Host-parasite interactions

Key concepts

- SIR compartment models
- R_0, density (in)dependent contact and transmission rates
- N_T, persistence mechanisms and the endemic equilibrium
- Herd immunity
- Transmission-virulence trade-off

The uninvited guest?

A huge proportion of species are parasitic. The word *parasite* is borrowed from the Greek word *parasitos* meaning "one who eats at the table of another". This gets to the very essence of parasites: they live in or on another species, and they have a negative impact on that species by using its resources. The large number of parasite species means they encompass a lot of diversity (taxonomic, size, life-span, life-cycle complexity, specialist *vs.* generalist etc.). The goal of this chapter is to focus on a subset of parasites (that are sufficiently well studied so that a good range of theory is developed) and explore the nature of the interaction between host and parasite. We'll focus on the factors that allow parasites to invade and persist in host populations, along with the consequences (to both species) of parasites that are more harmful to their hosts.

Phocine distemper virus outbreaks

Figure 1: The harbour seal (*Phoca vitulina*) has experienced dramatic outbreaks of a virus similar to human measles.

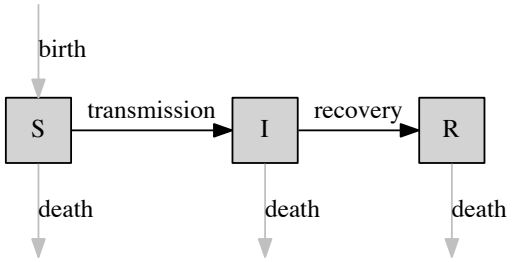
Phocine distemper virus is a morbillivirus (the same genus as measles) and has caused two large outbreaks in harbour seal populations in the North Sea in recent times. Transmission occurs when seals "haul out" on beaches. Given that mass mortality was associated with these events, disease ecologists (including population ecologists) set about trying to understand the factors that enabled the virus to invade these

populations along with assessing the potential for the virus to maintain itself over the long-term in the populations. We will periodically review their findings as we learn more about how to study such events through a population ecology lens.

Microparasites and the compartment model

One of way of organizing parasites is by size. Viruses and bacteria are relatively small (compared to ticks and worms) and are often termed microparasites. This term also usually implies that the microparasite completes a full life cycle (maybe more) within one host individual. Microparasites often reproduce inside the host's cells, and can illicit strong immune responses from the host.

Figure 2: Flow diagram for an SIR model including host demography (birth and death).



Because they are so small we don't aim to count microparasites (this is in stark contrast to all our population ecology so far!). Rather, we track the host individuals, which are then classified into different states - for example pre-, during and post-encounter with parasites. Pre-encouter, we refer to the hosts as *Susceptible (S)* to parasite infection. During the encounter we refer to the hosts as *Infectious (I)* and post-encouter we refer to the hosts as *Recovered (R)*, following clearance of the parasite by the host's immune response. This susceptible-infectious-recovered model is often referred to as the SIR model.

Although the Susceptible-Infectious-Recovered model applies to many host-parasite interactions, it is not the only such compartment model.

Contact rate: density-dependent or not?

A large proportion of microparasites rely on contact between host individuals in order to transmit to the next host. Transmission is essential to parasites as they consume resources in and on hosts and

trigger immune responses, meaning they can't use any host individual indefinitely. Because we use a host-centric model (SIR) to study the interaction between host and microparasite, it is vital to pause and consider whether contact rate between individuals in a host population scales with population size (i.e., is density-dependent) or not.

At this point we have to ask ourself what sort of contact we're talking about. Essentially, we mean the sort of contact that *could* result in transmission of the parasite. For some parasites this could require something like shaking hands, for others (for example when a virus becomes aerosolized during a sneeze) just being in the same building may be enough. Other parasites require more specific contact, such as sexually-transmitted infections. So the simple answer to the question: *does contact rate between individuals in a host population scale with population size?* is: *It depends!*

For a sexually-transmitted disease, we could make the reasonable assertion that the number of (sexual) contacts has little to nothing to do with population size and more to do with individual behaviors. For aerosolized virus transmission, large populations are likely to have more aggregation, whether it be infrastructure-related in humans (e.g. public transport) or resource-related in wildlife. Consequently, we may reasonably expect more contact in large populations, and therefore more transmission of such a parasite. We can conceptualize these two extremes of density-independent and density-dependent contact rates (Fig. 3). For density-independent contact, we just assume a constant rate parameter c applies at all population sizes. For density-dependent contact, we can assume a contact rate of the form cN where here c represents the slope of the relationship between contact rate and population size, N.

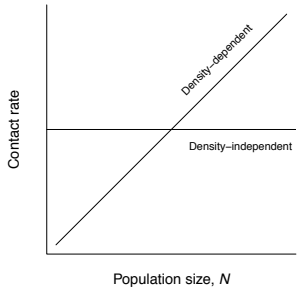


Figure 3: Examples of density-independent (constant=c) and density-dependent (linear, slope=c) forms of contact rate.

Transmission and the basic reproductive number

While contact is the pre-requisite for many types of parasite transmission, it is not the only requirement. Contact must also be between the *right* kind of individuals. In our SIR model context, this means contact between an I-type individual and an S-type individual. For each I individual, the probability of encountering an S individual is S/N, where N is the total host population size. Further, even if the right sort of contact does occur, transmission is not guaranteed. Rather, there is a probability (often termed the transmissibility) of transmission given appropriate contact. This could reflect, for example, the likelihood that virus particles move between individuals and bind to host cells in the second host individual.

Collectively then, the process of transmission requires contact (which occurs at some rate), the right sort of contact (a ratio deter-

mined by relative population sizes) and the 'favorable' outcome that the parasite establishes in the recipient host individual. Per infectious individual, we can write this as

$$\text{contact rate} \times \frac{\text{S}}{\text{N}}\text{a} \tag{1}$$

where the contact rate is possibly a function of N, and parameter a is the transmissibility. For all infectious individuals together we can multiply equation (1) by I to get the population-level transmission

$$\text{contact rate} \times \frac{\text{S}}{\text{N}}\text{aI}. \tag{2}$$

Conventionally, the contact rate and the transmissibility are multiplied together to give the transmission rate $\beta = \text{contact rate} \times \text{a}$.

We see that in the case of density-independent contact, the transmission term is $\beta SI/N$, whereas in the case of density-dependent transmission it is βSI. The rate of recovery of individuals is usually assumed to occur at a constant per capita rate, g. The simplest version of the SIR model ignores host demography. This may be a reasonable assumption if the rates associated with the parasite (transmission and recovery) occur much faster than the demographic rates of host birth and death. In this case we can write down the rate of change of the three host population classes as

Here, we are assuming a density-independent contact rate

$$\frac{dS}{dt} = -\beta\frac{SI}{N} \tag{3}$$

$$\frac{dI}{dt} = \beta\frac{SI}{N} - gI \tag{4}$$

$$\frac{dR}{dt} = gI \tag{5}$$

In order for the parasite to increase its representation at the host population level, we require that $dI/dt > 0$. In the case of density-independent contact, this is satisfied when

$$\beta\frac{SI}{N} > gI \tag{6}$$

which is equivalent to

$$\frac{\beta SI}{gIN} > 1. \tag{7}$$

Assuming that there is at least one infectious individual then we are safe to divide through by I

$$\frac{\beta S}{gN} > 1. \tag{8}$$

If we focus our attention on the initial invasion of the parasite into a host population then all individuals (perhaps save the initially

infected individual - or *index case*) are susceptible and $S \sim N$. Consequently, for initial invasion we require

$$\frac{\beta}{g} > 1. \tag{9}$$

This left-hand side of the inequality is the basic reproductive number (R_0) for the model with density-independent contact. Beyond being a threshold for parasite invasion ($R_0 > 1$), R_0 tells us the average number of secondary infections caused by one infectious individual in a wholly susceptible population. We see that R_0 is increased if β increases (high contact rate and/or transmissibility) or if g decreases. A decrease in g means a slow recovery from infection or equivalently a long infectious period. These attributes could occur by virtue of the parasite, the host or a combination of the two. In fact, R_0 is a measure of the parasite's *fitness* since it is related to parasite offspring (albeit measured at the level of the host).

In the case of density-dependent contact our model describing the dynamics of S, I and R become

$$\frac{dS}{dt} = -\beta SI \tag{10}$$

$$\frac{dI}{dt} = \beta SI - gI \tag{11}$$

$$\frac{dR}{dt} = gI \tag{12}$$

and analysis shows that for infection to grow in the host population we require

$$\beta SI > gI \tag{13}$$

which, dividing by I becomes

$$\beta S/g > 1 \tag{14}$$

Again at an initial invasion, $S \sim N$ and so we require

$$\beta N/g > 1 \tag{15}$$

defining the basic reproductive number as $R_0 = \beta N/g$. In this case, there is a third determinant of parasite invasion success (in addition to β and g): the host population size, N. For a given host-parasite species pair (when we can reasonably assume β and g are fixed) then the parasite may experience variable success in invading host populations (with success being associated with larger host population sizes). Formally, we can define the threshold host population size (N_T) for parasite invasion by considering the knife-edge situation where $R_0 = 1$.

$$1 = \beta N_T/g \tag{16}$$

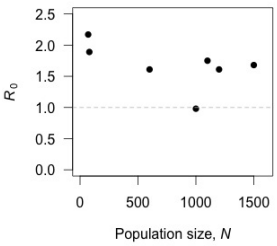


Figure 4: Data adapted from Heide-Jorgensen and Harkonen, 1992, *J. Appl. Ecol.* suggest no relationship between R_0 and population size, which implies that contact is not density-dependent in the phocine distemper system.

$$N_T = g/\beta \tag{17}$$

Therefore, provided $N_T > g/\beta$ the parasite will invade the host population and in cases where the transmission rate is small or the recovery rate is large, parasite invasion requires a corresponding augmentation in host population size to be able to invade.

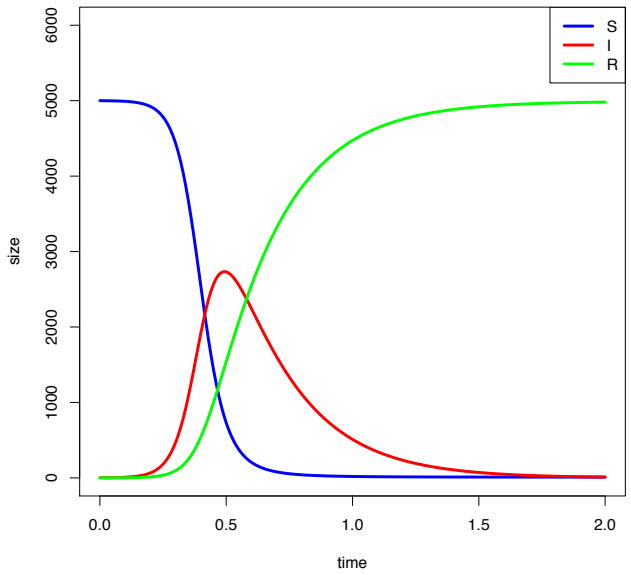


Figure 5: Solution of the SIR model without host demography. Parameters are $\beta = 25.0, g = 4.0, R_0 = 6.25$. Initial conditions are $S(0) = 5000, I(0) = 1, R(0) = 0$.

Note that the solution of the SIR model without host demography but with $R_0 > 1$ is a *disease outbreak* (Fig. 5, red "epidemic" curve) followed by the disappearance of the parasite.

R_0 *and insights into extinction threats and control opportunities*

Recap: the R_0 expressions based on density-independent and density-dependent contact rates are β/g and $\beta N/g$, respectively

We've seen that the form of transmission depends on our assumptions about how contact rate scales with population size. What do these different types of transmission mean for some of the critical issues of infectious disease? At their worst, parasites can threaten the existence of host species. We see that as host population sizes drop, the R_0 based on *density-dependent* contact will diminish (since it contains an N in the numerator). By contrast, the R_0 associated with *density-independent* contact will remain constant at all host population sizes (even small ones). Consequently, we may consider the latter more troubling in terms of host population extinction threats (though of

course, the details of the disease associated with the parasite need to be taken into account for a more accurate appraisal).

By a similar logic, differences emerge in the potential effects of control strategies. Culling can be an effective way of preventing further spread of wildlife and livestock diseases. By reducing population sizes, we reduce the potential for contact. This is likely to be most effective in the cases where parasite transmission responds to host population size via its effect on the contact rate.

Parasite persistence and the endemic equilibrium

So far, we've been studying parasite transmission in the absence of host demographic processes. When adding demography to equations describing transmission, we need to be clear about our assumptions (Which classes of S, I and R reproduce? Are individuals born susceptible? What would the host population do if the parasite were not present?). Here we'll assume that in the absence of the parasite, the host population would grow to its carrying capacity (due to density-dependence in the birth rate only). Additionally, we'll assume that all classes reproduce and that all individuals are born susceptible. This leads to the following model

Here, we're assuming a density-independent form of contact

$$\frac{dS}{dt} = (b_0 - b_1 N)N - d_0 S - \beta \frac{SI}{N} \tag{18}$$

$$\frac{dI}{dt} = \beta \frac{SI}{N} - gI - d_0 I \tag{19}$$

$$\frac{dR}{dt} = gI - d_0 R \tag{20}$$

where the carrying capacity is defined as $K = (b_0 - d_0)/b_1$. By following similar calculations to those above, we can write the basic reproductive number for this system as

$$R_0 = \frac{\beta}{g + d_0} \tag{21}$$

The inclusion of host demography means that now the parasite can invade *and* persist in the host population (Fig. 6). At this equilibrium (often called the endemic equilibrium) none of the states S, I or R are zero.

We can solve the three differential equations $dS/dt = 0, dI/dt = 0, dR/dt = 0$ simultaneously to get expressions for S, I, and R at equilibrium. The endemic number of infectious individuals is

$$\hat{I} = \frac{(d_0 - b_0)g + d_0^2 - (b_0 + \beta)d_0 + b_0\beta}{b_1\beta(g/d_0 + 1)} \tag{22}$$

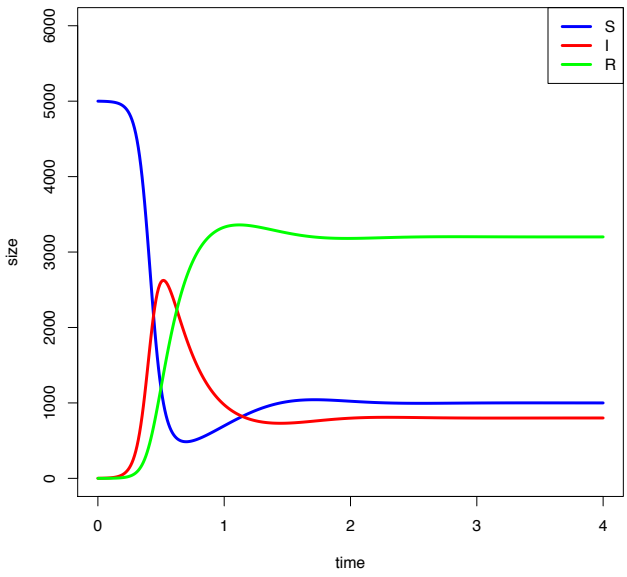


Figure 6: Solution of the SIR model with host demography. Parameters are $\beta = 25.0, g = 4.0, R_0 = 6.25, b_0 = 2.0, d_0 = 1.0, d_1 = 0.0002, K = 5000$. Initial conditions are $S(0) = 5000, I(0) = 1, R(0) = 0$.

which for the parameters used in Fig. 6 equates to $\hat{I} = 800$. While we may not routinely calculate the number of infectious individuals in a population at endemic equilibrium we not only see that it is possible, but that the amount of infection depends on parameters associated with the parasite (β, g) and those purely of the host (b_0, b_1 and d_0).

The birth of susceptible individuals replenishes the supply of hosts required by the parasite. Similar replenishment mechanisms can occur due to

- immigration of susceptible individuals into the host population
- waning immunity, whereby immune individuals eventually lose their immunity and become susceptible again
- parasite evolution, where mutations occur allowing the parasite to evade any immunity in recovered hosts

At a stable endemic equilibrium each infectious individual gives rise to exactly one replacement infectious individual on average. This means that the proportion of the population that is susceptible multiplied by R_0 equates to 1. For example, if $R_0 = 2$, then the infectious individuals must be encountering susceptibles with probability 0.5. Any more than this and the number of infectious individuals would grow, any less and it would decline. This means that

$$\frac{R_0 S}{N} = 1 \tag{23}$$

The definition of R_0 technically requires that the host population is at demographic equilibrium, e.g., at its stable carrying capacity

at the endemic equilibrium.

For infectious diseases at endemic equilibrium, if currently or previously infected individuals possess an enduring antibody, then the proportion of the population without this antibody allows an estimation of R_0

Remember: R_0 is the average number of secondary infections caused by one infectious individual in a wholly susceptible population

Herd immunity

The fact the many parasites (and their associated diseases) differ in their R_0 suggests that some are more easy to control than others. Estimates for some microparasite-associated diseases are provided in Table 1. While there are a range of practical factors that make some diseases more preventable (e.g. the ease of designing a vaccine), we can use R_0 to form a guiding principle regarding disease control.

Disease	R_0
Measles	12-18
Smallpox	5-7
Polio	5-7
HIV/AIDS	2-5
SARS	2-5
Influenza	2-3

Table 1: Values of R_0 for various diseases caused by microparasites.

Suppose there were a treatment that if administered to an individual would guarantee they were protected from infection. What proportion of the population would need to receive the treatment in order to protect the population? If we exceed this proportion (or even just meet it), then the parasite will not spread in the population.

If we consider one initially infectious individual, its effective R_0, which we'll call R_e, is going to be muted since the probability of encountering susceptible individuals is not 1, but rather $1 - p$.

$$R_e = R_0(1 - p) \tag{24}$$

For $R_e < 1$ (our condition to ensure the parasite doesn't spread in the host population), we require

$$R_0(1 - p) < 1 \tag{25}$$

which can be written as

$$p > 1 - \frac{1}{R_0} \tag{26}$$

Figure 7 shows how the critical proportion of hosts that must be immunized by a treatment increases with R_0. Importantly we see that this proportion is often well below 1.0. Treatment directly protects the treated individuals and indirectly protects the others. The concept of herd immunity explains why small pox (R_0~6) was eradicated. Although an incredible effort was made to treat all individuals, this was not possible. However, a sufficient proportion of the human population was immunized and small pox was eliminated.

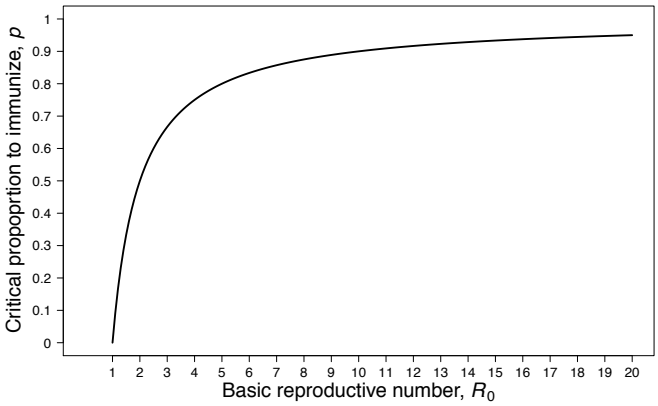


Figure 7: The critical proportion of the population that must be immunized to prevent parasite invasion and persistence increases with R_0

Disease-induced mortality (virulence) and the transmission-virulence trade-off

Many parasites (including phocine distemper virus) can kill their hosts. It is estimated that phocine distemper has killed up to 50% of some harbor seal populations. We can model this effect with an additional mortality term. For example,

$$\frac{dS}{dt} = (b_0 - b_1 N)N - d_0 S - \beta \frac{SI}{N} \quad (27)$$

$$\frac{dI}{dt} = \beta \frac{SI}{N} - gI - d_0 I - \alpha I \quad (28)$$

$$\frac{dR}{dt} = gI - d_0 R \quad (29)$$

where the basic reproductive number becomes

$$R_0 = \frac{\beta}{g + d_0 + \alpha} \quad (30)$$

Because it appears in the denominator for the expression for R_0, parasite virulence (α) decreases parasite fitness. By killing its host, the parasite deprives itself of transmission opportunities. This has led evolutionary ecologists to ask: *Why are all parasites not benign?* At first glance this indeed makes a lot of sense because the value of α that maximizes R_0 is $\alpha = 0$. However, a commonly-observed driver of virulence is a high replication rate of microparasites inside a host. While this may run the risk of host death, it also allows the parasite to produce a lot of transmissible copies of itself. So, while within-host parasite replication rate is negatively associated with parasite fitness due to virulence, it is positively associated with parasite fitness due to transmission. This trade-off between transmission and virulence appears to explain the *intermediate virulence* frequently observed in host-parasite interactions.

Test yourself

- What are the consequences of density-independent and density-dependent contact rates on parasite invasion?
- How does the data collected on phocine distemper virus provide evidence for density-independent contact rates of its seal hosts?
- Why is R_0 a measure of parasite fitness, and which factors act to increase and decrease parasite fitness?
- What mechanisms help parasites persist in host populations?
- How does the effective reproductive number, R_e, relate to R_0 and which one must be <1 to prevent a parasite establishing in a host population?

Further reading

- Swinton, J. et al. 1998. J. Anim. Ecol. "Persistence thresholds for phocine distemper virus infection in harbour seal *Phoca vitulina* metapopulations"
- Heide-Jorgensen, M.P. and Harkonen, T. 1992. J. Appl. Ecol. "Epizootiology of the seal disease in the Eastern North Sea"

Homework

1. In the boxes-and-arrows diagram (Fig. 2) add (and label) single arrows that represent: (i) waning immunity, (ii) vertical transmission, (iii) disease-induced mortality (virulence).

2. Using a common x-axis of "within-host replication rate", on one graph sketch the relationships between each of transmission, virulence, R_0 with x.

3. Assuming a density-dependent contact rate, what is the threshold host populations size, N_T, that must be exceeded for a parasite with a transmission rate of $\beta = 0.0005$ day^{-1} and an infectious period of 10 days, to invade?

4. For a parasite with $R_0 = 14$, what proportion of the host population needs to be immunized to prevent parasite invasion?