Introductory seminar on "Mathematical Population Genetics" winter term 2017/18

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6 Branching processes and absorption times

6.1 Alfred Lotka's (1931) population model

Alfred Lotka assumed a zero-modified geometric distribution to fit the offspring distribution of the 1920s American male population, where the probability to have $k > 0$ sons is given as $p_k = ab^{(k-1)}$ and $p_0 = 1 - \sum_k^\infty p_k$ with $0 < b < a + b < 1$.

a) Derive the mean number of sons of each male in his lifetime. If family names are inherited only via sons and the offspring distribution remains stable, derive the probability that the name will never die out, depending on the parameters a and b.

b) Lotka found that a good fit to the data is given by the values $a = \frac{1}{5}$ and $b = \frac{3}{5}$. What is the probability that a family name that goes back to 5 young male immigrants will survive in the long term?

6.2 Evolution of Antibiotics Resistance

Consider a population of bacteria, which grows in the presence of an antibiotic. In the beginning, we have N wild type bacteria, which are not resistant to the antibiotic. These have a birth rate b (a mother cell splits into two daughter cells) and a death rate $d > b$. Furthermore, wild type bacteria acquire a mutation that confers resistance to the antibiotic at rate m.

A resistant type has the same birth rate b, but a reduced death rate $d' < b$. We ignore mutations of the resistant type.

- Calculate the establishment probability of the bacterial population, which is the probability that the antibiotic fails.
- Assume the antibiotic sensitive strain dies at the 100-fold rate as it reproduces, whereas the resistant strain dies 100-fold less than the reproduction rate. Further assume that wild type bacteria acquire resistance at a rate of 10^{-6} and assume a starting population of 10^8 wild type cells. Calculate the probability that the bacterial population evades antibiotic treatment and a resistant strain establishes.

6.3 Mean Absorption Time

In the lecture we have obtained the ODE for mean fixation time in expression (9.38)

$$-1 = M(x_0)\frac{\partial \bar{t}(x_0)}{\partial x_0} + \frac{D(x_0)}{2}\frac{\partial^2 \bar{t}(x_0)}{\partial x_0^2}$$

with boundary conditions $\bar{t}(0) = \bar{t}(1) = 0$.

Prove that equation (9.39)

$$\bar{t}(x_0) = \int_0^1 \bar{t}(x|x_0)dx$$

together with expressions (9.40)

$$\bar{t}(x|x_0) = \bar{t}_<(x|x_0) = \frac{2P_0(x_0)\int_0^x \exp[-2\int^y \frac{M(z)}{D(z)}dz]dy}{D(x)\exp[-2\int^x \frac{M(z)}{D(z)}dz]}, \quad 0 \le x \le x_0$$

and (9.41)

$$\bar{t}(x|x_0) = \bar{t}_>(x|x_0) = \frac{2P_1(x_0)\int_x^1 \exp[-2\int^y \frac{M(z)}{D(z)}dz]dy}{D(x)\exp[-2\int^x \frac{M(z)}{D(z)}dz]}, \quad x_0 \le x \le 1$$

where $P_1(x_0) = 1 - P_0(x_0)$ is the fixation probability as given in (9.32, subsection Fixation probability), is a solution of this ODE.

6.4 Conditional Absorption Time

In population genetics, we are frequently interested in the absorption time of only those mutations that eventually reach fixation in $x = 1$. Let $\bar{t}_1(x_0)$ be the average time for such a mutation to reach $x = 1$ if it is initially in the population at frequency x_0. Similarly to the unconditioned fixation time $\bar{t}(x_0)$, one can also derive $\bar{t}_1(x_0)$ from the backward equation (see lecture notes). The solution is

$$\bar{t}_1(x_0) = \int_0^1 \bar{t}_1(x|x_0)dx$$

where

$$\bar{t}_1(x|x_0) = \frac{P_1(x)}{P_1(x_0)}\bar{t}(x|x_0)$$

is the "sojourn time density" (the density of the time spent at frequency x before fixation in $x = 1$). The probability of fixation $P_1(x_0)$ and the sojourn time density $\bar{t}(x|x_0)$ are as given above in Exercise 6.3, as well as in the lecture notes.

1. Consider first a neutral mutation and derive an explicit expression for the sojourn time density and the conditional fixation time. In particular, derive the fixation time for a single neutral mutant $\bar{t}_1(1/2N)$.

2. Consider now the case with selection, but without dominance ($h = 1/2$). Compare the conditional fixation times of a new beneficial allele with selection strength α, of a new deleterious allele with selection strength $-\alpha$ and a new neutral allele ($\alpha = 0$). Give an interpretation of the result.

3. Consider now a population without mutations initially. Assume that new mutations occur at some rate $2Nu = 0.5$. We assume that each mutation occurs at a new locus (infinite sites model) and that mutations at different loci never interfere. How long, on average, do we need to wait until a mutation reaches fixation if the mutants are all

   - neutral,
   - beneficial with $\alpha = 10$ and $h = 1/2$,
   - deleterious with $\alpha = -10$ and $h = 1/2$.

   You can ignore variance in the fixation time $\bar{t}_1$.