Lyapunov Theorem and HIV Infection Model

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Abstract

The goal of this work is to learn about stability of equalibrium solutions in HIV infection models, and understand the models themselves.

Outline of the Model

To model the spread of a disease such as HIV through the cells of a body, one could use an *age-structured HIV infection model* such as

$$\frac{dT(t)}{dt} = s - d \cdot T(t) - kV(t)T(t) \tag{1}$$

$$\frac{\partial i(a,t)}{\partial t} + \frac{\partial i(a,t)}{\partial a} = -\delta(a) i(a,t) \tag{2}$$

$$\frac{dV(t)}{dt} = \int_0^\infty p(a) i(a,t)\, da - cV(t) \tag{3}$$

$$\text{boundary condition: } i(0,t) = kV(t)T(t) \tag{4}$$

$$\text{initial conditions: } T(0) = T_s \tag{5}$$

$$i(a,0) = i_s(a) \tag{6}$$

$$V(0) = V_s \tag{7}$$

where

$T(t)$:	population of uninfected target cells T and time t
$i(a,t)$:	density of infected cells of infection age a at time t
$V(t)$:	population of infectious free virion at time t
s:	recruitment rate of healthy T cells
d:	per capita death rate of infected cells
$\delta(a)$:	age dependent per capita death rate of infected cells
c:	clearance rate of virions
k:	rate at which an uninfected cell becomes infected by an infectious virus
$p(a)$:	viral production rate of an infected cell with age a

Notice this model is a system involving partial differential equations. Solving Eq. (2) is not too difficult, but does require some knowledge of PDEs.

The important aspect of this model will be the equilibrium solutions, and analyzing the behaviour of the equilibrium solutions. This will have more of an analysis feel to it, and although you need not have already taken analysis, you will definitely be focussing on the model with some degree of rigor. This analysis will utilize the following theorem.

Theorem (Lyapunov) Let $x_e = 0$ be an equilibrium point for the system $dx(t)/dt = f(x(t))$. Let $V : \mathbb{R}^n \to \mathbb{R}$ be a positive definite continuously differentiable function.

- If $\nabla V(x) \cdot f(x)$ is negative semi-definite, then x_e is stable.
- If $\nabla V(x) \cdot f(x)$ is negative definite, then x_e is asymptotically stable.

The PDE model relates to an ODE model by removing the dependence on age, $\delta(a) = \delta_0$ and $p(a) = p_0$. Under this simplification, the model becomes

$$\frac{dT(t)}{dt} = s - d \cdot T(t) - kV(t)T(t) \tag{8}$$

$$\frac{dI(t))}{dt} = kV(t)T(t) - \delta_0 I(t) \tag{9}$$

$$\frac{dV(t)}{dt} = p_0 I(t) - cV(t) \tag{10}$$

$$\text{initial conditions: } T(0) = T_s \tag{11}$$

$$I(0) = I_s \tag{12}$$

$$V(0) = V_s \tag{13}$$

where $I(t) = \int_0^\infty i(a,t)\,da$ is the total number of infected cells at time t.

There are also *delay differential equation* (DDE) models, where there is a time delay in the infections.

Further Questions

- Are there some real world data that this could be applied to?
- From a modeling standpoint, are there significant benefits to using PDE or DDE models rather than ODE model? Are the dynamical properties of the models that much different?
- Since determining the Lyapunov function is an art form, what more can we learn about how Lyapunov functions are used/determined in modeling (either other HIV models or more generally)?

Prerequisites

- For this project, you should have completed at least Differential Equations.

What You Would Do

- You would start by reading Reference [1] and filling in all the details of the determining the equilibrium solutions. This would involve learning a bit about PDEs since you will need to solve a PDE to do this.
- You will learn some of the theory behind continuous dynamical systems, and also learn about Lyapunov's Theorem. This part (Lyapunov's Thoerem) could get quite complicated, so you'll want to carefully pick sources.
- You will examine how Lyapunov's Theorem is applied to the specific model being studied to examine the stability of the equilibrium solutions.
- Ideally, you would answer at least one of the *Further Questions*, or other questions that arose while you are filling in the details.
- If we feel you had learned something novel, you would finally create a poster of your results or give a talk at the URS.

References

[1] G. Huang, X. Liu, Y. Takeuchi *Lyapunov Functions and Global Stability for Age-Structured HIV Infection Model*, SIAM J. Appl. Math. **72** (2012), 25–38.