Population and Quantitative Genetics , Solutions

Worked answers to the problem set. Lessons 2 to 9.

Lesson 2

2.1 Gene frequencies by the gene-counting method, and the Hardy-Weinberg genotype frequencies expected in the offspring after random mating:

Breed	p(Z)	q(z)	ZZ (p^2)	Zz (2pq)	zz (q^2)
RDM	0.14	0.86	0.02	0.24	0.74
SDM	0.08	0.92	0.01	0.15	0.84
Jersey	0.46	0.54	0.21	0.50	0.29

2.2 $q^2 = 0.01 \rightarrow q = 0.1$, $p = 0.9$. a) Aa = 2pq = 0.18. b) Among the dominant phenotype, the heterozygotes are $2pq/(p^2+2pq) = 0.18/(0.81+0.18) = 0.18$.

2.3 q = 0.005. a) Healthy parents (A-) with affected (aa) offspring: $(2pq)^2 \cdot (1/4) = 2\times10^{-5}$. b) At least one affected parent with affected offspring: $2 \cdot (2pq) \cdot q^2 \cdot (1/2) + q^4 = 2\times10^{-7}$. c) Ratio a):b) = $p^2/(1-p^2) \approx 99$. Comment: affected individuals are usually born to normal (carrier) parents, so selection against the recessive removes it only slowly.

2.4 a) $q(r) = \sqrt{0.36} = 0.6$, p = 0.4; carriers = $2pq \cdot N = 48$. b) Probability the first pup is short-haired from two wire-haired parents with RR:Rr = 2:5 → $(5/7)^2 \cdot (1/4) = 0.13$.

2.5 For a sex-linked recessive, the gene frequency equals the phenotype frequency in the heterogametic (male) sex. a) $q(h) = 1/10\,000 = 10^{-4}$. b) Affected females $q^2 = 10^{-8}$. Men are affected far more often than women.

2.6 Mother B0 and father A0 (since they have an O child). Future children may be A0, B0, AB or O.

2.7 a) Gene-counting: p(red) = (13 655 + 678/2)/14 345 = 0.9755; q(black) = (12 + 678/2)/14 345 = 0.0245. b) Chi-square against H-W expectation: $\chi^2 = 1.43$ with df = 3 − 2 = 1 (two parameters, p and N, estimated). The 5% limit at df = 1 is 3.84, so there is no significant deviation from H-W equilibrium.

2.8 a) Expected genotype frequencies per locus:

Genotype	1/1	1/2	1/3	2/2	2/3	3/3
Locus A	0.01	0.06	0.12	0.09	0.36	0.36
Locus B	0.04	0.12	0.20	0.09	0.30	0.25

b) A1A2B1B2 = 0.06·0.12 = 0.0072; A3A3B3B3 = 0.36·0.25 = 0.09. c) Unlinked, offspring of A1A2B1B2 × A3A3B3B3: each of A1A3B1B3, A1A3B2B3, A2A3B1B3, A2A3B2B3 at 0.25.

d) Linked ($c = 0.2$), male carrying A1B1 in coupling: A1A3B1B3 = 0.40, A1A3B2B3 = 0.10, A2A3B1B3 = 0.10, A2A3B2B3 = 0.40.

2.9 a) Haplotypes: NE 0.3, Ne 0.1, ne 0.6. b) Removing all ne/ne pigs (0.36 of the population) raises susceptibility to oedema disease; remaining haplotype frequencies become NE 0.469, Ne 0.156, ne 0.375. After selection 79.7% of pigs are susceptible (vs 51% before), because removing nn (stress-sensitive, which are ne/ne here) also removes resistant e/e animals. c) Select pigs carrying the Ne haplotype (genotype N/N e/e), or use genotyping over ≥3-generation families to establish linkage phase; over generations the linkage disequilibrium between N and E decays toward zero, making the favourable haplotype easier to identify.

2.10 a) $D = f(AB) - p_A \cdot p_B = 0.4 - 0.5 \cdot 0.6 = 0.10$. b) D falls by a factor $(1 - c)$ each generation: 0.10, 0.07, 0.05, 0.03, 0.02, 0.02, 0.01, 0.01, 0.01, 0.00. c) At equilibrium $f(AB)=0.30$, $f(Ab)=0.20$, $f(aB)=0.30$, $f(ab)=0.20$. d) Double heterozygotes: $2[f(AB) \cdot f(ab) + f(Ab) \cdot f(aB)] = 0.28$ in the starting population, 0.24 at linkage equilibrium.

Lesson 3

3.1 a) $p(A) = 0.4944$, $q(a) = 0.5056$; the population is in H-W equilibrium ($\chi^2 < 0.1$, below 3.84). b) With $s(aa) = 0.1$, $q' = [\frac{1}{2} \cdot 2pq + q^2(1-s)]/(1 - sq^2)$: $q_1 = 0.4926$, $q_2 = 0.4799$, $q_3 = 0.4677$, $q_4 = 0.4558$, $q_5 = 0.4442$.

3.2 Halving the ee frequency means lowering q from a) 0.2 (4% red) to 0.1414 (2% red): $n = 1/0.1414 - 1/0.2 \approx 2.07$ generations. b) From 0.02 to 0.01414: $n = 1/0.01414 - 1/0.02 \approx 20.7$ generations. c) It takes about 10× longer to halve the frequency when the gene frequency is 10× lower: selection against a recessive is weak at low frequency.

3.3 Overdominance with $s_1 = 0.2$ (A1A1), $s_2 = 0.7$ (A2A2). a) $\hat{q} = s_1/(s_1+s_2) = 0.22$. b) Genotype frequencies before selection: A1A1 0.61, A1A2 0.34, A2A2 0.05. c) After selection (relative): 0.58, 0.40, 0.02 (sum 0.843 before rescaling).

3.4 Sickle-cell, $s_1 = 0.2$ (normal), $s_2 = 0.9$ (anaemic). a) $\hat{q}(Hbs) = 0.2/(0.2+0.9) = 0.18$. b) The number of newborns with sickle-cell anaemia will fall, since q^2 at equilibrium ($0.18^2 = 0.0324$) is below the current 0.05.

3.5 a) $p(C) = (10/2)/94\,000 = 5.32 \times 10^{-5}$. b) Fitness of dwarfs (Cc) $= (27/108)/(582/457) = 0.25/1.27 \approx 0.20$ relative to normal, i.e. $s \approx 0.80$. c) At mutation-selection balance, $\mu = p \cdot s = 5.32 \times 10^{-5} \cdot 0.80 = 4.26 \times 10^{-5}$.

3.6 Variance of the gene frequency is binomial over $2N = 80$: $Var = 0.6 \cdot 0.4/80$, $SD = 0.0548$. The 5% confidence limits are $0.6 \pm 2 \cdot 0.0548$, so the gene frequency in generation 1 lies between about 0.49 and 0.71.

3.7 a) $1/N_e = (1/4)(1/5 + 1/50) \rightarrow N_e = 18.18$, i.e. an equal-sex-ratio population needs about 9 males + 9 females. b) $\Delta F = 1/(2 \cdot 18.18) = 2.75\%$ per generation in both populations.

Lesson 4

4.1 Reducing the pedigree to the relevant individuals: A, B, C and D have no common ancestors, so no gene can reach X in double dose. X is not inbred, because its parents E and G are unrelated.

4.2 Inbred individuals are C, D and E. With A the common ancestor: aAB = 1/2, FC = 1/4. With A and B common: FD = 3/8. With A, B and C common (C inbred): FE = 1/2. The tabular method gives the same relationship matrix, and yields the recurrence F5 = a34/2 = (2F4 + 1 + F3)/4.

4.3 a) Arrow diagram for A. b) Inbred individuals are C and A: FC = aEG/2 = 1/8; FA = aBC/2 = $[(1/2)^2 + (1/2)^4 + (1/2)^4]/2$ = 3/16 (paths C-E-B of 2 generations, and C-G-H-E-B and C-G-J-F-B of 4 generations).

4.4 a) Wahl II is the common ancestor of Wahl 239 and cow no. 196. b) The calf's inbreeding is 1/8 (half-sib mating). c) Not recommended: practical animal breeding sets ~10% inbreeding as the acceptable limit, but this is acceptable here, so judge against herd context.

4.5 a) Animals A, B and E are inbred. b) FX = aAB/2 = $[4\cdot(1/2)^5 + 6\cdot(1/2)^6]/2$ = 0.11, summing over the ten paths (two of 5 generations and the rest of 6).

4.6 From the pedigree file, animals 10 and 11 have F = 0.25 and 0.187. Additive relationships of animal 11 with animals 1-10: 0.125, 0.125, 0.125, 0.312, 0.312, 0.250, 0.625, 0.500, 0.687, 0.812 (and a11,11 = 1.187).

4.7 a) Certain carriers are all parents of generation V: III 1, III 2, III 3 and IV 1. b) A phenotypically normal pup is a carrier with probability 2/3 (segregation 1:2:(1)). c) FA = aIII.1,III.2/2 = $(1/2)^3/2$ = 1/16; FB = aIII.3,IV.1/2 = $[(1/2)^1 + 2\cdot(1/2)^5]/2$ = 9/32. d) Additive relationship between two pups in litter A = $2\cdot(1/2)^2 + 2\cdot(1/2)^5$ = 9/16.

4.8 Mean inbreeding = (60·0 + 32·(1/8) + 8·(1/4))/100 = 0.06.

Lesson 5

5.1 a) IV 1 and IV 4 are aa; III 4 and III 8 are Aa (they have affected offspring); II 2 and II 5 are Aa (since II 1 and II 6 are AA). b) P(Aa | normal) = p(Aa)/(1 − p(aa)) = (1/2)/(1 − 1/4) = 2/3.

5.2 Sex-linked dominant: excluded. Sex-linked recessive: possible. Autosomal dominant: excluded. Autosomal recessive: possible. Sex-linked recessive is most likely, since only I 2 and II 2 need be heterozygous (autosomal recessive would require I 1, I 2, II 2 and III 1 all to be carriers); dominant modes are excluded as no generation-I parents are affected.

5.3 Sex-linked dominant: excluded (II 7 would be affected). Sex-linked recessive: excluded (III 3, III 6 could not be affected unless II 4 were). Autosomal dominant: likely. Autosomal recessive: not excludable but requires I 1, II 1, II 4 to be carriers, whereas autosomal dominant requires none, so autosomal dominant is most probable.

5.4 Sex-linked dominant: possible. Sex-linked recessive: excluded (III 4 is normal/common). Autosomal dominant: possible. Autosomal recessive: unlikely (I 2 and II 4 would have to be heterozygous). Verification: mate a generation-III male of the new fur quality with normal-fur females; the segregation reveals the mode of inheritance.

5.5 A sex-linked recessive mutant first appears in the heterogametic sex: a) in chickens, the hens (ZW); b) in rabbits, the males (XY).

5.6 a) Test whether the bull is AA or Aa by test matings with his own daughters (50% AA, 50% Aa, since the Danish population is AA). b) P(affected offspring) = 1/8, P(normal) = 7/8; $(7/8)^n = 0.05 \rightarrow n = 23$ offspring. c) If none of the 23 offspring is affected (aa), one can state with 95% certainty that the bull is not a carrier and must be AA.

5.7 At the 5% level: 1) recessive (aa) cows: $(1/2)^n = 0.05 \rightarrow n = 5$; 2) known heterozygous (Aa) cows: $(3/4)^n = 0.05 \rightarrow n = 11$; 3) own daughters: $(7/8)^n = 0.05 \rightarrow n = 23$.

5.8 a) I 1 and II 1 are carriers; III 1, III 3, III 5 are carriers with probability 2/3 (normal, from a 1:2 distribution). b) With q = 0.2, P(I 2 is Nn | not nn) = 2·0.2·0.8/(1 − 0.04) = 0.333. c) P(III 6 is NN | not nn) = [(1/2)(1 − 0.333/2)]/[1 − (1/2)·0.333/2] = 0.455.

5.9 Expected 1:2:1, $\chi^2 = (39-30)^2/30 + (51-60)^2/60 + (30-30)^2/30 = 4.05$ with df = 2; below the 5% value (5.99), so no significant deviation.

5.10 With 30 backcross individuals, recessive inheritance (1:1) is accepted where $\chi^2 = (x-15)^2/15 + ((30-x)-15)^2/15 < 3.84$ (df = 1), i.e. for splits between about 20:10 and 10:20 (the equation gives roots 20.37 and 9.63).

5.11 Two males and four females in a litter of six (binomial): $C(6,2)\cdot(1/2)^6 = 15/64 = 0.23$.

5.12 P(one polled + three horned from a heterozygous cow × heterozygous bulls) = $C(4,1)\cdot(3/4)^1\cdot(1/4)^3 = 12/256 = 0.05$.

5.13 Possible (AA, Aa, aa) counts among three siblings from Aa × Aa: (3,0,0), (0,3,0), (0,0,3), (2,1,0), (2,0,1), (1,2,0), (0,2,1), (1,0,2), (0,1,2), (1,1,1) , i.e. all partitions of three into the three genotype classes.

5.14 Test of 3:1 (recessive): totals 33 normal and 8 affected; $\chi^2 = (33-30.75)^2/30.75 + (8-10.25)^2/10.25 = 0.66$, df = 1, no significant deviation.

5.15 Because families were ascertained through at least one affected offspring, use the singles (Weinberg) method. With T = 53, A = 13, A1 = 9, A2 = 2, the test statistic is χ^2-distributed with df = 1: no significant deviation from 7:1.

5.16 The best hypothesis is autosomal recessive with 3:1 segregation; by the singles method (T = 51, A = 15, A1 = 1, A2 = 1) the χ^2 (df = 1) shows no significant deviation from 3:1.

Lesson 6

6.1 Mean riboflavin = Σ(genotype frequency × value) = 0.49·4.30 + 0.42·2.50 + 0.09·0.40 = 3.19 μg/g.

6.2 a) Population mean = 0.64·0.008 + 0.32·0.020 + 0.04·0.016 = 0.0110. b) Deviations from the mean: AA (genotype value 0.020) → +0.0090; Aa (0.016) → +0.0050; aa (0.008) → −0.0030. (Here the allele raising twinning is at frequency 0.2.) c) Splitting each genotypic value G into breeding value A and dominance deviation D gives, for example, AA: 0.0090 = 0.0116 + (−0.0026); Aa: 0.0050 = 0.0044 + 0.0006; aa: −0.0030 = −0.0028 + (−0.0002). The breeding value is twice the mean deviation of offspring under random mating; the dominance deviation is the remainder.

6.3 Response to individual selection $R = h^2(S_{sires} + S_{dams})/2$. Here $(89.5-88.5) = h^2[(102-88.5)+(93-88.5)]/2 \rightarrow h^2 = 0.11$.

6.4 Using $R = h^2(S)/2$ for two groups and subtracting: $266-259 = h^2(295-227)/2 \rightarrow h^2 = 0.21$.

6.5/6.6 Expected phenotypic correlations: half-sibs $r = (1/4)h^2$; full-sibs $r = (1/2)h^2 + c^2$; parent-offspring $r = (1/2)h^2$. For pig 6-week weight, half-sib $r = 0.05 \rightarrow h^2 = 0.20$; full-sib $r = 0.25 \rightarrow (1/2)(0.20) + c^2 = 0.25 \rightarrow c^2 = 0.15$. The full-sib estimate alone would give $h^2 = 0.5$, but since the half-sib estimate is 0.2 there must be a common-environment component for full-sibs, attributable to the shared maternal (litter) environment.

6.7 mother-offspring $r = (1/2)h^2 = 0.45 \rightarrow h^2 = 0.90$; father-offspring $r = (1/2)h^2 = 0.20 \rightarrow h^2 = 0.40$; regression on mid-parent $b = h^2 = 0.65$. The very high mother-offspring value suggests a shared mother-offspring environment; the low father-offspring value may reflect uncertain paternity; the mid-parent regression has been remarkably constant since such measurements began over a century ago.

Lesson 7

7.1 Using the squared accuracy of the breeding-value index $r^2_{AI} = n \cdot h^2 \cdot a'^2/[1 + (n-1)(a \cdot h^2 + c^2)]$: mother's performance $r = 0.25$; 50 half-sibs $r = 0.44$; 20 half-sib offspring $r = 0.76$. The 20 half-sib offspring give the greatest accuracy.

7.2 With population mean 4500 kg, $h^2 = 0.25$, $c^2 = 0.05$: 1) own 1st lactation (5000): EBV = 4625 kg, $r = 0.50$. 2) mean of 3 own lactations (4700): 4594 kg, $r = 0.68$. 3) mother's 3-lactation mean (5000): 4617 kg, $r = 0.34$. 4) 100 paternal half-sibs (4600): 4587 kg, $r = 0.47$. 5) combining 3) and 4): (4617+4587)/2 = 4602 kg, $r = \sqrt{[(0.34^2+0.47^2)/4]} = 0.29$. The 3-lactation own-record index is the most accurate.

7.3 Threshold trait scored 0/1. a) Population mean = 0.7; group means A 0.5, B 0.75, C 0.80. b) Half-sib-offspring EBVs ($a' = 1/2$): $A = 0.7 + [40 \cdot 0.20 \cdot 0.5/(1+39 \cdot 0.05)] \cdot (0.5-0.7) = 0.43$; B = 0.78; C = 0.80.

7.4 Squared accuracy for the five information sources across h^2 = 0.05-0.6:

h^2	0.05	0.1	0.2	0.4	0.6
own	0.05	0.10	0.20	0.40	0.60
5 own	0.15	0.27	0.45	0.66	0.78
200 half-sibs	0.17	0.20	0.22	0.23	0.24
10 offspring	0.11	0.20	0.34	0.52	0.63
200 offspring	0.71	0.83	0.91	0.95	0.97

Heritability matters less for accuracy when there are many records than when there are few.

7.5 With ancestral information only, the breeding-value expectation is the same in all cases ($\bar{P} + h^2(P - \bar{P})$), but the squared accuracy halves at each step back in the pedigree: own $r^2 = h^2$; two parents $h^2/2$; four grandparents $h^2/4$; eight great-grandparents $h^2/8$. Accuracy falls drastically the further back one goes.

Lesson 8

8.1 $R = h^2(S\_sires + S\_dams)/2 = 0.3[(1008-935)+(970-935)]/2 = 16$ g; expected offspring growth = 935 + 16 = 951 g.

8.2 Selection intensities (from tables): 5% males i = 2.06, 33% females i = 1.10. $S = i \cdot \sigma P$: males $2.06 \cdot 0.3 = 0.618$, females $1.10 \cdot 0.2 = 0.220$. $R = 0.4(0.618 + 0.220)/2 = 0.17$ kg per generation.

8.3 a) Selection differential = $i \cdot \sigma P = 1.4 \cdot 35.7 = 50$ eggs (i for top 20%). b) $R = 0.4(0 + 50)/2 = 10$ eggs. c) Daughters' mean = 230 + 10 = 240 eggs.

8.4 a) Taking 70% as a random sample for breeding: i = 0.50. b) $\Delta G = i \cdot h^2 \cdot \sigma P = 0.5 \cdot 0.3 \cdot \sigma P = 0.15$ σP-units. c) With 10% males (i = 1.75) selected by progeny test ($r = 0.79$, $\sigma A = 0.55$ σP) and 70% females (i = 0.5) by own record: $\Delta G = (1.75 \cdot 0.79 \cdot 0.55 \cdot \sigma P + 0.15 \cdot \sigma P)/2 = 0.46$ σP. d) Ratio c):b) ≈ 3-fold improvement.

8.5 Optimising offspring per father n at the progeny-test station (40 selected of the tested fathers): one maximises $i \cdot rAI$ subject to station capacity. Tabulating n vs proportion selected: n = 1 → 0.461, n = 2 → 0.540, n = 3 → 0.583, n = 4 → 0.583, n = 5 → 0.584, n = 6 → 0.568, n = 7 → 0.555. The optimum is about n = 5 offspring per father, though the peak is very flat.

8.6 a) Two phenotypes with values 0 and 4 (complete dominance) occur at 0.25 and 0.75, giving a mean of 3 and a variance $3^2 \cdot 0.25 + 1^2 \cdot 0.75 = 3.0$; the locus contributes 3% of the additive variance ($3/(\sigma A^2=100)$). b) Gene markers are worthwhile when the locus explains a large share of additive variance (much more than 3%) and the trait's heritability is low (of order 10% or less).

8.7 a) Genetic correlation = ratio of standardised indirect to direct response = $(0.693/0.88)/(2.34/1.13) = 0.38$ ($\sigma Ax = 1.13$, $\sigma Ay = 0.88$). b) From $R = h^2 \cdot i \cdot \sigma P$ over 9 generations, $i = (2.34/9)/(h^2 \cdot \sigma P) \rightarrow ix \approx 0.48$.

Lesson 9

9.1 Inbreeding (F = 0.25, Fpq = 0.04) shifts genotype frequencies toward homozygotes. a) Mean weight = $100 \cdot (0.64+Fpq) + 80 \cdot (0.32-2Fpq) + 50 \cdot (0.04+Fpq) = 91.2$ g. b) Mean without inbreeding = $100 \cdot 0.64 + 80 \cdot 0.32 + 50 \cdot 0.04 = 91.6$ g, so the inbreeding depression is 0.4 g.

9.2 a) Heterosis (%): 1) non-inbred lines $100 \cdot (22.8 - (22.7+20.1)/2)/((22.7+20.1)/2) = 6.5\%$; 2) inbred lines $100 \cdot (19.6 - (21.7+13.1)/2)/((21.7+13.1)/2) = 12.6\%$. b) Inbreeding depression: line A $100 \cdot (22.7-21.7)/22.7 = 4.4\%$; line B $100 \cdot (20.1-13.1)/20.1 = 34.8\%$.