Throughout this worksheet, assume that the population is HUGE, so even a very small difference in fitness will matter. Also assume that newly introduced alleles will not be immediately lost to drift. Finally, please write your answers on a separate sheet, not this one.

In West African populations, Cavalli-Sforza and Bodmer (1971) estimated relative fitness of different genotypes at the hemoglobin locus. (Example taken from Hartl and Clark textbook.) Hemoglobin S appears to protect against malaria in the heterozygote but causes sickle-cell anemia in the homozygote.

For the first two problems, consider only the two alleles A (normal) and S (sickle-cell trait). Expected counts were based on the allele frequencies in these populations.

Genotype	AA	AS	SS	Total
Observed count	25,374	5,482	67	30923
Expected count	25,607	5,065	251	30923

1. If we assign a fitness of 1.0 to AS, what are the relative fitnesses of AA and SS based on these data? (Hint: Do this in two steps. First find out, for each genotype, the ratio of individuals observed to individuals expected. Then normalize to give AS a value of 1, adjusting the others proportionately.)
2. What are the allele frequencies observed in these data?
3. What are the expected allele frequencies at the overdominant equilibrium? Do these seem to match the data? (You do not need to do a statistical test.)
4. Suppose that only A existed in a large population. If you introduced a few copies of S, what would be the expected outcome? Give a numeric estimate of the allele frequencies after a long time.
5. Suppose that A and S existed, at their equilibrium, in a large population. Suddenly, a medical breakthrough eliminated malaria, removing all disadvantage to the AA homozygote, but leaving the disadvantage of the SS homozygote. What would be the expected outcome after a long time?

   In the actual data, Cavalli-Sforza and Bodmer also observed a third, rarer allele, C. Here is their full table.

Genotype	AA	AS	SS	AC	SC	CC	Total
Observed count	25,374	5,482	67	1737	130	108	32,898
Expected count	25,615	4,967	307	1769	165	75	32,898

6. What are the relative fitnesses, assigning a fitness of 1.0 to AS? BE SURE to do at least four digits after the decimal or you will lose some important distinctions.

   In the following questions, you do not need to calculate equilibrium frequencies (they are quite tricky with three alleles). Just indicate the general direction things will go. Will the new allele tend to increase or decrease? Hint: when an allele is very rare, it exists almost solely in heterozygotes, and its future can be predicted by the fitness of the heterozygotes. The homozygous fitness of a very rare allele hardly matters.

7. Suppose that only A existed in a large population. If you introduced a few copies of C, what would be the expected outcome?
8. Suppose that only C existed in a large population. If you introduced a few copies of A, what would be the expected outcome?
9. Suppose that A and S existed, at their equilibrium, in a large population. If you introduced a few copies of C, what would be the expected outcome? (Hint: what is the mean fitness of the equilibrium population before C appears, and how does it compare to the mean fitness of individuals with the new C allele?)
10. Describe a situation in which, even in a large well-mixed population, natural selection will not produce the best possible outcome.