Are viral blips in HIV-1-infected patients clinically relevant?

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The initialization of Highly Active Antiretroviral Therapy (HAART) in HIV-1 patients is followed by an important decrease of the viral load below the detection limit (e.g. 50 copies/mL). However, this does not imply that the virus has been completely suppressed, supersensitive assays are able to detect the viral load below that limit. There have been observations of transient episodes of viremia above the detection limit ("blips")[1]. Different explanations have been suggested for explain the appearance of these viral blips, the first one was a drug failure, activation of latently infected cells when these cells encounter their relevant antigens[2,3], or simply that these blips represent biological fluctuations around the mean viral load or they are often the result of laboratory artifacts. Thus, there is a current discussion on the medical relevance of the viral blips. In this talk we try to throw some light on these two questions:

- Are they the product of random fluctuations or a different mechanism must be considered?
- Is their likelihood and frequency affected by laboratory procedures?

The previous models are homogeneous models in the blood stream. Latently cell activation has been studied by Perelson et al[2], they proposed a model that considers latently infected cell activation in response to stochastic antigenic stimulation and showed that programmed expansion and contraction of latently infected cells can generate intermittent viral blips. Conway and Coombs[3] formulated a stochastic model where cells and virions are supposed to be homogeneously distributed in the blood (well-stirred system assumption). Under this hypothesis, blips appear only under uncommonly high virion production.

Latent cells and virions are present in very low numbers. Thus, inhomogeneities in concentration are likely. We propose a compartmental model where the total volume of blood is divided in a number of compartments where a local stochastic population model (similar in its ingredients to the Conway-Coombs model), supplemented with random diffusion of cells and virions between compartments. We show two different compartmental models, just considering the healthy CD4+T cells, the latently infected cells, the productively infected cells and the viral load. One of the models taking into account just the dynamics in the body and the other one also taking into account the dynamics of the virus and cells in the blood sample after the extraction.

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