SIR epidemics with stages of infection

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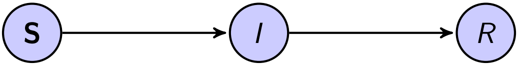
Table of contents

Table of contents

SIR models

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



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

SIR models with stages

We consider a SIR model with

- L stages of infection $1, 2, ..., L$
  (e.g. for different degrees of infectiousness).
- p types of elimination $\star_1, \star_2, ..., \star_p$.
  (e.g. death or immunization).

At the beginning : n susceptibles ans m_j infectives in phase j.

When contaminated, a susceptible begins in an initial stage given by $\boldsymbol{\alpha}$.

Transitions between stages

Contagion process

When in stage j, an infective contaminates the s available susceptibles according to a Poisson process with parameter $\frac{s\beta_j}{n}$.

Transitions for an infective

For each infective, a Markov process $\{\varphi(t)\}$ modulates the transitions between stages and the elimination time.
Defined on $\{\star_1, \star_2, \ldots, \star_p, 1, 2, \ldots, L\}$ and with generator

$$Q = \left[\begin{array}{cccc|c} & & 0 & & 0 \\ \hline \boldsymbol{a}_1 & \boldsymbol{a}_2 & \cdots & \boldsymbol{a}_p & A \end{array}\right].$$

Here, $t \in \mathbb{R}^+$ is the local time of an infection process.

Epidemic outcome

Let T be the ending time of the epidemic :

$$T = \inf\{t \geq 0 \mid I(t) = 0\}.$$

We aim to determine the joint distribution of the statistics :

- S_T : final size of the epidemic,
- $R_T^{(r)}$: final number of eliminations of type r,
- A_T : cumulative total duration of all infection periods.

Table of contents

Artificial time

Time change : We follow the infectives one after the other.

$\triangleright$ Discrete time $\tau = 0, 1, 2, ...$

- S_τ = number of susceptibles after τ infectives,
  $R_\tau^{(r)}$ = number of eliminations of type r after τ infectives,
  A_τ = cumulative duration of the first τ infection periods.
- Initially, $S_0 = n$, $A_0 = 0$, $R_0^{(r)} = 0$.

In this artificial time, the epidemic terminates at time

$$\tilde{T} = \inf\{\tau \,|\, \tau + S_\tau = n + m\}.$$

By the characteristics of the model,

$$(S_{\tilde{T}}, A_{\tilde{T}}, R_{\tilde{T}}^{(1)}, ..., R_{\tilde{T}}^{(p)}) \stackrel{d}{=} (S_T, A_T, R_T^{(1)}, ..., R_T^{(p)}).$$

Useful relations in the artificial time

Suppose that the τ-th infective begins in stage j. Then

$$\binom{S_\tau}{k} = \sum_{u=1}^{\binom{S_{\tau-1}}{k}} \mathbb{1}_j(k;u),$$
$$A_\tau = A_{\tau-1} + D_j,$$
$$R_\tau^{(r)} = R_{\tau-1}^{(r)} + 1_{j,r},$$

$\mathbb{1}_j(k) = \mathbb{I}$(a fixed group of k susceptibles escape from the infective)

$1_j(r) = \mathbb{I}$(the infective will become an eliminated of type r)

$D_j =$ infection duration of the infective.

Martingales for the epidemic outcome

With the preceding relations, one can show that for each $k = 0, 1, ..., n$, $\theta \geq 0$ and $\boldsymbol{z} \in \mathbb{R}^p$, the process

$$\left\{ \binom{S_\tau}{k} \frac{e^{-\theta A_\tau}}{q(k,\theta,\boldsymbol{z})^\tau} \prod_{r=1}^{p} {z_r}^{R_\tau^{(r)}} \;, \tau \geq m = m_1 + \cdots + m_L \right\}$$

is a martingale, provided that

$$\begin{aligned} q(k,\theta,\boldsymbol{z}) &= \sum_{j=1}^{L} \alpha_j \, q_j(k,\theta,\boldsymbol{z}), \\ q_j(k,\theta,\boldsymbol{z}) &= E\left[\mathbb{1}_j(k)\, e^{-\theta D_j} \prod_{r=1}^{p} {z_r}^{1_j(r)} \right]. \end{aligned}$$

Joint distribution of S_T, A_T and $R_T^{(r)}$

Applying the optional stopping theorem on this martingale for $\tilde{T} = \inf\{\tau \,|\, \tau + S_\tau = n + m\}$, after having considered the effect of the initial infectives :

Proposition

For $0 \leq k \leq n$, $\theta \geq 0$ *and* $\mathbf{z} \in \mathbb{R}^p$ *:*

$$E\left[\binom{S_T}{k} e^{-\theta A_T} q(k,\theta,\mathbf{z})^{S_T} \prod_{r=1}^{R} {z_r}^{R_T^{(r)}}\right] = \binom{n}{k} q(k,\theta,\mathbf{z})^n \prod_{j=1}^{L} q_j(k,\theta,\mathbf{z})^{m_j}.$$

Some consequences of the preceding formula

A triangular system to determine the distribution of S_T :

$$\begin{cases} \sum_{s=k}^{n} \binom{s}{k} q(k)^s \, \mathbb{P}(S_T = s) = \binom{n}{k} q(k)^n \prod_{j=1}^{L} q_j(k)^{m_j} \\ \sum_{s=0}^{n} \mathbb{P}(S_T = s) = 1 \end{cases},$$

where $q_j(k) \equiv q_j(k, 0, \mathbf{0})$.

The moments of A_T and $R_T^{(r)}$:

$$\mathbb{E}[A_T] = \sum_{j=1}^{L} m_j \mathbb{E}\left[D_j\right] + \left(n - \mathbb{E}[S_T]\right) \mathbb{E}[D_\alpha],$$

$$\mathbb{E}\left[R_T^{(r)}\right] = \sum_{j=1}^{L} m_j q(0, 0, \boldsymbol{e_r}) + \left(n - \mathbb{E}[S_T]\right) q_j(0, 0, \boldsymbol{e_r}).$$

Table of contents

Contagion per infective

To obtain the epidemic outcome, we only need the parameters

$$q_j(k,\theta,\boldsymbol{z}) = E\left[\mathbb{1}_j(k)\, e^{-\theta D_j} \prod_{r=1}^{p} {z_r}^{1_j(r)}\right].$$

→ We only need to analyse the behaviour of a unique infective facing k susceptibles, who are immediately removed when infected.

Let $N(k,t)$ be the number of infections generated by this single infective up to time t (t is the local time of the infectious period).

contagion process

$\{(N(k;t), \varphi(t)) \mid t \in \mathbb{R}^+\}$ is a Markov process with state space

$$\{\star_1, ..., \star_p, [(0,1), ..., (0,L)], \ldots, [(k,1), ..., (k,L)]\},$$

and its generator is

$$\left[\begin{array}{ccc|ccccc} & 0 & & & & 0 & & \\ \hline \mathbf{a_1} & \cdots & \mathbf{a_p} & A_0(k) & A_1(k) & 0 & \cdots & 0 \\ \mathbf{a_1} & \cdots & \mathbf{a_p} & 0 & A_0(k-1) & A_1(k-1) & \cdots & 0 \\ \mathbf{a_1} & \cdots & \mathbf{a_p} & 0 & 0 & A_0(k-2) & \cdots & 0 \\ \vdots & & \vdots & \vdots & \vdots & \vdots & & \vdots \\ \mathbf{a_1} & \cdots & \mathbf{a_p} & 0 & 0 & 0 & \cdots & A_1(1) \\ \mathbf{a_1} & \cdots & \mathbf{a_p} & 0 & 0 & 0 & \cdots & A \end{array}\right],$$

where $A_1(h) = \frac{h}{n}B$ and $A_0(h) = A - A_1(h)$.

Formula for the coefficients

By using the structure of this last generator, one can show that

Proposition

For $1 \leq j \leq L$,

$$q_j(k, \theta, \boldsymbol{z}) = \boldsymbol{e}_j \left[\theta I - A_0(k)\right]^{-1} \sum_{r=1}^{p} z_r \boldsymbol{a}_r.$$

The same formula holds for $q(k, \theta, \boldsymbol{z})$ *except that* α *is substituted for* $\boldsymbol{e}_j$.

Table of contents

Transitions between stages

The process $\{\varphi(t)\}$ is now a semi-Markov process with kernel

$$Q(t) = \left[\begin{array}{ccc|c} & I & & 0 \\ \hline \boldsymbol{a}_1(t) & \dots & \boldsymbol{a}_p(t) & A(t) \end{array}\right],$$

where, if δ denotes the first renewal time,

$$\begin{aligned} A_{j,v}(t) &= P[\delta \le t, \varphi(\delta) = v \mid \varphi(0) = j], \\ (\boldsymbol{a}_r)_j(t) &= P[\delta \le t, \varphi(\delta) = \star_r \mid \varphi(0) = j]. \end{aligned}$$

Epidemic outcome

- The martingales obtained in the Markovian case are still valid.
- We just need to adapt the formulae for the parameters

$$q_j(k,\theta,\mathbf{z}) = E\left[\mathbb{1}_j(k)\, e^{-\theta D_j} \prod_{r=1}^{p} {z_r}^{1_j(r)}\right].$$

- As before, we consider a unique infective facing k susceptibles

  $N(k,t)$ is be the number of infections generated by this infective ≪up to time t≫.

Contagion process

The semi-Markov kernel of $\{(N(k;t), \varphi(t))\}$ is

$$\left[\begin{array}{ccc|ccc} & I & & & 0 & \\ \hline \boldsymbol{u}_{kk}(t) & \cdots & \boldsymbol{u}_{k\,0}(t) & \mathcal{U}_{kk}(t) & \cdots & \mathcal{U}_{k\,0}(t) \\ \mathbf{0} & \cdots & \boldsymbol{u}_{k-1\,0}(t) & 0 & \cdots & \mathcal{U}_{k-1\,0}(t) \\ \vdots & & \vdots & \vdots & & \vdots \\ \mathbf{0} & \cdots & \boldsymbol{u}_{00}(t) & 0 & \cdots & \mathcal{U}_{00}(t) \end{array}\right],$$

where, if $Y(t)$ denotes the number of susceptibles at time t,

$$\begin{aligned} (\mathcal{U}_{hl})_{j,v}(t) &= P[\delta \leq t, Y(\delta) = l, \varphi(\delta) = v \mid Y(0) = h, \varphi(0) = j], \\ (\boldsymbol{u}_{hl})_{j}(t) &= P[\delta \leq t, Y(\delta) = l, \varphi(\delta) = \star \mid Y(0) = h, \varphi(0) = j]. \end{aligned}$$

Formula for the coefficients

Proposition

For $1 \leq j \leq L$,

$$q_j(k, \theta, \mathbf{z}) = \mathbf{e}_j \left[I - C_k(\theta) \right]^{-1} \sum_{r=1}^{p} z_r \mathbf{c}_{k,r}(\theta),$$

where for $0 \leq k \leq n$,

$$\begin{aligned} (C_k)_{j,v}(\theta) &= \widehat{A}_{j,v}(\theta + k\beta_j/n), \quad 1 \leq v \leq L, \\ (\mathbf{c}_{k,r})_j(\theta) &= (\widehat{\mathbf{a}}_r)_j(\theta + k\beta_j/n), \quad 1 \leq r \leq p, \end{aligned}$$

with $\widehat{A}_{j,v}$ *and* $(\widehat{\mathbf{a}}_r)_j$ *the Laplace transforms of* $A_{j,v}$ *and* $(\mathbf{a}_r)_j$.

End

Thank you for your attention.