MARKOV CELLULAR AUTOMATA AS MODELS FOR CHRONIC DISEASE PROGRESSION

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Abstract. We analyze a Markov cellular automaton that models the spread of viruses that often progress to a chronic condition, such as human immunodeficiency virus (HIV) or hepatitis C virus (HCV). We show that the complex dynamical system often produces a Markov process at the later stages, whose eigenvectors corresponding to the eigenvalue 1 have physical significance for the longterm prognosis of the virus. Moreover we show that drug treatment leads to chronic conditions that can be modeled by Markov shifts with more optimal eigenvectors.

Contents

1. Introduction 2
2. Preliminaries 4
  2.1. Mathematical background and notation 4
  2.2. Using CAs to model the immune response to a virus 6
3. Markov cellular automata used to model chronic illness 9
  3.1. Adding the probability measure to a topological Markov CA 11
  3.2. Medical interpretation of the measure on the Markov CA 11
4. Drug Intervention in the Model 15
5. The Markov model applied to chronic Hepatitis C 18
Appendix A. Stochastic Cellular Automata 20
  A.1. Measures governing the choices of CA used 23
  A.2. Equicontinuity points of stochastic CAs 23
References 24

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1. Introduction

When studying an extremely complex system it is frequently useful to develop a model which explains or illuminates statistical properties of the process rather than to follow the individual behavior of each of $10^{12}$ or more particles interacting with others nearby. This is the case for immunology and virology studies of diseases with underlying mechanisms often too complicated to model precisely; this statistical or global dynamics approach has been used by many authors [1, 4, 5, 6, 8, 9, 12, 11, 13, 16, 17, 22, 23, 33, 34, 35]. Often these models and computer simulations are used without rigorous analysis of their mathematical underpinnings. In this paper we discuss Markov cellular automata models as a noninvasive method for analyzing some aspects of chronic diseases. Cellular automata (CA) models used in the study of immune responses have been used for decades (eg., see the references listed above which also contain references to earlier studies). The authors (and Burkhead) introduced the use of Markov CAs to model end stage virus dynamics in [1], and to our knowledge this is the first analysis that shows it applies quite generally to chronic diseases.

In [35] a mathematical model for the spread of HIV within a lymph node was presented and studied. The paper [1] gives a rigorous mathematical study showing that the model accurately reflects the timing of the virus spread up to the terminal stages when AIDS sets in. The model works roughly as follows. An initial infection is simulated by introducing a random sprinkling of infected lymph cells (1’s) into a grid of healthy cells (0’s), with a density determined by clinical data [25]. At each time step one of three possible CAs is applied with certain data-driven probabilities and independently chosen at each site. Of the 3 CAs, labelled $\mathcal{N}$, $\mathcal{C}$, and $\mathcal{D}$, the CA $\mathcal{N}$ reflects the usual course of a disease such as a flu-virus, with the immune response fighting off the virus (and this CA receives the highest probability), $\mathcal{C}$ reflects that there are reservoirs of infected cells lying dormant that somewhat randomly (and rarely) spring to action, and the third, $\mathcal{D}$ represents the possibility that a depleted cell site remains in that state, instead of being replaced immediately by a healthy cell.

In [1] we established that once enough time has elapsed the more orderly view of the course of the disease disappears, and the state of a cell in the lymph node (actually a site of cells as explained in [1]) seems to evolve in a more random way that only depends on its current state. In the intervening years, many authors have worked on the model [24, 23, 16, 4, 5], inserting drugs into the model; this was also done in Section 6 of [1]. Most of the newer mathematical models
are far more complicated than the original one. Our goal in this paper is to simplify the model by turning our focus to the later stages and providing a model whose mathematical underpinnings come from some basic theorems in ergodic theory.

We focus on the CD4 cell counts because according to a large study using collaborative data involving over 75,000 HIV-infected adults ([20], p. 7):

"In all these studies, CD4 cell count was the strongest prognostic factor for disease progression; viral load was at best only weakly predictive of progression in models with time updated CD4 cell counts."

Often drugs are not introduced until the HIV has been present for some time and the CD4 count is already low; e.g. the levels remaining in the system used in [20] are 20%, 30%, and 50% of the healthy CD4 count, for drug treatment to be deemed essential, recommended, or worth considering respectively. Therefore according to [1] the three CAs have been interacting long enough that the big picture is somewhat random and the final stage model can be used.

One important advantage of this approach is that the model is a simple Markov shift whose relevant eigenvectors accurately reflect the final stage healthy CD4 cell count in patients. We showed in [1] that without drugs the final limiting CD4 count is barely above 14% which is well below the medically defined 20% AIDS-defining cut-off [19]. Secondly when drugs are introduced we can show how this affects the underlying Markov shift, the incidence matrix along with its dominant eigenvector, and the invariant probability measure, and estimate the new limiting CD4 cell counts. The model reflects the findings of the longitudinal cohort study done in [20]: namely patients with a lower beginning CD4 count are helped more, while patients with a moderately high starting CD4 level are only helped a little. This phenomenon is explained by the Birkhoff Ergodic theorem applied to the model, which shows that the limit is independent of the starting point. A conclusion to draw based on this mathematical model is that drug intervention should occur before the end stages.

Before the Markov stage has been reached, from [35] and [1] we know that the stochastic cellular automaton (SCA) models control the dynamics, and in that scenario the “healthy recovery model” (\(N\) described above and defined in Section 2.2 showing normal immune response) is the one that prevails. In that setting, before going over the threshold into the Markov dynamics, complete recovery is a mathematically possible outcome.
In the clinical setting, drug toxicity and reduction in drug effectiveness over time inhibit the search for a cure [28, 29], and in our model, the measures used to model the dynamics suggest that the optimal outcomes can be reached before this occurs (see Figure 8), reinforcing the idea that early drug intervention is best. Despite many disadvantages of an early rigorous drug treatment such as the potential for pill fatigue and short-term and long-term toxicity this hypothesis has been shown to have definite advantages in some patients ([2],[14]).

The paper proceeds as follows. In Section 2 we begin with some mathematical definitions for the model. Since we discuss limiting behavior it is important to have a metric; that is, a notion of what it means for one configuration of the system to approach a limit. We also describe the original model used in [35] and [1] to describe the dynamics of HIV in a lymph node. In Section 3 we turn to the model which simulates the chronic stages of HIV and give a brief mathematical description of how it works. Section 4 describes how the math model shows the effects of drug therapy. We apply the analysis in Section 5 to analyze the chronic hepatitis C dynamics. Finally we provide an appendix giving a mathematically rigorous definition of an SCA since this is important to understand how the dynamics progress before the chronic state is reached.

2. Preliminaries

One main claim of this paper is that despite the fact that many complicated models exist in the literature, the chronic stage of viral disease can be studied using a simple Markov model. In the appendix we review the original SCA model appearing in [35] and worked on rigorously in [1]. From both these studies the probabilistic laws governing a SCA will bring the dynamics to a Markov system when the virus is not eradicated completely, which can be expressed easily in terms of 7 constant CAs. Therefore using some data-driven analysis, we make a single simple model and show how drug therapy is consistent with, and explained by, this Markov CA as well. We introduce the basic mathematical building blocks for the models studied in this section, including a metric that explains what it means to discuss limiting behavior.

2.1. Mathematical background and notation. We begin by giving the mathematical setup for a cellular automaton (CA). Let \( \mathcal{A} \) denote a finite state space \( \mathcal{A} = \{0, 1, \ldots, m\} \). State 0 represents a healthy cell site in an organ, and states 1 through \( m - 2 \) represent infectious cells able to infect neighboring cells. State \( m - 1 \) represents an infected cell whose ability to infect a neighboring cell has weakened so that a
healthy cell needs many of these surrounding it (a parameter which we usually set to be 4) before it gets infected; that is, \( m - 1 \) is an infected and very weakly infectious cell. State \( m \) is a depleted (dead) cell.

We find that two dimensions captures most of the dynamics; this corresponds to thinking of a lymph node as a sort of cylinder. All of the math analysis that follows can be done for dimension \( d = 3 \) as well, but the analysis is the same. However using \( d = 2 \) makes the concepts and notation easier to explain in this paper. We define the space of vectors \( \mathbb{Z}^2 = \{ \vec{r} = (i, j), i, j \in \mathbb{Z} \} \). It is useful to think of \( \mathbb{Z}^2 \) as a lattice of integers in the plane (or on a surface, by identifying edges of a polygon in the plane). On \( \mathbb{Z}^2 \) we define length as: \( \| \vec{r} \| = \max\{|i|, |j|\} \), the larger absolute value of the two indices.

We define a CA on the space:

\[
X = \mathcal{A}^{\mathbb{Z}^2},
\]

which we should think of as the integer lattice \( \mathbb{Z}^2 \) with a coordinate from the state space \( \mathcal{A} \) placed at each \( (i, j) \) coordinate in the lattice. Since each location \( (i, j) \) is assigned exactly one state from \( \mathcal{A} \), mathematically we define \( X \) as the space of functions from \( \mathbb{Z}^2 \) to \( \mathcal{A} \). In this way each for each \( x \in X \) and \( \vec{r} = (i, j) \in \mathbb{Z}^2 \) we write \( x(\vec{r}) \) to denote the coordinate of \( x \) at \( \vec{r} \), with \( x(\vec{r}) \in \{0, \ldots, m - 1\} \).

Let \( E \subset \mathbb{Z}^2 \) be any finite set; by \( x_E \) we denote the block of coordinates \( \{x_{\vec{r}} : \vec{r} \in E\} \) i.e., \( x_E \in \mathcal{A}^{|E|} \) where \( |E| \) is the cardinality of \( E \). We define a neighborhood of radius \( k \in \mathbb{N} \cup \{0\} \) about \( \vec{0} \in \mathbb{Z}^2 \), by:

\[
N_k = \{\vec{r} = (i, j) : |i|, |j| \leq k\} = \{\vec{r} : \|\vec{r}\| \leq k\}.
\]

Note that \( |N_k| = (2k + 1)^2 \); it is just pairs of integers \( (i, j) \) with \( |i| \leq k \) and \( |j| \leq k \).

Now if \( u \) is a fixed \( (2k + 1)^2 \) square pattern of symbols from \( \mathcal{A} \), centered at \( \vec{0} \in \mathbb{Z}^2 \), then \( B_u = \{x \in X : x_{N_k} = u\} \) is the \( u \)-cylinder of radius \( k \) (centered at \( \vec{0} \)). \( B_u \) is precisely the set of points from \( X \) whose central block of coordinates extending out \( k \) units in each direction coincides with the fixed pattern \( u \).

The shift map on \( X \) corresponds to sampling different areas in the same affected organ (lymph node, liver, etc) and expecting the outcome to be more or less independent of the precise location of the sample. We define the shift maps on \( X \) as follows:

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

In order to discuss continuity of \( \sigma_{\vec{r}} \) we need to recall the classical metric on \( X \). For any pair of points \( x, v \in X \), \( d_X(x, v) = \frac{1}{2^k} \) where \( k = \min \{i : x_{N_i} \neq v_{N_i}\} \); \( X \) is compact with respect to the metric topology. This metric topology makes the points \( x \) and \( v \) close to each other if
and only if their central blocks of coordinates agree; i.e., \( x \) and \( v \) look the same when restricted to \( N_k \) for some \( k \in \mathbb{N} \).

We start with the first mathematical definition of a CA, but immediately follow it by an equivalent more practical one.

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

It is well-known that each CA is characterized by a local rule using the definition of continuity in the metric topology on \( X \). In the next theorem we use the symbol \( r \) to denote the radius of the local rule.

**Theorem 2.2.** [10] The map \( F \) on \( X \) is a CA if and only if there exists an integer \( r \geq 0 \) and a map \( f : A^{(2r+1)^2} \to A \) such that for every \( x \in X \),

\[
F(x)_{\vec{r}} = f(x_{N_r+\vec{r}}).
\]

The map \( f \) that appears in (2.1) is the local rule for the CA \( F \) as it describes it completely.

To summarize, a CA is a map or rule that updates each coordinate in \( X \) at each time step by looking only at nearby coordinates. If \( F \) is a CA, we iterate \( F \) using the notation \( F^k(x) = F \circ \cdots \circ F(x) \) to denote composition with itself \( k \) times.

### 2.2. Using CAs to model the immune response to a virus.

We describe a 2-dimensional CA, which we denote by \( \mathcal{N} \) for "normal immune response", and which is shown in Figure 1. It is a single CA where white represents 0, healthy cells; light blue cells represent state 1, the initial infection, as shown in the first frame. Each frame is labelled by 4 pieces of data in brackets above the frame. The first entry is the time step, showing how many increments of time have passed. The next 3 entries show percentages of cells in healthy (0), infected \((1 - 5)\), and depleted (6) states respectively. (Note that one increment of time varies according to the virus.) The blue gets darker as time passes showing the passage of time as a higher numbered state, revealing the spread of the virus; the darker color often represents the next generation of the mutated virus. In a healthy individual with a functioning immune system, after a time the infected cells die and are replenished by healthy ones at a rate faster than the infection. Therefore we see a return to all 0’s after a few more iterations. The local rule \( \nu \) that defines the CA \( \mathcal{N} \) is given here.
Figure 1. The CA $N$ represents a normal immune response to a virus, where infected cells are replenished by healthy ones and the virus is eradicated.

**Local rule for $N$.** Consider the state space $A = \{0, 1, \cdots, 6\}$ and define the local rule $\nu : A^{3 \times 3} \rightarrow A$ as follows:

\[
\begin{align*}
\nu (\begin{array}{ccc}
\ast & \ast & \ast \\
\ast & 0 & \ast \\
\ast & \ast & \ast \\
\end{array}) &= \begin{cases} 
1 & \text{if at least one } \ast \text{ is } 1, 2, 3, \text{ or } 4, \text{ or if at least } 4 \ast \text{'s are } 5 \text{'s} \\
0 & \text{otherwise}
\end{cases}, \\
\nu (\begin{array}{ccc}
\ast & \ast & \ast \\
\ast & a & \ast \\
\ast & \ast & \ast \\
\end{array}) &= a + 1 \text{ for } 1 \leq a \leq 5, \\
\nu (\begin{array}{ccc}
\ast & \ast & \ast \\
\ast & 6 & \ast \\
\ast & \ast & \ast \\
\end{array}) &= 0.
\end{align*}
\]

The CA $N$ occurs most of the time in the stochastic model discussed in [35] and [1]. Using the notion of distance coming from the metric described above, we showed in [1] that:

\[
\lim_{k \to \infty} A^k(x) = \overline{0}
\]

for every initial configuration $x \in X$ consisting of 0’s and 1’s, where $\overline{0}$ denotes the point with a zero in every coordinate. That is, initial infections are repaired by the normal immune response.

Similarly we use two small variations on this CA to model what happens if the immune system is compromised or if the virus mutates too fast for it to be wiped out. We call the two other CAs $C$ for weak response and $D$ for depleted response; we define them by their local
rules, \( c \) and \( d \) respectively Using the same state space \( \mathcal{A} \), we define the local rules \( c, d : \mathcal{A}^{3 \times 3} \to \mathcal{A} \) by:

\[
c, d \left( \begin{array}{ccc}
* & * & * \\
* & a & * \\
* & * & *
\end{array} \right) = \nu \left( \begin{array}{ccc}
* & * & * \\
* & a & * \\
* & * & *
\end{array} \right) \quad \text{for any } a \neq 6,
\]

while

\[
c \left( \begin{array}{ccc}
* & * & * \\
* & 6 & * \\
* & * & *
\end{array} \right) = 1, \quad d \left( \begin{array}{ccc}
* & * & * \\
* & 6 & * \\
* & * & *
\end{array} \right) = 6.
\]

Denote by \( \mathcal{N}, \mathcal{C}, \mathcal{D} : \mathcal{A}^{2 \times 2} \to \mathcal{A}^{2 \times 2} \) the CA with local rule \( \nu, c, \) or \( d \), respectively.

Figures 2 and 3 show the dynamics of \( \mathcal{C} \) and \( \mathcal{D} \); we proved in [1] that:

\[
\lim_{k \to \infty} \mathcal{D}^k(x) = \mathbf{6}
\]

for every initial configuration \( x \in \mathcal{X} \) consisting of 0’s and 1’s, where \( \mathbf{6} \) is the point with all 6’s. When an otherwise healthy person is infected with HIV, we combine these CAs randomly, using the rule \( \mathcal{N} \) slightly less than 99% of the time, to form a stochastic CA. The probabilities chosen for the model are data-driven. This is explained in detail in a variety of papers (see in particular [1]), but we provide a definition of an SCA in the Appendix.
Figure 3. The CA $\mathcal{D}$ represents the weakening of the immune system so that cells are not replenished.

3. Markov Cellular Automata Used to Model Chronic Illness

For this dynamical analysis we focus on the event that the immune system does not clear out the infection and therefore there is not a full set of equicontinuity points converging to the healthy state. Specifically we look at the dynamics of a chronic illness such as HIV or Hepatitis C and describe a model for the limiting viral presence in the lymph node or liver, with and without drug intervention.

We describe a dynamical system on $X = \mathcal{A}^\mathbb{Z}^2$, a CA of radius 0, determined by a single rule at each $\vec{r} \in \mathbb{Z}^2$. Our claim is that this CA provides an excellent simple model for the virus dynamics after the original stochastic CA has been iterated so many time steps that there are no longer coherent areas of healthy and unhealthy cells. We denote the CA on $X$ by $S$, and the local rule we write as $\sigma$ and define it to be a shift on a $\Sigma_B \subset \mathcal{A}^\mathbb{Z}$.

Under the assumption of no drug intervention, we use as the model the SCA given by $\mathcal{N}, \mathcal{C},$ and $\mathcal{D}_i$ (details are given in the Appendix), to give the incidence matrix $B = B_{ij}, i, j = 0, 1, \ldots, 6$, where $B_{ij} = 1$ if a cell can go from state $i$ to state $j$ in one time step, and 0 otherwise. In Figure 4 we show the incidence graph which determines the matrix (and vice versa). The directed graph in Figure 4 has vertices representing the possible states in $\mathcal{A} = \{0, 1, 2, 3, 4, 5, 6\}$ and vertices $i$ and $j$ are connected by a directed edge if a cell in state $i$ can transition to state $j$ in one time step of the stochastic CA.
Figure 4. The incidence matrix used to determine \( \Sigma_B \), assuming no drug intervention

The corresponding incidence matrix is given by:

\[
B = \begin{pmatrix}
1 & 1 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 1 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 1 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 1 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 1 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 1 \\
1 & 1 & 0 & 0 & 0 & 0 & 1
\end{pmatrix}
\]  

(3.1)

The graph or the matrix \( B \) defines a subshift (of finite type), \( \Sigma_B \subseteq \mathcal{A}^\mathbb{Z} \), given by \( \Sigma_B = \{ \alpha = \ldots a_0 a_1 \ldots \in \mathcal{A}^\mathbb{Z} : B_{a_i a_{i+1}} = 1 \} \). The natural dynamical system to consider on \( \Sigma_B \) is the shift \( s \); namely \( s(\alpha)_i = \alpha_{i+1} \). This shift will be used as the local rule in the Markov CA.

**Definition 3.1.** We define a (topological) Markov CA as follows: using the state space \( \mathcal{A} = \{0, 1, \ldots, 6\} \) define the local rule \( m : \mathcal{A}^{3 \times 3} \to \mathcal{A} \) as follows:

\[
m \begin{pmatrix}
* & * & * \\
* & a & * \\
* & * & *
\end{pmatrix} = s(\alpha)_0
\]

for all \( a \in \mathcal{A} \) and any \( \alpha \in \Sigma_B \) with \( a_0 = a \). We write \( M \) for the Markov CA with local rule \( m \).

We note that this is a rule of radius 0 since the state of a cell at time \( t + 1 \) depends only on its state at time \( t \) and not on the states of any of its neighbors. On the other hand we have that \( M \) is actually an SCA because if \( \alpha, \beta \in \Sigma_B \) with \( a = a_0 = \beta_0 \), then \( s(\alpha)_0 \) might not be the same as \( s(\beta)_0 \), for example if several successor states are allowed.
after $a$. There is a mathematical way to make this precise; we look at a larger space by playing which also includes a copy of $\Sigma_B$ over each coordinate $(i, j) \in \mathbb{Z}^2$ in $X$, and this is analyzed in [1]. It is also discussed in the Appendix of this paper. However to simplify the mathematics, we turn to the measure to finish the construction.

3.1. Adding the probability measure to a topological Markov CA. Given an incidence matrix such as $B$ above, we define a Markov probability measure $\mu$ on $\Sigma_B$ as follows. Assume we have a probability vector $p = (p_0, \ldots, p_6)$; this means $p_k > 0$ and $\sum_k p_k = 1$. In addition we have a stochastic matrix $P = (p_{ij})_{i,j = 0, \ldots, 6}$; by definition this means $p_{ij} \geq 0$ and all row sums are 1, and we assume that

$$(3.2) \quad pP = p.$$ 

From the pair $(p, P)$ we define a measure $\mu$ on $\Sigma_B$ by setting, for each finite sequence $c_0, c_1, \ldots, c_m$,

$$\mu(\{\alpha : a_k = c_k, k = 0, \ldots, m\}) = p_{c_0} \cdot p_{c_0} \cdot \cdots \cdot p_{c_{m-1} c_m}.$$ 

We call $(s, \mu)$ the $(p, P)$-Markov shift, and note that it is invariant for $s$ on $\Sigma_B$.

The matrix $P$ is irreducible if for each pair $i, j \exists l > 0$ such that $(P^l)_{ij} > 0$. That Markov measures can be found for any irreducible $P$ follows from the following result (cf. [32]).

**Theorem 3.2.** (Perron-Frobenius Theorem) Let $P$ be an irreducible stochastic matrix. Then 1 is an eigenvalue of $P$ such that:

1. 1 is a simple root of the characteristic polynomial of $P$,
2. 1 has strictly positive right and left eigenvectors,
3. these eigenvectors are unique up to constant multiple,
4. $1 \geq |\beta|$ for all other eigenvalues $\beta$ of $P$.

We note that the vector $p$ satisfying Eqn (3.2) is the left eigenvector for the eigenvalue 1 and satisfies the conclusions of the Perron-Frobenius Theorem.

3.2. Medical interpretation of the measure on the Markov CA. The left eigenvector for the left eigenvalue 1 for $P$, the probability vector $p$, represents the probability that if we sample a cell randomly from a lymph node, then the cell will be in state $a \in \{0, 1, \ldots, 6\}$. Recall that only 0 represents a healthy cell. The stochastic matrix $P$ represents the probability that if a cell is currently in state $i$, then with probability $p_{ij}$ after one time step it will be in state $j$. Since state 0 represents the healthy cells, then the first entry in $p$, $p_0$, is the proportion of healthy cells overall. The other entries of $p$ are not
as important because all the other states represent either infected or dead cells. It is therefore the leading term of the invariant vector \( p \) we would like to control. Amazingly enough, a classical theorem from ergodic theory, Theorem 3.5 below, gives us a tool for finding that leading entry.

Markov measures lead to understandable longterm behavior of a shift map, and they give information that is easy to estimate, as is shown in the next result.

**Lemma 3.3** ([32], Lemma 1.18). Let \( P \) be a stochastic matrix, having a strictly positive probability vector, \( p \), with \( pP = p \). Then

\[
Q = \lim_{N \to \infty} \frac{1}{N} \sum_{n=0}^{N-1} P^n
\]

exists. The matrix \( Q \) is also stochastic and \(QP = PQ = Q \). Any eigenvector of \( P \) for the eigenvalue 1 is also an eigenvector of \( Q \) and \( Q^2 = Q \).

The notion of an ergodic measure is important and reflects the indecomposable nature of the dynamical system; this corresponds to the fact that a virus spreads throughout a lymph node over time, and is not contained in one region. the Markov shifts we use here are more chaotic than that but we do not study that here.

**Definition 3.4.** We say that the shift \( s \) is ergodic on \( \Sigma_B \) with respect to an invariant probability measure \( \mu \) if: \( s^{-1}A = A \) for some measurable set \( A \subset \Sigma_B \) implies that \( \mu(A) = 0 \) or \( \mu(A) = 1 \).

**Theorem 3.5** ([32]). Consider the \( (p, P) \) Markov shift \( s \) on \( \Sigma_B \). Assume that \( p_i > 0 \) for each \( i \) where \( p = (p_0, \ldots, p_6) \). Let \( Q \) be the matrix obtained in Lemma 3.3. Then the following are equivalent:

1. \( s \) on \( \Sigma_B \) is ergodic with respect to the measure \( \mu \) determined by \( (p, P) \).
2. All rows of the matrix \( Q \) are identical and each row is \( p \).
3. Every entry in \( Q \) is strictly positive.
4. \( P \) is irreducible.
5. 1 is a simple eigenvalue of \( P \) with eigenvector \( p \).

For a patient with HIV, the analysis given in [1] gives rise to a matrix \( P \) with a set of parameters chosen that are well supported by the data available. We give a brief explanation of how we determine the entries in \( P \). We associate transition probabilities to the edges of the graph based on the local rules. Since each rule \( \nu, c, d \) has the rules 1 \( \to \) 2, 2 \( \to \) 3, 3 \( \to \) 4, 4 \( \to \) 5, and 5 \( \to \) 6, for all \( j \in \{1, 2, 3\} \), these directed
edges each have weight 1. The directed edges incident to 6 are weighted according to the probability of using \( \nu, c, \) or \( d \) when the site is in state 6. Therefore we weight the edge 6 \( \rightarrow \) 0 with \( p_1 = .9899 \), 6 \( \rightarrow \) 1 with \( p_2 = 9.9 \times 10^{-6} \), and 6 \( \rightarrow \) 6 with \( p_3 = .01 \) arrived at using the biological analysis in [1]. Finally, the weights of edges incident to 0 are determined by counting how many of the \( 7^8 \) total \( 3 \times 3 \) patterns with a center 0 update to 0 and how many update to 1. The transitions are the same under each local rule, (but can change across the board according to some parameter changes). We compute the number of patterns which update to 0. For this to be the case, none of the 8 neighbors can have value 1, 2, 3, or 4, and so each neighbor must have value 0, 5, or 6. Further, there must be no more than four 5’s and so we have \( z = \sum_{k=0}^{3} \binom{8}{k} 2^{8-k} = 4864 \) of the \( 3 \times 3 \) patterns with a center 0 which update to 0. Thus 0 \( \rightarrow \) 0 has weight \( \frac{z}{7^8} = \frac{4864}{5764801} \approx 0.000843741 \) and 0 \( \rightarrow \) 1 has weight \( 1 - \frac{z}{7^8} \).

\[
P = \begin{pmatrix}
8.43741 \times 10^{-4} & 0.999156 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\
.9899 & 9.9 \times 10^{-6} & 0 & 0 & 0 & 0 & 0 & .01
\end{pmatrix}
\]

(3.3) For this matrix a standard programming technique gives an accurate approximation to the vector, namely

\[
p = (0.142753, 0.142634, 0.142634, 0.142634, 0.142634, 0.142634, 0.144075)
\]

satisfying: \( pP = p \) and \( \sum_{k=0}^{6} p_k = 1 \). Therefore we can look at the first entry in this vector and see that if untreated, the healthy cells would drop to 14.2753% of the original healthy CD4 cell count. And further time increments would not change this percentage, by Theorem 3.5. However a patient has AIDS at 20% and is unlikely to survive long enough for the levels to reach this limiting value.

An important consequence of ergodicity is that for a set of initial values of full measure in \( \mathcal{A}^{2\mathbb{Z}} \), (which correspond to a large set of arbitrary points in time and space in which we start sampling the CD4 cells in a lymph node), after the system has entered its Markov stage and as time passes, the percentage of each state will approach their respective
Figure 5. This graph of time vs. % healthy cells shows the end stages of HIV, modeled by a Markov process; if at time 0 there are $20 - 25\%$ of healthy cells, then very soon less than $16\%$ of the cells are healthy.

Figure 6. The graph shows that if at time 0, $20\%$ of the cells are healthy, over time the percentage fluctuates around the limiting percentage of $\approx 14.3\%$.

limiting values. Figure 6 shows that there is some fluctuation about the limiting value. However in the case of an untreated patient the limit is medically unlikely to be reached because the immune system is usually fatally compromised before that time. We now turn to a discussion of how the drug intervention protocols developed over the past years have outcomes that are corroborated by this model, and with survivable limits for the percentages of healthy cells.
Figure 7. When drugs are introduced during the chronic stage of HIV, the Markov process shows that a much larger percentage of the cells are healthy at any given time.

4. Drug Intervention in the Model

In this section we analyze how the limiting value of the percentage of healthy CD4 cells increases under a drug regimen such as cART (combination antiretroviral therapy) [20] or HAART (highly active antiretroviral therapy) [24]. While it is desirable for the drugs to prevent infectivity in all cells attacked by the virus, so far this has remained elusive [29]. However it is fairly well accepted by now that for an enzyme inhibitor such as a protease or reverse transcriptase inhibitor, the IC50 (the concentration of a drug needed to produce 50% of the maximal inhibitory effect in vitro) can be calculated and realized in the drug applications [21, 29].

Due to the types of drugs administered we have a new incidence matrix for the underlying dynamical system. This is explained by the fact that the protease inhibitor drug causes immature non-infectious virions to be formed instead of active ones. Therefore a healthy cell which is touching a site that is infected may not be infected; mathematically, state 0 can go to state 0 or 1. The other type of drug, the reverse transcriptase inhibitor, prevents the virus from replicating; put simply in the incidence graph below, an infected cell site, instead of mutating through many generations of new virions, destroys the cell site and then typically the body produces a healthy cell to replace it. Mathematically this cuts out some generations of infected cells, and once the drug affects the virus-infected cell it goes to the depleted state immediately.
If at the time drug therapy is initiated, 25%, 35% or 45% of the cells are healthy, respectively, over time the percentage fluctuates around the limiting percentage of approximately 60%.

This is shown by the graph in Figure 9 sending all infected states to 5 as a possibility since 5 is the “cell will next die” state (a cell that is infected but only very weakly infectious). The new incidence graph is therefore:

The corresponding incidence matrix is:

\[
BD = \begin{pmatrix}
    1 & 1 & 0 & 0 & 0 & 0 & 0 \\
    0 & 0 & 1 & 0 & 0 & 1 & 0 \\
    0 & 0 & 0 & 1 & 0 & 1 & 0 \\
    0 & 0 & 0 & 0 & 1 & 1 & 0 \\
    0 & 0 & 0 & 0 & 0 & 1 & 0 \\
    0 & 0 & 0 & 0 & 0 & 0 & 1 \\
    1 & 1 & 0 & 0 & 0 & 0 & 1
\end{pmatrix}
\]  

Using the most conservative assumptions from [29] and [21] we assume that the drugs are each better than 50% effective but not close to 100% effective in their inhibitory effects. We assume each of the types of drugs is successful 55% of the time for this next calculation. Then
the stochastic matrix for determining the limiting values becomes, using the algorithm of [1],

Let

\[ PD = \begin{pmatrix}
0.8338 & 0.1662 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0.45 & 0 & 0 & 0.55 & 0 \\
0 & 0 & 0 & 0.45 & 0 & 0.55 & 0 \\
0 & 0 & 0 & 0 & 0 & 1 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 1 \\
0.9899 & 9.9 \times 10^{-6} & 0 & 0 & 0 & 0 & 0.01
\end{pmatrix} \]

The left eigenvector for \( PD \) corresponding to the eigenvalue 1 given in (4.2) is

\[ p_D = (0.615756, 0.102362, 0.0460633, 0.0207287, 0.00932799, 0.102364, 0.103399), \]

(compare with Eqn (3.4)) which shows that in the limit, in ideal conditions almost 62% of the CD4 cells could be functioning. This is illustrated in Figures 7 and 8, which shows that the same limit is reached with different starting levels of healthy cells. That is to say, these simulations show that assuming other causes of death are minimized, a person lives chronically with the disease as long as the drugs are taken at the appropriate regular intervals and dosages to maintain that drug effectiveness, a fact that has been established by large studies [20, 27].

The leading term in the stochastic eigenvector for the eigenvalue 1 shows that the percentage of healthy (state 0) cells is within a much safer range to ward off most opportunistic infections. According to many recent studies, [21]

\text{Antiretroviral therapy has changed human immunodeficiency virus type 1 (HIV-1) infection from a death sentence to a treatable chronic illness.}

As an example, we show that as long as there is some uncertainty about the ability of a dormant virus to reactivate, the longterm effectiveness of any given drug does not change too much. If we assume that \( \text{eff} \) denotes the effectiveness of the drug that inhibits replication (the reverse transcriptase inhibitor), the graph in Figure 10 shows that if the drug treatment starts when the viral spread has already entered the “Markov stage” then there is a limit to how much of the CD4 supply can be restored. Figure 10 shows a plot of the percentage of healthy CD4 cells (y-axis) vs. the effectiveness of the reverse transcriptase inhibiting drug (x-axis), while assuming that the protease inhibitor drug’s effectiveness is constant (above 50% effective) and that the reservoirs and mutations have not been completely controlled.
Figure 10. If the drug regimen is started late, even if one drug is fully effective the CD4 count can never be fully restored.

This shows the benefits of the combined drug therapy [24] as well as supports the studies showing advantages to starting the drug treatment early [2, 14].

5. The Markov model applied to chronic Hepatitis C

There are other chronic viral infections that can be studied using this Markov model; we focus on the hepatitis C virus (HCV) in this section. While many changes in the parameters of the model need to be made for the model to be consistent with the existing data on the course of the disease, we give an idea here of the connections between dynamics of the persistent viral levels of HCV and the Markov model developed above.

According to the Center for Disease Control, the hepatitis C virus (HCV) is a major health problem in the U.S. and worldwide. In the United States, around 3.2 million people are believed to be infected with chronic HCV and 12,000 each year die from it [3]. While some cases of HCV infection clear up on their own, around 75 – 85% of the instances of HCV infection become chronic cases [3, 15]; i.e., the virus persists in the system, sometimes causing no symptoms while still able to be spread. However 60 – 80% of the people who get infected with HCV develop chronic liver disease [30]. As is the case for HIV, in the early stages of HCV infection many of the patients show a typical “yo-yo” pattern of high to low viral infection [26], and this is captured by the stochastic CA (SCA) model discussed in [1] and in the appendix of this paper. Some trials of the SCA model result in chronic infection while occasionally the virus is eradicated [1]; in the model the probability of a chronic infection depends on the parameters chosen for the model which in turn are determined by available data. At the acute
stage of the infection (also in the SCA model and all the CA models) the immune response is operating in most patients; therefore it is difficult to predict at this early stage in which patients the infection will persist [15, 26]. This uncertainty in outcome is reflected in the stochastic nature of the model; i.e., the SCA provides a much better model than a single CA. A CA model of hepatitis B was described in [33] which is similar to the SCA HIV model given in [35] and [1].

It is not fully understood what causes 15 – 20% of the people infected with HCV to spontaneously be cured, or at least to go to an undetectable viral level, but many believe this early viral clearance is due to a strong and fast initial CD4 cell response against the virus (see [26] and the multiple studies referenced there). The progression of the virus has some similarities to that of HIV, so the SCA model, suitably adapted through parameter choices, does a good job of simulating the dynamics of this disease. In this paper we direct our focus on the chronic stage, the most common outcome of HCV infection; since chronic hepatitis C is most likely to end up in fibrosis or cirrhosis of the liver [31], understanding the dynamics is worthwhile. Our Markov model is consistent with the hypothesis that it is not a lack of an immune response from the start that causes chronic HCV presence, but rather a fast tapering off of the response which leaves viral levels at low and sometimes undetectable levels. These levels keep the person asymptomatic and relatively healthy for long periods of time while still able to spread the virus. This dynamic is evident in the model whose outcome is supported by Theorem 3.5.

The space $X = \mathcal{A}^{Z2}$ in this setting represents HCV-specific CD4 T-cell sites in the liver; we could use all T-cell sites, since the connection to CD4 cells is not as direct as in the case of HIV. Moreover there are a variety of complex interactions among T-cells that set off the immune response [30, 31]. However since there seems to be a distinct and specific connection between the immune response to the disease and the CD4 response [26], we use a configuration of CD4 cell sites in the liver to be represented by a point $x \in X$. According to [26] one cause of the chronic infection could be the lack of HCV-specific CD4 T-cells responding to the virus, which in our model corresponds to a shortage of coordinates in state 0; we call state 0 cells “healthy” CD4 cells. In any other state the cells are not able to launch an attack against the virus but may be strong enough to ward off most opportunistic infections of the liver. The precise number of states in a good Markov CA model of persistent HCV depends on the data-driven parameters; the viral dynamics are on a much shorter time scale than for HIV [18] but
they have many similarities in terms of the viral dynamics. An example of how they differ in timing is if HCV persists in the blood after 3 months or more, then chronic hepatitis is diagnosed. A similarity is that like HIV, HCV mutates quickly; drug resistant mutations have been observed as early as 2 days after the first administration of the drug, making treatment difficult [7].

If we use the same parameters in the stochastic matrix \( P \) as for the HIV setting, that is the matrix given in (3.3) before drugs are introduced, keeping in mind that we are only doing this at the third stage of the model when the length of one time step and the time to this stage are no longer relevant, then we see that only around 14% of the HCV-specific CD4 cells remain from the beginning of the infection. This could be enough to keep the infection from quickly destroying more liver cells but not enough to eradicate the virus. In other words, while the precise parameters could shed more light on the best treatment, the dynamics show that the steady state will not allow the immune system to completely eliminate the viral presence. Many studies give data to support this hypothesis, such as [15] and the references therein. Again the Markov model shows that a drastic intervention is needed, one that upsets the stochastic nature of the dynamics, to set the longterm prognosis of the patient on a new course.

Indeed in [18] it is noted that the most effective drug treatment seems to speed up the death of an infected cell, and this would lead to an incidence matrix such as the one in (4.1); in addition due to the efficacy of the drugs we expect to see (4.2) also apply to the HCV setting. Finally, though drug treatment brings the virus to undetectable quantities in the blood, it is widely assumed that the HCV persists and measurable quantities of the virus return in more than 50% of the patients. If the dynamics of HCV and HIV are as similar as they seem to be, continuing drug therapy for a patient carrying chronic HCV might be appropriate until new drugs assure the eradication of the virus from the liver. Since the drugs can have adverse side effects, this leaves the problem of calibrating the minimum effective dosage. A careful assessment of drug efficacy plugged into the Markov CA from Section 4 can help tackle this problem.

Appendix A. Stochastic Cellular Automata

In all the cellular automata models of virus dynamics referred to in this paper, starting with the one in [35] and analyzed rigorously in [1] there are numerous CAs: \( \mathcal{N}, \mathcal{C}, \) and \( \mathcal{D}, \) in this paper, but called \( F_1, \ldots, F_n \) in other papers, acting on the same space \( X. \) In [9] and
[1] a mathematical framework was given for this process of choosing from among these CAs independently and randomly at each lattice site. This dynamical system is called a stochastic CA, denoted SCA, and we outline the construction here. For details we refer the reader to [9] (in dimension one) or [1] in an arbitrary dimensional setting.

Suppose we have \( n \) different CAs, any one of which might occur with some probability (not all equal) at any given time unit. Then we denote by \( J \) the finite index set (alphabet) with \( |J| = n \), and we introduce the space of choices of CAs by:

\[
\Omega = J^{\mathbb{N} \cup \{0\}}.
\]

At each site \((i, j)\) in our integer lattice \( \mathbb{Z}^2 \) we choose randomly from among \( n \) different local rules, as defined in (2.1) for \( n \) CAs indexed by \( J \). The random selection is modeled by the space \((\Omega, \mathcal{S})\), the one sided shift space with metric \( d_{\Omega}(\omega, \zeta) = \frac{1}{2^k} \) where \( k = \min \{i \mid \omega_i \neq \zeta_i\} \). Different probability measures on \( \Omega \) reflect different weights of the CA that appear; the weights are determined by the disease, drug intervention, and other physical factors. For each \( \omega \in \Omega \), the usual shift map

\[
(A.1) \quad s(\omega)_j = \omega_{j+1}
\]
denotes the passage of time. While the probabilities remain the same over time, with each increment of time a different CA may be chosen.

Since at each location in the lattice \( \mathbb{Z}^2 \) we choose a new CA to apply, and we do this infinitely often, we model this using an infinite product of the spaces \( \Omega \). We set for each \( \vec{i} = (i_1, i_2) \), \( \Omega_{\vec{i}} = \Omega \), and we define

\[
\Omega = \prod_{\vec{i} \in \mathbb{Z}^d} \Omega_{\vec{i}}.
\]

Each coordinate is given by \( \omega_{\vec{i}} \equiv \omega^{(i)} \), so that each \( \omega^{(i)} = \{\omega_j^{(i)}\}_{j \in \mathbb{N}^{\cup} \{0\}} \) is itself a one-sided sequence from \( \Omega \). We denote the shift map by \( \sigma \) and define it by:

\[
(A.2) \quad [\sigma(\omega)]_j^{(i)} = \omega_j^{(i+1)} = [s(\omega^{(i)})]_j.
\]

Suppose we have \( n \) CAs \( F_1, \ldots, F_n \), on

\[
X = \mathcal{A}^{\mathbb{Z}^2}
\]

with associated local rules \( f_1, \ldots, f_n \) respectively and assume each \( F_j : X \to X \) has radius at most \( r \).

We define the SCA generated by \( F_1, F_2, \ldots, F_n \) on \( X \) as follows. On the space \( \Omega \times \mathcal{A}^{(2r+1)^d} \) we use the local rule for each \( x \in X \),

\[
(A.3) \quad g(\omega, x_{N_r}) = \pi_A (s(\omega), f_{\omega_0}(x_{N_r})) = f_{\omega_0}(x_{N_r}),
\]
where $\pi_\mathcal{A}$ denotes projection onto the second coordinate (which is in $\mathcal{A}$). By definition

$$g : \Omega \times \mathcal{A}^{N_r} \to \mathcal{A}$$

and the rule $g$ only depends on the $0^{th}$ coordinate of $\omega$.

$$\text{(A.4)} \quad [F(\vec{w}, x)]_{\vec{i}} \equiv [F_{\vec{w}}(x)]_{\vec{i}} = g(\omega^{(\vec{i})}, x_{N_r+\vec{i}}) = f_{\omega^{(\vec{i})}}(x_{N_r+\vec{i}}).$$

For each $\vec{i}$, we consider only the coordinate $\omega^{(\vec{i})}$ of $\vec{w}$ and the coordinate block $x_{N_r+\vec{i}}$ to choose and apply one of the $n$ local rules. We denote the stochastic CA by $F_{\vec{w}}$, and think of it as a process on $X$; with this definition $F_{\vec{w}}$ is not a true CA in the sense of Hedlund [10], but as Proposition A.1 shows it is close to one.

We consider the space

$$Y = (\Omega \times \mathcal{A})^{Z^d} = \Omega \times X$$

as a product space. A point in $Y$ has coordinates $y_{\vec{i}} = (\omega^{(\vec{i})}, x_{\vec{i}})$, for each $\vec{i} = (i_1, i_2) \in Z^2$, with $\omega^{(\vec{i})} \in \Omega$, $x_{\vec{i}} \in \mathcal{A}$. There is a natural way to define a metric on $Y$ such that $y, z \in Y$ are close in the metric if and only if the $x_{\vec{i}} = v_{\vec{i}}$ for $\parallel \vec{i} \parallel \leq k$, and $\omega^{(\vec{i})} = \zeta^{(\vec{i})}$ for $\parallel \vec{i} \parallel \leq k$ and for $p = 0, 1, \ldots t_{\vec{i}}$.

We summarize how a SCA behaves mathematically like a CA with the following result from [9] and [1].

**Proposition A.1.** Assume we have $n$ CAs $F_1, \ldots, F_n$, on $X = \mathcal{A}^{Z^d}$ with associated local rules $f_1, \ldots, f_n$ respectively, such that each $F_j : X \to X$ has radius bounded above by $r$. With the notation above, the map:

$$F : Y \to Y$$

defined using local rule:

$$\bar{\mathbf{g}} : (\Omega \times \mathcal{A})^{[N_r]} \to \Omega \times \mathcal{A},$$

$$(A.5) \quad \bar{\mathbf{g}}(\omega^{(N_r)}, x_{N_r}) = (s(\omega^{(0)}), f_{\omega^{(0)}}(x_{N_r}));$$

so that

$$(A.6) \quad F(y)_{\vec{i}} = \bar{\mathbf{g}}(\omega^{(N_r+\vec{i})}, x_{N_r+\vec{i}}) = (s(\omega^{(\vec{i})}), f_{\omega^{(\vec{i})}}(x_{N_r+\vec{i}}))$$

is a continuous shift commuting map of $Y$.

**Remark A.2.**

1. The shift map on the product space $Y$ is defined in the obvious natural way as described in [1].

2. Iterating an SCA $F$ is done as follows: $F_{\vec{w}}(x) \equiv F_{\vec{w}}^{n-1} \circ \cdots \circ F_{\vec{w}} \circ F_{\vec{w}}(x)$. 
(3) Proposition A.1 means that at any given moment in time, the same $n$ CAs govern the behavior at each point in the space. The same probabilities determine which CA is being applied, but at different coordinates in space different CA will be used.

A.1. Measures governing the choices of CA used. We assume there are $n$ CAs $F_1, \ldots, F_n$ with local rules $f_1, \ldots, f_n$ respectively, each with radius bounded above by $r$. Physical factors determine a $p = (p_1, \ldots, p_n)$ where $p_k$ indicates the probability that a random choice of one of the $n$ CAs will yield $F_k$; therefore $p_k \geq 0$ and $\sum_{k=1}^n p_k = 1$.

From this setup we obtain a measure $\mu$ on $\Omega$ characterized by: for each finite sequence $c_0, c_1, \ldots, c_m$, $\mu(\{\omega : \omega_k = c_k, k = 0, \ldots, m\}) = p_{c_0} \cdot p_{c_1} \cdots p_{c_m}$. This is just the usual shift invariant Bernoulli measure on $\Omega$ determined by $p$ and in turn gives an ergodic probability product measure $\widetilde{\mu}$ on $\Omega$ preserved by $\tau$. Recall that we define the shift $s$ to be ergodic with respect to a probability measure $\mu$ if for any measurable function $\phi$ on $\Omega$, $\phi \circ s = \phi$ a.e. $\Rightarrow \phi = \text{constant} \mu$ a.e.

Applying the Birkhoff Ergodic Theorem (cf. [32]) to this setting, for a point $x \in X$ we look at one coordinate $x_j$ and at time $t$ we roll an infinite die $\omega \equiv \omega(\overrightarrow{T})$ to see which of the local CA rules to apply at that time and location. We define

$$A_T^i(\overrightarrow{j}, x, \omega) = \frac{\# \text{times } f_i \text{ is applied to } x_{N_r+\overrightarrow{j}} \text{ in first } T \text{ iterations}}{T}$$

The next result tells us that in the limit we apply the CA $F_i$ approximately $100 p_i \%$ of the time for almost every $\omega$.

Theorem A.3. [1] For every $i \in \{1, \ldots, n\}$, $\lim_{T \to \infty} A_T^i(\overrightarrow{j}, x, \omega) = p_i$ for any $x \in X = A^{Z_d}$, any $\overrightarrow{j} \in Z_d$, and $\mu$-a.e. $\omega \in \Omega_j$.

A.2. Equicontinuity points of stochastic CAs. A point of equicontinuity in an iterated dynamical system is a point (i.e., a configuration of states) whose behavior can be predicted over time. Much of the paper [1] is concerned with determining when and how points of equicontinuity can be achieved as a disease progresses; however in this paper we take a different point of view so we only give a brief definition. A useful example to think of is that of a body naturally attacking cold virus cells and returning to the healthy state. This is usually independent of the initial dosage of the virus and shows the equicontinuity of the dynamical system. We have $Y = (\Omega \times A)^{Z^2}$ and $\overline{F} : Y \to Y$ defined by $\overline{F}(y)_\overrightarrow{j} = \overrightarrow{g}(\omega(\overrightarrow{i}), x_{N_r+\overrightarrow{j}}) = \left(s(\omega(\overrightarrow{i})), f_{\omega(\overrightarrow{i})}(x_{N_r+\overrightarrow{j}})\right)$. 

$\text{MARKOV MODELS OF CHRONIC DISEASE}$
Definition A.4. (1) We say $\mathcal{F}$ is equicontinuous at $y \in \mathcal{Y}$ if
\[
\forall \varepsilon = 2^{-k} > 0, \exists \delta > 0 \text{ such that } \rho(y,z) < \delta \implies d_X\left(\left\{[F^t_\omega(x)]_r \right\}_{r \in \mathbb{Z}^d}, \left\{[F^t_\xi(v)]_r \right\}_{r \in \mathbb{Z}^d}\right) < \varepsilon \forall t \geq 0.
\]
Note that the inequality for $d_X$ holds if and only if
\[
[F^t_\omega(x)]_r = [F^t_\xi(v)]_r
\]
for $\|r\| \leq k$ and for all integers $t \geq 0$.

(2) For any $\overline{\omega} \in \Omega$ with $\overline{\omega}_j = \omega(j)$, we say the stochastic CA $\mathcal{F}_{\overline{\Omega}}$ is equicontinuous at $x = \{x_j\}_{j \in \mathbb{Z}^d}$ if $\overline{F}$ is equicontinuous at $y \in (\Omega \times A)^{\mathbb{Z}^d}$ with $y_j = (\omega(j), x_j)$.

One of the main results of [1] is that while taken alone, each of the CAs $\mathcal{N}$, $\mathcal{C}$, or $\mathcal{D}$ has many points of equicontinuity. Combined into a stochastic CA, there are no predictable points, and they lead to a chaotic Markov dynamical system, but whose global properties can sometimes be understood via the Markov CA defined in Section 3 of this paper.

References


