Exercises: Mutation

Phenylthiocarbamide (PTC) is a chemical component involved in bitter taste. The human bitter taste receptor for PTC is coded by a single gene with two alleles. Consider an evolving population where the individuals who carry allele A have the taste receptor that allows them to detect bitterness, while B carriers do not.

(i) Let us first assume that this ability to taste bitterness does not have any impact on fitness, which is therefore the same regardless of the allele an individual carries. Assuming that during reproduction, allele A mutates to allele B with probability 0.01 and that the reverse event occurs with probability 0.02, *what is the frequency of allele* B *at an evolutionary equilibrium*?

In reality, the ability to taste bitter has evolved in multiple mammalian lineages, most likely by providing an evolutionary advantage in the natural environment of these lineages. Indeed, bitterness perception is associated with disgust and avoidance behaviours of natural toxins (mainly poisonous plants). Hence, the ability to taste bitter can not only be subject to mutation, but also selection.

(ii) Let us now assume that A individuals (who express the PTC receptor) have fitness 1, while B individuals (who do not express the PTC receptor) have fitness 0.99. Hence, there is frequency and density independent selection for the ability to taste bitter.

(1) Write down the equation for allele frequency change of the A *allele over one demographic time period due to selection and mutation. Recall that the overall change of allele frequency is the sum of change in allele frequency due to selection and mutation, i.e.* $\Delta p = \Delta p_{\mathrm{s}} + \Delta p_{\mu}$.

(2) Calculate Δp_{s} *and* Δp_{μ} *for* $p = 0.4$*, then* $p = 0.8$*. Are they of same or opposite sign? Compare the magnitude of the two evolutionary forces in each case.*

(3) Estimate the frequency of allele A *at equilibrium from figure 1 (see dashed line for bidirectional mutation). What do you think happens to the magnitudes of the two evolutionary forces (selection and mutation)? Explain in terms of the two evolutionary forces, why this equilibrium is unstable or stable.*

(iii) Let us further assume for simplification that mutation is unidirectional: the mutation rate from A to B is still 0.01, but now the mutation rate to the reverse direction is zero.

(1) Evaluate the frequency of allele A *at equilibrium when mutation is unidirectional. Is your result consistent with figure 1 (see solid line for unidirectional mutation)? Compare with the graphically estimated equilibrium for bi-directional mutation.*

(2) Explain in terms of the two evolutionary forces, why this equilibrium is unstable or stable.

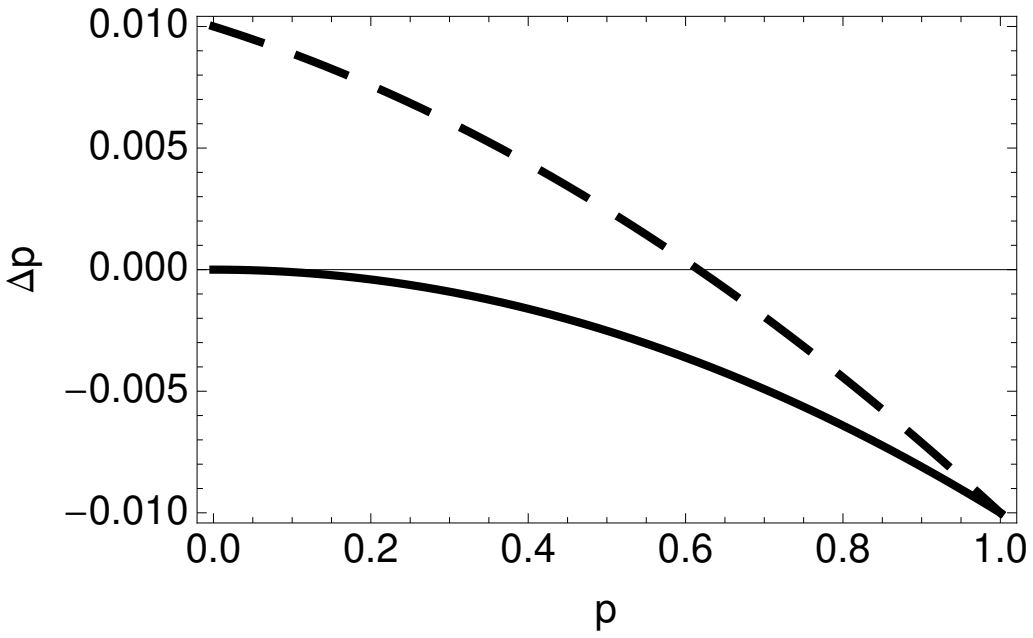

Fig. 1: Change in allele frequency as a function of allele frequency p, when mutation is in both directions ($\mu_A = 0.01$, $\mu_B = 0.02$, like in Exercise (ii)), A $\rightleftharpoons$ B (dashed line); or mutation is only in one direction ($\mu_A = 0.01$, $\mu_B = 0$, like in Exercise (iii)), A $\rightarrow$ B (solid line).

We have seen that the A allele has a selective advantage in the natural environment since it allows its carriers to detect bitterness and thus avoid potentially toxic plants. B carriers therefore have a comparatively smaller fitness due to higher risk of intoxication. What happens however in a modern environment, where technology can curtail this risk? Think for instance of how most of our food comes from well identified crops so that we need not worry about the edibility of the plants we eat. In such an environment, the fitness of individuals carrying B can be increased to match the fitness of individuals carrying A.

(iv) We assume that with probability k, an individual with allele B has the same fitness as a A carrier, and that with probability $1-k$, an individual with allele B has a "natural" fitness, here set to 0.8 (for example, if the B carrier gathers wild berries and is not able to recognize toxic ones from their bitter taste). In reality, mutation rate of human genes is much lower than the one we used earlier, so let us also decrease the mutation rate from A to B to 0.0001 (keeping the reverse rate of mutations to zero).

(1) Calculate the selection coefficient on A *in the natural environment and in the modern environment as a function of* k*.*

(2) Calculate the frequency of A *at a mutation-selection equilibrium as a function of* k*. Using this, determine the equilibrium frequency of* A*:*

(a) in the natural environment (i.e., with $k = 0$*).*

(b) in the modern environment, when the probability for a B *carrier to benefit from medicine is* $k = 0.999$*. For instance, when 99.9% of individuals that cannot taste bitter only get verified foods from the supermarket.*

(3) Calculate the genetic load of the modern population at equilibrium (question (iv.2.b)*), if individuals were put back in the natural environment (for instance if technology fails).*

Note that in native americans, about 2 percent of individuals are not able to taste bitter, while in Western societies, it is about 30 percent of the population that does not taste bitter Other examples of deleterious mutations that may have increased in modern human populations thanks to advances in science, medicine and technology include myopia, sickle-cell disease, diabetes type I, etc.

(v) Using your genetic load calculation (question (iv.3)), *reflect on the impact of technology on the evolution of human biology.*

(vi) Do you have the allele that codes for the PTC receptor? Ask one of the assistants to do the test!