Math 4600: Homework 6

Due: February 22nd

1. **(computing)** A simple model of HIV dynamics is

$$\frac{dV}{dt} = P - cV,$$

where P is virus production rate, V is virus concentration (per mL), and c is the clearance rate. Suppose a protease inhibitor drug is given, resulting in production becoming 0.

   (a) The text file ("hw6_data") on the website records how a patient's virus concentration changes with time. Time (measured in days) is scaled so that treatment begins on day 0. Use this data to estimate c, assuming that once treatment starts, $P = 0$. This can be done by plotting the natural log of virus concentration vs time after time 0, and fitting a line through the resulting scatter plot. Make a plot of this scatter plot, and a line going through the post-treatment points.
   Side note: Since P does not instantly go to 0 when the inhibitor is given, this is actually a lower bound of c. As we saw in class, a better estimate (found by fitting data to a more accurate model) is $c = 3.1$ per day.

   (b) Suppose that before treatment the virus production was in equilibrium. What was the production rate, P? (This requires estimating V_0, the steady state virus concentration, from the data.)

   (c) What is the total virus production per day (pre-treatment) if the person's fluid volume is estimated to be $15 \cdot 10^3$ mL?
   Note: Before these calculations were done, it was thought that virus production during the latent period was small. This calculation changed how people thought of HIV dynamics.

2. Here is the HIV dynamics model that we considered in class:

$$\begin{aligned}
\frac{dT}{dt} &= s + pT\left(1 - \frac{T}{T_{max}}\right) - d_T T - kVT \\
\frac{dT^*}{dt} &= kVT - \delta T^* \\
\frac{dV}{dt} &= N\delta T^* - cV.
\end{aligned}$$

Consider the model during the RT-inhibitor treatment. Assume that the inhibitor is perfect, i.e. it sets the appropriate parameter (k) to zero. In the resulting system the T^* and V equations are uncoupled from the T equation. Use this system to answer questions (a) and (b).

   (a) In the (T^*, V) system find the steady states and their stability analytically (by computing the eigenvalues). Then, draw a phase plane with nullclines and representative direction field arrows. Finally, draw qualitative time courses for $T^*(t)$ and $V(t)$ starting with some high initial values. (Assume $c = NkT_0$ if you need to).

   (b) In the T equation with $s = 0$ find the steady states (still assume that the inhibitor is present and perfect). Investigate the stability of these steady states analytically and using the phase line for different parameter values. Using these results, discuss the long-term condition of T-cell population under each parameter regime. Explain why these are reasonable outcomes at these parameter ranges.

The next problem focuses on the HIV-model we last considered in class: when the protease inhibitor completely blocks the production of infectious virus particles.

(As a side note: if you are wondering what happens when the drug is assumed to be only partially effective, for a look at some real data, and much more information, see the review article on canvas.)

3. **(computing)** As mentioned in class, V_I is infectious HIV, V_{NI} is non-infectious HIV. It has been estimated from data that $\delta = 0.5$ day^{-1}, $c = 3.1$ day^{-1}, and $V_0 = 130000$. Solve the model equations analytically for V_I and V_{NI} . Plot in MATLAB the total virus concentration $V(t) = V_{NI}(t) + V_I(t)$ as a function of time in regular and log-scale. Assume $T = T_0$, $T_0^* = kV_0T_0/\delta$ and $NkT_0 = c$ (with these assumptions, it is not necessary to know N, T_0, or T_0^*). Notice that there is a "shoulder" in the beginning, indicative of a slower initial decay rate of V. Suggest a possible reason for this observation.