SIR epidemics with stages of infection

Matthieu Simon (ULB)
Joint work with Claude Lefèvre (ULB)

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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 and $m_j$ infectives in phase $j$.

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

**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 $\{\star_1, \star_2, ..., \star_p, 1, 2, ..., L\}$ and with generator

$$Q = \begin{bmatrix} 0 & 0 \\ a_1 & a_2 & \cdots & a_p & A \end{bmatrix}.$$

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

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

- Discrete time $\tau = 0, 1, 2, \ldots$

- $S_\tau = \text{number of susceptibles after } \tau \text{ infectives},$
- $R^{(r)}_\tau = \text{number of eliminations of type } r \text{ after } \tau \text{ infectives},$
- $A_\tau = \text{cumulative duration of the first } \tau \text{ infection periods}.$

- Initially, $S_0 = n$, $A_0 = 0$, $R^{(r)}_0 = 0$.

In this artificial time, the epidemic terminates at time

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

By the characteristics of the model,

$$\left(S_{\tilde{T}}, A_{\tilde{T}}, R^{(1)}_{\tilde{T}}, \ldots, R^{(p)}_{\tilde{T}}\right) \overset{d}{=} \left(S_T, A_T, R^{(1)}_T, \ldots, R^{(p)}_T\right).$$
Suppose that the \( \tau \)-th infective begins in stage \( j \). Then

\[
\binom{S_{\tau}}{k} = \sum_{u=1}^{k} 1_j(k; u),
\]

\[
A_{\tau} = A_{\tau-1} + D_j,
\]

\[
R_{\tau}^{(r)} = R_{\tau-1}^{(r)} + 1_j, r,
\]

1. \( 1_j(k) = \mathbb{I}(\text{a fixed group of } k \text{ susceptibles escape from the infective}) \)
2. \( 1_j(r) = \mathbb{I}(\text{the infective will become an eliminated of type } r) \)
3. \( D_j = \text{infection duration of the infective.} \)
Martingales for the epidemic outcome

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

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

is a martingale, provided that

\[
q(k, \theta, z) = \sum_{j=1}^{L} \alpha_j q_j(k, \theta, z),
\]

\[
q_j(k, \theta, z) = E \left[ \mathbb{1}_j(k) e^{-\theta D_j} \prod_{r=1}^{p} z_r 1_j(r) \right].
\]
Joint distribution of $S_T$, $A_T$ and $R_T^{(r)}$

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

**Proposition**

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

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

$$= \binom{n}{k} q(k, \theta, z)^n \prod_{j=1}^{L} q_j(k, \theta, z)^{m_j}.$$
Some consequences of the preceding formula

A triangular system to determine the distribution of $S_T$:

\[
\begin{align*}
\sum_{s=k}^{n} \binom{s}{k} q(k)^s \mathbb{P}(S_T = s) &= \binom{n}{k} q(k)^n \prod_{j=1}^{L} q_j(k)^{m_j} \\
\sum_{s=0}^{n} \mathbb{P}(S_T = s) &= 1
\end{align*}
\]

where $q_j(k) \equiv q_j(k, 0, 0)$.

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

\[
\begin{align*}
\mathbb{E}[A_T] &= \sum_{j=1}^{L} m_j \mathbb{E}[D_j] + (n - \mathbb{E}[S_T]) \mathbb{E}[D_{\alpha}], \\
\mathbb{E}[R_T^{(r)}] &= \sum_{j=1}^{L} m_j q(0, 0, \bm{e}_r) + (n - \mathbb{E}[S_T]) q_j(0, 0, \bm{e}_r).
\end{align*}
\]
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To obtain the epidemic outcome, we only need the parameters

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

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

\[
\{(N(k; t), \varphi(t)) \mid t \in \mathbb{R}^+\} \text{ is a Markov process with state space }
\{\star_1, \ldots, \star_p, [(0, 1), \ldots, (0, L)], \ldots, [(k, 1), \ldots, (k, L)]\},
\]

and its generator is

\[
\begin{bmatrix}
0 & & & & & \\
& a_1 \cdots a_p & A_0(k) & A_1(k) & 0 & \cdots & 0 \\
& a_1 \cdots a_p & 0 & A_0(k-1) & A_1(k-1) & \cdots & 0 \\
& a_1 \cdots a_p & 0 & 0 & A_0(k-2) & \cdots & 0 \\
& \vdots & & & & & \vdots \\
& a_1 \cdots a_p & 0 & 0 & 0 & \cdots & A_1(1) \\
& a_1 \cdots a_p & 0 & 0 & 0 & \cdots & A_1(1) \\
\end{bmatrix},
\]

where \( A_1(h) = \frac{h}{n}B \) and \( A_0(h) = A - A_1(h) \).
By using the structure of this last generator, one can show that

**Proposition**

For $1 \leq j \leq L$,

$$q_j(k, \theta, z) = e_j \left[ \theta I - A_0(k) \right]^{-1} \sum_{r=1}^{p} z_r a_r.$$

The same formula holds for $q(k, \theta, z)$ except that $\alpha$ is substituted for $e_j$. 
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The process \( \{ \varphi(t) \} \) is now a semi-Markov process with kernel

\[
Q(t) = \begin{bmatrix}
I & 0 \\
\mathbf{a}_1(t) & \ldots & \mathbf{a}_p(t) & A(t)
\end{bmatrix},
\]

where, if \( \delta \) denotes the first renewal time,

\[
A_{j,v}(t) = P[\delta \leq t, \varphi(\delta) = v \mid \varphi(0) = j],
\]

\[
(a_r)_j(t) = P[\delta \leq t, \varphi(\delta) = *r \mid \varphi(0) = j].
\]
The martingales obtained in the Markovian case are still valid.

We just need to adapt the formulae for the parameters

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

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

\[
\begin{bmatrix}
I & 0 \\
\mathbf{u}_{k0}(t) & \mathbf{U}_{k0}(t) \\
\mathbf{0} & \mathbf{U}_{k-10}(t) \\
\vdots & \vdots \\
\mathbf{0} & \mathbf{U}_{00}(t)
\end{bmatrix},
\]

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

\[
(U_{hl})_{j, v}(t) = P[\delta \leq t, Y(\delta) = l, \varphi(\delta) = v \mid Y(0) = h, \varphi(0) = j],
\]

\[
(u_{hl})_{j}(t) = P[\delta \leq t, Y(\delta) = l, \varphi(\delta) = \star \mid Y(0) = h, \varphi(0) = j].
\]
The model
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Formula for the coefficients

Proposition

For $1 \leq j \leq L$,

$$ q_j(k, \theta, z) = e_j \left[ 1 - C_k(\theta) \right]^{-1} \sum_{r=1}^{p} z_r c_{k,r}(\theta), $$

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

$$ (C_k)_{j,v}(\theta) = \hat{A}_{j,v}(\theta + k \beta_j / n), \quad 1 \leq v \leq L, $$

$$ (c_{k,r})_j(\theta) = (\hat{a}_r)_j(\theta + k \beta_j / n), \quad 1 \leq r \leq p, $$

with $\hat{A}_{j,v}$ and $(\hat{a}_r)_j$ the Laplace transforms of $A_{j,v}$ and $(a_r)_j$. 
Thank you for your attention.