Approximation of epidemic models by diffusion processes and their statistical inference

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TALK 2-Part 2
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Size-normalized Process $Z_N(t)$

- Epidemic in a close population of size N
- p: Number of health states (or compartments)
- Jump Markov process on $E = \{0, \dots, N\}^p$
- Jump rates: $z \in E$, $z \rightarrow z + \ell$ at rate $\alpha_\ell(z)$.

Normalized process $Z_N(t) = \frac{1}{N} Z(t)$

- Pure Jump Markov State space $E_N = \{\frac{z}{N}, z \in E\}$,
- Jump rates : For $x \in E_N$, $x \rightarrow x + \frac{\ell}{N}$ at rate $\alpha_\ell(Nx)$.

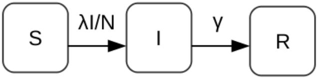
$Z_N(t)$ density dependent process if (H1) is satisfied

Assumption **(H1)**: $\forall (\ell, y) \in E^- \times [0,1]^p$, $\frac{1}{N}\alpha_\ell([Ny]) \rightarrow \beta_\ell(y)$.

Notation: if $u = (u_1, \dots, u_p) \in \mathbb{R}^p$, $[u] = ([u_1], \dots, [u_p])$; $[u_i]$= integer part of u_i.

Diffusion approximation of the *SIR* in a closed population

Population size $N \to Z_N(t) = (\frac{S(t)}{N}, \frac{I(t)}{N})$.



$(S, I) \to (S-1, I+1)$: $\alpha_{(-1,1)}(S, I) = \lambda S \frac{I}{N}$,
$(S, I) \to (S, I-1)$: $\alpha_{(0,-1)}(S, I) = \gamma I$

(1) Two transition rates corresponding to $\ell = (-1, 1), (0, -1)$

(2) Let $x = (s, i) \in [0, 1]^2$ and $\theta = (\lambda, \gamma)$
$\frac{1}{N}\alpha_{(-1,1)}([Nx]) \to \beta_{(-1,1)}(s, i) = \lambda si$; $\frac{1}{N}\alpha_{(0,-1)}([Nx]) \to \beta_{(0,-1)}(s, i) = \gamma i$.

(3) Computation of $b_\theta(x)$ for $x = (s, i)$

$$b_\theta(s, i) = \lambda si \begin{pmatrix} -1 \\ 1 \end{pmatrix} + \gamma i \begin{pmatrix} 0 \\ -1 \end{pmatrix} = \begin{pmatrix} -\lambda si \\ \lambda si - \gamma i \end{pmatrix}.$$

ODE: $x(t) = (s(t), i(t))$: $\frac{ds}{dt} = -\lambda si$ and $\frac{di}{dt} = \lambda si - \gamma i$.

Diffusion approximation of the *SIR* (2)

Recall that $\Sigma_\theta(x) := \sum_\ell \ell \; {}^t\ell \; \beta_\ell(x)$.

(4) Computation of the diffusion matrix $\Sigma_\theta(y)$

$$\Sigma_\theta(s,i) = \lambda si \begin{pmatrix} -1 \\ 1 \end{pmatrix} \begin{pmatrix} -1 & 1 \end{pmatrix} + \gamma i \begin{pmatrix} 0 \\ -1 \end{pmatrix} \begin{pmatrix} 0 & -1 \end{pmatrix} = \begin{pmatrix} \lambda si & -\lambda si \\ -\lambda si & \lambda si + \gamma i \end{pmatrix}.$$

Square root $\sigma_\theta(x)$ of $\Sigma_\theta(x)$ (i.e. $\sigma_\theta(x) \; {}^t\sigma_\theta(x)$) :

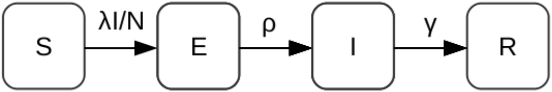
$$\sigma_\theta(s,i) = \begin{pmatrix} \sqrt{\lambda si} & 0 \\ -\sqrt{\lambda si} & \sqrt{\gamma i} \end{pmatrix}.$$

Diffusion approximation $X_N(t) = (S_N(t), I_N(t))$

$$\begin{aligned} dS_N(t) &= -\lambda S_N(t) I_N(t) dt + \frac{1}{\sqrt{N}} \sqrt{\lambda S_N(t) I_N(t)} dB_1(t), \\ dI_N(t) &= (\lambda S_N(t) I_N(t) - \gamma I_N(t)) dt \\ &+ \frac{1}{\sqrt{N}} \left(-\sqrt{\lambda S_N(t) I_N(t)} dB_1(t) + \sqrt{\gamma I_N(t)} dB_2(t) \right) \end{aligned}$$

SEIR model with temporal transmission rate

Camacho et al. PLoS Curr, 2015;7.



$(S, E, I) \to (S-1, E+1, I)$ at rate $S\ \lambda(t)\frac{I}{N}$,
$(S, E, I) \to (S, E-1, I+1)$ at rate $\rho\ E$
$(S, E, I) \to (S, E, I-1)$ at rate $\gamma\ I$

(1) Three transitions α_ℓ corresponding to $\ell = (-1,1,0)', (0,-1,1)', (0,0,-1)'$

(2) Set $x = (s, e, i) \in [0,1]^3$ and $\theta = (\lambda(t), \rho, \gamma)$. Then
$\beta_{(-1,,1,0)}(s,e,i) = \lambda(t)si$, $\beta_{(0,-1,1)}(s,e,i) = \rho e$ and
$\beta_{(0,0,-1)}(s,e,i) = \gamma i$.

(3) Computation of $b_\theta(t; x)$

$$b(\theta; s, e, i) = \lambda(t)si \begin{pmatrix} -1 \\ 1 \\ 0 \end{pmatrix} + \rho e \begin{pmatrix} 0 \\ -1 \\ 1 \end{pmatrix} + \gamma i \begin{pmatrix} 0 \\ 0 \\ -1 \end{pmatrix} = \begin{pmatrix} -\lambda si \\ \lambda si - \rho e \\ \rho e - \gamma i \end{pmatrix}.$$

$SEIR$ model with temporal transmission rate (2)

ODE $x(t) = (s(t), e(t), i(t))$
$\frac{ds}{dt} = -\lambda(t)si$, $\frac{de}{dt} = \lambda si - \rho e$ and $\frac{di}{dt} = \rho e - \gamma i$.

(4) Computation of the diffusion matrix $\Sigma_\theta(t; x)$ for $x = (s, e, i)$

$$\Sigma_\theta(t; x) = \begin{pmatrix} \lambda(t)si & -\lambda(t)si & 0 \\ -\lambda(t)si & \lambda(t)si + \rho e & -\rho e \\ 0 & -\rho e & \rho e + \gamma i \end{pmatrix}.$$

Choosing $\sigma_\theta(t; x) = \begin{pmatrix} \sqrt{\lambda(t)si} & 0 & 0 \\ -\sqrt{\lambda(t)si} & \sqrt{\rho e} & 0 \\ 0 & -\sqrt{\rho e} & \sqrt{\gamma i} \end{pmatrix}$

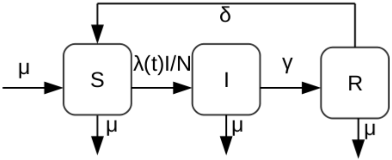
Then the diffusion is

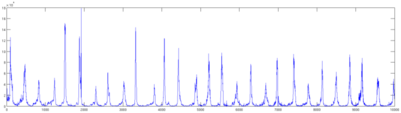
$$dS_N(t) = -\lambda(t)S_N I_N dt + \frac{1}{\sqrt{N}}\sqrt{\lambda(t)S_N I_N} dB_1(t),$$
$$dE_N(t) = (\lambda(t)S_N I_N - \rho E_N)dt + \frac{1}{\sqrt{N}}(-\sqrt{\lambda(t)S_N I_N} dB_1(t) + \sqrt{\rho E_N} dB_2(t)),$$
$$dI_N(t) = (\rho E_N - \gamma I_N)dt + \frac{1}{\sqrt{N}}(-\sqrt{\rho E_N} dB_2(t) + \sqrt{\gamma I_N} dB_3(t)).$$

$(B(t) = {}^t B_1(t), B_2(t), B_3(t)$ standard Brownian motion on $\mathbb{R}^3)$

A mechanistic model for recurrent epidemics

SIRS **model with seasonal forcing** (Keeling et Rohanni, 2011)





Notations supplémentaires

- δ: Immunity waning rate (per year)$^{-1}$,
- μ (Population renewal): birth rate and death rate (per decades)$^{-1}$
- $\lambda(t) = \lambda_0(1 + \lambda_1\, sin(2\pi \frac{t}{T_{per}}))$,
- λ_0 Baseline transition rate, λ_1 :intensity of the seasonal effect,
- T_{per}: period of the seasonal trend.

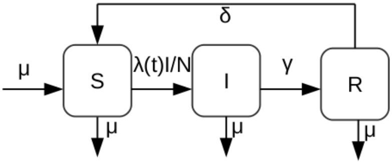
Important: $\lambda_1 = 0 \Rightarrow$ Damping out oscillations $\Rightarrow$ need to have a temporal forcing

Appropriate model for recurrent epidemics in very large populations

Key parameters: $R_0 = \frac{\lambda_0}{\gamma+\mu}$, $d = \frac{1}{\gamma}$,Average waning period: $\frac{1}{\delta T_{per}}$

SIRS model with seasonal forcing in a closed population

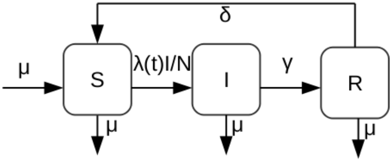
$\Rightarrow Z(t) = (S(t), I(t)) \in E = \{0, \ldots, N\}^2$,
$\ell = (-1, 1), (0, -1), (1, 0), (-1, 0)$.



$(S, I) \rightarrow (S-1, I+1) : \alpha_{(-1,1)}(t; S, I) = \lambda(t) S \, \frac{I}{N}$,
$(S, I) \rightarrow (S, I-1) : \alpha_{(0,-1)}(S, I) = (\gamma + \mu) I$,
$(S, I) \rightarrow (S+1, I) : \alpha_{(1,0)}(S, I) = \mu N + \delta(N - S - I)$,
$(S, I) \rightarrow (S-1, I) : \alpha_{(-1,0)}(S, I) = \mu S$.
$\lambda(t) = \lambda_0 (1 + \lambda_1 sin(2\pi \frac{t}{T_{per}})) \Rightarrow$ Time-inhomogeneous Markov process.

Remark: Simulations are easy with Gillespie's algorithm

Approximation of the *SIRS* model with seasonal forcing



$\beta_{(-1,1)}(s,i) = \lambda(t)si$; $\beta_{(0,-1)}(s,i) = (\gamma+\mu)i$; $\beta_{(-1,0)}(s,i) = \mu s$;
$\beta_{1,0}(s,i) = \mu + \delta(1-s-i)$.

Computation of $b_\theta(t;s,i)$ and $\Sigma_\theta(t;s,i) = \Sigma$.

$$b_\theta(t;s,i) = \begin{pmatrix} b_{\theta,1}(t;s,i) \\ b_{\theta,2}(t;s,i) \end{pmatrix} = \begin{pmatrix} -\lambda(t)si + \delta(1-s-i) + \mu(1-s) \\ \lambda(t)si - (\gamma+\mu)i \end{pmatrix}.$$

$$\Sigma = \begin{pmatrix} \lambda(t)si + \delta(1-s-i) + \mu(1+s) & -\lambda(t)si \\ -\lambda(t)si & \lambda(t)si + (\gamma+\mu)i \end{pmatrix}.$$

Diffusion approximation of the *SIRS* model (2)

Diffusion approximation $X_N(t)$

Time- dependent $b_\theta(t; s, i)$ $\Sigma_\theta(t, s, i)$

Let $\sigma_\theta(t, x)$ denote the Cholevski decomposition of Σ:
$\sigma_\theta(t, x)\,{}^t\sigma_\theta(t, x) = \Sigma_\theta(t, x)$ with $\sigma_{\theta,12}(t, x) = 0$.

$$dS_N(t) = b_{\theta,1}(t, S_N, I_N)dt + \frac{1}{\sqrt{N}}\sigma_{\theta,11}(t, S_N, I_N)dB_1(t)$$
$$dI_N(t) = b_{\theta,2}(t, S_N, I_N)dt + \sigma_{\theta,21}(t, S_N, I_N)dB_1(t) + \sigma_{\theta,22}(t, S_N, I_N)dB_2(t)$$