Differences in infectivity and susceptibility

This you can read as an introduction to Chapter 2 of the book (NOT a replacement to section 2.2, despite having the same title). I want to make it more explicit why variability in infectivity is easy to handle with a simple average, but variability in susceptibility or variation in both susceptibility and infectivity poses a harder problem. At the same time, this is preparation for Part II of the book.

If all hosts have the same susceptibility (before infection) and infectivity (while infected), then in a well-mixed population the dynamics of the disease follows

$$\dot{S}(t) = c\frac{S(t)}{N(t)}\int_0^\infty \dot{S}(t-\tau)A(\tau)d\tau \tag{1}$$

where the dot denotes the time derivative. Here c is the contact rate[1], $\frac{S(t)}{N(t)}$ is the probability that the contact is to a susceptible, $\dot{S}(t-\tau)d\tau$ is the negative of the number of hosts infected τ time ago (i.e., of those who have infection age τ; recall that S decreases so that $\dot{S}$ is negative), and $A(\tau)$ is the probability that the disease is communicated to a susceptible when an infected host with infection age τ makes a contact to a susceptible. Recall that $A(\tau)$ is zero if the infected host has recovered or died τ time after infection.

To investigate variability among hosts, assign a number $\xi \in \Omega$ to each host that characterizes its infectivity and susceptibility. The immune status of the host is a good example. Hosts with a weak immune system (low ξ) are highly susceptible (likely get the disease when making contact to an infected) and also highly infective when sick (their weak immune system cannot control the pathogen, so that they get a strong infection with many pathogens on their hands, in their cough etc.). Hosts with a strong immune system (high ξ) are less likely to contract the disease and are less infecious when infected. Let $f(\xi)$ denote the probability density of ξ among all hosts, and let $\tilde{S}(t,\xi)$ denote the density of susceptibles at ξ. This means that there are $\tilde{S}(t,\xi)\Delta\xi$ susceptible hosts with immune status between ξ and $\xi+\Delta\xi$. Obviously, the total number of susceptibles is

$$S(t) = \int_\Omega \tilde{S}(t,\xi)d\xi \tag{2}$$

and before the epidemic, we have $\tilde{S}(0,\xi)\Delta\xi = S(0)f(\xi)\Delta\xi$. During the epidemic, however, hosts with weak immune status get sick easier, and therefore $\tilde{S}(t,\xi)$ is no longer

[1] An individual makes $c\Delta t$ contacts in Δt time to anyone in the population. With constant c, this equation is for frequency-dependent transmission (epidemics in herds). In case of mass action as in the SIR model, $c = \gamma N(t)$, i.e., $N(t)$ cancels in (1). This makes no difference for what follows.

proportional to $S(t)$.

To generalize (1) to variable hosts, let $a(\tau, \omega, \xi)$ be the probability that infection happens when an infected individual with infection age τ and immune status ω makes a contact to a susceptible with immune status ξ. Recall that in equation (1), $\dot{S}(t-\tau)d\tau$ is the negative of the number of infecteds with infection age between τ and $\tau + d\tau$. Now the negative of the number of infecteds with infection age in $(\tau, \tau + d\tau)$ and immune status in $(\omega, \omega + \Delta\omega)$ is $\dot{\tilde{S}}(t-\tau, \omega)\Delta\omega d\tau$. Each of these infecteds makes a total of cdt contacts in dt time. A fraction $\tilde{S}(t, \xi)\Delta\xi/N(t)$ of these contacts go to susceptibles with immune status between ξ and $\xi + \Delta\xi$. Hence the number contacts between (τ, ω)-infecteds and ξ-susceptibles in dt time is

$$(cdt)\frac{\tilde{S}(t, \xi)\Delta\xi}{N(t)}\,\dot{\tilde{S}}(t-\tau, \omega)\Delta\omega d\tau$$

and in each such contact, the susceptible gets infected with probability $a(\tau, \omega, \xi)$. Integrating over all types of infecteds, the number of ξ-susceptibles who gets sick in dt is

$$d[\tilde{S}(t, \xi)\Delta\xi] = (cdt)\frac{\tilde{S}(t, \xi)\Delta\xi}{N(t)}\int_0^\infty \int_\Omega \dot{\tilde{S}}(t-\tau, \omega)a(\tau, \omega, \xi)d\omega d\tau$$

Dividing with dt and cancelling $\Delta\xi$, we arrive at the generalization of (1) to variable hosts,

$$\dot{\tilde{S}}(t, \xi) = c\frac{\tilde{S}(t, \xi)}{N(t)}\int_0^\infty \int_\Omega \dot{\tilde{S}}(t-\tau, \omega)a(\tau, \omega, \xi)d\omega d\tau \tag{3}$$

The total number of susceptibles (given in (2)) changes according to

$$\dot{S} = \int_\Omega \dot{\tilde{S}}(t, \xi)d\xi = c\int_\Omega \frac{\tilde{S}(t, \xi)}{N(t)}\int_0^\infty \int_\Omega \dot{\tilde{S}}(t-\tau, \omega)a(\tau, \omega, \xi)d\omega d\tau d\xi \tag{4}$$

Notice that this equation is pretty useless; to obtain the change of $S(t)$, we need to know $\tilde{S}(t, \xi)$ separately at all ξ. This is because $a(\tau, \omega, \xi)$ depends on ξ, the immune status of the susceptible. Hence we cannot dispense with the detailed dynamics in (3) when *susceptibility* is variable. We continue analysing models like (3) later in Part II of the book (Structured populations; here the host population is structured by differences in the immune status).

Assume, however, that the hosts do not differ in susceptibility, only the infecteds differ in their infectivity. This means that $a(\tau, \omega, \xi)$ does not depend on ξ (as a function of its

third argument, a is constant). With a slight abuse of notation, let $a(\tau, \omega)$ denote the probability that infection takes place in a contact where the infected has infection age τ and immune status ω (the same probability now holds for any susceptible). Then we can rewrite (3) as

$$\dot{\tilde{S}}(t, \xi) = c \frac{\tilde{S}(t, \xi)}{N(t)} \int_0^\infty \int_\Omega \dot{\tilde{S}}(t - \tau, \omega) a(\tau, \omega) d\omega d\tau \tag{5}$$

and (4) as

$$\begin{aligned} \dot{S}(t) &= c \int_\Omega \frac{\tilde{S}(t, \xi)}{N(t)} d\xi \cdot \int_0^\infty \int_\Omega \dot{\tilde{S}}(t - \tau, \omega) a(\tau, \omega) d\omega d\tau = \\ &= c \frac{S(t)}{N(t)} \int_0^\infty \int_\Omega \dot{\tilde{S}}(t - \tau, \omega) a(\tau, \omega) d\omega d\tau \end{aligned} \tag{6}$$

If we divide (5) with $\tilde{S}(t, \xi)$ and (6) with $S(t)$, then the same expression remains on their right hand sides. We therefore conclude that

$$\frac{\partial \ln \tilde{S}(t, \xi)}{\partial t} = \frac{d \ln S(t)}{dt} \tag{7}$$

holds for all t. This implies $\ln \tilde{S}(t, \xi) - \ln S(t) = const$, so that $\tilde{S}(t, \xi)/S(t)$ is constant over time. Before the epidemic, we have $\tilde{S}(0, \xi) = f(\xi) S(0)$ (see above); so also at any time during the epidemic, we still have $\tilde{S}(t, \xi) = f(\xi) S(t)$ at any time t. *This* is great relief. Now in (6) we get

$$\dot{S}(t) = c \frac{S(t)}{N(t)} \int_0^\infty \dot{S}(t - \tau) \int_\Omega f(\omega) a(\tau, \omega) d\omega d\tau \tag{8}$$

and defining $A(\tau) = \int_\Omega f(\omega) a(\tau, \omega) d\omega$, we recover (1). Importantly, $A(\tau)$ is the average of $a(\tau, \omega)$ over the distribution of the immune status ω.

Heuristically, simple averaging works when only infectivity is variable because the newly infecteds are a random sample from the current susceptibles, so that the distribution of the susceptibles does not change, i.e., it follows the distribution f at all times. However, if susceptibility also varies (i.e., depends on the immune status), then the newly infected tend to be those whose susceptility is higher (whose immune status is weaker). Not only the distribution of the newly infected differs from the rest of the susceptibles, the distribution of the susceptibles also changes during the epidemic as the more susceptible hosts are infected earlier.

When only infectivity varies, we have recovered the full dynamics in equation (1) with a simple average for $A(\tau)$; different levels of variability (with the same average) do not change the deterministic dynamics of the epidemic. As a consequence, there is no effect of variability on the basic reproduction number R_0, on the initial growth rate r, and on the final size $1 - s(\infty)$. There is an effect of variability, however, on the probability of a major outbreak ($1 - z_\infty$; see pp. 38-39 in the book). In the very beginning of the epidemic, ruled by a stochastic branching process, the number of new infections is small. The newly infecteds are a random sample from the susceptibles, but a *small* sample, subject to sampling error; i.e., just by chance, hosts with stronger or weaker immune status may be overrepresented among them. The more variability the population has, the more z_∞ is affected by the vagaries of sampling.

> **Exercise:** Show that when only susceptibility is variable (i.e., the probability of contracting the disease upon contact depends on the immune status of the susceptible partner but not on the immune status of the infected), then R_0 and r are still unaffected by variability in immune status but $s(\infty)$ is affected.

For simplicity, I tacitly assumed that the distribution of immune status has a probability density function f (i.e., no delta peaks). You can rewrite all of the above for measures ($\tilde{S}(t, \xi)$ must also be replaced with a measure).

I took immune status as the cause behind variability. Much of secion 2.1 of the book revolves around another mechanism that induces variability in infectivity but (importantly!) not in susceptibility: Infectivity varies among hosts with the same infection age if the infecteds move randomly between different classes, such as infectious and recovered/dead, or latent and infectious, etc. In this case, Ω would be the set of all possible routes and timing of these transitions, and we average over them. For example, in the SEIR model of exercise 2.2, infected hosts differ in when they move from the latent phase to the infectious phase (a random variable often denoted by T_1 in the book, exponentially distributed with parameter θ) and when they recover (ΔT after becoming infectious, exponentially distributed with parameter α in the book). In this model, we equip each host with a vector $\xi = (T_1, \Delta T)$, which contains his latency and infectious times should he become infected. The elements of ξ do not affect the host while susceptible, only infectivity varies due to the variable length of the infection. We can average over ξ as above.

In all of the above equations, we could factor the contact rate c into $a(\tau, \omega, \xi)$, and with this, we could also consider variability in host behaviour that affects the contact rate (e.g. outgoing hosts who make many contacts vs introvert hosts who make few). The

probability that two hosts make contact with each other depends on the behaviour of both of them, ω and ξ in $a(\tau, \omega, \xi)$. Hence with variable contact rate, we cannot simplify equation (3). Section 2.2 of the book presents a simple example to appreciate the consequences of variable contact rates. This example is also our first foray into models with structured host populations like the one in equation (3).

Solution: The probability $a(\tau, \omega, \xi)$ now does not depend on ω, the immune status of the infected partner. The full dynamics given by equation (3) reads

$$\begin{aligned} \dot{\tilde{S}}(t,\xi) &= c\frac{\tilde{S}(t,\xi)}{N(t)} \int_0^\infty a(\tau,\xi) \int_\Omega \dot{\tilde{S}}(t-\tau,\omega) d\omega d\tau \\ &= c\frac{\tilde{S}(t,\xi)}{N(t)} \int_0^\infty a(\tau,\xi) \dot{S}(t-\tau) d\tau \end{aligned} \tag{9}$$

Before the epidemic we have $\tilde{S}(0,\xi) = S(0)f(\xi)$, and this remains approximately true in the initial phase of the epidemic, when almost nobody is infected even among the most susceptible hosts. As long as we can take $\tilde{S}(t,\xi) = S(t)f(\xi)$, we have

$$\dot{\tilde{S}}(t,\xi) = c\frac{S(t)}{N(t)} \int_0^\infty f(\xi) a(\tau,\xi) \dot{S}(t-\tau) d\tau$$

and by integrating over ξ,

$$\dot{S}(t) = c\frac{S(t)}{N(t)} \int_0^\infty \dot{S}(t-\tau) \int_\Omega f(\xi) a(\tau,\xi) d\xi d\tau$$

which recovers (1) with $A(\tau) = \int_\Omega f(\xi) a(\tau,\xi) d\xi$. The initial phase of the epidemic is thus unaffected by the variation in ξ, only the average value of $a(\tau,\xi)$ matters. Since R_0 and r pertain to this initial phase, the are unaffected, too.

The final size of the epidemic is however affected by the variability; the above derivation cannot be extended beyond the initial phase where $\tilde{S}(t,\xi) = S(t)f(\xi)$ holds. To see a direct example for variability in susceptibilty affecting $s(\infty)$, consider an SIR epidemic without variability, and with R_0 sufficiently large such that $s(\infty) < 0.5$. Compare this to another epidemic, where half the hosts are not susceptible to the disease at all, and the other half has twice the probability of catching the disease upon contact compared to the first epidemic. The two epidemics have the same average susceptibility and the same R_0. In the second epidemic, by the assumption that half the hosts cannot get infected, $s(\infty)$ must be greater than 0.5.