SIR epidemics with stochastic infectious periods

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Table of contents

Table of contents

SIR models

SIR models : spread of an epidemic among a closed and homogeneous population, according to the scheme :

$$S \longrightarrow I \longrightarrow R$$

- S : healthy individuals, but susceptible to be contaminated.
- I : infected individuals, who can contaminate the healthy ones (independently of each other).
- R : infected individuals whose infection period is over. They take no longer part to the infection process (removed).

Stochastic infectious periods

Let X be a continuous time Markov process on $\mathcal{E} \cup \{\star\}$ where

- $\mathcal{E}$ is a set of transient states,
- the state $\star$ is absorbing.

When an individual i gets infected, a process X_i with the same evolution rules as X takes off to modulate his infectious period :

- The initial state of X_i is given by the cdf $\alpha(\cdot)$ on $\mathcal{E}$.
- When $X_i = x \in \mathcal{E}$, his instantaneous contamination rate is $S(t)\beta(x)$.
- When X_i is absorbed, the infected individual is removed.

$S(0) = n$, $R(0) = 0$ and $I(0)$ may be random, as well as the initial state of the initial infection processes.

Final epidemic outcome

The epidemic terminates at time $T = \inf\{t \geq 0 \mid I(t) = 0\}$.

Statistics of interest :

- the final number $S(T)$ of susceptibles,
- the final severity $\mathcal{A}(T) = \int_0^T \sum_{i=1}^{I(u)} a(X_i(u))\, du = \sum_{i=1}^{R(T)} D_i$

  where D_i is the total severity due to the i-th infected individual.

Assumptions :

- The processes $\beta(X)$ and $a(X)$ are càdlàg,
- $\tau_\star = \inf\{t \geq 0 \mid X(t) = \star\}$ is a.s. finite,
- The different versions X_i that activate throughout the epidemic are independent of each other.

Martingales

Let $\mathcal{F}$ be the filtration generated by the whole epidemic process.

Theorem

For each $k \in \{0, 1, 2, ..., n\}$ and $\theta \geq 0$, the process

$$\left\{ \binom{S(t)}{k} \rho(k,\theta)^{S(t)} \, e^{-\theta \mathcal{A}(t)} \prod_{i=1}^{I(t)} q(k,\theta,X_i(t)) \,\middle|\, t \in \mathbb{R}^+ \right\}$$

is a martingale with respect to $\mathcal{F}$ when

$$q(k,\theta,x) = \mathbb{E}\left[e^{-\int_0^{\tau_\star} \left(\theta a(X(u)) + k\beta(X(u))\right) du} \,\middle|\, X(0) = x \right],$$

$$\rho(k,\theta) = 1 - \int_{\mathcal{E}} d\alpha(y) + \int_{\mathcal{E}} q(k,\theta,y) \, d\alpha(y).$$

Final epidemic outcome

Applying the optional stopping theorem, for all $k \in \{0, ..., n\}$ and $\theta \geq 0$,

$$\mathbb{E}\left[\binom{S(T)}{k}\rho(k,\theta)^{S(T)}\, e^{-\theta\mathcal{A}(T)}\right] = \binom{n}{k}\rho(k,\theta)^n\,\mathbb{E}\left[\prod_{i=1}^{I(0)} q(k,\theta,X_i(0))\right].$$

▷ A triangular system to determine the distribution of $S(T)$:

$$\sum_{s=k}^{n}\binom{s}{k}\rho(k,0)^s\,\mathbb{P}\left(S(T)=s\right) = \binom{n}{k}\rho(k,0)^n\,\mathbb{E}\left[\prod_{i=1}^{I(0)} q(k,0,X_i(0))\right].$$

▷ The moments of the final severity. In particular,

$$\mathbb{E}\left[\mathcal{A}(T)\right] = \Big(n - \mathbb{E}\left[S(T)\right]\Big)\,\mathbb{E}\left[D \,|\, X(0)\sim\alpha\right] + \mathbb{E}\left[\sum_{i=1}^{I(0)}\mathbb{E}\left[D \,|\, X_i(0)\right]\right].$$

Example

Classical SIR model :

- Infectious periods of duration $L \sim F(\cdot)$,
- Contamination rate $\beta S(t)$ per infected individual.
- Probability p of detection for any newly infected individual.

Here,

- X is a Markov process with transient state space $\mathcal{E} = \mathbb{R}^+$,
  $X = s$ if the infectious period started s units of time ago ($X(0) = 0$).
- $\beta(x) = \beta$ and $a(x) = 1 \;\; \forall x \in \mathbb{R}^+$.

The coefficients $q(k, \theta) \equiv q(k, \theta, 0)$ are given by

$$q(k, \theta) = \mathbb{E}\left[e^{-(k\beta+\theta)D}\right] = \hat{F}(k\beta + \theta),$$

and $\rho(k, \theta) = p + (1 - p)q(k, \theta)$.

Example

Brownian infectious periods :

- X is a Brownian motion with negative drift $-d$ and variance σ^2,
- $\beta(x) = \gamma x$ and $a(x) = ax$ (for fixed $\gamma, a > 0$),
- $X(0) > 0$ and absorption occurs at time $\tau_\star = \inf\{t > 0 \,|\, X(t) = 0\}$.

Here,

$$q(k,\theta,x) = e^{\frac{d}{\sigma^2}x} Ai\left(\frac{\frac{d^2}{\sigma^2} + 2(k\gamma + a\theta)x}{(2\sigma(k\gamma + a\theta))^{\frac{2}{3}}}\right)\left[Ai\left(\frac{\frac{d^2}{\sigma^2}}{(2\sigma(k\gamma + a\theta))^{\frac{2}{3}}}\right)\right]^{-1}$$

where Ai is the standard Airy function :

$$Ai(y) = \frac{1}{\pi}\int_0^\infty \cos\left((t^3/3) + yt\right) dt.$$

Moreover,

$$\mathbb{E}\left[\tau_\star \,|\, X(0)=x\right] = \frac{x}{d} \quad \text{and} \quad \mathbb{E}\left[D \,|\, X(0)=x\right] = \frac{ax\sigma^2}{2d^2} + \frac{ax^2}{2d}.$$

Illustration :

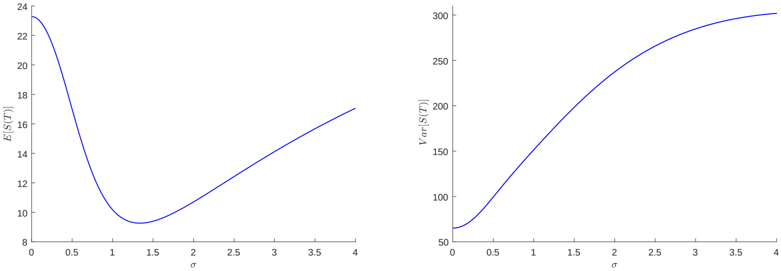

FIGURE – $S(0)=37$, $I(0)=3$, $X(0)=1$, $p=0$, $d=0.8$ and $\beta=0.05$.

Table of contents

Markov-modulated fluid flows (MMFF)

An MMFF is a process $(Y, \varphi) = \{(Y(t), \varphi(t)) \,|\, t \in \mathbb{R}^+\}$ in which

- φ is a Markov process on a finite space $\mathcal{S}$, with generator Q. To each phase $i \in \mathcal{S}$ one associates a rate $c_i \neq 0$.
- Y takes its values in $[0, B]$ and has the following dynamics :

$$\frac{d}{dt} Y(t) = \begin{cases} c_{\varphi(t)} & \text{if } 0 < Y(t) < B, \\ \max(0, c_{\varphi(t)}) & \text{if } Y(t) = 0, \\ \min(0, c_{\varphi(t)}) & \text{if } Y(t) = B. \end{cases}$$

Denoting by C the diagonal matrix of rates, we write Q and C according to the subdivision $\mathcal{S}_+ = \{i \in \mathcal{S} \,|\, c_i > 0\}$ and $\mathcal{S}_- = \{i \in \mathcal{S} \,|\, c_i < 0\}$:

$$Q = \begin{bmatrix} Q_{++} & Q_{+-} \\ Q_{-+} & Q_{--} \end{bmatrix}, \qquad C = \begin{bmatrix} C_+ & \\ & C_- \end{bmatrix}.$$

SIR model with fluid infectious periods

We consider the class of SIR model where

- $X = (Y, \varphi)$ is a two-sided MMFF and $\mathcal{E} = \{(y, i) \,|\, y \in [0, B], i \in \mathcal{S}\}$.
- $[0, B]$ is partitioned into $[v_0, v_1[, [v_1, v_2[, \cdots, [v_{N-1}, v_N]$ and

$$\beta(x, i) = \frac{\beta_{l,i}}{n} \;\; \text{when } x \in [v_l, v_{l+1}[,$$
$$a(x, i) = a_{l,i} \;\; \text{when } x \in [v_l, v_{l+1}[.$$

- The initial distribution vector is $\boldsymbol{\alpha} = [\boldsymbol{\alpha}_0 \;\; \boldsymbol{\alpha}_1 \;\; \cdots \;\; \boldsymbol{\alpha}_N]$ where

$$(\boldsymbol{\alpha}_l)_i = \mathbb{P}\left(Y(0) = v_l, \varphi(0) = i\right).$$

- (Y, φ) is absorbed at time $\tau_\star = \inf\{t > 0 \,|\, Y(t) = 0\}$.

Coefficients $q(k, \theta, x)$

let $\delta_y = \inf\{t > 0 \mid Y(t) = y\}$. The coefficients $q(\cdot)$ we need here may be written as

$$q(k, \theta, (v_l, i)) = \mathbb{E}\left[e^{-\int_0^{\delta_0} \left(\theta a(Y(t),\varphi(t)) + k\beta(Y(t),\varphi(t))\right) dt} \,\middle|\, Y(0) = v_l, \varphi(0) = i \right].$$

To compute them, we start by determining

$$W_{ij}(l) = \mathbb{E}\left[e^{-\int_0^{\delta_{v_{l-1}}} \left(\theta a(Y(t),\varphi(t)) + k\beta(Y(t),\varphi(t))\right) dt} \mathbb{1}_{\varphi(\delta_{v_{l-1}})=j} \,\middle|\, Y(0) = v_l, \varphi(0) = i \right]$$

for $0 \leq l \leq N$, $i \in \mathcal{S}$ and $j \in \mathcal{S}_-$. Then, for $1 \leq l \leq N$,

$$q(k, \theta, (v_l, i)) = \left[W(l) W_-(l-1) W_-(l-2) \cdots W_-(1) \mathbf{1} \right]_i.$$

Mean final severity

The total severity due to a single infected individual is

$$
\begin{aligned}
D &= \int_0^{\mathcal{T}_\star} a(Y(u), \varphi(u))\, du \\
&= \sum_{r=0}^{N-1} \sum_{j \in \mathcal{S}} a_{r,j} \int_0^{\mathcal{T}_\star} \mathbb{1}_{Y(u) \in [v_r, v_{r+1}], \varphi(u)=j}\, du.
\end{aligned}
$$

To compute $\mathbb{E}\left[\mathcal{A}(T)\right]$, we need to determine

$$
\mathbb{E}\left[D \mid Y(0) = v_l, \varphi(0) = i\right] = \sum_{r=0}^{N-1} \sum_{j \in \mathcal{S}} a_{r,j}\, M_{ij}(l, r),
$$

where

$$
M_{ij}(l, r) = \mathbb{E}\left[\int_0^{\mathcal{T}_\star} \mathbb{1}_{Y(u) \in [v_r, v_{r+1}], \varphi(u)=j}\, du \,\middle|\, Y(0) = v_l, \varphi(0) = i\right].
$$

Basic reproduction number

The matrices $M(l,r)$ also provide us with one of the most frequently used estimators of the virulence of the epidemic :

R_0 = average number of infections made by a single infected individual facing infinitely many susceptibles.

When $S = \infty$, an infected individual at level $x \in [v_l, v_{l+1}[$ in phase j makes contaminations at rate $\beta_{l,j}$. So,

$$R_0(\boldsymbol{\alpha}) = \mathbb{E}\left[\int_0^{\tau_\star} \sum_{r=0}^{N-1} \sum_{j\in\mathcal{S}} \beta_{r,j} \mathbb{1}_{Y(u)\in[v_r,v_{r+1}],\varphi(u)=j}\, du\right]$$
$$= \sum_{l=0}^{N} \sum_{r=0}^{N-1} \sum_{i\in\mathcal{S}} \sum_{j\in\mathcal{S}} (\boldsymbol{\alpha}_l)_i\, \beta_{r,j}\, M_{ij}(l,r).$$

Matrices $M(l, r)$

For $x > 0$ define

$$
\begin{aligned}
\Gamma_{ij}(x) &= \mathbb{P}\left(\delta_0 < \delta_x, \varphi(\delta_0) = j \,|\, Y(0) = 0, \varphi(0) = i\right) && (i \in \mathcal{S}_+, j \in \mathcal{S}_-),\\
\Gamma^*_{ij}(x) &= \mathbb{P}\left(\delta_x < \delta_0, \varphi(\delta_x) = j \,|\, Y(0) = x, \varphi(0) = i\right) && (i \in \mathcal{S}_-, j \in \mathcal{S}_+),\\
\Lambda_{ij}(x) &= \mathbb{P}\left(\delta_x < \delta_0, \varphi(\delta_x) = j \,|\, Y(0) = 0, \varphi(0) = i\right) && (i, j \in \mathcal{S}_+),\\
\Lambda^*_{ij}(x) &= \mathbb{P}\left(\delta_0 < \delta_x, \varphi(\delta_0) = j \,|\, Y(0) = x, \varphi(0) = i\right) && (i, j \in \mathcal{S}_-),\\
A_{ij}(x) &= \mathbb{P}\left(\varphi(\delta_x) = j \,|\, Y(0) = x, \varphi(0) = i\right) && (i \in \mathcal{S}_+, j \in \mathcal{S}_-).
\end{aligned}
$$

$$
\left.\begin{aligned}
M_+(l, r) &= \left(I - \Gamma(v_r - v_l)\Gamma^*(v_l)\right)^{-1} \Lambda(v_r - v_l) M_+(r, r)\\
M_-(l, r) &= \Gamma^*(v_l) M_+(l, r)
\end{aligned}\right. \qquad (r > l),
$$

$$
\left.\begin{aligned}
M_-(l, r) &= \left(I - \Gamma^*(v_l - v_{r+1}) A(v_l)\right)^{-1} \Lambda^*(v_l - v_{r+1}) M_-(r+1, r)\\
M_+(l, r) &= A(v_l) M_-(l, r)
\end{aligned}\right. \qquad (r < l-1).
$$

Matrices $M(l, r)$

Proposition $(r < N-1)$

$M_-(r,r) = \Gamma^*(v_r)M_+(r,r)$ *and* $M_+(r+1,r) = A(v_{r+1})M_-(r+1,r)$.

The matrices $M_+(r,r)$ *and* $M_-(r+1,r)$ *are given by*

$$\begin{bmatrix} M_+(r,r) \\ M_-(r+1,r) \end{bmatrix} = \begin{bmatrix} L(w_r) \\ \tilde{L}(w_r) \end{bmatrix} + \begin{bmatrix} \Gamma(w_r)\Gamma^*(v_r) & \Lambda(w_r)A(v_{r+1}) \\ \Lambda^*(w_r)\Gamma^*(v_r) & \Gamma^*(w_r)A(v_{r+1}) \end{bmatrix} \begin{bmatrix} M_+(r,r) \\ M_-(r+1,r) \end{bmatrix}$$

where $w_r = v_{r+1} - v_r$ *and*

- $L_{ij}(x)$ *is the average time spent in phase* $j \in \mathcal{S}$ *before reaching level zero or* x*, starting from* $(x, i \in \mathcal{S}_+)$,
- $\tilde{L}_{ij}(x)$ *is the average time spent in phase* $j \in \mathcal{S}$ *before reaching level zero or* x*, starting from* $(x, i \in \mathcal{S}_-)$.

Matrices $M(l, r)$

Proposition ($r = N-1$)

$$M_-(N-1, N-1) = \Gamma^*(v_{N-1}) M_+(N-1, N-1),$$
$$M_+(N, N-1) = [(-Q_{++})^{-1} \;\; 0] + (-Q_{++})^{-1} Q_{+-} M_-(N, N-1).$$

The matrices $M_+(N-1, N-1)$ *and* $M_-(N, N-1)$ *are given by*

$$\begin{bmatrix} M_+(N-1, N-1) \\ M_-(N, N-1) \end{bmatrix} = \begin{bmatrix} L(w_{N-1}) \\ \tilde{L}(w_{N-1}) \end{bmatrix} + \begin{bmatrix} \Lambda(w_{N-1}) \\ \Gamma^*(w_{N-1}) \end{bmatrix} \begin{bmatrix} (-Q_{++})^{-1} & 0 \end{bmatrix}$$
$$+ \begin{bmatrix} \Gamma(w_{N-1})\Gamma^*(v_{N-1}) & \Lambda(w_{N-1})(-Q_{++})^{-1} Q_{+-} \\ \Lambda^*(w_{N-1})\Gamma^*(v_{N-1}) & \Gamma^*(w_{N-1})(-Q_{++})^{-1} Q_{+-} \end{bmatrix} \begin{bmatrix} M_+(N-1, N-1) \\ M_-(N, N-1) \end{bmatrix}.$$

Example

The process (Y, φ) is an MMFF on the level space $[0, 1]$ and ruled by the matrices

$$Q = \begin{bmatrix} -1 & 1 \\ 1 & -1 \end{bmatrix}, \qquad C = \begin{bmatrix} 2 & \\ & -1 \end{bmatrix}.$$

The infectious periods start at level zero in the ascending phase, and

$$\beta_{l,i} = \begin{cases} \frac{\gamma}{n}\frac{l}{N} & \text{if } x \in [v_l, v_{l+1}[\text{ and } i \in \mathcal{S}_+, \\ 0 & \text{else,} \end{cases}$$

$$a(x,i) = \begin{cases} \frac{\alpha l}{N} & \text{if } x \in [v_l, v_{l+1}[\text{ and } i \in \mathcal{S}_-, \\ 0 & \text{else,} \end{cases}$$

Example

N	**10**	**20**	**50**	**100**	**200**	**500**	**1000**	**2000**
$\mathbb{E}[S(T)]$	7.70	6.84	6.37	6.23	6.16	6.12	6.10	6.10
$\mathbb{V}ar[S(T)]$	128	121	116	114	114	113	113	113
$\mathbb{E}[D]$	0.64	0.67	0.69	0.70	0.70	0.70	0.70	0.70
$\mathbb{E}[\mathcal{A}(T)]$	20.6	22.2	23.2	23.5	23.7	23.8	23.8	23.8
R_0	2.70	2.85	2.94	2.97	2.99	2.99	3.00	3.00

TABLE – $n = 37$, $m = 3$, $\gamma = 1.5$, $\alpha = 1$. Here, $\mathbb{E}[\tau_\star] = 3.6$.

End

Thank you for your attention.