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Causal tree of disease transmission and the spreading of infectious diseases

Alexei Vázquez

Abstract. We represent an epidemic outbreak by its causal tree of infection transmission, where nodes represent infected agents and arcs represent the disease transmission from an agent to another. The tree structure allows us to calculate different magnitudes quantifying the epidemic outbreak using iterative approaches. We focus on the expected outbreak size, and analyze its temporal evolution for different reproductive number and generation time distributions. We show that when the expected reproductive number is unbounded the outbreak size is proportional to agent population size and the temporal evolution is slower than exponential. The proposed framework can be used to model epidemic outbreaks using both empirical data obtained from previous outbreaks or by characterizing the contact process responsible for the disease transmission.

1. Introduction

A general framework for the mathematical modeling of epidemic spreading should allow us to understand the main features of the spreading dynamics, as well as being able to accommodate realistic spreading mechanisms and statistical properties obtained from empirical data. Mathematical approaches based on the mixed population hypothesis have been quite successful in this direction, determining the temporal evolution of the expected number of infected individuals with the estimation of a few parameters [**2, 10**]. These models have also been extended to include different transmission rates in a heterogeneous population [**21, 23**] and realistic distributions of infectious periods [**20**].

More recently, the partial mapping of several contact networks underlying the transmission of biological and computer viruses is making possible the development of network modeling frameworks. [**29, 22, 26, 3, 24, 12, 34**]. We can now perform numerical experiments modeling the possible outbreak scenarios of an infectious disease in a real environment, such as the spreading of an airborne virus within an urban settlement [**12, 24**] or a computer virus via email [**3, 34**]. Some analytical frameworks have also been developed to characterize the spreading dynamics on networks, explaining some features observed in the numerical simulations, such as

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the existence or absence of an epidemic threshold [**29, 28, 22, 5**], the final outbreak size [**25, 26, 24**], and the spreading velocity [**4**].

Yet, we are still lacking a general network approach that allows us to incorporate empirical distributions of disease transmission times and reproductive numbers. Some hints in this direction can be obtained from the Belmman-Harris age-dependent branching process [**15**]. Further work is, however, required to extend their results to the case of an unbounded expected reproductive number. This last point is of particular importance since it has been recently noted that several graph representations of real systems are characterized by a degree distribution with a power law tail [**1**], and in this case the expected reproductive number may be unbounded [**7, 29**].

In this work we study the spreading of an infectious diseases within an agent population. We use the generic term agent to identify the entity that can host and transmit the disease. In turn we use the generic term disease to identify the entity that can be hosted by an agent and transmitted from an agent to another. Obvious examples are the transmission of infectious diseases, such as SARS or AIDS, among humans. Less obvious examples are the spreading of ideas and rumors ("infections of the mind") among humans. Other examples are found within electronic communications, such as the spreading of computer viruses, chain letters and hoaxes among computer users [**14**].

We represent the spreading process by the causal tree of disease transmission. The causal tree is a rooted and weighted tree containing all the disease transmissions instances: agent A infected agent B, and their generation times, the time elapsed between the infection of B by A. Each individual in the causal tree is characterized by its reproductive number, giving how many other agents it infects, and the generation times. In Section 2 we characterize the statistical properties of the reproductive numbers and generation times, focusing on two different scenarios: 1- the disease spreading on a graph, such as the spreading of a virus on the Internet, and 2- the disease spreading through a contact process, such as sexual contacts. We emphasize that in several communication systems the expected reproductive number is unbounded, meaning that it diverges with increasing the system size. Next, in Section 3 we characterize the statistical properties of an epidemic outbreak exploiting the recursive iteration of the local spreading properties studied in Section 2. In particular, we determine the temporal evolution of the expected number of infected agents, leaving the calculation of higher moments for future work. For the case of a bounded expected reproductive number we reproduce some results obtained for the Bellman-Harris age-dependent branching process [**15**]. We also characterize the case of an unbounded expected reproductive number, which exhibit some new features. In this case the outbreak is extensive once it starts, meaning that the expected number of infected agents is proportional to the agent population size, while the temporal evolution of the initial epidemic growth is slower than exponential. The implications of these results to the disease spreading among humans and computers are discussed.

2. Local disease transmission

Consider the spreading of an infectious disease on a population of N_0 susceptible agents and, within that population, consider a probe agent i that became infected and potentially could transmit the disease to other agents (see inset of Figure 1).

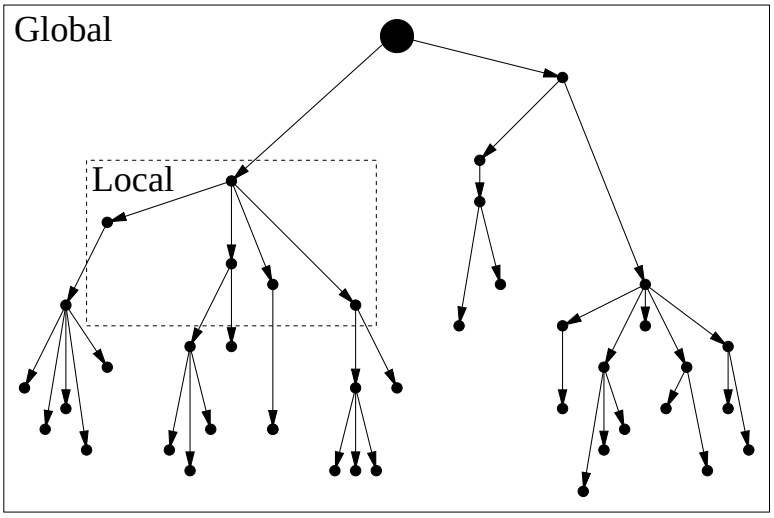

FIGURE 1. **Causal tree of disease transmission:** Schematic representation of a causal tree of disease transmission. Each node in the tree represents an infected agent and each arc represents the disease transmission from one agent to another: primary case → secondary case. We explicitly distinguish between patient zero (big circle) and other infected agents (smaller circles). Within the dashed square we consider a probe node, its out-degree giving its reproductive number and the arc's lengths giving the generation times.

We make an explicit distinction between the first infected agent ($i = 0$), or patient zero, and infected agents other than patient zero ($i = 1, \ldots, N_0 - 1$). The infection of patient zero comes from an exogenous source, such as an animal host in the case of human diseases or a hacker in the case of computer viruses. The infection of other agents, however, come from another agent that was infected at some previous time. Thus, we could imagine patient zero as any patient selected at random, while the disease transmission introduces some biases in the statistical properties of the agents being subsequently infected [**23, 2, 29**].

The probe agent will be characterized by the reproductive number and the generation time:

DEFINITION 2.1. The *reproductive number* $\mathcal{R}_i$ is the number of secondary infectious generated by agent i, given it is infected.

DEFINITION 2.2. The *generation time* $\mathcal{G}_{ij}$, is the time elapsed from the infection of a primary case i to the infection of a secondary case j.

We assume that the agent's reproductive numbers are independent random variables prescribed by the probability distributions $r_k = \mathbf{P}\{\mathcal{R}_0 = k\}$ and $\tilde{r}_k = \mathbf{P}\{\mathcal{R}_i = k | i > 0\}$, with expected reproductive number $R = \sum_k r_k k$ and $\tilde{R} = \sum_k \tilde{r}_k k$, respectively. We also assume that the generation times are independent random variables with the distribution functions $G(\tau) = \mathbf{P}\{\mathcal{G}_{0j} \leq \tau | j > 0\}$ and $\tilde{G}(\tau) = \mathbf{P}\{\mathcal{G}_{ij} \leq \tau | i, j > 0\}$, with probability density functions (pdf) $g(\tau) = dG(\tau)/d\tau$ and

$\tilde{g}(\tau) = d\tilde{G}(\tau)/d\tau$, respectively. In the following we are going to deduce expressions for the expected reproductive numbers and the generation time distributions for two different scenarios. The first one is the disease transmission on an existing structure, such as the spreading of a computer virus on the Internet. The second is the disease transmission through a contact process, such as the transmission of sexually transmitted diseases through sexual contacts.

2.1. Spreading on an existing graph. The statistical properties of the reproductive number of agents lying on a graph has been studied in [**7, 27, 26, 29, 28**]. We analyze then here to emphasize the observation of an unbounded reproductive number.

Consider a population of susceptible agents represented by a simple undirected graph, where vertices represent agents and edges represent disease transmission channels. The graph is assumed to be static, meaning that its adjacency matrix remain invariable during the course of the disease spreading. The degree of a vertex is given by the number of edges incident to it and represents the potential reproductive number of the corresponding agent. We make the following assumptions:

(*i*) The graph is a random graph with a given degree distribution p_s.
(*ii*) Given an infected vertex i and one of its neighbors j, the infection is transmitted from i to j with probability b, independently of the time when it happens.
(*iii*) Patient zero is any vertex selected at random.
(*iv*) The timing of the disease transmission from an infected vertex to its susceptible neighbors is independent of the graph topology.

Under these approximations we obtain that

THEOREM 2.3. *If (i)-(iv) are satisfied then*

$$R = b\sum_{s=1}^{\infty} p_s s \tag{2.1}$$

$$\tilde{R} = b\frac{\sum_{s=1}^{\infty} s(s-1)p_s}{\sum_{s=1}^{\infty} sp_s} \ . \tag{2.2}$$

PROOF. If the probe agent is represented by a vertex with degree s then from (*ii*) it follows that it infects k, $k = 1, \ldots, s$, of its neighbors with probability

$$v_k(s) = \binom{s}{k} b^k (1-b)^{s-k} \ . \tag{2.3}$$

If the probe agent is patient zero then from (*iii*) it follows that it has degree s with probability p_s, resulting in

$$r_k = \sum_{s=k}^{\infty} p_s v_k(s) \ . \tag{2.4}$$

From this equation we obtain the expected reproductive number in (2.1).

If the probe agent is an infected agent other than patient zero, represented by a vertex with degree s, then it can infect at most $s-1$ other agents, the remaining agent being the one from where it received the infection. Furthermore, this probe

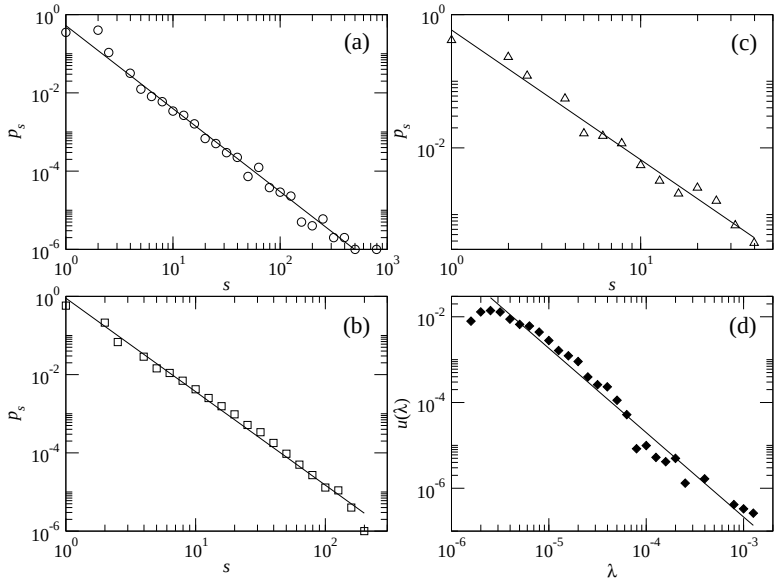

FIGURE 2. (a),(b),(c) Degree distribution of three graphs representing different communication networks. (a) Autonomous system representation of the Internet. (b) Router representation of the Internet. (c) Gnutella peer-to-peer network. For more information about the statistical properties of these graphs see [**33, 30**]. The continuous lines represent power law tails $p_s \sim s^{-\gamma}$ with $\gamma = 2.1$ (a), 2.4 (b) and 2.0 (c). (d) Probability density function $u(\lambda)$ of the rate λ at which email users send emails, as obtained from the dataset reported in [**11**]. The continuous line represents a power law tail $u(\lambda) \sim \lambda^{-\gamma}$ with $\gamma = 2.0$.

agent is not a vertex selected at random, but a vertex at the end of an edge selected at random. In the case of random graphs with a fixed degree distribution the vertex at the other end has degree s with probability $sp_s / \sum_{l=1}^{\infty} sp_s$ [**27**], resulting in

$$\tilde{r}_k = \sum_{s=k+1}^{\infty} \frac{sp_s}{\sum_{l=1}^{\infty} lp_l} v_k(s-1) \ . \tag{2.5}$$

From this equation we obtain the expected reproductive number in (2.2).

□

The degree distribution of many real graphs has the power law tail $p_s \sim s^{-\gamma}$, with $2 < \gamma < 3$ [**1**]. Some representative examples of electronic communication networks are shown in Figure 2(a),(b),(c). When $2 < \gamma < 3$ from (2.2) we obtain that $\tilde{R}$ is unbounded, where by unbounded we mean that $\tilde{R}_0 \to \infty$ when the agent population size tends to infinity. This fact has dramatic consequences on the global spreading of the disease (see Section 3).

EXAMPLE 2.4 (Email based computer worms). An email based computer worm is a "malicious" code that arrives to an email user (agent) via an infected email

and, when activated by the email user, self-broadcast to all the email addresses on its address book. In this case b represents the probability that the infected email is opened by the email user, and the graph is the address book graph [**3**]. An email user receiving an infected email could open it during one email access session. The duration of an email access session is generally much smaller than the time between to email access sessions and, therefore, each email access session can be considered as instantaneous. We model the sequence of $l = 1, 2, \ldots$ email access sessions as a renewal process [**13**], where the times $\mathcal{A}_l$ between the l and $l+1$ access sessions are independent random variables with a common distribution $A(\tau) = \mathbf{P}\{\mathcal{A}_l \leq \tau\}$, with expected value $\mu_{\rm A}$. The event of receiving an email is uncorrelated with the event having an email access session, implying that the time at which an email is received is any time selected at random. Thus, the generation time, the time elapsed until its opening, is the time interval till the next email access session. This time is the residual waiting time in renewal theory, and is distributed according to [**13**]

$$G(\tau) = \tilde{G}(\tau) = \frac{1}{\mu_{\rm A}} \int_0^\tau d\tau' \left[1 - A(\tau')\right] \ . \tag{2.6}$$

Hence, to model the spreading of an email based computer worm we need to collect empirical data about the email users' address books and the timing of their email access sessions.

2.2. Spreading through a contact process. Consider a population of N_0 susceptible agents and a contact process among them responsible for the disease transmission. A typical example is the spread, through sexual contact, of a sexually transmitted disease on a population of sexually active individuals. To model the disease spread we assume that:

- (*i*) Given an agent i, $i = 1, \ldots, N_0$, the sequence of times when it establishes a contact is modeled by a renewal process [**13**], with the inter-contact time distribution function $C_i(\tau)$, pdf $c_i(\tau) = dC_i(\tau)/d\tau$, and expected value Λ_i.
- (*ii*) Λ_i are independent random variables with the distribution function $U(\lambda) = \mathbf{P}\{\Lambda_i \leq \lambda\}$, pdf $u(\lambda) = dU(\lambda)/d\lambda$ and expected value μ_U.
- (*iii*) On each contact m, $m = 1, 2, \ldots$, other agents are simultaneously contacted with probability q_m, with expected value $M = \sum_{m=1}^{\infty} q_m m$.
- (*iv*) The agent's population is homogeneous regarding the disease transmission probability upon contact, characterized by the probability $b(t)$ that the disease is transmitted at time t given a contact is established and the agent became infected at time $t = 0$.
- (*v*) Patient zero is any agent selected at random.

The agent distinction in (*i*) and (*ii*) allows us to consider heterogeneous populations where different agents may establish contacts with different rates [**21, 23, 2**]. The fact that more than one agent can be contacted simultaneously (*iii*) allows us to consider contact processes with concurrency. This is the case of sexually transmitted diseases, where a sexually active individual may maintain sexual relations with more than one sexually active individual during a certain period of time [**2**], and of email contacts, where an email may be sent to more than one recipient. Under these approximations we obtain

THEOREM 2.5. *If (i)-(v) are satisfied then*

$$R = \int_0^\infty dt\beta(t) \tag{2.7}$$

$$G(\tau) = \frac{1}{R}\int_0^\tau dt\beta(t) \ , \tag{2.8}$$

where

$$\beta(t) = Mb(t)\frac{1}{N_0}\sum_{i=1}^{N_0}\sum_{l=1}^{\infty} c_i^{l\star}(t) \ ; \tag{2.9}$$

and

$$\tilde{R} = \int_0^\infty dt\tilde{\beta}(t) \tag{2.10}$$

$$\tilde{G}(\tau) = \frac{1}{\tilde{R}}\int_0^\tau dt\tilde{\beta}(t) \ , \tag{2.11}$$

where

$$\tilde{\beta}(t) = Mb(t)\frac{1}{N_0\mu_U}\sum_{i=1}^{N_0}\Lambda_i\sum_{l=1}^{\infty} c_i^{l\star}(t) \ . \tag{2.12}$$

where $\star$ denotes the convolution operation: $f\star g(t) = \int_0^\infty df(\tau)g(t-\tau)$ and $f^{l\star}(t)$ is the l-th order convolution of $f(t)$.

PROOF. Consider a probe agent i that became infected at $t = 0$. This agent establishes contacts at later times t_{i1}, t_{i2}, ... potentially infecting the contacted agents. Following (i) the contacting times are given by

$$t_{il} = \sum_{n=1}^{l}\tau_{in} \ , \tag{2.13}$$

where τ_{in} are independent random variables with the identical distribution $C_i(\tau)$. Let $\mathcal{R}_{il}$ be the number agents it actually infects on the l-th contact, resulting in the reproductive number

$$\mathcal{R}_i = \sum_{l=1}^{\infty}\mathcal{R}_{il} \ . \tag{2.14}$$

The number of agents infected on each contact is determined by q_m and $b(t)$, and therefore it is independent of i. Thus, in the following we drop the subscript i when writing $\mathcal{R}_{il}$. We obtain that

$$\mathbf{P}\{\mathcal{R}_l = s\}(t) = \sum_{m=s}^{\infty} q_m\binom{m}{s}b(t)^l[1-b(t)]^{m-s} \ . \tag{2.15}$$

If the probe agent is patient zero then from (v), (2.14) and (2.15) it follows that

$$r_k = \frac{1}{N_0}\sum_{i=1}^{N_0}\prod_{n=1}^{\infty}\int_0^{\infty} dC_i(\tau_n)\sum_{s_l=0}^{\infty}\delta_{k,\sum_{l=1}^{\infty}s_l}\prod_{l=0}^{\infty}\mathbf{P}\{\mathcal{R}_l = s_l\}\left(\sum_{n=1}^{l}\tau_n\right) , \tag{2.16}$$

where δ_{ij} is the delta Kronecker symbol ($\delta_{ii} = 1$ and $\delta_{ij} = 0$ for all $i \neq j$). From (2.16) we obtain the expected reproductive number in (2.7), where $\beta(t)$ is the expected number of agents that patient zero infects between time t and $t + dt$. Finally, by definition $G(\tau) = \int_0^{\tau} dt\beta(t)/\int_0^{\infty} dt\beta(t)$ resulting in (2.8).

If the probe agent is an infected agent other than patient zero then it is not an agent selected at random, but an agent that has already established a contact with an infected agent. In this case we take into account that agents with frequent contacts are more susceptible to become infected, and subsequently will transmit the disease at higher rates. To be more precise, the probability that agent i establishes a contact between time t and $t + dt$ is given by Λ_i. In turn the total number of agents establishing a contact between time t and $t + dt$ is given by $N_0\mu_U dt$. Thus, if an infected agent establishes a contact between time t and $t + dt$ with another agent then this other agent is i with probability $\Lambda_i/N_0\mu_U$. The rest of the proof is similar to that for patient zero after replacing $(N_0)^{-1}\sum_i$ by $(N_0\mu_U)^{-1}\sum_i \Lambda_i$.

□

Example 2.6 (Poisson contact process). If agent i establishes contacts at a constant rate Λ_i then $C_i(\tau) = 1 - e^{\Lambda_i\tau}$ [**13**]. In this case from (2.7)-(2.11) we obtain

$$R = \mu_U M\int_0^{\infty} b(t) , \tag{2.17}$$

$$\tilde{R} = \frac{\mu_{2U}}{\mu_U}M\int_0^{\infty} b(t) , \tag{2.18}$$

$$G(\tau) = \tilde{G}(\tau) = \frac{\int_0^{\tau} b(t)}{\int_0^{\infty} b(t)} , \tag{2.19}$$

where $\mu_{2U} = \int_0^{\infty} dU(\lambda)\lambda^2$ is the second moment of the contact rate distribution. Note that the generation time distributions are only determined by the transmission probability $b(t)$. Indeed, when the contacts are established at a constant rate the distribution of the time when an actual disease transmission takes place will only depend on $b(t)$. It is also worth noticing that in the long time limit a renewal process with renewal time distribution $C_i(\tau)$ can be approximated by a Poisson process with rate [**13**]

$$\Lambda_i = \frac{1}{\int_0^{\infty} dC_i(\tau)\tau} . \tag{2.20}$$

Hence, (2.17)-(2.19) may be a good approximation even when the contact process underlying the disease transmission is not a Poisson process.

When analyzing sexually transmitted diseases $u(\lambda)$ represents the pdf of the rate λ at which sexually active individuals acquires new sexual partners. Empirical data collected for several countries reveals that $u(\lambda)$ is characterized by a power law tail $u(\lambda) \sim \lambda^{-\gamma}$ [**18, 17, 31**]. The exponent γ resulting from the fit to the empirical data has values close to but larger than three. These observations should be considered with caution since γ is close to three and further refined measurements may reveal that γ is smaller than three, resulting in an unbounded $\tilde{R}_0$ in (2.18).

As sexually transmitted diseases spread via sexual contacts email viruses spread via email contacts, requiring us to investigate the contact rate distribution for the case of email contacts. The contact rate of an email user is given by the inverse of the average time between two consecutive email sent by that user. We have computed the distribution of this magnitude using a dataset containing the email history of 3180 email users within an university environment [**11**]. In Figure 2 we show that the distribution of email contact rate has also a power law tail, with exponent $\gamma \approx 2$, indicating that $\tilde{R}$ (2.18) is unbounded.

3. Global disease transmission

The recursive disease transmission, from one infected agent to some susceptible agents, from the new infected agents to other susceptible agents, and so on, may result in an outbreak with several infected agents (see Figure 1). We assume that to each infected agent, other than patient zero, we can assign one and only one infected agent from who he received the infection. In this case, we can represent an epidemic outbreak by an oriented weighted tree, where the root node $i = 0$ represents patient zero, nodes $i > 0$ represents infected agents other than patient zero, and each arc (i, j) represents the transmission of the disease from i to j. The number of arcs emanating from a node gives its out-degree and in turn the agent's reproductive number $\mathcal{R}_i$. Furthermore, to each arc (i, j) we assign a nonnegative real number $\mathcal{G}_{ij}$ giving the length of the time interval from the infection of i to the infection of j, *i.e.* the generation time. Since the out-degrees and arc's weights are random variables we thus obtain a set of random oriented weighted trees. More precisely:

Definition 3.1. A *random causal tree* is a rooted and weighted tree where:

(1) The node's out-degrees are independent random variables prescribed by the probability distributions $r_k = \mathbf{P}\{\mathcal{R}_0 = k\}$ and $\tilde{r}_k = \mathbf{P}\{\mathcal{R}_i = k | i > 0\}$.
(2) The arc's weights are independent random variables with the distribution functions $G(\tau) = \mathbf{P}\{\mathcal{G}_{0j} \leq \tau | j > 0\}$ and $\tilde{G}(\tau) = \mathbf{P}\{\mathcal{G}_{ij} \leq \tau | i, j > 0\}$.
(3) The tree has a diameter D.

The last hypothesis is introduced to take into account that the agent population is finite and, therefore, the causal tree diameter could be at most equal to the total number of agents. Furthermore, for the case of a disease spreading on a graph (2.1) D is given by the graph diameter.

Consider a random causal tree and one of its nodes i. There is one and only one path from the root to i. We say that node i belongs to generation d if there are d arcs in the path from the root to i, and we denote by Γ_d the set of all nodes in the d-th generation. In turn, focusing on the tree branch rooted at i, there is only and only one path from i to nodes j in that branch. The sum of the arc's weights in the path from i to j gives the infection time t_{ij} of j given i was infected

at time $t_{ii} = 0$. We then say that a node j is infected at time t if $t_{ij} \leq t$. Let $\mathcal{N}_i(t)$ be the number of infected nodes at time t in the branch rooted at i and $P_N^{(d)}(t) = \mathbf{P}\{\mathcal{N}_i(t) = N | i \in \Gamma_d\}$ be the probability distribution of $\mathcal{N}_i(t)$ given $i \in \mathcal{G}_d$. We introduce the generating functions

$$F^{(d)}(x,t) = \sum_{N=0}^{\infty} P_N^{(d)}(t) x^N \tag{3.1}$$

$$H(x) = \sum_{k=0}^{\infty} r_k x^k \tag{3.2}$$

$$\tilde{H}(x) = \sum_{k=0}^{\infty} \tilde{r}_k x^k \ . \tag{3.3}$$

We can exploit the recursive structure of a random causal tree to derive recursive relations for the generating function $F^{(d)}(x,t)$. More precisely

THEOREM 3.2. *$F^{(d)}(x,t)$ satisfies the recursive relations:*

$$F^{(d)}(x,t) = \begin{cases} xH\left(\int_0^t dG(\tau) F^{(d+1)}(x,t-\tau) + 1 - G(t)\right) \ , & d = 0 \\ x\tilde{H}\left(\int_0^t d\tilde{G}(\tau) F^{(d+1)}(x,t-\tau) + 1 - \tilde{G}(t)\right) \ , & 1 < d < D \\ x \ , d = D \ . \end{cases} \tag{3.4}$$

PROOF. Consider a node $i \in \Gamma_d$, with reproductive number $\mathcal{R}_i$, and let us denote by j, $j \in \{1, 2, \ldots, \mathcal{R}_i\}$, its neighbors in the $d+1$ generation. Thus

$$\mathcal{N}_i(t) = 1 + \sum_{j=1}^{\mathcal{R}_i} \mathcal{N}_j(t - \mathcal{G}_{ij}) \ . \tag{3.5}$$

$N_j(t - \mathcal{G}_{ij})$ are independent random variables with the distribution

$$\mathbf{P}\{\mathcal{N}_j(t - \mathcal{G}_{ij}) = N | j \in \Gamma_1\} = \int_0^t dG(\tau) P_N^{(1)}(t-\tau) + \delta_{N,0}\left(1 - G(t)\right) \tag{3.6}$$

for $d = 0$, and

$$\mathbf{P}\{\mathcal{N}_j(t - \mathcal{G}_{ij}) = N | j \in \Gamma_{d+1}\} = \int_0^t d\tilde{G}(\tau) P_N^{(d+1)}(t-\tau) + \delta_{N,0}\left(1 - \tilde{G}(t)\right) \tag{3.7}$$

for $d > 0$. From (3.5)- (3.7) we obtain

$$\begin{aligned} P_N^{(0)}(t) &= \sum_{k=0}^{\infty} r_k \sum_{N_1=0}^{\infty} \cdots \sum_{N_k=0}^{\infty} \delta_{\sum_{j=1}^k N_j + 1, N} \\ &\times \prod_{j=1}^{k} \left[\int_0^t dG(\tau) P_{N_j}^{(1)}(t-\tau) + \delta_{N_j,0}\left(1 - G(t)\right) \right] \end{aligned} \tag{3.8}$$

for $d = 0$, and

$$P_N^{(d)}(t) = \sum_{k=0}^{\infty} \tilde{r}_k \sum_{N_1=0}^{\infty} \cdots \sum_{N_k=0}^{\infty} \delta_{\sum_{j=1}^{k} N_j+1,N} \times \prod_{j=1}^{k} \left[\int_0^t d\tilde{G}(\tau) P_{N_j}^{(d+1)}(t-\tau) + \delta_{N_j,0} \left(1-\tilde{G}(t)\right) \right] \tag{3.9}$$

for $0 < d < D-1$. Since the causal tree ends at generation D we obtain the boundary condition.

$$P_N^{(D)}(t) = \delta_{N,1} \tag{3.10}$$

for $d = D$. Finally, substituting (3.8), (3.9) and (3.10) into the generating function (3.1) we obtain the recursive equations in (3.4).

□

This is a good point to mention the differences between our formalism and the Bellman-Harris age-dependent branching process [**15**]. First, in the Bellman-Harris process all the secondary cases are generated simultaneously, while in a random causal tree each secondary case has its own generation time. Second, in the Bellman-Harris process the number of generations is unbounded ($D \to \infty$) while we explicitly assume that there is a maximum number of generations D. Third, and final, Bellman and Harris obtain a self-consistent equation for the generating function of the number of new descendants generated between time t and $t + dt$, while we obtain recursive relations for the generating function of the total number of descendants up to time t.

3.1. Expected outbreak size. From the recursive relations (3.4) we can obtain recursive relations for the moments of $P_N^d(t)$. We focus our attention in the first moment (the expected outbreak size) leaving the calculation of higher moments for later work. Let $N(t)$ be the expected total number of infected nodes up to time, and $n(t)$ the expected number of nodes that are infected between time t and $t + dt$, which in turn satisfy

$$n(t) = \frac{dN(t)}{dt} \ . \tag{3.11}$$

We obtain the following result

THEOREM 3.3.

$$n(t) = \sum_{d=1}^{D} R\tilde{R}^{d-1} g \star \tilde{g}^{(d-1)\star}(t) \ . \tag{3.12}$$

PROOF. The expected number of infected agents in the branch rooted at $i \in \Gamma_d$, given that i became infected at $t = 0$, is given by

$$N^{(d)}(t) = \frac{\partial F^{(d)}(1,t)}{\partial x} \ . \tag{3.13}$$

Making use of the recursive relations (3.4) we obtain

$$N^{(d)}(t) = \begin{cases} 1 + R\int_0^t dG(\tau)N^{(1)}(t-\tau)\ , & d = 0 \\ 1 + \tilde{R}\int_0^t d\tilde{G}(\tau)N^{(d+1)}(t-\tau)\ , & 1 < d < D \\ 1\ , d = D\ . \end{cases} \tag{3.14}$$

Iterating these recursive relations from $d = D$ to $d = 0$ we obtain an expression for $N(t) = N^{(0)}(t)$. Finally, substituting this expression in (3.11) we obtain (3.12). □

3.2. Large population size. A fundamental concern in epidemiology is to determine whether an outbreak can result in an epidemic, infecting a significant number of susceptible agents in a short time. The final size of the outbreak is given by the expected value of the total number of infected agents, denoted by N_0. From (3.12) we obtain

$$N_0 = 1 + \int_0^\infty dt n(t) = 1 + R\frac{\tilde{R}^{D-1} - 1}{\tilde{R} - 1}\ . \tag{3.15}$$

If D, R and $\tilde{R}$ are finite then N_0 is finite. Yet, if one of these magnitudes becomes infinitely large then N_0 may also become infinitely large. We consider two possible scenarios:

3.2.1. *$R < \infty$, $\tilde{R} < \infty$ and $D \to \infty$:* First we focus in the case where it takes a large number of generations before the outbreak reaches all the susceptible agents. In this case we obtain the following series representation for the expected outbreak size:

COROLLARY 3.4. If $R < \infty$, $\tilde{R} < \infty$ and $D \to \infty$ then

$$n(t) = \sum_{d=1}^{\infty} R\tilde{R}^{d-1} g \star \tilde{g}^{(d-1)\star}(t)\ . \tag{3.16}$$

PROOF. Setting $D \to \infty$ in (3.12) we obtain (3.16). The question is whether this series converges and, therefore, it is a series representation of $n(t)$. Let $\hat{n}(\omega) = \int_0^\infty dt e^{-\omega t} n(t)$ be the Laplace transform of $n(t)$. In turn we denote by $\hat{g}(\omega)$ and $\hat{\tilde{g}}(\omega)$ the Laplace transforms of $g(\tau)$ and $\tilde{g}(\tau)$. From (3.16) we obtain

$$\hat{n}(\omega) = \frac{R\hat{g}(\omega)}{1 - \tilde{R}\hat{\tilde{g}}(\omega)}\ . \tag{3.17}$$

Since $g(\tau)$ and $\tilde{g}(\tau)$ are probability densities then $\hat{g}(\omega)$ and $\hat{\tilde{g}}(\omega)$ are defined and continuous for all $\omega \geq 0$. Yet, if the denominator in the *r.h.s.* of (3.17) equals zero then $\hat{n}(\omega)$ is not defined. Let α be the positive solution, if there is any, of the equation

$$\tilde{R}\hat{\tilde{g}}(\alpha) = 1\ . \tag{3.18}$$

If $\tilde{R} < 1$ then (3.18) has no positive solution and, therefore, $\hat{n}(\omega)$ in (3.17) is defined for all $\omega \geq 0$. If $\tilde{R} > 1$ then (3.18) has a positive solution and, therefore, $\hat{n}(\omega)$ in (3.17) is defined for all $\omega > \alpha$. In either case we can compute the inverse Laplace transform

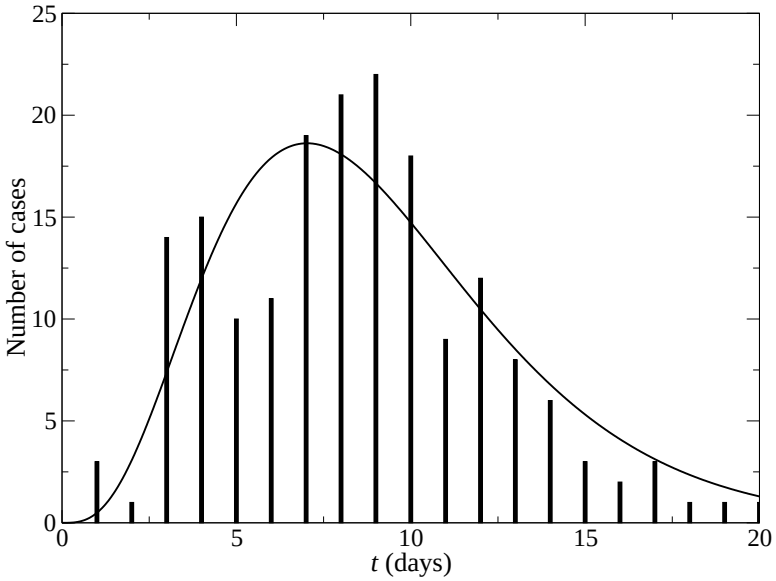

FIGURE 3. **Gamma distribution of generation times:** Number of secondary cases generated by a primary case for a SARS outbreak in Singapore, as reported in [**19**] (bars). The solid line is the best fit to the gamma pdf (3.20) times a pre-factor, resulting in $\theta \approx 4.3$.

$$n(t) = \frac{1}{2\pi\imath} \int_{\omega_0 - \imath\infty}^{\omega_0 + \imath\infty} e^{\omega t} \hat{n}(\omega) \ , \tag{3.19}$$

where $\omega_0 > 0$ for $\tilde{R} < 1$ and $\omega_0 > \alpha$ for $\tilde{R} > 1$. Since (3.19) is defined for all $t > 0$ then (3.16) converges for all $t > 0$ and it is a series representation of $n(t)$.

□

REMARK 3.5. (3.12) has two different long time asymptotic behaviors depending on the value of $\tilde{R}$:

- When $\tilde{R} < 1$ the Laplace transform of $n(t)$ is defined for all $\omega \geq 0$. Hence, $\int_0^\infty dt n(t) < \infty$ and, therefore, $n(t) = \mathcal{O}(1/t)$ when $t \to \infty$. This means that the epidemic outbreak will die out before a significant number of susceptible agents become infected.
- When $\tilde{R} > 1$ the Laplace transform of $n(t)$ is defined for $\omega > \alpha$ and, therefore, $n(t) \sim e^{\alpha t}$ when $t \to \infty$.

These two different asymptotic behaviors has already been obtained for the Hellman-Harris process [**15**].

EXAMPLE 3.6 (Gamma distribution of generation times). The empirical data often support the hypothesis of a gamma distribution of generation times [**19, 16**]. An example is shown in Figure 3 for a SARS outbreak in Singapore. Let us assume that $g(\tau) = \tilde{g}(\tau)$ and they are given by the gamma pdf

$$g(\tau) = \tilde{g}(\tau) = \frac{\theta}{\mu_{\rm G}\Gamma(\theta)} \exp\left(-\frac{\theta\tau}{\mu_{\rm G}}\right)\left(\frac{\theta\tau}{\mu_{\rm G}}\right)^{\theta-1}, \tag{3.20}$$

where $\mu_{\rm G}$ is the expected generation time and $\theta \geq 1$. Substituting (3.20) into (3.16) we obtain

$$n(t) = \frac{\theta R_0}{\mu_{\rm G}\tilde{R}_0^{1-1/\theta}} \exp\left(-\frac{\theta t}{\mu_{\rm G}}\right) \sum_{d=1}^{\infty} \frac{1}{\Gamma(\theta d)} \left(\frac{\tilde{R}_0^{1/\theta}\theta t}{\mu_G}\right)^{\theta d-1}. \tag{3.21}$$

In particular,

$$n(t) = \frac{R}{\mu_G} \exp\left(\frac{(\tilde{R}-1)t}{\mu_G}\right) \tag{3.22}$$

for $\theta = 1$ and

$$n(t) = \frac{2R}{\mu_{\rm G}\tilde{R}^{1/2}} \exp\left(-\frac{2t}{\mu_{\rm G}}\right) \sinh\left(\frac{\tilde{R}^{1/2}2t}{\mu_{\rm G}}\right). \tag{3.23}$$

for $\theta = 2$. This example illustrate how, in some cases, we can express $n(t)$ in terms of elementary functions. Whenever this is not possible, the series representation can be used to compute $n(t)$ numerically.

3.2.2. *$R < \infty$, $D < \infty$ and $\tilde{R} \to \infty$:* When $\tilde{R} \to \infty$ it may take just a few generations such that all the susceptible agents become infected. In this case, the temporal evolution of the expected number of new infected agents will be dominated by those terms in (3.12) with higher powers of $\tilde{R}$. More precisely

Corollary 3.7. If $R < \infty$, $D < \infty$, $\tilde{R} \to \infty$, and $g(\tau) > 0$ and $\tilde{g}(\tau) > 0$ for all $\tau > 0$ then

$$n(t) \sim N_0 g \star \tilde{g}^{(D-1)\star}(t) \left[1 + \mathcal{O}\left(\frac{1}{\tilde{R}}\right)\right]. \tag{3.24}$$

Proof. If $g(\tau) > 0$ and $\tilde{g}(\tau) > 0$ for all $\tau > 0$ then $g \star \tilde{g}^{(d-1)\star}(t) > 0$ for $t > 0$ and $d \geq 1$. From (3.12) and this fact it follows that

$$\frac{n(t) - R\tilde{R}^{D-1} g \star \tilde{g}^{(D-1)\star}(t)}{R\tilde{R}^{D-1} g \star \tilde{g}^{(D-1)\star}(t)} = \mathcal{O}\left(\frac{1}{\tilde{R}}\right). \tag{3.25}$$

Furthermore, from (3.15) we obtain

$$N_0 \sim R\tilde{R}^{D-1}\left[1 + \mathcal{O}\left(\frac{1}{\tilde{R}}\right)\right]. \tag{3.26}$$

Finally, from (3.25) and (3.26) we obtain (3.24).

□

REMARK 3.8. In this case the expected number of new infected agents is of the order of N_0 for $t > 0$, indicating that the outbreak can be considered as an epidemic from its starting time. In such a case it is more appropriate to work with the expected number of new infected agents relative to the population size. Thus, we define the pdf of the new infections between time t and $t + dt$

$$\rho(t) = \frac{n(t)}{N_0} = g \star \tilde{g}^{(D-1)\star}(t) \ , \tag{3.27}$$

where the second equality follows from (3.24) and it holds in the $\tilde{R} \to \infty$ limit.

REMARK 3.9. There may be cases where both $\tilde{R}$ and D diverges. An example is the spreading of a disease on a random graph with a given degree distribution, where the degree distribution has a power law tail $p_s \sim s^{-\gamma}$ with $2 < \gamma < 3$ and a maximum degree $k_{\max} = N_0^{\delta}$, where N_0 is the graph size. From (2.2) we obtain that $\tilde{R} \sim N_0^{\delta(3-\gamma)}$ when $N_0 \to \infty$, while D scale at most as $\log N_0$ [**8, 9**]. In this case (3.24) and (3.27) are still valid up to some logarithmic corrections to D.

EXAMPLE 3.10 (Gamma distribution of generation times). If the generation times are distributed according to the gamma distribution (3.20), then from (3.27) we obtain the gamma pdf

$$\rho(t) = \frac{\theta}{\mu_{\mathrm{G}}\Gamma(\theta D)} \exp\left(-\frac{\theta t}{\mu_{\mathrm{G}}}\right)\left(\frac{\theta t}{\mu_{\mathrm{G}}}\right)^{\theta D - 1} \ , \tag{3.28}$$

which is characterized by a polynomial growth of order $\theta D - 1$ followed by an exponential decay. This result completely departures from the exponential growth predicted by current mathematical approaches to the spreading dynamics [**35**].

4. Conclusions

The causal tree of infection transmission is a suitable object to characterize the spreading dynamics of infectious diseases. Its flexibility allow us to consider different generation time distributions, such as the gamma distribution of generation times that is often used to fit empirical data. It also allow us to extend previous studies of the Bellman-Harris age-dependent branching process to include the case when the expected reproductive number is unbounded. In this last case we obtain that the spreading dynamics is extensive from its very starting time, meaning that number of infected agents is proportional to the population size. Furthermore, the initial epidemic growth is not necessarily exponential as predicted by previous mathematical approaches, but depends on the shape of the generation time distribution. For instance, the initial epidemic growth is polynomial for a gamma distribution of generation times.

We find out contradictory evidence regarding the AIDS epidemics. While sexual network measurements suggest that $\tilde{R}$ is bounded, there is empirical evidence indicating that the AIDS epidemics exhibits a polynomial growth in certain countries [**23, 6, 32**]. Further work is required to determine whether this polynomial growth has a different origin or the sexual network data is incomplete. On the other hand, the empirical evidence indicates that $\tilde{R}$ is unbounded for several communication networks. Therefore, our predictions can be tested using empirical data for computer virus outbreaks.

While we have limited the analysis to the expected outbreak size, we can calculate higher order moments as well, and in principle the outbreak size probability distribution as a function of time. This point is extremely important to understand the initial phase of the outbreak were just a few agents are infected and the fluctuations around the expected outbreak size are significant.

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Department of Physics and center for Complex Networks Research, University of Notre Dame, IN 46556, USA
E-mail address: avazque1@nd.edu