

The early stage of an outbreak

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An epidemic does not have the branching property

- “Birth” in a branching process is “infection” in the epidemic.
- The rate at which an individual gives birth is age dependent. Before being adult this rate is 0. Then it increases and reaches a maximum, before decreasing with the age.
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Large population, small # of infectious

- Suppose that the total population N is large, and that the number of infectious $k = k(N)$ is of smaller order.
- We consider the *varying infectivity* epidemic model. If $\lambda(t)$ were deterministic, the law of the # of infections generated by one infectious would be $\text{Poi}(\int_0^\infty \lambda(t)dt)$. Otherwise, we call that law $\text{MixPoi}(\int_0^\infty \lambda(t)dt)$.
- Consider the Galton Watson process with offspring distribution $\text{MixPoi}(\int_0^\infty \lambda(t)dt)$. The mean number of offspring is $R_0 = \int_0^\infty \mathbb{E}[\lambda(t)]dt$.
- Let $\{\lambda_i(t), t \geq 0\}_{i=0,1,\dots}$ a sequence of i.i.d. copies of $\lambda(t)$, $\{Q_i, i = 0, 1, \dots\}$ an i.i.d. sequence of standard PRMs on \mathbb{R}_+^2 , $\{U_i, i = 1, 2, \dots\}$ an i.i.d. sequence of r.v. $\mathcal{U}([0, 1])$, the three being mutually independent.
We also define the r.v. $\eta_i = \sup\{t, \lambda_i(t) > 0\}$, $i \geq 0$.

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Compute the offspring distribution when

$$\lambda(t) = \lambda 1_{\mathcal{L} \leq t < \mathcal{L} + \mathcal{I}}(t),$$

with $\lambda > 0$ given, in the two cases \mathcal{I} deterministic, and $\mathcal{I} \sim \text{Exp}(\mu)$.

The branching process 1

- We start with an ancestor with label 0, to which we attach the pair (λ_0, Q_0) . The ancestor gives birth at the jump times of the process

$$\int_0^t \int_0^\infty 1_{u \leq \lambda_0(s)} Q_0(ds, du),$$

which we label $\tau_{0,1}, \tau_{0,2}, \dots$

- The first born indiv. at time $T_1 = \tau_{0,1}$ is given the label 1 and attached (λ_1, Q_1) , which describe the descent of indiv. 1, with births at times $T_1 + \tau_{1,1}, T_1 + \tau_{1,2}, \dots$
- The second born individual is born at time $T_2 = \inf\{\tau_{0,2}, T_1 + \tau_{1,1}\}$, to which is attached (λ_2, Q_2) , hence the descent at times $T_2 + \tau_{2,1}, T_2 + \tau_{2,2}, \dots$
- The third born individual is born at time

$$T_3 = \begin{cases} \inf\{\tau_{0,3}, T_1 + \tau_{1,1}, T_2 + \tau_{2,1}\}, & \text{if } T_2 = \tau_{0,2}, \\ \inf\{\tau_{0,2}, T_1 + \tau_{1,2}, T_2 + \tau_{2,1}\}, & \text{if } T_2 = T_1 + \tau_{1,1}. \end{cases}$$

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The branching process 2

- We now define (with $T_0 = 0$) for $t > 0$:

$$I(t) = \sum_{i \geq 0} 1_{T_i \leq t < T_i + \eta_i},$$

$$R(t) = \sum_{i \geq 0} 1_{T_i + \eta_i \leq t}.$$

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The epidemic model with N initially susceptibles 1

- Initially we have N susceptibles + one indiv. (= the ancestor of the BP) who is infected at time 0, to which is attached (λ_0, Q_0) . The first infectious contact is with the individual $[U_1 N] + 1$. This is individual 1, to which is attached (λ_1, Q_1) .
- The second potential infection hits individual $[U_2 N] + 1$. If $[U_2 N] + 1 = [U_1 N] + 1$, then nothing happens : we say that a *ghost* has been infected. Otherwise, $[U_2 N] + 1$ is the second infected individual, to which is attached (λ_2, Q_2) as in the branching process.
- We go on. When the contact is with an already infected individual, we say that a *ghost* appears, and the corresponding descent in the branching process is suppressed.

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The epidemic model with N initially susceptibles 2

- Let $\{i_j, j = 0, 1, 2, \dots\}$ denote the strictly increasing sequence starting from $i_0 = 0$, $i_1 = 1$ and such that for $j \geq 2$, $[U_{i_j} N] + 1 \notin \cup_{1 \leq k < i_j} \{[U_k N] + 1\}$, i.e. the i_j -th birth in the BP does not create a ghost in the N -epidemic.
- At time 0, we have $(S^N(0), I^N(0), R^N(0)) = (N, 1, 0)$. At each time T_{i_j} , $j \geq 1$, S^N decreases by 1 and I^N increases by 1. At each time $T_{i_j} + \eta_{i_j}$, $j \geq 0$, I^N decreases by 1 and R^N increases by 1. Recall that $\eta_{i_j} = \sup\{t > 0, \lambda_{i_j}(t) > 0\}$.
- The epidemic goes on until $I^N(t) = 0$. The final size equals the value of $R^N(t)$ at that time. Note that for all times, $S^N(t) + I^N(t) + R^N(t) = N + 1$.
- We have constructed the BP and the N -epidemic for all values of N jointly on the same probability space.

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The early stage 1

- The epidemic and the BP coincide until T^N = the time of appearance of the first ghost (= $+\infty$ in case no ghost appears). Let M^N denote the # of infections prior to the first ghost. We have

Theorem

For all $t \in [0, T^N)$, $(I^N(t), R^N(t)) = (I(t), R(t))$.

Moreover, $T^N \rightarrow \infty$ in probability, as $N \rightarrow \infty$. The same is true for M^N , unless the BP is (sub)critical, in which case $\mathbb{P}(T^N = +\infty) \rightarrow 1$.

- **Proof** The first statement is obvious. To prove the second statement, we first compute

$$\begin{aligned}\mathbb{P}(M^N > k) &= 1 \times \frac{N-1}{N} \times \cdots \times \frac{N-k}{N} = \prod_{j=0}^k \left(1 - \frac{j}{N}\right) \\ &\geq 1 - \sum_{j=1}^k \frac{j}{N} = 1 - \frac{k(k+1)}{2N}.\end{aligned}$$

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The early stage 2. End proof of Theorem

- We have $\mathbb{P}(M^N > k) \geq 1 - \frac{k(k+1)}{2N}$. So if $k(N) = o(\sqrt{N})$ (e.g. $k(N) = N^{1/3}$, $k(N) = \log(N)$), then $\mathbb{P}(M^N > k(N)) \rightarrow 1$, as $N \rightarrow \infty$.
- Let $Z(t)$ be the # of indiv. born on $[0, t]$ in the BP, and $Z^N(t) = N - S^N(t)$. We have $Z^N(t) = Z(t)$ for $t < T^N$. Since $\mathbb{P}(M^N > k(N)) \rightarrow 1$, $\mathbb{P}(\inf\{t; Z(t) = k(N)\} \leq T^N) \rightarrow 1$.
- If the BP is (sub)critical, then $Z(t)$ remains bounded, and $\mathbb{P}(T^N = +\infty) \rightarrow 1$.
- In the supercritical case, $\exists \rho > 0$ s.t. $\int_0^\infty \bar{\lambda}(t)e^{-\rho t} dt = 1$, $Z(t) \sim We^{\rho t}$, with $\{W = 0\} = \text{Ext}$. Now, with $W' > W$, $\mathbb{P}(k(N) \leq W'e^{\rho T^N}) \rightarrow 1$, hence $\mathbb{P}(T^N \geq \frac{\log k(N) - \log W'}{\rho}) \rightarrow 1$, and $T^N \rightarrow \infty$ in probability.

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The early stage 3

- Define $Z = Z(\infty)$, $Z^N = Z^N(\infty)$.
- We have first :

Corollary

If $R_0 \leq 1$, then with probability converging to 1 as $N \rightarrow \infty$, $(I^N(t), R^N(t)) = (I(t), R(t))$ for all $t \geq 0$. And $\mathbb{P}(Z^N = k) \rightarrow \mathbb{P}(Z = k)$ for all $k \geq 1$.

- We have next :

Corollary

If $R_0 > 1$, then $\mathbb{P}(Z^N = k) \rightarrow \mathbb{P}(Z = k)$ for all $k \geq 1$. Moreover

$$\mathbb{P}(\lim_N Z^N = +\infty) = \mathbb{P}(Z = +\infty) = 1 - \mathbb{P}(\text{Ext}).$$

- A BP approximation has been used for modeling the spread of EBOLA during an early stage in West Africa in 2014.

The early stage 3

- Define $Z = Z(\infty)$, $Z^N = Z^N(\infty)$.
- We have first :

Corollary

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Probability of a major / minor epidemic

- If $R_0 \leq 1$, then the BP goes extinct in finite time a.s. The N epidemic is upper bounded by the BP for all N , so there is no major outbreak, the proportion of the total number of individuals getting infected tends to 0 as N tends to ∞ .
- If $R_0 > 1$, with the probability $p_{Ext} \in (0, 1)$, the BP goes extinct in finite time (in which case there is no major outbreak). With probability $1 - p_{Ext}$, the BP goes off at exponential rate, and there is a major epidemic. How can we compute p_{Ext} ?
- p_{Ext} is also the probability of extinction of the discrete time BP, i.e. it is the solution of the equation $g(s) = s$, if g is the generating function of the number of offspring, which follows the $\text{MixPoi}(\int_0^\infty \lambda(t)dt)$ distribution. If $X \sim \text{Poi}(a)$, then $\mathbb{E}[s^X] = \exp([s - 1]a)$. So $g(s) = \mathbb{E} \left\{ \exp \left([s - 1] \int_0^\infty \lambda(t)dt \right) \right\}$.

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Exercise Compute $g(s)$ in the case of the Markov model, i.e. $\lambda(t) = \lambda 1_{t \leq \mathcal{I}}$, and \mathcal{I} follows the $\text{Exp}(\mu)$ distribution. Compute p_{Ext} in that case.

Remark p_{Ext} does not depend only upon $R_0 = \int_0^\infty \bar{\lambda}(t) dt$!