Quantifying Human Immunodeficiency Virus

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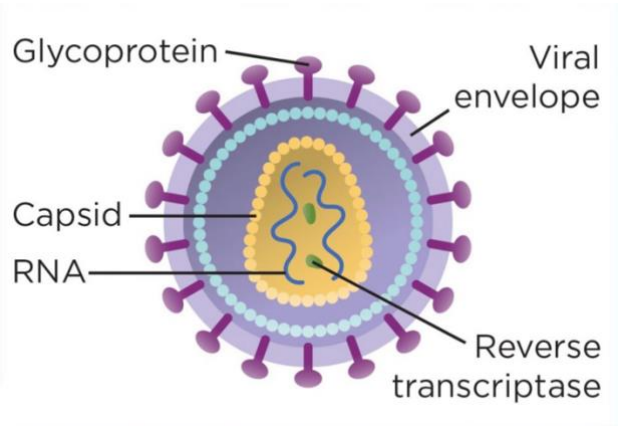
The Biology:

HIV is a virus of the immune system. Whether acquired via unsterilised needles, sexual intercourse or from a mother to a foetus, the crossing of bodily fluids provides a medium for the transmission of the HIV virus. HIV is a retrovirus; a virus whose DNA is stored as RNA. The Capsid of the HIV particle has the enzyme reverse transcriptase which, when the virus binds to the CD4 T cell, converts the synthesised RNA back into DNA, which is incorporated into the DNA of the host CD4 T cell. The HIV virus particle expresses the protein Gp120 on its cell membrane along with the glycoprotein Gp41. The Gp120 protein is complementary to the CD4 protein presented on certain T cells (helper), macrophages and dendritic cells. Once the GP120 receptor binds to CD4, the DNA that has been reverse transcribed enters the nucleus of the target cell and its DNA overtakes control of the cell. Once the HIV virus is in control of the cell it will trigger mechanisms causing cell death. One mechanism is necrosis, starving the cell of oxygen and the necessary molecules for chemical reactions within the cell. Another is apoptosis, which is programmed cell death (the cell commits suicide). This presents problems within the body as our main immune defence is comprised of CD4 T helper cells, macrophages and dendritic cells. This means the human body has relatively no defence against invading pathogens. What's left are our CD8 T killer cells. Once infected with the HIV virus, our bodies enter a phase called seroconversion. During seroconversion, the CD8 killer T cells detect the presence of the HIV virus and initiate an immune response against the virus called a CD8+ cytotoxic T cell (CTL) immune response. This is the crucial point. The CTL response kills virus infected cells. (Janeway, 2005)



The Maths:

The death rate of the HIV infected cell has been calculated showing that the life span of infected CD4+ T cells is one to two days which does not depend on the virus load, or immune response in these patients. The equations that represent the attack of the HIV virus on T cells are as follows:

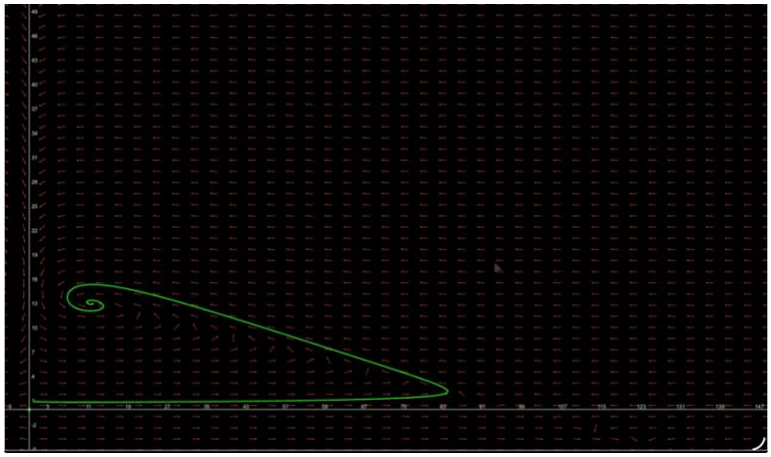
$$\frac{\mathrm{d}}{\mathrm{d}t}I = rI(1 - I/K) - \delta I$$
$$\frac{\mathrm{d}}{\mathrm{d}t}E_i = \frac{pE_i a_i I}{h + E_i + a_i I} - dE_i, \qquad i = 1, 2, \ldots$$

$$\delta = k \sum_{i=1}^{n} a_i E_i.$$

Where:

- I is the number of infected cells at time t. (x)
- E_i is the number of killer cells in the i^{th} immune response. (y)
- The proliferation rate of the immune responses is determined by a competitive saturation function allowing a maximum division rate, p when $a_i \gg h + E_i$, and requiring more infected cells at higher cell numbers.
- h = 100 cells.
- the parameter a_i is a number between 0 and a that measures the affinity of each response for the epitopes expressed by infected cells. A CTL with an affinity a_i = 1 requires the lowest amount of infected cells to become stimulated. (Lythe, 2016)

I then plotted these equations onto a phase plane plotter where you are able to modify some of the numbers in the equation to show how the destruction of T cells changes based on parameters.
The equations I inputted into the phase plane plotter are as follows: (Dews-Flick, 2019)

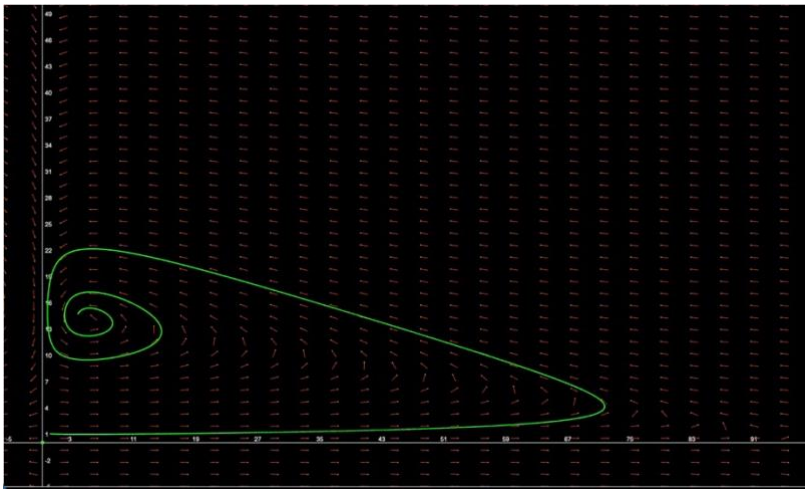


1. 1.5*x*(1 - x/100) - (0.1*1.0*y)*x
2. (1*y*1.0*x) / (100 + y + 1.0*x) – 0.1*y

- X range: -5,150
- Y range: -5,50
- Start Point: 1,1

The x axis represents the number of cells infected by HIV virus particles and the y axis represents the magnitude of your CTL response. The graph provides a quantitative representation of seroconversion. As the x axis (the amount of HIV infected cells) increases to a detectable number by the immune system, the y axis (magnitude of CTL response) increases and as it does so, the amount of HIV in the body decreases as the graph reverses its

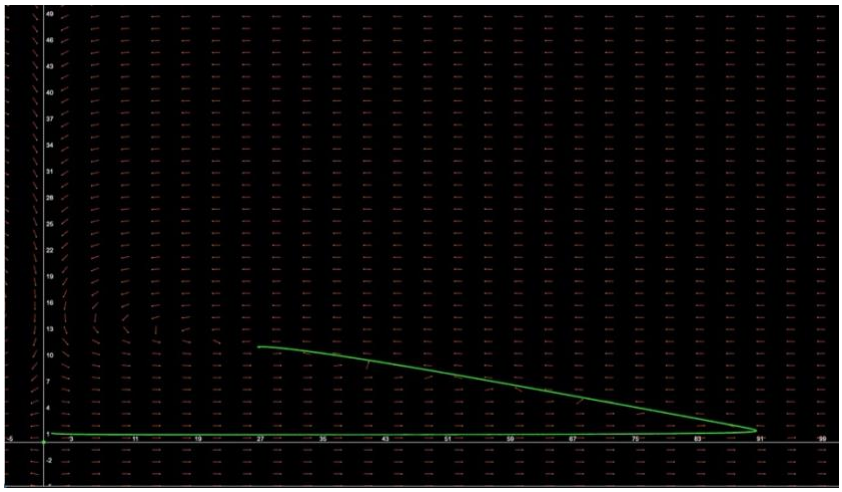
direction on the x axis. The limit to the number of cells infected until the equation no longer works is 100 cells, which, in reality, would of course be many more cells before death is reached. HIV is said to have developed into AIDS once the CD4 T cell count drops below 200 μl^{-1}. This equation can be manipulated to predict what different responses to HIV infection looks like by changing the numbers in the equation.
The graph now looks like this when I input the numbers:



1. 1.5*x*(1-x/100)-(0.1*1.0*y)*x
2. (1*y*2*x)/(100+y+1.0*x)-0.1*y

A_i, the affinity of the CTL response to infected cells increased from 1 to 2. The number of HIV infected cells before the CTL response is stimulated decreases. In addition, the magnitude of the CTL response (y axis) is much larger and reduces the number of HIV infected cells to zero, until the CTL response drops again and the HIV count rises. In reality, the HIV count would not be zero but very low (possibly undetectable). This makes the phase of seroconversion very difficult to detect because the infected human would be asymptomatic which could last for years before spiralling down into AIDS. This also makes it very difficult to trace the journey of the HIV virus as the point of infection could have been at any time in the decade before developing AIDS. The magnitude of a_i depends on the individuals' immune system and its speed/strength.

If I alter a_i once again so the second equation is (1*y*0.5*x)/(100+y+1.0*x)-0.1*y, the graph looks like this:



The affinity of your CTL response to the infection is decreased. Therefore, more cells are infected with HIV before the CTL response is initiated and the magnitude of the CTL response is greatly reduced. The CTL response also can't reduce the amount of HIV as far. This graph would represent someone with a weaker immune response.

What's my point?

This is key because individual (1), with an a_i of 2 would spend longer in the seroconversion phase than individual (2) with a_i: 0.5. This possibly indicates that there is

more time and opportunity to treat individual (1) so they have more of a chance of recovery, however, as their CTL response is much more effective than individual (2)'s their HIV would be virtually undetectable and is therefore more likely to go unnoticed. Person (2) may be experiencing flu-like symptoms which would possibly raise some flags. That being said, the awareness and defences we have implemented today against HIV would argue that both individuals would be treated and survive with the same success as each other. The medications we distribute, including reverse transcriptase inhibitors, are so successful in suppressing HIV that, provided the individual continues to take the drugs for life, they can live with HIV being practically undetectable and will not infect others should the opportunity arise.

Bibliography

Dews-Flick, J. (2019). *Phase Plane Plotter*. Retrieved from GitHub Pages Documentation: https://choosedews.github.io/PhasePlane/

Janeway, C. (2005). *Immunobiology.* New York: Garland Science Publishing.

Lythe, G. (2016). *Mathematical Biology.* Leeds.