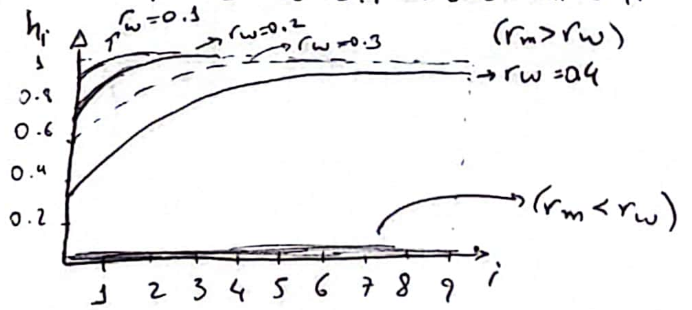
MATH 112B - HW6 (Raphael F. Levy - U1015 6477)

① Suppose a cell colony is described by the (const. pop.) Moran process. Suppose that if r_w is the division rate of the wild type cells and r_m is the division rate of mutants. Then the prob. of mutant fixation (mutants taking over) starting from i mutant cells out of n cells is given by:

$$h_i = \frac{1-\left(\frac{r_w}{r_m}\right)^i}{1-\left(\frac{r_w}{r_m}\right)^N}$$

a) Assume that $r_m > r_w$. Calculate the prob. of mut. fix. h_i for $0<i<10$ for very large pop sizes (take $\lim_{N\to\infty} h_i$). Plot this as a function of i.
b) The same with $r_m < r_w$.

⇒ a) When $r_m > r_w$, $\frac{r_w}{r_m} < 1$. Because of this, $\lim_{N\to\infty} \left(\frac{r_w}{r_m}\right)^N = 0$, so as N goes to ∞, the denominator goes to 1, so our fixation probability becomes $h_i = 1-\left(\frac{r_w}{r_m}\right)^i$. As $r_m + r_w = 1$, the plot below was done for $0.1 < r_w < 0.4 \Rightarrow 0.6 < r_m < 0.9$.



b) When $r_m < r_w$, $\frac{r_w}{r_m} > 1$, so $\lim_{N\to\infty}\left(\frac{r_w}{r_m}\right)^N = \infty$. Our denominator becomes $\lim_{N\to\infty}\left(1-\left(\frac{r_w}{r_m}\right)^N\right) = -\infty$.
Because the numerator remains finite, $\lim_{N\to\infty} h_i = \lim_{N\to\infty} \frac{\left(1-\left(\frac{r_w}{r_m}\right)^i\right)}{\left(1-\left(\frac{r_w}{r_m}\right)^N\right)} = 0$. Therefore the fixation prob. goes to 0 for any i when mutant cells divide less than wildtype cells.

② Consider a Moran process with two types: the wild type with fitness r_w and a mutant with fitness r_m. Suppose the mutant can experience a back mutation, where, as a result of a mutant cell division, a wild type daughter cell is created. We assume that this mutation happens with prob. β everytime a mutant divides, and no other mutations happen in the system. Consider the state space $j \in \{0, 1, \dots, N\}$, where j is the number of mutants. a) Write down the probs. $Prob(j\to j+1)$ and $Prob(j \to j-1)$ in a single step. b) What are the absorbing states of this system?

⇒ a) To go from $j \to j+1$, we have to consider the prob. that a wild-type dies, which is $\frac{N-j}{N}$, the prob. that a mutant divides, which is $\frac{r_m j}{r_m j + r_w(N-j)}$, but also consider that there is the probability for the mutant cell to generate a mutant daughter, which is $(1-\beta)$. Therefore, $Prob(j\to j+1) = \left(\frac{r_m j}{r_m j + r_w(N-j)}\right)(1-\beta)\left(\frac{N-j}{N}\right)$.
For $j \to j-1$, there is the prob. that a mutant cell is chosen to die, and that a mutant cell is chosen to divide and generates a wild-type daughter, or a mutant cell dies and a wild-type is chosen to divide. The full prob. is given by: $Prob(j\to j-1) = \left(\frac{r_m j}{r_m j + r_w(N-j)}\right)\beta\left(\frac{j}{N}\right) + \left(\frac{r_w(N-j)}{r_m j + r_w(N-j)}\right)\left(\frac{j}{N}\right)$.

b) In the Moran process with back mutation ($\beta > 0$), the only absorbing state will be at $j=0$, as no new mutant cells will be created.

3) Suppose a Markov Chain has states 0,1,2,3. Find the mean time to reach state 3 starting from state 0 for the Markov Chain whose transition matrix is given by

$$\begin{array}{c|cccc} & 0 & 1 & 2 & 3 \\ \hline 0 & 0.4 & 0.3 & 0.2 & 0.1 \\ 1 & 0 & 0.7 & 0.2 & 0.1 \\ 2 & 0 & 0 & 0.9 & 0.1 \\ 3 & 0 & 0 & 0 & 1 \end{array}$$

$\Rightarrow$ Let m_{ij} be the expected time to get to j starting from i:

$$\begin{cases} m_{03} = 0.1 + 0.4(1+m_{03}) + 0.3(1+m_{13}) + 0.2(1+m_{23}) \\ m_{13} = 0.1 + 0.7(1+m_{13}) + 0.2(1+m_{23}) \Rightarrow m_{13} = 0.1+0.7+0.7m_{13}+0.2+0.2(10) \to 0.3m_{13} = 1+2=3 \\ m_{23} = 0.1 + 0.9(1+m_{23}) \Rightarrow m_{23} = 0.1+0.9+0.9m_{23} \to 0.1m_{23} = 1 \to m_{23} = 10 \end{cases}$$

$m_{13} = 10$

$\to m_{03} = 0.1+0.4+0.4m_{03}+0.3+0.3(10)+0.2+0.2(10) \Rightarrow \cancel{m_{03}}\ 0.6m_3 = 1+3+2 = 6 \to m_{03} = 10$

$\Rightarrow$ The mean time to reach state starting at 0 is 10.

4) Suppose we have a continuous time birth process with immigration. That is, in time Δt, $Prob(j \to j+1) = (Lj+a)\Delta t$, $Prob(j \to j) = 1-(Lj+a)\Delta t$, and all other processes have prob. zero. Denote by $\varphi_j(t)$ the prob. to have j individuals at time t. Assume that, initially, there are zero individuals. a) Write down the master equation for $\frac{d\varphi_j(t)}{dt}$, including the equation for $j=0$ and the initial conditions for all $\varphi_j(t)$. b) Find $\varphi_j(t)$ for $j=0,1,2,\dots$ c) Derive the ODE for the mean number of individuals, $\langle X\rangle = \sum_{j=0}^{\infty} \varphi_j(t) j$, and the initial condition. d) Solve this ODE to find $\langle X\rangle$ as a function of time.

$\Rightarrow$ a) Since we have migration but we don't have death ($\underbrace{Prob(j \to j-1)=0}_{D=0}$), we can write $\frac{d}{dt}\varphi_j(t)$ as

$\varphi_{j-1}(L(j-1)+a) - \varphi_j(Lj+a) \Rightarrow j \geq 1$. For $j=0$, $\frac{d}{dt}\varphi_0(t) = \cancel{0}$, and we have that $\varphi_0(0) = 1$, $\varphi_K(0) = 0$ $\forall K \neq 0$

$-a\varphi_0(t) \Rightarrow \varphi_0(t) = e^{-at}$

b) $\frac{d}{dt}\varphi_1(t) = \varphi_0(L \cdot 0 + a) - \varphi_1(L+a) = \varphi_0(a) - \varphi_1(L+a)$

$= ae^{-at} - \varphi_1(L+a) \rightsquigarrow$ non-homogeneous linear dif. eq.

MATH112B – HW6 (Raphael F. Levy – U10156477)

(4) b) cont.: $\frac{d}{dt}\varphi_1(t) = ae^{-at} - \varphi_1(L+a) \Rightarrow \frac{d}{dt}\varphi_1(t) + \varphi_1(L+a) = ae^{-at}$. To solve this we use the integrating factor given by $\mu(t) = e^{\int (L+a)dt} = e^{(L+a)t}$. Now, multiplying both sides of the equation by the factor: $e^{(L+a)t}\frac{d\varphi_1(t)}{dt} + e^{(L+a)t}(L+a)\varphi_1(t) = ae^{(L+a)t}e^{-at} \Rightarrow \int \frac{d}{dt}\left(\varphi_1(t)e^{(L+a)t}\right) = \int ae^{Lt}$

$\Rightarrow \varphi_1(t)e^{(L+a)t} = \frac{a}{L}e^{Lt} + C \Rightarrow \varphi_1(t) = \frac{a}{L}e^{Lt}e^{-(L+a)t} + Ce^{-(L+a)t} = \frac{a}{L}e^{-at} + Ce^{-(L+a)t}$

given that $\varphi_1(0) = 0 \to \varphi_1(0) = \frac{a}{L}e^0 + Ce^0 = \frac{a}{L} + C = 0 \to C = -\frac{a}{L} \Rightarrow \varphi_1(t) = \frac{a}{L}e^{-at} - \frac{a}{L}e^{-(L+a)t}$
$= \frac{a}{L}\left(e^{-at} - e^{-(L+a)t}\right)$

↳ This will get complicated to calculate recursively, so let's use the mean number of individuals instead.

c) The mean number of individuals is given by $\langle X\rangle = \sum_{j=0}^{\infty}\varphi_j(t).j$, so taking the time derivative we get to: $\frac{d\langle X\rangle}{dt} = \sum_{j=0}^{\infty} j\frac{d\varphi_j(t)}{dt} = \sum_{j=0}^{\infty} j\left[\varphi_{j-1}(L(j-1)+a) - \varphi_j(Lj+a)\right]$

$= \sum_{j=1}^{\infty} j(L(j-1)+a)\varphi_{j-1} - \sum_{j=0}^{\infty} j(Lj+a)\varphi_j = \sum_{j=1}^{\infty} jL(j-1)\varphi_{j-1} + \sum_{j=1}^{\infty} ja\varphi_{j-1} - \sum_{j=0}^{\infty} Lj^2\varphi_j - \sum_{j=0}^{\infty} ja\varphi_j$

$= \sum_{j=0}^{\infty} Lj^2\varphi_j - \sum_{j=0}^{\infty} Lj\varphi_j + a\sum_{j=0}^{\infty}\varphi_j - a\sum_{j=0}^{\infty} j\varphi_j$. Using that $\sum_{j=0}^{\infty}\varphi_j(t) = 1$ and $\sum_{j=0}^{\infty} j\varphi_j(t) = \langle X\rangle$, we can rewrite the above as $\frac{d\langle X\rangle}{dt} = L\langle X\rangle + a - a\langle X\rangle = (L-a)\langle X\rangle + a$

d) To solve the ODE $\frac{d\langle X\rangle}{dt} = (L-a)\langle X\rangle + a$, we have the general solution $\langle X\rangle(t) = Ce^{(L-a)t} + \frac{a}{L-a} \rightsquigarrow \langle X\rangle(0) = 0 \Rightarrow C + \frac{a}{L-a} = 0 \to C = -\frac{a}{L-a}$

$\Rightarrow \langle X\rangle(t) = -\frac{a}{L-a}e^{(L-a)t} + \frac{a}{L-a} = \frac{a}{L-a}\left(1 - e^{(L-a)t}\right)$