Markov-modulated interactions in SIR epidemics

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14/07/15
The 5-th Workshop Quantum Days in Bilbao

University of the Basque Country (UPV-EHU).
Basque Center for Applied Mathematics (BCAM).
Basque Foundation for Science (IKERBASQUE).
Presentation based on the paper Markov-modulated interactions in SIR epidemics, by E. Almaraz and A. Gómez-Corral.
Our model: stochastic susceptible-infectious-recovered (SIR) model in a Markov-modulated context to incorporate correlated events in a closed finite community.

We work with non-exponential distributional assumptions on the contacts between an I and a S individual, and the duration of infectiousness, but keeping the dimensionality of the underlying Markov chain model tractable.
The epidemic SIR model has been widely applied to infectious diseases (measles, chickenpox, mumps...), among other situations where infection confers (typically lifelong) immunity.

SIR-models (deterministic and stochastic perspectives) have been studied by some authors like Allen (2003, 2007), Andersson and Britton (2000), Bailey (1975) and Keeling and Rohani (2008).

The SIR-model was first analyzed in depth by Kermack and McKendrick in 1927.

Britton (2010) and Isham (2005) made a review of the existing literature and some results about SIR model.
Stochastic perspective→ there are four important quantities of the SIR-model

- the quasi-stationary distribution.
- the final size distribution of an epidemic.
- the expected duration of an epidemic.
- the basic reproduction number $R_0$
Some authors have studied these quantities, for example:

- Neuts and Li (1996).
The basic SIR-model

In the SIR-model, individuals develop an immunity to the disease. At time $t$, the population consists of:

- $I(t) = i$ infectives.
- $S(t) = s$ susceptibles.
- $R(t) = r$ removed individuals.
Events:
- Contacts between an infective and a susceptible.
- Removal of an infective.

<table>
<thead>
<tr>
<th>Transitions</th>
<th>Events</th>
<th>Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>$i \rightarrow i + 1$, $s \rightarrow s - 1$, $r \rightarrow r$, for $i, s \in \mathbb{N}$</td>
<td>An infection</td>
<td>$\lambda_{i,s}$</td>
</tr>
<tr>
<td>$i \rightarrow i - 1$, $s \rightarrow s$, $r \rightarrow r + 1$, for $i \in \mathbb{N}, s \in \mathbb{N}_0$</td>
<td>A removal</td>
<td>$\mu_i$</td>
</tr>
</tbody>
</table>

**Table:** Stochastic transitions, events and rates in the basic SIR-model
Rates $\lambda_{i,s}$ and $\mu_i$ can be specified in many ways:

- $\lambda_{i,s} = \beta is$ and $\mu_i = \eta i$ (Bailey, 1975, Gani and Purdue, 1984).
- $\lambda_{i,s} = \beta i^{\alpha} s$ and $\lambda_{i,s} = \beta i \min\{s, \epsilon n\}$, $\alpha \in (0, 1)$ (Neuts and Li, 1996).
- $\lambda_{i,s} = (i + s)^{-1/2}$ (Saunders, 1980).
In the case of:
- closed population that is homogeneously mixed.
- two state variables.
- initial numbers of \( m > 0 \) infectives and \( n > 0 \) susceptibles.

the SIR-model is formulated as a time-homogeneous continuous-time Markov chain (CTMC)

\[
\mathcal{X} = \{ X(t) = (I(t), S(t)) : t \geq 0 \}
\]

defined on a finite state space

\[
S(m, n) = \{(i, s) \in \mathbb{N}_0 \times \mathbb{N}_0 : 0 \leq i \leq m+n, 0 \leq s \leq \min\{n, m+n-i\}\}
\]
The process $\mathcal{X}$, which is from now on termed *basic*, is uniquely specified by the transition rates $\lambda_{i,s}$ and $\mu_i$.

- states in $C_0(n) = \{(0, 0), (0, 1), \ldots, (0, n)\}$ are absorbing and are associated with the ultimate extinction of the epidemic.

- the irreducible class $C(m, n) = \{(i, s) \in \mathbb{N}_0 \times \mathbb{N}_0 : 1 \leq i \leq m + n, \ 0 \leq s \leq \min\{n, m + n - i\}\}$ consists of transient states. This class can be expressed in terms of *levels* as $\bigcup_{s=0}^{n} l(s)$, where the $s$th level corresponds to states with $s$ susceptibles present, that is, $l(s) = \{(i, s) \in \mathbb{N}_0 \times \mathbb{N}_0 : 1 \leq i \leq m + n - s\}$, for $0 \leq s \leq n$. 
If states are labeled so that states in \( l(s) \) precede states in \( l(s - 1) \), and transient states precede absorbing states, then the infinitesimal generator \( Q \) of \( X \) is given by

\[
Q = \begin{pmatrix}
Q_{C(m,n),C(m,n)} & Q_{C(m,n),C_0(n)} \\
0_{(n+1) \times J(m,n)} & 0_{(n+1) \times (n+1)}
\end{pmatrix},
\]

where \( J(m, n) = 2^{-1}(n + 1)(2m + n) \) is the cardinality of the class \( C(m, n) \).
The matrices $Q_{C(m,n),C(m,n)}$ and $Q_{C(m,n),C_0(n)}$ in (1) take the form

$$Q_{C(m,n),C(m,n)} = \begin{pmatrix} A(n) & B(n) \\ A(n-1) & B(n-1) \\ \vdots & \vdots \\ A(1) & B(1) \\ A(0) & 0_{(n+1)\times(m+n)} \end{pmatrix}$$

where the sub-matrices $A(s)$ and $B(s)$ record transition rates related to jumps of $X$ from states of the $s$th level to states of $l(s)$ and $l(s-1)$, respectively.
the column vector $\mathbf{t}(s)$ contains transition rates related to jumps of $\mathcal{X}$ from states of the $s$th level to the absorbing state $(0, s)$. 

$$
Q_{C(m,n),C_0(n)} = 
\begin{pmatrix}
\mathbf{t}(n) \\
\mathbf{t}(n-1) \\
\vdots \\
\mathbf{t}(1) \\
\mathbf{t}(0) \\
\mathbf{0}_{(n+1)}
\end{pmatrix},
$$
The basic SIR-model

Markov-modulated events in the SIR epidemic model

Numerical experiments and discussion

Conclusions

Bibliography

\[ A(s) = \begin{pmatrix}
-q_{m+n-s,s} & \mu_{m+n-s} \\
-q_{m+n-s-1,s} & \mu_{m+n-s-1} \\
\vdots & \vdots \\
-q_{2,s} & \mu_{2} \\
-q_{1,s}
\end{pmatrix}, \]

\[ B(s) = \begin{pmatrix}
\lambda_{m+n-s,s} \\
\lambda_{m+n-s-1,s} \\
\vdots \\
\lambda_{1,s} & 0
\end{pmatrix}. \]
Some extensions of the SIR classic model:

- SIR model with general distributed infection period (Clancy, 2014).
- PH, MAP general perspective: when there are "i" infected individuals we should consider "i" MAPs. As a result, the resulting problem is not tractable from a numerical perspective due to the underlying dimensionality.
The dynamics in the SIR-model can be explained in terms of \textit{scheduled} events. The process $\mathcal{X}$ enters state $(i, s) \in \mathcal{C}(m, n)$ at time $t$. The next transition $(i, s) \rightarrow (i', s')$ is triggered by two scheduled events:

- $E_{(i,s)}(1, -1)$: infection of a susceptible.
- $E_{(i,s)}(-1, 0)$: removal of an infective.

The occurrence instants of $E_{(i,s)}(1, -1)$ and $E_{(i,s)}(-1, 0)$:

- are independent and exponentially distributed.
- with mean values $\lambda_{i,s}^{-1}$ and $\mu_{i}^{-1}$, respectively.
- they are also independent of the story of $\mathcal{X}$ up to time $t$. 

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The basic process $\mathcal{X}$:

- spends in $(i, s)$ an exponentially distributed period of time, with expected length $(\lambda_{i,s} + \mu_i)^{-1}$.
- it then moves to state $(i', s') = (i + z_1, s + z_2)$ with probability:
  - $(\lambda_{i,s} + \mu_i)^{-1}\lambda_{i,s}$ if $(z_1, z_2) = (1, -1)$: a new infection.
  - $(\lambda_{i,s} + \mu_i)^{-1}\mu_i$ if $(z_1, z_2) = (-1, 0)$: the removal of an infective.
The basic state \((i, s) \in C(m, n)\) is actualized with the information of the observed value \((z_1, z_2)\) of a bivariate vector \((Z_1, Z_2)\):

\[
(i', s') = f((i, s), (Z_1, Z_2))
\]

with

\[
f((i, s), (z_1, z_2)) = (i + z_1, s + z_2)
\]

for pairs \((z_1, z_2) \in \{(1, -1), (-1, 0)\}\).

Distributional assumptions for \((Z_1, Z_2)\) are inherently linked to the superposition of two independent Poisson streams with arrival rates \(\lambda_{i,s}\) and \(\mu_i\).
Basic process $\mathcal{X}$ replaced by augmented version $(\mathcal{X}', \mathcal{Y})$ allowing a Markovian dependence on a finite number of phases. To do that:

- every basic state $(i, s) \in C(m, n)$ replaced by a set of augmented states $(i, s, y_1, y_2)$ with $1 \leq y_k \leq L_k$ for predetermined values $L_k \in \mathbb{N}$ and $k \in \{1, 2\}$.
- we construct the superposition from two independent MAP’s of orders $L_1$ and $L_2$ instead of Poisson processes.
- we introduce a third pair $(z_1, z_2) = (0, 0)$ that reflects a transition between phases, but it does not imply any transition in the basic state $(i, s)$. 

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→ Result: regular, time-homogeneous CTMC $(\mathcal{X}, \mathcal{Y})$, where the phase process $\mathcal{Y} = \{Y(t) = (Y_1(t), Y_2(t)) : t \geq 0\}$ can be thought of as a SD marked Markovian arrival process with two categories of marked events-type-$(z_1, z_2)$-:

- $(z_1, z_2) = (1, -1)$ if the infection of a susceptible individual is observed.
- $(z_1, z_2) = (-1, 0)$ if the removal of an infective is registered.
The state space $S^*$ of $(\mathcal{X}, \mathcal{Y})$ can be partitioned into:

- $C_0(n)$: set of absorbing states.
- $C^*(m, n)$: class of transient states, where:
  - $C^*(m, n) = \bigcup_{s=0}^{n} l^*(s)$.
  - $l^*(s)$: $s$th augmented level consists of states $(i, s, y_1, y_2)$ with $1 \leq i \leq m + n - s$ and $1 \leq y_k \leq L_k$ for $k \in \{1, 2\}$. 

\[ E.A.L, A.G-C. \]
We use two scaled MAP’s specified by characteristic matrices:

- \((C^*_0,(i,s), C^*_1,(i,s))\) for the occurrence of an infection.
- \((D^*_0,(i,s), D^*_1,(i,s))\) for the removal of an infective.

with

\[
C^*_{k,(i,s)} = \hat{\lambda}^{-1}(1)\lambda_{i,s}C_k,
\]
\[
D^*_{k,(i,s)} = \hat{\lambda}^{-1}(2)\mu_iD_k,
\]

for \(k \in \{1, 2\}\), where \((C_0, C_1)\) and \((D_0, D_1)\) are the characteristic matrices of two independent MAP’s of orders \(L_1\) and \(L_2\), respectively, and fundamental arrival rates \(\hat{\lambda}(1)\) and \(\hat{\lambda}(2)\).
The infinitesimal generator $Q^*$ of $(\mathcal{X}, \mathcal{Y})$ has the structured form of $Q$ in (1) with $A(s), B(s)$, and $t(s)$ in (2)-(3) replaced by suitably defined sub-matrices $A^*(s)$ and $B^*(s)$, and vectors $t^*(s)$. 
For every basic state \((i, s) \in C(m, n)\), the fundamental arrival rate of type-\((z_1, z_2)\) marks is given by

\[
\bar{\lambda}(i, s)(z_1, z_2) = \begin{cases} 
\lambda_{i, s}, & \text{if } (z_1, z_2) = (1, -1), \\
\mu_i, & \text{if } (z_1, z_2) = (-1, 0), 
\end{cases}
\]
and the fundamental arrival rate $\bar{\lambda}_{(i,s)}$ of the SD MMAP is given by

$$\bar{\lambda}_{(i,s)} = q_{i,s},$$

(5)

regardless of the initial MAPs with matrices $(C_0, C_1)$ and $(D_0, D_1)$. 
In the SIR-model defined by the rates $\lambda_{i,s} = \beta is$ and $\mu_i = \eta i$ with $\beta = N^{-1}\beta'$, the basic reproductive ratio $R_0 = \eta^{-1}\beta'$ separates the growing and shrinking behaviors and, consequently, it marks the epidemic *threshold* between regimes in which the disease either increases or dies out in the long run.
Based on works of Artalejo et. al (2013), we define $R_{\text{exact},0}$ as:

- the exact number of secondary cases generated by a typical infective individual during its infectious period.

Important:

- $R_0$ is related to the *time of invasion* (i.e., for a community with $(I(0), S(0)) = (1, N - 1)$ and $R(0) = 0$).
- $R_{\text{exact},0}$ can be appropriately defined at every time instant.
In the Markov-modulated SIR-model:

- the basic state \((1, N - 1)\) is replaced by the set of augmented states \((1, N - 1, y_1, y_2)\) with phases \(1 \leq y_k \leq L_k\) and \(k \in \{1, 2\}\).

- \textit{conditional} probability mass function

\[ x_{(1,N-1,y_1,y_2)} = \{x_{(1,N-1,y_1,y_2)}(j) : 0 \leq j \leq N - 1\} \]

of \(R_{\text{exact},0}\), provided that \((1, N - 1, y_1, y_2) \in C^*(m, n)\) is the initial state of \((X, Y)\), is defined by the probabilities

\[ P(R_{\text{exact},0} = j \mid (I(0), S(0), Y_1(0), Y_2(0)) = (1, N - 1, y_1, y_2)) \]

\[ 0 \leq j \leq N - 1. \]
We may define conditional probability mass functions $x(i,s,y_1,y_2)$ of $R_{\text{exact},0}$ in terms of probabilities $x(i,s,y_1,y_2)(j)$ for $0 \leq j \leq s$ and phases $1 \leq y_k \leq L_k$ with $k \in \{1, 2\}$, when initial basic states $(i, s) \in \mathcal{C}(m, n)$ are observed.

For every basic state $(i, s) \in \mathcal{C}(m, n)$ and values $0 \leq j \leq s$, we let $x(i,s)(j)$ be the column vector of order $L_1L_2$ with entries

$$(x(i,s)(j))(y_1-1)L_2+y_2 = x(i,s,y_1,y_2)(j)$$

for $1 \leq y_k \leq L_k$ and $k \in \{1, 2\}$.

By conditioning on the first transition of the augmented process $(X', Y') \rightarrow$ entries of $x(i,s)(j)$ satisfy
\[
\begin{align*}
0 \leq j \leq s \text{ and } (i, s) \in C(m, n)
\end{align*}
\]
where:

- $\lambda_{i,s}^*$: gives the individual rate at which a typical infective contacts with susceptibles.
- $\tilde{\lambda}_{i-1,s}$: reflects the superposition of the contact processes of the remaining $i - 1$ infectives.

in the special case $\lambda_{i,s} = \beta is$ with $\beta = N^{-1}\beta'$, they are given by:

- $\lambda_{i,s}^* = N^{-1}\beta's$.
- $\tilde{\lambda}_{i-1,s} = N^{-1}\beta'(i - 1)s$. 
Starting from \( x_{(i,0)}(0) = e_{L_1 L_2} \) for \( 1 \leq i \leq m + n \), the triangular system of equations (6) can be efficiently solved in the natural order \( j \geq 0 \), \( j \leq s \leq n \) and \( 1 \leq i \leq m + n - s \), and moments of \( R_{\text{exact},0} \) are then derived in an straightforward manner. The role of \( R_0 \) may be replaced by the *unconditional* expected value

\[
\overline{R}_{\text{exact},0} = \sum_{j=1}^{N-1} j (\eta(1) \otimes \eta(2)) x_{(1,N-1)}(j),
\]

where \( \eta(1) \otimes \eta(2) \) is the stationary probability vector of the phase process \( \mathcal{Y} \).
The population transmission number $R_p$

$R_p$ counts the exact number of secondary cases produced by all currently infective individuals prior to the first removal. For a fixed augmented state $(i, s, y_1, y_2) \in \mathcal{C}^*(m, n)$, we define the conditional probabilities $y_{(i,s,y_1,y_2)}(j)$ by

$$P\left( R_p = j \mid I(0), S(0), Y_1(0), Y_2(0) \right) = (i, s, y_1, y_2), \quad 0 \leq j \leq s,$$

from which we introduce vectors $y_{(i,s)}(j)$ with entries

$$(y_{(i,s)}(j))_{(y_1-1)L_2+y_2} = y_{(i,s,y_1,y_2)}(j) \quad \text{for} \quad 1 \leq y_k \leq L_k \quad \text{and} \quad k \in \{1, 2\}.$$
An appeal to a first-step argument yields

\[
- \left( \left( \hat{\lambda}^{-1}(1) \lambda_{i,s} C_0 \right) \oplus \left( \hat{\lambda}^{-1}(2) \mu_i D_0 \right) \right) y_{(i,s)}(j) = \\
= \delta_{0,j} \left( e_{L_1} \otimes \left( \hat{\lambda}^{-1}(2) \mu_i D_1 e_{L_2} \right) \right) \\
+ (1 - \delta_{0,j}) \left( \left( \hat{\lambda}^{-1}(1) \lambda_{i,s} C_1 \right) \otimes I_{L_2} \right) \ y_{(i+1,s-1)}(j-1),
\]

for values \(0 \leq j \leq s\) and basic states \((i, s) \in C(m, n)\), which can be routinely solved by starting from \(y_{(i,0)}(0) = e_{L_1L_2}\). The \textit{unconditional} expected value of \(R_p\) is then evaluated as

\[
\bar{R}_p = \sum_{j=1}^{N-1} j \left( \eta(1) \otimes \eta(2) \right) y_{(1,N-1)}(j),
\]
Numerical experiments and discussion

We assume:

- \( \lambda_{i,s} = \beta i s \) with \( \beta = N^{-1} \beta' \), \( \beta' > 0 \).
- \( \mu_i = \eta i \) with \( \eta = 1.0 \),
- sizes \( N \in \{10, 50, 100, 150\} \).
- Eight scenarios (see next table) defined in terms of standard Poisson processes, and positively and negatively correlated Markovian events, which are appropriately specified from two predetermined MAP’s of order \( L_1 = L_2 = 3 \) with values \( \rho_1 = 0.35016 \) and \(-0.35016\) for their correlation coefficients; in this setting, the basic SIR-model corresponds to scenario I.
<table>
<thead>
<tr>
<th>Scenario</th>
<th>Occurrence of an infection</th>
<th>Occurrence of a removal</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>$\hat{\lambda}^{-1}(1)\lambda_{i,s}C_1^+$</td>
<td>$\mu_i$</td>
</tr>
<tr>
<td>B</td>
<td>$\hat{\lambda}^{-1}(1)\lambda_{i,s}C_1^-$</td>
<td>$\mu_i$</td>
</tr>
<tr>
<td>C</td>
<td>$\lambda_{i,s}$</td>
<td>$\hat{\lambda}^{-1}(2)\mu_iC_1^+$</td>
</tr>
<tr>
<td>D</td>
<td>$\lambda_{i,s}$</td>
<td>$\hat{\lambda}^{-1}(2)\mu_iC_1^-$</td>
</tr>
<tr>
<td>E</td>
<td>$\hat{\lambda}^{-1}(1)\lambda_{i,s}C_1^+$</td>
<td>$\hat{\lambda}^{-1}(2)\mu_iC_1^-$</td>
</tr>
<tr>
<td>F</td>
<td>$\hat{\lambda}^{-1}(1)\lambda_{i,s}C_1^-$</td>
<td>$\hat{\lambda}^{-1}(2)\mu_iC_1^+$</td>
</tr>
<tr>
<td>G</td>
<td>$\hat{\lambda}^{-1}(1)\lambda_{i,s}C_1^+$</td>
<td>$\hat{\lambda}^{-1}(2)\mu_iC_1^+$</td>
</tr>
<tr>
<td>H</td>
<td>$\hat{\lambda}^{-1}(1)\lambda_{i,s}C_1^-$</td>
<td>$\hat{\lambda}^{-1}(2)\mu_iC_1^-$</td>
</tr>
<tr>
<td>I</td>
<td>$\lambda_{i,s}$</td>
<td>$\mu_i$</td>
</tr>
</tbody>
</table>

**Table:** Eight scenarios defined in terms of the matrices $C_{1,(i,s)}^*$ and $D_{1,(i,s)}^*$ for the occurrence of an infection and the removal of an infective, respectively.
Figure: 1 The expected value $\overline{R}_{\text{exact},0}$ versus the basic reproduction number $R_0$ for scenarios A, E and G and sizes $N \in \{10, 50, 100, 150\}$
**Figure: 4** The expected value $\bar{R}_p$ versus the basic reproduction number $R_0$ for scenarios A, E and G and sizes $N \in \{10, 50, 100, 150\}$
Figure: 2 The expected value $\overline{R}_{\text{exact},0}$ versus the basic reproduction number $R_0$ for scenarios B, F and H and sizes $N \in \{10, 50, 100, 150\}$
Figure: 5 The expected value $\bar{R}_p$ versus the basic reproduction number $R_0$ for scenarios B, F and H and sizes $N \in \{10, 50, 100, 150\}$
Figure: 3 The expected value $\overline{R}_{\text{exact},0}$ versus the basic reproduction number $R_0$ for scenarios C, D and I and sizes $N \in \{10, 50, 100, 150\}$
Figure: 6 The expected value $\bar{R}_p$ versus the basic reproduction number $R_0$ for scenarios C, D and I and sizes $N \in \{10, 50, 100, 150\}$
We develop a stochastic modeling framework that incorporates correlation between events into the dynamics of the SIR-model.

We construct Markov-modulated versions of the basic SIR-model $\mathcal{X}$ by allowing one to deal with non-exponential distributional assumptions on the contacts between I and S individual, and the random duration of infectiousness.
We construct an augmented Markovian process \((X, Y)\) describing the number of infectives and susceptibles in the basic SIR-model, and an auxiliary variable called phase.

The augmented process \((X, Y)\) is a regular, time-homogeneous CTMC exhibiting correlation between events, and the phase process \(Y\) amounts to a state-dependent version of a MMAP where the types of marked events correspond to either a new infection or the removal of an infective in the basic SIR-model.
The process $\mathcal{X}$ and its augmented version $(\mathcal{X}, \mathcal{Y})$ possess identical structural properties regarding the infinitesimal rates $\lambda_{i,s}$ and $\mu_i$, and the fundamental arrival rates $\bar{\lambda}_{(i,s)}(z_1, z_2)$ of type-$(z_1, z_2)$ marked events.

We study an alternative to the basic reproduction number $R_0 \rightarrow \bar{R}_{exact,0}$ and $\bar{R}_p$.

We compare $R_0$ with the expected values $\bar{R}_{exact,0}$ and $\bar{R}_p$ at the invasion time, that is, by assuming that the invasion starts at time $t = 0$ with $(I(0), S(0)) = (1, N - 1)$ and $R(0) = 0$. 

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Thank you for your attention.

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