Physica A 407 (2014) 303–311

Contents lists available at ScienceDirect

Physica A

journal homepage: www.elsevier.com/locate/physa

Modeling dynamics of HIV infected cells using stochastic cellular automaton

Monamorn Precharattana *, Wannapong Triampo

Institute for Innovative Learning, Mahidol University, Thailand
R&D Group of Biological and Environmental Physics (BIOPHYSICS), Department of Physics, Faculty of Science, Mahidol University, Thailand

HIGHLIGHTS

- The primary phase of HIV infection is simulated by two cellular automaton models.
- The new model incorporates effects of the cell-mediated immunity.
- Simulation results are shown in terms of both cell population and pattern formation.
- The obtained dynamics conform to the results from clinical evidence.

ARTICLE INFO

Article history:
Received 24 November 2013
Received in revised form 28 March 2014
Available online 13 April 2014

Keywords:
Stochastic
Cellular automata
Model
Simulation
Cell-mediated immunities

ABSTRACT

Ever since HIV was first diagnosed in human, a great number of scientific works have been undertaken to explore the biological mechanisms involved in the infection and progression of the disease. Several cellular automata (CA) models have been introduced to gain insights into the dynamics of the disease progression but none of them has taken into account effects of certain immune cells such as the dendritic cells (DCs) and the $CD8^+$ T lymphocytes ($CD8^+$ T cells). In this work, we present a CA model, which incorporates effects of the HIV specific immune response focusing on the cell-mediated immunities, and investigate the interaction between the host immune response and the HIV infected cells in the lymph nodes. The aim of our work is to propose a model more realistic than the one in Precharattana et al. (2010) [10], by incorporating roles of the DCs, the $CD4^+$ T cells, and the $CD8^+$ T cells into the model so that it would reproduce the HIV infection dynamics during the primary phase of HIV infection.

© 2014 Elsevier B.V. All rights reserved.

1. Introduction

Ever since the first case of HIV was diagnosed, several scientific works [1–3] have been carried out to understand the disease and answer questions concerning the biological mechanisms of the virus–host interactions. Since the majority of the virus resides in the lymphoid tissue [4], cellular automata (CA) models, taking into account the local interactions, have thus been introduced to understand those interactions and discover more in-depth knowledge of the infectious disease within the infected host.

In a CA model, the system of interest is represented by a grid in which each position takes on one of a number of specified states. The progress of the system is tracked by changing the states of the positions. The state of each position changes according to a set of local rules depending on the state of that position and those of its neighboring positions.

* Correspondence to: Institute for Innovative Learning, Mahidol University, 73170 Salaya, Nakhon Pathom, Thailand. Tel.: +66 865264623.
E-mail addresses: mprecharattana@hotmail.co.th, maewjee@hotmail.com (M. Precharattana).

http://dx.doi.org/10.1016/j.physa.2014.04.007
0378-4371/© 2014 Elsevier B.V. All rights reserved.

Many years ago, several CA models [5–7] were developed to explain the dynamics of HIV infection. However, few models successfully described the two timescales and three phases in the progression of the disease. The first CA model that can reproduce the entire dynamics of HIV infection was proposed by Santos et al. [8]. They described the dynamics of HIV infection based on the change of states of a type of white blood cell, namely the $CD4^+$ T lymphocyte ($CD4^+$ T cell). In their work the state of a position is healthy, infected-A1, infected-A2, or dead. To achieve a more realistic model, Shi et al. [9] modified the model of Santos et al. by incorporating two more states of the $CD4^+$ T cells, namely a latent state and an exposed but not infected state due to drug therapy. Shi et al. also calculated the number of free virus particles released from the infected cells which was then used to adjust the number of neighboring positions that influenced the infection rate at each time step. Definitely, Shi et al.'s model could simulate the three-phase dynamics of HIV infection.

As mentioned above, it seems that the prior models [8–10], processed by changing the states of only one kind of immune cell, i.e. the $CD4^+$ T cells, could completely describe the dynamics of HIV infection. Nevertheless, it was found that the simulation results of the entire dynamics of the models were artifacts of the spatial properties inherent in CA [10,11]. Moreover, they still did not realistically reflect the immune system's responses to viral attack, and their counter-responses.

It therefore becomes our primary objective in this work to propose a CA model to investigate the HIV infection dynamics among the immune cells in the lymphoid tissue. Our model is different from those in the earlier works in that the roles of the dendritic cells (DCs) and the $CD8^+$ T lymphocytes ($CD8^+$ T cells), among the basic immune cell types associated with HIV infection and generally present in the lymphoid organs, are incorporated into the model.

We focus on the dynamics of the DCs, the $CD4^+$ T cells, and the $CD8^+$ T cells residing in the lymph nodes within a human body. Since typically the majority of DCs, immune cells associated with HIV and the main route of HIV transmission, are located in the mucosa (including the oral and vaginal mucosal surface) and the lymphoid tissue, they can be classified as the first cells encountering HIV during sexual transmission [12]. Moreover, it has been suggested that DCs mediate the spread of HIV to $CD4^+$ T cells in the lymphoid tissue *in vivo*. They have also been identified as the most efficient antigen-presenting cells (APCs) during the course of infection [13,14]. Thus, we focus our attention on the influence of DCs in the trans-infection of $CD4^+$ T cells and the initiation of the virus-specific immune response. Besides, it was found that $CD4^+$ T cells are the main source of HIV replication and dissemination in the lymphoid tissue *in vivo* [15,16] and produce more than 98% of the newly free virus particles circulating in the blood stream [17–19]. In addition, several studies [20,21] have clearly demonstrated that the $CD8^+$ T cells play a key role as the primary effectors in the control of HIV after the primary attack.

The paper is organized as follows: first our previous model in Ref. [10], which took into account the states of only one kind of immune cell, namely the $CD4^+$ T cell, is described together with a discussion of desirable modification points. Then, our new CA model is presented, followed by the obtained simulation results.

2. Our previous model in Ref. [10]

In Ref. [10], we utilized a two-dimensional cellular automaton (CA) with a square grid of size $L \times L = 300 \times 300$ to represent a patch of lymphoid tissue within a lymph node. Each position in the lattice is a site randomly occupied by one of five $CD4^+$ T cell states, namely

Naïve $CD4^+$ T cell (N_{T4}) — a cell in an uninfected state,

Infected $CD4^+$ T cell stage 1 ($I1_{T4}$) — a cell that has been recently infected and could infect the healthy naïve $CD4^+$ T cells easily,

Infected $CD4^+$ T cell stage 2 ($I2_{T4}$) — an infected cell that has been weakened by the HIV-specific immune response such as $CD8^+$ T cells and DCs, (Therefore this type of cell could infect the healthy ones only in cases where the concentration is above a certain threshold.)

Latent $CD4^+$ T cell (L_{T4}) — the latent state of an infected cell, and

Dead (D) — an infected cell that is killed by the immune response system.

The initial configuration is depicted as a lymph node consisting of naive $CD4^+$ T cells (N_{T4}) contaminated by stage-1 infected $CD4^+$ T cells ($I1_{T4}$) with a fraction of $P_{I1_{T4}} = 0.005$. Then, the state of each position, which is affected by its Moore neighborhood, is updated according to the CA rules listed below, followed by counting the number of each cell state. Each time step is taken to be one week.

CA rules

Update rule for an N_{T4} cell

(1) *If an N_{T4} cell is in contact with at least one $I1_{T4}$ cell or at least $k = 4$ cells of $I2_{T4}$, the healthy cell becomes an $I1_{T4}$ cell with the probability $P_{\text{inf}} = 0.999$ or becomes an L_{T4} cell otherwise.*

Update rule for an $I1_{T4}$ cell

(2) *An $I1_{T4}$ cell becomes an $I2_{T4}$ cell after $\tau_{I1_{T4}} = 4$ time steps.*

Update rule for an $I2_{T4}$ cell

(3) *An $I2_{T4}$ cell becomes a D cell after $\tau_{I2_{T4}} = 1$ time step.*

Update rule for an L_{T4} cell

(4) *An L_{T4} cell becomes an $I1_{T4}$ cell with the probability $P_{act} = 0.0025$ after $\tau_{L_{T4}} \geq 30$ time steps. Otherwise, it stays unchanged.*

Download English Version:

https://daneshyari.com/en/article/975442

Download Persian Version:

https://daneshyari.com/article/975442

Daneshyari.com