

Mathematical Statistics Stockholm University

Competing epidemics in closed populations

Åke Svensson GianPaolo Scalia Tomba

Research Report 2001:8

ISSN 1650-0377

Postal address:

Mathematical Statistics Dept. of Mathematics Stockholm University SE-106 91 Stockholm Sweden

Internet:

http://www.matematik.su.se/matstat

Competing epidemics in closed populations

Åke Svensson

University of Stockholm

and

Gian-Paolo Scalia-Tomba

University of Rome

September 19, 2001

Abstract

If two infectious agents that causes cross-immunity spread simultaneously in a population they will compete for susceptible individuals. The outcome of the competition will depend on the strength and the speed with which the agents spread. Asymptotically, in a large population, a faster agent will be undeterred by a slower agent. However, if the agents spread equally fast, the proportion of the total number of infected that is infected by a particular of the two agents is a non–degenerate random variable. Its value depends on the early diffusion of the epidemic. It is shown how the distribution of this random variable can be calculated by numerical methods.

1. Introduction

We consider the simultaneous spread of two distinct infectious agents in a closed population. The setting is as follows. At time t = 0 the population consists of n individuals, all susceptible to both infections. At that time infected individuals enters the population from outside. Some of these individuals spread agent 1 and other agent 2. The two infectious agents interact in such a way that an individual which has been infected by one of the two agents can not be reinfected by any of the agents. Since the two agents infer immunity towards each other they will compete for susceptible individuals. Agents that are strong (i.e. has large total infectivity) and fast (i.e. spreads the infectivity shortly after being infected) have an advantage in this competition. Our aim is to study how these properties of the agents decide the relative outcome of the two epidemics.

The spread is assumed to follow the rules of a general epidemic model (cf. Bailey (1975) and Lefévre (1990)). This means that each infected individual is infectious with a constant infectivity during an exponentially distributed infectious time. After this the infected individuals are non–infectious and immune, i.e. they can not be re-infected. Important features of this model is that there are no latency times and no variation of infectivity during the infectious period.

We will study the proportion of the population that is finally infected and the distribution of the infections between the two agents. The main results are asymptotic, i.e., they give approximations that are valid in large populations. There are a number of studies on how cross immunity between different strains of infectious agents influences the equilibrium in a dynamic population (cf White et al. (1998), Adler and Brunet (1991), and Lin et al. (1999)). These studies are focused on properties of solutions to differential equations. In this paper we will study the non equilibrium situation where the an epidemic spread is started by a small number of infected persons entering a totally susceptible (closed) population. This force us to consider a non stationary situation where the randomness at the early stage of the spread has a decisive role for the progress of the epidemic. The paper Kendall and Saunders (1983) studies a situation similar to the one studied in this paper. However, they consider an epidemic that is started when a small proportion of the population being infected by the competing agents. Also in this situation the analysis is carried through by studying solutions to differential equations.

The presentation of the models and the proofs of the results are based on general theory for counting processes and limit theorems for martingales. An introduction to methods of this kind applied to infectious disease modelling can be found in Becker (1989) and in Svensson (1993).

In section 2 the notation is introduced and the epidemic model is defined with the use of counting processes. An equation of balance that the epidemic has several the possible final states is derived in section 3. The speed at which the infections spread initially is an important factor that influence the outcome of the competition between the agents. In fact, this decides which of the possible final states is attained. Section 4 contains a detailed analysis of the progress of the epidemic through four phases. This analysis is the basis for the derivation of asymptotic distributions for the final sizes of the two agents, the final size of the sum of the agents, and the final proportion of the infected by the two agents in section 5. The speed of convergence to the asymptotic results are slow.

In a forthcoming paper we will extend the results to models where the parameters that describe infectivity depend on the population size.

2. The general epidemic model with two infectious agents

The progress of the epidemic can be traced through counting processes that count the number of infected and the number of non–infectious immune individuals.

The two types of infections are distinguished by the subscripts 1 and 2. In order to indicate the dependence on the population size we will use n as superindex. Let $N_i^n(t)$, i = 1, 2, count the number of individuals in the population that are infected, by a specific agent, up till time t. This means that $N^n(t) = N_1^n(t) + N_2^n(t)$ is the number of individuals infected by any of the agents. Furthermore let $D_i^n(t)$ count the number of individuals in the population that, at time t, are non-infectious and immune after an infection with agent i.

We will assume that the spread starts at time t = 0. At that time C_i individuals spreading infectious agent *i* enters the population. Thus at time *t* the number of individuals actively spreading agent *i* is

$$E_i^n(t) = N_i^n(t) - D_i^n(t) + C_i, (2.1)$$

i = 1, 2.

The lengths of infectious periods are assumed to be independent and exponentially distributed with mean length $1/\gamma_i$, i = 1, 2. During the infectious period the (instantaneous) infectivity of an infectious individual is measured by the parameter α_i , i = 1, 2.

The epidemic model is defined by the intensities of the counting processes involved. We will assume that the intensities of the counting processes N_i^n are

$$\lambda_i^n(t) = \alpha_i (1 - N^n(t-)/n) E_i^n(t-), \qquad (2.2)$$

and that the intensities of the counting processes D_i^n are

$$\mu_i^n(t) = \gamma_i E_i^n(t-), \qquad (2.3)$$

i = 1, 2.

The strength of an infectious agent is measured as the mean amount of infectivity spread by an infectious individual. In the model considered here the infectious agents have the strengths

$$\theta_i = \alpha_i / \gamma_i \tag{2.4}$$

i = 1, 2. The strength is, in this case, equal to the basic reproduction number. This parameter is usually denoted by R_0 and can be interpreted as the expected number of individuals one infectious individual infects in a totally susceptible population. Throughout this paper we will assume that agent 1 is stronger than agent 2 and that both agents have strengths (R_0) greater than 1, i.e., $\theta_1 \ge \theta_2 > 1$.

When two infectious agents spreads simultaneous in a population it is not sufficient to consider their strengths. In such cases the speed of the spread is of importance. For this reason we consider

$$\rho_i = \alpha_i - \gamma_i, \tag{2.5}$$

i = 1, 2. As we shall see, ρ_i is related to the rate with which the agent spreads initially in a totally susceptible population.

3. The final sizes

Since the population is closed the epidemics will die out in finite time. The proportion of the population that eventually are infected by the agents are

$$\pi_i = N_i^n(\infty)/n,\tag{3.1}$$

i = 1, 2. These numbers are referred to as the final size of the agents. The total final size, i.e., the proportion of individuals finally infected by either of the agents is

$$\pi = \pi_1 + \pi_2. \tag{3.2}$$

We will also be interested the proportion of infections that comes from the two agents. For this reason we define the ratio

$$P = \frac{\pi_1}{\pi_1 + \pi_2}.$$
 (3.3)

This ratio will be called the final proportion.

In the general epidemic model with only one infectious agent it is well-known that the distribution of the final size can have a bimodal behavior. If the strength of the agent exceeds 1 the epidemic will either be small or reach a substantial proportion of the population. The final size will be one of two possible solutions to an equation of balance. With two infectious agents the situation is more complicated. However, also in this case there is a equation of balance, which is given in theorem 3.1 below.

First we will prove a lemma that will be used repeatedly in the following.

LEMMA 3.1. Let M^n be a sequence of martingales with means 0 and let t^n be a sequence of stopping times then

(a) $E([M^n](t^n)) \to 0 \text{ as } n \to \infty \text{ implies that}$

$$M^n(t^n) \to 0$$

in probability as $n \to \infty$, and

(b) $[M^n](t^n) \to 0$ and $\sup_{s < t^n} |\Delta M^n(s)| \to 0$ in probability as $n \to \infty$ implies that

$$\sup_{s \le t^n} \mid M^n(t^n) \mid \to 0$$

in probability as $n \to \infty$.

Proof. Since $E((M^n)^2(t^n)) = E([M^n](t^n))$ proposition (a) follows from Chebyshev's inequality.

The quadratic variation $[M^n]$ L-dominates $(M^n)^2$. According to Lenglard's inequality (see Jacod and Shiryaev (1987))

$$P(\sup_{s \le t^n} (M^n)^2(s) > \epsilon) \le \frac{1}{\epsilon} [\eta + \sup_{s \le t^n} |\Delta M^n(s)|^2] + P([M^n](t^n) \ge \eta).$$
(3.4)

for any $\eta > 0$ and $\epsilon > 0$. This proves proposition (b).

THEOREM 3.1. The asymptotic distribution of $(N_1^n(\infty)/n, N_2^n(\infty)/n)$ is concentrated on the solutions to the equation

$$-\ln(1-\pi) = \theta_1 \pi_1 + \theta_2 \pi_2. \tag{3.5}$$

Proof. Since the epidemics ends in finite time

$$N_i^n(\infty) = D_i^n(\infty) + C_i,$$

i = 1, 2. For each n we can define the martingales:

$$M^{n}(t) = \int_{0}^{t} \frac{dN^{n}(s)}{n - N^{n}(s - 1)} - \theta_{1}D_{1}^{n}(t)/n - \theta_{2}D_{2}^{n}(t)/n$$

The elementary inequality

$$\int_{n-N^{n}(t)}^{n} dx/x \ge \sum_{i=0}^{N^{n}(t)-1} 1/(n-i) \ge \int_{n-N^{n}(t)+1}^{n+1} dx/x,$$
(3.6)

implies that

$$-\ln(1-\pi) - \theta_1 \pi_1 - \theta_2 \pi_2 \geq M^n(\infty)$$

$$\geq -\ln(1 - n\pi/(n+1)) - \theta_1(\pi_1 + C_1/n) - \theta_2(\pi_2 + C_2/n).$$
(3.7)

Now

$$[M^{n}](t) = \int_{0}^{t} \frac{dN^{n}(s)}{(n - N^{n}(s -))^{2}} = \sum_{i=n-N^{n}(t)+1}^{n} 1/i^{2} \leq \int_{n-N^{n}(t)}^{n} dx/x^{2} = \frac{N^{n}(t)}{n(n - N^{n}(t))}.$$
(3.8)

First observe that $[M^n]$ is uniformly bounded by $\sum_{i=1}^{\infty} 1/i^2$, for all n. Thus $M^n(\infty)$ is uniformly bounded in probability and (3.7) implies that π is uniformly bounded away from 1. From (3.8) it follows that $[M^n](\infty) \to 0$ in probability as $n \to \infty$. Lemma 3.1 implies that $M^n(\infty) \to 0$. Together with (3.7) this proves the theorem.

We will say that an agent has asymptotically large (or epidemic) spread if has a final size is positive. Equation (3.5) gives the possible final sizes. First consider the equation

$$-\ln(1-\pi) = \theta_i \pi,$$

i = 1, 2. This equation has always the solution $\pi = 0$. Since $\theta_i > 1$ it also has a positive solution, $\overline{\pi}_i$. Evidently $(\pi_1, \pi_2) = (0, 0), (\overline{\pi}_1, 0)$ and $(0, \overline{\pi}_2)$ are possible solutions of (3.5). These solution corresponds to cases where none of the agents or only one of the agents have



Figure 3.1. Solutions of the balance equation for which both π_1 and π_2 are positive, which are possible final sizes. Here $\theta_1 = 2$ and $\theta_2 = 1.25$.

epidemic spread. However, there are also solutions such that both π_1 and π_2 are positive. These solutions define a curve in the (π_1, π_2) -plane. Elementary calculations shows that these solutions all lies on a concave curve connecting $(0, \overline{\pi}_2)$ and $(\overline{\pi}_1, 0)$. It is (at least heuristically) obvious that agent 2 can never spread more in case agent one also spreads in the population that if it were on its own. Similarly the spread of agent one will never be less than if agent 2 has optimal spread. This makes a further restriction on the possible final states for (π_1, π_2) .

Let $\underline{\pi}_1$ be the largest solution of

$$-\ln(1 - \pi_1 - \overline{\pi}_2) = \theta_1 \pi_1 + \theta_2 \overline{\pi}_2.$$
(3.9)

(as a function of π_1), An elementary analysis reveals that $\underline{\pi}_1 > 0$ if and only if $\theta_1 > 1/(1-\overline{\pi}_2)$ or equivalently

$$\theta_2 < \frac{\ln(\theta_1)}{1 - 1/\theta_1}.\tag{3.10}$$

Positive final sizes π_1 are contained in the interval $[\underline{\pi}_1, \overline{\pi}_1]$.

In figures 3.1 and 3.2 the possible solutions are indicated. In the first case $\underline{\pi}_1 > 0$ and in the second case $\underline{\pi}_1 = 0$.

4. The phases of an epidemic

To find out how large part of the total epidemic that is caused by the two agents we will divide the progress of the epidemic into four phases. The division is essentially the same as used by Barbour (1975) in his study of the duration of the general epidemic.



Figure 3.2. Solutions of the balance equation for which both π_1 and π_2 are positive., which are possible final sizes. Here $\theta_1 = 2$ and $\theta_2 = 1.5$.

During the initial phase the infectivity builds up in the population but still only a negligible part of the population is infected. In this paper the initial phase is defined to last until $\ln(n)^a$ individuals are infected. During the initial phase there is no interference between the spread of the two agents and the spread can be approximated by independent birth-and-death processes. Asymptotically this phase will last for a considerable time. The duration is of order $\ln(n)$. During the initial phase it is decided if the spread of an agent will be asymptotically large (i.e. $\pi_i > 0$) or not.

During the second phase the number of infected individuals grows to ϵn , where ϵ is a small positive number. The duration of this transitional phase is of size $\ln(\ln(n))$.

After the transitional phase follows an epidemic phase with rapid spread of the epidemic. At the start of this phase a small proportion of the population is infected and at the end a proportion of infected is close to a solution of (3.5). If both agents begins to spread in the initial phase there are two possibilities depending on the relative speeds and strengths of the two agents. One possibility is that the all epidemic spread takes place during a short time span, whose length is uniformly bounded independent of the population size. Another possibility, which takes place if and only if $\rho_1 < \rho_2$ and the inequality (3.10) holds, is that there are two distinct time intervals for epidemic spread. First the fastest agent approaches its final size, $\overline{\pi_2}$. During this time the lower, but stronger, agent 1 still has only infected a almost negligible proportion of the population. The spread of agent 1 passes through a transition phase and an epidemic phase after which it almost reaches its final size π_1 .

Finally there is a fading–out phase during which the spread stops due to lack of susceptible individuals in the population.

4.1 The initial phase

In the initial phase the two agents will not interfere with or deter each others spread. They can be studied separately. Technically we will approximate the spread of in the early phase by independent birth–and–death–processes.

Let $N_i^{(\epsilon)}(t)$ and $D_i^{(\epsilon)}(t)$ be counting processes with intensities

$$\lambda_i^{(\epsilon)}(t) = \alpha_i (1-\epsilon) E_i^{(\epsilon)}(t-), \qquad (4.1)$$

and

$$\mu_i^{(\epsilon)}(t) = \gamma_i E_i^{(\epsilon)}(t-) \tag{4.2}$$

where

$$E_i^{(\epsilon)}(t) = N_i^{(\epsilon)}(t) - D_i^{(\epsilon)}(t) + C_i,$$
(4.3)

i = 1, 2.

This means that $(N_i^{(\epsilon)}, D_i^{(\epsilon)})$, i = 1, 2 are two independent birth-and-death processes with birth intensities $\alpha_i(1 - \epsilon)$ and death intensities γ_i .

LEMMA 4.1. The inequalities

$$N_i^{(\epsilon)}(t) \le N_i^n(t) \le N_i^{(0)}(t), \tag{4.4}$$

$$D_i^{(\epsilon)}(t) \le D_i^n(t) \le D_i^{(0)}(t),$$
(4.5)

and

$$E_i^{(\epsilon)}(t) \le E_i^n(t) \le E_i^{(0)}(t)$$
 (4.6)

hold (in distribution) for i = 1, 2 and all t such that $N^n(t)/n \leq \epsilon$.

Proof. The proof is based on a coupling argument. We will construct a probability space on which all processes are defined and on which the inequalities hold for sure.

Let $(N_i^{(0)}, D_i^{(0)})$, i = 1, 2, be two independent birth-and-death processes. To the probability space where these processes are defined we add four independent sequences U_{i1}, U_{i2}, \ldots and V_{i1}, V_{i2}, \ldots of independent uniformly distributed random variables, i = 1, 2.

Let N_i^n jump each time the process $N_i^{(0)}$ jumps and

$$U_{iN_i^{(0)}(t)} \le \frac{(1 - N^n(t-)/n)E_i^n(t-)}{E_i^{(0)}(t-)}$$

and let D_i^n jump each time the process $D_i^{(0)}$ jumps and

$$V_{iD_i^{(0)}(t)} \le \frac{E_i^n(t-)}{E_i^{(0)}(t-)}$$

In the same way let $N_i^{(\epsilon)}$ jump each time the process $N_i^{(0)}$ jumps and

$$U_{iN_i^{(0)}(t)} \le \frac{(1-\epsilon)E_i^{(\epsilon)}(t-)}{E_i^{(0)}(t-)}$$

and let $D_i^{(\epsilon)}$ jump each time the process $D_i^{(0)}$ jumps and

$$V_{iD_i^{(0)}(t)} \leq \frac{E_i^{(\epsilon)}(t-)}{E_i^{(0)}(t-)}$$

With this construction $E_i^n(t) \leq E_i^{(0)}(t)$ for all t since if equality holds at some time t then $D_i^{(0)}$ jumps simultaneously with D_i^n and N_i^n jumps only if $N_i^{(0)}$ jumps. After the next jump the equality still holds or $E_i^n(t) < E_i^{(0)}(t)$.

From a similar argument it follows that $E_i^{(\epsilon)}(t) \leq E_i^n(t)$ for all t. This proves (4.6). Inequalities (4.4) and (4.5) then follow directly from construction.

We will say that a random variable has a $L(k, \theta)$ -distribution if it is the sum of k independent identically distributed random variables Z_1, \ldots, Z_k with distribution functions

$$P(Z_j \le z) = \frac{1}{\theta} I(z \ge 0) + (1 - \frac{1}{\theta})(1 - \exp\{-(1 - \frac{1}{\theta})z\}).$$
(4.7)

The distribution of Z_j is a mixture of a distribution with all mass at 0 and an exponential distribution such that the expectation of Z_j equals 1.

It is well-known that the speed at which the birth-and death processes grows is related to $\rho_i = \alpha_i - \gamma_i$. We will need the following lemma:

Lemma 4.2. As $t \to \infty$

$$E_i^{(0)}(t) / \exp\{\rho_i t\} \to \xi_i \tag{4.8}$$

and

$$N_i^{(0)}(t) / \exp\{\rho_i t\} \to \frac{\theta_i}{\theta_i - 1} \xi_i$$
(4.9)

almost surely where ξ_i has a $L(C_i, \theta_i)$ -distribution. Furthermore $N_i^{(0)}(\infty)$ is bounded with probability $\theta_i^{-C_i}$.

Proof. It follows from general theory of branching process that $E_i^{(0)}(t) / \exp\{\rho_i t\}$ converges almost surely, as $t \to \infty$, to a non-degenerate random variable (see Harris (1963)).

In case $C_i = 1$ the Laplace transform of $E_i^{(0)}(t) / \exp\{\rho_i t\}$ equals, (see Kendall (1948)),

$$\frac{\gamma_i (1 - e^{-\rho_i t}) + (\alpha_i e^{-\rho_i t} - \gamma_i) e^{-u \exp\{-\rho_i t\}}}{\alpha_i - \gamma_i e^{-\rho_i t} + \alpha_i (1 - e^{-\rho_i t}) e^{-u \exp\{-\rho_i t\}}}$$

As $t \to \infty$ this Laplace transform converges to

$$\frac{\rho_i + \gamma_i u}{\rho_i + \alpha_i u}$$

which is the Laplace transform of a random variable with a $L(1, \theta)$ -distribution.

If $C_i > 1$ the birth-and-death process can be regarded as the sum of C_i independent birth-and-death processes. In that case the limit distribution of $E_i^{(0)}(t)/\exp\{\rho_i t\}$, if it exists, is the convolution of C_i limit distributions.

THEOREM 4.1. N_i^n is uniformly bounded in n with probability $\theta_i^{-C_i}$, i = 1, 2, and N^n is uniformly bounded in n with probability $\theta_1^{-C_1}\theta_2^{-C_2}$.

Proof. If $N_i^n(t)/n \leq \epsilon$ for all t and some finite n then $N_i^{(\epsilon)}(t)$ is, according to Lemma 4.1, bounded for all t. This happens with probability $(\theta_i(1-\epsilon))^{-C_i}$. Thus $N_i^n(\infty)$ is bounded with a probability that is smaller than $(1/(\theta_i(1-\epsilon))^{-C_i})$.

Now $N_i^{(0)}(t)$ is bounded for all t with probability $\theta_i^{-C_i}$. According to lemma 4.1 N_i^n has the same bound.

Since ϵ can be made arbitrarily small the first part of the theorem follows. The uniform bound on $N^n = N_1^n + N_2^n$ follows since the processes $N_1^{(\epsilon)}$ and $N_2^{(\epsilon)}$ are independent as well as N_1^0 and $N_2^{(0)}$.

If $\rho_1 \neq \rho_2$ then the speed at which the two infectious agents spread differ initially. The speed at which the total epidemic grows is determined by

$$\tilde{\rho} = \max(\rho_1, \rho_2).$$

Let

$$g_n = \left(\ln(n)\right)^a,$$

for some a > 1.

LEMMA 4.3. If $t^n = \ln(n/g_n)/\tilde{\rho}$ then

$$\left(E_1^n(t^n)\left(\frac{g_n}{n}\right)^{\rho_1/\tilde{\rho}}, E_2^n(t^n)\left(\frac{g_n}{n}\right)^{\rho_2/\tilde{\rho}}\right) \to (\xi_1, \xi_2)$$
(4.10)

and

$$\left(N_1^n(t^n)\left(\frac{g_n}{n}\right)^{\rho_1/\tilde{\rho}}, N_2^n(t^n)\left(\frac{g_n}{n}\right)^{\rho_2/\tilde{\rho}}\right) \to \left(\frac{\theta_1}{\theta_1 - 1}\xi_1, \frac{\theta_2}{\theta_2 - 1}\xi_2\right)$$
(4.11)

in distribution, where ξ_1 and ξ_2 are independent random variables with distributions $L(C_1, \theta_1)$ and $L(C_2, \theta_2)$ respectively.

Proof. The proof is based on the coupling between the epidemic processes and birth–and–death processes described above.

It follows from lemma 4.2 that $N_i^{(0)}(t^n) / \exp\{\rho_i t^n\}$ is bounded in probability. Using the right-hand inequality (4.4) we find that

$$N_{i}^{n}(t^{n})/n^{\rho_{i}/\tilde{\rho}} \leq N_{i}^{(0)}(t^{n})/n^{\rho_{i}/\tilde{\rho}} = \left(N_{i}^{(0)}(t^{n})/\exp\{\rho_{i}t^{n}\}\right)g_{n}^{-\rho_{i}/\tilde{\rho}} \to 0$$
(4.12)

as $n \to \infty$.

Let $\epsilon^n = (\ln(n))^{-\tilde{a}}$, where $a \geq \tilde{a} > 1$. Then $\epsilon^n g^n \to \infty$ and $\epsilon^n t^n \to 0$ as $n \to \infty$.

It follows from (4.12) that $N^n(t^n) \leq \epsilon^n n$ with a probability that tends to 1. If this is the case lemma 4.1 implies that

$$E_i^{(\epsilon^n)}(t^n) \left(\frac{g_n}{n}\right)^{\rho_i/\tilde{\rho}} \le E_i^n(t^n) \left(\frac{g_n}{n}\right)^{\rho_i/\tilde{\rho}} \le E_i^{(0)}(t^n) \left(\frac{g_n}{n}\right)^{\rho_i/\tilde{\rho}}.$$
(4.13)

The upper bound converges to a random variable ξ_i which has a $L(C_i, \theta_i)$ -distribution (cf. lemma 4.2).

To prove that the lower bound in (4.13) has the same limit distribution we observe that

$$E_i^{(\epsilon)}(t) / \exp\{(\rho_i - \epsilon \alpha_i)t\}$$

are martingales with mean C_i . Combining this with inequality (4.6) we find that

$$\mathbb{E}\left(\left|\left(E^{(0)}(t^n) - E^{(\epsilon^n)}(t^n)\right)\right| \left(\frac{g_n}{n}\right)^{\rho_i/\tilde{\rho}}\right) = C_i(1 - e^{-\alpha_i\epsilon^n t^n}) \to 0$$

This L¹–convergence implies that

$$E_i^{(\epsilon^n)}(t^n) \left(\frac{g_n}{n}\right)^{\rho_i/\tilde{\rho}} \to \xi_i$$

in distribution as $n \to \infty$. Thus (4.10) follows from (4.13).

A similar argument shows (4.11).

We will say that an agent has large spread if $E_i^n(t^n) > 0$. A results that holds with a probability that tends to 1 on the subset $E_i^n(t^n) > 0$ is said to hold asymptotically if agent i has large spread. It may seem odd to use a definition that based on the duration of the epidemic spread rather than on its actual size. However, from lemma 4.1 and lemma 4.2 it follows that $E_i^n(t^n)$ and $N_i^n(t^n)$ are of the same size when $E_i^n(t^n) > 0$.

4.2 The transition phase

From lemma 4.3 we can derive the asymptotic distribution of the ratio $E_1^n(t^n)/E_2^n(t^n)$ in case both agents have large spread. In case $\rho_1 = \rho_2$ it is the same as the distribution of ξ_1/ξ_2 given that both ξ_1 and ξ_2 are positive. If $\rho_1 < \rho_2$ the asymptotic distribution has all mass at 0 and if $\rho_1 > \rho_2$ all mass is concentrated at ∞ .

Let

$$s_{\epsilon}^{n} = \inf\{t; N^{n}(t) \ge \epsilon n\}$$

$$(4.14)$$

The following lemma allows us to derive the distribution of $E_1^n(s_{\epsilon}^n)/E_2^n(s_{\epsilon}^n)$.

LEMMA 4.4. If $E_1(t^n) > 0$ and $E_2(t^n) > 0$ then

$$\frac{E_1^n(s_{\epsilon}^n)}{E_2^n(s_{\epsilon}^n)} \frac{E_2^n(t^n)}{E_1^n(t^n)} \exp\{(\alpha_2 - \alpha_1) \int_{t^n}^{s_{\epsilon}^n} N^n(s)/n \, ds + (\rho_1 - \rho_2)(s_{\epsilon}^n - t^n)\} \to 1$$

as $n \to \infty$

Proof. The martingale

$$\tilde{M}^{n}(t) = \int_{0}^{t} I(t > t^{n}) d(N_{1}^{n} - D_{1}^{n})(s) / E_{1}^{n}(s -)$$

$$- \int_{0}^{t} I(t > t^{n}) d(N_{2}^{n} - D_{2}^{n})(s) / E_{2}^{n}(s -)$$

$$+ (\alpha_{1} - \alpha_{2}) \int_{0}^{t} I(t > t^{n}) N^{n}(s) / n \, ds - (\rho_{1} - \rho_{2})(t - t^{n}) \vee 0 \qquad (4.15)$$

has mean 0.

The optional quadratic variation at time $t=s_{\epsilon}^{n}$ equals

$$\begin{split} [\tilde{M}^n](s_{\epsilon}^n) &= \int\limits_{0}^{s_{\epsilon}^n} \mathbf{I}(t > t^n) d(N_1^n + D_1^n)(s) / (E_1^n(s-))^2 \\ &+ \int\limits_{0}^{s_{\epsilon}^n} \mathbf{I}(t > t^n) d(N_2^n + D_2^n)(s) / (E_2^n(s-))^2 \end{split}$$

Let us do the same coupling as in lemma 4.1 but this time starting at time $t = t^n$, i.e. with $C_i = E_i^n(t^n)$. The birth-and-death process defined by $(N_i^{(\epsilon)}, D_i^{(\epsilon)})$ behaves after time t^n as the sum of C_i independent birth-and-death processes. If $\alpha_i(1 - \epsilon) > \gamma_i$ each of these processes has a positive probability to survive (and grow) indefinitely, i.e. it has at least one descendant. Let r_{ϵ} be a positive number smaller than the survival probability. According to the previous lemma $E_i^n(t^n)$ is (at least) of order $(n/g_n)^{\rho_i/\tilde{\rho}}$ if the *i*'th agent spreads. Since $E^n(t^n) \to \infty$ it follows from the law of large numbers that if $r_{\epsilon} > 0$ then

$$E_i^n(t) \ge r_\epsilon E_i^n(t^n) \tag{4.16}$$

for all $t \in [t^n, s^n_{\epsilon}]$ with a probability that tends to 1 as $n \to \infty$.

With a probability that tends to 1 as $n \to \infty$ none of the counting processes $N_i^n + D_i^n$ jumps more than $n^{\rho_i/\tilde{\rho}}$ times. This combined with the lower bound for $E_i^n(t)$ given in (4.16) implies that the quadratic variation given by (4.16) is (at most) of size $(g_n^2/n)^{\rho_i/\tilde{\rho}}$ and thus tends to 0 as $n \to \infty$. Since $|\Delta M^n(s)| \le 1/\min E_i^n(s)$ it follows from lemma 3.1 that $\tilde{M}^n(s_{\epsilon}^n) \to 0$ as $n \to \infty$.

The next step is to approximate the different terms of $\tilde{M}^n(s_{\epsilon}^n)$. Elementary calculations yield that

$$\int_{0}^{s_{\epsilon}^{n}} I(t > t^{n}) d(N_{i}^{n} - D_{i}^{n})(s) / E_{i}^{n}(s-)$$

$$= \sum_{j=E_{i}^{n}(t^{n})}^{E_{i}^{n}(s_{\epsilon}^{n})} 1/j + \int_{t^{n}}^{s_{\epsilon}^{n}} dD_{i}^{n}(s) / (E_{i}^{n}(s-)(E_{i}^{n}(s-)-1)).$$

Thus the first term on the right-hand side is approximated by $\ln(E_i^n(s_{\epsilon}^n)/E_i^n(t^n))$, cf (3.6). The second term tends to 0 as $n \to \infty$ due to the bound (4.16).

Applying the approximations above we find that

$$\ln(E_1^n(s_{\epsilon}^n)/E_1^n(t^n)) - \ln(E_2^n(s_{\epsilon}^n)/E_2^n(t^n)) + (\alpha_1 - \alpha_2) \int_0^{s_{\epsilon}^n} I(t > t^n) N^n(s)/n \, ds - (\rho_1 - \rho_2)(s_{\epsilon}^n - t^n) \lor 0 \to 0$$

as $n \to \infty$. This implies the lemma.

Lemma 4.5.

$$\lim_{\epsilon \to 0} \lim_{n \to \infty} \frac{1}{n} \int_{0}^{s_{\epsilon}^{n}} N^{n}(s) / n \, ds = 0$$
(4.17)

Proof. In the following $u_n^{(i)}$ denotes sequences of approximations such that $u_n^{(i)} \to 0$ as $n \to \infty$. The equalities are due to the fact that for any counting process Q, such that

Q(0) = 0, $\int_{0}^{t} Q(s)ds = \int_{0}^{t} (t-s)dQ(s).$ (4.18)

The inequalities comes from approximating integrals over a counting process with its compensator (and vice versa) and applying lemma 3.1. For any $t \leq s_{\epsilon}^n$

$$\int_{0}^{t} N_{i}(s) ds = \int_{0}^{t} (t-s) dN_{i}(s)$$

$$\leq \alpha_{i} \int_{0}^{t} (t-s) E_{i}(s) ds + nu_{n}^{(1)}$$

$$\leq \frac{\alpha_{i}}{\rho_{i} - \alpha_{i}\epsilon} \int_{0}^{t} (t-s) dE_{i}(s) + nu_{n}^{(2)}$$

$$= \frac{\gamma_{i}}{\rho_{i} - \alpha_{i}\epsilon} \int_{0}^{t} E_{i}(s) ds + nu_{n}^{(2)}$$

$$\leq \frac{\alpha_{i}}{(\rho_{i} - \alpha_{i}\epsilon)^{2}} E_{i}(t) + nu_{n}^{(3)}.$$

This implies that

$$\int_{0}^{s_{\epsilon}^{n}} N(s) ds \leq const(E_{1}(s_{\epsilon}^{n}) + E_{2}(s_{\epsilon}^{n}) + nu_{n}^{(4)})$$
$$\leq const(N_{1}(s_{\epsilon}^{n}) + N_{2}(s_{\epsilon}^{n}) + nu_{n}^{(4)})$$
$$\leq \epsilon n + nu_{n}^{(4)}.$$

The theorem follows directly after dividing the last relation with n.

THEOREM 4.2. If both epidemics are asymptotically large then: if $\rho_1 = \rho_2$

$$\lim_{\epsilon \to 0} \lim_{n \to \infty} \frac{E_1^n(s_{\epsilon}^n)}{E_2^n(s_{\epsilon}^n)} \to \frac{\xi_1}{\xi_2} \mid \xi_1, \xi_2 > 0,$$

where ξ_1 and ξ_2 are independent random variables with distributions $L(C_1, \theta_1)$ and $L(C_2, \theta_2)$ respectively;

if $\rho_1 < \rho_2$

$$\lim_{\epsilon \to 0} \lim_{n \to \infty} \frac{E_1^n(s_{\epsilon}^n)}{E_2^n(s_{\epsilon}^n)} \to 0;$$

if $\rho_1 > \rho_2$

$$\lim_{\epsilon \to 0} \lim_{n \to \infty} \frac{E_1^n(s_{\epsilon}^n)}{E_2^n(s_{\epsilon}^n)} \to \infty$$

Proof. According to lemma 4.3

$$\frac{E_1^n(t^n)}{E_2^n(t^n)} \exp\{(\rho_1 - \rho_2)t^n\} \to \frac{\xi_1}{\xi_2}$$

as $n \to \infty$.

The theorem is then a consequence of lemmata 4.4 and 4.5.

When studying the spread in the third or epidemic phase we will need approximations of the sizes of $N_1^n(s_{\epsilon}^n)$, $N_2^n(s_{\epsilon}^n)$, $E_1^n(s_{\epsilon}^n)$ and $E_2^n(s_{\epsilon}^n)$ when $E_1^n(s_{\epsilon}^n)/E_2^n(s_{\epsilon}^n)$ equals some fixed ratio ν . Observe that at time $t = s_{\epsilon}^n$ the total number of infected, i.e. $N_1^n(t) + N_2^n(t) = \epsilon n$.

THEOREM 4.3. If $\frac{E_1^n(s_{\epsilon}^n)}{E_2^n(s_{\epsilon}^n)} = v$ then as $n \to \infty$ and $\epsilon \to 0$

$$\frac{N_1^n(s_{\epsilon}^n)}{\epsilon n} \to \frac{v\alpha_1/\rho_1}{v\alpha_1/\rho_1 + \alpha_2/\rho_2}$$
(4.19)

$$\frac{N_2^n(s_{\epsilon}^n)}{\epsilon n} \to \frac{\alpha_2/\rho_2}{v\alpha_1/\rho_1 + \alpha_2/\rho_2} \tag{4.20}$$

$$\frac{E_1(s_{\epsilon}^n)}{\epsilon n} \to \frac{v}{v\alpha_1/\rho_1 + \alpha_2/\rho_2}$$
(4.21)

$$\frac{E_2(s_{\epsilon}^n)}{\epsilon n} \to \frac{1}{v\alpha_1/\rho_1 + \alpha_2/\rho_2} \tag{4.22}$$

Proof. Consider the martingale

$$N_i^n(t) - \theta_i D_i^n(t) + \alpha_i \int_0^t \frac{N^n(s)}{n} E_i^n(s) \, ds.$$

This martingale has a optional quadratic variation which is majorised by $(1+\theta_i^2)N_i^n(t)$. This implies that if $t \leq s_{\epsilon}^n$ the quadratic variation is smaller than a constant times ϵn and thus the martingale is itself bounded in probability by $\sqrt{\epsilon n}$. Since the integral

$$\frac{1}{n} \int_{0}^{t} \frac{N^{n}(s)}{n} E_{i}^{n}(s) \, ds$$

according to the proof of the preceding theorem is asymptotically smaller than ϵ^2 it follows that:

$$\lim_{\epsilon \to 0} \lim_{n \to \infty} \frac{N_i(s_{\epsilon}^n) - \frac{\alpha_i}{\rho_i} E_i(s_{\epsilon}^n)}{\epsilon n} \to 0.$$

This implies the theorem.

4.3 The epidemic phase

At the end of the transition phase a small proportion of the individuals in the population are infected. During the second (or epidemic) phase of the process there is a rapid spread of the infections. We will see that during this phase the epidemic develops almost deterministically. We are interested in the limit value of the proportion

$$P(t) = \frac{N_1^n(t)}{N_1^n(t) + N_2^n(t)}$$
(4.23)

This proportion changes during the epidemic phase but there are (asymptotically) be no random element in this change.

Let

$$X^{n}(t) = (N_{1}^{n}(t+s_{\epsilon}^{n})/n, N_{2}^{n}(t+s_{\epsilon}^{n})/n, D_{1}^{n}(t+s_{\epsilon}^{n})/n, D_{2}^{n}(t+s_{\epsilon}^{n})/n)$$

and let

$$X(t) = (X_1(t), X_2(t), X_3(t), X_4(t))$$

be a solution of the differential equations:

$$\dot{X}_{1}(t) = \alpha_{1}(1 - X_{1}(t) - X_{2}(t))(X_{1}(t) - X_{3}(t)),
\dot{X}_{2}(t) = \alpha_{2}(1 - X_{1}(t) - X_{2}(t))(X_{2}(t) - X_{4}(t)),
\dot{X}_{3}(t) = \gamma_{1}(X_{1}(t) - X_{3}(t)),
\dot{X}_{4}(t) = \gamma_{1}(X_{2}(t) - X_{4}(t))$$
(4.24)

with starting values $X(0) = X^n(s_{\epsilon}^n)$.

If $(X_1(0) - X_3(0))/(X_2(0) - X_4(0)) = v$ and $X_1(0) + X_2(0) = \epsilon$ then, according to theorem 4.3), the relevant starting values are:

$$X_{1}(0) = \epsilon \frac{v\alpha_{1}/\rho_{1}}{(v\alpha_{1}/\rho_{1} + \alpha_{2}/\rho_{2})},$$

$$X_{2}(0) = \epsilon \frac{\alpha_{2}/\rho_{2}}{(v\alpha_{1}/\rho_{1} + \alpha_{2}/\rho_{2})},$$

$$X_{3}(0) = \epsilon \frac{v\gamma_{1}/\rho_{1}}{(v\alpha_{1}/\rho_{1} + \alpha_{2}/\rho_{2})},$$

$$X_{4}(0) = \epsilon \frac{\gamma_{2}/\rho_{2}}{(v\alpha_{1}/\rho_{1}\alpha_{2}/\rho_{2})}.$$
(4.25)

It follows from general theory of differential equation that (4.24), with these starting values, has a unique solution. This solution will be used to approximate the random epidemic process during the epidemic phase. Even if we can not derive an explicit solution some important features of the solution are easily derived. First $X_i(t)$, i = 1, 2, 3, 4, are all non-decreasing functions. In the limit

$$X_{1}(\infty) = X_{3}(\infty), X_{2}(\infty) = X_{4}(\infty), -\ln(1 - X_{1}(\infty) - X_{2}(\infty)) = \theta_{1}X_{1}(\infty) + \theta_{2}X_{2}(\infty).$$
(4.26)

The last equation of (4.26) implies that $X_1(\infty) + X_2(\infty)$ is uniformly bounded away from 1 for all possible starting values.

Let $Y_1(t) = X_1(t) - X_3(t)$, and $Y_2(t) = X_2(t) - X_4(t)$. Then

$$Y_{1}(t) = \epsilon \frac{\nu}{\nu \frac{\alpha_{1}}{\rho_{1}} + \frac{\alpha_{2}}{\rho_{2}}} \exp\{\rho_{1}t - \alpha_{1} \int_{0}^{t} X(s)ds\},\$$

and

$$Y_{2}(t) = \epsilon \frac{1}{\nu \frac{\alpha_{1}}{\rho_{1}} + \frac{\alpha_{2}}{\rho_{2}}} \exp\{\rho_{2}t - \alpha_{2} \int_{0}^{t} X(s)ds\},\$$

Together with (4.26) this implies that, if $0 < \nu$ then $X(\infty) > \rho_1/\alpha_1$. In this case we can define

$$T = \inf\{t; \{\rho_1 t - \alpha_1 \int_0^t X(s) ds\} < 0\}.$$

If $\nu = 0$ we define

$$T = \inf\{t; \{\rho_2 t - \alpha_2 \int_0^t X(s) ds\} < 0\}$$

According to (4.24)

$$(\dot{X}_1 + \dot{X}_2)/(1 - X_1 - X_2) = \alpha_1 Y_1 + \alpha_2 Y_2 \ge \epsilon \frac{\alpha_1 \nu}{\frac{\alpha_1}{\rho_1} + \frac{\alpha_2}{\rho_2}}$$

for all $t \leq T$. Consequently

$$-\ln(1 - X_1(T) - X_2(T)) \ge \text{const} \quad \epsilon \nu T.$$

$$(4.27)$$

$$T \leq \frac{constant}{\nu\epsilon}$$

LEMMA 4.6. For any sufficiently small ϵ

$$\sup_{t \le T} |X^{n}(t) - X(t)| \to 0$$
(4.28)

as $n \to \infty$.

Proof. The function

$$F(a, b, c, d) = (\alpha_1(1 - a - b)(a - c), \alpha_2(1 - a - b)(b - d), \gamma_1(a - c), \gamma_2(b - d))$$

is Lipschitz-continuous, when $0 \leq a,b,c,d \leq 1,$ i.e.,

$$\mid F(X) - F(Y) \mid \leq M \mid X - Y \mid$$

for some finite constant M.

First observe that

$$X_{i}^{n}(t) - X_{i}^{n}(0) - \int_{0}^{t} F_{i}(X^{n}(s)) \, ds$$

are martingales with the optional quadratic variations

$$[X_i^n](t) = (X_i^n(t) - X_i^n(0))/n^2.$$

As a consequence of Lenglard's inequality

$$\sqrt{n} \mid X^{n}(t) - X^{n}(0) - \int_{0}^{t} F(X^{n}(s)) \, ds \mid$$

is uniformly bounded for all $t \in [0, T]$.

Since by definition

$$X(t) = \int_{0}^{t} F(X(s)) \, ds + X(0).$$

it follows that

$$|X^{n}(t) - X(t)| = |X^{n}(t) - \int_{0}^{t} F(X^{n}(s)) ds + \int_{0}^{t} \{F(X^{n}(s) - F(X(s))\} ds | A^{n}(s) - F(X(s))] ds$$

Thus if

$$\kappa_n = \sup_{t \le T} |X^n(t) - \int_0^t F(X^n(s)) \, ds|$$

then

$$|X^{n}(t) - X(t)| = \kappa_{n} + M \int_{0}^{t} |X^{n}(s) - X(s)| ds.$$

It follows from Gronwall's inequality that

$$\mid X^{n}(t) - X(t) \mid \leq \kappa_{n} e^{Mt}$$

for all t. Since $\kappa_n \to 0$ as $n \to \infty$ and since T is finite this inequality proves the lemma.

From theorem 4.2 it follows that $0 < \nu < \infty$ only in case $\rho_1 = \rho_2$ In case $\rho_1 \neq \rho_2$ we have to make some further considerations.

Let us first assume that $\rho_1 > \rho_2$, i.e. the strongest agent is also the fastest. If $E_2(t^n) > 0$ then $E_2^n(s_{\epsilon}^n)$ is of size n^{ρ_2/ρ_1} . Since T is finite at all infectious turns immune according to an exponential distribution $E_2(T)$ will be of the same size. However at time T agent 1 has already infected approximately $n\overline{\pi}_1$ members of the population. Even if there are many individuals still infectious with agent 2 they can never keep an epidemic going since $\theta_2(1-\overline{\pi}_1) < 1$.

Next assume that $\rho_2 > \rho_1$, i.e. the weaker agent spreads initially faster than the stronger. If $E_1(t^n) > 0$ then both $E_2^n(s_{\epsilon}^n)$ and $E_2^n(T)$ are of size n^{ρ_1/ρ_2} . If $\theta_1(1 - \overline{\pi}_2) < 1$ these infected can not keep the epidemic going. However if $\theta_1(1 - \overline{\pi}_2) > 1$ they will continue the epidemic spread after agent 2 the spread of agent 2 has seized. The number of individuals infective with agent 1 will grow to be of size n during a transitional phase and then there will be another epidemic phase where only agent 1 spreads. According to the equation of balance and equation (3.9) it will continue until the proportion $\underline{\pi}_1 > 0$ of the population has been infected by agent 1.

4.4 The fading-out phase

After the epidemic phase there are few infectious individuals spreading the two agents. In case there are any at all both $(1 - N^n)\theta_1$ and $(1 - N^n\theta_2)$ are less than 1. As during the initial phase the further progress of the process may be approximated by independent birth-and-death processes. However now the death intensities will be greater than the birth intensities. This implies that there will only a arbitrarily small proportions of the population that will be newly infected during this last phase.

Hence:

THEOREM 4.4. If $E_1(t^n) > 0$ and $E_2(t^n) > 0$ then if $\rho_1 = \rho_2$

$$\lim_{\epsilon \to 0} \lim_{n \to \infty} \frac{N_1^n(\infty)}{N_1^n(\infty) + N_2^n(\infty)} = \lim_{\epsilon \to 0} \frac{X_1(\infty)}{X_1(\infty) + X_2(\infty)}$$
(4.29)

if $\rho_1 \neq \rho_2$

$$\lim_{\epsilon \to 0} \lim_{n \to \infty} \frac{N_1^n(\infty)}{N_1^n(\infty) + N_2^n(\infty)} = \frac{\underline{\pi}_1}{\underline{\pi}_1 + \overline{\pi}_2}.$$
(4.30)

Solutions of equations like (4.24) have been studied by Kendall and Saunders (1983). They investigate how the final values $X_3(\infty)$ and $X_4(\infty)$ depend on the starting values of $X_1(0) - X_3(0)$ and $X_2(0) - X_4(0)$. Using a probabilistic argument they prove that $X_3(\infty)$ increases and $X_4(\infty)$ decreases if $X_1(0) - X_3(0)$ is increased by a number δ and if $X_2(0) - X_4(0)$ is decreased with the same number. Let us assume that the first agent is the strongest, i.e., $\theta_1 > \theta_2$. Then $X_1(0) - X_3(0)$ increases more than $X_2(0) - X_4(0)$ decreases this effect will be even stronger. It follows, in cases where the first agent is the strongest, that $X_1(\infty)$ increases and $X_2(\infty)$ decreases with v.

This will be an important observation when we derive the asymptotic distribution of ratio of the final sizes of the two epidemics. Combining this lemma with the observation on monotonicity made at the start of this section we conclude:

LEMMA 4.7. If $\rho_1 = \rho_2$, $\theta_1 > \theta_2$ and if $E_1(s_{\epsilon}^n) / E_1(s_{\epsilon}^n) = v$ for some small ϵ , then

$$N_1^n(\infty)/(N_1^n(\infty)+N_2^n(\infty))$$

is asymptotically increasing in v.

5. Distribution of the proportions of the final sizes

After the preparations in the previous sections we can now study the relation between the final sizes of the two infectious agents. We will derive the distribution of the proportion

$$P = \frac{\pi_1}{\pi_1 + \pi_2} \tag{5.1}$$

The distribution of this ratio depends on how many infectious agents of the two kinds that comes into the population.

The ratio P is only of interest if at least one of the agents have large spread. It may be the case that only one of the agents spread in the population. If only agent 1 spreads then P = 1 and if only agent 2 spreads P = 0. the interesting situation is when both agents has asymptotically large spread.

Let

$$P^{n}(t) = \frac{N_{1}^{n}(t)}{N_{1}^{n}(t) + N_{2}^{n}(t)}$$

If both agents have large spread the development of this function after time $t = s_{\epsilon}^{n}$ is asymptotically (for large n) determined by the ratio

$$\nu = \frac{E_1^n(s_\epsilon^n)}{E_2^n(s_\epsilon^n)}.$$
(5.2)

According the theorem 4.3

$$P^n(s_{\epsilon}^n) \to \frac{\nu \alpha_1 \rho_2}{\nu \alpha_1 \rho_2 + \alpha_2 \rho_1}$$

as $n \to \infty$ and $\epsilon \to 0$ if (5.2) holds..



Figure 5.1. Asymptotic trajectories for the number of infected of the two agents, i.e. $(N_1^n/n, N_2^n/n)$ for $P^n(s_{\epsilon}^n) = 0.1, 0.3, 0.5, 0.7$, and 0.9. Here $\theta_1 = 2$ and $\theta_2 = 1.25$. The possible final sizes are indicated by the dotted line. $(C_1 = C_2 = 1)$.

In order to find the asymptotic distribution of $P^n(\infty)$ we use lemma 4.2 to derive the asymptotic distribution of $P^n(s^n_{\epsilon})$ and solve the differential equation (4.24) to find out how $P^n(t)$ changes from $t = s^n_{\epsilon}$ till $t = \infty$.

It should be clear from the investigation above that we have to distinguish the two cases where $\rho_1 = \rho_2$ and $\rho_1 \neq \rho_2$. The first of these two cases will yield a non-degenerate distribution for P conditionally on that both agents have asymptotically large spread.

5.1 The case $\rho_1 = \rho_2$

The number of infected by the two agents will grow at different speed, depending on the strengths of the agents and of the initial phases of the epidemic , during the epidemic phase. Figures 5.1 and 5.2 shows the trajectories for $(X_1(t), X_2(t))$ during the epidemic phase for different starting values. These trajectories will be the approximate trajectories for $(N_1^n(t)/n, N_2^n(t))/n$ for large n.

Figures 5.3 and 5.4 illustrates how the final proportion of the two agents are related to the initial proportion at time $t = s_{\epsilon}^n$. The asymptotic distribution of P depends the distribution of the initial proportion.

5.1.1 The case $C_1 = C_2 = 1$ If both agents have asymptotically large spread the distribution of P(t) at the start of the epidemic phase is can be calculated using the result that $E_1(t^n)/E_2(t^n)$ is approximately distributed as the ratio between two independent exponential distributed random variables with intensities $1 - 1/\theta_1$ and $1 - 1/\theta_2$ respectively.

Let



Figure 5.2. Asymptotic trajectories for the number of infected of the two agents, i.e. $(N_1^n/n, N_2^n/n)$ for $P^n(s_{\epsilon}^n) = 0.1, 0.3, 0.5, 0.7$, and 0.9. Here $\theta_1 = 2$ and $\theta_2 = 1.25$. The possible final sizes are indicated by the dotted line. $(C_1 = C_2 = 1)$.



Figure 5.3. Relation between the initial proportion, $P^n(s_{\epsilon}^n)$, and the final proportion, $P^n(\infty)$. Here $\theta_1 = 2$ and $\theta_2 = 1.25$.



Figure 5.4. Relation between the initial proportion, $P^n(s_{\epsilon}^n)$, and the final proportion, $P^n(\infty)$. Here $\theta_1 = 2$ and $\theta_2 = 1.5$.

$$P^{n}(t) = \frac{N_{1}^{n}(t)}{N_{1}^{n}(t) + N_{2}^{n}(t)}.$$
(5.3)

Simple calculations yields that $P(t^n)$ and $P(s_\epsilon^n)$ has approximately the distribution function

$$Pr(P^n(s^n_{\epsilon}) \le z) \approx \frac{\alpha_2^2 z}{\alpha_1^2 + (\alpha_2^2 - \alpha_1^2) z}.$$
(5.4)

During the epidemic phase of the spread this "initial" distribution will be distorted in a way that is approximated by the differential equations (cf. theorem 4.4). Figures 5.5 and 5.6 below illustrates the distribution of the proportion at the initial phase and of the final sizes.

It is also of interest to study the distribution of the sum of the final sizes of the two agents separately, i.e. the distribution of the proportion of individuals who becomes infected by any of the two agents during the epidemic. This distribution is illustrated in figures 5.7 and 5.8.

5.2 The case $\rho_1 \neq \rho_2$

This case leads to simpler results since the distributions of $(N_1^n(\infty)/n, N_2^n(\infty)/n)$ will asymptotically be concentrated at at most four points. The probabilities are given in table 5.1.



Figure 5.5. Asymptotic distribution of the final proportion (unbroken line) and initial distribution (broken line) conditional on that both agents have large spread, when $\theta_1 = 2$ and $\theta_2 = 1.25$. ($C_1 = C_2 = 1$).



Figure 5.6. Asymptotic distribution of the final proportion (unbroken line) and initial distribution (broken line) conditional on that both agents have large spread, when $\theta_1 = 2$ and $\theta_2 = 1.5$. ($C_1 = C_2 = 1$).



Figure 5.7. Asymptotic distribution of the final sum of the two agents, when $\theta_1 = 2$ and $\theta_2 = 1.25$. $(C_1 = C_2 = 1)$.



Figure 5.8. Asymptotic distribution of the final sum of the two agents, when $\theta_1 = 2$ and $\theta_2 = 1.5$. $(C_1 = C_2 = 1)$.

(π_1,π_2)	P	probability
(0, 0)	undefined	$(heta_1 heta_2)^{-1}$
$(\overline{\pi}_1, 0)$	1	$(\theta_1 - 1)(\theta_1 \theta_2)^{-1}$
$(0,\overline{\pi}_2)$	0	$(\theta_2 - 1)(\theta_1 \theta_2)^{-1}$
$(\underline{\pi}_1, \overline{\pi}_2)$	$\underline{\pi}_1/(\underline{\pi}_1 + \overline{\pi}_2)$	$(\theta_1 - 1)(\theta_2 - 1)(\theta_1 \theta_2)^{-1}$

Table 5.1 Probabilities for possible outcomes when $\rho_1 \neq \rho_2$

As pointed out above the two last outcomes will be identical in case (3.10) holds. Their probabilities should then be added.

Acknowledgements

For this work Åke Svensson was supported by The Bank of Sweden Tercentenary Foundation.

References

- Adler, F. and Brunet, R. (1991). The dynamics of simultaneous infections with altered susceptibilities. *Theoretical population Biology* **40**, 360–410.
- Bailey, N. (1975). The mathematical Theory of Infectious Diseases and its Applications. Griffin, London.
- Barbour, A. (1975). The duration of the closed stochastic epidemic. *Biometrika* **62**, 477–482.
- Becker, N. (1989). Analysis of Infectious Disease Data. Chapman and Hall, London.
- Harris, T. E. (1963). The Theory of Branchibg Processes. Springer–Verlag, Berlin.
- Jacod, J. and Shiryaev, A. (1987). *Limit Theorems for Stochastic Processes*. Springer–Verlag, Berlin.
- Kendall, D. (1948). On the generalized "birth-and-death" process. AMS 19, 1–15.
- Kendall, W. and Saunders, I. (1983). Epidemics in competition ii: The general epidemic. JRSS Ser B 45, 238–244.
- Lefévre, C. (1990). Stochastic epidemic models for s–i–r infectious diseases: a brief survey of the recent theory. In Gabriel, J., Lefévre, C. and Picard, P., editors, *Stochastic Processes in Epidemic Theory*, volume 86 of *Lecture notes in Biomathematics*. Springer–Verlag, Berlin.
- Lin, J., Andreasen, V. and Levin, S. (1999). Dynamics of influenza a drift: the linear three-strain model. *Mathematical Biosciences* **162**, 33–51.

- Svensson, Å. (1993). Dynamics of an epidemic in a closed population. Adv. Appl. Prob. **25**, 303–313.
- White, L., Cox, M. and Medley, G. (1998). Cross immunity and vaccination against multiple microparasite strain. IMA Journal of Mathematics Applied in Medicine & Biology 15, 211–233.