Enhancement Epidemic Extinction by Random Vaccination

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Abstract

We investigate stochastic extinction in an epidemic model and the impact of random vaccinations in large populations. We show that, in the absence of vaccinations, the effective entropic barrier for extinction 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.

Motivation

Deterministic epidemic models do not account for some observed features, such as stochastic disease extinction. [1,2]

Markov chain theory proves extinction is inevitable in the asymptotic time limit. Numerical [3,4] and analytic work [5,6,7] shows extinction may occur in finite time.

Deterministic disease spread is characterized by the reproductive rate.

Fluctuations cause the extinct state (unstable) to be reached in finite time.

Problem

1. Study how extinction rates scale in stochastic epidemics with respect to reproductive rate
2. What is effect of randomly vaccinating new individuals on extinction rates?

1. Verdasca, et al., J. Theor. Bio. 233, 553 (2005)
2. Keeling, *Ecology, Genetcis and Evolution*, Elsevier, 2004.
3. West, et al., Math. Biosc., 141, 29 (1997)
4. Cummings, et al., ONAS PNAS 102, 10259 (2005)
5. Jacquez, et al., Math. Biosc., 163, 77, (2000)
6. Allen, et al., Math. Biosc. 163, 1 (2000)
7. Doering, et al., Multiscale Mod. 3, 283 (2005)

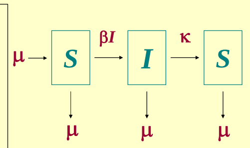
Model Setup

SIS model for epidemic spread

Transitions between states are assumed to be random

Variables and parameters:

- S: susceptibles
- I: infectives
- μ: birth and death rate
- β: contact rate (between S and I)
- κ^{-1}: mean infectious period
- N : Population size



Reproductive rate: $R_0=\beta/(\mu+\kappa)$

$R_0 > 1$ => Disease is endemic, extinct state is unstable.

Stochastic Variables

$X_1=S$, $X_2=I$, $\mathbf{X}=(X_1\ X_2)$

State Variable Increments

$\mathbf{r}=(r_1, r_2)$

Transition rates – W(X,r)

$W(\mathbf{X};(1,0)) = N(\mu-\xi(t))$	Birth
$W(\mathbf{X};(0,-1)) = \mu X_2$	Mortality of I
$W(\mathbf{X};(-1,1)) = \beta X_1 X_2$	Contact
$W(\mathbf{X};(-1,0)) = \mu X_1$	Mortality of S
$W(\mathbf{X};(1,-1)) = \kappa X_2$	Recovery

Vaccine assumption

Fraction of birth are removed stochastically with rate, $\xi(t)$.

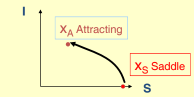
General Formulation

Master Equation Approach

$$\dot{\rho}(\mathbf{X}) = \sum_{\mathbf{r}}[W(\mathbf{X}-\mathbf{r};\mathbf{r})\rho(\mathbf{X}-\mathbf{r}) - W(\mathbf{X};\mathbf{r})\rho(\mathbf{X})]$$

Mean Field - N>>1

$$dX_1/dt = N(\mu-\xi(t)) - \mu X_1 + \kappa X_2 - \beta X_1 X_2/N$$
$$dX_2/dt = -(\mu+\kappa) X_2 + \beta X_1 X_2/N$$



Endemic State

$x_{1A} = (R_0)^{-1}$, $x_{2A} = 1-(R_0)^{-1}$

Extinct State

$x_{1s}= 1$, $x_{2s}= 0$ — Population normalized to 1

Eikonal Approximation

Assumptions:

N>>1, density $\rho(\mathbf{X})$ has a peak at $\mathbf{X}_A$ with width $\alpha\ N^{1/2}$

Tail of density for infected:

$\rho(\mathbf{X})\ \alpha\ \exp(-Ns(\mathbf{x}))$, $\mathbf{x}=\mathbf{X}/N$, normalized variables

$\rho(\mathbf{X}+\mathbf{r}) \approx \rho(\mathbf{X})\exp(-\mathbf{p}^T\mathbf{r})$, $\mathbf{p} = \partial_{\mathbf{x}} s$, s is the action

Effective Hamiltonian to O(1/N)

$$H(\mathbf{x},\mathbf{p};t) = \sum_{\mathbf{r}} w(\mathbf{x};\mathbf{r})(e^{\mathbf{p}\cdot\mathbf{r}}-1) \qquad \mathbf{W} \text{ - Transition rates per person}$$

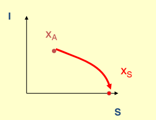
Need to solve Hamilton's equations for the action, s(x)

No Vaccine

Time independent case

Hamiltonian, $H=H_0$, Action, $s(\mathbf{x}_s) = \int_{-\infty}^{\infty} \mathbf{p}(t)\bullet\dot{\mathbf{x}}(t)dt$

$$H_0(\mathbf{x},\mathbf{p}) = 0$$



Trajectory is most probable sequence of events to extinction.

$Ns(x_s)$ is the entropic barrier

Solving the equations $\dot{\mathbf{x}} = \partial_{\mathbf{p}} H_0(\mathbf{x},\mathbf{p}), \dot{\mathbf{p}} = -\partial_{\mathbf{x}} H_0(\mathbf{x},\mathbf{p})$ gives the optimal path to extinction $-(x_{ext}(t),p_{ext}(t))$

Non-trivial momenta

Note: Solve $\partial_{\mathbf{p}} H_0(\mathbf{x},\mathbf{p}) = 0, \partial_{\mathbf{x}} H_0(\mathbf{x},\mathbf{p}) = 0$ for equilibria

Endemic State	Extinct State	Extinct State (nonzero momenta)
$\mathbf{x}_A$, p=0	$\mathbf{x}_s$, p=0	$\mathbf{x}_s$, $p=(0,-\ln(R_0))$ *

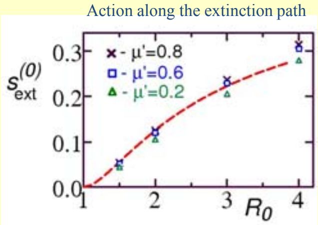
* Van Herwaarden,Grasman et al , JMB, 1995; Elgart, Kamenev, PRE, 2004

Scaling of extinction

If $|R_0-1|<<1$, optimal path may be approximated analytically.

$\boxed{\text{If } \eta = R_0-1, \text{ then } s(x_s) = \eta^2/\beta^2}$

Action along the extinction path



Vaccination Extinction Formulation

Full $H(x,p) = H_0(x,p)+H_1(x,p)$,

$H_1(x,p)=-\xi(t)(\exp(p_1)-1)$ is small due to noise.

Assuming action to be perturbed about the optimal path:

$$s(\mathbf{x}_s) = \underbrace{s^0(\mathbf{x}_s)}_{\text{Unperturbed action}} + \underbrace{\int_{-\infty}^{\infty}\xi(t)\chi_{ext}(t)dt}_{\text{Perturbed Hamiltonian along unperturbed orbits}}$$

Time averaged corrected density is

$$<\rho(\mathbf{X})>=A(\mathbf{X})\ \rho^0(\mathbf{X}),\ A(\mathbf{X}_s) = P_\xi[iN\chi_{ext}(t)]$$

$$P_\xi[k(t)] =< \exp\{i\int_{-\infty}^{\infty}\xi(t)k(t)dy\} >$$

To measure the random vaccination effect, we define

$\boxed{\text{Extinction factor: } A(\mathbf{X}_{ext}) = P_\xi[iN\chi_{ext}(t)]}$

Poisson Vaccine Case

Consider Poisson noise: Amplitude g, Average frequency: ν

For $k(t) = gN\chi_{ext}(t)$

The extinction factor is given by: $A(\mathbf{X}) = A_{av}A_{fl}$, where

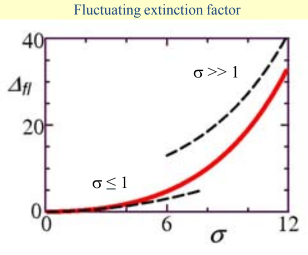
$$\underbrace{A_{av} = \exp\left\{\nu\int_{-\infty}^{\infty}k(t)dt\right\}}_{\text{Average part}} \qquad \underbrace{A_{fl} = \exp\left\{\nu\int_{-\infty}^{\infty}\left(e^{-k(t)}-1+k(t)\right)dt\right\}}_{\text{Fluctuating part}}$$

Some limiting results:

1. For $0 < \eta=R_0-1<<1$, $A_{av} = \exp[\nu\eta gN/\beta\mu]$
2. Letting
   - A. $\sigma \le 1$, $\ln A_{fl} \propto \eta^3 g^2 \nu N^2$
   - B. $\sigma >> 1$, $\ln A_{fl} \propto (4\nu/\eta)(\pi/\sigma)^{1/2}\exp(\sigma/4)$

Doubly exponential strong effect on *g*

Fluctuating extinction factor

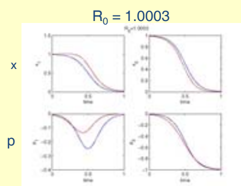


Conclusions/Numerics

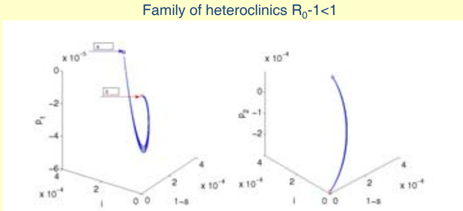
1. Considered fluctuations in full SIS model with and without vaccine
2. When $0<R_0-1<<1$, without vaccine, the extinction rate $\alpha\ (R_0-1)^2$. Numerical and analytic heteroclinic orbits agree.

-- Analytic
-- Numerical

$R_0 = 1.0003$



Family of heteroclinics $R_0-1<1$



3. Even weak random vaccination can exponentially affect the extinction rate.

   In deriving this, a general expression for the random extinction factor was obtained.

   Poisson distributed noise illustrates how strength of vaccine determines extinction exponents.