Modelling chemotherapy in leukaemia

In this simple stage-structured model we assume that all cells mature at a constant rate $g(x) = v$ and are killed by chemotherapy drugs at a rate $\mu(x,t)$ where

$$\mu(x,t) = \frac{K_1(x,t)c(t)}{K_2(x,t) + c(t)}$$

where x is a measure of the cells' maturity, $c(t)$ is the concentration of the drug and $K_1(x,t)$ and $K_2(x,t)$ relate to the cells' response to drugs. The governing equation for this structured cell population is

$$\frac{\partial n}{\partial t} = -v\frac{\partial n}{\partial x} - \mu n \tag{1}$$

for $0 < x < 1$. At $x = 1$ all cells divide so that

$$n(0,t) = 2n(1,t). \tag{2}$$

We assume that the drug acts equally effectively at all stages of the cell cycle and therefore we can let μ be independent of x so that $\mu = \mu(t)$. In the tx plane, sketch some typical characteristic curves for equation (1). Show clearly the region of the plane where valid solutions for $n(x,t)$ exist.

Assume that there is a solution with stable stage distribution for equation (1) with boundary condition (2). Use separation of variables to solve equation (1) and show that this stable stage distribution solution for $n(x,t)$ is

$$n(x,t) = Ae^{\lambda(t-\frac{1}{v}x)} \exp\left(-\int_0^t \mu(s)\,ds\right) \tag{3}$$

where λ and A are constants. Show that when boundary condition (2) is applied the solution becomes

$$n(x,t) = A2^{vt-x} \exp\left(-\int_0^t \mu(s)\,ds\right). \tag{4}$$

Let $N(t) = \int_0^1 n(x,t)\,dx$ be the total number of cells in the population. Show that as $t \to \infty$ (where the stable stage distribution solution is valid) the number of newly divided cells in the population is given by

$$n(0,t) = 2\ln 2\, N(t). \tag{5}$$

Hence show, by integration (1) or otherwise that the total population $N(t)$ is governed by the equation

$$\frac{dN}{dt} = v\ln 2N - \mu N. \tag{6}$$

Find the condition on $c(t)$, in terms of v, $K_1(x,t)$ and $K_2(x,t)$, such that the total number of cancer cells goes to zero as $t \to \infty$. (This will be an implicit relation.) Find an explicit relation when c, K_1 and K_2 are all constant.

Reference

Bischoff, K.B., Himmelstein, K.J. Dedrick, R.L. and Zaharko, D.S. (1973) Pharmacokinetics and cell population growth models in cancer chemotherapy. *Chem. Eng. Med. Biol., (Advances in Chemistry Series.)* **118**, 47–64.