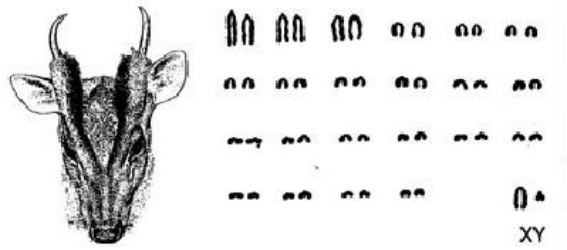
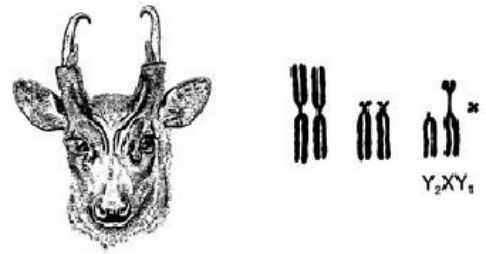
These are for your own information only; I won't be collecting or grading them. A solution key will be available on the Web. Some are a little longer and more open-ended than actual exam questions but otherwise they should be comparable.

1. In a hypothetical marine invertebrate, male offspring can be produced cheaply–a mother can generate 10 male offspring for the same energy and resource expenditure as 1 female offspring, because males come from smaller eggs. Assume that this creature is diploid, reproduces only by male-female mating, and cannot self-fertilize or clone. Also assume that offspring sex is determined by genes in the mother. What is the equilibrium sex ratio in this species? Why?

   Selection favors equal investment, which in this case would be making 1 female for every 10 males, or a sex ratio of 10:1 in favor of males. While the rare females will produce more grandchildren, they are more expensive. If females become rarer than 1 per 10 males, it will become advantageous to produce more females, and the female frequency will go up; if they become more common than 1 per 10 males, males will be more advantageous and the female frequency will go down. You can check this mathematically by counting grandchildren. At 10:1 an individual who specializes in male or female offspring will not gain more than the average number of grandchildren.



Chinese muntjac deer
Muntiacus reevesi



Indian muntjac deer
Muntiacus muntjak

2. Chinese muntjac deer have a fairly normal mammalian chromosome set. Indian muntjacs have very few, large chromosomes and unusual sex chromosomes. For each of the following (hypothetical) factors, explain how it might have contributed to the transition between the Chinese and Indian karyotypes:

   (a) Population bottleneck (tiny population size) *Large karyotype changes are usually bad in the heterozygote (underdominant). A bottleneck could enable rapid fixation of the new form due to strong genetic drift.*

   (b) Inbreeding *Karyotype changes are bad in the heterozygote. Inbred populations have fewer heterozygotes and thus suffer less from the bad consequences of such changes.*

   (c) Large numbers of transposons or other repeated sequences *Repeated sequences can lead to mis-pairing in meiosis and rearrangement of the genome. If the Indian muntjac had an abnormally large number of repeated sequences scattered across its chromosomes–perhaps due to a recently activated transposon, or a virus– that might explain how its genome became so massively rearranged.*

   (d) Mutations in genes involved in DNA repair *Failure of DNA repair might increase the frequency of chromosome rearrangements.*

(e) Habitat fragmentation *A fragmented habitat can encourage inbreeding and bottlenecks, both of which favor fixation of underdominant traits like karyotype changes.*

(f) Harem keeping by male muntjacs *Unequal reproductive success, such as one male monopolizing many females, reduces effective population size. This can promote fixation of underdominant traits. For example, if a successful male carries a new chromosome rearrangement, it may have a very high frequency in the next generation and get a big boost toward fixation.*

3. A short (fictional) DNA sequence is sampled from five primate species (only variable sites are shown):

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Species
Human (H)        GTC GCA ATA TGT
Chimpanzee (C)   GTA GCA TTC TGC
Bonobo (B)       GTA GCA TTC TGT
Gorilla (G)      ATA CCG TAC TGT
Rhesus (R)       ACA CTA TAG CCG
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(a) Make a distance matrix (raw distances with no corrections) for these five species.

	H	*C*	*B*	*G*	*R*
H	–	*4*	*3*	*7*	*11*
C	*4*	–	*1*	*5*	*9*
B	*3*	*1*	–	*4*	*9*
G	*7*	*5*	*4*	–	*7*
R	*11*	*9*	*9*	*7*	–

(b) Draw a UPGMA tree from your distances.

UPGMA will cluster C+B, then C+B+H, then C+B+H+G.

Reduced matrices for each step:

	H	*CB*	*G*	*R*
H	–	*3.5*	*7*	*11*
CB	*3.5*	–	*4.5*	*9*
G	*7*	*4.5*	–	*7*
R	*11*	*9*	*7*	–

	HCB	*G*	*R*
HCB	–	*5.75*	*10*
G	*5.75*	–	*7*
R	*10*	*7*	–

	HCBG	*R*
HCBG	–	*8.5*
R	*8.5*	–

In Newick format the final tree is:

(((((C:0.5,B:0.5):1.25,H:1.75):1.125,G:2.875):1.375),R:4.25):0.0;

We did not cover Newick format in class, but you can try to check your tree against this one.

(c) Modern genetic evidence suggests that humans, chimpanzees and bonobos group together on the tree (the "third chimpanzee" hypothesis). Previously it was thought that chimps, bonobos and gorillas must be closely related because they all walk on their knuckles, while humans do not. How could this disagreement between genetics and morphology be explained? Note that knuckle-walking is not purely a behavioral trait–if you try it yourself you will discover that human arms and legs have the wrong proportions for successful knuckle-walking. *Either humans lost knuckle-walking, perhaps as an adaptation to their plains lifestyle, or chimps and gorillas evolved it independently. A less likely possibility is species hybridization which allowed knuckle-walking to spread from, say, gorillas to chimps. Alternatively, the genetic evidence could be wrong for some reason, such as genetic convergent evolution, but across the whole genome this is highly unlikely.*

4. A morning glory plant is produced by fertilization of a normal haploid egg (1N) by an abnormal diploid sperm (2N), so that the resulting plant is triploid (3N).

(a) Give two ways in which this triploid plant could start a new species of morning glory. Be sure to explain how it could manage to reproduce successfully. *I know of at least four:*

i. Cloning, so no sexual reproduction required.

ii. Double all of its chromosomes so that it becomes hexaploid (6N) and can now go through meiosis normally.

iii. Double its chromosomes in oogenesis and halve them in spermatogenesis, or vice versa, so that sexual 3N offspring can be produced. I have never heard of a plant doing this–only amphibians–but theoretically it could happen.

iv. Lucky break in meiosis that produces a gamete with exactly 1N or 2N. (1N does not seem likely to produce anything new, but if two 2N gametes are made, you could get a tetraploid species.)

(b) Which of your two ways seems most promising in starting a species that will last for a long time? Why? *Cloning can lead to long-term problems (unless you are a rotifer) due to Muller's Ratchet. Hexaploidy and tetraploidy should be fine once they are established. The sexual-triploid strategy seems hard to get started but should be okay once it's established. If I had to bet, I'd bet on hexaploidy: this has happened in cultivated tobacco and wheat.*

(c) The plant hormone auxin is essential for normal plant development, but only one copy is needed. Would you expect the **allele frequency** of non-functional alleles of this gene to be higher or lower in a triploid morning glory species (assume that it has been triploid for many generations) than in the related diploid species? Why? (Please note that this question asks about allele frequency, not phenotype frequency!) *Higher. The alleles can hide in a heterozygote a lot more easily in a triploid. If it is asexual they would never risk coming together at all, and if it is sexual they would need to come together in 3's in order to be eliminated.*

Please be careful of questions like this. If you are asked for allele frequency, don't mistakenly give phenotype or genotype frequency instead.

5. As a researcher, you have three genetic markers to choose from:

A. A pseudogene with no function.
B. A gene coding for a moderately conserved protein, such as alcohol dehydrogenase.
C. A gene coding for an extremely conserved protein, such as cytochrome oxidase.

Which marker would you use for each of the following experiments? Briefly explain each answer. If you feel you need further information, explain what information you would need.

A general pattern in answers to this question is that many students want to make trees with sequences that are meaningful to the species splits. In fact these are probably the WORST choice. When we make a tree we'd like to see the inheritance of random differences; changes involved in speciation are far from random. For example, if two saltwater fishes both generate new freshwater subspecies, random genes are likely to show the right relationships among the species, but genes needed for freshwater adaptation may group the two freshwater forms together.

(a) A study to determine how the different orders of mammals (primates, bats, rodents, whales, etc) are related to each other. *Probably the moderately conserved protein is best. The pseudogene is unlikely to be recognizable among such distant species, and cytochrome oxidase will probably not have enough changes to be useful.*

(b) A coalescent analysis of migration patterns in humans. *I would prefer the pseudogene as it will have the most variability and no selection to confuse the issue. Even a moderately conserved protein won't vary among humans enough to help, unless it is selectively important (Duffy, hemoglobin, etc) and then I'd worry about convergent evolution.*

(c) An attempt to determine whether a newly-discovered hot-spring organism is a bacterium or an archaebacterium. *This must be a highly conserved protein (ribosomal RNA would also work). Nothing else will be reliably recognizable among such distantly related species.*

6. A variant form of the mosquito Y chromosome, called Y^*, is discovered. A male with Y^* transmits it to 100% of his offspring (who are therefore all sons).

We find a wild population of 1000 ordinary XY males and 1000 ordinary XX females, and in an attempt to destroy them, dump in 100 XY^* males. Assume that each male has an equal chance to reproduce and can produce an equal number of offspring.

(a) Initially, what are the relative frequencies of X, Y and Y^*? *Just by counting chromosomes, we find* $p(X) = 3100/4200 = 0.738$, $p(Y) = 1000/4200 = 0.238$, $p(Y^*) = 100/4200 = 0.024$. *Check that they add to 1.*

(b) After one generation, what will be the relative frequencies of X, Y and Y^*? (Remember that each mating must involve 1 male and 1 female.) *All females give X to their offspring so we can ignore them. All we care about is the relative frequency of XY males and XY^* males. We have 1100 males, 91% XY and 9% XY^*. So 91% of our offspring will come from normal males; half will be XX and half XY. 9% will come from supermales; all will be XY^*. This means* $p(X) = 3/4*0.91+1/2*0.09 = 0.7275$, $p(Y) = 1/4*0.91 = 0.2275$, $p(Y^*) = 1/2*0.09 = 0.045$. *The frequency of Y^* has approximately doubled due to its meiotic drive. Check that these add to 1.*

(c) Also after one generation, what will be the proportions of males and females? *We'll have 45.5% females and 54.5% males.*

(d) What kind of genetic event could save the mosquitoes from population extinction due to lack of females? *Females could develop the ability to recognize and reject XY^* males; a female who could do so would have daughters, which would spread her genes rapidly among a mostly-male population.*

An X^* chromosome mutation which overcame the meiotic drive of the Y^* so that X^*Y^* produced some daughters would also do the trick (though if all offspring inherited X^* you would just replace one problem with another!) There could be an "arms race" between X and Y; some researchers feel they see evidence of this in genomes.

An autosomal mutation that blocked the drive of Y^* would get into daughters and spread as a result.

Catching Wolbachia, which tends to transform males into females, could help–again, it might eventually replace one problem with another.

If the too-frequent sex were females, parthenogenesis (female cloning) could help, but as far as I know there are no species in which males can reproduce themselves without females.

7. Two visibly different types of butterfly exist in the same region. Hybrids between them are never found in the wild. Their caterpillars eat different host plants. When adults of different types are put together in the lab, they do not attempt to mate. Artificial insemination can produce viable and fertile hybrid offspring, but these offspring do not appear very healthy – they develop slowly and have a high mortality rate as caterpillars.

(a) Would you consider these butterflies separate species? Is there any additional evidence you need? *I would consider them species by just about any definition; they have separate gene pools and probably cannot share adaptations.*

(b) Can you say anything about likely modes of speciation? *There is strong pre-mating isolation and weaker post-mating isolation. This suggests species that arose in the presence of gene flow–parapatric, peripatric, or sympatric speciation. The different host plants make sympatric speciation, which is usually difficult, seem fairly likely here. By the way, if words like "peripatric" cause trouble you can use English phrases like "speciation of a tiny fringe population" instead.*

8. The Greek islands of Rhodos and Crete were connected to the mainland until about 5.3 million years ago, when the Mediterranean flooded. Since then they have been separated by salt water. Suppose that originally the area had one species of water frogs and one species of small songbirds. Water frogs cannot cross saltwater at all and were completely isolated after the flooding, whereas songbirds can occasionally fly from one island to another.

Today we observe that each island has its own species of frogs and of songbirds. In answering the following questions, you are not expected to use specific biological knowledge about birds and frogs; the essential difference is that birds can migrate and frogs, in this situation, cannot.

(a) Would we expect more pre-mating reproductive isolation in birds or in frogs? *In birds. Frogs don't have any selection for pre-mating isolation as they never meet each other.*

(b) Which mode or modes of speciation likely explain the bird species? If you don't remember the Latin names, paraphrase.

(c) Parapatric probably fits the best (speciation with some gene flow).

(d) A researcher proposes that the Rhodos water frog originated by peripatric (tiny isolated population) speciation. What would this predict about the genetic diversity of Rhodos frogs compared to mainland frogs? *If the Rhodos frogs came from a tiny isolated population, they should have low genetic diversity compared to the mainland because of lower population size.*

(e) We sample twenty protein-coding genes from the songbirds and draw a phylogenetic tree of each gene. To our surprise, the trees for different genes do not agree. About half the genes group Rhodos songbirds with Crete songbirds; the other half group Rhodos with the mainland. Give two different explanations for the discrepancies in these trees. Assume that we used an appropriate phylogeny method and that all of our trees have high bootstrap scores. *Rhodos songbirds could represent a hybrid population from the start. They could have become hybrid by later mixing. Or they could have maintained a large population and we could be seeing ancestral polymorphism, in which two different alleles were present in the ancestral species and have sorted out randomly in the descendants.*

9. The common ancestor of all modern human mtDNA appears to be about 200,000 years ago ("Mitochondrial Eve").

   (a) If we assume that this is about the expected value, roughly how long ago would we expect the common ancestor of a random nuclear locus to be? Don't forget that nuclear loci are diploid and are contributed by both parents, while mtDNA is haploid and only contributed by the mother. *About four times longer, or 800,000 years. One factor of two comes from diploidy and the other from inheritance through both males and females.*

   (b) Roughly how long ago would we expect the common ancestor of a Y chromosome gene to be? *The same as mtDNA, or 200,000 years.*

   (c) Give three (or more) reasons why the common ancestors of mitochondria and Y chromosomes might be at different time depths. *Statistical fluctuation (the coalescent has high random variability). Different effective population sizes in males and females due to either different survival or different reproductive success (Genghis Khan effect). Different migration rates in males and females. Natural selection on mitochondria or Y chromosomes.*

   (d) The common ancestor of the HLA locus HLA-DR is earlier than the human/chimpanzee split (6 to 8 million years ago). Why might this locus have a much older common ancestor than the average locus? (HLA genes are involved in immune system recognition of pathogens and cancer.) *Balancing selection. This gene probably has overdominant alleles (or alleles which are favored when rare–we can't be sure which) and therefore multiple alleles have been preserved throughout the history of both species, all the way back into the common ancestral population.*

10. In the bacterium *E. coli* and its relatives, housekeeping genes (genes which code for proteins involved in DNA replication, repair, transcription, translation, and basic metabolism) are seldom successfully transferred among species. Other genes (genes for exploiting a particular food source, resisting pathogens and toxins, antibiotic resistance, etc.) are frequently transferred among species, even nearly unrelated species.

    (a) If we draw a tree of a housekeeping gene, what kind of information will we be able to gain from it? *This probably carries information about the relationships between bacterial species, or at least the housekeeping parts of their genomes.*

    (b) If we draw a tree of an antibiotic resistance gene, what kind of information will we be able to gain from it? *This is more likely to give a history of gene transfer events, and may tend to clump together species which share a common set of environmental challenges, rather than ones whose genomes are overall closely related. For example, all hospital bacteria might cluster together.*

    (c) What would you expect from a tree made by mixing housekeeping and non-housekeeping genes? *Confusion! If you mix genes that come from different trees of descent, the resulting tree will be mixed up and impossible to interpret.*

11. We sample a specific smell-receptor gene from humans, mice, rats, and dogs. The length of the branch leading to humans is much greater than expected based on current theories of the relationship among primates, rodents and carnivores.

    (a) Why might this be? *The gene may be unused or even dysfunctional in humans, while it is still functional in the other species. Alternatively, it might be under rapid selection for a new function in humans, while it retains a conservative function in the other species. The first theory is more likely given that humans are known to have a poor sense of smell, but the second can't be ruled out.*

    (b) What traits would you look for in the DNA sequence in order to confirm or disconfirm your theory? *If the gene is a pseudogene in humans, it may have ω close to 1, and may also show damage such as stop codons, frameshifts, and very nonconservative changes. If it is being selected for a new function, it may have ω greater than 1, but will be free from blatant damage (unless the new function only requires the 5' end, which sometimes happens). In the other species where the gene is presumably functional, it will have ω less than 1.*

We could also do an HKA test using a non-selected sequence such as an intron as the control. If the polymorphism/divergence ratio in the human gene is similar to that of an intron, the gene is probably not important to humans.

A chimp or gorilla sequence would also be useful here, to see if this receptor is changing unexpectedly fast among other primates.

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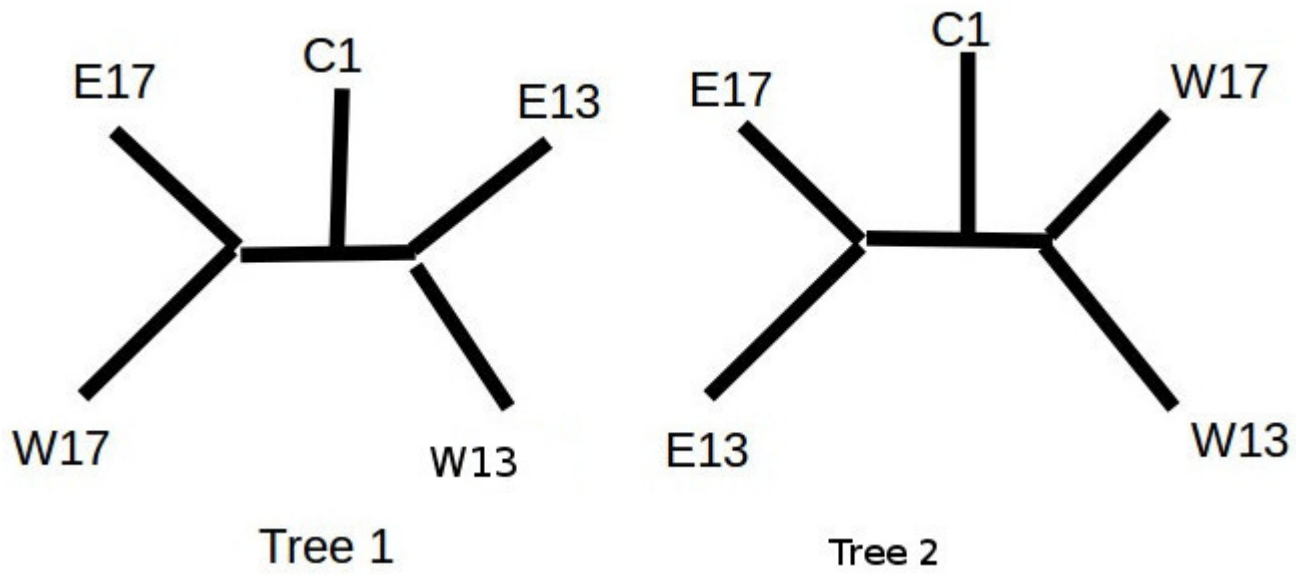
The remainder of these practice problems are the entire midterm from 2016. This should give an idea of the likely scope of a midterm.

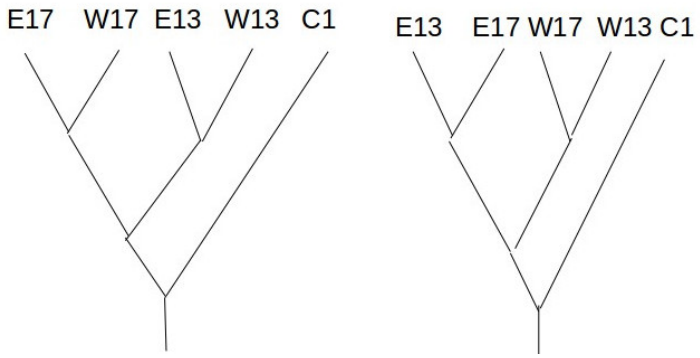
(The details of these problems are fictional, for exam purposes only; they don't represent real data. –Except for *P. esculentus*, which behaves just as described in the exam; I could never invent anything so weird.)

12. (23 pts) We search a country and find four species of periodic cicadas: eastern 17-year (E17), eastern 13-year (E13), western 17-year (W17), and western 13-year (W13). (The "year" designations tell how long the insect remains underground as a larva before emerging to mate and die.) We also find a species of one-year cicada (C1) which is clearly an outgroup to the periodic cicadas.

The following unrooted trees show two hypotheses about relationships between periodic cicadas. (There are other possibilities, but we will focus on these two.)



(a) (4 pts) Draw the two trees as rooted trees, using C1 as an outgroup. (Please draw them large!)



(b) (7 pts) We collect protein-coding sequences from the five species and find the following data (only variable sites are shown):

Position	1	2	3	4	5	6	7	8
E17	Val	Ser	His	Val	Arg	Glu	Gln	Trp
E13	Val	Lys	His	Val	His	Glu	Gln	Trp
W17	Val	Lys	Trp	Val	Arg	Ser	Gln	Trp
W13	Val	Lys	Trp	Ser	Arg	Ser	Val	Trp
C1	Ala	Lys	His	Val	Arg	Ser	Gln	Phe

Next to each of your trees on the previous page, write the parsimony score for these data on that tree. Circle the score of the tree that is preferred by parsimony. *Parsimony score is 10 for the left tree and 8 for the right, which is therefore the winner.*

Marking changes on the branches may be helpful for partial credit but is not required. NOTE: for your convenience, these data are reprinted on the tear-off sheet (last page of exam).

For the following two questions, make use of this additional information:

There is no geographic overlap between eastern and western cicadas due to a mountain range. In the east, however, E13 and E17 live in the same area, and in the west W13 and W17 live in the same area. C1 lives throughout the country.

The two 17-year species emerge in the same year; the two 13-year species also emerge in the same year (almost always a different year than the 17's).

When a cicada emerges in the wrong year it generally makes a mistake of 4 years. A 17-year cicada will thus occasionally emerge in 13 or 21 years. Genetic factors can influence how often a cicada makes a mistake, and whether it is early or late.

(c) (6 pts) If Tree 1 is correct, give a hypothesis for the origin of the four periodic cicada species. What speciation events probably happened, and in what order? *The periodic group arose first. Accumulation of errors caused it to split into 13- and 17-year forms, probably due to sympatric speciation based on separation in time. Subsequently, either the mountain range emerged or both 13- and 17-year cicadas crossed the mountains, and each speciated into an eastern and western form driven by the geographic barrier; this was probably allopatric given that they are still on the same schedule. (If they had gene flow, they'd probably have evolved to have different schedules to reduce it, assuming that hybrids are less fit.)*

(d) (6 pts) If Tree 2 is correct, give a hypothesis for the origin of the four periodic cicada species. What speciation events probably happened, and in what order?

The periodic group arose first. It was split by a mountain range into eastern and western species (probably allopatric speciation). Within each geographic area, time errors led to establishment of 13- and 17-year species by sympatric speciation.

I would have expected the first hypothesis to be true, as the second requires the 13 (or 17) year trait to evolve twice; but when real cicadas are studied the 13-year species is invariably related to the nearby 17-year species, suggesting that this is simply an event that can happen many times due to the insect's innate tendency to make 4 year mistakes.

13. (30 pts) The bacterium *Wolbachia* lives within insect cells, and is generally transmitted only from mother to offspring. In a certain gnat species, *Wolbachia* manipulates the sex ratio, causing 3/4 of offspring of an infected female to be female. This does not cause a reduction in total offspring produced.

(a) (6 pts) Suppose that gnat males are fully capable of fertilizing all females even when the males are only 1/4 of the population. Would there still be evolutionary pressure to return the sex ratio to 50/50? Explain briefly.

There would be pressure to return to 50/50 because in the 75/25 scenario, any individual who can get their genes into a male offspring will have more grandchildren. This will select for any trait that tends to produce male offspring. Yes, the species doesn't "need" more males, but for an individual it is most advantageous to produce a male offspring, so this will be selected for.

(b) (6 pts) Suppose that mutations in *Wolbachia* increase its ability to create female offspring, so that fewer and fewer males are produced. In response, infected female gnats might begin to produce fertile eggs by mitosis, creating offspring that are genetic copies of their mother. What long-term problem will this strategy cause for the gnats?

They will accumulate bad mutations (Muller's Ratchet). Their offspring will be less diverse. In the long term they may lose diploidy. If they need males to trigger egg development they will be reliant on foreign males who might let them down. They will not get the benefits of recombination.

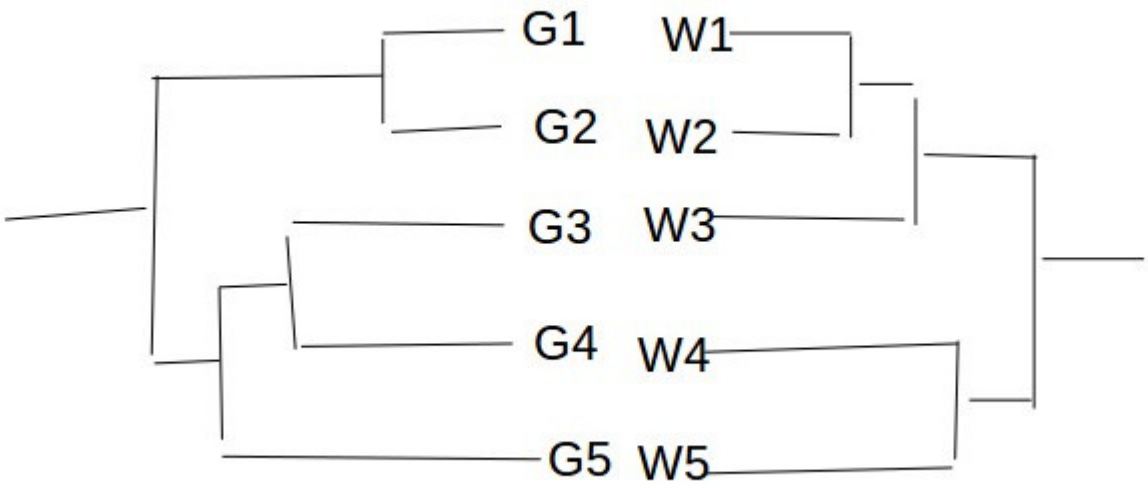
(c) (6 pts) Alternatively, infected gnats might become hermaphrodites that produce both eggs and sperm and self-fertilize. What long-term problem will this strategy cause for the gnats?

Homozygosity will increase, leading to loss of overdominant alleles and possible inbreeding depression. Offspring will be less diverse. While recombination will still occur, increasingly it will be between two identical copies, so it will not do much to produce new allele combinations. Note that self-fertilization does NOT lead to loss of diploidy; if one copy of a gene goes bad, this will pair up in the offspring and be eliminated. I took points off for this.

(d) (6 pts) No one has ever found a strain of *Wolbachia* that transforms insects into males. Why not?

It would self-destruct, since males can't transmit Wolbachia.

(e) (6 pts) A researcher wishes to know if gnat *Wolbachia* is ever able to infect a new host (as opposed to being inherited from the mother). She draws phylogenetic trees of gnat species and the *Wolbachia* that infect them, with the following results:



In these trees, G1 is gnat species 1, and W1 is the *Wolbachia* that infects it; similarly for G2, G3, etc. Do these data support the theory that gnat *Wolbachia* occasionally infects new hosts? Explain briefly. You may want to circle aspects of the trees that support your answer.

It does infect new hosts. In particular, while G3 is related to G4 and G5, it has been infected by a Wolbachia similar to that in G1 and G2. If there were no infections, the two trees should be identical.

14. (32 pts) The frog *Pelophylax esculentus* arose from an ancient hybridization of two species, which for simplicity I will call L and R. As far as we know, the original hybridization only happened once.

In preparation for meiosis, *P. esculentus* destroys its L genome and duplicates its R genome (in germ line cells). It then undergoes meiosis and mates with an L individual. The offspring therefore have one L genome and one R genome, and are *P. esculentus* again. This has been going on for thousands of years and has produced a widespread population of *P. esculentus*. An illustration:

	P. esculentus		"L"
somatic	RL		LL
germ line	RR	x	LL
		produces	
		RL	

(a) (4 pts) We catch several *P. esculentus* frogs and sequence their L and R genomes. Would we expect more linkage disequilibrium (non-random association of alleles along the chromosome) among the L genomes or the R genomes? Explain briefly. *The R genomes. While R can recombine, it is always recombining with an identical copy of itself, which is useless for reassorting alleles. Thus when a mutation arises in R it will be permanently associated*

with whatever alleles were already present on that copy of R. The L genomes come from the sexual L species and recombine normally, reducing disequilibrium.

This question gave students a lot of trouble, ranging from forgetting what linkage disequilibrium is, to forgetting where the L chromosome came from (always species L, which is a normal kind of frog and has recombination), to forgetting what effect recombination has on disequilibrium.

For the following three questions, please predict if the new mutation will **increase** due to natural selection, **decrease** due to natural selection, or **drift randomly,** and explain your answer briefly.

(b) (5 pts) A mutation arises in the L species which causes it to reject mating with *P. esculentus*. Assume that L x *P. esculentus* matings and L x L matings produce the same number of surviving offspring on average. What will happen to this mutation in the L population?

This will increase. Mating with P. esculentus is useless to an L individual as his/her genome will just be discarded; animals which don't do this are likely to have more successful matings and more grandchildren, so the allele will spread. Some students also argued that this mutation will tend to eliminate P. esculentus and reduce competition for habitat–whether this is true depends on the ecology of the species, but it is hard to select for a long-term effect like this.

(c) (5 pts) A **harmful recessive** mutation arises in the **R genome** of a *P. esculentus* individual. Assume that this mutation does not act in the germ line, and that it does not exist in the L species. What will happen to this mutation in the *P. esculentus* population? *It will drift randomly. It will only be homozygous briefly after the R genome duplicates in the germ line, and as it does not act in the germ line this should be harmless. Otherwise it permanently hides in the heterozygote.*

I gave some points for the argument that L might not have this gene at all, in which case the mutation will die out rapidly; but in fact L and R are rather similar (otherwise the hybrid would probably be unfit) and it's likely there is a corresponding gene in L. I did not give points for this answer unless accompanied by a solid explanation, however.

(d) (4 pts) A paracentric (non-centromere-containing) inversion arises in the **R genome** of a *P. esculentus* individual. Assume that the inversion itself does not change any genes. What will happen to this mutation in the *P. esculentus* population? *Drift randomly. Inversions are only harmful when recombination happens in a heterozygote, and by the time recombination happens in P. esculentus, it is always a homozygote (it just duplicated its R genome).*

(e) (4 pts) A paracentric (non-centromere-containing) inversion arises in the **L genome** of a *P. esculentus* individual. Assume that the inversion itself does not change any genes. What will happen to this mutation in the *P. esculentus* population? *This goes extinct instantly as the L genome is discarded.*

(f) (5 pts) Given your answers to the previous questions, what do you predict the R genome of *P. esculentus* will look like if this species lasts for a long time?

It should have a lot of inversions and recessive bad mutations, as there is no selection against them.

(g) (5 pts) Logically, crossing two *P. esculentus* should produce an R individual:

	P. esculentus		*P. esculentus*
somatic	RL		RL
germ line	RR	x	RR
		produces	
		RR	

P. esculentus prefer not to mate with each other, but when they do, the tadpoles (baby frogs) always die early in development. Based on your answers so far, what is a likely reason for the inviable tadpoles?

Apparently in a few thousand years the R genome of P. esculentus has already accumulated too many bad recessives, and pairing them up is lethal. (Some students argued that the inversions were responsible, but inversions prevent grandchildren, not children.)

15. (15 pts) Three children with the same father, but different mothers, all have abnormal brain development. When their genomes are sequenced, each child is found to have one normal copy of chromosome 3 and one abnormal copy which is missing several genes and has extra copies of several other genes.

The mothers are developmentally normal, and each has two normal copies of chromosome 3.

The father is developmentally normal, but unfortunately his genome is not available. The clinician who collected these data is very surprised that the three children appear to have inherited their problem from their **unaffected** father.

(a) (5 pts) If we could sequence the father's copies of chromosome 3, what do you predict we would find? Be as specific as possible, and be sure to account for both copies. You may draw a picture, but it is not required.

I expected the answer that he is heterozygous for a pericentric inversion on chromosome 3. I took off a few points for answers that didn't establish what kind of inversion, or thought he could be a homozygote.

I also had to give full points to answers that said his two copies of chromosome 3 have rearranged so that they still have all genes, but not equally distributed (a reciprocal translocation). This does not make it as obvious why the kids have both duplications AND deletions, but it does help explain why all three kids are affected. I had not thought of this answer but it does fit the facts.

(b) (5 pts) Does your explanation predict that future children of his will all be developmentally abnormal, or might some healthy children be produced? If so, how would they be produced? (Assume that any child with a deletion/duplication genotype will be abnormal.)

If it is a pericentric inversion, normal kids can be produced if there is no recombination in the inversion or if they inherit non-recombinant chromatids.

If it is a translocation, there's little hope as he is essentially homozygous: kids will only get one or the other chromosome and neither is normal.

(c) (5 pts) Is the father's genetic abnormality likely to be due to a recent event (for example, in him or one of his parents) or is it plausibly an ancient variant in the human population? Explain briefly. *It is almost surely recent as it clearly gives rise to unhealthy offspring and should be eliminated by selection. The pericentric inversion is known to be underdominant; the translocation would be even worse. Students noted that the most likely scenario for the translocation is that it happened in the father, as otherwise he'd have had to inherit an abnormal chromosome from each parent and they would likely not have been healthy themselves. The pericentric inversion could be a bit older but they are quickly selected out of the population.*

It's interesting to note that many inversions and translocations in humans have been identified by examining children with unexplained developmental disabilities – Dr. Evan Eichler in this deparment has several papers on this.