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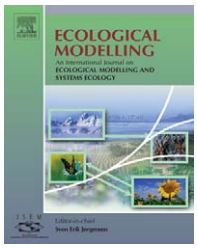

Short communication

Big cities: Shelters for contagious diseases

L.H.A. Monteiro[a,b,*], *H.D.B. Chimara*[a], *J.G. Chaui Berlinck*[c]

[a] *Universidade Presbiteriana Mackenzie, Escola de Engenharia, Pós-Graduação em Engenharia Elétrica, Rua da Consolação, n.896, Edifício Amantino Vassão, Térreo, CEP 01302-907, São Paulo, SP, Brazil*

[b] *Universidade de São Paulo, Escola Politécnica, Departamento de Engenharia de Telecomunicaçõese Controle, Av. Prof. Luciano Gualberto, Travessa 3, n.380, CEP 05508-900, São Paulo, SP, Brazil*

[c] *Universidade de São Paulo, Instituto de Biociências, Departamento de Fisiologia, Rua do Matão, Travessa 14, n.321, CEP 05508-900, São Paulo, SP, Brazil*

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ABSTRACT

People infected with chickenpox or measles can die; however, they usually become cured and no longer contract and, consequently, propagate them. Then, why are such diseases not naturally eradicated, since almost the entire adult population is immune to them? Here, we propose an epidemiological model based on probabilistic cellular automata (CA) for studying the spreading of a viral contagious disease. We concluded that its maintenance strongly depends on the number of individuals that can be infected. We also analyze the set of ordinary differential equations corresponding to the CA model and derive links between these two approaches.

1. Introduction

Cellular automata (CA) models have been employed for investigating the evolution of diseases in humans, because it is possible to propose rules of state transitions that are biologically motivated and easily programmable in digital computers. For example, Patel et al. (2001) simulate tumor growth; Zornenon dos Santos (1998) deals with the HIV infection. CA models have also been employed for studying the spreading of infectious diseases among humans. For example, Ahmed et al. (1998) examine hepatitis B transmission; Boccara and Cheong (1993), Fuentes and Kuperman (1999) , Sirakoulis et al. (2000), Willox et al. (2003) and Yakowitz et al. (1990) model a generic infectious disease. In these models, individuals usually live in a toroidal surface: a square matrix formed by $n \times n$ cells with periodic boundary conditions. The population is divided into three groups, as in classical SIR models based on differential equations (e.g. Anderson and May, 1991; Murray, 2003). Thus, each cell represents an individual that can be in one of three states: *S*, when the individual is susceptible and thus subjected to infection by neighbors; *I*, when the individual is infected and can transmit the disease for neighboring susceptible cells; and *R*, when the individual is recovered. The neighborhood of a cell is formed by its eight surrounding cells. The main goal of the investigations is to determine the influence of the parameters of the models on the behaviors of $S(t)$, $I(t)$, $R(t)$ in order to find control strategies.

* *Corresponding author*. Tel.: +55 11 3236 8711; fax: +55 11 3236 8600.
E-mail addresses: luizm@mackenzie.br, luizm@usp.br (L.H.A. Monteiro).

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CA models have been proposed as an alternative to represent the spatiotemporal dynamics described by some well-known partial differential equations, namely, the Fourier equation (Chopard and Droz, 1991) ; the Laplace equation (Danikas et al., 1996); the Poisson equation (Chen et al., 1990); the Korteweg-de Vries equation (Tokihiro et al., 1996); the Weyl, Dirac, and Maxwell equations (Bialynicki-Birula, 1994). And it is also possible to map continuous processes on CA lattices such as circular wavefront propagation (Sirakoulis et al., 2005).

Some epidemiological studies present a set of ordinary differential equations (ODEs) that would correspond to the proposed CA model (Ahmed et al., 1998; Fuentes and Kuperman, 1999). Here, explicit connections between these two approaches are stressed in a SIR model representing diseases for which the cure confers long-lasting immunity, as chickenpox and measles.

In Section 2, the probabilistic CA model is described. In Section 3, the corresponding ODEs are analyzed and relationships with the CA model are derived. In Section 4, the influence of the lattice size on the asymptotical solutions are investigated. Our main conclusion is: big cities can live together with contagious diseases that would be naturally eradicated in small ones.

2. Probabilistic CA model

The disease evolution is governed by a set of probabilities of state transitions. Thus, at each time step t, there is a probability P_i of a S-cell being infected according to $P_i(v) = (1 - e^{-Kv})$, where v is the number of infected neighbors and K is a parameter related to the infectivity of the disease (observe that P_i is a monotone increasing function of v; and that $P_i(0) = 0$, but $P_i(8) < 1$). Each I-cell has probability P_c per time step of becoming cured and probability P_d per time step of dying because of the disease. At each iteration, infected and recovered cells may die for other causes with probability P_n. When infected and recovered individuals die, susceptible ones replace them. Therefore, the total number of individuals $N = n^2$ remains constant. The states of all cells are simultaneously updated. Notice that the parameter P_n is a feature of the population; while K, P_c and P_d characterize the disease evolution in such a population. The boundary conditions are periodic; thus, the lattice is spatially homogeneous.

Fig. 1a shows the dynamical behavior of the CA model for $n = 200$, $K = 1$, $P_c = 60\%$, $P_d = 30\%$, $P_n = 10\%$. At $t = 0$, S, I and R-cells are randomly distributed according to the proportions $S(0)/N = 99.5\%$, $I(0)/N = 0.5\%$, $R(0)/N = 0\%$. With these choices, the amount of cells in each class remains fluctuating around a non-null value for $t \to \infty$. In this case, the disease survives. By taking $K = 0.1$, $S(0)/N = 50\%$, $I(0)/N = 50\%$, $R(0)/N = 0\%$ the disease tends to disappear as shown in Fig. 2a. Simulations performed for $n \geq 10$ and $0 < I(0) \leq 100\%$ (with $R(0) = 0\%$) revealed that the future of the disease is independent of n and $I(0)$. Its fate is determined only by the probabilities related to the state transitions.

3. Deterministic ODE model

When S, I and R-individuals are homogeneously distributed over the space, ODEs can be used for representing the population dynamics. The set of ODEs corresponding to the CA model is:

$$\frac{dS(t)}{dt} = -aS(t)I(t) + cI(t) + eI(t) + eR(t),$$
$$\frac{dI(t)}{dt} = aS(t)I(t) - bI(t) - cI(t) - eI(t), \qquad \frac{dR(t)}{dt} = bI(t) - eR(t) \tag{1}$$

where a is the infection rate, b the recovering rate, c the death rate related to the disease, and e is the death rate related to other causes. The total number of individuals remains constant because:

$$\frac{dS(t)}{dt} + \frac{dI(t)}{dt} + \frac{dR(t)}{dt} = 0 \to S(t) + I(t) + R(t) = N \tag{2}$$

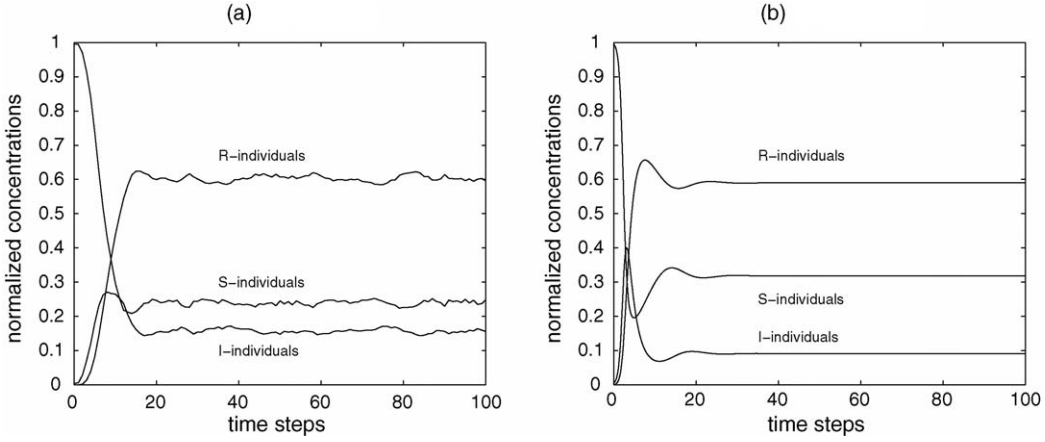

Fig. 1 – (a) Normalized concentrations of S, I and R-individuals obtained by simulating the CA model. Parameter values: $K = 1$, $P_c = 60\%$, $P_d = 30\%$, $P_n = 10\%$. Total number of individuals: $N = 4 \times 10^4$. Initial condition: $S(0) = 99.5\%$, $I(0) = 0.5\%$, $R(0) = 0\%$. (b) Normalized concentrations of S, I and R-individuals obtained by numerically integrating the ODE model. Parameter values: $a = 7.8 \times 10^{-5}$, $b = 0.60$, $c = 0.30$, $e = 0.093$. Initial condition: $S(0) = 99.5\%$, $I(0) = 0.5\%$, $R(0) = 0\%$. In this case, the asymptotical solution is an endemic state.

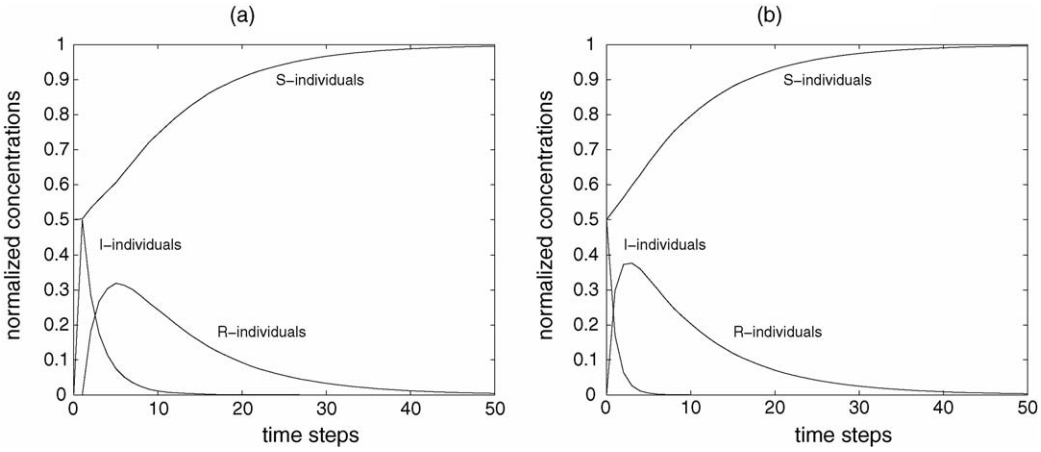

Fig. 2 – (a) Normalized concentrations of *S*, *I* and *R*-individuals obtained by simulating the CA model. Parameter values: $K = 0.1$, $P_c = 60\%$, $P_d = 30\%$, $P_n = 10\%$. Total number of individuals: $N = 4 \times 10^4$. Initial condition: $S(0) = 50\%$, $I(0) = 50\%$, $R(0) = 0\%$. (b) Normalized concentrations of *S*, *I* and *R*-individuals obtained by numerically integrating the ODE model. Parameter values: $a = 0$, $b = 0.60$, $c = 0.30$, $e = 0.10$. Initial condition: $S(0) = 50\%$, $I(0) = 50\%$, $R(0) = 0\%$. In this case, the asymptotical solution is a disease-free state.

A stationary solution is given by $(S(t), I(t), R(t)) = (S^*, I^*, R^*)$, where S^*, I^*, R^* are constants satisfying $dS(t)/dt = 0$, $dI(t)/dt = 0$, $dR(t)/dt = 0$ for any instant t. This kind of solution is called equilibrium point because it is represented by a point fixed in the state space $S \times I \times R$.

The equilibrium points of Eq. (1) are

$$S^* = N; \qquad I^* = 0; \qquad R^* = 0 \tag{3}$$

and

$$S^* = \frac{N}{R_0}; \qquad I^* = \frac{eN}{e+b}\left(1 - \frac{1}{R_0}\right); \qquad R^* = \frac{bN}{e+b}\left(1 - \frac{1}{R_0}\right) \tag{4}$$

where

$$R_0 \equiv \frac{aN}{b+c+e} \tag{5}$$

Observe that Eq. (3) represents a disease-free stationary solution and Eq. (4) represents an endemic stationary solution. Numerical examples of Eqs. (4) and (3) are shown in Figs. 1b and 2b, respectively.

The stability of (S^*, I^*, R^*) can be determined by calculating the eigenvalues of the Jacobian matrix corresponding to the system linearized around this point. An equilibrium point is asymptotically stable when all eigenvalues have negative real parts (e.g. Guckenheimer and Holmes, 1983). Asymptotical stability of an equilibrium point means that, in the state space, there is a ball centered on this point so that any solution starting from an initial condition within this ball would converge to such a point. Stability analysis of Eq. (1) shows that the disease-free state is asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$; the endemic state is unstable if $R_0 < 1$ and asymptotically stable if $R_0 > 1$. Thus, there is transcritical bifurcation (e.g. Guckenheimer and Holmes, 1983) for $R_0 = 1$. The bifurcation parameter R_0 is usually called basic reproduction rate (e.g. Murray, 2003).

In the case of uniformly mixed classes, Eq. (1) can be used for producing dynamical behaviors similar to those obtained by the CA model, because ODEs are a mean-field approximation for CA (see Toffoli (1984) for a discussion). The difficulty is to find appropriate numerical values corresponding to the ones used in CA simulations. However, by inspection of Eq. (1), we verify that these values can be estimated from the CA simulations by the following expressions:

$$a \simeq \frac{\Delta I(t)_{S\to I}}{S(t)I(t)\Delta t}, \qquad b \simeq \frac{\Delta R(t)_{I\to R}}{I(t)\Delta t},$$
$$c \simeq \frac{\Delta S(t)_{I\to S}}{I(t)\Delta t}, \qquad e \simeq \frac{\Delta S(t)_{I\to S;R\to S}}{[I(t)+R(t)]\Delta t} \tag{6}$$

where $\Delta I(t)_{S\to I}/\Delta t$ is the increase per time step of susceptible individuals due to the contamination process, $\Delta R(t)_{I\to R}/\Delta t$ the increase per time step of recovered individuals due to the healing process, $\Delta S(t)_{I\to S}/\Delta t$ the increase per time step of susceptible individuals due to the death caused by the disease, and $\Delta S(t)_{I\to S;R\to S}/\Delta t$ is the increase per time step of susceptible individuals due to the death for other causes. By assuming that the probability of a state transition at each iteration can be estimated from the relative frequency of its occurrence, then $\bar{P}_i \simeq \Delta I(t)_{S\to I}/[\Delta t S(t)]$; $P_c \simeq \Delta R(t)_{I\to R}/[\Delta t I(t)]$; $P_d \simeq \Delta S(t)_{I\to S}/[\Delta t I(t)]$; $P_n \simeq \Delta S(t)_{I\to S;R\to S}/[\Delta t(I(t)+R(t))]$. Therefore:

$$a \simeq \frac{\bar{P}_i}{I(t)} = \frac{\sum_{v=0}^{8} P_i S_v}{I(t)\sum_{v=0}^{8} S_v}; \qquad b \simeq P_c; \qquad c \simeq P_d; \qquad e \simeq P_n \tag{7}$$

where S_v is the number of susceptible cells with v infected neighbors.

Thus, the parameters b, c, e appearing in the linear terms of Eq. (1) are the probabilities of recovering and dying. The parameter a is related to the average infection probability $\bar{P}_i$ and to $I(t)$ and, consequently, to N.

CA simulations can be used for estimating a, b, c, e. For instance, the asymptotical values of these parameters determined from Fig. 1a are $a = (7.8 \pm 0.1) \times 10^{-5}$, $b = (0.60 \pm 0.01)$,

$c = (0.30 \pm 0.01)$, $e = (0.093 \pm 0.004)$. These average values and the corresponding standard deviations are computed from Eq. (6) by taking into account the last 20 time steps of the CA evolution (similar results are obtained by considering more time steps after discarding the transient behavior). Fig. 1b was plotted by numerically solving Eq. (1) with the average values of a, b, c, e from the same initial condition chosen in Fig. 1a. Fig. 2b corresponds to Fig. 2a. Observe the qualitative agreement found in the two approaches.

The numerical values obtained for the parameters are influenced by the (usual) choice of taking the time step $\Delta t = 1$. For instance, $b \simeq 0.6$ means that the probability of an infected individual to become cured after one iteraction is 60%; after two iteractions is 84% and so on, where one time step can correspond to 12 h or 3 days or 1 week. Thus, the parameter values are normalized in relation to the time unity characterizing the disease.

The values of b, c, e are easily determined from P_c, P_d, P_n and the value a can be easily derived when $0 < K \ll 1$ and the endemic state is the asymptotically stable solution. In this case, $R_0 \simeq 1$. Thus:

$$a \simeq \frac{P_c + P_d + P_n}{N} \equiv a_{\min} \tag{8}$$

An example: a simulation of the CA model with $K = 0.20$, $P_c = 60\%$, $P_d = 30\%$, $P_n = 10\%$, $n = 32$ yields $a = (1.0 \pm 0.1) \times 10^{-3}$. By using Eq. (8), the estimated value is $a \simeq 0.98 \times 10^{-3}$; therefore, both results agree. If $a < a_{min}$, then $R_0 < 1$, and the endemic state is not the asymptotical solution. In fact, by taking $K = 0.19$, $P_c = 60\%$, $P_d = 30\%$, $P_n = 10\%$ the CA evolution tends to the disease-free solution in a lattice with $n = 32$. However, in a lattice with $n = 200$, a disease with $K = 0.19$ usually survives. These results led us to the next question.

4. Where does a disease usually survive?

By using our CA model, we investigated how the asymptotical concentrations of S, I and R-cells vary in function of P_d, P_c and K. We found that $I^* \neq 0$ only if $P_c < P_{c(\max)}$, $P_d > P_{d(\min)}$, and $K > K_{(\min)}$. When $P_c > P_{c(\max)}$ or $P_d < P_{d(\min)}$ or $K < K_{(\min)}$ the stationary state with $I^* = 0$ is reached. For instance, when $P_c = 60\%$, $P_d = 30\%$, $P_n = 10\%$, $n = 32$ the asymptotical solution is usually the disease-free state if $K < K_{(\min)} = 0.19$ and it is usually the endemic state if $K \geq 0.20$.

The interesting results are that the critical values $P_{d(\min)}$ and $K_{(\min)}$ diminish when the total number of individuals N increases; and that the critical value $P_{c(\max)}$ increases with N. Table 1 illustrates these results, which are not influenced by the initial proportions of S and I-cells. The value of $P_{d(\min)}$ for each N was numerically obtained as follows (the values of $P_{c(\max)}$ and $K_{\min}$ were determined by a similar way). All parameter values were kept fixed except P_d. We started choosing an initial value $P_d(0)$ great enough for supporting the disease in 10 of 10 simulations. Each simulation was performed during $3n$ time steps, which is large enough for eliminating the transient behavior. Then, we reduced $P_d(0)$ from 0.5% and performed a new simulation using $P_d(1) = P_d(0) - 0.5\%$. In the next simulation, we used $P_d(2) = P_d(1) - 0.5\%$. This procedure of reducing P_d by a fixed amount before starting a new simulation was repeated until obtaining a value of P_d for which the disease was eliminated. We found 10 critical values of P_d for each N. Then, we computed the average $P_{d(\min)}$ and its standard deviation as shown in Table 1.

Table 1 – Critical values of P_c, P_d and K in function of N

N	$P_{c(\max)}$(%)	$P_{d(\min)}$(%)	$K_{\min}$
1×10^3	11.0 ± 4.0	68.1 ± 1.5	0.278 ± 0.082
5×10^3	13.4 ± 4.1	64.6 ± 2.4	0.220 ± 0.060
1×10^4	19.2 ± 2.9	60.5 ± 2.3	0.173 ± 0.027
5×10^4	24.9 ± 1.0	52.2 ± 2.1	0.169 ± 0.002
1×10^5	27.8 ± 1.6	46.1 ± 2.0	0.169 ± 0.001
5×10^5	32.5 ± 0.8	41.4 ± 1.6	0.169 ± 0.001
1×10^6	34.6 ± 0.7	35.8 ± 0.9	0.170 ± 0.001

Parameter values used in each investigation: $K = 1$, $P_d = 3\%$, $P_n = 1\%$ for $P_{c(\max)}$; $K = 1$, $P_c = 60\%$, $P_n = 1\%$ for $P_{d(\min)}$; and $P_c = 60\%$, $P_d = 30\%$, $P_n = 10\%$ for $K_{(\min)}$.

The CA algorithm was written in Visual Basic 6.0 and ran in a 2.4 GHz processor/512 MB RAM personal computer platform. The processing time of the algorithm strongly depends on N: for $N = 1 \times 10^3$, each critical number is obtained in a few hours; for $N = 1 \times 10^6$ in several weeks.

5. Conclusions

By using CA and ODEs, we investigated the evolution of diseases for which the cure leads to permanent immunity. We derived relationships among the parameters of both approaches and showed that by appropriately taking the parameter values, both models give similar results. Then, we used the CA model for investigating why diseases confering permanent immunity are not naturally eradicated.

Our model revealed that big cities can live together with contagious diseases that would be eradicated in small ones. Thus, big cities serve as reservoirs, supporting those diseases of low death rate, low infectivity and short recovering time, because the turnover of their populations is above some critical value. By contrast, in small cities, some contagious diseases (as chickenpox and measles) cannot permanently remain; they need to be reintroduced from time to time. The determination of the critical size of a city capable of supporting a contagious disease can guide prophylatic strategies and vaccination campaigns for combating its spreading.

It is relevant to note that empirical biological studies of infectious diseases propagation disclose similar features as those we are describing here. The maintenance of infective agents in populations is strongly influenced by the size of such populations (Biggs, 1985; Tadei et al., 1998; Lopez et al., 2005), and not by the relative frequency of infected individuals within the population (Ryder et al., 2005).

This model can be improved by considering long-range interactions between CA cells, with a regular connection topology, like an extended Moore neighborhood with radius greater than one; or random, like a “small-world” coupling topology (Watts and Strogatz, 1998).

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