A new model for the dynamics of HIV infection

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Medical Introduction

The first cases of Acquired Immunodeficiency Syndrome - AIDS became known at the end of the 20th century. Since that time the number of infected people has been menacingly growing. In the absence of cure, this disease has spread out and has became a major concern in the area of public health.

For a patient to develop AIDS, it is necessary to have acquired the HIV, human immunodeficiency virus. To reproduce itself, this virus needs to invade the nucleus of a certain kind of animal or plant cells to use the machinery of the cell. Thus, when the cell produces a copy of its genetic code to reproduce itself, it ends up creating a copy of the virus.

Two important classes of white blood cells are T and B cells. There are two types of T cells, the CD4+ T cells and the CD8+ T cells. In the case of the virus of HIV the main target cells are the CD4+ T cells.

The presence of HIV starts a process of disease, which may lead to the development of AIDS. It is usual to claim that this last stage of the disease is achieved when the concentration of T cells is less than 30%, see [1]. The following situations may occur in the process of disease:

- (1) if an individual with HIV does not develop AIDS, the infection has two phases: the primary response, characterized by a growth of the population of the virus during the first weeks, followed by a sharp decline due to the reaction of the immune system; and the period of clinical latency, in which a low concentration of HIV is observed for a long time, see [1] and [2];
- (2) if the individual with HIV develops AIDS, two cases are possible: (2.1) the individual develops AIDS right after the primary response without a period of clinical latency, and (2.2) the individual develops AIDS after the two phases, namely the primary response and the period of clinical latency, always in this order.

To check, in which stage of disease a patient is, it is necessary to observe the concentration of CD4 T and CD8 T cells. We concentrate on CD4 T cells, because they are atacked by this virus more often. Usually it is assumed that a CD4 T cell can be in one of the following states:

- (1) healthy;
- (2) infected;
- (3) removed if it underwent apoptosis, lysis or left the lymphatic organ.

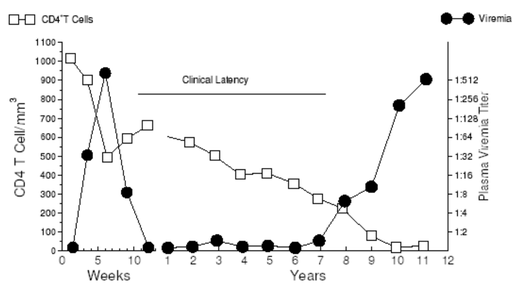

Figure 1: Experimental data from [3] for three phases of the disease. Viremia is the density of virus in the blood, see [4]. The black balls indicate the viremia and the white squares indicate the density of CD4 T cells.

Existing Models

Many studies have been made to describe various aspects of the infection and spread of the HIV virus in the body. Most existing mathematical models use ordinary or partial differential equations.

Other studies use interacting particle systems with discrete time, known as cellular automata, see [1]. [1] described the evolution of concentration of healthy, infected and removed cells observed during a computational experiment and compare them with data obtained *in vivo*.

Our Model

Our model follows the idea of [1] in using a sistem of interacting particles, but unlike [1] our time is continuous. The behavior of our model is described by a system of differential equations with stochastic coefficients, see [5].

We denote by $H(t)$, $I(t)$ and $R(t)$ the numbers of healthy, infected and removed cells at time t respectivelly. We assume that $H(t)$, $I(t)$ and $R(t)$ are so large that they may be treated as real differentiable functions of time t. In our model we assumed:

- (1) any healthy cell becomes infected with a rate γ if it is in contact with an infected one;
- (2) any infected cell may be removed with a rate α or remain infected;
- (3) any removed cell may remain removed or may be restored either as a healthy cell with a rate p_1 or as an infected cell with a rate p_2. Throughout our experiment we assumed that $p_1 = (H(t))^{p_0}$, where $p_0 \in [1, 1.7]$. This condition was obtained by means of our computational experiments.

We interpret p_1 as the responsiveness of the immune system. We denote by p_{max} the maximal possible value of p_1.

We use the following random variables

$$\beta_1(t) = \begin{cases} 1, & \text{if } u_1(t) \leq p_1 \\ 0, & \text{in other cases} \end{cases} \quad \text{and} \quad \beta_2(t) = \begin{cases} 1, & \text{if } u_2(t) \leq p_2 \\ 0, & \text{in other cases,} \end{cases}$$

where $u_1(t)$ and $u_2(t)$ are independent random variables distributed uniformly in $[0, 1]$.

These assumptions lead us to the following system of differential equations:

$$\begin{cases} \dfrac{dH}{dt} = -\gamma HI + \beta_1(t)R, \\ \dfrac{dI}{dt} = \gamma HI - \alpha I + \beta_2(t)R, \\ \dfrac{dR}{dt} = \alpha I - (\beta_1(t) + \beta_2(t))R. \end{cases}$$

Results of Simulation

These differential equations define the functioning of our model. We study them numerically. We note that if $p_{max} = 0.94$ (see figure 2), the patient will certainly develop AIDS in the first stage. If $p_{max} \in [0.95, 0.99]$ (see figure 3), we have the dynamics with the three phases described above. When $p_{max} = 1$ (see figure 4), the infected patient remains with HIV, but does not develop AIDS and therefore shows no signs of disease.

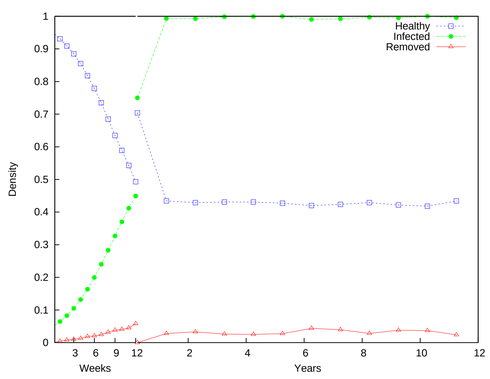

Figure 2: Dynamics of the model with $p_{max} = 0.94$. It is an average of 11 independent computer experiments, which we conducted.

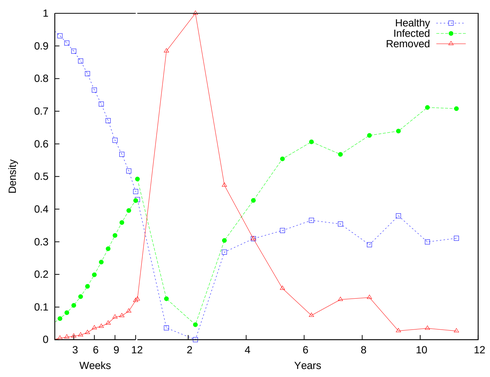

Figure 3: Dynamics of the model with $p_{max} = 0.95$. It is an average of 11 independent computer experiments, which we conducted.

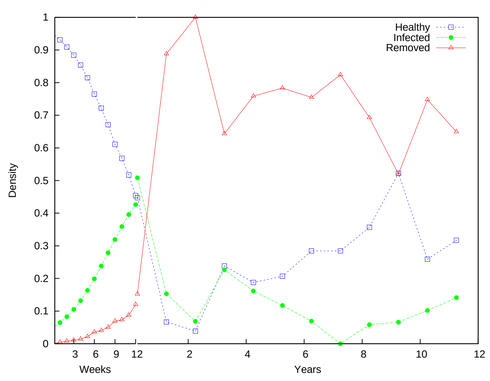

Figure 4: Dynamics of the model with $p_{max} = 1$. It is an average of 11 independent computer experiments, which we conducted.

Figures 2, 3, and 4 show the HIV viral dynamics of our model, and each one of these results was an average of 11 experiments conducted by us. Figure 3 ($p_{max} = 0.95$) shows the three phases. Thus our computer experiments correspond real data shown on figure 1: in both cases we have three phases. To illustrate this dynamics better, we show on the figures 5 and 6 two individuals experiments out of those 11 experiments used to generate figure 3.

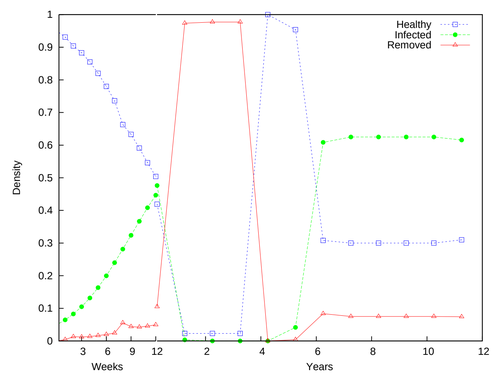

Figure 5: Dynamics of one experiment with $p_{max} = 0.95$.

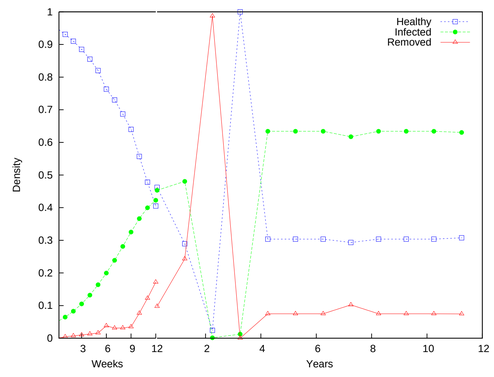

Figure 6: Dynamics of one experiment with $p_{max} = 0.95$.

Conclusion

Our model shows the process of HIV infection. An advantage of our work, as compared with [1], is the following: in [1] the number of cells was constant. Unlike this, in our experiment the densities of healthy, infected and removed cells were variable. In this respect, our model has a better potential to fit real situations.

Acknowledgements

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