1. A population of 100 diploid individuals contains 100 A alleles and 100 a alleles. If there is no mutation and the three genotypes are selectively equivalent (neutral), what would you expect the genotype frequencies to be 10,000 generations in the future?

   The overwhelming probability is that the population will be fixed for either A or a. This can be seen by calculating the expected heterozygosity at t = 10,000 (equivalently, the probability of heterozygosity).

2. What is the heterozygosity (H) in each of the following populations?

	Genotype Frequency		
Pop'n	AA	Aa	aa
1	25	50	25
2	50	0	50
3	0	50	50
4	0	0	100

   1. H= 2pq = 0.5
   2. 0.5
   3. 0.375
   4. 0

3. If the neutral rate is 10^{-8} at a locus, what is the rate of neutral evolution at that locus if the population size is a)100, b) 1000.

   The neutral rate of evolution is independent of population size and equal to the neutral mutation rate.

4. Why is the neutral theory confined to molecular evolution, rather than being applied to all evolution?

   Because many changes at the molecular sequence level are expected to have little or no effect on the phenotype, the focus of natural selection.

5. What facts about molecular evolution led to the proposal of the neutral theory of molecular evolution?

   Constancy of rate of molecular sequence evolution, as opposed the non-constancy of morphological (phenotypic) evolution.

   The fact the molecular sequences can undergo changes with little or no expected effects on phenotype.

6. What facts about molecular evolution led to the proposal of the nearly neutral theory of molecular evolution?

   The molecular clock ticks per year, not per generation for amino acid sequences.

   Also, genetic variation (a measured by H) is too low in species with large N. (This is explained by neutral theory as the result of more effective purifying selection in large populations preventing the fixation of slightly deleterious mutations).

7. Explain the relationship between the degree of functional constraint on a molecule (or a region of a molecule) and its rate of evolution according to the neutral theory.

   More constrained sites have lower rates of neutral mutation. Therefore the rate of evolution by neutral substitution is also lower.

   In particular, silent sites are expected to be less constrained than non-silent sites, because changes at silent sites may have little or no effect on phenotype, whereas changes at non-silent sites may often have effects on phenotype.

8. Do synonymous sites show pan-neutral evolution (in the sense that all mutations are neutral) [see pp 260-262 in your text]? Why does this not invalidate the argument that synonymous sites evolve according to the neutral theory?

   No.

   Because the expectation is that less constrained sites will shower higher rates of evolution under neutral theory. The fact that synonymous sites are not completely unconstrained does not alter the prediction.

9. Three genes have dN/dS ratios of a) 0.2, b) 1, c) 10. What inferences can we make about the evolution of these genes?

   a. Purifying selection against non-synonmous substitutions is indicated. This is the common observation for most genes.

   b. This observation suggests equal substitution rates at both synonyomous and non-synonymous sites. For a gene which is under selection to maintain a specific function, this is an unlikely observation. Usually, this observation results from calculating dN/dS for a sequence where some sites are under postive selection and most sites are under purifying selection, resulting in an intermediate value.

   c. Positive selection is driving non-synonymous substitutions over the rate expected under neutrality.