

Stochastic dynamics of cholera epidemics

Sandro Azaele,^{1,2} Amos Maritan,^{3,*} Enrico Bertuzzo,^{4,5} Ignacio Rodriguez-Iturbe,¹ and Andrea Rinaldo^{4,5,6,†}

¹*Department of Civil and Environmental Engineering, E-Quad, Princeton University, Princeton, New Jersey 08544, USA*

²*Institute of Integrative and Comparative Biology, University of Leeds, Leeds LS2 9JT, United Kingdom*

³*Dipartimento di Fisica G. Galilei and INFN, Università di Padova, Via Marzolo 8, I-35151 Padova, Italy*

⁴*Laboratory of Ecohydrology, ECHO/ISTE/ENAC, Faculté ENAC, École Polytechnique Fédérale Lausanne (EPFL), Lausanne (CH), Switzerland*

⁵*Laboratory of Ecohydrology, ECHO/IEE/ENAC, Faculté ENAC, École Polytechnique Fédérale Lausanne (EPFL), Lausanne (CH), Switzerland*

⁶*Dipartimento IMAGE, Università di Padova, I-35131 Padova, Italy*

(Received 21 November 2007; revised manuscript received 12 April 2010; published 3 May 2010)

We describe the predictions of an analytically tractable stochastic model for cholera epidemics following a single initial outbreak. The exact model relies on a set of assumptions that may restrict the generality of the approach and yet provides a realm of powerful tools and results. Without resorting to the depletion of susceptible individuals, as usually assumed in deterministic susceptible-infected-recovered models, we show that a simple stochastic equation for the number of ill individuals provides a mechanism for the decay of the epidemics occurring on the typical time scale of seasonality. The model is shown to provide a reasonably accurate description of the empirical data of the 2000/2001 cholera epidemic which took place in the Kwa Zulu-Natal Province, South Africa, with possibly notable epidemiological implications.

DOI: [10.1103/PhysRevE.81.051901](https://doi.org/10.1103/PhysRevE.81.051901)

PACS number(s): 87.18.Tt, 87.19.X-, 05.40.-a

I. INTRODUCTION

Large-scale public health projects that involve infectious disease, such as cholera, pose a major practical problem in the need to provide models of the epidemic reliably accounting for real-life epidemiological and environmental complexity in a reliable predictive fashion. Deterministic models of the susceptible-infected-recovered (SIR) type [1,2] are the standard framework for a wide array of spreading diseases, including cholera. They have a great deal of usefulness in coping with different epidemiological situations in dealing with both epidemic and endemic situations [3,4]. In spite of these achievements, however, there still exists a lack of complete analytical predictability (of, say, total infected individuals or times to infection peaks) which may allow one to handle the temporal dynamics governing a spreading disease in a given region. Unless at the cost of additional, parameter-riddled modeling efforts, deterministic models of the SIR type [1] cannot directly cope with a range of epidemiological situations dominated by environmental fluctuations in the forcings or in the controlling parameters, which are intrinsic to the phenomenon [4,5]. To that end, stochastic SIR models have proved valuable in estimating asymptotic expressions for the probability of occurrence of a major outbreak and for the expected time of extinction [6], including the probability that an infectious disease will eventually disappear [7].

Especially in recent years, upon notable increase in the extent of suitable observational databases, it has been also stressed that cholera epidemics exhibit complex spatial-temporal patterns mostly encoded in environmental forcings and in the constraints of the ecological corridors provided by

the river networks where the pathogens disperse from the autochthonous regions [8–12]. Seasonality, endogenous oscillations, and climate variability may dynamically interact to produce regular or irregular disease cycles [13–15]. Furthermore, the interplay between nonlinearity and noise can yield stochastic amplifications which may give rise to population oscillations that are comparable to those due to seasonal forcing in deterministic systems [16].

In this paper, we focus on the role of stochasticity within a single cholera outbreak and propose a different mechanism for the turn-around of the epidemic, which contrasts with the prevailing idea that the waning of the disease is substantially due to the depletion of susceptibles. We will assume that the number of susceptible individuals is always very large, i.e., comparable to the population of the spatial region taken into account, and suggest that infected individuals are depleted because of the demographic stochasticity of the disease. The source of this variability rests on the highly unpredictable spatial and environmental pathways coupled to the intrinsic discreteness of the population, which can potentially jeopardize the predictions of classical deterministic approaches. The presence of a susceptible pool of individuals as well as the seasonal factors related to environmental drivers still remain crucial for the onset of the outbreak, but they may become less important, compared to stochasticity, for the extinction of the disease. Indeed, there exist relevant time scales corresponding to seasonal factors and we suggest that below the smallest seasonal time scale stochastic dynamics dominates the evolution of the disease.

In order to test this hypothesis, we set up a minimalist stochastic model derived from a traditional picture of cholera dynamics and compare it to the empirical data of an epidemic which took place in South Africa. Our approach implicitly accounts for the spatial distribution of the disease and is valid when the following hypotheses hold: (i) the number of susceptibles is much larger than that of the infected ones;

*amos.maritan@pd.infn.it

†andrea.rinaldo@epfl.ch; andrea.rinaldo@unipd.it

TABLE I. Model parameters and values.

Description	Symbol	Value	Reference
Total human population	H	3.3×10^6 ind	[27]
Population natality and mortality rate	n	5×10^{-5} day $^{-1}$	[9]
Rate of ingestion of contaminated water	a	variable	[28]
<i>V. cholerae</i> concentration that yields 50% chance of catching cholera	V_0	$\sim 10^6$ cell/ml	[17]
Rate of recovery from cholera	r	0.2 day $^{-1}$	[20,28]
(Net) Mortality rate of <i>V. cholerae</i> in the aquatic environment	β	0.033 day $^{-1}$	[20,28]
Contribution of infecteds to <i>V. cholerae</i> concentration in the aquatic environment	e	~ 0.1 cell/ml day individuals	[9,17,28]
Characteristic population	$J \equiv \frac{\beta V_0}{e}$	$\sim 3 \times 10^5$ individuals	

(ii) a well-defined separation of time scales occurs allowing the decoupling of the infected individuals and the vibriions, i.e., the causative organisms of cholera; (iii) the spatial regional patterns of infection may be collapsed to yield a meaningful regional temporal evolution, an assumption whose validity is assessed by computing the speed of traveling waves of infection [10]. Our model describes the time evolution of the infected individuals following a single initial outbreak and takes into account only a minimal number of key ingredients for epidemic spreading in order to keep it analytically tractable. Although the assumed flux of susceptibles suggests a demographic dynamics untenable in the absence of cholera and the presence of asymptomatic cases is troublesome toward model calibration against data, the exact nature of the proposed solutions is believed to provide clues relevant to various epidemiological matters.

II. THEORETICAL BACKGROUND

We proceed to a derivation of the framework starting from a deterministic model which is a traditional picture of cholera dynamics [17]. This will allow us to give a physical interpretation to the parameters of the stochastic setting. It is well known that the causative organism of cholera, in the present case the *Vibrio cholerae* 01 El Tor Ogawa, thrives in warm waters [18,19], thus we assume that there exists an environmental reservoir of vibriions which is coupled to the dynamics of infected and susceptible individuals according to the following system of deterministic differential equations:

$$\frac{dS}{dt} = n(H - S) - a \frac{V}{V + V_0} S, \quad (1a)$$

$$\frac{dI}{dt} = a \frac{V}{V + V_0} S - rI, \quad (1b)$$

$$\frac{dV}{dt} = -\beta V + e(H)I, \quad (1c)$$

where I , S , and V are the numbers of infected individuals, susceptible individuals, and the vibriion concentration (cells/

ml), respectively, n is the human birth and death rate, and H is the population size of the region in which the disease is present. The system (1) explains a cholera epidemic according to the following mechanisms. Susceptible individuals ingest contaminated water at a rate a and have the probability of 50% to catch cholera when the concentration of vibriions in water is V_0 . When infected, people recover at a rate r but simultaneously shed vibriions into water at a rate $e(H)$, increasing the concentration of contaminated water on the basis of the total population H (see Refs. [9,10]). In the aquatic environment, vibriions have a mean lifetime β^{-1} .

Interestingly, from a numerical integration of the system (1) with the realistic parameters listed in Table I, one can see that vibriions and infectives can roughly be considered proportional to each other. As a first approximation, we can substitute Eq. (1c) simply with $V \approx eI/\beta$. This means that vibriions' dynamics is fast and the *V. cholerae* concentration is driven by infectives. In this case, we can focus on the coupled dynamics of susceptible and infected individuals, considering the concentration of vibriions proportional to the number of infectives. Thus, the system (1) now reads

$$\frac{dS}{dt} = n(H - S) - a \frac{I}{I + J} S, \quad (2a)$$

$$\frac{dI}{dt} = a \frac{I}{I + J} S - rI. \quad (2b)$$

Equation (2b) indicates that an infection will be able to spread through a population in a full-blown outbreak only when the number of susceptibles is greater than Jr/a , so that the basic reproductive number is $R_0 = aH/rJ$, being the entire population supposedly susceptible. Unfortunately, in the system of Eqs. (2), the estimation of J is a hard task because it strongly depends on the epidemiological characteristics of the particular *V. cholerae* strain as well as its coupling to human beings and environment. However, from the available literature (see Table I), we can roughly estimate $J \sim 10^5$ (individuals). As the number of infectives is usually much smaller than J , we can assume that Eq. (2b) is simply

$$\frac{dI(t)}{dt} = \left(\frac{aS(t)}{rJ} - 1 \right) rI(t). \quad (3)$$

This equation shows that infected individuals grow whenever $S > rJ/a$, such that within this deterministic framework, the number of infectives blows up if $S \approx H > rJ/a$, which is one of our main assumptions. However, in the following, we will show that by introducing some meaningful stochastic and deterministic terms, the divergence disappears.

III. STOCHASTIC MODEL

In this section, we define the stochastic model which we will compare to data in order to validate our previous assumptions. First, we assume that at the beginning of the outbreak, the infected individuals increase with the constant rate $b = k(aH/J - r) = rk(R_0 - 1)$, where k is a constant of order 1. This is simply inferred from Eq. (3) when assuming that initially the entire population is susceptible to the disease. Second, we present the characteristic time scale, τ , of the epidemic outbreak related to the balance of (i) the rate of infection of susceptibles due to the contact with one infected individual and (ii) the loss rate of infected individuals owing to recovery, death, or isolation. We will assume that the contribution of these factors always result in the loss of infected individuals. Finally, we bring stochasticity in the evolution of infectives: the nature of disease transmission is intrinsically discrete, involving at least pairs of individuals. The discreteness of the process naturally brings about stochasticity, whose effects can be described, within a first rough approximation, by a birth and death process [21]. At least when the population of infectives is large, a natural choice for the rate of producing (depleting) an infected individual is $b_I = bI$ ($d_I = dI$) because one expects that the larger the infected population, the more likely to get one new infected individual within the next small time interval and, correspondingly, one new recovered or dead individual. These rates define a discrete Markov process whose fluctuations are proportional to \sqrt{I} in the continuum approximation [21]. Therefore, if we want to accommodate stochastic effects in the dynamics of the infectives, we should introduce in our framework the fluctuating term $\sqrt{DI(t)}\xi(t)$, where $\xi(t)$ is a delta-autocorrelated Gaussian noise. More general functions, e.g., I^c with $c \neq 1/2$, can certainly be used to describe the fluctuations. They are not considered here as they usually weaken the analytical tractability as well as the physical transparency.

When adding all these terms, one obtains the following Langevin equation, which combines both the deterministic and the stochastic contributions:

$$\frac{dI}{dt} = b - \frac{I}{\tau} + \sqrt{DI}\xi(t). \quad (4)$$

In this equation, $\xi(t)$ is a Gaussian white noise with zero mean and autocorrelation function $\langle \xi(t)\xi(t') \rangle = 2\delta(t-t')$. Equation (4) defines our stochastic model which we will use to test whether stochastic effects may be responsible for the waning of the outbreak. Notice that had we used $DI(t)\xi(t)$ in Eq. (4), the second moment of the infected individuals could

diverge; if we use a repulsive potential or no potential at all (instead of the current potential), all moments (at least from the second one) diverge. Additionally, note that for Eq. (4) to hold, we need the number of susceptibles to be much larger than that of infected ones for avoiding finite size effects during the evolution. In addition, note that when setting $D=0$, one gets a trivial deterministic evolution for the infecteds. In this sense, the combination of both deterministic and stochastic terms gives rise to the interesting behavior which we will show [22,23].

This equation is analytically tractable and depends on three free parameters, namely, b , D , and τ : b takes into account a constant immigration rate of new infected individuals and/or a flow of water contaminated with vibriions that a given delimited region may experience—hence it summarizes the overall connectivity provided to water-borne infective agents by the network of waterways. Interestingly, the deterministic condition for an outbreak to occur, $R_0 > 1$, translates into a positive flux of infectives, $b > 0$, which we will estimate from empirical data. D is a positive constant, assumed to be independent of time, which accounts for the stochasticity arising from largely unpredictable factors such as environmental fluctuations and intrinsic variability [18,19,25]. It measures the strength of the noise in the infected population.

Equation (4) is a stochastic differential equation with a multiplicative noise which should be interpreted *a la* Itô, i.e., equivalent to the Fokker-Planck equation

$$\dot{p} = \partial_I[(I\tau - b)p] + D\partial_I^2(Ip), \quad (5)$$

where $p \equiv p(I, t | I_0, 0)$ is the conditional probability distribution function (PDF) of finding I -infected individuals in a spatially delimited (and epidemiologically connected) region at time t , given that at time $t=0$, there were I_0 infectives therein. Because in this framework recovered individuals do not participate in the evolution of the infection and we are interested only in the dynamics of epidemics after a single initial outbreak, we consider the evolution of the infected population until the number of infected reaches zero for the first time. This is equivalent to study the absorbing solution of Eq. (4), without taking account of any effect due to seasonality or endogenous frequency. By assuming that the epidemics initially commences with I_0 infected individuals, one obtains the following distribution [24] which is amenable to statistical analysis:

$$p(I, t | I_0, 0) = \frac{(D\tau)^{-1}}{1 - e^{-t/\tau}} \exp \left[- \frac{\frac{1}{D\tau}(I + I_0 e^{-t/\tau})}{1 - e^{-t/\tau}} \right] \times \left(\frac{I}{I_0} e^{t/\tau} \right)^{b/2D-1/2} \mathcal{I}_{1-b/D} \left[\frac{2}{D\tau} \sqrt{I_0} e^{t/\tau} \right], \quad (6)$$

where $\mathcal{I}_\sigma(z)$ is the modified Bessel function of the first kind [26]. In order that Eq. (6) exists, it must be $b/D < 1$, which interestingly translates into an upper bound for the basic reproductive number of the disease, i.e., $R_0 < 1 + D/kr$. The fact that the above solution is obtained with absorbing

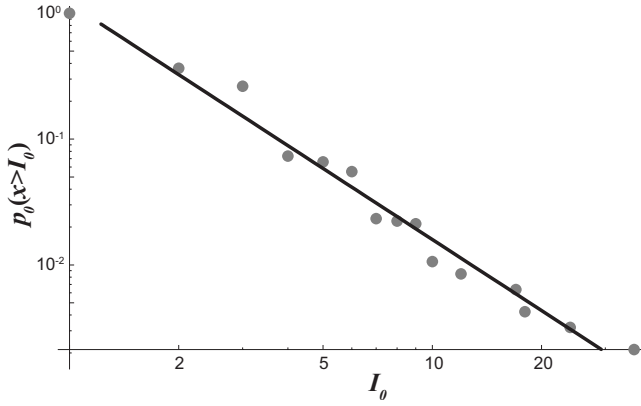


FIG. 1. In the log-log plot, dots represent the empirical probability that a given SHD has an initial infected population greater than I_0 . The empirical data pertain to the 2000/2001 cholera epidemics which took place in South Africa. The straight line is the best fitted power law [see Eq. (7)] with slope $\alpha=2.87$.

boundary conditions is proved by the fact that $P(I, t|I_0, 0)$ tends to zero at large times, i.e., the infected population, sooner or later, gets extinct.

IV. STOCHASTIC MODEL VS DATA

Now we benchmark our model against the empirical data pertaining to the 2000/2001 cholera epidemics that spread through the eastern and northeastern parts of South Africa. The causative organism *Vibrio cholerae* 01 *El Tor* *Ogawa* mostly affected the Kwa Zulu-Natal province, where the first case was confirmed as well. The epidemic data were gathered within sub health districts (SHDs), where the number of new cholera cases was daily updated. The time at which the first infected case occurred varies from district to district depending on the spatial spreading of the epidemic. Thus, in order to compare the data to the exact solution, we shifted all the times of the onset of the local epidemics so as to obtain a unique initial time for all the SHDs. This allowed us to get an ensemble average which is coherent with the type of spatial coarse-graining postulated by the model. On the other hand, in order to get the actual number of infected individuals per day, we assigned a mean lifetime for the disease throughout the population. According to epidemiological studies [20], the lifetime varies from 3 to 6 days, but it is more likely confined to be between 4 and 5 days. Thus we assigned to each case a disease period of 3 or 6 days with probability 0.30 (0.15+0.15) and a duration of 4 or 5 days with probability 0.7 (0.35+0.35). After these manipulations, the initial probability distribution of the infected individuals throughout the SHDs is found to be well represented by a power law (Fig. 1), i.e.,

$$p_0(I_0) = c(I_0/\bar{I}_0)^{-\alpha}, \quad (7)$$

where $c=(\alpha-1)/\bar{I}_0$, $\bar{I}_0=1$, and $\alpha=2.87$. This initial PDF summarizes the information about the highly heterogeneous spatial distribution of infectives across the SHDs and has to be encapsulated in our aggregated description of the disease.

Accordingly, the time dependent-distribution of infectives is modified into the new PDF which reads

$$q(I, t) \equiv \int_0^\infty p(I, t|I_0, 0)p_0(I_0)dI_0.$$

Notably, the total infected individuals of a given district are poorly correlated ($\rho \approx 0.05$) with the respective total population. This means that one can find very populated SHDs with a small number of infecteds as well as SHDs with small populations and a lot of infected individuals. Although it may be somehow surprising at a first sight, this pattern might stem from better sanitary conditions present in populated SHDs. On the other side, this observation also points out that the stochasticity involved in the outbreak is not trivially related to the actual total population of a SHD. Under the previous initial conditions, the average number of infectives at time t in a given district is simply

$$\langle I(t) \rangle = \int_0^\infty I p(I, t|I_0, 0)p_0(I_0)dI_0 dI,$$

which can be calculated by exploiting the analytic solution in Eq. (6). In order to be more restrictive on the model validation and obtain a more reliable set of parameters, we studied also the probability that a given district has at least one infected individual at time t , which reads

$$q(t) \equiv \int_0^\infty p(I, t|I_0, 0)p_0(I_0)dI_0 dI.$$

Least-square errors statistics were carried out on all SHDs so as to yield the parameters of the model. By resorting to a weighted mean of the χ^2 statistics, we simultaneously best fitted the data of the mean value of the infected individuals per SHD at time t and the empirical probability that a given district has at least one infected individual at time t with the corresponding quantities predicted by the model. The obtained parameters are $b=0.48$ individuals/day, $D=0.69$ individuals/day, and $\tau=19.1$ days. The comparative results are shown in Fig. 2.

V. DISCUSSION

The model correctly explains the time scales for the peak and the extinction of the epidemic ($\langle I(t_{end}) \rangle \sim 1$ when $t_{end} \approx 200$ days) without resorting to the depletion of susceptible individuals as customary in deterministic SIR models [11,17]. Assuming that $k \approx 1$, we obtain $R_0 \approx 3.4$ which is consistent with previous works [9,10,13,25,29], but smaller than the one suggested by Hartley *et al.* [28], who explained a cholera epidemic by incorporating a state of hyperinfectivity in the Codeço model [17]. In addition, the human-environment coupling captured by the parameter $a \approx 0.07$ (days) $^{-1}$ turns out to be quite small compared to the previously suggested range of values [17,28].

Unlike deterministic SIR frameworks, within our scenario, the epidemic peaks and declines even though the number of susceptible individuals is always larger than a critical threshold, i.e., rJ/a . While the epidemiological significance

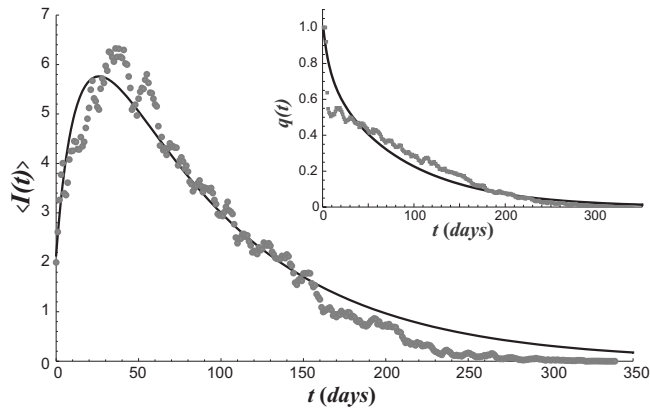


FIG. 2. Dots show the mean value, $\langle I(t) \rangle$, of the infected individuals per SHD at time t , whereas the solid line is the best fitted curve provided by the model. Inset shows the empirical and theoretical probabilities that a given SHD has at least one infected individual at time t . The two curves were obtained by simultaneously best-fitting the empirical data with both the analytical predictions yielded by the model.

of seasonality on the onset of the outbreak is present and well recognized [19], we suggest here that stochasticity itself may be able to automatically provide a mechanism, occurring at the same time scale, for the extinction of the epidemics. Indeed, the Codeço model in the form of the system of deterministic Eq. (1) is not able to explain quantitatively the initial behavior of the disease and predicts a final endemic state of about 800 infected individuals for the present epidemics. The model we have discussed here also shows how one can analytically explain the dynamical evolution of an epidemic outbreak without explicit reference to the complex spatial patterns which may exist in the presence of factors such as a structural network underlying the spatial dynamics [8,9]. Such environmental matrix, however, has to be taken into account to provide a suitable connection between spatial

and temporal scales of the epidemics [10]. Indeed SHDs are connected by several possible infectious processes and *V. Cholerae* is a water-borne disease native to coastal ecosystems where it thrives in warm waters of limited salinity [18,19]. Such strong correlation reasonably suggests that an infection network related to the spatial connectivity of the SHDs is needed to fully understand the spatial spreading of the cholera outbreak including the role of infective corridors played by the river network should the time needed by the traveling cholera wave to reach all susceptibles be comparable (or larger) than the intrinsic disease lifetime [9]. Under certain conditions which we have made explicit here, however, networks involving a large number of nodes, i.e., infected individuals within a spatially extended region, may exhibit a markedly coherent behavior extending well beyond the local scale. In this manner, when a large number of interacting factors leads to substantial mutual influences, the result may be that the impact in the evolution due to the interactions is smoothed out and a collective dynamics emerge. Under such circumstances, the spreading of infections may indeed be described by models with an aggregated dynamics which does not explicitly take into account complex spatial patterns. These conditions allow analytical predictions of peaks and duration of infections of the type presented herein and suggest powerful developments on general approaches related to network dynamics.

ACKNOWLEDGMENTS

We are thankful to the Kwa Zulu-Natal Department of Health, South Africa for providing the cholera epidemic data. We also thank Mercedes Pascual for insightful comments and suggestions. A.M. acknowledges support from a grant of CARIPARO foundation. A.R. and E.B. acknowledge funding from ERC Advanced Grant No. RINEC-22761 and from the Swiss National Science Foundation Grant No. 200021_124930/1.

-
- [1] J. D. Murray, *Mathematical Biology* (Springer, Berlin, 2002), Vol. I, Chap. 10.
- [2] H. W. Hethcote, in *Lecture Notes in Biomathematics* Vol. 100, edited by S. A. Levin (Springer-Verlag, Heidelberg, 1994), pp. 119–144.
- [3] R. M. Anderson and R. M. May, *Infectious Diseases of Humans: Dynamics and Control* (Oxford University Press, Oxford, 1992).
- [4] N. T. J. Bailey, *The Mathematical Theory of Infectious Disease and its Applications* (Griffin, London, 1975).
- [5] K. G. Kendall, Proceedings of the 5th Berkeley Symposium on Mathematical Statistics and Probability, 1956, Vol. 4, p. 149 (unpublished); P. Whittle, *Biometrika* **42**, 116 (1955); D. Ludwig, *J. Appl. Probab.* **10**, 263 (1973); *SIAM Rev.* **17**, 605 (1975); J. Grasman, *Math. Biosci.* **152**, 13 (1998).
- [6] O. A. van Herwaarden and J. Grasman, *J. Math. Biol.* **33**, 581 (1995).
- [7] O. A. van Herwaarden, *J. Math. Biol.* **35**, 793 (1997).
- [8] E. Bertuzzo *et al.*, *Water Resour. Res.* **43**, W04419 (2007).
- [9] E. Bertuzzo *et al.*, *Water Resour. Res.* **44**, W01424 (2007).
- [10] E. Bertuzzo *et al.*, *J.R. Soc., Interface* **7**, 321 (2010).
- [11] M. Pascual, X. Rodó, S. P. Ellner, R. Colwell, and M. J. Bouma, *Science* **289**, 1766 (2000).
- [12] M. J. Bouma and M. Pascual, *Hydrobiologia* **460**, 147 (2001).
- [13] K. Koelle, X. Rodó, M. Pascual, Md. Yunus, and G. Mostafa, *Nature (London)* **436**, 696 (2005).
- [14] I. B. Schwartz, *J. Math. Biol.* **30**, 473 (1992).
- [15] D. J. D. Earn, P. Rohani, B. M. Bolker, and B. T. Grenfell, *Science* **287**, 667 (2000).
- [16] D. Alonso, A. J. McKane, and M. Pascual, *J. R. Soc., Interface* **4**, 575 (2007).
- [17] C. T. Codeço, *BMC Inf., Dis.* **1**, 1 (2001).
- [18] R. R. Colwell, *Science* **274**, 2025 (1996).
- [19] E. K. Lipp, A. Huq, and R. R. Colwell, *Clin. Microbiol. Rev.* **15**, 757 (2002).
- [20] J. B. Kaper, J. G. Morris, and M. M. Levine, *Clin. Microbiol.*

- Rev. **8**, 48 (1995).
- [21] N. G. van Kampen, *Stochastic Processes in Physics and Chemistry* (Elsevier, New York, 2004).
- [22] J. C. Cox, G. E. Ingersoll, and S. A. Ross, *Econometrica* **53**, 385 (1985).
- [23] S. Azaele, S. Pigolotti, J. R. Banavar, and A. Maritan, *Nature (London)* **444**, 926 (2006).
- [24] W. Feller, *Ann. Math.* **54**, 173 (1951).
- [25] K. Koelle and M. Pascual, *Am. Nat.* **163**, 901 (2004).
- [26] N. N. Lebedev, *Special Functions and their Applications* (Dover, New York, 1972).
- [27] C. Mugero and A. Hoque, *Review of Cholera Epidemic in South Africa with Focus on Kwazulu-Natal Province* (Kwazulu-Natal Department of Health Report, Durban, 2001).
- [28] D. M. Hartley, J. G. Morris, Jr., and D. L. Smith, *PLoS Med.* **3**, e7 (2006).
- [29] A. A. King, E. L. Ionides, M. Pascual, and M. J. Bouma, *Nature (London)* **454**, 877 (2008).