Intermittent HIV-1 Viremia (Blips) and Drug Resistance in Patients Receiving HAART

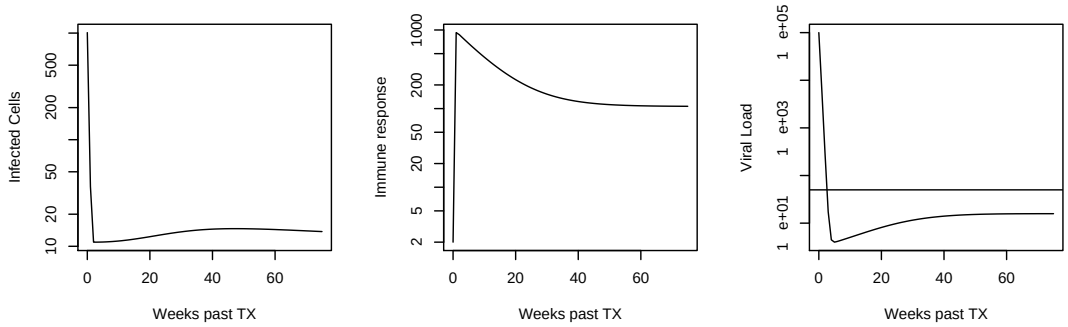
Nettles RE et.al JAMA 2005

Example: A model which produces low level viral steady state after Tx

$$\begin{aligned}
\frac{dX}{dt} &= (1-\epsilon)k_T T - \delta_X X - \gamma X Z \\
\frac{dY}{dt} &= (1-\epsilon)k_M M - \mu M \\
\frac{dZ}{dt} &= s + \alpha X Z - \delta_Z Z \\
\frac{dV}{dt} &= p_X X + p_Y Y - cV
\end{aligned}$$

- X and Y are (short,long)-lived infected cells
- Z is (some measure of) the immune response
- V is the population of viral RNA
- ϵ is drug efficacy
- γ is effectiveness of immune response, α is stimulation of the immune response

Example: A model which produces low level viral steady state after Tx



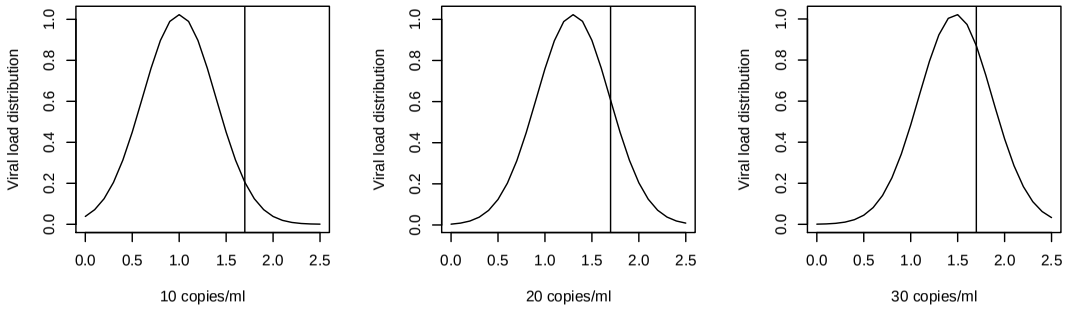
Variance Components in observed viral load

- **Measurement error or assay error** - Different measurements on the same sample will give different results.
- **Sampling error** - Different samples from the same person will give different results
- **Process error** - The true viral load is changing over time. Different time points actually have different levels of viral load - but not deterministically, or according to a model.
- Discussion/Question. Which of these does the CV from the test kit describe?
- Disccusion/Question. Which of there are Nettles et.al trying to describe?

Assumptions used to generate Table 2

- Viral load after treatment reaches a steady state and measurements are normally distributed around that steady state - ie process error = 0.
- Each viral load measurement is independent i.e a measurement just after an observed blip is no more likely to be a blip than one just after a non-blip measurement.
- Variance around that steady state (presumably sampling error and measurement error) is given by 0.39 - computed from the CV from the testing kit.
- Question/Discussion - CV from sampling kit should be for measurement error only - not sampling error - Is this appropriate as used?

Distributions used for calculations in Table 2



Patient 154

- Five episodes, 12 blips total.
- Episodes: 3 blips, 2 blips, 5 blips, 1 blip, 1 blip.
- Recall: Assumes all measurements are independent, ie, a blip is no more or less likely to occur just after another blip.

Six simulated data sets from distribution with mean 30 copies per ml