KEY **MID-TERM BIO 434: March 4, 2004**

POINTS: Q1:20; Q2:12; Q3:20; Q4:12; Q5:16; Q6:20

1. For each of the following comparisons, identify which situation would be expected to allow **more** genetic variance. Circle either the left- or right-hand side if it would have more genetic variance. Circle both left- and right-hand sides if the genetic variance should be approximately equal.

A.	
Population with 20 males and 4 females	Population with 4 males and 20 females
B.	
Locus experiencing underdominant Selection	Locus experiencing overdominant selection
C.	
Locus experiencing positive frequency Dependence	Locus experiencing negative frequency dependence
D.	
A population with effective population size 100 and census size 200	A population with effective population size 200 and census size 100
E.	
A population of 100 individuals with variance in reproductive success equal to 2	A population of 150 individuals with variance in reproductive success equal to 4

In this last case, the effective population sizes are approximately the same (slightly higher for the right-hand case), so having circled both is an OK answer.

2. A population of vampire bats starts with genetic variance at one locus equal to 0.37. It varies in effective size over 5 generations, with N_e being 10, 20, 15, 50, and 30 in the five generations.

A. If this population were closed to migration, what would we expect its genetic variance at this locus to be after these five generations?

The effective population size can be found approximately by the harmonic mean of N_e over generations:

$$\tilde{N} = \frac{1}{(1/10 + 1/20 + 1/15 + 1/50 + 1/30)/5} = 18.5$$

$$V_t = \left(1 - \frac{1}{2N_e}\right)^t V_0$$

$$V_5 = \left(1 - \frac{1}{2(18.5)}\right)^5 (0.37) = 0.323$$

B. At the end of the five generations, the genetic variance at this locus was measured again and found to be 0.42. Assuming that this is not the answer you found in the part A., why might the observed number be different from the expected answer?

The best answer is that with genetic drift, allele frequencies can change in any direction. Since genetic variance is a function of allele frequency, it is possible that sometimes genetic variance can increase with genetic drift in a given population. The answer given in part A is the *expectation* , but a given locus in a single population can vary from that expectation by quite a lot.

3. The Norway rat, *Rattus norvegicus*, is a worldwide agricultural and domestic pest. The anticoagulant warfarin has been used to control the Norway rat, but after a decade the rats developed resistance to the pesticide. A single gene determines resistance to warfarin, and heterozygotes for the gene are resistant to the pesticide. However, homozygotes for the resistant allele have a 20-fold increase in their need for vitamin K and, therefore, have low viability. In populations exposed to warfarin, fitness values are estimated to be 0.82 for wild-type, 1.20 for heterozygotes, and 0.44 for homozygous-resistant individuals.

A. If this population reached equilibrium without migration or mutation, what would we expect the frequency of the warfarin-resistant allele to be?

This is a case of heterozygote advantage, so first find the relative fitnesses of the genotypes, by standardizing by the heterozygote fitness.

$$\frac{0.82}{1.2} = 0.68;\ \frac{1.2}{1.2} = 1;\ \frac{0.44}{1.2} = 0.37$$

$$1 - s = 0.68 \qquad 1 - t = 0.37$$

$$s = 0.32 \qquad t = 0.63$$

Therefore the equilibrium allele frequency of the wild-type allele is $\frac{t}{s+t} = 0.66$, so the frequency of the resistant allele would be 1-0.66 = 0.34.

B. Imagine now that the population was no longer exposed to warfarin. If this population reached equilibrium without migration or mutation, what would we expect the frequency of the warfarin-resistant allele to be?

Without warfarin, there would be selection against the resistance allele because of its increased need for vitamin K. Without migration or mutation to re-introduce the allele, the population would eventually be expected to lose its warfarin resistance allele. In other words the equilibrium frequency of the resistance allele would be zero,

C. Let us now include mutation from the wild-type allele to the warfarin-resistant allele **and back**, both at rate 10^{-6}. In a population exposed to warfarin, what would we expect the equilibrium allele frequency of the resistant allele to be?

Mutation at such a low rate would not affect the equilibrium frequency of the alleles, given that the locus is experiencing strong overdominance selection. So the frequency of the warfarin allele would be the same as without mutation, or 0.34.

D. Again including mutation at the same rates as in part C, what would we expect the equilibrium frequency of the warfarin-resistant allele to be in a population **not** exposed to warfarin?

Without warfarin the resistance allele would be selected against, but we can't tell from the information given how strong that selection might be. The allele would not reach

frequency of zero, however, because mutation would constantly introduce it to the population. The equilibrium allele frequency in this case would be either m/hs (if the selection against the resistance allele was partially expressed in the heterozygote) or $\sqrt{\mu/s}$ if the deleterious effects were completely recessive.

4. In Mukai's mutation accumulation experiment, the effective population size was kept at a minimum value. What was Mukai trying to measure in this experiment, and why was a small N_e important?

Mukai was trying to measure both the rate and effects on fitness of new mutations.

Small N_e was important because if caused most new mutation to be nearly neutral, and therefore less likely to be eliminated by selection. As a result, Mukai was able to measure a more complete spectrum of new mutations than would have been possible if selection had already eliminated the deleterious effects.

5. In the McDonald–Kreitman test, the neutral model predicts 2 t μ_{syn} n synonymous substitutions. Explain what each of these terms means ("neutral", t, μ_{syn}, n, "synonymous", "substitution"). Explain why 2 t μ_{syn} n is the prediction.

Neutral: alleles are not under selection

t: number of generations since the most recent common ancestor of the two species

μ_{syn} : the mutation rate to synonymous mutations

n : the length of sequence being studied

synonymous : a DNA sequence change that, owing to the redundancies of the genetic code, does not change amino acid sequence.

substitution: A fixed difference in DNA sequence between two species.

2 t μ_{syn} n is the predicted number of synonymous substitutions between two species for neutral alleles, because for neutral alleles the substitution rate per base pair per generation is equal to the mutation rate per base pair per generation. There are t generations since the species shared a common ancestor, which is multiplied by 2 because a substitution in either species would result in a difference between them. For each of those 2t generations there is a μ_{syn} chance per base pair of a synonymous mutation, and there are n bases in the sequence. So the overall number of synonymous substitutions is the product of these numbers.

6. A locus in a diploid population has three alleles: *A, S*, and *C*. In one generation, the fitnesses of the genotypes formed by these alleles are:

AA 0.976; *AS* 1.138; *AC* 1.103; *SS* 0.192; *SC* 0.407; *CC* 0.550

A. If the population is randomly mating and the allele frequencies of the three alleles are $p_A = 0.8$, $p_S = 0.15$, and $p_C = 0.05$, calculate allele frequencies of each in the next generation after selection.

One way to calculate allele frequencies in the next generation is to use the formula $p'_A = p_A w_A / \overline{w}$. First calculate the marginal fitnesses of each allele, and the mean fitness:

$$w_A = 0.8(0.976) + 0.15(1.138) + 0.05(1.103) = 1.00665$$
$$w_S = 0.8(1.138) + 0.15(0.192) + 0.05(0.407) = 0.95955$$
$$w_C = 0.8(1.103) + 0.15(0.407) + 0.05(0.550) = 0.97095$$
$$\overline{w} = 0.8(1.00665) + 0.15(0.95955) + 0.05(0.97095) = 0.9978$$

Then we get:

$$p_A' = (0.80)\frac{1.00665}{0.9978} = 0.807096$$
$$p_S' = (0.15)\frac{0.95955}{0.9978} = 0.14425$$
$$p_C' = (0.05)\frac{0.97095}{0.9978} = 0.05$$

B. Look at the fitnesses of the six genotypes. At equilibrium, would you expect one of these alleles to be fixed in the population? Why, or why not?

We would not expect fixation at equilibrium. Each of the homozygotes has a heterozygote containing that allele that is more fit, so alternate alleles would always be maintained in the population by selection.