Disease as an evolutionary weapon

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Disease and predation are both highly important in ecology, yet their interplay has received little attention from biophysicists. Here, we analyse a model of a predator-prey system with disease in both prey and predator populations and determine reasonable parameter values using allometric mass scaling relations. We find that if the predator is a specialist, epidemics frequently drive the predator species to extinction. If the predator has an additional, immune prey species, predators will usually survive. Coexistence of predator and disease is impossible in the single-prey model. We conclude that for the prey species, carrying a pathogen can be an effective weapon against predators, and that being a generalist is a major advantage for a predator.

Keywords: predator, prey, disease, Lotka-Volterra, evolution

INTRODUCTION

Predation is one of the fundamental modes of interaction among living organisms. Mechanisms similar to predation are found in anything from mammals to bacteria. Another equally important factor is epidemic disease, which is also found on all scales in the ecosphere. In recent years it has become clear that many epidemic pathogens are shared between several species [1], of which some presumably prey on each other. If the predator runs a risk of becoming infected when eating infected prey, it is possible that the prey species will be able to use the pathogen as a weapon against the predator. This could even be a very effective evolutionary strategy, given that prey species are often much more numerous than their predators, leading to a high infection pressure against the predator species [2]. On this basis, we propose the hypothesis that a disease shared between a prey species and its predator will often turn out to be a major problem for the predator, and thus perhaps a long term advantage for the prey. However, if the predator has several prey options, epidemics should pose much less of a threat to it, as it can just feed on an immune prey species in the event of an epidemic.

Despite the ubiquity of the two mechanisms, the interplay between predation and disease has been studied relatively little in quantitative biology. Only a few dynamical models exist, most of which primarily concern themselves with single-host epidemics affecting either the predator or the prey [3–5]. Others deal specifically with parasitism rather than epidemic pathogens [6]. Hsieh and Hsiao [7] have constructed a predator-prey-disease model similar to the one we will put forward in this paper. However, their parameterisation and mathematical treatment is different from ours.

A further novelty of our study will be the parameterisation of the model. Previous works on this subject have made few attempts at estimating biologically reasonable model parameters. We will use the well-known allometric scaling of several biological quantities with animal mass to make such estimates. It has been known for decades that quantities such as reproduction rate and metabolic effect scale with animal mass to some quarter power [8]. Attempts have been made in ecology to use this to predict the behaviour of predator-prey systems [9–11]. More recently, it has been shown that disease recovery and death rates also scale with animal mass [12], which is useful in epidemiological modelling [13]. The parameterisation that we will use here will be based in part on our previous work on parameterising the Lotka-Volterra predator-prey equations [11].

In summary, the questions that we will try to answer here will be whether prey species can use epidemic diseases as a weapon against their predators, and if so, for what parameter values this weapon will be most effective. We also want to examine the effect of a predator being a generalist, i.e. having an alternative prey option that is not affected by the epidemic.

MODELS

The first classic theory upon which we will base our study is the Lotka-Volterra predator-prey model

$$\frac{dx}{dt} = \alpha x(1 - x/K) - \phi x \frac{y}{x+\epsilon} \tag{1}$$

$$\frac{dy}{dt} = \nu y \frac{x}{x+\epsilon} - \delta y \frac{\epsilon}{x+\epsilon} \tag{2}$$

where x is prey, y is predator, α is the per capita prey reproduction rate and δ is the predator starvation rate in the absence of prey. K is the prey carrying capacity and ϵ is the half-saturation constant for predators. $\phi \frac{y}{x+\epsilon}$

gives the rate of prey being eaten (the so-called functional response) and $\nu\frac{x}{x+\epsilon}$ gives the predator reproduction rate as a function of prey population (the numerical response) [14]. We have here chosen to modify the original Lotka-Volterra model to account for the natural limit on prey growth and the fact that predators do not grow infinitely fast when there is infinite available prey, nor do they starve when there is enough prey.

We will combine these equations with the equally classic SIR model, which gives the following equations for the changes in population during an epidemic:

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

$$\frac{dI}{dt} = \beta SI - \gamma I \tag{4}$$

$$\frac{dR}{dt} = \gamma I. \tag{5}$$

Here, S denotes susceptible individuals, I infected, and R recovered or dead individuals. β gives the rate at which each infected individual infects susceptible individuals, and γ gives the death or recovery rate of the infected [15].

When constructing our model, we shall make the assumption that the disease is always deadly, as the possibility of recovery with immunity will vastly complicate the analysis in a predator-prey system. Furthermore, we assume that infection from predator to prey is impossible, as any close encounters between the two species are likely to cause the immediate death of the prey. For the sake of simplicity we assume that the majority of predator infections stem from prey, and thus neglect predator-predator infections. This is reasonable, as the density of prey will usually be a lot higher than that of predators, leading to a high prey-predator infection pressure [2, 11]. We also let only healthy animals reproduce, although both healthy and infected predators eat prey. Combining the SIR and Lotka-Volterra models, we end up with the following equations for the single-prey system:

$$\frac{dS_x}{dt} = \alpha S_x(1-(S_x+I_x)/K) - \beta_{xx}S_xI_x - \phi\frac{S_y+I_y}{S_x+I_x+\epsilon}S_x \tag{6}$$

$$\frac{dI_x}{dt} = \beta_{xx}S_xI_x - \phi\frac{S_y+I_y}{S_x+I_x+\epsilon}I_x - \gamma_xI_x \tag{7}$$

$$\frac{dS_y}{dt} = \nu\frac{S_x+I_x}{S_x+I_x+\epsilon}S_y - \beta_{yx}S_yI_x - \delta\frac{\epsilon}{S_x+I_x+\epsilon}S_y \tag{8}$$

$$\frac{dI_y}{dt} = \beta_{yx}S_yI_x - \gamma_yI_y - \delta\frac{\epsilon}{S_x+I_x+\epsilon}I_y. \tag{9}$$

The equations for the number of dead individuals have been dropped, as they add no information when the disease is universally fatal. Subscripts here denote the species, with β_{ij} being the coefficient for infection from species j to species i. If we set the probability of infection when eating an infected prey equal to 1, the infection coefficient β_{yx} becomes equal to $\frac{\phi}{S_x+I_x+\epsilon}$, as the number of infected prey eaten equals the number of predators infected.

If we are to derive any information from these equations, it will be necessary to estimate realistic parameter values, and this is what we will do in the following.

From [8, 11] we can find relations between predator and prey mass (m_x and m_y), and the parameters α, δ, ϕ and ν. We want α and ν to represent theoretical maximal reproduction rates for prey and predators respectively. Instead of using the data from growing populations in the wild, where starvation, disease and other complications practically always play a role, we believe that the theoretical cap on reproduction should be set by the gestation period. α and ν should thus be the inverse gestation period [8]:

$$\alpha \approx 1/t_g \approx \frac{1}{50}m_x^{-1/4} \quad , \quad \nu \approx \frac{1}{50}m_y^{-1/4} \qquad [1/days]. \tag{10}$$

Our intuition tells us that when the predator is satisfied ($S_y \approx \epsilon$), predator reproduction should be equal to predator death, giving us $\nu \approx \frac{1}{50}m_y^{-1/4}$ as well. In order to calculate how many prey the predators need to eat to reproduce this much, we must know the ecological efficiency η. The ecological efficiency, defined as the fraction of consumed prey biomass converted into predator biomass, we estimate to be 10 % although the quantity varies significantly with trophic level and the specifics of the species [16, 17]. Knowing the efficiency, we can calculate the number of prey eaten as $\phi\frac{S_x}{S_x+\epsilon}S_y = \frac{m_y}{\eta m_x}\nu\frac{S_y}{S_x+\epsilon}S_x$, which implies $\phi = \frac{10m_y}{m_x}\nu = \frac{m_y^{3/4}}{5m_x}$ Finally, also from Peters [8], we have the following approximate relation for prey carrying capacity:

$$K \approx 200m_x^{-3/4} \qquad [prey/km^2]. \tag{11}$$

Thus, we have finally decided that the units of the population densities are $[km^{-2}]$. ϵ is difficult to determine, and we therefore choose to set $\epsilon = K/2$. We believe this to be reasonable, as it allows the predator population growth to saturate before the prey population reaches its carrying capacity. However, as can be seen in the supplement, we can set ϵ to practically any value between $0.3K$ and K and still get similar results.

To extend the predator-prey model to the predator-prey-disease case, we also need to know the scaling relations for disease duration. According to Cable *et al.*

[12], both the time until first symptoms and the time until recovery or death scale as $t = cm^{1/4}$, where c is an experimental constant. Here, we shall use the constants appropriate for rabies. Rabies is able to infect predators orally when they eat prey [18] and fulfills our assumption of nearly 100 % mortality [19]. At the same time, rabies infects most mammal species and extensive data for mass scaling relations therefore exist [12]. Rabies can only be passed on when the virus has reached the brain and salivary glands and thus causes symptoms [20]. Therefore, we will assume that the duration of the period during which the infected individual can pass on the disease can be written as $t_I \approx t_D - t_S = (c_2 - c_1)m^{1/4}$, where c_1 and c_2 are the scaling coefficients appropriate for time until first symptoms and death, respectively. These constants have been determined using statistical analysis by Cable *et al.*, and their values are $c_1 = 9\ \ (4, 19)$ and $c_2 = 16\ \ (7, 32)$, where the numbers in parentheses are the boundaries of the confidence interval from $p = 2.5$ % to $p = 97.5$ % [12]. γ_i can now be found as $1/t_{I,i}$.

Finally, to make the parameterisation more intuitive, we choose to express infectivity in terms of the *basic reproduction number* (R) of the disease instead of the coefficient β. The basic reproduction number represents the number of animals infected when exposing an infected individual to a completely susceptible population. The reproduction number is related to the infection coefficient as $R_{ij} = \frac{\beta_{ij} S_{i,0}}{\gamma_j}$ [2], where $S_{i,0}$ is the initial density of susceptible individuals of species i. R ranges from 1, where an epidemic is barely able to sustain itself, up to 18 in measles [21]. We therefore intend to vary R_{xx} from 1 to 10, as we believe this covers a wide range of all epidemics. The cross-species reproduction number R_{yx} will be determined by the number of prey eaten by predators which in turn depends on their mass ratio.

By using this parameterisation, we are now left with only five parameters: Prey mass, predator mass, ϵ, prey-prey disease reproduction number, and the infection probability when predators eat infected prey. If we set this probability to 1, we save another parameter. We believe that this is a reasonable thing to do, since the pathogen load transferred from prey to predator upon consumption must be very large. At the same time, we have ensured that the values of the parameters used are at least biologically plausible. All this will be highly advantageous when we examine parameter space.

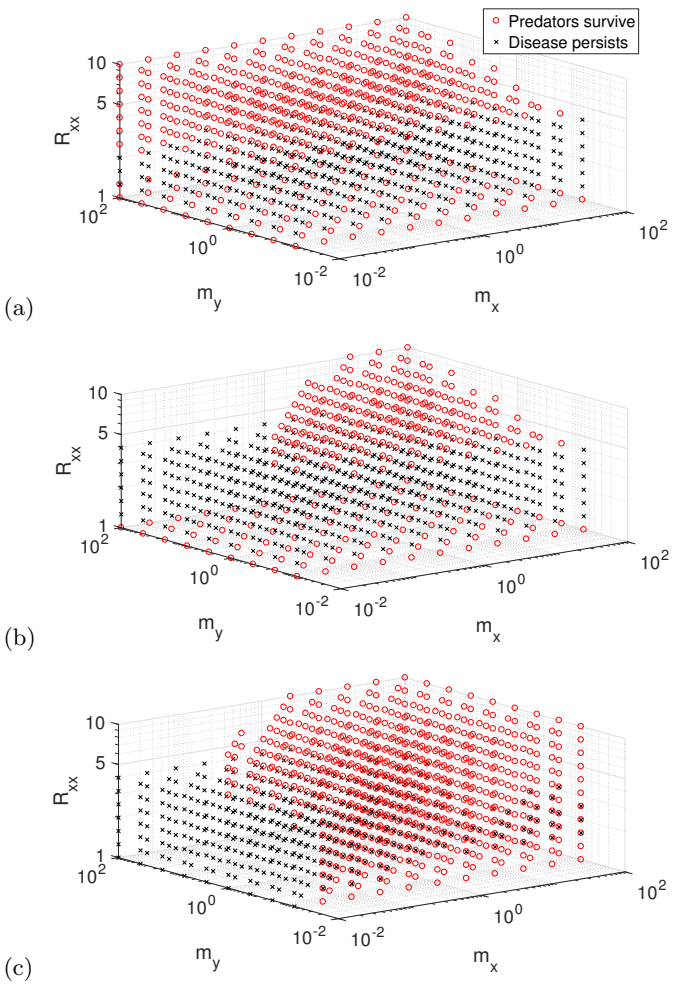

FIG. 1. The distribution of scenarios with predator survival (red circles) and disease persistence (black crosses) in (predator mass) - (prey mass) - (disease reproduction number) space. If (a) the predators are immune, large predators survive at high R_{xx}. On the other hand, if (b) the predators are susceptible, they survive if they are large and about the same size as the prey. In (c), an immune prey is included alongside the susceptible one. The susceptible predators survive regardless of disease infectivity, so long as the predator is not too large compared to the prey. If the predator is not susceptible, it always survives.

EXAMINING PARAMETER SPACE

To derive information about parameter space most effectively, we perform a parameter sweep where we let the different quantities vary logarithmically. This ensures that we probe each order of magnitude equally, rather than each absolute interval. We believe that in biological systems, relative size differences are more meaningful than absolute differences. For example, it probably makes a bigger difference whether a predator eats a mouse or a rabbit than whether it eats a rabbit or a hare, even though the absolute size difference between the latter two might be larger. We scan a region of parameter space that we believe to be relevant for the largest possible number of diseases and predator-prey ecosystems. An overview of the parameter ranges and increments can be seen in table I. As initial condition, we choose the classical Lotka-Volterra equilibrium to avoid introducing large artificial oscillations into the system.

In the analysis of our model, we have found that when

	Min. value	Increment	Max. value
$\log(m_x)$	-2	0.4	2
$\log(m_y)$	-1.2	0.4	2
$\log(R_{xx})$	0	0.1	1

TABLE I. (a) The ranges of parameters examined in our logarithmic parameter sweep. m_i is the mass of species i, and R_{xx} is the disease reproduction number characterising infection from prey to prey. 1089 parameter sets were tested.

using reasonable parameter values, the populations will usually perform damped oscillations of initially large amplitude around some equilibrium, or approach a limit cycle with some possibly large amplitude. Although the equilibria might be stable, after a disease outbreak the populations often temporarily reach such low values that it would lead to extinction in any system with a discrete number of individuals. Also, an equilibrium with a very low population density would lead to extinction in the real world. If we introduce an extinction threshhold to our model to account for the finite and discrete number of individuals found in real populations, this changes the dynamics significantly. Instead of carrying out a linear stability analysis of the fixed points, we will therefore focus on the existence of the various populations.

We introduce an extinction threshhold of 10^{-5}. If a population dips below this value, we consider it extinct. It should be noted that the precise value of the threshhold makes a relatively small difference in the end result. After solving the equations numerically over $T = 20000$ days, we classify the end state of the system into one of four categories: Scenarios with predator survival, disease persistence, disease-predator coexistence, and scenarios where only the healthy prey population survives. Since coexistence of disease and predator appears to be transient, we let the simulation run up to 10^5 days if there is still coexistence initially. Plots of the regions of parameter space with predator survival and disease persistence can be seen in fig. 1.

First and foremost, we observe that the prey species practically always survives the epidemic. Therefore, there are a few scenarios where the prey ends up with no natural enemies and thus will grow to the carrying capacity and dominate the ecosystem. As another point, it should be noted that the pathogen never coexists with the specialist predator.

From the plots, we see that the survival of predators is strongly dependent on the reproduction number of the disease among prey and the mass of the predator species. When the epidemic does not directly affect the predators (fig. 1 (a)), the predators can survive at high R_{xx}. A high mass is advantageous to the predator, as this ensures that it is not affected as much by starvation when the epidemic lowers the prey population. We see a "zone of exclusion" at intermediate R_{xx} where the disease keeps the predator away. This gap is evidence of competitive exclusion between predator and disease, which both subsist on the same resource, the susceptible prey.

In the case where predators are susceptible to the disease (fig. 1 (b)), on the other hand, the predator species can sometimes survive at high R_{xx}, but only if its mass is in the same range as or smaller than the prey. Being large is otherwise an advantage for the predator, but only up until about 10 times the prey mass. Above this threshhold, the predator needs to eat so many prey to survive that it is almost guaranteed to be infected. These diagrams show us that sharing a pathogen with a prey species will most often cause the predator to go extinct. In fact, even an outbreak of a prey-specific epidemic can cause predator extinction, at least if the predator is a specialist.

The effect of additional prey species could be interesting to study, since a large part of the reason why epidemics are so deadly to predators appears to be that specialist predators starve if prey population drops. We do not expect this effect to be present, or at least not nearly as powerful in the presence of two prey species, of which one is immune. To test this hypothesis, we modify the equations (6)-(9) to include another prey that is unaffected by the disease. We assume that the immune prey is identical to the susceptible prey, as predators will probably hunt similar sized prey species most of the time. The route of infection from prey to predator is the same as before, and the initial combined prey population is also the same. Scanning the parameter space as before, we get the results seen in fig. 1 (c)

There is a striking difference compared to the case with only susceptible prey. In the two-prey model, predators will always survive, so long as they are small enough (less than 50-100 times the prey size at high R_{xx} and less than the prey size at low R_{xx}). We here see the same effect as in fig. 1 (b), that predators bigger than this need to eat a lot of prey and will therefore almost always end up eating an infected individual. We can confirm that this is the mechanism by making predators immune to the disease. In such a case, we always see predator survival. Furthermore, coexistence of predator and pathogen is now possible, as they no longer compete for a single resource. The conclusion that disease is usually an effective weapon against predators thus has to be modified. It holds for the specific case of specialist predation. If we add an additional prey species, carrying a disease can still be effective against predators, but only if they are large.

DISCUSSION

The most striking conclusion to be drawn from this study is that an emerging epidemic in a specialist predator-prey system will tend to drive the predator, *but not the prey*, to extinction. Furthermore, the parame-

ter sweeps show that disease and predators cannot coexist. We believe this to be an example of competitive exclusion. Both the pathogen and the predator share a resource - the susceptible prey - and in such cases, long-term coexistence is impossible [22]. The obvious implication of these two conclusions is that we should see very few ecosystems with specialist predators, prey, and a shared pathogen in the real world, as they are inherently unstable. Indeed, when examining existing literature, we have found quite few examples of predators and prey sharing a deadly pathogen. Our model provides a reasonable explanation for the absence of such ecosystems.

Quite often when the predator goes extinct but the epidemic persists, the resulting prey-pathogen equilibrium will have a lower prey population than the prey-predator equilibrium. Nonetheless, carrying the pathogen may still turn into an advantage for the prey species. From evolutionary biology, we know that when a pathogen becomes endemic in a given species, there will be a pressure for it to evolve to become less lethal over time [23]. This allows the pathogen to live longer in each host, and possibly to spread more effectively. An initially fatal epidemic can thus end up becoming harmless to its primary host species. If it has wiped out the predator in the process, this will represent a win-win situation for the prey species.

Possibly, we could expand our conclusion and simply state that specialist predators generally are extremely vulnerable to any changes in prey population. It is a well-known fact of ecology that specialists are the most vulnerable to extinction in the event of changes such as disease outbreaks [24]. Predator species that subsist entirely on one prey species should therefore also be rare in nature. This is supported by the fact that even predators which are usually noted as specialists, such as the weasels (*Mustela nivalis*) of northern Scandinavia that often form the basis of predator-prey models [25], tend to switch prey in times when their preferred prey is scarce [26].

Finally, as an additional and somewhat curious result, predators that are much bigger than the size of their prey are a lot more vulnerable to infection with a shared pathogen from their prey, since they need to eat more potentially infected individuals to survive. This, in addition to energetic concerns about hunting very small animals, could lead to an evolutionary pressure for predators to not grow too large compared to their prey.

Given all of the above, we conclude that epidemic diseases can serve as a powerful evolutionary weapon against specialist predators. A pathogen infecting a prey species will often competitively exclude the predator species, even when the predator is not itself susceptible to the pathogen. This is coupled with the direct impact that the epidemic may have on the predator if it is susceptible. Although the prey will often end up afflicted by the endemic pathogen instead of the predator, this may through coevolution end up being a net advantage for the prey species. Shared epidemics between predator and prey may help impose an upper limit on the predator-prey size ratio, since eating a lot of small prey is dangerous if the prey is infectious. The uneasy coexistence of predators and pathogens should make predator-prey-disease systems rare in the real world, and this is indeed what we see. Our study supports the conclusion that being a specialist predator is a highly vulnerable position, and that being a generalist should be evolutionarily favourable for predator species. The effectiveness of disease as a weapon is significantly diminished when letting the predator have an alternative, immune prey. Normally, one would expect that competitive exclusion presents a drive towards speciation and specialisation [27]. Our model, on the contrary, provides an example of how the inherent vulnerability of specialists will drive species towards generalisation.

In conclusion, our study supports the idea that shared epidemic diseases could be a much more important factor in the coevolution of predator and prey species than they are usually given credit for.

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