Population and Quantitative Genetics , Problem Set

Exercises for a master's-level course in animal breeding and population genetics. Lessons 2 to 9.

Lesson 2 , Gene frequencies and Hardy-Weinberg equilibrium

2.1 Consider the cattle Zz blood-type system with the three blood types ZZ, Zz and zz. The table below gives the blood-type distribution in three samples from the breeds RDM, SDM and Jersey. How is the blood-type distribution expected to be in the following generation after random mating within each breed?

Blood-type distribution (counts)	ZZ	Zz	zz
RDM	28	340	1 032
SDM	2	55	318
Jersey	56	129	75

2.2 Consider a large, randomly mated population. At a locus with two alleles A and a, where A is dominant over a, the frequency of homozygous recessive individuals (aa) is 1%. a) What is the frequency of heterozygous individuals (Aa)? b) What proportion of individuals with the dominant phenotype do these (Aa) represent?

2.3 In a randomly mating population a recessive disease gene (a) occurs at a frequency of 0.005. a) State the probability of finding, in the population, healthy parents (A-) with affected offspring (aa). b) State the probability of finding parents of whom at least one is affected (aa) with affected offspring (aa). c) State the numerical ratio between the probabilities found under a) and b) and comment on the result.

2.4 In dachshunds there is a pair of alleles R and r determining coat type, with R dominant over r. The phenotypes are wire-haired (R-) and short-haired (rr) respectively. a) Among 100 dachshunds in Hardy-Weinberg equilibrium, 64 wire-haired and 36 short-haired were found. How many dachshunds must be assumed to be carriers of a hidden allele for short hair in this population? b) In another population of dachshunds it has been established that the ratio between the genotypes RR and Rr is 2:5. What is the probability that the first pup will be short-haired after mating two randomly chosen wire-haired dogs?

2.5 In a population it was found that 1 in 10 000 men suffered from haemophilia, while no affected women were found. (Haemophilia is a sex-linked recessive trait.) a) What is the frequency of the gene for haemophilia (h) among men? b) What is the probability that women with haemophilia are born, assuming the gene frequency is the same in men and women?

2.6 A couple, where the mother has blood type B and the father blood type A, have a child with blood type O. Which blood types can their possible future children have?

2.7 From a Russian fox population, 14 345 foxes were caught. Of these, 12 were black, 678 intermediate and 13 655 red. a) Calculate the frequency of the gene for red and for black colour respectively. b) Test, using a chi-square test, whether the observed numbers agree with those expected under Hardy-Weinberg equilibrium.

2.8 In the following it is assumed that there is random mating in the Danish German Shepherd population. Microsatellite locus A is autosomal and has three alleles A1, A2 and A3 with frequencies 0.1, 0.3 and 0.6 respectively. Microsatellite locus B is likewise autosomal, with three alleles B1, B2 and B3 at frequencies 0.2, 0.3 and 0.5 respectively. a) State the expected genotypes and expected genotype frequencies in the population for each locus. b) State the expected frequency of genotype A1A2B1B2 and of genotype A3A3B3B3 in the population. A male dog with genotype A1A2B1B2 is mated to a number of bitches with genotype A3A3B3B3. c) State the expected genotypes among the offspring of these matings and the expected segregation of these genotypes among the offspring, assuming the two loci are not genetically linked. d) State the expected genotypes among the offspring and the expected percentage distribution, assuming the two loci are linked with a recombination frequency of 0.20, and that the male carries genes A1 and B1 on the same chromosome (i.e. A1 and B1 are in coupling phase).

2.9 On the pig's chromosome 6 there are two closely linked disease genes. One gene, the Calcium Release Channel (CRC), is responsible for the recessive disorder Porcine Stress Syndrome (stress sensitivity). Pigs with genotype n/n are stress-sensitive, while pigs with genotypes N/n and N/N are normal. The other gene, 1,2-alpha-fucosyltransferase 1 (FUT1), determines whether pigs become susceptible to oedema disease. Susceptibility to oedema disease is inherited dominantly, so that pigs with genotypes E/E and E/e are susceptible while pigs with genotype e/e are resistant. a) In a rare pig breed the CRC allele N and the FUT1 allele E are always in coupling phase. The frequency of the N allele is 0.4 and that of the E allele is 0.3. State the haplotypes and their frequencies. b) A breeder of the rare breed removes all stress-sensitive pigs (nn) in one generation. What effect will this have on the pigs' susceptibility to oedema disease? Calculate the haplotype frequencies after selection. c) The genetic distance between CRC and FUT1 is 5 map units. DNA tests exist so that both the CRC and FUT1 genotypes can be determined. How can these DNA tests be used to breed pigs that are both stress-free and resistant to oedema disease?

2.10 Two loci A and B are genetically linked with a recombination frequency of 0.3. In a randomly mating population the following gamete frequencies are found: AB = 0.4, Ab = 0.1, aB = 0.2, ab = 0.3. a) Calculate the linkage disequilibrium D. b) Calculate D in each of the following 10 generations. c) Calculate the gamete frequency at linkage equilibrium (i.e. when D = 0). d) Calculate the frequency of double heterozygotes in the starting population and at linkage equilibrium.

Lesson 3 , Selection and changes in gene frequency

3.1 In a population the following genotype distribution was found: AA = 110, Aa = 225, aa = 115. a) Is the population in Hardy-Weinberg equilibrium? b) Selection then acts against aa with selection coefficient s = 0.1. Calculate the gene frequencies in the next five generations.

3.2 Within the SDM breed there is an undesirable colour mutant such that individuals with genotype ee are red-and-white, while the black-and-white animals have genotype E-. Within a randomly mating herd of black-and-white cattle, where the gene frequency of E is p, red-and-white cattle are completely eliminated from each new offspring generation. a) How many generations will it take to halve the frequency of red-and-white calves if the frequency p0 = 0.80? b) Same question as a) with p0 = 0.98. c) Comment on the numerical relationship between the answers in a) and b).

3.3 In an autosomal, two-allele system with overdominance there is the following relationship between genotypes and fitness:

Genotype	A1A1	A1A2	A2A2
Fitness	0.8	1	0.3

a) Calculate the gene frequencies at gene-frequency equilibrium. b) Calculate the genotype frequencies before selection. c) Calculate the genotype frequencies after selection.

3.4 In a population the frequency of sickle-cell anaemia is found to be 0.05 among newborns. Because of resistance to malaria, the heterozygotes have most offspring, so that the normal individuals (Hba/Hba) and the anaemic individuals (Hbs/Hbs) contribute only 80% and 10% offspring respectively relative to the offspring of heterozygotes (Hba/Hbs). a) What will the frequency of Hbs be when the population is in equilibrium? b) Will the number of newborns with sickle-cell anaemia rise or fall?

3.5 In a Danish survey of 94 000 births, 10 cases of chondrodystrophic dwarfs (a dominantly inherited malformation) were found. It is assumed that the observed dwarfs are heterozygotes. a) What is the gene frequency of the disease gene? b) Find the fertility (which in this case equals fitness) of the dwarfs (Cc) relative to normal animals (cc), given that another Danish study found that 108 adult dwarfs had 27 children, while 457 normal siblings had 582 children. c) Assume the Danish population is in mutation-selection equilibrium for this disease. From the results in a) and b), give an estimate of the mutation frequency from c to C.

3.6 A closed population comprises in each generation 20 breeding males and 20 breeding females. In generation 0 the gene frequencies at a given locus are p = 0.6 and q = 0.4. Generation 1 is formed by random mating. State the possible outcomes of gene frequencies in generation 1, using confidence limits corresponding to a probability of p = 5% in a normal distribution.

3.7 A closed population consists of five breeding males and 50 breeding females generation after generation. One wishes to assemble another closed population consisting of breeding males and females in the ratio 1:1. a) How many individuals must the latter population comprise if the effective population size is to be unchanged? b) How large is the change in the rate of inbreeding per generation in the two populations?

Lesson 4 , Inbreeding and relationship in pedigrees

4.1 What is the inbreeding coefficient of individual X in the diagram below?

4.2 Calculate the inbreeding coefficient for all individuals in the following pedigree:

Animal	1	2	3	4	5
Sire	0	1	1	3	3
Dam	0	0	2	2	4

(0 = unknown)

4.3 On the basis of the pedigree below (with A = 1, B = 2, C = 3, D = 4, E = 5, 0 = unknown), answer the following: a) Set up an arrow diagram for individual A. b) Calculate the rate of inbreeding for all inbred individuals.

4.4 Consider the following two pedigrees. a) Who is the common ancestor of bull Wahl 239 and cow no. 196? b) How large will the inbreeding coefficient be of a calf out of Wahl 239 and cow no. 196? c) Can the bull Wahl 239 be recommended for insemination of cow no. 196?

4.5 On the basis of the following mink pedigrees, answer: a) State which animals are inbred. b) Set up an arrow diagram and calculate the inbreeding coefficient of offspring out of IV A and IV B.

4.6 In the pedigree below, the original designations of the individuals have been replaced by the numbers 1 to 11. Calculate the inbreeding coefficient for animals no. 10 and 11, and calculate the additive relationship between animal no. 11 and the other animals in the pedigree.

4.7 In the genealogical diagram below, V 12 (proband) represents the first recognised German-Shepherd dwarf in Denmark. This dwarfism is inherited as an autosomal recessive trait. a) State the individuals that must with certainty be heterozygous carriers. b) What is the probability that a randomly chosen phenotypically normal pup in one of the two litters (A or B) in generation V is a heterozygous carrier of dwarfism? c) What is the rate of inbreeding for 1) a randomly chosen pup in litter A, and 2) a randomly chosen pup in litter B? d) What is the relationship coefficient between two randomly chosen pups in litter A?

4.8 On a mink farm there are 100 breeding animals, of which 60 are unrelated, eight are offspring of full-sib mating, and 32 are offspring of half-sib mating. Calculate the average rate of inbreeding for the 100 breeding animals.

Lesson 5 , Qualitative traits, Mendelian genetics and statistical tests

5.1 Below is a pedigree showing the autosomal defect ataxia (aa) in dogs in a litter out of normal (A-) but related parents III 4 and III 8. Since this defect is rare, it can be assumed that II 1 and II 6 do not carry the gene a. a) Give a list of the dogs whose genotype can be determined, and state the type. b) What is the probability that the clinically healthy animal IV 2 is a carrier?

5.2 At a clinic for small domestic animals, a rare enzyme defect has been demonstrated in a male dog IV 1. On the basis of the owner's information and laboratory examination of all living siblings and ancestors, the genealogical diagram below could be constructed. Which monofactorial mode of inheritance must be considered most probable for the occurrence of the enzyme defect? The possibilities are to be treated separately.

5.3 In humans and rabbits, an anomaly has been found that manifests itself, among other things, in the shape of the leucocytes. The pedigree below shows the occurrence of "diseased" and normal individuals. Give a detailed justification of which mode of inheritance is most probable, and which can probably be excluded (monofactorial inheritance assumed).

5.4 Fur-animal breeders have demonstrated a new fur quality in a male, I 1, and have further obtained the results shown in the genealogical diagram. A filled symbol denotes the new fur quality. a) Assuming monofactorial inheritance, give an account of the mode of inheritance of the newly arisen trait. b) Describe a breeding method that can be used to verify the mode of inheritance.

5.5 In which sex would one expect a recessive sex-linked mutant trait to appear? a) In chickens? b) In rabbits?

5.6 A bull imported from Canada is suspected of being a carrier of an undesirable recessive trait that is very rare within the breed in question in this country. a) Sketch a method for testing the bull for the trait. b) Calculate the number of individuals needed in the study to be able to state with 95% certainty. c) Give a clear formulation of the possible result of the study.

5.7 One wishes through a progeny test to determine whether a bull is a carrier of a particular recessive gene. This can be done by mating the bull with a) cows of the recessive type (aa); b) cows known to be heterozygous (Aa); c) his own daughters. If all the offspring are normal, how many offspring must the bull produce in each of these three different tests for the probability that he is not a carrier to be 95%?

5.8 In the genealogical diagram, I 1 and I 2 represent a randomly chosen boar and a randomly chosen sow within the Danish Landrace in the mid-1980s, when the frequency of the recessive halothane gene n was high, with 4% halothane-sensitive pigs (genotype nn) being born. All pigs in the diagram were halothane-tested at 6 to 7 weeks of age. The test showed that III 2 and III 4 were halothane-sensitive. In the population as a whole there was random mating. a) State the individuals that must with certainty be carriers of the halothane gene n, and state the probability that III 1, III 3 and III 5 respectively are carriers. b) What is the probability that I 2 is a carrier, given that 4% halothane-sensitive pigs are born in the population? c) Assuming that II 2 is a carrier, what is the probability that III 6 is genotypically normal (i.e. genotype Hal NN)?

5.9 Among 120 offspring of heterozygous parents (mating type Aa × Aa) the following segregation ratio was found: AA = 39, Aa = 51, aa = 30. Test, using a chi-square test, whether there is a statistically significant deviation from the expected segregation.

5.10 A backcross is carried out (homozygote × heterozygote) to test whether a character is inherited recessively. There are 30 backcross individuals in total. Using a chi-square test, determine for which numerical ratios the hypothesis of recessive inheritance (1:1 segregation) can be accepted, using the 5% significance level.

5.11 State the probability of a sex distribution of two males and four females in a litter of six mink pups. The sex ratio is taken to be 50%.

5.12 In cattle, polled (P-, without horns) is dominant over horned (pp). What is the probability that a heterozygous cow gets one polled + three horned calves after insemination with heterozygous bulls?

5.13 State the possible combinations of AA, Aa and aa in families of three siblings from a mating between heterozygous parents.

5.14 Offspring of a phenotypically normal boar and four phenotypically normal sows, all five of which were known carriers of the gene for crooked hindlimbs, showed the following segregation ratios:

	Normal	Affected
Sow 1	6	3
Sow 2	10	2
Sow 3	12	3
Sow 4	5	0

Using a statistical test, examine whether these segregation ratios are consistent with a hypothesis of recessive inheritance.

5.15 Examine whether the segregation of recessives in the cattle family material below is consistent with a 7:1 segregation, assuming that both the father and the maternal grandfather are carriers. The families were found on the basis of at least one affected offspring.

Family size	2	2	2	2	2	3	5	6	6	8	15
No. affected	1	1	1	1	1	1	1	1	1	2	2

5.16 In pigs, a form of lameness of the forelegs has been demonstrated that occurs sporadically in litters out of normal parents. In a larger herd the anomaly was found in pigs in six litters, distributed as follows:

Litter no.	1	2	3	4	5	6
Normal	5	4	4	7	7	9
Affected*	3	3	1	3	3	2

(*equally distributed between male and female pigs). State the genetic hypothesis that best matches the collected data. A statistical test of this hypothesis is required.

Lesson 6 , Genotypic value, breeding value, dominance deviation and heritability

6.1 In a chicken population there are three genotypes corresponding to the genes Rd and rd at the riboflavin locus. The average content of riboflavin in micrograms per gram of egg yolk is 4.30 for Rd/Rd hens and 0.40 for rd/rd hens, while it is 2.50 for heterozygous hens. The frequencies of Rd and rd are 0.7 and 0.3 respectively. What is the average riboflavin content per gram of yolk, assuming all hens lay the same number of eggs and that the yolk weight is the same for all eggs?

6.2 In SDM dairy cattle a QTL with an effect on the frequency of twin births has been found. The QTL allele that has a positive influence on twin births has an allele frequency of 0.2. The following effects were found:

Genotype	AA	Aa	aa
Frequency of twins	0.008	0.020	0.016

a) Calculate the population frequency of twins. b) Calculate the deviations of the three genotypic values from the population mean. c) Split the deviation of the genotypic values from the population mean into an additive part (breeding value) and a dominance deviation.

6.3 In a pig herd the pigs' weight at five months is on average 88.5 kg. The gilts used in breeding weigh on average 93.0 kg, and the boars used weigh 102.0 kg at five months. The offspring weigh on average 89.5 kg at five months. Calculate the heritability for weight at five months.

6.4 A bull was used on two groups of cows whose average butterfat (bf.) yields were: Group I: 295 kg bf.; Group II: 227 kg bf. The offspring of the two groups yielded 266 and 259 kg bf. respectively. Calculate h2 for butterfat.

6.5 Draw an arrow diagram of the relationship between half-sibs and between full-sibs respectively. State the expected phenotypic correlation between half-sibs and between full-sibs, expressed in terms of the additive relationship (a), h2 and c2.

6.6 On the basis of a large observation set, the correlation between related individuals for weight at 6 weeks in pigs has been calculated. The results were: between half-sibs 0.05; between full-sibs 0.25. Calculate the heritability in the two cases, referring to the formula for the expected correlation between related individuals. Is there a common-environment component for full-sibs, and if so why?

6.7 On the basis of an observation set, the correlation and regression between related individuals for height in veterinary students and their parents in 1998 have been calculated. The results were: correlation mother-offspring 0.45; father-offspring 0.20; regression offspring on mid-parent 0.65. Calculate h2 in the three cases and discuss reasons for the differences between the results.

Lesson 7 , Estimation of breeding values and their accuracy

7.1 When choosing between alternative methods of assessing an animal's breeding value, it is essential to know the accuracy of the breeding-value estimate. Assume that a trait with heritability h2 = 0.25 can be assessed on the basis of: 1) the mother's performance; 2) the performance of 50 half-sibs; 3) 20 offspring that are mutually half-sibs (cf. figure, where the animal whose breeding value is to be determined is marked in black). Which of the three methods gives the greatest accuracy?

7.2 Calculate the breeding-value estimate for milk yield for the following animals ($h2$ = 0.25, $c2$ = 0.05 and population mean = 4500 kg), basing the estimate on knowledge of own yield or the yield of related individuals: 1) own yield, 1st lactation: 5000 kg 2) mean of own yield in three lactations: 4700 kg 3) mean of mother's yield in three lactations: 5000 kg 4) mean of 100 paternal half-sibs: 4600 kg 5) offspring of 3) and 4) Which of the breeding-value estimates is computed with the greatest accuracy?

7.3 In Swedish sport horses the syndrome osteochondrosis (OCD) occurs with a frequency of 30% (i.e. 30% OCD, 70% OCD-free). The population can be regarded as the result of random mating. The genetic disposition is polygenic with a heritability of 0.20. The relative value of individuals with OCD is set to 0, while the value of OCD-free individuals is 1. A has 40 offspring, of which 20 are OCD-free and 20 have OCD. B has 60 offspring, of which 45 are OCD-free and 15 have OCD. C has 20 offspring, of which 16 are OCD-free and 4 have OCD. a) Calculate the population mean and the means of the three offspring groups. b) Calculate the breeding-value estimate of the three stallions (A, B and C), all individuals within each offspring group being paternal half-sibs.

7.4 Calculate the squared accuracy of the breeding-value estimates for five individuals with the following observation sets: 1) own performance; 2) mean of 5 own performances; 3) mean of 200 paternal half-sibs; 4) mean of 10 offspring that are mutually half-sibs; 5) mean of 200 offspring that are mutually half-sibs, with $h2$ = 0.05, 0.1, 0.2, 0.4 and 0.6 and $c2$ = 0.10. Comment on the results.

7.5 Derive a formula for the breeding-value index and the squared accuracy for four individuals with information from: 1) own performance; 2) the two parents' performances; 3) the four grandparents' performances; 4) the eight great-grandparents' performances. Comment on the results.

Lesson 8 , Selection response, intensity and correlated response

8.1 The heritability for growth (20-90 kg) in pigs is set to 0.30. In a herd the average growth is 935 g. The gilts used in breeding had an average growth of 970 g, and the boars used a growth of 1008 g. What average growth is expected for the offspring of the selected individuals?

8.2 In a mink population, 5% of males and 33% of females are used for breeding. Selection is for body size, which has σP of 0.3 and 0.2 kg for males and females respectively. The heritability for body size is 0.40. How large a genetic change is expected per generation?

8.3 Assume that a population of hens has an annual average yield of 230 eggs. The phenotypic standard deviation is 35.7 eggs. A heritability of 0.40 is assumed for annual egg yield. Selection is based solely on hens, and 20 percent of the highest-yielding hens are used for breeding. Calculate: a) The selection differential (number of eggs). b) The genetic change (number of eggs) from the mother to the daughter generation. c) The daughters' average egg yield per year.

8.4 Hip dysplasia in dogs is a threshold trait with a heritability of 0.3. About 30% of all German Shepherds have hip dysplasia. The 70% that are phenotypically healthy are assigned the same breeding value, if the breeding value is based solely on a simple (either/or) interpretation of the X-rays of the individual dogs. a) Assume that among the 70% healthy German Shepherds a random sample is taken as breeding animals. How large is the selection intensity? b) State the expected genetic change in phenotypic standard-deviation units per generation if the 70% healthy German Shepherds are used as breeding animals. c) Calculate delta-G in σP-units if the females are selected by individual testing while the males are selected on the basis of a progeny test (20 half-sib offspring), using 10% for breeding. d) Calculate the ratio between delta-G computed under c) and b).

8.5 A progeny-test station for mink is planned to improve a fur trait with a heritability of 0.2. The station is to have a capacity of 800 offspring per generation, i.e. at most 800 fathers can be tested. Selection is to be carried out so that 40 of the tested fathers are selected for breeding. Only paternal half-sib groups are placed at the station, and from the above it follows that the number of offspring per father can vary between 1 and 20. How many offspring per father should be tested for the genetic change per generation to be as large as possible?

8.6 Two alleles each have a frequency of 0.5. The gene pair gives rise to variation in a quantitative trait, such that there is a difference of 4 kg in the quantitative trait between the two types of homozygote. There is complete dominance at the locus in question. The quantitative trait has σA = 10 kg and σP = 20 kg. a) What proportion of the quantitative trait's additive variance is due to the locus in question? b) Comment on when it is useful to apply gene markers.

8.7 In a selection experiment with mice, run over nine generations, individual selection was applied for growth (x), and over the nine generations a genetic change of 2.34 g was measured. As a correlated effect, a change in litter size (y) of 0.693 young per litter was measured over the same nine generations.

Trait	Heritability	Variance(P)
x	0.23	5.59
y	0.15	5.18

a) Calculate the genetic correlation between growth and litter size. b) Calculate the selection intensity ix.

Lesson 9 , Inbreeding depression and crossbreeding

9.1 In a guinea-pig population, where an inbreeding coefficient of F = 0.25 is maintained, there are three weight classes: 100 g, 80 g and 50 g, corresponding to the genotypes A1A1, A1A2 and A2A2. The frequencies of A1 and A2 are 0.8 and 0.2 respectively. a) How large is the average weight? b) Calculate the inbreeding depression.

9.2 In a crossbreeding experiment with pigs, the following average weights in kg at 80 days of age were found:

	Line A	Line B	Cross F1 (A × B)
Not inbred	22.7	20.1	22.8

	Line A	Line B	Cross F1 (A × B)
Inbred	21.7	13.1	19.6

a) Calculate the degree of heterosis for crosses between 1) non-inbred lines and 2) inbred lines. State the results in both absolute and relative terms. b) Calculate the inbreeding depression in percent.