Ancestral process for infectious disease outbreaks with superspreading

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Running title: Ancestry for outbreaks with superspreading

Keywords: infectious disease epidemiology modelling; offspring distribution; superspreading; outbreaks; lambda-coalescent model; multiple mergers

Abstract

When an infectious disease outbreak is of a relatively small size, describing the ancestry of a sample of infected individuals is difficult because most ancestral models assume large population sizes. Given a set of infected individuals, we show that it is possible to express exactly the probability that they have the same infector, either inclusively (so that other individuals may have the same infector too) or exclusively (so that they may not). To compute these probabilities requires knowledge of the offspring distribution, which determines how many infections each infected individual causes. We consider transmission both without and with superspreading, in the form of a Poisson and a Negative-Binomial offspring distribution, respectively. We show how our results can be incorporated into a new lambda-coalescent model which allows multiple lineages to coalesce together. We call this new model the omega-coalescent, we compare it with previously proposed alternatives, and advocate its use in future studies of infectious disease outbreaks.

1 Introduction

An outbreak of an infectious disease typically starts when a single or a small number of infected individuals appear within a susceptible population. Each infected individual may come in contact and transmit the disease to each of the susceptible individuals, who will then become infected in their turn and spread the disease further. Most mathematical models of infectious diseases describe situations where the disease is at an equilibrium, when the number of infected individuals is high and/or with a significant part of the population already infected (Anderson and May 1991; Keeling and Rohani 2008). Here however we focus on the early stages of an epidemic, where the number of infected individuals is small and the number of susceptibles comparatively high and constant. In this situation it is useful to consider the number of new infections that each infected individual is likely to cause, and the probabilistic distribution for this number is often called the offspring distribution (Grassly and Fraser 2008). The mean of the offspring distribution is called the basic reproduction number R_0 and has been given much attention especially since it determines how likely the outbreak is to spread, and how much effort would be needed to bring it under control (Fraser et al. 2004; Ferguson et al. 2006).

If we consider that all individuals are infectious for the same duration and with the same transmission rate, the offspring distribution is Poisson distributed with mean R_0, in which case the variance of the offspring distribution is also R_0. We would then say that there is no transmission heterogeneity. However, in practice there are many reasons why this may not be the case, with some individuals being infectious for longer than others, or being more infectious than others, or having more frequent contacts with susceptibles, or being less symptomatic and therefore less likely to reduce contact numbers, etc. All these factors cause the offspring distribution to be more dispersed than it would otherwise be, that is to have a variance greater than its mean R_0. A frequent choice to capture this overdispersion is to model the offspring distribution using a Negative-Binomial distribution with mean R_0 and dispersion parameter r (Lloyd-Smith et al. 2005; Grassly and Fraser 2008). When r is close to zero the variance is high compared to the mean, whereas when r is high the variance becomes close to the mean. This transmission heterogeneity is often called superspreading, although this is perhaps misleading as it is the rule rather than the exception of how infectious diseases spread. Superspreading has indeed been described in many diseases (Woolhouse et al. 1997; Stein 2011; Kucharski and Althaus 2015; Wang et al. 2021), and most recently for SARS-CoV-2 (Wang et al. 2020; Lemieux et al. 2021; Gómez-Carballa et al. 2021; Du et al. 2022).

As an outbreak unfolds forward-in-time, a transmission tree is generated representing who-infected-whom, in which each node is an infected individual and points towards a number of nodes distributed

according to the offspring distribution. Here we consider the reverse problem of the transmission ancestry, going backward-in-time, from a sample of infected individuals, until reaching the last common transmission ancestor of the whole sample. Given a set of n sampled individuals, we show how to calculate the probability that a given subset of size k have the same infector, either inclusively (so that the remaining $n-k$ may also have the same infector or not) or exclusively (so that none of the remaining $n-k$ have the same infector). We start by considering the general case of an offspring distribution with arbitrary form, and then the specific cases of offspring distributions that follow a Poisson and a Negative-Binomial distribution. The main novelty of our approach is that we consider that the overall population size is small, but we show that in the limit where the population size is large, our results agree with several previous studies (Volz 2012; Koelle and Rasmussen 2012; Fraser and Li 2017). Finally, we show how our results can be incorporated into a new lambda-coalescent model (Pitman 1999; Sagitov 1999; Donnelly and Kurtz 1999) and compare it with previously proposed models.

2 General offspring distribution case

Let time be measured in discrete units and denoted t. Each discrete value of t corresponds to a unique non-overlapping generation of infected individuals, so that individuals infected at t have offspring at $t+1$, etc. Let N_t denote the number of infectious individuals at time t. Each of them creates a number $s_{t,i}$ of secondary infections at time $t+1$, following the offspring distribution $\alpha_t(s)$. The mean of this distribution is the basic reproduction number R_t and the variance is V_t. The total number of infected individuals at time $t+1$ is given by:

$$N_{t+1} = \sum_{i=1}^{N_t} s_{t,i} \tag{1}$$

2.1 Inclusive coalescence probability

We define the inclusive coalescence probability $p_{k,t}(N_t, N_{t+1})$ as the probability that a specific set of k individuals from generation $t+1$ have the same infector in generation t, conditional on population sizes N_t and N_{t+1}. Given full information about offspring counts from individuals in generation t, $\mathbf{s}_t = (s_{t,1}, \dots s_{t,N_t})$, we have:

$$
\begin{aligned}
p_{k,t}(\mathbf{s}_t, N_t) &= \sum_{i=1}^{N_t} \frac{\binom{s_{t,i}}{k}}{\binom{N_{t+1}}{k}} \\
&= \sum_{i=1}^{N_t} \frac{s_{t,i}!}{(s_{t,i}-k)!} \frac{(N_{t+1}-k)!}{N_{t+1}!}
\end{aligned} \tag{2}
$$

Full information $\{s_{t,i}\}$ yields the population size N_{t+1} as shown in Equation 1, but this is not available in practice. We can instead express the inclusive coalescence probability conditioning on the next population size N_{t+1} by summing over possible offspring counts $\mathbf{s}_t = (s_{t,1}, \dots s_{t,N_t})$ conditional on the total generation size. Let $S_t^{-(1)} = (S_{t,2}, \dots, S_{t,N_t})$:

$$
\begin{aligned}
p_{k,t}(N_t, N_{t+1}) &= \sum_{\mathbf{s}_t \in \mathbb{N}_0^{N_t}} \mathbb{P}\left[\mathbf{S}_t = \mathbf{s}_t \middle| \sum_{i=1}^{N_t} S_{t,i} = N_{t+1}\right] p_{k,t}(\mathbf{s}_t, N_t) \\
&= \sum_{\mathbf{s}_t \in \mathbb{N}_0^{N_t}} \mathbb{P}\left[\mathbf{S}_t = \mathbf{s}_t \middle| \sum_{i=1}^{N_t} S_{t,i} = N_{t+1}\right] \sum_{i=1}^{N_t} \frac{\binom{s_{t,i}}{k}}{\binom{N_{t+1}}{k}} \\
&= \sum_{i=1}^{N_t} \sum_{\mathbf{s}_t \in \mathbb{N}_0^{N_t}} \frac{\binom{s_{t,i}}{k}}{\binom{N_{t+1}}{k}} \mathbb{P}\left[S_{t,1} = s_{t,1}, \mathbf{S}_t^{-(1)} = \mathbf{s}_t^{-(1)} \middle| \sum_{i=1}^{N_t} S_{t,i} = N_{t+1}\right] \\
&= \frac{N_t}{\binom{N_{t+1}}{k}} \sum_{\mathbf{s}_t \in \mathbb{N}_0^{N_t}} \binom{s_{t,1}}{k} \mathbb{P}\left[S_{t,1} = s_{t,1} \middle| \sum_{i=1}^{N_t} S_{t,i} = N_{t+1}\right] \\
&\qquad \times \mathbb{P}\left[\mathbf{S}_t^{-(1)} = \mathbf{s}_t^{-(1)} \middle| S_{t,1} = s_{t,1}, \sum_{i=1}^{N_t} S_{t,i} = N_{t+1}\right] \\
&= \frac{N_t}{\binom{N_{t+1}}{k}} \sum_{s_{t,1}=0}^{N_{t+1}} \binom{s_{t,1}}{k} \mathbb{P}\left[S_{t,1} = s_{t,1} \middle| \sum_{i=1}^{N_t} S_{t,i} = N_{t+1}\right] \\
&\qquad \times \underbrace{\sum_{\mathbf{s}_t^{-(1)} \in \mathbb{N}_0^{N_t - 1}} \mathbb{P}\left[\mathbf{S}_t^{-(1)} = \mathbf{s}_t^{-(1)} \middle| \sum_{i=2}^{N_t} S_{t,i} = N_{t+1} - s_{1,t}\right]}_{=1} \\
&= \frac{N_t}{\binom{N_{t+1}}{k}} \mathbb{E}\left[\binom{S_{t,1}}{k} \middle| \sum_{i=1}^{N_t} S_{t,i} = N_{t+1}\right] \\
&= N_t \frac{(N_{t+1}-k)!}{N_{t+1}!} \mathbb{E}\left[\frac{S_{t,1}!}{(S_{t,1}-k)!} \middle| \sum_{i=1}^{N_t} S_{t,i} = N_{t+1}\right]
\end{aligned} \tag{3}
$$

The k-th falling factorial moments $\mathbb{E}\big[\frac{S_{t,1}!}{(S_{t,1}-k)!}\big|\sum_{i=1}^{N_t} S_{t,i} = N_{t+1}\big]$ in Equation 3 can be readily obtained by differentiating the probability generating function of $S_{t,1}|(\sum_{i=1}^{N_t} S_{t,i} = N_{t+1})$.

2.2 Exclusive coalescence probability

Generally, we observe a sample of individuals from each generation rather than the entire population. In this case, we are interested in the exclusive coalescence probability $p_{n,k,t}(N_t, N_{t+1})$ that a specific subset of k individuals amongst n sampled individuals arose from a common infector one generation in the past given knowledge of the total population sizes N_t and N_{t+1}. Let us first assume full knowledge about offspring counts of the individuals at time N_t amongst the sample at time N_{t+1}, namely $\mathbf{x}_t = (x_{t,1}, \ldots, x_{t,N_t})$ such that $x_{t,1} + ... + x_{t,N_t} = n$. Note that $X_{t,i}$ does not follow the same offspring distribution as $S_{t,i}$. We have:

$$\begin{aligned} p_{n,k,t}(\mathbf{x}_t, N_t) &= \sum_{i=1}^{N_t} \frac{\binom{x_{t,i}}{k}}{\binom{n}{k}} \mathbb{I}\{x_{t,i} = k\} \\ &= \sum_{i=1}^{N_t} \frac{x_{t,i}!}{(x_{t,i}-k)!} \frac{(n-k)!}{n!} \mathbb{I}\{x_{t,i} = k\} \end{aligned} \tag{4}$$

Similarly to the inclusive coalescence probability in Equation 3, we can use this to evaluate the exclusive probability given N_t and N_{t+1} by summing over possible parent offspring configurations (for $k \leq n$):

$$
\begin{aligned}
p_{n,k,t}(N_t, N_{t+1}) &= \sum_{\mathbf{x}_t \in \mathbb{N}_0^{N_t}} \mathbb{P}\left[\mathbf{X}_t = \mathbf{x}_t \middle| \sum_{i=1}^{n} X_{t,i} = n\right] p_{n,k,t}(\mathbf{x}_t, N_t) \\
&= \sum_{\mathbf{x}_t \in \mathbb{N}_0^{N_t}} \mathbb{P}\left[\mathbf{X}_t = \mathbf{x}_t \middle| \sum_{i=1}^{n} X_{t,i} = n\right] \sum_{i=1}^{N_t} \frac{\binom{x_{t,i}}{k}}{\binom{n}{k}} \mathbb{I}\{x_{t,i} = k\} \\
&= \frac{N_t}{\binom{n}{k}} \sum_{\mathbf{x}_t \in \mathbb{N}_0^{N_t}} \binom{x_{t,1}}{k} \mathbb{P}\left[\mathbf{X}_t = \mathbf{x}_t \middle| \sum_{i=1}^{N_t} X_{t,i} = n\right] \mathbb{I}\{x_{t,1} = k\} \\
&= \frac{N_t}{\binom{n}{k}} \sum_{\mathbf{x}_t^{-(1)} \in \mathbb{N}_0^{N_t - 1}} \binom{k}{k} \mathbb{P}\left[X_{t,1} = k, \mathbf{X}_t^{-(1)} = \mathbf{x}_t^{-(1)} \middle| \sum_{i=1}^{N_t} X_{t,i} = n\right] \\
&= \frac{N_t}{\binom{n}{k}} \mathbb{P}[X_{t,1} = k \middle| \sum_{i=1}^{N_t} X_{t,i} = n] \underbrace{\sum_{\mathbf{x}_t^{-(1)} \in \mathbb{N}_0^{N_t - 1}} \mathbb{P}\left[\mathbf{X}_t^{-(1)} = \mathbf{x}_t^{-(1)} \middle| \sum_{i=1}^{N_t} X_{t,i} = n, X_{t,1} = k\right]}_{=1} \\
&= \frac{N_t}{\binom{n}{k}} \mathbb{P}\left[X_{t,1} = k \middle| \sum_{i=1}^{N_t} X_{t,i} = n\right] \qquad (5)
\end{aligned}
$$

2.3 Complementarity of exclusive coalescence probabilities

If we consider one of the lines observed amongst a set of n, it can either remain uncoalesced with probability $p_{n,1,t}(N_t, N_{t+1})$ or coalesce in an event of size k with probability $p_{n,k,t}(N_t, N_{t+1})$ with any set of $k-1$ lines among the $n-1$ other lines, leading to the following complementarity equation:

$$
\sum_{k=1}^{n} \binom{n-1}{k-1} p_{n,k,t}(N_t, N_{t+1}) = 1 \qquad (6)
$$

We can show that it is indeed satisfied by the formula in Equation 5:

$$
\begin{aligned}
\sum_{k=1}^{n}\binom{n-1}{k-1}p_{n,k,t}(N_t,N_{t+1}) &= \sum_{k=1}^{n}\binom{n-1}{k-1}\frac{N_t}{\binom{n}{k}}\mathbb{P}\left[X_1=k\middle|\sum_{i=1}^{N_t}X_i=n\right]\\
&= \sum_{k=1}^{n}N_t\frac{k}{n}\mathbb{P}\left[X_1=k\middle|\sum_{i=1}^{N_t}X_i=n\right]\\
&= \frac{N_t}{n}\sum_{k=0}^{n}k\mathbb{P}\left[X_1=k\middle|\sum_{i=1}^{N_t}X_i=n\right]\\
&= \frac{N_t}{n}\mathbb{E}\left[X_1\middle|\sum_{i=1}^{N_t}X_i=n\right]\\
&= \frac{1}{n}\sum_{i=1}^{N_t}\mathbb{E}\left[X_i\middle|\sum_{i=1}^{N_t}X_i=n\right]\\
&= \frac{1}{n}\mathbb{E}\left[\sum_{i=1}^{N_t}X_i\middle|\sum_{i=1}^{N_t}X_i=n\right]\\
&= 1
\end{aligned}
\tag{7}
$$

3 Poisson offspring distribution case

In this section we consider that the offspring distribution is $\alpha_t = \text{Poisson}(R_t)$. In this case, we have:

$$
\sum_{i=1}^{N_t}S_{t,i} \sim \text{Poisson}(N_tR_t) \tag{8}
$$

and the conditional distribution:

$$
\begin{aligned}
\mathbb{P}\left[S_{t,1}=s\middle|\sum_{i=1}^{N_t}S_{t,i}=N_{t+1}\right] &= \frac{\mathbb{P}\left[S_{t,1}=s,\sum_{i=1}^{N_t}S_{t,i}=N_{t+1}\right]}{\mathbb{P}\left[\sum_{i=1}^{N_t}S_{t,i}=N_{t+1}\right]}\\
&= \frac{\alpha_t(s)\,\mathbb{P}\left[\sum_{i=2}^{N_t}S_{t,i}=N_{t+1}-s\right]}{\mathbb{P}\left[\sum_{i=1}^{N_t}S_{t,i}=N_{t+1}\right]}\\
&= \frac{\frac{R_t^s e^{-R_t}}{s!}\cdot\frac{((N_t-1)R_t)^{N_{t+1}-s}}{(N_{t+1}-s)!}}{\frac{(N_tR_t)^{N_{t+1}}e^{-N_tR_t}}{N_{t+1}!}}
\end{aligned}
$$

$$= \binom{N_{t+1}}{s} \left(\frac{1}{N_t}\right)^s \left(1 - \frac{1}{N_t}\right)^{N_{t+1}-s} \tag{9}$$

105

106 This is the probability mass function of a Binomial distribution and therefore we deduce that:

$$S_{t,1} \Bigg| \left(\sum_{i=1}^{N_t} S_{t,i} = N_{t+1} \right) \sim \text{Binomial} \left(N_{t+1}, \frac{1}{N_t} \right) \tag{10}$$

107 The k-th falling factorial moments of $X \sim \text{Binomial}(n, p)$ are (Potts 1953):

$$\mathbb{E}\left[\frac{X!}{(X-k)!}\right] = \binom{n}{k} p^k k! \tag{11}$$

108 By applying this formula to the Binomial distribution in Equation 10 and injecting into Equation 3,
109 we deduce that the inclusive probability of coalescence for k lines is:

$$p_{k,t}(N_t, N_{t+1}) = \frac{1}{N_t^{k-1}} \tag{12}$$

110 In addition, following a similar reasoning as for Equation 10 we can show that:

$$X_{t,1} \Bigg| \left(\sum_{i=1}^{N_t} X_{t,i} = n \right) \sim \text{Binomial} \left(n, \frac{1}{N_t} \right) \tag{13}$$

111 By injecting the probability mass function of this Binomial distribution into Equation 5 we deduce
112 that the exclusive probability of coalescence for k lines from a sample of n ($n \geq k$) is:

$$p_{n,k,t}(N_t, N_{t+1}) = \frac{(N_t - 1)^{n-k}}{N_t^{n-1}} \tag{14}$$

113 It is interesting to note that neither the inclusive nor the exclusive coalescence probability depend on
114 the mean R_t of the Poisson offspring distribution or the size N_{t+1} of the population at time $t+1$. The
115 inclusive coalescent probability in Equation 12 can also be obtained conceptually by considering that
116 among the k lines, the first one has an ancestor with probability one, and the remaining $k-1$ need to

have the same ancestor among a set of N_t from which they choose uniformly at random so that the probability of picking the same ancestor is $1/N_t$. The exclusive coalescent probability in Equation 14 can be derived likewise by considering that in addition to the above, each of the $n-k$ other lines need to choose a different ancestor, which happens with probability $(N_t-1)/N_t$.

Figure 1 illustrates the inclusive and exclusive coalescence probabilities for the Poisson case for a set of size $k=1$ to $k=10$ amongst a total of $n=10$ observed lines, in a population of size $N_t=10$, $N_t=20$ or $N_t=30$.

4 Negative-Binomial offspring distribution case

In this section we consider that the offspring distribution is $\alpha_t = \text{Negative-Binomial}(r,p)$ with parameters (r,p) set by moment-matching the mean R_t and variance V_t of the offspring distribution which are assumed constant over time. The resulting parameters for this distribution are $r = R_t^2/(V_t-R_t)$ and $p=R_t/V_t$. In this case, we have:

$$\sum_{i=1}^{N_t} S_{t,i} \sim \text{Negative-Binomial}(N_t r, p) \tag{15}$$

and similarly to the Poisson offspring distribution case we identify that the conditional distribution of $S_{t,1}|\sum_{i=1}^{N_t} S_{t,i}$ is as follows:

$$\begin{aligned}
\mathbb{P}\left[S_{t,1}=s \middle| \sum_{i=1}^{N_t} S_{t,i} = N_{t+1}\right] &= \frac{\alpha_t(s)\cdot \mathbb{P}\left[\sum_{i=2}^{N_t} S_{t,i} = N_{t+1}-s\right]}{\mathbb{P}\left[\sum_{i=1}^{N_t} S_{t,i} = N_{t+1}\right]} \\
&= \frac{\dfrac{\Gamma(r+s)}{s!\Gamma(r)}(1-p)^s p^r \cdot \dfrac{\Gamma\big((N_t-1)r+(N_{t+1}-s)\big)}{(N_{t+1}-s)!\Gamma((N_t-1)r)}(1-p)^{N_{t+1}-s}p^{(N_t-1)r}}{\dfrac{\Gamma(N_t r+N_{t+1})}{N_{t+1}!\Gamma(N_t r)}(1-p)^{N_{t+1}}p^{N_t r}} \\
&= \frac{N_{t+1}!}{s!(N_{t+1}-s)!}\frac{\Gamma(r+s)\Gamma\big((N_t-1)r+(N_{t+1}-s)\big)}{\Gamma(N_t r+N_{t+1})}\frac{\Gamma(N_t r)}{\Gamma(r)\Gamma\big((N_t-1)r\big)} \\
&= \binom{N_{t+1}}{s}\frac{\mathrm{B}(s+r, N_{t+1}-s+(N_t-1)r)}{\mathrm{B}(r,(N_t-1)r)}
\end{aligned} \tag{16}$$

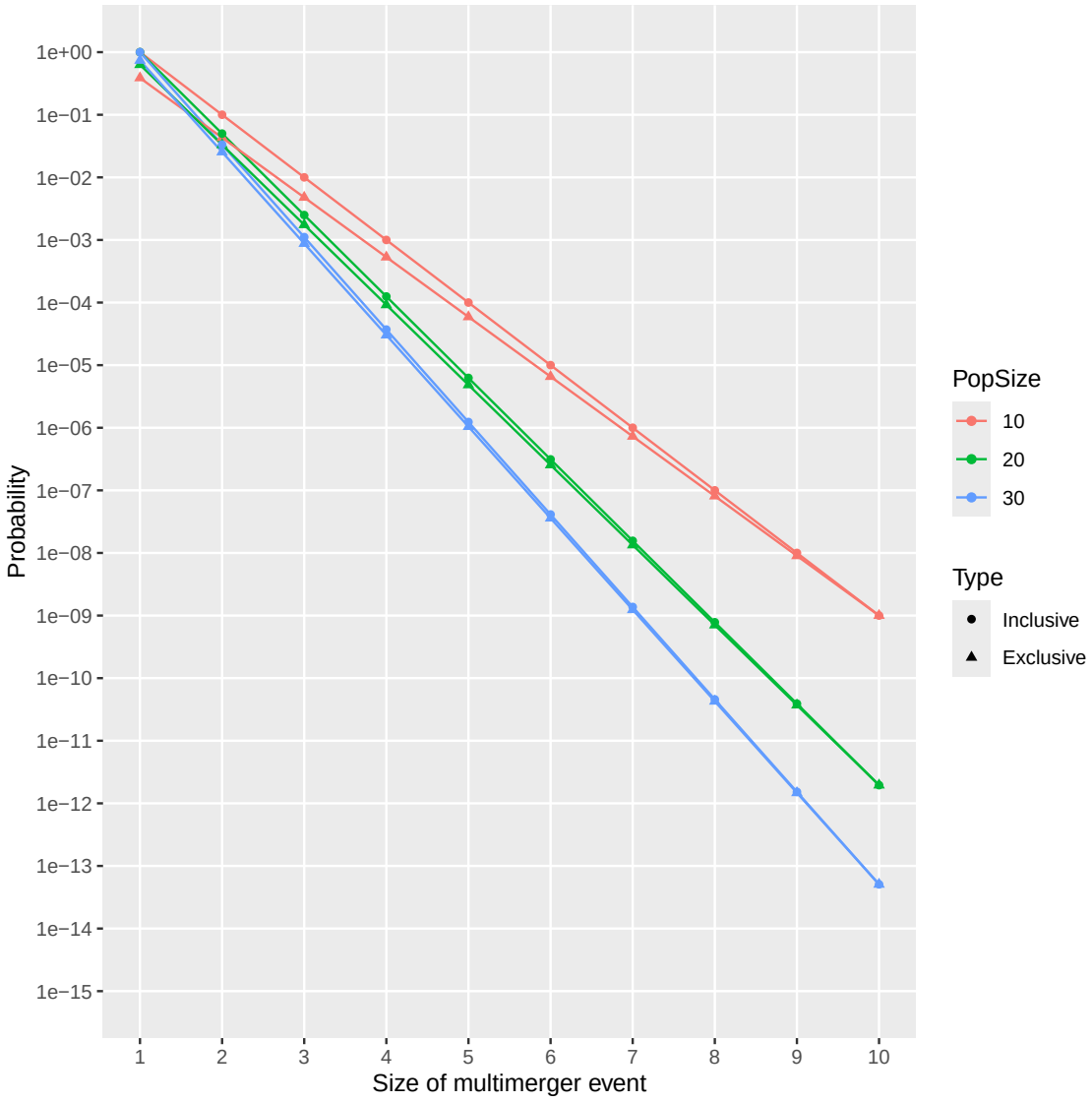

Figure 1: Inclusive and exclusive coalescence probabilities for the Poisson case.

where $\mathrm{B}(x, y)$ denotes the Beta function defined as $\mathrm{B}(x, y) = \Gamma(x)\Gamma(y)/\Gamma(x+y)$. This is the probability mass function of a Beta-Binomial distribution and therefore we deduce that:

$$S_{t,1} \Bigg| \left(\sum_{i=1}^{N_t} S_{t,i} = N_{t+1} \right) \sim \text{Beta-Binomial}(N_{t+1}, r, (N_t - 1)r) \tag{17}$$

The k-th falling factorial moments of $X \sim \text{Beta-Binomial}(n, \alpha, \beta)$ are (Tripathi et al. 1994):

$$\mathbb{E}\left[\frac{X!}{(X-k)!}\right] = \binom{n}{k} \frac{\mathrm{B}(\alpha + k, \beta)k!}{\mathrm{B}(\alpha, \beta)} \tag{18}$$

By applying this formula to the Beta-Binomial distribution in Equation 17 and injecting into Equation 3, we deduce that the inclusive probability of coalescence for k lines is:

$$p_{k,t}(N_t, N_{t+1}) = \frac{\mathrm{B}(N_t r + 1, r + k)}{\mathrm{B}(r + 1, N_t r + k)} \tag{19}$$

In addition, following a similar reasoning as for Equation 17, we can show that:

$$X_{t,1} \Bigg| \left(\sum_{i=1}^{N_t} X_{t,i} = n \right) \sim \text{Beta-Binomial}(n, r, (N_t - 1)r) \tag{20}$$

By injecting the probability mass function of this Beta-Binomial distribution into Equation 5 we deduce that the exclusive probability of coalescence for k lines is:

$$p_{n,k,t}(N_t, N_{t+1}) = \frac{N_t \mathrm{B}(k + r, n - k + N_t r - r)}{\mathrm{B}(r, N_t r - r)} \tag{21}$$

It is interesting to note that as for the Poisson case, the inclusive and exclusive coalescence probabilities do not depend on the size N_{t+1} of the population at time $t + 1$. They both depend on the Negative-Binomial offspring distribution only through the dispersion parameter r. If we consider that r is large in Equations 19 and 21, we can derive that the asymptotic behaviour is the same as in the Poisson case shown in Equations 12 and 14. For example this can be derived by rewriting the Beta functions

using Gamma functions, and using the following form of Stirling's approximation:

$$\lim_{a\to\infty} \frac{\Gamma(a+b)}{\Gamma(a)} = a^b \mathrm{e}^{-b} \tag{22}$$

Figure 2 illustrates the inclusive and exclusive coalescence probabilities for the Negative-Binomial case for a set of size $k = 1$ to $k = 10$ amongst a total of $n = 10$ observed lines, in a population with size $N_t = 20$. Several Negative-Binomial offspring distributions are compared, all of which have the same mean $R_t = 2$, and with the dispersion parameter equal to $r = 0.1$, $r = 1$, $r = 10$ and $r = 100$. When $r = 1$ the Negative-Binomial reduces to a Geometric distribution. When r is high (for example $r = 100$ as shown in Figure 2) the dispersion is low and the Negative-Binomial case behaves almost like the Poisson case. When r is lower the dispersion of the offspring distribution increases, so that both the inclusive and exclusive probabilities of larger multimerger events increase.

5 Limit when the population size is large

If we consider that the population size N_t is fixed and large, we can show the connections between our results and several previous studies. In the Poisson case, from Equations 12 and 14 we can see that both inclusive and exclusive probabilities are of order $\mathcal{O}(N_t^{1-k})$. We can therefore ignore events with $k > 2$ and retain only the events with $k = 2$ which occur with probability:

$$p_{2,t}(N_t, N_{t+1}) = p_{n,2,t}(N_t, N_{t+1}) = \frac{1}{N_t} \tag{23}$$

For the Negative-Binomial case, from Equations 19 and 21 we can rewrite using Gamma functions and apply the form of Stirling's equation given in Equation 22 to show that once again both inclusive and exclusive probabilities are also of order $\mathcal{O}(N_t^{1-k})$. We can therefore once again ignore events with $k > 2$ and retain only the events with $k = 2$ which occur with probability:

$$p_{2,t}(N_t, N_{t+1}) = p_{n,2,t}(N_t, N_{t+1}) = \frac{r+1}{N_t r + 1} \approx \frac{r+1}{N_t r} \tag{24}$$

Koelle and Rasmussen (2012) derived the rates of coalescence of two lineages for several epidemiological models, assuming a large population at equilibrium. For each model they use the equation $N_\mathrm{e} = N/\sigma^2$

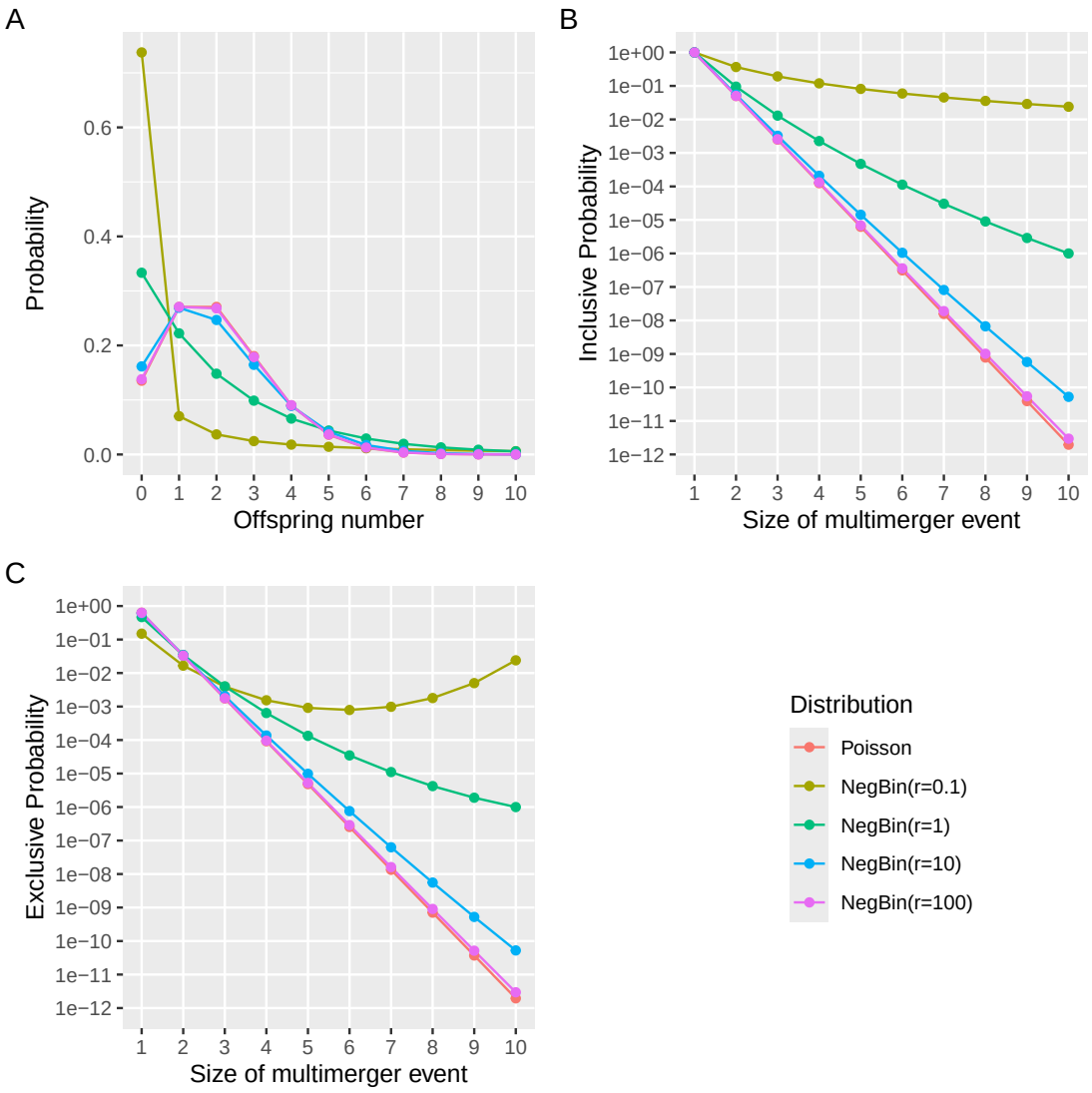

Figure 2: (A) Offspring distributions with mean $R_t = 2$. (B) Inclusive probability of coalescence for $N_t = 20$ and $n = 10$. (C) Exclusive probability of coalescence for $N_t = 20$ and $n = 10$.

to relate the effective population size N_e to the actual population size N and the variance σ^2 in the number of offspring. This relationship was first established by Kingman (1982a) to derive the backward-in-time coalescent model from the forward-in-time Cannings exchangeable models (Cannings 1974). From Equation 24 we can take $R_t = 1$ to achieve equilibrium of the population size and the method of moments estimator $r = R_t^2/(V_t - R_t) = 1/(V_t - 1)$ to deduce the equivalent $p_{2,t} = V_t/N_t$.

Volz (2012) showed that the rate of coalescence for two lineages under a continuous-time epidemic coalescent model is $2f(t)/I(t)^2$ where $f(t)$ is the incidence and $I(t)$ the prevalence. Setting in this formula the prevalence as $I(t) = N_{t+1} = N_t R_t$ and the incidence as $f(t) = R_t N_{t+1} = R_t^2 N_t$ we get a coalescent rate of $2/N_t$. To apply our methodology we need to consider that the offspring distribution is Geometric, since the epidemiological models considered have successes (offspring) happening until the first failure (removal). We therefore set $r = 1$ in Equation 24 to make the Negative-Binomial offspring distribution reduce to a Geometric distribution and the same result follows.

Fraser and Li (2017) calculated the effective population size $N_e(t)$ as a function of the actual population size $N(t)$ and the mean and variance of the offspring distribution R and σ^2. This formula was used to estimate the dispersion parameter of a Negative-Binomial offspring distribution from genetic data (Li et al. 2017). In our notation, their formula is equivalent to the inclusive coalescence probability for two lineages:

$$p_{2,t}(N_t, N_{t+1}) = \frac{\sigma^2/R + R - 1}{N_t R} \tag{25}$$

In the Poisson case we have $\sigma^2 = R$ so that Equation 25 simplifies to $1/N_t$ which agrees with Equation 23. In the Negative-Binomial case we have $\sigma^2/R = 1/p = (r + R)/r$ so that Equation 25 simplifies to $(r+1)/(N_t r)$ which agrees with our Equation 24. Conversely, if we substitute the method of moments estimator $r = R^2/(\sigma^2 - R)$ in Equation 24 we obtain the Equation 25.

6 Definition of a new lambda-coalescent model

The coalescent model (Kingman 1982a,b) describes the ancestry of a sample from a large population evolving according to many forward-in-time models such as the Wright-Fisher model (Wright 1931; Fisher 1930), the Moran model (Moran 1958) and the Cannings exchangeable model (Cannings 1974). Since the coalescent considers a large population in which each individual only has a number of

offspring that is small compared to the population size, coalescent trees are always binary and do not feature multimergers, making them unsuitable to represent the ancestry of outbreaks considered in this study. However, the lambda-coalescent models are an extension of the coalescent model that do allow multimergers (Pitman 1999; Sagitov 1999; Donnelly and Kurtz 1999).

A lambda-coalescent model is defined by a probability measure $\Lambda(\mathrm{d}x)$ on the interval $[0, 1]$, from which we can deduce the rate $\lambda_{n,k}$ at which any subset of k lineages within a set of n observed lineages coalesce:

$$\lambda_{n,k} = \int_0^1 x^{k-2}(1-x)^{n-k}\,\Lambda(\mathrm{d}x) \tag{26}$$

The beta-coalescent (Schweinsberg 2003) is a specific type of lambda-coalescent that has been used recently in several studies analysing genetic data from infectious disease agents (Hoscheit and Pybus 2019; Menardo et al. 2021; Helekal et al. 2025; Zhang and Palacios 2024). The beta-coalescent model has a single parameter $\alpha \in [0, 2]$ and is defined as:

$$\Lambda(\mathrm{d}x) = \frac{x^{1-\alpha}(1-x)^{\alpha-1}}{\mathrm{B}(2-\alpha, \alpha)}\mathrm{d}x \tag{27}$$

By combining Equations 26 and 27 we can deduce that:

$$\lambda_{n,k} = \frac{\mathrm{B}(k-\alpha, n-k+\alpha)}{\mathrm{B}(2-\alpha, \alpha)} \tag{28}$$

Special cases of the beta-coalescent include $\alpha = 2$ corresponding to the Kingman coalescent, $\alpha = 1$ which is known as the Bolthausen-Sznitman coalescent and $\alpha = 0$ for which the phylogeny is always star-shaped.

We now define a new lambda-coalescent based on the Negative-Binomial case described previously. We call this new lambda-coalescent model the omega-coalescent (where omega stands for outbreak). For ease of comparison with other coalescent models, we consider that time is continuous and that the population size remains constant equal to N_t. The exclusive coalescent probability $p_{n,k,t}(N_t, N_{t+1})$ in the Negative-Binomial case given by Equation 21 can be used to determine the corresponding rate of the omega-coalescent, if we consider that the probability of each event in discrete time is the result of

the event happening at a constant rate in continuous time:

$$\lambda_{n,k} = -\log(1 - p_{n,k,t}(N_t, N_{t+1})) \tag{29}$$

In order to compare the omega-coalescent defined in Equation 29 with other models such as the beta-coalescent defined in Equation 28, we consider the distribution of the size k of the next event among a set of n lineages. For any lambda-coalescent this can be computed as:

$$p(k|n) = \frac{\binom{n}{k}\lambda_{n,k}}{\sum_{i=2}^{n}\binom{n}{i}\lambda_{n,i}} \tag{30}$$

Figure 3 compares this distribution for $n = 10$ in the beta-coalescent with parameter $\alpha \in \{0.5, 1, 1.5\}$ and for the omega-coalescent with parameters $N_t \in \{10, 20, 30\}$ and $r \in \{0.1, 1, 10\}$. In the beta-coalescent, the distribution shifts towards more larger multimerger events as the parameter α decreases. In the omega-coalescent a wider range of behaviours is obtained when varying the two parameters N_t and r. For a given value of N_t, decreasing the value of r results in more larger events. Conversely, for a given value of r we can see that increasing the value of N_t reduces the probability of larger events.

Genealogies can be simulation from the omega-coalescent model defined in Equation 29 using the same algorithm as for other lambda-coalescent models (Pitman 1999). Figure 4 shows examples of trees simulated for a sample of size $n = 20$, constant population size $N_t = 30$ and dispersion parameter $r \in \{0.1, 1, 10, 100\}$. It is already clear from these single realisations that the lower values of r result in trees with more larger multimerger events and lower time to the most recent common ancestor, but to quantify these properties we need to consider many trees.

Figure 5 shows summary statistics for 10,000 trees simulated in the same conditions as the individual trees shown in Figure 4. As the dispersion parameter increases from $r = 0.1$ to $r = 100$ multimerger events become less and less likely and large. Simultaneously, the time to the most recent common ancestor increases, as well as the stemminess of the tree (ie the proportion of branch lengths in non-terminal branches).

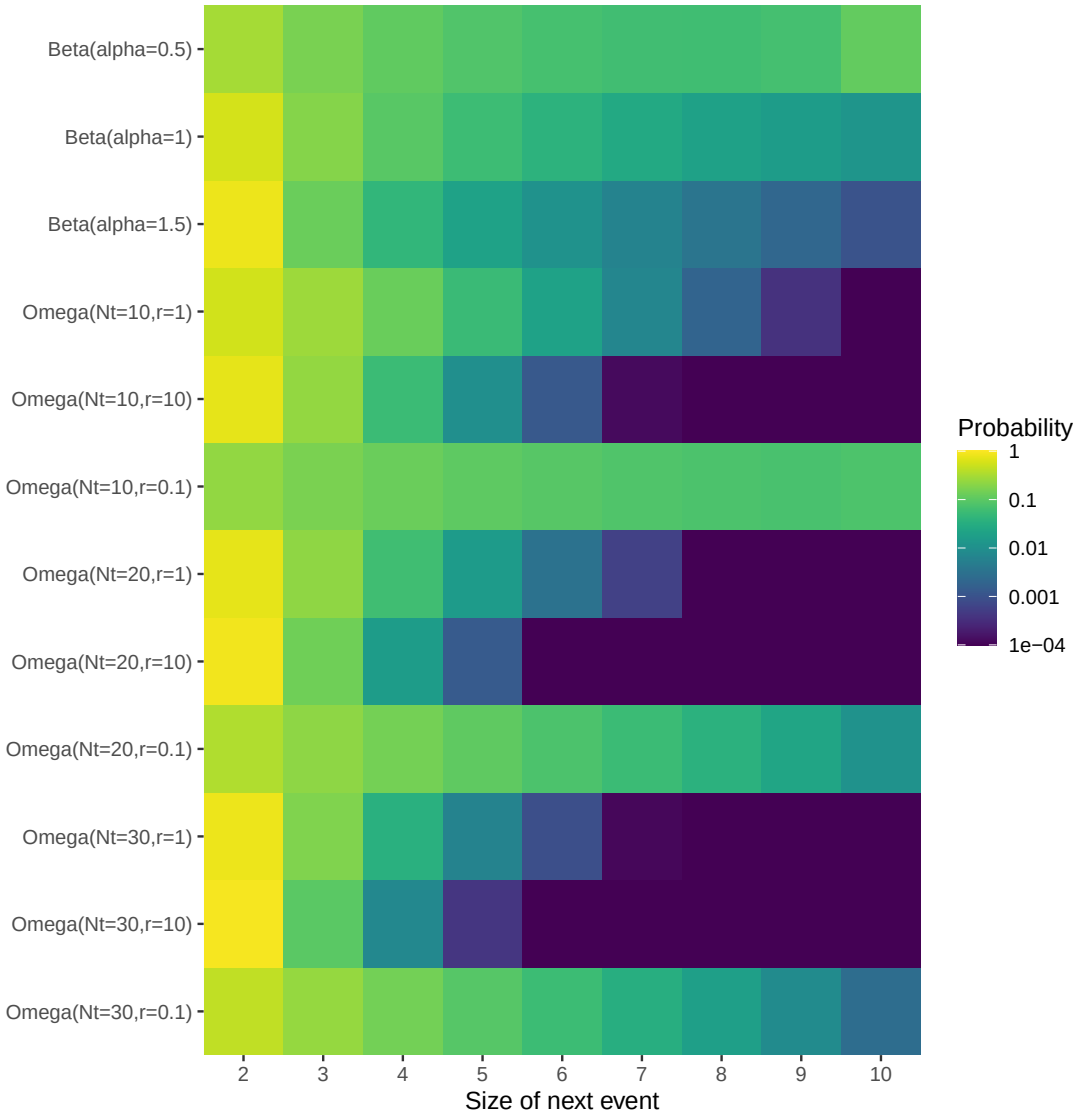

Figure 3: Distribution of the size of the next event among a set of $n = 10$ lineages, compared between the beta-coalescent and the omega-coalescent model with various parameters.

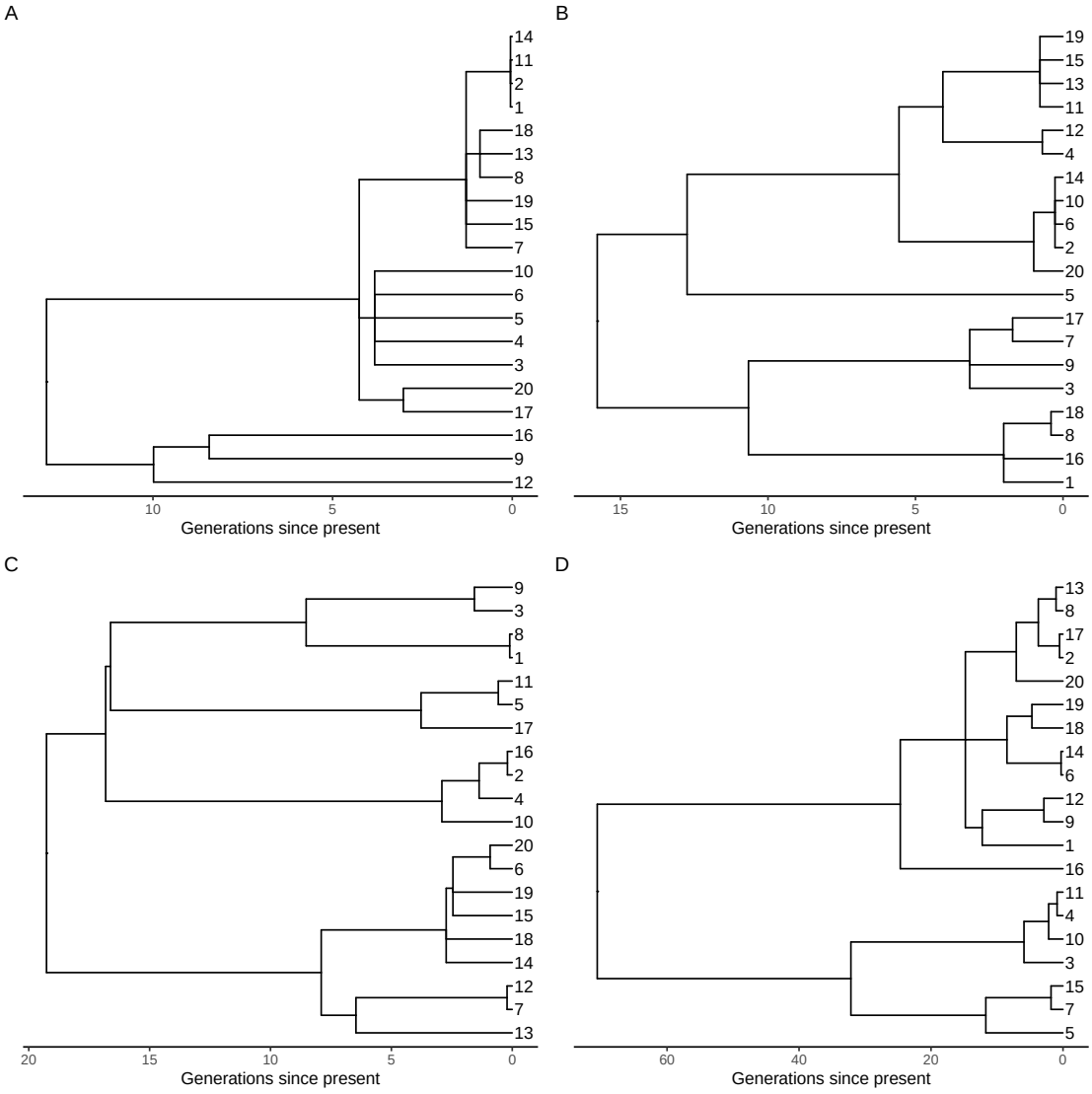

Figure 4: Example of trees simulated under the omega-coalescent with $r = 0.1$ (A), $r = 1$ (B), $r = 10$ (C) and $r = 100$ (D).

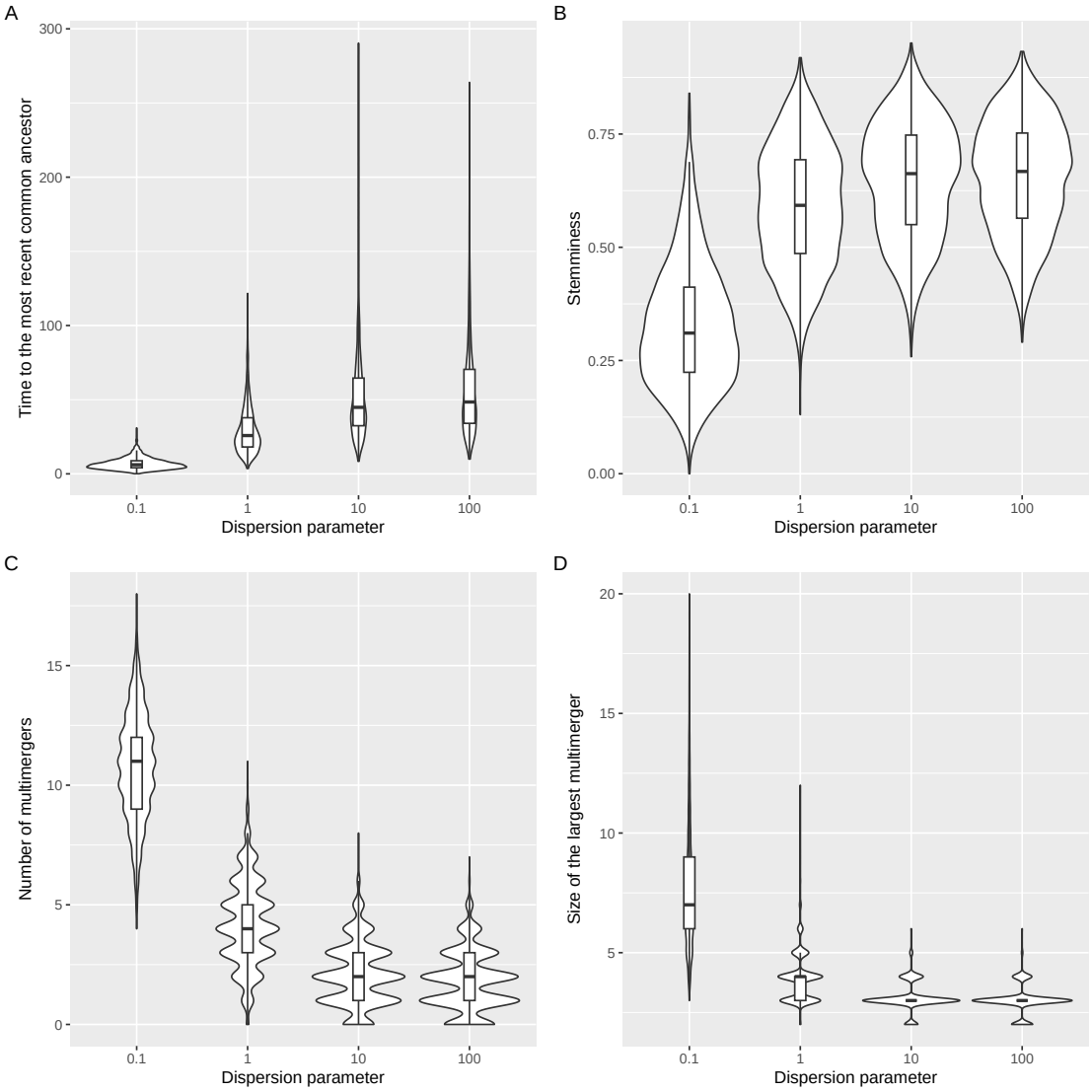

Figure 5: Summary statistics for trees simulated under the omega-coalescent with $r = 0.1$, $r = 1$, $r = 10$ and $r = 100$, namely the time to the most recent common ancestor (A), stemminess (B), number of multimergers (C) and the size of the largest multimerger (D).

7 Parameter inference

Consider a genealogy T with n leaves and c coalescent nodes, with $t_0 = 0$ the sampling time, $t_1, ..., t_c$ the times of the coalescent nodes in increasing order and k_i the number of lineages coalescing at time t_i. The number of lineages existing between time t_{i-1} and t_i is then $n_i = n - \sum_{j=1}^{i-1} k_j$. Under a lambda-coalescent model, the genealogy T has likelihood:

$$p(T|\Lambda) = \prod_{i=1}^{c} \lambda_{n_i,k_i} \exp\left(-\sum_{j=2}^{n_i} \binom{n_i}{j} \lambda_{n_i,j}(t_i - t_{i-1}) \right) \tag{31}$$

Note that in Equation 31 the term $\binom{n_i}{k_i}$ term from the coalescent rate cancels out with its reciprocal from the probability of sampling k_i specific lineages to coalesce within a set of n_i. Estimating the lambda measure in general is a difficult problem (Koskela 2018; Miró Pina et al. 2023). Here however we focus on estimation under the omega-coalescent model, where the $\lambda_{n,k}$ terms are given by Equation 29. There are therefore two parameters to estimate which have direct and important biological meaning: the effective population size N_t (which remains constant) and the dispersion parameter r of the Negative-Binomial offspring distribution. We perform estimation simply by maximising the likelihood in Equation 31, using the Brent algorithm (Brent 1971) when estimating a single parameter and the L-BFGS-B algorithm when (Byrd et al. 1995) estimating both parameters.

We simulated 100 genealogies from the omega-coalescent model each of which had $n = 100$ leaves, with parameter N_e drawn uniformly at random between 100 and 500 and parameter r drawn uniformly at random between 0.01 and 2. If we assume knowledge of the dispersion parameter, then estimating the population size works really well (Figure 6A). Conversely we obtain good result when estimating the dispersion parameter given a known population size (Figure 6B). However, attempting to estimate both parameters at the same time performed significantly less well (Figures 6C and D). To illustrate the cause of this, we consider a simulation for which the true N_t was 200 and the true r was 0.5, and we construct the likelihood surface (Figure 6E). This shows a strong inverse tradeoff between the two parameters, which explains why one can be estimated given the other, but not jointly.

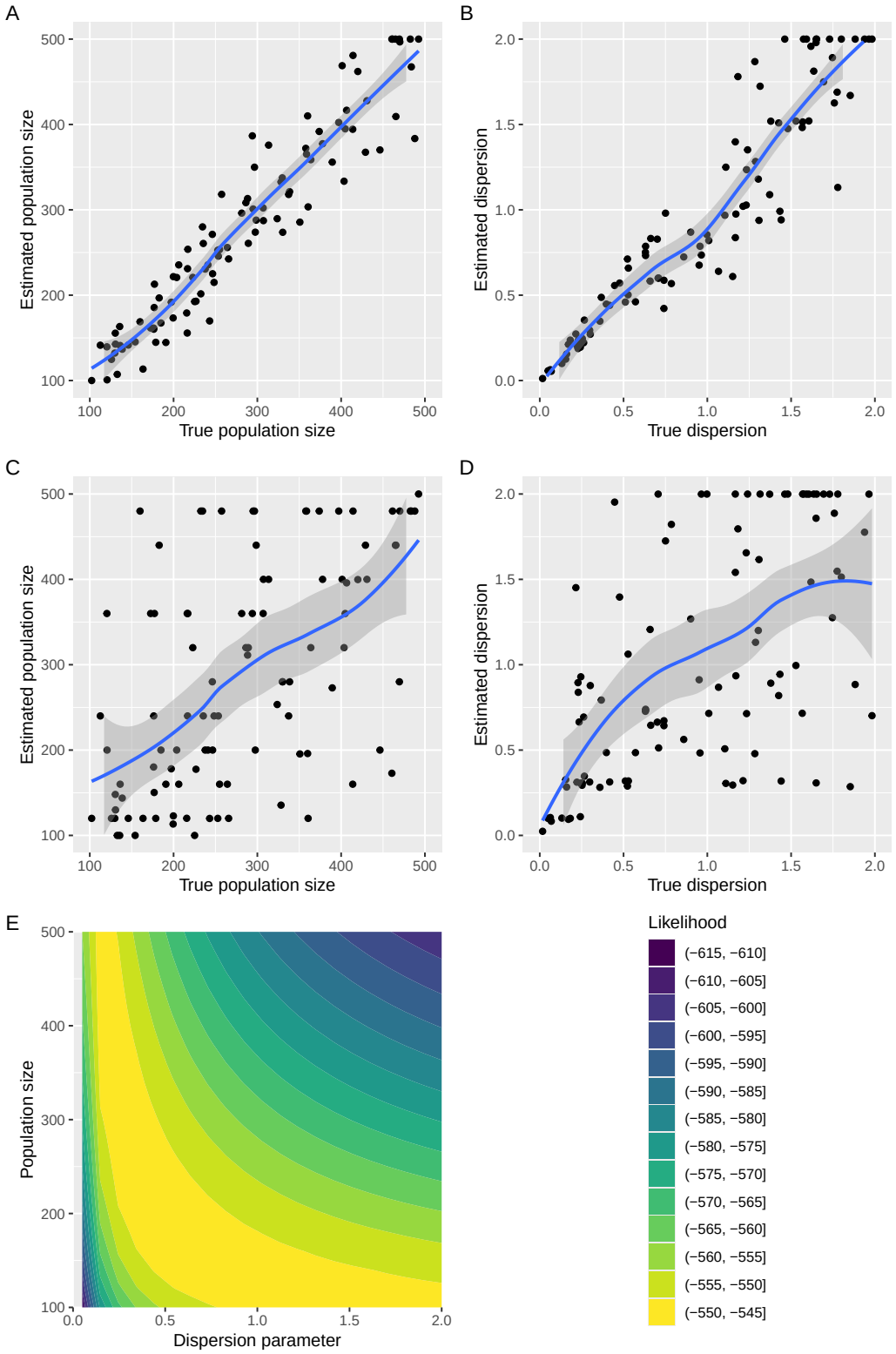

Figure 6: Maximum likelihood estimation of parameters. (A) Estimation of the population size given the dispersion parameter. (B) Estimation of the dispersion parameter given the population size. (C and D) Joint estimation of both the population size and dispersion parameters. (E) Example of likelihood surface as a function of both parameters.

8 Implementation

We implemented the analytical methods described in this paper in a new R package entitled *EpiLambda* which is available at `https://github.com/xavierdidelot/EpiLambda` for R version 3.5 or later. All code and data needed to replicate the results are included in the "run" directory of the *EpiLambda* repository. The R package `ape` was used to store, manipulate and visualise phylogenetic trees (Paradis and Schliep 2019).

9 Discussion

The omega-coalescent could be extended to allow temporally offset leaves following work on the coalescent (Drummond et al. 2003) and the beta-coalescent (Hoscheit and Pybus 2019). It could also be defined in a varying population size following the same approach as previously described for the coalescent (Griffiths and Tavare 1994; Pybus et al. 2000; Ho and Shapiro 2011) and the beta-coalescent (Hoscheit and Pybus 2019; Zhang and Palacios 2024). This could be even more useful for the omega-coalescent than for the beta-coalescent since in the omega-coalescent the probability of multimerger events of various size depends explicitly on the population size (see for example Figure 3).

We compared the omega-coalescent only to the beta-coalescent (Schweinsberg 2003) but it could also be compared to the Dirac coalescent aka psi-coalescent (Eldon and Wakeley 2006), the Durrett-Schweinsberg coalescent (Durrett and Schweinsberg 2005) or the extended Beta-coalescent (Helekal et al. 2025).

The xi-coalescent models admit multiple simultaneous mergers (Schweinsberg 2000).

Difference between transmission tree and phylogenetic tree (Jombart et al. 2011). Modelling within-host evolution to bridge the gap (Didelot et al. 2014; Hall et al. 2015; Didelot et al. 2017). Superspreading individuals vs superspreading events (Riley et al. 2003; Wallinga and Teunis 2004; Ho et al. 2023).

Acknowledgements

We acknowledge funding from the National Institute for Health Research (NIHR) Health Protection Research Unit in Genomics and Enabling Data.

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