These are for your own information only; I won't be collecting or grading them. Some are a little longer and more open-ended than actual exam questions but otherwise they should be comparable.

1. As a teenager I attempted to show Mendelian segregation by crossing pure-breeding normal-wing fruit flies with pure-breeding vestigal-wing fruit flies (vestigal-wing flies have small, stubby wings and cannot fly). My first generation consisted of 100% normal-wing flies. In my second generation I saw something like this:

Phenotype	Number of flies
Normal	180
Vestigal	20

   (a) Using the information that this is a single-gene Mendelian trait, calculate the expected flies in each category and perform a statistical test to see if the observed flies match expectations. (Note that this was a controlled cross, **not** a random population of flies.)

   I know that this should be a cross of two heterozygotes so I expect 3/4 normal and 1/4 vestigal. I do not need to estimate the allele frequencies from the offspring, luckily, so the test can be done.

Phenotype	*Number of flies*	*Expected*	$(o-e)^2/e$
Normal	*180*	*150*	*6.0*
Vestigal	*20*	*50*	*18.0*
Total	*200*	*200*	$\chi^2 = 24.0$

   With 1 df this is highly significant; these results are not consistent with my expected 3:1 ratio.

   (b) Assuming that offspring were conceived in the expected ratios, calculate the fitness of vestigal-winged flies in my experimental setup.

   Observed/expected = 20/50 so the absolute fitness would be 0.4. Divide by the fitness of the best phenotype (normal), which was 1.2, to give a relative fitness of 0.33. I think the fly medium was too sticky and the vestigal-winged flies got stuck in it and died, whereas the others could fly to the top of the tube (I did find dead vestigal-winged flies in the medium when I cleaned it out later).

2. Suppose that naked mole rats have one breeding female and about three breeding males per colony. A geographic region has 100 colonies of average size 80 individuals.

   (a) What is the census (headcount) population size of this region? *8000 individuals.*

   (b) What is the effective population size? (It will be useful to know that if the sex ratio is unequal, the effective population size is $4N_mN_f/(N_m + N_f)$, where N_m is the count of breeding males and N_f is the count of breeding females.) *We have 100 breeding females and 300 breeding males, for $N_e = 300$.*

   (c) A related species of mole rat is solitary, with all individuals able to reproduce. If the two species had the same census population size, would you expect the solitary species to contain more, less, or the same amount of neutral genetic variability? *More; it has a much higher N_e so is less likely to lose neutral alleles by drift.*

   (d) What advantage might naked mole rats gain by being eusocial (only a few individuals reproduce)? *They may be more altruistic and thus able to cooperate better to dig tunnels and exploit rare, large food sources.* What disadvantage might they face? *Small N_e makes them vulnerable to drift fixing bad alleles; low diversity makes then vulnerable to diseases. The politics when the queen dies are intense! Also, their breeding system might be vulnerable to "cheater" alleles.*

3. In Hawaiian fruit flies, we sampled a gene of unknown function. 60% of our flies were homozygous GG; 40% were homozygous gg. Despite a lengthy search we never found any heterozygotes.

   (a) List as many possible explanations for this result as you can. Try to be specific.

   Selection: Gg could be lethal. G and g could be linked to something else which is lethal when combined. The two kinds of flies could be separate species which are not interfertile. Non-random mating: GG and gg flies could refrain from mating, or fail to mate successfully–again, they might even be different species. Geographic separation: We might have two populations of flies, such as lowland and highland, which never meet so never mate, even though they could if we put them together. Ecological separation: we might have two kinds of flies in different niches–such as papaya orchards and mango orchards–which never meet even though they live nearby.

(b) Which of your explanations would still be plausible if we sampled newly laid eggs and found some heterozygotes? *This suggests strongly that Gg is lethal or linked to something lethal. Clearly matings between GG and gg did occur to produce these eggs.*

4. An agricultural geneticist tried to select for resistance to leaf rust in tobacco. He started with a gene pool that clearly contained lots of genetic variability: some individuals were very susceptible, others were very resistant. He imposed strong artificial selection in favor of resistance for several generations, but there was no improvement in average resistance.

   (a) What are at least two possible explanations for this result? *The resistant form may be a heterozygote. Or, natural selection may favor the susceptible form so that it opposes his artificial selection.*

   (b) For each of your reasons, is there something the experimenter can try in order to improve his results, or is it hopeless? *If resistance is due to a heterozygous genotype, there are several things to try, though none are perfect. He could clone his resistant tobacco rather than breeding it. He could isolate pure strains of the two homozygotes and cross them to get resistant F1 (which would then not breed true). He could wait for a new mutation which might not be overdominant. He could use genetic engineering to put both alleles on the same chromosome. He could try to find a non-overdominant resistance allele in another species or strain and introduce it into his plants.*

   If his problem is natural selection, he could try to weaken the selection by changing the environment. For example, if resistant plants take up nutrients badly, he could use more fertilizer. He could also wait for a new mutation, either a non-harmful form of leaf rust resistance, or a mutation at another gene which makes the plants better able to survive having the resistance allele. He could try to find a better resistance allele in some other plant and cross or engineer it into his plants.

5. A cat breeder discovers several kittens with curled ears. She attempts to establish a new breed of curled-ear cats by selling off all normal-eared kittens and breeding only the curled-ear kittens. Ten generations later, she is frustrated to find that crosses between two of her curled-ear cats still produce 67% curled and 33% normal kittens.

   She measures V_E for the curled-ear trait and finds that it is nearly 0. Identical twin kittens invariably have the same kind of ears. She also notes that her breed is not as fertile as expected.

   (a) What is a likely explanation for her results? *The curl/curl genotype is an early lethal; she never sees them because they die before birth.*

   (b) Is there anything she could do to obtain pure-breeding curled-ear cats? *One trick is to pair this with another lethal on the same chromosome so that the normal/normal genotype is also lethal, but the resulting cats will be only 50% fertile. (You are still producing normal-eared kittens; you just don't see them because they die, which at least saves on catfood.) Otherwise she could try changing the environment to save curl/curl kittens (change the mother's diet, maybe?) but there is not much hope if they die so early. She can wait for a better mutation (very slow), or search in other kinds of cats to find one that already exists.*

   (This is a real situation. I am a bit surprised that cat breeders didn't figure it out right away.)

6. The well-known form of hemophilia is a recessive X-linked gene. Homozygous recessive females and hemizygous recessive males are gravely ill. However, there are also autosomal (not sex linked) recessive genes which can cause hemophilia when defective.

   (a) We examine two human populations of the same size. Population R has a 10% frequency of the X-linked hemophilia allele, and population S has a 10% frequency of the autosomal hemophilia allele. What is be the initial frequency of hemophiliac individuals in each population (assume H-W)? What proportion would be males? *In R, 10% of males have hemophilia, and 1% of females. Assuming equal sex ratios, 5.5% of people will have hemophilia, and 91% of those affected will be males. In S, 1% of everyone has hemophilia, and 50% of those affected will be males.*

   (b) Which population would tend to lose the harmful allele more rapidly? Why? *R would, because there are a lot more hemophiliac individuals present, and when they die, copies of the gene are removed from the gene pool. In S the gene hides in heterozygotes; in R, the copies in males are revealed to selection.*

(c) If a complete cure for hemophilia were discovered so that these alleles became selectively neutral, would there be any expected difference in the length of time the hemophilia allele would take to fix or be lost in the two populations? Why or why not? (Hint: count gene copies.) *Genetic drift is stronger in R because the effective population size is smaller. 100 people have 200 autosomal gene copies but only 150 X-linked gene copies. So the allele will fix or be lost sooner in R than in S, on average.*

7. In humans, BB and Bb individuals have brown eyes, and bb individuals have blue eyes. We survey 1000 Northern Europeans and find the following: 824 brown-eyed people, 176 blue-eyed people.

   (a) If we can assume Hardy-Weinberg, what are the allele frequencies of B and b? *At HW, the frequency of blue-eyed homozygotes (0.176) should be the square root of the allele frequency. So* $p(blue) = 0.420$. $p(brown) = 0.580$.

   (b) There are a number of reasons the HW assumption could be wrong. Give two possible reasons. For each one, say whether it would cause you to over-estimate the frequency of the blue allele, or under-estimate it. *We could have population subdivision such that this is a mixture of people from a mostly brown-eyed population and people from a mostly blue-eyed population. If so, homozygotes are proportionally more frequent than we expected, and we overestimated* $p(blue)$. *At the limit* $p(blue)$ *might be only 0.176 if there are no heterozygotes at all.*

   We could have non-random mating such that brown-eyed people marry other brown-eyed people; this would also lead us to overestimate $p(blue)$.

   We could have the other kind of non-random mating, such that brown-eyed people marry blue-eyed people; this would lead us to underestimate $p(blue)$. *(This seems unlikely.)*

   We could have selection against heterozygotes, so that there are more homozygotes in our sample than expected; this would overestimate.

   We could have selection in favor of heterozygotes, so that there are fewer homozygotes than expected; this would underestimate.

   Other deviations involving mutation or drift are much less likely to make a significant difference than these. The first reason I gave is the most likely in practice, and it's likely enough to make our result quite unreliable.

8. In the social amoeba *Dictyostelium discoideum*, individual free-swimming amoebae, not necessarily related to each other, come together to form fruiting bodies with a stem and a tip. Only the amoebae in the tip reproduce. An individual amoeba can be "selfish" or "altruistic" depending on an allele at the gene *csA*. Selfish amoebae have a greater chance to end up in the tip, which increases their individual fitness. Altruistic amoebae have a greater chance to end up in the stem, which increases the fitness of the amoebae in the tip.

   (a) Would you expect the altruism allele to be able to spread, if introduced into a population of mostly selfish alleles? *Probably not. If amoebae have no special relationship to the ones they are helping, the gene won't benefit from kin selection, and its effect on the individual is negative. Group selection would be its only hope, and the conditions needed for group selection are quite rare.*

   (b) If fruiting bodies were made up of closely related amoebae, would this change your conclusion? Supposing that the cost of being altruistic is 50% and the benefit is 1% each to 1000 other amoebae, how closely related would the amoebae have to be, on average, to make altruism superior to selfishness? (The example is real, but these numbers are fictional.) *Altruism could spread. The key equation is* $Br - C > 0$, *but be sure to remember that a 1% benefit to 1000 amoeba is a 10-fold benefit. So B=10, C=0.5. Solving for r we see that the gene will spread if the amoeba are more closely related to each other than r=0.05. The benefit is to so many relatives, each one does not have to be closely related.*

   (c) Remarkably, individual amoebae with the altruistic allele of *csA* can recognize each other (they literally stick together). This enables them to be less altruistic when surrounded by selfish amoebae, and more altruistic when surrounded by altruistic amoebae. Does this change your conclusion about whether altruism can spread? *Altruism could spread more easily in this case because the amoeba can avoid being altruistic when it would not benefit their kin. It may even be able to spread when the fruiting body is made up of unrelated amoeba, as a "greenbeard gene."*

9. In Japan, there is a strong correlation between a father's height and his sons' height. Heritability is high: $h^2 = 0.8$.

   We sampled a group of fathers and sons who were all of Japanese ancestry (with no European admixture). The fathers were all born and raised in Japan; some of the sons were raised in Japan, others were raised in California. In this study, heritability was low: $h^2 = 0.1$. The height of a father did not predict the height of his sons well.

The mothers of these children were also Japanese with no European admixture. How can this result be explained?

If you don't understand this problem, please study it carefully! People are often confused by heritability and this problem is a fine example of why.

Heritability in Japan was high because V_E was low; the environment was relatively constant. The environment differs more between California and Japan than it did within Japan, so V_E is higher, making heritability lower. Remember that heritability is $V_A/(V_A + V_D + V_E)$. This shows that heritability is only meaningful for a specific environment; if the environment changes, heritability may change too.

This is a real effect and can be seen clearly in my husband's family; the boys raised in Japan are much shorter than their relatives raised in California. The key environmental variable is believed to be diet early in life. This environmental effect is so big that it drowns out the genetic resemblance between fathers and sons; the genetic effect is still there, but hidden by the much larger environmental effect. We would see it if we considered the Japan-raised boys and California-raised boys separately, thus controlling for the effects of environment.

10. Plants can be either zinc-sensitive or zinc-resistant based on alleles at the z locus. The sensitive allele, zS, is dominant over the resistant allele zR.

    (a) On a zinc-contaminated mine site, we collect random seeds and find 17 zinc-sensitive seeds (these are either zS/zS or zS/zR) and 105 zinc-resistant seeds (these are zR/zR). Assuming that the seeds are in Hardy-Weinberg proportions, what are the allele frequencies of zS and zR? $p(zR) = 0.924$, $p(zS) = 0.076$
    Here are fitnesses on different types of soil. The death due to selection happens while the plants are growing and before they can flower.

Genotype	zS/zS	zS/zR	zR/zR
Fitness on zinc soil	0.5	0.5	1.0
Fitness on regular soil	1.0	1.0	0.9

    (b) If we plant these seeds on zinc soil, what genotype frequencies will we expect in the flowering adults? $p(zS/zS) = 0.003$, $p(zS/zR) = 0.076$, $p(zR/zR) = 0.921$.

    (c) After one generation of selection, what will the new allele frequencies be? $p(zR) = 0.959$, $p(zS) = 0.041$.

    (d) Suggest a theory for why zS alleles are still present on this mine site.
    It is possible that the zR allele has newly arisen and has not yet had time to fix. But most likely the zS alleles are entering by migration from a nearby non-mine population where that allele is superior. Eventually the mine population may evolve self-fertilization or reproductive isolation to shut off this flow of unfit alleles from outside.
    People often try "There is selection in favor of zS" as an answer, but if the fitnesses given in the problem are assumed to be correct, we can see that there is no selection in favor of zS–at least not on zinc soil. Your theory has to be consistent with the given observations.

11. Researchers find a gene for which mutant alleles in modern humans are associated with inability to speak. They wonder whether change in this gene was important in the development of human speech abilities.

    (a) One approach is to calculate $\omega = D^N/D^S$ for this gene within modern humans. Supposing that the gene really is essential for human-like speech abilities, what general result would you expect? Why? (I.e. would ω tend to be greater than 1, less than 1, or approximately equal to 1?) *Since inability to speak is a severe disability in humans, I would expect ω to be much less than 1. While directional selection can cause $\omega > 1$ it seems unlikely that directional selection for this trait would be seen in the* **current** *human population.*

    (b) Another approach is to compare this gene between humans and chimpanzees via a Hudson-Kreitman-Aguade test (HKA). Supposing that change in this gene partially explains the superior speech abilities of humans, would you expect it to show higher polymorphism or higher divergence, compared to a neutral control gene? Why? *If this gene is responsible for rapid changes between humans and chimps, I would expect divergence to be higher compared to the neutral locus. Rapid directional change tends to increase divergence and wipe out polymorphism.*

    (c) Suppose that when the gene sequences were compared, the human and chimpanzee alleles were found to code for exactly the same protein product. Would this rule out a role of this gene in development of human speech? Why or why not? *No. The same protein product, expressed in a different tissue, at a different time, at a different level, or otherwise regulated differently, could produce a significantly different phenotype. Selection can act on non-coding variation as long as it has some effect on the phenotype.*