Stochastic dynamics of dengue epidemics

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We use a stochastic Markovian dynamics approach to describe the spreading of vector-transmitted diseases, such as dengue, and the threshold of the disease. The coexistence space is composed of two structures representing the human and mosquito populations. The human population follows a susceptible-infected-recovered (SIR) type dynamics and the mosquito population follows a susceptible-infected-susceptible (SIS) type dynamics. The human infection is caused by infected mosquitoes and vice versa, so that the SIS and SIR dynamics are interconnected. We develop a truncation scheme to solve the evolution equations from which we get the threshold of the disease and the reproductive ratio. The threshold of the disease is also obtained by performing numerical simulations. We found that for certain values of the infection rates the spreading of the disease is impossible, for any death rate of infected mosquitoes.

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I. INTRODUCTION

Dengue is a vector-borne infectious disease with very complex dynamics, whose spreading is a relevant problem of public health. The disease is transmitted to human mainly by the mosquito *Aedes aegypti*. Many factors are determinant for the transmission of dengue in urban centers, such as the climatic conditions for the vector proliferation, and the human concentration and mobility. Although much effort is expended in the development of a vaccine against the four types of virus, until now the only available strategy to reduce the spreading of the disease [1] is the control of the vector population. Therefore, it is very important to analyze the effect of vector control in avoiding the occurrence of dengue epidemics. In this context, the interhost modeling of dengue dynamics and control may be a very useful tool for helping our understanding and for the establishment of vector control strategies.

Different techniques and approaches are used to model the dynamics of transmitted diseases [2,3] such as deterministic differential equations [4], stochastic dynamics [5–7], cellular automata [8], and complex networks [9]. Concerning vector transmitted diseases including dengue modeling, there are also different schemes and approaches [2,3] based on deterministic models of differential equations [10–12], probabilistic cellular automata [13–16], and complex networks [17,18]. Although a description in terms of a master equation defined on a lattice has been used to investigate epidemic models of direct transmitted diseases [5], this approach has not been explored in the investigation of a vector-borne infectious disease. This approach takes into account in an explicit way the spatial structure of the environment and, in contrast to mixing models, it predicts stochastic fluctuations and correlations in the number of individuals, features that are inherent in real population dynamics. As we shall see, it allows a definition of the basic reproduction ratio in terms of conditional probability, which is nontrivial only when correlations are taken into account.

As in other works [10–12,15], the present approach is also motivated by actual data of dengue epidemics [19]; in particular, by two outbreaks of dengue that occurred in Salvador, Bahia, Brazil in 1995 (without vector control) and 2002 (with vector control). Those data had also motivated a previous analysis based on the basic reproductive ratio [10].

The first dengue model was proposed by Newton and Reiter [20] in 1992 assuming a susceptible-exposed-infected-recovered (SEIR) structure for humans and susceptible-exposed-infected (SEI) structure for mosquitoes due to the fact that the mosquitoes die before being removed. This framework has been followed by other continuous and discrete dengue models [10–12,14,15]. Here we consider a simpler model, illustrated in Fig. 1, assuming a susceptible-infected-recovered (SIR) structure for humans and susceptible-infected-susceptible (SIS) structure for mosquitoes. The infection of humans is due to mosquitoes and the infection of mosquitoes is due to humans. In other words the infection reactions, $S \to I$, on both structures are catalytic and not autocatalytic as happens in the original SIR and SIS models [5–7]. The other reactions, $I \to R$ in the SIR structure and $I \to S$ in the SIS structure, are spontaneous reactions. The mosquito structure has been simplified by suppressing the death and the birth of mosquitoes which amounts to saying that a dead mosquito is immediately replaced by a newborn (susceptible) mosquito. We are, therefore, assuming that the number of mosquitoes remains constant throughout the outbreak of the epidemics.

The features of our model that differ from that of Newton and Reiter [20] are as follows. First, we do not distinguish between susceptible and exposed states both for humans and mosquitoes. Second, deaths of humans are not considered since the human lifetime is much larger than the period of the disease. The deaths of the mosquitoes are implicit in the model in the following sense. The reaction $I \to S$ for the mosquitoes is to be interpreted as the death of an infected mosquito and the simultaneous birth of a susceptible mosquito. The major difference, however, rests on the use of a stochastic lattice model, which takes into account the spatial distribution of humans and mosquitoes.

After setting up the master equation we develop two truncation schemes to solve the evolution equations from which we get the threshold of the disease and the reproductive ratio. From the second truncation scheme we found that, for

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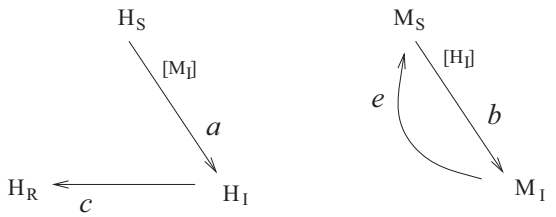

FIG. 1. Illustration of the reactions. Left panel: SIR structure. A susceptible human (H_S) becomes infected (H_I) through a catalytic reaction mediated by infected mosquitoes (M_I). An infected human becomes recovered (H_R) spontaneously and remains permanently in this state. Right panel: SIS structure. A susceptible mosquito (M_S) becomes infected through a catalytic reaction mediated by infected humans. An infected mosquito spontaneously becomes susceptible.

a range of values of the infection rates, the disease does not spread no matter how small is the rate at which the infected mosquitoes disappear. This result is confirmed by numerical simulations performed on a square lattice.

This paper is organized as follows. In Sec. II, we introduce the model and derive from the master equations the evolution equations for the densities. We also define in this section the quantities that characterize the spreading of the epidemics, the reproductive ratio, and the size of the epidemics. In Sec. III, we develop the simplest truncation scheme and show how some classic results are obtained. In Sec. IV, we introduce the second truncation scheme and set up the evolutions equations for densities and pair correlations. The stability analysis of these equations allows us to obtain the threshold of epidemics from which we get the phase diagram. Section V is reserved for the numerical simulations of the model on a square lattice. Concluding remarks and discussion are placed in the last section.

II. MODEL AND EVOLUTION EQUATIONS

The modeling of disease spreading that we consider here corresponds to a continuous time stochastic Markovian process defined on a lattice, with periodic boundary conditions, where the sites are occupied by human individuals or by mosquitoes. In order to properly describe the human and mosquito populations we consider two sublattices of the whole lattice, one for each population. The sublattices, named H and M, are interpenetrating in such a way that the nearest neighbor sites of a site of one sublattice belong to the other sublattice. The number of nearest neighbors, the coordination number γ, is the same for both sublattices. Each site of the sublattice M can be in one of two states, either occupied by a susceptible mosquito (M_S) or by an infected mosquito (M_I). Each site of the sublattice H can be in one of three states, occupied by a susceptible human (H_S), occupied by an infected human (H_I), or occupied by a recovered human (H_R). The system evolves in time according to the following stochastic dynamics.

Each site changes its state, independently of the others, at waiting times distributed exponentially with rates that depend on the state of the site and its neighborhood. (a) If a site is occupied by a susceptible human then it becomes infected at rate a times the fraction of infected mosquitoes in its neighborhood. If the site is occupied by an infected human then it recovers spontaneously with rate c. Once recovered the individual remains permanently in this state which means that, if the site is occupied by a recovered human, it remains unchanged. (b) If a site is occupied by a susceptible mosquito then it becomes infected at a rate b times the fraction of infected humans in its neighborhood. If the site is occupied by an infected mosquito it spontaneously becomes susceptible with rate e. Our simple model is therefore described by four parameters a, b, c, and e. In the applications we will further simplify by setting $a + e = b + c$.

For convenience we introduce a stochastic variable η_i associated with each site i of the lattice that takes the values 0, 1, 2, 3, or 4 according to whether the site i is occupied, respectively, by a susceptible mosquito, an infected mosquito, a susceptible human, an infected human, or a recovered human. The time evolution of the probability distribution $P(\eta)$ of configuration $\eta = \{\eta_i\}$ is governed by the master equation

$$\frac{d}{dt}P(\eta) = \sum_i \{w_i(\mathcal{A}_i^- \eta)P(\mathcal{A}_i^- \eta) - w_i(\eta)P(\eta)\}, \quad (1)$$

where $w_i(\eta)$ is the transition rate from η to $\eta' = \mathcal{A}_i\eta$, and $\mathcal{A}_i$ is the operator that changes $\eta_i \to \eta_i'$ as follows: 0→1, 1→0, 2→3, 3→4; and $\mathcal{A}_i^-$ is the inverse of $\mathcal{A}_i$. The transition rate $w_i(\eta)$ is defined according to the rules stated above. The time evolution of an average $\langle f(\eta)\rangle = \sum_\eta f(\eta)P(\eta)$ is obtained from the master equation and is given by

$$\frac{d}{dt}\langle f(\eta)\rangle = \sum_i \langle [f(\mathcal{A}_i\eta) - f(\eta)]w_i(\eta)\rangle. \quad (2)$$

Instead of using the full probability distribution $P(\eta)$ we consider an equivalent description in terms of the various marginal probability distributions, obtained from $P(\eta)$. The time evolution of the several marginal probability distributions is obtained from the master equation (1) and comprises a hierarchic set of coupled equations which is equivalent to the master equation. This approach is convenient because it allows us to obtain a solution of the set of equations by a truncation scheme to be explained shortly. In what follows we assume invariance of the properties by a translation of the lattice by two lattice spacings so that a site of one sublattice goes into another site of the same sublattice. Isotropy is also assumed. At $t = 0$, a fraction ϵ of the mosquito sites, which we consider to be very small, are infected and all the human sites are susceptible.

Let us denote by $P(\eta_i)$ the marginal one-site probability that represents the probability that a site i is in state η_i and by $P(\eta_i,\eta_j)$ the marginal two-site probability that represents the probability that site i is in state η_i and a neighboring site j is in state η_j. Other marginal probabilities are denoted in an analogous way. The evolution equation of the one-site probability $P(1)$, which represents the density of infected mosquitoes, can be obtained from Eq. (2) if we recall that $P(1) = \langle\delta(\eta_i,1)\rangle$ and is given by

$$\frac{d}{dt}P(1) = bP(03) - eP(1), \quad (3)$$

where we used the definition $P(03) = \langle\delta(\eta_i,0)\delta(\eta_j,3)\rangle$. The notation $\delta(x,y)$ stands for the Kronecker delta. The time evolution equation for $P(0)$, the density of susceptible

mosquitoes, can be obtained from Eq. (3) by using the property $P(0)+P(1)=1$.

The evolution equations for $P(2)$ and $P(3)$, the densities of susceptible and infected humans, respectively, are obtained similarly from Eq. (2) and are given by

$$\frac{d}{dt}P(2) = -aP(12), \tag{4}$$

$$\frac{d}{dt}P(3) = aP(12) - cP(3). \tag{5}$$

The evolution equation for $P(4)$, the density of recovered humans, is

$$\frac{d}{dt}P(4) = cP(3) \tag{6}$$

and can also be obtained from Eqs. (4) and (5) by taking into account the property $P(2)+P(3)+P(4)=1$.

To characterize the threshold of the epidemic it is convenient to write Eq. (3) for the density of infected mosquitoes and Eq. (5) for the density of infected individuals in the forms

$$\frac{d}{dt}P(1) = bP(0|3)P(3) - eP(1), \tag{7}$$

$$\frac{d}{dt}P(3) = aP(2|1)P(1) - cP(3), \tag{8}$$

where $P(2|1)=P(12)/P(1)$ is the conditional probability of occurrence of a susceptible individual given an infected neighboring mosquito and $P(0|3)=P(03)/P(3)$ is the conditional probability of occurrence of a susceptible mosquito given an infected neighboring individual. Using the simplified notation $x=P(1)$ and $z=P(3)$ the set of equations (7) and (8) can be written as

$$\begin{pmatrix} dx/dt \\ dz/dt \end{pmatrix} = \begin{pmatrix} -e & bP(0|3) \\ aP(2|1) & -c \end{pmatrix} \begin{pmatrix} x \\ z \end{pmatrix}. \tag{9}$$

At the early stages of the epidemic the cross-transmission probabilities $P(0|3)$ and $P(2|1)$ can be considered to be constant (independent of time) and the set of equations (7) and (8) becomes a linear set of equations. A fundamental quantity that characterizes the spreading of the disease is the so-called reproductive ratio R_0, which is defined here as

$$R_0 = \frac{ab}{ce}P(2|1)P(0|3). \tag{10}$$

The threshold of epidemic is determined by the largest eigenvalue λ of the matrix (9), which is related to the reproductive ratio by

$$R_0 = \left(1+\frac{\lambda}{e}\right)\left(1+\frac{\lambda}{c}\right), \tag{11}$$

or by

$$\lambda = \tfrac{1}{2}\{-(e+c)+\sqrt{(e-c)^2+4ecR_0}\}. \tag{12}$$

According to the linear analysis, the threshold of epidemic occurs when the largest eigenvalue vanishes, which happens, according to Eq. (11), when $R_0=1$. Moreover, when $\lambda<0$ there is no transmission of disease. According to Eq. (11) this happens when $R_0<1$. The spreading of the disease occurs when $\lambda>0$, that is, when $R_0>1$. The reproductive ratio characterizes not only the threshold of the disease but also its strength.

An epidemic is usually characterized by the epidemic curve defined as the number of cases occurring in unit time, for instance, in a day or in a weak, plotted as a function of time. In other terms it is the number of susceptible individuals that are being infected per unit time. In the place of number of individuals we may use the density of individuals so that the epidemic curve is defined as the density of individuals that are being infected per unit time $\zeta=-dy/dt$, where $y=P(3)$ is the density of susceptible individuals. Using the initial conditions $x=\epsilon$, $y=1$, and $z=0$ where ϵ is a small quantity, ζ increases and then decreases in time and vanishes when $t\to\infty$.

The density of recovered individuals $\rho=P(4)$ increases with time, as implied by Eq. (6), and approaches its maximum value in the limit $t\to\infty$. This final density of recovered individuals is the integral of the epidemic curve, that is,

$$\int_0^\infty \zeta\, dt = \rho, \tag{13}$$

obtained by integrating $\zeta=-dy/dt$, and by using the initial condition $y(0)=1$ and the result that the final density of infected individuals vanishes, $z(\infty)=0$, and the constraint $\rho+y+z=1$. The final density of recovered individuals, which is a measure of the size of the epidemic, may be understood in this approach as the order parameter in the sense that it vanishes in the nonspreading regime and is nonzero in the regime where the disease spreads. Strictly speaking the vanishing only occurs when ϵ vanishes. Notice that the limit $\epsilon\to 0$ should be taken after the limit $t\to\infty$, which is the proper way to get the transition from the spreading to the nonspreading regime.

III. SIMPLE MEAN-FIELD APPROXIMATION

The three equations for the time evolution of $P(1)$, $P(2)$, and $P(3)$ are not a set of closed equations because they depend on the two-site probabilities $P(12)$ and $P(03)$. To get closed equations, we first use a scheme, called the simple mean-field (SMF) approximation, which consists of writing a two-site probability as the product of one-site probabilities; that is, $P(\eta_i,\eta_j)=P(\eta_i)P(\eta_j)$. Using the abbreviations $P(1)=x$, $P(2)=y$, and $P(3)=z$, respectively, the densities of infected mosquitoes, susceptible individuals, and infected individuals, this approximation gives $P(12)=xy$ and $P(03)=(1-x)z$ so that Eqs. (3), (4), and (5) are reduced to the forms

$$\frac{dx}{dt} = b(1-x)z - ex, \tag{14}$$

$$\frac{dy}{dt} = -axy, \tag{15}$$

$$\frac{dz}{dt} = axy - cz. \tag{16}$$

To describe the spreading of the disease we consider an initial condition such that all individuals are susceptible so that $y=1$ and $z=0$. Moreover we consider a very small density of infected mosquitoes, that is, $x=\epsilon$ where $\epsilon\ll 1$.

Then, we look for solutions for x, y, and z in the limit $t \to \infty$. In this limit the densities of infected mosquitoes and infected individuals vanish, $x \to 0$ and $z \to 0$. If the density of recovered individuals $\rho = 1 - y - z$ approaches a nonzero value than the disease spreads. On the other hand if ρ approaches zero (when $\epsilon \to 0$) the disease does not spread. This means that the stationary solution $x = 0$, $z = 0$, $y = 1$ ($\rho = 0$) is the solution corresponding to the nonspreading regime.

To obtain the stability of this solution we linearize the above equations around this solution to obtain

$$\frac{dx}{dt} = bz - ex, \tag{17}$$

$$\frac{d\rho}{dt} = ax, \tag{18}$$

$$\frac{dz}{dt} = ax - cz. \tag{19}$$

A linear analysis of stability amounts to determining the eigenvalues of the matrix composed of the coefficients of the right-hand side of these equations, given by

$$\begin{pmatrix} -e & 0 & b \\ a & 0 & 0 \\ a & 0 & -c \end{pmatrix}. \tag{20}$$

One eigenvalue is zero and the others are the roots of

$$\lambda^2 + (e + c)\lambda + ec - ab = 0, \tag{21}$$

that is,

$$\lambda_{\pm} = \tfrac{1}{2}\{-(e + c) \pm \sqrt{(e - c)^2 + 4ab}\}. \tag{22}$$

The solution is stable as long as $\lambda_+ < 0$, that is when $ec > ab$. The threshold of the spreading occurs when

$$\frac{ab}{ec} = 1. \tag{23}$$

For $a + e = b + c$, the threshold line is described by $e = b$ as shown in the phase diagram of Fig. 2.

The threshold obtained by the above linear analysis can equivalently be obtained from the condition $R_0 = 1$; that is, when the reproductive ratio R_0 given by Eq. (10) equals 1. In the present case of the simple mean-field approach, $P(2|1) = P(2)$ and $P(0|3) = P(0)$. The initial condition gives $P(2) = 1$ and $P(0) = 1$ so that

$$R_0 = \frac{ab}{ce}, \tag{24}$$

which coincides with the condition (23) when $R_0 = 1$.

Near the threshold of epidemic the density of infected mosquitoes is much smaller than unity and we may neglect x in the first term on the right-hand side of Eq. (14). The evolution equation for x becomes then

$$\frac{dx}{dt} = bz - ex, \tag{25}$$

which together with Eqs. (15) and (16) allows us to determine explicitly the size of the epidemic ρ. This is possible because these equations imply a conservation law obtained as follows.

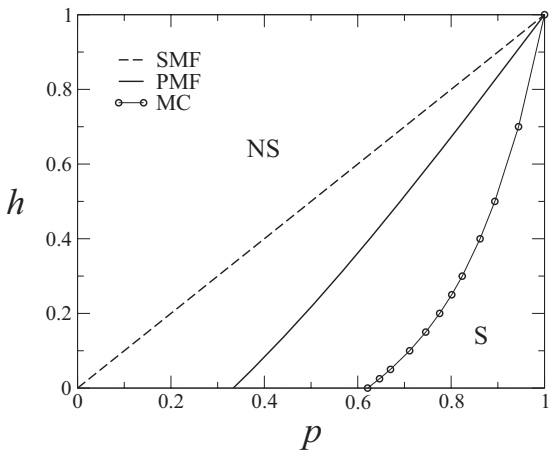

FIG. 2. Phase diagram in the plane $h = e/(e + a)$ vs $p = b/(b + c)$ for the case $e + a = b + c$, showing the regions of spreading (S) and nonspreading (NS) of the disease for the SMF approximation, PMF approximation for coordination number $\gamma = 4$, and Monte Carlo (MC) simulations on a square lattice. When $e \to 0$, the value of b approaches zero for the SMF, the value $p = 1/3$ for the PMF, and the value $p = 0.621$ for numerical simulations.

We start by defining the quantity $\phi = cx + bz$. From Eqs. (25) and (16) its evolution equation is given by

$$\frac{d\phi}{dt} = -cex + abxy. \tag{26}$$

The ratio of Eqs. (26) and (15) gives

$$\frac{d\phi}{dy} = \frac{ce}{ay} - b, \tag{27}$$

which can be integrated to give

$$cx + bz = \frac{ce}{a} \ln y + b(1 - y), \tag{28}$$

which is the desired conservation law. The constant of integration was obtained by remembering that at $t = 0$, $x = \epsilon \to 0$, $y = 1$, and $z = 0$.

When $t \to \infty$, then $x = 0$, $z = 0$, and $1 - y = \rho$ so that

$$\ln(1 - \rho) + R_0\rho = 0, \tag{29}$$

where we used the relation $R_0 = ab/ce$. This equation determines the size of the epidemic ρ and may be written in the form

$$1 - \rho = e^{-R_0\rho}. \tag{30}$$

This equation is the same equation obtained by Kendall [21] for the model introduced by Kermack and McKendrick [22] to describe directed transmitted epidemics [2,3] and also obtained by means of the simple mean-field approach to the SIR model on a lattice [7]. Near the threshold it is given by $\rho = 2(R_0 - 1)$.

IV. PAIR MEAN-FIELD APPROXIMATION

Next we set up equations for the pair mean-field (PMF) approximation. To this end we begin by writing the equations for the two-site probabilities. The evolution equation for the probability $P(03)$ of a site being occupied by a susceptible mosquito and a neighboring site by an infected individual is

given by

$$\frac{d}{dt}P(03) = eP(13) - (c+rb)P(03) + (1-r)aP(021) - (1-r)bP(303), \quad (31)$$

where $r = 1/\gamma$, and γ is the coordination number of the lattice. The notation $P(\eta_i,\eta_j,\eta_k)$ stands for the joint three-site probability where i and k are nearest neighbor sites of j. The evolution equation for the probability $P(12)$ of a site being occupied by an infected mosquito and a neighboring site by a susceptible individual is given by

$$\frac{d}{dt}P(12) = -(e+ra)P(12) + (1-r)bP(302) - (1-r)aP(121). \quad (32)$$

The equations for the other two-site probabilities, $P(02)$, $P(04)$, $P(13)$, and $P(14)$ are not necessary because they can be written in terms of $P(03)$, $P(12)$, $P(1)$, $P(2)$, and $P(3)$.

Let us consider now the evolution equations for $P(1)$, $P(2)$, $P(3)$, $P(03)$, and $P(12)$, given by Eqs. (3), (4), (5), (31), and (32). These five equations are not closed because (31) and (32) include three-site probabilities. To get a set of closed equations we now use a truncation at the level of two-site probabilities [23–25]. This truncation amounts to use the following approximation for the three-site probability:

$$P(\eta_i,\eta_j,\eta_k) = \frac{P(\eta_i,\eta_j)P(\eta_j,\eta_k)}{P(\eta_j)}. \quad (33)$$

This approximation is used in Eqs. (31) and (32) to get a set of closed equations in the variables $P(1) = x$, $P(2) = y$, $P(3) = z$, $P(03) = u$, and $P(12) = v$. With this approximation the model is described by the set of five equations

$$\frac{dx}{dt} = bu - ex, \quad (34)$$

$$\frac{dy}{dt} = -av, \quad (35)$$

$$\frac{dz}{dt} = av - cz, \quad (36)$$

$$\frac{du}{dt} = e(z-u) - (c+rb)u + (1-r)a\frac{(y-v)v}{y} - (1-r)b\frac{u^2}{1-x}, \quad (37)$$

$$\frac{dv}{dt} = -(e+ra)v + (1-r)b\frac{u(y-v)}{1-x} - (1-r)a\frac{v^2}{y}. \quad (38)$$

We have solved the above set of equations using the initial condition $x = 10^{-4}$, $y = 1$, $z = 0$, $u = 0$, and $v = 10^{-4}$. From the numerical solution we have obtained the epidemic curve; that is, the density of individuals that are being infected per unit time, $\zeta = -dy/dt$. Figure 3 shows examples of the epidemic curve obtained in the PMF approximation for $b/c = 2$ and $a + e = b + c$.

To obtain the threshold of the spreading of the disease we analyze the stability of the solution $x = 0$, $y = 1$, $z = 0$, $u = 0$, and $v = 0$, which characterizes the state where the disease does not spread. To get the stability of this equation we linearize

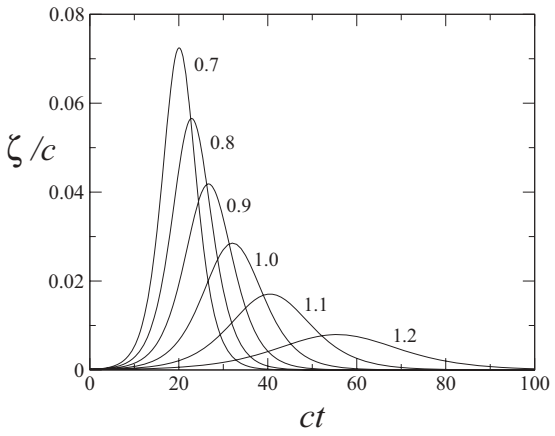

FIG. 3. Epidemic curves according to the PMF approximation. Each curve represents the density of individuals that are being infected per unit time $\zeta = -dy/dt$ as a function of time for the values of e/c indicated and for $b/c = 2$ and $a + e = b + c$. The area below the epidemic curve ζ equals the final density of recovered individuals ρ and becomes negligible as one approaches the threshold of epidemic.

the evolution around this solution to obtain

$$\frac{dx}{dt} = -ex + bu, \quad (39)$$

$$\frac{d\rho}{dt} = av, \quad (40)$$

$$\frac{dz}{dt} = -cz + av, \quad (41)$$

$$\frac{du}{dt} = ez - (e+c+rb)u + (1-r)av, \quad (42)$$

$$\frac{dv}{dt} = (1-r)bu - (e+ra)v, \quad (43)$$

where $\rho = 1 - y - z$. A linear analysis of stability amounts to calculating the eigenvalues of the matrix composed of the linear coefficients of the right-hand side of the above equations, given by

$$\begin{pmatrix} -e & 0 & 0 & b & 0 \\ 0 & 0 & 0 & 0 & a \\ 0 & 0 & -c & 0 & a \\ 0 & 0 & e & -(e+c+rb) & (1-r)a \\ 0 & 0 & 0 & (1-r)b & -(e+ra) \end{pmatrix}. \quad (44)$$

Two eigenvalues are $\lambda_1 = 0$ and $\lambda_2 = -e$. The others are the roots of

$$-(\lambda+c)(\lambda+e+c+rb)(\lambda+e+ra) + ea(1-r)b + (\lambda+c)(1-r)^2ab = 0. \quad (45)$$

The line of stability is obtained by setting $\lambda = 0$ in this equation, to get

$$-c(e+c+rb)(e+ra) + (1-r)abe + (1-r)^2abc = 0. \quad (46)$$

As before, we consider $b + c = a + e$ and write the equation that describes the threshold line as

$$rc^2 + [e - (1-2r)b]c - (1-r)(b-e)e = 0. \quad (47)$$

In Fig. 2 we show the line described by this equation for the case of coordination number $\gamma = 4$. This line represents the phase transition between the spreading and nonspreading regimes. Below the transition line the nonspreading solution becomes unstable, giving rise to the spreading solution. Comparing the pair and simple mean-field approximations we see that the inactive region of the phase diagram is larger for the pair approximation, as can be seen in Fig. 2.

When $e = 0$, the threshold of the disease occurs at $b/c = r/(1-2r)$, a nonzero value. In terms of the quantity $p = b/(b+c)$, used in the phase diagram of Fig. 2, it occurs at $p = r/(1-r) = 1/(\gamma-1)$. This result leads us to conclude that there is a range of values of b/c, as can be seen in Fig. 2, for which there is no spreading of the disease for any e/c. This result is qualitatively distinct from the SMF result for which the threshold occurs at $b = 0$ when $e = 0$. As we shall see this PMF prediction is confirmed by numerical simulations.

The threshold of epidemic obtained by the above linear analysis can equivalently be obtained in terms of the reproductive ratio. In the present case of the pair mean-field approach, $P(2|1) = P(12)/P(1) = v/x$ and $P(0|3) = P(03)/P(3) = u/z$ so that

$$R_0 = \frac{abuv}{ecxz}. \tag{48}$$

The reproductive ratio R_0 depends on the parameters a, b, c, and e only through the ratios e/c, b/c, and a/c. Indeed, if we substitute λ given by Eq. (11) into Eq. (45) we get an equation that gives R_0 in an implicit form. It is easy to see that this equation contains the parameters a, b, c, and e only through the ratios e/c, b/c, and a/c.

It is worth mentioning that in the early stages of spreading of epidemics the quantities x, z, u, and v increase exponentially, that is, the increase in time of each of these quantities is proportional to $e^{\lambda t}$, where λ is the largest eigenvalue of the matrix (44). From this behavior we see that the ratios $v/x = P(2|1)$ and $u/z = P(0|3)$ are independent of time at the early stage of the spreading of disease, and so is the reproductive ratio R_0.

An important aspect of our pair approach concerns the relation of the epidemic curve to the conditional probabilities $P(2|1)$ and $P(0|3)$, which are treated exactly in this approach. Remember that $P(2|1)$ is the conditional probability of the occurrence of a susceptible individual in the presence of a infected mosquito and $P(0|3)$ is the conditional probability of the occurrence of a susceptible mosquito in the presence of a infected individual.

V. NUMERICAL SIMULATIONS

Numerical simulations were performed on a square lattice according to the following rules. At each time step, a site is chosen from a list of infected sites; that is, a list of sites that are either occupied by an infected mosquito or by an infected human individual. (i) If the chosen site is M_I then with probability h it becomes M_S and, with the complementary probability $1-h$, a neighboring site is chosen at random; if this neighboring site is H_S then it becomes H_I. (ii) If the chosen site is H_I then with probability q it becomes H_R and with the complementary probability $p = 1-q$, a neighboring site is chosen at random; if this neighboring site is M_S then it becomes M_I. The time is then increased by $1/N_I$ where N_I is the number of sites in the list. These rules are not the most general that one can conceive from the original definition of the model but are very simple and valid as long as $e + a = b + c$. Since the transition rates must be proportional to the transition probabilities, it follows that $a = \alpha(1-h)$, $b = \alpha(1-q)$, $c = \alpha q$, and $e = \alpha h$. From these relations we see that $e + a = b + c = \alpha$ and may write $h = e/(e+a)$, $q = c/(b+c)$, and $p = b/(b+c)$.

At $t = 0$ all sites of sublattice H were occupied by susceptible human individuals and all sites of sublattice M were occupied by susceptible mosquitoes except one site which is occupied by an infected mosquito. We use lattice sizes sufficiently large so that the cluster of infected sites never reached the border of the lattice. The simulation was repeated a number of times, on the order of a thousand, and the averages of relevant quantities were obtained. For instance, we measured the mean number of infected human individuals and the mean number of infected mosquitoes as functions of time. The location of the critical point was obtained by assuming an algebraic behavior of these quantities at the critical point.

The results are shown in the phase diagram of Fig. 2. When $h = 0$ ($e = 0$), we have obtained for p a nonzero value, a result qualitatively distinct from the SMF approximation and similar to the PMF approximation, although the value is a bit larger than that of the PMF approach, namely $p = 0.621$. Therefore, our model predicts a range of values of $p = b/(b+c)c$ for which the epidemic is impossible for any h.

VI. CONCLUDING REMARKS AND DISCUSSION

In this work we have applied stochastic dynamics to a dengue bipartite lattice model to analyze the transition between epidemic and nonepidemic states in terms of the probability of human-mosquito and mosquito-human transmission and vector control parameters. We have presented a precise definition of the reproductive rate R_0 which is appropriate for systems described by stochastic dynamics, that characterizes the spreading of the disease, and we have related it to the largest eigenvalue of the matrix associated with the evolution equations. This definition can be generalized to other types of disease transmission and seems to be promising in the analysis of epidemics. According to our definition, the reproductive rate is directly related to the conditional probability of the occurrence of a susceptible human (mosquito) given the presence in the neighborhood of an infected mosquito (human). At the early stages of the epidemic, these conditional probabilities are simply equal to unity in the SMF approach but are nontrivial in the PMF, which makes this approach a richer description when compared to the SMF. Another quantity that characterizes the epidemic is ρ, the quantity that measures the size of the epidemic and vanishes in the nonspreading regime. It was also determined by means of the SMF and PMF approaches.

It is worth mentioning that the initial conditions we have used in the mean-field approach are translational invariant. If we had used an initial condition such that a finite number of mosquito sites were infectious, the initial state would not be translational invariant and the mean-field calculation we have employed here would no longer be valid. For this initial

condition the disease may go to an early extinction even if $R_0 > 1$, and the growth of the epidemic may no longer be exponential.

A qualitative relevant result that we have obtained from the PMF approximation, and confirmed by numerical simulations, is that for small values of p there is no epidemic. The minimum value for the spreading of the disease, that occurs for $h = 0$, is $p^* = 1/(\gamma - 1)$ for the PMF approximation and $p^* = 0.621$ for numerical simulations on a square lattice. This result can be understood by relating the present model with percolation. It is well established that the SIR model has a close relation with percolation [6,7], so that it is to be expected that the present model is also related to percolation growth.

To appreciate the relation with percolation we consider the spreading of the disease on a Cayley tree of coordination γ when $h = 0$, starting from one single infected mosquito, and observing the growth of the cluster of infected mosquitoes and infected individuals. A site M_I will remain forever in this state because $e = 0$, and a site H_I will eventually become H_R, so that in the stationary state the percolating cluster is formed by infected mosquitoes in sites belonging to sublattice M and recovered individuals in sites belonging to sublattice H. In the process of cluster growth we may ask for the probability that a site next to the border of the growing cluster will belong to the stationary cluster. If the site belongs to the H sublattice the probability is 1. If the site belongs to the M sublattice, a calculation similar to that of Tomé and Ziff [6], gives the value

$$p_M = \frac{p}{\gamma - (\gamma - 1)p}. \tag{49}$$

Therefore, we may say that the present model as defined on a Cayley tree can be exactly mapped into an inhomogeneous site percolation on a Cayley tree such that a site of sublattice H is permanently active and a site of sublattice M is active with probability p_M. The critical value of p_M for percolation in such a lattice is $1/(\gamma - 1)^2$ instead of $1/(\gamma - 1)$, as happens in homogeneous site percolation [26]. If we substitute this value into Eq. (49), we get $p = 1/(\gamma - 1)$, which is the critical value we have found by means of the PMF approximation.

The relation to percolation allowed us to understand the existence of the minimum value of p for the spreading of the disease and therefore a range of values of infection rates for which the epidemic is impossible for any death rate of infected mosquitoes. This result might be relevant in order to get the optimal intervention scenario in the control of the disease. In future work we intend to analyze other important issues such as the role of diffusion. Specifically, we wish to know whether this scenario is preserved or not by the inclusion of diffusion.

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