2nd year, winter semester

3rd week October 21, 22 and 23, 2008

P O P U L A T I O N

G E N E T I C S

II.

Repetition I

a) estimates of gene frequencies – different procedure of calculation at

- three distinct phenotypes (*e.g.* in MN blood group system).

$$p = \frac{2 \times \text{number of homozygotes } (AA) + \text{number of heterozygotes } (Aa)}{2 \times \text{number of all individuals in the sample}}$$

- complete dominance (Rh blood group system, tasting of PTC or AR diseases)

$$q = \sqrt{\frac{\text{number of recessive homozygotes}}{\text{number of all individuals in the sample}}} =$$

$$= \sqrt{\text{frequency in population}}$$

Repetition II

b) Selection

- **against recessive homozygotes** (the dropping of frequency of recessive allele is inicially rapide, then slowering, majority of deleterious alleles in heterozygotes, paradoxical result in an inappropriate application of the model)
- **against both types of homozygotes = selection favouring heterozygotes** - conditions of equilibrium; while in CF the selection mechanism against ca 2 % of dominant homozygotes is not clear (cholera epidemy speculated about), in sickle-cell anemia in Africa the malaria is functioning as the selection factor.

Results of homework I

Selection favouring heterozygotes - Task 8/pp. 143-144

a) Estimates of gene frequencies (HbS, HbA):

$$q = \frac{2 \times 29 + 2\,993}{2 \times 12\,387} = 0.123$$

$$p = 1 - q = 1 - 0.123 = 0.877$$

expected frequencies (fractions) of individual genotypes

HbA HbA	*HbA HbS*	*HbS HbS*
p^2	$2pq$	q^2
0,769	0,216	0,015

expected rates (numbers) of individual genotypes

9525,0	2674,3	187,7

Results of homework II

Selection favouring heterozygotes - Task 8/pp. 143-144

Statistical evaluation

Genotype	*HbA HbA*	*HbA HbS*	*HbS HbS*
Observed (O)	9365	2993	29
Expected (E)	9525	2674,3	187,7
Difference (O - E)	-160	318,7	-158,7
Relation (O/E)	0,983	1,119	0,155

$\chi^2 = 174.9 \quad P < 0.01$

Interpretation of χ^2 test: incidence (observed frequencies) of individual genotypes and their (at C-H-W equilibrium) expected numbers are statistically significantly different – therefore, we may suppose that this sample is in a balance elicited by mechanisms other then C-H-W equilibrium.

Results of homework III

Selection favouring heterozygotes - Task 8/pp. 143-144

b) Estimates of s_1 a s_2 selection coeficients

Reproductive abilities of individual genotypes

Genotypes	*HbA HbA*	*HbA HbS*	*HbS HbS*
Relation (O/E)	0,983	1,119	0,155

Adjustment to relative reproductive ability by dividing with reproductive ability of most fertile genotype

0,879	1,0	0,138

s_1 a s_2 as additions of relative reproductive abilities to 1

$$s_1 = 1 - w_1 = 1 - 0.879 = 0.121$$

$$s_2 = 1 - w_2 = 1 - 0.138 = 0.862$$

Results of homework IV

Selection favouring heterozygotes - Task 8/pp. 143-144

Sickle-cell anaemia as stable polymorphism by heterozygous advantage

Errata

- p. 141, line 1 and 2 bot, in formula
  = is twice missing, instead 10 place 1
- p. 143, line 3 bot instead â place β
- p. 145, line 3 top instead *í* place ν
- p. 147, line 2 bot (question b)
  replace their offspring by them

Equilibrium of mutations and selections I

a) for AR mutant alleles

Selection against recessive homozygotes

$$q' = \frac{q\,(1 - qs)}{1 - q^2 s}$$

For rare diseases, q is too small, and therefore

$$q^2 s \ll 1$$

$$1 - q^2 s \doteq 1$$

$$\Delta q = q' - q = \frac{-\,pq^2 s}{1 - q^2 s} \doteq -\,pq^2 s$$

Mutations

A $\xrightarrow{\mu}$ a

$$p' = p - \mu p$$

$$\Delta p = p' - p = p - \mu p - p = -\mu p$$

Equilibrium

$$-\mu p = -\,pq^2 s \quad \Rightarrow\Rightarrow\Rightarrow \quad q_{equil} = \sqrt{\frac{\mu}{s}}$$

Equilibrium of mutations and selections II

a) for AR mutant alleles

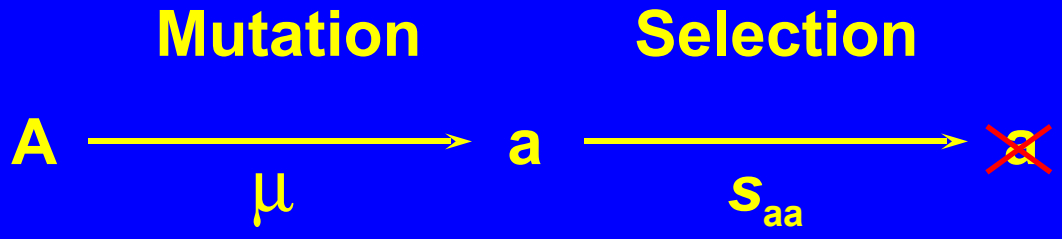
Estimation of mutation frequency μ for albinism

– Task 9/p.146

$s_{aa} = 0.1$

$q^2_{equil.} = 1/20\,000$

μ = ???



Equilibrium

$$q_{equil} = \sqrt{\frac{\mu}{s_{aa}}} \Rightarrow\Rightarrow\Rightarrow \mu = q^2_{equil} \times s_{aa}$$

$$\mu = \frac{1}{20\,000} \times 0.1 = \frac{1}{200000} = 5 \cdot 10^{-6}$$

Equilibrium of mutations and selections III

b) for AD mutant alleles

Selection against dominant phenotype

$$p' = \frac{p\,(1 - s)}{1 - 2\,ps}$$

for rare AD diseases, p is small, and therefore $1 - 2\,ps \doteq 1$

$$\Delta p = p' - p = \frac{p(1-s) - p(1-2ps)}{1-2ps} = \frac{-ps + 2p^2 s}{1-2ps} = \frac{-ps\,(1-2p)}{1-2ps} \doteq -ps$$

Mutations

a $\xrightarrow{\nu}$ A

$$q' = q - \nu q$$

$$\Delta q = q' - q = q - \nu q - q = -\nu q$$

Equilibrium

$$-\nu q = -ps$$

$q \doteq 1$

$\Rightarrow \Rightarrow \Rightarrow$

$$p_{equil} = q \cdot \frac{\nu}{s} \doteq \frac{\nu}{s}$$

Simple model of gene drift I

Drift – changes in gene frequencies in small populations elicited by random processes

- modelling of random use of alleles (gametes)
- random mechanism – dice throw
- small population $N = 3$, and original $p = q = ½$
    - allele A picked out … side 1, 2 or 3 cast
    - allele a picked out … side 4, 5 or 6 cast
- 6 throws each time – results of series mark in the table
- According to the result (ratio, new frequencies) p_A / q_a change the rules for next series of throws (generation)
- continue until one allele fixed

Simple model of gene drift II

– Task 14/p. 148

Into your protocols, prepare this table, at the least to the 10th generation

Generation		1		2		3			10 (20)	
Alelle		*A*	*a*	*A*	*a*	*A*	*a*		*A*	*a*
side casted		1, 2, 3	4, 5, 6							
throw No.	1									
	2									
	3									
	4									
	5									
	6									
Total										

Simple model of gene drift III

– Task 14/p. 148

An example of results after the firts series of throws and the change of the rules for next series

Generation		1		2		3			10 (20)	
Alelle		*A*	*a*	*A*	*a*	*A*	*a*		*A*	*a*
side casted		1, 2, 3	4, 5, 6	1, 2, 3, 4	5, 6					
throw No.	1	/								
	2		/							
	3	/								
	4	/								
	5		/							
	6	/								
Total		4	2							

Simple model of gene drift IV

– Task 14/p. 148

An example of results after the firts series of throws and the change of the rules for next series

Generation		1		2		3			10 (20)	
Alelle		*A*	*a*	*A*	*a*	*A*	*a*		*A*	*a*
side casted		1, 2, 3	4, 5, 6	1, 2, 3, 4	5, 6	1, 2, 3, 4, 5	6			
throw No.	1	/		/						
	2		/	/						
	3	/		/						
	4	/			/					
	5		/	/						
	6	/		/						
Total		4	2	5	1					

Simple model of gene drift IV

– Task 14/p. 148

- work in pairs, one is throwing, the other is recording
- remind you the change of rules, where according to the result the gene frequencies are changing for next series of throws and consequently which sides of the dice will represent the allele *A* or *a*
- continue in experiment until the point of fixation of one allele
- now, swap your roles, this way one pair will finish and evaluate at least two experiments, each experiment and result visualize in a graph
- for whole classroom calculate average time of fixation as weighted mean of results of all partial experiments, the ratio of fixed *A* and *a* alleles should be approx. 1 : 1

Simple model of gene drift V – Task 14/p. 148

Conclusion of experiments

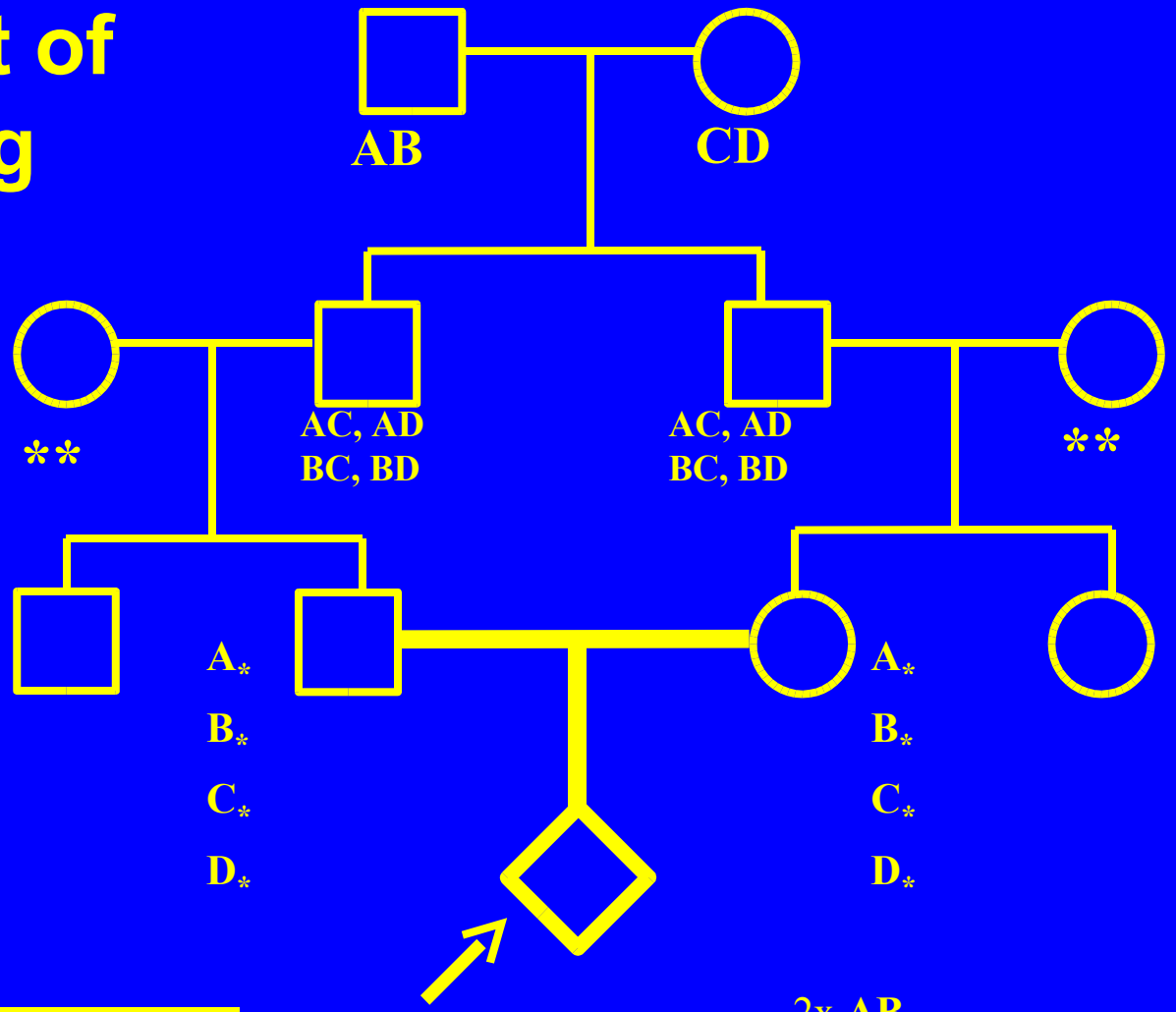
number of generations to fixation	1	2	3	4	5	6	7	8	9	10	11
represented in practicals											

12	13	14	15	16	17	18	19	20				

Number of fixation *A*		Total of experiments	0
Number of fixation *a*		Total of *A* + *a*	0

Average time of fixation

Coefficient of inbreding *F*

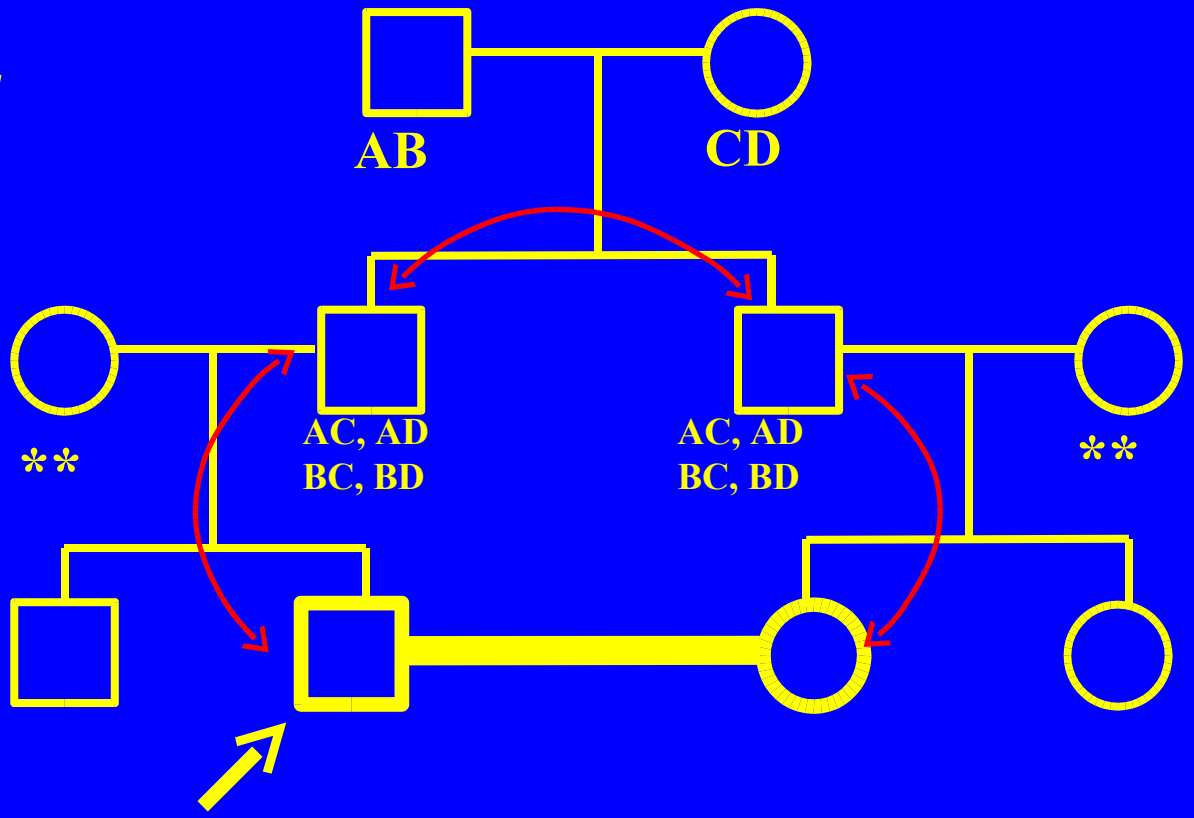


$$F = \frac{4}{64} = \frac{1}{16}$$

4x { AA, BB, CC, DD } { 8x A*, 8x B*, 8x C*, 8x D*, 16x ** } { 2x AB, 2x AC, 2x AD, 2x BC, 2x BD, 2x CD } 60x

Coefficient of relationship

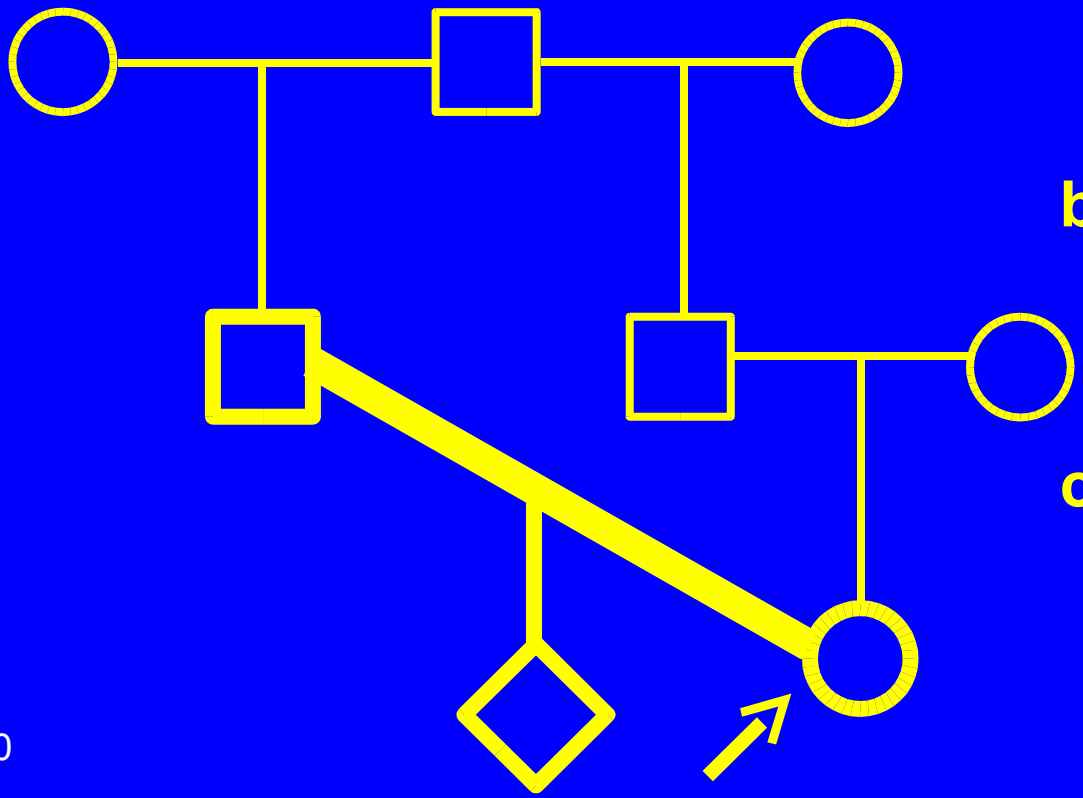
r



$$r = \left(\frac{1}{2}\right)^3$$

Coefficients of inbreeding (*F*) and of relationship (*r*)

According to the ”motto” one (*F*) vs. two genomes (*r*)
In the formula for *r* , the *n* express the number of connecting lines in pedigree chart.
Task 12a, b, c/p. 147



b) *r* for an half-uncle and his half-niece is 1/8

c) *F* for an offspring of an half-uncle and his half-niece is 1/16

Migration – Task 13/p. 148

Population		Frequency of *Rh*^{0}
Caucasoid (USA)	(p)	0,03
Negroid (Africa)	(p_i)	0,63
Negroid (USA)	(p_i')	0,45

$$p_i' - p_i = -m(p_i - p)$$

$$m = \frac{p_i' - p_i}{p - p_i} = \frac{0{,}45 - 0{,}63}{0{,}03 - 0{,}63} = 0{,}3 = 30\ \%$$

7. Conclusion

- **Home work: Tasks 10 and 11/p. 146 and 147**
- **Home study – the test will be next week!!!**