Modeling the progression of HIV to AIDS in individuals during the AIDS Epidemic

Lily Nelson, Shae Delany, Charlotte Jordan

MATH102 Ordinary Differential Equations

Disease description

Brief Description

- The 1980s AIDS epidemic was a major global health crisis
- It is caused by the Human Immunodeficiency Virus (HIV)
- In early years, AIDS affected men who had sexual contact with other men, intravenous drug users, and recipients of contaminated blood products
- Targets the immune system by infecting helper T cells, weakening the immune system
- The depletion of helper T cells leaves the body vulnerable to infections, which ultimately defines the onset of AIDS

Epidemiology Characteristics

- Not highly contagious in casual contact – it is transmitted primarily through blood, sexual contact (80%), and from mother to child during birth or breastfeeding
- It has a long incubation period – takes years before symptoms of AIDS develop after initial infection
- High mortality rate – life expectancy after diagnosis was 1-2 year
- Lack of diagnostic tools and treatment

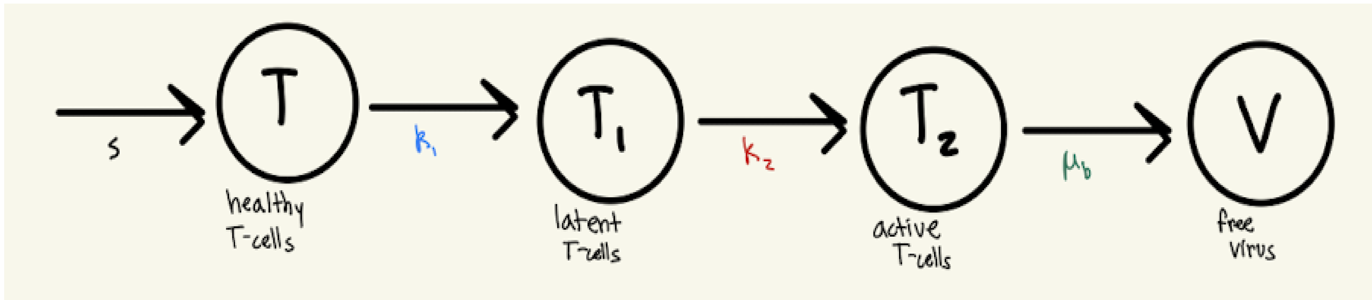
Ryan, Nicole. "Modeling Immune System Dynamics during HIV Infection and Treatment with Differential Equations," *CODEE Journal:*, 1 Apr. 2023

Sharp, Paul M, and Beatrice H Hahn. "Origin of HIV and the AIDS pandemic," *Cold Spring Harbor Perspectives in Medicine*. 1 Sept. 2011

Diagram of our compartments and flows

T-cells function in the human immune system to coordinate the immune response and signal the site of an infection. HIV infects T-cells and uses them as viral replicated hosts. An HIV infected T-cell can no longer notify the immune system of an infection which makes HIV infected people more susceptible to other infections.

The path of HIV infection in T-cells is modeled below



$T(t)$	T-cells of the healthy immune system
$T_1(t)$	latently infected T-cells
$T_2(t)$	actively infected T-cells
$V(t)$	free HIV virus

The system of differential equations

$$\begin{cases} \dfrac{dT}{dt} &= s + rT\left(1 - \dfrac{T+T_1+T_2}{T_{max}}\right) - \mu_T T - k_1 VT \\ \dfrac{dT_1}{dt} &= k_1 VT - \mu_T T_1 - k_2 T_1 \\ \dfrac{dT_2}{dt} &= k_2 T_1 - \mu_b T_2 \\ \dfrac{dV}{dt} &= N\mu_b T_2 - k_1 VT - \mu_V V. \end{cases}$$

Parameters:

s	supply rate of T-cells from the thymus	$10\ day^{-1}mm^{-3}$
r	growth rate parameter of T-cells	$0.03\ day^{-1}$
μ_T	death rate parameter of T-cells	$0.02\ day^{-1}$
k_1	infection rate parameter of the virus	$2.4 \times 10^{-5} mm^3 day^{-1}$
k_2	rate of transforming from T_1 to T_2	$3 \times 10^{-3} day^{-1}$
μ_b	death rate parameter of infected T-cells	$0.24\ day^{-1}$
μ_v	viral clearance rate parameter	$2.4\ day^{-1}$
N	bursting number parameter	varies (50 - 1500)

Important info:
- CD4 (helper) T-cell count in healthy person: 500-1500 /mm^3
- Considered AIDS when T-cell count reaches 200 or lower
- Takes HIV on average 5-10 years to progress to AIDS

Deriving the system of equations

To model the infection of HIV into the immune system, we begin with a mathematical model describing the rate of change of T-cells in a healthy human immune system, assuming logistic growth of T-cells. This model was first suggested by Perelson, Kirschener, and DeBoer.

$$\frac{dT}{dt} = s + rT\left(1 - \frac{T}{T_{max}}\right) - \mu_T T,$$

To incorporate HIV, we introduce the variables T1 = T1(t), T2 = T2(t), and V = V(t) (defined in the compartment model and shown below in yellow).

$$\frac{dT}{dt} = s + rT\left(1 - \frac{T+T_1+T_2}{T_{max}}\right) - \mu_T T - k_1 VT$$

k1 is the rate at which free virus infects T-cells. We subtract the term k1VT from the model of a healthy immune system to account for the infection of healthy T-cells with HIV. As T-cells get infected, they become latent (T1), so this same term is added to our equation modeling the rate of change of latent cells (T1), shown below:

$$\frac{dT_1}{dt} = k_1 VT - \mu_T T_1 - k_2 T_1$$

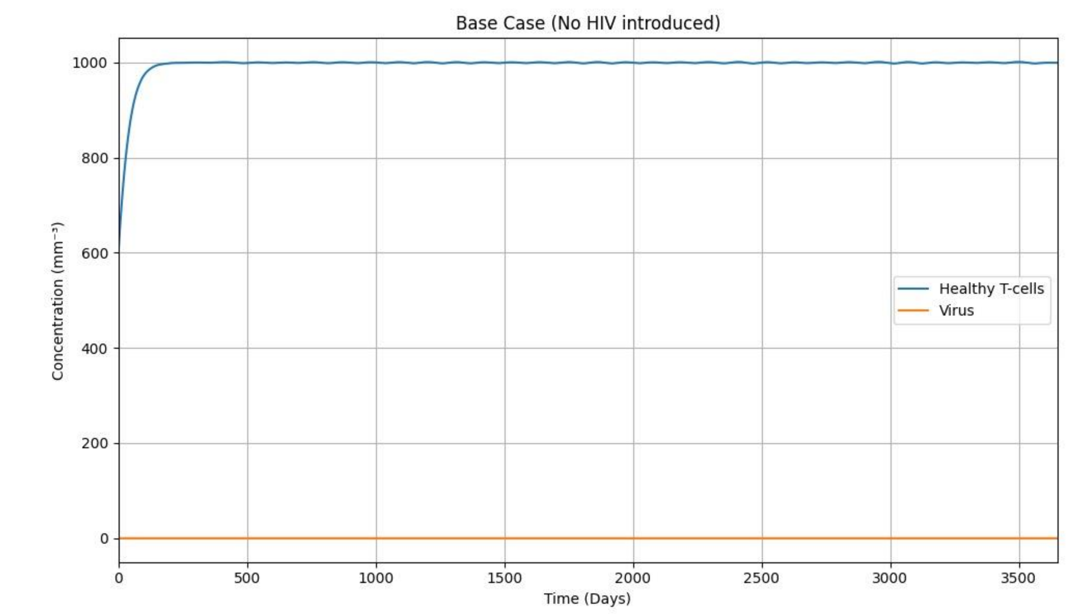
This equation models the rate of change of latent, infected cells (T1). Latent cells are assumed to die at the same rate as uninfected T-cells, shown by the parameter μb. K2 is the rate at which latent T-cells become active hence the last term is subtracted to account for the activation of latent T-cells. This same term is added to our equation modeling the rate of change of active cells (T2), shown below:

$$\frac{dT_2}{dt} = k_2 T_1 - \mu_b T_2$$

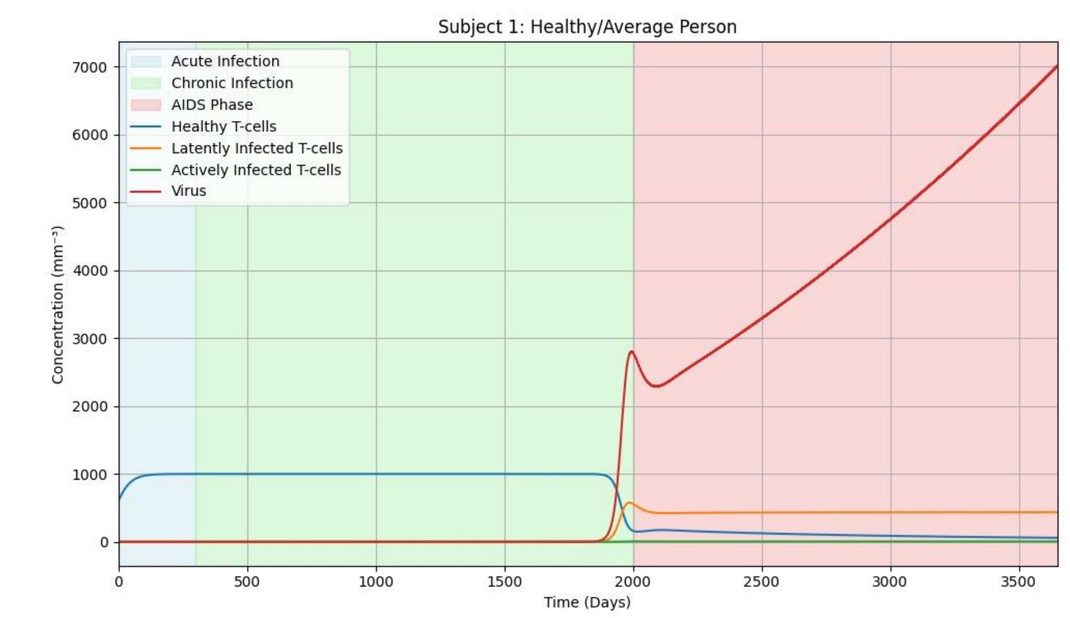
This equation models the rate of change of active, infected cells (T2). The second term models the rate at which T2 cells die. When a T2 cell dies, it has released N amount of free virus in its lifetime. Thus, the rate of T2 cells dying is used in our final equation to model the rate of free virus in the bloodstream, shown below:

$$\frac{dV}{dt} = N\mu_b T_2 - k_1 VT - \mu_v V$$

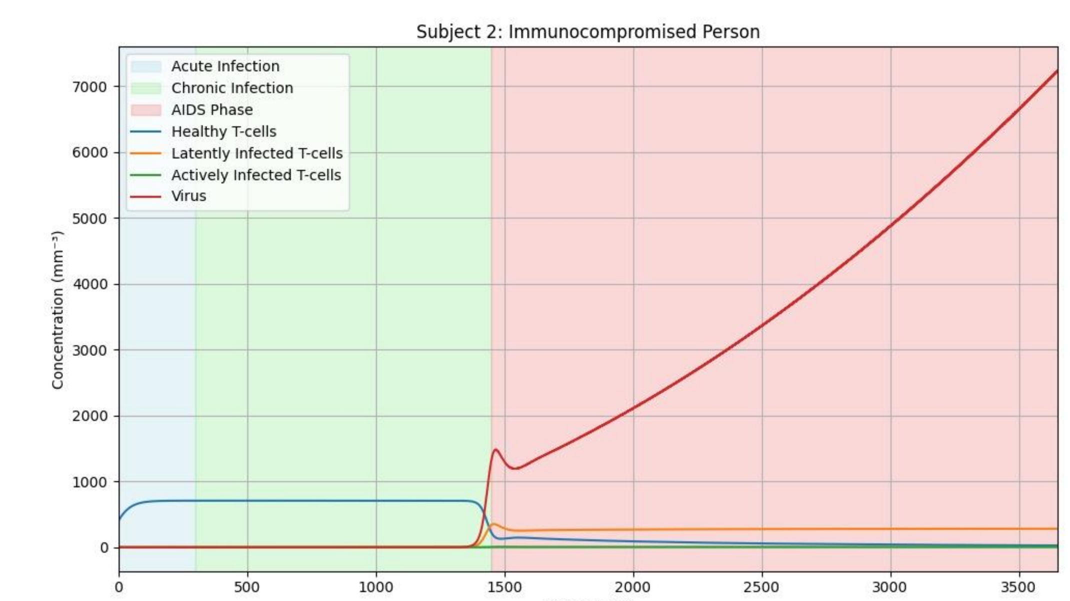
Solutions under different initial conditions



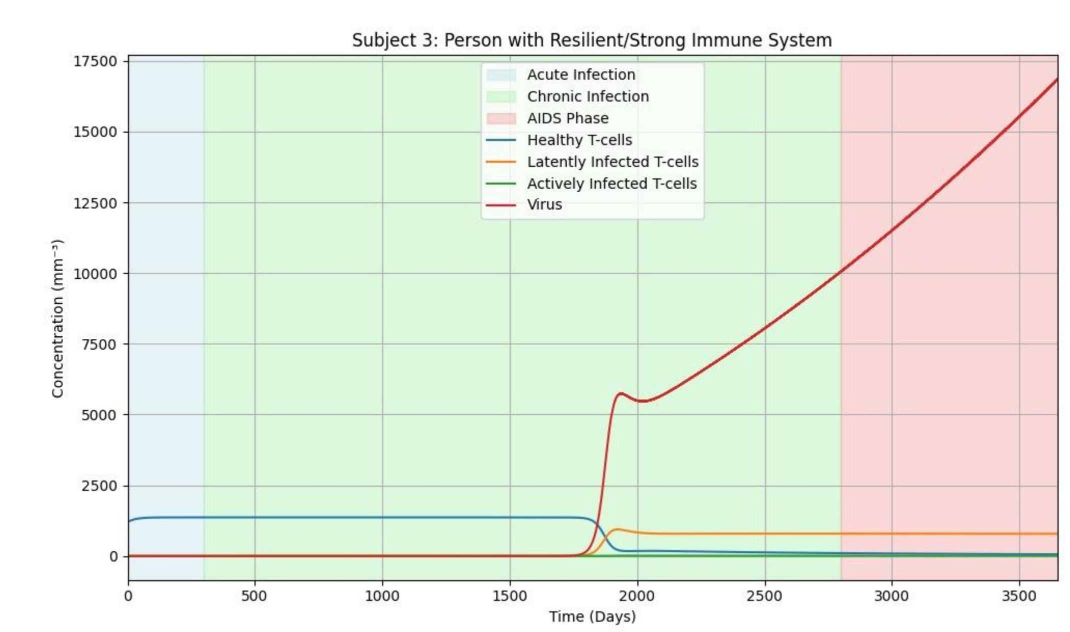
Initial Conditions/Parameters: T=600, V=0
Semantic Meaning: No virus introduced; progression to AIDS does not occur



Initial Conditions/Parameters: T=600, V=.001, muT=0.02, muv=2.4, k1=2.4e-5, k2=0.003
Semantic Meaning: Avg T-cell count/reproduction rate, avg virus load/reproduction rate; progression to AIDS in about 5.5 years



Initial Conditions/Parameters: T=400, V=10, muT=0.03, muv=2.5, k1=5e-5, k2=0.005
Semantic Meaning: A lower initial T-cell count with a higher virus load and faster T-cell death-rate; progression to AIDS in about 4 years



Initial Conditions/Parameters: T=1200, k1=1e-5, muT=0.01, muv=1.8
Semantic Meaning: high T0, slow virus replication, longer T-cell life; progression to AIDS in about 8 years