MATH-449 - Biostatistics
EPFL, Spring 2025
Problem Set 12

1. Show that the standard stochastic SIR model for the number of susceptibles ($X(t)$), and the number of infectives ($Y(t)$), introduced during the lecture, has the Markov property, if and only if, the (continuous) random variable I, denoting infectious period of infectives, is exponentially distributed.

   Solution The Markov property for $(X(t), Y(t))$ means that

$$P(X(t+dt) = i', Y(t+dt) = j'|\mathcal{F}_t) = P(X(t+dt) = i', Y(t+dt) = j'|X(t) = i, Y(t) = j),$$

holds for all $h > 0$, $i, j, i', j' \in \mathcal{S}$, where $\mathcal{F}_t$ stands for the filtration ("history" up to time t), and $\mathcal{S}$ denotes the state space of the Markov chain. We have for the standard stochastic SIR model $E_{n,m}(\lambda, I)$ without specifying the distribution of I that

$$P(X(t+dt) = i', Y(t+dt) = j'|X(t) = i, Y(t) = j) = \begin{cases} P(X(t+dt) = i-1, Y(t+dt) = j+1|X(t) = i, Y(t) = j) \\ P(X(t+dt) = i, Y(t+dt) = j-1|X(t) = i, Y(t) = j) \\ o(dt) \quad \text{if } (i', j') \notin \{(i-1, j+1), (i, j-1)\}. \end{cases}$$

By construction, a new infection occurs when the total infection pressure $A(t + dt)$ exceeds the threshold of a still susceptible individual, that is

$$\begin{aligned} P(X(t+dt) = i-1, Y(t+dt) = j+1|X(t) = i, Y(t) = j) &= \sum_{k=1}^{i} P(Q_k < A(t+dt)|Q_k > A(t)) + o(dt) \\ &= \sum_{k=1}^{i} P(Q_k < A(t+dt)|\mathcal{F}_t) + o(dt), \end{aligned}$$

where we used that the thresholds are exponentially distributed, hence they have the memoryless property ($P(Z > t + s|Z > t) = P(Z > s)$).

The last sum can be further simplified as

$$\begin{aligned} \sum_{k=1}^{i} P(Q_k < A(t+dt)|Q_k > A(t)) + o(dt) &= \sum_{k=1}^{i} 1 - \exp(-A(t+dt) + A(t)) + o(dt) \\ &= \sum_{k=1}^{i} 1 - \exp\Big(-\frac{\lambda}{n} j dt\Big) + o(dt) \\ &= \frac{\lambda}{n} ij dt + o(dt), \end{aligned}$$

giving the correct rate of transition.

Similarly, an infective becomes removed, when the time exceeds their infectious time, that is

$$\begin{aligned} P(X(t+dt) = i, Y(t+dt) = j-1|X(t) = i, Y(t) = j) &= \sum_{k=1}^{j} P(I_k < t+dt|I_k > t) + o(dt) \\ &= \sum_{k=1}^{j} P(I_k < t+dt|\mathcal{F}_t) + o(dt), \end{aligned}$$

where the second line holds, if and only if, I is exponentially distributed, as a continuous random variable has the memoryless property, if and only if its distribution is exponential. If

$I \sim Exp(\gamma)$

$$\begin{aligned}\sum_{k=1}^{j} P(I_k < t+dt | I_k > t) + o(dt) &= \sum_{k=1}^{j} P(I_k < dt) + o(dt)\\ &= \sum_{k=1}^{j} 1 - \exp\Big(-\gamma dt\Big) + o(dt)\\ &= j\gamma dt + o(dt),\end{aligned}$$

again giving the correct rate of transition.

2. Compute P_0^n, P_1^n and P_2^n numerically using the recursive formula given during the lecture (Equation 2.4 in the notes), assuming $n = 10$, $m = 1$, $\lambda = 2$ and that the infectious period I is:

   (a) exponentially distributed (the Markovian case) with mean 1 time unit.

   (b) $\Gamma(2, 2)$-distributed (i.e. with mean 1).

   (c) constant and equal to 1.

   Hint: You are welcome to calculate everything by hand, but I would advise using some programming language to derive these probabilities recursively.

   Solution Denote the probability that out of the n many initial susceptible, k becomes infected by the end of the epidemic, given that there were initially m many infections as P_k^n, where m is left implicit.

   Equation 2.4 gives the recursive formula for P_k^n as

$$\sum_{k=0}^{l} \frac{\binom{n-k}{l-k} P_k^n}{\phi\Big(\frac{\lambda(n-l)}{n}\Big)^{k+m}} = \binom{n}{l}, \qquad 0 \le l \le n,$$

   where $\phi(\cdot)$ is the Laplace transform of I, and λ/n is the rate of contact between individuals.

   The Laplace transform of the different I-s are

   (a) $\phi_{Exp(1)}(\theta) = \int_0^\infty \exp(-\theta x)\exp(-x)\mathrm{d}x = \big[\frac{-1}{\theta+1}\exp(-(\theta+1)x)\big]_{x=0}^\infty = \frac{1}{\theta+1}$

   (b) $\phi_{Gamma(2,2)}(\theta) = \int_0^\infty \exp(-\theta x)\frac{2^2}{\Gamma(2)}x\exp(-2x)\mathrm{d}x$
   $= \big[\frac{2^2}{\Gamma(2)}x\frac{-1}{\theta+2}\exp(-(\theta+2)x)\big]_{x=0}^\infty - \int_0^\infty \frac{2^2}{\Gamma(2)}\frac{-1}{\theta+2}\exp(-(\theta+2)x)$
   where we used integration by parts. Solving the integral and using the fact that $\Gamma(2) = (2-1)! = 1$ we have
   $-\big[2^2\frac{1}{(\theta+2)^2}\exp(-(\theta+2)x)\big]_{x=0}^\infty = \Big(\frac{2}{\theta+2}\Big)^2.$

   (c) $\phi_1(\theta) = E[\exp(-\theta)] = \exp(-\theta)$

   See the code (`shiny_sellke.R`) for calculating the values with the different distributions of I. In particular P_0^n, P_1^n and P_2^n are

   (a) $(0.3333, 0.085, 0.047)$

   (b) $(0.25, 0.0748, 0.0436)$

   (c) $(0.1353, 0.0495, 0.0321)$

   Please note that for certain parameter/initial values, the recursive formula breaks down even if it is performed on the log scale.

3. Consider the Markovian version of the standard SIR epidemic (m fixed, n large). Without referring to the branching approximation, approximate the process of infectives $Y_n(t)$ during the initial stage of the epidemic with a suitable simple birth and death process. What is the probability of extinction/explosion of this approximating process?

   Hint: $X_n(t) \approx n$ during the initial stage of the epidemic.

   Birth and death processes are continuous-time Markov chains, with transition probabilities such that $P_{ij}(t) = 0$ if $|i-j| > 1$. In particular

$$\begin{aligned} P_{i,i+1}(dt) &= \lambda_i dt + o(dt), \\ P_{i,i-1}(dt) &= \mu_i dt + o(dt), \\ P_{j,j}(dt) &= 1 - (\lambda_j + \mu_j)dt + o(dt). \end{aligned}$$

Solution Consider the Markovian version of the standard SIR model where $I \sim Exp(\gamma)$. In this setup, the process (X, Y) is governed by the rates

from	**to**	**at rate**
(n, j)	$(n, j+1)$	λj
(n, j)	$(n, j-1)$	γj

where we used that in the initial stage of the epidemic, $X_n(t)$ is approximately equal to the initial number of infections, n.

We can define a birth and death process $Y(t)$ for the number of infections in the population, with linear rates, that is

$$\begin{aligned} P_{j,j+1}(dt) &= (\lambda \cdot j)dt + o(dt), \\ P_{j,j-1}(dt) &= (\mu \cdot j)dt + o(dt), \\ P_{j,j}(dt) &= 1 - j(\lambda + \mu)dt + o(dt), \end{aligned}$$

which agrees with the marginal transition rates of the infectives in the Markovian SIR model.

Denote the extinction probability of infectives, given that initially there were $Y(0) = m$ many of them with $q_m = \lim_{t\to\infty} P(Y(t) = 0|Y(0) = m)$. Using the law of total probability, we can rewrite q_m as

$$\begin{aligned} q_m &= \lim_{t\to\infty} P(Y(t) = 0|Y(0) = m) \\ &= \lim_{t\to\infty} P(Y(t) = 0|Y(dt) = m-1)P(Y(dt) = m-1|Y(0) = m) \\ &+ P(Y(t) = 0|Y(dt) = m+1)P(Y(dt) = m+1|Y(0) = m) \\ &+ P(Y(t) = 0|Y(dt) = m)P(Y(dt) = m|Y(0) = m) \\ &= (q_{m-1}\mu m)dt + (q_{m+1}\lambda m)dt + q_m(1 - (\lambda m - \mu m)dt) + o(dt). \end{aligned}$$

After simplification, we get the equation

$$0 = q_{m+1}m\lambda - (\lambda+\mu)mq_m + \mu m q_{m-1} = q_{m+1}\lambda - (\lambda+\mu)q_m + \mu q_{m-1}.$$

Solving the characteristic equation of the recursive formula, we derive the second-order polynomial

$$0 = q^{m+1}\lambda - q^m(\lambda+\mu) + \mu q^{m-1} \implies 0 = q^2\lambda - q(\lambda+\mu) + \mu,$$

which gives the solutions

$$q = \frac{\lambda + \mu \pm \sqrt{(\lambda+\mu)^2 - 4\lambda\mu}}{2\lambda} = \begin{cases} 1 \\ \frac{\mu}{\lambda} \end{cases}$$

Therefore, the extinction probability of the infectives $q_m = q^m$ is equal to 1 if $\mu \geq \lambda$, otherwise it is $\left(\frac{\mu}{\lambda}\right)^m$.

4. **Challenging Exercise:**
Suppose that $X = \{X(t); t \geq 0\}$ and $X' = \{X'(t); t \geq 0\}$ are two **birth and death processes** on the set of nonnegative integers. The process X has birth rates λ_i and death rates μ_i,

$$P(X(t+dt) - X(t) = +1 \mid X(t) = i) = \lambda_i dt + o(dt),$$
$$P(X(t+dt) - X(t) = -1 \mid X(t) = i) = \mu_i dt + o(dt),$$

$X(0) = m$, and likewise X' has birth rates λ'_i, death rates μ'_i and initial value m'.

Coupling is a mathematical technique via which we define highly dependent random elements, facilitating the comparison between random variables. Formally, given:

- Two probability spaces: $(\Omega, \mathcal{F}, \mathbb{P})$ and $(\Omega', \mathcal{F}', \mathbb{P}')$
- Random elements: $X : \Omega \to E$, and $X' : \Omega' \to E$
- State space E (e.g. $\mathbb{N}$, $\mathbb{R}$, $\mathbb{R}^{\mathbb{N}}$, $D[0, \infty)$, etc.),

then we define the **coupling** of X and X' as:

- A new probability space $(\widehat{\Omega}, \widehat{\mathcal{F}}, \widehat{\mathbb{P}})$
- A pair of random elements $(\widehat{X}, \widehat{X}') : \widehat{\Omega} \to E^2$
- Such that:
$$\widehat{X} \stackrel{d}{=} X \quad \text{and} \quad \widehat{X}' \stackrel{d}{=} X'$$
(i.e. marginal distributions preserved)

We could use coupling to show that if $\lambda_i \leq \lambda'_i$ for all $i \geq 0$ and $\mu_i \geq \mu'_i$ for all $i \geq 1$, then $X(t)$ is stochastically smaller than $X'(t)$ for all t (provided also $m \leq m'$).

Define a bivariate process $(\hat{X}, \hat{X}')$ with initial value (m, m') and with the following intensity table:

from	**to**	**at rate**
(i, j)	$(i+1, j)$	λ_i
(i, j)	$(i, j+1)$	λ'_j
(i, j)	$(i-1, j)$	μ_i
(i, j)	$(i, j-1)$	μ'_j
(i, i)	$(i+1, i+1)$	λ_i
(i, i)	$(i, i+1)$	$\lambda'_i - \lambda_i$
(i, i)	$(i-1, i-1)$	μ'_i
(i, i)	$(i-1, i)$	$\mu_i - \mu'_i$

Check that the process $(\hat{X}, \hat{X}')$, is indeed a coupling of the birth and death processes X and X', i.e. that the marginal distributions coincide with the distributions of X and X', respectively.

Hint: Try to compute the marginal intensities of the joint Markov chain.

Solution From the Kolmogorov forward equation, it follows that if two Markov chains, in this case twp birth and death processes, have the same initial distribution and intensities, then they share the same distribution.

By assumption $X(0) = m = \hat{X}(0)$ and $X'(0) = m' = \hat{X}(0)$, therefore we only have to show that the intensities coincide.

We will use the notation $\alpha^X_{(i),(i')}(t) = \lim_{dt \to 0^+} \frac{1}{dt} \mathbb{P}(X(t+dt) = i' | X(t) = i)$ and $P^{X'|X}_{j|i}(t) = \mathbb{P}(X'(t) = j | X(t) = i)$, and analogously for the joint Markov chains, (X, X'), $\alpha^{X,X'}_{(i,j),(i',j')}(t) = \lim_{dt \to 0^+} \frac{1}{dt} \mathbb{P}(X(t+dt) = i', X'(t+dt) = j' | X(t) = i, X'(t) = j)$.

Using the Kolmogorov forward equation for the joint Markov chain $(\hat{X}, \hat{X}')$ one can show that the marginal intensity $\alpha^{\hat{X}}_{(i),(i')}(t)$ of $\hat{X}$ is equal to

$$\alpha^{\hat{X}}_{(i),(i')}(t) = \sum_j P^{X'|X}_{j|i}(t) \sum_{j'} \alpha_{(i,j),(i',j')}$$

In particular, from i to $i+1$ is

$$\begin{aligned}
\alpha^{\hat{X}}_{(i)(i+1)}(t) &= \sum_{j,j'} \alpha^{\hat{X},\hat{X}'}_{(i,j)(i+1,j')}(t) P^{\hat{X}'|\hat{X}}_{j|i}(t) \\
&= \sum_{j \neq i} \alpha^{\hat{X},\hat{X}'}_{(i,j)(i+1,j)}(t) P^{\hat{X}'|\hat{X}}_{j|i}(t) + \alpha^{\hat{X},\hat{X}'}_{(i,i)(i+1,i+1)}(t) P^{\hat{X}'|\hat{X}}_{i|i}(t) \\
&= \lambda_i \sum_j P^{\hat{X}'|\hat{X}}_{j|i}(t) = \lambda_i.
\end{aligned}$$

From i to $i-1$ is

$$\begin{aligned}
\alpha^{\hat{X}}_{(i)(i-1)}(t) &= \sum_{j,j'} \alpha^{\hat{X},\hat{X}'}_{(i,j)(i-1,j')}(t) P^{\hat{X}'|\hat{X}}_{j|i}(t) \\
&= \sum_{j \neq i} \alpha^{\hat{X},\hat{X}'}_{(i,j)(i-1,j)}(t) P^{\hat{X}'|\hat{X}}_{j|i}(t) + \alpha^{\hat{X},\hat{X}'}_{(i,i)(i-1,i-1)}(t) P^{\hat{X}'|\hat{X}}_{i|i}(t) + \alpha^{\hat{X},\hat{X}'}_{(i,i)(i-1,i)}(t) P^{\hat{X}'|\hat{X}}_{i|i}(t) \\
&= \mu_i \sum_{j \neq i} P^{\hat{X}'|\hat{X}}_{j|i}(t) + P^{\hat{X}'|\hat{X}}_{i|i}(t)(\mu_i' + (\mu_i - \mu_i')) \\
&= \mu_i \sum_j P^{\hat{X}'|\hat{X}}_{j|i}(t) = \mu_i.
\end{aligned}$$

Similarly for $\hat{X}'$,

$$\begin{aligned}
\alpha^{\hat{X}'}_{(j)(j+1)}(t) &= \sum_{i,i'} \alpha^{\hat{X},\hat{X}'}_{(i,j)(i',j+1)}(t) P^{\hat{X}|\hat{X}'}_{i|j}(t) \\
&= \sum_{i \neq j} \alpha^{\hat{X},\hat{X}'}_{(i,j)(i,j+1)}(t) P^{\hat{X}|\hat{X}'}_{i|j}(t) + \alpha^{\hat{X},\hat{X}'}_{(j,j)(j+1,j+1)}(t) P^{\hat{X}|\hat{X}'}_{j|j}(t) + \alpha^{\hat{X},\hat{X}'}_{(j,j)(j,i+1)}(t) P^{\hat{X}|\hat{X}'}_{j|j}(t) \\
&= \lambda_j' \sum_{i \neq j} P^{\hat{X}|\hat{X}'}_{i|j}(t) + P^{\hat{X}|\hat{X}'}_{j|j}(t)(\lambda_j + (\lambda_j' - \lambda_j)) = \lambda_j' \sum_i P^{\hat{X}|\hat{X}'}_{i|j}(t) = \lambda_j'
\end{aligned}$$

$$\begin{aligned}
\alpha^{\hat{X}'}_{(j)(j-1)}(t) &= \sum_{i,i'} \alpha^{\hat{X},\hat{X}'}_{(i,j)(i',j-1)}(t) P^{\hat{X}|\hat{X}'}_{i|j}(t) \\
&= \sum_{i \neq j} \alpha^{\hat{X},\hat{X}'}_{(i,j)(i,j-1)}(t) P^{\hat{X}|\hat{X}'}_{i|j}(t) + \alpha^{\hat{X},\hat{X}'}_{(j,j)(j-1,j-1)}(t) P^{\hat{X}|\hat{X}'}_{j|j}(t) \\
&= \mu_j' \sum_i P^{\hat{X}|\hat{X}'}_{i|j}(t) = \mu_j'.
\end{aligned}$$

Thus both the initial states and marginal intensities of $(\hat{X}, \hat{X}')$ agree with X and X', therefore $X \stackrel{d}{=} \hat{X}$ and $X' \stackrel{d}{=} \hat{X}'$, as desired.