2nd year, winter semester
1st week October 14 – 16, 2008

P O P U L A T I O N
G E N E T I C S
I.

The lecture has taken place in the last semester – see short introductory text and formulas [3] and [4] on pp. 138 and 139.

1. Introduction to population genetics – estimates of gene frequencies

a) Task 1/p.139 – frequencies of alleles in MN blood group system

b) Task 3/p. 139 – gene frequencies in the Rh blood group system

c) Task 2/p. 139 – gene frequencies in the dominant system (*T*, *t*)

d) Task 4/p. 140 – estimates of frequencies of deleterious (recessive) alleles

Castle-Hardy-Weinberg law

$$p^2_{(AA)} + 2\,pq_{(Aa)} + q^2_{(aa)} = 1$$

Applied on panmictic population under the assumption of limiting conditions

Castle-Hardy-Weinberg law

Basic relation for a system with two alleles in a given gene

$$p_{(A)} + q_{(a)} = 1$$

$$p_{(A)} = 1 - q_{(a)}$$

approximation

$$2\,pq_{(Aa)} \doteq 2q$$, **if** $p_{(A)}$ **approaches** 1

Task 1/p.139 – frequencies of alleles in MN blood group system

Phenotype	Number of persons
M	406
MN	744
N	332

Task 1/p.139 – frequencies of alleles in MN blood group system

Solution:

- **direct calculation of the frequency of one of alleles according to formula [3] on p. 138**

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

- **Calculation of the frequency of the second allele as addition to 1.**

Task 1/p.139 – frequencies of alleles in MN system

phenotype	Number of		
	persons	alleles M	alleles N
M	406	812	0
MN	744	744	744
N	332	0	664
Total	1 482	1 556	1 408

$$p = \frac{2 \times 406 + 744}{2 \times 1482} = \frac{1556}{2964} = 0.525$$

$$q = 1 - p = 0.475$$

Task 3/p. 139 – gene frequencies in the Rh blood group system

- In a population, 16 % of persons were Rh negative (Rh-) – for better calculating, otherwise in Czech population it is 13.4 %
- Rh- individuals ……. recesive homozygotes *dd*
- Rh+ individuals ……. homozygotes *DD*
  or heterozygotes *Dd*

Estimates: $q^2_{(dd)} = 0.16 \Rightarrow q_{(d)} = 0.4$

$p_{(D)} = 1 - q = 0.6$

$p^2_{(DD)} = 0.36$

$2pq_{(Dd)} = 0.48$

Task 3/p. 139 – gene frequencies in the Rh blood group system

♂ \ ♀	*DD* p^2	*Dd* $2pq$	*dd* q^2
DD p^2			*Dd* p^2q^2
Dd $2pq$			*Dd* pq^3 *dd* pq^3
dd q^2			*dd* q^4

Results:

b) **84 %**; *i.e.* $p^2 + 2pq$

c) **13.44 %**; *i.e.* $0.16 \times 0.84 = q^2 \times (p^2 + 2pq)$

d) **60 %**; *i.e.* $p = 0.6 = (p^2q^2 + pq^3)/(p^2q^2 + 2pq^3 + q^4)$

e) **36 %**; *i.e.* $p^2 = 0.36 = p^2q^2/(p^2q^2 + 2pq^3 + q^4)$

Task 2a/p. 139 – Estimation of gene frequencies in the dominant system

30 % of persons unable to recognize the bitter taste of PTC in a given population (non-tasters)

phenotype → genotypes ⇒ *TT*, *Tt* – tasters; *tt* – non-tasters

$q^2_{(tt)} = 0.3 \quad \Rightarrow \quad q_{(t)} = \sqrt{0.3} = 0.548$

$p_{(T)} = 1 - q = 0.452$

$p^2_{(TT)} = 0.205$

$2pq_{(Tt)} = 0.495$

Estimation of gene frequencies in two-allele polymorphism (*T*, *t*)

in the population sample of students

phenotyping of PTC tasting in students in the classroom:
one drop of saturated solution of phenylthiocarbamide (PTC) on the tip of the tongue

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portion of non-tasters $[q^2_{(tt),\ class}] = \dfrac{\text{non-tasters in the class}}{\text{total of students in the class}}$

frequency of recessive allele $[q_{(t),class}] = \sqrt{q^2_{(tt),\ class}}$

$p_{(T),class} = 1 - q$ $\quad$ $p^2_{(TT),class}$ $\quad$ $2pq_{(Tt),class}$

Task 4/p. 140 – estimates of frequencies of deleterious (recessive) alleles

Disease	Abbrev.	population frequency
phenylketonuria	PKU	1/8100
cystic fibrosis (mucoviscidosis)	CF	1/2500

Task 4/p. 140 – estimates of frequencies of deleterious (recessive) alleles

Solution: the estimate calculated according to formula [4] on p. 139 (top),

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

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

Task 4/p. 140 – estimates of frequencies of deleterious (recessive) alleles

disease	Frequency in population	estimate		
		q	$p = 1 - q$	$2pq \doteq 2q$
PKU	1/8100	1/90	$89/90 \doteq 1$	2 x 1 x 1/90 = 1/45
CF	1/2500	1/50	$49/50 \doteq 1$	2 x 1 x 1/50 = 1/25

2. Selection against (recessive) homozygotes

Intensity of selection against genotype *i* (i.e. *AA, Aa* or *aa*)

$$\boxed{s_i = 1 - w_i}$$

w_i … fitness, average relative reproduction ability of the genotype i

$$w_i = \frac{\text{average number of offspring of the genotype } [i]}{\text{average number of offspring of the genotype with maximal fertility}}$$

	AA	*Aa*	*aa*	$\sum$
	p^2	$2pq$	q^2	1
s_i	0	0	s	
w_i	1	1	$1 - s$	
	p^2	$2pq$	$q^2(1 - s)$	$1 - q^2s$

Gene frequency of recessive alelle <u>*a*</u> after one generation of selection of intensity *s* :

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

Intergenerational change of gene frequency as consequence of selection of intensity *s* :

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

If $\Delta q = 0$ ⇨ gene frequency does not change ⇨ polymorphism is stable ⇨ thereafter must be :

$$\boxed{-pq^2 s = 0}$$

1. *p* = 0 (population formed only by homozygotes <u>*aa*</u>)
2. $q^2 = 0$, i.e. *q* = 0 (population formed only by homozygotes <u>*AA*</u>)
3. *s* = 0, (considered type of selection does not take place)

If $\Delta q \neq 0$, gene frequencies change from generation to generation – population polymorphism is of transitional type

When s = 1, it is a case of a system with recessive lethal effect

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

After two generation of selection proceeding this way

$$q'' = \frac{q'}{1 + q'} = \frac{\dfrac{q}{1 + q}}{1 + \dfrac{q}{1 + q}} = \frac{\dfrac{q}{1 + q}}{\dfrac{1 + q + q}{1 + q}} = \frac{q}{1 + 2q}$$

After three generations of lethal effect

$$q''' = \frac{q}{1 + 3q}$$

Selection by/against cystic fibrosis (mucoviscidosis)

Task 6a,b/p. 142

Extension of preceding consideration – after many (*t*) generations of selection (*t* - time)

$$q \xrightarrow[t \text{ generations}]{} q_{(t)}$$

$$q_{(t)} = \frac{q}{1 + tq}$$

Arrangement of the formula

$$t = \frac{q - q_t}{q \times q_t}$$

Calculation :

$$t = \frac{q - q_t}{q \times q_t} = \frac{\frac{1}{50} - \frac{1}{2} \times \frac{1}{50}}{\frac{1}{50} \times \frac{1}{2} \times \frac{1}{50}} = 50$$

Answer a) : 50 generations **b) : 7450 generations**

Selection by/against cystic fibrosis (mucoviscidosis)

Task 6c/p. 142

Other extension of initial consideration – before many (*t*) generations of selection (*t* - time)

$$q_0 \xleftarrow[t \text{ generations}]{} q_{(t)}$$

$$q_{(t)} = \frac{q_0}{1+tq}$$

Arrangement of the formula

$$q_0 = \frac{q_{(t)}}{1-tq_{(t)}}$$

Calculation :

$$q_0 = \frac{q_{(t)}}{1-tq_{(t)}} = \frac{\frac{1}{50}}{1-\frac{49}{50}} = 1$$

Answer: the frequency was 1 ⇨ ⇨ 49 generations ago (ca 1 000 yr) the entire population was affected by CF

Paradoxical result can be commented *e.i.* as an **inappropriate application of the model**

If, 49 generations ago (some time arround the years 900 to 1000), there has been formed the entire population (exactly according to the result q = 1) by recessive homozygotes,

which is i) a nonsense, because there have been no reports, that all people have suffered with CF at that time,

then ii) any selection itself could not change anything on that state.

3. Selection favouring heterozygotes - I

Task 7/p. 142

Genotypes	*AA*	*Aa*	*aa*	Σ
before	p^2	$2pq$	q^2	1
s_i	s_1	0	s_2	
w_i	$1 - s_1$	1	$1 - s_2$	
after	$p^2(1 - s_1)$	$2pq$	$q^2(1 - s_2)$	$1 - p^2 s_1 - q^2 s_2$

$$q' = \frac{2pq + 2q^2(1 - s_2)}{2(1 - p^2 s_1 - q^2 s_2)} = \frac{pq + q^2 - q^2 s_2}{1 - p^2 s_1 - q^2 s_2} =$$

$$= \frac{q(p+q) - q^2 s_2}{1 - p^2 s_1 - q^2 s_2} = \frac{q - q^2 s_2}{1 - p^2 s_1 - q^2 s_2} = \frac{q(1 - q s_2)}{1 - p^2 s_1 - q^2 s_2}$$

Selection favouring heterozygotes - II

Task 7/p. 142

$$\Delta q = q' - q = \frac{q(1 - qs_2)}{1 - p^2 s_1 - q^2 s_2} - q =$$

$$= \frac{q(1 - qs_2) - q(1 - p^2 s_1 - q^2 s_2)}{1 - p^2 s_1 - q^2 s_2} =$$

$$= \frac{q(1 - qs_2 - 1 + p^2 s_1 + q^2 s_2)}{1 - p^2 s_1 - q^2 s_2} =$$

$$= \frac{q(p^2 s_1 + q^2 s_2 - qs_2)}{1 - p^2 s_1 - q^2 s_2} = \frac{q(p^2 s_1 + qs_2(q - 1))}{1 - p^2 s_1 - q^2 s_2} =$$

$$= \frac{q(p^2 s_1 - pqs_2)}{1 - p^2 s_1 - q^2 s_2} = \frac{pq(ps_1 - qs_2)}{1 - p^2 s_1 - q^2 s_2}$$

Selection favouring heterozygotes - III

Task 7/p. 142

$$\Delta q = q' - q = \frac{pq(ps_1 - qs_2)}{1 - p^2 s_1 - q^2 s_2}$$

If $\Delta q = 0$ ⇨ gene frequency does not change ⇨ polymorphism is stable ⇨ thereafter must be :

$$pq\,(ps_1 - qs_2) = 0$$

1. p = 0 (population formed only by homozygotes <u>*aa*</u>)
2. q = 0 (population formed only by homozygotes <u>*AA*</u>)
3. $ps_1 - qs_2 = 0$, from it follows

$$(1 - q)s_1 - qs_2 = s_1 - qs_1 - qs_2 = s_1 - q(s_1 + s_2) = 0$$

$$s_1 = q(s_1 + s_2)$$

$$s_1/(s_1 + s_2) = q$$

$$\hat{q} = q_{equil.} = \frac{s_1}{s_1 + s_2} = \frac{s_{AA}}{s_{AA} + s_{aa}}$$

Selection favouring heterozygotes - IV

Task 8/pp. 143-144

Sickle-cell anaemia as stable polymorphism by heterozygous advantage

a) Gene frequencies :

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

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

Selection favouring heterozygotes - V

Task 8/pp. 143-144

Genotype	AA	Aa	aa
Observed (O)	9365	2993	29
Expected (E)	9523.87	2675.6	187.87
Difference (O - E)	-158.87	317.4	-158.87
Relation (O/E)	0.983	1.119	0.154

$$\chi^2 = 174.9$$

The population is not in C-H-W equilibrium

Selection favouring heterozygotes - VI

Task 8/pp. 143-144

b) Estimation of values of selection coefficients

Relations O/E in the table represent reproduction ability of individuals with different genotypes

Fitness of *AA* $w_1 = 0.983/1.119 = 0.879$

and *aa* $w_2 = 0.154/1.119 = 0.138$

Selection coefficients

$$\boxed{\begin{aligned} s_1 &= 1 - w_1 = 1 - 0.879 = 0.121 \\ s_2 &= 1 - w_2 = 1 - 0.138 = 0.862 \end{aligned}}$$

Study of population genetics required – no other lecture with this topic will be.