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Ring vaccination

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Abstract. Based on the description of an outbreak of foot-and-mouth disease (FMD), a particle model is developed describing the most important properties of this epidemic. Also control measures (mass and ring vaccination) are implemented. This model shows the expected behavior in simulations. Since it is impossible to treat this model analytically, we use ideas of branching processes on two levels to derive a caricature of the particle model. In simulations it is shown that this caricature exhibits similar behavior as the particle system. It is possible to analyze the caricature and, in this way, to obtain expressions for the most important quantities like the reproduction number or the expected final number of infected individuals etc. In this way mass vaccination and ring vaccination can be compared and control strategies can be optimized.

1. Introduction

While there is abundant literature addressing the mechanisms of mass vaccination programs, little is known about properties of ring vaccination [12, 26, 10, 22]. In contrast to mass vaccination, ring vaccination does not neglect but is highly based on the contact structure between single individuals. The idea is that individuals who have close contact to an infected individual are at a high risk to become infected, and thus should be protected. Essentially, only individual based stochastic models are able to capture this situation [12]. Unfortunately, not many tools for the analysis of such models are available. The most frequently used analytical methods are the mean field approximation [8, 23] and the rapid stirring limit [9]. Both approaches destroy the contact structure, and thus are not well suited to address ring vaccination.

We shall develop a model incorporating most of the features of ring vaccination. We concentrate on foot-and-mouth disease (FMD) since ring vaccination is frequently used for the control of this disease. We do not claim to consider a detailed model, but a model that takes into account many of the known properties

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of FMD and ring vaccination. However, one can expect that the basic structure of our approach can be adapted to more elaborate models. The model is based on a particle system; it cannot be analyzed directly. We shall only consider subcritical scenarios where we are able to develop a caricature of the primary model, based on the theory of branching processes [18] and models for epidemics on two levels [15, 6, 5]. The particle model and the branching process show good agreement in numerical simulations. It is possible to analyze the latter with standard methods. In the second section we list facts about the disease and consider an outbreak of FMD that has happened 1987/88 near Hannover, Germany. Taking into account these observations we develop a spatially structured particle model in Section 3. In the fourth section we derive a linear stochastic caricature of the particle model, that is valid only in a certain parameter range but can be treated analytically. Finally, in Section 5, we compare ring and mass vaccination with respect to certain features.

2. Foot-and-mouth disease

FMD is eliminated in the United States and Europe, while it is still endemic in Africa, South America and Asia. However, even in regions where the disease is not endemic, there are frequent outbreaks [25]. These outbreaks cause considerable economic loss since the export markets are closed for a country, in which the disease is present. Only after eliminating the disease, export is again possible. Hence efficient control strategies are of high interest. Recently, the European Union changed its policy: there is no mass vaccination any more but import controls, quarantine, and, in case of a local outbreak, emergency vaccinations and massive local control measures like ring vaccination.

2.1. Some basic facts

FMD is a highly infectious disease for all clovenhooved animals like cattle, sheep and pigs. At outbreaks, even within vaccinated herds, the reproduction number R_0 (defined by the mean number of secondary cases infected by one primary case in an uninfected but vaccinated herd) was estimated in some cases to be 11.1 and even 72.8 [29]. The latent period varies between two and 14 days; the animals are only one or two days infectious before showing clinical symptoms like fever, blisters at mouth, tongue and feet etc., which point at FMD quite clearly [29]. Mortality is rather low (about one to three percent), and the recovered animals are immune for the rest of their lives. Meanwhile, about thirty different strains are known (mainly recently created under the evolutionary pressure of vaccines), but an animal recovered from one strain has aquired a certain degree of immunity against the other strains. There is almost no natural resistance against the virus. FMD can be transmitted by direct contacts, contacts with infected tools or food, but also aerosol and air borne transmission are important.

An animal can develop a “carrier state”: it may carry the virus one to three years without showing symptoms. This happens more frequently if an animal is challenged in the first few days after vaccination by contacts with infected animals. These carriers are in principle able to transmit the disease, but it seems that their

infectivity is negligible [7]. Vaccines are very effective: vaccinated animals develop sufficient immunity in about four days [7, 29]. There are hardly any vaccination failures. However, the immunity vanishes rather fast, after three months half of the animals are susceptible again [29].

2.2. Description of an outbreak

An outbreak of FMD occured 1987/88 near Hannover (Germany) [19]. At that time a mass vaccination program was performed. Altogether six herds were detected to be infected.

1. The first two infected herds were discovered on October 8, 87, and all animals of the diseased farms were subsequently slaughtered. In a radius of three kilometers all animals were vaccinated. Moreover, this region was closed off for animal transports. A screening program was started within 10 km of the outbreak.
2. On January 1, 1988 two other infected herds were found on farms 18 km away from the place of the initial outbreak. The control measures were the same as in the initial case.
3. On January 5, 1988 the next discovery of an infected herd took place, 8 km from the initial case. From then on, the control measures were stricter: not only all cattle and pigs at the diseased farm were slaughtered, but also animals within 10 km were vaccinated and the area was closed off.
   The last case appeared January 10, 1988, in the same village as the case of January 5. The control measures remained the same.
4. After no other cases were discovered, the region was declared disease free on February 12, 1988.

The structure of this outbreak can be described as consisting of three different local outbreaks (LO) which took place far away from each other, with a possible large delay (there are two and a half month between the first and the second LO) and two infected herds per LO. This interpretation suggests that there are two mechanisms for infection. The first mechanism is effective only over short distances, but at a high rate. It seems that here real contacts occur (due to direct contacts or airborne spread) since the two infections per outbreak occured more or less at the same time. Due to this first way of transmission, it is very likely that, once a herd is infected, very soon other herds in the immediate neighborhood become also infected. The second mechanism of transmission does not occur at such a high rate but acts at longer distances and with a possible delay in transmission: even though the first LO was eliminated at the beginning of October, two months later other LOs occured far away. This way of transmission may be contact with infected tools or food, transport of infected gear or animals together with airborne spread, or may be caused by an unrecognized local epidemic in wildlife (such mechanisms are known to play a role for e.g. rinderpest (cattle plaque) [24]). In our model we will not take into account the indirect way of the long distance contacts which lead to the possible delay in the creation of secondary outbreaks, but only distinguish between (direct) short distance contacts at a high rate and (direct) long distance contacts at a low rate.

The control measures that are called "ring vaccination" consist of

1. A general screening program independent of the disease (this "screening" program may consist only of the farmer, calling the veterinarian if suspicious symptoms are discovered).
2. Slaughtering the animals at diseased farms.
3. Vaccination in a ring with a certain radius around diseased farms.
4. Closing off a region around the farm.
5. Setting up a screening program in a region around the diseased farm.

There are other scenarios, which are also called ring vaccination, like slaughtering all animals within a certain radius r_1 of the primary case and only vaccinating the farms within a distance between two radii r_2 and r_3, with $r_1 \leq r_2 < r_3$. However, these different scenarios have more or less similar features as the previous one.

3. The spatial model

3.1. Without control measures

We use a particle model [8] with a fixed, finite but large contact graph Γ. This graph may be an $N \times N$ square lattice or a more complex finite graph. Each site of the graph represents a farm. Since there is almost no natural resistance to the disease and moreover the disease is very infectious, we can assume that once an infected animal appears on a farm, very soon a high percentage of all animals are diseased. In view of this fact it is sensible to consider the whole farm as susceptible, infected or (after vaccination) immune. For sake of simplicity, we neglect the latency period. We expect that the results do not change much, if this property of the disease is also taken into account. A farm, where infected animals are discovered can be considered as immune after slaughtering the animals, since there are no more susceptible or infectious animals (we neglect the infectivity of this farm by infected tools etc.). Also, on this farm, there will be - after a certain time - again new, susceptible animals. This transition corresponds to a loss of immunity. We will also neglect the carrier state, since these animals seem to have a very low infectivity. Hence we get a simple SIRS-Model for each farm: each site (farm) can assume one of three states: susceptible 'S', infected 'I' or recovered 'R'.

In the view of the different ways of transmission, we define two rates β_s and β_l for short and long distance infections. While short distance infections occur only in an infection neighborhood N_i (N_i is the Moore neighborhood in the case of a square lattice), long distance contacts may take place to any other site of the graph with the same probability.

3.2. With control measures

The control of the disease has two independent components: mass vaccination and ring vaccination. Ring vaccination itself has again five components: a general screening of all farms, the slaughtering of the animals of diseased farms, vaccination and intensive screening of all farms nearby and the closure of a region around the initial case.

It is easy to introduce mass vaccination. This kind of vaccination corresponds to a fixed rate ψ_m for the transition of a farm from susceptible to recovered.

More difficult is the implementation of ring vaccination. In order to model the general screening program, we introduce a rate σ. An infectious site is discovered at this rate. Once an infected site is discovered, all processes but ring vaccination are stopped. This can be done, since ring vaccination runs on a much faster time scale than the other processes. At the discovered farm, all animals are slaughtered (i.e. the site undergoes a transition $I \to R$). Furthermore, in a control neighborhood N_c, which is in general larger than the infection neighborhood N_i, every site is screened and the uninfected sites are vaccinated (and thus become recovered). If an infected site is found, ring vaccination is performed around this second infected farm as well. The procedure stops if no more infected sites are discovered. Now all other processes are allowed to start again.

Since we stop time as long as the ring vaccination procedure runs, the implementation of ring vaccination is synchronous. All other events occur asynchronous (see [8], Section 2). The synchronism of ring vaccination is justified by a time scale argument: within one or two days after discovery of an infected farm, the control measures are carried out. Furthermore, the emergency vaccine protects quite soon after vaccination. Hence it is appropriate to consider the time scale of ring vaccination to be faster than that of all other processes.

3.3. Specification of the transition rates

We denote by x a site of the graph Γ, by $\phi(x)$ the state of the site x, by $N_i(x)$ the infective neighborhood and $N_c(x)$ the control neighborhood of site x.

- Infection, $S \to I$: there are short distance contacts at a rate β_s within the infective neighborhood N_i, and long distance contacts at rate β_l all over the graph, i.e. we obtain the total rate of infection $\beta_s \#\{y \in N_i(x) \mid \phi(y) = I\} + \beta_l \#\{y \in \Gamma \mid \phi(y) = I\}$.
- Recovery, $I \to R$: the recovery rate is denoted by α.
- Observation of infected farms: an infected site is discovered at rate σ. All animals at this farm are slaughtered at once, i.e. the site undergoes a transition to R. Moreover, in the control neighborhood N_c of this site, all susceptible sites are vaccinated, i.e. undergo a transition from S to R. Ring vaccination is also performed around any infected site that was discovered in the original control neighborhood N_c.
- Loss of immunity, $R \to S$: loss of immunity occurs at rate γ.
- Vaccination $S \to R$: a transition from S to R occurs as the consequence of vaccination. This vaccination may be mass vaccination (at rate ψ_m) or ring vaccination (caused by discovery of an infected site).

Technically spoken, a system like this with synchronous processes (ring vaccination) is no more a particle system in the strict sense, but can be approximated by a sequence of particle systems. However, we will refer to this simulation model as particle system.

3.4. Example of a simulation

For the simulation, we choose as parameter values $\beta_s = 1.453$, $\beta_l = 0.0492$, $\alpha = 0.03$, $\gamma = 0.00743$, $\psi_m = 0.0$ (no mass vaccination program), $\sigma = 0.071$. The graph is chosen as a 50 times 50 square lattice with periodic boundary conditions (topology of a torus), the infectious neighborhood as the Moore neighborhood $N_i(x) = \{y \mid \|x - y\|_\infty \leq 1\}$, and the control neighborhood as an extended Moore neighborhood $N_c(x) = \{y \mid \|x - y\|_\infty \leq 2\}$ ($\|.\|_\infty$ denotes the maximum norm: If $x = (x_1, x_2)^T$, $\|x\|_\infty = \max\{|x_1|, |x_2|\}$). We show the trajectory of an outbreak in Fig. 1.

We find the typical picture of LOs which create other LOs. Furthermore, an observed LO is very likely to be eradicated by ring vaccination. This behavior is typical for the particle model, and agrees with that of the described outbreak near Hannover. Furthermore, it underlines the importance of contact tracing for ring vaccination.

4. Caricature of the spatial model

In this section we reduce the spatial structure, which is a possibly very large grid, to a system with a finite number of patches. Two kinds of contacts can be distinguished: short range and long range. One (primary) case creates with a high rate other cases by means of short range contacts. This mechanism yields a cluster of infected sites. Since the cluster is clumped together, it can be treated as one individual: E.g. this individual "dies", if one of its infected farms is observed. In contrast, a successful long range contact will start a new LO far away from the first cluster. Hence it is very likely that ring vaccination of the first cluster does not affect the second LO. One LO can be described independently of the others [4].

Since we assume that the disease can be controlled by ring vaccination, one LO cannot grow too much and, in addition, creates less than one new LO on average. Therefore it is possible to model the intra LO dynamics as well as the inter LO dynamics as a linear process (see also discussion in the next section and in Section 4.1.3). Note, that the assumption of linearity leads only to an approximation of the spatial process. Since the infectious neighborhood is finite, already a few infected sites produce a considerable nonlinear effect. Nonetheless, simulations will show that at least in a certain parameter range the linear approximation is well suited as a description of the full process.

This concept resembles that of a metapopulation [14], where each LO corresponds to one patch. Essentially the population dynamics within one patch can be described independent from that of all other patches. However, empty patches can be invaded by residents of active patches (i.e. long distance contacts create new LOs).

4.1. Intra-outbreak dynamics

Once an LO is created either by invasion from the outside or by another LO, its dynamics are assumed to be independent of the remaining part of the system. Since we assume that the disease can be controlled by ring vaccination, the LOs are not

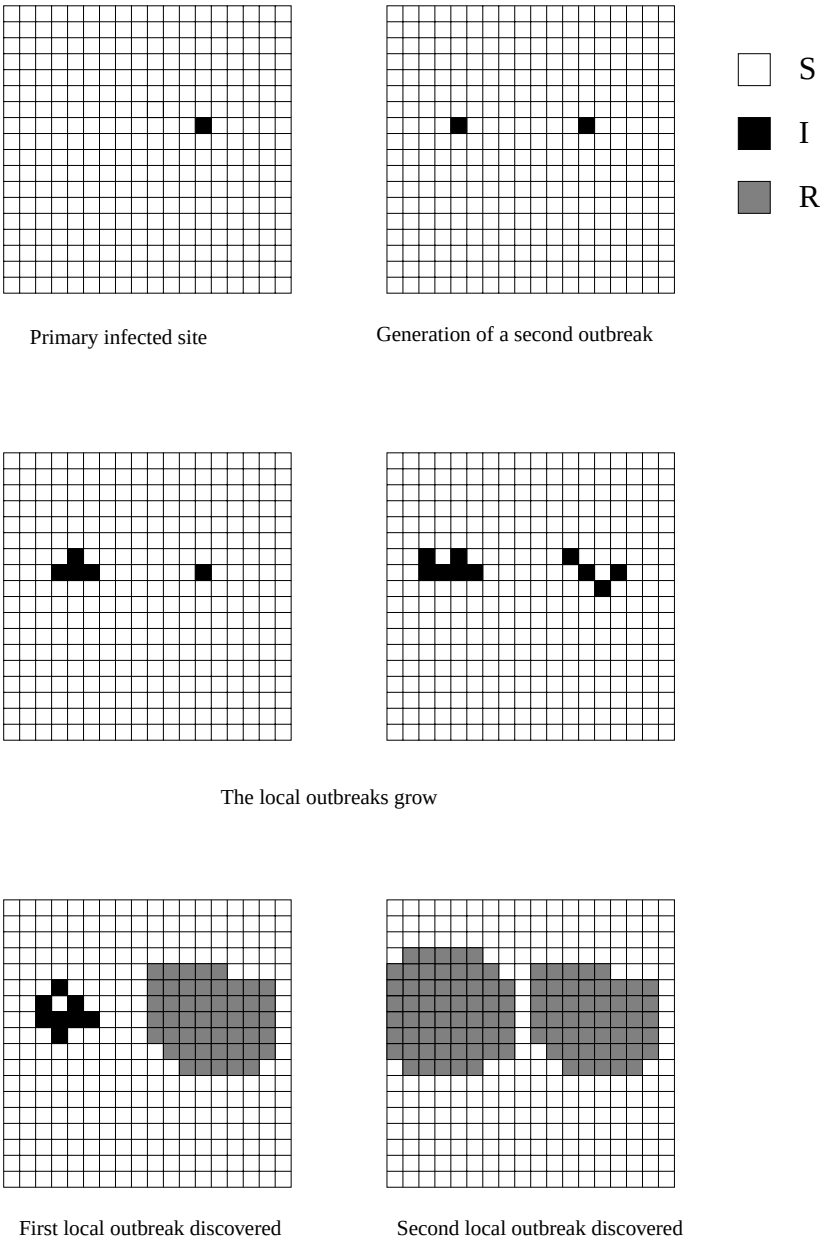

Fig. 1. Simulation of an outbreak.

likely to become large and we can more or less neglect nonlinear effects. Moreover, the LO is localized in one single cluster, and hence we also neglect its spatial structure. Basically, the dynamics can be described by a linear birth and death pro-

cess. In addition, we incorporate the event of discovery of the LO. Once the LO is observed, control measures (ring vaccination) ensure that very soon after discovery the disease dies out at the place of this LO.

It is possible to reformulate the particle model, such that the description of the time evolution of an LO is close to the formulation of a birth and death process: We define states $\mathscr{I}_i$ of $i = 0, 1, 2, ...$ infected sites, where so far no site of the LO has been discovered as infected. In addition, we define a state $\mathscr{D}$ that corresponds to an observation of at least one infected site. In the following, we will use the nomenclature of infectious processes (infection/recovery) as well as that of birth and death processes (birth/death). The per capita mortality rate is $\overline{\mu}$ and the screening rate $\overline{\sigma}$. Births do not occur with a constant per capita rate: Infectious sites attempt to infect neighbored sites at some constant per capita rate β_s^0, but it depends on the spatial distribution of infected and recovered cells whether or not such an attempt is successful or not. Thus, not only the state of an LO at time t but also the per capita birth "rate" $\tilde{\beta}_{s,i}$ in state $\mathscr{I}_i$ is a random variable. In Fig. 2 we show the distribution of $\tilde{\beta}_{s,i}$ for $i = 1, 5, 10, 15$.

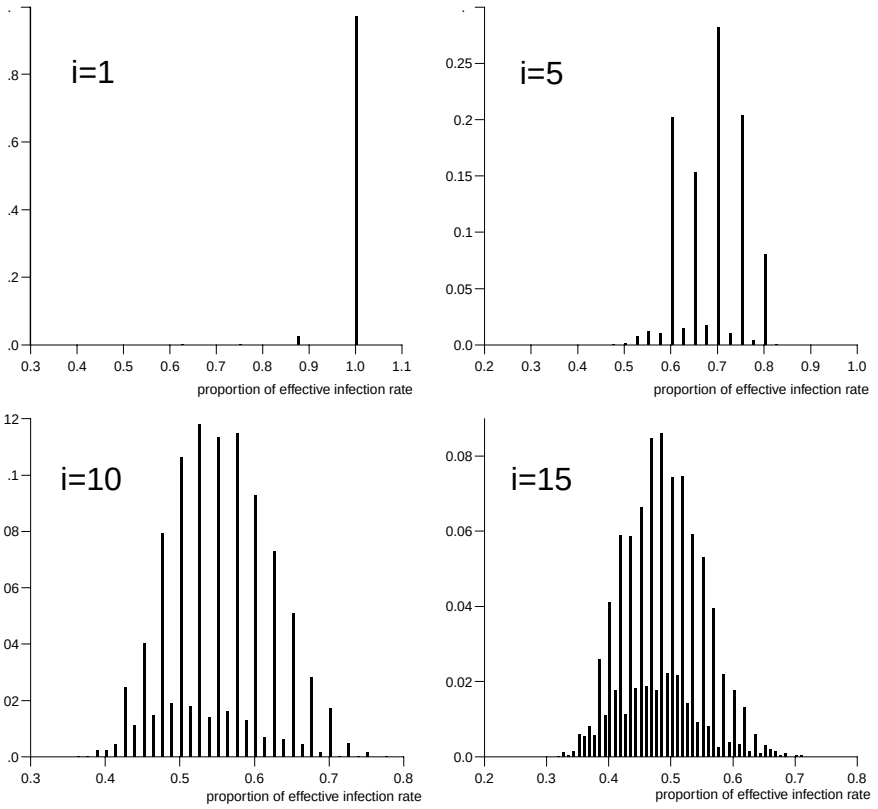

Fig. 2. Distribution of $\tilde{\beta}_{s,i}/\tilde{\beta}_s^0$ for $i = 1, 5, 10, 15$. Please note that the scale of the x-axis is different. The parameters are $\beta_s = 50.0$, $\alpha = 4.5$, $\sigma = 5.0$, $\gamma = 0.05$, $\psi_m = 0.0$, $N = 40$. Number of runs: 10000.

For $i = 1$, the distribution $\tilde{\beta}_{s,1}$ resembles the exponential distribution: If there is no recovered site in state $\mathscr{I}_1$, all neighbors of the infected cell are susceptible, i.e. in this case we have

$$P(\tilde{\beta}_{s,1} = \beta_s^0 \mid \text{no recovered in state } \mathscr{I}_1) = 1.$$

If there is one recovered cell in state $\mathscr{I}_1$, then this recovered cell must be in the neighborhood of the infected cell and reduces the number of susceptible cells that can be infected by one, i.e. for the More neighborhood

$$P(\tilde{\beta}_{s,1} = (7/8)\,\beta_s^0 \mid \text{one recovered in state } \mathscr{I}_1) = 1.$$

If there are two recovered cells, the effective birth rate $\tilde{\beta}_{s,1}$ is not unique any more, since there are different possible spatial structures (all in one row or all clumped), which lead to different rates, but still

$$P(\tilde{\beta}_{s,1} \in \{(7/8)\,\beta_s^0, (6/8)\,\beta_s^0\} \mid \text{two recovered in state } \mathscr{I}_1) = 1.$$

The random variable $\tilde{\beta}_{s,1}$ assumes only values $k\beta_s^0/8$, $k = 0, \ldots, 8$ and looks nearly exponential distributed. Note that the mass of $\tilde{\beta}_{s,1}$ is concentrated on $k = 8$.

In a similar way, also the random variables $\tilde{\beta}_{s,i}$ for i large are discrete random variables. However, for states with a high number of infected cells, the distribution of $\tilde{\beta}_{s,i}$ looks approximately normal. More precisely, the distribution approximates a superposition of several Gaussian distributions, accordingly to the distribution of the number of recovered cells in state $\mathscr{I}_i$.

So far we have only reformulated the spatial model – the spatial structure of an LO is still reflected by the distribution of $\tilde{\beta}_{s,i}$. The first step toward a simple caricature that can be analyzed is to replace the random variables $\tilde{\beta}_{s,i}$ by constant rates $\overline{\beta}_{s,i}$. Since the number of transitions from state $\mathscr{I}_i$ to $\mathscr{I}_{i+1}$ depend on the product of the probability to be in state $\mathscr{I}_i$ and the random variable $\tilde{\beta}_{s,i}$, there is no straight forward way to choose $\overline{\beta}_{s,i}$ (in general, the mean values of $\tilde{\beta}_{s,i}$ would not do it). However, even if we assume constant per capita rates $\overline{\beta}_{s,i}$, the birth and death process will in general not be feasible for analytic tools. That's why we assume in a second step of approximation of the original system that the birth rates do not depend on i,

$$\overline{\beta}_{s,i} = \overline{\beta}_s.$$

Of course, this assumption is a cruel simplification which will not work for all parameter values. However, in Section 4.1.3 we will compare numerical simulations with the outcome of the described birth and death process (for a flow diagram of the latter see Fig. 3), and find good agreement for certain interesting parameter values.

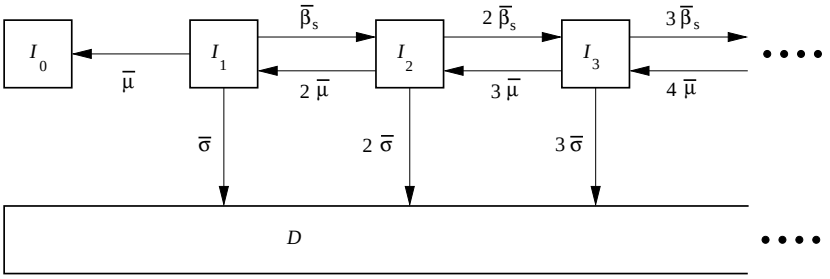

Fig. 3. Linear birth and death process stopped by the discovery of infection.

Let $p_i(t)$ be the probability for states $\mathscr{I}_i$ at time t and $q(t)$ the probability for state $\mathscr{D}$ at time t. The evolution of these probabilities are described by

$$\frac{d}{dt}p_0 = \overline{\mu}p_1 \tag{1}$$

$$\frac{d}{dt}p_i = -i(\overline{\mu}+\overline{\beta}_s+\overline{\sigma})p_i + (i-1)\overline{\beta}_s p_{i-1} + (i+1)\overline{\mu}p_{i+1} \quad \text{for} \quad i \geq 1 \tag{2}$$

$$\frac{d}{dt}q = \overline{\sigma}\sum_{i=0}^{\infty} i p_i. \tag{3}$$

If we assume that at time $t = 0$ exactly m individuals are infected (mostly we will deal with $m = 1$), the initial conditions are

$$p_i(0) = \delta_{i,m}, \qquad q(0) = 0.$$

The generating function $u(x, t)$ for this process is

$$u(x,t) = \sum_{i=0}^{\infty} x^i p_i(t). \qquad u(x,t)|_{t=0} = x^m. \tag{4}$$

Note that $u(1, t) < 1$ for $\overline{\sigma}$, $t > 0$, since there are not only the states $\mathscr{I}_i$ in the system but also the state $\mathscr{D}$. We obtain for $m = 1$ the generating function (see Appendix A.1)

$$\varphi(x,t) = \frac{x(z_+ - z_- e^{\Lambda t}) + (z_+ z_-(e^{\Lambda t}-1))}{(z_+ e^{\Lambda t} - z_-) + x(1-e^{\Lambda t})} \tag{5}$$

where Λ and $z_\pm$ are defined in equation (18) in the appendix. For $m > 1$ we have $u(x, t) = \varphi^m(x, t)$. If we choose $\overline{\sigma} = 0$, i.e. no screening at all, we recover the usual linear birth and death process [11]. Since $u(1, t) + q(t) = 1$,

$$p_i(t) = \frac{1}{i!}\partial_x^i u(x,t)|_{x=0}, \quad q(t) = 1 - u(1,t).$$

Therewith we have a complete description of the stochastic process.

4.1.1. Time to extinction or observation

The distribution of the time to extinction without observation of the LO, denoted by $F_e(t)$, is given by

$$F_e(t) = \overline{\mu} p_1(t),$$

and the distribution of the time to discovery (before extinction), $F_d(t)$, by

$$F_d(t) = \overline{\sigma} \sum_{i=0}^{\infty} i p_i(t) = \overline{\sigma} \langle i \rangle(t),$$

where $\langle i \rangle(t)$ denotes the mean value of the number of infected sites at time t. We derive expressions for p_1 and $\langle i \rangle$ from the generating function, $p_1(t) = \partial_x u(x,t)|_{x=0}$ and $\langle i \rangle(t) = \partial_x u(x,t)|_{x=1}$, i.e.

$$\begin{aligned} p_1(t) &= m \left(\frac{(z_+ - z_-)^2 e^{\Lambda t}}{[z_+ e^{\Lambda t} - z_-]^2} \right) \left(\frac{z_+ z_- (e^{\Lambda t} - 1)}{z_+ e^{\Lambda t} - z_-} \right)^{m-1} \\ \langle i \rangle(t) &= m \left(\frac{(z_+ - z_-)^2 e^{\Lambda t}}{[(z_+ - 1) e^{\Lambda t} - (z_- - 1)]^2} \right) \\ &\quad \left(\frac{z_-(z_+ - 1) e^{\Lambda t} - z_+(z_- - 1)}{(z_+ - 1) e^{\Lambda t} - (z_- - 1)} \right)^{m-1} \end{aligned}$$

and thus

$$F_e(t) = m \overline{\mu} \frac{(z_+ - z_-)^{m+1} e^{\Lambda t} (e^{\Lambda t} - 1)^{m-1}}{[z_+ e^{\Lambda t} - z_-]^{m+1}} \tag{6}$$

$$F_d(t) = m \overline{\sigma} \frac{(z_+ - z_-)^2 e^{\Lambda t} [z_-(z_+ - 1) e^{\Lambda t} - z_+(z_- - 1)]^{m-1}}{[(z_+ - 1) e^{\Lambda t} - (z_- - 1)]^{m+1}}. \tag{7}$$

The distributions of the time to extinction without observation F_e is always monotone decreasing. For the distribution of the time to discovery F_d there are two qualitatively different possible shapes: Either it is monotonously decreasing or has exactly one maximum at a positive time point before it decrease exponentially in time (for the latter case, see e.g. Fig. 6). If F_d just decreases, this does mean that most LOs die out unobserved, i.e. even without ring vaccination the disease is not able to spread. The other case is a sign that the disease is about to take off: A new infected LO is small and thus not likely to be observed. Later on the size of the LOs become large such that also the probability per time interval for an observation becomes large. At this point of time the peak appears in the distribution F_d. The tail in the distribution declines with $e^{-\Lambda t}$. This exponential decrease reflects the fact that in our model all processes are Poisson with constant rates, where particles may survive arbitrary long by chance.

The difference between situations where the disease would – without ring vaccination – take off respectively die out anyway will be discussed further in the next section.

4.1.2. Distribution of infected sites at discovery of an outbreak

The dynamics of an LO is that of a usual birth and death process until one infected site is observed or all infected sites died out without control measures. If it is observed, the cost for the treatment of this LO will depend on the number of infected sites. In this section we investigate this distribution.

Let $\overline{q}_i$ be the probability to find i infected sites in the LO at the time of the first observation for $i > 0$. Let furthermore $\overline{q}_0$ be the probability that the LO dies out without being observed. Hence

$$\begin{aligned}
\overline{q}_i &= \int_0^\infty i\,\overline{\sigma}\,P(\mathscr{I}_i \text{ at time } t)\,dt = \overline{\sigma}\frac{1}{(i-1)!}\partial_x^{i-1}\int_0^\infty \partial_x u(x,t)\,dt\Big|_{x=0} \\
&= \overline{\sigma}\frac{1}{(i-1)!}\partial_x^{i-1}\int_0^\infty \frac{(z_+ - z_-)^2 e^{\Lambda t}}{[(z_+ - x)e^{\Lambda t} - (z_- - x)]^2}\,dt\Big|_{x=0} \\
&= \overline{\sigma}\frac{1}{(i-1)!}\partial_x^{i-1}\frac{(z_+ - z_-)^2}{\Lambda}\int_1^\infty \frac{1}{[(z_+ - x)\tau - (z_- - x)]^2}\,d\tau\Big|_{x=0} \\
&= \frac{\overline{\sigma}}{\overline{\beta}_s}\frac{1}{(i-1)!}\partial_x^{i-1}\,\frac{1}{z_+ - x}\Big|_{x=0} = \frac{\overline{\sigma}}{\overline{\beta}_s}\frac{1}{z_+^i} \\
\overline{q}_0 &= \lim_{t\to\infty} u(0,t) = z_-.
\end{aligned}$$

The process of an LO consists more or less of two parts: one part describes the linear birth and death process (the dynamics without observation), the other part describes the observation events. The disease itself may be sub- or supercritical ($\overline{\beta}_s/\overline{\mu} < 1$ respectively $\overline{\beta}_s/\overline{\mu} > 1$). The total process is always subcritical in the sense that an LO always dies, either due to an observation or since the epidemic dies out anyway. We can find this fact in the quantity z_-. If $\overline{\beta}_s/\overline{\mu} < 1$, i.e. if the branching process for the disease without observation is subcritical, then $z_- \to 1$ as $\overline{\sigma} \to 0$, i.e. the disease dies out, even if there is no observation (see Fig. 4). In the other case, z_- stays below one: if $\overline{\sigma} = 0$, a certain fraction of the realizations of the process will grow for all times.

In this spirit we can define a *major outbreak* as an LO that is observed, and thus the probability for a major outbreak is

$$\text{Probability for a major outbreak} = \sum_{i=1}^{\infty}\overline{q}_i = 1 - z_-.$$

Furthermore, the expected number of infected sites of an LO by discovery i_{exp} is

$$i_{\text{exp}} = \sum_{i=1}^{\infty} i\overline{q}_i = \frac{\overline{\sigma}}{\overline{\beta}_s}\,\frac{z_+}{(z_+ - 1)^2}$$

If $\overline{\mu} = 0$, this expression simplifies to $i_{\text{exp}} = 1 + \overline{\beta}_s/\overline{\sigma}$. This formula is remarkable, since in absence of the dependency of the individuals within an LO, $\overline{\beta}_s/\overline{\sigma}$ would just be the number of secondary cases one primary infected individual produces

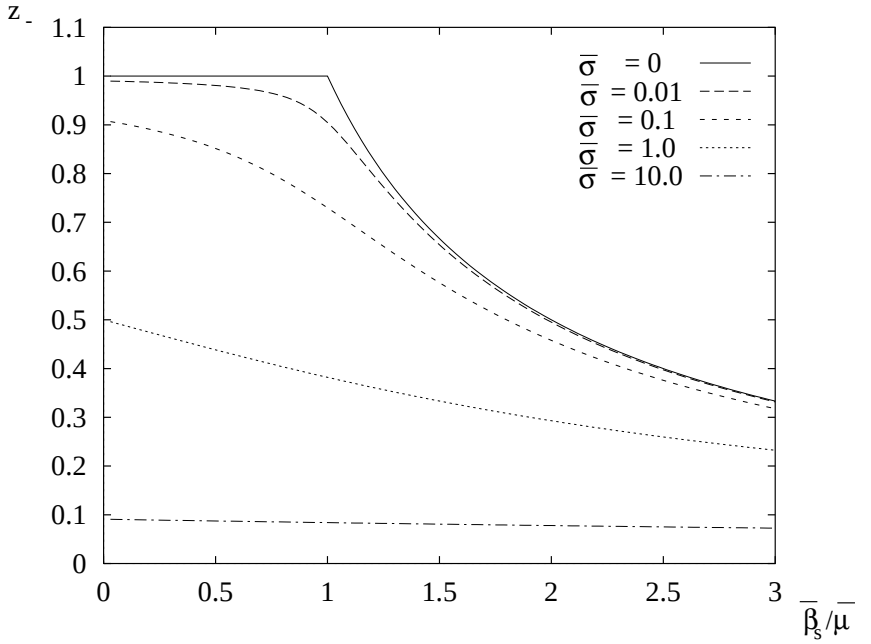

Fig. 4. Dependence of the factor z_- on $\overline{\beta}_s/\overline{\mu}$ for the disease in an LO without observation.

for $\overline{\mu} = 0$. In this setting, i_{exp} is equal to the primary case (one) plus the cases of the second generation ($\overline{\beta}_s/\overline{\sigma}$).

It is technically a little bit more complex to compute the distribution and the mean value of affected (infected or recovered) sites at the moment of observation but straightforward using the same ideas as before. Since for FMD among cattle unobserved farms do not play a major role, we skip this computation.

4.1.3. Comparison of the spatially structured model with its caricature

In order to compare the particle model with the caricature, we link the parameters $\overline{\mu}$, $\overline{\beta}_s$ and $\overline{\sigma}$ to those of the particle model. Then we look at simulations of some distributions to find similarities and differences.

Parameters:
We assume here that only short distance contacts occur, i.e. $\beta_l = 0$. The simplest parameter is $\overline{\sigma}$: this is just the screening rate,

$$\overline{\sigma} = \sigma.$$

We assume that the screening rate is not changed by the discovery of another outbreak. An infected site looses its infectivity at rate $\overline{\mu}$,

$$\overline{\mu} = \alpha.$$

$\overline{\beta}_s$ is the per capita "birth" rate of infected individuals. We assume that the population is vaccinated by a mass vaccination program with vaccination rate ψ_m. Hence, the expected number of susceptible neighbors of a site in the uninfected situation is $\gamma/(\psi_m + \gamma)$ times the number of all neighbors. However, the average number of susceptible neighbors is not only reduced by the mass vaccination program but also by infection. To take this fact into account, we define

$$\overline{\beta}_s = \theta \frac{\gamma}{\psi_m + \gamma} \beta_s,$$

where $0 < \theta \leq 1$ denotes the typical reduction of susceptible neighbors due to the disease. Of course, this reduction depends on the spatial distribution and especially on the number of infected and immune cells. In our approximation we assume only one constant factor for all states $\mathcal{I}_i$. The comparison with simulations will show that this assumption is not too rough. For simplicity, we fit θ by eye such that the curves of the distributions become similar. We do not use optimization methods to obtain θ, since the fitting by eye yields satisfying results.

It is astonishing that it is possible to describe the nonlinear particle model by a linear birth death process. Note that we assume in the following usually $\theta = 0.75$; $\theta = 1$ would result in considerably worse approximations. This does mean that the described procedure of approximation of the particle model by the birth and death process is not merely a hidden kind of linearization but that the nonlinearity in the particle model cannot be neglected. However, it seems enough for the chosen parameter values to adapt θ (i.e. to rescale the parameters of the birth death process) in order to capture the nonlinear effects within the particle system.

Of course, a birth and death process where the per capita birth rate depends on the number of infected sites would lead to even better approximations; but since the result of the simple model is quite satisfying there is no real need for more complex models. Also, a bigger neighborhood N_i would diminish the nonlinear effects and in this way the approximation of the caricature would become better. Again, we will see below that even for the Moore neighborhood the approximation is well enough to be interesting as a caricature of the particle model.

Simulations:
Two scenarios are considered: one with mass vaccination and one without mass vaccination ($\psi_m = 0$). For the first we choose $\psi_m = \gamma$, such that on average half of the sites of the uninfected grid are protected. The other parameter values are the same as in Section 3.4, with the exception of $\beta_l = 0$. At time $t = 0$ one infected site is randomly chosen. We performed 10000 runs to obtain the results. We compare three types of distributions: the probability to find i infected sites at time t for $i = 1, \ldots, 4$, the probability density of the time to extinction (either with or without observation of infected sites) and the distribution of the number of infected sites at the moment of the observation.

In Fig. 5 we show the probabilities to have one, two, three or four infected sites in an LO at certain time. In addition to the simulated values we show the computed values for the birth and death process. We find a good agreement for $\theta = 0.75$, independently of $\psi_m = 0$ or $\psi_m = \gamma$. Similarly, in Fig. 6 the time to extinction is

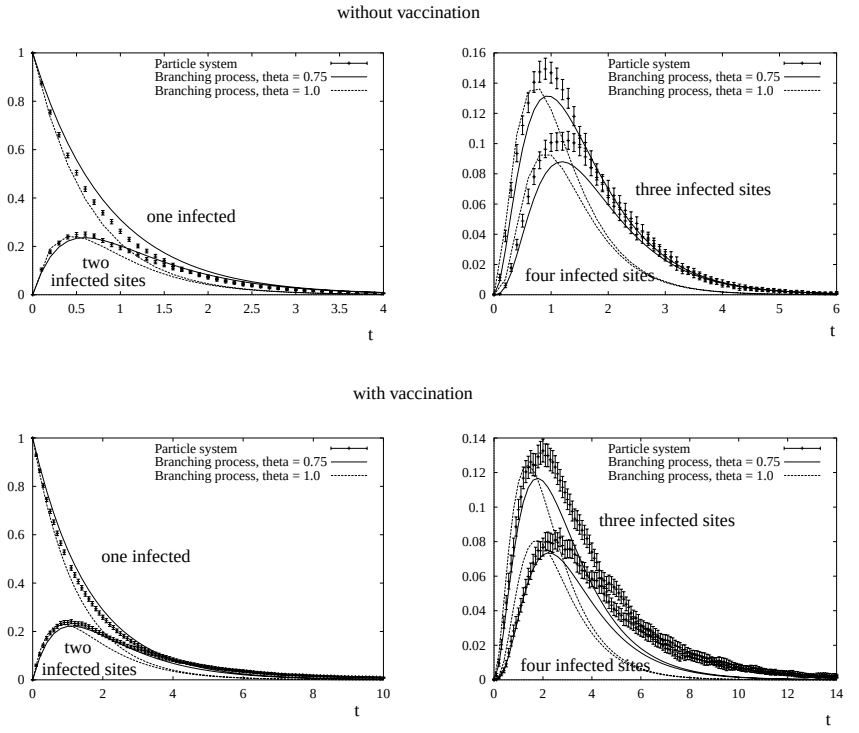

Fig. 5. Comparison of the probability to have one, two, three or four infected sites in one LO at time t. The curves correspond to simulations of the branching process ($\theta = 1$ and $\theta = 0.75$). The measured probabilities of the simulation model are shown together with the 95% confidence interval. Note, that the graphs have different time scales.

compared. Again, we use $\theta = 0.75$ and obtain a good agreement. The situation is slightly different in case of the distribution of the number of infected sites at the moment of observation (Fig. 7). The figures show the densities of the distribution of the particle model together with the distributions for the caricature with $\theta = 1$, $\theta = 0.75$ and $\theta = 0.5$. We find, that the curve for $\theta = 0.5$ agrees much better with the particle system than the curves with $\theta = 1$ or $\theta = 0.75$ (equally for $\psi_m = 0$ and $\psi_m = \gamma$). This fact can be explained: while the distributions for the probability to have i infected sites at time t and the time to extinction depends mainly on the grid states with a small number of infected sites, the number of discovered infected sites also depends on the states with a higher number of infected sites. For the latter the average reduction of susceptibles in the contact neighborhood is larger, and thus for θ a smaller value should be chosen. However, in all cases θ seems not to depend strongly on ψ_m, a fact that allows one to compare different vacination strategies easily.

4.2. Inter-outbreak dynamics

In general, an LO assumes more than one state before it dies. This implies for the dynamics of the population of LOs that the lifecycle of a single LO must be

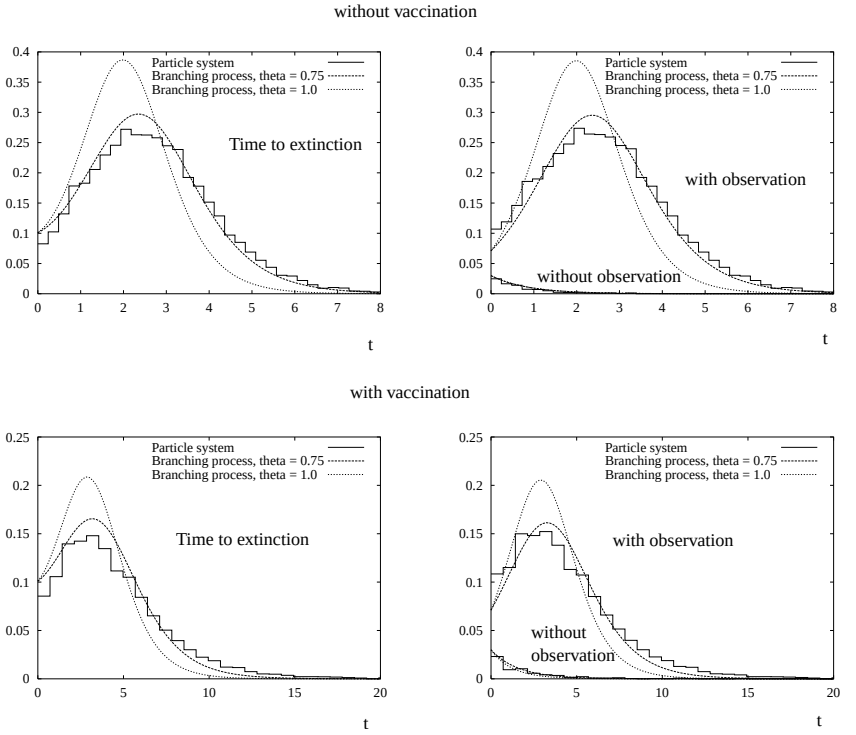

Fig. 6. Time to extinction. The extinction of an LO may be due to an observation or the LO may die out spontaneously. In the left figures, the distibution of the time to extinction is shown in total, while in the right figures the time to extinction is distinguished by the two reasons for dying out. Again, $\theta = 1$ and $\theta = 0.75$.

taken into account, a fact, that leads to similar difficulties as the generalized age structured branching process: The process generating function cannot be computed explicitly. However, we basically concentrate on properties independent of time (like reproduction number R_{LO} for LOs, i.e. the average number of LOs created by one typical LO, or the probability of major outbreaks etc.). To descibe these properties it is enough to know the embedded Galton-Watson process. In the next section we derive the generating function for the latter process.

4.2.1. The embedded Galton-Watson process

In order to obtain the reproduction number for LOs we consider the embedded Galton-Watson process, i.e. we do not work with time but only with the number of generations. The Galton-Watson process is determined by the distribution of the number of secondary LOs,

$$\overline{p}_j := P(\text{one LO creates exactly } j \text{ secondary LOs}).$$

To compute the generating function for this process, we investigate the birth process of LOs. Let $\mathscr{I}_i^j$ be the state where the primary LO consists of i infected sites and

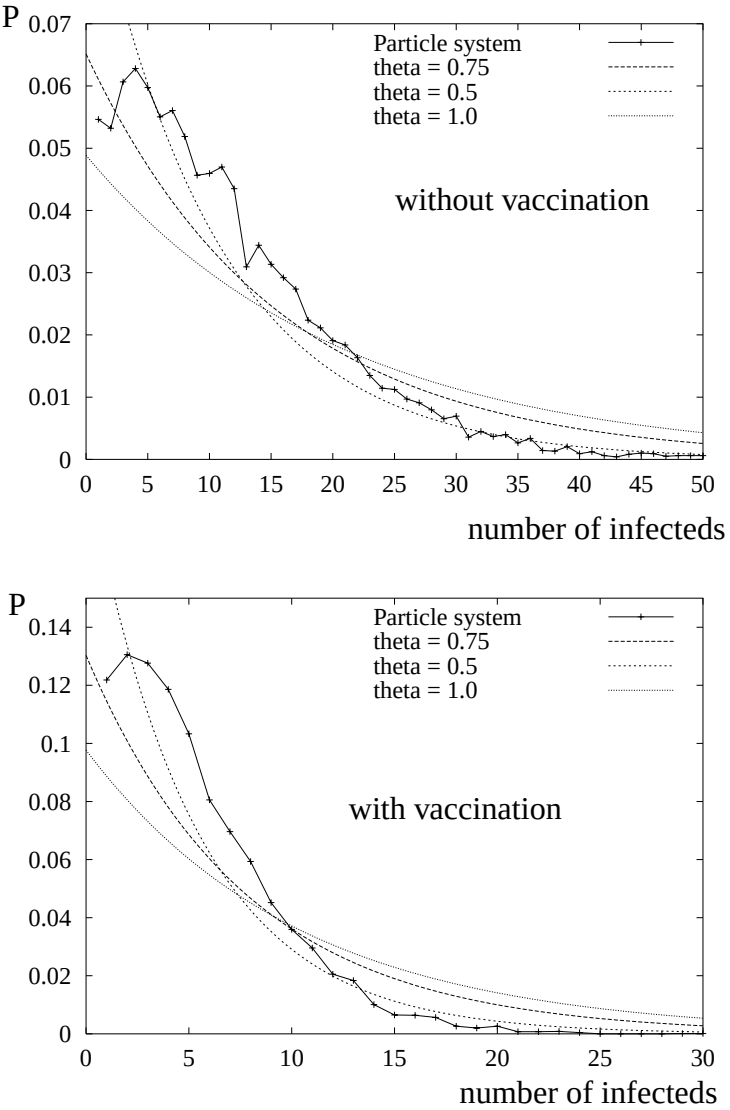

Fig. 7. Comparison of the spatial model and the caricature with respect to the distribution of the number of infected sites at the moment of observation.

has created already j secondary LOs and is not discovered. Furthermore let $\mathscr{D}^j$ be the state where the LO has been discovered (and thus the LO is "dead"), but has created j secondary LOs before. The transition graph between these states is shown in Fig. 8. Defining the probabilities $\tilde{p}_i^j(t) = P(\mathscr{I}_i^j \text{ at time } t)$ and $\tilde{q}^j(t) = P(\mathscr{D}^j \text{ at time } t)$, we obtain the system of ordinary differential equations

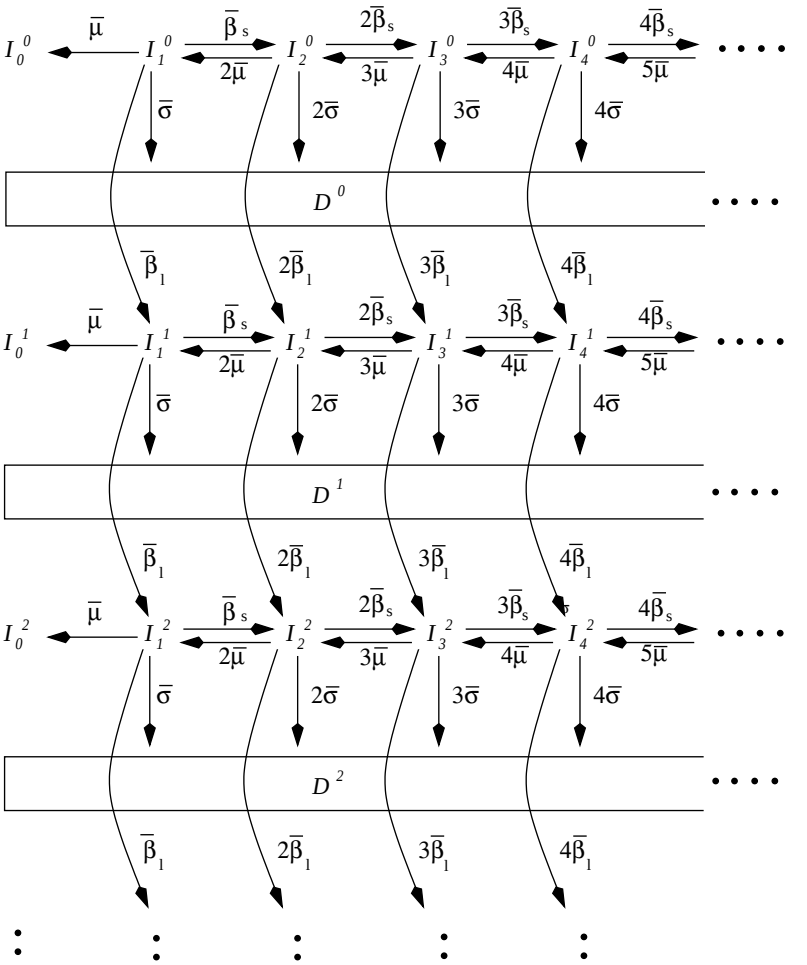

Fig. 8. Births generated by one LO.

$$\frac{d}{dt}\tilde{p}_i^j = -i(\overline{\mu}+\overline{\beta}_s+\overline{\sigma}+\overline{\beta}_l)\tilde{p}_i^j + (i+1)\overline{\mu}\tilde{p}_{i+1}^j$$
$$+(i-1)\overline{\beta}_s\tilde{p}_{i-1}^j + i\overline{\beta}_l\tilde{p}_i^{j-1} \quad \text{for} \quad i \geq 1$$
$$\frac{d}{dt}\tilde{p}_0^j = \overline{\mu}\tilde{p}_1^j$$
$$\frac{d}{dt}\tilde{q}^j = \overline{\sigma}\sum_{i=0}^{\infty} i\,\tilde{p}_i^j$$

The distribution of offspring $\overline{p}_j$ reads

$$\overline{p}_j = \lim_{t\to\infty}(\tilde{p}_0^j(t) + \tilde{q}^j(t)).$$

Let u be the generating function, $u(x, y, t) = \sum_{i=0}^{\infty} \sum_{j=0}^{\infty} x^i y^j \tilde{p}_i^j(t)$. We obtain (Appendix A.2)

$$u(x, y, t) = \frac{x(z_+(y) - z_-(y)e^{\Lambda(y)t}) - z_+(y)z_-(y)(1 - e^{\Lambda(y)t})}{(z_+(y)e^{\Lambda(y)t} - z_-(y)) + x(1 - e^{\Lambda(y)t})}. \tag{8}$$

where $\Lambda(y)$ and $z_\pm(y)$ are defined in equations (19), (20). Let $\phi(y)$ be the generating function for the embedded Galton-Watson process, $\phi(y) = \sum_{j=0}^{\infty} \overline{p}_j y^j$. From $\lim_{t\to\infty} u(x, y, t)$ it is possible to derive an expression for $\phi(y)$ (see Appendix A.2),

$$\phi(y) = z_-(y) + \frac{\overline{\sigma}}{\overline{\beta}_s} \frac{1}{z_+(y) - 1} = \frac{\overline{\mu} - \overline{\sigma} + \overline{\beta}_s + (1 - y)\overline{\beta}_l - \Lambda(y)}{\overline{\mu} + \overline{\sigma} - \overline{\beta}_s + (1 - y)\overline{\beta}_l + \Lambda(y)}. \tag{9}$$

The generating function of the embedded Galton-Watson process will be used in the next sections to find characteristic quantities of the whole process.

4.2.2. The reproduction number

It does not make sense to consider the secondary cases of one primary infected *site*, since the assumption of time-homogeneity does not hold: The discovery of one infected site will change the situation for all infected sites within an LO dramatically (they are mostly erased after the event has happend). Hence the reproduction number for farms infected early in the history of a certain LO will be considerably higher than that of farms infected later. However, the stability of the uninfected situation is well described by the number of secondary LOs, created by one primary LO. This reproduction number R_{LO} is defined similarly to the reproduction number for households R_{HO} in [6] (the number of secondary infected households, infected by one typical primary infected household) or R_T in [5] (the reproduction number for the second level of a two-level epidemic model).

The reproduction number is defined as $R_{LO} = \phi'(1)$, i.e.

$$R_{LO} = \phi'(1) = \overline{\beta}_l \left(\frac{z_-(1)}{\Lambda(1)} + \frac{\overline{\sigma}}{\overline{\beta}_s} \frac{z_+(1)}{(z_+(1) - 1)^2 \Lambda(1)} \right) = \frac{\overline{\beta}_l}{\overline{\beta}_s} \frac{1}{z_+(1) - 1}. \tag{10}$$

Note, that this expression is the same as

$$\overline{\beta}_l \int_0^{\infty} \langle i \rangle(\tau)\, d\tau = \frac{\overline{\beta}_l}{\overline{\beta}_s} \frac{1}{z_+(1) - 1} = R_{LO}.$$

This formula does mean that the avarage number of infected sites $\langle i \rangle(t)$ in an LO produce newly infected LOs at rate $\overline{\beta}_l$. In order to obtain the reproduction number one has to integrate over time. If there is no natural recovery, i.e. $\overline{\mu} = 0$, the expression for R_{LO} simplifies to

$$R_{LO} = \overline{\beta}_l / \overline{\sigma}, \tag{11}$$

i.e. R_{LO} does not depend on $\overline{\beta}_s$. At first glance, this result seems counterintuitive, since a high $\overline{\beta}_s$ does mean that the disease is very contagious and thus one should expect that also R_{LO} is large. However, for $\overline{\beta}_s$ high the LOs grow fast and thus are likely to be observed soon. These two effects, the growth and the observability, balance in such a way that for $\overline{\mu} = 0$ the rate $\overline{\beta}_s$ drops out.

4.2.3. Probability for a major outbreak

Let $R_{LO} > 1$ and P_M be the probability for a major outbreak. The magnitude $1 - P_M$ is the positive root of $\phi(y) = y$, i.e.

$$1 - P_M = \phi(1 - P_M) = \frac{\overline{\mu} - \overline{\sigma} + \overline{\beta}_s + P_M\overline{\beta}_l - \Lambda(1 - P_M)}{\overline{\mu} + \overline{\sigma} - \overline{\beta}_s + P_M\overline{\beta}_l + \Lambda(1 - P_M)}.$$

Even though $R_{LO} > 1$, the probability for the disease to take off is only P_M. In order to get some insight in the magnitude of P_M we again consider the special case $\overline{\mu} = 0$: The expression for P_M simplifies considerably, that is

$$P_M = 1 - 1/R_{LO}.$$

In this special case an LO behaves like a particle that dies at rate $\overline{\sigma}$ and gives birth to other particles at rate $\overline{\beta}_l$.

4.2.4. Expected number of observed infected farms

We have already computed the expected number of infected sites per LO i_{exp}. Let $R_{LO} < 1$. From R_{LO} we obtain that the expected number of LO is $1/(1 - R_{LO})$. Hence the expected total number of observed infected farms I_{exp} becomes

$$I_{\text{exp}} = \frac{1}{1 - R_{LO}} \frac{\overline{\sigma}}{\overline{\beta}_s} \frac{z_+}{(z_+ - 1)^2}. \tag{12}$$

Also here, for $\overline{\mu} = 0$ this expression becomes more simple, $I_{\text{exp}}|_{\overline{\mu}=0} = (1 + \overline{\beta}_s/\overline{\sigma})/(1 - \overline{\beta}_l/\overline{\sigma})$, i.e. the expected number of infected sites within an LO multiplied by the expected number of LOs.

4.2.5. Time-dependent behavior

Up to now we only considered properties derived from the embedded Galton-Watson process, i.e. from the sequence of generations. Other properties which are connected with time and not with generations, like time to extinction, cannot be determined in this way. Therefore one needs information about the process generating function of the full process on two levels. There are two ways to look at this problem. One could interprete LO's as age-dependend particles, which leads to a general (Crump–Mode–Jagers) branching process [18]. This approach is suggested by F. Ball [3]. Instead we will look at it as a multitype branching process [2] with infinitely many types. The numbering of the types is obvious: a particle of type i

is an LO with i infected sites, $i = 0, 1, 2, ...$ Let $\underline{s} = (s_0, s_1, s_2, ...)$ be an infinite dimensional vector of real variables s_i, and

$$F(\underline{s}; t) = F(s_0, s_1, s_2, \dots ; t)$$

be the process generating function. A particle of type i may have a short range contact at rate $i\overline{\beta}_s$, a long range contact at rate $i\overline{\beta}_l$, it may be observed at rate $i\overline{\sigma}$ or the site may recover spontaneously at rate $i\overline{\mu}$. Hence the time until some event happens is exponentially distributed at rate a_i,

$$a_i = i(\overline{\beta}_s + \overline{\beta}_l + \overline{\sigma} + \overline{\mu}).$$

If a short range infection takes place, one particle of type i becomes a particle of type $i+1$ while a long range contact creates a new particle of type one. Furthermore, the observation changes the type number to zero. Hence we obtain the infinitesimal generating function

$$u^i(\underline{s}) = i[\overline{\sigma}s_0 + \overline{\beta}_l s_1 + \overline{\mu}s_{i-1} - (\overline{\beta}_s + \overline{\sigma} + \overline{\mu})s_i + \overline{\beta}_s s_{i+1}],$$

and therefore

$$\partial_t F = \sum_{i=0}^{\infty} u^i \partial_{s_i} F = \sum_{i=0}^{\infty} i[\overline{\sigma}s_0 + \overline{\mu}s_{i-1} - (\overline{\beta}_s + \overline{\sigma} + \overline{\mu})s_i + \overline{\beta}_s s_{i+1}]\partial_{s_i} F, \; F(\underline{s}; t) = s_1.$$

Defining the operator $\mathscr{L}$ by

$$\mathscr{L} = \sum_{i=0}^{\infty} i[\overline{\sigma}s_0 + \overline{\mu}s_{i-1} - (\overline{\beta}_s + \overline{\sigma} + \overline{\mu})s_i + \overline{\beta}_s s_{i+1}]\partial_{s_i},$$

the equation for F reads

$$\partial_t F = \mathscr{L}F + \overline{\beta}_l s_1 \sum_{i=0}^{\infty} i\,\partial_{s_i} F.$$

To obtain a better representation of the solution, we look again at generations. Let

$$\partial_t F^0 = \mathscr{L}F^0, \qquad F^0(\underline{s}; t) = s_1,$$

$$\partial_t F^n = \mathscr{L}F^n + \overline{\beta}_l s_1 \sum_{i=0}^{\infty} i\,\partial_{s_i} F^{n-1}, \qquad F^n(\underline{s}; t) = 0, \quad n = 1, 2, ...$$

Then F^0 describes the primary infected particles, and F^n the nth generation of particles. The generating function F is just the sum of the functions F^n,

$$F(\underline{s}; t) = \sum_{n=0}^{\infty} F^n(\underline{s}; t).$$

In order to derive a recursion formula we solve the equation

$$\partial_t G(\underline{s}; t) = \mathscr{L}G(\underline{s}; t), \qquad G(\underline{s}; 0) = G_0(\underline{s}), \tag{13}$$

for some smooth initial condition $G_0(\underline{s})$. Let $G^m(\underline{s}; t)$ be the solution for $G_0(\underline{s}) = s_m$. In some sense, we already know this solution, because G^m describes the fate of a single LO starting at time $t = 0$ with m infected sites, i.e. with φ defined in (5),

$$G^m(\underline{s}; t) = \sum_{i=0}^{\infty} s_i \frac{1}{i!} \partial_s^i \left[\varphi(s, t) + 1 - \varphi(1, t)\right]^m \Big|_{s=0}.$$

Since $F^0(\underline{s}; 0) = s_1$, it follows that $F^0(\underline{s}; t) = G^1(\underline{s}; t)$. Defining

$$\underline{G}(\underline{s}; t) := \left(G^0(\underline{s}; t), G^1(\underline{s}; t), G^2(\underline{s}; t), \ldots\right),$$

it follows for the initial value problem (13) that

$$G(\underline{s}; t) = G_0(\underline{G}(\underline{s}; t)).$$

With Duhamel's principle we rewrite the inhomogeneous systems for F^k as

$$F^k(\underline{s}; t) = \overline{\beta}_l \int_0^t G^1(\underline{s}; t - \tau) \sum_{i=0}^{\infty} i \, \partial_{s_i} F^{k-1}(\underline{G}(\underline{s}; t - \tau); \tau) \, d\tau. \qquad (14)$$

This formula gives an explicit expression for $F(\underline{s}, t)$, since we know F^0, and F^k can be contructed out of F^{k-1}. Furthermore, LOs are not likely to grow very much, i.e. for practical purposes it is possible to restrict the number of states from an infinite number to a relatively small number. Alike, it is possible to restict the effective live time of an LO from an infinite time to a finite maximal live span. These restrictions yield a finite sum as well as a finite integral in equation (14), which make it well suited for numerical methods to approximate the process generating function.

4.2.6. When is the population disease-free?

Assume that for a time interval Δt no LO is observed. If one wants to decide whether the population is disease free or not, one has to estimate the probability that infected sites were able to stay unobserved for a time Δt,

$$\begin{aligned} &P(\#\text{infected sites} > 0 \text{ at time } t \mid \text{no observations in } (t - \Delta t, t]) \\ &= \sum_{i=1}^{\infty} P(\{\#\text{inf.} > 0 \text{ at time } t\} \text{ and } \{\#\text{inf.} = i \text{ at time } t - \Delta t\} \mid \\ &\qquad \text{no observ. in } (t - \Delta t, t]) P(\#\text{inf.} = i \text{ at time } t - \Delta t). \end{aligned}$$

Starting at time $t = 0$ with i infected sites and assuming one LO, we compute for one LO the probability

$$\begin{aligned} &P(\#\text{infected sites} > 0 \text{ at time } \Delta t \mid \text{no observations up to time } \Delta t) \\ &= \frac{P(\{\#\text{infected sites} > 0 \text{ at time } \Delta t\} \cap \{\text{no observations up to time } \Delta t\})}{P(\text{no observations up to time } \Delta t)} \\ &= \frac{P(\#\text{infected sites} > 0 \text{ at time } \Delta t)}{P(\text{no observations up to time } \Delta t)} = \frac{\varphi^i(1, \Delta t) - \varphi^i(0, \Delta t)}{\varphi^i(1, \Delta t)}. \end{aligned}$$

Since $\varphi(1, \Delta t) > \varphi(0, \Delta t)$, the latter function is increasing in i. Thus

$$\begin{aligned}
&P(\#\text{infected sites} > 0 \text{ at time } t \mid \text{no observations in } (t - \Delta t, t]) \\
&\leq (\varphi(1, \Delta t) - \varphi(0, \Delta t))/\varphi(1, \Delta t) \sum_{i=0}^{\infty} P(\#\text{inf.} = i \text{ at time } t - \Delta t) \\
&= (\varphi(1, \Delta t) - \varphi(0, \Delta t))/\varphi(1, \Delta t) \\
&\sim \frac{(z_+ - z_-)^2}{z_+ z_- (z_+ - 1)} e^{-\Lambda \Delta t} \quad \text{for} \quad \Delta t \to \infty,
\end{aligned}$$

where Λ and $z_\pm$ are defined in (18). Of course, this estimate is very rough. Taking the sequence of observations into account, it may be possible to derive much better bounds for the probability that no infected site exists any more.

4.2.7. Comparison of the spatially structured model and the caricature

In Section 4.1.3 we already identified the rates $\overline{\beta}_s$, $\overline{\sigma}$ and $\overline{\mu}$ with parameters of the particle model. Here, we define in addition the rate $\overline{\beta}_l$,

$$\overline{\beta}_l := \frac{\gamma}{\psi_m + \gamma} \beta_l.$$

This time a correction with a factor θ is not necessary, at least not in the subcritical case: In [4] it is shown that for subcritical epidemic processes in a large enough population, the approximation with a branching process becomes exact. In the supercritical case the agreement holds only up to a time T, that grows logarithmically with population size.

5. Comparison of mass and ring vaccination

For sake of simplicity, we assume $\alpha = 0$ throughout this section. The aim is to compare mass and ring vaccination. We define a control strategy as a pair of rates (ψ_m, σ), i.e. we choose a mass vaccination rate and an observation rate. The question of how to determine such a control strategy in an optimal way comes forward immediately. In order to answer this question, one has to pin down a concept for optimality.

One possible approach is to concentrate on the costs only. The idea is to choose a certain time horizon T, to add up the costs for the control strategy (resulting from the number of vaccinations etc.) and the expected costs caused by outbreaks of FMD up to the time T, and to minimize these total costs [27, 28]. Though this point of view may be natural, especially for agricultural problems, it is very hard to find realistic estimates especially of the expected costs due to outbreaks of FMD.

Here, we use another approach: Consider two strategies, (ψ_m^1, σ^1) and (ψ_m^2, σ^2). It is obvious that for $\psi_m^1 < \psi_m^2$ and $\sigma^1 < \sigma^2$, the second strategy protects the population better than the first. But, since also the effort of (ψ^2, σ^2) is higher than that of (ψ^1, σ^1), it is not appropriate to compare these two strategies directly. To overcome this problem, only strategies which guarantee the same level for R_{LO}

are considered, and – within this class – the costs are minimized. This concept is frequently used in the literature, see for example [1,17,13,16,20,21]. The idea is to guarantee a certain stability of the uninfected situation at lowest costs. To realize this concept, we first define costs for observation and mass vaccination.

Costs for observations: Let N be the total number of farms in the system and c_1 the average costs for one observation. We define the costs for the observations per time unit as

$$C_o(\sigma) = c_1 \sigma N. \tag{15}$$

Note, that c_1 will be very small, since one "observation" corresponds basically to the fact that the farmer looks after his cattle from time to time. Costs basically arise if the veterinarian is called in because of suspicious animals.

Costs for mass vaccination: Let c_2 be the average costs for vaccinating the cattle of one farm. Then the costs for mass vaccination read

$$C_m(\psi_m) = c_2 \frac{\psi_m}{\gamma + \psi_m} N. \tag{16}$$

Now we fix R_{LO}, i.e. ask for all strategies (ψ_m, σ) with $R_{LO} = R_*$, for some given constant R_*. According to Section 4.2.7 we have $\overline{\beta}_l = \beta_l \gamma/(\gamma + \psi_m)$. Since $\alpha = 0$, i.e. $\overline{\mu} = 0$, the expression for R_{LO} (11) becomes fairly simple

$$R_* = R_{LO} = \left(\frac{\gamma}{\gamma + \psi_m} \beta_l \right) \Big/ \sigma \qquad \Rightarrow \qquad \sigma = \left(\frac{\gamma}{\gamma + \psi_m} \beta_l \right) \Big/ R_*.$$

Hence, the total costs for the control strategy (ψ_m, σ) under the condition $R_{LO} = R_*$ reads

$$\begin{aligned} C_o(\sigma) + C_m(\psi_m) &= c_1 \sigma N + c_2 \frac{\psi_m}{\gamma + \psi_m} N \\ &= c_1 \frac{\gamma}{\gamma + \psi_m} \beta_l N / R_{LO} + c_2 \frac{\psi}{\gamma + \psi_m} N \\ &= \frac{c_1 \gamma \beta_l / R_{LO} + c_2 \psi_m}{\gamma + \psi_m} N. \end{aligned}$$

This function is increasing in ψ_m if $c_2 - c_1 \beta_l / R_{LO} > 0$ and decreasing otherwise.

Result: *If $c_2 > c_1 \beta_l / R_*$, then all effort should go into ring vaccination. Otherwise all effort should be used for mass vaccination.*

Since in general c_1 as well as β_l are small, these considerations seem to indicate that in our situation ring vaccination is better suited than mass vaccination to guarantee a certain stability of the uninfected situation. This result is somehow astonishing, since herd immunity is lost without mass vaccination. The reason may be the fact that we consider the uninfected situation only. Here it is cheaper to react fast on immigration of the disease than to protect the whole population all the time.

6. Discussion

We developed a particle model for FMD and ring vaccination. This model assumes an SIRS–type infectious disease that takes into account especially the contact structure of FMD. An SEIRS–type model would be more appropriate, but complicates the mathematical structure. Up to now a square lattice was used for simulations. In future work the stability of the results against different topologies of the graph will be checked. Simulations of the particle model showed similar characteristics as the outbreak near Hannover 1987/88. Note, that this outbreak took place in a vaccinated population. It is possible that properties are different in totally naive populations.

Since the particle model cannot be analyzed directly, we derived a linear branching process that approximates the particle model in certain parameter regions. The nonlinear aspects of the particle system are summerized in one parameter. This parameter was chosen *ad hoc*. Simulations show good agreement. However, it is the aim of future work to investigate the approximation properties in more detail. Especially the interplay between size of outbreak, correlations between infected particles and nonlinearity are interesting. For the branching process, it is possible to derive many interesting measures analytically like the reproduction number or the number of infected, observed farms.

The last section compared mass and ring vaccination. The chosen approach was not to minimize the total costs for control measures and disease but to minimize the costs of strategies which guarantee a certain level for the reproduction number. Here, ring vaccination seems to be superior to mass vaccination. However, we emphasize that the model was developed for the case of a vaccinated population and it has to be checked again for totally naive situations.

A. Computation of generating functions

Since the computation of generating functions is rather standard and in some case somewhat lengthy, some of these derivations are shifted to this appendix.

A.1. Generating function for one single LO

Assuming for the generating function $u(x,t)$ the form

$$u(x,t) = \sum_{i=0}^{\infty} x^i p_i(t). \qquad u(x,t)|_{t=0} = x^m,$$

this function satisfies the partial differential equation

$$\begin{aligned} \partial_t u &= x^0 \overline{\mu} p_1 - (\overline{\mu} + \overline{\beta}_s + \overline{\sigma}) \sum_{i=1}^{\infty} i x^i p_i + \overline{\beta}_s \sum_{i=1}^{\infty} (i-1) x^i p_{i-1} \\ &\quad + \overline{\mu} \sum_{i=1}^{\infty} (i+1) x^i p_{i+1} \\ \Rightarrow \quad 0 &= \partial_t u - [\overline{\beta}_s x^2 - (\overline{\mu} + \overline{\beta}_s + \overline{\sigma}) x + \overline{\mu}] \partial_x u. \end{aligned} \tag{17}$$

Let $Q(x)$ be the polynomial

$$Q(x) = \overline{\beta}_s x^2 - (\overline{\mu} + \overline{\beta}_s + \overline{\sigma})x + \overline{\mu}.$$

The characteristic equation of the partial differential equation reads $\frac{d}{dt}x = Q(x)$, $x(0) = x_0$. The roots $z_\pm$ of $Q(z)$ are

$$\Lambda := \sqrt{(\overline{\mu} + \overline{\beta}_s + \overline{\sigma})^2 - 4\overline{\beta}_s\overline{\mu}}, \quad z_\pm := (\overline{\mu} + \overline{\beta}_s + \overline{\sigma} \pm \Lambda)/(2\overline{\beta}_s). \quad (18)$$

Separation of the variables yields

$$t = \int_{x_0}^{x} \frac{1}{Q(y)} dy = \frac{1}{\Lambda} \{\log(z_+ - x) - \log(z_+ - x_0) - \log(z_- - x) + \log(z_- - x_0)\}$$

i.e.

$$x(t; x_0) = \frac{x_0(z_+ - z_- e^{\Lambda t}) - (z_+ z_-(1 - e^{\Lambda t}))}{(z_+ e^{\Lambda t} - z_-) + x_0(1 - e^{\Lambda t})}.$$

Thus we obtain for $m = 1$ that the generating function assumes the form (5).

A.2. Generating function for the embedded Galton-Watson process of the whole process

The generating function $u = \sum_{i=0}^{\infty} \sum_{j=0}^{\infty} x^i y^j \tilde{p}_i^j(t)$ satisfies the partial differential equation

$$\partial_t u = [\overline{\beta}_s x^2 - (\overline{\mu} + \overline{\beta}_s + \overline{\sigma} + (1 - y)\overline{\beta}_l)x + \overline{\mu}]\partial_x u, \quad u(x, y, 0) = x.$$

Let $Q(x) = \overline{\beta}_s x^2 - (\overline{\mu} + \overline{\beta}_s + \overline{\sigma} + (1 - y)\overline{\beta}_l)x + \overline{\mu}$. The characteristic equation of the partial differential equation reads $\frac{d}{dt}x = Q(x)$, $x(0) = x_0$. The roots $z_\pm(y)$ of $Q(z)$ are

$$z_\pm(y) := [\overline{\mu} + \overline{\beta}_s + \overline{\sigma} + (1 - y)\overline{\beta}_l \pm \Lambda(y)]/(2\overline{\beta}_s), \quad (19)$$

$$\Lambda := \sqrt{(\overline{\mu} + \overline{\beta}_s + \overline{\sigma} + (1 - y)\overline{\beta}_l)^2 - 4\overline{\beta}_s\overline{\mu}}. \quad (20)$$

Note that $z_\pm(1) = z_\pm$ and $\Lambda(1) = \Lambda$, where $z_\pm$ and Λ are defined in equation (18). Separation of variables yields

$$t = \int_{x_0}^{x} \frac{1}{Q(z)} dz = \frac{1}{\Lambda}(y) \{\log(z_+ - x) - \log(z_+ - x_0) - \log(z_- - x) + \log(z_- - x_0)\}$$

i.e.

$$x(t; x_0) = \frac{x_0(z_+ - z_- e^{\Lambda(y)t}) - z_+ z_-(1 - e^{\Lambda(y)t})}{(z_+ e^{\Lambda(y)t} - z_-) + x_0(1 - e^{\Lambda(y)t})}.$$

Thus we obtain expression (8) for $u(x, y, t)$. Hence $\tilde{p}_0^j = \frac{1}{j!}\partial_y^j u(0, y, t)|_{y=0}$ and

$$\sum_{i=0}^{\infty} i\,\tilde{p}_i^j(t) = \sum_{i=0}^{\infty} i\,\frac{1}{i!j!}\partial_x^i\partial_y^j u(x, y, t)\Big|_{x=0,\,y=0} = \frac{1}{j!}\partial_y^j\partial_x e^{\partial_x} u(x, y, t)\Big|_{x=0,\,y=0}$$
$$= \frac{1}{j!}\partial_y^j\partial_x u(x, y, t)\Big|_{x=1,\,y=0}.$$

We obtain the expression for $\overline{p}_j$

$$\overline{p}_j = \lim_{t\to\infty}\frac{1}{j!}\partial_y^j\left(u(0, y, t) + \overline{\sigma}\int_0^t \partial_x\, u(x, y, \tau)\Big|_{x=1} d\tau\right)\Big|_{y=0}.$$

Let $\phi(y)$ be the generating function for the Galton-Watson process. Since u is smooth and the limit $t \mapsto \infty$ converges fast enough, we are allowed to exchange the time limit and the derivative with respect to y, i.e. $\phi(y)$ can be written as

$$\phi(y) = u(0, y, \infty) + \overline{\sigma}\int_0^{\infty} \partial_x\, u(x, y, \tau)\Big|_{x=1} d\tau.$$

Since $\Lambda(0) > 0$ the first term yields

$$\lim_{t\to\infty} u(0, y, t) = z_-(y)$$

and the second term is

$$\int_0^{\infty} \partial_x\, u(x, y, \tau)\Big|_{x=1} d\tau$$
$$= \int_0^{\infty} \partial_x\left(\frac{x(z_+ - z_- e^{\Lambda(y)t}) - z_+ z_-(1 - e^{\Lambda(y)t})}{z_+ e^{\Lambda(y)t} - z_- + x(1 - e^{\Lambda(y)t})}\right)\Big|_{x=1} dt$$
$$= \int_0^{\infty} \frac{(z_+ - z_-)^2 e^{\Lambda(y)t}}{[z_+ e^{\Lambda(y)t} - z_- + 1 - e^{\Lambda(y)t}]^2}\, dt$$
$$= \frac{(z_+ - z_-)^2}{\Lambda(y)}\int_1^{\infty} \frac{1}{[(z_+ - 1)\tau - (1 - z_-)]^2}\, d\tau = \frac{1}{\overline{\beta}_s}\,\frac{1}{z_+ - 1}.$$

where we used the transformation $\tau = e^{\Lambda(y)t}$. Hence the generating function $\phi(y)$ is given by (9).

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