Large deviations for Poisson driven processes in epidemiology

Peter Kratz
joint work with Etienne Pardoux

Aix Marseille Université

CEMRACS Luminy. August 20, 2013

Overview

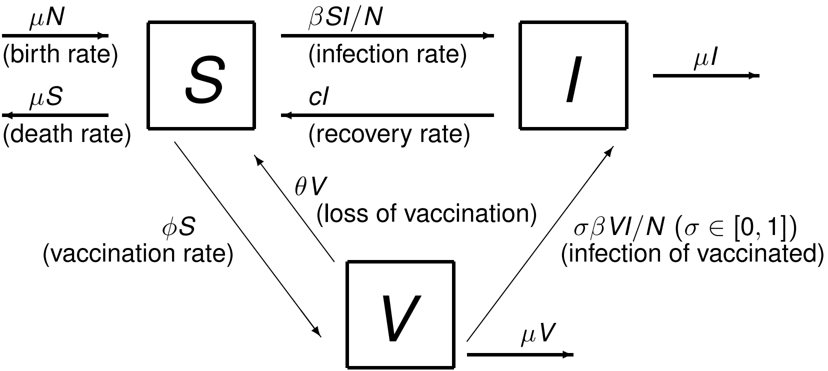
1. Motivation
   - Deterministic compartmental models
   - Long-term behavior
   - Stochastic models
   - Dynamically consistent finite difference schemes
2. General models
   - Poisson models
   - Law of large numbers
3. Large deviations
   - Rate function
   - Large deviations principle (LDP)
   - Exit from domain
4. Diffusion approximation

Overview

1. Motivation
   - Deterministic compartmental models
   - Long-term behavior
   - Stochastic models
   - Dynamically consistent finite difference schemes
2. General models
   - Poisson models
   - Law of large numbers
3. Large deviations
   - Rate function
   - Large deviations principle (LDP)
   - Exit from domain
4. Diffusion approximation

A model with vaccination

- SIV model by Kribs-Zaleta and Velasco-Hernández (2000)
- S =# of susceptibles, I = # of infectives,
  V = # of vaccinated, $N = S + I + V$ population size



ODE representation

- $$
\begin{aligned}
S' &= \mu N - \beta \frac{SI}{N} - (\mu + \phi) S + cI + \theta V \\
I' &= \beta \frac{(S + \sigma V) I}{N} - (\mu + c) I \\
V' &= \phi S - \sigma \beta \frac{VI}{N} - (\mu + \theta) V
\end{aligned}
\tag{1}
$$

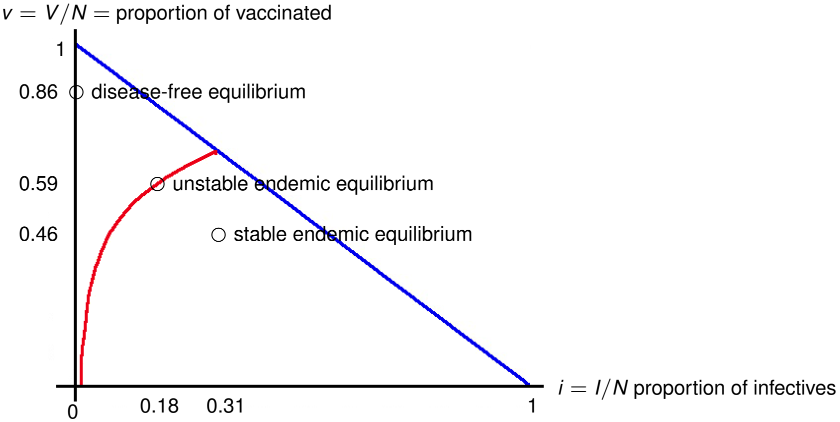
- Equation (1) has a unique solution satisfying $0 \leq S, I, V \leq S + I + V = N$

ODE and equilibria

- We are interested in the long-term behavior of the model
  - Does the disease become extinct or endemic?
- Find equilibria of the ODE (1)
  - $R_0 =$ basic reproduction number
    = "# of cases one case generates in its infectious period"
    a disease-free equilibrium ($I = 0$) of (1) exists
    $R_0 < 1 \Rightarrow$ the equilibrium is asymptotically stable
  - $\tilde{R}_0 =$ basic reproduction number without vaccination
    $\tilde{R}_0 > 1 \Rightarrow$ the disease-free equilibrium is unstable
  - $R_0 < 1 < \tilde{R}_0$ (and appropriate parameter choice)
    $\Rightarrow$ two endemic equilibria ($I > 0$) exist
    One is asymptotically stable, one is unstable

Equilibria of the ODE

- Reduction of dimension
  $s = S/N = 1 - i - v =$ proportion of susceptibles



Stochastic models

- Stochastic model corresponding to the deterministic model
- Replace the deterministic rates by (independent) non-homogenous Poisson processes
  - An individual of type S becomes of type I at the jump time of the respective processes
  - Jump rates are constant in-between jumps
  - Example. Infection rate (at time t): $\beta \frac{S(t)I(t)}{N}$
- Questions
  - What is the difference between the two processes for large N?
  - Can the stochastic process change between the domains of attraction of different stable equilibria (for large N)?
  - When does this happen?
  - For which population size N is it possible/probable?

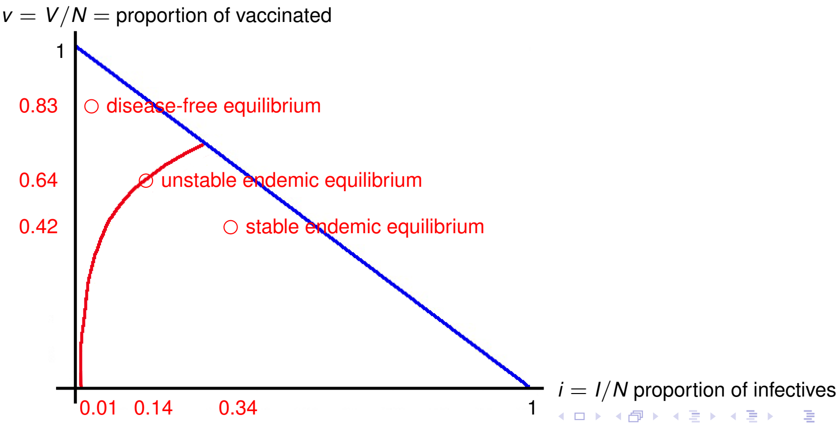
Alternative model with immigration

- We require a modification of the SIV-model in order to ensure that the process doesn't get stuck at $I = 0$
- Immigration of infectives at rate $\alpha > 0$ (small)

$$
\begin{aligned}
S' &= \mu N - \beta \frac{SI}{N} - (\mu + \phi + \alpha) S + cI + \theta V \\
I' &= \alpha N + \beta \frac{(S + \sigma V) I}{N} - (\mu + c + \alpha) I \\
V' &= \phi S - \sigma \beta \frac{VI}{N} - (\mu + \theta + \alpha) V
\end{aligned} \tag{2}
$$

Equilibria with immigration

- For $\alpha \approx 0$ (but $\alpha > 0$ sufficiently small) the equilibria and the regions of attraction remain similar
- The "disease-free" equilibrium satisfies $I \approx 0$ (but $I > 0$)



Numerical solution of the ODE

- We require a numerical method for solving the ODE
- Anguelov et al. (2014): Non-standard finite difference scheme which is *elementary stable*
  - The standard denominator h of the discrete derivatives is replaced by a more complex function $\phi(h)$
  - Nonlinear terms are approximated in a nonlocal way by using more than one point of the mesh
  - The equilibria and their local stability is the same as for the ODE

Overview

Poisson models

$$Z^N(t) := x + \frac{1}{N}\sum_{j=1}^{k} h_j P_j\Big(\int_0^t N\beta_j(Z^N(s))ds\Big) \tag{3}$$

$$= x + \int_0^t b(Z^N(s))ds + \frac{1}{N}\sum_j h_j M_j\Big(\int_0^t N\beta_j(Z^N(s))ds\Big)$$

- $d =$ number of compartments (susceptible individuals, ...)
  $N =$ "natural size" of the population
  $Z_i^N(t) =$ proportion of individuals in compartment i at time t
  $A =$ domain of process (compact)
- P_j ($j = 1, \ldots, k$): independent standard Poisson processes
- $M_j(t) = P_j(t) - t$: compensated Poisson processes
- $h_j \in \mathbb{Z}^d$: jump directions
  $\beta_j : A \to \mathbb{R}_+$: jump intensities
  $b(x) = \sum_j h_j \beta_j(x)$

Law of large numbers

- Deterministic model

$$\phi(t) := x + \int_0^t b(\phi(s))ds = x + \int_0^t \sum_{j=1}^k h_j \beta_j(\phi(s))ds \qquad (4)$$

Theorem (Kurtz)

$x \in A$, $T > 0$, $\beta_j : \mathbb{R}^d \to \mathbb{R}_+$ bounded and Lipschitz. There exist constants $C_1(\epsilon), C_2 > 0$ ($C_1(\epsilon) = \Theta(1/\epsilon)$ as $\epsilon \to 0$, C_2 independent of ϵ) such that for $N \in \mathbb{N}$, $\epsilon > 0$

$$\mathbb{P}\Big[\sup_{t \in [0,T]} |Z^N(t) - \phi(t)| \geq \epsilon\Big] \leq C_1(\epsilon) \exp\Big(-C_2 \frac{N}{\log N} \epsilon^2\Big).$$

In particular, $Z^N \to \phi$ almost surely uniformly on $[0, T]$.

Overview

Rare events

- Recall (LLN): $Z^N \to \phi$ almost surely uniformly on $[0, T]$
- But: A (large) deviation of Z^N from the ODE solution ϕ is nevertheless possible (even for large N, cf. Campillo and Lobry (2012))
- Fix $T > 0$; $D([0,T];A) := \{\phi : [0,T] \to A | \phi \text{ càdlàg}\}$;
- Quantify

$$\mathbb{P}[Z^N \in G], \quad \mathbb{P}[Z^N \in F]$$

for $G \subset D$ open, $F \subset D$ closed (N large)

Legendre-Fenchel transform

- Legendre-Fenchel transform
  $x \in A$ position, $y \in \mathbb{R}^d$ direction of movement

$$L(x, y) := \sup_{\theta \in \mathbb{R}^d} \ell(\theta, x, y)$$

  for

$$\ell(\theta, x, y) = \langle \theta, y \rangle - \sum_j \beta_j(x)(e^{\langle \theta, h_j \rangle} - 1)$$

- $L(x, y) \geq L\big(x, \sum_j \beta_j(x) h_j\big) = 0$
- $L(x, y) < \infty$ iff
  $\exists \mu \in \mathbb{R}_+^k$ s.t. $y = \sum_j \mu_j h_j$ and $\mu_j > 0 \Rightarrow \beta_j(x) > 0$
- “Local measure” for the “energy” required for a movement from x in direction y

Rate function

- Rate function ($x \in A$)

$$I_{x,T}(\tilde{\phi}) := \begin{cases} \int_0^T L(\tilde{\phi}(t), \tilde{\phi}'(t))dt & \text{for } \tilde{\phi}(0) = x \text{ and } \tilde{\phi} \text{ is abs. cont.} \\ \infty & \text{else} \end{cases}$$

- $I_{x,T}(\phi) = 0$ iff ϕ solves (4) on $[0, T]$
- Interpretation of $I_{x,T}(\tilde{\phi})$: the “energy” required for a deviation from ϕ

Large deviations principle

- For appropriate assumptions (which are satisfied for the SIV-model with immigration)

Theorem (work in progress)

For $G \subset D([0,T];A)$ open and $x \in A$,

$$\liminf_{N\to\infty} \frac{1}{N} \log \mathbb{P}[Z^N \in G] \geq -\inf_{\tilde{\phi}\in G} I_{x,T}(\tilde{\phi}).$$

For $F \subset D([0,T];A)$ closed and $x \in A$,

$$\limsup_{N\to\infty} \frac{1}{N} \log \mathbb{P}[Z^N \in F] \leq -\inf_{\tilde{\phi}\in F} I_{x,T}(\tilde{\phi}).$$

- Problem: $\beta_j(x) \to 0$ for $x \to \partial A$ is possible

Exit from domain

- $G =$ domain of attraction of an equilibrium x^*; $x \in G$
- When does Z^N exit from G (and enter the domain of attraction of another equilibrium)?
  - $\tau^N := \inf\{t > 0 | Z^N(t) \in A \setminus G\}$
- Where does Z^N exit G (and "on" which trajectory)?
- $T > 0$, $y, z \in A$.

$$V(y, z, T) := \inf_{\phi:\, \phi(0)=y, \phi(T)=z} I_{y,T}(\phi)$$

$$V(y, z) := \inf_{T>0} V(y, z, T)$$

$$\bar{V} := \inf_{z \in \partial G} V(x^*, z)$$

- The minimal energy required to go from y to z in $[0, T]$, respectively from y to z, respectively form x^* to the boundary

Time of exit

- For appropriate assumptions:

Corollary (work in progress)

$x \in G$, $\delta > 0$.

$$\lim_{N\to\infty} \mathbb{P}[e^{N(\bar{V}+\delta)} > \tau^N] = 1, \quad \lim_{N\to\infty} \mathbb{P}[e^{N(\bar{V}-\delta)} < \tau^N] = 1.$$

- This follows from the LDP (once it is completely established)

Place of exit

- For appropriate assumptions:

Theorem (work in progress)

$x \in G$, $F \subset \partial G$ closed, $\inf_{z \in F} V(x^*, z) > \bar{V}$.

$$\lim_{N \to \infty} \mathbb{P}[Z^N(\tau^N) \in F] = 0.$$

In particular, if there exists a $z^* \in \partial G$ such that for all $z \neq z^*$ $V(x^*, z^*) < V(x^*, z)$, then for $\delta > 0$,

$$\lim_{N \to \infty} \mathbb{P}[|Z^N(\tau^N) - z^*| < \delta] = 1.$$

- Problem: ∂G is the "characteristic boundary" of G, i.e., for $x \in G$, $\lim_{t \to \infty} \phi(t) \neq x^*$.

Overview

Diffusion approximation

$$Y^N(t) = x + \int_0^t b(Y^N(s))ds + \frac{1}{N} \sum_j h_j W_j\Big(\int_0^t N\beta_j(Y^N(s))ds\Big),$$

- W_j ($j = 1, \dots, k$): standard independent Brownian motions

Theorem (Kurtz)

There exists a RV $X = X(N, T)$ whose distribution is independent of N with $\mathbb{E}[\exp(\lambda X)] < \infty$ for some $\lambda > 0$ such that

$$\sup_{0 \le t \le T} |Z^N(t) - Y^N(t)| \le X \frac{\log N}{N}.$$

- Problem: Kurtz' Theorem does not explain the long-term behavior of the process
  - Pakdaman et al. (2010):
    Z^N and Y^N can differ not only quantitatively but also qualitatively

Literature

R. Anguelov, Y. Dumont, J. Lubuma, and M. Shillor. Dynamically consistent nonstandard finite difference schemes for epidemiological models. *Journal of Computational and Applied Mathematics*, 255:161–182, 2014.

F. Campillo and C. Lobry. Effect of population size in a predator-prey model. *Ecological Modelling*, 246:1–10, 2012.

C. M. Kribs-Zaleta and Velasco-Hernández. A simple vaccination model with multiple endemic states. *Math. Biosci.*, 164(2):183–201, 2000.

K. Pakdaman, M. Thieullen, and G. Wainrib. Diffusion approximation of birth-death processes: Comparison in terms of large deviations and exit points. *Statistics & Probability Letters*, 80(13-14):1121–1127, 2010.