Enhancement of epidemic spread by noise and stochastic resonance in spatial network models with viral dynamics

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We extend a previous dynamical viral network model to include stochastic effects. The dynamical equations for the viral and immune effector densities within a host population of size n are bilinear, and the noise is white, additive, and Gaussian. The individuals are connected with an $n \times n$ transmission matrix, with terms which decay exponentially with distance. In a single individual, for the range of noise parameters considered, it is found that increasing the amplitude of the noise tends to decrease the maximum mean virion level, and slightly accelerate its attainment. Two different spatial dynamical models are employed to ascertain the effects of environmental stochasticity on viral spread. In the first model transmission is unrestricted and there is no threshold within individuals. This model has the advantage that it can be analyzed using a Fokker-Planck approach. The noise is found both to synchronize and uniformize the trajectories of the viral levels across the population of infected individuals, and thus to promote the epidemic spread of the virus. Quantitative measures of the speed of spread and overall amplitude of the epidemic are obtained as functions of the noise and virulence parameters. The mean amplitude increases steadily without threshold effects for a fixed value of the virulence as the noise amplitude σ is increased, and there is no evidence of a stochastic resonance. However, the speed of transmission, both with respect to its mean and variance, undergoes rapid increases as σ changes by relatively small amounts. In the second, more realistic, model, there is a threshold for infection and an upper limit to the transmission rate. There may be no spread of infection at all in the absence of noise. With increasing noise level and a low threshold, the mean maximum virion level grows quickly and shows a broad-based stochastic resonance effect. When the threshold within individuals is increased, the mean population virion level increases only slowly as σ increases, until a critical value is reached at which the mean infection level suddenly increases. Similar results are obtained when the parameters of the model are also randomized across the population. We conclude with a discussion and a description of a diffusion approximation for a model in which stochasticity arises through random contacts rather than fluctuation in ambient virion levels.

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INTRODUCTION

There have been many recent studies of coupled nonlinear dynamical systems in the absence or presence of additive or multiplicative noise [1]. In a recent communication [2] we considered a mathematical model for the spread of viral infection within human or other populations in which both the dynamics of viral (or bacterial) growth within individuals and the interactions between individuals are taken into account. We thus bridged the classical macroscopic approach, as typified by *S*, *I*, and *R* models [3], to the growth and population dynamics of disease at the microscopic level. Although in that work we incorporated the stochastic nature of the transmission process, expectations were used in interpretations of the transmission matrix, and this resulted in a deterministic system which was integrated numerically. Of interest were the results obtained on threshold effects in the parameters describing microscopic viral growth and microscopic antibody production.

In the present study we examine truly stochastic effects on the dynamical process of viral growth and the transmission of virions among population members. We will see that noise even of a small amplitude serves to accelerate the spread of the virus and to synchronize the development of disease across the population. In Ref. [4] heterogeneous spatial effects were taken into account in deterministic and stochastic *S*, *E*, *I*, and *R* frameworks. In contrast, our approach involves dynamical variables at the microscopic level, and complements approaches in which disease is considered to percolate through a social network as in Ref. [5]. However, the advantage of our approach is that one can study the spread of a virus at the population level in such a way that viruses with different growth patterns within individuals may be distinguished.

STOCHASTIC MODEL WITH UNRESTRICTED TRANSMISSION

It is known [6,7] that the immune reaction to viral infection entails a complex set of reactions involving specific and nonspecific responses. In the case of the influenza-*A* virus, a complete study of the dynamical system requires a system of ten differential equations [8]. A simplified but useful approach in the mathematical modeling of these phenomena is to suppose that there are only two dynamical variables required to describe the state of the system of interest [2,6]. Thus we let each member i of a population of n individuals be represented by a vector function of time whose compo-

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nents are effector numbers $A_i(t)$ and the virion level $V_i(t)$. The term ''effector'' is used to incorporate the gamut of host defense particles, which may include antibodies [6], that lead directly or indirectly to the destruction of virus particles. These quantities evolve according to $2n$ differential equations which are coupled via a transmission matrix **B** with elements $\beta_{ij}, i,j=1,\ldots,n$, such that $\beta_{ij}V_i$ is the expected rate of transmission of infectious particles from individual i to individual j.

Network equations

The equation describing the evolution of the effector population within the ith individual is

$$\frac{dA_i}{dt}=\lambda_i-\mu_iA_i+\epsilon_iA_iV_i. \tag{1}$$

In Ref. [2] we made the capturing of virions by any individual depend upon a nonlinear function of the total number of virions transmitted to that individual by all the other members of the population. Adopting the same approach here, we have

$$\frac{dV_i}{dt}=r_iV_i\left(1-\frac{V_i}{k_i}\right)-\gamma_iA_iV_i+F\left[\sum_{j\neq i}\beta_{ji}V_j\right]+\sigma_iw_i. \tag{2}$$

The parameters have the following meanings for individual i: λ_i is the rate of production and/or transport of effectors, μ_i is the death (clearance) rate of effectors, ϵ_i is the rate of production of effectors in response to a unit viral population, r_i is the intrinsic growth rate (measure of ''virulence'' and referred to as the virulence parameter) of the viral population, k_i is the saturation value of the viral population, and γ_i is the clearance rate of virus particles. We have inserted an additive white noise term, with variance parameter σ_i^2, in each viral equation as a first approximation to a study of stochastic effects. The latter may result from random variations in the processes of viral growth within individuals, or random environmental effects. Here $w_i=dW_i/dt, i=1,2,\ldots$ are white noises, $\{W_i\}$ being assumed to be n independent standard Wiener processes. The function F is usually, as in our previous deterministic study, nonlinear and saturating to represent an upper limit to the rate at which virus particles can be absorbed by any individual. Here we will consider two possibilities for F. In the first model of the effects of noise, we will assume that the capture process is purely linear and additive; the justification for this approach is that the populations under consideration are of small sizes so that, especially because the number of transmitted particles is multiplied by an exponentially decreasing function of the distance between individuals, and saturation and nonlinear effects are not expected to be important. This approach also has the advantage of not requiring a specially constructed function F which carries with it a certain degree of arbitrariness. In the model to be developed below, F is assumed to be a step function.

We will consider the case of transmission which declines exponentially with distance, whereupon

$$\beta_{ij}=\beta(1-\delta_{ij})e^{-\alpha|i-j|}, \tag{3}$$

where $\delta_{ij}=0$ if $i\neq j$ and $\delta_{ij}=1$ if $i=j$. This incorporates a truly spatial effect, and represents an averaging of the effects of various members of the community on each other, as the distances between them fluctuate. Although in general the nonstochastic source terms for virus production in the ith individual are all bounded for any finite n, we will find solutions for relatively small population sizes and assume $k_i=\infty$ for all i. The viral dynamical equations are now

$$\frac{dV_i}{dt}=r_iV_i-\gamma_iA_iV_i+\beta\sum_{j=1}^{n}V_j(1-\delta_{ij})e^{-\alpha|i-j|}+\sigma_iw_i. \tag{4}$$

In the numerical work described below we have, in the first instance, made the dynamical parameters the same for all members of the population with the following values: $\lambda_i=0.5$, $\mu_i=0.05$, $r_i=1$, $\gamma_i=0.1$, $\epsilon_i=0.01$, and $k_i=\infty$. The network parameters were set at $\beta=0.1$ and $\alpha_i=0.75$. Changes in the values of r_i and σ_i are considered below and we will, in the second model (see below), allow the dynamical parameters to be drawn from probability distributions.

FOKKER-PLANCK APPROACH

As the system of $2n$ stochastic differential equations defined by Eqs. (1) and (4) is in fact a $2n$-component temporally homogeneous Markov process, we may define a transition probability density function

$$p(a_1,a_2,\ldots,a_n,v_1,v_2,\ldots,v_n,t|a_1^0,a_2^0,\ldots,a_n^0,v_1^0,v_2^0,\ldots,v_n^0),$$

where a_k^0 and v_k^0 are initial values, which satisfies a Fokker-Planck or forward Kolmogorov equation

$$\begin{aligned}\frac{\partial p}{\partial t}=&-\sum_{k=1}^{n}\frac{\partial}{\partial a_k}[(\lambda_k-\mu_ka_k+\epsilon_ka_kv_k)p]\\&-\sum_{k=1}^{n}\frac{\partial}{\partial v_k}[[r_kv_k-\gamma_ka_kv_k+\beta f(v_1,v_2,\ldots,v_n)]p]\\&+\frac{1}{2}\sum_{k=1}^{n}\sigma_k^2\frac{\partial^2p}{\partial v_k^2}.\end{aligned} \tag{5}$$

Here we have defined

$$f(\mathbf{v})=\beta\sum_{j=1}^{n}v_j(1-\delta_{ij})e^{-\alpha|i-j|}.$$

Although the partial differential equation (5) can in principle be solved numerically, it is expeditious to proceed by direct simulation of the stochastic integrals of Eqs. (1) and (4)—see below.

One individual

Because we are adding noise to the entire system of connected hosts, it is of interest to attempt to distinguish the effects of noise upon a single individual from those which arise through network phenomena; that is, by means of contact with all the other individuals in the population. Thus for one individual we set

$$\frac{dA}{dt} = \lambda - \mu A + \epsilon AV, \tag{6}$$

$$\frac{dV}{dt} = rV - \gamma AV + \sigma \frac{dW}{dt}, \tag{7}$$

where W is a standard Wiener process. For this system the transition probability density function $p(a,v,t|a_0,v_0)$ defined through

$$p(a,v,t|a_0,v_0)da\,dv = \Pr\{A(t) \in [a,a+da), V(t) \in [v,v+dv) | A(0) = a_0, V(0) = v_0)\},$$

satisfies the forward Kolmogorov or Fokker-Planck equation

$$\frac{\partial p}{\partial t} = -\frac{\partial}{\partial a}[(\lambda - \mu a + \epsilon a v)p] - \frac{\partial}{\partial v}[(rv - \gamma a v)p] + \frac{\sigma^2}{2}\frac{\partial^2 p}{\partial v^2}. \tag{8}$$

Solution of this equation, which is also not difficult using numerical methods, with appropriate boundary and initial conditions gives the joint probability density of the effector and virion densities, and thus enables one to determine quantities such as their moments at time t for a given starting pair (a_0,v_0).

NUMERICAL SOLUTIONS

We have integrated the pair of coupled stochastic differential equations (6) and (7) using a strong Euler method. We have done this for the same values of λ, μ, ϵ, r, and γ as above, and with the various values of σ which are to be used in the network equations. Without noise there are in general two equilibrium points for this system $P_1 = (\lambda/\mu, 0)$ and $P_2 = [r/\gamma, (\mu r - \lambda\gamma)/\epsilon r]$. For the above choice of parameters there is only one equilibrium point at $P_1 = P_2 = (10,0)$, and this is an asymptotically stable node. The initial virion level was set at $V(0) = 0.5$ with probability 1. The results of this integration are shown in Fig. 1(a), and are somewhat surprising. In this figure the values of the maximum mean virion level (20 trials) are plotted against the noise parameter σ. The error bars in this figure are not indicative of true 95% confidence intervals, but represent ± 1.96 times the maximum standard deviation of the virion level. It is seen that the deterministic maximum virion level is 79.63, but that the maximum decreases as the noise increases. The extent of the error bars increases from 0 in the deterministic case to 24.16 when $\sigma = 0.5$. We also noted the time at which the mean virion level achieved its maximum level. This declined from 6.72 days in the deterministic case to 6.4 days when $\sigma = 0.4$. Thus the maximum is attained more somewhat rapidly in the presence of noise, but it has a smaller magnitude. The question arises as to whether this phenomenon is due to the particular choice of parameters which make the critical points coincide. To examine this, we numerically solved the stochastic equations with the same parameters as before, but with $\mu = 0.1$, and the corresponding results are shown in Fig. 1(b). With this new value of μ there are two equilibria: the point (5,0) is an unstable saddle, and (10,5) is an asymptotically stable spiral point. Thus the virus cannot be extinguished as the death rate of effectors is lowered. For this different configuration, with an extra critical point away from $V = 0$, we again find that the maximum of the mean virion level tends downward as the noise level is increased and the speed at which the maximum is attained is slightly increased.

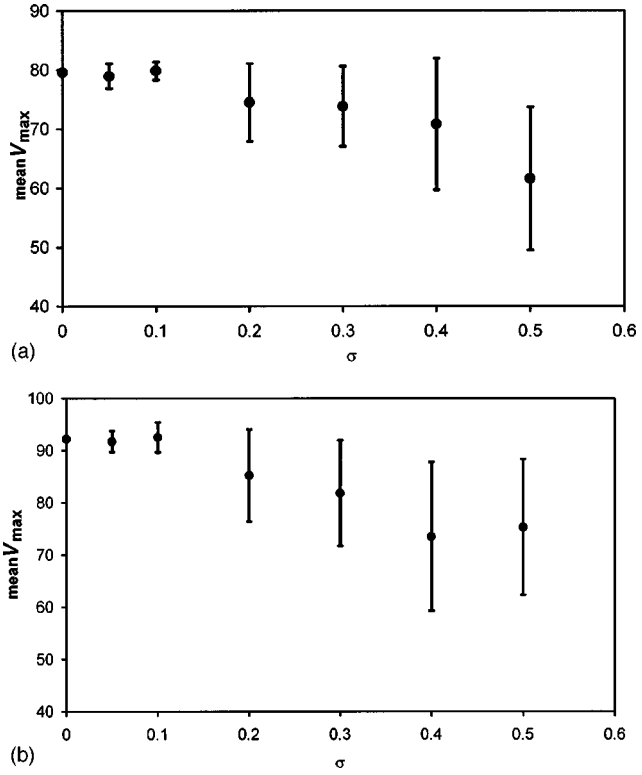

FIG. 1. (a) Illustrating the effects of increased noise on the response in a single individual. The maximum mean virion level is plotted against increasing values of the noise parameter σ. The error bars, which are not exact confidence intervals, are explained in the text. Here there is one equilibrium point at (10,0) which is an asymptotically stable node. The parameter values are $\lambda = 0.5$ effectors/day, $\mu = 0.05$ days^{-1}, $r = 1$ days^{-1}, $\gamma = 0.1$ days^{-1} effectors^{-1}, $\epsilon = 0.01$ days^{-1} virions^{-1}, and $k = \infty$ virions. Here and in all subsequent figures the units of viral load may be taken as those appropriate for certain influenza viruses, namely, 10^{11} per ml of infected tisue [8]. The units for σ throughout are virions ml^{-1} time$^{-1/2}$. (b) As in (a) except with $\mu = 0.10$. There are now two equilibria, one of which at (10,5) is an asymptotically stable spiral point, the other being an unstable saddle point at zero virions.

NETWORK RESPONSE WITH NOISE

With the same values of the parameters as above, the system of stochastic differential equations (1) and (4) was numerically solved using a strong Euler method [9]. It was assumed that there was initially one infected individual at the center of a population of $n = 31$ individuals, resulting in a system of 62 coupled stochastic differential equations. Each individual, infected or not, had an initial effector density count of zero, and again the initial value of virion density in the first individual to be infected was set at 0.5. The parameters σ_i were all changed from zero (a deterministic case as

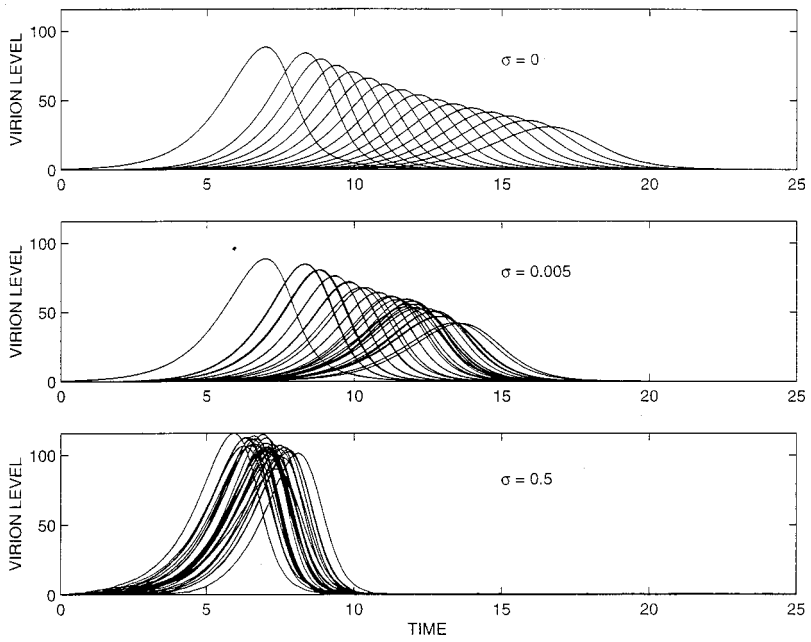

FIG. 2. Showing the effects of increasing noise level on the spread of virus across the population. In the top part of the figure are shown the results in the deterministic case ($\sigma=0$). In the middle records, a small amount of noise $\sigma=0.005$ speeds up the spread of virions and causes a slight increase in the average amplitude. In the lowest record, with a much larger value of $\sigma=0.5$, the spread across the population is greatly increased and the maximum virion level attained in individuals is uniform.

in Ref. [2]) to 0.05 to examine the effects of noise on the spread of the epidemic through the population. Note that because there is no artificially imposed threshold, the entire population is infected to some extent even in the absence of noise. However, the parameter values given above, in the absence of noise, are such that the infection invades the whole population in the absence of noise, but the individual response, as measured by the peak viral load, becomes smaller as distance from the initially infected individual increases. This can be seen in the top part of Fig. 2, where the virion level is plotted against time with $\sigma_i=0$—for one half of the population. The individual responses are well distinguished. In the initially infected individual the peak viral density reaches a maximum value more than double that attained in the individuals furthest from the source. Furthermore, the time interval between the occurrences of the peak viral loads in the initially infected individual and in the last infected is about ten days. The fact that in the absence of

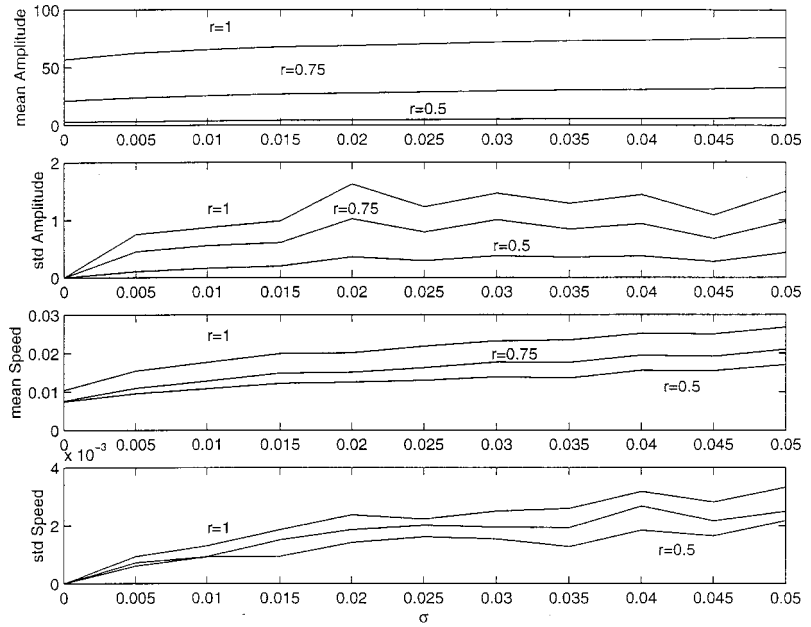

FIG. 3. For three values of the virulence parameter r, we show the variation in measures of the network response as the noise parameter σ increases. From top to bottom are shown the mean value of the amplitude $\mathcal{A}$ [see Eq. (9)], the standard deviation of this quantity, and the mean and standard deviation of the speed $\mathcal{V}$ as defined in Eq. (10). Units for r may be taken as $(5h)^{-1}$.

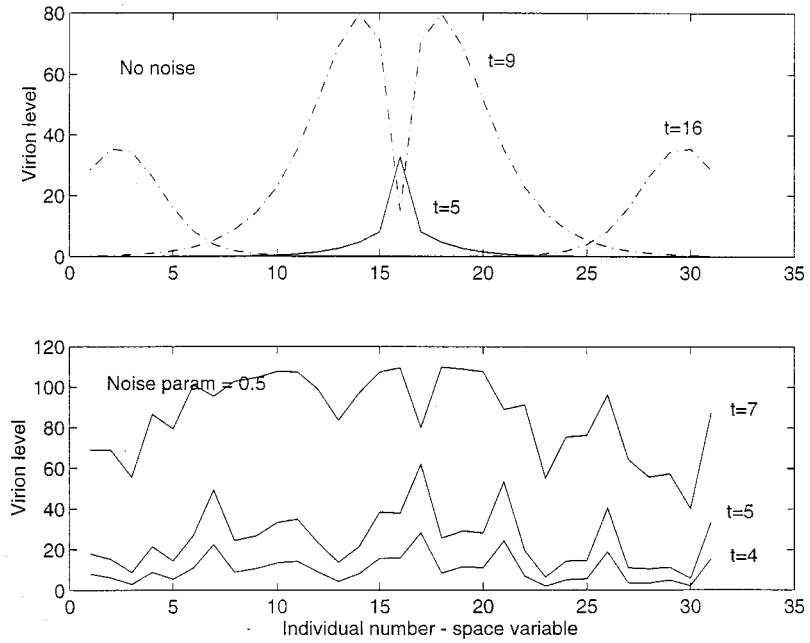

FIG. 4. Here we show the spatiotemporal development of the epidemic wave for the standard parameter values as given in the text.

noise individuals more remote from the initially infected one attain smaller virion levels is considered to be a deficiency in this first simpler unrestricted model.

When the noise is switched on at a low level, with $\sigma_i = 0.005$, the spread of infection throughout the population is more rapid and the responses are more uniform. The corresponding time courses of viral loads are shown in the middle part of Fig. 2. Thus a small amount of stochasticity in the background virion levels leads to an enhancement in both the amplitudes of the individual responses and in the alacrity with which the infection propagates throughout the noninfected parts of the population. When the noise parameters are increased to $\sigma_i = 0.5$, the enhancement is much greater, as can be seen in the bottom part of Fig. 2. Here the amplitudes of the individual responses differ little among themselves, and the speed with which the maximum virion level propagates is greatly augmented. It can be seen that the spread across the population is almost immediate. It is also noteworthy that the acceleration and increase in the response occurs despite the fact that the noise terms are additive and have zero mean.

These phenomena are reflected in the time courses of the mean virion levels (not shown). When there is no noise ($\sigma_i = 0$) the mean rises slowly to a maximum level of about 25. With a small amount of noise ($\sigma_i = 0.005$) the mean virion level rises more rapidly to attain a higher peak. With greatly increased noise ($\sigma_i = 0.5$) a truly epidemic phenomenon occurs, as the mean virion level reaches a very large peak value in a very short time and subsides equally rapidly. One thus observes, in this simple model, two phenomena in relation to the effects of noise on the spread of disease through a viral dynamical network that are seen in neural networks, namely, an enhancement and a synchronization of the individual responses.

AMPLITUDE AND SPEED

In order to more accurately quantify the effects of noise on the spread of virions throughout the host population, we compute, as a function of the noise parameters, the mean and standard deviation, across trials, of the amplitude $\mathcal{A}$ of the response. Let the maximum virion level in individual i be the random variable $V_{\max,i}$. Then we put

$$\mathcal{A} = \frac{1}{n} \sum_{i=1}^{n} V_{\max,i}. \tag{9}$$

Also, we compute the mean and standard deviation of the speed $\mathcal{V}$ of spread. The latter is here pragmatically defined as follows. Let $T_{\max,i}$ be the time at which the virion level attains its maximum value in the ith individual. Then let $T_{\max}$ be the largest of the $T_{\max,i}$, and let $T_{\min}$ be the smallest of these same random variables. The speed is

$$\mathcal{V} = \frac{1}{T_{\max} - T_{\min}}. \tag{10}$$

In Fig. 3 we show the variation in $\mathcal{A}$ and $\mathcal{V}$ as the noise level increased from $\sigma = 0$ to 0.05 for the three values of the viral intrinsic growth parameter $r = 0.5$, 0.75, and 1.0. It can be seen from the plot of mean amplitude that increasing r has a dramatic effect, which was already noted as a threshold phenomenon in Ref. [2]. In fact one can also observe that the rate of change of the mean amplitude with increasing noise is relatively small for all values of r investigated. There is also a gentle increase in the standard deviation of $\mathcal{A}$. However, the relative increases in the means are greater than the corresponding increases in the standard deviations, so that the coefficient of variation of the maximal virion level must decrease as σ_i increases. Thus the response across the population becomes more uniform. The effects of increased noise on the speed of spread are more pronounced. For $r = 1$ (the standard value), increasing the noise parameter from 0 to 0.5 results in a nearly threefold increase in the speed of spread and an extremely large concomitant increase in the standard deviation of the spread. Further increases in σ resulted in a

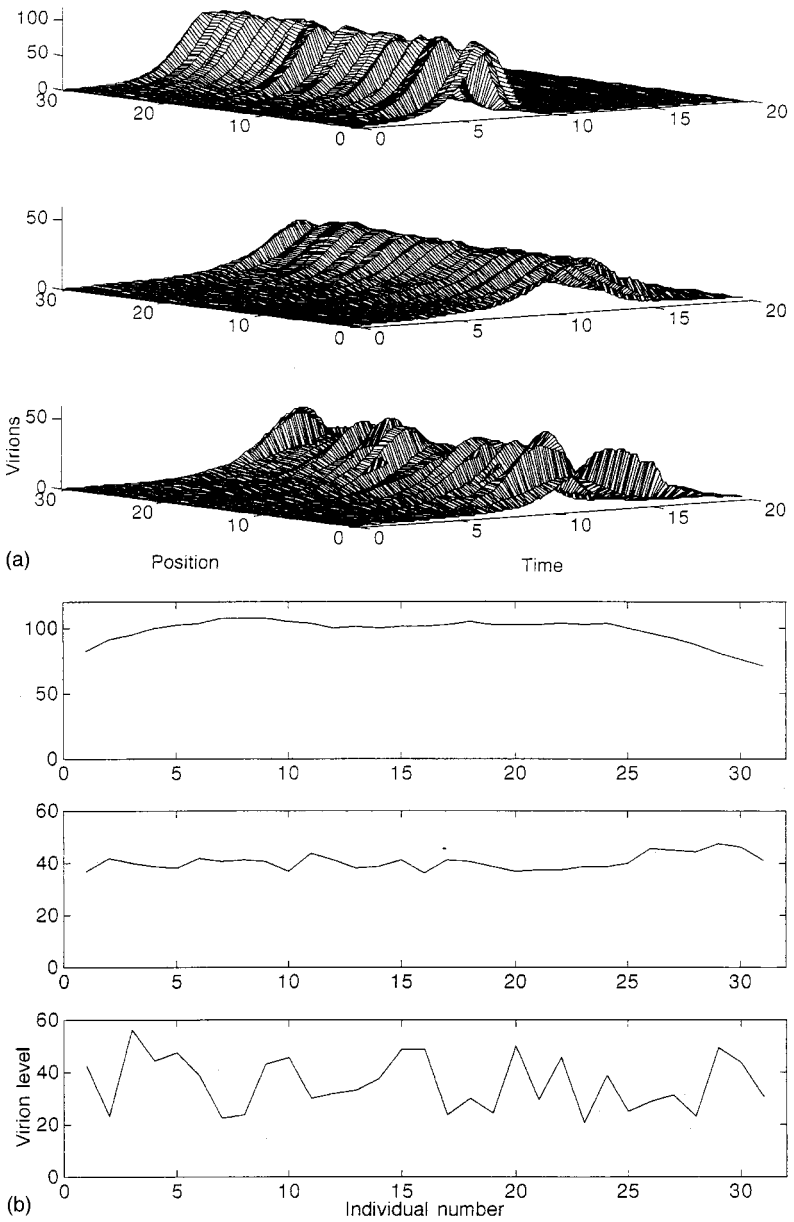

FIG. 5. (a) The virion levels are shown as functions of time for each member of the population of 31 individuals when only the middle individual is initially infected. In all three records, $\sigma=0.5$. The upper set of results is for the unrestricted model, the middle set is for the second model (with threshold) with the same parameters, and the third set is for that same model with randomized parameters. (b) The maximum virion levels attained within the individuals in the three cases depicted in part (a).

continued growth in the overall amplitude of the response with no evidence of a stochastic resonance [10] effect. Similar results were found for the less virulent cases $r=0.75$ and $r=0.5$. In Fig. 4 we show the profiles of the virion levels across the population. In the top part, there is no noise ($\sigma=0$), and the wavelike spread of the virus from the central initially infected individual throughout the population is discernible. In the lower part of Fig. 4 the results are shown for $\sigma=0.5$, at the times $t=4$, 5.5, and 7. The progressive wave is replaced by a stochastic and relatively haphazard growth pattern.

MODEL WITH THRESHOLD

Although the model employed above has the advantages of simplicity and having a straightforward Fokker-Planck framework, it has two major shortcomings. First, there is no threshold for the growth of a viral population within an individual. Thus any contact with an infected individual leads immediately to a new infection. Second, there is theoretically no upper limit to the rate at which virions can be transmitted to an individual from all other infected individuals, regardless of the virion population already present. We have therefore considered a second stochastic dynamical network model which has both a threshold and an upper limit for the rate of transmission of virions to any individual. The effector equations (1) are assumed to be unaltered but the virion equations are changed as follows. Define

$$T_i=\beta\sum_{j=1}^{n} V_j(1-\delta_{ij})e^{-\alpha|i-j|}+\sigma_i w_i\,. \tag{11}$$

Then

$$\frac{dV_i}{dt} = r_i V_i - \gamma_i A_i V_i + H(T_i - v_{i,\mathrm{thresh}}) \min(T_i, T_{i,\max}), \tag{12}$$

where $v_{i,\mathrm{thresh}} \geqslant 0$ is the threshold level of rate of viral transmission required to make a successful colonization in the ith host, and $T_{i,\max}$ is the maximal rate at which virions may be transmitted into the ith host. Here $H(\cdot)$ is a unit step function at the origin.

Equations (1) and (12) were also integrated numerically, and the noise parameter varied as for the above unrestricted model. A comparison of results for the two models is shown in Figs. 5(a) and 5(b). In Fig. 5(a) we show three-dimensional plots of virion levels against time in all the members of the population, all for a noise level of $\sigma = 0.5$. The top set of results is for the first model with standard parameters (as above); in the middle part are the results for the threshold model with the same set of parameters; and the third set of results are for the second model with randomized parameters. Here the five parameters λ_i, r_i, γ_i, μ_i, and ϵ_i were drawn randomly from normal distributions with mean values as in the deterministic case, and with standard deviations equal to one-tenth of the mean value. In Fig. 5(b) are shown the maximum virion levels across the population for the three corresponding cases of Fig. 5(a).

In Fig. 6(a) we show the mean values of the maximum virion levels (MMVL's) attained in the various individuals plotted against the noise parameter σ. For the unrestricted (first) model, discussed partly above, the MMVL is large even in the absence of noise. Increasing the value of σ from 0 to 0.3 makes the MMVL increase, in a linear fashion, to approximately 1.7 times its value without noise. After $\sigma = 0.3$, the MMVL continues to increase with the noise amplitude at all values up to $\sigma = 10$, and there is no evidence of stochastic resonance in this model. In contrast, for the chosen values of the parameters, with a low threshold ($v_{i,\mathrm{thresh}} = 0.01$), there is no spread of disease at all either without noise or with very low levels of noise, it being emphasized that the noise added has zero mean. A rapid increase occurs in the MMVL as σ increases, until about the value $\sigma = 0.25$, whereupon the MMVL attains a maximum. The detail of this maximum is shown in Fig. 6(b). Thus a broad based stochastic resonance effect does occur, presumably in keeping with the nonlinearities induced by the threshold and maximal transmission rate. For the higher threshold case investigated, with $v_{i,\mathrm{thresh}} = 0.1$, there is no spread of virus throughout the population until considerable noise is present (again with zero mean), with an apparent threshold of about $\sigma = 0.2$. With greater values of the noise amplitude, the MMVL rises quite sharply, but reaches a maximum at about $\sigma = 1.25$ after which it again declines significantly as detailed in the lower part of Fig. 6(b). Thus there is again a broad-based stochastic resonance. A similar behavior was observed when, as indicated in the figure, the five parameters were chosen randomly as described above. Standard deviations of the maximum virion levels (SMVL's), were also obtained for the unrestricted model or the three cases of the second model mentioned above. In the first model, the SMVL decreased rapidly at first as σ increased, reflecting the uniformization

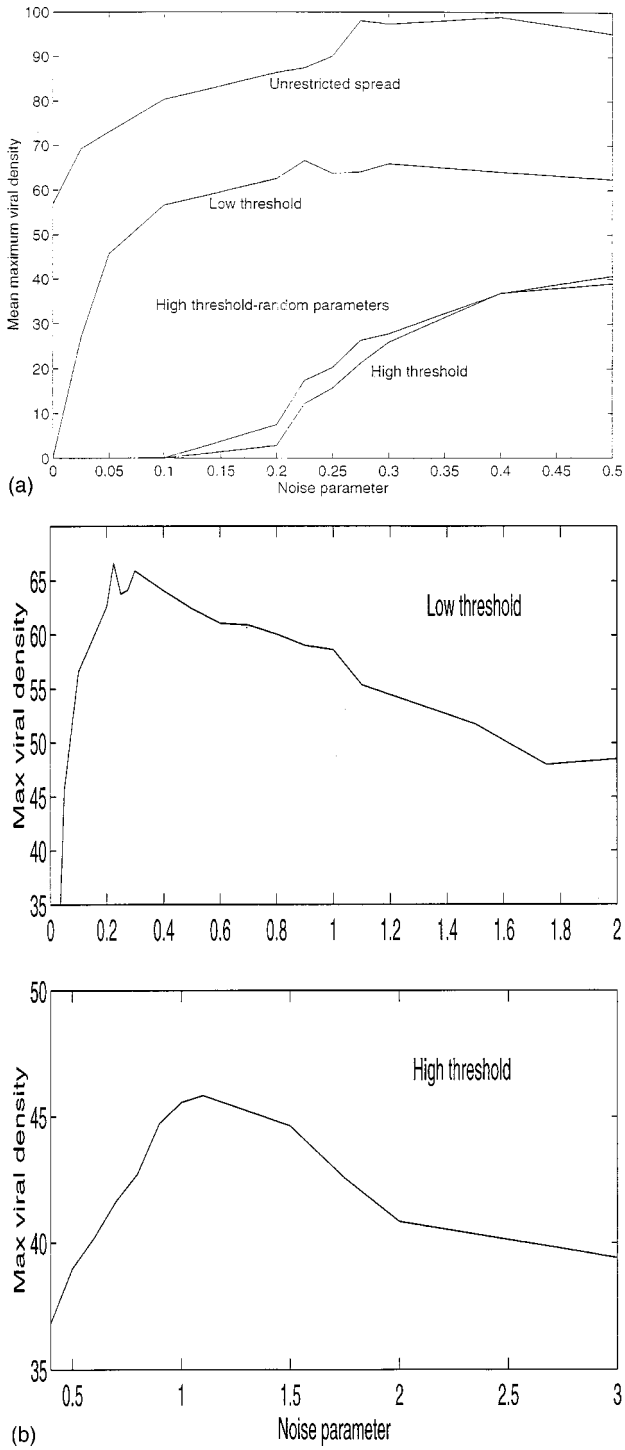

FIG. 6. (a) Comparison of results for the unrestricted model [Eqs. (1) and (4)] with those of the model with a threshold and a maximum transition rate [Eqs. (1) and (12)]. Mean values of the maximum virion levels are plotted against the noise parameter σ. The uppermost curve is for the first model, whereas all other curves are for the second model. For the curve marked *low threshold*, $v_{i,\mathrm{thresh}} = 0.01$ for all i's. For the remaining curves $v_{i,\mathrm{thresh}} = 0.1$ for all i's and in one case, as indicated, the parameters are randomized across the population. (b) Detail of the maxima in the mean maximum virion levels for the model with a threshold for the cases of low and high thresholds. For explanations, see text.

of the response amplitude already noted above. For values of the noise parameter greater than about 0.5, the SMVL increased, probably because the deterministic component was masked by the noise. In the second model, with a low threshold, the SMVL grew quickly with σ, but remained very small, never exceeding a value of 4.6 or $\frac{1}{10}$ of the mean. In the high threshold case, the SMVL remained very small, attaining a maximum value of about 10% of the mean when $\sigma=0.4$. With randomized parameters the SMVL is, as expected, much greater, being as large as 33% of the mean. Thus one sees that, in the second model, the noise is more crucial for spreading the disease but that the variation in individual responses is, for nonrandom parameters, small. The variability in responses is only significant if the five parameters themselves are drawn from probability distributions.

DISCUSSION AND CONCLUSIONS

The spread of disease by virus or bacteria in human and other populations involves two main components, both of which must be included in a mathematical treatment. First, the dynamical processes which describe the within-host growth of the population of invading, disease-causing particles (e.g., virions). This is necessary because each disease has its particular temporal pattern of development, a factor which has been ignored in classical (*SIR* or *SEIR*) models. Second, a plausible model must contain a description of the dynamics of spread from infected to uninfected individuals. In our previous communication [2] we endeavored to introduce models with these two components by employing a dynamical systems approach to both the within-host development of a viral population and the transmission of virions from infected to uninfected hosts. Whereas previously we considered only deterministic effects, here we have addressed the inclusion of stochastic effects by the addition of white Gaussian noise to the dynamical equation satisfied by the virion numbers for each individual. Although there are many possibilities for the way in which noise is introduced, we chose the simplest as a useful starting point which gave the first model. The effects of noise on the growth of a viral population in an isolated individual were studied first, and led to the surprising result that the mean virion level was depressed as the amplitude of the noise increased. In many cases noise acts to increase the mean of a dynamical variable—for example, it increases the firing rate in neurons with subthreshold voltage modeled by an Ornstein-Uhlenbeck process [11]. However, the effect of noise varies depending on the mathematical properties of the system [12]. When noise was added to the viral epidemic network as in Eqs. (1) and (4) above, its most noticeable effect was to accelerate the spread of the disease across the population and to make the amplitude of the response individuals more uniform across the population. No stochastic resonance was observed in this unrestricted transmission model. We also considered a more realistic but less tractable model in which there is a threshold rate required to instigate a new viral infection and a maximum rate of transmission to any individual from other host. Here the effect of noise was more dramatic, as it could give rise to an epidemic under circumstances where there was no spread of infection in the absence of noise. Furthermore, a broad-based stochastic resonance was found in this model. There are many factors which we did not have the space to discuss, such as the effects of various geometrical patterns of initial infection—see Ref. [2], where we reported some details of this aspect for a deterministic model with threshold.

We remark that noise or stochastic efects may be introduced into a viral epidemic dynamical spatial network in several ways. For example, apart from the additive noise considered in this paper the transmission coefficients can be made into random processes. This can be achieved by making the number of encounters between individual i and individual j a Poisson process, N_{ij}, with rate parameter $\lambda_{ij}=e^{-\alpha|i-j|}$. In the absence of threshold or limiting effects, the equations for the viral dynamics then become

$$\frac{dV_i}{dt}=r_iV_i-\gamma_iA_iV_i+\beta\sum_{j=1}^{n}V_j(1-\delta_{ij})\frac{dN_{ij}}{dt}, \qquad (13)$$

or there may be additive noise as well. An interesting diffusion approximation is obtained for Eq. (13), namely,

$$\frac{dV_i}{dt}=r_iV_i-\gamma_iA_iV_i+\beta\sum_{j=1}^{n}V_j(1-\delta_{ij})\lambda_{ij}+\beta\sqrt{\sum_{j=1}^{n}V_j^2(1-\delta_{ij})\lambda_{ij}^2}\frac{dW_i}{dt}. \qquad (14)$$

A threshold may be introduced as above, but a more convenient way to do this is to introduce a cubic nonlinearity as in Ref. [2],

$$\frac{dV_i}{dt}=r_iV_i\left(1-\frac{V_i}{k_i}\right)(V_i-\theta)+\beta\sum_{j=1}^{n}V_j(1-\delta_{ij})\lambda_{ij}+\beta\sqrt{\sum_{j=1}^{n}V_j^2(1-\delta_{ij})\lambda_{ij}^2}\frac{dW_i}{dt}, \qquad (15)$$

where θ is a threshold viral density. The use of Eq. (15) makes clear the analogy between neural and epidemic network models. We will pursue this aspect in future papers.

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