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?