

Please show your work as this will make it easier to give partial credit.

The enzyme alcohol dehydrogenase (ADH) is used by fruit flies (and people) to detoxify alcohol. Without it, alcohol can cause fatal poisoning. Call the wild-type, working version of the gene $ADH+$ and a broken, non-working copy $ADH-$.

1. Suppose that we raise fruit flies on carefully sterilized food so that they do not encounter any alcohol, and the ADH enzyme is not needed.

- (a) (2 pts) If the mutation rate from working $ADH+$ to broken $ADH-$ is 10^{-7} and from $ADH-$ back to $ADH+$ is 10^{-9} , what will be the long-term equilibrium frequency of $ADH+$? (Ignore the possibility of multiple mutations in the same copy.)

$$pA = \nu / (\nu + \mu) = 0.0099$$

- (b) (1 pt) Will this happen quickly? Why or why not?

Very slowly, as the change per generation is on the order of 10^{-7} . Mutation is a weak force when the rates are this low.

2. We have managed to breed a population of lab flies which have allele frequencies as follows:

$ADH+$ 0.7
 $ADH-$ 0.3

- (a) (2 pts) What will the genotype frequencies be in our population, assuming it is in Hardy-Weinberg equilibrium?

$$p(AA) = 0.7^2 = 0.49$$

$$p(Aa) = 0.7 * 0.3 * 2 = 0.42$$

$$p(aa) = 0.3^2 = 0.09$$

- (b) (2 pts) We now release the flies into the cafeteria, where their main food source is alcohol-rich spoiled fruit. Their fitnesses are as follows:

Genotype	+/+	+/-	-/-
Fitness	1.0	1.0	0.4
H-W	0.49	0.42	0.09
After deaths	0.49	0.42	0.036
Over new total	0.518	0.444	0.038

After one generation, what genotype frequencies do we expect in adult flies? (Assume that flies which die of alcohol poisoning do so before adulthood.) *See table above.*

- (c) (1 pt) What allele frequencies will be present in adults of this new generation? $p(A) = 0.74$, $p(a) = 0.26$
- (d) (3 pts) If we sample 1000 adult flies and they conform exactly to the post-selection genotype frequencies and allele frequencies you computed in the previous two subquestions, will they be significantly different from H-W at the 5% level? (Round fractional flies so as to keep the total at 1000.) Please show your χ^2 table, and use the post-selection allele frequencies to calculate expectations, not the allele frequencies from the original release population.

Allele frequencies are 0.74 and 0.26. Hardy-Weinberg:

Genotype	"Observed"	Expected	χ^2
+/+	518	547.6	1.6
+/-	444	384.8	9.1
-/-	38	67.6	13.0
total	1000	1000	23.7

This has 1 df (since we used the data twice, once to get totals and once to get allele frequencies) and is clearly significant. The selection has pushed the population off of H-W. (Please state your df when doing a problem of this kind.)

If we had assumed the allele frequencies of the original population we would have 2 df; the result of that test is also significant. The flies are not in H-W for either their parents' allele frequencies or their own, due to the selection.

- (e) (2 pts) What is the expected long-term fate of $ADH-$ in the cafeteria environment? (Assume the population is very large.) *Eventually it will reach mutation/selection equilibrium. As it is recessive, this will be at $\sqrt{\frac{\mu}{s}} = \sqrt{\frac{10^{-7}}{0.6}} = 0.0004$. I accepted any answers that talked about slow decline, but it is possible to be much more specific here.*
3. A new mutation of ADH , which we will call ADH^* , arises in our cafeteria. It is dominant, and flies with at least one copy benefit from a super-active ADH protein which gives them a 10% advantage (in the cafeteria environment) over wild-type $ADH + /ADH +$.

- (a) (2 pts) Write out fitnesses for each genotype found in a population with all three alleles present. Set the fitness of the most fit genotype to 1.0. *I started with the fitnesses given above, added the new allele, and renormalized to the new best genotype.*

Genotype	Raw fitness	Normalized fitness
$+/+$	1.0	0.909
$+/-$	1.0	0.909
$-/-$	0.4	0.364
$*/*$	1.1	1.0
$*/+$	1.1	1.0
$*/-$	1.1	1.0

Many people got the wrong fitnesses. One mistake is to assume that a fitness of 1.0 is 10% better than a fitness of 0.9, but it isn't (it's about 11% better). Another mistake is to subtract 0.1 from everyone's fitness, giving $-/-$ a fitness of 0.3, but this is incorrect. (Imagine if a new fly were twice as fit as before—that doesn't mean all other flies have a fitness of 0.) Instead, you should divide all fitnesses by the new maximum fitness (in this case 1.1). This preserves the ratios. I graded subsequent parts using whatever fitnesses were given here.

- (b) (3 pts) If the pre-selection frequencies of the three alleles are as shown below, what will the post-selection frequencies be?

$ADH+$ 0.9
 $ADH-$ 0.09
 ADH^* 0.01

Genotype	$+/+$	$+/-$	$-/-$	$*/*$	$*/+$	$*/-$
Fitness	0.909	0.909	0.364	1.0	1.0	1.0
$H-W$	0.8100	0.1620	0.0081	0.0001	0.0180	0.0018
After deaths	0.7363	0.1473	0.0029	0.0001	0.0180	0.0018 (total 0.9064)
Over new total	0.8123	0.1625	0.0031	0.00011	0.0199	0.0020

$$ADH+ = 0.8123 + (0.5)(0.1625) + (0.5)(0.0199) = 0.9035$$

$$ADH- = 0.0031 + (0.5)(0.1625) + (0.5)(0.0020) = 0.0854$$

$$ADH^* = 0.00011 + (0.5)(0.0199) + (0.5)(0.0020) = 0.01106$$

- (c) (2 pts) Will ADH^* zoom straight to fixation (allele frequency of 1.0) or will it slow down eventually? Explain briefly. *It will slow down when the other two alleles have become very rare, as then they are rare recessives and hide from selection.*