Two questions, not too hard either.

1. (13 points) You can work backwards from the formula for the equilibrium frequency of a deleterious allele and infer the mutation rate to it.

   (i) Imagine a deleterious recessive allele with selection coefficient $s$ and observed to be at gene frequency $q$. If this is the equilibrium gene frequency under this pattern of selection, derive the formula for the estimate of the mutation rate to this allele, explaining as you go.

   (ii) But now suppose that the allele actually has a fitness $1 - hs$ in the heterozygote as well, and that that is what affects its equilibrium frequency, and you just didn’t know that. Instead of the correct mutation rate, what mutation rate would you get? (Write it as an expression in the true mutation rate $u$ and the values of $h$ and $s$). Will that be higher or lower than the truth?

2. (12 points) Bacteria grow by doubling. Suppose that a bacterial population has its DNA have $n$ sites that are under selection and need to be maintained in their current state. If fitnesses at the different sites are multiplicative (the assumption I used in class), what is the largest mutation rate per site per generation (to other base states, all of which are deleterious) you can have and still have the most-fit class just barely be able to reproduce itself (i.e. just be able to have the average bacterium have one fully-fit descendant). *Hint* – you won’t need to compute mutational loads, just try to figure out the expected number of nonmutant, fully-fit descendants and ensure that it is 1. That number would be 2 if there were no mutation.

   What would this mutation rate be if $n = 5 \times 10^6$? (By the way, this argument is from a famous 1971 paper by Manfred Eigen and Peter Schuster – it’s the paper that introduced the hypercycles scheme for the Origin Of Life and the notion of a “quasispecies”).