Comment on "Dynamics of HIV Infection: A Cellular Automata Approach"

In a recent Letter [1], dos Santos and Coutinho propose a cellular automaton (CA) model of HIV infection. They claim that this model exhibits two time scales that differ 100-fold, corresponding to two time scales in HIV pathogenesis.

The dynamics observed in HIV infection occurs in three phases. After an initial infection with a variable inoculum, the amount of virus in the host grows exponentially in both HIV [2,3] and SIV [4] infections, with a doubling time T_2 of about 0.5 day. Defining the initial fraction of cells infected as p_{HIV}, the duration of this exponential rise is approximately $T_2 \log_2(1/p_{\mathrm{HIV}})$; this period is seen to be approximately 3 weeks, suggesting that p_{HIV} may be as small as 10^{-10}. The viral load then drops to the "set point," corresponding to a fraction of infected cells of the order of 10^{-3} [5]. Throughout the clinically latent period, lasting 6–10 years in most patients, the amount of virus in the body increases slowly, accelerating near the onset of AIDS. The remarkable feature of these dynamics is that nearly all patients progress to disease after several years, of the order of 1000 times the infected cell lifetime of 1–2 days [6,7].

The dos Santos–Coutinho model exhibits a biphasic behavior for certain parameter values. The infected cell density initially grows approximately *linearly* in their model, as infection spreads to nearest-neighbor lattice sites in each time step. They point out that the duration of this phase is proportional to the mean distance between initially infected cells, which scales as $1/\sqrt{p_{\mathrm{HIV}}}$. Thus, for the value $p_{\mathrm{HIV}} \approx 10^{-10}$ estimated above from experiments, the initial infection peak does not occur in the dos Santos–Coutinho model. More generally, the duration of the initial transient is only of the order of 1–10 time steps if $p_{\mathrm{HIV}} \lesssim 10^{-2}$. An example is shown in Fig. 1.

The predictions of the dos Santos–Coutinho model are similarly sensitive to the parameter p_{infec}, corresponding to the fraction of cells that are infected. The authors claim to base the parameter choice $p_{\mathrm{infec}} = 10^{-5}$ on the fraction of infected cells observed *in vivo;* however, this quantity is in the range of 10^{-2} to 10^{-4} in untreated infection [5]. Figure 1 shows the dynamics of the CA for these parameter values. The time scale of the slow increase in infected site density depends strongly on p_{infec} and thus agrees with experiments only for values near that used in their Letter.

The dos Santos–Coutinho model represents a novel approach to the modeling of a preeminent scientific problem. However, we have been unable to find a robust correspondence between the dynamics of their model and the dynamics of HIV infection *in vivo.*

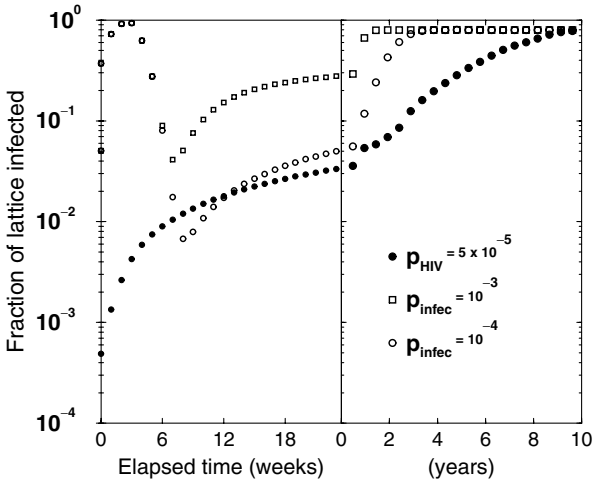

FIG. 1. Sensitivity of the dos Santos–Coutinho model to the initial condition parameter (p_{HIV}) and the influx parameter (p_{infec}). If the initial number of infected lattice sites is too small, there is no distinct first-phase dynamics; the value $p_{\mathrm{HIV}} = 5 \times 10^{-5}$ shown corresponds to $> 10^5$ infected cells in the body. The time scale of the slow increase varies approximately linearly p_{infec}. All other parameter values are as given in Fig. 2 of [1].

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