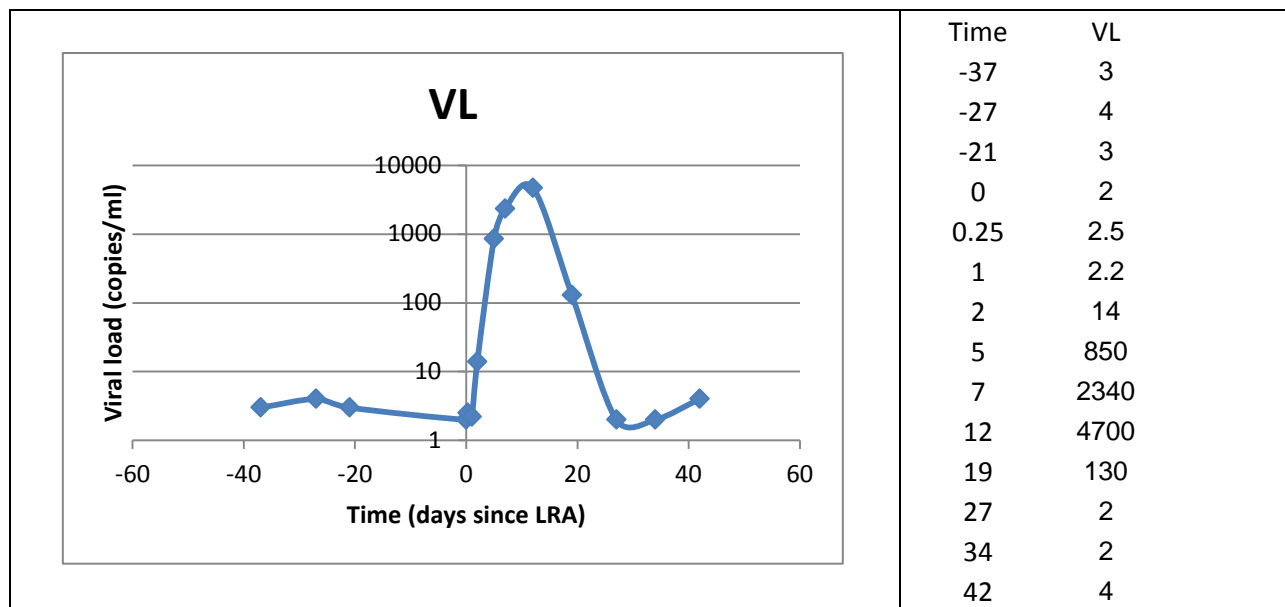


## MODELING LATENCY REVERSAL IN HIV-1 INFECTION

One of the main obstacles to the successful cure of a HIV-1 infected person with eradication of the virus from that person is the existence of a latently infected cellular state. In this state, HIV-1 DNA is stably integrated into the genome of resting T cells and can survive for many months to several years – a state known as latency. Thus, when an infected person is treated with antiretroviral drugs, the viral load can decline to very low undetectable levels, but a reservoir of infected cells is maintained. When the person stops treatment, the eventual activation of a latently infected cell leads to viral production and rekindling of the infection, often to levels similar to before treatment.

An important goal of HIV-1 research is to find ways to stimulate the activation of latent cells, so that HIV-1 DNA can be flushed out of this reservoir. This is currently attempted with so-called 'latency reversal agents' (LRA). In a recent trial with a SIV-macaque model of HIV-1 infection, the following observations were made: 1) The viral load is controlled below detection (<30 copies/ml) without treatment (likely by the immune responses); 2) When an activation agent (LRA) is administered the viral load increases in a pattern similar to primary infection (but at much lower levels). Below we show an example of this behavior.



The objective is to develop a model based on the standard model of viral dynamics that captures this behavior to understand in quantitative detail what is the effect of the LRA. A possible first model is given by

$$\begin{aligned}\frac{dT}{dt} &= \lambda - dT - \beta VT \\ \frac{dI}{dt} &= \beta VT + \alpha L - (\gamma + \delta)I \\ \frac{dL}{dt} &= \gamma I - \alpha L \\ \frac{dV}{dt} &= pI - cV\end{aligned}$$

More details and more complex models can be found in Rong and Perelson, PLoS Comp Biol 5: e1000533. doi:10.1371/journal.pcbi.1000533.

Find the steady state of this model as a starting point, using the data and this steady state as a constraint for one or more parameters. Then simulate the model under different sets of parameter values to find out if it ever displays the behavior observed in the data.