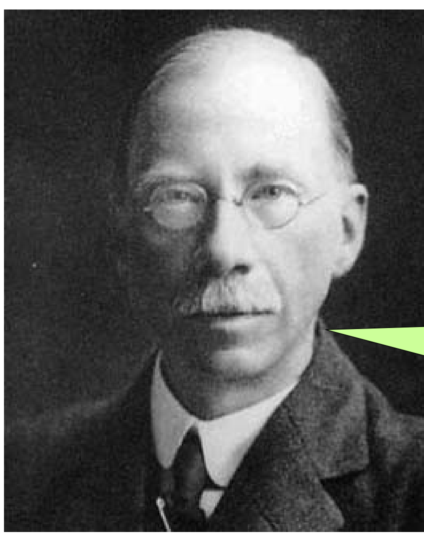
Paradox:

for evolutionary biologists important to study phenotypes

for geneticists easier to directly study molecules

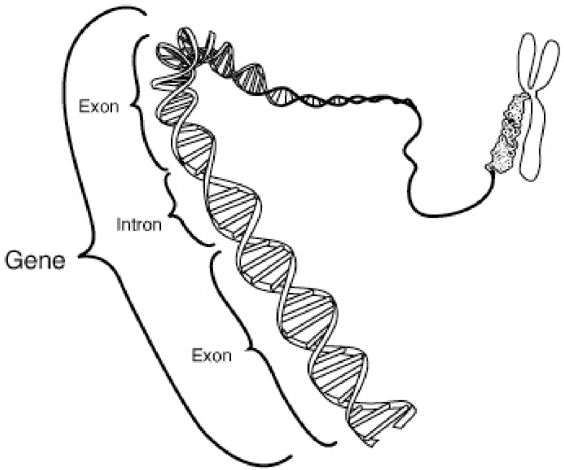
Reginald C. Punnett: brachydactyly

	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 or any other molecular trait

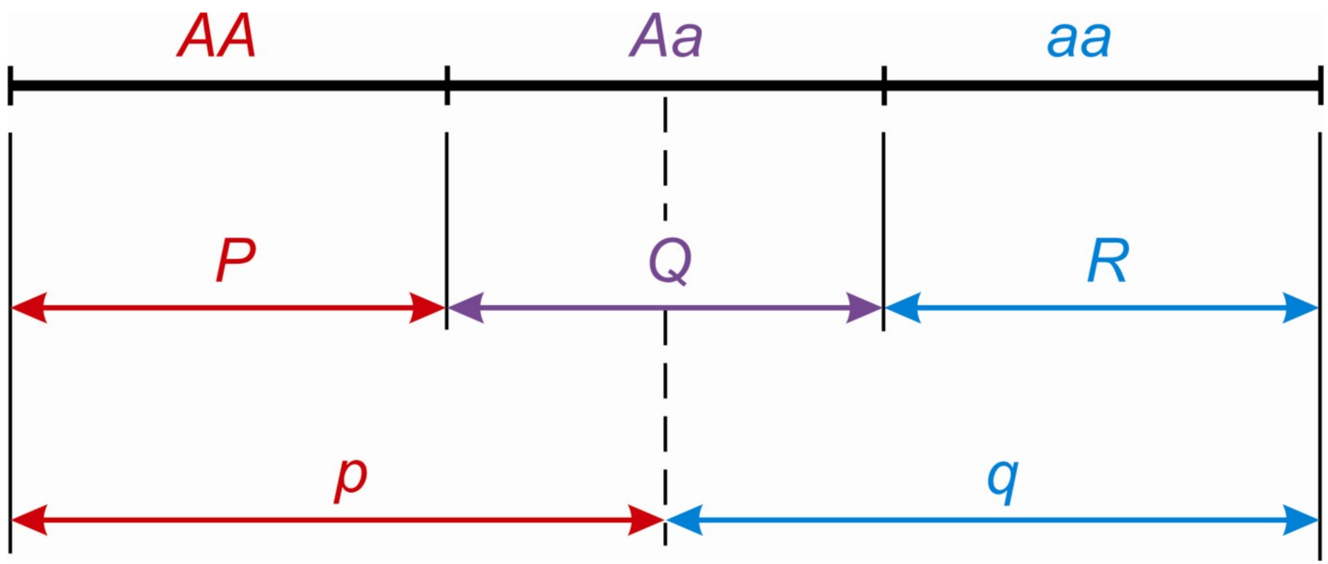
alleles = alternative forms of genes (now broader meaning – segment of DNA)

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

genotype = set of alelles of one or more genes of an individual

haplotype (haploid genotype) = combination of alelles inherited together

Genotype and allele frequencies



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

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

$P + Q + R = 1$

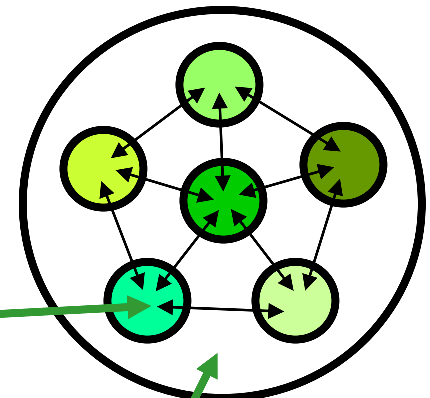
$p + q = 1$

Evolution takes place in populations…

T. Dobzhansky, E. Mayr:

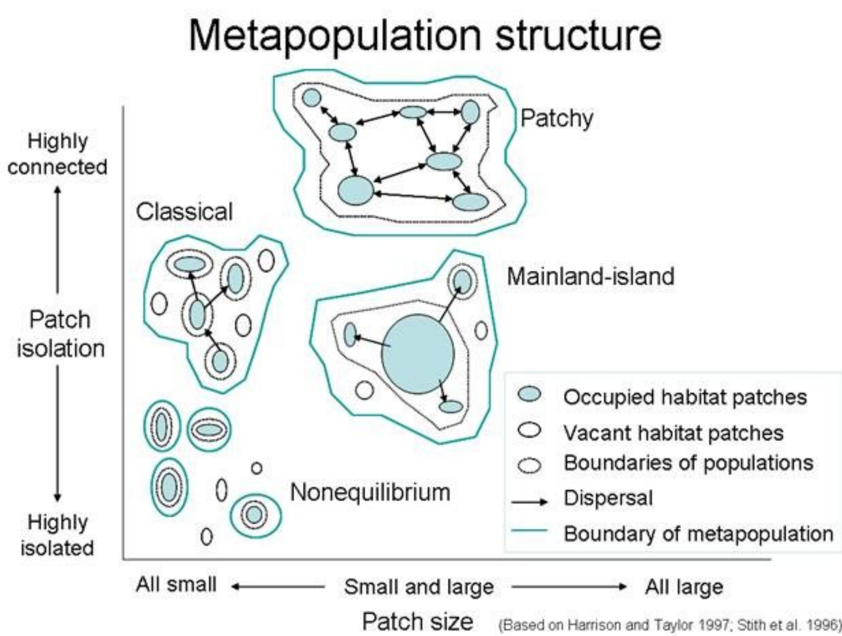
population as a shared gene pool

≈ set of shared alelles or gametes



local populations (subpopulations, demes)

global population, metapopulation



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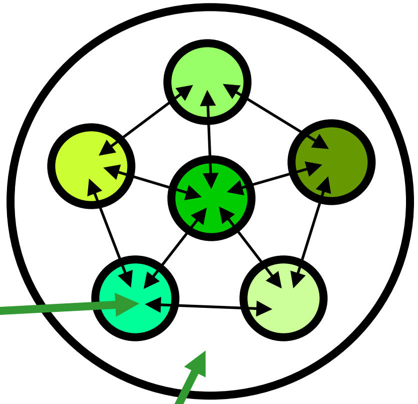


local populations (subpopulations, demes)

global population, metapopulation

Local populations also share a system of mating

populations natural, experimental, agricultural, model

Model populations – Hardy-Weinberg population

Characteristics:

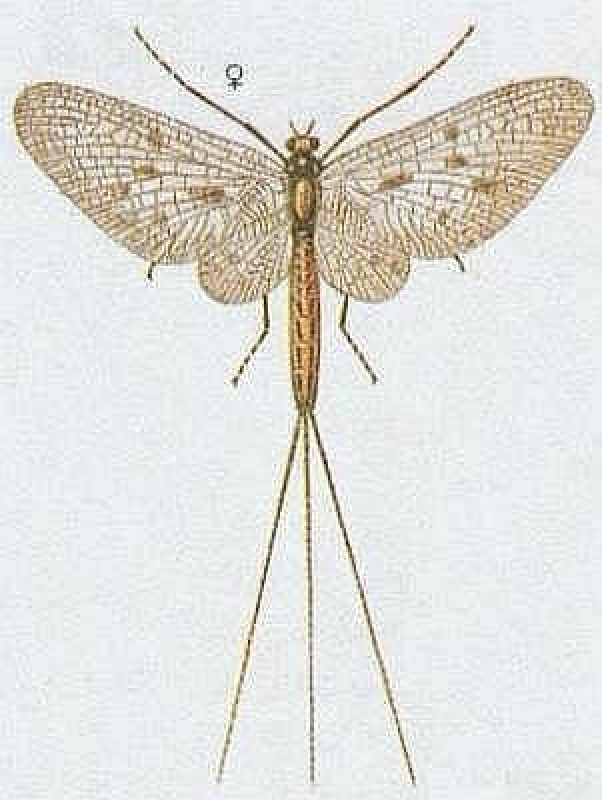
diploid

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

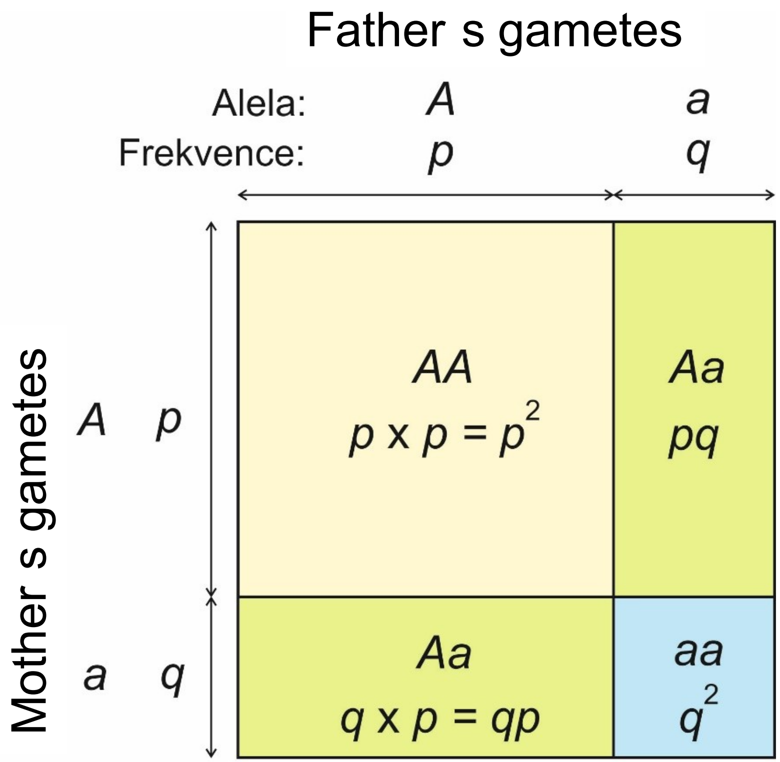
Why don t we observe the Mendelian ratios in nature?

R. C. Punnett

1908

Godfrey Harold Hardy

HARDY-WEINBERG PRINCIPLE



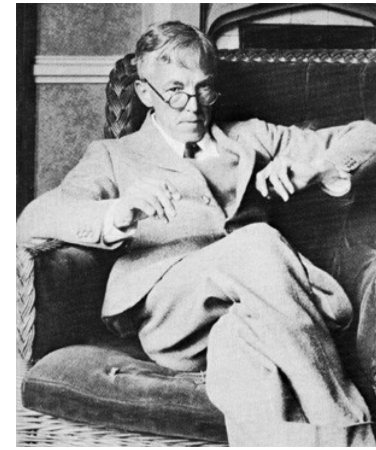
Genotype frequencies in zygotes:

$f'_{AA} = p^2$

$f'_{Aa} = pq + qp = 2pq$

$f'_{aa} = q^2$

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



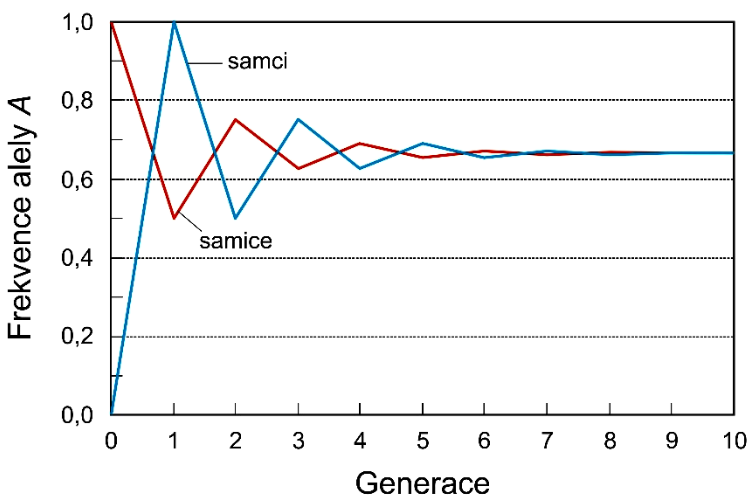
Godfrey Harold Hardy
(1877-1947)

Wilhelm Weinberg
(1862-1937)

HARDY-WEINBERG PRINCIPLE

1. Alelle frequencies stable across generations
   = Hardy-Weinberg equilibrium (HWE)

2. HWE achieved within a single generation of random mating



Generalization:

X-linked genes:

females: $p^2 + 2pq + q^2$

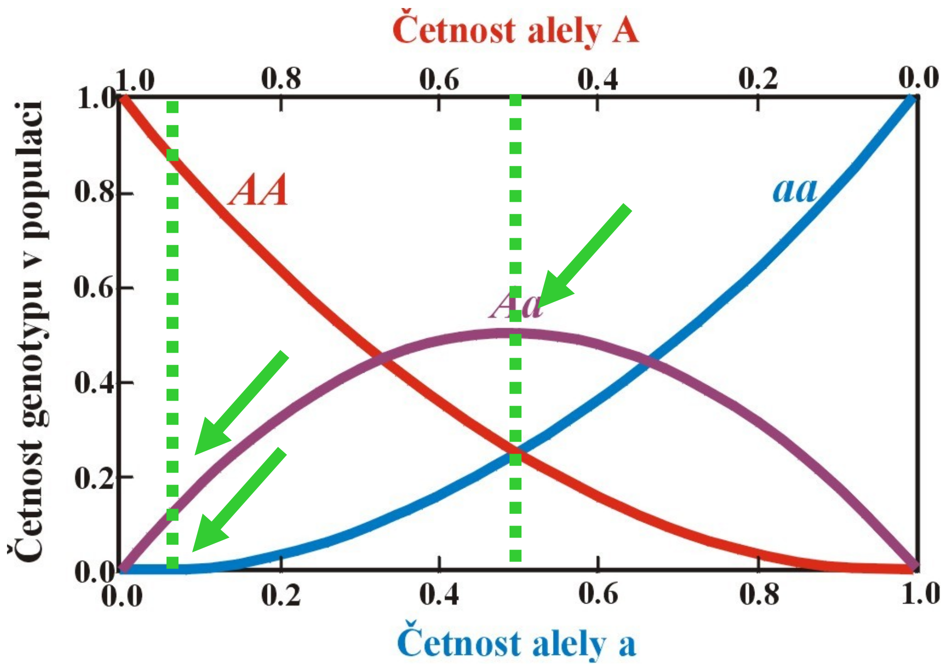
males: $p + q$

more than 2 alleles:

3 alleles: $p^2 + q^2 + r^2 + 2pq + 2pr + 2qr$

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:

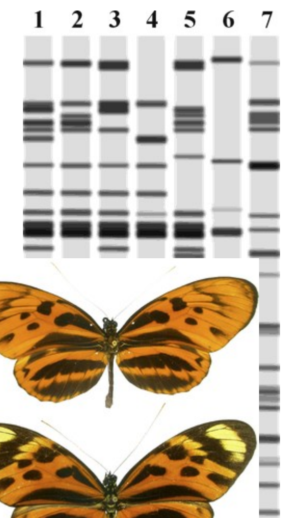
selection in favour of heterozygotes
nonrandom mating (outbreeding, negative assortative mating)
migration
mutation

GENETIC VARIATION IN POPULATIONS

Methods of the study of genetic variation:

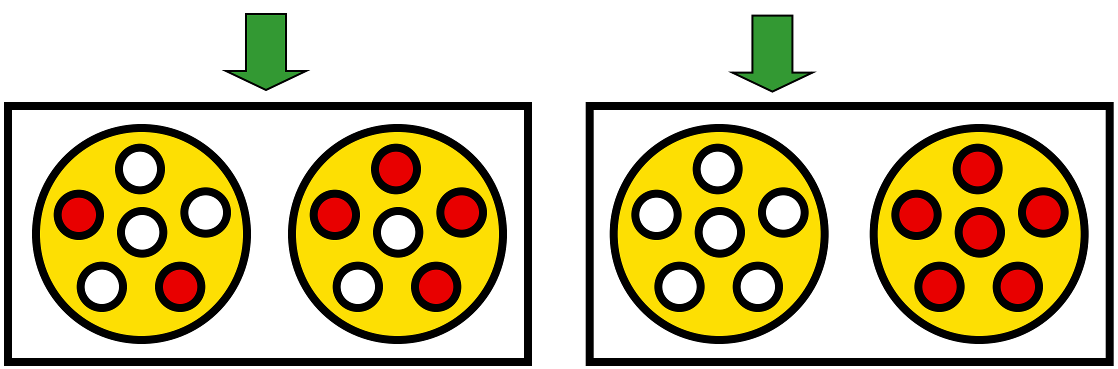
protein electrophoresis

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



PCR, sequencing, NGS, microsatellites ...

Polymorfism and polytypy



Polymorfism:

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 (θ)

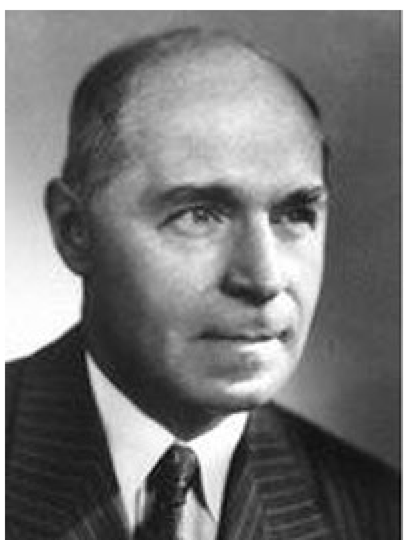
nucleotide diversity (π)

GENETIC VARIATION IN NATURAL POPULATIONS

Issue of the extent of variation in natural populations:

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

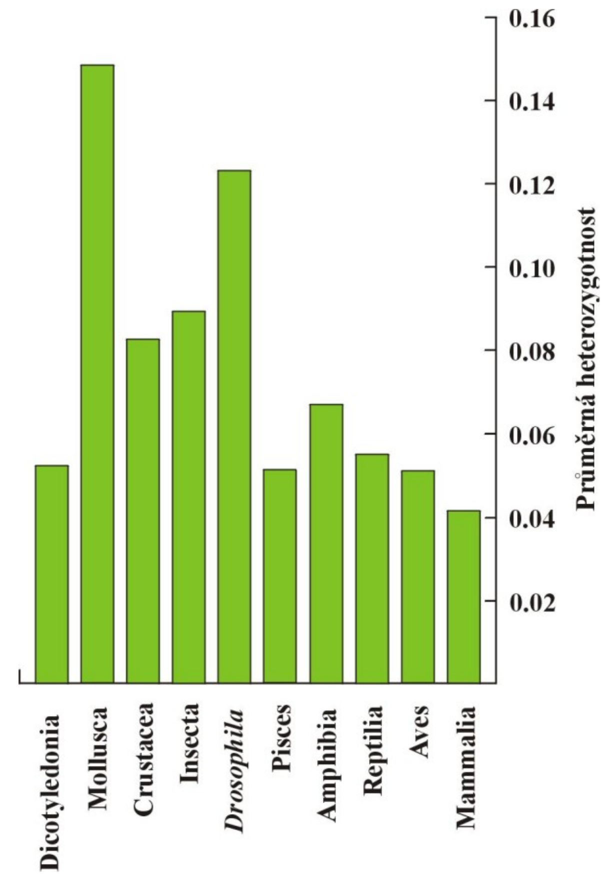
A. Sturtevant, T. Dobzhansky:
„equilibrium“ model
variation widespread

GENETIC VARIATION IN NATURAL POPULATIONS

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

Taxon	Počet zkoumaných druhů	Podíl lokusů polymorfních	Průměrná heterozygotnost
Bezobratlí			
mořští plži	5	0.175	0.083
suchozemští plži	5	0.437	0.150
ostatní mořští bezobratlí	9	0.587	0.147
haplodiploidní blanokřídlí	6	0.243	0.062
Drosophila	43	0.431	0.140
ostatní hmyz	23	0.329	0.074
bezobratlí celkem	93	0.397	0.112
Obratlovci			
ryby	51	0.152	0.051
obojživelníci	13	0.269	0.079
plazi	17	0.219	0.047
ptáci	7	0.150	0.047
hlodavci	26	0.202	0.054
savci	46	0.147	0.036
obratlovci celkem	135	0.173	0.049
Rostliny celkem	473	0.505	–



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

VARIATION AT MORE LOCI

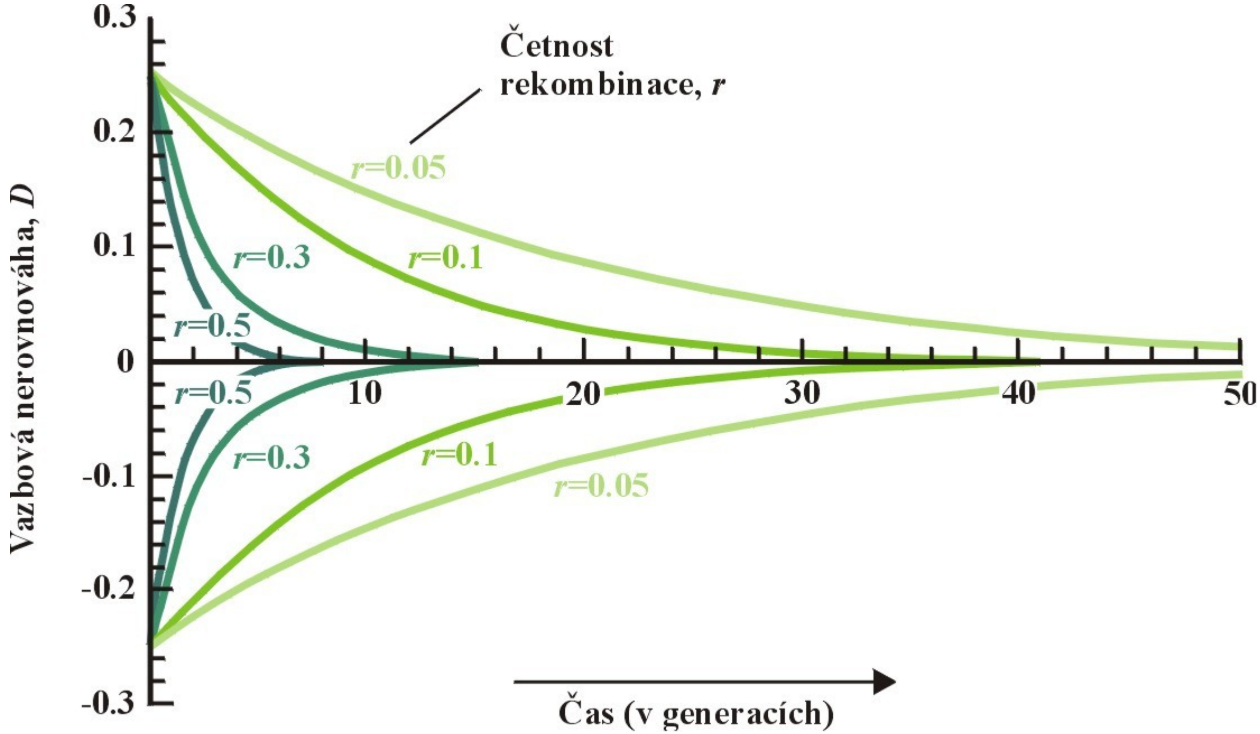
proximity of loci = linkage

valid H-W assumptions ⇒ formation of linkage equilibrium

this proces can be slow ⇒ linkage disequilibrium (LD)

coefficient of LD: *D*

relation of *D* to recombination *r* :



Causes of linkage disequilibrium:

LD needn t exist only between loci on the same chromosome!

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

INBREEDING

= mating between relatives

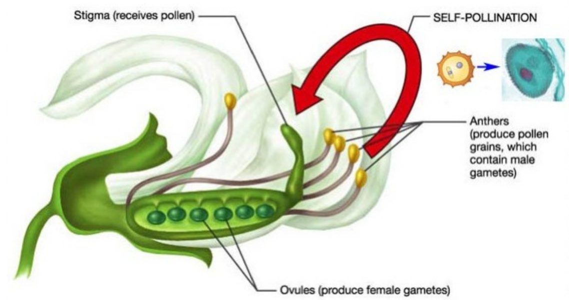
eg. repeated autogamy (self-fertilization, self-pollination):

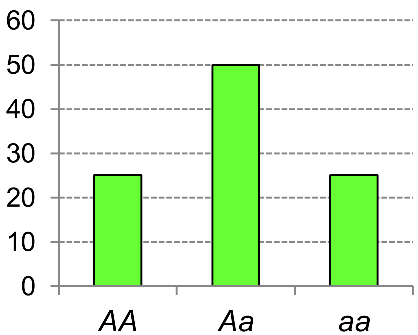
initial generation (HWE): 1/4 *AA*, 2/4 *Aa*, 1/4 *aa*

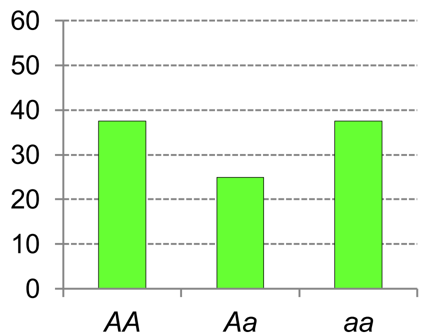
1. gen. of selfing: 3/8 *AA*, 2/8 *Aa*, 3/8 *aa*

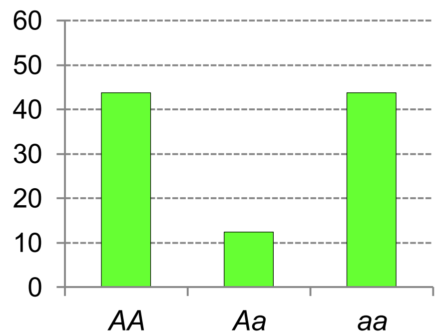
2. gen. of selfing: 7/16 *AA*, 2/16 *Aa*, 7/16 *aa*

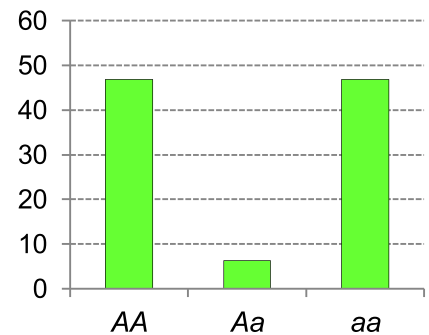
3. gen. of selfing: 15/16 *AA*, 2/32 *Aa*, 15/16 *aa*







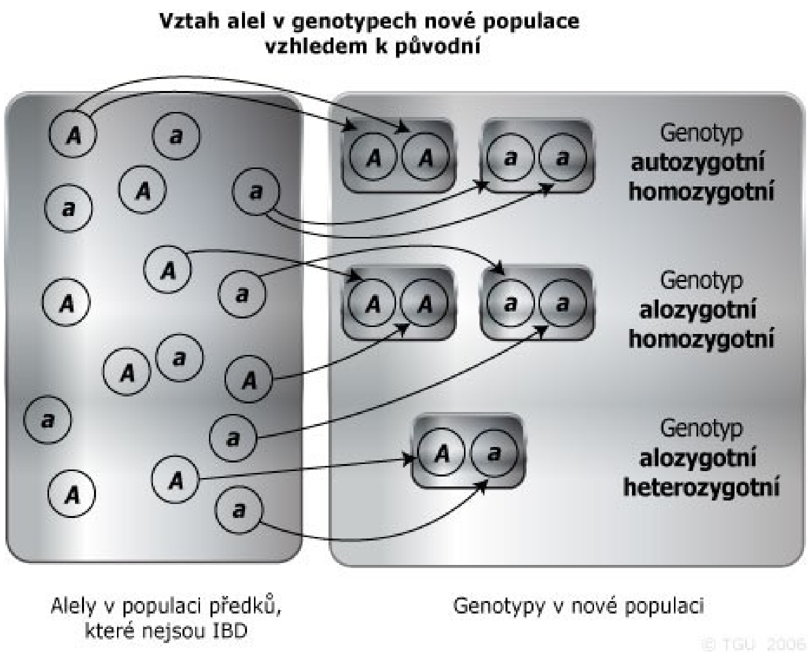




INBREEDING COEFFICIENTS

1. Pedigree inbreeding, *F*:

= probability of autozygosity



autozygosity:

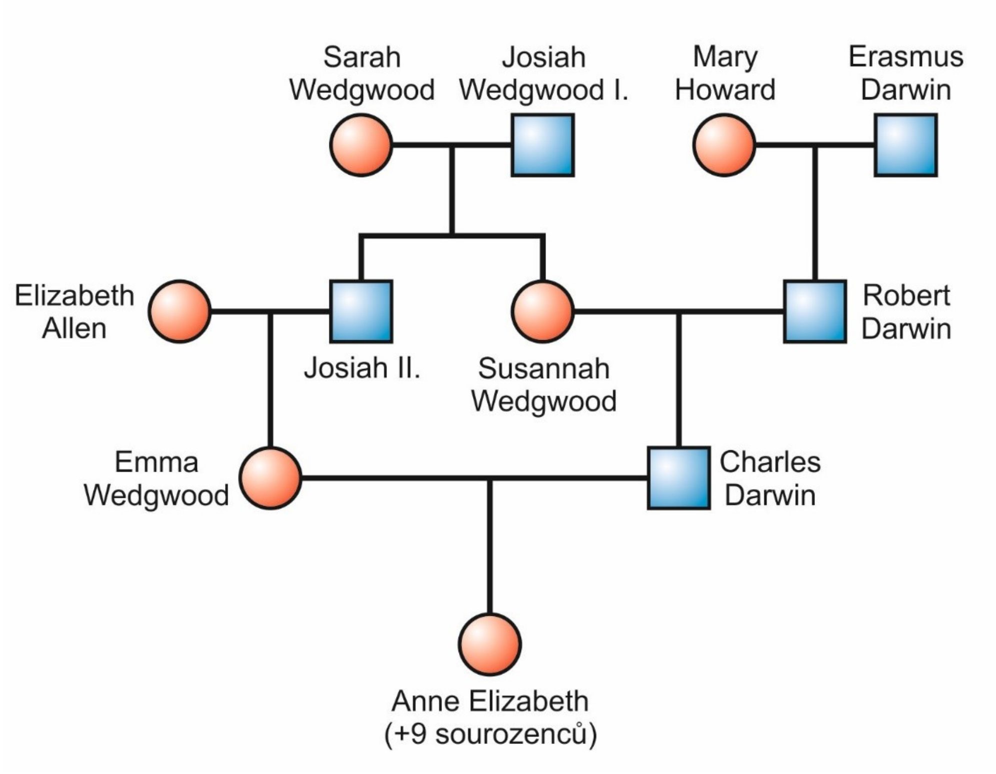
alleles identical by descent (IBD), always homozygous

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)



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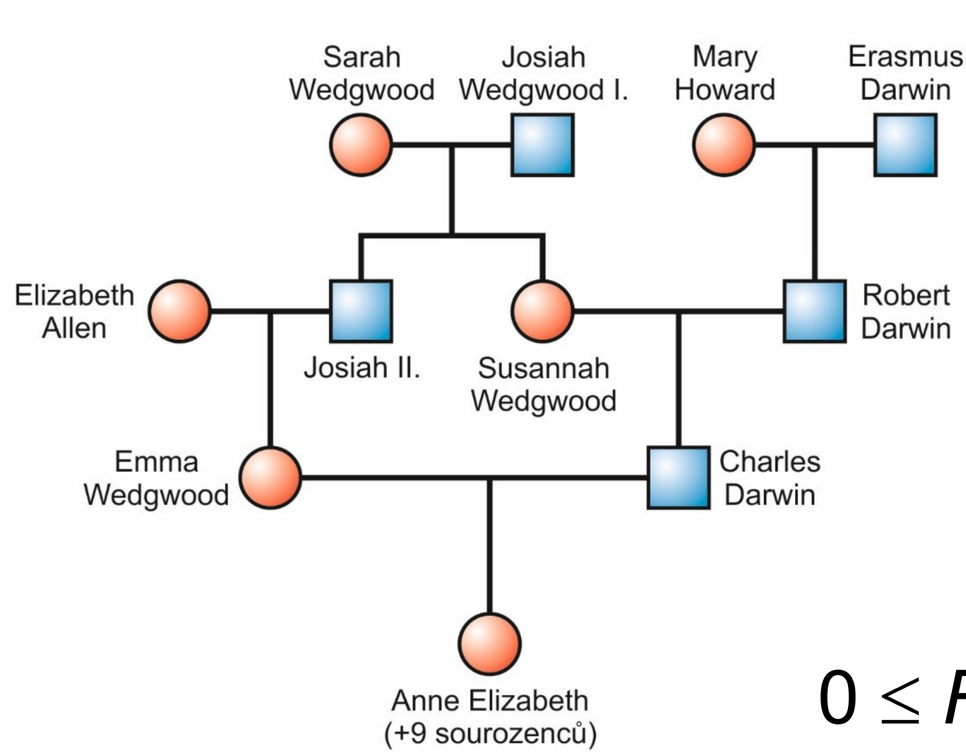
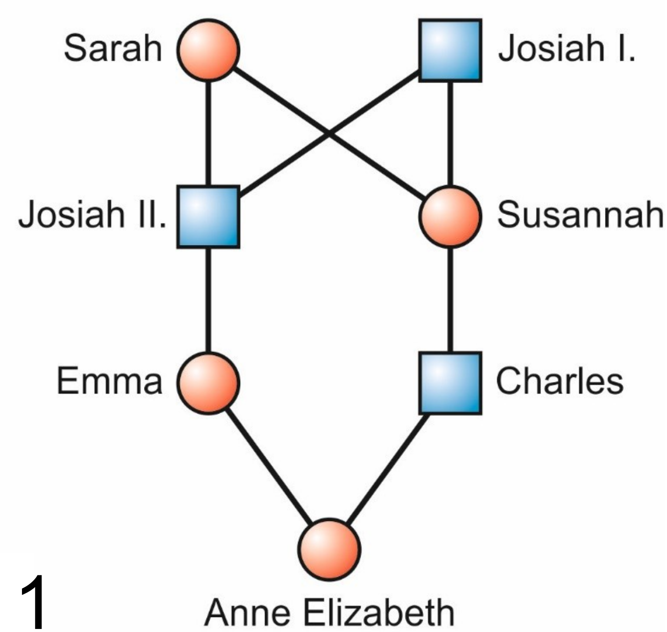
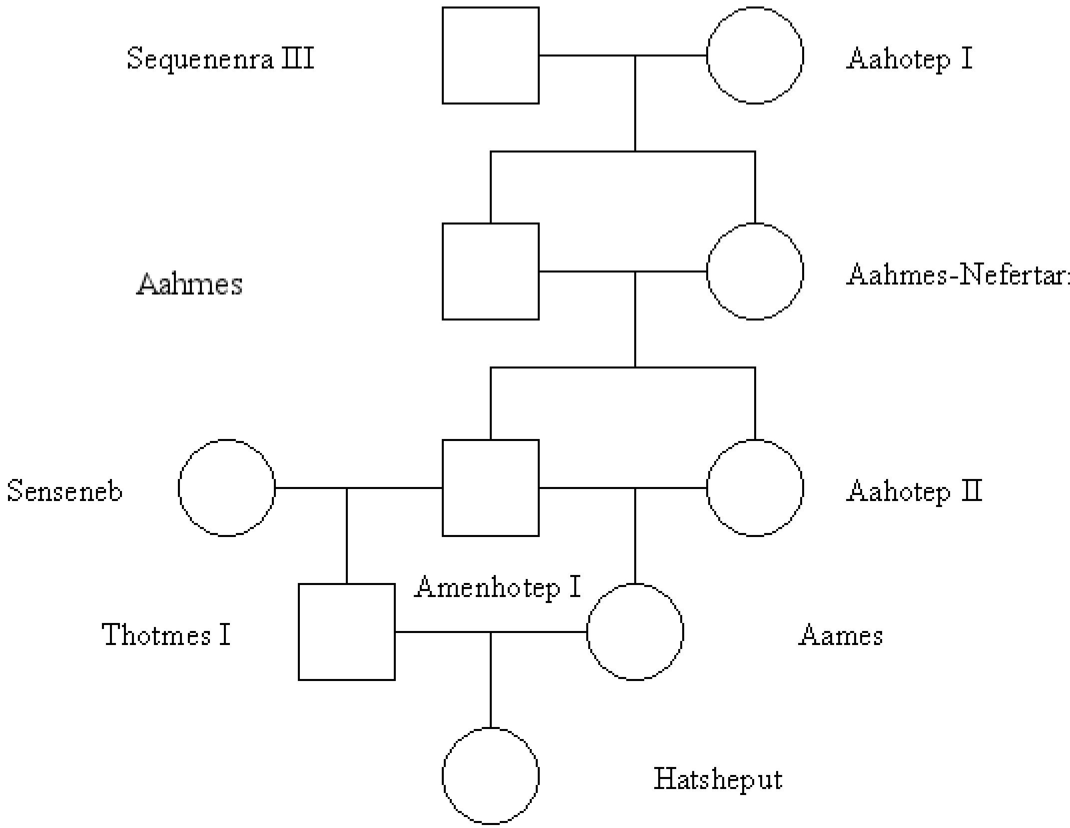


$0 \leq F \leq 1$





a) Amenhotep I. and Aahotep II. 25%

b) Aames 37.5%

c) Hatsheput 25%

d) Remaining in the pedigree are not inbred, ie $F = 0$

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

= deviation from HWE

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

H_o= observed
H_e= expected heterozygosity

F and F_{IS} don t measure the same thing!

F is the <u>individual</u> measure, F_{IS} is the <u>group</u> measure

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

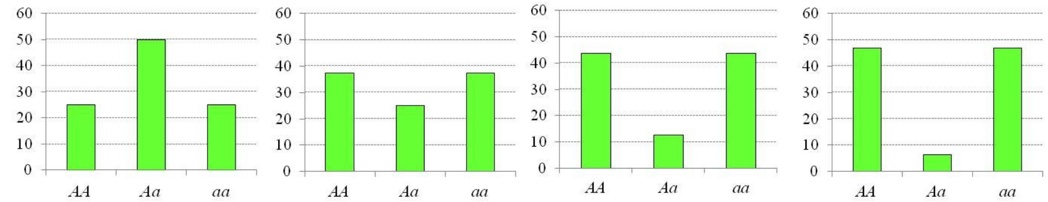
- in spite of respecting the incest taboo this is one of the most inbred human groups known (F = 0,0255)
- caused by a small number of founders (Protestants from Tyrol and Carinthia, 16th century)

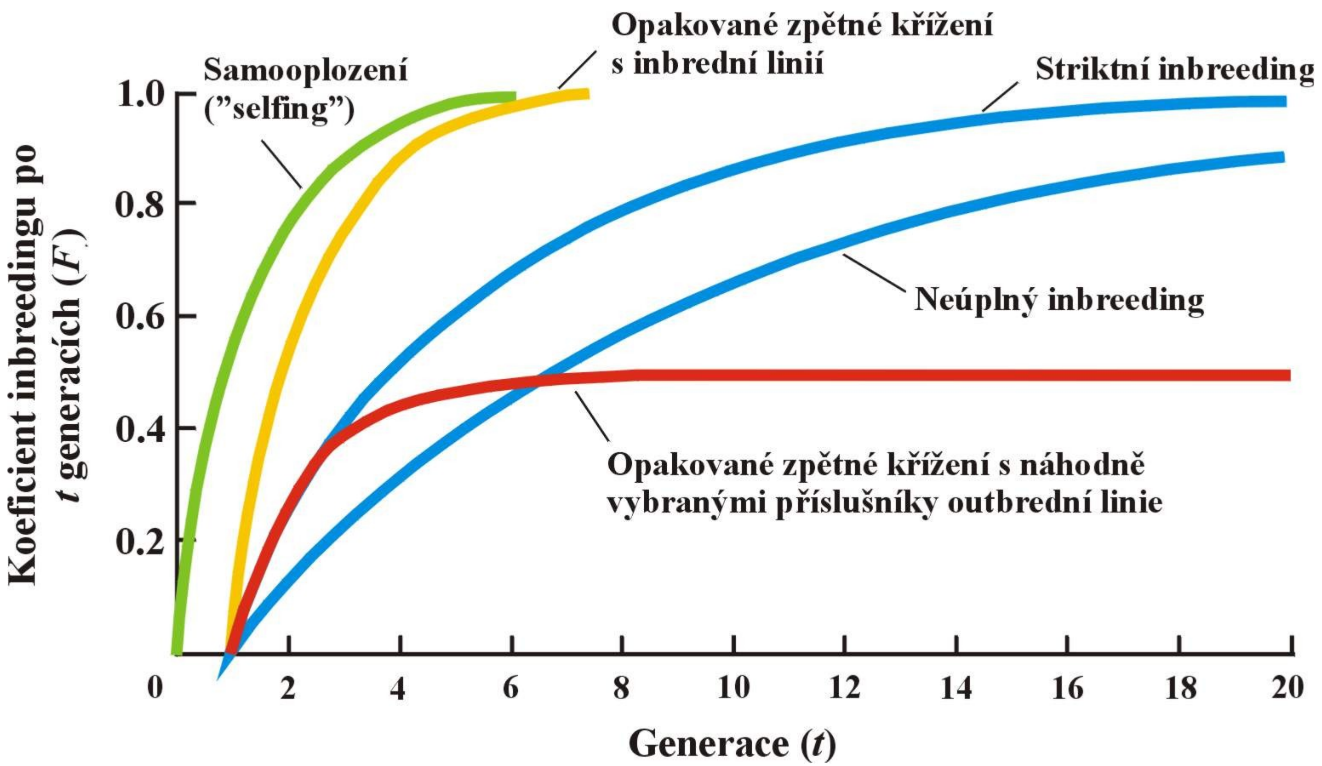
Genetic effects of inbreeding:

inbreeding changes <u>genotype</u> frequencies (increase of homozygote freq.)

× <u>allele freqs. don t change</u>

affects all loci

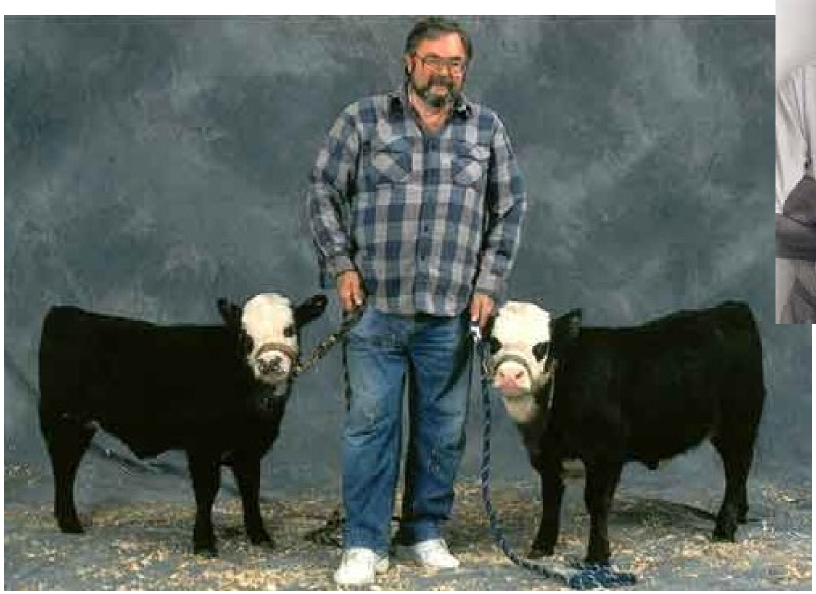




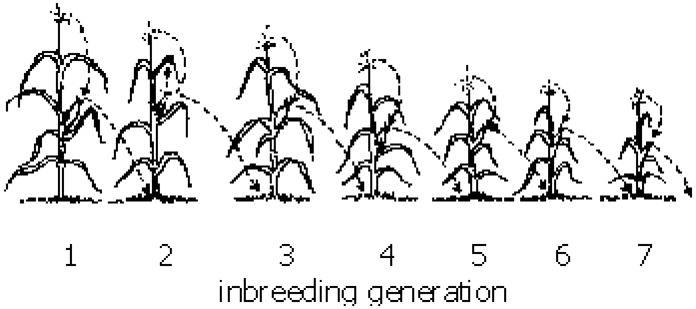
Phenotypic effects of inbreeding:

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 (dwarfness, 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 assistence

Maria Theresa

Francis I of Lorraine

hybrid vigour
(heterosis)

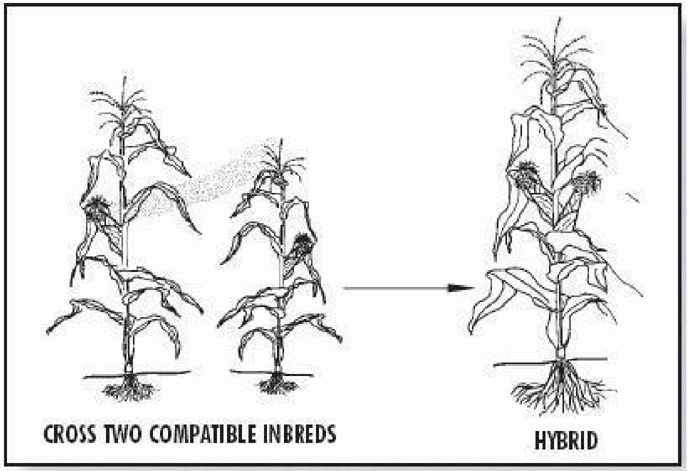


Figure 6. Cross pollination of two inbreds to produce a vigorous hybrid.

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 <u>only locus (loci) connected with preferred phnotype</u> inbreeding affects <u>all loci</u>

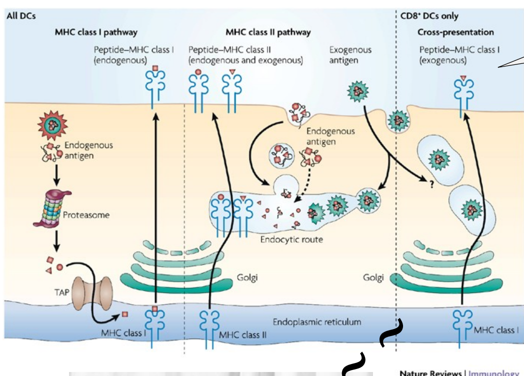
ass. mating is <u>a powerful evolutionary force </u>(strong LD at more loci) × inbreeding only strenghtens existing LD, and only in the case of selfing, in other cases recombination „more succesful“ → reduction of LD

NEGATIVE ASSORTATIVE (DISASSORTATIVE) MATING

= preference of mates with different phenotypes

results in <u>intermediary allele frequencies</u>, <u>reduces LD</u>

eg. preference of males with different MHC (mouse, man)



MHC