

Probabilistic cellular automaton describing a biological immune system

Tânia Tomé

*Instituto de Física, Universidade de São Paulo, Caixa Postal 66318
05389-970 São Paulo, São Paulo, Brazil*

J. R. Drugowich de Felício

*Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto, 14040-901 Ribeirão Preto, São Paulo, Brazil
and Instituto de Física de São Carlos, Universidade de São Paulo, 13560-000 São Carlos, São Paulo, Brazil*

(Received 21 August 1995)

We have analyzed a probabilistic cellular automaton to describe the T -helper cells response under parasitic infections. The evolution rules are of totalistic type and possess “up-down” symmetry. The automaton displays a dynamical phase transition, from a disordered state to an ordered one, which takes place through a spontaneous symmetry breaking. In the ordered phase, one type of T -helper cells predominates over the others. The phase transition was studied both by a pair approximation and by Monte Carlo simulations. In addition, we were able to obtain some exact results for the densities of T -helper cells.

PACS number(s): 87.10.+e

I. INTRODUCTION

The use of cellular automata and stochastic lattice gas models to mimic systems in the area of biological sciences [1–10] gives us a better explanation of the microscopic mechanisms that lead to the macroscopic behavior of the systems. These statistical-mechanical treatments, with probabilistic local rules, take into account the fluctuations that play an important role in determining the critical behavior of the system. From the point of view of nonequilibrium statistical mechanics these models are very useful because they are simple and can display very intricate behavior not well understood yet. In the present work we pursue this approach by studying a probabilistic cellular automaton to describe one part of the cellular immune system [4,9–13]. The automaton explains some cellular mechanisms of the immune system that are of interest in biological sciences by exploring features of nonequilibrium phase transitions present in the model.

Recently Brass *et al.* [9,10] have introduced a cellular automaton that models the polarization of the T -helper cells when mice are exposed to parasitic infections. Their model considers three subsets of T -helper cells and the processes that result in the change from one type of cell to another one. T -helper cells that have not yet been presented to the antigen are denoted by T_{H0} . Two different antigen presentation routes, in which T_{H0} cells develop into T_{H1} or T_{H2} cells are included in the model to represent the populations of antigen presentation cells. In order to mimic the competition between mature T -helper cells, the induction $T_{H0} \rightarrow T_{H1}$ (T_{H2}) is prohibited when a T_{H0} cell has a majority of T_{H2} (T_{H1}) neighbors. This happens because mature cells produce cytokines, which support neighboring cells of the same kind but suppress cells of different type. Finally, a cutoff N_T is introduced such that cells not restimulated by appropriate antigen within this time die (substituted by T_{H0} cells). Starting

from a system composed only of T_{H0} cells, via Monte Carlo simulation in cubic lattices, the model can display a steady state with a predominance of one type of cells (polarization). The polarization occurs as one varies the antigen density or the cutoff N_T , even in the case of equal populations of presenting antigen cells. In this case, a spontaneous symmetry breaking occurs in agreement with experimental results obtained by Else *et al.* [14] for the $B10.D2n$ strain of mice.

Here we propose a modified version of the model devised by Brass *et al.* by considering a *probabilistic* cellular automaton where we allow the death of cells T_{H1} and T_{H2} to happen at each time step with a given probability r . This rule is distinct from that considered by Brass *et al.* in the sense that the cutoff N_T (lifetime of the cells T_{H1} and T_{H2}) was eliminated in favor of a *mean* lifetime related to a probability r . The cells T_{H0} develop into T_{H1} or T_{H2} cells with a probability that depends on the type of neighboring cells and on a parameter p , related to the antigen density.

We were able to find some exact results for such a model. For instance, under any parasitic conditions (any values of p and r) and for any spatial dimension, the density of T_{H0} cells and the probability of having any agglomeration of T_{H0} cells were obtained exactly. We have also studied the steady states of the system by using a pair approximation and by performing Monte Carlo simulations in square lattices.

II. MODEL

The system we have studied is a probabilistic cellular automaton that evolves in time according to local stochastic rules. We consider a lattice with N sites in which each site can be occupied by three kinds of cells: T_{H0} , T_{H1} , or T_{H2} . To each site i we attach a variable

σ_i that takes the value 0, 1, or -1 according to whether the site is occupied by a T_{H0} , a T_{H1} , or a T_{H2} cell. The microscopic state of the system is represented by $\sigma = (\sigma_1, \sigma_2, \dots, \sigma_N)$.

The time evolution of the probability $P_\ell(\sigma)$ of state σ at time ℓ is governed by the equation

$$P_{\ell+1}(\sigma') = \sum_{\sigma} W(\sigma'|\sigma)P_\ell(\sigma), \quad (1)$$

where $W(\sigma'|\sigma)$ is the transition probability from state σ to state σ' that must obey the condition

$$\sum_{\sigma'} W(\sigma'|\sigma) = 1. \quad (2)$$

A system described by a cellular automaton evolves at discrete time steps and all the sites are updated simultaneously. Using this condition, the transition probability is written as

$$W(\sigma'|\sigma) = \prod_{i=1}^N w_i(\sigma'_i|\sigma), \quad (3)$$

where $w_i(\sigma'_i|\sigma)$ is the conditional probability that site i , at time $\ell + 1$, be in the state σ'_i given that, at time ℓ , the state of the system is σ . The transition probability $w_i(\sigma'_i|\sigma)$ obeys the property

$$w_i(0|\sigma) + w_i(1|\sigma) + w_i(-1|\sigma) = 1, \quad (4)$$

so that Eq. (2) is fulfilled. Usually, the transition probability w_i depends only on a neighborhood of site i .

The cellular automaton considered here belongs to the class of totalistic cellular automata [15] for which $w_i(\sigma'_i|\sigma)$ depends on σ_i and on the sum $\sum_{\delta} \sigma_{i+\delta}$ of dynamical variables of the neighborhood of i . Actually, it is a special kind of totalistic automaton that depends only on the sign of this sum. More specifically, if we define $s_i(\sigma)$ by

$$s_i = S\left(\sum_{\delta} \sigma_{i+\delta}\right) \text{ where } S(\xi) = \begin{cases} 1 & \text{if } \xi > 0 \\ 0 & \text{if } \xi = 0 \\ -1 & \text{if } \xi < 0, \end{cases} \quad (5)$$

then the transition probability will be denoted by $w_i(\sigma'_i|\sigma_i, s_i)$.

The transition probabilities are given by the rules

$$w_i(+1|\sigma_i, s_i) = p\delta(\sigma_i, 0)\{\delta(s_i, +1) + \frac{1}{2}\delta(s_i, 0)\} + (1-r)\delta(\sigma_i, +1), \quad (6)$$

$$w_i(-1|\sigma_i, s_i) = p\delta(\sigma_i, 0)\{\delta(s_i, -1) + \frac{1}{2}\delta(s_i, 0)\} + (1-r)\delta(\sigma_i, -1), \quad (7)$$

$$w_i(0|\sigma_i, s_i) = (1-p)\delta(\sigma_i, 0) + r\{\delta(\sigma_i, 1) + \delta(\sigma_i, -1)\}. \quad (8)$$

These rules have ‘‘up-down’’ symmetry

$$w_i(\sigma'_i|\sigma_i, s_i) = w_i(-\sigma'_i|-\sigma_i, -s_i), \quad (9)$$

so that we expect, following Grinstein *et al.* [16], that this probabilistic cellular automaton is in the same universality class as kinetic Ising models.

Our aim is to study the automaton defined by these rules. We are primarily interested in such averages as the number of cells of each type and correlations of cells placed in neighboring sites. We consider the case where the system is homogeneous and denote by x_ℓ , y_ℓ , and z_ℓ the mean occupation number of cells of types T_{H1} , T_{H2} , and T_{H0} , respectively, at time ℓ (notice that $x_\ell + y_\ell + z_\ell = 1$). The correlation between T_{H1} and T_{H0} cells placed on neighboring sites is denoted by u_ℓ and that between T_{H2} and T_{H0} is denoted by v_ℓ .

From the evolution equation for $P_\ell(\sigma)$ we get the following equations for the time evolution of the mean occupation number of cells and for the correlations. The evolution equation for x_ℓ and y_ℓ are given formally by

$$x_{\ell+1} = \langle w_i(1|\sigma_i, s_i) \rangle_\ell \quad (10)$$

and

$$y_{\ell+1} = \langle w_i(-1|\sigma_i, s_i) \rangle_\ell. \quad (11)$$

The evolution equations for the two-site correlations u_ℓ and v_ℓ are given formally by

$$u_{\ell+1} = \langle w_i(1|\sigma_i, s_i)w_j(0|\sigma_j, s_j) \rangle_\ell \quad (12)$$

and

$$v_{\ell+1} = \langle w_i(-1|\sigma_i, s_i)w_j(0|\sigma_j, s_j) \rangle_\ell, \quad (13)$$

where i and j are nearest-neighbor sites. All other nearest-neighbor two-site correlation functions are given in a similar way.

III. EXACT RESULTS

From the dynamical rules we see that the transition probability $w_i(0|\sigma_i, s_i)$ to the state $\sigma'_i = 0$ does not depend on s_i , i.e., it depends only on the state of site i . This leads to conservation laws that we will deduce below.

Let us define the random variable η_i that takes the value 0 when $\sigma_i = 0$ and the value 1 when $\sigma_i = \pm 1$, i.e., $\eta_i = \sigma_i^2$. The joint probability $Q_\ell(\eta) = Q_\ell(\eta_1, \eta_2, \dots, \eta_N)$ is then defined by

$$Q_\ell(\eta) = \sum_{\sigma} \prod_{i=1}^N \delta(\eta_i, \sigma_i^2) P_\ell(\sigma). \quad (14)$$

From the evolution equation for $P_\ell(\sigma)$, it is possible to obtain the time evolution of $Q_\ell(\eta)$, which is given by

$$Q_{\ell+1}(\eta') = \sum_{\eta'} \prod_{i=1}^N \tilde{w}_i(\eta'_i|\eta_i) Q_\ell(\eta), \quad (15)$$

where

$$\tilde{w}_i(\eta'_i|\eta_i) = \delta(\eta'_i, 0)\{\delta(\eta_i, 0)(1-p) + \delta(\eta_i, 1)r\} + \delta(\eta'_i, 1)\{\delta(\eta_i, 0)p + \delta(\eta_i, 1)(1-r)\}, \quad (16)$$

and is interpreted as the probability of changing the state of site i from state η'_i to state η_i .

The time evolution equation for $Q_\ell(\eta)$ can be solved exactly. The solution is $Q_\ell(\eta) = \prod_i Q_\ell(\eta_i)$, where $Q_\ell(\eta_i)$ evolves as

$$Q_{\ell+1}(\eta'_i) = \sum_{\eta_i=\pm 1} \tilde{w}_i(\eta'_i|\eta_i) Q_\ell(\eta_i), \quad (17)$$

or

$$Q_{\ell+1}(0) = (1-p)Q_\ell(0) + rQ_\ell(1) \quad (18)$$

and

$$Q_{\ell+1}(1) = pQ_\ell(0) + (1-r)Q_\ell(1). \quad (19)$$

In the stationary state

$$Q(0) = \frac{r}{p+r}, \quad Q(1) = \frac{p}{p+r}, \quad (20)$$

so that the stationary solution $Q(\eta)$ will be

$$Q(\eta) = \prod_{i=1}^N Q(\eta_i). \quad (21)$$

Under stationary conditions we get then the exact result

$$\sum_{\sigma} P(\sigma) \prod_{i=1}^N \delta(\eta_i, \sigma_i^2) = \prod_{i=1}^N Q(\eta_i) \quad (22)$$

concerning the stationary probability $P(\sigma)$. It follows that the probability of any cluster of M sites occupied by T_{H0} cells is obtained exactly and is given by

$$P(\underbrace{0, 0, \dots, 0}_M) = [Q(0)]^M = \left(\frac{r}{p+r}\right)^M. \quad (23)$$

In particular, the density of T_{H0} cells is given by

$$P(0) = \frac{r}{p+r}. \quad (24)$$

Other exact results that can be obtained from Eq. (22) are

$$P(10) + P(-10) = Q(10) = Q(1)Q(0), \quad (25)$$

$$P(11) + P(1-1) + P(-11) + P(-1-1)$$

$$= Q(1, 1) = [Q(1)]^2 \quad (26)$$

and

$$P(\underbrace{1, 0, 0, \dots, 0}_M) + P(\underbrace{-1, 0, 0, \dots, 0}_M) = Q(1)[Q(0)]^M. \quad (27)$$

IV. STEADY STATES

The system evolves in time according to the local Markovian rules given by Eqs. (6)–(8) and eventually attains a steady state. The steady states of this model can be of two types: a disordered steady state, characterized by $\alpha = 0$, and an ordered phase, characterized

by $\alpha \neq 0$, where $\alpha = x - y$ is the order parameter. The ordered phase characterizes the system when one type of cells predominates: either T_{H1} or T_{H2} .

We point out that, for any value of the parameters p and r , the density of T_{H0} cells at the steady state is obtained exactly from Eq. (24) and is given by

$$z = P(0) = \frac{r}{p+r}. \quad (28)$$

As a consequence of the above result, the sum $\beta = x + y$ of the densities x and y of T_{H1} and T_{H2} cells at the stationary state is obtained exactly, since $x + y = 1 - z$, and is given by

$$\beta = \frac{p}{p+r}. \quad (29)$$

A. Disordered steady state

In the disordered state the numbers of T_{H1} and T_{H2} cells are the same ($\alpha = 0$). The densities x , y , and z can be obtained exactly and are given by

$$x = y = \frac{p}{2(p+r)}; \quad (30)$$

z is given by the expression (28).

The probability $u = P(10)$ of finding a nearest-neighbor pair of T_{H1} and T_{H0} cells and $v = P(-10)$ of finding a nearest-neighbor pair of T_{H2} and T_{H0} cells can also be obtained exactly. Indeed, from the exact results given by Eq. (25), and since $P(10) = P(-10)$ in the disordered state, we have

$$u = v = \frac{1}{2}Q(1)Q(0) = \frac{1}{2}(1-z)z = \frac{pr}{2(p+r)^2}. \quad (31)$$

Notice that not all the probabilities of any set of dynamic variables $\{\sigma_i\}$ (corresponding to a cluster of three or more sites) can be obtained exactly. If it were possible to find all such probabilities, we would obtain the stationary probability $P(\sigma)$ exactly for the disordered state. But this does not seem to be possible since the present model does not satisfy detailed balance.

B. Ordered state

At a given instant ℓ , the sites occupied by T_{H1} and T_{H2} cells form clusters of several sizes. As long as these clusters are finite, it is not possible for the system to sustain an ordered state. Only when these clusters grow until the appearance of an infinite one, which is the percolating cluster, will the occurrence of an ordered state be possible. If ρ_c is the critical concentration for site percolation for the given lattice, then the ordered state can exist only if

$$x + y = \frac{p}{p+r} > \rho_c \quad (32)$$

or

$$\frac{r}{p} < \frac{1}{\rho_c} - 1. \quad (33)$$

For a one-dimensional model we therefore expect no ordered phase since $\rho_c = 1$.

In the ordered state, where $x \neq y$ or $\alpha \neq 0$, the average number of one type of cells, T_{H1} or T_{H2} , predominates. Even in this state the mean number of T_{H0} cells is given by the exact result (28).

Next, we use an analytical approach to study the ordered state and find the transition line in the phase diagram in the space of parameters (r, p) . To calculate the averages on the right-hand sides of Eqs. (10) and (11), we need the probability of a cluster composed by a central site and its nearest-neighbor sites. We approximate the probability of this cluster by using a dynamical mean-field approximation [17–19] at the level of two-site correlations, the so-called pair approximation. By using the pair approximation the probability of a cluster composed by a central site i and its nearest neighbors is written as

$$P(\sigma_i) \prod_{\delta} \frac{P(\sigma_i, \sigma_{i+\delta})}{P(\sigma_i)}, \quad (34)$$

where the product is over the nearest-neighbor sites of site i .

We consider a regular square lattice and obtain a closed set of evolution equations for the densities x_{ℓ} and y_{ℓ} and the pair correlations u_{ℓ} and v_{ℓ} . From Eqs. (10)–(13) and using the approximation above we get the closed set of equations for the variables $\alpha_{\ell} = (x_{\ell} - y_{\ell})$, $\beta_{\ell} = (x_{\ell} + y_{\ell})$, $\phi_{\ell} = (u_{\ell} - v_{\ell})$, and $\psi_{\ell} = (u_{\ell} + v_{\ell})$,

$$\alpha_{\ell+1} = (1-r)\alpha_{\ell} + pz_{\ell}^{-3}\{4w_{\ell}^3 + 6w_{\ell}^2\psi_{\ell} + \frac{1}{2}(4w_{\ell} + \psi_{\ell})(3\psi_{\ell}^2 - \phi_{\ell}^2)\}, \quad (35)$$

$$\beta_{\ell+1} = p + (1-r-p)\beta_{\ell}, \quad (36)$$

$$\begin{aligned} \phi_{\ell+1} = & r(1-r)\alpha_{\ell} + (1-r)(1-p-r)\phi_{\ell} \\ & + p(1-p)z_{\ell}^{-3}\phi_{\ell}\{3w_{\ell}^3 + 3\psi_{\ell}w_{\ell}^2 + \frac{1}{2}(3\psi_{\ell}^2 - \phi_{\ell}^2)w_{\ell}\} \\ & + prz_{\ell}^{-3}\phi_{\ell}\{w_{\ell}^3 + 3\psi_{\ell}w_{\ell}^2 \\ & + \frac{1}{4}(3\psi_{\ell}^2 - \phi_{\ell}^2)(2\psi_{\ell} + 3w_{\ell})\}, \end{aligned} \quad (37)$$

and

$$\psi_{\ell+1} = p(1-p) + (r-p)(1-p-r)\beta_{\ell} + (1-p-r)^2\psi_{\ell}, \quad (38)$$

where $z_{\ell} = 1 - \beta_{\ell}$ and $w_{\ell} = 1 - \beta_{\ell} - \psi_{\ell}$. The stationary solution is obtained by an iterative procedure.

For a fixed value of p , the trivial solution corresponding to the disordered state and given by Eqs. (30) and (31), or by

$$\alpha = 0, \quad \beta = \frac{p}{p+r}, \quad \phi = 0, \quad \psi = \frac{pr}{(p+r)^2}, \quad (39)$$

is stable for high values of r . As the parameter r decrease, the trivial solution loses its stability when a spontaneous symmetry breaking takes place at a critical value r_c . The critical parameter can be obtained by performing a linear stability analysis around the trivial solution. Due to structure of the set of Eqs. (35)–(38) it suffices to study the eigenvalues of the 2×2 matrix

$$\begin{pmatrix} A_{11} & A_{12} \\ A_{21} & A_{22} \end{pmatrix}, \quad (40)$$

where

$$A_{11} = 1 - r, \quad (41)$$

$$A_{12} = pz^{-3}(4w^3 + 6\psi w^2 + 6\psi^2 w + \frac{3}{2}\psi^3), \quad (42)$$

$$A_{21} = r(1-r), \quad (43)$$

and

$$\begin{aligned} A_{22} = & (1-r)(1-p-r) + 3p(1-p)z^{-3}(w^3 + \psi w^2 + \frac{1}{2}\psi^2 w) \\ & + prz^{-3}(w^3 + 3\psi w^2 + \frac{9}{4}\psi^2 w + \frac{3}{2}\psi^3), \end{aligned} \quad (44)$$

where $z = r/(p+r)$, $w = r^2/(p+r)^2$, and $\psi = pr/(p+r)^2$.

The same analysis can be done in the more realistic situation in which r is fixed and p is varied. In order to make a comparison with the results obtained by Brass *et*

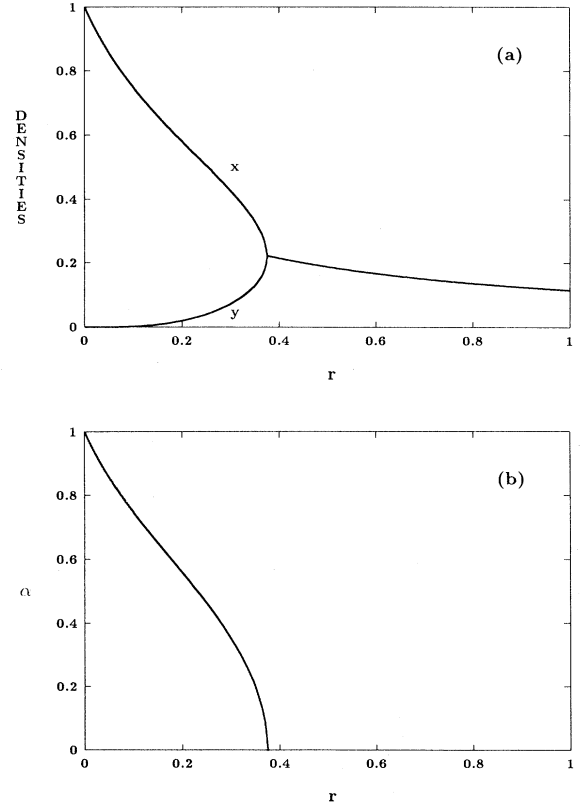


FIG. 1. (a) Densities x and y of T_{H1} and T_{H2} cells, respectively, according to the pair approximation, as functions of r , for $p = 0.3$. (b) Order parameter $\alpha = (x - y)$, according to the pair approximation, as a function of r , for $p = 0.3$.

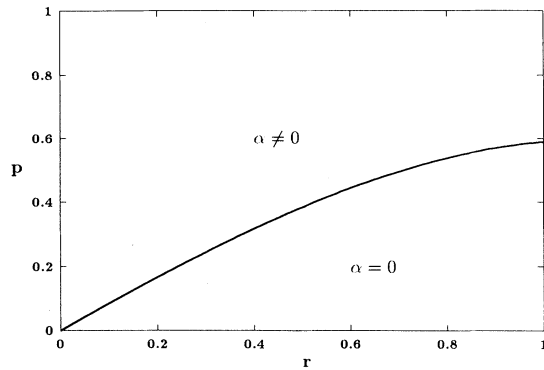


FIG. 2. Phase diagram in the r - p plane according to the pair approximation.

al. easy we have chosen the death probability r as the variable.

The behavior of the densities x and y of T_{H1} and T_{H2} cells, respectively, as functions of r (for a fixed value of p) is shown in Fig. 1(a). The density of one of the cells (T_{H1} or T_{H2}) approaches 1 in the limit where $r \rightarrow 0$ with p fixed. The densities become identical when $r = r_c$. In Fig. 1(b) we show the behavior of α , the order parameter, as a function of r . In Fig. 2 we show the phase diagram for the present model defined on a square lattice in the pair approximation. The critical line was obtained by analyzing the eigenvalues of the matrix (40). We observe that the critical points on the transition line in the phase diagram are always located according to Eq. (33). The conjecture made in Sec. IV B is accomplished if we identify the pair approximation in a square lattice with the solution coming from a Bethe lattice of coordination number 4. For a Bethe lattice of coordination 4 the critical concentration for site percolation is $\rho_c = 1/3$ [20], which leads to $p/r_c > 1/2$.

V. MONTE CARLO SIMULATIONS

We have performed Monte Carlo simulations for several values of p and r . The implementation of the rules was done in a synchronized way. In one dimension we found no ordered state, as expected from the analysis of the preceding section. In two dimensions, however, the ordered state is present in the numerical experiments and we observe a phase diagram very similar to that obtained by the pair approximation, at least for low values of p . Simulations run on a square lattice at high values of r , for instance, have led to a steady state in which both T_{H1} and T_{H2} cells were present [see Fig. 3(a)]. For simulations done at low values of r the numbers of T_{H1} cells and T_{H2} cells at the stationary state are completely different [see Fig. 3(b)], which suggests that one consider the mean difference between the number of T_{H1} and T_{H2} cells as the order parameter of this nonequilibrium phase transition.

In Fig. 4 we plot the densities of T_{H1} and T_{H2} cells against the value of the death probability r , when

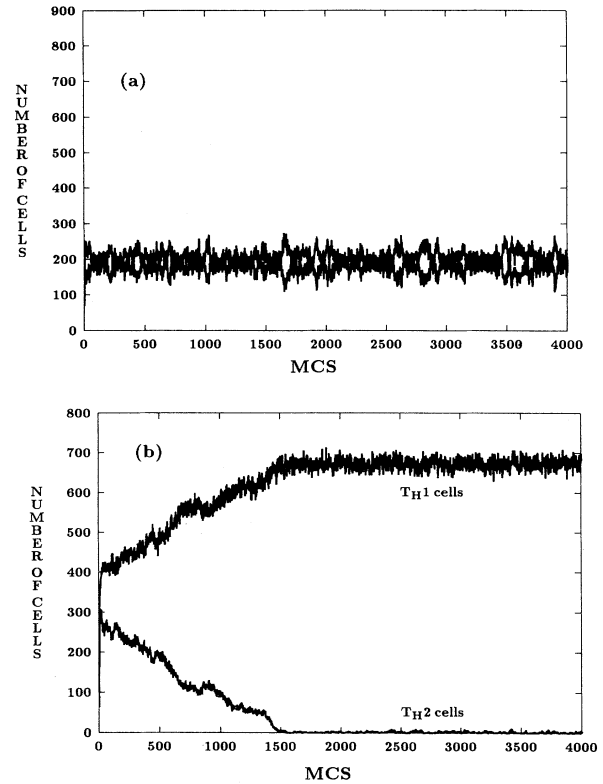


FIG. 3. Number of T_{H1} and T_{H2} cells as a function of the number of Monte Carlo steps (MCS) with $p = 0.3$ for (a) $r = 0.4$ and (b) $r = 0.1$.

$p = 0.3$. It is worthwhile to notice that the critical value $r_c = 0.19$ satisfies Eq. (33). Indeed, for a square lattice $\rho_c = 0.593$ [20] and for $p = 0.3$ it follows from (33) that $r_c < 0.206$, which is satisfied here. In addition, the equilibrium values of the densities for $r > r_c$ are in complete agreement with the exact results contained in

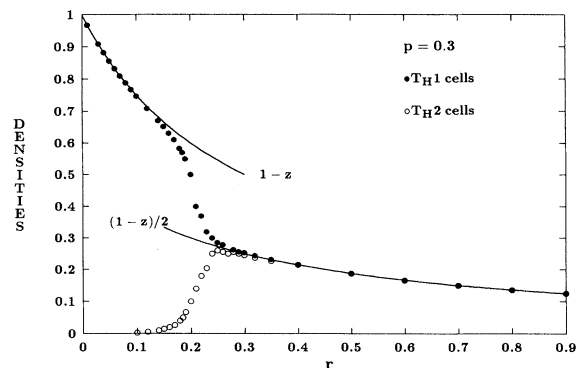


FIG. 4. Densities of T_{H1} and T_{H2} cells as functions of the death probability r , when $p = 0.3$. The dots are data obtained through Monte Carlo simulations. The line $(1-z)/2$ is the exact result for the cell population densities. The line $1-z$ corresponds to the asymptotic (small r) result for one of the densities, where $z = r/(p+r)$.

Eqs. (28) and (30). In contrast to the clean results obtained for high values of r , we found strong fluctuations at the vicinity of the critical parameter r_c . However, when $r < r_c$ results are again in agreement with exact results [Eqs. (28) and (29)].

VI. CONCLUSION

We have analyzed a three-state probabilistic cellular automaton whose dynamical rules are invariant under the permutation between two of three states. As one varies the parameters, the automaton displays a spontaneous symmetry breaking between these two states, giving rise to a nonequilibrium phase transition. The model we dealt with, similar to the one devised by Brass *et al.*, has the purpose of describing the polarization of the T -helper cells in terms of the local interactions occurring at the lymph node, as a consequence of different cytokines produced by the mature cells. The present model exhibits the same features of the Brass *et al.* automaton, but it is amenable to an analytical approach.

The states of the model correspond to the occupation of each site, in the lattice, by one of the three types of T -helper cells T_{H0} , T_{H1} , and T_{H2} . At each time step each cell T_{H1} or T_{H2} has the probability r of changing to a T_{H0} cell and each T_{H0} cell can change into a T_{H1} or T_{H2} cell with a probability that depends on the neighborhood of the site and on a parameter p . Moreover, the evolution rules have transition probabilities with “up-down” ($T_{H1} \leftrightarrow T_{H2}$) symmetry. We have constructed the evolution equation for the average numbers of T_{H0} , T_{H1} , and T_{H2} cells, as well as the evolution equation for the correlation functions. The system evolves in time and eventually reaches a steady state that can be of two types: (a) disordered, in which the average numbers of T_{H1} and T_{H2} cells are equal, and (b) ordered, in which either T_{H1} or T_{H2} cells predominate.

The average number of T_{H0} cells under stationary conditions was obtained exactly and is given by $r/(p+r)$. This result does not depend on the dimension of the lat-

tice and it is true for any conditions of parasitic infection. Another exact result is that the probability of an agglomeration of T_{H0} cells, of any size M , can be obtained exactly, under stationary conditions, and it is given by $[r/(p+r)]^M$.

In the disordered state (low level of infection) the density of each type of cell can also be obtained exactly and does not depend on the space dimension. Also the probabilities of agglomeration of two cells, one being a T_{H1} or a T_{H2} cell and the other being a T_{H0} cell, are obtained exactly and are the product of the densities of these two types of cells (under the conditions cited above).

The state where the T_{H1} or T_{H2} cells predominate (polarized state) can exist only for lattices of two or more space dimensions. The fact that this state cannot be stable in one dimension can be explained by looking to the mechanism that leads to the possibility of an ordered phase. An agglomerate of T_{H1} cells or an agglomerate of T_{H2} cells is always a part of the cluster of T_{H1} and T_{H2} cells. Since in the ordered phase the former must be an infinite agglomerate, so must the latter. Therefore, the ordered state exists only when an infinite cluster of T_{H1} or T_{H2} cells occurs, that is, only when the concentration of these cells $p/(p+r)$ is larger than the percolation concentration ρ_c for the corresponding lattice. In one dimension there will be no transition since in this case an infinite percolation cluster exists only when $\rho_c = 1$.

The ordered state was studied in a square lattice by using a pair approximation and by performing Monte Carlo simulations. The results are in agreement with each other. Both approaches show that the disordered state is stable when the ratio r/p is sufficiently large. As the death probability r is decreased, at fixed p , it reaches a critical value r_c for which a symmetry breaking takes place. For $r < r_c$, the system is in the ordered phase. As a consequence of the up-down symmetry exhibited by the transition rules we expect that this transition is in the same universality class of the kinetic Ising model. The analysis of the critical behavior as well as of the spreading of the damage in this model is planned to be the object of a future work.

-
- [1] S. A. Kauffman, *J. Theor. Biol.* **22**, 437 (1969).
 - [2] G. Weisbuch and H. Atlan, *J. Phys. A* **21**, L189 (1988).
 - [3] P. Grassberger, *Math. Biosci.* **63**, 157 (1983).
 - [4] F. Celada and P. E. Seiden, *Immunol. Today* **13**, 56 (1992).
 - [5] D. Stauffer and G. Weisbuch, *Physica A* **180**, 42 (1992).
 - [6] D. Stauffer and M. Sahimi, *Int. J. Mod. Phys.* **4**, 401 (1993).
 - [7] J. E. Satulovsky and T. Tomé, *Phys. Rev. E* **49**, 5073 (1994).
 - [8] R. M. Zorzenon dos Santos, *Physica A* **196**, 12 (1993).
 - [9] A. Brass, R. K. Grencis, and K. J. Else, *J. Theor. Biol.* **166**, 189 (1994).
 - [10] A. Brass, A. J. Bancroft, M. E. Clamp, R. K. Grencis, and K. J. Else, *Phys. Rev. E* **50**, 1589 (1994).
 - [11] T. R. Mosmann and R. L. Coffman, *Adv. Immunol.* **46**, 111 (1988).
 - [12] K. J. Else and R. K. Grencis, *Immunology* **72**, 508 (1991).
 - [13] P. Scott and H. E. Kaufmann, *Immunol. Today* **12**, 346 (1991).
 - [14] K. J. Else, G. M. Entwistle, and R. K. Grencis, *Parasite Immunol.* **15**, 595 (1993).
 - [15] S. Wolfram, *Rev. Mod. Phys.* **55**, 601 (1983).
 - [16] G. Grinstein, C. Jayaprakash, and H. Yu, *Phys. Rev. Lett.* **55**, 2527 (1985).
 - [17] R. Dickman, *Phys. Rev. A* **34**, 4246 (1986).
 - [18] H. A. Gutowitz, J. D. Victor, and B. W. Knight, *Physica D* **28**, 18 (1987).
 - [19] T. Tomé and M. J. de Oliveira, *Phys. Rev. A* **40**, 6643 (1989).
 - [20] D. Stauffer, *Introduction to Percolation Theory* (Taylor & Francis, London, 1985).