Further Mathematical Biology: Problem Sheet 6
Michaelmas Term 2020

Question 1.

Suppose that the number of individuals in a population changes due to births, deaths and immigration, where the rate of births is λ per unit time, the rate of deaths is μ per unit time, and immigration occurs at rate β per unit time. Suppose that there are N_0 individuals in the population at time $t = 0$.

(a) Derive the master equation satisfied by $p_n(t)$, the probability that there are n cells in the population at time t.

(b) Use the master equation to derive a first order partial differential equation for the probability generating function $G(s,t) = \sum_{n=0}^{\infty} p_n(t)s^n$, where $|s| \leq 1$.

(c) Given that the solution of this partial differential equation is, for $\lambda \neq \mu$,

$$G(s,t) = \frac{(\lambda-\mu)^{\beta/\lambda}\left[\mu\left(e^{(\lambda-\mu)t}-1\right) - s\left(\mu e^{(\lambda-\mu)t}-\lambda\right)\right]^{N_0}}{\left[\lambda e^{(\lambda-\mu)t} - \mu - \lambda s\left(e^{(\lambda-\mu)t}-1\right)\right]^{N_0+\beta/\lambda}}, \tag{1}$$

derive an expression for the mean number of individuals in the population, $M(t)$.

(d) Describe the range of possible behaviours displayed by the model as λ, μ and β are varied.

Question 2.

Consider a population of proliferating cancer cells, which is composed of two subpopulations: Type I cells which are drug sensitive (S) and Type II cells which are drug resistant (R). We can summarise the proliferative behaviour of the cells using the following "chemical equations":

$$\mathrm{S} \xrightarrow{\lambda(1-\mu)} \mathrm{S}+\mathrm{S}, \qquad \mathrm{S} \xrightarrow{\lambda\mu} \mathrm{S}+\mathrm{R}, \qquad \mathrm{R} \xrightarrow{\lambda} \mathrm{R}+\mathrm{R}. \tag{2}$$

(a) Write down the biological assumptions underpinning the model.

(b) Derive the master equation for $p_{n,m}(t)$, the probability that there are n sensitive and m resistant cells in the population at time t, given a single sensitive cell at time $t = 0$.

(c) Use the master equation to determine the how the mean numbers of sensitive and resistant cells in the population evolve over time.

(d) Describe the biological implications of your results.

Question 3.

Consider a population of cells undergoing a random walk on a one-dimensional lattice along the x-axis, where the lattice sites are all of width $\mathrm{d}x$, and $\mathrm{d}x$ is approximately equal to the cell diameter so that at most one cell can occupy any lattice site. Let $p(A_n,t)$ be the probability that lattice site n is occupied at time t, with $p(A_n,0) = p_n(0)$

During a time interval $[t, t+\mathrm{d}t)$, an individual in lattice site n attempts to move left into lattice site $n-1$ with probability $P_l\mathrm{d}t$, and attempts to move right into lattice site $n+1$ with probability $P_r\mathrm{d}t$. Attempted moves into occupied sites are aborted.

In addition, during $[t, t+\mathrm{d}t)$ a cell attempts to reproduce with probability $P_b\mathrm{d}t$, placing a daughter cell into either site $n-1$ or $n+1$ with equal probability, and aborting the proliferation attempt if the target site is filled. Finally, a cell dies with probability $P_d\mathrm{d}t$ during $[t, t+\mathrm{d}t)$.

(a) Use the principle of mass balance to deduce discrete conservation equations for $p(A_n, t)$.

(b) By taking the limit as $\mathrm{d}x$ and $\mathrm{d}t$ tend to zero show that the lattice site occupancy evolves approximately according the advection-diffusion-reaction equation

$$\frac{\partial n}{\partial t} = D\frac{\partial^2 n}{\partial x^2} - v\frac{\partial}{\partial x}\left[n(1-n)\right] + rn\left(1 - \frac{n}{K}\right), \tag{3}$$

where n is the occupancy probability location x at time t, and D, v, r and K are non-negative constants that you should define. State clearly any assumptions you make in deriving this equation.