Computational Molecular Medicine

Assignment 5

Due April 18

Problem 1: Consider a simple Galton-Watson branching process for a population of (normal) stem cells with the following parameters:

- The population starts from one cell : $N(0) = 1$.
- At each generation, each stem cell can either die with probability $\frac{1}{2}$ or divide into two stem cells with probability $\frac{1}{2}$.

Simulate this process from generation $t = 0$ to generation $t = 1000$.

- Compare the analytical expression of the expected value of the size of population at each generation t with the value estimated with simulations.
- Do the same thing for the probability of extinction of the population by considering $t = 1000$ as $t = \infty$.

Using the recursive equation between the MGF $F(t+1, z)$ of $N(t+1)$ and the MGF $F(t, z)$ of $N(t)$:

- Derive a method to compute $P(N(t) > 0)$.
- Compare the computed probability with the values estimated from simulations for $t = 15$.

Problem 2: Consider the same setting as Problem 1 with the difference that the probability of death is now $\frac{20}{41}$.

- Answer the same questions posed in Problem 1.
- Compare the approximation of $E(N(t)|N(t) > 0)$ derived in class for large values of t with its estimated values from your simulations.

Problem 3: In this problem we will take into account mutations of normal stem cells and simultaneously consider both normal and mutant populations. More specifically, we will consider the process $N(t) = (N_0(t), N_1(t))$ where $N_0(t)$ (respectively, $N_1(t)$) is the number of normal (respectively mutant) stem cells at generation t. The definitions and dynamics are:

- Each normal stem cell can either die with probability $\frac{100}{201}$ or divide into two cells. When a normal stem cell divides, there is a possibility that exactly one of the two daughter cells acquires a mutation and becomes a mutant cell. This event has probability $\frac{1}{5000}$ and in this case a cell is added to the mutant population and hence only one normal cell is generated.
- Mutant cells have a fitness advantage: they can either die with probability $\frac{20}{41}$ or divide into two mutant cells. We will not consider the possibility that mutant cells acquire another mutation.
- Every mutant cell whose parent is a normal cell is the founder cell of a mutant "clone" consisting of all the descendants of the mutant founder cell.
- We define the time T of the appearance of cancer as first time t at which there exists a mutant clone of size at least 10^6. (Note: $T = \infty$ if no such t exists.)

Starting from 100 normal cells and no mutant cells, simulate this process for 500 generations, i.e., $t = 1$ to $t = 500$.

- Plot the "cancer incidence" curve $t \to P(T \leq t)$, where each generation represents two months. The overall cancer incidence is $P(T \leq 500)$.