
Answers

Q1

1. Suppose that mutation increases the additive genetic variance by $V_m = 0.001 V_e$ per generation.

i) What heritability would be maintained at equilibrium, in a population of $N_e = 1000$ diploid individuals, assuming no selection?

ii) Is it plausible that heritability is maintained by a balance between mutation and random drift?

iii) If instead, heritability is maintained by a balance between selection and mutation, roughly what selection coefficient must act on the underlying alleles?

iv) Suppose that we select on a population that is initially completely inbred; we select the top

35% of individuals, so that with a normal distribution, the selection differential is 0.5 phenotypic standard deviations. How much does the population mean change after 50 generations (i.e., what is the response to selection?)

i) Genetic variance, and hence heritability, decreases by a factor $(1 - \frac{1}{2N_e})$ per generation, and is replenished by $V_m = 0.001 V_e$. Therefore, at equilibrium $V_g = 2 N_e V_m = 2000 \times 0.001 V_e = 2 V_e$. Therefore, $h^2 = V_g / (V_g + V_e) = 2/3$ (assuming variation is entirely additive).

ii) Under this neutral model, V_g should be proportional to N_e . Yet, heritabilities do not show this strong relation with population size; in particular, large populations do not show extremely high heritability. Much the same argument applies to sequence variation. This argument is known as *Lewontin's paradox*.

iii) Detailed models for the interaction between selection and mutation can get complicated.

However, a very rough argument is that if mutation builds up variance over a timescale of $\sim 1/0.001 = 1000$ generations, then selection must remove it over the same timescale, implying $s \sim 0.001$. To be a bit more precise: deleterious alleles decrease in frequency by $\Delta p \sim -spq$, and so if they are rare ($p \ll 1$), genetic variance ($\sim pq$) decreases by a factor $(1 - s)$ per generation. Hence, at equilibrium $V_g \sim V_m / s$, implying that $s \sim 0.001$ if $h^2 \sim 1/2$.

iv) With a selection differential $S = 0.5 \sqrt{V_p}$, $\Delta z = h^2 S = (V_g / V_p) S = 0.5 V_g / \sqrt{V_p}$ per generation.

Initially $V_g = 0$, but it increases by V_m per generation, reaching $50 \times 0.001 V_e = 0.05 V_e$ after 50 generations. Thus, $V_p \sim V_e$, and so summing over the generations, $\sum_{t=1}^{50} \Delta z = \sum_{t=1}^{50} 0.5 t V_m / \sqrt{V_e} = (50 \times 51/2) 0.5 \times 0.001 \sqrt{V_e} = 0.625 \sqrt{V_e}$. Because genetic variance accumulates linearly with time, the response increases quadratically with time. Eventually, though, selection and finite population size would limit the genetic variance.

Q2

2. In Weber and Diggins' (1990) experiment, the 20% of mated females with the highest ethanol resistance were selected to found the next generation.

i) Assuming that the trait is normally distributed, what is the mean of the selected females, in standard deviations ?

ii) If the initial heritability of ethanol resistance was 50%, what would be the predicted change in mean resistance after 65 generations, in a very large population?

iii) By how much would this be reduced in a smaller population, with effective size $N_e = 50$ individuals ?

iv) If a mutation arose, which increased ethanol resistance by 0.05 standard deviations, what would its ultimate probability of fixation be? What is its expected contribution to the response? What determines the relative contribution of large vs small effect mutations?

Note: Weber and Diggins (1990) give detailed explanations of their experimental design, and its effect on genetic variation. Here, you should can make simpler arguments, but give your assumptions.

i) A normal distribution has 20% of its mass above 0.84 standard deviations; this mass has a mean 1.4 s.d. You can find this by solving the integral, using tables of the normal distribution, or just by drawing the graph on squared paper and measuring the area. Yet another method: draw a large # of random numbers from a normal distribution and take the mean of the top 20%.

ii) The change in mean is $\Delta z = h^2 S$. Presumably, females mated at random, and so selection is effectively only on females, not males, halving the selection differential. (Actually, for X linked genes, there are two copies in females and one in males, so the selection differential is divided by 2/3). Assuming that genetic variances stay constant, we predict $65 \times 0.5 \times 1.4/2 = 23$ s.d.

iii) In a population with $N_e=50$, genetic variance decreases by $(1 - 1/(2 N_e))$ per generation, to $(1 - \frac{1}{2 N_e})^{65} \sim 52\%$ of its original value. The total response after 65 generations is $0.5 \times \frac{1.4}{2} \times \sum_{t=0}^{64} (1 - \frac{1}{2 N_e})^t \sim 13.8$ s.d. (Actually, one should allow for the decreasing variance which influences the selection differential - but this is a small effect).

iv) Suppose that this new allele increases the trait by 0.05 s.d. in the heterozygote. A random female had a 20% chance of being above the threshold of 0.84 s.d.; we need to find the probability that an individual with an extra 0.05 s.d. gets selected - which is just the area under a normal distribution, above $0.84 - 0.05$ s.d. This is 0.214, and so the selection coefficient is $s = \frac{0.214}{0.2} - 1 = 0.07$. We need to halve this, since only females are selected, so $s \sim 0.035$. The probability of fixation is ~ 2

$s = 0.07$. Thus, it is expected to contribute $2 \cdot 0.05 \cdot 0.07 = 0.007$ s.d. to the selection response. Clearly, a very large number of such mutations are required to have a significant influence. The contribution of small-effect alleles depends on the distribution of mutational effects, $\psi[\alpha]$, and specifically, on the contribution to the genetic variance generated by mutation, $V_m = \sum 2 \mu \alpha^2 \psi[\alpha]$. The shape of this distribution is an unresolved empirical question.