AMC In-host model for HIV infection practive exercise

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1. A within host mathematical model for HIV interration with the immune system is given below where T, I, V denotes the Healthy T cells, Infected T Cells and Virus populations respectively:

$$\begin{aligned}\dot{T} &= \pi - \mu T - \beta_1 TV - \beta_2 TI,\\ \dot{I} &= (\beta_1 V + \beta_2 I)T - (\mu + \alpha)I\\ \dot{V} &= N\alpha I - \mu_V V,\end{aligned}$$

   (a) Construct a table of variables and parameters and state the units of each of them making sure that the units on both sides of each equation balance.

   (b) State all the assumptions used to construct the model.

   (c) Define a set of mathematically and biologically meaningful solutions of the model and prove that the set if a feasible region of the model.

   (d) Compute all the equilibrium points and state the conditions for existence of nonnegative solutions.

   (e) Compute the thresholds $\mathcal{R}_0$ and N_{crit} using the

      i. Next generation operator method.

      ii. Next generation matrix method.

      iii. Local stability of the uninfected equilibrium via the Jacobian method.

   (f) Dertemine the local stability of the equilibrium points using the Jacobian matrix method and the centre-manifold theory.

   (g) Prove the global stability of the uninfected equilibrium point using the method given in the lectures.

   (h) To prove the global stability of the infected equilibrium point, do the following:

      i. Define a function

$$L(t) = T - T^* - T^* \ln\left(\frac{T}{T^*}\right) + a(I - I^* - I^* \ln\left(\frac{I}{I^*}\right)) + b(V - V^* - V^* \ln\left(\frac{V}{V^*}\right))$$

      ii. Show that $L(t)$ is positive definate.

      iii. Show that the infected equilibrium point is a global minimum point of the function $L(t)$.

iv. Find $\frac{dL(t)}{dt}$ and find the appropriate values of a and b so that

$$\frac{dL(t)}{dt} \leq 0.$$

Determine the condition where $\frac{dL(t)}{dt} = 0$. You have actually used a Lyapunov function to prove the global stability of the infected equilibrium point.

(i) The infected T cells usually go through a period of latency before they become actively infectious. Modify the given model to incorporate latency in the infected cells. Compute the thresholds $\mathcal{R}_0$ and N_{crit} using the Next generation operator method.

(j) The Cytotoxic T cells (CTLs) kill the actively infectious T cells using a predator-prey kind of relationship. Modify the model in part (i) to incoporate the effects of CTLs and carry out the full analysis of the model using t methods mentioned above.

(k) The B cells produces neutralising antibodies to kill the actively free circulating virus using a predator-prey kind of relationship. Modify the model in part (j) to incoporate the effects of neutralising antibodies and carry out the full analysis of the model using methods mentioned above.

(l) Carry out numerical simulations using either MATLAB, R or Python for all the models formulated in this exercise to illustrate the evolution of solutions over time.