

Stochastic amplification in epidemics Supplementary Material

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Supplementary Material

This supplementary online information is organized into the following four sections:

1. The stochastic SIR model with immigration.
2. The peak of the power spectra: analytic approach.
3. The master equation and the large- N expansion.
4. Bifurcation diagrams.

1 The stochastic SIR model with immigration

Here we will describe in detail an individual based model which takes the form of a non-spatial stochastic model, but mimics spatial coupling by considering external infection. We will then show that, in the limit where the size of the system (the largest possible number of individuals that the system can support), N , becomes very large and the system is closed to immigration, it becomes the population level SIR model of epidemics (Anderson & May 1991; Bauer & Castillo-Chavez 2001). We will be interested in the situation where N is large, but where there are still significant departures from the mean field description.

To obtain a stochastic version of the SIR model we divide the population into three classes. The first are the susceptibles: those susceptible to disease, but who are not yet infected at a time t . The second are the infectives: those which are infected with the disease, and are able to spread it through contact with susceptibles. The final class are the recovered: those which have recovered from the infection and can no longer spread the infection (for instance, because they are immunized). At a given time, a realization of the model will consist of m individuals of type S (the susceptibles), n individuals of type I (the infectives) and l individuals of type R (the recovered). In order for all three of these classes to be independent dynamical variables, we have to introduce a fourth class, E (denoting “empty”). There will be $(N - l - m - n)$ of these passive constituents of the system. If this class was not introduced, the number of S, I and R individuals would not be independent, for instance, n would be given by $n = N - l - m$, where N is fixed.

As in the population level SIR model, we now need to list the possible processes that can take place within the system, and introduce rate constants for each of these processes. A schematic representation of this is shown in Fig. 1 (main text). The processes may be divided into four groups:

1. Infection. An infected individual may come into contact with an susceptible individual giving rise to two infected individuals. This is assumed to take place with a rate β . A susceptible may also be infected by an external agent (that is, from the environment). This is assumed to happen with a rate η . These two mechanisms may be expressed as $SI \xrightarrow{\beta} II$ and $S \xrightarrow{\eta} I$.
2. Death. This is a demographic effect rather than an epidemiological one, and consequently all three types of individuals are assumed to have the same death rate. These are represented by $S \xrightarrow{\delta} E$, $I \xrightarrow{\delta} E$ and $R \xrightarrow{\delta} E$.
3. Birth. This is again a demographic effect, but with all newly-born individuals being susceptible: $E \xrightarrow{b} S$.

4. Recovery. The rate of recovery of individuals from the infected class is taken to be γ :
 $I \xrightarrow{\gamma} R$.

It is now straightforward to carry out numerical simulations of this model (Gillespie 1976). The dynamics is defined by performing a large number of events in which constituents (either S, I, R or E) are chosen at random and allowed to interact through one of the processes defined above. This implies that the probabilities that these processes take place only depend on the probabilities of choosing the various constituents and on the rates at which these processes take place. For example, the probability of a susceptible dying in a time dt is $\delta m dt$, assuming that dt is so small that only one event can occur during that time interval. Since the state of the system is defined by the three integers (l, m, n) we may define a transition rate from the state (l, m, n) to the state $(l, m - 1, n)$ mediated by this process as $T(l, m - 1, n | l, m, n) = \delta m$. Note in our convention, initial states are on the right and final states are on the left. All other transition rates may be defined in the same way. If we list them according the four processes defined above they are:

1. Infection:

$$T(l, m - 1, n + 1 | l, m, n) = \left(\beta \frac{m}{N} n + \eta m \right). \quad (1)$$

2. Death:

$$\begin{aligned} T(l - 1, m, n | l, m, n) &= \delta l, \\ T(l, m - 1, n | l, m, n) &= \delta m, \\ T(l, m, n - 1 | l, m, n) &= \delta n. \end{aligned} \quad (2)$$

3. Birth:

$$T(l, m + 1, n | l, m, n) = b(l + m + n). \quad (3)$$

4. Recovery:

$$T(l + 1, m, n - 1 | l, m, n) = \gamma n. \quad (4)$$

Since the transition rates (1)-(4) only depend on the state of the system when the process began, and not on any previous states, this is a Markov process and may be modeled using a master equation (Nisbet & Gurney 1982; Renshaw 1991; Van Kampen 1992). This equation has the general form

$$\frac{d}{dt} P(\underline{\sigma}, t) = \sum_{\underline{\sigma}' \neq \underline{\sigma}} T(\underline{\sigma} | \underline{\sigma}') P(\underline{\sigma}', t) - \sum_{\underline{\sigma}' \neq \underline{\sigma}} T(\underline{\sigma}' | \underline{\sigma}) P(\underline{\sigma}, t), \quad (5)$$

where $\underline{\sigma}$ represents the state of the system, in our case $\underline{\sigma} = (l, m, n)$. This equation has a simple interpretation: the first term on the right hand is the sum of the transition rates into the state $\underline{\sigma}$ from all other states $\underline{\sigma}'$ and the second term is the sum of the transition rates out of the state $\underline{\sigma}$ into all other states $\underline{\sigma}'$. The explicit form for the master equation involving the processes (1)-(4) is given in section 3.

It is straightforward to obtain the deterministic version of the model, valid in the limit of very large N , from the master equation. Essentially, all that is required is to multiply (5) by l, m and n in turn and to sum over all the states. This generates rate equations which are the deterministic equations if correlations between the variables are ignored. The details are given

in Section 3, but these equations, together with the results (1)-(4), give

$$\begin{aligned}\frac{dI}{dt} &= \beta \frac{S}{N} I + \eta S - \delta I - \gamma I, \\ \frac{dS}{dt} &= -\beta \frac{S}{N} I - \eta S - \delta S + b(I + S + R), \\ \frac{dR}{dt} &= -\delta R + \gamma I,\end{aligned}\tag{6}$$

which is the usual SIR model. Adding up these three equations we find that

$$\frac{d}{dt}(I + S + R) = -\delta(I + S + R) + b(I + S + R),\tag{7}$$

so if we choose $b = \delta$, then $I + S + R$ remains constant, and so we may express one of the variables, say R , in terms of the other two. This is completely standard in the context of the deterministic model (Bauer & Castillo-Chavez 2001). In the context of the individual based model, it corresponds to a zero sum rule: whenever a death takes place, a birth must also take place so that the number of individuals in the population remains fixed. This means that the E become irrelevant: processes 2 and 3 become tightly coupled. Consequently, we can do away completely with the E and simply have S, I and R individuals with $l + m + n = N$. This means that now not all of the variables are independent, and the R may be eliminated through the relation $l = N - n - m$. In this way we may work with only the m and n variables, and the role of the E variables is now played by the R variables. The processes may now be divided into three groups:

1. Infection: $SI \xrightarrow{\beta} II$ and $S \xrightarrow{\eta} I$.

$$T(m-1, n+1|m, n) = \left(\beta \frac{m}{N} n + \eta m \right).\tag{8}$$

2. Birth/Death: $I \xrightarrow{\delta} S$ and $R \xrightarrow{\delta} S$.

$$\begin{aligned}T(m+1, n|m, n) &= \delta(N - m - n), \\ T(m+1, n-1|m, n) &= \delta n.\end{aligned}\tag{9}$$

3. Recovery: $I \xrightarrow{\gamma} R$.

$$T(m, n-1|m, n) = \gamma n.\tag{10}$$

The deterministic limit of these equations are obtained as before and are given explicitly in section 3. Writing these out using Eqs. (8)-(10) gives

$$\begin{aligned}\frac{dS}{dt} &= -\beta \frac{S}{N} I - \eta S + \delta(N - S), \\ \frac{dI}{dt} &= \beta \frac{S}{N} I + \eta S - \delta I - \gamma I,\end{aligned}\tag{11}$$

which, as expected, is exactly what we obtain from (6) by eliminating R from the first two equations using $R = N - S - I$. In the remainder of the paper we will only consider this latter version of the model, where the zero-sum rule is implemented by equating the birth and death rates.

Our aim is to go beyond the mean-field equations (11), by including fluctuations within a systematic expansion in $1/\sqrt{N}$ which is due to Van Kampen (Van Kampen 1992; Alonso & McKane 2002; Chen & Bokka 2005). The equations (11) are those found to leading order, and for our purposes it will only be necessary to go to the next-to-leading order. At this order the fluctuations can be described by a Fokker-Planck equation which is *linear*. By this we mean that it describes Brownian-like motion in a potential which is quadratic, so the deterministic forces are linear. The probability distributions obtained from Fokker-Planck equations such as these are Gaussian. An intuitive picture of what this means can be obtained by imagining a plot of the probability that the system is in state (m, n) at time t , $P(m, n, t)$, on the vertical axis against m and n on the horizontal axes, for different values of t . At $t = 0$ the distribution is a delta-function spike at the given initial values of m and n , which we denote by m_0 and n_0 . As the system evolves with time, the position of the peak changes according to the mean-field equations, and it broadens due to fluctuations. Therefore what we are doing is replacing the master equation by (i) a set of deterministic equations (Eqs. (11)) which specifies the position of the peak of the probability distribution, and (ii) a Fokker-Planck equation which specifies the width of the broadening of the distribution (since the distribution is Gaussian with a specified mean, the variance completely determines it). We wish to stress that this approximation is justified within the $1/\sqrt{N}$ expansion — the higher order corrections simply give deviations from the Gaussian form, which from numerical simulations we find must be very small for reasonable values of N .

From a mathematical point of view, the Van Kampen large- N expansion involves moving from the discrete variables m and n to continuous variables x and y , which are the variables used to specify the probability distribution function. Essentially the method involves the replacements $m/N = \phi + x/\sqrt{N}$ and $n/N = \psi + y/\sqrt{N}$ in the transition probabilities that appear in the master equation. The $1/\sqrt{N}$ terms are present since, by the central-limit theorem, we expect fluctuations to be of the order of $1/\sqrt{N}$ when the variables m and n are expressed in terms of fractions m/N and n/N . As $N \rightarrow \infty$, these fluctuations vanish, and the system is entirely described by $\phi(t)$ and $\psi(t)$, which are simply $S(t)/N$ and $I(t)/N$ in this limit. Once these have been subtracted out (by moving the origin to the peak of the distribution) and the $1/\sqrt{N}$ factored out, we may once again take $N \rightarrow \infty$. In this way x and y become continuous variables, and terms of different orders in $1/\sqrt{N}$ can be identified in the master equation.

The implementation of the $1/\sqrt{N}$ expansion is straightforward, and is discussed in Van Kampen's book (Van Kampen, 1992) and in some detail, for a system very similar to that being considered here, in a recent paper (McKane & Newman 2004). We give an outline of the application of the method in section 3. As we have already mentioned, to leading order we obtain the equations (11). It is useful to eliminate one of the parameters by a suitable choice of time scale, and this we do by defining a dimensionless time $\tau = \gamma t$. Rescaled versions of the other parameters may then be introduced:

$$\hat{\beta} = \frac{\beta}{\gamma}, \quad \hat{\delta} = \frac{\delta}{\gamma}, \quad \hat{\eta} = \frac{\eta}{\gamma}. \quad (12)$$

Notice that $\hat{\beta}$ is the model R_0 to a very good approximation. After this rescaling, the deterministic equations read

$$\begin{aligned} \frac{d\phi}{d\tau} &= -\hat{\beta}\phi\psi - \hat{\eta}\phi + \hat{\delta}(1 - \phi), \\ \frac{d\psi}{d\tau} &= \hat{\beta}\phi\psi + \hat{\eta}\phi - \hat{\delta}\psi - \psi. \end{aligned} \quad (13)$$

If the infection by external agents is absent ($\hat{\eta} = 0$), then there are two fixed points: a trivial one ($\phi^* = 1, \psi^* = 0$) which corresponds to having no infected individuals and a non-trivial one

($\phi^* \neq 0, \psi^* \neq 0$) which is the one of interest to us (we use asterisks to denote fixed point values). Having a small, but non-zero $\hat{\eta}$ changes ψ in the previously trivial fixed point to a small non-zero value, but this state remains now of little interest to us —it corresponds to a situation with a very small number of infected individuals which is kept in this state only by the continuous supply of external infection (the “sink” phase). Our interest is still focused on the non-trivial state, whose value is slightly changed from its value when $\hat{\eta} = 0$ by terms of order $\hat{\eta}$. It is simple enough to calculate ϕ^* and ψ^* , and they are given in section 3, but there is no need to record their explicit form here for what follows.

At next order, rather than write down the Fokker-Planck equation, it is simpler to give the set of Langevin equations to which it is equivalent (Van Kampen 1992). They take the form

$$\begin{aligned} \frac{dx}{d\tau} &= a_{11}x + a_{12}y + \eta_1(\tau) \\ \frac{dy}{d\tau} &= a_{21}x + a_{22}y + \eta_2(\tau). \end{aligned} \quad (14)$$

These are a pair of differential equations which describe the stochastic behavior of the model at large, but finite N . The variables $x(t)$ and $y(t)$ are stochastic corrections to the deterministic behavior of the susceptible and infected population numbers respectively, and the $\eta_i(t), i, j = 1, 2$, are Gaussian white noises with zero mean and a correlation function which is defined in terms of a noise covariance matrix B_{ij} . The constants a_{ij} appearing in Eq. (14) can also be given in terms of the rate constants. It turns out that the a_{ij} are exactly the same coefficients found from a linear stability analysis about the non-trivial fixed point of Eq. (11). The matrix B_{ij} , which is responsible for generating the large-scale oscillations, cannot be determined from Eq. (11) and is derived from the master equation using the Van Kampen expansion. Since the noise is white, B_{ij} is independent of the frequency ω . The explicit expressions for these constants are given in section 3.

Since we are interested in cycles it is natural to work in terms of $\tilde{x}(\omega)$ and $\tilde{y}(\omega)$ which are the Fourier transforms of $x(\tau)$ and $y(\tau)$, respectively. Furthermore, taking the Fourier transform of the equations (14) allows us to solve for these variables very simply. We can now calculate the power spectra of the fluctuations about the mean-field values for the susceptibles and infectives to be

$$P_S(\omega) = \langle |\tilde{x}(\omega)|^2 \rangle = \frac{\alpha_S + B_{11}\omega^2}{[(\omega^2 - \Omega_0^2)^2 + \Gamma^2\omega^2]}, \quad (15)$$

and

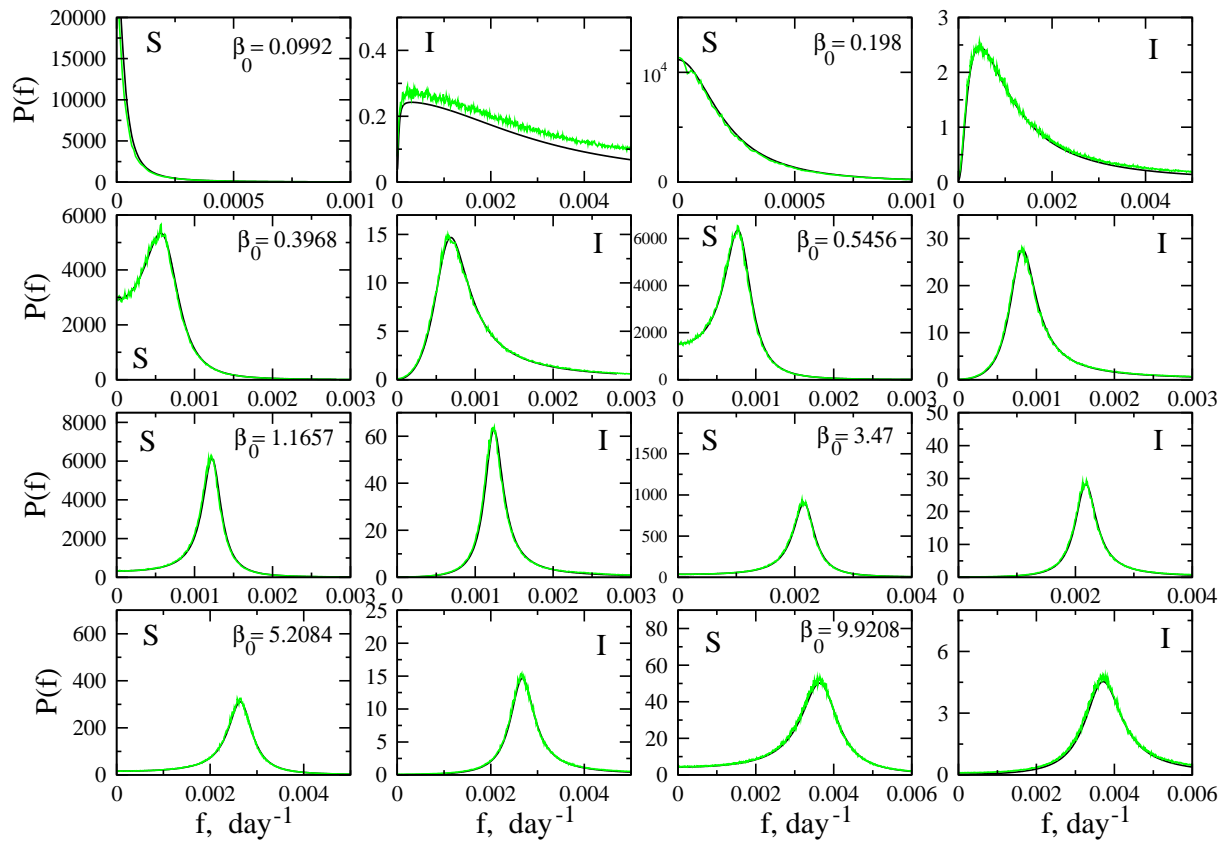
$$P_I(\omega) = \langle |\tilde{y}(\omega)|^2 \rangle = \frac{\alpha_I + B_{22}\omega^2}{[(\omega^2 - \Omega_0^2)^2 + \Gamma^2\omega^2]}, \quad (16)$$

respectively. The constants α_S and α_I are defined in section 3. They depend on the a_{ij} and B_{ij} which themselves depend on the three parameters of $\hat{\beta}, \hat{\delta}$ and $\hat{\eta}$. However, what is of principal interest to us is the denominator $[(\omega^2 - \Omega_0^2)^2 + \Gamma^2\omega^2]$ which depends on the frequencies $\Omega_0^2 = a_{11}a_{22} - a_{12}a_{21}$ and $\Gamma = |a_{11} + a_{22}|$. It should be noted that these frequencies only depend on the a_{ij} , and not on the B_{ij} , and that since the a_{ij} can be obtained from a linear stability analysis of the mean-field equations, there is no need to consider fluctuations to find these quantities, even though the effects we will be exploring most certainly need fluctuations to exist.

In Fig S1 and for increasing values of β , we show the very good agreement between the theoretical predictions given by expressions (15) and (16) and numerically averaged power spectral densities calculated over an ensemble of stochastic simulations.

Fig S2 is analogous to Fig 2 (main text), but a larger city has been considered. The theoretical prediction still captures the qualitative behavior of the PSD for decreasing values of

$$\gamma = 0.077 \quad \delta = 5.5 \cdot 10^{-5} \quad \beta_1 = 0. \quad \eta = 10^{-5} \quad N = 3000000$$



Supplementary Figure 1. Large city. The agreement between the analytic PSD and the numerical averaged PSD without introducing seasonality is perfect for large cities.

the transmission rate. As in Fig 2 of the main text, whenever numerical simulations without seasonal forcing has been performed (middle plot) an effective transmission rate has been calculated (Keeling, Rohani & Grenfell 2001). This enables a fair comparison with the seasonal forced case (lower plot).

The forms (15) and (16) are classic illustrations of resonant phenomena: if we differentiate the denominator with respect to ω^2 we see that it has a minimum when $\omega^2 = \Omega_0^2 - (\Gamma^2/2)$. Thus fluctuations will have maximum enhancement at a resonant frequency defined by $\omega_0 \equiv \sqrt{\Omega_0^2 - (\Gamma^2/2)}$. Including the ω dependence in the numerator changes the position of the peak, so that the actual position of the peak can deviate from ω_0 depending on the values of the model parameters. To study this, a full analysis is needed and this is provided in the next section.

2 The peak of the power spectra: analytic approach

The PSD of both susceptibles and infectives, given by Eqs. (15) and (16) as a function of the angular frequency, ω , takes the general form:

$$P(\omega) = \frac{\alpha + B\omega^2}{[(\omega^2 - \Omega_0^2)^2 + \Gamma^2\omega^2]}, \quad (17)$$

where the two parameters in the numerator are different depending on whether we are dealing with the PSD for susceptibles ($\alpha = \alpha_S$ and $B = B_{11}$) or infectives ($\alpha = \alpha_I$ and $B = B_{22}$). In an earlier article on endogenous stochastic fluctuations for two interacting predator-prey species (McKane and Newman 2005) it was found that, for parameter values of interest, the two peaks for prey and predators were almost coincident. This is not true in general (see Fig S3), and the positions of the respective peaks and the condition for the existence of a peak at nonzero ω in the spectra can be derived easily enough analytically.

To find the condition for the existence of a peak in the PSD, as well as its position, we introduce the new variable $z = \omega^2$. Since

$$\frac{dP}{d\omega} = \frac{dP}{dz} \frac{dz}{d\omega} = \frac{dP}{dz} 2\omega = 0,$$

extrema at non-zero values of ω are found by solving $dP/dz = 0$. Since the power spectra are even functions (reflecting the fact that these fluctuations are real valued) any solution to this equation will give rise to two values of ω : $\omega = \pm\sqrt{z}$. The equation $dP/dz = 0$ has the form

$$Bz^2 + 2\alpha z + [\alpha(\Gamma^2 - 2\Omega_0^2) - B\Omega_0^4] = 0. \quad (18)$$

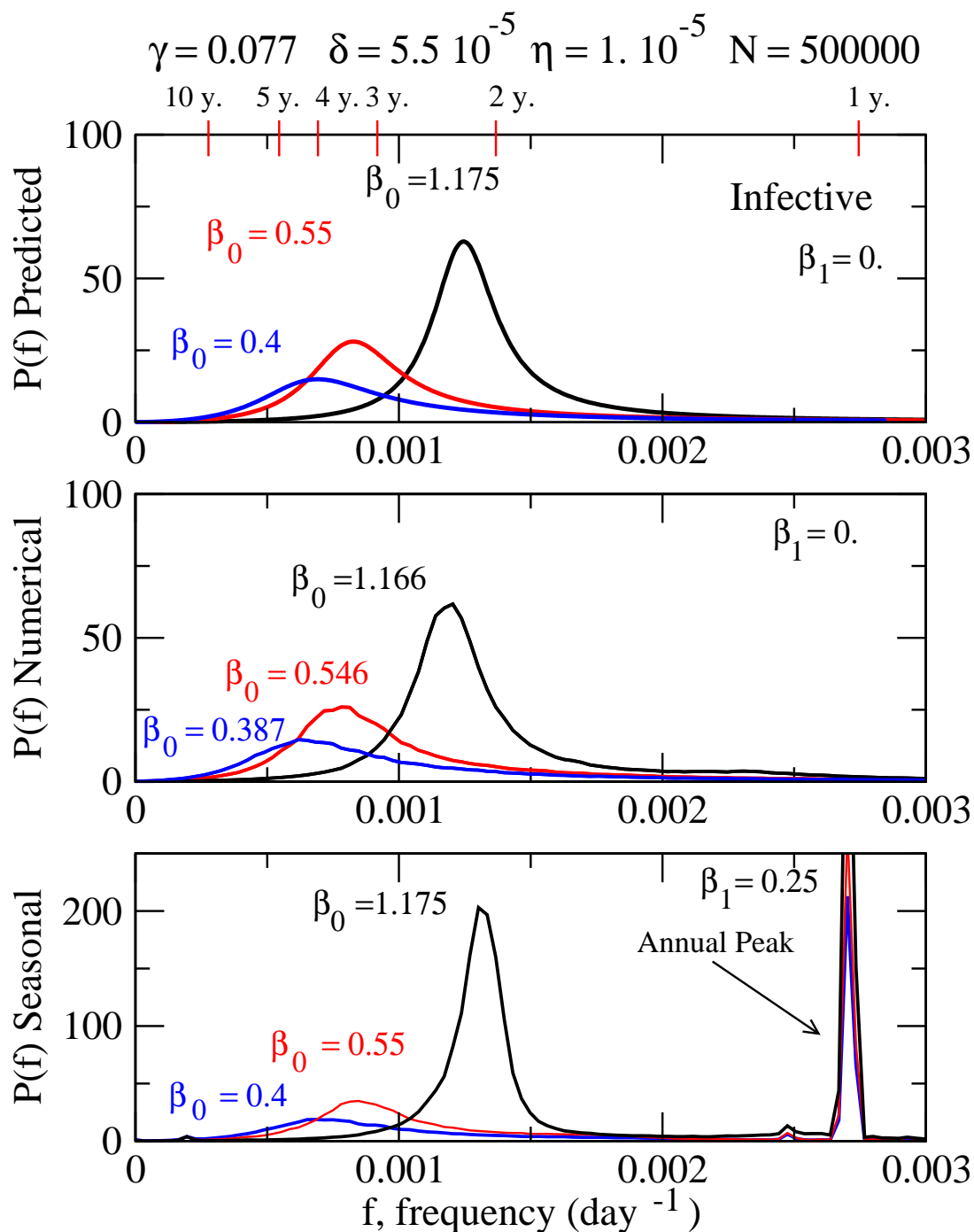
The roots of Eq. (18) are real if $\alpha^2 - \alpha B(\Gamma^2 - 2\Omega_0^2) + B^2\Omega_0^4 > 0$. If we suppose this is the case, then since the sum of the roots equals -2α , and since we can show that α is always positive, it follows that at least one of the roots is negative. We require a positive root ($z = \omega^2$), and the condition for this to happen is that the last term on the left-hand side of Eq. (18) be negative, that is,

$$-\alpha(\Gamma^2 - 2\Omega_0^2) + B\Omega_0^4 > 0, \quad (19)$$

which also implies the condition for the reality of the roots given earlier.

In summary, there is never more than one extremum of the PSD at non-zero values of ω (positive values of z). The condition for it to exist is given by (19). If it does exist it is given by

$$z = -\frac{\alpha}{B} + \frac{S}{B}, \quad (20)$$



Supplementary Figure 2. Large city. The equivalent to Fig 2 (main text) for a larger city. Notice again that the numerically averaged PSD calculated with school term seasonal forcing shows a pronounced and clear annual signature. The same parameters as in Fig 2 (main text) have been used, which are typical values for measles.

where

$$S \equiv \sqrt{\alpha^2 - B [\alpha (\Gamma^2 - 2\Omega_0^2) - B\Omega_0^4]}. \quad (21)$$

To check that the extremum is a maximum we may use

$$\left. \frac{d^2 P}{dz^2} \right|_{\text{extremum}} = \frac{-2S}{[(z - \Omega_0^2)^2 + \Gamma^2 z]^2} < 0. \quad (22)$$

Thus if a real positive solution in z exists, then it is automatically a maximum.

We can write the solution (20) in another way, if we determine the position of the peak simply by finding the zeros of the denominator of the PSD (this is equivalent to taking $B = 0$). Then from (18), the extrema at non-zero ω occurs when

$$\omega_0^2 = z_0 = \frac{1}{2} (2\Omega_0^2 - \Gamma^2). \quad (23)$$

In this case we require that $2\Omega_0^2 - \Gamma^2 > 0$ for z_0 to be real and positive. Using Eqs. (20) and (23) leads to another expression for the peak of the PSD:

$$\omega_p^2 = \frac{\alpha}{B} \left[-1 + \sqrt{1 + 2\frac{B}{\alpha}\omega_0^2 + \left(\frac{B}{\alpha}\Omega_0^2\right)^2} \right]. \quad (24)$$

This expression is different for susceptibles and infectives because the parameters B and α are different in both cases. By contrast, ω_0^2 does not depend on α or B and so is the same for infectives and susceptibles. When B is small,

$$\omega_p^2 \sim \omega_0^2 + \frac{1}{2} \frac{B}{\alpha} (\Omega_0^4 - \omega_0^4) + \mathcal{O}(B^2), \quad (25)$$

and the position of the peaks for infective and susceptible PSD tend to be very similar: $\omega_p \sim \omega_0$.

Writing Eq. (19) as

$$\Omega_0^2 \left[1 + \frac{1}{2} \frac{B}{\alpha} \Omega_0^2 \right] - \frac{1}{2} \Gamma^2 > 0, \quad (26)$$

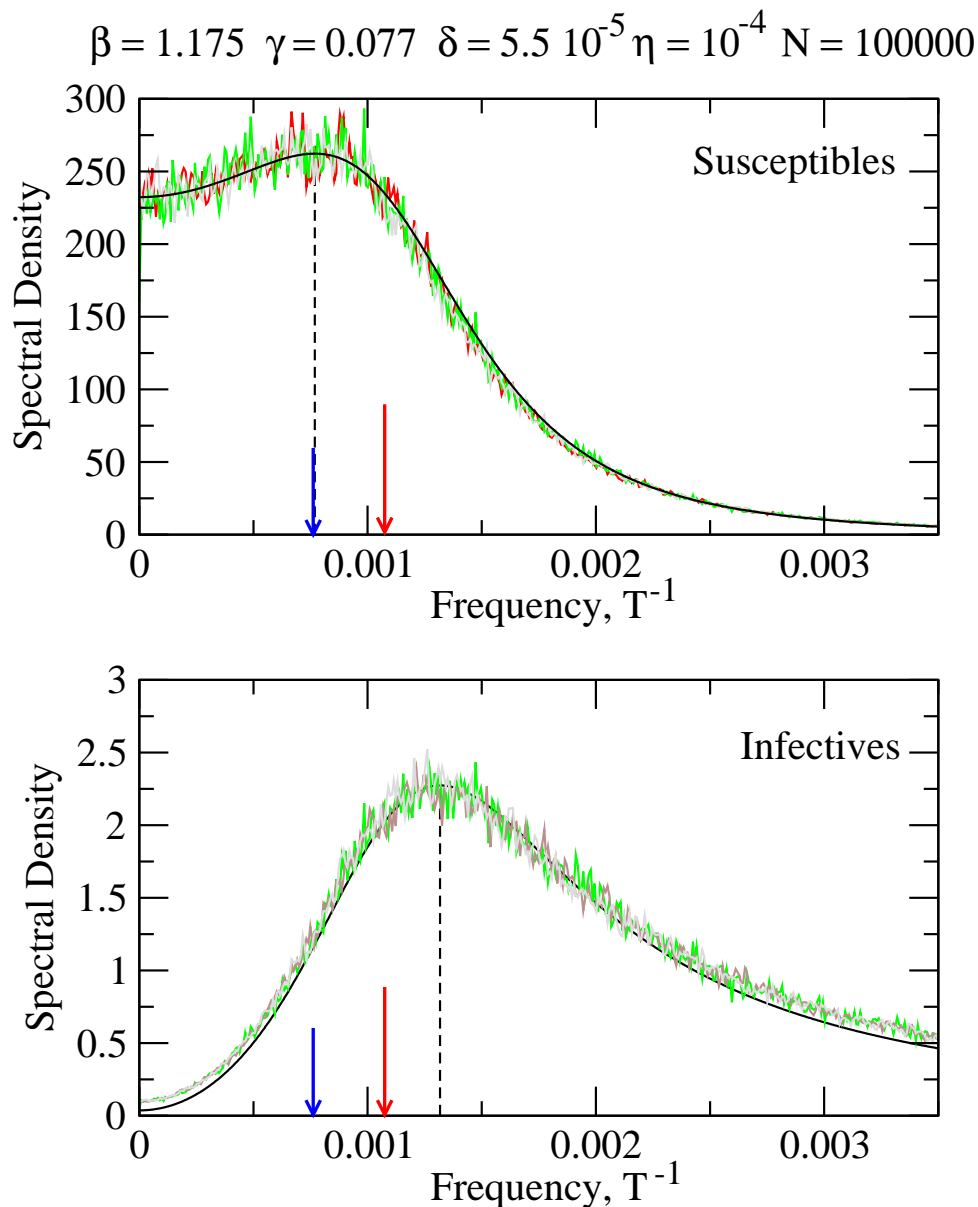
then it can be seen that when $B/\alpha \Omega_0^2 \ll 1$ for both infectives and susceptibles, condition (26) converges to a common simple condition for both susceptibles and infectives: $\Omega_0^2 - \frac{1}{2} \Gamma^2 > 0$. In this case both spectra will peak at the same frequency $\omega_p = \omega_0$. This more restrictive condition was used in Fig 4B of the main text.

In Fig. S3, we choose a parameter set of our open SIR model where the PSD for infectives and susceptibles are very different.

3 The master equation and the large- N expansion

In this section we will give details concerning the explicit form of the master equation and carry out the large- N expansion to leading and next-to-leading order.

We begin with the full stochastic model, that is, with the master equation (5) where the states are specified by $\underline{\sigma} = (l, m, n)$. The form of the equation can be made a little more elegant by introducing the step operators \mathcal{E} which are defined by their actions on functions of n, m and l by $\mathcal{E}_R^{\pm 1} f(l, m, n, t) = f(l \pm 1, m, n, t)$, $\mathcal{E}_S^{\pm 1} f(l, m, n, t) = f(l, m \pm 1, n, t)$, and



Supplementary Figure 3. The dominant frequency of stochastic oscillations. The PSD for susceptible and infective individuals are represented here. On thick black the analytic predictions are represented. In the PSD for the infectives, the red arrow represents the characteristic frequency value for the damped oscillations to the stable attractor of the corresponding deterministic system. The blue arrow is the predicted dominant frequency ω_0 (Eq. 23) for the stochastic oscillation given by McKane and Newman, 2005

$\mathcal{E}_I^{\pm 1} f(l, m, n, t) = f(l, m, n \pm 1, t)$. Then for the processes (1)-(4), the general form of the master equation (5) may be written as

$$\begin{aligned} \frac{dP(l, m, n, t)}{dt} &= (\mathcal{E}_S \mathcal{E}_I^{-1} - 1) [T(l, m - 1, n + 1 | l, m, n) P(l, m, n, t)] \\ &+ (\mathcal{E}_R - 1) [T(l - 1, m, n | l, m, n) P(l, m, n, t)] \\ &+ (\mathcal{E}_S - 1) [T(l, m - 1, n | l, m, n) P(l, m, n, t)] \\ &+ (\mathcal{E}_I - 1) [T(l, m, n - 1 | l, m, n) P(l, m, n, t)] \\ &+ (\mathcal{E}_S^{-1} - 1) [T(l, m + 1, n | l, m, n) P(l, m, n, t)] \\ &+ (\mathcal{E}_R^{-1} \mathcal{E}_I - 1) [T(l + 1, m, n - 1 | l, m, n) P(l, m, n, t)] . \end{aligned} \quad (27)$$

The deterministic limit of this stochastic model may be obtained by multiplying (27) by l, m and n in turn, and then summing over all the states of the system. This gives equations for the mean values $R = \langle l \rangle$, $S = \langle m \rangle$ and $I = \langle n \rangle$ in the limit $N \rightarrow \infty$ if we make the replacement $\langle mn \rangle \rightarrow \langle m \rangle \langle n \rangle$. For $R(t) = \langle l \rangle = \sum_{l, m, n} l P(l, m, n, t)$ this mean field theory takes the form

$$\begin{aligned} \frac{dR}{dt} &= \sum_{l, m, n} \{ -T(l - 1, m, n | l, m, n) P(l, m, n, t) \\ &+ T(l + 1, m, n - 1 | l, m, n) P(l, m, n, t) \} , \end{aligned} \quad (28)$$

where the summation variables have been shifted by ± 1 to simplify the expressions. A similar shift of variables in the equations for $S(t) = \langle m \rangle$ and $I(t) = \langle n \rangle$ gives

$$\begin{aligned} \frac{dS}{dt} &= \sum_{l, m, n} \{ -T(l, m - 1, n + 1 | l, m, n) P(l, m, n, t) \\ &- T(l, m - 1, n | l, m, n) P(l, m, n, t) \\ &+ T(l, m + 1, n | l, m, n) P(l, m, n, t) \} , \end{aligned} \quad (29)$$

and

$$\begin{aligned} \frac{dI}{dt} &= \sum_{l, m, n} \{ T(l, m - 1, n + 1 | l, m, n) P(l, m, n, t) \\ &- T(l, m, n - 1 | l, m, n) P(l, m, n, t) \\ &- T(l + 1, m, n - 1 | l, m, n) P(l, m, n, t) \} . \end{aligned} \quad (30)$$

As we described in the main text, we may reduce the number of independent degrees of freedom from 3 to 2, by implementing a zero-sum rule: every death of an individual is accompanied by the birth of a susceptible. The state of the system is now described by only two integers: $\underline{\sigma} = (m, n)$, with the number of recovered given by $l = N - m - n$. Then for the processes (8)-(10), the general form of the master equation (5) may be written as

$$\begin{aligned} \frac{dP(m, n, t)}{dt} &= (\mathcal{E}_S \mathcal{E}_I^{-1} - 1) [T(m - 1, n + 1 | m, n) P(m, n, t)] \\ &+ (\mathcal{E}_S - 1) [T(m + 1, n | m, n) P(m, n, t)] \\ &+ (\mathcal{E}_I \mathcal{E}_S^{-1} - 1) [T(m, n - 1 | m, n) P(m, n, t)] \\ &+ (\mathcal{E}_I - 1) [T(m, n - 1 | m, n) P(m, n, t)] . \end{aligned} \quad (31)$$

The deterministic limit of this reduced stochastic model may be obtained by multiplying (31) by m and n in turn, and then summing over all the states of the system just as for the full model.

This gives

$$\begin{aligned} \frac{dS}{dt} &= \sum_{m,n} \{-T(m-1, n+1|m, n)P(m, n, t) \\ &+ T(m+1, n|m, n)P(m, n, t) \\ &+ T(m+1, n-1|m, n)P(m, n, t)\}, \end{aligned} \quad (32)$$

and

$$\begin{aligned} \frac{dI}{dt} &= \sum_{m,n} \{T(m-1, n+1|m, n)P(m, n, t) \\ &- T(m+1, n-1|m, n)P(m, n, t) \\ &- T(m, n-1|m, n)P(m, n, t)\}. \end{aligned} \quad (33)$$

We now wish to analyze the master equation (31) using the $1/N$ expansion. An intuitive explanation of the method is given in the main text, an application of the method to a system very similar to the one we are considering here has been discussed in some detail in other papers (Alonso & McKane 2002; McKane & Newman 2004) and the method is also clearly discussed in Van Kampen (1992). So here we merely give the explicit expressions that are obtained through an application of the method. At leading order we obtain the deterministic equations for

$$\phi(t) = \lim_{N \rightarrow \infty} \frac{S(t)}{N} ; \quad \psi(t) = \lim_{N \rightarrow \infty} \frac{I(t)}{N}, \quad (34)$$

to be $d\phi/dt = \alpha_{1,0}(\phi, \psi)$ and $d\psi/dt = \beta_{1,0}(\phi, \psi)$, where the two functions $\alpha_{1,0}$ and $\beta_{1,0}$ are given below. This gives Eq. (13) after rescaling time by $\tau = \gamma t$. At next-to-leading order we obtain a Fokker-Planck equation which is given explicitly in Appendix A of McKane and Newman (2004), but now with the α and β functions given by

$$\begin{aligned} \alpha_{1,0}(\phi, \psi) &= -\hat{\beta}\phi\psi - \hat{\eta}\phi + \hat{\delta}(1 - \phi), \\ \beta_{1,0}(\phi, \psi) &= \hat{\beta}\phi\psi + \hat{\eta}\phi - \hat{\delta}\psi - \psi, \\ \alpha_{2,0}(\phi, \psi) &= \hat{\beta}\phi\psi + \hat{\eta}\phi + \hat{\delta}(1 - \phi), \\ \beta_{2,0}(\phi, \psi) &= \hat{\beta}\phi\psi + \hat{\eta}\phi + \hat{\delta}\psi + \psi, \\ \gamma(\phi, \psi) &= -\hat{\delta}\psi - \hat{\eta}\phi - \hat{\beta}\psi\phi, \end{aligned} \quad (35)$$

after rescaling time and using the rescaled parameters defined by Eq. (12).

However we wish to Fourier analyze the fluctuations about the deterministic model, and for this purpose we require to describe the fluctuations in terms of a set of Langevin equations, rather than in terms of a Fokker-Planck equation. If we use the following correspondence between the Fokker-Planck equation:

$$\frac{\partial \Pi}{\partial t} = - \sum_i \frac{\partial}{\partial r_i} (A_i(\underline{r}) \Pi) + \frac{1}{2} \sum_{i,j} B_{ij} \frac{\partial^2 \Pi}{\partial r_i \partial r_j}, \quad (36)$$

where $\underline{r} = (x, y)$ and $i, j = 1, 2$, and the Langevin equations

$$\frac{dr_i}{dt} = A_i(\underline{r}) + \eta_i(t), \quad (37)$$

where $\langle \eta_i(t)\eta_j(t') \rangle = B_{ij}\delta(t-t')$, then we find the equations (14) given in the main text. Here $A_i(\underline{x})$ is a linear function of x and y and the B_{ij} is a constant matrix. Their explicit forms are $A_1 = a_{11}x + a_{12}y$ and $A_2 = a_{21}x + a_{22}y$ where

$$\begin{aligned} a_{11} &= \left. \frac{\partial \alpha_{1,0}}{\partial \phi} \right|_{FP}, & a_{12} &= \left. \frac{\partial \alpha_{1,0}}{\partial \psi} \right|_{FP}, \\ a_{21} &= \left. \frac{\partial \beta_{1,0}}{\partial \phi} \right|_{FP}, & a_{22} &= \left. \frac{\partial \beta_{1,0}}{\partial \psi} \right|_{FP}, \end{aligned} \quad (38)$$

all evaluated at the fixed point (FP) values, and where

$$\begin{aligned} B_{11} &= \alpha_{2,0}(\phi^*, \psi^*), & B_{12} &= \gamma(\phi^*, \psi^*), \\ B_{21} &= \gamma(\phi^*, \psi^*), & B_{22} &= \beta_{2,0}(\phi^*, \psi^*). \end{aligned} \quad (39)$$

Once we know the a_{ij} and B_{ij} in terms of the parameters defining the stochastic model, we know all we need to about the fluctuations for large N . All that remains is to find the fixed points ϕ^* and ψ^* , defined by $\alpha_{1,0} = 0$ and $\beta_{1,0} = 0$, from Eq. (35), and substitute them into the expressions for a_{ij} and B_{ij} given by Eqs. (38) and (39). Adding $\alpha_{1,0} = 0$ and $\beta_{1,0} = 0$, we see that

$$\psi^* = \frac{\hat{\delta}(1 - \phi^*)}{1 + \hat{\delta}}, \quad (40)$$

and so

$$(\phi^*)^2 - \left[1 + \frac{\hat{\eta}(1 + \hat{\delta})}{\hat{\delta}\hat{\beta}} + \frac{(1 + \hat{\delta})}{\hat{\beta}} \right] \phi^* + \frac{(1 + \hat{\delta})}{\hat{\beta}} = 0. \quad (41)$$

Clearly it is straightforward to solve the quadratic equation (41) for ϕ^* and then obtain the corresponding values of ψ^* from Eq. (40), but since for the most part we will be evaluating the a_{ij} and B_{ij} numerically, there is no need to give the explicit form here. However, it is instructive to write out the solutions as a linear expansion in $\hat{\eta}$, since this parameter will typically be very small. One finds:

$$\begin{aligned} \phi_+^* &= 1 + \frac{(1 + \hat{\delta})}{\hat{\delta}(\hat{\beta} - 1 - \hat{\delta})} \hat{\eta} + O(\hat{\eta}^2), \\ \phi_-^* &= \frac{1 + \hat{\delta}}{\hat{\beta}} \left\{ 1 - \frac{(1 + \hat{\delta})}{\hat{\delta}(\hat{\beta} - 1 - \hat{\delta})} \hat{\eta} + O(\hat{\eta}^2) \right\}. \end{aligned} \quad (42)$$

The presence of external infection ($\eta \neq 0$) decreases the stable level of susceptibles observed for the closed system which is $\phi_0^* = (1 + \hat{\delta})/\hat{\beta}$ when $\hat{\beta} > 1 + \hat{\delta}$. Consequently, the incidence of the disease increases ($\psi_-^* > \psi_0^*$). Otherwise, we have a stable incidence level, ψ_+^* , which is only maintained by external infection. The population acts as a sink rather than as a reservoir or source for infections. It is actually the situation where the disease is internally self-maintained that we are interested in ($\hat{\beta} > 1 + \hat{\delta}$). In this case, it is also illustrative to write these solutions in terms of the fixed point in absence of external immigration (ψ_0^* and ϕ_0^*):

$$\begin{aligned} \phi^* &= \phi_0^* - \frac{(1 + \hat{\delta})^2}{\hat{\beta}\hat{\delta}(\hat{\beta} - 1 - \hat{\delta})} \hat{\eta} + O(\hat{\eta}^2), \\ \psi^* &= \psi_0^* + \frac{(1 + \hat{\delta})}{\hat{\beta}(\hat{\beta} - 1 - \hat{\delta})} \hat{\eta} + O(\hat{\eta}^2). \end{aligned} \quad (43)$$

Using Eq. (35), the a_{ij} and B_{ij} given by Eqs. (38) and (39) may be written as

$$\begin{aligned} a_{11} &= -\hat{\beta}\psi^* - \hat{\eta} - \hat{\delta}, & a_{12} &= -\hat{\beta}\phi^*, \\ a_{21} &= \hat{\beta}\psi^* + \hat{\eta}, & a_{22} &= \hat{\beta}\phi^* - (1 + \hat{\delta}), \end{aligned} \quad (44)$$

and

$$\begin{aligned} B_{11} &= 2\hat{\delta}(1 - \phi^*), & B_{12} &= -(2\hat{\delta} + 1)\psi^*, \\ B_{21} &= -(2\hat{\delta} + 1)\psi^*, & B_{22} &= 2(1 + \hat{\delta})\psi^*, \end{aligned} \quad (45)$$

where we have simplified the expressions for the B_{ij} by using the equations defining the fixed points in Eq. (35). From these last two equations, in conjunction with Eqs. (40) and (41) — or Eqs. (40) and (42) for small $\hat{\eta}$ — we can find the a_{ij} and B_{ij} in terms of the parameters $\hat{\beta}, \hat{\delta}$ and $\hat{\eta}$.

Taking the Fourier transform of (14) gives

$$\begin{aligned} (-i\omega - a_{11})\tilde{x} - a_{12}\tilde{y} &= \tilde{\eta}_1, \\ -a_{21}\tilde{x} + (-i\omega - a_{22})\tilde{y} &= \tilde{\eta}_2, \end{aligned} \quad (46)$$

where

$$\langle \tilde{\eta}_i(\omega)\tilde{\eta}_j(\omega') \rangle = B_{ij}(2\pi)\delta(\omega + \omega'). \quad (47)$$

Solving Eqs. (46) we obtain

$$\begin{aligned} \tilde{x}(\omega) &= \frac{a_{12}\tilde{\eta}_2 - a_{22}\tilde{\eta}_1 - i\omega\tilde{\eta}_1}{D}, \\ \tilde{y}(\omega) &= \frac{a_{21}\tilde{\eta}_1 - a_{11}\tilde{\eta}_2 - i\omega\tilde{\eta}_2}{D}, \end{aligned} \quad (48)$$

where the denominator, D , is given by

$$D(\omega) = (-i\omega)^2 - [a_{11} + a_{22}](-i\omega) + [a_{11}a_{22} - a_{12}a_{21}]. \quad (49)$$

Averaging the squared moduli of \tilde{x} and \tilde{y} gives the power-spectrum:

$$\begin{aligned} P_S(\omega) &= \langle |\tilde{x}(\omega)|^2 \rangle = \frac{\alpha_S + B_{11}\omega^2}{|D(\omega)|^2}, \\ P_I(\omega) &= \langle |\tilde{y}(\omega)|^2 \rangle = \frac{\alpha_I + B_{22}\omega^2}{|D(\omega)|^2}, \end{aligned} \quad (50)$$

where

$$\begin{aligned} \alpha_S &= B_{11}a_{22}^2 + B_{22}a_{12}^2 - 2B_{12}a_{12}a_{22}, \\ \alpha_I &= B_{22}a_{11}^2 + B_{11}a_{21}^2 - 2B_{12}a_{21}a_{11}. \end{aligned} \quad (51)$$

We may write $|D(\omega)|^2$ in the form $(\omega^2 - \Omega_0^2)^2 + \Gamma^2\omega^2$, as in earlier sections. This gives the identification

$$\Omega_0^2 = a_{11}a_{22} - a_{21}a_{12}, \quad \Gamma = |a_{11} + a_{22}|. \quad (52)$$

Finally, as we have already remarked, the matrix with entries a_{ij} is the stability matrix of the deterministic equation around the fixed point of interest to us. From Eq. (49) it is clear that the eigenvalues of the matrix, λ , satisfy $D(i\lambda) = 0$. Writing this out explicitly gives

$$\begin{aligned} \lambda^2 &+ \left[\hat{\beta}(\psi^* - \phi^*) + \hat{\eta} + 2\hat{\delta} + 1 \right] \lambda \\ &+ \left[\hat{\beta}(\hat{\delta} + 1)\psi^* - \hat{\beta}\hat{\delta}\phi^* + (\hat{\delta} + 1)(\hat{\delta} + \hat{\eta}) \right] = 0. \end{aligned} \quad (53)$$

4 Bifurcation Diagrams

In our model, it can be easily shown that a vaccination of a proportion of the population p , changes both contact rates and the external infection parameter, η , so that:

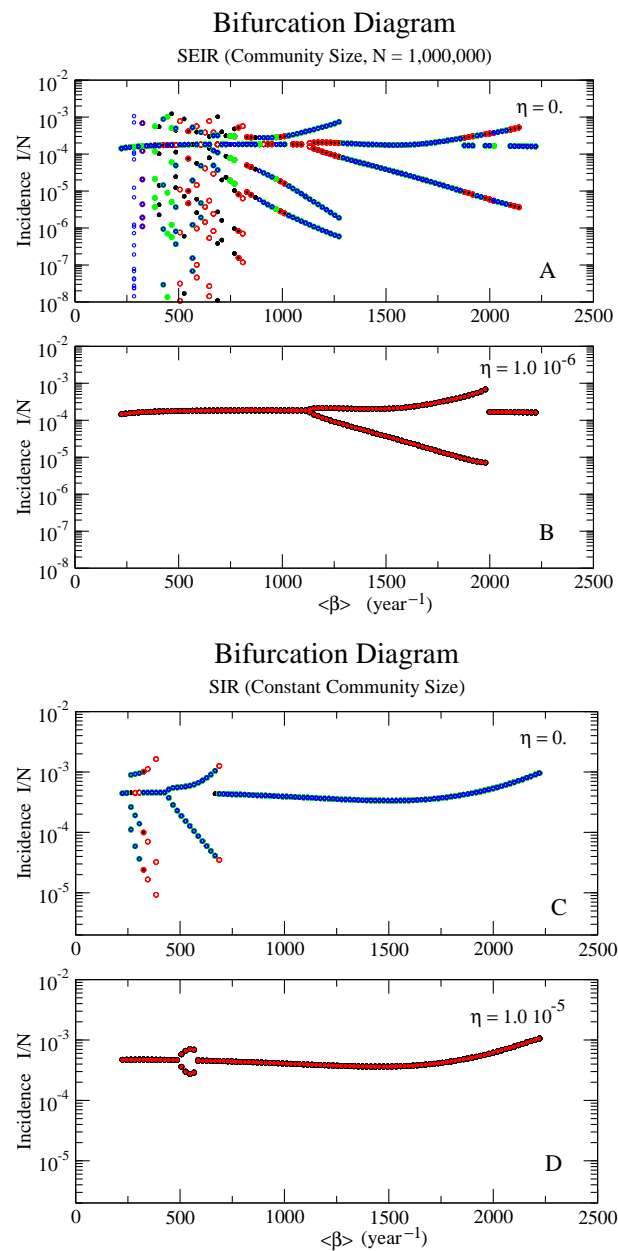
$$\begin{aligned}\langle\beta\rangle &\longrightarrow (1-p)\langle\beta\rangle \\ \eta &\longrightarrow (1-p)\eta\end{aligned}\tag{54}$$

However, a realistic determination of how vaccination decreases transmission rates is difficult. The linear scaling assumed by the above transformation relies on the same mixing mechanism (mass action) for both local and global levels. This is probably unrealistic. Vaccination can affect internal transmission ($\langle\beta\rangle$) and the probability of acquiring the infection from an external source (η) in very different ways. It is reasonable to assume that the ‘‘mass action principle’’ applies locally (within a city) but not globally, where other mechanisms are at play, including complex individual movements enhancing long distance contacts. Since vaccination was a global campaign, transmission rates decreased everywhere. If, rather than assuming that the factor $(1-p)$ affected both rates, we consider instead that $\langle\beta\rangle \longrightarrow (1-p)\langle\beta\rangle$ but η remained constant, we emphasize the effect of vaccination on local transmission relative to external infection. Examples of mechanisms that might have promoted this type of scenario include an increase in the mean age of infection in the vaccination era (Rohani *et al*, 1999), and other social causes linked to a better communication system in modern times, leading to the synergy of greater movement and mixing of susceptible and infective individuals. We report here primarily on the case for a constant and small η but we have also considered smaller values of this parameter, as well as the case where it decreases in the same proportion as β . Qualitative results are for the most part robust to these changes. Specifically, longer periods and less overall amplification are also observed at low transmission rates. However, when vaccination decreases both rates β and η in the same proportion, the PSD maintains a coherent dominant frequency for lower values of the effective transmission rates. In our work, we have taken η values of $10^{-5} - 10^{-6}$ which correspond to a coupling parameter ξ in Rohani *et al.* (1999) of around 0.05 in cities with a community size of $10^5 - 10^6$.

In the bifurcation diagrams of Fig S4 (B and D) it is assumed, for simplicity, that the external infection rate η is not affected by the introduction of vaccination:

$$\begin{aligned}\langle\beta\rangle &\longrightarrow (1-p)\langle\beta\rangle \\ \eta &\longrightarrow \eta.\end{aligned}\tag{55}$$

If we assume that vaccination affects both rates linearly (Eq. 54), similar bifurcation diagrams as those shown in Fig S4 (B and D) are obtained. When external infection is taken into account, the coexistence of different stable attractors (see Fig S4 A, for low betas, see also Fig 1. in Earn *et al* 2000) is lost and a simple one-year stable attractor is observed instead (compare Fig S4 A and C with B and D, respectively)



Supplementary Figure 4. Bifurcation Diagrams. Different diagrams for SEIR (upper panels) and SIR (lower panels) epidemic deterministic models with ($\eta = 1.10^{-6}$) and without ($\eta = 0.$) external infection are represented. For low values of the transmission rate the deterministic system shows a set of coexisting multi-annual attractors (plots A and C, when there is no external infection, Earn *et al.* 2000). This diagram is not robust to external infections. The same bifurcation diagrams are calculated with a small value of the immigration parameter (plots B and D) and an annual simple attractor is the only structure observed for low values of the transmission rate $\langle\beta\rangle$

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