Contact Matrices and Epidemic Dynamics

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- Imagine an epidemic circulating in a stratified population with I strata. Typically i will be used to denote the strata of an uninfected individual, j the strata of the infectious.
- Assuming mass action dynamics (everything extends straightforwardly to the Reed-Frost case).
- Rate of change in the number of susceptibles in strata i is:

$$\frac{dS_i}{dt}(t) = -S_i(t)\sum_j \beta_{ij}(t)I_j(t) \tag{1}$$

- $\beta_{ij}(t)$ therefore has the interpretation of the time-t hazard of infection faced by a susceptible individual of strata i of being infected by an infectious individual in strata j.
- A related, but different quantity is the reproductive number, R, the number of secondary infections caused by one typical infection in a fully susceptible population.
- In a stratified population, this is not a straightforward quantity to understand, as the number of second generation infections will depend on the strata occupied by a typical initial infection.
- Setting a single initial infection to be in strata j, in (1) set vector $\boldsymbol{I} = \boldsymbol{e}^{(j)}$, where $\boldsymbol{e}^{(j)}$ has k^{th} component $e_k^{(j)} = \delta_{jk}$. The rate of infection acting upon strata i in this case is $N_i\beta_{ij}(0)$. After one generation you could expect to see a number of new infections in strata i given by

$$N_i\beta_{ij}(0)d_I$$

  Where d_I is the duration of the infectious period.
- However, this quantity is not R because it is dependent on the strata to which the initial infective belongs.
- Define the time-t **next generation matrix**, $\boldsymbol{\Lambda}$ to have entries

$$\Lambda_{ij}(t) = N_i\beta_{ij}(t)d_I \tag{2}$$

- If none of the parameters vary over time, the number of infected individuals in each strata after n generations would be given by the vector

$$\Lambda^n \boldsymbol{e}^{(j)}$$

- If Λ is of full rank, then as n gets large, the total number of infectives would tend towards R_0^n with a distribution over strata given by the normalised vector $\hat{\boldsymbol{\nu}}$. Here R_0 is the dominant eigenvalue of Λ and is the time-0 reproductive number. $\hat{\nu}$ is the corresponding 'dominant' eigenvector.

- We don't know $\beta_{ij}(0)$ to calculate the reproductive number, R_0.

What is $\beta_{ij}(t)$

- Introduce a time-t contact matrix, $M(t) = \{M_{ij}(t)\}$. The elements describe rates of contact between any one individual of strata i with any one individual of strata j.

- Then $N_i M_{ij}(t)$ gives the total number of contacts with strata i for any one infected individual in strata j.

- If $b_{ij}(t) = \mathbb{P}\{\text{transmission}|\text{contact between } i \text{ and } j \text{ at time } t\}$, then the expected number of transmission events to members of strata i in one time unit from a single infectious individual in strata j is given by $b_{ij}(t)N_i M_{ij}(t)$.

- Multiplying by the duration of infectiousness, gives $b_{ij}(t)N_i M_{ij}(t)d_I$, the total number of secondary infections in strata j from a single primary infection in strata i.

- Setting

$$\beta_{ij}(t) = b_{ij}(t)M_{ij}(t) \tag{3}$$

  we can see that this is equivalent to equation (2).

- Simple case, consider $b_{ij}(t)$ to be a constant, $b_{ij}(t) = b$. Define a matrix $\boldsymbol{M}^*$, s.t. $M^*_{ij} = N_i M_{ij} d_I$. Then if R^* is the dominant eigenvalue of $\boldsymbol{M}^*$, we have that

$$b = \frac{R_0}{R^*}$$

- Alternatively: allow variation over time $b_{ij}(t) = b(t)$. Case of environmental stochasticity. Commonly handled by presuming $b(t)$ to be a stochastic (usually a Wiener) process.

- Variation over strata, e.g. $b_{ij}(t) = b_{ij} = b_0\sigma_i\tau_j$.
  - σ_i describes the susceptibility of individuals of strata i (how easy they are to infect).
  - τ_j describes the transmissibility of individuals of strata j (how good this strata is at infecting others).

How the RTM Estimates Transmission

- The real-time model has as 'free' parameters (in as much as they can be free when constrained by a prior distribution): infectious period d_I, exponential growth rate ψ and parameters, $\boldsymbol{m}$ of the contact matrix as it changes over time (i.e. $\boldsymbol{M}(t) \equiv \boldsymbol{M}(t; \boldsymbol{m})$).
- There is a functional relationship between ψ and R_0.
- Parameters of the contact model $\boldsymbol{m}$ are described below.

Scaling the Contact Matrix, $\boldsymbol{M}$

- Consider $\boldsymbol{M}' = k\boldsymbol{M}$.
- Transmission dynamics are determined by $\beta_{ij}(t)$.
- Under constant b, from (3)

$$\begin{aligned}\beta_{ij}(t) &= bM_{ij}(t) \\ &= \frac{R_0}{R^*}\frac{1}{k}M'_{ij}(t) \\ &= \frac{R_0}{R'^*}M'_{ij}(t)\end{aligned}$$

  where $R^{'*}$ is the dominant eigenvalue of $N_i M'_{ij}(0)d_I = kN_i M_{ij}(0)d_I$ (and so $R^{'*} = kR^*$). So, transmission dynamics are independent of the scaling of the matrix M.

- *Edwin has previously been picking k s.t $R^{'*} = 1$.*
- *Rather than using a Wiener process as suggested above, we currently have a time-varying $b(t)$ such that*

$$b(t) = \begin{cases} b_0 & \text{if } t \leq t_{\text{lock}} \\ mb_0 & \text{if } t > t_{\text{lock}} \end{cases}$$

  Transmission dynamics are now governed by

$$\beta_{ij}(t) = \begin{cases} \frac{R_0}{R^*}M_{ij}(t) & \text{if } t \leq t_{\text{lock}} \\ \frac{mR_0}{R^*}M_{ij}(t) & \text{if } t > t_{\text{lock}} \end{cases}$$

  Noting that R^* is as estimated from the time-0 NGM, under exponential growth. As the matrix $\boldsymbol{M}$ changes over time it just plugs into the above expression.

- In the above, scalar m could represent a decrease in transmissibility due to environmental factors (perhaps nicer weather? Shorter duration of contacts?)

- R_t is found to be the dominant eigenvalue of the time t next-generation matrix, the matrix with $(i,j)^{\text{th}}$ entry

$$\Lambda^*_{ij}(t) = S_i(t)\beta_{i,j}(t)d_I$$

- $M_{ij}(t)$ represents the probability of a contact between a random individual in strata i with a random individual in strata j at time t. The total number of contacts between individuals in strata i and j at time t is then $N_iN_jM_{ij}(t)$. The average number of contacts by any individual is calculated as the total number of contacts in the population, divided by the size of the population ($\sum_{ij} N_iN_jM_{ij}(t)/\sum_i N_i$).