Evolutionary Genetics Midterm I, February 2nd 2012

P1:	/6
P2:	/8
P3:	/14
P4:	/7
P5:	/5
TOT:	/40

KEY

How to review your exam

An outlined key for midterm I is included below.

Please do the following to ensure your exam was properly graded:

- **Check the page totals for each page against the front page. Note that page 4 was out of 7 and page 5 was out of 5.**
- **Check the sum on the front page.**
- **If you find an error in the summing, please attach a note to the front of your exam that says which page the error is on.**

Go through your exam and compare your answers with the key.

If you think there has been an error in applying the grading scheme, attach a note to the front of your exam describing what you think the error is. Write clearly on the note, but DO NOT write on your exam. If you wish, you may circle the relevant parts of your answer on your exam in red, but no other markings should appear on your exam.

Hand in your exam for regarding to Jeannette. You can hand these in in class or drop off your exam at my office (Biodiversity 221). Feel free to slide your exam under my door, but do not leave your exam with a TA or with the other instructors. I would prefer to get these back by March 6th.

When you get your exam back, you may follow up with questions during office hours.

Improving your grade based on the final:

The class average for this exam was 57%. This is on the low end for my exams, but this exam was very similar to those of previous years, and the review materials were also similar. I am concerned that the exam may not have accurately measured your understanding of the material, but other factors can't be discounted. I do believe that the exam was fair, and that you had the necessary materials to do well. Very few student came to office hours, and I don't know what this reflects.

Based on this concern, this is what the teaching team has decided: The final exam includes a 19% cumulative section. If your grade on this section of the final is better by 10% or more compared with your grade on midterm I, 50% of the weight for exam I will be replaced using the % you got on the cumulative part of the final.

For example:
You got 52% on the midterm
You get 70% on the cumulative portion of the final

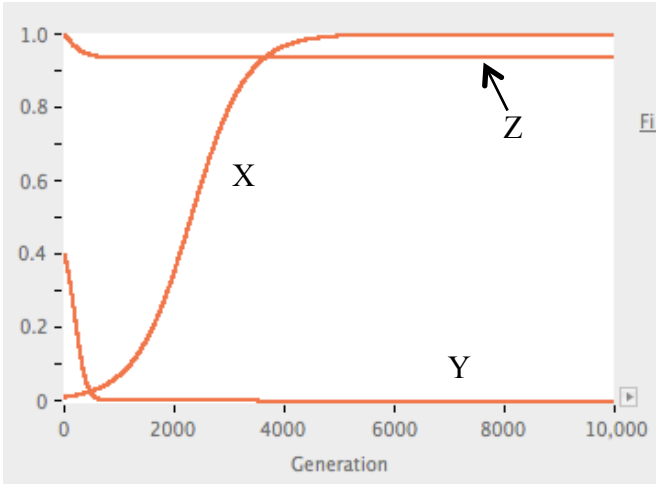
70-52 = 18, therefore you qualify to have part of midterm I replaced.

Normally, midterm I would count for 16% of your final grade. Now, it will only count for 8% and the cumulative part of the final will count for 27% of your final grade.

This will be assessed automatically for every student.

1. The graph to the right shows the change in the frequency of allele A under three scenarios (labeled X, Y and Z) that differ in various population genetic variables.

   Each of the lines corresponds to a single scenario described below. Determine the scenario (a-e) that best predicts each of the lines (X,Y,Z). **Briefly explain your choice in the space provided**. (6 marks)



a) $N = 500$; $W_{AA} = 1.0005$, $W_{Aa} = 1.000$, $W_{aa} = 1.000$; μ=0

b) N = 1000000; $W_{AA} = 1$, $W_{Aa} = 0.99$, $W_{aa} = 1.01$; μ=0

c) $N = 1000000$; $W_{AA} = 0.95$, $W_{Aa} = 1$, $W_{aa} = 0.95$; μ=0

d) $N = 1000000$; $W_{AA} = 1$, $W_{Aa} = 1$, $W_{aa} = 0.95$; μ=0.0002

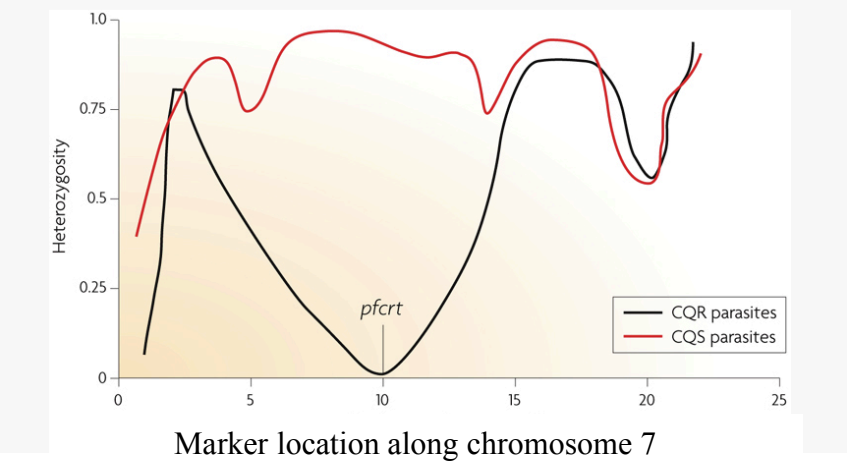
e) $N = 1000000$; $W_{AA} = 1.004$, $W_{Aa} = 1.002$, $W_{aa} = 1$; μ=0

*Note that μ is the mutation rate from A to a.

Line	Best matches scenario… [(a-e) from above]	Explanation
X	(e)	This line shows direction selection in a very large population, in which A is favored. Fixation is achieved; therefore there must be no mutation.
Y	(b)	Because A is lost, this has to be an example of either directional selection in favor of a (but there are no examples of this), or it could be a situation in which there is het disadvantage, and we are starting with the frequency of A below the polymorphic equilibrium. This fits scenario b.
Z	(d)	This line shows a polymorphic equilibrium. Of the scenarios we have seen, only het advantage or mutation-selection balance allow for polymorphism. The fact that the line is close to p=1 suggests mutation-selection balance, but this is confirmed by noting that the particular het advantage scenario shown would lead to p-hat = 0.5. Therefore, the only possible match is (d).

2. The parasite that causes malaria, *Plasmodium falciparum*, infects more than 200 million people worldwide. Some malaria strains can be treated with chloroquine, but resistance of the parasite to chloroquine has arisen in many of the areas where the drug is used to treat malaria.

   The graph below shows data from sequencing of several *P. falciparum* strains that are either resistant (lower line) or susceptible (upper line) to chloroquine. The mutation "pfcrt", at marker location 10, is thought to be responsible for conferring resistance to chloroquine.



Marker location along chromosome 7

a. Considering the sequence across the whole chromosome, describe the key feature of this graph that suggests that selection is responsible for the spread of chloroquine resistant strains of *P. falciparum*. Explain in 1-2 sentences. (2 marks)

The key feature is the sharp decline in heterozygosity surrounding "location 10" (which is the hypothesized target of selection). Note that it is not enough to say that location 10 is homozygous. As you know, drift alone is expected to lead to fixation. The fact that hitchhiking has occurred indicated a rapid process of fixation, which is what we expect if selection has acted to favour resistance.

b. Assuming that chloroquine continues to be used to treat malaria, how would you expect the regions surrounding Marker 10 to change over the next 1000 generations? Explain. (2 marks)

We expect that over time, recombination will break down linkage disequilibrium. Therefore, over time, the markers around location 10 should increase in heterozygosity. This means that the graph will spike down more sharply at pfcrt.

3. Consider the fate of a novel mutation that is not subject to selection, present in a single copy in a population of finite size. (Assume no further mutation occurs.)
   a. Does the mutant allele have a greater probability of eventually reaching fixation in a population of size 100 or 10,000? Explain in one sentence. (2 marks)

The probability of fixation with drift alone (no mutation and no selection) is given by n/N (haploid) or n/2N (diploid). In the case described, this means 1/100 compared with 1/10,000 (or 1/200 compared with 1/20,000). From this, it can be seen that the probability of fixation is greater in the smaller population.

b. Is the mutation more likely to be lost in a population of size 100 or 10,000? Explain in one sentence. (2 marks)

Given that there is only one copy of the allele in each case, the probability of loosing the allele is greater in the larger population. This is intuitive as the frequency of the allele in the larger population is 100

times lower than in the smaller population, and the probability of loosing the allele is a function of its frequency.

c. Assume that the allele drifts to a frequency of 0.1 in a population of size 10,000. The population undergoes a sudden decline to a size of 50 in a single generation. What can you say about whether you expect the frequency of the mutant allele to be greater or less than 0.1 in the new population of 50 individuals? (2 marks)

This scenario describes taking a random sample of 50 from a population of 10,000. Given that you are doing this only once (1 sample), you can't say whether the frequency will be greater than 0.1 or smaller than 0.1 in the sample. This is like saying that you toss a coin 50 times, and asking you to guess whether you will likely toss more than 25 heads or fewer than 25 heads. You simply don't know which is more likely.

d. Based on these answers, explain how genetic drift has both predictable and unpredictable effects on allele frequencies in finite populations. (3 marks)

In the first two scenarios, you were asked about the likelihood of specific outcomes over the long term. We have learned that we can say that the probability of eventual fixation or loss is related to the frequency of an allele at the present time. This is an example of the predictable nature of drift. We know that alleles will be lost by drift, that heterozygosity is expected to decline according to certain models, etc.
The unpredictable nature of drift was illustrated by part c, in which it is clear that while there are general long term expectations, because of the chance effects of drift from one generation to the next, the outcome of a specific scenario, especially looking at a specific generauo cannot be predicted

4. The following data show the frequencies of four haplotypes for two neutral loci, A and B, in a large gamete pool.

Haplotype	Observed frequency
A_1B_1	0.1
A_1B_2	0.4
A_2B_1	0.2
A_2B_2	0.3

a. Calculate the coefficient of linkage disequilibrium, D, for the data. (2 marks)

D = 0.05

b. What are the frequencies of the four alleles in this population of gametes? (2 marks)

A1 = 0.1+0.4 = 0.5
A2 = 0.2 + 0.3 = 0.5 (note that the frequencies at this locus sum to 1)

B1 = 0.1 + 0.2 = 0.3
B2 = 0.4+0.3 = 0.7 (these two also sum to 1)

c. Considering only the A locus, how many generations will it take for the three genotypes A_1A_1, A_1A_2 and A_2A_2 to be in Hardy-Weinberg proportions in a population of zygotes generated from these gametes? Briefly explain your answer. (2 marks)

Just one generation of random mating.

[Parts B and C were meant to test your understanding of the fact that each of these loci on its own acts according to the single locus expectations].

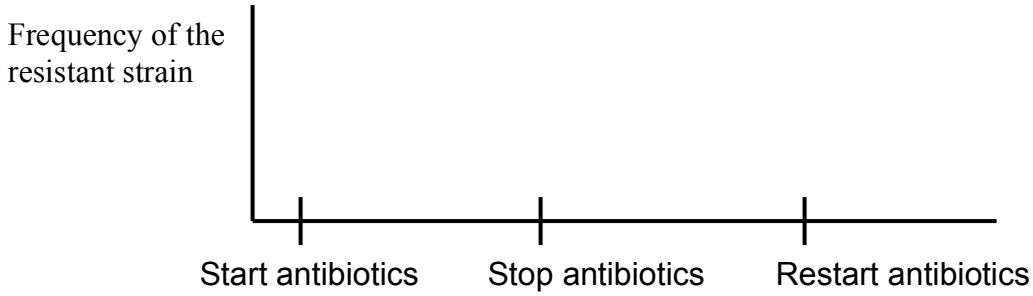
5. Can an individual evolve? Explain in 2-3 sentences, including a definition of evolution in your answer. (3 marks)

Evolution is a concept that applies to a population, not an individual. Most of you defined evolution as a change in allele frequencies from one generation to the next, and thus said that an individual could not evolve. If you incorrectly said that evolution was the same as natural selection, or implied that natural selection was the only mechanism of evolution, you lost at least 1 mark.

6. Alleles that are advantageous in one situation might be disadvantageous in another. This has been found, for example, with in some case of antibiotic resistance in bacteria, in which resistant strains are most fit well when the antibiotic is present, but less fit (relative to the antibiotic susceptible strain) when the antibiotic is absent (sometimes referred to as the *cost of resistance*). Given this scenario, if a patient is found to carry a resistant bacterial strain, one strategy involves stopping antibiotic treatment for a time.

Sketch a graph that describes the trend that you would expect in the frequency of the antiobiotic resistant strain over time. Note the points at which antiobiotic treatment starts and stops, and assume that the resistant strain is initially rare, and that neither strain reaches fixation over this time span. Recall that bacteria are haploid, so we only have to think about two fitnesses, W_R, the fitness of the

resistant allele, and W_S, the fitness of the susceptible allele. (4 marks)



Explain the pattern that you drew in 2-3 sentences.

You should have drawn a curve that started with a low frequency of antibiotic resistance, then rose in a sigmoidal shape once antibiotics were started, to reach a high frequency.

When antibiotics are stopped, this changes the advantage so that the most fit type is the antibiotic-sensitive strain, so the frequency of the resistant strain drops (again, in a sigmoidal form) to ear zero. When antibiotics are restarted, the frequency of the resistant strain again rises.

7. A group of researchers is interested in a locus associated with the ability of bed bugs to resist blasting with insecticide. They estimate the fitnesses of three genotypes as follows

$W(Blast^a/Blast^a)$ =1.0

$W(Blast^a/Blast^b)$ =0.9 [You should see right away that this is a case of het disadvantage]

$W(Blast^b/Blast^b)$ =1.15

a. In a very large, randomly mating population with an initial frequency of $Blast^a$ = 0.35, what are the expected genotype frequencies after one generation of selection? (2 marks)

Calculate the allele frequencies after one generation of selection using:

$$p[t+1] = \frac{p[t]^2 W_{AA} + p[t]q[t]W_{Aa}}{p[t]^2 W_{AA} + 2p[t]q[t]W_{Aa} + q[t]^2 W_{aa}}$$

you should get p[t+1] = 0.32; q[t+1] = 0.68

The genotype frequencies are then $(p[t+1])^2 = 0.10$

$2pq = 0.44$

$q^2 = 0.46$

b. If a population has an initial frequency of $Blast^b$ = 0.17, what will the frequency of this allele be after a large number of generations (assume large population, no mutation)? (1 mark)

With het disadvantage, you first need to determine the value of the polymorphic equilibrium

$$p = \frac{W_{Aa} - W_{aa}}{2W_{Aa} - W_{AA} - W_{aa}}$$

This value is p=0.71 (the polymorphic equilibrium value for *Blast*^{a}). The actual equilibrium with het disadvantage depends on whether you start above or below the equilibrium (slide 23 in lecture 4). Here, you start with *Blast*^{b} = 0.17, so *Blast*^{a}=0.83, above the polymorphic equilibrium, so you expect the frequency of *Blast*^{a} = 1 at equilibrium, and therefore *Blast*^{b}=0.

8. Climate change is expected to have a major impact on species, requiring that they evolve in response to changing environmental conditions. Genetic variation is often described as "*crucial for allowing species to survive the impacts of changing climate*".
   a. Why is genetic variation generally considered to be such a good thing? Briefly describe the key benefit of genetic variation in allowing populations to deal with the impacts of climate change? (1 mark)

   When the environment changes, the fitness of an allele (or a trait) may also change. Therefore, having variation present in a population is thought to increase the chance that an allele that is beneficial in the new environment will be present in the population.

   b. Collared Pikas live on isolated rocky slopes at high elevations of northern BC, Yukon and Alaska. They have a limited ability to tolerate high temperatures, and will die if they experience temperatures above 28C for prolonged periods. The narrow sense heritability of thermal tolerance has been estimated for a population in Kluane National Park in Yukon. The value of h^2 was found to be 0.53. Can conservation managers use this finding to suggest that populations of the species will likely to be able to adapt to warmer temperatures across the species range? Explain in 1-2 sentences. (2 marks)

   Key idea: heritability is not transferable, but applies only to the population and environment in which it was measured.

   You can't say anything about the heritability (and therefore the potential for adaptation) in this trait in environments or populations other than the population at Kluane. So, NO, managers can't use this specific value to make general conclusions about adaptability across the species range.

   c. Collared Pikas rarely disperse between populations, and populations are typically quite small. This population structure has both positive and negative consequences for the species potential to adapt to future climates. Describe a possible **benefit** of this type of population structure that might help the Collared Pika adapt to climate change. [Hint: think about Buri's experiment]. (2 marks)

Buri's experiment showed that each small population went to fixation for the locus under study, but different populations lost one of the other allele.

Linking the point from a about genetic variation being important for evolution, the expected answer here was that the benefit might come form the fact that while each population would tend to go to fixation for one allele at each locus, different populations might end up with different alleles. Therefore, the benefit

is that an allele that may turn out to be beneficial in the future has a better chance of being preserved in at least one of these small isolated population.

Biol 336
Formula Sheet for Population Genetics
Midterm I Version

Hardy-Weinberg and Null Models:

$X^2 = \sum \frac{(obs - \exp)^2}{\exp}$ Critical X^2-value for α=0.05 is 3.84

Linkage Disequilibrium with recombination:

$D' = (1 - r)D$

$D[t] = (1 - r)^t D[0]$

$$x_{11}[t+1] = x_{11}[t] - rD_t$$
$$x_{12}[t+1] = x_{12}[t] + rD_t$$
$$x_{21}[t+1] = x_{21}[t] + rD_t$$
$$x_{22}[t+1] = x_{22}[t] - rD_t$$

Mutation-Selection Balance:

$\hat{q} = \frac{\mu}{hs}$ (h>0)

$\hat{q} = \sqrt{\frac{\mu}{s}}$ (h=0)