LUNDS UNIVERSITET

Inspiration Coffee

Disease control in a heterogeneous population

Alain Govaert

Meanwhile, during the lockdown...

RESPECT THE UNSTABLE: DELAYS AND SATURATION IN CONTACT TRACING FOR DISEASE CONTROL *

RICHARD PATES†, ANDRES FERRAGUT‡, ELIJAH PIVO§, PENGCHENG YOU¶, FERNANDO PAGANINI‡, AND ENRIQUE MALLADA¶

Simple control for complex pandemics: the impact of testing and contact tracing on heterogeneous networks

Sarah C. Fay,* Dalton J. Jones, Munther A. Dahleh, and A.E. Hosoi

Why consider contact heterogeneity?

- Human contact networks are typically not homogeneous (nor constant).
- Is really only the mean relevant for disease spread, or other moments as well?

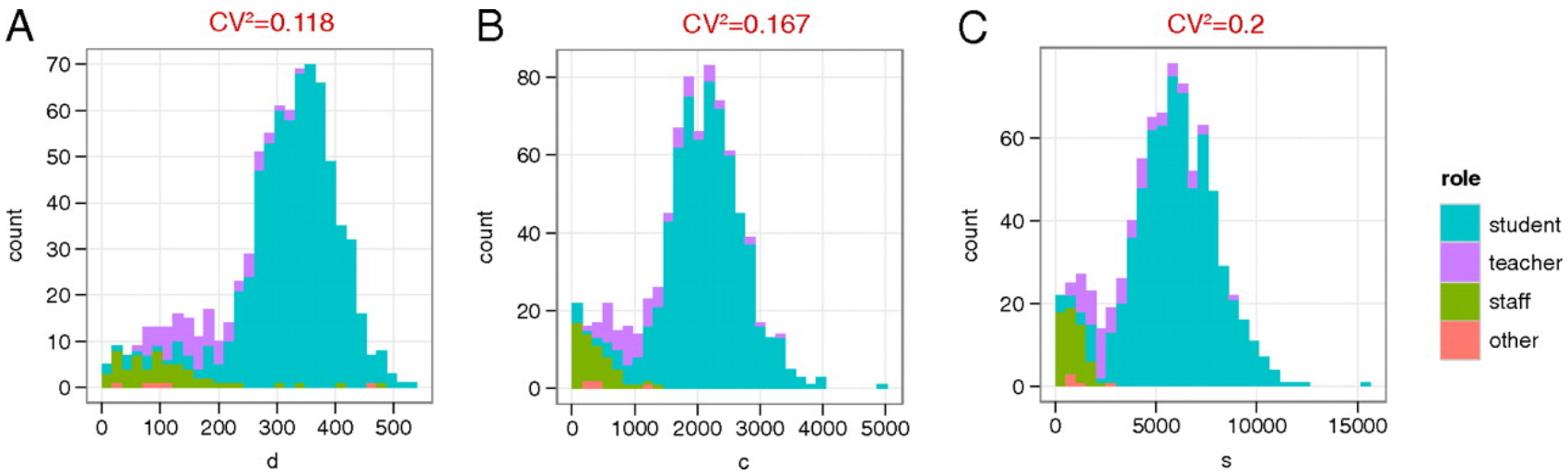

Figure: Proximity-based human contact network in an American high school: PNAS December 21, 2010 107 (51) 22020-22025

Heterogeneous population SIR model

The answer was hidden deep in the archives of *Nature* (80s HIV epidemic)

- N_k: fixed number of individuals with k contacts per time unit;
- X_k and Y_k: number of susceptible and infectious individuals in partition $k = 1, 2, \ldots, n$;
- $\rho \in (0, 1]$: infection probability per contact;
- $\gamma > 0$: recovery rate.

$$\frac{d}{dt}\begin{bmatrix} X_k \\ Y_k \end{bmatrix} = \begin{bmatrix} -k\lambda & 0 \\ k\lambda & -\gamma \end{bmatrix}\begin{bmatrix} X_k \\ Y_k \end{bmatrix}, \quad \lambda = \rho \frac{\sum_{k=1}^{n} kY_k}{\sum_{k=1}^{n} kN_k}, \quad \rho \in (0, 1]$$

- $\lambda \in [0, 1]$: probability of acquiring an infection from any randomly chosen contact per unit time—*now more likely to come from those with high number of contacts!*

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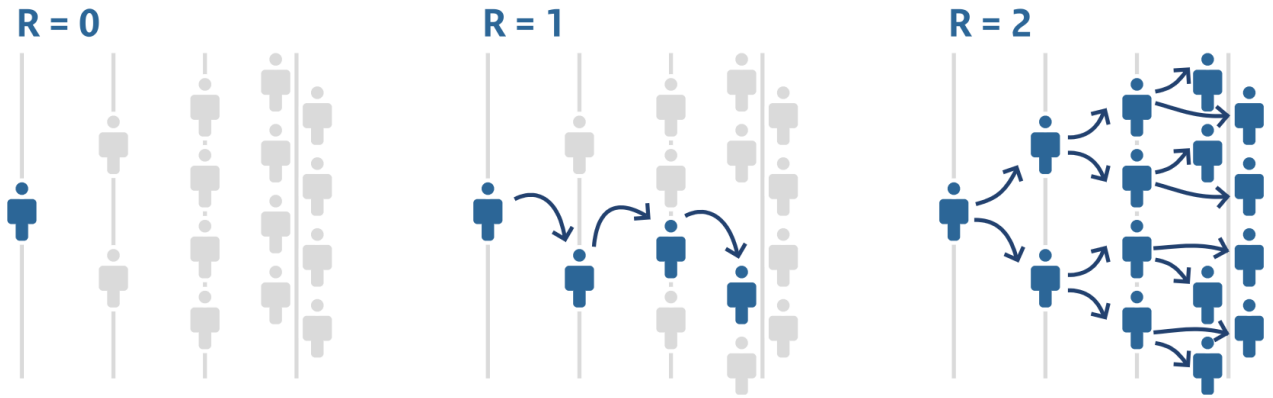
Homogeneous population SIR model

- For $z \in \mathbb{N}$, if $N_z = N >> 1$ then the z-homogeneous SIR model is retrieved:

$$\frac{d}{dt}\begin{bmatrix} S \\ I \end{bmatrix} = \begin{bmatrix} -\beta I & 0 \\ \beta I & -\gamma \end{bmatrix}\begin{bmatrix} S \\ I \end{bmatrix}, \quad R = 1 - I - S,$$

  with $S = X/N$, $I = Y/N$, and $\beta = \rho z > 0$;

- Linearization about all-susceptible equilibrium is asymptotically stable if $\mathcal{R}_0 = \beta/\gamma < 1$.



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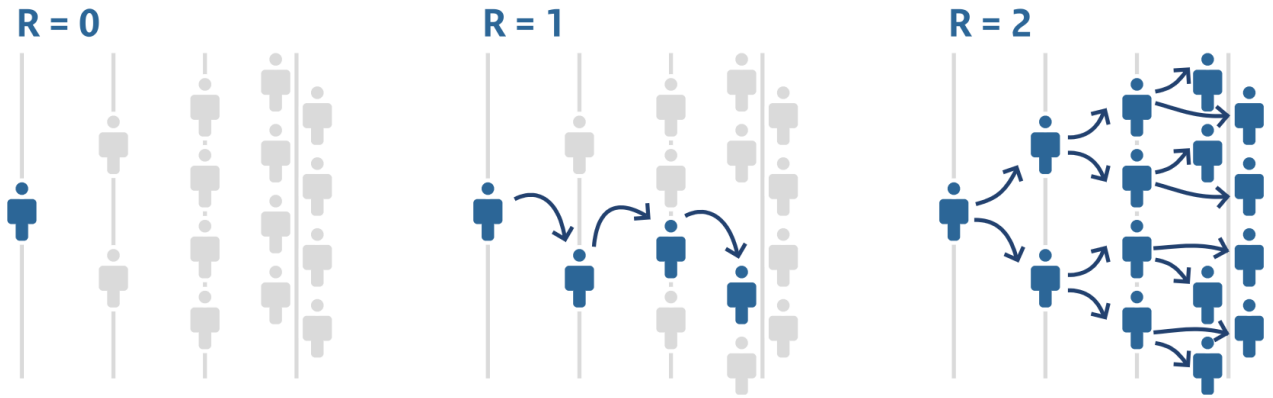

Implementing case isolation

- Isolate a fraction α of individuals that were infected T_{delay} time units ago:

$$Y_k(t) - Q_k(t), \quad Q_k(t) = \alpha e^{-\gamma T_{\text{delay}}} Y_k(t - T_{\text{delay}}).$$

- Probability of acquiring an infection becomes

$$\rho \sum_k k(Y_k(t) - Q_k(t)) / \left(\sum_k k N_k \right). \tag{1}$$

- Infections in the partitions are described by:

$$\frac{d}{dt} \begin{bmatrix} Y_1 \\ Y_2 \\ \vdots \\ Y_n \end{bmatrix} = \frac{\rho}{\sum_k N_k} \begin{bmatrix} X_1 \cdot 1 \\ X_2 \cdot 2 \\ \vdots \\ X_n \cdot n \end{bmatrix} \begin{bmatrix} 1 \\ 2 \\ \vdots \\ n \end{bmatrix}^\top \begin{bmatrix} Y_1 - Q_1 \\ Y_2 - Q_2 \\ \vdots \\ Y_n - Q_n \end{bmatrix} - \gamma \mathbf{I}_n \begin{bmatrix} Y_1 \\ Y_2 \\ \vdots \\ Y_n \end{bmatrix}. \tag{2}$$

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Stability of all-susceptible equilibrium

Lemma (Homogeneous vs. heterogeneous population model)

About the all-susceptible equilibrium $S_k = N_k$ *for all* $k = 1, \ldots, n$*, the heterogeneous SIR model with delayed case isolation* (2) *is asymptotically stable if and only if the linearization of the homogeneous model about the all-susceptible equilibrium* $(S, I, R, Q) = (1, 0, 0, 0)$ *is asymptotically stable with mixing parameter* $\beta = \rho\mu(c_v^2 + 1)$*.*

Proof sketch: derive the delayed differential equations at a population level $I = \frac{1}{N}\sum_i Y_i$. Compare its characteristic equation around healthy equilibrium with that of the homogeneous model.

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Stability conditions

Proposition (Delay upper bound)

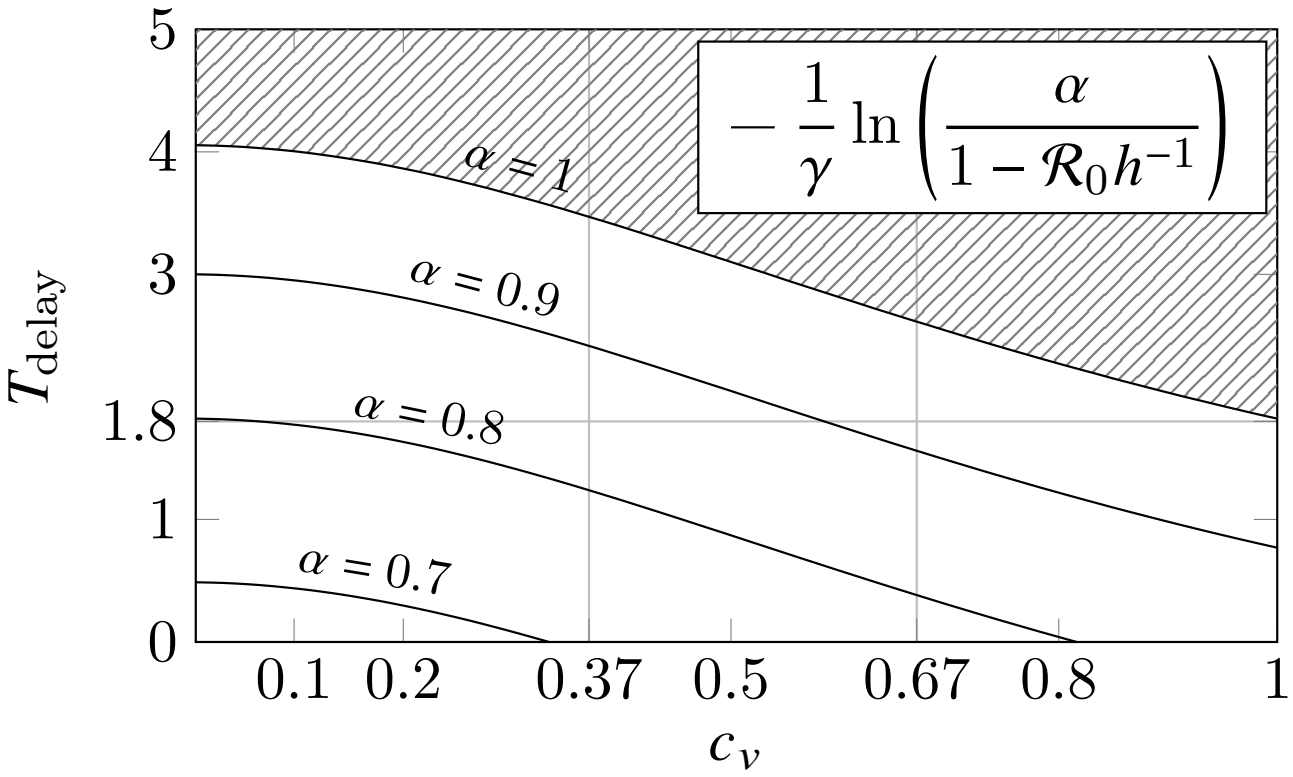
The linearization of the heterogeneous population model (2) *about the all-susceptible equilibrium is asymptotically stable if and only if*

$$T_{delay} < \frac{1}{\gamma} \ln\left(\frac{\alpha\beta h}{\beta h - \gamma}\right), \quad h = (c_v^2 + 1),$$

where $c_v = \sigma/\mu$ *is the the coefficient of variation, or relative standard deviation and* $\beta = \rho\mu$.

Numerical example

Parameters chosen to be representative for SARS-CoV-2: $\mathcal{R}_0 = 3$ and $\gamma = 0.1$



When is a delay allowed?

Corollary

For a basic reproduction number $\mathcal{R}_0 > 1$ of the corresponding homogeneously interacting population and $\alpha \in [0, 1)$, a positive delay is allowed in the heterogeneous population if and only if the coefficient of variance of the number of contacts satisfies

$$c_v^2 < \frac{1}{\mathcal{R}_0(1-\alpha)} - 1. \tag{3}$$

Again, for $\mathcal{R}_0 = 3$ and $\gamma = 0.1$ the maximum $c_v \approx 0.82$.

Some preliminary conclusions

- Stability of the healthy equilibrium does **not only** depend on mean number of contacts;
- Variance in number of contact matters—**things get worse**!
- In empirical human contact networks, only small delays in case isolation schemes are possible.
- *Transient behaviors can be quite bad*: Jonas, Emma, Richard know more!

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Social network perspective

The simple heterogeneous population model assumes:

- Contacts are a result of random mixing;
- One-off random contacts don’t last.

Social contacts are not (always) like this:

- Long-lasting group of friends, family, etc;
- A fixed social network limit.

Can the heterogeneous population model provide some insight here?

Thought experiment

Think of:

- Your set of friends $\mathcal{F}$, e.g., $\{Jonas, Erik, Celie\} \neq \emptyset$;
- A randomly chosen friend from your set of friends, e.g. $Erik$;
- How many friends, d, your randomly chosen friend has.

Question:

- Is $|\mathcal{F}|$ larger, smaller, or equal, to d?

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The friendship paradox

- In non-regular social networks, your friends have more friends than you (in expectation):

$$\mathbb{E}(|\mathcal{F}|) < \mathbb{E}(d) = \frac{\sigma^2}{\mu} + \mu.$$

- That looks familiar:

$$\mathbb{E}(d) = \frac{\sigma^2}{\mu} + \mu = \mu(c_v^2 + 1), \quad c_v = \frac{\sigma}{\mu}.$$

- It is the scaling of the mixing parameter of homogeneous population model in which all individuals have μ contacts!

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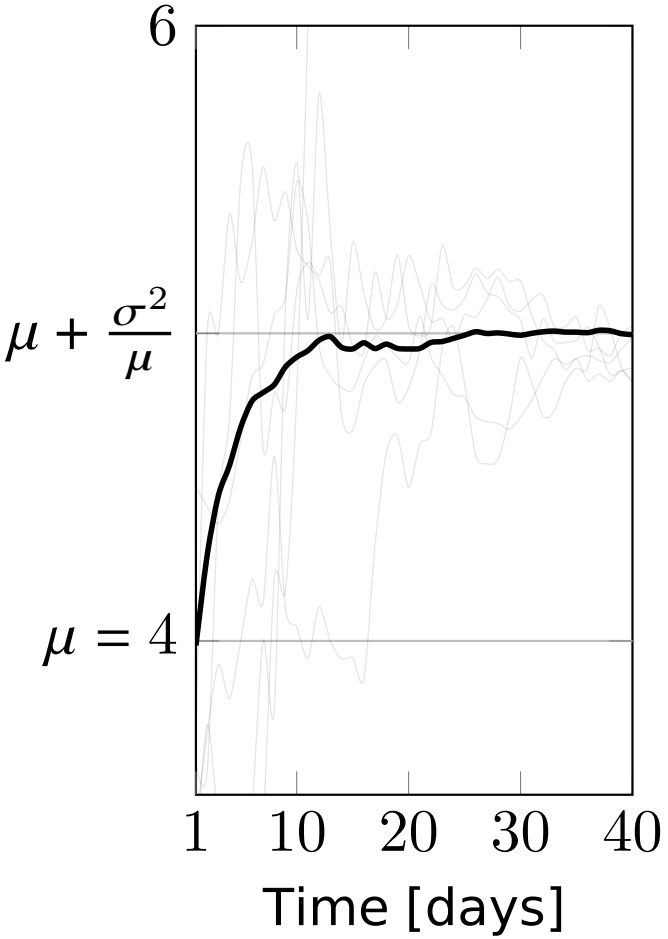
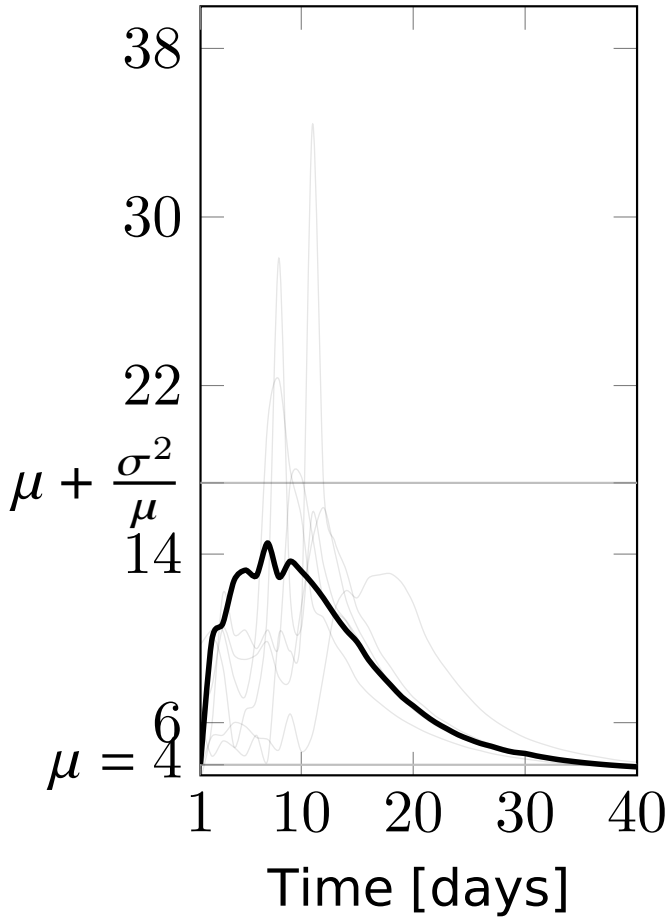
Simulation examples



(a) Average degree of infected in Poisson configurator model network



(b) Average degree of infected in Barabási–Albert graph

Conclusions and extensions

- On fixed contact networks, heterogeneity matters for the early spread of the disease.
- Simulations suggest that mean dynamics on fixed networks are lower (resp. upper) bounded by the homogeneous (resp. heterogeneous) population model.
- More precisely: for infinite random graphs generated by configurator model the correction factor is:

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Credits and thanks to...

Collaborators:

- Jonas
- Richard
- Kristian
- Emma

And, of course, you for attending the Friday seminar.

Population level model

Around the healthy equilibrium, at a population level $I = \frac{1}{N}\sum_i Y_i$, new infectious satisfy

$$\frac{d}{dt}\begin{bmatrix} I \\ \lambda \end{bmatrix} = \underbrace{\begin{bmatrix} -\gamma & \mu \\ 0 & \rho\left(\frac{\sigma^2}{\mu}+\mu\right)-\gamma \end{bmatrix}}_{\mathbf{A}_0}\begin{bmatrix} I \\ \lambda \end{bmatrix} + \underbrace{\begin{bmatrix} 0 & -\mu\alpha e^{-\gamma T_{\text{delay}}} \\ 0 & -\rho\left(\frac{\sigma^2}{\mu}+\mu\right)\alpha e^{-\gamma T_{\text{delay}}} \end{bmatrix}}_{\mathbf{A}_1}\begin{bmatrix} I(t-T_{\text{delay}}) \\ \lambda(t-T_{\text{delay}}) \end{bmatrix}, \quad (4)$$