

Stochastic epidemic models: introducing heterogeneities

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Outline

- Introduction
 - The infectivity profile (recap)
 - Key quantities of interest
- Multi-type models
 - Next-generation matrix
 - Basic reproduction number
 - Final size
 - Growth rate
- Network models
 - Local interactions
 - Basic reproduction number
- Households models
 - Model formulation
 - Reproduction numbers
 - Basic reproduction number
 - Comparisons between reproduction numbers
- Advanced concepts
 - Final size for the households model
 - Extensions: households-workplaces models

The infectivity profile (recap)
Key quantities of interest

INTRODUCTION

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The Reed-Frost model

- Assumptions:
 - Latency of 1 time unit, instantaneous infectious period (discrete)
 - Each susceptible escapes infection from each infectious independently with probability q (non-random)
 - X_k, Y_k = random number of susceptibles and infective in gen k

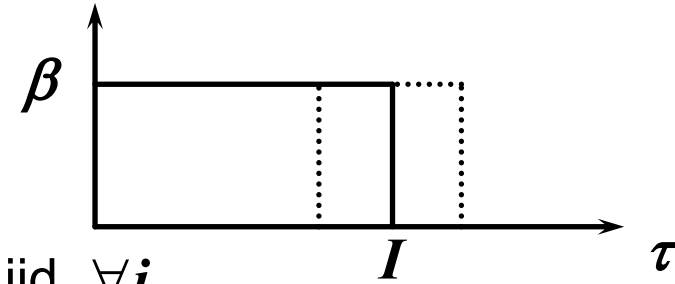
- Then:

$$\begin{aligned} & \mathbb{P}(Y_{k+1} = \mathbf{y}_{k+1} \mid X_0 = \mathbf{x}_0, Y_0 = \mathbf{y}_0, \dots, X_k = \mathbf{x}_k, Y_k = \mathbf{y}_k) \\ &= \mathbb{P}(Y_{k+1} = \mathbf{y}_{k+1} \mid X_k = \mathbf{x}_k, Y_k = \mathbf{y}_k) \\ &= \binom{\mathbf{x}_k}{\mathbf{y}_{k+1}} (1 - q^{y_k})^{y_{k+1}} (q^{y_k})^{x_k - y_{k+1}} \end{aligned}$$

Standard stochastic S/R model

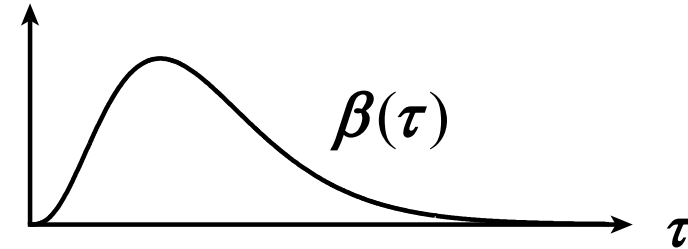
- Population of n individuals
- Upon infection, each case i :
 - remains infectious for a duration $I_i \sim I$, iid $\forall i$
 - makes infectious contacts with each person in the population at the points of a homogeneous Poisson process with rate $\lambda = \beta/n$
- Contacted individuals, if susceptible, become infected
- Recovered individuals are immune to further infection

- Special cases:
 - Constant infectious period: $I \equiv t$
 - Markovian case: $I \sim \text{Exp}(\gamma)$



Time-varying-infectivity model (TVI)

- Population of n individuals
- At time τ after infection, each case i :
 - makes infectious contacts with each person in the population at the points of an inhomogeneous Poisson process with rate

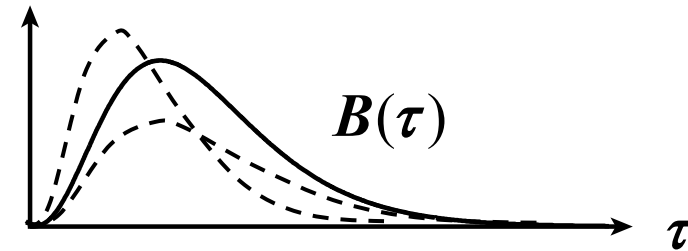


$$\lambda(\tau) = \beta(\tau)/n$$

- Contacted individuals, if susceptible, become infected
- Individuals do not recover (often you make them recover after a fixed amount of time)
- Special cases:
 - Constant infectivity: $\beta(\tau) = \beta \mathbb{I}_{\{0 < \tau < l\}}$

Random TVI model

- Population of n individuals
- At time τ after infection, each case i :
 - makes infectious contacts with each person in the population at the points of an inhomogeneous Poisson process with rate



$$\Lambda(\tau) = B(\tau)/n$$

- Contacted individuals, if susceptible, become infected
- Individuals do not recover (often you make them recover after a fixed amount of time)
- Special cases:
 - sSIR: $B(\tau) = \beta I_{\{0 < \tau < I\}}$

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Key epidemiological quantities

Now focus on single (fast) epidemic in a large populations with few initial infectives only.

Can we provide some summary information of the full dynamics?

- Time-independent quantities:
 - Threshold condition
 - Probability of a large outbreak
 - Epidemic final size
 - Critical vaccination coverage

- Time-dependent quantities:
 - Real-time growth rate
 - Duration of an epidemic

Next-generation matrix

Reproduction number

Final size

Growth rate

MULTI-TYPE MODELS

Multi-type models

- Distinguish individuals in “types”:
 - Identify epidemiologically relevant characteristics (age, sexual activity, geographical location...)
 - Describe the interaction of each type towards each other type
- Note that “type” may be dependent or independent of infection
 - sometimes susceptibles have a type (e.g. age)
 - sometimes the type is attributed at the time of infection (e.g. strain)
- Most ideas carry on from single-type models:
 - Infectivity profiles
 - Small vs large population
 - Key epidemiological quantities of interest

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Multitype epidemic model

- Different types of individuals
- Define the next generation matrix (NGM):

$$\mathbf{K} = \begin{pmatrix} k_{11} & k_{12} & \cdots & k_{1n_t} \\ k_{21} & k_{22} & & \vdots \\ \vdots & & \ddots & \vdots \\ k_{n_t 1} & \cdots & \cdots & k_{n_t n_t} \end{pmatrix}$$

where k_{ij} is the average number of type- i cases generated by a type- j case, throughout the entire infectious period, in a fully susceptible population

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where k_{ij} is the average number of type- i cases generated by a type- j case, throughout the entire infectious period, in a fully susceptible population

Properties of the NGM:

- Non-negative elements
- We assume the matrix is primitive

Perron-Frobenius theory

- Single dominant eigenvalue $\Lambda = \rho(\mathbf{K})$, which is positive and real
- “Dominant” eigenvector \mathbf{v} has non-negative components
- For every starting condition, after a few generations, the proportions of cases of each type in a generation converge to the components of the dominant eigenvector \mathbf{v} , with per-generation multiplicative factor Λ

Exercise: find R_0 by iterations

$$\mathbf{K} = \begin{pmatrix} 1 & 2 \\ 3 & 4 \end{pmatrix}$$

$$\mathbf{I}_0 = \begin{pmatrix} 1 \\ 0 \end{pmatrix} = \mathbf{m}_0 \mathbf{v}_0$$

$$\mathbf{m}_0 = |\mathbf{I}_0| = 1$$

$$\mathbf{v}_0 = \frac{\mathbf{I}_0}{\mathbf{m}_0} = \begin{pmatrix} 1 \\ 0 \end{pmatrix}$$

Exercise: find R_0 by iterations

$$\mathbf{K} = \begin{pmatrix} 1 & 2 \\ 3 & 4 \end{pmatrix} \quad \mathbf{I}_0 = \begin{pmatrix} 1 \\ 0 \end{pmatrix} = \mathbf{m}_0 \mathbf{v}_0 \quad \mathbf{m}_0 = |\mathbf{I}_0| = 1 \quad \mathbf{v}_0 = \frac{\mathbf{I}_0}{\mathbf{m}_0} = \begin{pmatrix} 1 \\ 0 \end{pmatrix}$$
$$\mathbf{I}_1 = \mathbf{K}\mathbf{I}_0 = \begin{pmatrix} 1 & 2 \\ 3 & 4 \end{pmatrix} \begin{pmatrix} 1 \\ 0 \end{pmatrix} = \begin{pmatrix} 1 \\ 3 \end{pmatrix} = (\mathbf{m}_0) \mathbf{m}_1 \mathbf{v}_1 \quad \mathbf{m}_1 = 4 \quad \mathbf{v}_1 = \begin{pmatrix} 0.25 \\ 0.75 \end{pmatrix}$$

Exercise: find R_0 by iterations

$$\mathbf{K} = \begin{pmatrix} 1 & 2 \\ 3 & 4 \end{pmatrix} \quad \mathbf{I}_0 = \begin{pmatrix} 1 \\ 0 \end{pmatrix} = m_0 \mathbf{v}_0 \quad m_0 = |\mathbf{I}_0| = 1 \quad \mathbf{v}_0 = \frac{\mathbf{I}_0}{m_0} = \begin{pmatrix} 1 \\ 0 \end{pmatrix}$$

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$$\mathbf{I}_2 = \mathbf{K}\mathbf{I}_1 = \begin{pmatrix} 1 & 2 \\ 3 & 4 \end{pmatrix} \begin{pmatrix} 1 \\ 3 \end{pmatrix} = \begin{pmatrix} 7 \\ 15 \end{pmatrix} = (m_0 m_1) m_2 \mathbf{v}_2 \quad m_2 = 5.5 \quad \mathbf{v}_2 \approx \begin{pmatrix} 0.32 \\ 0.68 \end{pmatrix}$$

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$$\mathbf{I}_3 = \mathbf{K}\mathbf{I}_2 = \begin{pmatrix} 1 & 2 \\ 3 & 4 \end{pmatrix} \begin{pmatrix} 7 \\ 15 \end{pmatrix} = \begin{pmatrix} 37 \\ 81 \end{pmatrix} = (m_0 m_1 m_2) m_3 \mathbf{v}_3 \quad m_3 \approx 5.36 \quad \mathbf{v}_3 \approx \begin{pmatrix} 0.31 \\ 0.69 \end{pmatrix}$$

Exercise: find R_0 by iterations

$$K = \begin{pmatrix} 1 & 2 \\ 3 & 4 \end{pmatrix} \quad I_0 = \begin{pmatrix} 1 \\ 0 \end{pmatrix} = m_0 v_0 \quad m_0 = |I_0| = 1 \quad v_0 = \frac{I_0}{m_0} = \begin{pmatrix} 1 \\ 0 \end{pmatrix}$$

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$$m_k \xrightarrow{k \rightarrow \infty} \Lambda \approx 5.37$$

$$v_k \xrightarrow{k \rightarrow \infty} v = \begin{pmatrix} 0.31 \\ 0.69 \end{pmatrix}$$

where

$$Kv = \Lambda v$$

Perron-Frobenius theory

- Single dominant eigenvalue $\Lambda = \rho(\mathbf{K})$, which is positive and real
- “Dominant” eigenvector \mathbf{v} has non-negative components
- For every starting condition, after a few generations, the proportions of cases of each type in a generation converge to the components of the dominant eigenvector \mathbf{v} , with per-generation multiplicative factor Λ



- Define $R_0 = \Lambda$
- Interpret “typical” case as a linear combination of cases of each type given by \mathbf{v}

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Basic reproduction number R_0

Naïve definition:

*“ Average number of new cases generated by a **typical** case, throughout the entire infectious period, in a large and otherwise **fully susceptible** population ”*

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What is a **typical** case?

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What is a **typical** case?

What do we mean by **fully susceptible** population?

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Final size

➤ Given:

- n_i = number of individuals of type i , $i = 1, 2, \dots, n_t$
- $h_i = n_i / N$ = fraction of population of type i
- k_{ij} = elements of the NGM

➤ Let:

- z_i = fraction of type i population ultimately infected

➤ Then:

$$1 - z_i = e^{-\sum_j \frac{k_{ij}}{n_i} n_j z_j} = e^{-\sum_j \frac{h_j}{h_i} k_{ij} z_j} \quad i = 1, 2, \dots, n_t$$

and the overall fraction of the population infected is $z = \sum_{i=1}^{n_t} h_i z_i$

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Real-time growth rate

➤ Single-type model:

- r is the implicit solution of the Euler-Lotka equation

$$L_{\beta}(\theta) = \int_0^{\infty} \beta(\tau) e^{-\theta\tau} d\tau = 1$$

➤ Multitype model:

- Construct the matrix

$$H_{\theta} = \left(\int_0^{\infty} \beta_{ij}(\tau) e^{-\theta\tau} d\tau \right) = \begin{pmatrix} L_{\beta_{11}}(\theta) & \dots & L_{\beta_{1n}}(\theta) \\ \vdots & \ddots & \vdots \\ L_{\beta_{n1}}(\theta) & \dots & L_{\beta_{nn}}(\theta) \end{pmatrix}$$

- Compute its dominant eigenvalue $\rho(H_{\theta})$, which depends on θ
- r is the implicit solution of

$$\rho(H_{\theta}) = 1$$

Fraction of types in real-time

- Once we have found r , we know that H_r has dominant eigenvalue 1
- The corresponding eigenvector \mathbf{v}_r gives the (constant) proportions of individuals of each type present at any point during the exponentially growing phase

➤ Simple case:

- If $\beta_{ij}(\tau) = k_{ij}\omega(\tau)$, then

$$H_r = \left(\int_0^\infty \beta_{ij}(\tau) e^{-r\tau} d\tau \right) = \left(\int_0^\infty k_{ij}\omega(\tau) e^{-r\tau} d\tau \right) = (k_{ij}) \left(\int_0^\infty \omega(\tau) e^{-r\tau} d\tau \right)$$

i.e.

$$H_r = \frac{1}{R_0} K$$

- so $\mathbf{v}_r = \mathbf{v}$, even if generations tend to overlap

Local interactions

Basic reproduction number

NETWORK MODELS

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The problem of small mixing groups

- For large populations the concept of R_0 , r , small/large outbreak are useful, but result from a linearisation process (e.g. BP)
- In small populations, the linearisation is not possible but also not useful
- But if the population is large AND the number of individuals one interact with is small, the linearisation is useful, but not trivial
- Basic idea is still to imbed a branching process, though this is not always possible
- In general, one needs to solve the local dynamics, which are non-linear because of **local depletion of susceptibles**

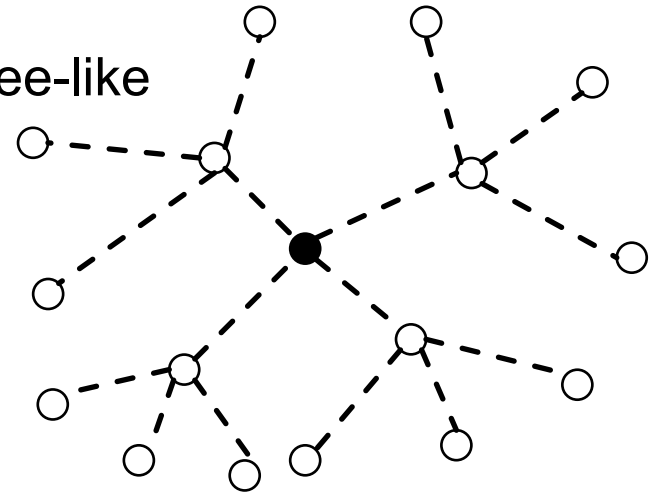
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Network models

- People connected by a static network of acquaintances
- **Simple case:** no short loops, i.e. locally tree-like
 - Repeated contacts
 - First case is special
 - $E[X_1] = 1$ is not a threshold
 - Define:

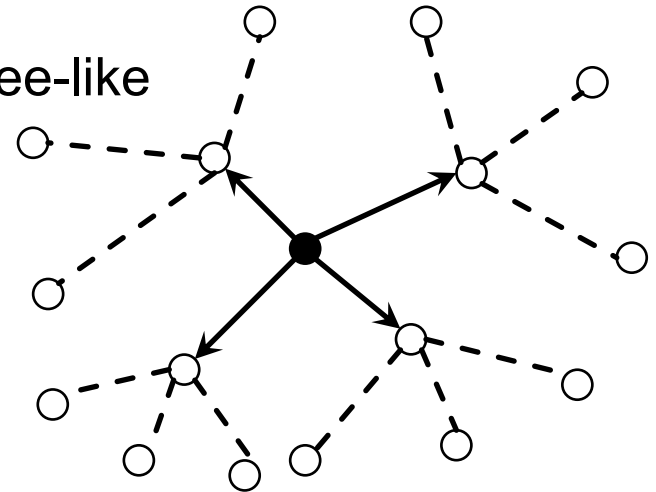
$$R_0 = E[X_2 | X_1 = 1]$$



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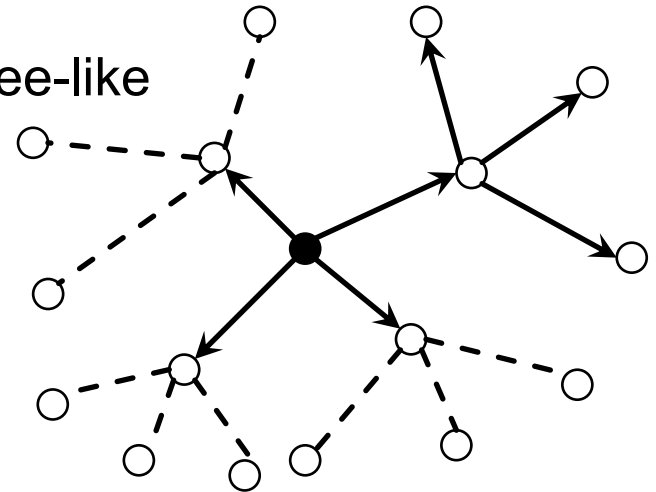
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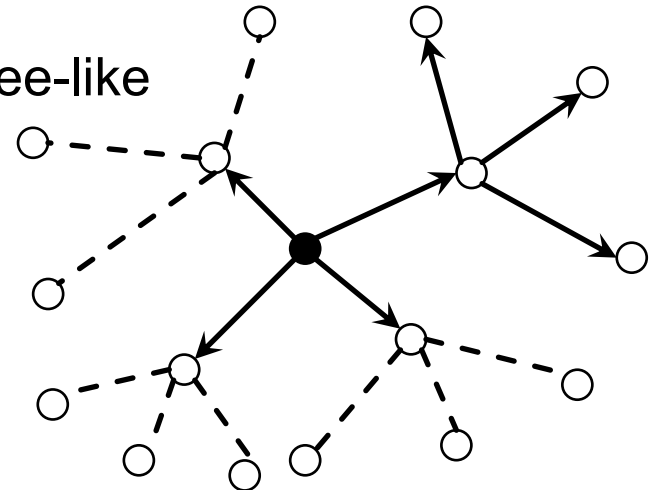
What do we mean by **fully susceptible** population?

Network models

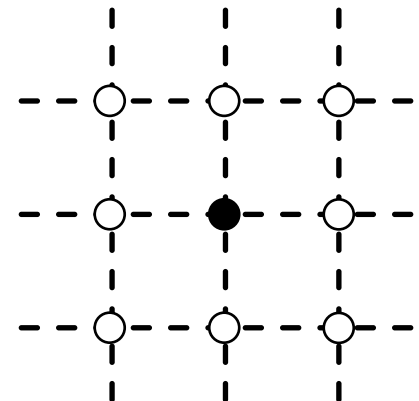
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- Define:

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- **Difficult case:** short loops, clustering
 - Maybe not even possible to use branching process approximation or define R_0



Introduction

Reproduction numbers

Basic reproduction number

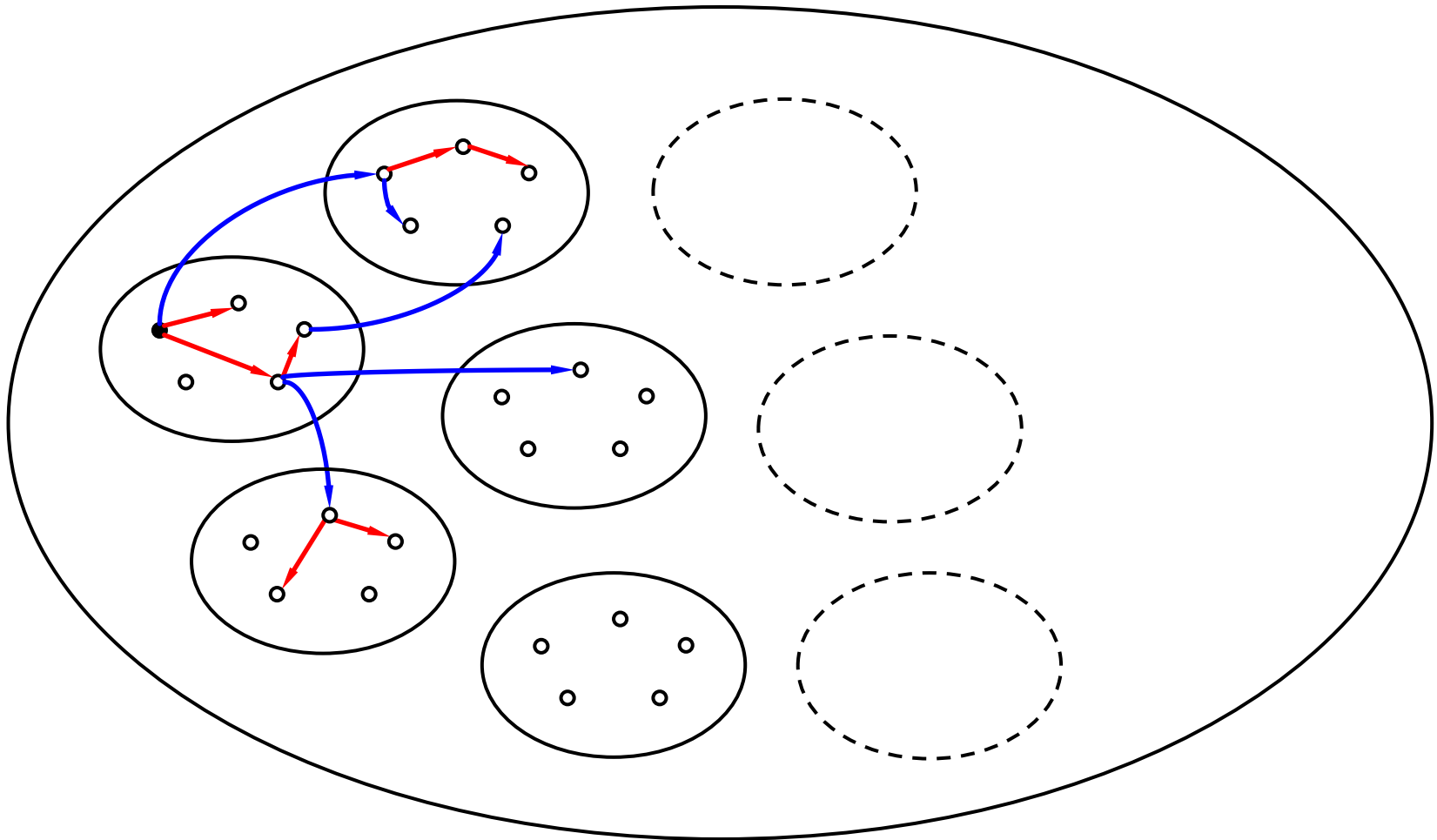
Comparison between reproduction numbers

THE HOUSEHOLDS MODEL

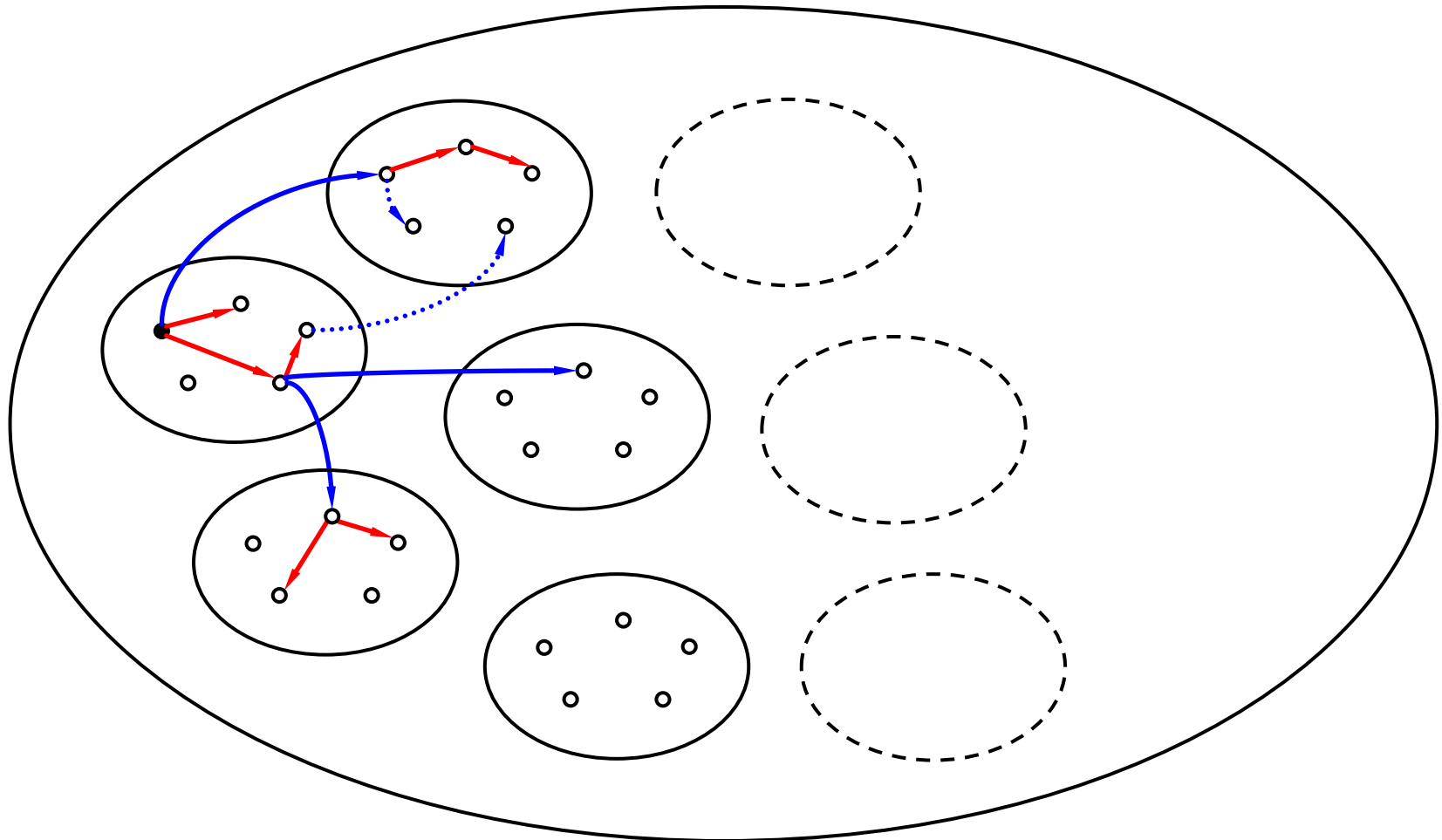
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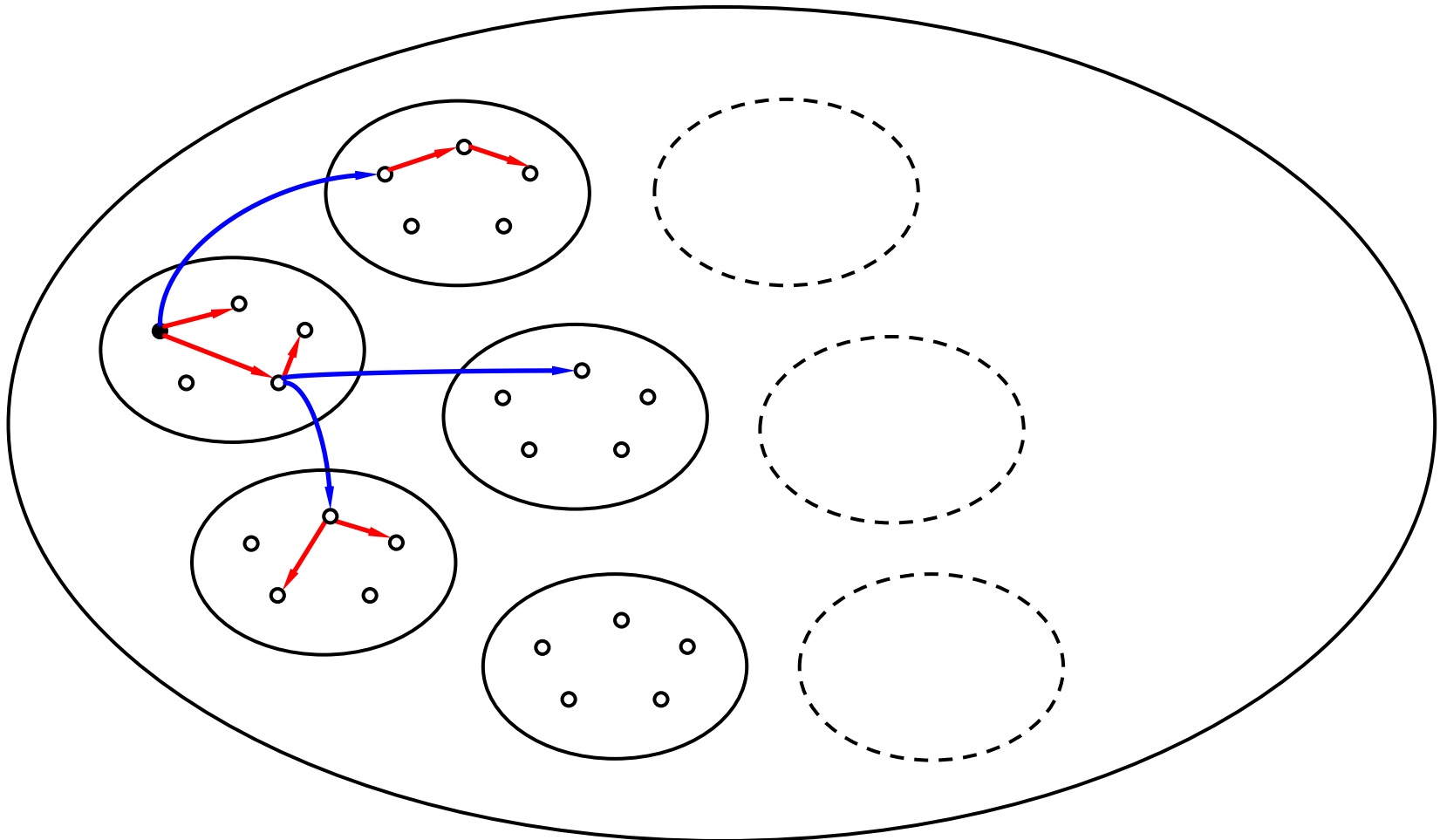
Model illustration



Model illustration



Model illustration



sSIR households model

- Population of m households with of size n_H
- Upon infection, each case i :
 - remains infectious for a duration $I_i \sim I$, iid $\forall i$
 - makes infectious contacts with each household member according to a homogeneous Poisson process with rate $\lambda_L = \beta_L / n_H$
 - makes contacts with each person in the population according to a homogeneous Poisson process with rate $\lambda_G = \beta_G / N$
- Contacted individuals, if susceptible, become infected
- Recovered individuals are immune to further infection

Household size distribution

- n_H = maximum size of a household
- h_n = probability that a randomly selected household has size n
- Then the probability that the household of a randomly selected individual has size n is:

$$\pi_n = \frac{nh_n}{\sum_{n=1}^{n_H} nh_n}$$

- Every quantity of interest should simply be average over this distribution, e.g.
 - $\mu_L^{(n)}$ = average epidemic size in a household of size n
 - then

$$R_* := \mu_G (1 + \mu_L) \quad \text{where} \quad \mu_L = \sum_{n=1}^{n_H} \pi_n \mu_L^{(n)}$$

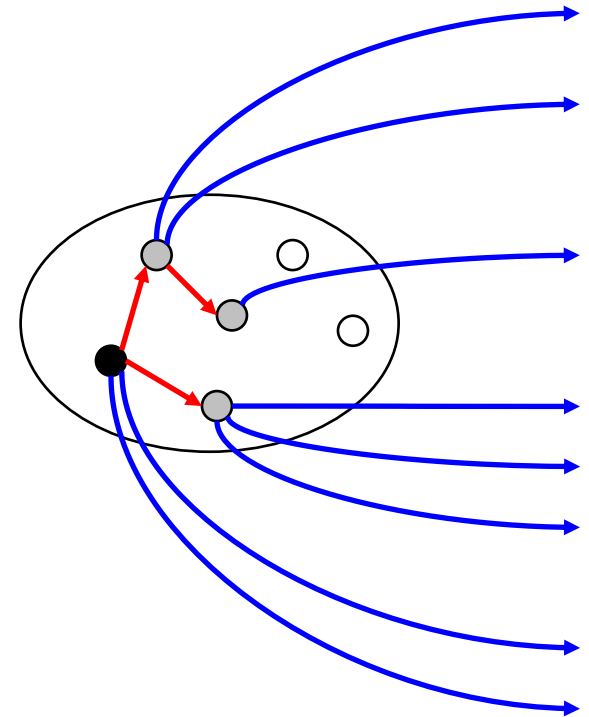
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Household reproduction number R^*

- Consider a within-household epidemic started by one initial case
- Define:
 - μ_L = average household final size, excluding the initial case
 - μ_G = average number of global infections an individual makes
- “Linearise” the epidemic process at the level of households:

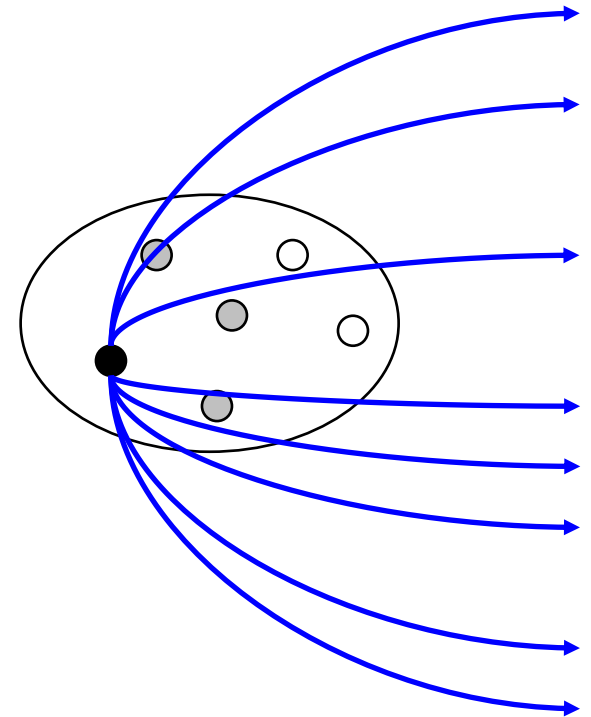
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Individual reproduction number R_I

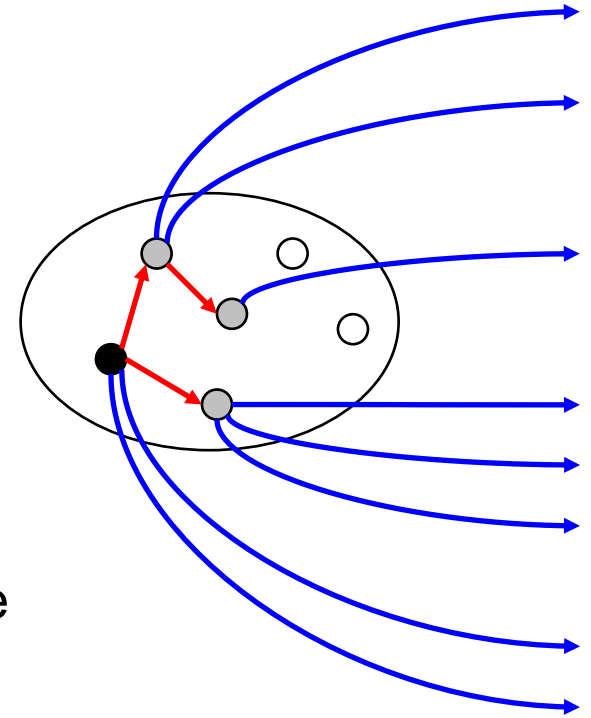
- Attribute all further cases in a household to the primary case

$$M_I = \begin{pmatrix} \mu_G & \mu_G \\ \mu_L & 0 \end{pmatrix}$$

- R_I is the dominant eigenvalue of M_I :

$$R_I = \frac{\mu_G}{2} \left(1 + \sqrt{1 + \frac{4\mu_L}{\mu_G}} \right)$$

- More weight to the first case than it should be



Individual reproduction number R_I

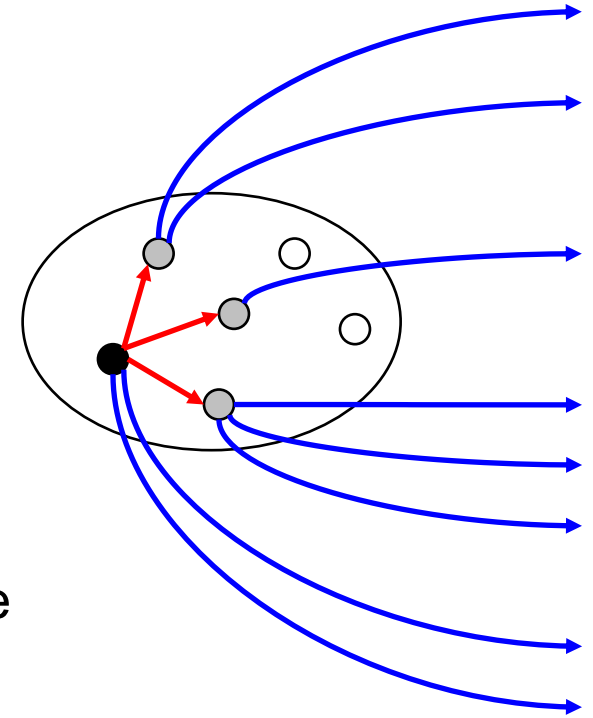
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$$M_I = \begin{pmatrix} \mu_G & \mu_G \\ \mu_L & 0 \end{pmatrix}$$

- R_I is the dominant eigenvalue of M_I :

$$R_I = \frac{\mu_G}{2} \left(1 + \sqrt{1 + \frac{4\mu_L}{\mu_G}} \right)$$

- More weight to the first case than it should be



Further improvement: R_2

- Approximate tertiary cases:
 - μ_1 = average number of cases infected by the primary case
 - Assume that each secondary case infects b further cases
 - Choose $b = 1 - \mu_1 / \mu_L$, such that

$$\mu_1 (1 + b + b^2 + b^3 + \dots) = \frac{\mu_1}{1 - b} = \mu_L,$$

so that the household epidemic yields the correct final size

- Then:

$$M_2 = \begin{pmatrix} \mu_G & \mu_G \\ \mu_1 & b \end{pmatrix}$$

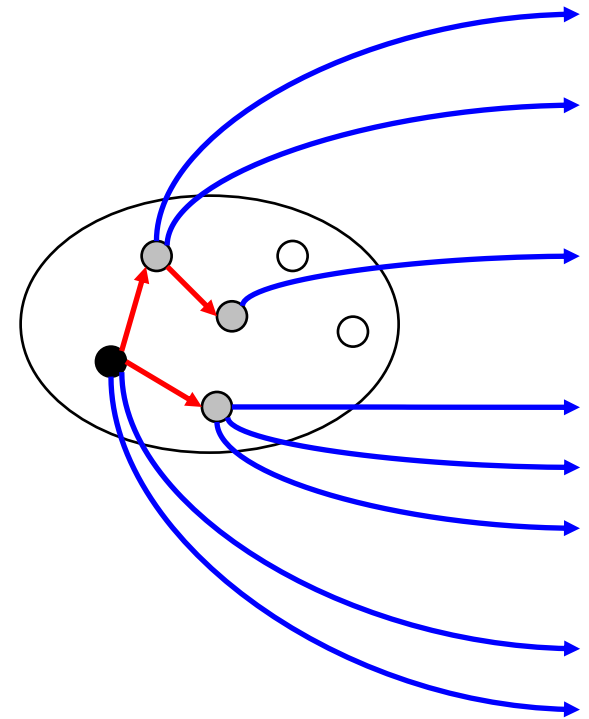
and R_2 is the dominant eigenvalue of M_2

Opposite approach: R_{HI}

- All household cases contribute equally

$$R_{HI} := \mu_G + \frac{\mu_L}{1 + \mu_L}$$

- Less weight on initial cases than what it should be

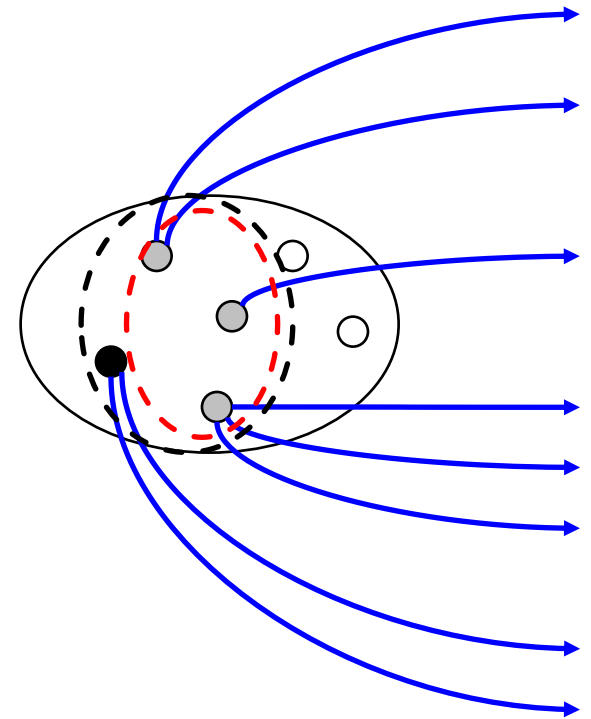


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Vaccine-associated reproduction numbers R_V and R_{VL}

Perfect vaccine

- Assume $R_* > 1$
- Define p_C as the fraction of the population that needs to be vaccinated to reduce R_* below 1
- Then

$$R_V := 1 - \frac{1}{p_C}$$

Leaky vaccine

- Assume $R_* > 1$
- Define E_C as the critical vaccine efficacy (in reducing susceptibility) required to reduce R_* below 1 when vaccinating the entire population
- Then

$$R_{VL} := 1 - \frac{1}{E_C}$$

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Naïve construction of R_0

- Consider a within-household epidemic started by a single initial case. Type = generation they belong to.
- Define $\mu_0 = 1, \mu_1, \mu_2, \dots, \mu_{n_H-1}$ the expected number of cases in each generation
- Let μ_G be the average number of global infections from each case
- The next generation matrix is:

$$K = \begin{pmatrix} \mu_G & \mu_G & \mu_G & \mu_G & \mu_G \\ \mu_1 & & & & 0 \\ & \mu_2 / \mu_1 & & & \vdots \\ & & \ddots & & \vdots \\ & & & \mu_{n_H} / \mu_{n_H-1} & 0 \end{pmatrix}$$

More formal approach (I)

➤ Notation:

- $x_{k,i}$ = average number of cases in generation k and household-generation i
- $x_k = \sum_{i=0}^{n_H-1} x_{k,i}$ = average number of cases in generation k and any household-generation

➤ System dynamics:

$$x_{k,0} = \mu_G \sum_{i=0}^{n_H-1} x_{k-1,i}$$

$$x_{k,i} = \mu_i x_{k-i,0} \quad 1 \leq i \leq n_H - 1$$

➤ Derivation:

$$x_{k,0} = \mu_G x_{k-1}$$

$$x_{k,i} = \mu_i \mu_G x_{k-i-1} \quad 1 \leq i \leq n_H - 1$$

$$x_k = \sum_{i=0}^{n_H-1} x_{k,i} = \mu_G \sum_{i=0}^{n_H-1} \mu_i x_{k-i-1}$$

More formal approach (II)

- System dynamics: $\mathbf{x}_{k,0} = \mu_G \mathbf{x}_{k-1}$
 $\mathbf{x}_{k,i} = \mu_i \mu_G \mathbf{x}_{k-i-1} \quad 1 \leq i \leq n_H - 1$
 $\mathbf{x}_k = \sum_{i=0}^{n_H-1} \mathbf{x}_{k,i} = \mu_G \sum_{i=0}^{n_H-1} \mu_i \mathbf{x}_{k-i-1}$

- Define $\underline{\mathbf{x}}^{(k)} = (\mathbf{x}_k, \mathbf{x}_{k-1}, \dots, \mathbf{x}_{k-n_H+1})$

- System dynamics:

$$\underline{\mathbf{x}}^{(k)} = A_{n_H} \underline{\mathbf{x}}^{(k-1)}$$

where

$$A_{n_H} = \begin{pmatrix} \mu_G \mu_0 & \mu_G \mu_1 & \mu_G \mu_2 & \cdots & \mu_G \mu_{n_H-1} \\ 1 & & & & 0 \\ & 1 & & & \vdots \\ & & \ddots & & \vdots \\ & & & 1 & 0 \end{pmatrix}$$

More formal approach (III)

- Let
 - $\Lambda = \rho(A_{n_H})$ = dominant eigenvalue of A_{n_H}
 - $V = (v_0, v_1, \dots, v_{n_H-1})$ = “dominant” eigenvector

- Then, for $k \rightarrow \infty$:

$$\begin{aligned}\underline{\mathbf{x}}^{(k)} / \|\underline{\mathbf{x}}^{(k)}\| &\rightarrow V \\ \|\underline{\mathbf{x}}^{(k)}\| / \|\underline{\mathbf{x}}^{(k-1)}\| &\rightarrow \Lambda \\ \mathbf{x}_k / \mathbf{x}_{k-1} &\rightarrow \Lambda\end{aligned}$$

- Therefore:

$$\Lambda = R_0$$

Similarity

➤ Recall:

$$K = \begin{pmatrix} \mu_G & \mu_G & \mu_G & \mu_G & \mu_G \\ \mu_1 & & & & 0 \\ & \mu_2 / \mu_1 & & & \vdots \\ & & \ddots & & \vdots \\ & & & \mu_{n_H} / \mu_{n_H-1} & 0 \end{pmatrix}$$

$$A_{n_H} = \begin{pmatrix} \mu_G \mu_0 & \mu_G \mu_1 & \mu_G \mu_2 & \cdots & \mu_G \mu_{n_H-1} \\ 1 & & & & 0 \\ & 1 & & & \vdots \\ & & \ddots & & \vdots \\ & & & 1 & 0 \end{pmatrix}$$

➤ Define:

$$S = \begin{pmatrix} \mu_0 & & & & \\ & \mu_1 & & & \\ & & \ddots & & \\ & & & \mu_{n_H-2} & \\ & & & & \mu_{n_H-1} \end{pmatrix}$$

➤ Then:

$$K = S A_{n_H} S^{-1}$$

➤ So:

$$\rho(K) = \rho(A_{n_H}) = R_0$$

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Comparison between reproduction numbers

- Goldstein *et al* (2009) showed that

$$R_* = 1 \Leftrightarrow R_{VL} = 1 \Leftrightarrow R_r = 1 \Leftrightarrow R_V = 1 \Leftrightarrow R_{HI} = 1$$

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- In a **growing** epidemic:

$$R_* \geq R_{VL} \geq R_V \geq R_{HI}$$

$$R_* \geq R_r$$

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$$R_* = 1 \Leftrightarrow R_{VL} = 1 \Leftrightarrow R_r = 1 \Leftrightarrow R_V = 1 \Leftrightarrow R_{HI} = 1$$

- To which we added

$$\Leftrightarrow R_I = 1 \Leftrightarrow R_0 = 1 \Leftrightarrow R_2 = 1$$

- In a **growing** epidemic:

$$\geq R_I \geq R_V \geq R_{HI} \geq R_2 \geq$$

Comparison between reproduction numbers

- Goldstein *et al* (2009) showed that

$$R_* = 1 \Leftrightarrow R_{VL} = 1 \Leftrightarrow R_r = 1 \Leftrightarrow R_V = 1 \Leftrightarrow R_{HI} = 1$$

- To which we added

$$\Leftrightarrow R_I = 1 \Leftrightarrow R_0 = 1 \Leftrightarrow R_2 = 1$$

- In a **growing** epidemic:

$$R_* \geq R_I \geq R_V \geq R_0 \geq R_2 \geq R_{HI}$$

- To which we added that, in a **declining** epidemic:

$$R_* \leq R_I \leq R_V \leq R_0 \leq R_2 \leq R_{HI}$$

Fundamental interpretation

- For each reproduction number R_A , define a r.v. X_A describing the generation index of a randomly selected infective in a household epidemic

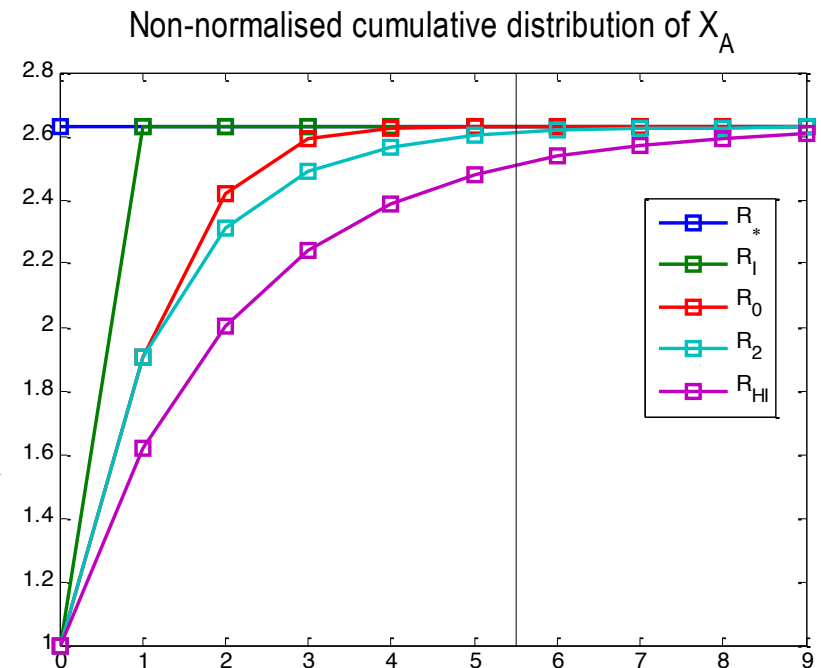
- Distribution of X_A is $P\{X_A = k\} = \frac{\mu_k^A}{1 + \mu_L}$, $0 \leq k \leq +\infty$

- Nice result:

$$X_A \stackrel{st}{\leq} X_B \Rightarrow R_A \geq R_B$$

- Therefore:

$$R_* \geq R_I \geq R_0 \geq R_2 \geq R_{HI}$$



Practical implications

- $R_V \geq R_0$, so vaccinating $p = 1 - \frac{1}{R_0}$ is not enough
- Goldstein *et al* (2009):

$$R_* \geq R_V \geq R_{HI}$$

- Now we have sharper bounds for R_V :

$$R_* \geq R_I \geq R_V \geq R_0 \geq R_{HI}$$

Why so long to come up with R_0 ?

Basic reproduction number R_0

Naïve definition:

*“ Average number of new cases generated by a **typical** case, throughout the entire infectious period, in a large and otherwise **fully susceptible** population ”*

What is a **typical** case?

What do we mean by **fully susceptible** population?

Why so long to come up with R_0 ?

- Typical infective:
 - “Suitable” average across all cases during a household epidemic

$$K = \begin{pmatrix} \mu_G & \mu_G & \mu_G & \mu_G & \mu_G \\ \mu_1 & & & & 0 \\ & \mu_2 / \mu_1 & & & \vdots \\ & & \ddots & & \vdots \\ & & & \mu_{n_H} / \mu_{n_H-1} & 0 \end{pmatrix}$$

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 - not defined *a priori*
 - appear only in real-time

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- Types are given by the generation index:
 - not defined *a priori*
 - appear only in real-time
- “Fully” susceptible population:
 - the first case is never representative
 - need to wait at least a few full households epidemics

Final size of households model

Extensions: households-workplaces model

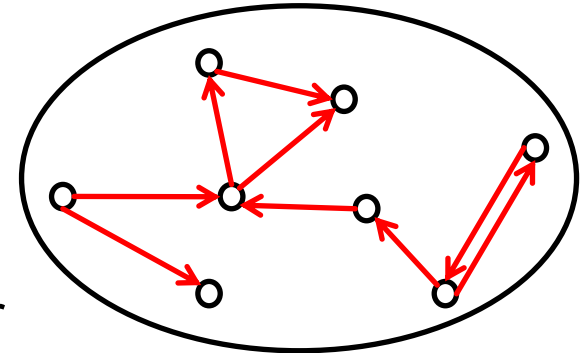
ADVANCED TOPICS

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Household epidemic with external infection

- Consider a household of size n
- Consider the epidemic graph
- Consider infections from outside as they occur during the epidemic
- Notice that in the end the within-household final size is the same you would obtain if all external infections occurred at the beginning
- $\alpha_n(\varepsilon)$ = expected final size assuming that each individual escapes infection from outside independently with probability ε
 - the number of initial cases is $Y_0 \sim \text{Bin}(n, 1 - \varepsilon)$
- α_{x_0, y_0} = expected epidemic size in a household with x_0 and y_0 initial susceptibles and infectives, and no infection from outside

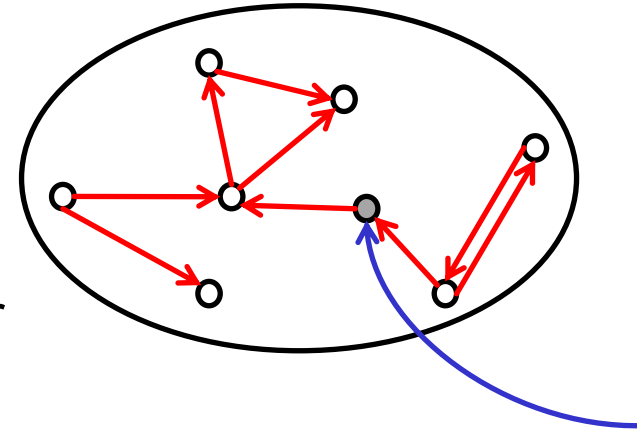


➤ Then

$$\alpha_n(\varepsilon) = \sum_{k=0}^n \binom{n}{k} (1 - \varepsilon)^k \varepsilon^{n-k} \alpha_{n-k, k}$$

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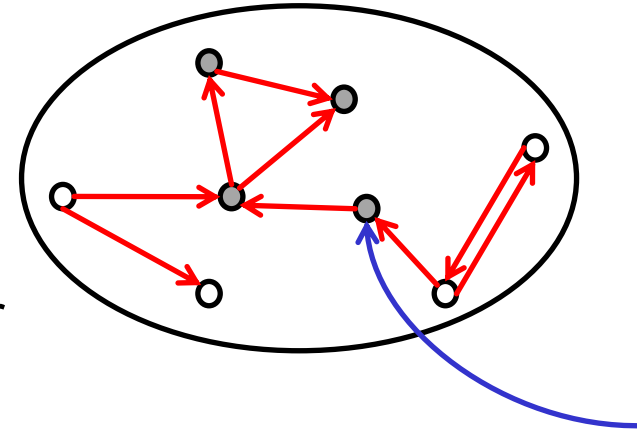


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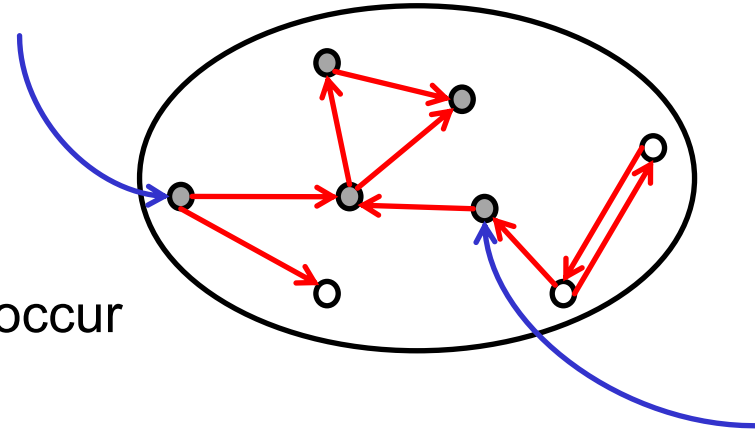


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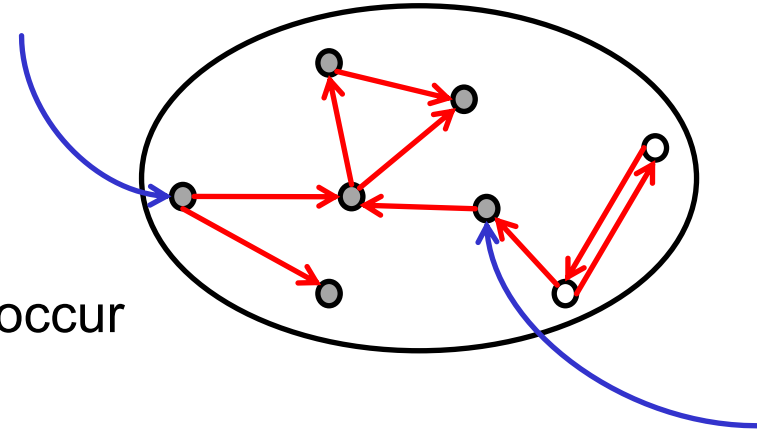


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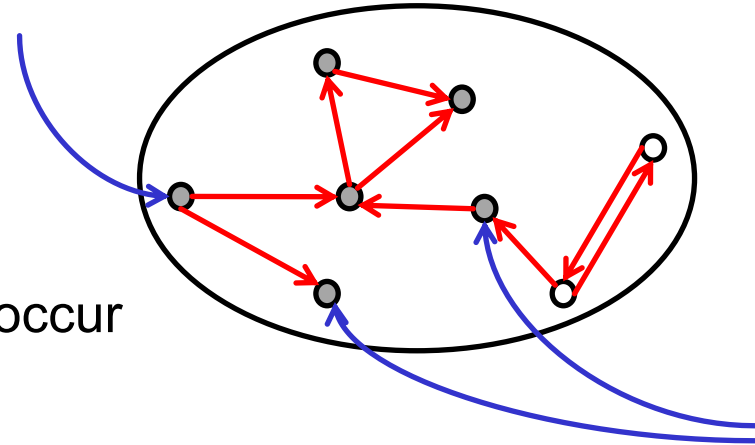
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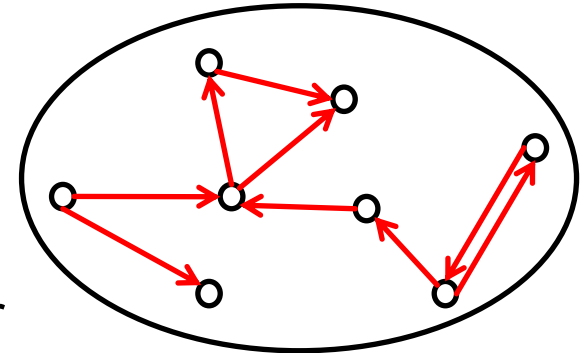


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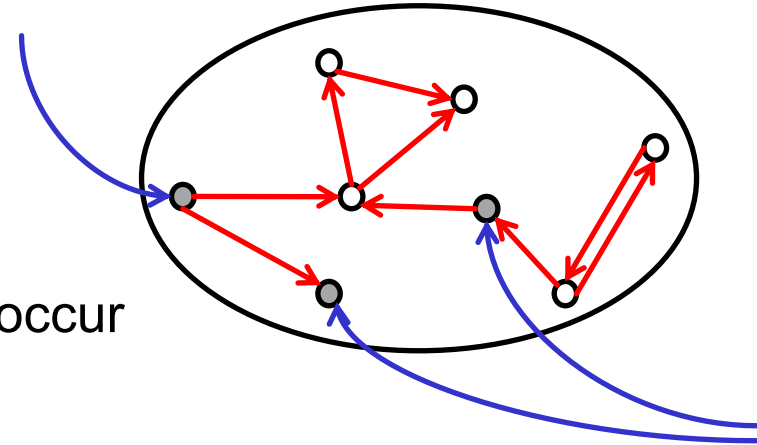
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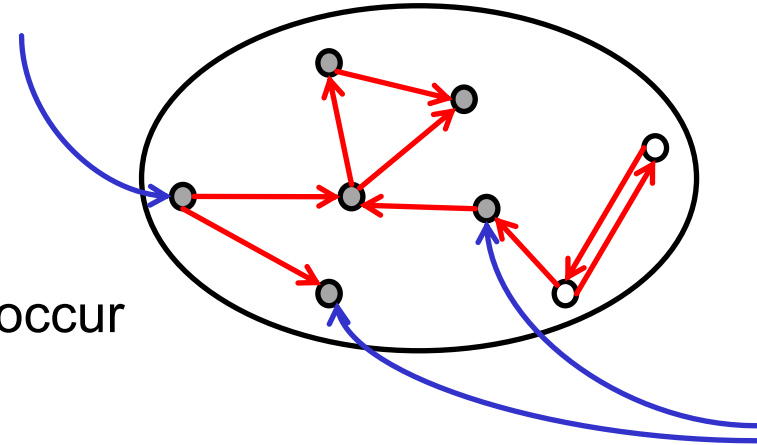


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Average epidemic final size

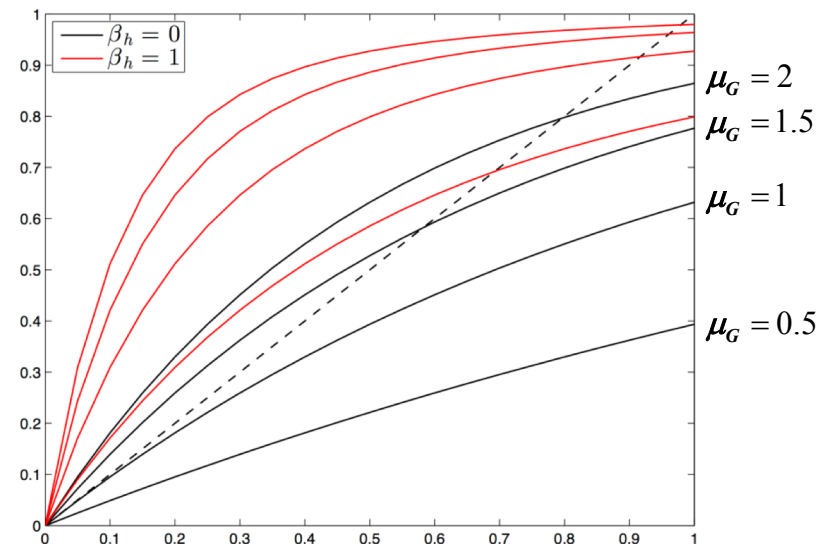
- z = expected fraction of the population infected
- Then, approximately,

$$\varepsilon(z) = \exp\left(-\frac{\mu_G}{N} Nz\right) = e^{-\mu_G z}$$

- But because (almost) all households are identical and fully susceptible, z must also be the expected fraction of infectives in each household
- The expected final size z must be the largest solution in $[0,1]$ of

$$\theta = \alpha_n(\varepsilon(\theta))/n$$

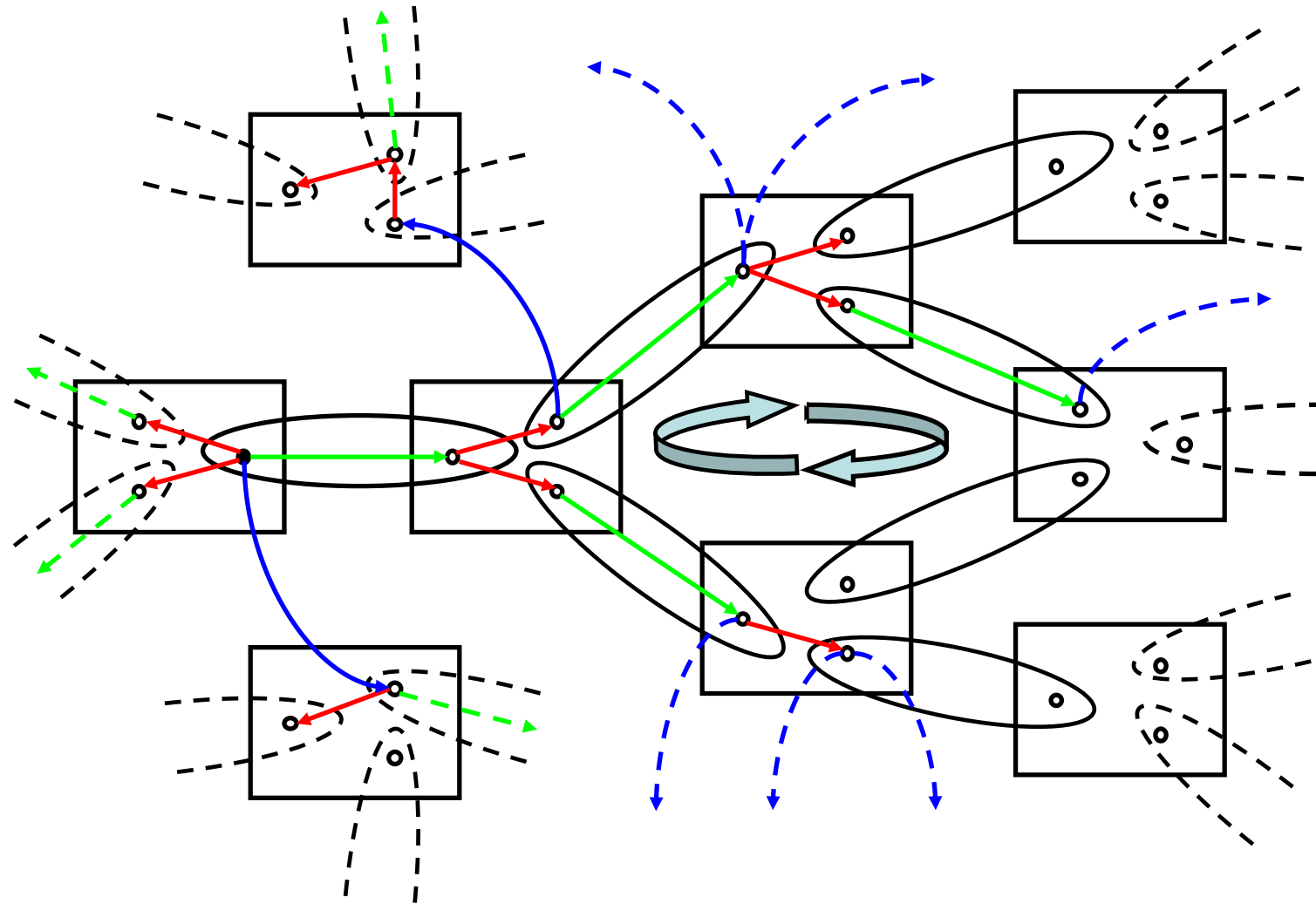
- It is possible to prove that $z > 0$ if and only if $R_* > 1$



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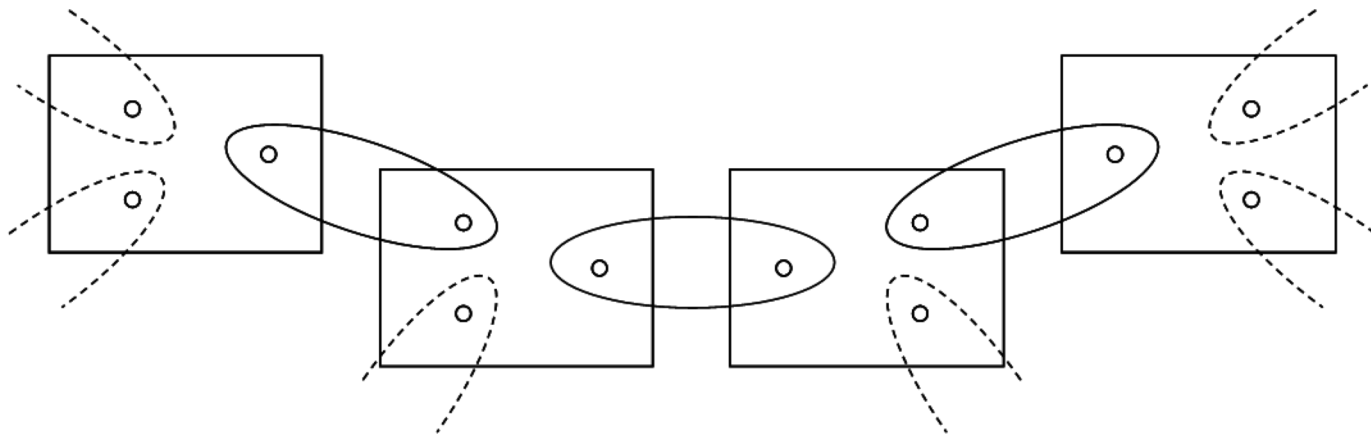
Households-workplaces model



Model description

Assumptions:

- Each individual belongs to a household and a workplace
- Rates λ_H, λ_W and λ_G of making infectious contacts in each environment
- No loops in how households and workplaces are connected, i.e. locally tree-like



Construction of R_0

- Define $\mu_0^H = 1, \mu_1^H, \mu_2^H, \dots, \mu_{n_H-1}^H$ and $\mu_0^W = 1, \mu_1^W, \mu_2^W, \dots, \mu_{n_W-1}^W$ for the households and workplaces generations
- Define $n_T = n_H + n_W$
- Then R_0 is the dominant eigenvalue of

$$A_{n_T} = \begin{pmatrix} c_0 & c_1 & \cdots & c_{n_T-3} & c_{n_T-2} \\ 1 & & & & 0 \\ & 1 & & & \vdots \\ & & \ddots & & \vdots \\ & & & 1 & 0 \end{pmatrix},$$

where $c_k = \mu_G \sum_{\substack{i+j=k \\ 0 \leq i \leq n_H-1 \\ 0 \leq j \leq n_W-1}} \mu_i^H \mu_j^W + \sum_{\substack{i+j=k+1 \\ 1 \leq i \leq n_H-1 \\ 1 \leq j \leq n_W-1}} \mu_i^H \mu_j^W, \quad 0 \leq k \leq n_T - 2$