

Assignment 5**due: January 20****Changes in birth and death rates and evolutionary rescue (4 P.)**

Imagine a population of haploid individuals where the wildtype has birth rate $\lambda_a < \mu_a$ such that the population size declines. A rescue mutant with $\lambda_A > \mu_A$ can have an increased birth rate or a reduced death rate (or both might be different from the wildtype traits). Explore how this influences the probability of evolutionary rescue by *de novo* mutations. Is the probability of rescue higher if the mutation increases the birth rate or if it decreases the death rate or is it equal in both cases?

Rescue from pre-existing mutants (4 P.)

A population gets exposed to a very harsh change in its environment that immediately kills all wild-type individuals. Mutants that can rescue the population may pre-exist in the population. In the new environment, mutant individuals have a Poisson distributed number of offspring with mean $1 + s$. Denote by $\{p_k\}$, $k = 0, 1, 2, \dots$ the probability distribution for the number of mutants prior to the environmental change, i.e. p_k is the probability that there are k mutants in the population when the environment changes.

- Give the formula for the probability of evolutionary rescue under these circumstances.
- Now set $p_0 = 0.2$, $p_1 = 0.3$, $p_{100} = 0.5$, and $s = 0.01$. What is the probability of evolutionary rescue?

The evolution of antibiotic resistance (4 P.)

Consider a bacterial population of N_0 sensitive bacteria that is treated with antibiotics. The antibiotic concentration is denoted by c . The per-cell death rate is μ . The per-cell birth rate is $\lambda_s(c) = \mu + S_s(c)$ with

$$S_s(c) = S_{\max}^s - \frac{(S_{\max}^s - S_{\min}) \left(\frac{c}{c_{\text{MIC}}^s}\right)^\kappa}{\left(\frac{c}{c_{\text{MIC}}^s}\right)^\kappa - \frac{S_{\max}^s}{S_{\min}}}$$

(It holds that $S_{\max} > 0$ and $S_{\min} < 0$.)

- What is the minimal concentration required to cause a population decline?

Through mutation, resistant bacteria may appear. The mutation probability at cell division is u . Assume that resistant bacteria have the same death rate as sensitive bacteria. But their birth rate is different and given by $\lambda_r(c) = \mu + S_r(c)$ with

$$S_r(c) = S_{\max}^r - \frac{(S_{\max}^r - S_{\min}) \left(\frac{c}{c_{\text{MIC}}^r}\right)^\kappa}{\left(\frac{c}{c_{\text{MIC}}^r}\right)^\kappa - \frac{S_{\max}^r}{S_{\min}}}$$

- Determine the probability of resistance evolution (= evolutionary rescue).

Now use the following parameter values: $S_{\max}^s = 0.5$, $S_{\max}^r = 0.49$, $S_{\min} = -0.2$, $\kappa = 2$, $c_{\text{MIC}}^s = 5$, $c_{\text{MIC}}^r = 20$, $\mu = 1.0$, $N_0 = 10^9$, $u = 10^{-9}$.

- What is the probability of resistance evolution for $c = 5.5$, $c = 10$, $c = 25$?

In this scenario, the probability of resistance evolution decreases with the antibiotic dose c .

- Give one reason why this might not always be true.