1 Dynamics of a recessive allele

We consider the dynamics of a diploid population of \(N\) individuals, i.e. \(2N\) alleles with two types: \(A_1\) and \(A_2\), with \(A_2\) corresponding to a genetic disease. At each generation, individuals are generated by independently drawing each one of the two alleles at random from random individuals. We note \(x\) the fraction of allele \(A_2\) in the total pool of alleles, and \(p_{\nu\mu}\) the fraction of \(A_\nu A_\mu\) individuals, with \((\nu, \mu) \in \{1, 2\}^2\).

a. Assuming no allele presents any advantage, write down the Hardy-Weinberg prediction for steady-state in terms of \(x\) and the \(p_{\nu\mu}\).

We now assume that having allele \(A_2\) reduces the chances of individuals to reproduce regardless of the other allele. The probability of picking an \(A_1A_2\) individual for reproduction is reduced by a factor \(\omega_1\). Similarly, the probability of choosing an \(A_2A_2\) individual for reproduction is reduced by a factor \(\omega_2\).

b. Write down the expressions for \(p_{11}\), \(p_{12}\) and \(p_{22}\) (their sum should be unity by normalization) at generation \(n + 1\) as function of the \(p_{\nu\mu}\) at generation \(n\).

c. What are the two steady-states of this system of equations?

d. Show that the homozygous state \(p_{22} = 1\) is linearly unstable, e.g. if \(p_{22} = 1 - \varepsilon\) and \(p_{12} = \varepsilon\) (with \(\varepsilon \ll 1\)) then \(\varepsilon\) grows over the generations. What do you expect if you initially take \(p_{22} = 1 - \varepsilon\) and \(p_{11} = \varepsilon\)?

e. Show that the homozygous state \(p_{11} = 1\) is linearly stable. This points to the fact that in the limit \(N \to \infty\) the allele \(A_2\) will disappear. Is that true if \(N\) is finite?

f. Reach the previous conclusion by assuming Hardy-Weinberg and using (b.) to write down the expression for \(x'\) (the fraction \(x\) at the generation \(n + 1\)) as a function of \(x\) at the generation \(n\). Show that \(x' \geq x\). Write down the expression for the rate of decrease of the \(A_2\) allele.
g. We now assume that only bi-allelic $A_2A_2$ individuals suffer a reproductive $\omega^2$ penalty. Does the property (f.) still hold? Make the proof general by removing the assumption Hardy-Weinberg and still showing that $x' \geq x$. Discuss the stability of the $p_{11} = 1$ state.

h*. We now assume that bi-allelic individuals suffer a reproductive penalty $\alpha$ but that the mono-allelic version of the mutation $A_1A_2$ have a reproductive advantage, i.e. the probability to be picked for reproduction increases by a factor $\beta$. Show that the steady-state distribution of alleles is the solution of two coupled equations of degree 3 (you do not necessarily have to compute the solution). Intuitively, how is this solution going to differ from Hardy-Weinberg? Can you think of a famous disease with similar dynamics?