Enhanced extinction processes in the presence of non-Gaussian controls

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We investigate stochastic extinction processes in the presence of non-Gaussian noise. Motivated by the process of natural disease extinction in epidemics, we examine the impact of random vaccinations in large populations. We show that, in the absence of vaccinations, the effective entropic barrier for extinction in an SIS model displays scaling with the distance to the bifurcation point, with an unusual critical exponent. Even a comparatively weak Poisson-distributed vaccination leads to an exponential increase in the extinction rate, with the exponent that strongly depends on the vaccination parameters. We make a direct comparison between predictions and numerical simulation in both 1 and 2 dimensional models.

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INTRODUCTION

On the major goals in stochastic population dynamics,especially in modeling epidemic spread in a population, is that of predicting finite extinction times, when one or more components of the population go to zero. Practically all diseases of interest exhibit randomness resulting in observed fluctuations. Childhood diseases [1–3], meningitis [4], dengue fever and malaria [5] are but a few examples where incidence rates fluctuate with significant amplitude. These fluctuations arise from random contacts within a population, uncertainty in epidemic parameters, and stochastic flux changes from external coupled populations [6, 7]. As diseases evolve in large populations, there is the possibility of finite time extinction and reintroduction of the disease [8, 9]. Extinction occurs where the number of infectives become so small that there is insufficient transmission to keep the disease in its endemic state [10–12]. Therefore, in the absence of disease reintroduction, the epidemic dies out.

For epidemic models where only susceptibles (S) and infectives (I) (and possibly recovered (R)) are present, (called SIS or SIR models) [13], the disease spread can be characterized by the reproductive rate of infection, R_0. In its deterministic form, R_0 can be defined so that, for an endemic state to exist along with the disease free equilibrium (DFE), $R_0 >1$. When $R_0 < 1$, the disease becomes extinct. For appropriate parameters where both states co-exist, the disease free state is unstable, and the endemic state is attracting. For the models we consider here, the it is assumed the endemic state is globally attracting.

In the presence of fluctuations, the situation becomes more complicated. Fluctuations cause the disease free state to be reached albeit for a limited time, as indicated by both numerical [14–17] and analytic [13, 18–21] results for various models. Such an extinction process occurs even when R_0 is greater than unity.

A major characteristic of fluctuation-induced extinction in the SIS stochastic model for large populations is the extinction rate, or the reciprocal mean first time the number of infectives approaches zero. It has been studied by approximating the full two dimensional stochastic system as a continuous one, with fluctuations induced by noise in the Langevin approach. A discrete birth-death SIS model was investigated recently and a comparison with the continuous model was performed by Doering *et al.* [21]. The analysis referred to a one-variable model, which allows one to obtain an explicit solution in various regimes of R_0. However, this model does not reveal some generic features of the full discrete SIS system, including the scaling behavior of the extinction rate.

It is the purpose of this paper to analyze in full the general SIS discrete model, and obtain explicit scaling behaviors of extinction rates in the neighborhood of disease onset; i.e., when the reproductive rate is greater than but close to unity. Using these scaling results, we will study the effect of vaccination on the extinction rate. Since vaccine scheduling is inherently random despite the best policy controls, we will examine the important case where the vaccine schedule is a Poisson process. As we show, even a comparatively weak vaccination can affect the extinction rate exponentially strongly. The analysis of both problems requires developing methods, to the best of our knowledge, have not been previously used in the theory of large rare fluctuations of multivariable systems.

THE DISCRETE MODEL

We consider a model where susceptibles (S) are born at rate μ, both susceptibles and infectives (I) die at the same rate μ, and infectives recover at rate $\varkappa$ and immediately become susceptible. If susceptibles contact infectives, they may become infected at rate β. Time-dependent vaccination of incoming susceptibles reduces their probability to become infected at rate $\xi(t)$. This rate will be assumed small, on average. We also assume that once vaccinated, they are recovered.

Since the events of birth, death, and contact happen at random, we model the process discretely. Letting vector $\mathbf{X} = (X_1, X_2)$ with components $X_1 = S, X_2 = I$ and vector $\mathbf{r} = (r_1, r_2)$ with components r_1 and r_2, we show, respectively, the increments in S and I in a single transition. They are transitions between the states of the system with different S and I. Therefore the quantity of interest is the probability $\rho(\mathbf{X}, t)$ to have given S and I at time t. Its evolution is given by the master equation

$$\dot{\rho}(\mathbf{X}, \mathbf{t}) = \sum_r \left[W(\mathbf{X} - \mathbf{r}; \mathbf{r})\rho(\mathbf{X} - \mathbf{r}, t) - W(\mathbf{X}; \mathbf{r})\rho(\mathbf{X}, \mathbf{t})\right] \ , \tag{1}$$

and the transition rates $W(\mathbf{X}, \mathbf{r})$ are

$$\begin{aligned} &W\big(\mathbf{X}; (1,0)\big) = N[\mu - \xi(t)], \quad W\big(\mathbf{X}; (-1,0)\big) = \mu X_1, \\ &W\big(\mathbf{X}; (0,-1)\big) = \mu X_2, \quad W\big(\mathbf{X}; (1,-1)\big) = \varkappa X_2, \\ &W\big(\mathbf{X}; (-1,1)\big) = \beta X_1 X_2/N, \end{aligned} \tag{2}$$

where N is the scaling factor which we set equal to the average population, $N \gg 1$.

For sufficiently large $S, I \propto N$, fluctuations of S, I are small on average. If these fluctuations are disregarded, one arrives at the deterministic (mean-field) equations for the mean values of S, I

$$\dot{X}_1 = N[\mu - \xi(t)] - \mu X_1 + \varkappa X_2 - \beta X_1 X_2/N, \tag{3}$$

$$\dot{X}_2 = -(\mu + \varkappa) X_2 + \beta X_1 X_2/N. \tag{4}$$

These are standard equations of the SIS model [1]. In the absence of vaccination, $\xi(t) = 0$, for $R_0 = \beta/(\mu + \varkappa) > 1$ they have a stable solution $\mathbf{X}_A = N\mathbf{x}_A$ with $x_{1A} = R_0^{-1}, x_{2A} = 1 - R_0^{-1}$. It describes the endemic disease. In addition, Eqs. (3) have an unstable stationary state (saddle point) $\mathbf{X}_\mathcal{S} = N\mathbf{x}_\mathcal{S}$ with $x_{1\mathcal{S}} = 1, x_{2\mathcal{S}} = 0$. This state corresponds to extinction of infectives.

For $N \gg 1$ and for small vaccination rate the steady state +distribution $\rho(\mathbf{X})$ has a peak at the stable state $\mathbf{X}_A$ with width $\propto N^{1/2}$. This peak is formed over a typical relaxation time $t_\mathrm{r} = \max[\mu^{-1}, (\beta - \mu - \varkappa)^{-1}]$. However, we are interested in the probability of having a small number of infected, $X_2 \ll X_{2A}$. It is determined by the tail of the distribution. The tail can be obtained by seeking the solution of Eq. (1) in the eikonal form,

$$\begin{aligned} &\rho(\mathbf{X}) = \exp[-Ns(\mathbf{x})], \qquad \mathbf{x} = \mathbf{X}/N, , \\ &\rho(\mathbf{X} + \mathbf{r}) \approx \rho(\mathbf{X}) \exp(-\mathbf{pr}), \qquad \mathbf{p} = \partial_\mathbf{x} s. \end{aligned} \tag{5}$$

For time-independent parameters W this formulation was used in a number of papers [20–26].

To leading order in N^{-1}, the equation for s has a form of the Hamilton-Jacobi equation $\dot{s} = -H(\mathbf{x}, \partial_\mathbf{x} s; t)$, where s is the effective action, and the effective Hamiltonian is

$$H(\mathbf{x}, \mathbf{p}; t) = \sum_\mathbf{r} w(\mathbf{x}; \mathbf{r}) \left(e^{\mathbf{pr}} - 1\right), \tag{6}$$

with $w(\mathbf{x}; \mathbf{r}) = N^{-1} W(\mathbf{X}; \mathbf{r})$ being the transition rates per person. Action $s(\mathbf{x})$ can be found from classical trajectories of the auxiliary system with Hamiltonian H,

$$\begin{aligned} H(\mathbf{x}, \mathbf{p}; t) = \mu(e^{p_1} - 1) + \mu x_1(e^{-p_1} - 1) + \mu x_2(e^{-p_2} - 1) + \\ \kappa x_2(e^{(p_1 - p_2)} - 1) + \beta x_1 x_2(e^{(p_2 - p_1)} - 1)/N^2 \end{aligned} \tag{7}$$

that satisfy equations

$$\dot{\mathbf{x}} = \partial_\mathbf{p} H(\mathbf{x}, \mathbf{p}; t), \qquad \dot{\mathbf{p}} = -\partial_\mathbf{x} H(\mathbf{x}, \mathbf{p}; t). \tag{8}$$

EXTINCTION IN THE ABSENCE OF VACCINE

In this section, we assume there is no vaccine, $\xi(t) = 0$, and the fluctuations are from the random contacts. Here, the transition rates $w = w^{(0)}$ and the Hamiltonian $H = H^{(0)}$ are independent of time, and we consider the stationary distribution. The function $s = s^{(0)}$ is then independent of time. It has the form [23–26],

$$s^{(0)}(\mathbf{x}_f) = \int_{-\infty}^{t_f} \mathbf{p}\,\dot{\mathbf{x}}\,dt, \qquad H^{(0)}(\mathbf{x},\mathbf{p}) = 0. \tag{9}$$

Here, the integral is calculated for a Hamiltonian trajectory $\big(\mathbf{x}(t),\mathbf{p}(t)\big)$ that starts at $t \to -\infty$ at $\mathbf{x} \to \mathbf{x}_A, \mathbf{p} \to \mathbf{0}$ and arrives at time t_f at a state $\mathbf{x}_f$. This trajectory describes the most probable sequence of elementary events $\mathbf{X} \to \mathbf{X}+\mathbf{r}$ bringing the system to $N\mathbf{x}_f$. It provides the absolute minimum to $s^{(0)}(\mathbf{x}_f)$, and $s^{(0)}(\mathbf{x}_f)$ is independent of t_f. The quantity $Ns^{(0)}(\mathbf{x})$ is the entropic barrier for reaching $N\mathbf{x}$; it gives also the exponent in the expression for the mean first passage time for reaching $N\mathbf{x}$ from the vicinity of the attractor $\mathbf{X}_A$ [27].

The extinction rate is determined by $s^{(0)}$ by taking the limit $x_2 \to 0$. It is intuitively clear, and can be shown from Eq. (6) that the maximum of $s^{(0)}(\mathbf{x})$ over x_1 for $x_2 \to 0$ is reached at the saddle point $\mathbf{x}_\mathcal{S}$ of the fluctuation-free motion (3). Thus the entropic barrier for extinction is $Ns^{(0)}_{\rm ext} = Ns^{(0)}(\mathbf{x}_\mathcal{S})$.

The Hamiltonian trajectory $\mathbf{x}_{\rm ext}(t), \mathbf{p}_{\rm ext}(t)$ that gives $s^{(0)}(\mathbf{x}_\mathcal{S})$ is the optimal extinction trajectory. One can show that it approaches $\mathbf{x}_\mathcal{S}$ as $t \to \infty$. This is similar to other problems of an optimal trajectory leading from a deterministic stable state to a saddle point [25, 28]. However, in contrast to the more common situation, for $t \to \infty$ the momentum $\mathbf{p}_{\rm ext}$ does not go to zero. Instead $\mathbf{p}_{\rm ext}(t) \to \mathbf{p}_\mathcal{S}$, with $\mathbf{p}_\mathcal{S} = \big(0, -\ln R_0\big)$. This is in spite of the fact that, along with $(\mathbf{x}_\mathcal{S}, \mathbf{p}_\mathcal{S})$, the Hamiltonian $H^{(0)}$ has a "standard" fixed point $(\mathbf{x}_\mathcal{S}, \mathbf{p} = \mathbf{0})$.

To show that this is indeed the case in the multidimensional system under consideration we note that the optimal extinction trajectory should lie on the stable manifold of the appropriate fixed point. It is straightforward to show that the stable manifold of $(\mathbf{x}_\mathcal{S}, \mathbf{p} = \mathbf{0})$ lies in the plane $x_2 = p_1 = 0$. An optimal path does not reach this plane at any finite time. From Eq. (8), x_2 approaches zero exponentially as $t \to \infty$, but for $t \to \infty$ the system as a whole approaches a fixed point. Therefore the optimal extinction trajectory does not lie on the stable manifold of $(\mathbf{x}_\mathcal{S}, \mathbf{p} = \mathbf{0})$. It may only lie on the stable manifold of the fixed point $(\mathbf{x}_\mathcal{S}, \mathbf{p}_\mathcal{S})$, which is not confined to a plane in the $(\mathbf{x}, \mathbf{p})$ space.

The situation where an auxiliary Hamiltonian system has two fixed points with the same $\mathbf{x}_\mathcal{S}$ was first noticed for a system described by the Fokker-Planck equation with a singular diffusion matrix at $\mathbf{x}_\mathcal{S}$ [18], and the "right" point was chosen based on numerical simulations. This situation was also found for a system described by a one-variable master equation, where the Hamiltonian dynamics is integrable [20]; it occurs also in a two-variable susceptible-infected-recovered (SIR) model concurrently studied by Kamenev and Meerson [29].

Equations (8) allow finding the extinction rate for any values of the parameters of the system. An explicit analytical solution in the absence of vaccination can be obtained close to a bifurcation point where the number of the stationary solutions of the deterministic equations changes [25]. In the present case it corresponds to $0 < \eta \ll 1, \eta = \beta - \mu - \varkappa \equiv (\mu + \varkappa)(R_0 - 1)$. For $\eta \ll 1$ the mean-field value of x_2 in the stable state $x_{2A} = \eta/\beta \ll 1$ is close to $x_{2\mathcal{S}}$. The relaxation time of x_2 near the stable state is η^{-1}. It is much longer than the relaxation time of x_1, which is μ^{-1}, i.e., x_2 is a soft mode. Coordinate x_1 follows x_2 adiabatically on the time scale that largely exceeds μ^{-1}.

The solution of Hamiltonian equations (8) in the adiabatic approximation is simplified by the fact that $x_2 \ll 1$ and $|p_2| \ll 1$. To leading order in η we have $x_1 = 1 - x_2, p_1 = \beta x_2 p_2/\mu$, while the equations for slow variables x_2, p_2 have the Hamiltonian form

$$\dot{x}_2 = \partial H^{\rm ad}/\partial p_2, \quad \dot{p}_2 = -\partial H^{\rm ad}/\partial x_2 \tag{10}$$

with Hamiltonian $H^{\rm ad} = \eta x_2 p_2 - \beta x_2 p_2 (x_2 - p_2)$. The Hamiltonian trajectory is

$$p_2(t) = x_2(t) - \frac{\eta}{\beta}, \quad x_2(t) = x_{2A}\left(1 + e^{\eta(t-t_0)}\right)^{-1}. \tag{11}$$

The solution in Eq. 11 describes in particular the optimal extinction trajectory as depicted in Fig. 1. The full Hamiltonian system using Eqns. **??**,8 was also computed to get the optimal path from the attractor to the extinct state. The solution compared with the adiabatic time series is shown Fig. 2, where the control parameter, η,is small.

From Eqs. (9), (11) we derive our first main result:

$$s^{(0)}_{\rm ext} = s^{(0)}(\mathbf{x}_\mathcal{S}) = \eta^2/2\beta^2. \tag{12}$$

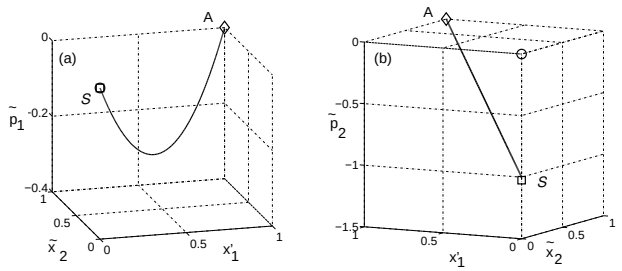

Figure 1: 3D projections of the optimal extinction trajectory in Eqs. (8), (11) in scaled coordinates $\tilde{x}_2 = x_2/(R_0-1)$, $\tilde{p}_2 = p_2/(R_0-1)$, $x_1' = (R_0-1)(1-x_1)$, $\tilde{p}_1 = (\mu/\beta)(R_0-1)^2 p_1$. Panels (a) and (b) show x_1, x_2, p_1 and x_1, x_2, p_2 projections. The trajectory goes from point A that corresponds to the stable state of the system with coordinates $\mathbf{x}_A$ and zero momentum to point $\mathcal{S}$ that corresponds to extinction of the disease, with coordinate $\mathbf{x}_\mathcal{S}$ and with nonzero momentum $\mathbf{p}$.

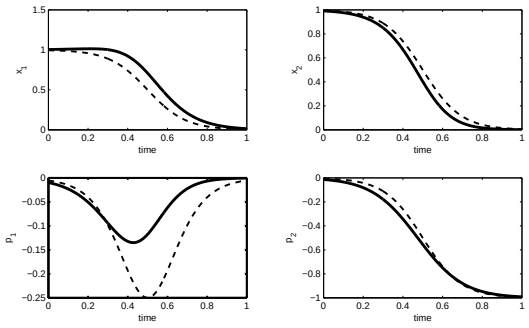

Figure 2: Time series of the heteroclinic orbits. The time series in bold represents those of the adiabatic equations 11. The dashed lines were computed using the full Hamiltonian system in Eq. 8. Here the coordinates are un-scaled. The parameters valued in the numerical computations were $\mu = 0.02, \gamma = 100.0, \beta = 100.05, \eta = 0.0308$.

The entropic barrier for extinction $Ns^{(0)}_{\rm ext}$ (12) scales with the distance to the bifurcation point $\eta \propto R_0 - 1$ as η^2. This is in contrast to the standard scaling of the activation energy of escape near a saddle-node bifurcation point, where the critical exponent is 3/2 [25]. Such unusual scaling is related to $\mathbf{p}_\mathcal{S}$ being nonzero. It emerges also in the SIR model [29].

VACCINE ENHANCED EXTINCTION

If $\xi(t)$ is a stationary noise, the distribution $\langle \rho(\mathbf{X}) \rangle$ averaged over noise realizations is stationary, too. However, for a given realization $\xi(t)$, $\rho(\mathbf{X}) \equiv \rho(\mathbf{X}, t)$ is time-dependent, as is also $s \equiv s(\mathbf{x}, t)$. We are interested in the region of $\mathbf{x}$ where the mean first time of reaching $\mathbf{x}$ from the vicinity of the stable state largely exceeds the correlation time $t_{\rm corr}$ of $\xi(t)$. Then arrivals to a given $\mathbf{x}$ are uncorrelated with each other.

The full Hamiltonian of the system that determines s can be written as $H = H^{(0)} + H^{(1)}$, with

$$H^{(1)}(\mathbf{x}, \mathbf{p}, t) = -\xi(t) h(\mathbf{x}, \mathbf{p}), \qquad h = \exp(p_1) - 1. \tag{13}$$

The term $H^{(1)}$ is small for weak noise $\xi(t)$. Because $s(\mathbf{x}_f, t_f)$ provides a minimum to the integral over time of $\mathbf{p}\,\dot{\mathbf{x}} - H$, to first order in $\xi(t)$ we have [30]

$$s(\mathbf{x}_f, t_f) \approx s^{(0)}(\mathbf{x}_f) + \int_{-\infty}^{t_f} dt \xi(t) \chi_f(t). \tag{14}$$

Here, $\chi_f(t) = h\big(\mathbf{x}(t|\mathbf{x}_f, t_f), \mathbf{p}(t|\mathbf{x}_f, t_f)\big)$; the functions $\mathbf{x}(t|\mathbf{x}_f, t_f), \mathbf{p}(t|\mathbf{x}_f t_f)$ are unperturbed Hamiltonian trajectories given by Eq. (8) with $H = H^{(0)}$ and with boundary conditions $\mathbf{x}(t) \to \mathbf{x}_A, \mathbf{p}(t) \to 0$ for $t \to -\infty$ and $\mathbf{x}(t_f) = \mathbf{x}_f$.

From Eq. (14) the logarithm of the distribution $\rho(\mathbf{X}_f, t_f)$ is linear in the force $\xi(t)$. The proportionality coefficient is $\propto \chi_f(t)$, and therefore we call $\chi_f(t)$ the logarithmic susceptibility, as for systems where fluctuations are induced by Gaussian noise [31]; it is convenient to set $\chi_f(t) = 0$ for $t > t_f$.

Equations (**??**), (14) lead to a simple general expression for the distribution averaged over realizations of noise,

$$\langle\rho(\mathbf{X})\rangle = A(\mathbf{X})\rho^{(0)}(\mathbf{X}), \quad A(\mathbf{X}_f) = \tilde{\mathcal{P}}_\xi[iN\chi_f(t)], \tag{15}$$

where $\rho^{(0)}$ is the distribution for $\xi(t) = 0$ and $\tilde{\mathcal{P}}_\xi[\kappa(t)] = \left\langle \exp\left[i\int \kappa(t)\xi(t)dt\right]\right\rangle$ is the characteristic functional of $\xi(t)$. Because $N \gg 1$, an already weak noise $\xi(t)$ can significantly change the distribution, the factor A can be exponentially large. This happens because an outburst of noise of an appropriate temporal shape can largely increase the probability of the chain of reactions $\mathbf{X} \to \mathbf{X} + \mathbf{r}$ that brings the system to a given state.

The above analysis can be extended also to the problem of extinction. A physically reasonable formulation is to study the probability of reaching a small vicinity of $\mathbf{x}_\mathcal{S}$ where, nevertheless, $|\mathbf{x}_f - \mathbf{x}_\mathcal{S}|$ largely exceeds $N^{-1/2}$ and the typical amplitude of $\xi(t)$-induced fluctuations, so that corrections to $s(\mathbf{x}_f, t_f)$ remain small. The unperturbed Hamiltonian trajectories leading to this area form a narrow tube around the optimal extinction path $(\mathbf{x}_{\rm ext}, \mathbf{p}_{\rm ext})$. If we choose $\mathbf{x}_f$ close to this path and to $\mathbf{x}_\mathcal{S}$, from Eq. (15) the noise-induced change of the probability of reaching $N\mathbf{x}_f$ is described by the factor

$$A_{\rm ext} = \tilde{\mathcal{P}}_\xi[iN\chi_{\rm ext}(t)], \quad \chi_{\rm ext}(t) = h\big(\mathbf{x}_{\rm ext}(t), \mathbf{p}_{\rm ext}(t)\big) \tag{16}$$

We call $A_{\rm ext}$ the *noise-induced extinction factor*. It is independent of the precise choice of $\mathbf{x}_f$, because $h\big(\mathbf{x}_{\rm ext}(t), \mathbf{p}_{\rm ext}(t)\big)$ is small for $\mathbf{x}_{\rm ext}(t_f)$ close to $\mathbf{x}_\mathcal{S}$, and therefore the integral over time in the noise-induced correction to the action (14) can be extended to infinity.

To illustrate the effect of noise on extinction we consider an important model where the noise is a Poisson process, $\xi(t) = g\sum_j \delta(t - t_j)$ with average pulse frequency ν. For such noise, $A_{\rm ext}$ has a form [32]

$$A_{\rm ext} = A_{\rm av}A_{\rm fl}, \qquad A_{\rm av} = \exp\left[-\nu\int_{-\infty}^{\infty} dt\,\kappa(t)\right], \tag{17}$$
$$A_{\rm fl} = \exp\left[\nu\int_{-\infty}^{\infty} dt\,\left(e^{-\kappa(t)} - 1 + \kappa(t)\right)\right]$$

with $\kappa(t) = gN\chi_{\rm ext}(t)$. The factor $A_{\rm av}$ describes the effect of the average noise $\langle\xi(t)\rangle = \nu g$, whereas the term $A_{\rm fl}$ describes the effect of the fluctuating part of $\xi(t)$ with zero mean.

It is seen from Eq. (17) that $A_{\rm fl} > 1$; this agrees with the qualitative picture described above in which even zero-mean noise leads to the increase of the probability of fluctuations in the system and specifically, of the extinction rate. In the limit of small noise amplitude g, where $|\kappa(t)| \ll 1$, we have $A_{\rm fl} = \exp\left[\nu\int dt\,\kappa^2(t)/2\right]$, implying $\ln A_{\rm fl} \propto g^2$. In the opposite limit where $\max[-\kappa(t)] \gg 1$ we have $A_{\rm fl} = \exp\left[\nu(2\pi/\ddot{\kappa}_m)^{1/2}\exp(-\kappa_m)\right]$, where $-\kappa_m \equiv -\kappa(t_m)$ is the maximum of $-\kappa(t)$ and $\ddot{\kappa}_m = \ddot{\kappa}(t_m)$. In this case $\ln A_{\rm fl}$ is exponential in the noise amplitude g.

An explicit expression for $A_{\rm ext}$ can be obtained near the bifurcation point. It follows from Eq. (11) that here $\chi_{\rm ext} = \dot{x}_2/\mu$. This gives $A_{\rm av} = \exp[\nu\eta gN/\beta\mu]$. The exponent in $A_{\rm av}$ linearly scales with the distance to the bifurcation point η and the noise amplitude g.

The fluctuation part of the extinction factor $A_{\rm fl}$ is determined by the parameter $\sigma = g\eta^2 N/\mu\beta$. For $\sigma \lesssim 1$ we have $A_{\rm fl} \approx \exp[\nu\sigma^2/12\eta]$. Here $\ln A_{\rm fl} \propto \eta^3 g^2 \nu N^2$. In the opposite limit of $\sigma \gg 1$ we have $A_{\rm fl} \approx \exp[(4\nu/\eta)(\pi/\sigma)^{1/2}\exp(\sigma/4)]$. Here the dependence of $A_{\rm fl}$ on the vaccination amplitude g is double exponential, which is extremely strong.

CONCLUSIONS AND DISCUSSION

In summary, we have considered fluctuations in the full two-variable SIS model and found the rate of extinction of disease with and without vaccination. The problem has been reduced to the analysis of dynamics of an auxiliary Hamiltonian system, with nontrivial boundary conditions. We showed that, where the reproductive rate of infection R_0 is close to one, the extinction rate displays scaling with R_0 in the absence of vaccination, with the logarithm of the rate being $\propto (R_0 - 1)^2$. We showed that even comparatively weak vaccination can exponentially strongly affect the extinction rate. A general expression that describes this effect for random vaccine in terms of its characteristic functional has been obtained. For a Poisson distributed vaccine, the change of the exponent of the extinction rate may itself depend on the vaccine strength exponentially.

One of the important aspects of our work shows not only how random vaccinations improve the time to disease extinction, but it also shows how limited resources may be implemented in order to achieve a particular extinction rate. For example, it may be possible to vaccinate a limited fraction of new susceptibles every year, but maybe apply

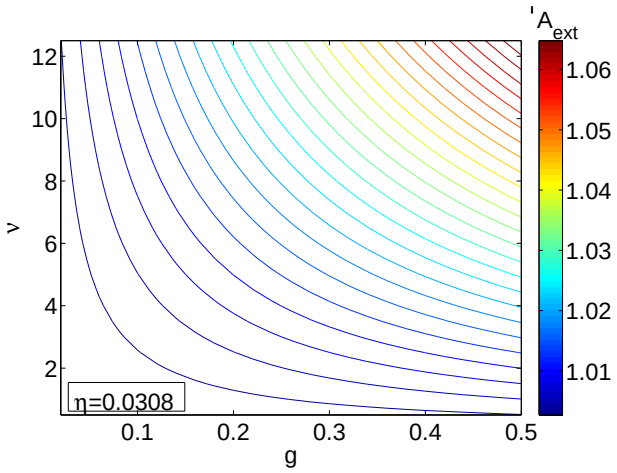

Figure 3: Extinction factor based on the asymptotic results in Eqns. 11 and 17. Parameters used are the same as in Fig. 2

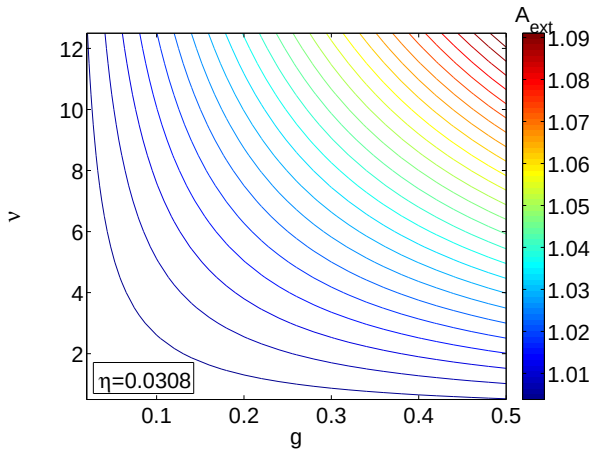

Figure 4: Extinction factor based on computed heteroclinic orbits plotted in Fig. 2 (dashed lines) and Eq. 16

it more frequently. Conversely, it may be possible to one vaccination per year that is massive (a current approach for most childhood diseases). Other approaches for slow diseases may require vaccination that is intermittent. The analysis predicts just just how much the strength and application frequency of the vaccine is needed to enhance disease extinction. For small η,or slowly propagating diseases, Figs. 3 and 4 show the dependency of the extinction factor on the amplitude A and frequency μ. Figure 3 is computed with the analytic adiabatic approximation while Fig. 4 is computed based the exact optimal path. The agreement is excellent, and the contours show the explicit dependence of the extinction factor.

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