A within-host mathematical model of HIV infection during combination therapies

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Motivation:

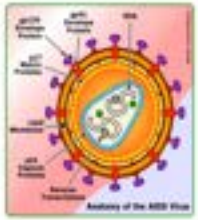
For this model we wanted to study HIV dynamics on the immunological level within a host whilst undergoing treatment for HIV infection.

Introduction:

HIV Biology

Basic Facts

- Enveloped retrovirus
- Causative agents of AIDS
- Systematically destroys the immune system
- Without the immune system, host is more susceptible to diseases and infections



Retrovirus Immunology

- Viral genes can become a permanent part of the host cell's genome
- HIV has a high mutation rate
- HIV infects CD4 lymphocytes, monocytes, macrophages, and B lymphocytes
- Direct action from virus causes destruction of T cells and other white blood cells and damage to the central nervous system

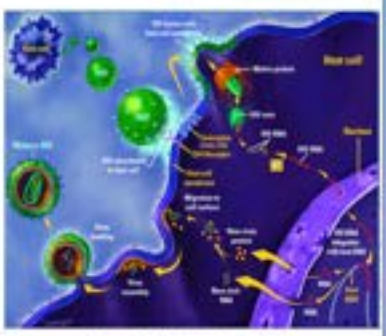


Figure 1 : Life cycle of HIV virus

Math:

- Figure 2 is a visual representation of the HIV model

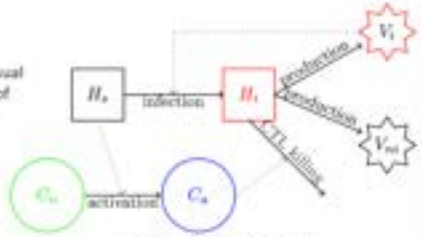


Figure 2 : Theoretical diagram

The Model:

This model combines two standard HIV models, a viral dynamics model in the presence of drugs as well as a model of T cell dynamics (Perelson pg 30,32). We also considered immunological response to viral infection within a host.

$$\text{Susceptible Helper T-cell} \quad \frac{dH_u}{dt} = H_0 - (1-\varepsilon_{rt})\lambda H_u V_i - d_h H_u$$

$$\text{Infectious Helper T-cell} \quad \frac{dH_i}{dt} = (1-\varepsilon_{rt})\lambda H_u V_i - bH_i C_a - kd_h H_i$$

$$\text{Naive Cytotoxic T-cell} \quad \frac{dC_u}{dt} = C_0 - gH_i C_u - d_c C_u$$

$$\text{Active Cytotoxic T-cell} \quad \frac{dC_a}{dt} = gH_i C_u - bH_i C_a - md_c C_a$$

$$\text{Infectious virus} \quad \frac{dV_i}{dt} = (1-\varepsilon_{pi})pH_i - cV_i$$

$$\text{Noninfectious virus} \quad \frac{dV_{ni}}{dt} = \varepsilon_{pi} pH_i - cV_{ni}$$

Two Drugs

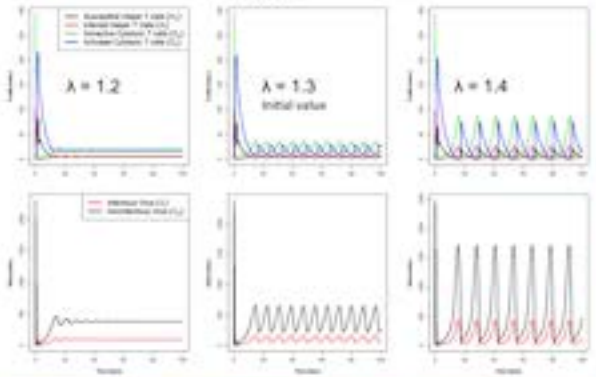
- Reverse transcriptase inhibitors block HIV's ability to infect a cell ($\sim \varepsilon_{rt}$)
- Protease inhibitors cause the production of non-infectious viral particles ($\sim \varepsilon_{pi}$)

Results:

- These graphs were obtained using the mathematical software program R. As illustrated below, the dynamics of the model change drastically with minimal variation in the parameters (in this case, the infection rate (λ))

Parameters	Values
Helper cell supply (H_0)	100
CT cell supply (C_0)	100
Treatment (ε_{rt})	0.82
Treatment (ε_{pi})	0.8
Helper cell death (d_h)	0.14
Helper cell death (k)	7
Infection rate (λ)	1.3
Interaction rate (b)	1
CT cell death rate (d_c)	0.14
CT cell death rate (m)	1.5
Activation rate (g)	1
Viral production rate (p)	1000
Viral clearance (c)	12.00

Initial values



Conclusions:

- Dynamics are very sensitive to parameters
  When the parameters (m, λ, p) are varied the period and amplitude of oscillations change before dampening out
- Clearly observed oscillations that disappear with variation in m, λ, and p when increased and b and g when decreased
- Efficacy of drug(s) has a strong effect on the dynamics (if efficacy is >90%, viral particles are quickly destroyed)
- Infection rate (λ) and T-cell interaction rate (g) appear to be important in this model (little variation needed for drastic changes in output)

Future Directions:

- Introduction of more drugs and more susceptible cell types to model
- Continue to study the unique oscillations and try to further understand their biological meaning
- Stochastic model on the probability of starting and sustaining an HIV infection
- Development of partial differential equations model to study effects of time since infection or activation of cells

Acknowledgements:

- CURE-STEM for funding this research
- Student Travel Grant for the 2014 Joint Mathematics Meetings
- The University of Central Oklahoma for providing a supportive undergraduate research environment

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