

Stochastic epidemic modelling and analysis Part 2: beyond the initial phase

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Assumptions/focus:

Focus on where stochastic models are needed/preferred

SIR or SEIR (not SIS or SIRS)

n = (approximate) population size assumed large

Unless mentioned: non-changing behavior

Biased towards my own interests

Stochastic finite population models always relevant for estimation.

However: focus on inference in other talk(s)

Short term outbreaks: Local structures

Suppose an outbreak gets going. What can happen?

Assume no intervention or change in behavior

If outbreak is very quick the population is more or less fixed so eventually it will die out (epidemic situation)

Then it makes sense to talk about *final size*

What will the final size be as a function of model parameters?

For many models the final size is obtained from deterministic models (except fluctuations of order \sqrt{n}): e.g. homogeneous mixing and multitype epidemics

Example: SIR with transmission rate λ and recovery rate γ
 \implies final size τ solves

$$1 - \tau = e^{-\tau\lambda/\gamma}$$

Household epidemics

However: models having certain local structures have a final size distribution genuinely depending on stochasticity

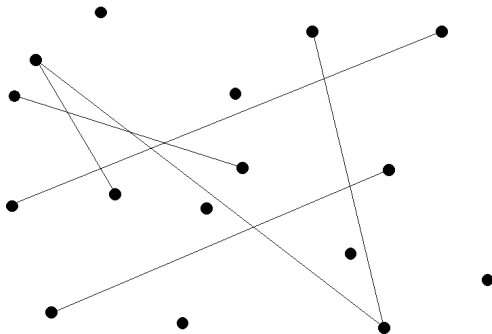
Household models:

- Much higher transmission rate within households
- Outbreak sizes within households genuinely stochastic
- Even R_0 (or R_* ...) depends on outbreak size distribution within households

Longini and Koopman (1982) and Ball et al. (1997)

Network epidemics

Network epidemics: Underlying social structure defined by a suitable random network (having desired properties)



Network epidemics

Given the network, an epidemic model can be defined "on" the network

E.g. R-F: infected individuals infect each neighbour independently with probability p

The final size has a complicated expression depending on network structures

Open problems

Open stochastic problems for final size

- Models having households and/or networks with a spatial component: community transmission distance dependent
- Models having adaptive behavior: individuals take precautions the more people get infected
- Estimation: E.g. in partially observed networks
- Network models with different type of individuals and/or different type of edges (some work exists)
- Prove conjecture by Ball et al (1997): Optimal vaccination strategy for household epidemics is to reduce the largest number of unvaccinated (top-to-bottom)

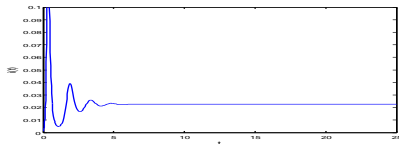
Extinction in first trough

Beyond first outbreak: If outbreak is not very short new susceptible individuals enter community (birth and/or immigration)

This influx of new susceptibles may give rise to *endemic situation*

Either the epidemic dies out in first trough or else it will reach endemicity

Extinction in first trough



Open problem (Diekmann): What is the chance of epidemic going extinct in first trough as function of epidemic and population parameters? (Not well solved even for simplest model!)

Time to extinction (\iff Critical community size)

Dynamic populations: in order to reach endemic state influx of new individuals needed

Either a growing population or a population of approximately constant size

In the former disease may persist forever (endemic) but in the latter the epidemic will always die out (possibly after a long time): quasi-endemic

Classical problem: Derive expression for time to extinction T (i.e. determine c in $E(T) = e^{cn}$), Nåsell (1997). Large deviations?

Open problem: Extend model to meta-populations and/or spatially distributed population

Some work exists

Endemic (quasi-)equilibrium

For some models the (quasi-) endemic state can be derived from deterministic model

Example SIR with demography:

- new individuals are "born" at constant rate n and each individual dies at rate 1 (time unit = life-length)
- individuals who get infected immediately get infectious and recover at rate γ
- while infectious the individual has infectious contacts (with uniformly selected individuals) at rate λ

Endemic (quasi-)equilibrium, cont'd

Corresponding system of differential equations (for fractions):

$$s'(t) = 1 - \lambda s(t)i(t) - s(t)$$

$$i'(t) = \lambda s(t)i(t) - \gamma i(t) - i(t)$$

$$r'(t) = \gamma i(t) - r(t)$$

The system has the stable endemic state

$$(\hat{s}, \hat{i}, \hat{r}) = \left(\frac{\gamma + 1}{\lambda}, \frac{1}{\gamma + 1} - \frac{1}{\lambda}, 1 - \hat{s} - \hat{i} \right)$$

$$\text{if } R_0 = \frac{\lambda}{\gamma + 1} > 1$$

Endemic (quasi-)equilibrium, cont'd

If the endemic equilibrium is reached it stays there forever in growing populations and for a very long time in large but \approx fixed populations (Cholera, chicken-pox, measles, hiv, clamidia, malaria, dengue, ...)

Possible to do the same thing for multitype case

Much less is known for dynamic populations with local structures (households, network, spatial, ...)

Then the endemic state often will depend on local random properties

Special case with pair-formation models has been analysed using deterministic models (e.g. Kretschmar & Morris, 1996)

Dynamic network epidemics

Epidemic model for a growing dynamic network population

- *Population*: Super critical linear birth and death process: individuals give birth at rate ν and die at rate μ ($\nu > \mu$)
- *Network*: New-born have no edges. During life an individual creates new edges to uniformly selected individuals at rate α and edges disappear at rate β
- *Epidemic*: An individual who gets infected becomes infectious and recovers at rate γ . While infectious he/she infects each susceptible neighbour at rate λ

Model parameters: Pop: ν, μ . Network: α, β . Epidemic: λ, γ

Dynamic network epidemics (cont'd)

(Some) asymptotic properties of network known (B, Lindholm, Turova, 2010+1): asymptotic degree distribution, asymptotic degree-degree correlation, threshold for existence of giant component

Some results for early stages of outbreak (B+Trapman, 201?):
Three regimes:

1. no epidemic possible,
2. epidemic possible but slower epidemic growth than population growth,
3. epidemic possible and epidemic growth initially faster than population growth

Open problem: Existence and characterization of endemic equilibrium (for this or other models)

Dynamic household epidemic model

A possible Dynamic household epidemic model:

Population model:

- Individuals reside in households of size 1, 2, ...
- *Birth*: each household increases size by 1 at rate ν
- *Death*: each household decreases size by 1 at rate μ (or $h\mu$)
- *Splitting*: each household of size h decreases by one and a new household of size 1 is formed at rate $(h - 1)\sigma$
- Perhaps also rate for joining two singles

Epidemic model:

- *Infection and recovery*: an individual who gets infected becomes infectious and recovers at rate γ
- *Transmission*: while infectious an individual has infectious contacts with each household member at rate λ_L and with uniformly selected individuals at rate λ_G

Dynamic household epidemic model (cont'd)

Open problems: This or similar models have never been analysed(?)

- Criterion for sub-critical, critical and super-critical population?
- R_0 ?
- How many different regimes?
- Description of (quasi-) endemic state?
- Time to extinction?

(Deterministic methods may be used for solving some of these questions)

Spatial epidemics

There exists stochastic epidemic models allowing for transmission

1. along network-links and/or
2. within households and/or
3. uniformly in community

(Ball and co-authors)

Much less has been done for transmission related to **space**

(see however e.g., Meester & Trapman, 2011 + ref on next slide)

Spatial epidemic model

A simple **spatial epidemic model**:

- Suppose n individuals are distributed on unit circle (or higher dimensional torus)
- initially: one random infective, and other $n - 1$ are susceptible
- an individual i who gets infected infects any other susceptible individual j independently, with probability $p = f_n(d_{ij})$, where d_{ij} is the distance between i and j and $f_n(d_{ij})$ is a suitably decreasing function of the distance

Relation to percolation models and some to small world model

Related work: Mollison (1977 and comments by Kelly), Ball and Neal (2003)

Open stochastic problems for spatial epidemics

Open problems:

- For model above: P (major outbreak), description of final outbreak
- Similar models also having local structures
- Dynamic epidemic models with spatial component

(Some may be solved using deterministic models)

Adaptation, control and genetic evolution

As soon as large numbers get infected individuals start taking precautions (**adaptation**): improving hygiene, fewer contacts, ...

At least for harmful diseases also health authorities aim to reduce spreading (**control**): vaccination, isolation of cases, promotion of improved hygiene, ...

The infectious agent might **mutate** and spreading potential as well as symptoms may change (and/or different competing strains, ...)

Much more modelling is needed for these type of effects

Both stochastic and deterministic models may apply

Vaccine response models

If a vaccine is available, its effect on susceptibility, infectivity (and symptoms, ...) is usually random among individuals and over time

Models exist (leaky, all-or-nothing, all-partial-none, ..., Longini and Halloran) but in particular *waning* of immunity needs more modelling.

However: there is a limit to what can be estimated, so estimation methods should be studied simultaneously

Prevention at criticality

Several diseases have gone extinct (by vaccination) in many countries (but remain endemic in others)

The diseases are kept away by continuous vaccination

If vaccination coverage drops down to the critical level: small outbreaks start appearing

These outbreaks have $R_E \approx 1$

Motivates analysis of **critical epidemics**. Some theoretical results exist (Martin-Löf 1998, van der Hofstad et al. 2010) but

More attention to applications needed:

- For what over-all coverage does the risk of outbreaks start?
- Which sub-groups are most important to increase coverage in?
- Should vaccine boosters or new vaccinees be prioritized?

Summary: important open problems (from both parts)

- More **realistic mathematically tractable models** for households/workplaces and clustered networks.
- **Real-time growth rate** for models with small mixing groups (and estimation in emerging epidemics).
- Finite population **interpretation** of branching process results.
- **Adaptive dynamics**: individuals take precausive measures, society intervenes, genetic evolution, ...
- **Spatial epidemics**: Short and long term behavior for epidemics with spatial component
- **$P(\text{extinction in first trough})$** : simple models, seasonality, meta-populations
- **Endemic state** in dynamic populations with local structures: households, networks, spatial models
- **Prevention**: vaccine response models, vaccination schemes in structured communities, critical epidemics