Physica A xx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Physica A

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

A cellular automata model of Ebola virus dynamics

Q1 Emily Burkhead [a,1], Jane Hawkins [b,*]

[a] Department of Mathematics and Computer Science, Meredith College, United States
[b] Department of Mathematics, University of North Carolina at Chapel Hill, CB #3250, Chapel Hill, NC 27599-3250, United States

HIGHLIGHTS

- We construct a stochastic cellular automaton model for the Ebola virus.
- Basic dynamical rules governing viral spread are adapted to the Ebola setting.
- Rigorous results are given about the dynamics.
- Model output simulates the timeline of the infection and captures fatality rates.

ARTICLE INFO

Article history:
Received 2 June 2015
Available online xxxx

Keywords:
Ebola
Cellular automata
Virus spread

ABSTRACT

We construct a stochastic cellular automaton (SCA) model for the spread of the Ebola virus (EBOV). We make substantial modifications to an existing SCA model used for HIV, introduced by others and studied by the authors. We give a rigorous analysis of the similarities between models due to the spread of virus and the typical immune response to it, and the differences which reflect the drastically different timing of the course of EBOV. We demonstrate output from the model and compare it with clinical data.

1. Introduction

Ebola virus (EBOV) is a filovirus that causes severe illness in most humans who are exposed to it. A filovirus is a negative, single-stranded RNA virus whose genome is configured linearly, which differs from a retrovirus such as HIV (human immunodeficiency virus) in its method of replication [1,2]. On the other hand, similarities between these two types of viruses, especially in terms of their negative effect on the immune system, have been studied for some time [3]. In October of 2014 the World Health Organization (WHO) Ebola Response Team published a report estimating the fatality rate of Ebola Virus Disease (EVD) to be around 70.8% [4], but hospitalized patients during the recent outbreak in West Africa had a slightly lower fatality rate. Due to the difficulty in gathering accurate data, differences among patient care, and individual responses to treatment, there is a wide range of fatality rates reported, from 25% to 90% [5].

Because of the extreme virulence of EBOV, autopsies and handling of fluids of infected patients are limited and avoided when possible [5], making mathematical and computer models of the disease a particularly valuable tool. In Ref. [6], a computer model first introduced in 2001 by Zorzenon dos Santos and others [7] for HIV, was amended and studied rigorously to show precisely which viral dynamics were being modeled, how the set of infected cells spreads, and how immune response and drug therapy affects the dynamics. The authors of Ref. [6] extracted some results that apply independently

* Corresponding author.
E-mail addresses: burkhead@unc.edu (E. Burkhead), jmh@math.unc.edu (J. Hawkins).
[1] Current address: Department of Mathematics, University of North Carolina at Chapel Hill, CB #3250, Chapel Hill, NC 27599-3250, United States.

http://dx.doi.org/10.1016/j.physa.2015.06.049
0378-4371/

of the virus in question and showed how varying parameters changed the model. The spread of HIV, as well as the effect of administering drugs, has been modeled by SCAs (see for example, Refs. [6,8–10] and references therein). In Refs. [11,10] the later chronic stages of viral infection were isolated from the model and studied further; these studies involved Markov processes reflecting randomness in the development and control of a chronic viral condition. The EBOV time scale is much shorter and there seems to be no chronic residual disease that has been observed in survivors of the acute illness up to now. Therefore the early viral dynamics control the progression and outcome. In this paper we adapt the early stages of the viral dynamics model in Ref. [6] to EBOV.

A cellular automaton (CA) model is an agent-based model, a computer simulation of the process of the viral spread in an organ based on simple rules. For example, a rule that all viral models have in common is that if a cell is contiguous to an actively infected cell, it becomes infected in the next time step. An SCA uses a small number of simple rules chosen randomly using data-based probabilities, to emulate differences in immune responses to viral spread. By running an SCA simulation, we achieve a variety of outcomes from a single model.

In this paper, we modify the original (HIV) SCA model to use parameters and cellular automata rules specific to the spread of EBOV within an individual organ. While much is still unknown about EBOV, we can use features of existing models for the general properties of viral spread and the body's typical immune response to it. We change some of the salient features of the HIV model as needed for this setting. As of this writing, it is believed that viral mutation occurs much less with EBOV than with HIV though the possibility that EBOV mutations might affect future diagnosis and treatment is being studied [12]. In contrast, it has been known for some time that HIV shows extensive genetic variation even within individual hosts, making HIV one of the fastest evolving of all organisms [13]. Therefore, one of the main modifications we make is to remove the rule leading to viral reservoirs due to mutating viruses, a characteristic property of HIV. We eliminate that as a mathematically possible rule and replace it with a rule that reflects a delayed or slower immune response to the virus. The rest of the rules in the SCA stay the same and this small change immediately speeds up the course of the viral infection to a fairly rapid recovery or death.

The paper is organized as follows. In Section 2 we give the basic definitions of CAs and SCAs, introduce the rules used in our model of EBOV dynamics, and present theoretical results. The output obtained by various computer simulations utilizing different parameters is analyzed in Section 3, and we discuss some conclusions in Section 4.

2. Theory of cellular automata models

2.1. Cellular automata

Let $\mathcal{A}$ denote the finite state space or *alphabet*, $\mathcal{A} = \{0, 1, 2, 3\}$. We use state 0 to represent a healthy cell site in an organ, and states 1 and 2 to represent infectious cells able to infect neighboring cells. State 3 represents a depleted (dead) cell site. Then, we define the integer lattice $\mathbb{Z}^2 = \{\vec{\imath} = (i, j),\ i, j \in \mathbb{Z}\}$, viewed as a subset in the plane (or on a surface, by identifying edges of a polygon). The length of a vector in $\mathbb{Z}^2$ is taken as $\|\vec{\imath}\| = \max\{|i|, |j|\}$. The space on which a cellular automaton acts is $X = \mathcal{A}^{\mathbb{Z}^2}$, which we think of as the integer lattice $\mathbb{Z}^2$ in the plane with exactly one value from the state space $\mathcal{A}$ placed at each coordinate (i, j) in the lattice. The space X is mathematically equivalent to the set of functions from $\mathbb{Z}^2$ to $\mathcal{A}$. So, for each $x \in X$ and $\vec{\imath} = (i, j) \in \mathbb{Z}^2$ we write $x_{(i,j)}$ to denote *the coordinate of x at* $\vec{\imath}$, with $x_{(i,j)} \in \{0, 1, 2, 3\}$. Similarly for any finite set $E \subseteq \mathbb{Z}^2$, we define x_E to be the block of coordinates $\{x_{\vec{\imath}} : \vec{\imath} \in E\}$; i.e., $x_E \in \mathcal{A}^{|E|}$ where $|E|$ is the cardinality of E.

We make X into a compact space by using the classical metric on X, which is defined so that two points are close if their coordinates agree on a large central region. First, we define a neighborhood of radius $k \in \mathbb{N} \cup \{0\}$ about $(0, 0) \in \mathbb{Z}^2$, by $N_k = \{\vec{\imath} = (i, j) : |i|, |j| \le k\} = \{\vec{\imath} : \|\vec{\imath}\| \le k\}$. Then, *the metric* d_X *on* X is defined as follows: for any pair of points $x, \upsilon \in X$, $d_X(x, \upsilon) = \frac{1}{2^k}$ where $k = \min\left\{m : x_{N_m} \ne \upsilon_{N_m}\right\}$. We call a *pattern* any fixed $(2k + 1)^2$ square block of states from $\mathcal{A}$ (or a finite union of $(2k+1)^2$ square blocks), $k \in \mathbb{N}$. We form a basis for the metric topology from the following collection of sets. For any pattern u, define $B_u = \{x \in X : x_{N_k} = u\}$ to be the *u-cylinder of radius k* (centered at $(0, 0)$). B_u is precisely the set of points from X whose central block of coordinates extending out k units in each direction from $(0, 0)$ coincides with the fixed pattern u.

The space X provides a model for an organ that is susceptible to the virus such as liver, spleen, lungs, or skin [5,14]. Each point $x \in X$ represents a configuration of the healthy, infected, and depleted cells of the organ at any given time, and each coordinate $x_{(i,j)}$ shows the state of the organ at that location where a coordinate is either a cell or a site of cells, depending on the organ. In order to dynamically move around within an organ and sample the state at any location, we define the *shift maps on* X as follows:

$$\forall \vec{\imath} = (i, j) \in \mathbb{Z}^2, \quad [\sigma_{\vec{\imath}}(x)]_{(k,l)} = x_{(i+k,j+l)}.$$

With respect to the metric d_X, each shift $\sigma_{\vec{\imath}}$ is a continuous transformation on X. With all this structure in place, we are now able to define a CA.

Definition 2.1. A **2-dimensional cellular automaton (CA)** is a continuous transformation F on X such that for every $\vec{\imath} \in \mathbb{Z}^2$, $F \circ \sigma_{\vec{\imath}} = \sigma_{\vec{\imath}} \circ F$.

It is well-known that each CA is characterized by a local rule (of radius $r \ge 0$), based on the definition of continuity in the metric topology on X. In the next theorem this is made precise.

Please cite this article in press as: E. Burkhead, J. Hawkins, A cellular automata model of Ebola virus dynamics, Physica A (2015), http://dx.doi.org/10.1016/j.physa.2015.06.049