Homework 5
due Wednesday February 8, 2017

Do these problems, and email the results (if you can, in a PDF or else in Word .DOC or .DOCX format. PDF is best as I cannot read some .docx files). Like all of the weekly homeworks this one totals 25 points and is due at the end of that day (at midnight).

1. (13 points) For a simple model of change in DNA, suppose that the mutation rate at a site from any one of the four bases is μ, and that these mutations are equally likely to change to any of the other three bases. So if the base is A, the probability that it changes to something that isn't A is μ. If it is, say T, the probability that it changes to something else is also μ.

   (i) In terms of μ, what is the probability that, in one generation, the base that we know starts out as T changes to an A? *(Be careful, and take into account the symmetry of the changes to the other three nucleotides).*

   (ii) If we lump the nucleotides into two groups, A and not-A (where not-A means "either C or G or T") If we start with an A, what is the probability of changing in one generation from A to not-A? If we start with one of the not-A bases, what is the probability of changing in one generation from that to A? *(Be careful!)*

   (iii) Considering that as a two-allele locus, what is the expected mutational equilibrium of these two alleles? Does this make intuitive sense to you? Why or why not?

   (iv) If the site starts with its base being A and after some number of generations it is not-A, what fraction of that time do you expect the base to turn out to be G?

   (v) How many generations does it take to go halfway to the equilibrium frequencies? (Use the exact formula, not the one which uses the approximation involving $e^{-(u+v)}$. You can solve for this by taking logarithms.)

   (vi) If $\mu = 10^{-8}$, how many generations is this? Make sure to take enough decimal places in your computation.

2. (12 points) It is often argued that by curing genetic diseases, we are allowing disease alleles to continue to exist in the population, and that the frequency of those diseases will then increase. Let's try to work out how fast that process will be. Imagine a locus with two alleles, A and a, where the fitnesses are multiplicative so that they are

$$\begin{array}{ccc} AA & Aa & aa \\ \hline 1 & 1-s & (1-s)^2 \end{array}$$

   (i) If we have mutation from A to a at rate u, but no back mutation, what will be the equilibrium frequency of allele a?

   (ii) If the mutation continues but the disease is cured, so that all genotypes now have fitness 1, what will be the gene frequency in the next generation? In the generation after that? *(Be careful to take into account what fraction of the population has the A allele).*

   (iii) If we have the values $u = 10^{-6}$ and $s = 0.05$, what will the equilibrium gene frequency be, and what will be the gene frequencies of a in the two generations following the cure?

   (iv) (No points, I am just curious about people's opinions) Given that a generation in humans is about 27 years, is this an alarming rate of increase? Why or why not?