Exercises 4

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Problem 1

a)

Let X_i be the probablity of i state **without** CIN, and Y_i be the probablity of i state **with** CIN.

1) neutral CIN

For $X_i, i \in \{0, 1, 2\}$:

$$\frac{\mathrm{d}X_o}{\mathrm{d}t} = -(u_1 + u_c)X_0$$
$$\frac{\mathrm{d}X_1}{\mathrm{d}t} = u_1 X_0 - (u_c + N \cdot u_2)X_1$$
$$\frac{\mathrm{d}X_2}{\mathrm{d}t} = N \cdot u_2 \cdot X_1$$

For $Y_i, i \in \{0, 1, 2\}$:

$$\frac{\mathrm{d}Y_0}{\mathrm{d}t} = u_c \cdot X_0 - u_1 \cdot Y_0$$
$$\frac{\mathrm{d}Y_1}{\mathrm{d}t} = u_1 \cdot Y_0 + u_c \cdot X_1 - N \cdot u_3 \cdot Y_1$$
$$\frac{\mathrm{d}Y_2}{\mathrm{d}t} = N \cdot u_3 \cdot Y_1$$

The solution to the ODE above is approximately:

$$X_2(t) = \frac{N u_1 u_2 t^2}{2}$$
$$Y_2(t) = u_1 u_2 t^2$$

The ratio C is calculated as $\frac{NY_2(t)}{NX_2(t)} = \frac{2u_c}{Nu_2} = \frac{2(2n_1+n_2)}{N}$

2) costly CIN in small compartments

Let r be the relative fitness of CIN cells, the fixation probablity of a Moran process: $p = \frac{1-r^{-1}}{1-r^{-N}}$.

From the lecture slides, we have:

$$X_2(t) = \frac{N u_1 u_2 t^2}{2}$$
$$Y_2(t) = N p u_1 u_c t^2$$

The ratio C is calculated as $\frac{NY_2(t)}{NX_2(t)} = \frac{2pu_c}{u_2} = \frac{4p(2n_1+n_2)u}{2u} = 2p(2n_1 + n_2)$

3) costly CIN in large compartments

Fixation of intermediate CIN will not be reached in large compartment and the population will tunnel from X_1 to Y_2 at a rate of $R = \frac{Nu_c u_3 r}{1-r}$

From the lecture slides, we have:

$$X_2(t) = \frac{Nu_1u_2t^2}{2}$$
$$Y_2(t) = \frac{Ru_1t^2}{2}$$

The ratio C is calculated as $\frac{NY_2(t)}{NX_2(t)} = \frac{R}{Nu_2} = \frac{Nu_cu_3r}{(1-r)Nu_2} = \frac{(2n_1+n_2)r}{100(1-r)}$

Obviously, the ratio C for the three CIN scenarios is independent of time.

b)

The ratio for three cases c_1, c_2, c_3 can be calculated

$$c_1 = \frac{2(2n_1+n_2)}{N} = 3$$
$$c_2 = 2p(2n_1+n_2) = 2\frac{1-r^{-1}}{1-r^{-N}}(2n_1+n_2) = 2 \cdot 0.06 \cdot 15 = 1.8$$
$$c_3 = \frac{(2n_1+n_2)}{100(1-r)} = \frac{15 \cdot 0.9}{100 \cdot 0.1} = 1.35$$

Problem 2

Assuming there are 365.25 days on average in a year

a)

Let $P(t)$ be the probablity of crypts being neoplastic at time t

Time: $t = 365.25 \cdot 50 = 18262.5$, The probablity of fixation in a Moran process: $p = \frac{1-r^{-1}}{1-r^{-N}} = 0.048$

$P(t) = 1 - \exp(-Nupt) = 0.00873$ $E(\text{number of neoplastic crypts}) = M \cdot P(t) = 8.73 \times 10^4$

b)

Let $P(t)$ be the probablity of crypts being transformed at time t

Time: $t = 365.25 \cdot 50 \cdot \frac{1}{10} = 1826.25$,

$P(t) = 1 - \exp(-ut) = 1.83 \times 10^{-5}$ $E(\text{number of neoplastic crypts}) = M \cdot P(t) = 183$

c)

Let $P(t)$ be the probablity of crypts being transformed at time t

Time: $t = 365.25 \cdot 50 \cdot \frac{1}{10} = 1826.25$, $N = 5$, $p = \frac{1-r^{-1}}{1-r^{-N}} = 0.22$

$P(t) = 1 - \exp(-Nupt) = 2.01 \times 10^{-5}$ $E(\text{number of neoplastic crypts}) = M \cdot P(t) = 201$

When the cells in each crypt originate from a single stem cell, the expected number of neoplastic crypts at age 50 is minimum. Thus this kind of tissue architecture prevents best the initiation of cancer.

Problem 3

a)

In Moran process, the average fixation time of the first mutation is N, and the average waiting time for the second mutation is $\frac{1}{Nu_2}$. When $N << \frac{1}{\sqrt{u_2}}$, it means $N << \frac{1}{Nu_2}$, so type 1 cells reach fixation before a type 2 cell arises.

b)

Given the initial condition, the equtions can be solved numerically using `ode45` in Matlab

The figure above can be reproduced using

https://github.com/wyq977/evolutionary-dynamics-2019/Exercises/Ex4.m

$X_0 = 0.90484, X_2 = 0.059662, X_3 = 0.035501$

Code is available on github repo: (https://github.com/wyq977/evolutionary-dynamics-2019)

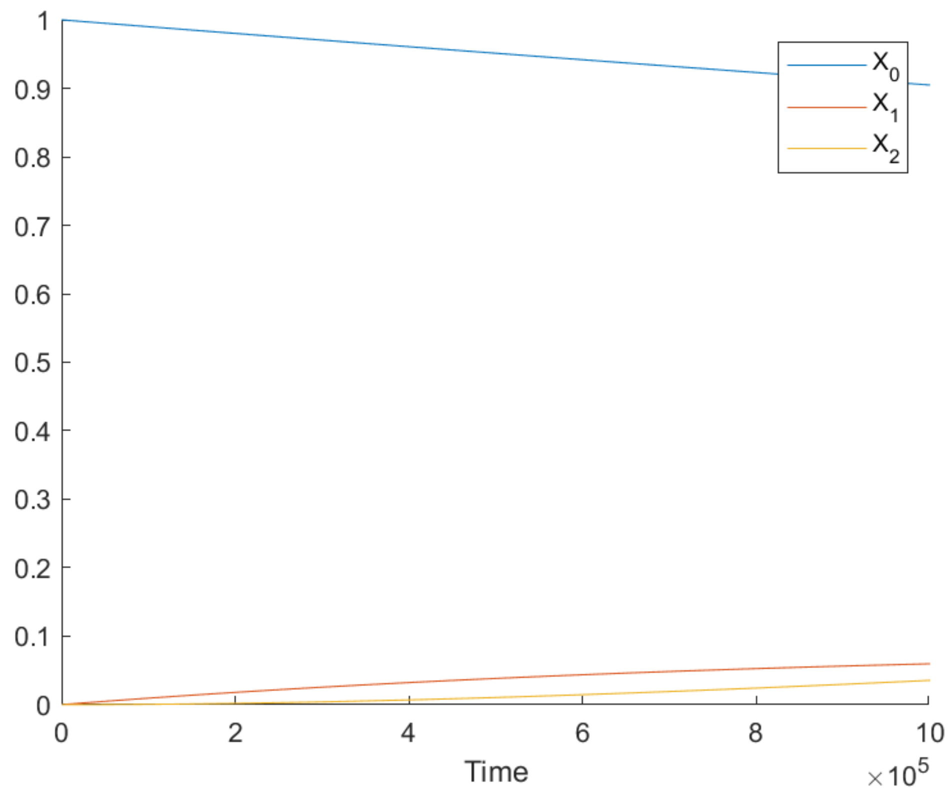

Figure 1: N=100. t=1e6