An epidemic model with short-lived mixing groups

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Introduction

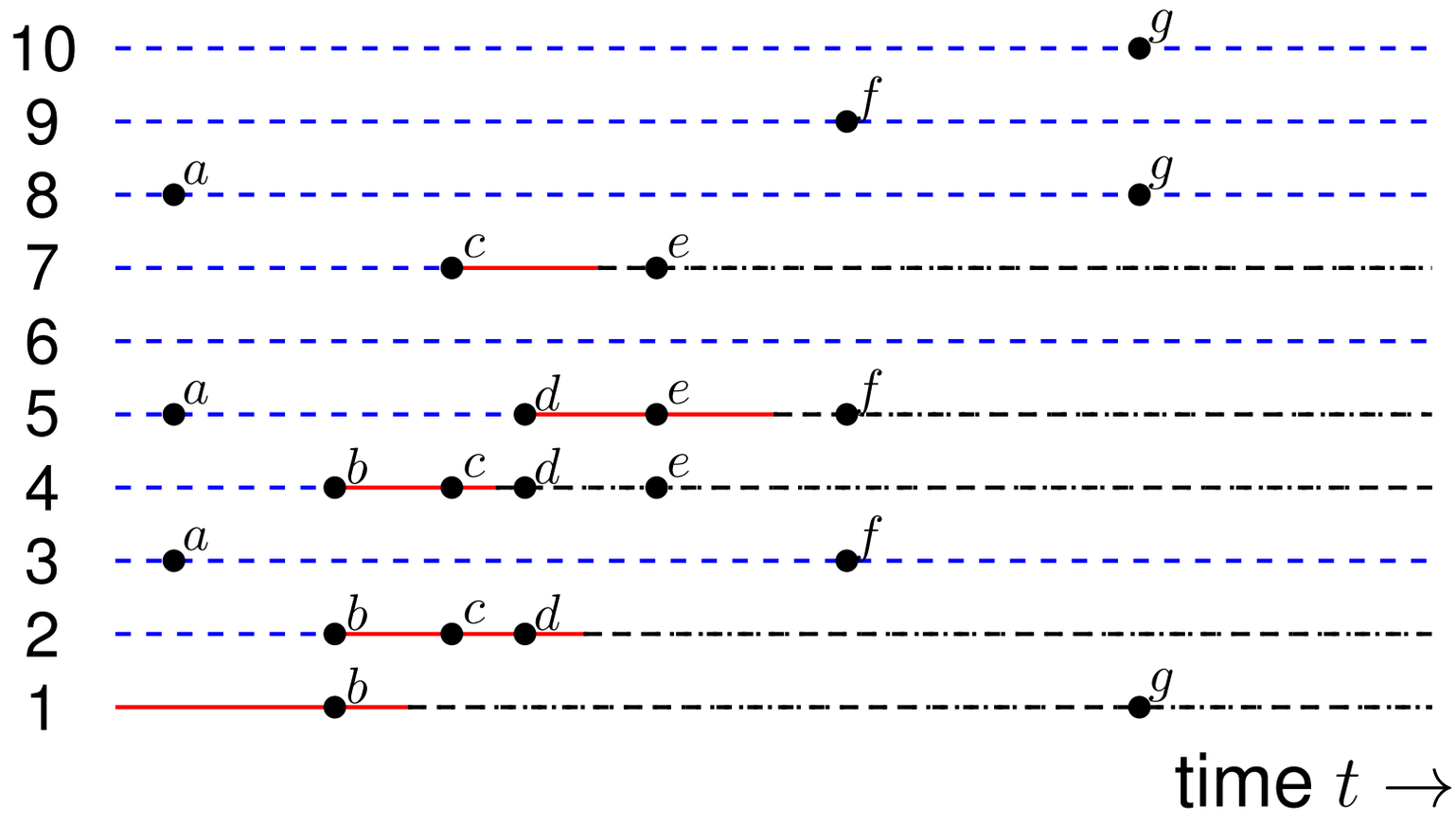
- Most epidemic models assume infection occurs via pairwise interaction of individuals.
  - mass action models λxy
  - Network models
- In practice, mixing occurs in groups larger than 2.
- Aim of talk – develop and analyse a model in which mixing events can involve > 2 people.
- Other models with non-pairwise transmission include
  - Greenwood chain-bimomial model
  - Highly infectious household model (Becker and Dietz(1995))
  - Replace λxy by $\lambda f(x, y)$ (e.g. λxy^{α} – O'Neill and Wen (2012)).

Epidemic model

- SIR model with infectious period $\sim \mathrm{Exp}(\gamma)$ among a population of size n.
- Mixing events occur at the points of a Poisson process having rate $n\lambda$.
- Sizes of successive mixing events $C_1^{(n)}, C_2^{(n)}, \ldots \overset{\text{i.i.d.}}{\sim} C^{(n)}$, where $C^{(n)}$ takes values in a subset of $\{2, 3, \ldots, n\}$. Suppose $C_i^{(n)} = c$. Then c individuals are chosen uniformly at random from the population to form the mixing event.
- At a mixing event of size c, any infective has probability π_c of making an infectious contact with any given susceptible, with all such contacts occurring independently.
- Infectives cannot infect susceptibles at the mixing event in which they were infected.
- Initially, m_n infectives and $n - m_n$ susceptibles.

(Ball and Neal (2022), Cortez (2022))

Example with $\mathrm{P}(C^{(n)} = 3) = 1$ and $\pi_3 = 1$



Susceptible – blue dashed, infective – red, recovered – black dot-dash.

Special case – $\mathrm{P}(C^{(n)} = 2) = 1$

- Suppose $\mathrm{P}(C^{(n)} = 2) = 1$, so all mixing events have size 2.
- If there are s susceptibles and i infectives at time t, the probability that a mixing event involves one infective and one susceptible is $si/\binom{n}{2} = \frac{2si}{n(n-1)}$, so the rate at which new infections occur is $n\lambda \times \frac{2si}{n(n-1)} \times \pi_2 = \frac{2\lambda\pi_2}{n-1}si$.
- Model reduces to a standard homogeneously mixing stochastic SIR epidemic with individual-to-individual infection rate $\frac{2\lambda\pi_2}{n-1}$ and recovery rate γ.

Outline of talk

- Derive model properties
  - Early stages of an epidemic – branching process approximation
  - Main body of an epidemic – approximating deterministic model and functional CLT
  - Final outcome – CLT
- Effect of π and distribution of C on epidemic properties – comparison with standard homogeneously mixing model
- SEIR model and model with demography
- Concluding comments

Approximating branching process $\mathcal{B}$

- Suppose $C^{(n)} \xrightarrow{\mathrm{D}} C$ as $n \to \infty$, where $\mathrm{P}(C = c) = p_C(c)$ $(c = 2, 3, \dots)$.
- The early stages of an epidemic can be approximated by a branching process $\mathcal{B}$, which assumes every mixing event that contains infectives has one infective with all others at the mixing event being susceptible.
- Consider a typical infective i_*. The probability a mixing event of size c involves i_* is $\frac{c}{n}$, so mixing events involving i_* occur at rate $n\lambda \sum_{c=2}^{\infty} p_C(c)\frac{c}{n} = \lambda\mu_C$, where $\mu_C = \mathrm{E}[C]$, and the size $\tilde{C}$ of a typical mixing event involving i_* has the size-biased distribution

$$p_{\tilde{C}}(c) = \mathrm{P}(\tilde{C} = c) = \mu_C^{-1} c p_C(c) \qquad (c = 2, 3, \dots).$$

- Thus in $\mathcal{B}$, an individual has lifetime $\sim \mathrm{Exp}(\gamma)$, during which they have birth events at rate $\lambda\mu_C$. The number of offspring $\tilde{Z}$ produced at a typical birth event has the mixed-binomial distribution $\mathrm{Bin}(\tilde{C} - 1, \pi_{\tilde{C}})$.

Basic reproduction number R_0

- Let R be the number of offspring of a typical individual in $\mathcal{B}$. Then,

$$R = \tilde{Z}_1 + \tilde{Z}_2 + \cdots + \tilde{Z}_G,$$

where $\tilde{Z}_1, \tilde{Z}_2, \cdots \overset{\text{i.i.d.}}{\sim} \text{Bin}(\tilde{C} - 1, \pi_{\tilde{C}})$ and G has the geometric distribution

$$\text{P}(G = k) = \frac{\gamma}{\gamma + \lambda\mu_C} \left(\frac{\lambda\mu_C}{\gamma + \lambda\mu_C} \right)^k \qquad (k = 0, 1, \dots).$$

- $R_0 = \text{E}[R] = \text{E}[G]\text{E}[\tilde{Z}] = \frac{\lambda\mu_C}{\gamma}\text{E}[(\tilde{C} - 1)\pi_{\tilde{C}}] = \frac{\lambda}{\gamma}\sum_{c=2}^{\infty} \pi_c c(c-1)p_C(c)$.
- If the infection probability π_c is independent of mixing event size (i.e. $\pi_c = \pi$ for all c), then

$$R_0 = \frac{\lambda\pi}{\gamma}\text{E}[C(C-1)].$$

Extinction probability of $\mathcal{B}$

- Let z be the extinction probability of $\mathcal{B}$ given a single ancestor.
- By standard branching process theory, z is given by the smallest solution in $[0,1]$ of $f_R(s) = s$, where

$$f_R(s) = \sum_{k=0}^{\infty} \frac{\gamma}{\gamma + \lambda\mu_C} \left(\frac{\lambda\mu_C}{\gamma + \lambda\mu_C} \right)^k (f_{\tilde{Z}}(s))^k = \frac{\gamma}{\gamma + \lambda\mu_C \left(1 - f_{\tilde{Z}}(s)\right)},$$

with (recall $\tilde{Z} \sim \mathrm{Bin}(\tilde{C} - 1, \pi_{\tilde{C}})$)

$$f_{\tilde{Z}}(s) = \sum_{c=2}^{\infty} p_{\tilde{C}}(c)(1 - \pi_c + \pi_c s)^{c-1} = \frac{1}{\mu_C} \sum_{c=2}^{\infty} p_C(c) c (1 - \pi_c + \pi_c s)^{c-1}.$$

- If $\pi_c = \pi$ for all c,

$$f_R(s) = \frac{\gamma}{\gamma + \lambda\mu_C - \lambda f'_C(1 - \pi + \pi s)}.$$

Exponential growth rate r of $\mathcal{B}$

- Let $L \sim \mathrm{Exp}(\gamma)$ denote a typical lifetime. The mean rate that an individual produces offspring at age t is

$$\mathrm{P}(L > t)\lambda\mu_C \mathrm{E}[\tilde{Z}] = \mathrm{e}^{-\gamma t}\gamma R_0 \qquad (t > 0),$$

  so the Lotka-Euler equation is $\int_0^\infty \mathrm{e}^{-rt}\gamma \mathrm{e}^{-\gamma t} R_0 \, \mathrm{d}t = 1$, yielding

$$r = \gamma(R_0 - 1).$$

- If R_0 and γ are fixed, then the exponential growth rate r is the same for all corresponding choices of the distribution of C and (π_c), and equals that of a standard homogeneously mixing epidemic.

Threshold theorem

Theorem 1 Suppose that $m_n = m$ for all sufficiently large n, $C^{(n)} \xrightarrow{\mathrm{D}} C$ and $\mathrm{E}[(C^{(n)})^2] \to \mathrm{E}[C^2]$ as $n \to \infty$, where $E[C^2] < \infty$. Suppose also that

$$\lim_{n\to\infty} \sqrt{n} \sum_{c=2}^{\infty} c \left| p_C^{(n)}(c) - p_C(c) \right| = 0 \quad \text{and} \quad \lim_{n\to\infty} \sum_{c=2}^{\infty} \pi_c c^3 p_C^{(n)}(c) = \sum_{c=2}^{\infty} \pi_c c^3 p_C(c) < \infty.$$

(a) Let $T^{(n)}$ be the final size of the epidemic $\mathcal{E}^{(n)}$. Then

$$\mathrm{P}(T^{(n)} \geq \log n) \to 1 - z^m \quad \text{as } n \to \infty.$$

(b) If also $R_0 > 1$, then there exists $\delta > 0$ such that

$$\mathrm{P}(T^{(n)} \geq \delta n \mid T^{(n)} \geq \log n) \to 1 \quad \text{as } n \to \infty.$$

Outcome of mixing event

Lemma 1 Consider a mixing event of size c, in which individuals are independently susceptible, infective or recovered with probabilities x, y and $1-x-y$. Let Z be the number of new infectives created at the mixing event, $\mu_c(x,y) = \mathrm{E}[Z]$ and $\mu_{c,2}(x,y) = \mathrm{E}[Z^2]$. Then,

$$\mu_c(x,y) = cx\left[1-(1-y\pi_c)^{c-1}\right]$$

and

$$\mu_{c,2}(x,y) = cx\left[1-(1-y\pi_c)^{c-1}\right] + c(c-1)x^2\left\{1-2(1-y\pi_c)^{c-2}+[1-y\pi_c(2-\pi_c)]^{c-2}\right\}.$$

Proof Label the individuals at the event $1, 2, \ldots, c$. Let

$$\chi_i = \begin{cases} 1 & \text{if individual } i \text{ is infected at the event} \\ 0 & \text{otherwise .} \end{cases}$$

Then

$$\mathrm{E}[Z] = \mathrm{E}[\chi_1+\chi_2+\cdots+\chi_c] = c\mathrm{P}(\chi_1=1) = c\mathrm{P}(1 \text{ is susceptible})\mathrm{P}(1 \text{ is infected}|\ 1 \text{ is susceptible})$$
$$= cx\left[1-(1-y\pi_c)^{c-1}\right].$$

Epidemics with many initial infectives

- Let $S^{(n)}(t)$ and $I^{(n)}(t)$ be the numbers of susceptibles and infectives at time t.
- $\{(S^{(n)}(t), I^{(n)}(t))\} = \{(S^{(n)}(t), I^{(n)}(t)) : t \geq 0\}$ is an (asymptotic) density dependent population process (Ethier and Kurtz (1986), Pollett (1990)).
- Suppose $n^{-1}m_n \to \varepsilon > 0$ as $n \to \infty$. Then, for any $t_0 > 0$,

$$\sup_{0 \leq t \leq t_0} \left| n^{-1}(S^{(n)}(t), I^{(n)}(t)) - (x(t), y(t)) \right| \xrightarrow{\text{p}} 0 \quad \text{as} \quad n \to \infty,$$

where $\{(x(t), y(t)) : t \geq 0\}$ satisfies the following ODE:

$$\frac{dx}{dt} = -\lambda x g(y), \qquad \frac{dy}{dt} = \lambda x g(y) - \gamma y, \qquad (x(0), y(0)) = (1 - \varepsilon, \varepsilon), \quad (1)$$

where

$$g(y) = \sum_{c=2}^{\infty} p_C(c) g_c(y), \qquad \text{with} \qquad g_c(y) = c\left[1 - (1 - y\pi_c)^{c-1}\right].$$

- Models of the general form (1) were studied by Capasso and Serio (1978).

Functional CLT

- In the limit as $n \to \infty$, the process $\{(S^{(n)}(t), I^{(n)}(t))\}$ has infinitesimal drift function

$$\boldsymbol{F}(x,y) = (-\lambda x g(y), \lambda x g(y) - \gamma y)$$

and infinitesimal variance/covariance matrix

$$\boldsymbol{G}(x,y) = \lambda h(x,y) \begin{bmatrix} 1 & -1 \\ -1 & 1 \end{bmatrix} + \gamma y \begin{bmatrix} 0 & 0 \\ 0 & 1 \end{bmatrix}, \quad \text{where} \quad h(x,y) = \sum_{c=2}^{\infty} p_C(c) \mu_{c,2}(x,y).$$

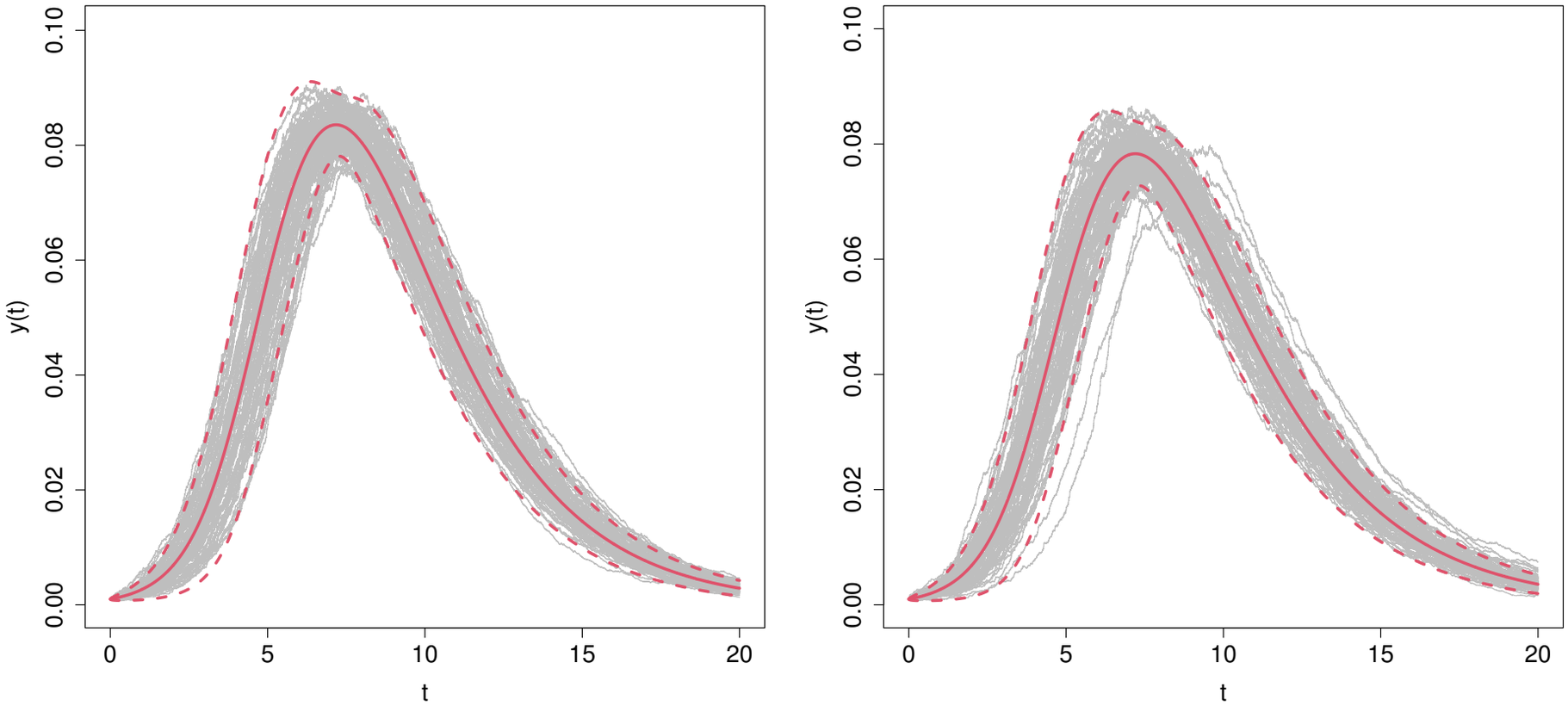
- Suppose that $\sqrt{n}(n^{-1} m_n - \varepsilon) \to \varepsilon_0$ as $n \to \infty$, where $\varepsilon > 0$. Then,

$$\left\{ \sqrt{n} \left[n^{-1} (S^{(n)}(t), I^{(n)}(t)) - (x(t), y(t)) \right] : t \geq 0 \right\} \Rightarrow \{\boldsymbol{V}(t) : t \geq 0\} \quad \text{as } n \to \infty,$$

where $\{\boldsymbol{V}(t) : t \geq 0\}$ is a zero-mean Gaussian process with $\boldsymbol{V}(0) = (-\varepsilon_0, \varepsilon_0)$. Further, $\boldsymbol{\Sigma}(t) = \mathrm{var}\,(\boldsymbol{V}(t))$ satisfies the ODE

$$\frac{d\boldsymbol{\Sigma}}{dt} = \boldsymbol{G}(x(t), y(t)) + \boldsymbol{\partial F}(x(t), y(t)) \boldsymbol{\Sigma} + \boldsymbol{\Sigma} [\boldsymbol{\partial F}(x(t), y(t))]^{\top}, \qquad \boldsymbol{\Sigma}(0) = \mathbf{0}.$$

Illustration of functional CLT



100 simulated realisations of trajectories of fraction infected $y(t)$ in population of size $n = 100,000$, with 100 initial infectives, $R_0 = 2$ and $\pi = 1$. Left panel: $C \sim$ logarithmic distribution with $\mu_C = 3.95$. Right panel: $C \sim$ geometric distribution with $\mu_C = 5$.

Final outcome

- Let $\tau^{(n)} = \inf\{t > 0 : I^{(n)}(t) = 0\}$. Then the final size $T^{(n)}$ of the epidemic is given by $T^{(n)} = n - S^{(n)}(\tau^{(n)})$.
- Suppose $n^{-1}m_n \to \varepsilon > 0$ as $n \to \infty$. Then $\tau^{(n)} \xrightarrow{\mathrm{p}} \infty$ as $n \to \infty$.
- Let $\{(\tilde{S}^{(n)}(t), \tilde{I}^{(n)}(t))\}$, be the random time-scale transformation of $\{(S^{(n)}(t), I^{(n)}(t))\}$ in which, at any time $t \geq 0$, the clock is speeded up by a factor $\frac{n}{I^{(n)}(t)}$.
- $T^{(n)} \stackrel{D}{=} \tilde{T}^{(n)}$, where $\tilde{T}^{(n)} = n - \tilde{S}^{(n)}(\tilde{\tau}^{(n)})$ and $\tilde{\tau}^{(n)} = \inf\{t > 0 : \tilde{I}^{(n)}(t) = 0\}$.
- $n^{-1}\{(\tilde{S}^{(n)}(t), \tilde{I}^{(n)}(t))\} \xrightarrow{\mathrm{p}} \{(\tilde{x}(t), \tilde{y}(t))\}$ as $n \to \infty$, where

$$\frac{d\tilde{x}}{dt} = -\lambda\tilde{x}\tilde{g}(\tilde{y}), \quad \frac{d\tilde{y}}{dt} = \lambda\tilde{x}\tilde{g}(\tilde{y}) - \gamma, \quad (\tilde{x}(0), \tilde{y}(0)) = (1 - \varepsilon, \varepsilon),$$

with

$$\tilde{g}(y) = \begin{cases} y^{-1}g(y) & \text{if } y \neq 0, \\ \sum_{c=2}^{\infty} p_C(c)c(c-1)\pi_c & \text{if } y = 0. \end{cases}$$

Final outcome LLN and CLT

- Time-transformed deterministic model

$$\frac{d\tilde{x}}{dt} = -\lambda\tilde{x}\tilde{g}(\tilde{y}), \quad \frac{d\tilde{y}}{dt} = \lambda\tilde{x}\tilde{g}(\tilde{y}) - \gamma, \quad (\tilde{x}(0), \tilde{y}(0)) = (1-\varepsilon, \varepsilon).$$

- For $t \geq 0$, we have $\tilde{x}(t) = 1 - \tilde{y}(t) - \gamma t$, so $\tilde{y}(t)$ satisfies

$$\frac{d\tilde{y}}{dt} = \lambda(1 - \tilde{y} - \gamma t)\tilde{g}(\tilde{y}) - \gamma, \qquad \tilde{y}(0) = \varepsilon.$$

- Note $\tilde{\tau}_\varepsilon = \inf\{t > 0 : \tilde{y}(t) = 0\} < \infty$, so the deterministic final size is $1 - \tilde{x}(\tilde{\tau}_\varepsilon) = \gamma\tilde{\tau}_\varepsilon$.
- $n^{-1}T^{(n)} \xrightarrow{\mathrm{p}} \gamma\tilde{\tau}_\varepsilon$ as $n \to \infty$.
- If $m_n = m$ for all n and $R_0 > 1$, then $n^{-1}T^{(n)} \mid T^{(n)} \geq \log n \xrightarrow{\mathrm{p}} \gamma\tilde{\tau}_0$ as $n \to \infty$.
- Corresponding CLTs are available using a functional CLT for $\{(\tilde{S}^{(n)}(t), \tilde{I}^{(n)}(t))\}$ and solving the associated boundary crossing problem.

Force of infection when $\pi_c = \pi$ for all c

- Force of infection acting on an individual is

$$\lambda g(y) = \lambda \sum_{c=2}^{\infty} p_C(c) g_c(y) = \lambda \sum_{c=2}^{\infty} p_C(c) c \left[1 - (1 - y\pi)^{c-1}\right].$$

- Recall $R_0 = \frac{\lambda\pi}{\gamma}\mathrm{E}[C(C-1)]$.
- Hence,

$$\lambda g(y) = \frac{\gamma R_0}{\pi \mathrm{E}[C(C-1)]} \sum_{c=2}^{\infty} p_C(c) c(c-1) \int_{1-\pi y}^{1} u^{c-2}\,\mathrm{d}u = \gamma R_0 U(y),$$

where

$$U(y) = \frac{1}{\pi} \int_{1-\pi y}^{1} \sum_{c=2}^{\infty} \frac{p_C(c)c(c-1)}{\mathrm{E}[C(C-1)]} u^{c-2}\,\mathrm{d}u = \frac{1}{\pi} \int_{1-\pi y}^{1} f_{\hat{C}-2}(u)\,\mathrm{d}u = \int_0^y f_{\hat{C}-2}(1-\pi v)\,\mathrm{d}v$$

and $\hat{C}$ has the "size-biased" distribution

$$\mathrm{P}(\hat{C} = c) = \frac{p_C(c)c(c-1)}{\mathrm{E}[C(C-1)]} \qquad (c = 2, 3, \ldots).$$

Model comparisons – effect of π

- Recall,

$$U(y) = \int_0^y f_{\hat{C}-2}(1-\pi v)\,\mathrm{d}v.$$

- Final size $\tilde{\tau}_\varepsilon = \tilde{\tau}_\varepsilon(R_0, C, \pi) = \inf\{t > 0 : \tilde{y}(t) = 0\} < \infty$, where $\tilde{y}(t)$ satisfies

$$\frac{d\tilde{y}}{dt} = \gamma R_0 \frac{U(\tilde{y})}{\tilde{y}}(1 - \tilde{y} - \gamma t) - \gamma, \qquad \tilde{y}(0) = \varepsilon.$$

- Extinction probability $z = z(R_0, C, \pi)$ is the smallest solution in $[0, 1]$ of

$$\frac{1}{1 + R_0 U(1-s)} = s.$$

- For fixed R_0 and event size distribution C,
  - $\tilde{\tau}_\varepsilon(R_0, C, \pi)$ decreases with π and $z(R_0, C, \pi)$ increases with π.
  - When $\mathrm{P}(C = 2) = 1$, $\tilde{\tau}_\varepsilon$ and z are independent of π, say $\hat{\tau}_\varepsilon(R_0)$ and $\hat{z}(R_0)$.
  - $\tilde{\tau}_\varepsilon(R_0, C, \pi) \uparrow \hat{\tau}_\varepsilon(R_0)$ and $z(R_0, C, \pi) \downarrow \hat{z}(R_0)$ as $\pi \downarrow 0$.

Model comparisons – effect of C

- Recall,

$$U(y) = \frac{1}{\pi} \int_{1-\pi y}^{1} f_{\hat{C}-2}(u)\, \mathrm{d}u.$$

- PGF ordering of random variables

$$C' \overset{g}{\leq} C \quad \text{if and only if} \quad f_{C'}(s) \geq f_C(s) \quad \text{for all } 0 \leq s \leq 1.$$

- Suppose π is fixed and $\hat{C}' \overset{g}{\leq} \hat{C}$. Then,
  - $\tilde{\tau}_\varepsilon(R_0, C', \pi) \geq \tilde{\tau}_\varepsilon(R_0, C, \pi)$, with strict inequality if $C \overset{D}{\neq} C'$.
  - $z(R_0, C', \pi) \leq z(R_0, C, \pi)$, with strict inequality if $R_0 > 1$ and $C \overset{D}{\neq} C'$
- For any C with $\mathrm{P}(C = 2) < 1$ and any $\pi \in (0, 1]$,
  - $\tilde{\tau}_\varepsilon(R_0, C, \pi) \leq \hat{\tau}_\varepsilon(R_0)$, with strict inequality if $\varepsilon > 0$ or $R_0 > 1$.
  - $z(R_0, C, \pi) \geq z(R_0)$, with strict inequality if $R_0 > 1$.

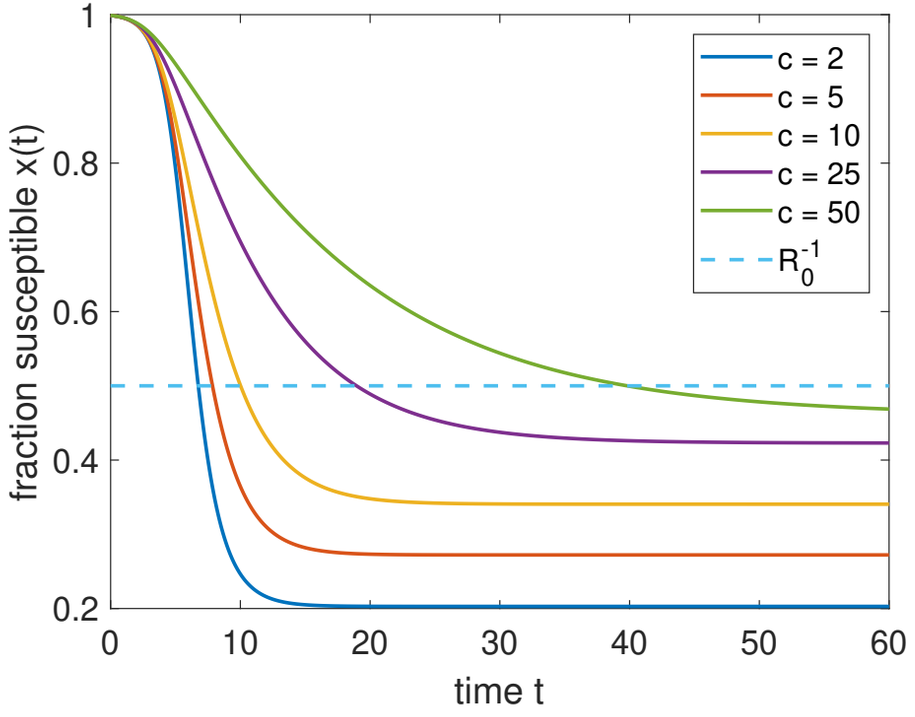
Large mixing events

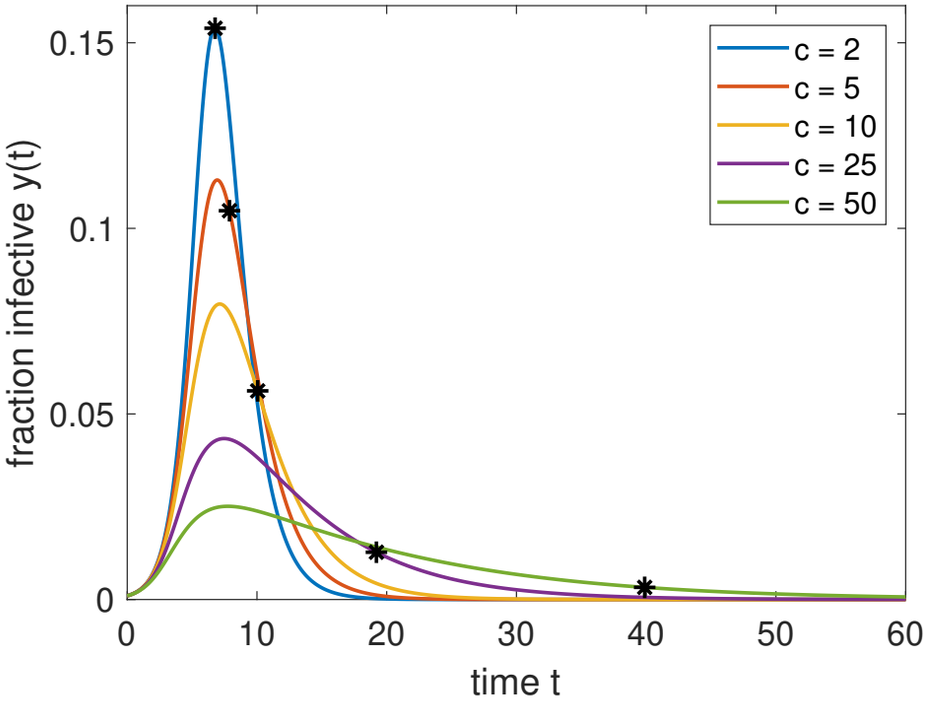
- Suppose all mixing events have size c. Then in the deterministic model

$$\begin{aligned}\frac{dy}{dt} &= \frac{\gamma R_0}{(c-1)\pi}\left[1-(1-y\pi_c)^{c-1}\right]x-\gamma y\\ &\leq \gamma\left[\frac{R_0}{(c-1)\pi}-y\right]\\ &\Longrightarrow\ y(t)\leq\frac{R_0}{(c-1)\pi}\quad\text{for all } t.\end{aligned}$$

- If c is large,
  - epidemics have long duration,
  - size of epidemic is only just greater than $1-\frac{1}{R_0}$.

Large mixing events





Trajectories of fraction susceptible $x(t)$ and fraction infective $y(t)$ when $R_0 = 2$, $\gamma = 1$, $\pi = 1$ and initial fraction infective $\varepsilon = 0.001$. * indicates when $x(t) = 1/R_0$.

Event size distributions

- Logarithmic $C \sim \text{Log}(\alpha)$.

$$p_C(c) = \kappa_\alpha \frac{(1-\alpha)^c}{c} \qquad (c = 2, 3, \ldots),$$

where $\kappa_\alpha = [-\log(\alpha) - (1-\alpha)]^{-1}$.

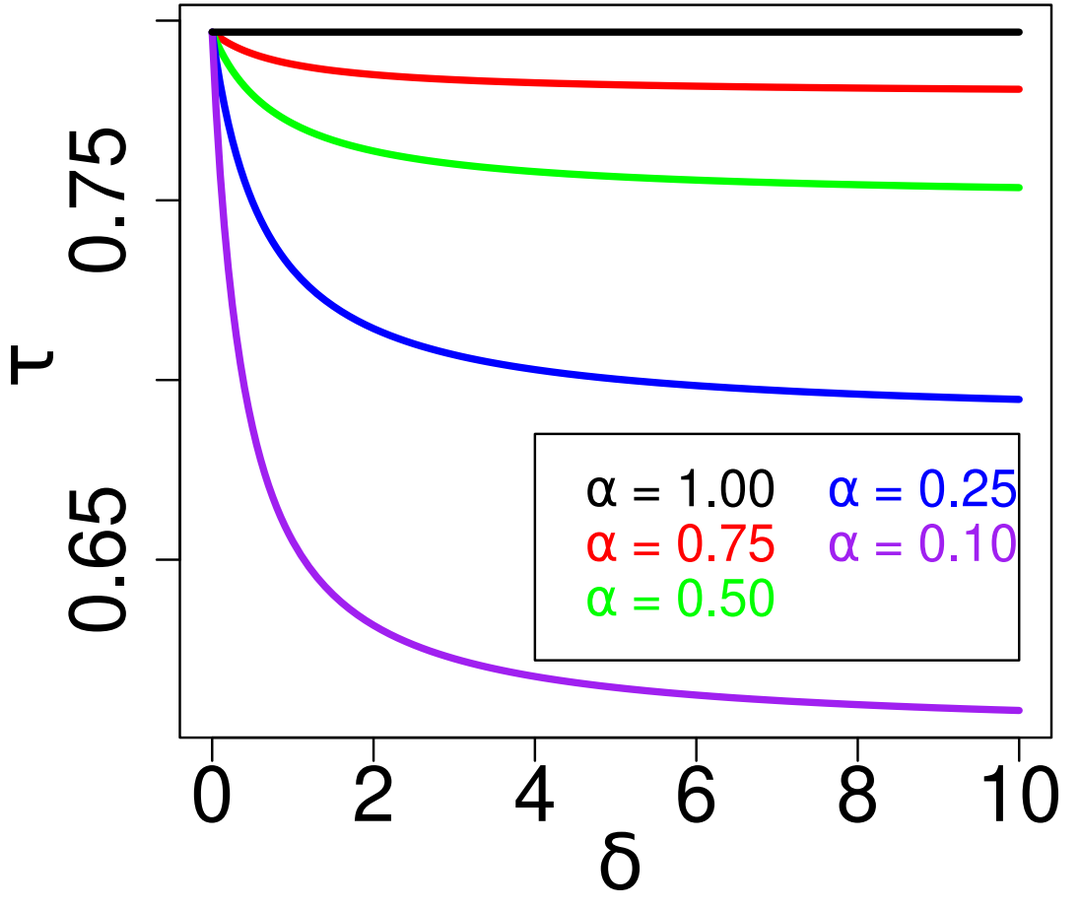
  - $\mu_C = \frac{\kappa_\alpha (1-\alpha)^2}{\alpha}$, $\quad R_0 = \frac{\lambda \pi \kappa_\alpha (1-\alpha)^2}{\gamma \alpha^2}$,
  - $U(y) = \frac{\alpha y}{\alpha + (1-\alpha)\pi y}$, $\quad f_{\hat{C}-2}(s) = \left(\frac{\alpha}{1-(1-\alpha)s}\right)^2$.
  - Deterministic model explicitly soluble in the (x, y) plane (Capasso and Serio (1978), Cortez (2022)).

- Geometric $C \sim \text{Geom}(\alpha)$

$$p_C(c) = (1-\alpha)^{c-2}\alpha \qquad (c = 2, 3, \ldots).$$

  - $\mu_C = 1 + \alpha^{-1}$, $\quad R_0 = \frac{2\lambda\pi}{\gamma\alpha^2}$,
  - $U(y) = \frac{\alpha y[2\alpha + (1-\alpha)\pi y]}{2[\alpha + (1-\alpha)\pi y]^2}$, $\quad f_{\hat{C}-2}(s) = \left(\frac{\alpha}{1-(1-\alpha)s}\right)^3$.

SEIR final size $\tilde{\tau}_0$



$C \sim Log(\alpha)$, $\alpha = 1, 0.55, 0.35, 0.2, 0.1$ ($\mu_C = 2.00, 2.21, 2.59, 3.54, 5.78$),

$R_0 = 2$, $\gamma = 1$, latent period $\sim \mathrm{Exp}(\delta)$

Concluding comments

- New class of epidemic models in which disease transmission is via mixing events
- For fixed R_0, the distribution of mixing event size C has a significant impact on epidemic properties
- Standard homogeneously mixing model ($C \equiv 2$) is a worst-case scenario
- Extensions
  - non-exponentially distributed infectious periods
  - Other models for transmission at mixing events
  - household models
  - multitype models