Solution of epidemic models with quenched transients

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We consider a model for single-season disease epidemics, with a delay (latent period) in the onset of infectivity and a decay (''quenching'') in host susceptibility described by time-varying rates of primary and secondary infections. The classical susceptible-exposed-infected (SEI) model of epidemiology is a special case with constant rates. The decaying rates force the epidemics to slow down, and eventually stop in a ''quenched transient'' state that depends on the full history of the epidemic including its initial state. This equilibrium state is neutrally stable (i.e., has zero-value eigenvalues), and cannot be studied using standard equilibrium analysis. We introduce a method that gives an approximate analytical solution for the quenched state. The method uses an interpolation between two exactly solvable limits and applies to the whole, five-dimensional parameter space of the model. Some applications of the solutions for analysis of epidemics are given.

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I. INTRODUCTION

Epidemic models with latency and decaying rates of infection (''quenching'') [1,2] characterize a range of plant [3] and animal diseases [4] in which epidemic spread is limited by a decay in susceptibility as the host, or cohort, matures. The *susceptible-exposed-infected* (SEI) model of classical epidemiology [5] is a special case with constant rates, appropriate for describing single-season epidemics. In this paper we study the SEI model with quenching, which we denote by SEIq.

The introduction of quenching is motivated by the following question: why is it that so often epidemics do not invade whole populations in the absence of any control measures or apparent antagonistic organisms? The evidence for this behavior comes, for example, from observations of plant diseases in seasonal crops in the field, in glasshouses, and in controlled experiments [1,2,6]. A plausible explanation for quenching is that it results from a change in susceptibility, which decays as hosts age and become more resistant [7]. It is likely that quenching also occurs with human and animal diseases [4], but on time scales much larger than the duration of a single outbreak. One possible exception, though, is the attenuation of pathogenicity of certain viruses with successive passage through the host [8].

In the long term, quenching causes the epidemic to ''freeze'' in a transient state with a disease level (fraction of the population which is infected) that depends on the state of the epidemic at every point in time (the ''dynamic path'') since the initial condition. We refer to these long-term states as quenched transients, because the dependence on the initial condition (and the spatial distribution of disease in spatially explicit populations) is typical of transient states. This situation is analogous to that of physical systems which, when rapidly cooled (quenched), stabilize in a state that is thermodynamically out of equilibrium [9]. Mathematically, these states can be defined as being neutrally stable (the corresponding eigenvalues have zero or imaginary value); they are different from the most-commonly found equilibrium states, which are fixed points towards which a system evolves regardless of its initial state. This feature makes solving the SEIq model a difficult mathematical problem: standard methods of analysis, such as equilibrium analysis, which relies on the existence of stable-equilibrium states, and power-series expansions, which rely on knowledge of the long-term asymptotic limit, do not apply.

In this work we derive an explicit solution for the level of disease of the quenched state in terms of the model parameters and initial condition. The solution is based on an approximation which interpolates between two exact limiting solutions that bound the general solution above and below. Despite being an approximation, this result is shown to be accurate over large sections of parameter space. The explicit solution allows easier and more transparent analyses of sensitivity and trade-offs between parameters than is possible with numeric solution of the differential equations governing the model. We apply the solution to address questions relevant to epidemiological applications. Specifically: (1) how does the final level of disease vary with the initial amount of inoculum and initial condition, and with the strength of quenching? (2) What are the trade-offs between the latent period and the strength of quenching?

In addition to examining the consequences of quenching on epidemics, this paper also revisits an older unsolved problem, that of solving the SEI model. Some analytical progress has been possible (e.g., Refs. [10,11]) with the standard *susceptible-infected-removed* (SIR) model of epidemiology, which is essentially a nonspatial forest-fire model. However, very few results have been reported on the solution of epidemic models with a latent period, such as the SEI and SEIR models. The combination of nonlinearity (in the infectious contacts) and delay in infection make such models particularly intractable. The method introduced in this paper provides a starting point.

The study and solution of epidemic models has been a long-standing interest to theoretical physicists motivated by analogies between spreading phenomena in epidemic and physical systems and by the application of analytical techniques (e.g., Refs. [12–15]). Quenched transients, as studied

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here, are not restricted to epidemics but appear in a broad class of systems in physics, chemistry, and biochemistry, such as rapidly cooled (quenched) systems [9,16], thermal explosions [17], and catalytic reactions [18–20]. The method of solution examined here, therefore applies to a range of systems including those governed by differential equations, for which explicit bounding solutions are available.

The outline of the paper is as follows: definition of the model and exploration of the formalism (Sec. II), exact solution of the model in special cases (Sec. III), derivation and testing of an approximation to the full solution (Sec. IV), and a discussion (Sec. V).

II. SEIq EPIDEMIC MODEL

We consider a model, denoted by SEIq, that is an extension of the standard deterministic and compartmental SEI model for one-season epidemics [5], with quenched rates of infection [1]. The model represents a host population, that is homogeneous and large enough that it can be assumed to be infinite, and in which each individual can be either in a susceptible (S), exposed (E), or infectious (I) state. We denote the corresponding *fractions* of the population in each state at time t by $S(t)$, $E(t)$, and $I(t)$, respectively. The dynamics of the model are described by the following system of ordinary differential equations (ODEs):

$$\frac{dS}{dt} = -S(\alpha+\beta I)e^{-qt}, \tag{1}$$

$$\frac{dE}{dt} = S(\alpha+\beta I)e^{-qt} - l\,E, \tag{2}$$

$$\frac{dI}{dt} = l\,E, \tag{3}$$

with initial condition: $S(0)=S_0$, $I(0)=I_0=1-S_0$, and $E(0)=0$. Note that, since $S+E+I=1$, only two of the equations are independent. Also, $\alpha+\beta I_0>0$ is a necessary condition for the epidemic to take off, with α representing the initial inoculation rate and I_0 being an initial import of infected hosts, which, in botanical epidemics, is usually subdominant.

Infections may be of primary or secondary type. *Primary infections* may be caused by external inoculum, arriving from outside the host population, or by internal inoculum, persisting in the environment for long periods; in agriculture, for example, the latter may occur from inoculum surviving in the soil from previous crops. *Secondary infections* are those resulting from contact between susceptible and infectious hosts in the population. This model assumes that primary and secondary infections occur at rates $\alpha\exp(-qt)$ and $\beta\exp(-qt)\,I(t)$ per susceptible, respectively. The proportionality of the latter rate to I invokes the mean-field, or *mass-action* principle, according to which infectives and susceptibles mix homogeneously. The exponential factor accounts for the temporal decay (with host age) of the probability of infection of hosts (given that contact with the pathogen has occurred); all hosts are assumed to have the same age. The susceptible state of an isolated host has a lifetime $1/q$, and the latent period has an exponential distribution with mean $\kappa=1/l$.

Reformulation of the model

Next we derive two formal modifications of the compartmental model. First, we define a new time variable that is convenient for describing the dynamics of susceptibles and exposed and for taking the long-term limit. Second, we introduce a new state variable that obeys a single, higher-order equation equivalent to the original system of ODEs. Reformulation of the compartmental model as a single differential equation allows direct comparison with standard nonlinear ODEs to check whether explicit solutions are known (in general it may also facilitate application of various analytical methods).

We define the transformed time variable

$$\tau(t) = \int_0^t dt' e^{-qt'} = [1-e^{-qt}]/q. \tag{4}$$

Note that $\tau(\infty)=1/q$ and $\lim_{q\to 0}\tau(t)=t$. Then, using the relation $S+E+I=1$, model (1)–(3) can be recast in the form

$$\frac{dS}{d\tau} = -S(\alpha+\beta I), \tag{5}$$

$$\frac{dI}{d\tau} = (l/x)(1-S-I), \tag{6}$$

where $x=\exp(-qt)=1-q\tau$, $dS/d\tau=(1/x)dS/dt$.

Equation (5) can be formally solved to give

$$S(\tau) = S_0 e^{-\alpha\tau-\beta\phi(\tau)}, \tag{7}$$

where

$$\phi(\tau) = \int_0^\tau d\tau' I \tag{8}$$

is a new state variable that depends explicitly on the full history of the system. The other state variables can also be written in terms of ϕ, as follows:

$$I = \phi', \tag{9}$$

$$E = (x/l)\,\phi'', \tag{10}$$

where $\phi'=d\phi/d\tau$, etc. Substituting Eqs. (7), (9), and (10) into $S+E+I=1$ gives an equation for ϕ,

$$(x/l)\,\phi'' + \phi' + S_0 e^{-\alpha\tau-\beta\phi} = 1. \tag{11}$$

This single, second-order ODE, with initial condition: $\phi(0)=0$, $\phi'(0)=I_0$, is equivalent to the system of equations (5)–(6). The original variables S, E, and I are recovered by replacing the solution of Eq. (11) back into Eqs. (7)–(10). Although Eq. (11) resembles the Poisson-Boltzmann equation [17], the correspondence is not exact and there is no

known explicit solution of this nonlinear ODE [21], and thus to the system of equations (5)–(6).

III. SOLVABLE LIMITING CASES

We first derive explicit solutions for two limiting cases: one in the absence of a delay, and the other in the absence of nonlinearity. These are then shown to provide upper and lower bounds on the solution.

A. No latent period, $\kappa=0$

When there is no latent period ($\kappa=1/l=0$) and, therefore, susceptibles become infectious immediately on contact with the disease, the model reduces to SIq form [1,2]. Substituting $I=1-S$ in Eq. (5) yields the Bernoulli equation

$$\frac{dS}{d\tau}=[-(\alpha+\beta)S+\beta S^2], \tag{12}$$

with solution, written in terms of $I=1-S$,

$$I(t)_{\kappa=0}=1-\frac{S_0 c e^{-c\tau(t)}}{c-\beta S_0[1-e^{-c\tau(t)}]}, \tag{13}$$

with $\tau(t)$ given by Eq. (4), and

$$c=\alpha+\beta. \tag{14}$$

B. No secondary infection, $\beta=0$

In the absence of secondary infections ($\beta=0$) the model is linear. The solution is obtained from Eqs. (7) and (11), which is now a first-order equation for $\phi'=I$, and reads

$$S(t)_{\beta=0}=S_0 \mathrm{e}^{-\alpha\tau(t)}, \tag{15}$$

$$I(t)_{\beta=0}=1-S_0[\mathrm{e}^{-\alpha\tau(t)}+\alpha H(t)], \tag{16}$$

with $E(t)_{\beta=0}=S_0\alpha H(t)$ and

$$H(t)=e^{-lt}\int_0^t dt' e^{(l-q)t'}e^{-\alpha\tau(t')}. \tag{17}$$

Note that the term $H(t)$ is purely transient, since $\lim_{t\to\infty}H=0$. In the limit when $q\to 0$ the integral in Eq. (17) can be made explicitly, giving $H=[\exp(-\alpha t)-\exp(-lt)]/[l-\alpha]$, and hence $\lim_{q\to 0}I(t)_{\beta=0}=1-S_0[l\exp(-\alpha t)-\alpha\exp(-lt)]/[l-\alpha]$.

C. Consequences of quenching

Various behavioral features can be discerned from the above exact solutions, some of which are shared by the general solution of the model. The long-term level of disease, $I_\infty=\lim_{t\to\infty}I(t)$, is obtained by taking $\tau=1/q$ and (for $\kappa>0$) $H_\alpha=0$. This limit has a nontrivial value $I_\infty<1$ that, in the above special cases, only depends on I_0 and on the parameter combinations α/q and β/q, although, in general, it will depend on all parameters of the model. Only in the absence of quenching, when $q\to 0$, does the whole population become infected: $I_\infty\to 1$ and $S_\infty\to 0$.

During transients, there are two additional arguments, qt and lt [note that $q\tau(t)$ is a function of qt]. It is also apparent that the natural temporal variable for S is $\tau(t)$, while the natural temporal variable for $E=1-S-I$ (when $\kappa>0$) is t, a consequence of the fact that S and I have nonzero asymptotic limits (for $q>0$), while the number of exposed E vanishes in the long term. These features reflect the result (derived from asymptotic expansions in the Appendix) that there are two time scales involved in the approach to the asymptotic limit, $1/q$ and $1/l=\kappa$; which time scale dominates the approach to this limit depends on which process is slower, secondary infection (controlled by q) or latency.

When there are primary but no secondary infections ($\beta=0$), the long-term level of infection is independent of κ, although the transient level of infection depends on κ. In fact, there is a simple asymptotic relationship between the two solutions (13) and (16): $I(\infty)_{\beta=0}=\lim_{\beta\to 0}I(\infty)_{\kappa=0}$. The frequency of secondary infections depends on κ, because infectious contacts are conditioned by the current number of infectious individuals, which depends on κ. Hence, in the presence of quenching, a latent period reduces the final number of infections resulting from secondary contacts. However, if only primary infections take place, the effect of a latent period is solely to delay the time when the level of infection stabilizes.

D. Bounds on the general solution

The two limiting-case solutions derived above provide *upper* and *lower* bounds to the full solution of the model for any given time and over the whole parameter space. Specifically, since secondary infection provides an additional route of infection and latency delays infections (both primary and secondary), we expect the following relations to hold at any given time t:

$$S(t)_{\kappa=0}\leqslant S(t)\leqslant S(t)_{\beta=0}=1-I(t)_{\beta=0}, \tag{18}$$

$$I(t)_{\beta=0}\leqslant I(t)\leqslant I(t)_{\kappa=0}, \tag{19}$$

where the left- and right-hand sides are given by Eqs. (13), (15), and (16). Bounds on the asymptotic values, S_∞ and I_∞, are obtained by replacing $\tau=1/q$ and $H_\alpha=0$ in the exact solutions. When $q\to 0$, the upper and lower bounds equalize, implying that $S_\infty=0$ and $I_\infty=1$. Figure 1 shows the gap between bounds on I_∞ in the parameter subspace $(\alpha/q,\beta/q)$. The gap is large when both α and β have low values relative to q, but is comparatively small elsewhere in parameter space. Figure 2 illustrates the bounds on a transient solution for given parameter values; although no formal test is available, the bounds provide a reasonably tight envelope around the actual solution. From Eq. (18), using $E+I=1-S$ and $E(t)_{\kappa=0}=0$, we also have

$$E(t)_{\beta=0}+I(t)_{\beta=0}\leqslant E(t)+I(t)\leqslant I_{\kappa=0}(t), \tag{20}$$

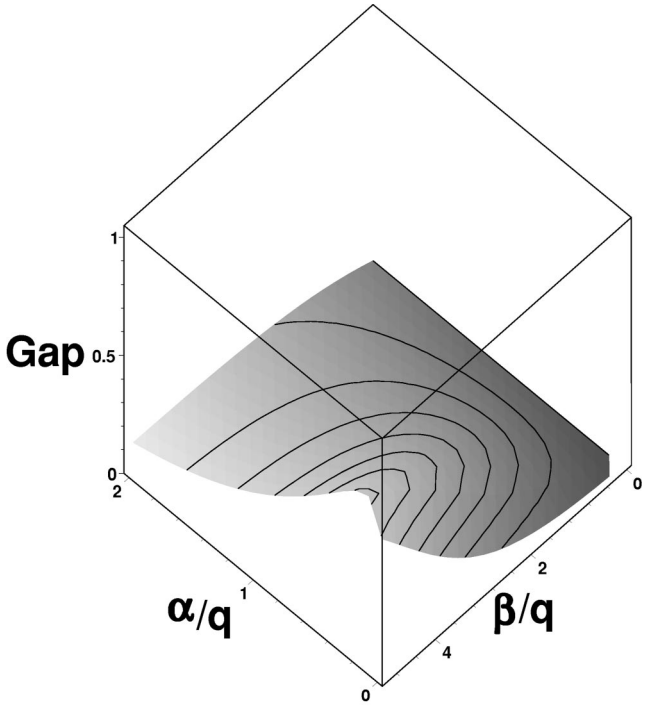

FIG. 1. Gap in I_∞ between upper and lower bounds for the solution of the SEIq model, in the parameter subspace $(\alpha/q,\beta/q)$ with $I_0=0$. The bounds do not depend on κ.

which, together with Eq. (19), is a necessary but not a sufficient condition for having $E(t)_{\beta=0}\leqslant E(t)$. This inequality holds in the case shown in Fig. 2 but does not hold in general.

We briefly outline an heuristic proof of conjecture (18)–(19). Consider the formal solution $S(t)=S_0\exp[-\alpha\tau(t)-\beta\phi(t)]$ [Eq. (7)]. Since $\tau(t)$ and $\phi=\int_0^{\tau(t)}d\tau' I$ (where $I\geqslant 0$) are monotonically increasing functions of time, $S(t)$ is a monotonically decreasing function of time that decreases

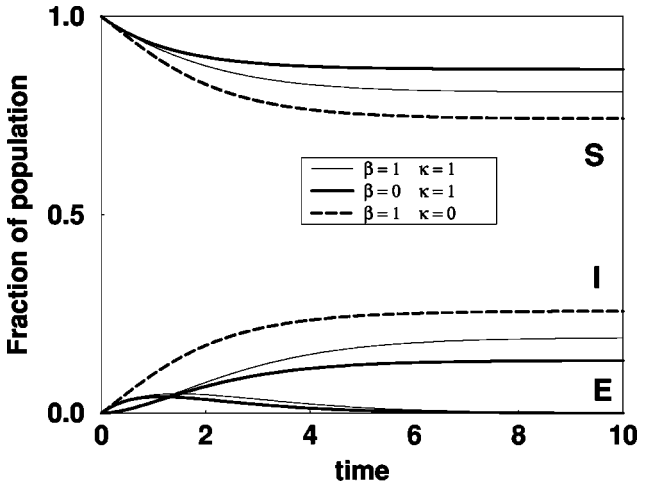

FIG. 2. Bounds on the model solution (obtained numerically) provided by the two exactly solvable limiting cases. Fixed parameters: $I_0=0$, $\alpha=0.1$, $\beta=1$, $\kappa=1=l$, and $q=0.7$. Similarly tight bounds were found for other parameter values. The groups of curves correspond to compartments *S*, *I*, and *E* (top to bottom).

more slowly when $\beta=0$ for any given values of the other parameters. Hence, $S(t)\leqslant S(t)_{\beta=0}$. Conversely, the formal solution of Eq. (6),

$$I(t)=1-S_0e^{-lt}-le^{-lt}\int_0^t dt' e^{-lt'}S(t') \tag{21}$$

is sufficient to prove that if $S(t)\leqslant S(t)_{\beta=0}$ then $I(t)_{\beta=0}\leqslant I(t)$. On the other hand, $I(t)$ necessarily increases faster when $\kappa=0$. Hence, $I(t)\leqslant I(t)_{\kappa=0}$, which in turn implies, via Eq. (7), that $S(t)_{\kappa=0}\leqslant S(t)$.

IV. APPROXIMATE SOLUTION

The two, exact and bounding solutions obtained so far can be used to construct two perturbative solutions in power series of β and κ, respectively. These solutions approximate the full solution in confined regions, where these parameters are small relative to some combination of the remaining parameters. However, without a precise idea of the values, the parameters are likely to take, such confined parameter regions can be too restrictive for general use. Accordingly, we propose a different approach, that does not assume a particular relation between parameters and applies, in principle, to the whole parameter space of the model. For ease of reference and understanding, we present the sequence and steps in deriving this approximate solution.

A. Interpolation

We exploit the fact that the solution of the model must lie between the two bounds, and that the gap between the bounds is not very wide in most parameter regions (Fig. 1). It is natural then to construct a solution that interpolates between the bounds. A first guess is to approximate the solution by the middle point between bounds,

$$I_{approx}(t)=\frac{I_{\kappa=0}(t)+I_{\beta=0}(t)}{2}. \tag{22}$$

However, this approximation has some drawbacks: it assumes that the solution is always equidistant from the two bounds, and, most importantly, lacks any long-term dependence on the latent period κ (since neither bound depends on κ when $t\to\infty$). We compared expression (22), as well as perturbative solutions based on power series of κ and β, with the numeric solution of Eqs. (1)–(3), and found that neither of them approximated the latter qualitatively well, except in restricted parameter regions.

A more promising approach is to use a nonlinear form of interpolation, in which the two solutions are weighted by coefficients that depend nonlinearly on the parameters. This takes the general form

$$I_{approx}(t)=B\,I_{\kappa=0}(t;\beta,\mathbf{a})+K\,I_{\beta=0}(t;\mathbf{a}), \tag{23}$$

where B and K may be functions of time and any of the parameters, and $\mathbf{a}=\{I_0,\alpha,q\}$. We require that

$$\lim_{\beta=0}B=0 \quad \text{and} \quad \lim_{\kappa=0}B=1,$$

$$\lim_{\kappa=0} K=0 \quad \text{and} \quad \lim_{\beta=0} K=1, \tag{24}$$

so that I_{approx} equals $I_{\beta=0}$ and $I_{\kappa=0}$, respectively, in each of the limits. One way of formalizing these requirements is to write

$$B=\frac{\beta(\cdots)_1}{\beta(\cdots)_1+\kappa(\cdots)_2}, \quad K=\frac{\kappa(\cdots)_2}{\beta(\cdots)_1+\kappa(\cdots)_2}, \tag{25}$$

where $(\cdots)_1$ and $(\cdots)_2$ represent arbitrary mathematical expressions which may depend on any of the parameters; however, they must not alter the above limiting requirements, and must be such that B and K are dimensionless quantities. The latter condition implies that k, which has dimension ''time,'' must appear multiplied by q, α, t, or τ. Similarly, β, which has dimension ''1/time,'' must appear multiplied by $1/q$, etc.

Next, we select a form for $(\cdots)_1$ and $(\cdots)_2$. We focus on the *long-term* behavior, although the proposed solution still applies to transients (see the Discussion). We do so to exclude the possibility that B and K might depend on time, and, in particular, to avoid taking into account additional constraints, such as the form we expect B and K to have in limit when $t\to 0$. In this context the simplest possible choice seems to be $(\cdots)_1=1$ and $(\cdots)_2=q^2$, which leads to the following ansatz for approximating the full solution of the model:

$$\begin{aligned} I_{approx}(t) &= \frac{\beta}{\beta+\kappa q^2} I_{\kappa=0}(\beta,\mathbf{a}) + \frac{\kappa q^2}{\beta+\kappa q^2} I_{\beta=0}(\mathbf{a}) \\ &= I_{\beta=0}(\mathbf{a}) + \frac{\beta}{\beta+\kappa q^2}[I_{\kappa=0}(\beta,\mathbf{a}) - I_{\beta=0}(\mathbf{a})]. \end{aligned} \tag{26}$$

This expression has the expected limit, 1, when $q\to 0$. A less simple choice for correct dimensionalization would be $(\cdots)_2=(q+\alpha)^2$, while the choice $(\cdots)_2=\alpha^2$ would not satisfy the appropriate limits.

Figure 3 compares ansatz (26) with the numeric solution of the model represented by contour plots in various two-dimensional parameter subspaces. A parameter has the same value in all graphs in which it is kept constant. In particular, the values of I_0 and α, both of which may contribute to the start of an epidemic, were chosen to be very small to maximize the nonlinearity of the model and provide very demanding conditions on the performance of the approximation. We see that the ansatz captures the qualitative, and even the quantitative behavior of the model extremely well; it did so much better than any of the above alternative approaches. Note that the dependence of expression (26) on the latent period κ is very simple, and yet picks up the essential features of behavior.

B. Exploration of the epidemic surface

The availability of an explicit expression for I_∞, given by the limit $t\to\infty$ of Eq. (26), in terms of the model parameters, makes it possible to explore this surface in detail with great ease. It is often important to carry out a sensitivity analysis to assess how the long-term disease level changes with variation in each of the parameters. Such analysis involves evaluation of the derivatives of I_∞ with respect to the parameters; this is trivial using the approximate solution, but would be considerably more difficult through numeric solution. Figures 4(a) and 4(b) illustrate the sensitivity of I_∞ with respect to the latent period (κ) and the initial condition (or initial infecteds, I_0), respectively; note that the sensitivity of epidemic size is maximal for a nonzero amount of quenching and for $\kappa=0$ and $I_0=0$, respectively. A second important feature is the trade-off between parameters, which reflects a trade-off between biological processes: how much does one parameter have to change to compensate for change in another parameter in order that the long-term level of disease remains unchanged (even thought the duration of the transient may differ)? The answer to this question can be found graphically by examining the contours, ''isobars,'' in Fig. 3. For example, the same level of disease observed in a system with latent period κ and amount of quenching q, may be observed in another system with longer latency but weaker quenching [Figs. 3(a), 3(b)]. It is also clear that the trade-off can be quite different at different points in parameter space: for example, contours in regions with large β and small κ can be almost orthogonal to contours in regions with small β and large κ [Figs. 3(i), 3(j)].

V. DISCUSSION

In this paper we examined a nonstandard, SEIq, compartmental model for disease epidemics comprising latency and temporal decay in the rates of infection, also known as quenching [1]. The model is motivated by field and experimental botanical epidemiological data which supports the biological assumption that the host susceptibility decreases with host age [1,2,6,7]. The main contribution of the paper is the derivation of an approximation to the full solution in the long term. In Sec. IV we showed how to use this result to answer generic epidemiological questions formulated in the Introduction.

Quenched transients. The most important behavioral feature of the model considered here is that, as the rates of infection decrease with time, the epidemic gradually slows down and eventually stops in a quenched transient state. This long-term state is not an equilibrium state in the usual sense: it is characterized by a disease level that depends on the whole history of the epidemic including the initial condition. Mathematically, this state is a neutrally stable equilibrium, and there is an infinite number of such solutions depending on the initial condition, so some properties cannot be studied via standard equilibrium or asymptotic analyses which rely on solving equations at (or in the vicinity of) a single point. On the other hand, although numerical solution of Eqs. (1)–(3) is trivial for given parameter values, a full study of behavior over all dimensions of parameter space is a tedious

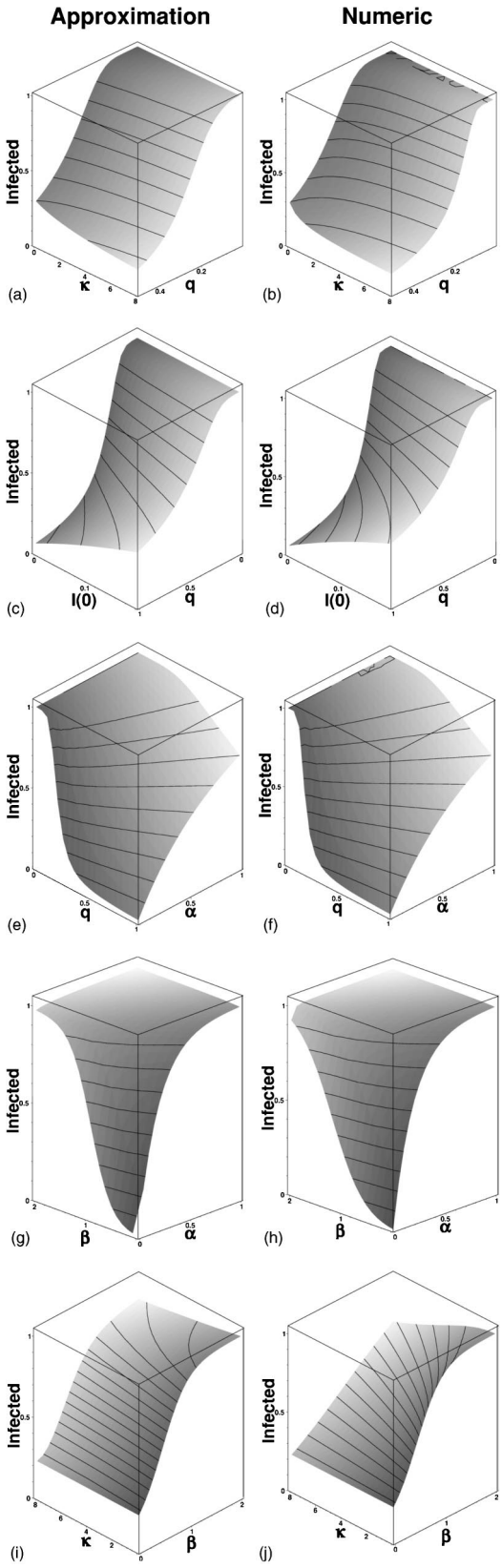

FIG. 3. Comparison of the approximate (left) and numeric (right) solutions to the long-term level of infection, I_∞, in the SEIq model. Fixed parameters: $I(0)=I_0=0.01$, $\alpha=0.05$, $\beta=1$, $\kappa=1=l$, and $q=0.2$, except where indicated otherwise. Lines represent contours of constant values of I_∞.

and inefficient way of gaining insight even for such a simple model.

Analysis. We proposed a different way of studying quenched transients, by considering an explicit approximate solution describing how the level of disease of the quenched state depends on all parameters of the model. This is given by Eq. (26), which is the central result of the paper. The solution was constructed as an interpolation between two exactly solvable limiting cases, one without latency and another without nonlinearity, shown to provide upper and lower bounds to the exact solution. We demonstrated, in several two-dimensional parameter subspaces (Fig. 3), that the approximation follows the numeric solution of the model very closely. Since the approximation is free from assumptions about the magnitude of the parameters, it is not restricted to particular parameter regions in the same way that a power-series perturbative solution would be. The regions in which the approximation might perform less well are likely to be those in which the gap between bounds (illustrated in Fig. 1) is greater. Future work will provide more understanding as to why the approximation works well and under which conditions it may break down when applied to other models. One possible route, is to derive an exact equation for the mixing coefficient B [Eq. (25)], currently given by $\beta/[\beta+\kappa q^2]$. It is worth pointing out an analogy between the current interpolative solution and an approximate solution [15] to related spatially explicit epidemic models. The latter method also formulates a solution by combining upper and lower bounds; however, the bounds are not exact solutions, they rely on the use of cluster approximations [22], and the derivation of the weighing coefficients is different from the current one.

Analysis of transient dynamics. The approximation given by Eq. (26) was applied to the long-term limit I_∞ and examined in detail in this case, but, in principle, it can also be applied to transients. Application of Eq. (26) to transients revealed, as expected, that the approximation, in its current form, performs less well than in the long term, as it tends to show more limited agreement with the numeric solution. Transient behavior is more general and complex than long-term behavior, and therefore more difficult to approximate; in this case the mixing coefficients B and K may be time dependent and have to satisfy additional constraints (e.g., on their limit as $t\rightarrow 0$). Investigating how to extend these coefficients to the transient case will be the subject of further work.

Other applications. Quenched-transient states have considerable practical relevance not only in epidemiology but in other areas concerned with invasive organisms or species [10,11,18–20]. The existence of decaying rates of spread could, however, be difficult to establish in practice as there may be competing factors limiting the spread of invasive species. Nevertheless, the model and method of approximation presented here do have wider application than the simple epidemic system, which is analogous to an irreversible chemical reaction. We note that the essential effect of the decaying rates could also be achieved by bifurcating the flow from the susceptible compartment; for example, allowing susceptibles to become resistant at certain rates. Systems in which mass flows monotonically from one compartment to

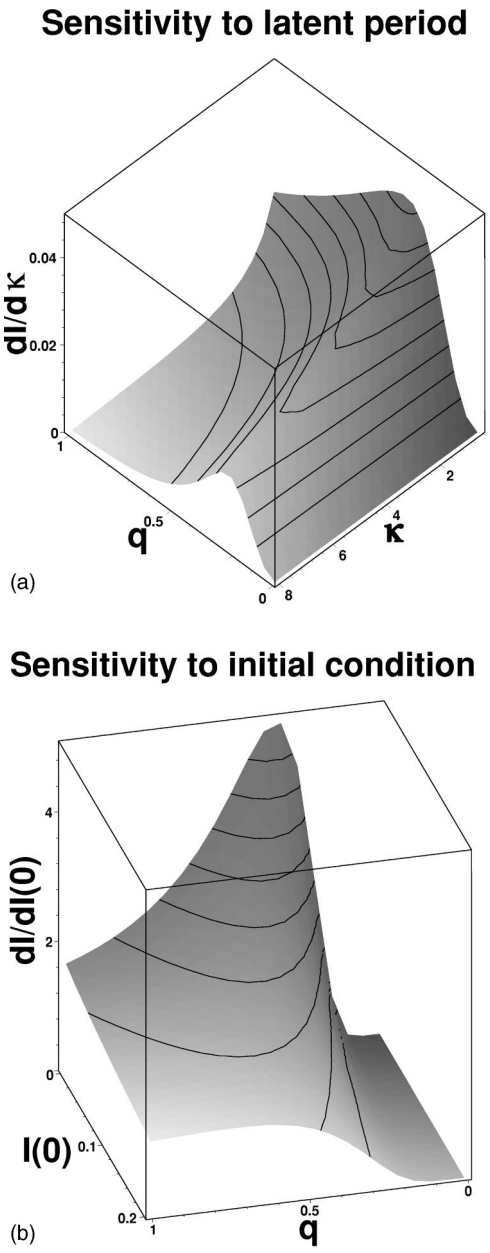

FIG. 4. Sensitivity of the epidemic with respect to (a) the latent period, $\partial I_\infty/\partial\kappa$, in the parameter subspace (q,κ); (b) the initial condition, $\partial I_\infty/\partial I_0$, in the parameter subspace (q,I_0) (maximum at $I_0=0$ and $q\approx 0.65$). Fixed parameters, $I(0)=I_0=0.01$, $\alpha=0.05$, $\beta=1$, and $\kappa=1=l$.

another, or to several others, and have an intermediate, transient state could also exhibit upper and lower solvable bounds which could, in principle, be used to construct similar approximate solutions.

Extensions. Although the SEIq model fits into the framework of standard epidemiological models [5], it is still a considerable oversimplification of real epidemiological systems. For example, the model relies on a mean-field or perfect-mixing assumption, i.e., it does not account for the spatial distribution of infectives which is known to affect disease spread, in particular, when secondary infections occur within a small neighborhood of the source [22]. However, the current model is driven by requirements of tractability, and we believe that the insight gained from the analysis can, in essence, be transposed to a spatial context, where such an analysis would not be feasible. A challenge that remains open is to extend the interpolation approximation to describe the transient dynamics. Such an extension would be welcome for both theoretical and practical reasons: it would lead to a more complete study; it would also trivialize the task of estimating the latent period and other parameters by fitting an explicit (rather than a numeric) solution to epidemic time series. Finally, it could allow an extension of the analysis to models with recurrent epidemics, such as the SIR and SEIR models.

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APPENDIX: TEMPORAL ASYMPTOTICS

In this appendix we examine the approach to the long-term state of the model, and illustrate the emergence of two time scales, $1/q$ and $1/l$, in the asymptotic dynamics.

Assuming that a power-series expansion about the long-term level of disease exists in the form $I(t)=I_\infty+a_1x+a_2x^2+\cdots$, with x being a time-decaying quantity such as $\exp(-qt)$, we obtain recursive equations for the coefficients a_n that involve the leading term $a_0=I_\infty$. Since I_∞ cannot be determined by this or other exact methods that we know of, none of the coefficients can be determined explicitly in terms of the parameters of the model. Since q and l are the parameters naturally arising in transient expressions (Sec. III A), the general term in an asymptotic power series is more likely to be of the form $a_{nm}x^ny^m$, with $x=\exp(-qt)$ and $y=\exp(-lt)$, but this more elaborate form would not change the above conclusion. Therefore, derivation of a power-series solution is not appropriate for this model. However, it is possible to derive the leading asymptotic terms in the approach to the long-term state, without assuming the nature of those terms; we succeeded in doing so at least in the case when $l<q$. Consider the following expression:

$$E(t)=e^{-lt}\int_0^t dt' e^{-(q-l)t'}S(t')[\alpha+\beta I(t')], \qquad \text{(A1)}$$

which results from formal integration of Eq. (2). When $l<q$ the integral in Eq. (2) has a finite limit as $t\to\infty$. Hence, expressing the integral as $\int_0^\infty dt'\cdots-\int_0^t dt'\cdots$, replacing $S(\alpha+\beta I)$ in the second integral by its dominant term as $t\to\infty$, and simplifying, gives the leading terms

$$E(t)=Ae^{-lt}-Be^{-qt}+\cdots(t\to\infty), \qquad \text{(A2)}$$

where

$$A=\int_0^\infty dt' e^{-(q-l)t'} S(t')[\alpha+\beta I(t')],$$

$$B=\frac{S_\infty(\alpha+\beta I_\infty)}{q-l}=-\frac{S'_\infty}{q-l},$$

and $A<(\alpha+\beta)/(q-l)$. Expression (A2) implies, via Eq. (3) and $S=1-E-I$, that

$$I(t)=I_\infty-Ae^{-lt}+\frac{l}{q}Be^{-qt}+\cdots,$$

$$S(t)=S_\infty-\frac{S'_\infty}{q}e^{-qt}+\cdots(t\to\infty). \tag{A3}$$

Derivation of an analogous result in the case of $q<l$ appears technically less straightforward, but would not modify the qualitative message from the above results, i.e., the emergence of two time scales.

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