Separable Mixing

weighted at random $\Rightarrow$ scalar variables
(despite heterogeneity)

See Section 8.4 of DHB book mentioned on P2.11

Assume

$$A(\tau, x, \xi) = a(x) g(\tau, \xi)$$

Interpretation: the properties of the two individuals involved have independent influence on the likelihood of transmission.

Consequences: ① The operators K_λ have one-dimensional range spanned by a. Hence

$$R_0 = N \int_\Omega \left(\int_0^\infty g(\tau, \xi) \, d\tau \right) a(\xi) \, \Phi(d\xi)$$

Euler-Lotka $\quad 1 = N \int_\Omega \left(\int_0^\infty g(\tau, \xi) e^{-\lambda \tau} \, d\tau \right) a(\xi) \Phi(d\xi)$

$\text{sign}(R_0 - 1) = \text{sign } r \quad$ is easy to prove

②
$$s(t, x) = e^{-a(x) w(t)}$$

with w a solution of the

scalar RE $\quad w(t) = N \int_0^\infty \int_\Omega g(\tau, \xi) \left[1 - e^{-a(\xi) w(t-\tau)} \right] \Phi(d\xi) \, d\tau$

with $w(-\infty) = 0$
So the cumulative f-o-i on individuals with trait x
equals $\quad a(x) w(t)$

Note that we can discretize the RE for w as described on P1.10

③ Final Size : $s(\infty, x) = e^{-a(x)w(\infty)}$ with (P4.2

$$w(\infty) = N \int_{\Omega} \left(\int_0^{\infty} g(\tau, \xi) d\tau \right) \left[1 - e^{-a(\xi)w(\infty)} \right] \Phi(d\xi)$$

Assume

$$g(\tau, \xi) = b(\tau) c(\xi)$$

Define

$$\Psi(w) := \int_{\Omega} c(\xi) \left(1 - e^{-a(\xi)w} \right) \Phi(d\xi)$$

then the RE for w reads

$$w(t) = N \int_0^{\infty} b(\tau) \Psi(w(t-\tau)) d\tau$$

Gamma Distribution

- J.O. Lloyd-Smith, S.J. Schreiber, P.E. Kopp, W.M. Getz, Superspreading and the effect of individual variation on disease emergence, Nature (2005) 438 (7066) : 355-359
- A.S. Novozhilov, On the spread of epidemics in closed heterogeneous populations, Math. Biosc. 215 (2008) 177-185
- M.G.M. Gomes & various co-authors, preprints on medRxiv, arXiv
- A.V. Tkachenko e.a., Time-dependent heterogeneity leads to transient suppression of the COVID-19 epidemic, not herd immunity, PNAS (2021) 118 (17) e2015972118
- J. Neipel e.a., Power-Law population heterogeneity governs epidemic waves, PLoS ONE (2020) 15 (10) e0239678
- T. Britton, F. Ball, P. Trapman, A mathematical model reveals the influence of population heterogeneity on herd immunity to SARS-CoV2 Science (2020) 369 : 846-849

$\Omega = (0, \infty)$ Φ is the Gamma Distribution with

$$\boxed{\text{mean} = 1}$$

so Φ has density $\qquad x \longmapsto \dfrac{P^P}{\Gamma(P)} x^{P-1} e^{-Px}$

and $\qquad \boxed{\text{variance} = \dfrac{1}{P}}$

So small p corresponds to much heterogeneity !

The $\boxed{\text{Laplace Transform}}$ is $\qquad \overline{\Phi}(\lambda) = \left(\dfrac{\lambda}{P} + 1\right)^{-P}$

and $\quad \overline{\Phi}'(\lambda) = -\left(\dfrac{\lambda}{P} + 1\right)^{-P-1}$, so $\overline{\Phi}'(0) = -1$,

$$\overline{\Phi}''(\lambda) = \dfrac{P+1}{P}\left(\dfrac{\lambda}{P} + 1\right)^{-P-2}$$

We discuss / contrast the following three cases

I. no heterogeneity : $a(\zeta) = 1$, $c(\zeta) = 1$

II. heterogeneity in susceptibility, but not in infectiousness : $a(\zeta) = \zeta$, $c(\zeta) = 1$

III. correlated heterogeneity in susceptibility and infectiousness : $a(\zeta) = \zeta$, $c(\zeta) = \zeta$

in particular with respect to the $\boxed{\text{Effective Reproduction Number}}$

and the $\boxed{\text{Herd Immunity Threshold}}$

On page 1.3 the Basic Reproduction Number R_0 was defined as the expected number of secondary cases per primary case. It was left implicit that this concerns the start of an outbreak in a *fully* susceptible host population. On P3.2, 3.3 we considered a partly vaccinated population and introduced $\tilde{R}_0$ as a first example of an Effective Reproduction Number. Now we want to consider an ongoing outbreak and try to quantify the effect of immunity of those that were infected so far. To do so, we simply pretend that the current susceptible subpopulation is the entire population in which the pathogen is introduced and call the corresponding reproduction number $R_{eff}(t)$. For instance, for the SIR model of page 1.5 we have

$$R_{eff}(t) = \frac{\beta \, S(t)}{\alpha} = s(t) \, R_0 \quad \text{with } s(t) := \frac{S(t)}{N}$$

The Herd Immunity Threshold (HIT) corresponds, by definition, to $R_{eff}(t) = 1$ so in the present special case to

$$s(t) = \frac{1}{R_0}$$

(Please keep in mind that upon reaching the HIT during an actual outbreak, the epidemic does not stop, there is an overshoot due to the reservoir of already infected individuals, see the phase plane picture on page 1.5.)

For the RE for w from P4.2 we define

$$R_{eff}(t) = N \int_0^\infty b(\tau) \, d\tau \; \Psi'(w(t)) = R_0 \, \frac{\Psi'(w(t))}{\Psi'(0)}$$

$$= R_0 \, \frac{\int_\Omega c(\xi) a(\xi) \, e^{-a(\xi) w(t)} \, \Phi(d\xi)}{\int_\Omega c(\xi) a(\xi) \, \Phi(d\xi)}$$

We consider $R_{eff} = 1$ as an equation for w and denote the solution of this equation by $\bar{w}$.

The fraction of the population that is still susceptible when the HIT is reached is given by

$$\bar{s} = \int_0^\infty e^{-\alpha(\xi)\bar{w}} \, \Phi(d\xi)$$

	$\Psi(w)$	R_0	$R_{eff}(w)$	$\bar{w}$	$\bar{s}$
I	$1 - e^{-w}$	1	$R_0 e^{-w}$	$\ln R_0$	R_0^{-1}
II	$1 - \left(\frac{w}{p} + 1\right)^{-p}$	1	$R_0 \left(\frac{w}{p} + 1\right)^{-p-1}$	$p\left(R_0^{\frac{1}{p+1}} - 1\right)$	$R_0^{-1 + \frac{1}{p+1}}$
III	$1 - \left(\frac{w}{p} + 1\right)^{-p-1}$	$1 + \frac{1}{p}$	$R_0 \left(\frac{w}{p} + 1\right)^{-p-2}$	$p\left(R_0^{\frac{1}{p+2}} - 1\right)$	$R_0^{-1 + \frac{1}{\frac{1}{2}p+1}}$

Note that in the "uniform"/homogeneous case I, the HIT for vaccination and for natural immunity (induced by infection) is exactly the same, while for cases II, III and random vaccination, the vaccination HIT R_0^{-1} differs substantially from the HIT for infection induced immunity, especially for small p ~ strong heterogeneity. The reason is, of course, that among the individuals infected so far the highly susceptible individuals are over-represented. This effect plays already a role in the early stage of the outbreak. This can be seen by expanding the

formula for $R_{eff}(t)$ at the bottom of P4.4 while
assuming that $w(t)$ is small and, likewise, expanding

$$s(t) = \int_0^\infty e^{-a(\xi)w(t)} \bar{\Phi}(d\xi) = 1 - \int_0^\infty a(\xi)\bar{\Phi}(d\xi)w(t) + \cdots$$

Eliminating $w(t)$, and using that for all three cases
$\int_0^\infty a(\xi)\bar{\Phi}(d\xi) = 1$, we obtain

$$R_{eff}(t) = R_0\left(1 - \theta(1-s(t)) + o(1-s(t))\right)$$

with

$$\theta = \frac{\int_0^\infty c(\xi)a^2(\xi)\bar{\Phi}(d\xi)}{\int_0^\infty c(\xi)a(\xi)\bar{\Phi}(d\xi)} = \begin{cases} 1 & \text{case I} \\ 1 + \frac{1}{P} & \text{II} \\ 1 + \frac{2}{P} & \text{III} \end{cases}$$

A.V. Tkachenko e.a. write: "We named the coefficient
θ the immunity factor because it quantifies the effect
that a gradual buildup of population immunity has
on the spread of an epidemic."
 We re-iterate the message of the Exercise on P3.5, 3.6:
if the most susceptible individuals are also the most
infectious (in the sense of having many contacts) individuals,
heterogeneity has a large impact on R_0, see second column,
third row entry of the matrix scheme.

Assume $\boxed{b(\tau) = \beta e^{-\alpha\tau}}$ $\Rightarrow$ $\boxed{\dfrac{dw}{dt} = -\alpha w + \beta N\Psi(w)}$

Assume $\boxed{b(\tau) = \beta\dfrac{\gamma}{\alpha-\gamma}\left(e^{-\gamma\tau} - e^{-\alpha t}\right)}$ $\Rightarrow$ $\boxed{\begin{aligned} \frac{dw}{dt} &= f \\ \frac{df}{dt} &= \beta N\gamma\Psi(w) \\ &\quad -(\alpha+\gamma)f - \alpha\gamma w \end{aligned}}$

In the paper of J. Neipel e.a., see P4.2, the SIR ODE is related to Covid data of Germany.

See A. Cori, N.M. Ferguson, C. Fraser, S. Cauchemez
A new framework and software to estimate time-varying reproduction numbers during epidemics
American J. of Epidemiology (2013) 178(9): 1505-1512
for general methodology for estimating R_{eff} from data.

Other relevant references are
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Statistical Methods in Medical Research (2021) 09622800221103770
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H. Nishiura, G. Chowell, The effective reproduction number as a prelude to statistical estimation of time-dependent epidemic trends, pp 103-121 In: G. Chowell e.a., editors, Mathematical and Statistical Estimation Approaches in Epidemiology, Springer, 2009