Stochastic population genetics: homework 1

To be returned on April 9, 2019

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 ω^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 $p_{\mu\nu}$ 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 ε 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 $x' \geqslant x$. 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 ω^2 penalty. Does the property (f.) still hold? Make the proof general by removing the assumption Hardy-Weinberg and still showing that $x' \geqslant x$. Discuss the stability of the $p_{11} = 1$ state.

h*. We now assume that bi-allelic individuals suffer a reproductive penalty α 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 β. 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?