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Weekly Problem 01
Computational

HIV Lab

Derivation of $N_v(t) = Xe^{-k_i t} + (N_{vo} - X)e^{-k_v t}$ with explanation of steps and assumptions

First we need to define variables that will be used for this equation in the context of the HIV study.

$t = time;\ N_I(t) = number\ of\ infected\ T-cells\ at\ time,\ t;\ N_V(t) = number\ of\ free\ virions\ in\ the\ blood\ (viral\ load)$

$k_I =\ clearance\ constant\ for\ infected\ T-cells;\ k_V\ = clearance\ constant\ for\ virions;$

$\gamma = rate\ constant\ for\ virion\ production/T-cells;\ \beta =\ \gamma N_{I,0}$

Looking into how to visualize and quantify HIV treatment, we must understand where the process starts and ends. The patient starts at a quasi-steady state where the production of infected T-cells equals the clearance process before the commencement of treatment. Thus, the rate of clearance equals the rate of production. This is an important start for our equation since after they administer the antiviral drug the number of infected T-cells will decrease depending on the time passed and the amount started with time of 0 being when the drug was administered.

1. $\frac{dN_I}{dt} = \ -k_I N_I$

$\frac{dN_I}{N_I} = -k_I dt$

$\int \frac{dN_I}{N_I} = \int -k_I dt$

$N_I(t) = N_{I,0} e^{-k_I t}$

At the same time, we must consider the production and clearance of virions, which is similar to the T-cells. But there is also another consideration that must go into the equation for the virions. The number of virions produced is dependant upon the population of T-cells at that time interval.

2. $\frac{dN_V}{dt} = -k_V dt + \gamma N_I$

Using the above solution of the first differential equation, we can substitute N_I in the second differential equation.

$\frac{dN_V}{dt} = -k_V dt + \gamma N_{I,0} e^{-k_I t}$

Here is where they use β to represent two unknown quantities that are not actually measured, $\gamma\ and\ N_{I,0}$.

3. $\frac{dN_V}{dt} = -k_V dt + \beta e^{-k_I t}$

Solution:

$\int \frac{dN_V}{dt} = \int -k_V dt + \beta e^{-k_I t}$

$N_V(t) = N_{V,0} e^{k_V t} - C e^{-k_V t} + C\beta e^{-k_I t}$

Using X as they do:

$$N_V(t) = Xe^{-k_I t} + (N_{V,0} - X)e^{-K_V t}$$

Questions:

1. List the key assumptions in derivation
    a. One main assumption made is assuming that the drug actually stops completely the T-cell's infection. Assuming that the treatment will cease infections of new T-cells, they do not need to consider the non-infected T-cells since they will, at that point, be safe from infection and thus need not be considered. They also assume that each infected T-cell has a fixed chance of being cleared in a short time interval. This is dependant upon the time interval. For the virions, similar assumptions are made such as a fixed probability of clearance per virion per time unit.
2. Consequences in relaxing the assumptions listed in question one. How does it change the approach?
    a. If we relax some of these assumptions, there would be other added problems which need to be considered. The largest one being if the antiviral drug did not stop the production of the infection. The model will have to make sure to add an element that represents the on-going production of infected T-cells. Also, if the infected t-cells and the virions did not have a fixed probability of being cleared, there would be a more randomness to it and that would need to be considered in the equation as well and it would not necessarily be proportional per unit time interval.
3. How did the two limiting cases simplify the problem?
    a. With the two limiting case being when the two constants are brought to extreme values. Let's say that the clearance of infected T-cells was far greater than the clearance of the virions, then the second term would dominate and the first term goes to zero. Saying, the number of virions at a given point is controlled by the decay rate constant of the virions. Vice versa, the first term would dominate and the second term would go to zero showing the number of virions would decrease by the decay rate of the infected T-cells. The limiting cases helps us visualize what is occurring with this function and how we are to expect to fit the model to real data.