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Predator–prey oscillations can shift when diseases become endemic

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HIGHLIGHTS

- Consider a density dependent disease of a host in a predator–prey oscillation.
- Basic reproductive number (R_0) is based on time average of the oscillations.
- In particular, R_0 is not based on the equilibrium it oscillates around.
- The reason is that time-averaged host density differs from equilibrium density.
- This undermines the usual equilibrium-based 'R_0' for predator–prey cycles.

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ABSTRACT

In epidemiology, knowing when a disease is endemic is important. This is usually done by finding the basic reproductive number, R_0, using equilibrium-based calculations. However, oscillatory dynamics are common in nature. Here, we model a disease with density dependent transmission in an oscillating predator–prey system. The condition for disease persistence in predator–prey cycles is based on the time-average density of the host and not the equilibrium density. Consequently, the time-averaged basic reproductive number $\overline{R_0}$ is what determines whether a disease is endemic, and not on the equilibrium-based basic reproductive number R_0^*. These findings undermine any R_0 analysis based solely on steady states when predator–prey oscillations exist for density dependent diseases.

1. Introduction

In epidemiology, the classical method of determining whether a disease will be endemic or die out is by finding the basic reproductive number R_0. The basic reproductive number is understood as the number of secondary infections from an infected individual, during its infectious period, in an otherwise purely susceptible host population (although more general definitions are available, see Bacaër and Ait Dads, 2012; Inaba, 2012). If the basic reproductive number is less than one, the disease will not survive, whereas if the basic reproductive number is greater than one, the disease will spread. Typically, this is calculated based on a constant population. However, not all populations are at equilibrium.

Oscillatory dynamics has recently become the focus of many epidemiologists studying both human and wildlife diseases. Although endogenous oscillations like predator–prey oscillations are mentioned occasionally (for example Greenman and Norman, 2007), the investigations that follow are invariably on exogenous oscillations caused by external forcing. These exogenous oscillations include periodic or stochastic forcing caused by seasonality, multi-annual periodic events like El Niño and anthropogenic interventions (Altizer et al., 2006; Greenman and Norman, 2007). Of these, seasonality is probably the most prominent. For example, Grassly and Fraser (2006) state that there are four types of causes of seasonality in human infectious diseases: (a) survival of pathogen outside host; (b) host behaviour; (c) host immune function; and (d) abundance of vectors and non-human hosts.

Within this body of work, it has been shown that some exogenous oscillations can shift the endemic threshold (Greenman and Norman, 2007; Bacaër and Abdurahman, 2008; Nakata and Kuniya, 2010, for example). However, populations frequently cycle as the result of endogenous mechanisms. Density-dependence, delay effects and ecological interactions are probably the most prominent of numerous examples (Turchin, 2003). Predator–prey oscillations are particularly iconic,and the field of eco-epidemiology has begun studying the impact diseases have on ecological relationships like predator–prey interactions (and vice versa). So far, it has largely been assumed that the criteria for the disease becoming endemic is the same for

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predator–prey equilibria and oscillations. For example, papers based on Rosenzweig–MacArthur dynamics have ignored the possibility that they are different (for example Chattopadhyay and Arino, 1999; Chattopadhyay et al., 2003; Haque and Chattopadhyay, 2007; Bairagi et al., 2007). However, Hadeler and Freedman (1989) noted that the endemic thresholds are different for equilibria and oscillations, but they did not explain why. This phenomenon has only recently been rediscovered by Kooi et al. (2011), where they briefly noted that the endemic thresholds are not the same, but they did not explain why either. In short, the consequences of oscillatory dynamics caused by predator–prey oscillations on disease establishment have not been thoroughly investigated and have often been overlooked.

In this paper, we find that the basic reproductive number for a disease is different from the value derived from the (unstable) equilibrium when the host is involved in predator–prey oscillations. This is the result of the basic reproductive number being based on the time average of the predator–prey oscillations and not on the corresponding predator–prey equilibrium. Two eco-epidemiological models are developed to demonstrate these results. One considers an SI disease in the predators, whereas the other considers an SI disease in the prey. In both models, transmission is density dependent, although we later consider the frequency dependent case as well.

Throughout this paper, we will refer to the equilibrium-based basic reproductive number as R_0^* and the time-averaged basic reproductive number as $\overline{R_0}$. These 'decorations' allow us to distinguish these numbers from the actual basic reproductive number, R_0.

2. The models

The models used are based on the Rosenzweig–MacArthur model, i.e. logistic growth of prey, Holling type II functional response and exponential decay of the predator without prey. Hence, the underlying scaled predator–prey model is

$$\frac{dN}{dt} = rN(1-N) - \frac{NP}{h+N}, \tag{1}$$

$$\frac{dP}{dt} = \frac{NP}{h+N} - mP, \tag{2}$$

where N is the prey density and P is the predator density, r is the per-capita growth rate for the prey (when rare), m is the per-capita natural death rate for the predator, and h is the half-saturation density for the Holling type II functional response.

We will assume that there is an SI disease with density dependent transmission. This means that the disease will split the host population into a susceptible population (S) and an infected population (I). There is one model where the disease infects predators and an equivalent model with the disease infecting the prey. Here we will assume in both models that the disease causes more deaths, but that infected individuals are otherwise identical to susceptible individuals (unless otherwise stated, like in Section 4). On top of this, all newborns are assumed to be susceptible, i.e. there is no vertical transmission.

We will formulate the models in terms of the total predator and prey populations and the prevalence of the disease in the host population, i.e. the fraction of hosts that are infected. In other words $i_P = \frac{I_P}{P} = \frac{I_P}{S_P+I_P}$ and $i_N = \frac{I_N}{N} = \frac{I_N}{S_N+I_N}$,

where I_P (I_N) and S_P (S_N) are the infected and susceptible predator (prey) densities, respectively (the original SI models can be found in Appendix A). This scaling is used to demonstrate the effect the disease has on the host in the predator–prey system, something that is not immediately clear when the host population is in two classes. Notice that i_P and i_N can take any value between 0 and 1, where a value of zero means that there is no disease and a value of one means that every host is infected.

The scaling and parameters are equivalent to those in Hilker and Schmitz (2008); their model being the same as the diseased predators model except they used frequency dependent infection.

2.1. Diseased predators model

$$\frac{dN}{dt} = rN(1-N) - \frac{NP}{h+N}, \tag{3}$$

$$\frac{dP}{dt} = \frac{NP}{h+N} - mP - \mu P i_P, \tag{4}$$

$$\frac{di_P}{dt} = i_P\left((\beta P - \mu)(1-i_P) - \frac{N}{h+N}\right). \tag{5}$$

2.2. Diseased prey model

$$\frac{dN}{dt} = rN(1-N) - \frac{NP}{h+N} - \mu N i_N, \tag{6}$$

$$\frac{di_N}{dt} = i_N((\beta N - \mu)(1-i_N) - r), \tag{7}$$

$$\frac{dP}{dt} = \frac{NP}{h+N} - mP. \tag{8}$$

In both models, μ is the disease-induced death rate and β is the disease transmissibility. In the diseased prey model, r is defined as a per capita birth rate instead of a growth rate, i.e. there is no density independent mortality (see A.3 for details). This means that susceptible prey only experience mortality via predation and competition.

Parameter values are chosen such that the predator–prey system has a stable limit cycle in the absence of the disease (i.e. $m < (1-h)/(1+h)$). Throughout this paper, any variable that is 'starred', e.g. P^*, refers to the (unstable) steady state of that variable. Likewise, any variable that has a 'bar', e.g. $\overline{P}$, is the time-average of that variable. In this paper, the time-average (of P, say) is defined as $\overline{P} = (1/T)\int_0^T P\,dt$, where T is the period of the predator–prey limit cycle.

3. Results

Several papers have calculated R_0 in a periodic environment (Bacaër and Guernaoui, 2006; Wang and Zhao, 2008; Wesley and Allen, 2009, for example). Here, we find $\overline{R_0}$ by using a Floquet theory argument. However, we only need to focus on the infecteds/prevalence equations since the predator–prey cycles are stable in the original Rosenzweig–MacArthur model (1)–(2). The details of this argument are in A.3. However, it is worth noting that all $\overline{R_0}$'s can be found directly by using the method in Bacaër and Guernaoui (2006, Eq. (31)).

3.1. Diseased predators

Fig. 1a shows when a disease establishes in an oscillating predator host, as a function of transmissibility, β. For low transmissibility, the disease is not endemic and only disease-free predator–prey oscillations are stable. At $R_0^* = 1$, an unstable endemic equilibrium bifurcates from the unstable disease-free predator–prey equilibrium. For some region after this (the grey region), we have stable disease-free oscillations with an unstable endemic equilibrium, i.e. the disease is not endemic despite $R_0^* > 1$. At $\overline{R_0} = 1$, a stable endemic limit cycle bifurcates from

the stable disease-free predator–prey limit cycle. Beyond this, the disease is endemic in oscillation until the stable oscillations and unstable equilibrium collide at a Hopf bifurcation, giving rise to a stable endemic equilibrium.

The crucial point of Fig. 1a is that the system remains disease-free (zero prevalence) in a parameter range well beyond $R_0^* > 1$, where R_0^* is the equilibrium-based basic reproductive number $R_0^* = \beta P^*/(m+\mu)$ and P^* is the predator density at the disease-free predator–prey equilibrium. This means that the system remains disease-free for a larger parameter range because of the oscillatory dynamics.

Fig. 1b demonstrates that this difference can be attributed to the difference in the time-averaged density of the predator between the equilibrium and oscillations (a corollary of results in Armstrong and McGehee, 1980). A disease is endemic only when the time-averaged basic reproductive number $\overline{R_0} = \beta \overline{P}/\ (m+\mu) \geq 1$, where $\overline{P}$ is the time-average predator density for the disease-free predator–prey oscillations (see Appendix A). The dotted line representing $R_0(\beta) = 1$ gives the invasion condition for a disease, i.e. the critical host density required for the disease to establish. This means that a disease can only become endemic if the time-averaged predator density is above the dotted line. Note that the dotted line intersects both the (unstable) predator–prey equilibrium and the time-average of the predator–prey oscillations at the transcritical bifurcations where the disease becomes endemic. This is consistent with the fact that R_0^* and $\overline{R_0}$ differ only because the (time-averaged) host densities of the disease-free equilibrium and oscillations are different.

3.2. Diseased prey

Fig. 2a demonstrates that the (stable) endemic oscillations bifurcate from the disease-free predator–prey oscillations before the (unstable) endemic equilibrium bifurcates from the disease-free equilibrium. This contrasts with Fig. 1a where the oscillations bifurcate after the unstable equilibrium bifurcates. Hence there is a region (the grey region) where the disease is endemic in oscillations despite $R_0^* < 1$. This means that a disease in the prey host becomes endemic at a smaller transmissibility (β) than expected from the standard calculation of the equilibrium-based basic reproductive number $R_0^* = \beta N^*/(\mu + P^*/(h+N^*) + rN^*)$, which can be simplified to $R_0^* = \beta N^*/(\mu + r)$, where N^* and P^* are the respective prey and predator densities at the disease-free predator–prey equilibrium. Instead, the invasion criterion is $\overline{R_0} = 1$, where $\overline{R_0} = \beta \overline{N}/(\mu + \overline{P/(h+N)} + r\overline{N}) = \beta \overline{N}/(\mu + r)$ is the time-averaged basic reproductive number (see Appendix A). Since the predator–prey oscillations have a larger time-averaged prey density than the equilibrium (Armstrong and McGehee, 1980), $\overline{R_0}$ has a smaller threshold value of β to become endemic. This means that the disease will find it "easier" to become endemic because of the oscillatory dynamics. The dotted line in Fig. 2b demonstrates that this change in critical β can be solely attributed to the difference between N^* and $\overline{N}$.

3.3. Summary

In this section, we have described the difference between the equilibrium-based basic reproductive number R_0^* and the time-averaged basic reproductive number $\overline{R_0}$ for predator–prey oscillations. In all cases we have that $R_0 = \overline{R_0}$. At equilibrium, $R_0 = \overline{R_0} = R_0^*$. However, in oscillations, we generally have $R_0 = \overline{R_0} \neq R_0^*$.

On a side issue, both the diseased predator and diseased prey models demonstrate that the disease can stabilise an oscillating predator–prey system by increasing total host mortality (for a

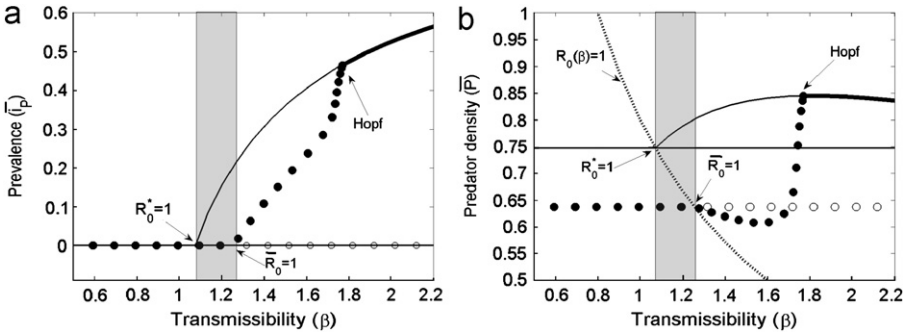

Fig. 1. Diseased predators model: Time-averaged bifurcation diagram of (a) prevalence and (b) predator (host) density, with respect to the disease transmission parameter β. The grey region highlights where the disease is *not* endemic despite the equilibrium-based reproductive number being greater than one, i.e. $i_P = 0$ and $R_0^* > 1$. Thick lines mean stable equilibria, thin lines mean unstable equilibria, black (white) circles are time-averages of stable (unstable) oscillations. The dotted line in (b) represents $R_0(\beta) = 1$ and goes through both $R_0^* = 1$ and $\overline{R_0} = 1$, demonstrating that host time-averaged density alone explains the difference in disease invasion. (Parameter values: $\mu = 0.5$, $r = 2$, $h = 0.3$ and $m = 0.3$.)

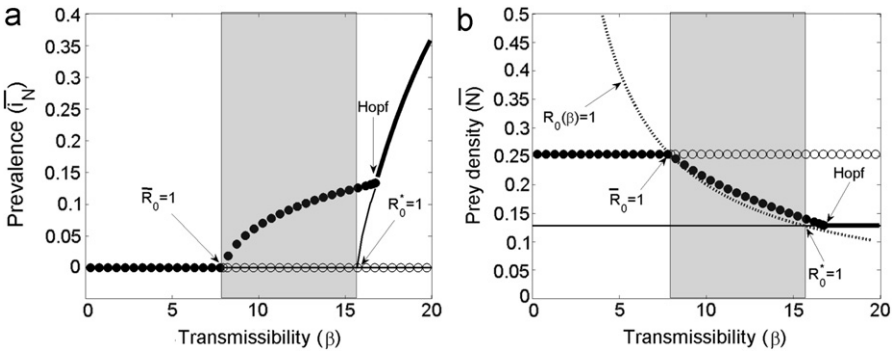

Fig. 2. Diseased prey model: Time-averaged bifurcation diagram of (a) prevalence and (b) prey (host) density, with respect to the disease transmission parameter β. The grey region highlights where the disease is endemic despite the equilibrium-based reproductive number being less than one, i.e. $\overline{i_N} > 0$ and $R_0^* < 1$. The lines and circles have the same meaning as those in Fig. 1. (Parameter values: $\mu = 1$, $r = 1$, $h = 0.3$ and $m = 0.3$.)

sufficiently large μ and β), in a manner similar to that in Hilker and Schmitz (2008).

4. Extensions

4.1. Disease alters density dependent mortality in prey host

Previously, infected prey experienced the same density dependence as susceptible prey. We will now change this assumption by letting infected prey experience a different level of density dependence than susceptible prey. Henceforth, we will assume that susceptible prey have a density dependent mortality term of rSN (since the carrying capacity has been scaled to one), whereas infected prey have a density dependent term $rcIN$ (see Appendix A). Here, c is a coefficient that defines the density dependent mortality infected prey experience relative to susceptible prey. If $c=1$, then the total density dependent mortality becomes rN^2, which is the same as in the original diseased prey model.

While this formulation accounts for different competitive pressures experienced by susceptible and infected individuals, it implies that both susceptibles and infected exert the same competitive strength on an individual they interact with. This is a simplifying assumption and in general is not true. In fact, (Hochberg, 1991) argues that there are four different terms of density dependence in an SI model; the density dependence that (i) susceptibles inflict on susceptibles (called α_{SS}), (ii) susceptibles inflict on infected (α_{IS}), (iii) infected inflict on susceptibles (α_{SI}) and (iv) infected inflict on infected (α_{II}). However, since we can assume that there are negligibly few infected individuals when finding R_0^* or $\overline{R_0}$, the density dependent mortalities caused by infected individuals (cases (iii) and (iv)) are negligible on the calculation of R_0^* and $\overline{R_0}$. This means that R_0^* and $\overline{R_0}$ found here are the same as those in a full four-case density dependent model, where $r=\alpha_{SS}$ and $rc=\alpha_{IS}$.

Now, incorporating this assumption into the diseased prey model, we get

$$\frac{dN}{dt} = rN(1-N((1-i_N)+c\,i_N)) - \frac{NP}{h+N} - \mu N i_N, \tag{9}$$

$$\frac{di_N}{dt} = i_N((\beta N - \mu - rN(c-1))(1-i_N) - r), \tag{10}$$

$$\frac{dP}{dt} = \frac{NP}{h+N} - mP. \tag{11}$$

In A.3, we demonstrate that

$$\overline{R_0} = \frac{\beta \overline{N}}{\mu + r + r(c-1)\overline{N}}, \tag{12}$$

as well as $R_0^* = \beta N^*/(\mu + r + r(c-1)N^*)$.

If $c \neq 1$, then the denominator of $\overline{R_0}$ depends on $\overline{N}$ and we get an overall expression for $\overline{R_0}$ that is hyperbolic rather than linear in $\overline{N}$. If we assume that infected suffer more from density dependent mortality than susceptibles (because they are at a disadvantage in competition), then we have $c>1$. The expression for $\overline{R_0}$ is then much like a Holling type II functional response. This means that $\overline{R_0}$ still monotonically increases with respect to $\overline{N}$, but it saturates to $\overline{R_0}_{max} = \beta/r(c-1)$. A corollary of this is that the disease can never be endemic if $\beta < r(c-1)$. However, saturation happens beyond all feasible values of $\overline{N}$; consequently, we have $\overline{R_0}$ is 'sublinear' with respect to $\overline{N}$ (Fig. 3).

Now suppose $c<1$, i.e. infected prey are better competitors than susceptible prey. (While this assumption seems unrealistic at first glance, Sieber, Malchow and Hilker (in preparation) find that this is possible if density dependence is due to exploitative competition where infected take up less resources. If infected take up less resources, one would expect that infected would have a smaller reproductive rate than susceptibles. Here, however, both populations have the same birth rate. Hence this may not be compatible with $c<1$.) Notice that although $\overline{R_0}$ does have an asymptote and can be negative for large enough $\overline{N}$, such values of $\overline{N}$ can never be attained since $\overline{N}$ is bounded above by the disease-free carrying capacity, i.e. $\overline{N} \leq 1$. This means that $\overline{R_0}$ is 'super-linear' and monotonically increasing for all feasible values of $\overline{N}$ (Fig. 3).

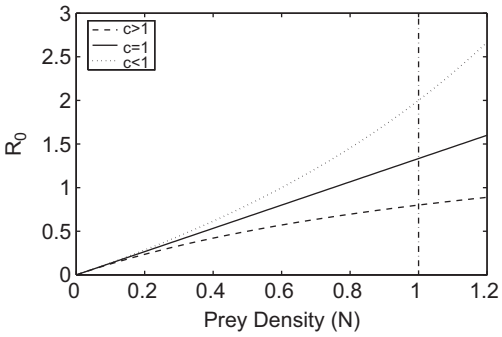

Fig. 3. Density dependent mortality: plots of R_0 as a function of host density. This figure demonstrates, with respect to N, R_0 is sublinear for $c>1$, linear for $c=1$ and superlinear for $c<1$. Replace R_0 and N with R_0^* and N^* or $\overline{R_0}$ and $\overline{N}$ to get the equivalent figure of R_0^* and $\overline{R_0}$, respectively. The vertical line represents the disease-free carrying capacity of the prey. Parameter values: $\beta=2$, $\mu=0.5$, $r=1$, $c=2$ (sublinear) and $c=0.5$ (superlinear).

Using $(\partial/\partial i_N)(dN/dt)$, we get that N increases with i_N if $\mu + r(c-1)N < 0$. In particular, if $\mu < r(1-c)$, the prey host at disease-free carrying capacity (i.e. no predators) will increase in density as the disease establishes in the population. This means a disease that reduces density dependent mortality can benefit the infected host if this reduction is greater than the additional disease-induced mortality. If this is the case (which at the moment is hypothetical), the disease will increase the total host population.

4.2. Frequency dependent transmission

One key assumption in all the previous models in this paper is density dependent transmission. Incorporating frequency dependent transmission into the model (9-11), the prevalence equation becomes:

$$\frac{di_N}{dt} = i_N((\beta - \mu - rN(c-1))(1-i_N) - r). \tag{13}$$

The only difference between this and the previous prevalence equation is that βN has become just β. Using the same arguments as before, we get that $R_0^* = \beta/(\mu + r + r(c-1)N^*)$ and $\overline{R_0} = \beta/(\mu + r + r(c-1)\overline{N})$. If $c=1$, i.e. we are working with the frequency dependent transmission version of the original diseased prey model, we have that $R_0^* = \overline{R_0} = \beta/(\mu + r)$. This means that the basic reproductive number is independent of host density, whether oscillatory or not. However, if $c>1$, we have that $\overline{R_0}$ is monotonically decreasing with host density $\overline{N}$. This means that disease is endemic when the population is sufficiently small, i.e. $\overline{N} < (\beta - \mu - r)/r(c-1)$. If $c<1$, then $\overline{R_0}$ is monotonically increasing with host density. Here, the disease is endemic if the population is sufficiently large, i.e. $\overline{N} > (\beta - \mu - r)/r(1-c)$.

5. Discussion

We have demonstrated that the conditions for a disease to become endemic in a host involved in a predator–prey relationship

depend on the time-averaged host density. Rosenzweig–MacArthur predator–prey dynamics are used to show this. Oscillations in such a model have a greater time-averaged prey density and lower time-averaged predator density compared to the corresponding (unstable) equilibrium. This means that predator–prey oscillations make a disease easier to become endemic in a prey host and harder to become endemic in a predator host.

These explanations could also explain the differing basic reproductive numbers observed in Kooi et al. (2011) and make some progress towards explaining the basic reproductive number argument from Hadeler and Freedman (1989). The latter is not straightforward since the disease in their model infects both the prey and predator and only by cross-infection (i.e. infected prey infect susceptible predators and infected predators infect susceptible prey), which complicates the pattern of transmission (see Appendix B for a model description). However, Fig. 4a demonstrates that the disease is not endemic when the hosts cycle despite having an equilibrium-based basic reproductive number greater than one, i.e. $R_0^* > 1$ (like the diseased predator model). Likewise, Fig. 4b shows that the disease is endemic when the hosts cycle despite having an equilibrium-based basic reproductive number less than one (like the diseased prey model). This means that the equilibrium-based basic reproductive number does not give either an upper nor lower bound for when a disease is endemic in predator–prey oscillations. With two infected compartments, the model in Hadeler and Freedman (1989) is considerably more complicated that the diseased predators or diseased prey models. In another model with two infected compartments (Bacaër, 2007, a malaria model with seasonality in the vector), it was shown that the actual endemic threshold is based on the time-averaged reproductive number with a correction based on the size of the oscillations. Assuming something similar occurs here, the difference in endemic thresholds between predator–prey oscillations and equilibria in Hadeler and Freedman (1989) can largely be explained by the difference in the time-averages, but this difference alone does not give the full picture.

This can have major consequences for disease management and epidemiology. Firstly, it undermines the idea that the equilibrium-based basic reproductive number determines whether a disease would invade deterministically. This somehow resembles the scenario of a backward bifurcation, where a disease may persist (depending on initial conditions or the "history" of the population) even though $R_0 < 1$. Conversely, other bifurcations like saddle-node bifurcations or homoclinic bifurcations can lead to the disappearance of disease even though $R_0 > 1$, but this typically involves host extinction as well (Hilker et al., 2009; Hilker, 2010). Consequently, if oscillations exist in the disease-free predator–prey system, care must be taken when using reproductive number arguments based on equilibria as one cannot assume that they are the same for oscillations (like those in Hilker and Schmitz, 2008; Das et al., 2011).

Secondly, there can be profound consequences for the eradication of diseases within predators. A common strategy to help eradicate a disease from a wildlife host is indiscriminate culling or harvesting of the host. For example, hunting/harvesting/culling has been used for controlling chronic wasting disease in some species of deer and elk (Williams et al., 2002), bovine tuberculosis in badgers (Woodroffe et al., 2002) and facial tumour disease in Tasmanian devils (Beeton and McCallum, 2011). However, harvesting/indiscriminate culling corresponds to effectively increasing the constant per-capita death rate. Applying this to a predator population will not decrease, but rather increase the time-average predator density, if the system is cyclic. (This phenomenon is called the hydra effect Abrams, 2009; Sieber and Hilker, 2012.) Hence, harvesting will increase disease prevalence in predators and is therefore counter-productive as a control approach.

In contrast, a management action that can be recommended on the basis of this paper is to enforce endogenous oscillations in an otherwise stable population. The oscillations could bring the time-averaged basic reproductive number $\overline{R_0}$ below one, even though without oscillations R_0^* is greater that one, resulting in long term disease eradication. One such way of forcing oscillations is to utilise the *paradox of enrichment* by increasing the prey's carrying capacity, which will destabilise the predator–prey system.

Lastly, for prey as a host population, a disease will spread more easily under predator–prey oscillations than at equilibrium, thus making eradication harder. Actions that stabilise predator–prey oscillations such as reducing the prey's carrying capacity or increasing the predators death rate can combat this. In particular, indiscriminate culling or harvesting of predators can help eradicate a disease of the prey by stabilising the predator–prey oscillations. This contradicts the 'keeping the herds healthy' hypothesis in

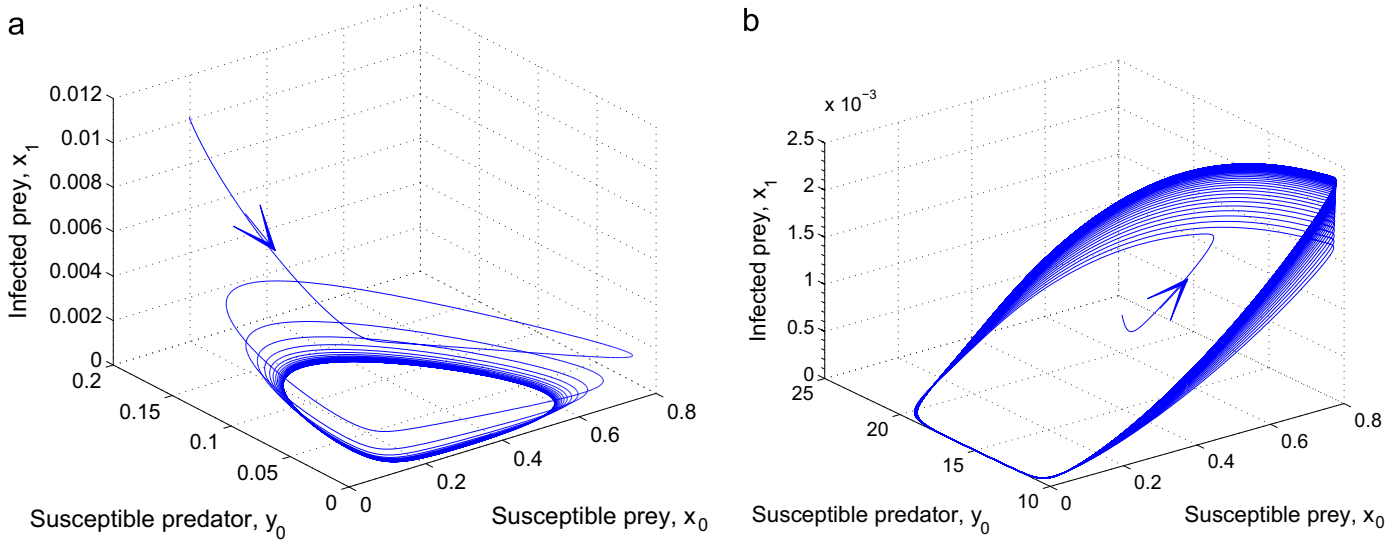

Fig. 4. Disease in both predator and prey: State space diagrams of (a) a disease that does not become endemic in the prey (likewise predator) despite $R_0^* > 1$ ($R_0^* = 1.26$) and (b) a disease that becomes endemic in the prey (likewise predator) despite $R_0^* < 1$ ($R_0^* = 0.8055$). For model details/equations, see Appendix B. Parameter values: (a) $\beta = 3$, $a = 0.1$ and $\rho = 1$ and (b) $\beta = 1.4$, $a = 50$ and $\rho = 10$. Other parameters: $K = \kappa = c = 1$ and $A = B = 0.3$.

Packer et al. (2003), where the predator removal is suggested to result in more infections in the prey.

The effect of shifting the threshold for the establishment of disease described in this paper is only due to the difference in the time-averaged host density. Hence, assumptions about the disease (e.g. increased mortality, reduced fertility, vertical transmission or host manipulation) should not change this. Consequently, the difference between R_0^* and $\overline{R_0}$ is largely independent of model assumptions. In fact, the phenomenon reported here does not depend on the predator–prey dynamics itself, but on the fact that the host is oscillating at a different time-averaged density when compared to the equivalent equilibrium density.

One important assumption made in the diseased prey model is that susceptible and infected prey are equally good intra-specific competitors. However, this assumption is likely to be unrealistic in many cases. In the Extensions, using different strengths of density dependence for susceptibles and infecteds, we demonstrate that although the relationship between time-averaged host density and the time-averaged basic reproductive number is no longer linear, they still monotonically increase with each other. This suggests that density dependence does not alter the rule that higher time-averaged densities have higher values of $\overline{R_0}$.

There is one curious result in the case where infected individuals experience significantly less density dependence than susceptibles ($c \ll 1$); in this case, the disease can increase host density. Here, the reduction in density dependent mortality more than offsets the additional disease-induced mortality, giving a total reduction in host mortality. In particular, this means that infection will result in increasing the carrying capacity of the host population beyond that of a disease-free host population (the per capita growth rate ($r-\mu i_N$) still decreases with prevalence). This scenario of a disease increasing rather than decreasing the host carrying capacity challenges the typically detrimental impact associated with diseases. We have not searched for any empirical evidence for this theoretical prediction, but we believe this could be an interesting over-looked indirect effect of infectious diseases.

However, there is one crucial assumption throughout this paper; namely density dependent disease transmission. For a frequency dependent disease, the basic reproductive number would be independent of host density, whether time-averaged or otherwise. If we put together frequency dependent transmission and infected individuals experiencing greater density dependent mortality, we get that the basic reproductive number R_0 is a monotonically decreasing function of host density. This means that the disease is endemic if the host population is below some threshold density. This is contrary to typical epidemiological models where a disease is endemic when above some threshold density.

Frequency dependent transmission and density dependent mortality are common in epidemiological and ecological systems, respectively. Hence, it seems reasonable that a maximum viable host density should exist in some wildlife diseases. In these cases, attempts to eradicate a disease by reducing the (time-averaged) host density (e.g. by indiscriminate culling) could actually help keep a disease endemic. A more general discussion of this effect is in preparation.

The diseased predator model also exhibits bistability and saddle-node bifurcations (Bate and Hilker, in preparation; Hurtado et al., in preparation), which further undermine the use of basic reproductive numbers in determining the long term dynamics of an eco-epidemiological system.

In summary, density dependent diseases can only become endemic in an oscillating predator–prey system if the time-averaged density of the disease free oscillation is large enough. The time-averaged density is different from the equilibrium-based density that the disease-free oscillations cycle around. This means endemicity cannot be determined by the equilibrium-based basic reproductive number. These results can have major consequences on disease management and conservation in oscillating populations.

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Appendix A. Model formulation and calculation of $\overline{R_0}$

For all models, the equilibrium-based basic reproductive number R_0^* can be found from $\overline{R_0}$ by setting the time-averaged densities ($\overline{N}$ or $\overline{P}$) as the equilibrium value (since the time-average of something at equilibrium is the equilibrium). The converse is generally not true; for example $(P^2)^* = P^{*2}$ but generally $\overline{P^2} \neq (\overline{P})^2$. This example is equivalent to the variance of one data point against (infinitely) many data points, where variance is zero in the former, but variance is non-zero in the latter unless P is constant.

A.1. Diseased predator

Incorporating the assumptions in the main text for a disease in the predators, we get

$$\frac{dN}{dt} = rN(1-N) - \frac{N(S+I)}{h+N}, \tag{A.1}$$

$$\frac{dS}{dt} = \frac{N(S+I)}{h+N} - mS - \beta SI, \tag{A.2}$$

$$\frac{dI}{dt} = \beta SI - (m+\mu)I. \tag{A.3}$$

From an eco-epidemiological point of view, one key question is what a disease does to the host population. This is not entirely clear when the host is split into two different classes. Hence, we will gather all predators, whether susceptible or infected, into one class. This is done by replacing the equation for dS/dt with $dP/dt = d(S+I)/dt$. Consequently, we have

$$\frac{dP}{dt} = \frac{NP}{h+N} - mP - \mu I. \tag{A.4}$$

From this, we establish that the disease only adds an addition mortality term to the host population. On top of this, by replacing infected predators with disease prevalence, we get the diseased predator equations (3)–(5) in the main text.

Along the predator–prey limit cycle, if we integrate over the period T of the limit cycle, then the cycle is back where it has started. The same is true if we take the 'per-capita' of the limit cycle. This means that both $\int_0^T (1/P)(dP/dt)\,dt = 0$ and $\int_0^T (1/N)(dN/dt)dt = 0$ by the Fundamental Theorem of Calculus, noting that $(1/P)(dP/dt) = d(\ln P)/dt$. Armed with this information we get

$$\overline{R_0} = \frac{\frac{1}{T}\int_0^T \beta P\,dt}{\mu+m} = \frac{\beta\overline{P}}{\mu+m}, \tag{A.5}$$

which can be derived from

$$\frac{1}{T}\int_0^T \frac{1}{I}\frac{dI}{dt}\,dt = \frac{1}{T}\int_0^T \frac{d(\ln I)}{dt}\,dt = 0,$$

where I is negligibly small.

There is an equivalent formulation of $\overline{R_0}$ from the prevalence equation (5) which can be found by substituting $(1/T)\int_0^T (1/P)(dP/dt)\,dt = 0$ into the denominator of the above $\overline{R_0}$. However, this

formulation is a more complicated formulation of $\overline{R_0}$ and therefore has been omitted.

A.2. Diseased prey

Following the modelling assumptions in the main text for a disease in the prey, we get

$$\frac{dS}{dt} = r(S+I)(1-S) - \frac{SP}{h+(S+I)} - \beta SI, \tag{A.6}$$

$$\frac{dI}{dt} = \beta SI - \frac{IP}{h+(S+I)} - (\mu + r(S+I))I, \tag{A.7}$$

$$\frac{dP}{dt} = \frac{(S+I)P}{h+(S+I)} - mP. \tag{A.8}$$

Recall that there is no vertical transmission, i.e. infected individuals reproduce into the S-class with the same per-capita birth rate r as susceptible individuals. Moreover, both susceptible and infected individuals experience density-dependent mortality (described by the parameter r since the carrying capacity has been scaled to one) and mortality due to predation, but no density-independent mortality.

Like the diseased predator model, it is more convenient to work with N instead of S. Consequently, we have

$$\frac{dN}{dt} = rN(1-N) - \frac{NP}{h+N} - \mu I. \tag{A.9}$$

Again, by replacing infected prey with disease prevalence, we get the diseased prey equations (6)–(8) in the main text.

Just like for the diseased predator results, we integrate over the period T of the limit cycle for the 'per capita' of the limit cycle. Using $\frac{1}{T}\int_0^T \frac{1}{I}\frac{dI}{dt}\,dt = \frac{1}{T}\int_0^T \frac{d(\ln I)}{dt}\,dt = 0$,

where I is negligibly small, we get that

$$\overline{R_0} = \frac{\frac{1}{T}\int_0^T \beta N\,dt}{\mu + \frac{1}{T}\int_0^T \left(\frac{P}{h+N} + rN\right)dt} = \frac{\beta\overline{N}}{\mu + \overline{\left(\frac{P}{h+N}\right)} + r\overline{N}}. \tag{A.10}$$

By using $r = \overline{(P/(h+N))} + r\overline{N}$ (from $(1/T)\int_0^T (1/N)(dN/dt)\,dt = 0$, where I (i_N) is negligibly small), $\overline{R_0}$ can be greatly simplified to

$$\overline{R_0} = \frac{\frac{1}{T}\int_0^T \beta N\,dt}{\mu + r} = \frac{\beta\overline{N}}{\mu + r}. \tag{A.11}$$

This formulation demonstrates that $\overline{R_0}$ is in fact linear with $\overline{N}$, something that could not be seen from the original formulation of $\overline{R_0}$. It is also the formulation of $\overline{R_0}$ that can be found directly from the prevalence equation (7) found in the main text.

A.3. Density dependent mortality

Here, we will allow infected prey to be weaker (or stronger) intra-specific competitors than susceptible prey, and see the effect this has on $\overline{R_0}$ and its relationship with $\overline{N}$.

Starting with the diseased prey model, suppose that infected experience density dependence differently to susceptibles. Doing so, we have that the infected population follows:

$$\frac{dI}{dt} = \beta(N-I)I - rcNI - \mu I - \frac{IP}{h+N}, \tag{A.12}$$

where rc is reflects the density dependence infected suffer. The corresponding N,i_N,P equations are given in Section 4 of the main text (9)–(11).

Working with the infected population equation (or its logarithm), and assuming that I is negligibly small, we get

$$\overline{R_0} = \frac{\frac{1}{T}\int_0^T \beta N\,dt}{\mu + \frac{1}{T}\int_0^T \frac{P}{h+N} + rcN\,dt} = \frac{\beta\overline{N}}{\mu + \overline{\left(\frac{P}{h+N}\right)} + rc\overline{N}}. \tag{A.13}$$

This in itself is not enlightening. However, by substituting $(1/T)\int_0^T (1/N)(dN/dt)\,dt = 0$, where I (i_N) is negligibly small or by using the prevalence equation we get

$$\overline{R_0} = \frac{\frac{1}{T}\int_0^T \beta N\,dt}{\mu + r\left(1 - \frac{1}{T}\int_0^T N\,dt\right) + rc\frac{1}{T}\int_0^T N\,dt} = \frac{\beta\overline{N}}{\mu + r + r(c-1)\overline{N}}. \tag{A.14}$$

Linking back to the original diseased prey model (when $c=1$), we had that $\overline{R_0}$ is linear (with respect to $\overline{N}$). This means that the original $\overline{R_0}$ is the transition between the sublinear ($c>1$) and superlinear ($c<1$) cases, which makes sense.

Appendix B. Disease in both predators and prey

The model is from Hadeler and Freedman (1989). It has notable differences to the other models in this paper beyond just being a disease infecting both predators and prey. Disease transmission is interspecific only, where susceptible predators become infected by feeding on infected prey, and susceptible prey are infected by infected predators. However, the disease-free dynamics are the same (up to rescaling) as the models considered in this paper, and thus have the same type of oscillations.

Keeping the original notation from Hadeler and Freedman (1989), we have

$$\frac{dx_0}{dt} = ax\left(1 - \frac{x_0}{K}\right) - \frac{x_0}{A + x_0 + \rho x_1}y - \beta x_0 y_1, \tag{B.1}$$

$$\frac{dy_0}{dt} = -c\frac{B}{B+A}y_0 + c\frac{x_0 + \rho x_1}{A + x_0 + \rho x_1}y - \kappa\frac{\rho x_1}{A + x_0 + \rho x_1}y_0, \tag{B.2}$$

$$\frac{dx_1}{dt} = \beta y_1 x_0 - \frac{axx_1}{K} - \frac{\rho x_1}{A + x_0 + \rho x_1}y, \tag{B.3}$$

$$\frac{dy_1}{dt} = -c\frac{B}{B+A}y_1 + \kappa\frac{\rho x_1}{A + x_0 + \rho x_1}y_0, \tag{B.4}$$

where $x = x_0 + x_1$ is the total prey density, x_0 is the susceptible prey density and x_1 is the infected prey density. Likewise, $y = y_0 + y_1$ is the total predator density, y_0 is the susceptible predator density and y_1 is the infected predator density. Many of the parameters have abstract definitions chosen for analytical simplicity; but some parameters do have important definitions. For example, ρ is the vulnerability to predation of infected prey relative to the susceptible prey (Hadeler and Freedman, 1989 stipulated that $\rho > 1$, a restriction we will ignore here), κ is the transmissibility from feeding on infected prey, β is the transmissibility of the disease from infected predator to prey, K is the carrying capacity of the prey, and B is the prey density at the disease-free predator–prey equilibrium (when $B < K$).

In this model, oscillatory disease-free predator–prey dynamics occurs when $B < (K-A)/2$. Likewise, the condition where the (equilibrium-based) basic reproductive number $R_0^* = 1$ is

$$\beta\kappa = \frac{cB}{A+B}\frac{ax^*(A+x^*) + \rho K y^*}{\rho K x^* y^*} = \frac{cB}{A+B}\frac{B + \rho(K-B)}{B\rho(K-B)}, \tag{B.5}$$

where (x^*, y^*) is the disease-free (unstable) equilibrium.

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