# Disease Extinction as a Dynamical System: Stochastic control to enhance epidemic die-out

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E. Forgoston, S. Bianco, L.B. Shaw and I.B. Schwartz,Bulletin of Mathematical Biology, 73:495-514
I.B. Schwartz, E. Forgoston, S. Bianco, L.B. Shaw, J. Royal. Roc. INTERFACE. 65: 1699-1707.

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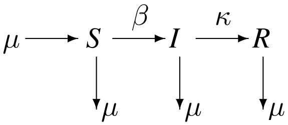
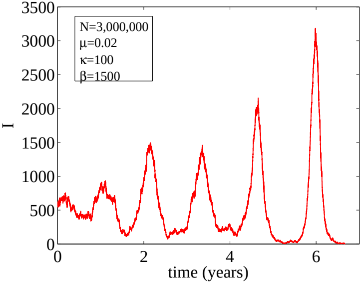
# Introduction

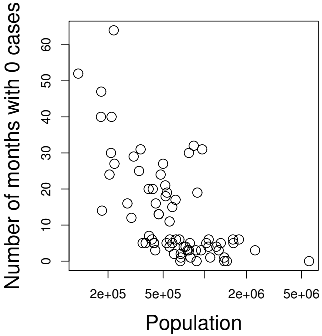
- Control and eradication of infectious diseases are important public health goals.
  - The global eradication of smallpox has been achieved.
  - It is difficult to accomplish, and remains a goal for polio, malaria, childhood diseases, etc.
- There are other extinction processes besides global disease eradication.
  - A disease may become locally extinct, but can be reintroduced-measles in Thailand.
  - Extinction of individual strains of multi-strain diseases - influenza and dengue fever.
  - Extinction of species.

# Example of Epidemic Extinction - SIR



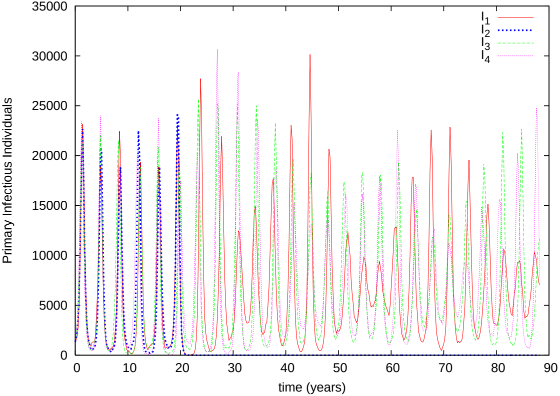




Population size = 3 million




Data courtesy of D. Cummings

# Example of Epidemic Extinction - Multi-strain Disease

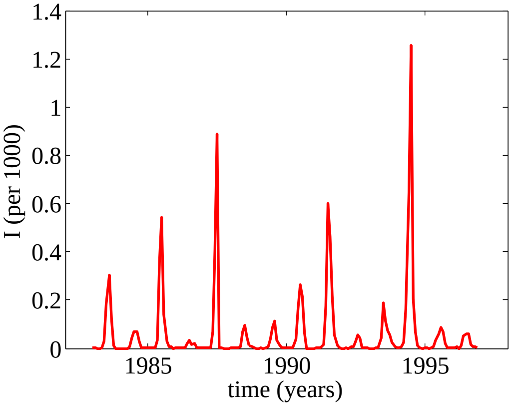



Four strain model (Dengue Fever with antibody dependent enhancement)
Population size is 100 million

Only one strain (blue) goes extinct

Figure courtesy of S. Bianco

# *Example of Epidemic Extinction - Dengue Fever Data*




Data showing incidence (per 1000 individuals) of Dengue Fever for Chiang Mai province, Thailand.

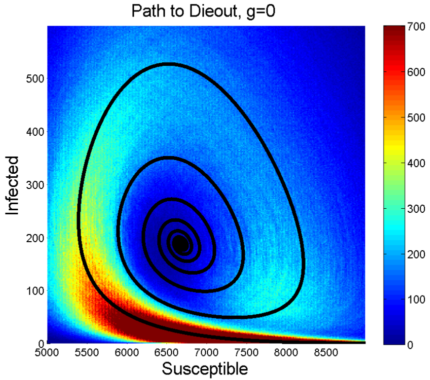
Data courtesy of D. Cummings

# Problem and Objective

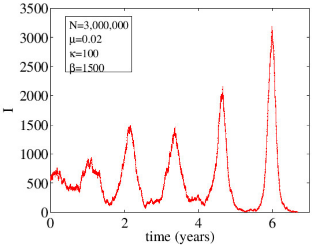
- Extinction of an epidemic is assumed to be rare event that occurs due to a large, rare stochastic fluctuation.
- The problem is to find the most likely trajectory in state space to extinction (the optimal path).
  - Equivalent to maximizing local sensitive dependence to initial data
- Show that the path which maximizes the probability to extinction (optimal path) also has a finite-time Lyapunov exponent (FTLE) that attains its local maximum on the optimal path.
- Therefore, we can use the geometry of the FTLE as a constructive tool to evolve naturally toward the optimal path.


1. Verdasca et al, J. Theor. Bio. 233, 553 (2005)
2. Keeling, Ecology, Genetics, and evolution , Elsevier, 2004.
3. West et al, Math. Biosc., 141, 29 (1997)
4. Cummings et al, 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)

# Optimal Path for Stochastic SIR




Color bar is a pre-history histogram of 2000 runs that go extinct.




$$\beta = 1500, \gamma = 100, R_0 \approx 15$$

An iterative action minimizing method for computing optimal paths in stochastic dynamical systems

BS Lindley, IB Schwartz - arXiv preprint arXiv:1210.5153, 2012 - arxiv.org

# Outline

- Optimal path to extinction.
  - Theory developed using example of a branching - annihilation process.
  - Analytical results.
- Optimal path and sensitive dependence to initial conditions.
  - Ideas developed using example of simple pendulum.
  - Quantifying sensitive dependence using FTLE.
- Return to example of branching-annihilation process.
- A second example (SIS/SIR epidemic models).
- Control using treatment in SIS model
- Conclusions and future work.

# Stochastic Branching-Annihilation Process- An Example

$$A \xrightarrow{\lambda} 2A \qquad \text{and} \qquad 2A \xrightarrow{\mu} \emptyset$$

branching                annihilation

$\lambda$, $\mu > 0$ are the reaction rates.

This is a single species process that can be thought of as a simplified model of population growth.

Illustrates the role of the optimal path to extinction in large fluctuations of a stochastic population, and more generally, in stochastic systems far from equilibrium.

# *Stochastic Branching-Annihilation Process*

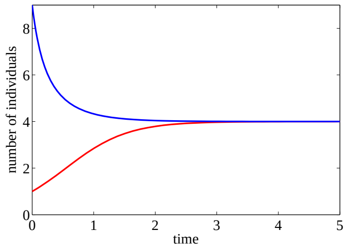
The deterministic (mean-field) rate equation is given by

$$\dot{X} = \lambda X - \mu X^2$$

There are two fixed points:

A repelling, zero-population (extinct) state at $X_S = 0$

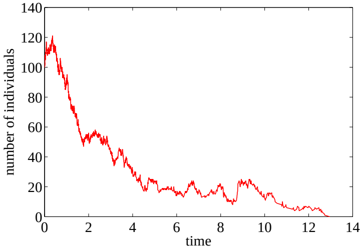
An attracting, non-trivial (endemic) state at $X_A = \lambda/\mu$




Deterministic

$\lambda = 2.0$

$\mu = 0.5$




Stochastic

# *Master Equation for* $A \xrightarrow{\lambda} 2A, \quad 2A \xrightarrow{\mu} \emptyset$

The deterministic picture misses the fact that the true, asymptotic state of the stochastic system is the zero-population (extinct) state.

Stochastic effects occur as a result of random interactions.

Transition rates:

| | |
|---|---|
| $W(X,-1) = \mu X^2$ | Annihilation |
| $W(X,+1) = \lambda X$ | Creation |

Assaf, Meerson PRE 70,041106 (2008)

Elgart, Kamenev, PRE 78, 041123 (2004)

# Solving the General Master Equation (ME)

$X \epsilon R^m$ are individual numbers of population

Transitions occur as $\boldsymbol{X} \to \boldsymbol{X} + \boldsymbol{r}$ at rate $W(\boldsymbol{X}, \boldsymbol{r})$

Mean field equations ($N \to \infty$)

$$\frac{d\boldsymbol{X}}{dt} = \sum_{\boldsymbol{r}} \boldsymbol{r} W(\boldsymbol{X}, \boldsymbol{r}) \qquad (1)$$

Probability evolves according to master equation

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

# *Eikonal Approximation to the Master Equation*

Assumptions: Large population limit $N >> 1$ *

Density $\rho(X)$ has central peak at endemic $\boldsymbol{X_A}$ of width $\alpha N^{1/2}$

Density of ME is approximated as the exponential of a function, $s(\boldsymbol{x})$ called the action:

$$\begin{aligned} \rho(\boldsymbol{X}) \quad &\alpha \quad exp(-Ns(\boldsymbol{x})), & \boldsymbol{p} = \partial s / \partial \boldsymbol{x} \\ \rho(\boldsymbol{X} + \boldsymbol{r}) \quad &\approx \quad \rho(\boldsymbol{X}) exp(-\boldsymbol{p}^t \boldsymbol{r}), & \boldsymbol{X} \gg \boldsymbol{r} \\ \frac{\partial s}{\partial t} \quad &= \quad -H(\boldsymbol{x}, \partial s / \partial \boldsymbol{x}), & Hamilton - Jacobi \;\; Equation \end{aligned}$$

with Hamiltonian as a function of population fraction $\boldsymbol{x}$ and conjugate momenta $\boldsymbol{p}$ :

$$H(\boldsymbol{x}, \boldsymbol{p}) = \sum_r w(\boldsymbol{x}, \boldsymbol{r})(e^{\boldsymbol{p}^t r} - 1)$$


* Gang, PRA 36 5782 (1987)

Dykman et al, J. Chem. Phys. 100, 5735 (1994).

Elgart et al PRE, 70 041106 (2004)

Dykman, Landsman, Schwartz PRL, 101 078101 (2008)

# Hamiltonian for $A \xrightarrow{\lambda} 2A, \quad 2A \xrightarrow{\mu} \emptyset$

Using a Legendre transformation*, we have

$$H(q,p) = \left(\lambda(1+p) - \frac{\mu}{2}(2+p)q\right) qp$$

$$\dot{q} = \frac{\partial H}{\partial p} = q[\lambda(1+2p) - \mu(1+p)q],$$
$$\dot{p} = -\frac{\partial H}{\partial q} = p[\mu(2+p)q - \lambda(1+p)]$$

$q$ is a coordinate, while $p$ is a conjugate momentum.

Since $H$ is independent of time, it is conserved: $H = E = \text{const.}$

We consider zero-energy orbits, so that $H = E = 0$.

* Gang, PRA 36 5782 (1987)

# Steady States of Hamiltonian Flow

Zero fluctuations correspond to momentum $p = 0$ and the dynamics are described by

$$\dot{q} = \lambda q - \mu q^2$$

with attracting fixed point $q = \lambda/\mu$
and repelling fixed point $q = 0$.

There are three zero-energy fixed points of the Hamiltonian flow:

| | |
|---|---|
| $h_1 = (q, p) = (\lambda/\mu, 0)$ | deterministic, endemic state |
| $h_0 = (q, p) = (0, 0)$ | deterministic, zero-population state |
| $h_2 = (q, p) = (0, -1)$ | fluctuational, zero-population state |

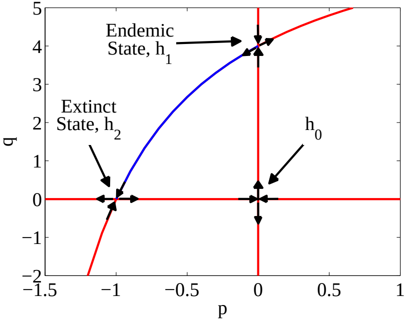
All three points are hyperbolic (saddles) in $2d$.

Extinction requires fluctuational orbits with non-zero momentum.(Absorbing state)

# Geometry of the Optimal Path

Three zero-energy curves given as:

$$p = 0, \quad q = 0, \quad \text{and} \quad q = \frac{2\lambda(1+p)}{\mu(2+p)}$$




The path from the endemic state to extinction must leave point $h_1$ and reach the extinction line $q = 0$.

Of all such trajectories, the optimal path reaches $q = 0$ at point $h_2$ and describes the most probable sequence of events which evolves the system to extinction.

# Outline

- Optimal path to extinction.
  - Theory developed using example of a branching - annihilation process.
  - Analytical results.
- Optimal path and sensitive dependence to initial conditions.
  - Tutorial using example of simple pendulum.
  - Quantifying sensitive dependence using FTLE.
- Return to example of branching-annihilation process.
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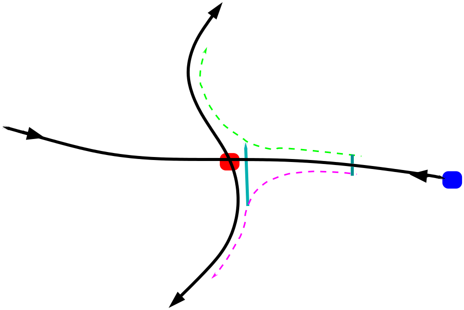
# Optimal Path and Sensitive Dependence to IC

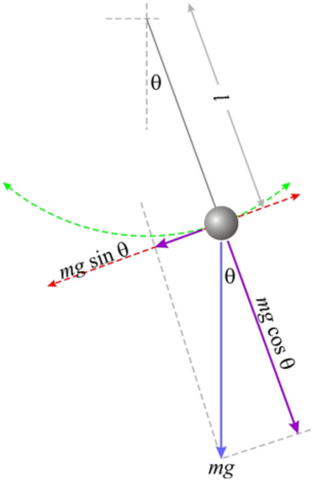
The optimal path is a heteroclinic orbit that connects two saddles (endemic state to extinct state).



Dynamically, the heteroclinic orbit (optimal path) exhibits maximal sensitivity to initial conditions.

We quantify the sensitive dependence to initial conditions by computing finite-time Lyapunov exponents (FTLE).

# Example - Simple Pendulum



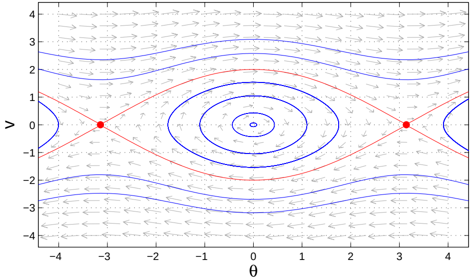

$$\ddot{\theta} + \sin\theta = 0$$

Write as $\dot{\boldsymbol{x}} = f(\boldsymbol{x})$ with $\boldsymbol{x} = (\theta, v)$;

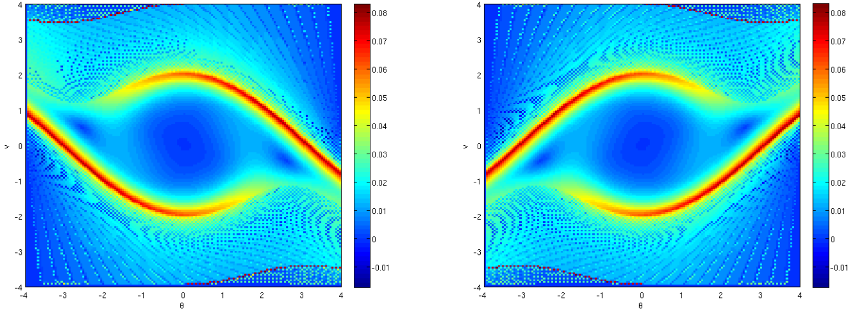
$$\dot{\theta} = v,$$

$$\dot{v} = -\sin\theta$$

Look at trajectories in phase space.



# *FTLE for Simple Pendulum*



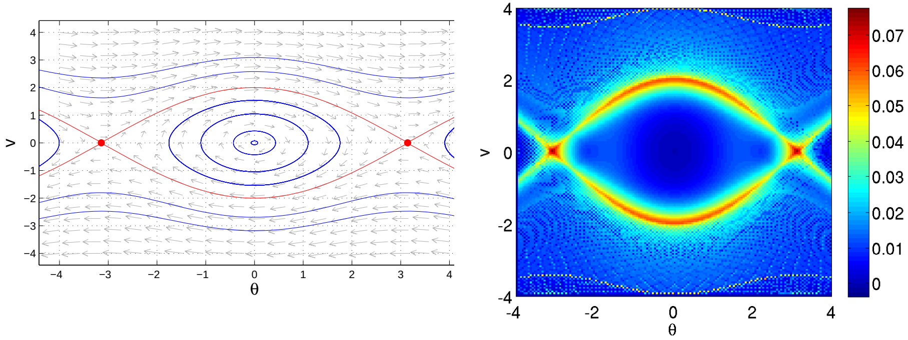

Forward FTLE

Backward FTLE

Attracting structures when one integrates forward in time.

Repelling structures when one integrates backwards in time.

# FTLE for Simple Pendulum




The “ridges” of maximal FTLE values (coherent structures) correspond to the invariant manifolds.

# How to Compute FTLE

Consider a vector field $\boldsymbol{v}$ defined over the time interval $I = [t_i, t_f]$.

Trajectories satisfy:
$$\dot{\boldsymbol{x}}(t; t_i, \boldsymbol{x}_0) = \boldsymbol{v}(\boldsymbol{x}(t; t_i, \boldsymbol{x}_0), t),$$
$$\boldsymbol{x}(t_i; t_i, \boldsymbol{x}_0) = \boldsymbol{x}_0$$

Integration of the system from $t_i \to t_i + T$ yields the flow map:

$$\phi_{t_i}^{t_i+T} : \boldsymbol{x}_0 \mapsto \phi_{t_i}^{t_i+T}(\boldsymbol{x}_0) = \boldsymbol{x}(t_i + T; t_i, \boldsymbol{x}_0)$$

Consider a perturbed point $\boldsymbol{y} = \boldsymbol{x} + \delta\boldsymbol{x}(0)$. After time $T$:

$$\delta\boldsymbol{x}(T) = \phi_{t_i}^{t_i+T}(\boldsymbol{y}) - \phi_{t_i}^{t_i+T}(\boldsymbol{x}) = \frac{d\phi_{t_i}^{t_i+T}(\boldsymbol{x})}{d\boldsymbol{x}}\delta\boldsymbol{x}(0) + \mathcal{O}(||\delta\boldsymbol{x}(0)||^2)$$

# How to Compute FTLE

Magnitude of the perturbation is:

$$||\delta \boldsymbol{x}(T)|| = \sqrt{\left\langle \frac{d\phi_{t_i}^{t_i+T}(\boldsymbol{x})}{d\boldsymbol{x}} \delta \boldsymbol{x}(0), \frac{d\phi_{t_i}^{t_i+T}(\boldsymbol{x})}{d\boldsymbol{x}} \delta \boldsymbol{x}(0) \right\rangle} = \sqrt{\left\langle \delta \boldsymbol{x}(0), \frac{d\phi_{t_i}^{t_i+T}(\boldsymbol{x})}{d\boldsymbol{x}}^{*} \frac{d\phi_{t_i}^{t_i+T}(\boldsymbol{x})}{d\boldsymbol{x}} \delta \boldsymbol{x}(0) \right\rangle}$$

Maximum stretching from max eigenvalue of deformation matrix.

$$\max_{\delta \boldsymbol{x}(0)} ||\delta \boldsymbol{x}(T)|| = \sqrt{\lambda_{\max}(\Delta)} ||\bar{\delta} \boldsymbol{x}(0)|| = \exp\left(\sigma_{t_i}^{T}(\boldsymbol{x})|T|\right) \cdot ||\bar{\delta} \boldsymbol{x}(0)||$$

The (largest) finite-time Lyapunov exponent is therefore:

$$\sigma_{t_i}^{T}(\boldsymbol{x}) = \frac{1}{|T|} \ln \sqrt{\lambda_{\max}(\Delta)}$$

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# Back to Branching-Annihilation Problem

Three zero-energy curves given as:

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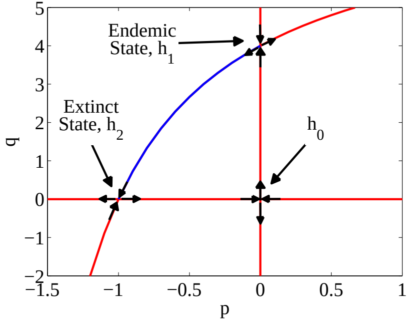
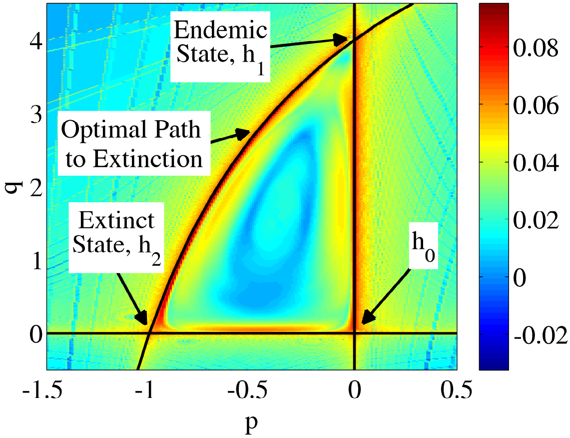
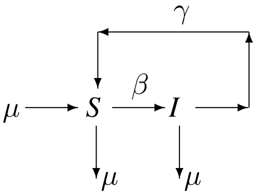


# FTLE for Branching-Annihilation Problem




Color bar depicts the FTLE values

# SIS Epidemic Model




$$\dot{S} = \mu N - \mu S + \gamma I - \beta IS/N,$$
$$\dot{I} = -(\mu + \gamma)I + \beta IS/N$$

Assume constant population so that $S + I = N$

$$\dot{I} = -(\mu + \gamma)I + \beta I(1 - I)/N, \qquad R_0 = \beta/(\mu + \gamma)$$

# *Hamiltonian for Stochastic SIS*

The Hamiltonian is

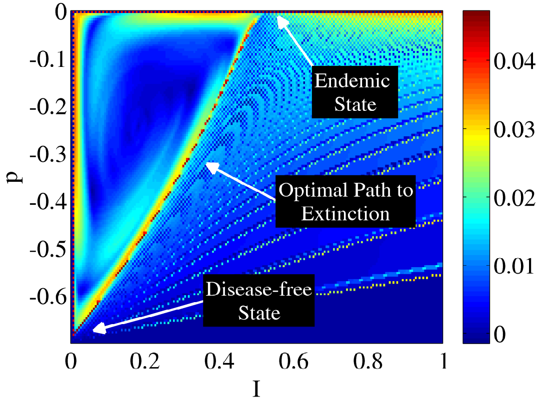
$$H(I,p) = (\mu+\gamma)I(e^{-p}-1) + (\beta/N)I(1-I)(e^{p}-1)$$

Hamilton's equations are

$$\dot{I} = \frac{\partial H}{\partial p} = -(\mu+\gamma)Ie^{-p} + (\beta/N)I(1-I)e^{p},$$

$$\dot{p} = -\frac{\partial H}{\partial I} = -(\mu+\gamma)(e^{-p}-1) + (\beta/N)(e^{p}-1)(2I-1)$$

# *Optimal Path for Stochastic SIS-1-D model*

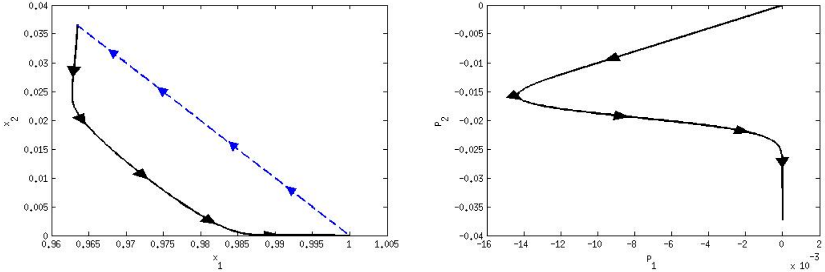


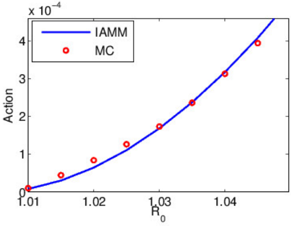

Color bar values of FTLE at each point.

Optimal path to extinction lies along a maximal ridge of the FTLE.

When p = 0, the system follows its deterministic path (no fluctuations)

# *Optimal Path for Stochastic SIS-2-D model*



[1]

[1] Monte Carlo simulations courtesy of L. Billings.

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# *Treatment model - scaled treatment $gX_2$*

## Infectives receive treatment $\Longrightarrow$ group removal.

Approximate susceptibles $S = N - I$ using the mean population size $N$.

Consider the dynamics in the one-dimensional state $\mathbf{X} = I = X_2$.

Remove a percentage of the infectives ($gx_2$) at frequency ($\nu$).

## Transition rates for stochastic control:

$$\begin{aligned} W\big(X_2; -1\big) &= (\mu + \kappa) X_2, && \text{removal by death or recovery} \\ W\big(X_2; 1\big) &= \beta X_2 (N - X_2)/N, && \text{infection event} \\ W\big(X_2; -gX_2\big) &= \nu, && \text{treatment} \end{aligned} \tag{2}$$

Let:

$\tau = t/(\mu + \kappa)$ (time) $q = X_2/N$. (infective fraction)

$R_0 = \beta/(\mu + \kappa)$ (spread rate) $\omega = \nu/(\mu + \kappa)$ (Normalized treatment frequency).

## Hamiltonian:

$$H(q, p) = R_0 q(1 - q)(e^p - 1) + q(e^{-p} - 1) + \frac{\omega}{N}(e^{-gNqp} - 1)$$

# Treatment model - Higher order approximation

Assuming $g \ll 1$, the optimal path to extinction:

$$p_a(q) = -\ln(R_0(1-q))\left(1 - \frac{\omega g}{R_0(1-q)-1}\right) + \mathcal{O}(g^2)$$

The higher order terms in the approximation of the probability distribution:

$$\rho(\mathbf{X}, t) = \exp(-N\mathcal{S}(\mathbf{x})) = \exp(-NS(q) - S_1(q) - ...),$$

We can approx $S_1(q)$ by*

$$S_1(q) = \int_{q_1}^{q} \frac{H_{qp}(\xi, p_a) + \frac{1}{2}H_{pp}(\xi, p_a) - \frac{\omega}{N}(e^{-gN\xi p_a} - 1)}{H_p(\xi, p_a)} d\xi$$

*Escudero and Kamenev, Phys. Rev. E, 79 (2009); Assaf and Meerson, Phys. Rev. E, 81 (2010).

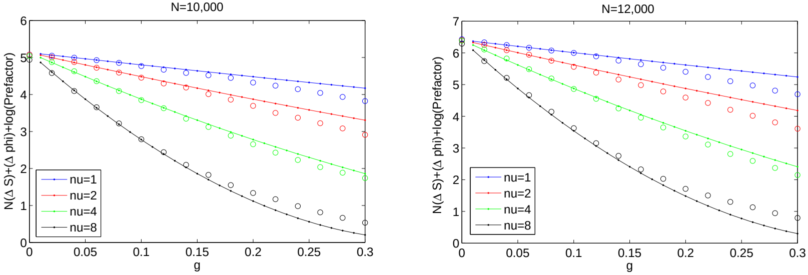
# *Treatment model-Enhanced mean time to extinction*

## Mean time to extinction with pre-factor*

$$\tau = Ke^{N[S(0)-S(q_1)]+(\phi(0)-\phi(q_1))}$$

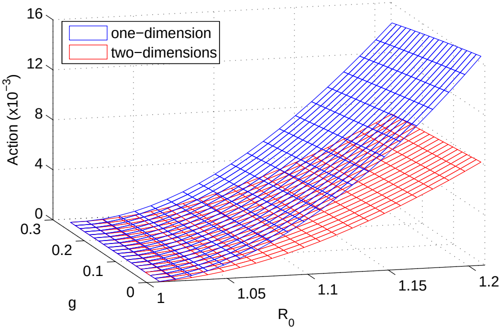
for $\phi(q) = S_1(q) - \ln q$ and $K = \dfrac{(\frac{1}{R_0-1})\sqrt{2\pi}}{(\mu+\kappa)(\frac{R_0-1-\omega g}{R_0})\sqrt{\frac{N\ln(1+\omega g)R_0}{\omega g}}}$

Parameters: $\beta = 104$, $\mu = 0.2$, and $\kappa = 100$.




*Assaf and Meerson, Phys. Rev. E, 81 (2010).

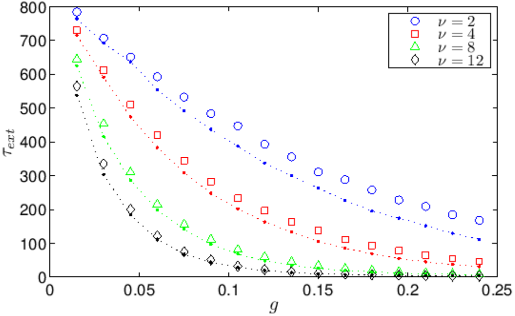
# *Treatment control-Relaxing the fixed population assumption*




The action of 1D SIS model as a function of $R_0$ and treatment fraction $g$. Population is assumed to be fixed size $N$

The action 2D SIS model as a function of $R_0$ and treatment fraction $g$. Population fluctuates.

# *Comparing periodic and random treatment effectiveness*




Mean time to disease extinction
Random treatment (dotted lines)
Periodic treatment (symbols)

Parameters: N = 8,000, $R_0 = 1.05$

Random schedule had a faster mean time to extinction over the range of frequencies

# *Conclusions*

- Extinction occurs when fluctuations due to random transitions act as an effective force to drive one or more components or species to vanish.
- We have shown that even though the extinction process is random, it follows an optimal path which:
  - (1) maximizes the probability to extinction, and
  - (2) is equivalent to the dynamical systems idea of having maximum sensitive dependence to IC.
- The relation between sensitive dependence and the path to extinction allows one to evolve naturally toward the optimal path using FTLE.
- Showed how random controls enhance the time to extinction in simple stochastic models.
- One and two dimensional models possess different scalings as functions of $R_0$ and $g\nu$.

# Some Recent Epidemiology References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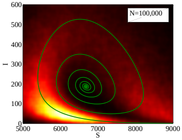
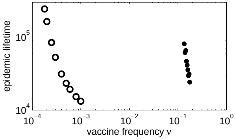
# *Future Work*

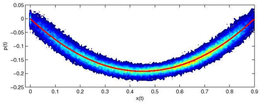
- Apply method to higher-dimensional models, such as SIR and multi-strain models.
- Devise improved control methods which promote disease extinction.
- Extend to non-Markovian dynamical systems
  Stochastic differential delay equations
  State dependent stochastic delay equations




SIR Optimal Path and PDF- With Shaw and Bianco




Adaptive network vaccine control-With Leah Shaw




Stochastic delayed logistic optimal path-With Thomas Carr, SMU

# *Sketch of Proof of Equivalence*

Consider the n-dimensional Langevin problem with vector field $V(\boldsymbol{x})$ with additve noise. Eikonal equations of motion and Hamiltonian are:

$$\begin{aligned}
\dot{\boldsymbol{x}} &= \boldsymbol{p} + \boldsymbol{V}(\boldsymbol{x}) \\
\dot{\boldsymbol{p}} &= -\boldsymbol{V}'(\boldsymbol{x})\boldsymbol{p} \\
H(\boldsymbol{x},\boldsymbol{p}) &= \frac{\|\boldsymbol{p}\|^2}{2} + \boldsymbol{p} \cdot \boldsymbol{V}(\boldsymbol{x})
\end{aligned}$$

Optimal path lies along the $H(\boldsymbol{x},\boldsymbol{p}) = 0$ surface

$$C_{(\boldsymbol{x},\boldsymbol{p})} = \{t \in (-\infty,\infty) \,|\, \boldsymbol{p}(t) = -2\boldsymbol{V}(\boldsymbol{x}(t))\},$$

Local geometry assumptions:

- $\boldsymbol{V}(\boldsymbol{x})$ is smooth,
- $\boldsymbol{V}(\boldsymbol{x}_a) = \boldsymbol{V}(\boldsymbol{x}_s) = \boldsymbol{0}$,
- $\boldsymbol{V}'(\boldsymbol{x}_a)$ has eigenvalues with negative real parts, and $\boldsymbol{V}'(\boldsymbol{x}_s)$ has at least one eigenvalue with positive real part.

# *Sketch of Proof of Equivalence (Cont'd)*

Assume that the optimal path has a direction on $H(\boldsymbol{x}(t),\boldsymbol{p}(t)) = 0$:

$$\lim_{t\to+\infty}(\boldsymbol{x}(t),\boldsymbol{p}(t)) = (\boldsymbol{x}_s,\boldsymbol{0}),$$

$$\lim_{t\to-\infty}(\boldsymbol{x}(t),\boldsymbol{p}(t)) = (\boldsymbol{x}_a,\boldsymbol{0}).$$

Shift optimal path to the origin by using the $2n$-dimensional transformation:

$$\boldsymbol{u} = \boldsymbol{x},$$
$$\boldsymbol{w} = \boldsymbol{p} + 2\boldsymbol{V}(\boldsymbol{x}),$$
$$\hat{H}(\boldsymbol{u},\boldsymbol{w}) = \frac{\|\boldsymbol{w}\|^2}{2} - \boldsymbol{w}\cdot\boldsymbol{V}(\boldsymbol{u}).$$

The new equations of motion are now:

$$\dot{\boldsymbol{u}} = \partial\hat{H}/\partial\boldsymbol{w} = \boldsymbol{w} - \boldsymbol{V}(\boldsymbol{u}),$$
$$\dot{\boldsymbol{w}} = -\partial\hat{H}/\partial\boldsymbol{u} = \boldsymbol{V}'(\boldsymbol{u})\boldsymbol{w}.$$

The optimal path now is described by the curve

$$C_{(\boldsymbol{u},\boldsymbol{w})} = \left\{t\in(-\infty,\infty)\,|\,\boldsymbol{w}(t)=\boldsymbol{0},\dot{\boldsymbol{u}}(t) = -\boldsymbol{V}(\boldsymbol{u}(t))\right\},$$

# *Sketch of Proof of Equivalence (Cont'd)*

Linearized variation along the optimal path $C_{(\boldsymbol{u},\boldsymbol{w})}$:

$$\dot{\boldsymbol{X}} = \begin{bmatrix} -\boldsymbol{V}'(\boldsymbol{u}(t)) & \boldsymbol{I}_n \\ \boldsymbol{0} & \boldsymbol{V}'(\boldsymbol{u}(t)) \end{bmatrix} \boldsymbol{X} \equiv \boldsymbol{J}(\boldsymbol{u}(t), \boldsymbol{0})\boldsymbol{X}, \quad \boldsymbol{X}(\boldsymbol{0}) = \boldsymbol{I}. \qquad (3)$$

The eigenvalues of $\boldsymbol{J}(\boldsymbol{u}_0, \boldsymbol{0})$ are given by $\{\pm\lambda_i\}_{i=1}^{n}$, where $\lambda_i$ are eigenvalues of $\boldsymbol{V}'(\boldsymbol{u}_0)$.
Diagonalizing and ordering the eigenvalues, the solution about $(\boldsymbol{u}, \boldsymbol{w}) = (\boldsymbol{u}_0, \boldsymbol{0})$ for $0 < t \ll 1$ is $\boldsymbol{X}(t) \approxeq \exp\left(t\boldsymbol{J}(\boldsymbol{u}_0, \boldsymbol{0})\right)$.
For any initial value, $\boldsymbol{x}_0$, the solution is

$$\begin{aligned} \boldsymbol{x}_p(t; \boldsymbol{x}_0) &= (x_1(t), x_2(t), \cdots, x_{2n}(t)) \\ &= (e^{\lambda_{\max} t} x_{10}, e^{\lambda_2 t} x_{20}, \cdots, e^{\lambda_n t} x_{n0} \\ & e^{-\lambda_n t} x_{(n+1)0}, \cdots, e^{-\lambda_2 t} x_{(2n-1)0}, e^{-\lambda_{\max} t} x_{2n0}). \end{aligned}$$

Here $\lambda_{max} > 0$ dominates the eigenvalues.

# *Sketch of Proof of Equivalence (Cont'd)*

Apply FTLE definition on $2n$-dimensional hypercube $D = [-1, 1]^{2n}$:
If the initial condition lies within a distance $\delta$ of the unstable manifold with $0 < \delta << 1$, then the time to escape from the domain for an arbitrary non-zero initial condition is given by

$$t_f \approxeq -\frac{\log(\delta)}{\lambda_{\max}}.$$

Using the definition of the FTLE given by :

$$\sigma(t_f; \boldsymbol{x}_0) = \frac{1}{t_f} \ln\left(||\boldsymbol{x}_p(t_f; \boldsymbol{x}_0 + \boldsymbol{\epsilon}) - \boldsymbol{x}_p(t_f; \boldsymbol{x}_0)||\right),$$

Since $|\lambda_{\max}| >> |\lambda_i|$, and since $\pm\lambda_{\max}$ dominates the expanding and contracting directions,

$$\frac{\partial \sigma(t_f; \boldsymbol{x}_0(\delta))}{\partial \delta} \approx \frac{\lambda_{\max} \ln\left(\epsilon_1^2\right)}{2\delta \left(\ln \delta\right)^2} \left(1 + \frac{\delta^4 \epsilon_{2n}^2}{\epsilon_1^2}\right),$$

which can be shown to be negative assuming $\epsilon_1 << 1$.