

## Problem Set 11

1. In class, we looked at sequence variation for the cytochrome B gene in different human populations.
  - a. Of the total number of variable sites, changes at which codon position contributed to most of the sequence variation in the data? (1 pt)
  - b. Explain why this result is expected under the neutral theory of molecular evolution (3 pts)
  
2. Why is the rate of fixation of neutral mutations ( $\mu$ ) independent of population size? (4 pts)
  
3. If most mutations are deleterious (i.e. alleles of negative effect) and have a low probability of fixation, you would expect positive alleles to have a high probability of fixation given the fitness advantage that they engender to the individual carrying the allele.
  - a. Why is the rate of fixation for positive alleles so low according to the neutral theory? (3 pts)
  - b. Which evolutionary process governs the rate of fixation for alleles with positive or negative effects? For neutral alleles? (2 pts)
  
4. Compare the % sequence divergence observed in two genes in a pair of salamander species. The histone protein requires a precise structure to function properly, while the structure of the zinc finger gene depends on only a few key amino acids. You can assume that most of the observed variation in these genes has no effect on fitness.
  - a. Fill in the blanks below with  $>$ ,  $<$  or  $=$  to indicate the relative divergence expected in these comparison. (3 pts)
 

3 <sup>rd</sup> codon positions in the histone gene	_____	1 <sup>st</sup> codon positions in histone gene
3 <sup>rd</sup> codon positions in the histone gene	_____	3 <sup>rd</sup> codon positions in the zinc finger gene
1 <sup>st</sup> codon positions in the histone	_____	1 <sup>st</sup> codon positions in the zinc finger gene
  - b. Explain the reasoning that you used in filling in the blanks above. (3 pts)
  - c. Suppose that you discover a gene in which most mutations that change the protein sequence increase fitness. How would you expect the rate of divergence at 1<sup>st</sup> codon positions in the gene under positive selection compare to the rate of divergence at 1<sup>st</sup> codon positions in the histone and zinc finger genes? Why? (3 pts)
  - d. How would you expect the rate of divergence at 1<sup>st</sup> codon positions to compare to the rate of divergence at 3<sup>rd</sup> codon positions in the gene under positive selection? Why? (3 pts)
  
5. Suppose that the neutral mutation rate is measured to be  $3 \times 10^{-9}$  in a gene encoding a milk protein and as  $1 \times 10^{-9}$  in a gene encoding a DNA binding protein.
  - a. Give two biological explanations for why the neutral mutation rate could be higher in the milk gene. (4 pts)
  - b. How could you distinguish between these two explanations? (4 pts)
  
6. Molecular clock estimates (calibrated using the bird-mammal divergence) for the age of major groups of placental mammals suggests that these groups radiated more than 100 million years ago. This conflicts with the fossil evidence that major lineages of mammals diverged from each other after the non-avian dinosaurs went extinct 65 million years ago.
  - a. Assuming that the molecular clock dates are correct, describe two ways you could explain the gap in the fossil record. (4 pts)
  - b. Assuming that the current understanding of the fossil record is correct, give a specific explanation of what could have changed at the molecular level to cause the inflated estimates of divergence times. (4 pts)

