The Ecological and Evolutionary Consequences of Parasites that Manipulate their Hosts

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Abstract

Infectious disease is prevalent in nature and can significantly alter human, animal, plant and bacteria populations. Parasites are a leading cause of infection, so understanding parasite evolution is vital for disease surveillance, control and limitation. The field of host-parasite relationships is vast; however, there are still unanswered questions, for example, about the effect of other species' interactions and complex transmission processes. Therefore, increasing our knowledge of these topics is beneficial for the field and for limiting the spread of infectious diseases.

In this thesis, I utilise mathematical models to study the evolution of host-parasite relationships when the transmission route is complex within the context of wider community interactions. Trophic parasites will transmit to a definitive predator host via an intermediate prey host. The predators in this system form an important part of the parasite's life cycle. Parasites can harbour manipulation as an adaptive trait and alter the appearance or behaviour of the prey host to increase predation risk. We extend a model of shared parasite infection in a predator-prey system and explore the scenarios where parasites evolve to manipulate their prey hosts to facilitate transmission. My three key research questions in this thesis are as follows:

- When are parasites most likely to evolve a higher degree of manipulation? (chapter 2)

- When will hosts evolve defence mechanisms against parasitic infection when faced with the threat of predation? (chapter 3)

- Do parasites go extinct in regions on cyclic dynamics when stochastic effects are accounted for? (chapter 4)

Our key results are that there exists an important feedback loop between ecological and evolutionary dynamics, emphasised by the fact that population densities are evolutionary drivers. Also, we highlight the significant evolutionary effect of fluctuating dynamics. The theoretical results in this thesis provide important contributions to the field and expand our understanding of host-parasite relationships that include complex transmission routes and other species interactions that can be used as a foundation for future experimental work.

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Chapter 1

Introduction

Infectious disease is ubiquitous in nature and affects humans, animals, plants, and bacteria. It can significantly impact public health, the economy, agriculture, and conservation. This is not an exhaustive list. Therefore, it is an important area of research to understand disease spread, conduct surveillance, and consider ways to control and limit transmission. Mathematical models are a key tool for investigating infection systems and forecasting how disease incidence may change in different conditions. The recent coronavirus pandemic, with over 7,000,000 recorded deaths worldwide (WHO 2024), emphasises the vitality of this field since modelling work was integral to government policy decisions to limit infection spread (GOV.UK 2023) (see, for example, SPI-M-O (2020)). The coronavirus pandemic is an accessible example of disease evolution as it rapidly progressed through different variants, and we witnessed policy changes in accordance (Markov et al. 2023). I utilise mathematical models in this thesis to explore host-parasite evolution and contribute knowledge about complex transmission processes to infectious disease research.

In our models, we tend to divide our population into hosts and parasites. Parasites are a leading cause of infectious diseases. A parasite is an organism that uses another organism - the host - for habitat and food whilst causing some degree of harm (Poulin 2007). This harm is known as virulence and shortens the

host's lifespan. We can divide parasites into two groups: microparasites and macroparasites. The first describes viruses, bacteria, protozoans and fungi. These are usually small in size, have a short generation time and have a high reproduction rate within the host (Anderson & May 1979, May & Anderson 1979, Anderson & May 1981). The latter group, macroparasites, are bigger and do not directly reproduce inside the host, but instead, infection depends on how many parasites the host is harbouring (Anderson & May 1979, 1981). Helminths (worms) and arthropods (invertebrates) are macroparasite infections (Anderson & May 1979). Learning more about parasites and how they interact with their hosts deepens our understanding of the diseases that they cause. This will allow for improved measures to control infectious diseases.

Within host-parasite relationships, evolution can be studied from the parasite's point of view (Levin & Pimentel 1981, Bremermann & Pickering 1983, Bremmerman & Thieme 1989, Frank 1996, Boots & Sasaki 1999, Gandon, Mackinnon, Nee & Read 2001, Day 2001, 2003, Boots & Sasaki 2003, Day & Proulx 2004, Miller et al. 2006, Day & Gandon 2007, Kamo et al. 2007, Messinger & Ostling 2013, Leggett et al. 2013, Berngruber et al. 2013, 2015, Hasik et al. 2023). Virulence, broadly defined to be a reduction in host fitness due to infection (Read 1994), is a major topic in this field to understand why, and the extent to which, parasites evolve to harm their host. This knowledge is vital for informing public health decisions about preventative measures against particular parasites that can become more dangerous than others. The trade-off hypothesis underpins a substantial proportion of parasite evolution research and states that virulence is an unavoidable consequence of transmission (Anderson & May 1982). It replaced conventional wisdom (May & Anderson 1983) where it was believed that all parasites would eventually evolve to become avirulent (Smith 1904). Around the same time, trade-off links between transmission and virulence were also drawn (Bremermann & Pickering 1983, Massad 1987) whereby parasites that evolved greater transmission would also be more virulent. As a result, the 1990s beheld a lot of research on the trade-off hy-

pothesis (Bull 1994, Ewald 1994, Read 1994, Ebert & Herre 1996, Frank 1996). While trade-offs between virulence and recovery have been investigated (Anderson & May 1982, Frank 1996), the relationship between transmission and virulence remains the most widely studied trade-off (Anderson & May 1982, Frank 1996, Alizon et al. 2009, Cressler et al. 2016).

Much theoretical parasite research has focused on virulence evolution (see review by Cressler et al. (2016)). A widely accepted prediction is that increased background host mortality will result in increased parasite transmission and thus increased virulence under the transmission-virulence trade-off (Anderson & May 1982, Kakehashi & Yashinaga 1992, Lenski & May 1994, Ebert & Weisser 1997, Gandon, Jansen & van Baalen 2001, Cressler et al. 2016, Hasik et al. 2023). However if increased virulence can influence host mortality caused by something other than infection, such as predation for example, then other outcomes are possible: one of which is decreased virulence (Choo et al. 2003, Cressler et al. 2016). Despite this neat set of results, empirical studies are limited and have contrasting results (Cressler et al. 2016, Hasik et al. 2023). Some agree with theoretical findings (Chen et al. 2004, Shim & Galvani 2009, Nidelet et al. 2009, Wasik et al. 2015) whereas Ebert & Mangin (1997) conducted experimental tests using monocultures of the water flea *Daphnia magna* and its *Glugoides intestinalis* parasite and found that replacing 80% of a host population led to a reduction in virulence owing to reduced within-host competition (Gandon, Jansen & van Baalen 2001). Population structure is another important influence on virulence evolution. A population of hosts with restricted movement leads to parasites self-shading which means they infect local susceptible hosts and end up surrounded by infecteds with no suitable hosts left to transmit to. They evolve high transmission and thus lower virulence (Boots & Mealor 2007). In contrast, a less structured population where hosts have more freedom of movement gives rise to highly virulent parasite strains (Claessen & de Roos 1995, Lipsitch et al. 1995, Boots & Sasaki 2000, Boots et al. 2004, Caraco et al. 2006, Kamo et al. 2007, Messinger & Ostling

2013, Cressler et al. 2016). Empirical work shows considerable support for this finding (Cressler et al. 2016). For example, Dennehy et al. (2007) showed that in bacteria-phage systems, less virulent strains are favoured when the population structure is rigid, moreover, Kerr et al. (2006), Eshelman et al. (2010), Berngruber et al. (2015) evidenced that lower virulence will evolve. Theoretical work predicts that virulence will be higher during the early stages of an epidemic since susceptible hosts are abundant. As this population is depleted, virulence evolves to decrease as the infection moves to endemic equilibrium (Lenski & May 1994, Day & Proulx 2004, Day & Gandon 2007, Bull & Ebert 2008, Bolker et al. 2010, Cressler et al. 2016, Gowler et al. 2023). It is challenging to find studies that support these findings since they must conduct observations for the entirety of an epidemic (Cressler et al. 2016). The most notable study used in evidence is the myxoma virus, where highly virulent strains domineered when it was first introduced to control Australian rabbit populations but then evolved to be less virulent (Fenner & Ratcliffe 1965, Cressler et al. 2016, Gowler et al. 2023). The pathogen, in this case, was introduced by humans, and so Gowler et al. (2023) studied virulence evolution of *Pasteuria ramosa* during a naturally occurring outbreak amongst *Daphina* (zooplankton) hosts. They did not find evidence to support theoretical findings of virulence evolution during an epidemic.

Notice that we cannot always draw neat links between theory and empirical studies. Reviews by Alizon et al. (2009) and Cressler et al. (2016) highlight that a major issue causing a lack of synergy between the two disciplines is that virulence is often defined differently, so it can be difficult to connect the results from both areas. Mathematical models often use parasite-induced host mortality or reduced production rate to measure virulence. In contrast, empirical work may measure host anaemia, weight loss, or death as indicators of parasitic harm (Cressler et al. 2016). This stark difference between theoretical and empirical methods is highlighted in bacteria-phage coevolution experiments since the virulence equivalent in these systems is measured

based on the number of bacterial genotypes that phage can infect (Buckling & Rainey 2002*a*,*b*, Koskella & Brockhurst 2014). Despite this difference, interest in microbial experiments has grown in the last twenty years because phages are abundant in nature (Thomas et al. 2011, Williamson et al. 2013, Engelhardt et al. 2014, Koskella & Brockhurst 2014), bacteria can evolve phage-mediated defence mechanisms, and bacteria-phage interactions can be comparable with host-parasite relationships (Koskella & Brockhurst 2014). The most intensely studied bacteria-phage interaction is *Pseudomonas fluorescens* SBW2S and T7-like podovirus, Φ2 (Buckling & Rainey 2002*a*, Brockhurst et al. 2007, Koskella & Brockhurst 2014). In coevolution experiments, these species exhibit arms race dynamics that tend to be observed, characterised by both species' ongoing escalation of defence and broadness of infectiousness (Dawkins & Krebs 1979, Woolhouse et al. 2002, Gandon et al. 2008, Koskella & Brockhurst 2014). Bacteria-phage experiments are important to test theoretical predictions in host-parasite relationships because coevolution loops can be observed quickly; in other words, we witness evolution in real-time (Koskella & Brockhurst 2014).

Parasites can transmit via various modes, such as direct and sexual contact, through vertical transmission, carried by vectors, or free-living infective stages picked up from the environment. Since transmission is so often modelled in a trade-off with virulence, it is unsurprising that it influences virulence evolution (Cressler et al. 2016). For example, the 'Curse of the Pharaoh' hypothesis (Bonhoeffer et al. 1996) was developed from work by Ewald (1983) and states that virulence will evolve to be greater when free-living infective stages are capable of surviving for longer in the environment. In contrast, vertical transmission can reduce virulence since host survival and reproduction are imperative to avoid parasite extinction (Ebert 2013, Cressler et al. 2016). The risk of eradication of the parasite means that, in reality, mixed mode transmission is more likely than vertical transmission alone, so horizontal transmission and higher virulence are selected for when the susceptible host

population is large, but vertical transmission and lower virulence evolve when this population is depleted (Lipsitch et al. 1996, Berngruber et al. 2013, 2015). These are just selected examples of what is known about how transmission affects parasite evolution, but these alone highlight the significant impact that transmission mode can have on parasite evolution. Despite this, less is known about more complicated processes, such as trophic transmission, even though many parasites utilise intermediate hosts (see Moore (2002)). So this should be studied theoretically and empirically to clarify the evolutionary effect of this transmission mode.

Many theoretical works investigate host evolution of defence against parasitic infection (Antonovic & Thrall 1994, Bowers et al. 1994, van Baalen 1998, Boots & Bowers 1999, 2004, Boots & Haraguchi 1999, Bowers 1999, 2001, Gandon & Michalakis 2000, Roy & Kirchner 2000, Gandon et al. 2002, Restif & Koella 2003, Miller et al. 2005, 2006, Boots et al. 2009, Boots 2011, Koskella et al. 2012, Donnelly et al. 2015, Best et al. 2017, Ferris & Best 2018, Singh & Best 2021, 2023). Defence can be divided into different mechanisms: avoidance, tolerance, recovery and acquired immunity. Their respective functions are as follows: preventing infection, reducing the severity of parasitic effects, increased parasite clearance rate and immune memory to prevent reinfection. Some hosts will not evolve any defence, and those that do display a variation in the level of defence they harbour. This variation strongly suggests that this trait must incur some cost but theoretical and empirical work provide the evidence that these costs exist and are in the form of a reduction of another component of the host's fitness (Stearns 1992, Boots & Begon 1993, Biere & Antonovics 1996, Fellowes et al. 1998, Kraaijeveld & Godfray 1997, Webster & Woolhouse 1999, Rolff & Siva-Jothy 2003, Siva-Jothy et al. 2005). Evolving increased parasitic resistance has been experimentally shown to negatively impact development time (Boots & Begon 1993), fecundity (Boots & Begon 1993, Biere & Antonovics 1996, Webster & Woolhouse 1999) and competitive ability of the host (Kraaijeveld & Godfray 1997, Fellowes et al. 1998). When

investigating snails that had evolved increased resistance against schistosomes, Webster & Woolhouse (1999) found that they produced fewer offspring when compared to the control lines. This trade-off between birth or growth rate and resistance is included in theoretical models. For example, Boots & Haraguchi (1999) found that resistance is most likely to evolve when parasites cause a low level of virulence, whereas a high birth rate is more beneficial when parasites are highly virulent because the reduced lifespan of infected hosts means that susceptible hosts are less at risk of infection. In contrast, van Baalen (1998) found that host defence was maximised at an intermediate level of virulence, but unlike Boots & Haraguchi (1999), they assumed no parasite-induced sterility. Rather than two opposing extremes in infected host fertility, Best et al. (2017) considered a gradient of sterility and found this a key evolutionary driver with higher sterility selecting for higher host resistance. Miller et al. (2007) discovered that if the infected population is large, resistance mechanisms are unlikely to evolve because this poses such a significant infection risk that defences could be rendered futile. Increasing the birth rate would be more beneficial to replace those lost individuals. These studies tend to consider the host and parasite relationship in isolation, but in reality, these relationships are part of a wider community. It is interesting to consider host evolution when the host is faced with not only the threat of infection but also from another source, such as a predator.

Both host and parasite evolution can be looked at when the host faces two enemies in the population. An example of a multi-enemy population is one comprised of a host that is at risk of infection from more than one parasite strain or species. These are multiple infections and are known to occur commonly in nature, affecting not only humans but also bacteria (Turner & Duffy 2008), plants (Malpica et al. 2006) and animals (Sharp et al. 1997). They are important to study because theory predicts that they can have a significant impact on virulence evolution, often concluding that more virulent strains are selected for, because of the within-host competition for resources (Alizon et al.

2009, Choisy & Roode 2010, Alizon et al. 2013). When these co-infecting parasite strains cooperate, often because they are closely related and collective action is beneficial for all, it is documented that virulence can evolve to lower levels (Frank 1996, Chao et al. 2000, Brown et al. 2002, West & Buckling 2003, Ewald & Cochran 2004, André & van Baalen 2007, Alizon et al. 2009, Choisy & Roode 2010). Knowledge about more complex population structure comprised of multiple enemies is clearly very important for understanding how infections can evolve.

Multiple enemies could be the simultaneous risk of infection and predation. Parasite evolution has been examined in this context to find that the presence of an immune predator can result in the evolution of highly virulent parasites (Morozov & Adamson 2011), branching that leads to parasite diversity (Morozov & Best 2012, Kisdi et al. 2013) and also evolutionary cyclic behaviour (Kisdi et al. 2013). Some parasites use the food chain to transmit to a predator host via an intermediate prey host. These are trophically transmitted parasites and have been documented to develop manipulation strategies to alter host behaviour or appearance to increase the likelihood of predation, thus successful parasite transmission to the predator host (Moore 2002). Empirical work tends to provide examples of manipulative behaviour (Bethel & Holmes 1973) and to demonstrate the existence of costs for parasites to evolve these strategies (Vizoso & Ebert 2005, Frost et al. 2008, Franceschi et al. 2010, Maure et al. 2011). For example, Frost et al. (2008) and Franceschi et al. (2010) support Poulin (1994)'s theoretical findings that manipulation evolution requires energy diversion from other important parasite functions since they show that manipulation investment is at the expense of parasite growth and spore production. Theoretical models explore manipulative parasite systems such as that by Fenton & Rands (2006). They looked at the population dynamics and found that these manipulative strategies can induce oscillatory dynamics and imply that this could cause stochastic extinction of either the predator or the prey species. Vries & van Langevelde (2018) use the model by Fenton

& Rands (2006) to explore predation suppression and predation enhancement. When they vary one of these strategies they find that enhancement, which increases the likelihood of predation on the infected intermediate host, is most beneficial to the parasite - and so potentially most likely to evolve - when the predator population is respectively small. While we know these manipulation mechanisms exist and some of the effects that they may have, there has not yet been a full evolutionary analysis that explores when parasites will evolve greater levels of manipulation strategies.

In a similar vein, we can explore host evolution of defence mechanisms against parasitic infection when also faced with the threat of predation. Experimental work elucidates how the composition of the enemy population will influence the selection of resistance and how defence against one enemy will reduce defence mechanisms against another (Stinchcombe & Rausher 2001, Craig et al. 2007, Friman & Buckling 2013). By way of illustration Friman & Buckling (2013) found that bacteria evolved greater defences against both phage and protists in single-enemy populations than when both enemies were present. Toor & Best (2016) draw similar conclusions from their model, stating that whichever enemy poses a greater risk to the host determines which defence mechanism will evolve. Other theoretical work documents how predator-mediated branching can arise in the host and that the evolution of host defence against infection can result in the extinction of one of the enemy populations (Hoyle et al. 2012) and is maximised at intermediate levels of predation (Toor & Best 2015). Although parasitic defence mechanisms in the presence of predators have been researched, the predators are always assumed to be immune to infection. Less is known about how defence mechanisms will evolve when the predator is no longer immune and is part of the trophically transmitted parasite's life cycle.

I will consider a population where a host is simultaneously faced with the threat of infection and predation. We assume that the predators are non-immune and will form part of the parasite's life cycle which trophically transmit from prey to predator. Parasites in this scenario have been documented to evolve to

manipulate prey to increase the likelihood of predation and, thus, successful parasite transmission from prey to predator. Extending the model by Fenton & Rands (2006) that readily exhibits fluctuating ecological dynamics, I will explore the scenarios where parasites evolve to manipulate their prey hosts to facilitate transmission. My three key research questions are:

- When are parasites most likely to evolve a higher degree of manipulation? (chapter 2)

- When will hosts evolve defence mechanisms against parasitic infection when faced with the threat of predation? (chapter 3)

- Do parasites go extinct in regions on cyclic dynamics when stochastic effects are accounted for? (chapter 4)

1.1 Modelling Host-Parasite Relationships

Compartment models are a useful tool for modelling infection. The main idea of the framework, formalised by Dietz (1967) but based on the studies by Kermack & Mckendrick (1927), is to divide a population according to their infection status. We can utilise this framework for modelling host-parasite relationships, and the diagram in figure 1.1 depicts how we may divide our host population into two categories - susceptible (S) and infected (I). Susceptible means the host is vulnerable to the parasite's infection, and infected represents those currently infected. This model can be extended by adding further host categories. For example, a latent period can be added using an exposed category so that there is a time delay between exposure to the parasite and the onset of symptoms or for the host to be contagious. Recovered is another possible category for hosts that can clear the infection and are immune from further exposure. Recovery may not always lead to immunity and the host

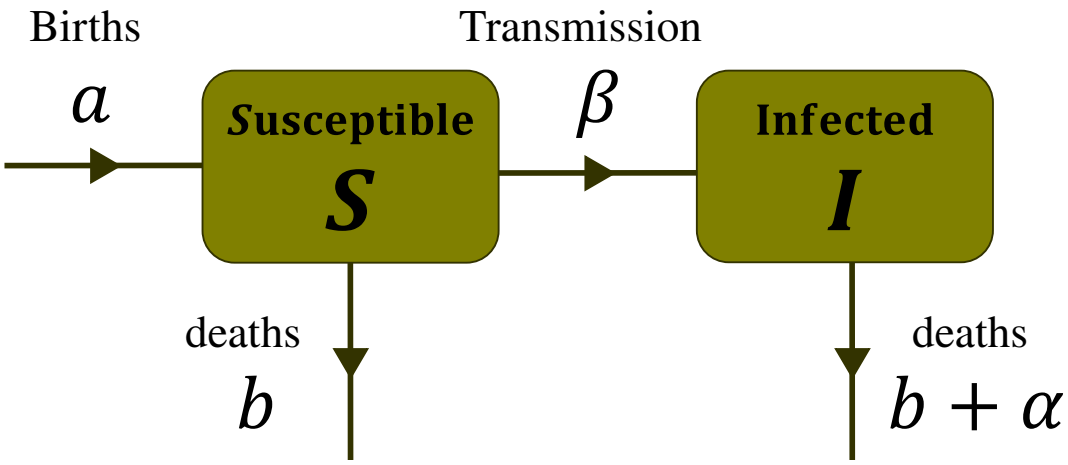

Figure 1.1: A general SI framework used to model infection.

may return to being susceptible and be at risk from infection again. These are just two ways these models can be adapted. Still, they could be extended in numerous ways to represent different infection systems, highlighting why they are such a key tool for studying infectious diseases.

How hosts move between the categories in figure 1.1 can be described by the following two ordinary differential equations,

$$\frac{dS}{dt} = a(1 - qN)S - bS - \beta SI, \tag{1.1}$$

$$\frac{dI}{dt} = \beta SI - (b + \alpha)I, \tag{1.2}$$

where S and I are susceptible and infected hosts respectively and N represents the total population size thus $N = S + I$. New susceptible individuals are birthed into the population at a rate a and this birth rate is limited by the effects of crowding represented by the parameter q. Susceptible individuals will become infected through contact with infected individuals we call this density-dependent transmission (Anderson & May 1981) where β is the coefficient of transmission. All hosts have a natural mortality rate b, but infected hosts have an additional mortality term α, which is a result of damage to the host by the parasite, and this is known as virulence. We assume that infected hosts do not reproduce or recover.

Model Parameter	Description
S	Density of susceptible hosts
I	Density of infected hosts
a	Host birth rate
b	Host mortality rate
β	Coefficient of transmission
α	Host virulence
q	Coefficient of crowding acting on susceptible hosts

Table 1.1: Descriptions for the dependent variables (S and I) and each parameter used in the general SI model.

There are three equilibrium points in this system representing the following scenarios:

- **extinction**, $(S^*, I^*) = (0, 0)$,
- **disease-free**, $(S^*_{df}, I^*_{df}) = \left(\frac{a-b}{aq}, 0\right)$,
- **endemic**, $(S^*_{de}, I^*_{de}) = \left(\frac{b+\alpha}{\beta}, \frac{a(1-qS^*)-b}{\beta+aq}\right)$.

In this model, for infection to persist in the population, the extinction and disease-free equilibrium points should be unstable, whereas the endemic equilibrium should be stable. However, these are not the only conditions that will support infection persistence. For example, some models may exhibit oscillatory behaviour, and in this scenario, none of the equilibria are stable.

Returning to our example model, we need to calculate the Jacobian matrix and eigenvalues to perform stability analysis on the system. If we set $f = \frac{dS}{dt}$ and $g = \frac{dI}{dt}$ then,

$$J = \begin{pmatrix} \frac{\partial f}{\partial S} & \frac{\partial f}{\partial I} \\ \frac{\partial g}{\partial S} & \frac{\partial g}{\partial I} \end{pmatrix} = \begin{pmatrix} a - aqN^* - aqS^* - b - \beta I^* & -S^*(aq+\beta) \\ \beta I^* & \beta S^* - (b+\alpha) \end{pmatrix}. \quad (1.3)$$

In the case of the extinction equilibrium point, we find,

$$J_{(0,0)} = \begin{pmatrix} a-b & 0 \\ 0 & -(b+\alpha) \end{pmatrix}. \quad (1.4)$$

Our model parameters are all greater than zero, so $\lambda_2 = -(b+\alpha) < 0$. Hence, for the extinction equilibrium point to be unstable, we must have that $\lambda_1 = a - b > 0$, satisfied whenever $a > b$. Considering instead the disease-free equilibrium point,

$$J_{\left(S^*_{df}, I^*_{df}\right)} = \begin{pmatrix} b-a & -S^*_{df}(aq+\beta) \\ 0 & \beta S^*_{df} - (b+\alpha) \end{pmatrix}, \tag{1.5}$$

we see that $\lambda_1 = b - a < 0$ whenever $S^*_{df} > 0$. Thus for the disease-free equilibrium to be unstable, we must find that

$$\lambda_2 = \beta S^*_{df} - (b+\alpha) = \frac{\beta(a-b)}{aq} - (b+\alpha) > 0 \tag{1.6}$$

Now, to see if the endemic equilibrium is stable, thus allowing infection to persist, instead of working from the Jacobian matrix, we can utilise the basic reproduction number, R_0, which is defined to be the average number of secondary infections arising from one primary infection in an otherwise entirely susceptible population (Anderson & May 1991). R_0 is a useful quantity in disease modelling since if $R_0 > 1$, infection can spread amongst a population whereas if $R_0 < 1$, infection will die out. Anderson & May (1981) calculate the basic reproductive number as the expected number of secondary infections multiplied by the length of the infectious period, which for our model are βS and $\frac{1}{b+\alpha}$, respectively. Thus, for the disease to spread, we require,

$$R_0 = \frac{\beta S^*_{df}}{b+\alpha} = \frac{\beta(a-b)}{aq(b+\alpha)} > 1, \tag{1.7}$$

which, if rearranged, gives us the condition from equation 1.6, and so the infection will persist in this system as long as $a > b$.

1.1.1 Numerical Analysis

The model we use throughout this thesis often exhibits fluctuating dynamics. It is not unusual for these dynamics to be stiff. By stiff, we mean that the dynamics can suddenly and dramatically change, meaning that some numerical solvers are unstable and require increasingly smaller time steps to solve the equations. This may result in the dynamics having an extremely long run-time. One way we can try to overcome this is by taking the final host density values from the last run as our new initial conditions to try and speed up the dynamics. More specialist ODE solvers are designed to cope better with these stiff dynamics. For example, we utilise the `SciPy Integrate` Python library for numerical integration and within our `solve_ivp` solver we use the argument `method = Randau`. Another remedy to tackle slow run times is to take the logarithm of the model equations, as this can make their rate of change less extreme. For example, figure 1.2 shows an exponential function and then the log-transform of this function. This transformation means that time steps do not need to be as small. We show this log-transformation on our example model in Equations 1.1 and 1.2 We set $X = \ln(S)$ and $Y = \ln(I)$ and our equations become,

$$\frac{dX}{dt} = a(1 - q(e^{X+Y})) - b - \beta e^{Y}, \tag{1.8}$$

$$\frac{dY}{dt} = \beta e^{X} - (b + \alpha). \tag{1.9}$$

To return to our non-logarithmic model, we can simply reverse this transform using $S = e^{X}$ and $I = e^{Y}$ to get the host densities.

1.2 Adaptive Dynamics

Adaptive dynamics is a classical, evolutionary framework (Metz et al. 1996, Dieckmann & Law 1996, Marrow et al. 1996, Geritz et al. 1998). It works under the assumption of a separation of ecological and evolutionary timescales. Thus,

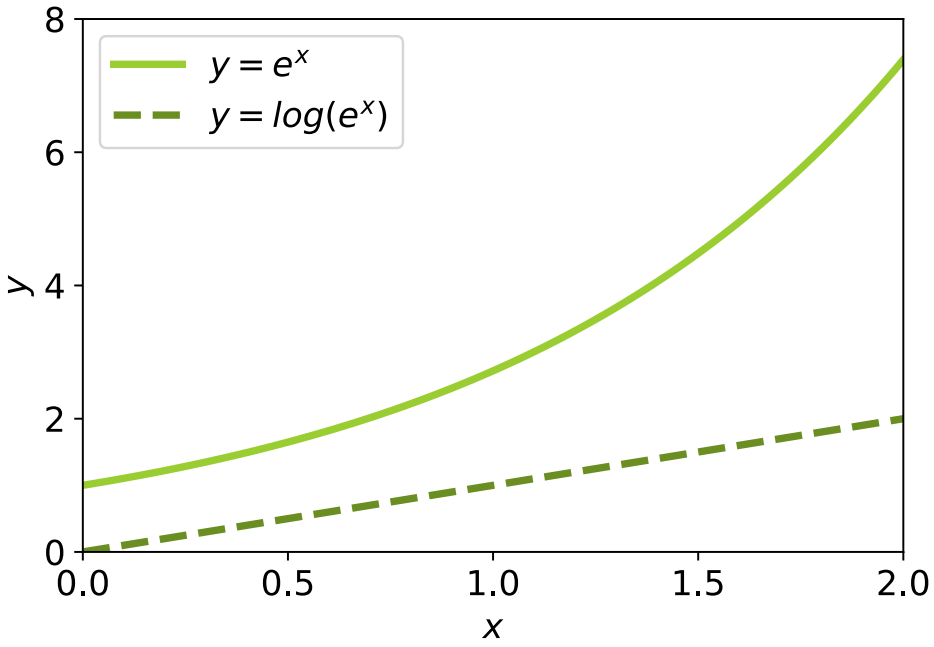

Figure 1.2: An example of how a log-transform reduces the rate of change of the exponential function.

we suppose that the long-term behaviour of the resident dynamics has settled to a stable equilibrium before a rare mutant arises. The mutant usually has a marginally different trait from the resident. We can calculate the local selection gradient to determine whether the mutant is successful and can invade the resident, or not. This is usually called mutant invasion fitness and is denoted by r for a parasite and s for a host. This thesis uses different methods to calculate the mutant invasion fitness depending on what is most appropriate for that model. The full calculation of fitness will be outlined clearly in Chapter 2, and 3 in box 2.1, and equation 3.6 respectively. The mutant has positive fitness when $r, s > 0$ and may invade the resident, whereas when $r, s < 0$, it has negative fitness and cannot invade. A singular strategy occurs when the local selection gradient is zero.

Evolutionary Behaviour	Evolutionary Stable	Convergence Stable
Continuously Stable Strategy (CSS)	✓	✓
Repeller	✗	✗
Garden of Eden	✓	✗
Evolutionary Branching Point	✗	✓

Table 1.2: The possible evolutionary outcomes at a singular strategy.

1.2.1 Singular Strategies

Recall that a singular strategy occurs when the local selection gradient is zero. However, there are four different types of singular strategy classifications which were first defined by Metz et al. (1996) and Geritz et al. (1998). Pairwise Invasion Plots (PIPs) are a graphical tool used to plot and classify singular strategies. A continuously stable strategy (CSS) (figure 1.3, top left) is attracting, since it is convergence stable, and so the population will evolve to this singular strategy and, once there, no local mutant strains can invade, since it is evolutionary stable. This is a long-term end-point of evolution. A Garden of Eden (figure 1.3, bottom left) also cannot be invaded, but since it is not attracting like a CSS, a population will never evolve to this strategy. Evolution will always take the population away from a repeller (figure 1.3, top right) since it is not attracting and can be invaded by mutant strains. The final evolutionary behaviour is a branching point (figure 1.3, bottom right), which is convergence stable, so the population will evolve towards this singular strategy, but mutants can invade at this singular strategy. This results in the population dividing into two coexisting populations. Throughout this thesis, I am mostly interested in looking for CSS points.

1.2.2 Floquet Exponents

Calculating fitness as in subsection 1.2 relies on a rare mutant attempting to invade the resident only when the system has settled to its long-term behaviour at a stable equilibrium. This allows an assumption to be made where

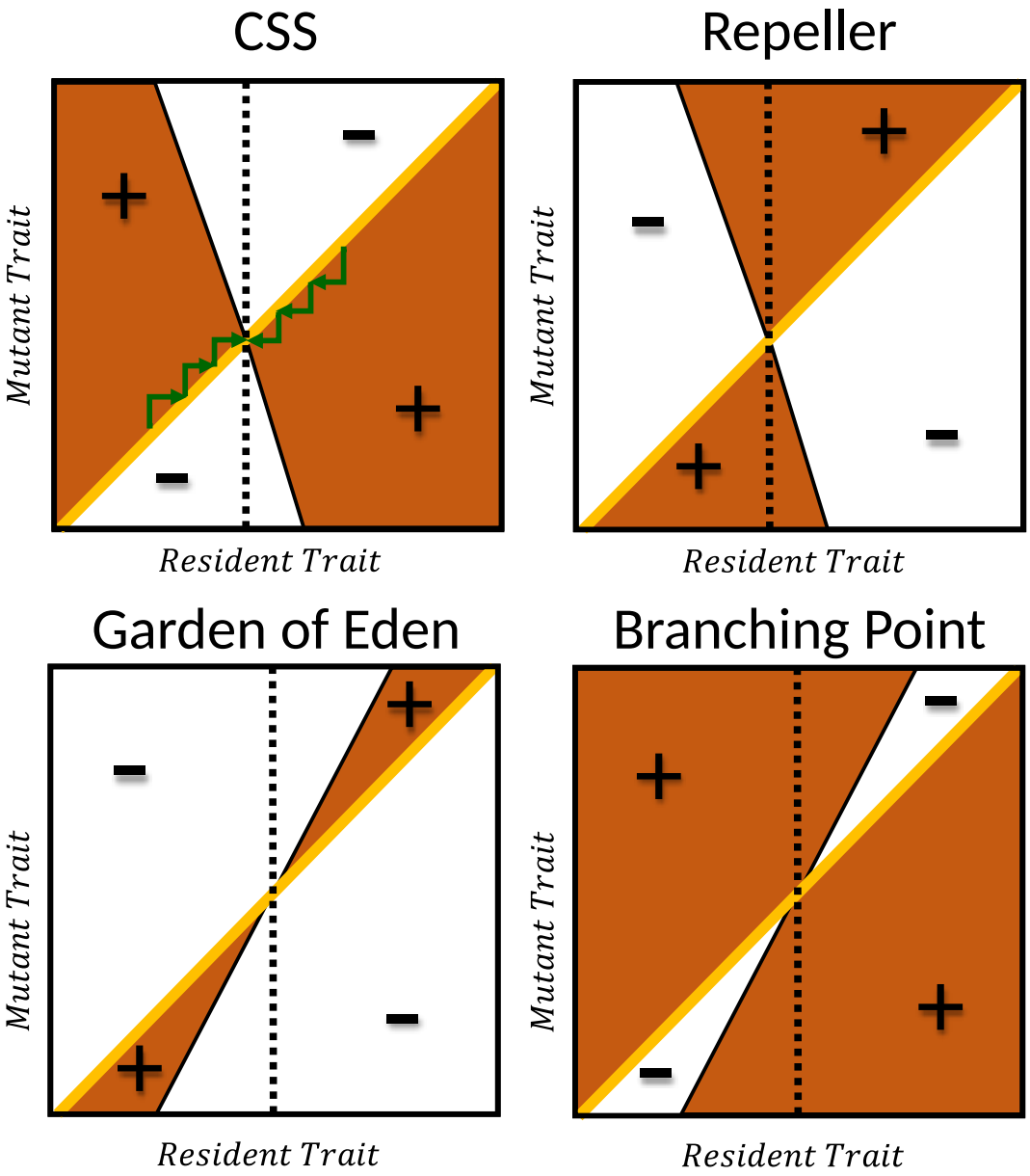

Figure 1.3: These Pairwise Invasion Plots (PIPs) show the four different types of evolutionary behaviour. Mutant invasion fitness is positive in the orange regions and negative in the white regions. The yellow line on the main diagonal represents the case where the mutant trait is equivalent to the resident trait. The dotted black line indicates if we have evolutionary stability when it lies in regions of negative mutant fitness. The green arrows on the CSS PIP show how this evolutionary outcome is convergence stable. There are regions of positive mutant fitness above and below the main diagonal on the left and right sides of the singular strategy, respectively.

the ecological and evolutionary timescales can be separated. So, single-point estimates of the resident densities at equilibrium can be used to calculate mutant invasion fitness. If the population dynamics do not settle to a stable equilibrium but fluctuate, an issue arises whereby the single point estimate will vary depending on where on the cycle it is taken. Then mutant invasion fitness will also fluctuate with it.

In this scenario, it was noticed by Metz et al. (1992) that, when population dynamics fluctuate, mutant invasion fitness can be calculated by finding the exponent with the largest absolute value which is referred to as the dominant Lyapunov exponent. We refer to these Lyapunov exponents as floquet exponents. Ferris & Best (2018) used this key result and applied it to host-parasite systems to formalise the method for calculating mutant invasion fitness when fluctuations are induced by seasonal variation in births. The numerical routine for finding these floquet exponents is outlined in the work by Best & Ashby (2023) and supplemented with two worked examples. We also present the numerical routine, specific to our system and mutant equations, in box 2.2, Chapter 2 and box 3.1, Chapter 3. Part of the routine involves creating a vector of mutant dynamics at time t and then, assuming the dynamics have a cycle of period T, the dynamics at time $t + T$ would be

$$X(t + T) = P(t)e^{\mu_i T}. \tag{1.10}$$

Here, $P(t)$ is a periodic function. Therefore, mutant density depends on the floquet multipliers, $e^{\mu_i T}$, which create an envelope around the oscillating dynamics from which they cannot escape. The floquet exponents, μ_i decide which direction the mutant density grows. If $\mu_i > 0$ for all i, then the envelope around the dynamics grows, and so does the mutant population, whereas if $\mu_i < 0$ for all i, the envelope shrinks asymptotically towards zero, and the mutant will die out (Best & Ashby 2023). Hence the rest of the numerical routine serves to calculate μ_i so that we can take the dominant value as mutant invasion fitness.

1.3 Trade-offs

An organism cannot invest in all beneficial life-history traits that will increase its survival; thus, an important assumption when modelling host-parasite relationships is that the evolution of one trait incurs a cost that is detrimental to another trait (Stearns 1989). This relationship is represented by trade-off functions and is incorporated in models for additional biological realism.

Intuitively, these costs must exist; otherwise, a parasite species, for example, would have evolved identical traits to ensure the maximum chance of survival. Since parasite species have great diversity, we can assume this is not the case. For example, some parasites evolve manipulative traits to increase transmission from prey to predator hosts, whereas others do not. Experimental work by Frost et al. (2008) and Franceschi et al. (2010) suggests a trade-off exists and that investment in manipulation strategies is detrimental to parasite growth and spore production. There is also experimental evidence for other trade-offs such as between host resistance and other life-history traits (Boots & Begon 1993, Rigby & Jokela 2000, Kraaijeveld & Godfray 1997, Mealor & Boots 2006, Tschirren & Richner 2006), and between different defence systems when there are multiple enemies in the population (Rigby & Jokela 2000, Yin et al. 2011, Friman & Buckling 2013), and between transmission and parasite virulence (Mackinnon & Read 1999, Fraser et al. 2007, Roode et al. 2008).

Although experiments demonstrate the existence of trade-offs, it is still difficult to determine their exact shape. Hence in theoretical studies, approximations of the trade-off function are used. I have chosen the form of function similar to the one used by Hoyle et al. (2012), Toor & Best (2015, 2016), and Singh & Best (2021). If we were to use a transmission-virulence trade-off, then our function would have the following form,

$$\alpha(\beta) = \alpha(\beta^*) - \frac{\alpha'(\beta^*)^2}{\alpha''(\beta^*)} \left[1 - \exp\left(\frac{\alpha''(\beta^*)(\beta - \beta^*)}{\alpha'(\beta^*)} \right) \right]. \tag{1.11}$$

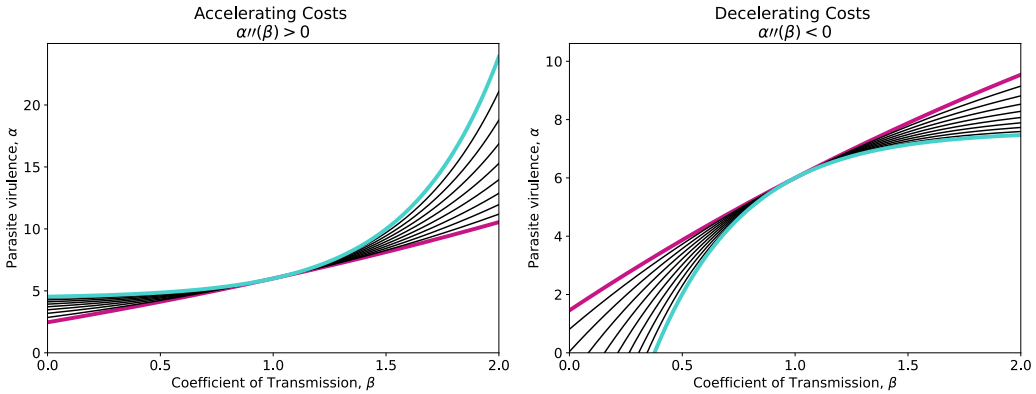

Figure 1.4: The shapes of a transmission-virulence trade-off function $\alpha(\beta)$ with positive gradient ($\alpha'(\beta) = 4$) for both accelerating (left) and decelerating (right) costs. We vary the curvature $\alpha''(\beta)$ between 1 (pink) and 10 (turquoise) for accelerating costs and the negative equivalent for decelerating costs. We choose the singular strategy as $(\alpha^*, \beta^*) = (6, 1)$.

This trade-off function requires that an initial singular strategy (β^*, $\alpha(\beta^*)$) is fixed. Then I can investigate how the trait evolves from this initial point by considering which direction selection is acting in and whether investment in the trait increases or decreases. I must also select values to determine the shape of our curve since $\alpha'(\beta^*)$ and $\alpha''(\beta^*)$ are the gradient and curvature respectively. If we choose $\alpha''(\beta^*) < 0$, we have a convex curve meaning that we have decelerating costs to evolve this trait, whereas a concave curve given by $\alpha''(\beta^*) > 0$ means costs are accelerating instead (see figure 1.4.) We often see the latter case being chosen over the former since the idea of continuing to invest in a trait and it becoming less costly to do so is not intuitive. However, decelerating costs are explored in Chapter 3. The shape of these functions is imperative since it is influential on the dynamics of host-parasite interactions and the evolutionary outcomes (Boots & Haraguchi 1999, Rueffler et al. 2004, de Mazancourt & Dieckmann 2004, Bowers et al. 2005, Kisdi 2006, Hoyle et al. 2008, Best et al. 2015, Ashby & King 2017).

1.4 Model Framework

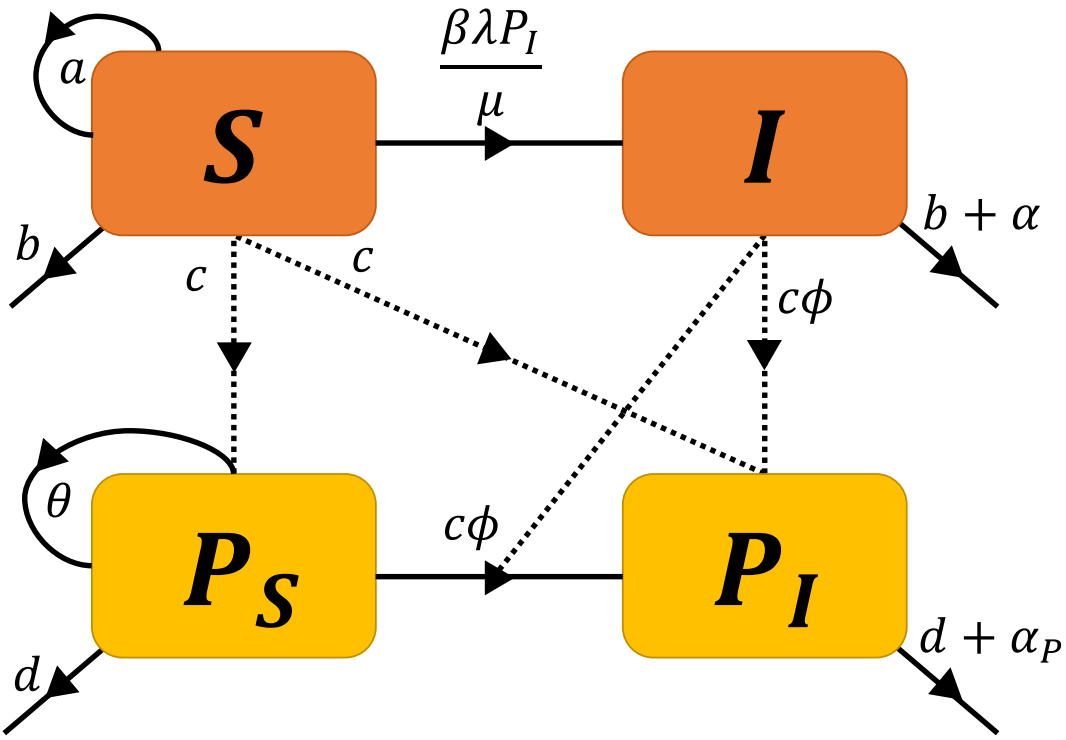

Figure 1.5: The schematic diagram for the host-parasite model. Here S and I (orange) represent the susceptible and infected intermediate prey hosts, respectively, and similarly, P_S and P_I (yellow) represent the susceptible and infected definitive predator hosts, respectively. The dotted lines represent predation.

The framework I use throughout my thesis is presented in the diagram in figure 1.5. I use it to model trophically transmitted parasites with an intermediate prey host and a definitive predator host in their life cycle. This model is developed from work by Fenton & Rands (2006) and is represented by the following equations,

$$\frac{dS}{dt} = aS(1 - qS) - \rho_S(S, I)(P_S + P_I) - \frac{\beta\lambda S P_I}{\mu} - bS, \tag{1.12a}$$

$$\frac{dI}{dt} = \frac{\beta\lambda S P_I}{\mu} - (b + \alpha)I - \rho_I(S, I)(P_S + P_I), \tag{1.12b}$$

$$\frac{dP_S}{dt} = \theta\rho_S(S, I)P_S - \rho_I(S, I)P_S - dP_S, \tag{1.12c}$$

$$\frac{dP_I}{dt} = \rho_I(S, I)P_S - P_I(d + \alpha_P), \tag{1.12d}$$

where S, I, P_S and P_I represent the host densities for susceptible prey, infected prey, susceptible predators and infected predators, respectively. The model parameters are summarised in table 1.3. Prey hosts reproduce at a rate a and die at a rate b. They also suffer additional mortality due to parasite virulence, α. Predators convert predation into new predator hosts at a rate θ, die at a rate d, and suffer parasite-induced death at a rate α_P. Since the intermediate hosts are preyed upon, the model incorporates predation using Holling functional responses (Holling 1959) in the terms ρ_S and ρ_I. In the simplest case, these equations are linear and take the form $\rho_S = cS$ and $\rho_I = c\phi I$, where c is the baseline predation rate and ϕ is the change in predation due to manipulation strategies which are documented in nature and can facilitate parasite trophic transmission from prey to predator hosts. Predators become infected by eating infected prey, and prey become infected by consuming spores from the environment with parameter β. This term is the spore consumption rate in alignment with the framework of Fenton & Rands (2006) in chapter 2; however, we also think of it as the level of susceptibility of prey hosts in chapter 3. These spores are produced at a rate λ in the predator host and will decay in the environment at a rate μ if not picked up by prey.

This model is interesting because it exhibits cyclic population dynamics. We cannot use traditional methods to calculate the mutant invasion fitness because this relies on the long-term behaviour settling to a stable equilibrium. Instead, we use Floquet exponents in the method outlined in section 1.2.2. Figure 1.6 displays the two types of behaviour we expect from this model: equilibria or fluctuations. I also utilise the stochastic framework for this system in chapter 4.

1.5 Thesis Outline

Chapter 2

In Chapter 2, I study trophically transmitted parasite evolution of manipulation mechanisms to increase transmission from intermediate prey hosts to

Model Parameter	Description
S	Density of susceptible intermediate prey hosts
I	Density of infected intermediate prey hosts
P_S	Density of susceptible definitive predator hosts
P_I	Density of infected definitive predator hosts
μ	Free-living parasite spore decay rate
b	Prey mortality rate
d	Predator mortality rate
β	Prey host susceptibility to infection
α	Virulence for Prey
α_P	Virulence for Predator
a	Prey birth rate
θ	Conversion of predation into births of new predators
q	Strength of intraspecific density dependence acting on prey
c	Baseline predation rate
ϕ	Scale factor of predation due to host manipulation
λ	Rate at which parasites produce infective stages (spores) in predators
ρ_S, ρ_I	Holling Type I response in predators

Table 1.3: Descriptions for our dependent variables (S, I, P_S, and P_I) and each model parameter used in the model.

definitive predator hosts. I include a trade-off between manipulation and spore production rate. Both traits are vital for parasite transmission since prey will pick up the free-living spores from the environment. I find that the population densities of the susceptible prey and the total predator population are vital evolutionary drivers. The work from this chapter is published in the *Journal of Evolutionary Biology*, see Oliver & Best (2024).

Chapter 3

I use the same model framework in Chapter 3, but now I consider host evolution of defence mechanisms to prevent infection when non-immune predators are present. The impact of parasite manipulation strategies on evolution is also considered. A trade-off between prey host birth rate and prey host susceptibility to infection is included in the model. I again find that population densities are key evolutionary drivers, and prey hosts will tend to increase the birth rate

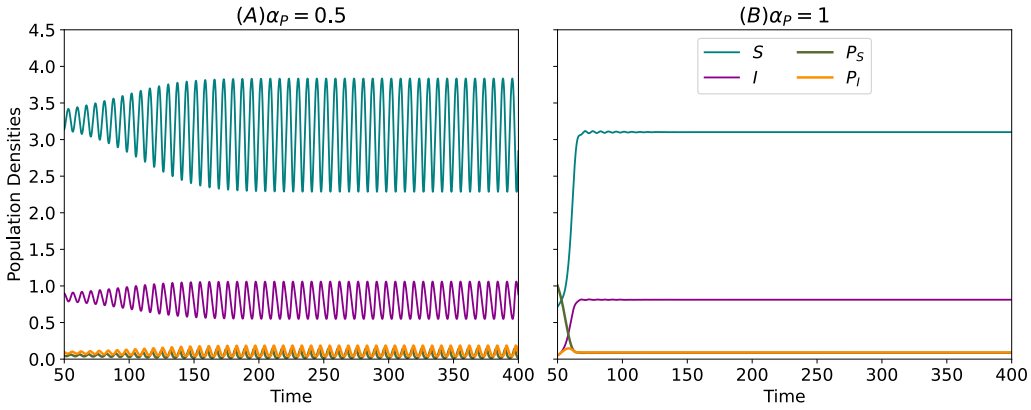

Figure 1.6: Time courses showing how the model can exhibit both (A) cyclic and (B) equilibrium population dynamics. We emit the early time dynamics to emphasise the focus on the system's long-term behaviour. Parameter values are as follows: $\mu = 0.15$, $b = 0.2$, $d = 0.4$, $\beta = 0.95$, $\alpha = 0.8$, $a = 2$, $\theta = 0.5$, $q = 0.2$, and $c = 1.2$.

when the threat of both predation and infection is high as this strategy will replace individuals lost to either of these risks, whereas infection defence only protects against a single enemy. I also find that if costs are decelerating then the system is bistable and will display starkly different population dynamics and levels of host defence dependent on the initial conditions.

Chapter 4

In previous chapters, I have seen that fluctuating population dynamics are a possible outcome of the deterministic model. I have presented results that show how these cycles can influence evolution and have important ecological effects since host densities can get very small, putting the parasite at risk of extinction. In Chapter 4, I, therefore, consider the stochastic model of the framework used throughout this thesis to look at how often the parasite can survive in these fluctuating regions. I, and other theoretical studies, have results that depend on parasite survival when the dynamics fluctuate; hence, understanding if the parasite can survive and under what conditions is vital for utilising these previous results.

Chapter 2

The evolution of a parasite to manipulate the host

2.1 Abstract

Trophically transmitted parasites often infect an intermediate prey host and manipulate their behaviour to make predation more likely, thus facilitating parasite transmission to the definitive host. However, it is unclear when such a manipulation strategy should be expected to evolve. We develop the first evolutionary invasion model to explore the evolution of manipulation strategies that are in a trade-off with parasite production of free-living spores. We find that the size of the susceptible prey population, together with the threat of predation, drives manipulation evolution. We find that selection favours manipulation strategies over spore production only when the susceptible prey population is large, and the threat of predation is relatively small. We also confirm that the system exhibits cyclic population dynamics and this can influence the qualitative direction of selection. The work from this chapter is published in the *Journal of Evolutionary Biology*, see Oliver & Best (2024).

2.2 Introduction

Many parasite species are known to manipulate the hosts they infect to increase their transmission success. We define host manipulation as a parasite-induced change in the host's phenotype that has fitness benefits for the parasite (Dawkins 1999, Poulin 2010, Poulin & Maure 2015). Trophically transmitted parasites often demonstrate such manipulation, as they will manipulate an intermediate prey host to become more vulnerable to predation due to an alteration in appearance or behaviour by a definitive host, thereby facilitating transmission (Fenton & Rands 2006, Thomas et al. 2005, Moore 2002). Host manipulation has been a buzz topic of parasite research since the 1970s when Bethel & Holmes (1973) first documented this phenomenon in their studies as a parasitic adaption (Moore 2002, Thomas et al. 2005, Poulin & Maure 2015, Doherty 2020). As the literature on this topic has grown, manipulation is now broadly accepted as an adaptive mechanism (Poulin 1994, Poulin & Maure 2015) that is widespread throughout nature rather than some spectacular happenstance (Moore 2002, Poulin 2010, Gopko & Mikheev 2017).

Manipulator parasites appear common in nature (see Moore (2002)); for example, experiments by Bethel & Holmes (1973) found that infection from *Polymorphus paradoxus* turns photophobic crustaceans photophilic so ducks more easily see them, ants are more vulnerable to grazing sheep when infected by *Dicrocoelium dendriticum* (Carney 1969, Wickler 1976, Poulin 2007) and rodents infected by *Toxoplasma gondii* become attracted to cat odours (Berdoy et al. 2000). Although there are many instances of manipulator parasites, not every parasite will evolve to alter host behaviour (Poulin 2010). A reason for this may be the associated costs to evolve this strategy. There is evidence that these costs do exist (Vizoso & Ebert 2005, Maure et al. 2011) and they are likely to come in the form of energy diversion from other important functions such as reproduction, growth and tackling the host's immune system (Poulin 1994). Experimental work by Frost et al. (2008) and Franceschi et al. (2010)

is in support as they show that manipulation investment is at the expense of parasite growth and spore production. Further, a possible consequence of host manipulation is that an infected intermediate host may be consumed by a so-called dead-end predator (Seppälä & Jokela 2008) which may be considered as a different form of cost to the parasite. Against the backdrop of the existence of these costs, Poulin (1994) claimed that the likely outcome is that parasites will not necessarily maximise manipulation but rather selection will favour an optimum investment that will instead maximise fitness. Hence, a key research question is to investigate when parasite manipulation strategies evolve.

A theoretical study by Fenton & Rands (2006) developed a model based on work by Lafferty (1992) to investigate population dynamics when a parasite can evolve to be manipulative. They found that altering the intermediate host behaviour can result in oscillatory dynamics that may cause stochastic extinction of either the predator or the prey species since, in the dynamical troughs, they can dip to meagre numbers. They also found that the extent to which manipulation alters these dynamics depends on the relationship between a predator's feeding rate and prey density (Holling 1959). Vries & van Langevelde (2018) use the model by Fenton & Rands (2006) to explore how the population dynamics are altered if one of two host manipulation strategies, predation suppression and predation enhancement, are varied. They find that manipulation enhancement, which increases the likelihood of predation on the infected intermediate host, is most beneficial to the parasite - and so potentially most likely to evolve - when the predator population is respectively small. However, there is yet to be a formal evolutionary invasion analysis of this system. Due to the aforementioned oscillatory dynamics generated by the inclusion of free-living spores (Anderson & May 1981), investigating parasite evolution is challenging because it requires the use of a method reliant on Floquet exponents, such as that developed by Ferris & Best (2018), to find invasion fitness (see also Lion & Gandon 2022). This method is formalised in a numerical routine by Best & Ashby (2023) that is appropriate for calculating invasion

fitness (Metz et al. 1992) in a varying environment. Other theoretical studies, while they do not directly model manipulation, have focused on parasite evolution in the presence of immune predators, and they have demonstrated that the inclusion of this enemy population can have a significant effect on evolution (Choo et al. 2003, Morozov & Adamson 2011, Morozov & Best 2012, Kisdi et al. 2013, Best 2018). Morozov & Adamson (2011) concluded that the presence of a predator could lead to the evolution of highly virulent parasites and predator extinction, Morozov & Best (2012) reported predator-mediated branching that can lead to diverse parasite strains with differing virulence and Kisdi et al. (2013) confirmed the findings of parasite diversity but also found evolutionary cycles can arise between predator density and parasite virulence.

Using a model similar to Fenton & Rands (2006), we include a trade-off between investment in manipulation strategies and spore production (free-living infective stages), building on preliminary research by Toor (2016). We investigate when a parasite is most likely to invest in behavioural alteration methods of intermediate hosts by varying ecological parameters that will alter the environment of the system to decide which characteristics promote manipulative traits. Our key finding is that population densities are drivers of manipulation evolution. We verify that these conclusions hold in regions where we have fluctuating dynamics and check what happens to the trend of the change in the level of manipulation across the boundary between equilibrium and cyclic dynamics.

2.3 Model

The parasites in this system are trophically transmitted, so we consider intermediate and definitive hosts that are prey and predators, respectively. We are interested in parasite evolution of manipulation strategies that cause the intermediate host to change their appearance or behaviour to be more vulnerable to predation, thus facilitating parasite transmission from prey to predator.

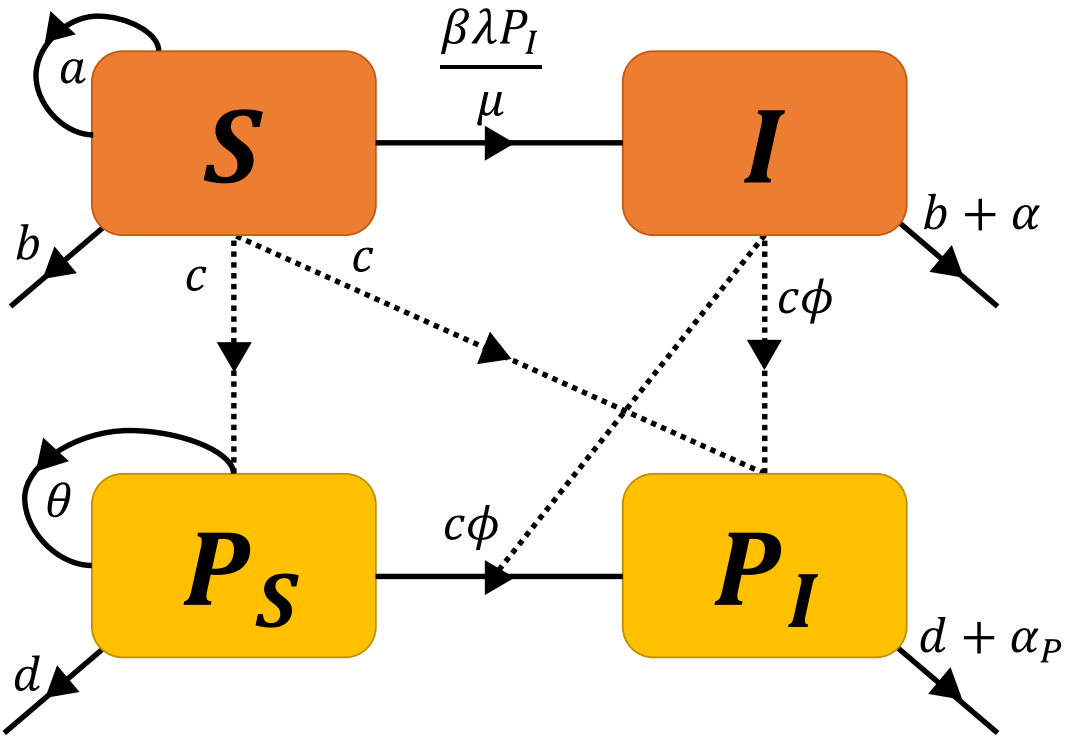

Figure 2.1: The schematic diagram for the host-parasite model. Here S and I (orange) represent the susceptible and infected intermediate prey hosts respectively and similarly, P_S and P_I (yellow) represent the susceptible and infected definitive predator hosts respectively. The dotted lines represent predation.

The model is analogous to the framework by Fenton & Rands (2006) is presented schematically in figure 2.1 is governed by the following equations,

$$\frac{dS}{dt} = aS(1 - qS) - \rho_S(S, I)(P_S + P_I) - \frac{\beta\lambda S P_I}{\mu} - bS, \tag{2.1a}$$

$$\frac{dI}{dt} = \frac{\beta\lambda S P_I}{\mu} - (b + \alpha)I - \rho_I(S, I)(P_S + P_I), \tag{2.1b}$$

$$\frac{dP_S}{dt} = \theta\rho_S(S, I)P_S - \rho_I(S, I)P_S - dP_S, \tag{2.1c}$$

$$\frac{dP_I}{dt} = \rho_I(S, I)P_S - P_I(d + \alpha_P), \tag{2.1d}$$

where S, I, P_S and P_I represent the host densities for susceptible prey, infected prey, susceptible predators and infected predators, respectively. The model parameters are summarised in table 2.1. New prey hosts are introduced to the system at a rate a and die at a rate b. They also suffer additional mor-

tality due to parasite virulence, α. The parameters for a predator are similar, although their birth rate, θ, is defined as the conversion of predation into new predator hosts. Predators are removed from the system at a rate $(d + \alpha_P)$ arising from natural and parasite-induced deaths. We make the simplifying assumptions that there is no recovery for either host and that infected individuals do not reproduce. Further research should explore the impact of these assumptions since it is noted that they can have important impacts on selection (Boots & Bowers 2004, Donnelly et al. 2015, Best et al. 2017), though we note that Fenton & Rands (2006) found that models where infected prey hosts could reproduce showed no qualitative differences in dynamics. Since the intermediate hosts are preyed upon, the model incorporates predation in the terms ρ_S and ρ_I. These are Holling functional responses (Holling 1959); our main focus is the linear Type I case where predation increases with prey density, and there is no limitation on predation (see figure 2.2). We also consider the hyperbolic Type II responses later. In the first instance, the predation equations take the form $\rho_S = cS$ and $\rho_I = c\phi I$, where c is the baseline predation rate and ϕ acts like a scaling factor for predation resulting in an increase or decrease in predation due to host manipulation. We allow ϕ to vary between 1 and 2 so that when $\phi = 1$ the likelihood that a predator eats a susceptible prey is equal to the likelihood that a predator will eat an infected prey as the predation equations are both solely reliant on the baseline predation rate, and so no manipulation strategies have evolved, and we take $\phi = 2$ as the maximum so that predation of infected prey hosts is twice as likely due to manipulation strategies. Also, note here that we assume manipulation is instantaneous upon infection. Predators become infected by eating infected prey, and prey become infected by consuming spores with parameter β that have been released into the environment. We refer to this term as the spore consumption rate to align with the framework of Fenton & Rands (2006), but it can be considered as a combination of the probability that a prey host comes into contact with a spore and the probability of infection given a contact has occurred. Parasites

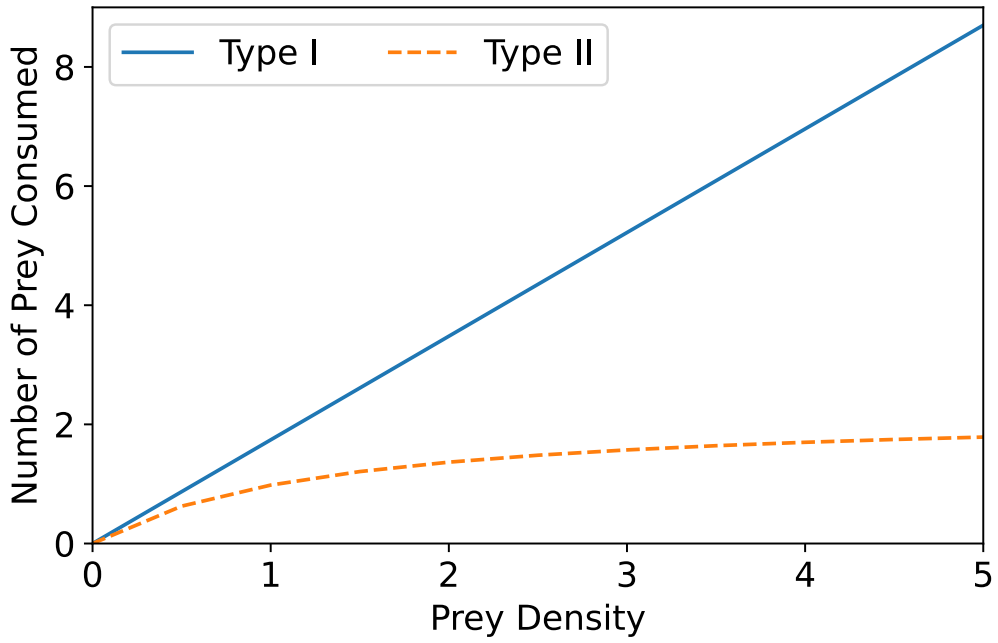

Figure 2.2: The number of prey consumed as prey density is varied when we use both Holling (1959) Type I and Type II functional responses. Parameter values are as follows: $c = 1.2$, $h_S = 0.6$, $h_I = 0.1$, and $\phi = 1.5$.

produce these spores at a rate λ in the predator host. If the spores are not consumed by prey, they decay at a rate μ. Fenton & Rands (2006) simplified the model by assuming that these spore, free-living stages' dynamics are fast and do not need to be explicitly modelled. Thus, assuming that the free-living parasite density is at equilibrium, the infection term is, therefore, $\frac{\beta\lambda P_I}{\mu}$.

We do also consider Holling Type II functional responses (Holling 1959). These are hyperbolic equations of the form $\rho_S = \frac{cS}{1+ch_SS+c\phi h_II}$ and $\rho_I = \frac{c\phi I}{1+ch_SS+c\phi h_II}$. Here, h_S and h_I are predator handling times of susceptible and infected prey, respectively. These responses now limit predator consumption because intake of prey decelerates as prey density increases. A graphical representation of this relationship can be seen in figure 2.2.

For our evolutionary model, we include a trade-off between spore production λ and the scale factor of predation due to host manipulation ϕ. The function,

Model Parameter	Description
S	Density of susceptible intermediate prey hosts
I	Density of infected intermediate prey hosts
P_S	Density of susceptible definitive predator hosts
P_I	Density of infected definitive predator hosts
μ	Free-living parasite spore decay rate
b	Prey mortality rate
d	Predator mortality rate
β	Prey host susceptibility to infection
α	Virulence for Prey
α_P	Virulence for Predator
a	Prey birth rate
θ	Conversion of predation into births of new predators
q	Strength of intraspecific density dependence acting on prey
c	Baseline predation rate
ϕ	Scale factor of predation due to host manipulation
λ	Rate at which parasites produce infective stages (spores) in predators
ρ_S, ρ_I	Holling Type I response in predators

Table 2.1: Descriptions for our dependent variables (S, I, P_S, and P_I) and each model parameter used in the model.

$\lambda(\phi)$, has the following form similar to that used by Hoyle et al. (2012), Toor & Best (2015, 2016), and Singh & Best (2021),

$$\lambda(\phi) = \lambda(\phi^*) - \frac{\lambda'(\phi^*)^2}{\lambda''(\phi^*)}\left[1 - \exp\left(\frac{\lambda''(\phi^*)(\phi - \phi^*)}{\lambda'(\phi^*)}\right)\right], \tag{2.2}$$

where we fix the singular strategy at $(\phi^*, \lambda^*) = (1.5, 0.6)$ and we choose the other components so that the trade-off function is,

$$\lambda(\phi) = 0.6 - \frac{(-0.3)^2}{0.2}\left[1 - \exp\left(\frac{0.2(\phi - 1.5)}{-0.3}\right)\right]. \tag{2.3}$$

Figure 2.3 shows that as ϕ increases, $\lambda(\phi)$ decreases. This means that an increase in predation due to manipulation will cause a decrease in parasite spore production. Due to limited energy, the parasite cannot maximise all desirable traits hand so it can only maximise either the spore production rate or manipulation level. The curve is concave meaning that we assume that manipulation

becomes increasingly costly as the strategy evolves to higher levels. We model the trade-off so that the default singular strategy is an intermediate value for both the spore production rate and the change of predation due to manipulation for our chosen default parameter values and then our analysis looks to see if the direction of selection results in the degree of manipulation increasing or decreasing from this intermediate level.

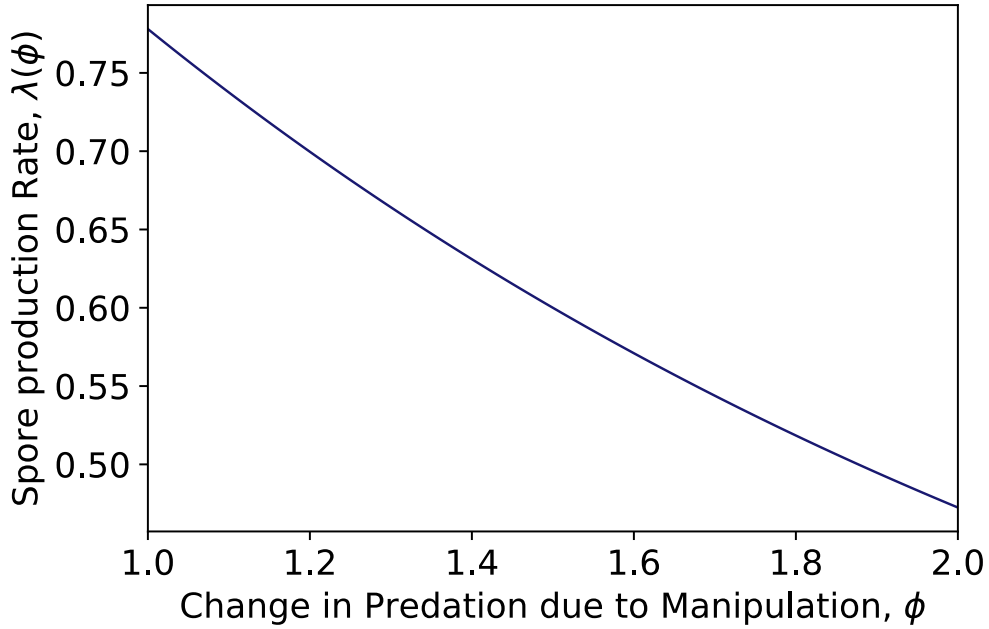

Figure 2.3: The shape of the trade-off function from Equation 2.3, where $\lambda(\phi)$ is the parasite spore production in predators, and ϕ is the scaling factor of predation due to host manipulation. We choose $(\phi^*, \lambda^*) = (1.5, 0.6)$, $\lambda'(\phi^*) = -0.3$, and $\lambda''(\phi^*) = 0.2$.

We will vary the ecological parameters and investigate the effect on the population dynamics and parasite evolution of manipulation strategies. We must find the Continuously Stable Strategies (CSS) for the latter. This is when the local selection gradient is zero, and the strategy is both evolutionary and convergence stable (Geritz et al. 1997, Best & Ashby 2023). At these CSS points, we can calculate the level of manipulation from mutant invasion fitness. We still work within the classical adaptive dynamics framework (Metz et al. 1996,

Dieckmann & Law 1996, Marrow et al. 1996, Geritz et al. 1998) to calculate fitness. As such, we consider the invasion of a rare mutant into a resident population and look to calculate mutant invasion fitness. For our model, the fitness equation has the form,

$$r(\hat{\lambda}, \hat{\phi}, \lambda, \phi) = -(d + \alpha_P)(b + \alpha + c\hat{\phi}(P_S + P_I)) + \frac{c\hat{\phi}\beta\hat{\lambda}SP_S}{\mu}, \tag{2.4}$$

where we denote our mutant traits as $\hat{\lambda}$ and $\hat{\phi}$. The full calculation for the derivation of mutant invasion fitness is in box 2.1. The mutant has positive fitness when $r > 0$ and may invade the resident, whereas when $r < 0$, it has negative fitness and cannot invade. Most studies usually rely on the long-term behaviour of the resident dynamics settling to a stable equilibrium before a mutant arises. This allows a simple assumption of a separation of ecological and evolutionary timescales so that we can take a point estimate of resident densities required in the mutant fitness calculation. However, due to free-living infective stages, this system displays fluctuating dynamics for some parameter regions (Anderson & May 1981, Fenton & Rands 2006) meaning that we can no longer take a single-point estimate of these resident densities since they will cycle and consequently mutant fitness will too. So, because of this cyclic behaviour, we calculate Lyapunov (Floquet) exponents since Metz et al. (1992) reported that the largest of these can be taken as mutant invasion fitness. These methods have been used before by Ferris & Best (2018) when fluctuations are brought about by seasonal variation in births, but we now use them for fluctuations caused by free-living stages. We give a general overview of the method in Chapter 1, subsection 1.2.2, and we provide an outline of how we use floquet theory to calculate the mutant invasion fitness when the dynamics fluctuate in box 2.2. In this case, the numerical routine to calculate these exponents was formally developed by Ferris & Best (2018, 2019) and outlined in full detail by Best & Ashby (2023). We then look for those aforementioned CSS points.

Box 2.1 Calculating Mutant Invasion Fitness

To calculate mutant invasion fitness, we follow a proof similarly outlined in Appendix S1 in Hoyle et al. (2012). For our model, the mutant invasion matrix is given by

$$J = \begin{pmatrix} -(b+\alpha) - c\hat{\phi}(P_S + P_I) & \frac{\beta\hat{\lambda}S}{\mu} \\ c\hat{\phi}P_S & -(d+\alpha_P) \end{pmatrix} = \begin{pmatrix} A & B \\ C & D \end{pmatrix}, \tag{2.5}$$

where $\hat{\phi}$ and $\hat{\lambda}$ are the mutant traits. The matrix shows that $A, D < 0$ and $B, C > 0$. To find the mutant invasion fitness we can calculate the dominant eigenvalue of our invasion matrix:

$$\begin{vmatrix} A-\lambda & B \\ C & D-\lambda \end{vmatrix}$$

$$= (A-\lambda)(D-\lambda) - BC = \lambda^2 + (A+D)\lambda + (AD - BC) = 0. \tag{2.6}$$

From this we find that our eigenvalues are

$$\begin{aligned} \lambda_\pm &= \frac{A + D \pm \sqrt{(A+D)^2 - 4(AD - BC)}}{2}, \\ &= \frac{A + D \pm \sqrt{(A+D)^2 + 4BC}}{2}. \end{aligned} \tag{2.7}$$

The discriminant is positive and so both eigenvalues are real and since $A, D < 0$, $\lambda_- < 0$. It is clear that $\lambda_+ > \lambda_-$ and so this must mean that λ_+ is our dominant eigenvalue and thus our fitness term (Metz et al. 1996, Geritz et al. 1998). We refer to mutant invasion fitness as r and so $r = \lambda_+$. If the determinant of $(J - \lambda I) = (\lambda_+ - \lambda)(\lambda_- - \lambda)$ then it follows that setting $\lambda = 0$ means that the determinant of J is simply the product of our two eigenvalues, $\lambda_+\lambda_-$. In all, the sign of the determinant is reliant on the sign of λ_+.

- If $\lambda_+ < 0$, the mutant does not invade and $|J| = \lambda_+\lambda_- > 0$.
- If $\lambda_+ > 0$, the mutant will invade and $|J| = \lambda_+\lambda_- < 0$.

Hence the mutant invasion fitness expression, which we take as the dominant eigenvalue λ_+, is sign equivalent to the negative determinant of the invasion matrix. This is the fitness proxy used in my analysis and shown in equation 2.4.

Box 2.2 Numerical Routine to Calculating Mutant Invasion Fitness

Metz et al. (1992) noted that mutant invasion fitness can be calculated by finding the dominant Lyapunov exponent when population dynamics fluctuate. Work by Ferris & Best (2018) used this result to formalise a way of calculating mutant invasion fitness when the population dynamics fluctuate. We present an outline of how this method works.

If the mutant dynamics were to be given by a single ODE we would have,

$$\frac{dX_m}{dt} = r(t)X_m, \tag{2.8}$$

where $r(t)$ would be the average growth rate of the mutant over one cycle and thus could be taken as an expression for fitness.

If we apply this to our fluctuating system where we would have two equations for the mutant, we would use vector notation so that our mutant densities are,

$$X(t) = \begin{pmatrix} I_m(t) \\ P_{I_m}(t) \end{pmatrix}. \tag{2.9}$$

If the cycles have period T then the initial mutant dynamics at time $t+T$ would be given by,

$$X(t+T) = P(t)e^{\mu_i T}. \tag{2.10}$$

Here, $P(t)$ is a periodic function. Thus, the mutant density depends on the term $e^{\mu_i T}$ and, more specifically, μ_i, which are the Lyapunov exponents, which we call Floquet exponents. If $\mu_i > 0$ for all i, then the mutant population will grow, whereas if $\mu_i < 0$ for all i, the mutant density will decrease. If then instead, we write the system as,

$$X(t+T) = X(t)C, \tag{2.11}$$

and numerically run our mutant dynamics twice for the length of the period T using initial conditions reliant on the last value of the resident densities and two linearly independent values for the mutant, we can calculate this matrix C. We take the mutant densities at the end of the two numerical simulations so that,

$$C = \begin{pmatrix} I_{m1} & P_{I_{m1}} \\ I_{m2} & P_{I_{m2}} \end{pmatrix}. \tag{2.12}$$

The matrix C has eigenvalues $\rho_i = e^{\mu_i T}$. From this, the Floquet exponents, μ_i, can be calculated, and we take the dominant eigenvalue as our expression for mutant invasion fitness. The full numerical routine is presented clearly, and the associated code is linked, in the work by Best & Ashby (2023).

2.4 Results

2.4.1 Holling Type I Predation Equations

We aim to investigate how the parasite may evolve to change its investment in manipulation strategies when it is in a trade-off with the spore production rate. We investigate all model parameters, and we outline the most interesting trends in the main text, although further plots feature in Appendix A.

In figure 2.4A, we show the change in CSS investment in manipulation (white dots) as the model parameter is altered, and we plot them against a colour map that depicts when we have equilibrium population dynamics (dark-purple regions) and cyclic population dynamics (lighter-coloured regions) and in the latter case the period of these cycles. In figures 2.4B and 2.4C, we plot the minimum, average and maximum densities of the susceptible prey and total predator population at this CSS point. In Appendix A, we also include the equivalent population density plots of infected prey and predators. Considering only the equilibria region, we see that as β increases, selection favours an increase in the degree of manipulation that the parasite evolves (figure 2.4A) and infected prey density increases (figure A.3A, appendix A) because the prey population are consuming more spores. This means that predators are more likely to eat infected prey, ultimately resulting in reduced predator (average) lifespan and this population (figure 2.4C) which simultaneously allows the susceptible prey population to grow (figure 2.4B). Coupling the fact that the susceptible population is large and the spore consumption rate by prey is increasing, prey hosts are likely to be exposed to the infection allowing the parasite to persist among them. Because of this, selection pressure is stronger for increased manipulation than for increased spore production, to facilitate parasite transmission from prey to predator. Manipulation strategies are particularly important here because there are fewer predators, and encouragement to eat infected prey over susceptible prey helps ensure the parasite can survive amongst this limited predator population. The direction of selection is contin-

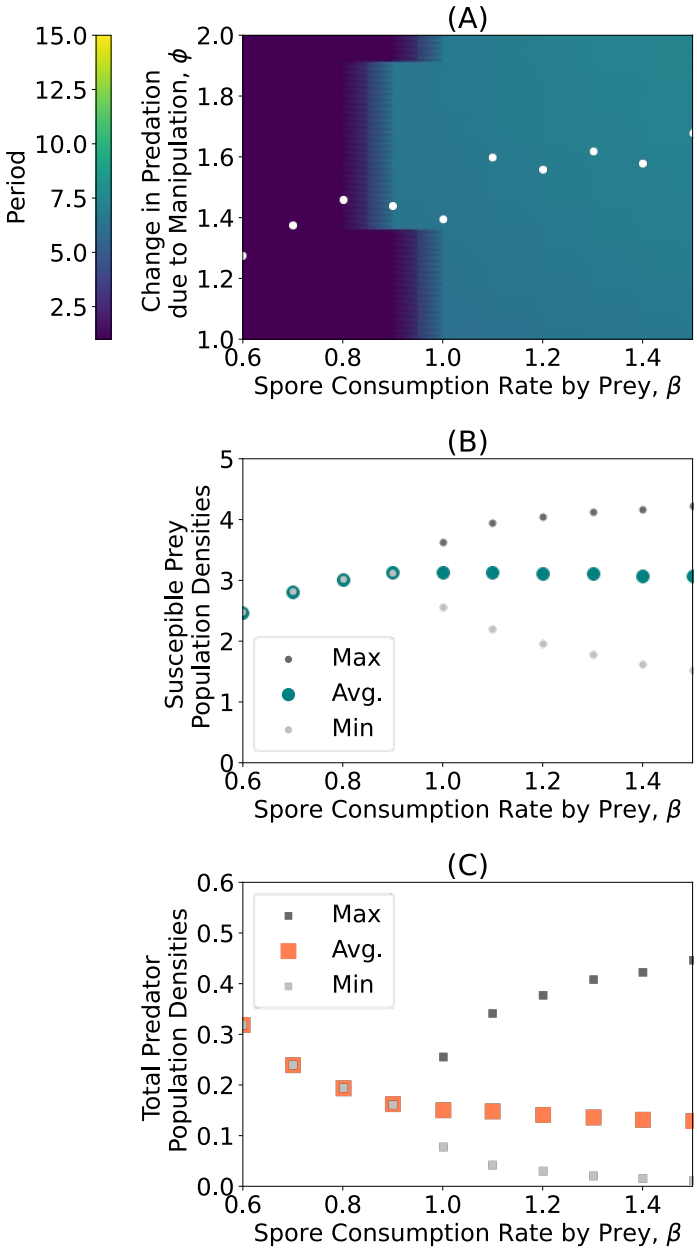

Figure 2.4: The spore consumption rate by prey, β is varied to see how it affects the singular strategy ϕ^* (A), the susceptible prey population densities (B) and the total predator population densities (C). The x-axis is limited since the parasite cannot persist in the population for values smaller than this. Standard parameter values are $\mu = 0.15$, $b = 0.2$, $d = 0.4$, $\beta = 0.95$, $\alpha = 0.8$, $\alpha_P = 0.7$, $a = 2$, $\theta = 0.5$, $q = 0.2$, and $c = 1.2$. Parameter values were chosen so that infection is present in the population and to ensure we were in a region where cyclic dynamics occur.

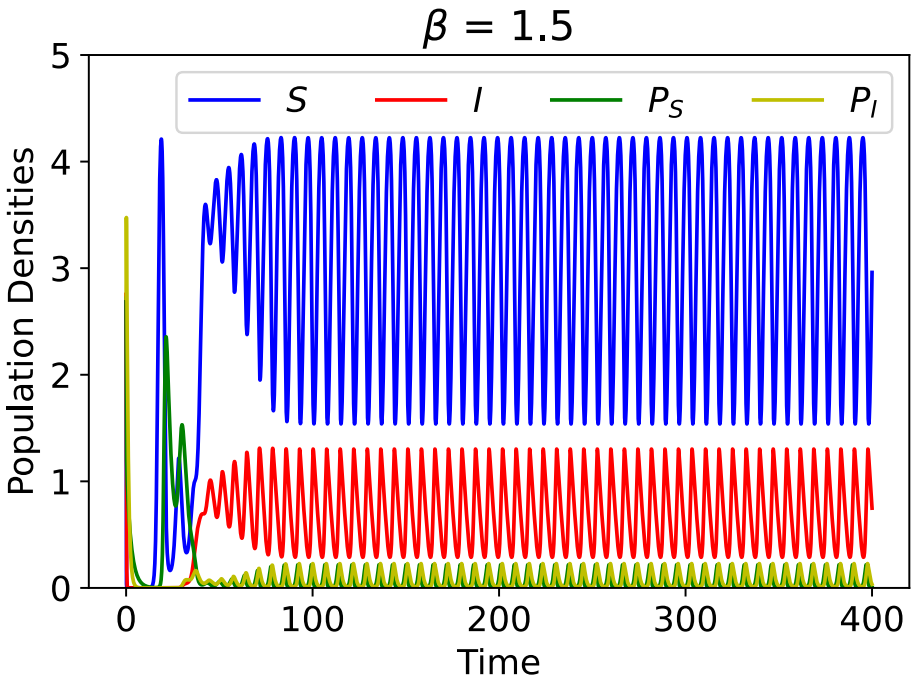

Figure 2.5: Population Dynamics at the CSS point for $\beta = 1.5$. Other parameters take the standard values outlined in figure 2.4.

uous across the boundary between the equilibrium and cyclic regions. We see that while both the susceptible prey and total predator populations plateau on average, the maximum and minimum densities they can reach continue to increase and decrease, respectively. As the susceptible prey population cycles between reasonably high densities, there will always be enough hosts to pick up spores, and selection remains in favour of manipulation strategies. Notice that there are time periods when the predator population is extremely small. We evidence this further by plotting a time course at the CSS point when $\beta = 1.5$ in figure 2.5. It is clearly visible here that the troughs of the cycles put the predator densities perilously close to zero, making it difficult for parasites to complete their life cycle, whereas the prey population densities remain relatively large even at their minimum values.

If the transmission efficiency of spores is compromised in any way, there is selection for an increased spore production rate. Factors that affect spores

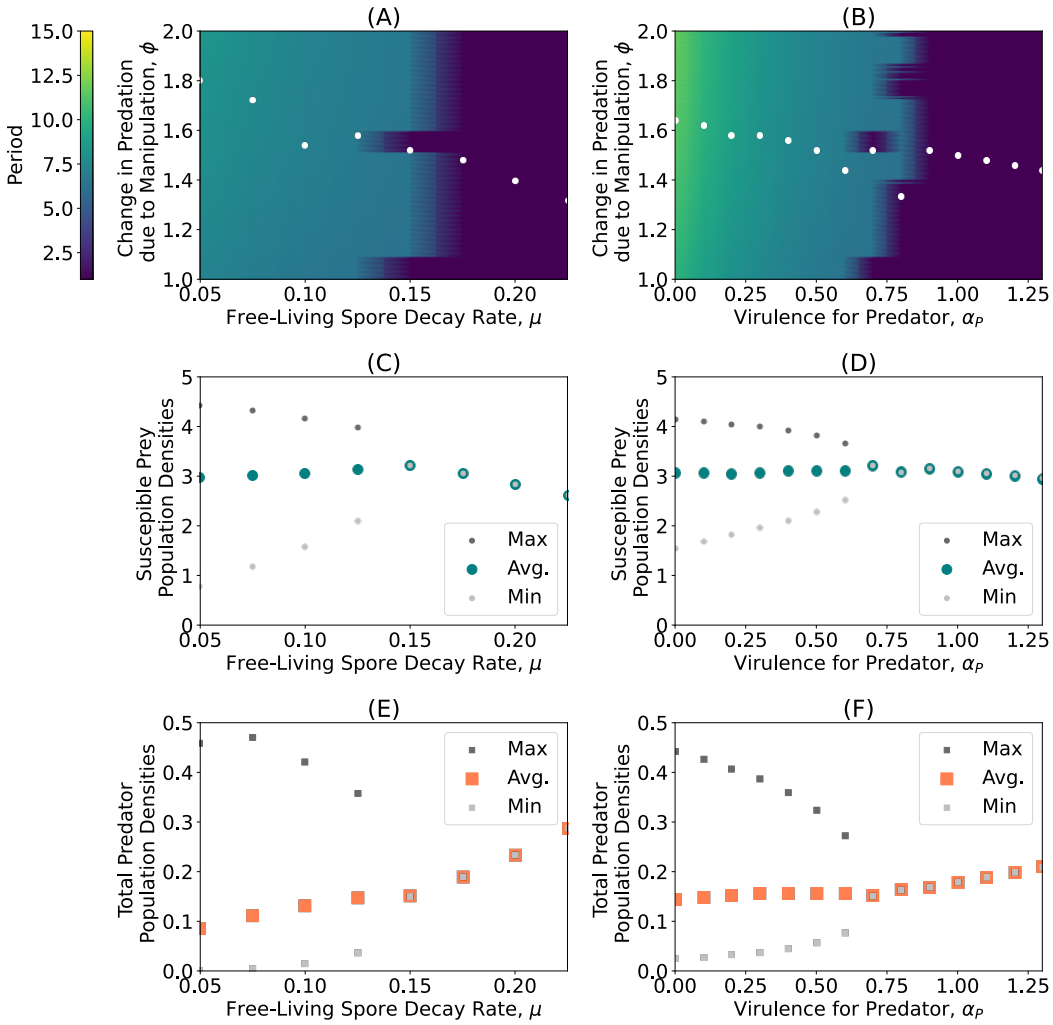

Figure 2.6: The decay rate of free-living parasite spores, μ and predator virulence, α_P are each varied to see how it affects the singular strategy ϕ^* (A-B), the susceptible prey population densities (C-D) and the total predator population densities (E-F). The x-axis is limited since the parasite cannot persist in the population for $\mu < 0.05$. Standard parameter values are as in figure 2.4.

in this way are an increase in the spore decay rate, μ, which means that the spores decay faster in the environment, and an increase in predator virulence, α_P, which means that the organism in which these spores are produced does not survive for as long. In both cases, selection will not prioritise manipulation strategies that facilitate transmission from prey to predator but instead favour increasing the spore production rate (figures 2.6A and 2.6B) to ensure that the infection is present in the prey population. As both μ and α_P are increased, we see that the threat of predation also increases (figures 2.6E and 2.6F respectively). The latter result is non-intuitive but arises because increased predator virulence only shortens infected predators' lifespan. This means the growth in the predator population must predominantly be coming from the susceptible predators (see figure A.4D, Appendix A). Susceptible predators can thrive because we can see from figure 2.6D that there is always sufficient prey in the population to ensure they can feed. In all, we see selection favouring spore production instead of costly manipulation strategies because having a greater predator population already increases the likelihood that infected prey will be eaten. As shown in figure 2.4, the trend in the parasite's level of manipulation continues across both the equilibrium and cyclic regions. In both cases, the investment in manipulation is reduced further since the susceptible prey population continues to decline whereas predation becomes increasingly likely.

We next look at prey mortality rate b and virulence α. If we consider what happens in the equilibrium regions (right-hand side) of the plots figure 2.7A and 2.7B, we see that as prey mortality rate and prey virulence decrease, investment in manipulation increases, albeit only slightly in the case of α. If the prey lifespan is increasing, then, of course, the susceptible population grows (figure 2.7C). The predator population simultaneously shrinks (figure 2.7E), which could be due to an increase in infection since we see the infected prey population rapidly increase (see figure A.5, Appendix A). As prey virulence decreases in this equilibrium region, infected prey will survive for longer, and thus, predators are likely to have an increased chance of eating infected prey

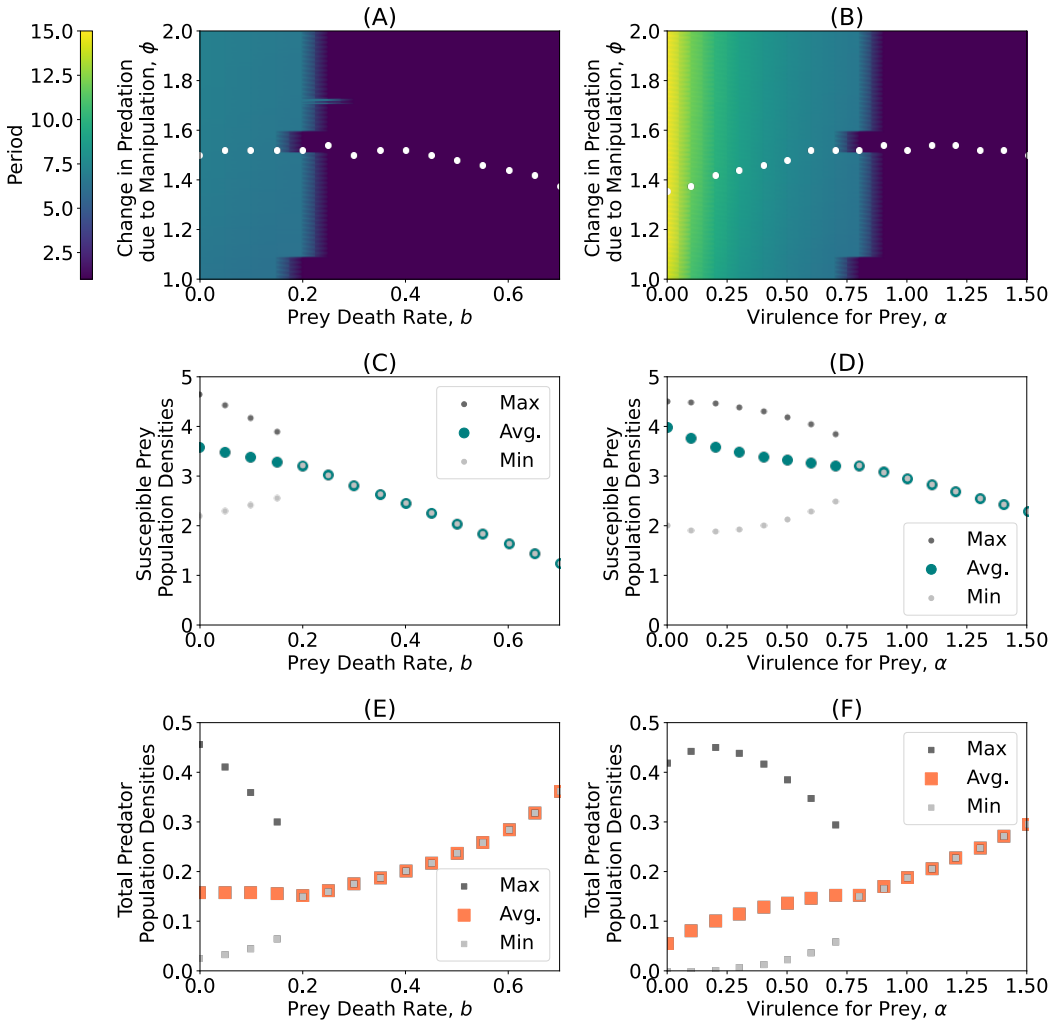

Figure 2.7: The prey death rate, b and prey virulence, α are each varied to see how it affects the singular strategy ϕ^* (A-B), the susceptible prey population densities (C-D) and the total predator population densities (E-F). Standard parameter values are as in figure 2.4.

before they die due to parasite damage. Infection among predators may increase and explain the reduction in predator density (figure 2.7F). Moreover, the susceptible prey population can thrive (figure 2.7D) as the predation threat is reduced. In both cases, we see a sufficient prey population that is likely to pick up spores, meaning that the parasite can persist amongst them, resulting in selection favouring manipulation strategies to maintain infection within the predator population.

As the cycles emerge we see the direction of selection change. In the case of continuing to reduce b, the degree of manipulation evolved decreases slightly but remains relatively stable. The susceptible prey population continues to grow, and the predator population remains stable on average. However, the maximum predator densities get very large and the minimum susceptible prey densities simultaneously relatively small as the prey mortality rate shrinks. A plot displaying how the peaks and troughs of these densities coincide can be found in figure 2.8A. This extreme predation risk at certain time points in this cycling region explains why selection looks to start favouring an increase in spore production to ensure that the parasite can persist even in the time periods when prey density is dramatically reduced. Extreme maximum predator densities and minimum susceptible prey densities during the cycles are also visible in the case of continuing to reduce prey virulence α. Couple this with the fact that the parasite has longer to transmit to the predator hosts due to infected prey having a longer lifespan explains why we see a decrease in the degree of manipulation that evolves. Selection favours spore production to ensure the parasite can persist in the prey population even during the times when the densities are at the minimum point on the cycles.

As the prey birth rate, a, begins to increase, we see an increase in manipulation (figure 2.9A). We know from previous discussions that selection acts in favour of manipulation when the susceptible prey population is large (figure 2.9C) and when the predator population is relatively small (figure 2.9E). This is because transmission to prey is sufficient but facilitating transmission from prey

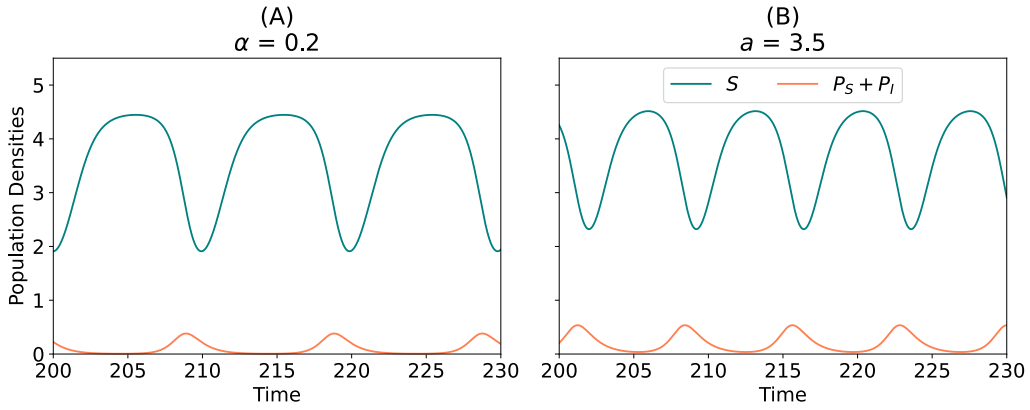

Figure 2.8: A small subsection of the susceptible prey and total predator population dynamics to show how the minimum prey densities coincide with the maximum predator densities for two values of prey virulence α and prey birth rate a.

to predator may be necessary to ensure that the limited number of predators eat infected prey so that infection remains amongst the definitive hosts. Continuing to increase the birth rate causes the dynamics to fluctuate and we see a change in trend in the qualitative direction of selection since the parasite reduces investment in manipulation in favour of spore production instead. This change occurs because the susceptible prey population growth slows down, with minimum densities becoming increasingly small (figure 2.9C), the predator population begins to grow, with maximum densities becoming increasingly large (figure 2.9E), and the peaks and troughs of the predator and susceptible prey densities coincide (figure 2.8B). Since we model predation so that it grows linearly with prey density (see figure 2.2) we find that predation increases as more prey are birthed into the population. Infected prey are more at risk from predation now, so selection would not favour costly manipulation strategies. Increasing spore production is necessary here to keep infection present in the prey population.

Similarly, when the strength of intraspecific density dependence acting on prey, q is small, the susceptible prey population can grow (figure 2.9D) since there

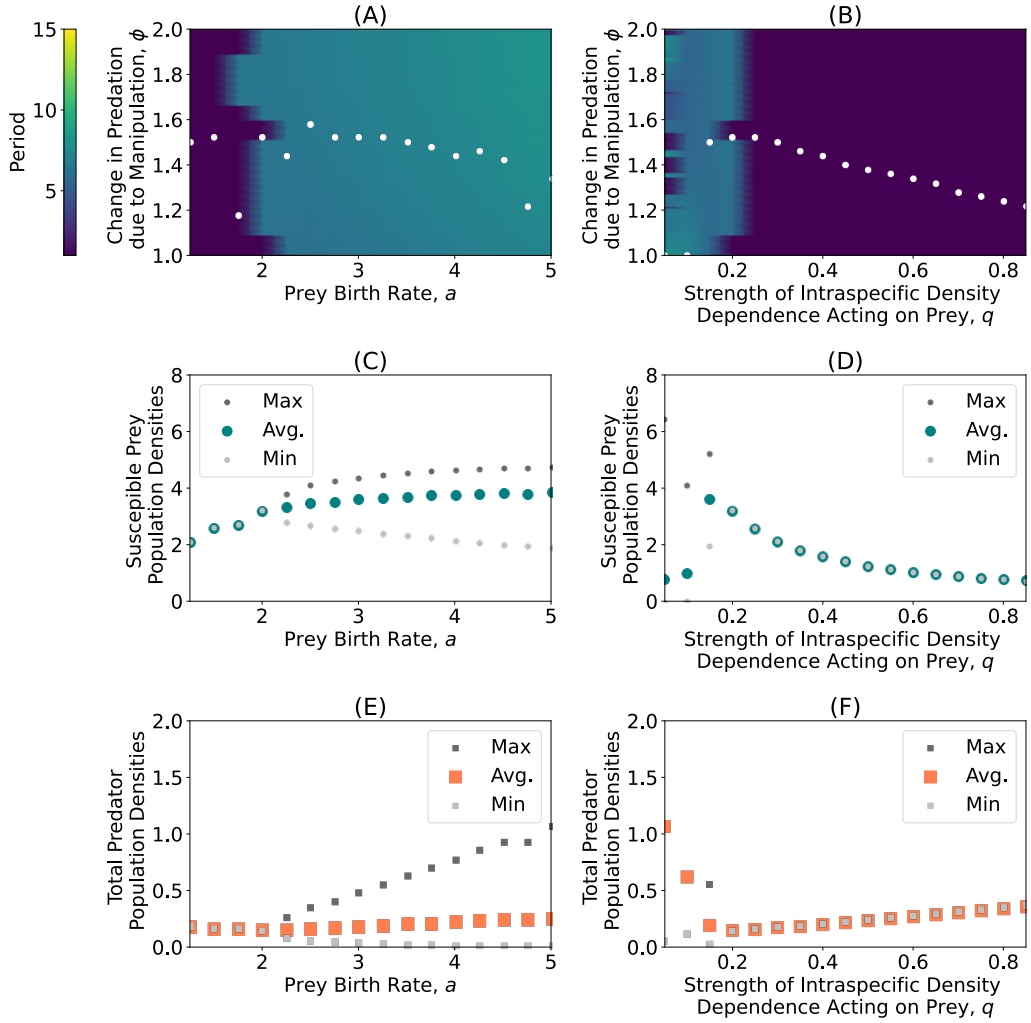

Figure 2.9: The prey birth rate, a and strength of intraspecific density acting on prey, q are each varied to see how it affects the singular strategy ϕ^* (A-B), the susceptible prey population densities (C-D) and the total predator population densities (E-F). The x-axis is limited in both cases since the parasite cannot persist in the population for values smaller than this. Standard parameter values are as in figure 2.4.

are little to no limiting competition factors. Hence manipulation strategies will evolve for the reasons outlined before, only this time, the population dynamics are cyclic rather than at equilibrium (figure 2.9B); this is likely to be since there are not any strong limiting competition factors acting on the population so it can grow quite large for certain time periods. As q continues to increase, we get population dynamics at equilibrium, but the susceptible prey population densities decline severely. As competition for food and habitat increases, prey will die sooner due to a reduced quality of life. Hence increasing spore production is prioritised for parasite survival in the prey population.

2.4.2 Holling Type II Predation Equations

We repeat the analysis but instead use hyperbolic Holling Type II functional response equations (Holling 1959) where handling times limit predation by accounting for the time predators take to catch and consume prey. In the Type I case, predation linearly increased with prey density, but now we have that predation decelerates as prey density increases (see figure 2.2).

The figures for the Type II case are in Appendix A. When we alter each model parameter, we still find that the same patterns emerge as in the Type I case. Overall, the results are very similar to the Type I model, but a notable difference in the Type II case is that manipulation will always evolve to a higher degree, and the susceptible prey population densities are greater when compared with the Type I case. Since there are now limits on predation that did not exist in the Type I case, it makes sense that the susceptible prey population can grow because their risk of being eaten is minimised. This large susceptible prey population is more likely to pick up spores and sustain infection within the prey population. Predation is limited and so selection favours a higher degree of manipulation to encourage predators to eat infected prey so that infection does not die out in the predator population. Overall, a reduction in predation risk coupled with larger susceptible prey densities results in the evolution of a higher degree of manipulation, which is similar to

our findings in the Type I case.

We also find that fluctuating dynamics occur significantly more frequently for our chosen parameter ranges and manipulation will evolve to cycling regions even if it is possible to evolve to regions of equilibrium dynamics. Considering only the predator densities, the minimum numbers can get very small, but the maximum numbers, when compared to the Type I case and the respective average predator density in the Type II case, can get relatively large. Fluctuating dynamics may allow the predator to reach large enough densities when at the peaks of the cycles to maintain infection amongst this population even when predation is limited, which is why we may see selection favouring a degree of manipulation that results in cyclic dynamics when it would be possible to remain in a region of equilibria.

When we compare the level of infection between the Type I and Type II case, the infection level is consistently lower in the Type II case (see figures A.13, A.14, A.15, A.16 and A.17 in Appendix A.) When the population dynamics fluctuate, the minimum and maximum infected densities are almost always very close to zero and significantly larger than the average density, respectively. Since cyclic dynamics occur more frequently in the Type II case, infection levels seem to be more unstable and sometimes there may not be enough infected hosts in the system. Figure A.18, Appendix A depicts how these minimum densities of infected prey and predator hosts coincide. Because of this, there are certain time periods where the parasite may be at risk of extinction; thus, we see the parasite evolving to a higher degree of manipulation.

2.4.3 Summary of Results

Our investigation presents a clear conclusion that the size of the susceptible prey population coupled with the threat of predation based on the relative size of the total predator population governs whether the parasite will evolve to a higher degree of manipulation. When the predator population is large,

infected prey will likely be eaten, so selection does not favour costly manipulation strategies. With predation threat high, the susceptible prey population will likely shrink, so spores have a reduced chance of being picked up from the environment because there are less suitable hosts. Hence, increasing spore production is essential to ensure infection persists amongst the prey population. When predation risk is low, and the susceptible prey population is large enough to guarantee contact with spores, selection favours manipulative behaviour to boost infection in the predator population. In our results, ϕ is always greater than one; hence, infected prey hosts are always more likely to be eaten than susceptible prey hosts to some extent, but selection tends to favour higher levels of spore production rate rather than higher levels of manipulation. However, when we use the Type II predation equations where we introduced predation limitations, manipulation evolves significantly. This is because the susceptible prey population can grow to larger densities since the predation threat is reduced compared to the Type I case, where predation is not limited and increases linearly with prey density.

When we look at what happens to the manipulation level on the boundary between cyclic and equilibrium dynamics, we sometimes see that the trend in the direction of selection remains the same and continues across the boundary, whereas other times, we see the trend change. Interestingly, the direction only changes when we alter parameters that directly affect the prey population, namely prey mortality rate b, prey virulence, α, prey birth rate, a, and the strength of the intraspecific density dependence acting on prey, q in figures 2.7A, 2.7B, 2.9A, and 2.9B respectively. We see cycles with large amplitude in both the susceptible prey and predator populations. However, the predator cycles can reach maximum values significantly bigger than the average densities compared to the susceptible prey population (see figure 2.6 as an example). Similarly, it would seem that the minimum densities are reduced more severely compared to the average in the susceptible prey population than in the predator population. Having more predators in the population means

the susceptible prey are at greater risk of being consumed which will reduce an already small prey population during those periods of time at the trough of the cycle. This illustrates the impact these cycles have on the susceptible prey population and alludes to why we only see a change in the direction of selection of the manipulation level on the boundary between cyclic and equilibrium dynamics for these parameters that directly affect the prey population.

2.5 Discussion

Our model predicts that parasites are most likely to evolve high levels of manipulation when the susceptible prey population is large, and the threat of predation is relatively low. Hence, we find the susceptible prey and total predator densities to be evolutionary drivers. An important factor to consider when looking at when host manipulation will evolve in parasites is the costs associated with the strategy. Work by Vizoso & Ebert (2005) and Maure et al. (2011) have provided empirical evidence to support the existence of these costs and, to add to this, experiments by Frost et al. (2008) and Franceschi et al. (2010) highlight that trade-offs exist in these systems between investment in manipulation and parasite growth rate and spore production. To our knowledge, empirical studies have yet to investigate the ecological conditions under which parasites will evolve to be manipulative. Instead, empirical studies tend to describe examples and provide evidence of host manipulation of intermediate hosts to increase predation but have been unable to elucidate the specific mechanism or the underlying evolutionary triggers (Carney 1969, Bethel & Holmes 1973, Lafferty & Morris 1996, Berdoy et al. 2000, Moore 2002, Poinar & Yanoviak 2008, Yanoviak et al. 2008). In one such instance, work from Poinar & Yanoviak (2008) and Yanoviak et al. (2008) reveals that the nematode *Myrmeconema neotrpicum* infects ants to turn their abdomen from black to red to induce fruit mimicry and make the ants vulnerable to predation by birds. Some empirical studies provide possible extensions of our theoretical

model, for example, a focus on host manipulation when there is a switch in strategy from predation suppression to enhancement as parasites mature (Dianne et al. 2011, Weinreich et al. 2013), or in the presence of other parasites when parasites can work together to lower manipulation accordingly to share costs or potentially sabotage one another (Hafer & Milinski 2015, Gopko et al. 2017) and also in the presence of non-host predators (Seppälä et al. 2008). It is reported that a paradox exists in that the empirical work available to us emphasises that parasites that manipulate their intermediate hosts to increase predation are widespread in nature, whereas theoretical work contradicts this since manipulator parasites are at risk from stochastic extinction and may not actually be so persistent (Fenton & Rands 2006, Iritani & Sato 2018). In the ongoing effort to achieve synergy between empirical and theoretical work, it would be beneficial if, for those predator-prey systems where we know manipulation strategies are at play, empirical work focused on elucidating the ecological conditions that allow this strategy to evolve.

There are limited theoretical investigations of manipulation evolution, especially those where ecological dynamics are included explicitly. Our model is built on the framework by Fenton & Rands (2006), who consider only the population dynamics when looking at host manipulation by parasites. They highlight how altering intermediate host behaviour can induce oscillatory dynamics. Furthermore, the minimum densities of either the predator or prey populations can become so close to zero that it may result in the stochastic extinction of one of these species. Our analysis shows a similar result since, during the troughs of the cycles, the densities of the prey and predator populations can be very close to zero. We also show that it is possible for a parasite to evolve from equilibria to cycle regions even though there is an increased risk of parasite extinction. Moreover, in the case of Type I functional responses, where predation is not limited and grows linearly with prey density, the predator is most at risk of extinction, whereas when we have more extreme fluctuations, as in the Type II case when the predation rate is decelerating as

prey density increases since predators are limited by handling times of prey, we see the risk extended to both predator and prey populations.

Other works consider manipulation evolution but do not include population dynamics. Poulin (1994) exhibits a cost/benefit argument to conclude that host manipulation will evolve to higher levels when infection prevalence increases, or when parasite or host longevity after infection, parasite population size, passive transmission rates, or parasite fecundity decreases. Reduction in parasite fecundity in favour of manipulation is incorporated in our model as our trade-off function, and we also find evidence that investment in host manipulation strategies decreases as host longevity after infection decreases and as passive transmission increases from our results of altering prey and predator virulence and baseline predation rate respectively in our model. Parker et al. (2009) elucidate a switch in the type of manipulation strategy from predation suppression to enhancement upon parasite maturity in an intermediate host so that there is a delay between a host that is infected and infectious. We consider only predation enhancement, and they find the evolution of this strategy to depend upon the parasite having some fixed lifespan and whether they die in their intermediate host as they reach the end of said lifespan or if they randomly die before this lifespan is reached. If parasites die upon reaching the end of a fixed lifespan, then predation enhancement will evolve because there are fewer infected definitive hosts in the population (Parker et al. 2009), and enhancement can ensure that infection is maintained in the predator population, which is similar to the results that we find.

To our knowledge, the only other study of parasite manipulation to simultaneously consider evolutionary and ecological dynamics explicitly is Vries & van Langevelde (2018), although this looks at changes to model behaviour as manipulation is varied when the system is already at equilibrium rather than an evolutionary invasion analysis thus their model framework does not have manipulation in a trade-off function. They also built upon the model by Fenton & Rands (2006) but instead considered this aforementioned switch in strategy

from predation suppression to enhancement so that the parasite has enough time to develop in the intermediate host before consumption by a predator. They find that when the definitive predator population is large, this additional strategy, predation suppression, is more beneficial to the parasite and so more likely to evolve than enhancement. This is because there is greater predation pressure on this intermediate host population which may mean infected hosts are consumed before they are infectious. Although we only consider predation enhancement in our work, we still find that investment in host manipulation strategies is not favoured when the predator population is large, which is not as extreme as evolving to suppress predation in this circumstance, but predation certainly is not facilitated.

Our system exhibits fluctuating dynamics which could be attributed to the inclusion of free-living spores in the environment (Best & Ashby 2023), the inclusion of a predator (Kisdi et al. 2013) or the mechanism of manipulation (Fenton & Rands 2006). Highlighted by Best & Ashby (2023), cycles in population dynamics can alter evolutionary dynamics. We also find this feedback between ecological and evolutionary dynamics since the trend in what happens to the level of manipulation can change across the boundary between equilibrium and cyclic dynamics. For example, a small prey birth rate induces cyclic dynamics and increasing this parameter does not seem to affect manipulation evolution, but once it is large enough, the dynamics begin to fluctuate, and investment in manipulation strategies begins to decrease instead. However, we also show examples of where the trend does not change across this boundary, such as when we increase the spore consumption rate by prey. This increases investment in manipulation across the entire parameter range, even when we move from equilibrium to cyclic dynamics. Ultimately cycles change the qualitative direction of selection only when we alter parameters that directly affect the prey population, and we believe this is due to cycles having a more severe effect on the prey dynamics compared to the predator dynamics.

We know that the evolution of manipulation strategies comes at a cost for

the parasite in the form of energy diversion away from other important functions such as growth, reproduction and tackling host defence (Poulin 1994). A parasite may evolve these strategies but transmit to the wrong definitive host because the prey gets eaten by a non-host predator (Mouritsen & Poulin 2003, Seppälä et al. 2008, Vries & van Langevelde 2018). Dead-end hosts are another cost for the parasite that we do not consider in our model and may limit selection for manipulation. Some studies have considered modelling specific manipulation (Seppälä & Jokela 2008, Parker et al. 2009), but a key question we might like to ask is how targeted specific predators may affect the evolution of these manipulation strategies in both regions of equilibria and cyclic dynamics. Our interest lies with parasite evolution, but it would be interesting if future work looked at this model but considered host evolution of defence mechanisms against manipulator parasites instead, as well as an obvious extension of a co-evolutionary study that looked at how these intermediate hosts and parasites could evolve defence and manipulation mechanisms simultaneously. Running parallel with increasing the number of theoretical studies, it would be beneficial for experimental work to provide more evidence of the costs for a parasite to evolve manipulation and investigate whether the degree of manipulation depends on susceptible prey and predator densities, as we have found in this study.

Chapter 3

The evolution of host defence against parasite manipulation

3.1 Abstract

Many host-parasite models explore when a host may evolve defence mechanisms against parasitic infection. Some studies have considered how the presence of a predator impacts evolution but usually assume that the predator is immune to the infection. I, therefore, investigate when a host evolves defence mechanisms against trophically transmitted parasites when a non-immune predator is present and the predators in the system selectively choose to consume infected prey. I put prey host susceptibility to infection in a trade-off with prey birth rate and find that population densities are significant evolutionary drivers. I also present results to show that the system is bistable when costs to evolve defences are decelerating.

3.2 Introduction

A substantial body of work exists concerning the evolution of host defence mechanisms against parasitism (Boots & Begon 1993, Boots & Haraguchi

1999, Boots & Bowers 1999, Miller et al. 2007, Boots 2011, Hoyle et al. 2012, Koskella et al. 2012, Toor & Best 2015, 2016, Gorter et al. 2015). Many of the results have focused on host-parasite relationships in isolation, not necessarily accounting for underlying community structure. Still, more recently, studies have begun to measure the impact of other interactions on these relationships, such as the presence of a predator, for example (Morozov & Adamson 2011, Morozov & Best 2012, Kisdi et al. 2013). Moreover, some investigations have focused on host defence evolution when hosts are simultaneously at risk from infection and predation (Hoyle et al. 2012, Toor & Best 2015, 2016). The assumption is often that predators are immune, but this is not always the case in natural systems. For example, there is substantial work on trophically transmitted parasites that use manipulation strategies to increase predation on infected prey hosts to facilitate transmission to their definitive predator hosts, which form an important stage in the parasite's life-cycle (Moore 2002, Fenton & Rands 2006, Poulin 2010, Vries & van Langevelde 2018). Hence, we investigate how defence evolution is impacted when predators pose a second threat to the prey and are non-immune to parasitic infection.

There is a multitude of empirical support for the result that host evolution of defence mechanisms leads to constraints on another component of the host's fitness (Boots & Begon 1993, Biere & Antonovics 1996, Kraaijeveld & Godfray 1997, Rolff & Siva-Jothy 2003, Siva-Jothy et al. 2005, Friman & Buckling 2013). Friman & Buckling (2013) conducted bacteria-phage experiments that highlighted how bacteria in a system with both a predator (protist) and a virus (phage), evolving defence against one of these enemies would reduce defence against the other. While this work sheds light on the cost of defence mechanisms, particularly when they are in a trade-off with each other, we still do not have experimental evidence of what would happen to defence evolution if the predator forms a vital stage of the parasite's life cycle. Other studies demonstrate the existence of trophically transmitted parasites that can evolve manipulation strategies since they can often be observed in nature (see

Moore (2002)) and shown experimentally (Carney 1969, Bethel & Holmes 1973, Wickler 1976, Berdoy et al. 2000, Moore 2002, Poulin 2007); for example, experiments by Bethel & Holmes (1973) found that infection from *Polymorphus paradoxus* turns photophobic crustaceans photophilic so ducks more easily see them. Overall empirical work has highlighted how host evolution of defence mechanisms is costly and that both trophic and manipulative parasites exist. They also highlight that host defences in a multi-enemy population can be in a trade-off with each other but leaves the question about what will happen to host infection defences when one of these enemies - the predator - forms part of the parasite's life cycle and so is non-immune.

Theoretical studies have considered the conditions under which hosts are more likely to evolve defence mechanisms against parasitic infection. In their work, Boots & Haraguchi (1999) show that infection resistance is likely to evolve against parasites with low to intermediate levels of virulence whereas high reproduction is more beneficial than defence against highly pathogenic parasite strains. Miller et al. (2007) found that resistance mechanisms are not beneficial when the infected population is large because hosts are highly likely to get infected regardless of their evolved defences. Some studies consider the impact of predator inclusion on host-parasite relationships. Morozov & Adamson (2011) demonstrated that the presence of a predator can lead to the evolution of highly virulent parasites and predator extinction, Morozov & Best (2012) showed that it is possible to have populations of parasite strains with differing virulence as a result of predator-mediated branching and Kisdi et al. (2013) also reported parasite diversity and documented evolutionary cyclic behaviour between predator density and parasite virulence. Some studies investigate host defence against a parasite and others consider what effect the presence of a predator can have on host-parasite relationships. Combining these two research questions, it is possible to consider how hosts evolve defence mechanisms against parasitic infection when a predator is present. Hoyle et al. (2012) concluded that the evolution of host defence against infection can result in either

parasite or predator extinction and also obtained evidence of branching in the host in the presence of a predator. Toor & Best (2015) noted that host defence against parasitism is maximised at intermediate levels of predation. Moreover, Toor & Best (2016) found that if prey can evolve defences against both the parasite and the predator, selection varies depending on the composition of the enemy population: whichever risk is bigger determines which mechanism will evolve. Despite these important findings, to our knowledge, the multiple enemy population studies that exist tend to assume predators are immune to infection. Hence, the question remains about how host defences evolve in the presence of non-immune predators subject to manipulative parasites that promote predation on infected prey. Findings by Oliver & Best (2024) show that cyclic ecological dynamics can alter the qualitative direction of parasite trait evolution. We then want to find out what, if any, effect these cycles will have on host evolution.

We investigate the evolutionary behaviour of prey hosts in a population with multiple enemies: parasites and non-immune predators. We assume that increasing defence against manipulative parasites constrains prey birth rate. Using the framework by Fenton & Rands (2006) and including this trade-off function, we vary ecological parameters to see the effect on evolution to decide which system characteristics mean that defence mechanisms evolve. Our key finding is that population densities are drivers of evolution, and we demonstrate that the population dynamics can fluctuate, likely owing to the free-living stages (Anderson & May 1981).

3.3 Model

We are interested in how prey hosts evolve defence mechanisms against trophically transmitted parasites. We assume that infected prey are more likely to be consumed than susceptible prey. Predators may selectively eat infected prey because weaker prey are easier to catch (Hudson, Dobson & Newborn 1992,

Murray et al. 1997, Johnson et al. 2006, Otti et al. 2012). While results can be generalised, we assume that in our system the infected prey are more likely to be eaten because the trophic parasites have evolved manipulative mechanisms that alter infected prey behaviour or appearance to make them more likely to be consumed by predators. Parasites utilise this strategy to increase their transmission from intermediate prey hosts to definitive predator hosts.

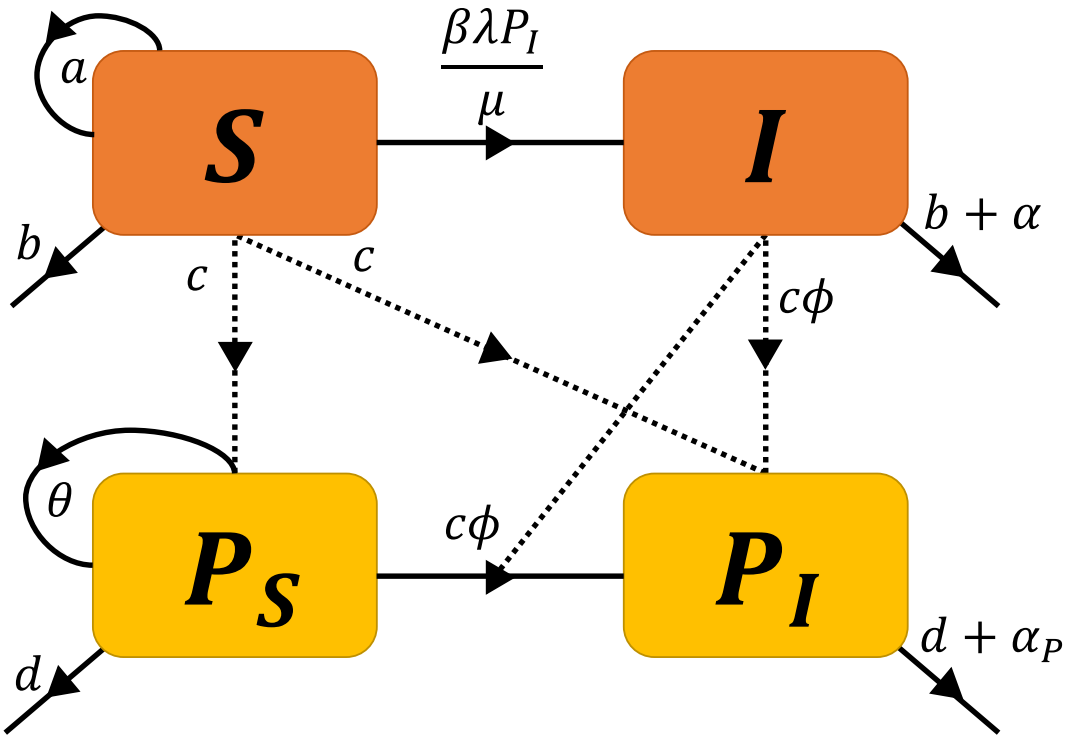

Figure 3.1: The schematic diagram for the host-parasite model. Here S and I (orange) represent the susceptible and infected intermediate prey hosts, respectively, and similarly, P_S and P_I (yellow) represent the susceptible and infected definitive predator hosts, respectively. The dotted lines represent predation.

Our model is based on the framework by Fenton & Rands (2006). We present

the diagram in figure 3.1 and the model equations are as follows,

$$\frac{dS}{dt} = aS(1-qS) - \rho_S(S,I)(P_S+P_I) - \frac{\beta\lambda SP_I}{\mu} - bS, \tag{3.1a}$$

$$\frac{dI}{dt} = \frac{\beta\lambda SP_I}{\mu} - (b+\alpha)I - \rho_I(S,I)(P_S+P_I), \tag{3.1b}$$

$$\frac{dP_S}{dt} = \theta\rho_S(S,I)P_S - \rho_I(S,I)P_S - dP_S, \tag{3.1c}$$

$$\frac{dP_I}{dt} = \rho_I(S,I)P_S - P_I(d+\alpha_P), \tag{3.1d}$$

where S, I, P_S and P_I represent the host densities for susceptible prey, infected prey, susceptible predators and infected predators respectively. Table 3.1 summarises the model parameters. Prey hosts have a birth rate a and mortality rate b with an additional mortality rate (virulence) α that only affects infected prey as a result of infection by the parasite. Similarly, predator hosts convert predation into births of new predators at a rate θ, d is the mortality rate, and α_P is parasite-induced death. We assume that there is no recovery for prey or predators and that infected individuals cannot reproduce. These assumptions aim to simplify our analysis, and future work should explore the impact of these assumptions since they can have important impacts on evolution (Boots & Bowers 2004, Donnelly et al. 2015, Best et al. 2017). It should be noted that Fenton & Rands (2006) found that models where infected prey hosts could reproduce showed no qualitative differences in dynamics. Predation on intermediate prey hosts is incorporated into the model through the predation terms ρ_S and ρ_I, which are Holling functional responses (Holling 1959). We only consider the linear type I case where predation increases with prey density; thus, there are no limits on predation. These have the form $\rho_S = cS$ and $\rho_I = c\phi I$, where c is the baseline predation rate and ϕ acts like a scaling factor for predation resulting in an increase or decrease in predation on infected prey hosts. This could be selective predation but we are referring to this parameter as the change in predation due to host manipulation by parasites. If $\phi = 1$, susceptible and infected prey are equally likely to be eaten but whenever $\phi > 1$,

infected prey have an increased likelihood of being predated on. We assume that manipulation is instantaneous upon infection by the parasite. Infection of predators occurs when predators eat infected prey. Parasites produce spores inside predators at a rate λ. These spores are released into the environment and are vital for parasite transmission, highlighting the importance of non-immune predators' role in the parasite's life cycle. Prey become infected when they come into contact with these spores. Hence, the parameter β is prey host susceptibility to infection and can be considered as a combination of the probability that a prey host comes into contact with a spore and the probability of infection given that a contact has occurred. If spores are not picked up by prey, they decay in the environment at a rate μ. Like Fenton & Rands (2006) we assume that the dynamics of the free-living stages do not need to be modelled explicitly because they are fast. Because the free-living parasite density is at equilibrium, the infection term is, therefore, $\frac{\beta\lambda P_I}{\mu}$.

Model Parameter	Description
S	Density of susceptible intermediate prey hosts
I	Density of infected intermediate prey hosts
P_S	Density of susceptible definitive predator hosts
P_I	Density of infected definitive predator hosts
μ	Free-living parasite spore decay rate
b	Prey mortality rate
d	Predator mortality rate
β	Prey host susceptibility to infection
α	Virulence for Prey
α_P	Virulence for Predator
a	Prey birth rate
θ	Conversion of predation into births of new predators
q	Strength of intraspecific density dependence acting on prey
c	Baseline predation rate
ϕ	Scale factor of predation due to host manipulation
λ	Rate at which parasites produce infective stages (spores) in predators
ρ_S, ρ_I	Holling Type I response in predators

Table 3.1: Descriptions for our dependent variables (S, I, P_S, and P_I) and each model parameter used in the model.

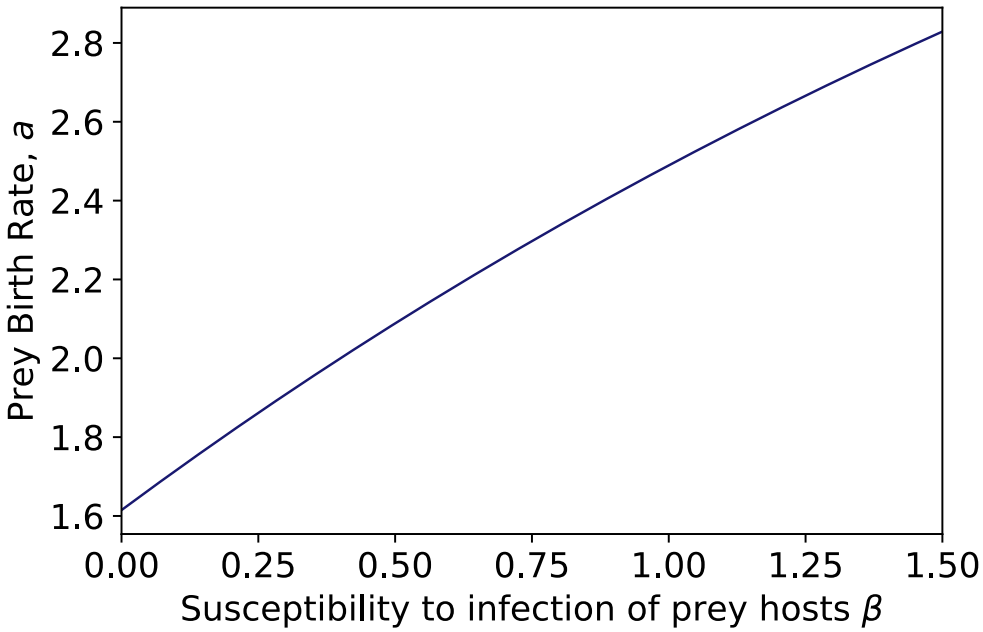

Figure 3.2: The trade-off function, $a(\beta)$ between prey host susceptibility to infection β and prey birth rate a when costs are accelerating. We choose $(\beta^*, a^*) = (0.4, 2)$, $a'(\beta^*) = 0.9$, and $a''(\beta^*) = -0.3$.

We wish to investigate how prey hosts evolve defence mechanisms against parasitic infection, we include a trade-off in our model between prey birth rate a and prey host susceptibility to infection β. We assume that a host which is highly susceptible has little or no defence against infection whereas those who are not very susceptible will be relatively resistant to infection. Our trade-off function, $a(\beta)$, has a form similar to that utilised by Hoyle et al. (2012), Toor & Best (2015, 2016), and Singh & Best (2021),

$$a(\beta) = a(\beta^*) - \frac{a'(\beta^*)^2}{a''(\beta^*)}\left[1 - \exp\left(\frac{a''(\beta^*)(\beta - \beta^*)}{a'(\beta^*)}\right)\right]. \tag{3.2}$$

Here, $a'(\beta^*)$ and $a''(\beta^*)$ are the gradient and curvature of the function respectively. This function becomes,

$$a(\beta) = 2 - \frac{(0.9)^2}{-0.3}\left[1 - \exp\left(\frac{-0.3(\beta - 0.4)}{0.9}\right)\right], \tag{3.3}$$

when we fix a singular strategy at $(\beta^*, a^*) = (0.4, 2)$ and choose the other components of the function. Figure 3.2 shows that as prey hosts susceptibility β increases, prey birth rate a also increases. This means that prey can either maximise defence against infection (low susceptibility) or birth rate or have an intermediate value in both. We assume that the cost to birth rate becomes increasingly costly as prey evolve to have lower susceptibility, thus accelerating costs. We also investigate what happens if costs are decelerating. We model the trade-off so that the default singular strategy means that prey have relatively high levels of defence against infection and an intermediate value of birth rate. Our analysis looks to see if the direction of selection results in the level of defence against infection increasing or decreasing.

We investigate how the population dynamics and prey host evolution of defence mechanisms are affected by varying the ecological parameters of our model. To see how the host evolves, we must find the Continuously Stable Strategies (CSS), which occur when the local selection gradient is zero, and the strategy is simultaneously evolutionary stable and convergence stable (Geritz et al.

1997, Best & Ashby 2023). At these CSS points, we can use classical adaptive dynamics methods (Metz et al. 1996, Dieckmann & Law 1996, Marrow et al. 1996, Geritz et al. 1998) to calculate mutant invasion fitness and find the host's level of parasitic defence. As such, we consider the invasion of a rare mutant into a resident population and look to calculate mutant invasion fitness. For our model, the mutant equations are,

$$\begin{aligned}\frac{dS_m}{dt} &= aS_m(1-q(S_r+S_m)) - \rho_{S_m}(S_m,I_m)(P_S+P_I) \\ &\quad - \frac{\beta\lambda S_m P_I}{\mu} - bS_m, \end{aligned} \tag{3.4}$$

$$\frac{dI_m}{dt} = \frac{\beta\lambda S_m P_I}{\mu} - (b+\alpha)I_m - \rho_{I_m}(S_m,I_m)(P_S+P_I). \tag{3.5}$$

Mutant invasion fitness is just the growth rate of the mutant susceptible prey hosts because infected hosts do not recover or reproduce, and so they do not directly contribute to fitness. The expression for mutant invasion fitness, therefore, has the form,

$$s(\hat{a},\hat{\beta},a,\beta) = \hat{a}(1-qS) - c(P_S+P_I) - \frac{\hat{\beta}\lambda P_I}{\mu} - b, \tag{3.6}$$

where we denote our mutant traits as $\hat{a}$ and $\hat{\beta}$. A mutant can invade the resident with positive fitness when $r > 0$, and when $r < 0$, the mutant cannot invade since fitness is negative. Usually, we assume that the resident dynamics settle into long-term equilibria dynamics before a mutant arises to assume the separation of ecological and evolutionary timescales. This assumption means that point estimates of resident densities can be used in the mutant invasion fitness calculation. In our analysis, we cannot rely on the resident dynamics settling to equilibria since the free-living infective stages induce fluctuations in our dynamics for some parameter regions (Anderson & May 1981, Fenton & Rands 2006). We cannot take single-point estimates for our resident densities because these will cycle, thus so will mutant fitness. As a result, we instead calculate Lyapunov (Floquet) exponents since Metz et al. (1992) reported that the

largest of these can be taken as mutant invasion fitness. Ferris & Best (2018) have used these methods when seasonal variation in births causes fluctuations. This work led the formal development of the numerical routine (Ferris & Best 2018, 2019) outlined in full detail by Best & Ashby (2023). We include a general overview of this method in Chapter 1, subsection 1.2.2 and we also provide more detail on the numerical method specific to our system in box 3.1. Once we numerically calculated the mutant invasion fitness, we looked for the aforementioned CSS points. We used pairwise invasion plots (PIPs) to check for branching. We did not see this behaviour in our chosen parameter space.

Box 3.1 Numerical Routine to Calculating Mutant Invasion Fitness

In rapidly changing environments, it is possible to calculate the dominant Lyapunov (Floquet) exponent and use this for the mutant invasion fitness (Metz et al. 1992). Ferris & Best (2018) built on this, formalising a routine for calculating the mutant invasion fitness when the ecological dynamics fluctuate. We present an outline of how this method works.

Since we do not consider infected births or recovery, the growth of the mutant relies solely upon the change in the mutant susceptible density. This is similar to the method used by Donnelly et al. (2015) since only the mutant infected density was important for finding the fitness. Hence, the mutant dynamics are,

$$\frac{dS_m}{dt} = r(t)S_m(t), \tag{3.7}$$

where $S_m(t)$ is the mutant density at time t and $r(t)$ would be the average growth rate of the mutant over one cycle and thus could be taken as an expression for fitness.

If the cycles have period T the the initial mutant dynamics at time $t+T$ would be given by,

$$S_m(t+T) = P(t)e^{\mu T}. \tag{3.8}$$

Here, $P(t)$ is a periodic function. Thus, the mutant density depends on the term $e^{\mu T}$ and, more specifically, μ, which is the Floquet exponent. If $\mu > 0$, then the mutant population will grow, whereas if $\mu < 0$, the mutant density will decrease. Hence, we can take the logarithm to find μ, which will be the mutant invasion fitness. The full numerical routine is presented clearly, and the associated code is linked in the work by Best & Ashby (2023).

3.4 Results

3.4.1 Decreased Host Defence

We vary our model parameters and determine the CSS level (white circles) of prey host susceptibility to infection. We plot this against a colour map that shows the period of the underlying population dynamics. This highlights regions where we get cyclic dynamics (lighter colours) and those where the dynamics are at equilibrium (dark purple).

In figure 3.3, the CSS level of host susceptibility to infection β increases as we increase prey death rate b, the baseline predation rate c, and the conversion of predation into the births of new predators θ. All else being equal, increasing these parameters will decrease the prey population either because the prey lifespan is shorter, their predation risk is increased, or there are more predators in the population, which also increases predation risk. We consider why a mutant with increased susceptibility β can invade the resident, and in figure 3.4, we look at how this change to β affects the population dynamics for the baseline predation rate at $c = 0.6$ (figures 3.4A & B). The patterns in the dynamics were similar for b and θ. Early-time dynamics are ignored under the adaptive dynamics framework, as mutants are assumed to arise only when the resident dynamics have reached their long-term behaviour. Increasing host susceptibility β results in an increase in susceptible and infected prey hosts but also a favourable decline in predators. Likely, this is owing to increased parasite-induced death. In general, an increase in any of these parameters will negatively impact the prey population, meaning that infection numbers will decrease naturally as parasite-induced deaths occur and fewer susceptible hosts are in the population. Simultaneously, it may also have a positive impact on the predator population. Increasing the baseline predation rate c and conversion of predation into the births of new predators θ are linked, meaning increasing either one of these leads to a larger predator population. Prey death rate b, on the other hand, is likely to decrease all host classes because prey

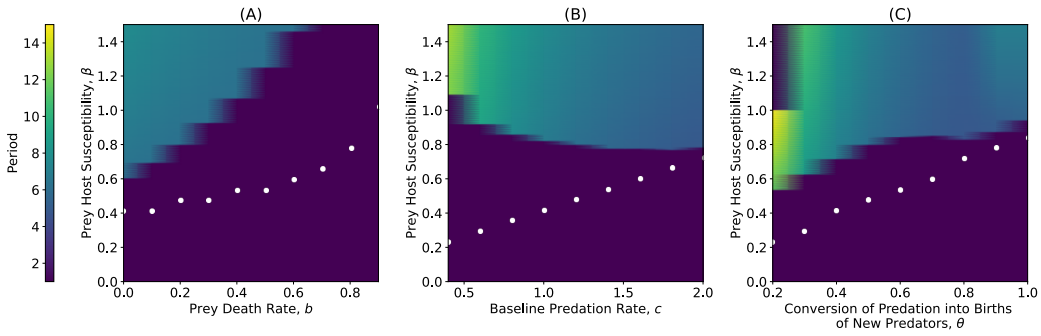

Figure 3.3: Varying prey death rate b (A), baseline predation rate c (B), and the conversion of predation into the births of new parameters θ (C) to see the effect on the evolution of prey host susceptibility β and the period of the population dynamics. Standard parameter values throughout this analysis are $b = 0.2$, $c = 1.2$, $\theta = 0.5$, $\mu = 0.1$, $\alpha = 0.9$, $\alpha_p = 0.7$, $\lambda = 0.6$, $d = 0.4$, $q = 0.2$, and $\phi = 1.2$.

are dying sooner, reducing the pool of food available to predators. However, the decline in predators may be relatively lower than the decline in prey since predator mortality is not directly targeted. This means a mutant with higher susceptibility is likely to be selected for and invade again because, despite infection levels increasing due to lower parasitic defences, the reduction in predator numbers as a knock-on effect of increased susceptibility is extremely beneficial to the prey. In addition, an increase in births due to the trade-off function also allows prey numbers to regroup after diminishing from infection and predation. This is evidence of a feedback between the ecological and evolutionary dynamics. We note that the CSS level of host susceptibility β remains in the regions of equilibrium dynamics and does not cross the boundary into cyclic dynamics - this is something we see throughout our results.

Increasing parasite mortality rate μ, prey virulence α and predator virulence α_P results in an increase in the CSS level of host susceptibility to infection (figure 3.5). If the parasite mortality rate increases, spores will decay faster in the environment, meaning fewer spores will be picked up by prey. If prey

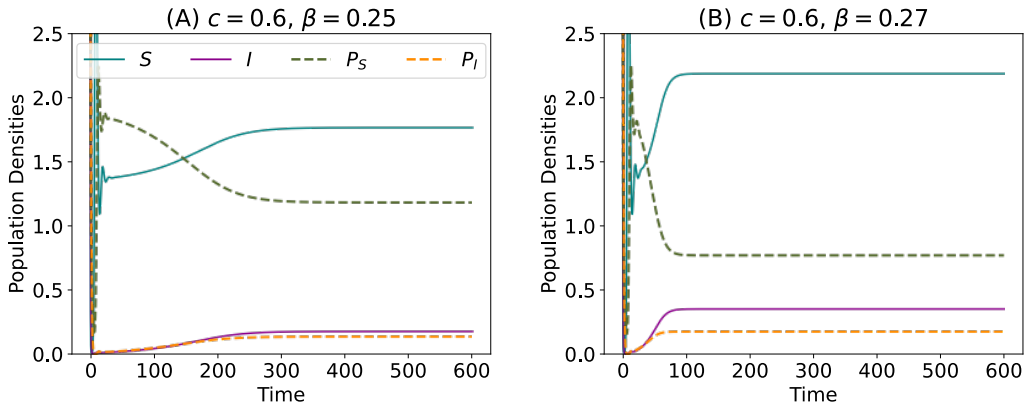

Figure 3.4: Population dynamics for a value of the baseline predation rate, ($c = 0.6$) as we alter the host susceptibility β (A-B).

virulence is greater, infected prey will die sooner from infection, potentially before a susceptible predator eats them. If predator virulence increases, then the duration of the infection is shorter, and parasites have less time to produce spores before the predator dies, so less will be released into the environment. Increasing any of these parameters ultimately compromises transmission at some stage of the parasite's life cycle. Moreover, as each of these parameters increases, selection will not favour costly defence mechanisms against parasitic infection when the level of infection in the population is reduced due to a decline in the duration of time that infected hosts and free-living infective stages survive. Due to the trade-off, an increase in susceptibility leads to an increase in prey birth rate. This result is supported by Boots & Haraguchi (1999) since they also found increasing prey virulence leads to increased reproduction as it is more beneficial against highly pathogenic strains than infection resistance.

3.4.2 Increased Host Defence

Some of our model parameters result in greater host defence and a lowered birth rate when they are increased. More spores will be released into the environment when we consider increasing the spore production rate, λ in figure 3.6A. Thus, the infection risk to prey is increased. Logically, it follows

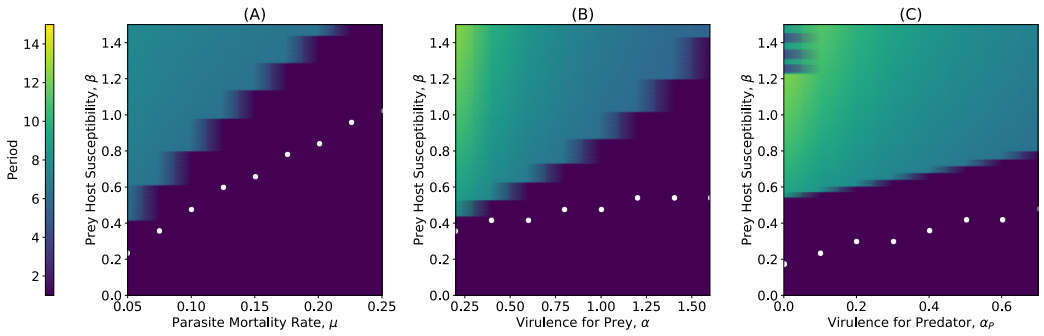

Figure 3.5: Varying parasite mortality rate μ (A), prey virulence α (B), and predator virulence α_P (C) to see the effect on the evolution of prey host susceptibility β and the period of the population dynamics.

that selection would favour greater prey defence mechanisms against infection by lowering host susceptibility, β. Inspecting the population dynamics at $\lambda = 0.8$ you can see that there is a high infected prey density (figure 3.7A) and increasing infection defence will reduce this population (figure 3.7B). As spore production increases, infection numbers will rise again. Thus, a mutant with lower susceptibility will invade again to increase defence, and this trend repeats for the entirety of our chosen values or λ.

Increasing predator death rate, d shortens predator lifespan and increases prey host defences against infection (figure 3.6B). Infected prey death can be inflicted in three ways: natural mortality, parasite-induced mortality, or predation. If infected predator death increases, fewer predators are around to eat infected prey. Reducing one avenue in which infected prey can die means that they potentially can survive longer in the environment; thus, infection risk is greater. Moreover, selection increases defence mechanisms by lowering host susceptibility, β. Looking at the population dynamics (figure 3.7C & D), the susceptible prey population reaches significant numbers, so reducing the prey birth rate of this host type in favour of defences will not be detrimental to prey numbers. Reducing susceptibility (figure 3.7D) reduces the maximum infected prey density, as we would expect, but also reduces maximum predator density,

and the susceptible prey population remains large. This is advantageous to the prey because predator numbers are reduced. This means that a mutant with lower susceptibility will continue to invade as the predator death rate increases.

What is striking about this result is that this is the only time we see prey evolve to a level of susceptibility in regions of fluctuating dynamics, albeit just past the boundary between cycles and equilibria. Figure B.2 in Appendix B may allude to why we see this occurring. For the smaller values of predator death rate, we can see that when prey hosts have a level of susceptibility β that lies in the equilibrium region, infection is not present, susceptible predator numbers are very large, and there are minimal numbers of susceptible prey. However, when the prey evolves to regions of cyclic dynamics, where predators have a longer lifespan, prey numbers can increase and predator numbers are more limited.

Interestingly, despite our focus on the long-term resident dynamics, the population dynamics in figure 3.7 initially stay near the disease-free equilibrium before switching to the endemic state. This may arise because the endemic state is initially only weakly attracting, so the dynamics remain where the disease is not viable. Eventually, we see this switch where the number of infection cases can increase and clearly, the endemic state becomes attracting. This is a feature in the majority of our results.

3.4.3 No Change to Host Defence

Altering some of our parameters, such as the strength of intraspecific density acting on prey q (figure 3.8A) and the change in predation due to manipulation ϕ (figure 3.8B) appears to have little effect on the evolution of prey host susceptibility. Instead, selection opts to maintain a reasonable level of defence against infection. For q, increasing this parameter increases crowding that directly acts to reduce births of susceptible prey; this will also mean the pool

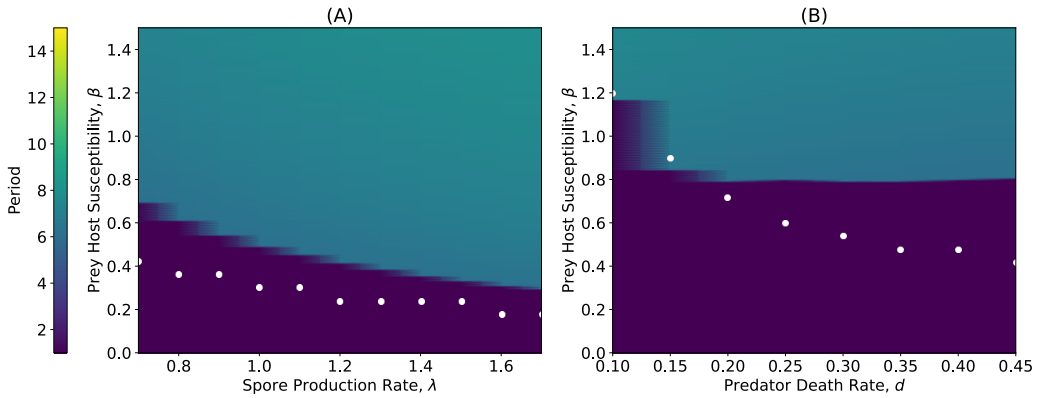

Figure 3.6: Varying spore production rate λ (A), and predator death rate d (B) to see the effect on the evolution of prey host susceptibility β and the period of the population dynamics.

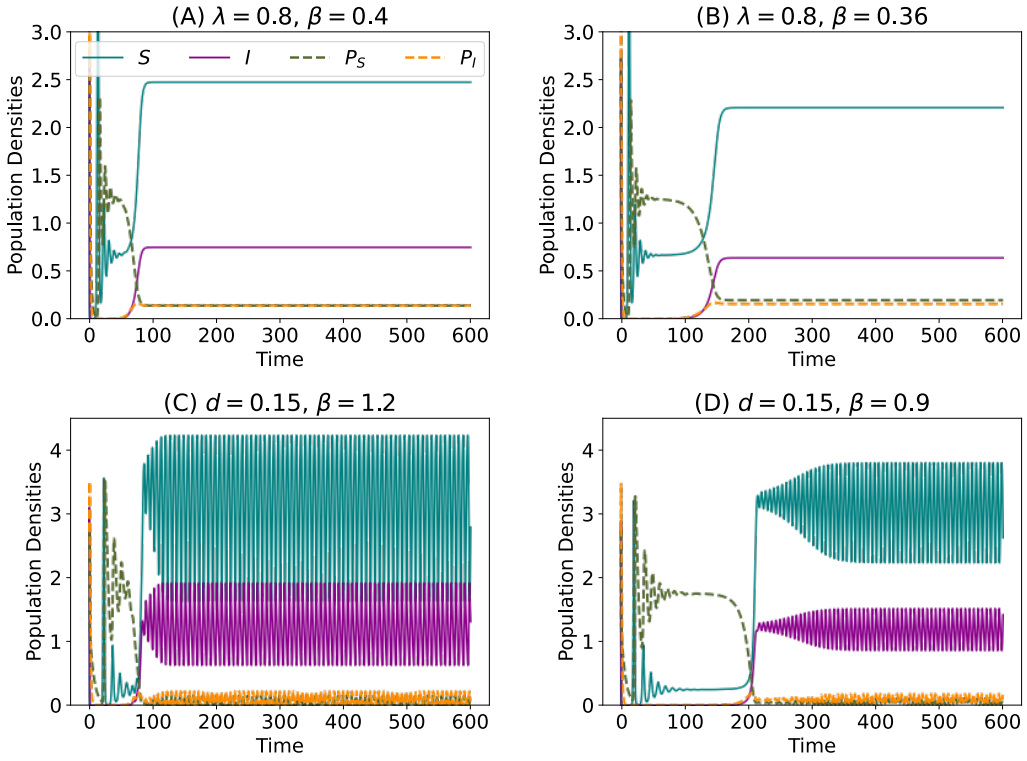

Figure 3.7: Population dynamics for a value of the spore production rate λ (A-B) and of the predator death rate d (C-D) and host susceptibility β is altered.

of available hosts to pick up spores is reduced. The population dynamics in figures 3.9A and 3.9B show the effect of increasing q whilst the host susceptibility level stays constant and the prey population decreases. The predator population does increase, but similarly to our analysis for the spore production rate (figures 3.7A & B), this increase is marginal when compared to the decrease in infection. Thus, selection will not favour increasing costly defence mechanisms when infection levels are reduced naturally with increasing q so β remains relatively stable. When q reaches the larger values, we get lower infection prevalence (see figure B.3, Appendix B). This means that selection favours lower investment in defence mechanisms in response to the lower infection prevalence.

Increasing the change in predation due to manipulation ϕ also maintains a reasonable level of host susceptibility β (figure 3.8B). Increasing ϕ increases the likelihood that a predator will selectively choose to eat infected prey, increasing the infection risk to predators. This leads to more spores in the environment and an increased infection risk to prey, so we see an increase in the infected prey population (figure 3.9D). Susceptible prey numbers grow (figure 3.9D) since, if they avoid spore contact, they are increasingly less likely to be eaten by a proportion of the predator population, so their survival chance will be slightly greater. This means the parasite has a substantial pool of susceptible hosts to infect. Parasite-induced death will decrease the number of predators. Still, the decrease in predators and the increase in infected prey are both marginal changes: the ratio of the equilibrium densities of infected prey to predators remains very similar, so the risks posed by the parasite and the predator are balanced. Since infection levels remain stable, selection does not change, which is why we see this sustained investment in the level of host susceptibility (figure 3.8B).

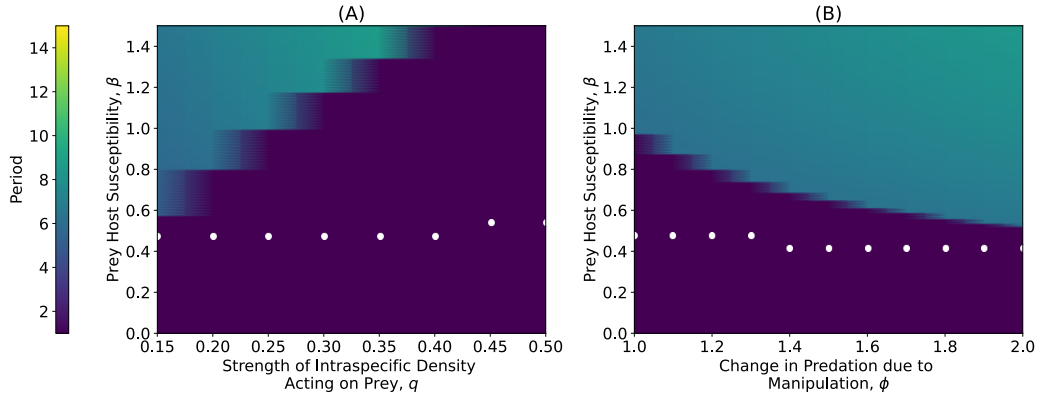

Figure 3.8: Varying the strength of the intraspecific density dependence acting on prey (competition) q (A), and the change in predation due to manipulation ϕ (B) to see the effect on the evolution of prey host susceptibility β and the period of the population dynamics.

3.4.4 How does Manipulation Alter Prey Host Evolution of Susceptibility to Infection?

In figure 3.8B, we saw that increasing ϕ resulted in selection maintaining a relatively stable level of defence. Despite this, we repeat our previous analysis but compare how altering parameters affects susceptibility evolution when there is no manipulation ($\phi = 1$, figure 3.10A) versus when manipulation is maximised and infected prey are twice as likely to be eaten as susceptible prey ($\phi = 2$, figure 3.10B). We find that host infection defences will evolve to be higher when manipulation is higher. When parasites harbour a higher degree of manipulation, infection leads to predation mainly targeting infected prey, so predator infection risk is greater. Thus, we see that the infected predator numbers at the CSS level of host susceptibility are always the same or lower when manipulation is high (figure 3.10F) compared to when it is not present (figure 3.10E) due to an increased number of parasite-induced deaths. We can use the same argument presented in the analysis about our manipulation parameter ϕ previously in figure 3.8B: increased predation on infected prey will eventually lead to more spores in the environment so greater infection preva-

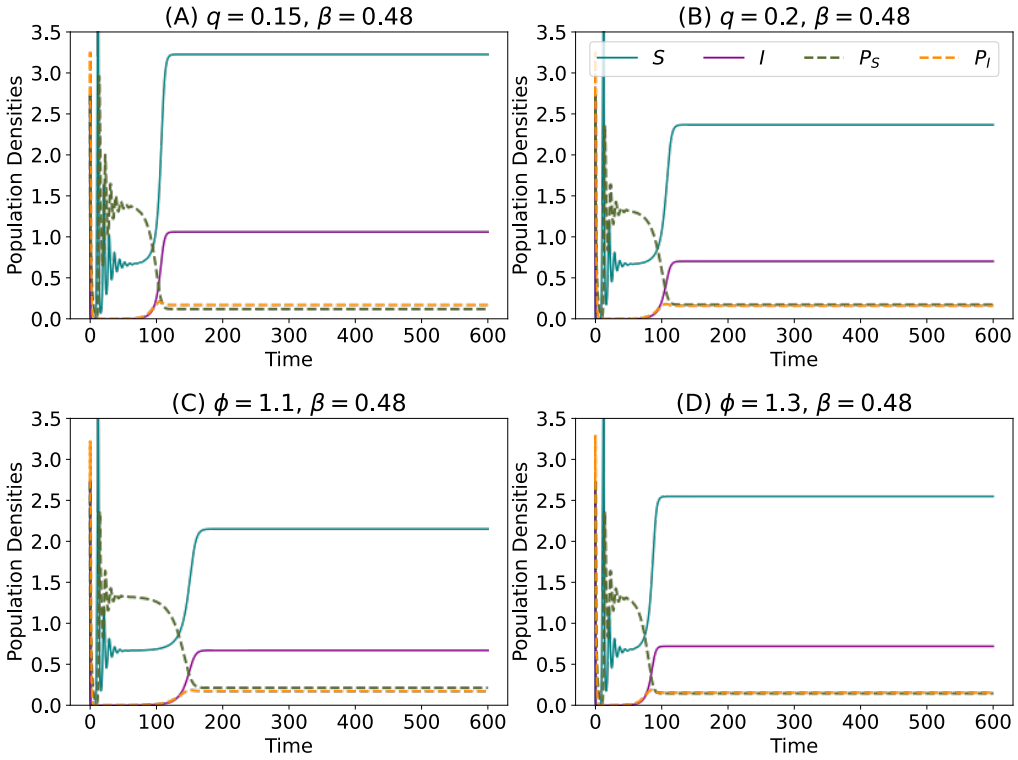

Figure 3.9: Population dynamics where host susceptibility β is held constant but different values of the strength of the intraspecific density dependence acting on prey (competition) q (A-B) and the change in predation due to manipulation ϕ (C-D) are considered.

lence among prey that leads to greater parasite-induced deaths. This explains why we see smaller CSS densities of infected prey when ϕ is maximised (figure 3.10D) compared to when it is minimised (figure 3.10C). This pattern is repeated when we consider all model parameters in Appendix B (figures B.4, B.5, and B.6) and compare manipulation levels. We also see that while cycling occurs more frequently across all the possible parameter regions when manipulation is maximised, the host still never evolves into the cyclic regions and remains below or on the boundary between equilibria and cyclic behaviour.

3.4.5 Decelerating Costs

We now alter our trade-off so that costs to evolve defence mechanisms against infection are decelerating instead. The function has the form,

$$a(\beta) = 2 - \frac{(0.4)^2}{0.6}\left[1 - \exp\left(\frac{0.6(\beta - 0.4)}{0.4}\right)\right], \tag{3.9}$$

and we can see from figure 3.11 that prey host birth rate is reduced more when susceptibility is decreased at the higher end of the range of values for β compared to at the lower end of the range. It is less common to consider decelerating costs since the assumption that a host could evolve a low-level defence against infection and this would be more detrimental to the birth rate than if they were to evolve very high defences is unlikely.

Repeating the analysis from the previous section, we find similar trends in the CSS level of host susceptibility as we vary each model parameter, so we only include one example (figure 3.12) where we vary prey death rate b. Results for the other model parameters can be found in Appendix B (figures B.8, B.9, B.10, and B.11). The interesting occurrence is that our system is bistable when costs are decelerating; hence, on the colour map in figure 3.12A, there are two sets of singular points: the CSS points in the equilibrium region (circles) and another set that lies in the cyclic region (triangles). The Pairwise Invasion Plot (PIP) in figure 3.12B for $b = 0.2$ indicates that the latter set are repeller singular

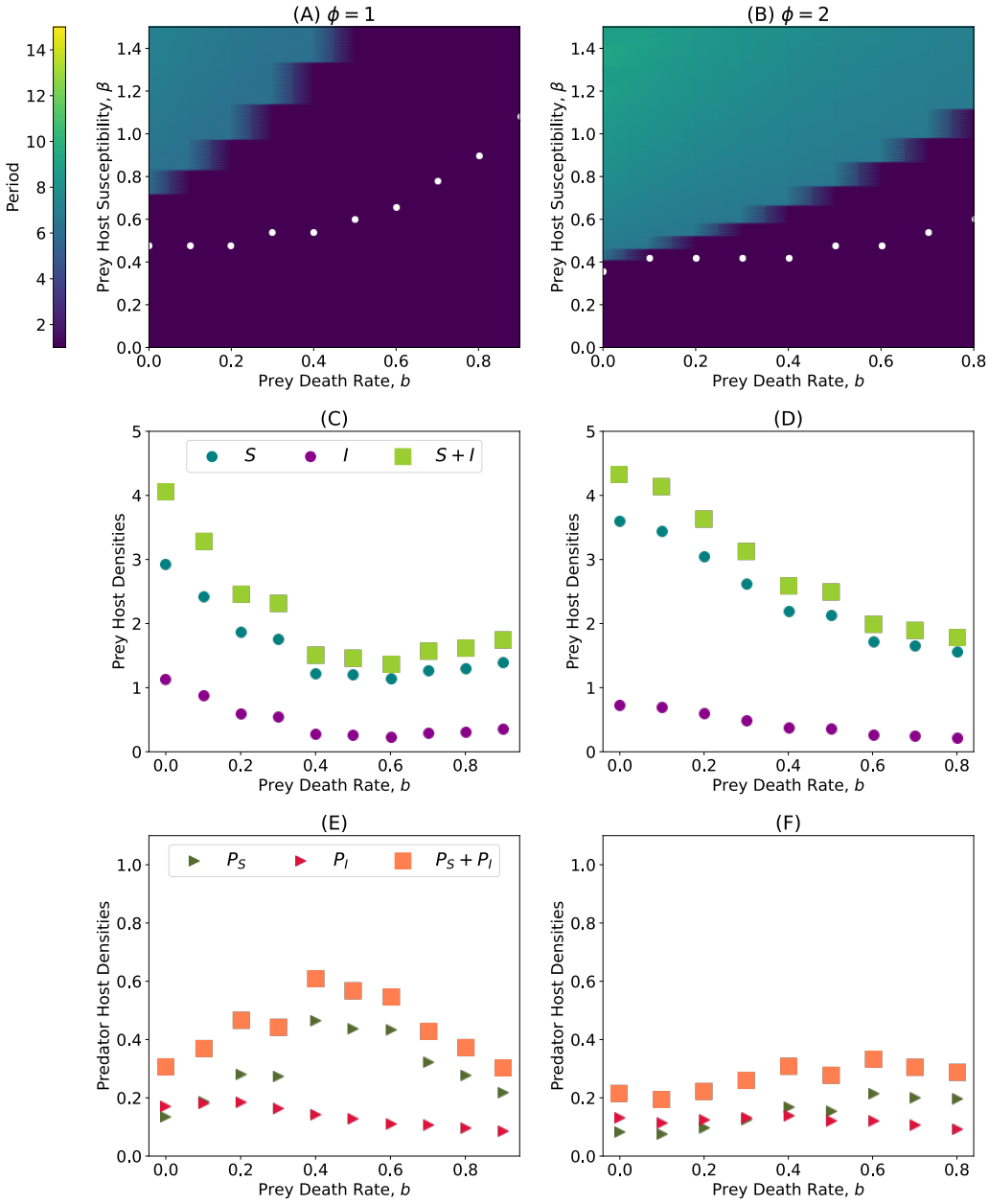

Figure 3.10: Comparing prey host evolution of host susceptibility β (A-B) and the population dynamics (B-E) as we vary the prey death rate b when the parasite does not manipulate its host ($\phi = 1$) and when manipulation is maximised ($\phi = 2$).

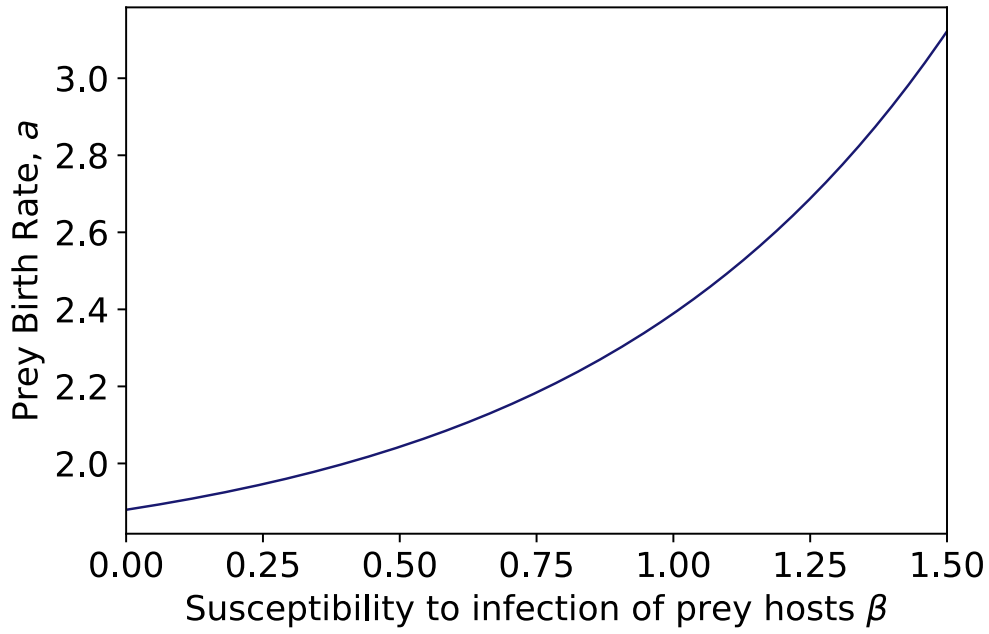

Figure 3.11: The trade-off function, $a(\beta)$ between prey host susceptibility to infection β and prey birth rate a when costs are decelerating.

points. Hoyle et al. (2008) demonstrated that decelerating trade-offs generally result in repellers, so this interesting result is not surprising. The prey host population will either evolve to remain in the equilibrium region with some intermediate level of defence or will evolve to have maximum susceptibility β, which means that they will have no defence against infection instead, favouring a maximal birth rate. Where our system ends up will be dependent upon the initial conditions.

Depending on the direction of host evolution, the population dynamics will look significantly different (figure 3.12C & D). Figure 3.12D shows cyclic dynamics with great amplitude; hosts evolve to maximise susceptibility in this region. Figure 3.13 is a subsection of the cyclic dynamics and shows how the peaks of the infected prey and both the susceptible and infected predators all coincide with the troughs on the susceptible prey population. Thus, prey face the threat of both infection and predation simultaneously. Evolving defence

mechanisms in regions where prey are highly likely to be eaten is futile. In this scenario, maximising the birth rate is more beneficial than infection defence since it replaces individuals lost to both predation and infection; thus, increasing the birth rate is a preventative measure to avoid prey numbers getting detrimentally small when costs are decelerating.

3.4.6 Summary of Results

Accelerating costs and a substantial level of infection in the population means that the size of the predator population can determine whether defence levels will increase or decrease. If predator numbers are low, parasitic infection poses a bigger threat to prey, so defence mechanisms will evolve. However, if predator numbers grow and the prey faces the simultaneous risk of infection and predation, we see infection defences evolve to reduce. We also observe that lowering infection defence to increase infection can benefit the prey population due to parasite-induced predator deaths.

Analysis considering the effect of parasite manipulation strategies on host defence evolution shows that prey always evolve to have a greater level of defence against infection when as the degree of manipulation increases. This is likely because becoming infected also means prey are more likely to be eaten, and so protecting against infection will reduce the predation risk from infected predators at least - but there are still susceptible predators posing a threat. This may indicate why we have not observed maximal infection defences evolving.

Our system is bistable when costs to evolve host defence are decelerating. Hence, in addition to the CSS points lying in the equilibrium region, we also get a set of repeller singularities that are more likely to lie in the cyclic regions. This means that, dependent on the initial state of the population, prey hosts will either evolve some intermediate level of defence or evolve maximum susceptibility and have no defences against infection at all. In the cyclic regions there are coinciding, significant risks to prey from predation and infection.

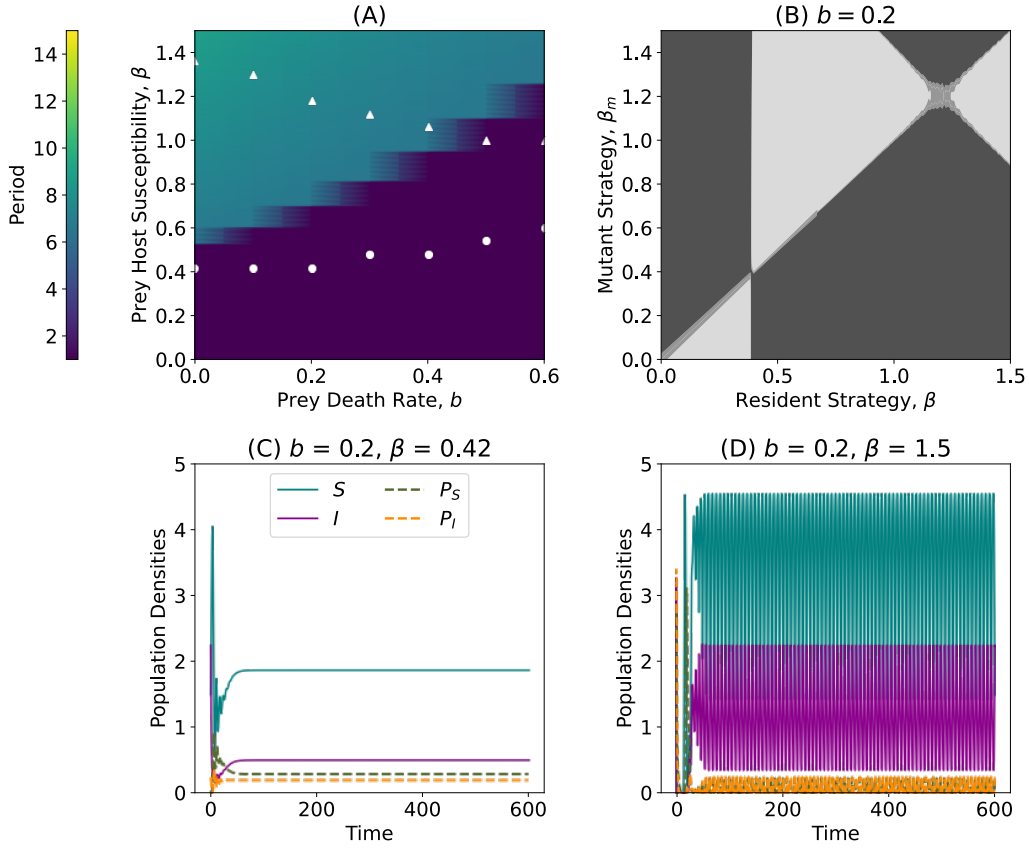

Figure 3.12: When costs are decelerating and we vary prey death rate b (A) is the colour map that displays how host susceptibility β evolves against the period of the population dynamics. (B) At $b = 0.2$ we show the Pairwise Invasion Plot (PIP) where the dark regions are when the mutant invasion fitness is positive and the lighter regions are when it is negative. We get two singular strategies: a CSS (bottom-left) and a repeller (top-right). We also plot two-time courses (C) at the CSS level of host susceptibility and (D) at maximal host susceptibility, where the system goes due to the repeller.

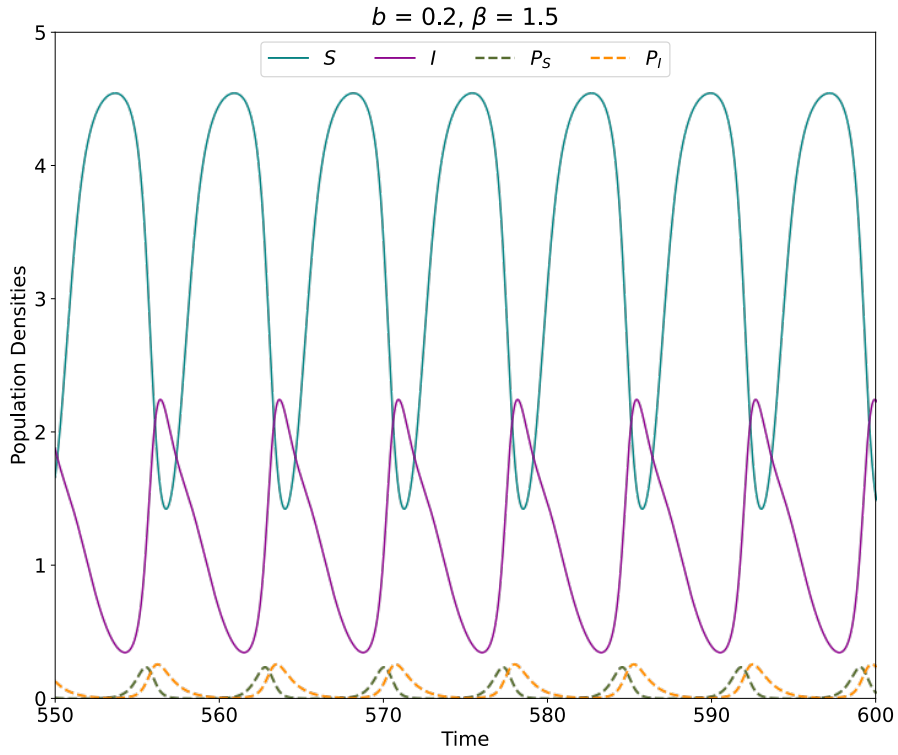

Figure 3.13: A subsection of the population dynamics from figure 3.12(D) to show how the peaks of the infected prey and both the susceptible and infected predators coincide with the troughs of the susceptible prey population.

Hence, a maximal birth rate in these regions is a multi-faceted strategy to replace individuals lost from either threat.

3.5 Discussion

Our research finds that host densities govern defence evolution and that prey tend to evolve lower defences against infection when ecological changes lead to more predation and lower infection. While lowering defence introduces more infection into the population, this is somewhat beneficial to the prey since predator numbers will also be reduced from greater infection levels. As per the trade-off, the birth rate will increase to replace individuals lost from the population due to both infection and predation. We find that defences against parasitism evolve when predator numbers are extremely small and infection levels are respectively large. This resembles a result from Toor & Best (2016) whereby they found that defence mechanisms against parasites or predators would vary depending on the greater threat. Our results, albeit we do not include direct defence against predation, differ slightly since we can find that even when infection levels are high and could be deemed the dominant threat, a mutant with a greater birth rate will invade as opposed to one with greater infection defences (see, for example, figure 3.5B and B.1A-B). This could be due to a result presented by Miller et al. (2007), who noted that when infection levels are high, defence mechanisms are no longer beneficial because hosts are likely to get infected regardless. This also supports our earlier reasoning in that increased reproduction replaces prey hosts lost from the population due to both infection and predation and infection defences could be a wasted investment if prey are highly likely to be consumed anyway. Hoyle et al. (2012) found that parasite and predator extinction is possible when host defence mechanisms evolve in the presence of a predator. We do find examples where infection can be eliminated from the population (see Appendix B, figure B.2). Still, we did not find any instances of the complete eradication of predators, only that this

population can drop to very low numbers. We caveat that this could be for our chosen parameter regions and a further analysis would be needed to determine whether this result is true in general.

An interesting result is that when costs to evolve defence mechanisms accelerate, prey hosts do not tend to evolve beyond the boundary between equilibrium and cyclic dynamics; moreover, the CSS points lie within the regions of equilibria dynamics. This outcome is robust to parameter changes since we have investigated many possible parameter combinations (see the example in Appendix B, figure B.7). While we are not sure about the underlying mechanisms that cause avoidance of fluctuating dynamics, it is a result that has been reported before by Singh (2023). In their coevolutionary model, where sterility tolerance is in a trade-off with transmission, they discovered that fluctuating dynamics can prevent coexisting dimorphic host and parasite strains from reaching their extremes. This means that evolution takes both the parasite and host strain to a region where the population dynamics converge to equilibrium and lie close to the boundary between the cyclic and equilibrium dynamics regions. Since we only consider host evolution in our model and see similar patterns of behaviour, it may be the case that the host dynamics are driving this mechanism in the coevolutionary model. Work by Oliver & Best (2024) adds further support to this claim since they consider only parasite evolution of manipulation strategies, and crossing this boundary and going to regions of fluctuating dynamics occurs frequently, even if parasite numbers can get extremely small. We highlight this as an avenue for further research.

In our system, the underlying mechanism parasites use to facilitate transmission from intermediate prey hosts to definitive predator hosts are manipulation strategies. When we vary the manipulation parameter ϕ, we found that it did not significantly influence host evolution of defence mechanisms, and instead, an intermediate level of defence was sustained. We repeated our analysis to compare our results when manipulation strategies are not present and when they are maximised. Here we saw that manipulation does matter for certain

parameter regions, such as high prey death rate (figure 3.10) and can impact evolution. We found that prey still only evolved to regions of equilibrium population dynamics, even though cycling occurs across a greater region of the possible parameter space when manipulation is maximised, and that defences against infection are greater when manipulation is present since becoming infected also means prey are more likely to be eaten so protecting against infection will also provide some level of protection against predation. To our knowledge, no studies look at how defence mechanisms evolve in prey when parasites can manipulate their hosts. However, one study by Poulin et al. (1994) looked at hosts evolving to oppose manipulation once they had become infected and noted that infected hosts with an expected future high reproductive success are more likely to invest in defence mechanisms. While the types of defence mechanisms that have evolved are different, these results both suggest that defence mechanisms will evolve to a greater level when manipulation is present. While we assume these mechanisms that increase predation on infected individuals are parasite manipulation strategies, these results could be considered more generally with selective predation owing to reasons other than manipulation, such as infected prey being easier to catch, for example.

If we instead look at decelerating costs for hosts to evolve defence mechanisms, our system is bistable with prey hosts either investing in the CSS level of relatively intermediate levels of defence or, the singular strategy is instead a repeller and host susceptibility is maximised hence they have no infection defence in favour of a greater birth rate instead. Decelerating trade-offs leading to repellers is a result known to hold in general (Hoyle et al. 2008). When hosts have maximal susceptibility, the population dynamics tend to fluctuate, so infection levels and predator numbers can simultaneously get extremely high. In this scenario, infection defence could be a wasteful investment since it is very likely that prey hosts will be consumed by predators anyway and, as we have highlighted before, an increased birth rate will replace individuals lost due to both threats. Theoretical work by Miller et al. (2007) reaffirms our

findings since, as well as finding lower defence when infection levels are significantly high, they also documented bistability in the level of host avoidance of infection.

We only consider a linear Holling's Type I functional response in our analysis (Holling 1959), but a Type II and III response should also be investigated, especially since Fenton & Rands (2006) and Oliver & Best (2024) noted that the effect manipulation strategies have on the population dynamics and oscillatory behaviour is due to the relationship between a predator's feeding rate and prey density. In a similar vein, an extension to this work would be to include host recovery and allow infected individuals to reproduce, as we know that this can have significant effects on the outcomes of selection (Poulin et al. 1994, Boots & Bowers 2004, Donnelly et al. 2015, Best et al. 2017). The latter case would be particularly interesting to explore when the prey birth rate is in a trade-off with host defence mechanisms. In nature, numerous documented examples show defence mechanisms by hosts to avoid parasitism, such as altering foraging activity, moving habitat, changes in social interactions or overt displays of defensive behaviour (Moore 2002). To our knowledge, no explicit empirical studies consider examples of host defences to infection by manipulative parasites when the host is also at risk from non-immune predators. This is unsurprising since this could be difficult to observe in nature and replicate in experimental conditions. For example, the behaviour of a host residing near the surface instead of deep in bodies of water can be a sign of manipulation by parasites in some systems (amphipods infected by *Polymorphus paradoxus* parasites ((Bethel & Holmes 1973))) and a sign of parasite avoidance in others (stickleback fish and *Argulus canadensis* parasites ((Poulin & FitzGerald 1989, Moore 2002))). Despite this, for future empirical work, our model suggests that low predator numbers and high infection levels would indicate that host defences against parasitism may have evolved. Another interesting research question relating to our work would be instead to consider the evolution of predator defences against infection when parasites have evolved manipula-

tion strategies. Moore (2002) provides some suggestion that predators could display this defence mechanism since oystercatchers have been documented to reject highly parasitised clams (the trematodes are visible as white cysts in the clam) even if these infected clams are much easier to locate due to behaviour alterations induced by the parasite. As well as developing more theoretical results to help us discover how hosts evolve defence mechanisms against infection when considered in conjunction with a complex community structure that involves interactions with predators and parasites that display manipulative tendencies, it would also be beneficial to have empirical work specifically look to see what defence mechanisms may evolve in this community structure.

Chapter 4

Do fluctuating ecological dynamics result in parasite extinction when stochastic effects are accounted for?

4.1 Abstract

In previous chapters, I observed that fluctuating ecological dynamics were a possible outcome of the modelling system. In the regions of oscillatory dynamics, host densities can become very small, putting the parasite at risk of extinction. Motivated by this work, I consider the stochastic model to investigate how likely the parasite can survive when the dynamics oscillate when we introduce some random effects. I have also documented in this thesis how these cycles can have important evolutionary effects, so it is important to understand whether and under what conditions parasite survival is possible for these effects to be seen.

4.2 Introduction

Many host-parasite models assume that the long-term behaviour of the ecological dynamics goes to equilibrium. However, fluctuating dynamics can frequently occur in many natural systems induced by several factors, including seasonality (Dietz 1976, Focks et al. 1995, White et al. 1996, Hoshen & Morse 2004, Donnelly et al. 2013, Ferris & Best 2018), free-living infective stages (Anderson & May 1981, Best & Ashby 2023), the inclusion of a predator (Anderson & May 1981, Kisdi et al. 2013), and parasite manipulation strategies (Fenton & Rands 2006). In general, cycles can have significant ecological effects since they can often cause low host numbers. Important evolutionary effects of cycles have also been documented (Donnelly et al. 2013, Ferris & Best 2018, Best & Ashby 2023, Oliver & Best 2024). Largely motivated by the studies by Fenton & Rands (2006) and Oliver & Best (2024) that show in these regions, predator and prey densities can drop close to zero, potentially putting the parasite at risk of extinction, we ask how often will the parasite survive if random effects are taken into account? We use a stochastic model that accounts for these random effects since probability determines event occurrence and population sizes are discrete, meaning extinction is likely when population sizes are small. A natural second question then arises: how often will the evolutionary effects be seen in reality if the parasite is unlikely to survive under fluctuating dynamics necessary for them to occur?

Intuitively, it makes sense that fluctuations in dynamics would be observed in real-world systems since a great range of factors can induce changes that would perturb dynamical equilibrium (Hudson, Dobson & Newborn 1992). In some host-parasite relationships, such as red grouse *Lagopus lagopus scoticus* in Scotland and the parasitic nematode *Trichostrongylus tenuis*, empirical studies have found that interactions with parasites can induce fluctuations in their host densities (Hudson, Newborn & Dobson 1992, Dobson & Hudson 1992, Hudson et al. 1998). Yoshida et al. (2003) conducted experiments on planktonic

rotifers, *Brachionus calyciflorus*, who consume green algae, *Chlorella vulgaris* and observed cycles in the population dynamics in a live predator-prey system. They also highlighted the importance of studying ecological and evolutionary dynamics in parallel since rapid prey evolution can alter the period of population cycles; these cycles can cause fluctuations in selection, which can mean that rapid prey evolution continues indefinitely and the feedback loop with the population dynamics continues. Other experimental work evidences this important feedback between ecological and evolutionary dynamics, too, and how they must be considered in concert. For example, Dwyer et al. (1990) demonstrated this link for coevolving populations of wild rabbits and myxoma virus in Australia. Hesse & Buckling (2016) conducted bacteria-phage experiments and documented phage extinction as a possible outcome when they coevolve with hosts with reduced diversity due to genetic bottlenecking events that remove highly susceptible individuals from the population. Frickel et al. (2016) looked at the infectivity and resistance of virus and algae and found that population dynamics oscillated during periods of arms race dynamics. The populations stabilised when the coevolutionary dynamics became trade-off dependent. Another system where cycles are possible, and links between ecological and evolutionary dynamics are important, include trophically transmitted parasites that can evolve host-manipulation strategies to facilitate their transmission from prey to predator. The first documented example of manipulation by Bethel & Holmes (1973) described how photophobic crustaceans become photophilic upon infection by *Polymorphus paradoxus* parasites making them more easily predated on by hunting ducks. There are many other examples in nature of this parasite adaption (see Moore (2002)). Manipulation has been a focal point of previous chapters in this thesis where parasite evolution of these strategies, how cycles can impact selection for manipulation, and how host defence is impacted by parasites harbouring this trait have been considered. From this, a natural question arises - how general are these results? Thus we want to explore how often the parasite can survive in regions

of cyclic dynamics.

Cyclic ecological dynamics is an important area of host-parasite research because they can affect host densities, generally causing them to fall to low numbers. Fenton & Rands (2006) developed a deterministic framework studying trophically transmitted parasites that use host manipulation strategies to facilitate transmission by increasing predation on infected prey. They attributed manipulative behaviour as a cause of cyclic dynamics that can force predator and prey densities close to zero. In reality, the parasite could be driven to stochastic extinction due to these strategies. As we stated, this is not the only system where cyclic behaviour has been theoretically demonstrated. Seasonality is another causal factor of population cycles (Dietz 1976) and there is a wealth of seasonal changes that have been considered from changes in birth rate (White et al. 1996, Donnelly et al. 2013, Ferris & Best 2018), to changes in host immunity (Dowell 2001), to changes in temperature that can affect vector-borne diseases (Focks et al. 1995, Hoshen & Morse 2004). For example, the study by Focks et al. (1995) found that the replication rates of mosquito-transmitted dengue viruses were greater when temperatures were higher. Altizer et al. (2006) emphasised that in cooler temperatures, it may be the case that adult parasites may not mature before adult mosquitoes die, thus reducing infection risk since the proportion of mosquitoes that are infected is reduced. Cyclic behaviour is also known to impact evolution (Donnelly et al. 2013, Ferris & Best 2018, Best & Ashby 2023, Oliver & Best 2024) thus highlighting the importance of the development of eco-evolutionary models that incorporate underlying population dynamics to create links with evolution when investigating host-parasite systems (Gokhale et al. 2013, Song et al. 2015, Papkou et al. 2016, Best et al. 2017, MacPherson & Otto 2018, Ashby et al. 2019, Best & Ashby 2023). Despite this, theoretical studies in this field tend to consider fluctuating ecological dynamics with a focus on host-parasite co-evolution and fluctuating selection (Red Queen; see Lively (2010*b*)) dynamics rather than how these oscillations can impact host or parasite selection individually (Hamilton 1980,

May & Anderson 1983, Galvani et al. 2003, Lively 2010*a*, Ashby & Boots 2017, Best et al. 2017, Seppälä et al. 2020). The few studies that do consider the effects on evolution have found several important results. For example, Best & Ashby (2023) suggested that rapidly changing environments can result in increased parasite prevalence and severity since Donnelly et al. (2013) documented higher degrees of virulence and Ferris & Best (2018) found lower host avoidance when the amplitude of seasonal forcing increases. Oliver & Best (2024) studied parasite evolution of manipulation strategies and found that the qualitative direction of selection can alter across the boundary between equilibrium and cyclic dynamics. Therefore, the existing theoretical studies highlight the importance of the effects of oscillating dynamics on ecological dynamics and host and parasite evolution.

Fluctuating ecological dynamics can put the parasite at risk of extinction because host densities can drop to meagre numbers. In a stochastic model, populations are discrete, which means that these host populations close to zero are at risk of extinction. Probabilities will determine which events, such as births and deaths, for example, will occur in this model, meaning that despite using the same parameter values and initial conditions, we can produce different time courses. We use this modelling system to investigate whether, and if so, how often, the parasite can survive in these rapidly changing ecological landscapes or whether the parasite will always go extinct when stochastic effects are accounted for. This is an important research question because we want to understand how general the results are that arise in these regions of cyclic dynamics or if they can only be applied under particular conditions that support parasite survival.

4.3 Model

Including infective free-living parasite stages means that the deterministic model exhibits cyclic dynamics (Anderson & May 1981) that result in infected

densities dropping perilously close to zero. We are interested in investigating this framework's stochastic model to see if the introduction of some randomness will result in parasite extinction during the troughs of the cycles rather than recouping and growing again, as in the deterministic model.

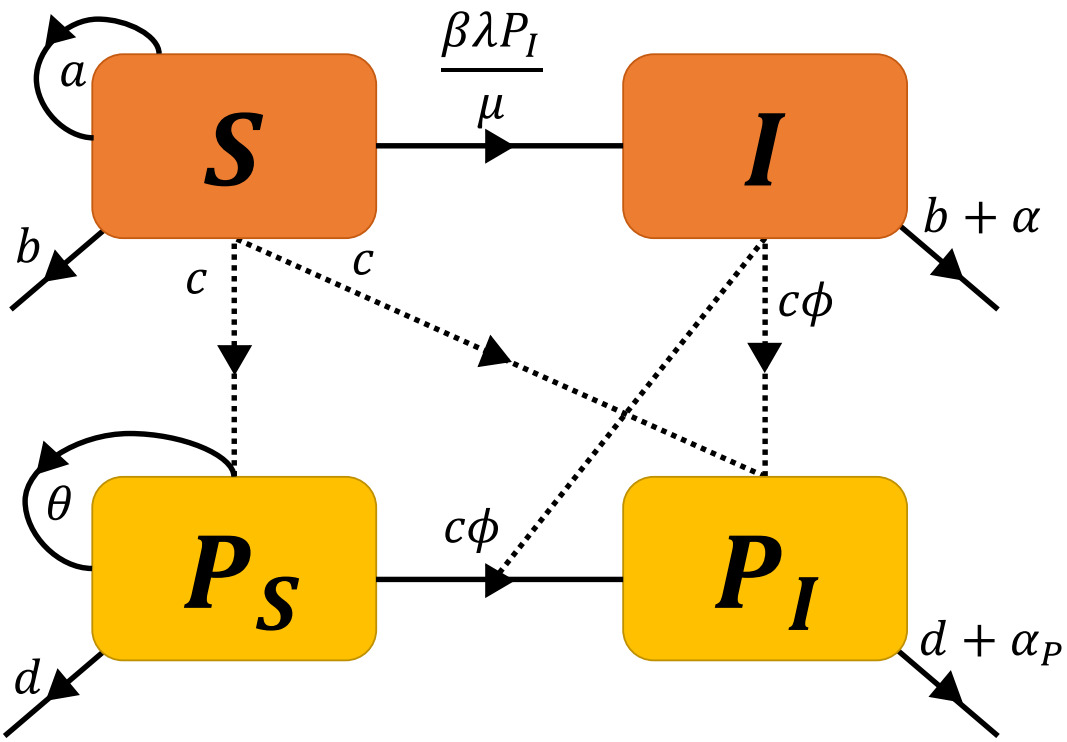

Figure 4.1: The schematic diagram for the host-parasite model. Here S and I (orange) represent the susceptible and infected intermediate prey hosts, respectively, and similarly, P_S and P_I (yellow) represent the susceptible and infected definitive predator hosts, respectively. The dotted lines represent predation.

We utilise a model framework from Fenton & Rands (2006). We present the diagram of the deterministic model in figure 4.1, and the model equations are

as follows,

$$\frac{dS}{dt} = aS(1 - qS) - \rho_S(S, I)(P_S + P_I) - \frac{\beta\lambda SP_I}{\mu} - bS, \tag{4.1a}$$

$$\frac{dI}{dt} = \frac{\beta\lambda SP_I}{\mu} - (b + \alpha)I - \rho_I(S, I)(P_S + P_I), \tag{4.1b}$$

$$\frac{dP_S}{dt} = \theta\rho_S(S, I)P_S - \rho_I(S, I)P_S - dP_S, \tag{4.1c}$$

$$\frac{dP_I}{dt} = \rho_I(S, I)P_S - P_I(d + \alpha_P), \tag{4.1d}$$

where S, I, P_S and P_I represent the host densities for susceptible prey, infected prey, susceptible predators and infected predators, respectively. Table 4.1 displays the model parameters and their associated descriptions. Prey birth and mortality rates are a and b, respectively. Predators convert predation into the births of new predator hosts at a rate θ and die at a rate d. Both prey and predators suffer parasite-induced death represented by the virulence terms α and α_P, respectively. We assume that neither infected host can recover or reproduce to simplify our analysis, although other works do show that these assumptions can influence evolution (Boots & Bowers 2004, Donnelly et al. 2015, Best et al. 2017); however, Fenton & Rands (2006) do find that including reproduction by infected hosts does not exhibit qualitative differences in dynamics. Consumption of prey is captured using Holling (1959) Type I functional responses $\rho_S = cS$ and $\rho_I = c\phi I$ where predation grows linearly with prey density and c is the baseline predation rate, and ϕ is the change in predation due to manipulation strategies. Predators become infected as a result of consuming infected prey; hence, manipulation strategies are used by parasites to increase predation on infected individuals. If $\phi = 1$, susceptible and infected prey are equally likely to be eaten, but whenever $\phi > 1$, infected prey are more likely to be consumed. In the predator host, parasites produce spores at a rate λ, which are released into the environment. These free-living infective stages are picked up by prey as they forage for food; thus, this is how the parasite transmits to prey, and β is the rate at which prey consume spores. If spores

are not picked up by prey, they decay in the environment at a rate μ. Like Fenton & Rands (2006), we assume that the dynamics of the free-living stages do not need to be modelled explicitly because they are fast.

Model Parameter	Description
S	Density of susceptible intermediate prey hosts
I	Density of infected intermediate prey hosts
P_S	Density of susceptible definitive predator hosts
P_I	Density of infected definitive predator hosts
μ	Free-living parasite spore decay rate
b	Prey mortality rate
d	Predator mortality rate
β	Prey host susceptibility to infection
α	Virulence for Prey
α_P	Virulence for Predator
a	Prey birth rate
θ	Conversion of predation into births of new predators
q	Strength of intraspecific density dependence acting on prey
c	Baseline predation rate
ϕ	Scale factor of predation due to host manipulation
λ	Rate at which parasites produce infective stages (spores) in predators
ρ_S, ρ_I	Holling Type I response in predators

Table 4.1: Descriptions for our dependent variables (S, I, P_S, and P_I) and each model parameter used in the model.

We have presented the deterministic framework but are interested in the stochastic model. This may be a more realistic framework because it will produce different time courses each time we run the model despite using the same initial conditions and parameter values. There are several ways to build a stochastic model. The first is to begin with an individual-based model that involves random events that control whether the population increases or decreases, and then use this to derive an ODE model (for example, Filho et al. (2017)). The second is to instead begin with an ODE model and add extrinsic noise to arrive at a stochastic differential equation (SDE) model (Ditlevsen & Samson 2013). The third is to take an ODE model again and utilise the Gillespie Algorithm (Gillespie 1976) to give a statistically correct stochastic implementation.

Label	Event	Model Term	Change to Population
E_1	Susceptible Prey Birth	$aS(1-qS)$	$S+1$
E_2	Susceptible Prey Death	bS	$S-1$
E_3	Susceptible Prey Infection	$\frac{\beta\lambda SP_I}{\mu}$	$S-1$ $I+1$
E_4	Susceptible Prey eaten by Susceptible Predator and Susceptible Predator Birth	$\rho_S P_S$	$S-1$ P_S+1
E_5	Susceptible Prey eaten by Infected Predator	$\rho_S P_I$	$S-1$
E_6	Infected Prey Death	$(b+\alpha)I$	$I-1$
E_7	Infected Prey eaten by Susceptible Predator and Susceptible Predator Infection	$\rho_I P_S$	$I-1$ P_S-1 P_I+1
E_8	Infected Prey eaten by Infected Predator	$\rho_I P_I$	$I-1$
E_9	Susceptible Predator Death	dP_S	P_S-1
E_{10}	Infected Predator Death	$(d+\alpha_P)P_I$	P_I-1

Table 4.2: The possible events that can occur in our stochastic model.

As we already have an ODE model the first method is not preferable and we choose to use the third method as we can directly compare our deterministic and stochastic models. It is important to note that in our stochastic implementation, the population sizes are discrete so values close to zero are at risk of extinction. Hence, in our code, it is imperative to prevent population sizes from taking a negative value by adding an `if/else` statement that ensures the population is truly extinct when it hits zero and cannot decrease below zero if an event is drawn that would usually reduce that population by one.

We introduce randomness into the system by calculating probabilities to determine when an event will occur. Events are occurrences such as prey death or prey birth: an exhaustive list of events and the resulting change to the population densities is displayed in table 4.2. Recall that the conversion of predation into the births of new predators is represented by the parameter θ so that the event 'predator birth' has the model term $\theta\rho_S P_S$. We take $\theta = 1$ for ease since we can consider the predation of a susceptible prey host, which has the model term $\rho_S P_S$, and predator birth as one single event that decreases the susceptible prey population by one and increases the susceptible predator

population by one simultaneously. We let the parameter ϵ be the sum of all the possible model outcomes,

$$\begin{aligned}\epsilon &= aS(1-qS) + bS + \frac{\beta\lambda SP_I}{\mu} + \theta\rho_S P_S + \rho_S P_I + (b+\alpha)I + \rho_I P_S \\ &\quad + \rho_I P_I + dP_S + (d+\alpha_P)P_I, \\ &= E_1 + E_2 + E_3 + E_4 + E_5 + E_6 + E_7 + E_8 + E_9 + E_{10}.\end{aligned}$$

We wish to observe the change in infected prey host density until our chosen time point to see if this host class survives. How this density changes depends on which events from table 4.2 occur and at what time point. As a result, we ask the question: If the current time is t, what time $t+\tau$ will the next event occur? So, we must generate random numbers representing these waiting times τ. This can be done by utilising the Gillespie Algorithm (Gillespie 1976) since it has been demonstrated in Gillespie (1977) that the waiting times can be distributed exponentially with mean $\frac{1}{\epsilon}$, where ϵ is the sum of all the possible model outcomes. So,

$$F(\tau) = e^{-\epsilon\tau},$$

and, since we assume that τ is a continuous variable from the interval $[0,\infty)$, then $F(\tau)$ must take a value from the interval $[0,1]$. Hence, if we were to draw a random number r uniformly distributed between 0 and 1, we can use this to calculate τ since,

$$r = F(\tau) = e^{-\epsilon\tau},$$

and so,

$$\tau = \frac{1}{\epsilon}\ln\left(\frac{1}{r}\right).$$

We numerically implement the Gillespie algorithm; the routine is presented in box 4.1.

Box 4.1 Gillespie Algorithm

1. Set the initial time, $t(0) = 0$, and initial population densities $S(0)$, $I(0)$, $P_S(0)$, and $P_I(0)$.
2. Draw a random number r_1 from a uniform distribution $(0, 1)$.
3. Calculate the total sum of all the possible event outcomes, ϵ.
4. Set the time τ until the next event occurs: $\tau = \frac{1}{\epsilon} \ln\left(\frac{1}{r_1}\right)$.
5. Check that we have not reached the endpoint of the simulations $t+\tau < 50$. If this condition is not met, exit the algorithm.
6. Draw a second random number from the uniform distribution $(0, 1)$ and scale it by multiplying by ϵ. Label this r_2.
7. Now to determine which event occurs (This a summary of the possible outcomes - see table 4.2 for a full list of possible events that could be chosen and how they each alter the host densities).
   (a) If $r_2 < E_1$ then prey birth occurs. Set $S(t+\tau) = S(t)+1$, $I(t+\tau) = I(t)$, $P_S(t+\tau) = P_S(t)$, $P_I(t+\tau) = P_I(t)$, and $t = t+\tau$. Return to step 2.

   $\vdots$

   (j) If $r_2 < E_1 + E_2 + E_3 + E_4 + E_5 + E_6 + E_7 + E_8 + E_9 + E_{10}$ then infected predator death occurs. Set $S(t+\tau) = S(t)$, $I(t+\tau) = I(t)$, $P_S(t+\tau) = P_S(t)$, $P_I(t+\tau) = P_I(t) - 1$, and $t = t+\tau$. Return to step 2.

4.4 Results

The model framework by Fenton & Rands (2006) is known to exhibit fluctuating dynamics (Fenton & Rands 2006, Vries & van Langevelde 2018, Oliver & Best 2024) likely due to the inclusion of free-living infective stages (Anderson & May 1981). Figure 4.2A shows an example of these oscillations. During these cycles, the troughs can mean that certain host classes, such as the infected prey hosts, can drop to meagre numbers putting the parasite at risk of potential stochastic extinction. In the deterministic framework, the numbers will grow again as the dynamics progress to the peaks of the cycles. However, in reality, can infected host numbers grow again when the parasite essentially goes extinct, albeit somewhat momentarily? Because of this, we look at the stochastic model to see, in this situation, how often the infection will go ex-

tinct and how often the parasite can recoup and survive. In figure 4.2B, we compare the deterministic and the stochastic time course for the infected prey for a particular set of parameter values. While the infection remains in the population for the entire time in the deterministic case, in the stochastic case, the infected prey are wiped out before the end of the fifty runs of our stochastic model. We mark on a line at $t = 50$ as this is what we determine to be our endpoint of the simulations – any infected prey still present in the population at this time point are classified as surviving. We note that this is a modelling choice and if we were to extend this endpoint, it is increasingly likely that the infected prey, moreover the parasite, will go extinct.

We run fifty stochastic simulations and present the time course of the infected prey in figure 4.3. We divide the time into smaller intervals and count how many simulations result in the extinction of infected prey in each interval. This is when the infected prey density is zero and is indicated by the grey circle on the plot. We reaffirm that if infected prey are still present in the population at the end time point ($t = 50$), we classify this as infected prey survival. We also count how many simulations the infected prey survives in. We then present this information as a pie chart (figure 4.3).

We are interested in how our ecological parameters affect parasite survival. Using the aforementioned method, we simultaneously vary two parameters and create a pie chart for each possible pair of values. Although we investigated varying all possible pairs of model parameters, we only included four examples. In Appendix C, we provide the results by varying a single model parameter. We choose the standard parameter values that give the parasite the best chance of survival: for instance, we take prey virulence and predator virulence to be very small to reduce infected host death. The possible ranges for these values are often small, so we add the caveat that using a broader range means parasite extinction is more likely.

We first consider varying prey virulence α together with our manipulation pa-

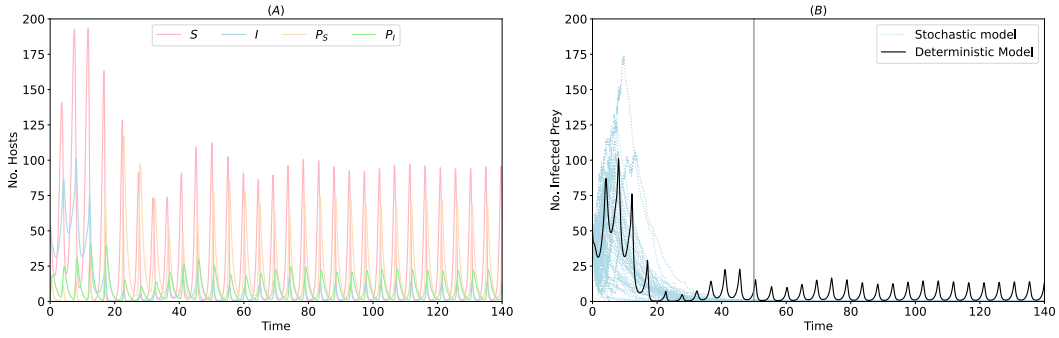

Figure 4.2: Time courses showing (A) population numbers using the deterministic model and (B) comparing the infected prey numbers when we use both the deterministic and stochastic model. Parameter values used are as follows: $\alpha = 0.1$, $\alpha_P = 0.01$, $b = 0.05$, $d = 1.1$, $a = 3$, $c = 0.06$, $\theta = 1$, $\phi = 1$, $\beta = 1.2$, $\mu = 0.1$, $q = 0.004$, and $\lambda = 0.01$.

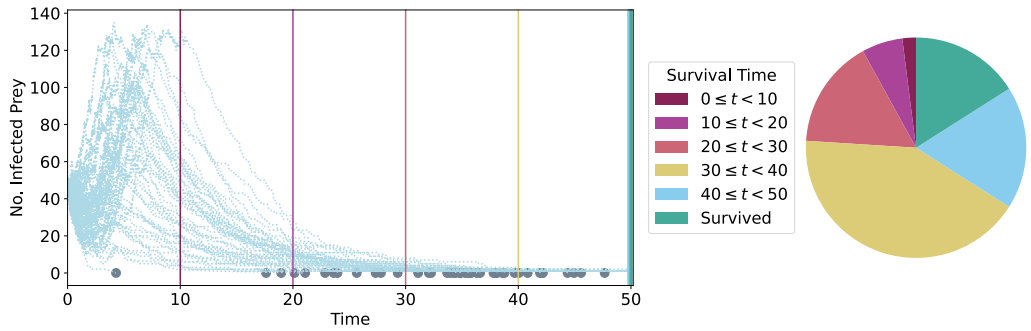

Figure 4.3: The Time course shows infected prey numbers when we run our stochastic model 50 times. The grey circles indicate if the infected prey goes extinct and in which time interval this occurs. The coloured vertical lines mark the time intervals. The number of extinctions in each time interval, or the number of times the infected prey survived, is displayed on the pie chart.

rameter ϕ (figure 4.4). Immediately from the pie charts, we see that α seems to have the greatest influence on whether parasite extinction occurs or not, and extinction is more likely as we increase the parameter. Increasing prey virulence, α decreases the duration of infection, meaning there is less time for infected prey to be consumed by predators before the prey host succumbs to parasite damage and dies. Since the predator is a vital stage of the parasite's life cycle, failing to transmit to this host and instead dying inside the prey means that eradication of the infection is more likely. While our manipulation parameter ϕ does not seem to have quite as significant an effect as α, when $\alpha > 0$, it seems that increasing manipulation strategies positively impact parasite survival to some intermediate value of ϕ ($\phi = 1.4$, $\alpha = 0.1$) and then reduces survival chance for higher degrees of manipulation. This could equally be due to random effects, and actually, the impact of increasing manipulation has levelled off for larger values of ϕ, so we might expect that selection would not favour a parasite to evolve to these higher levels of manipulation if the survival change is minimal. Increasing ϕ means increasing the likelihood that an infected prey will be eaten over a susceptible prey, thus increasing parasite transmission to its definitive host. An intermediate degree of manipulation will facilitate parasite transmission to predator hosts but will mean that less susceptible predators will become infected than when manipulation is maximised so that there are still predators to reproduce and introduce new susceptible hosts into the population. Thus, small prey virulence coupled with parasites that have evolved intermediate manipulation strategies appears to give the parasite the best chance of survival. Despite this, considering all the possible parameter pairs in this plot, parasite extinction is still more likely than parasite survival.

Figure 4.5 shows the outcome of simultaneously varying predator virulence α_P and the spore production rate λ. Increasing predator virulence α_P increases parasite-induced deaths of this population. A reduction in infected predators in the population means that the predation risk to infected prey is reduced,

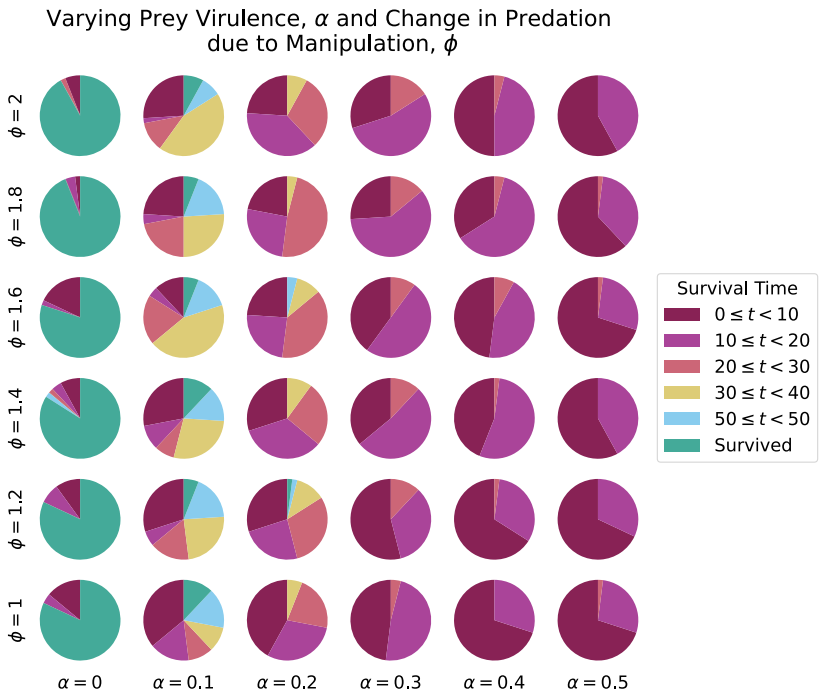

Figure 4.4: Pie charts showing infected prey survival times in 50 stochastic simulations when we vary prey virulence α and the change in predation due to manipulation ϕ. Standard parameter values are $\alpha = 0.05$, $\alpha_P = 0.05$, $a = 3$, $b = 0.03$, $d = 1.1$, $\theta = 1$, $c = 0.06$, $q = 0.005$, $\phi = 1$, $\beta = 1$, $\lambda = 0.01$, and $\mu = 0.15$.

especially when the parasites harbour manipulative strategies. Thus, infected prey survival is increased for larger values of α_P. We find that a small value of spore production is optimal for infected prey survival. Initially, increasing λ positively impacts infected prey survival. If more spores are released into the environment, prey are more likely to pick them up, so the proportion of infected prey individuals in the population will increase. As λ gets larger, it negatively impacts infected prey since their survival chance is reduced, and we also see instances of predator extinction marked by the white circles on the pie charts. An increase in infection prevalence will also affect the predator population. Both prey and predators will suffer parasite-induced effects which increases their mortality. As more susceptible prey become infected this pool of suitable hosts will deplete. Food for predators reduces and it becomes increasingly likely that they will eat infected prey. Eventually, predators die out either from infection or lack of food. This reduction of predators will see fewer spores in the environment, despite the increased production rate, and will reduce the number of infected prey. When predators go extinct, no more spores will be produced or released and thus parasite transmission to prey is ceased. So, while there are some simulations where a proportion of the infected prey are recorded as surviving when predators go extinct, actually, infected prey will die out at some later time point. Hence, the parasite will go extinct due to an increased spore production rate. Keeping the spore production and predator virulence relatively small is preferable for boosting parasite survival chances.

Parasite mortality rate μ can be varied with the spore consumption rate by prey β (figure 4.6). Parasite mortality rate determines how long spores can survive in the environment. When parasite survival is maximised for very small values of μ the stochastic simulations result in predator extinction. If spores can survive until they are picked up by prey from the environment, then it is very likely that most of them will cause an infection, thus increasing the infected prey population. Similar to our analysis for figure 4.5, this results

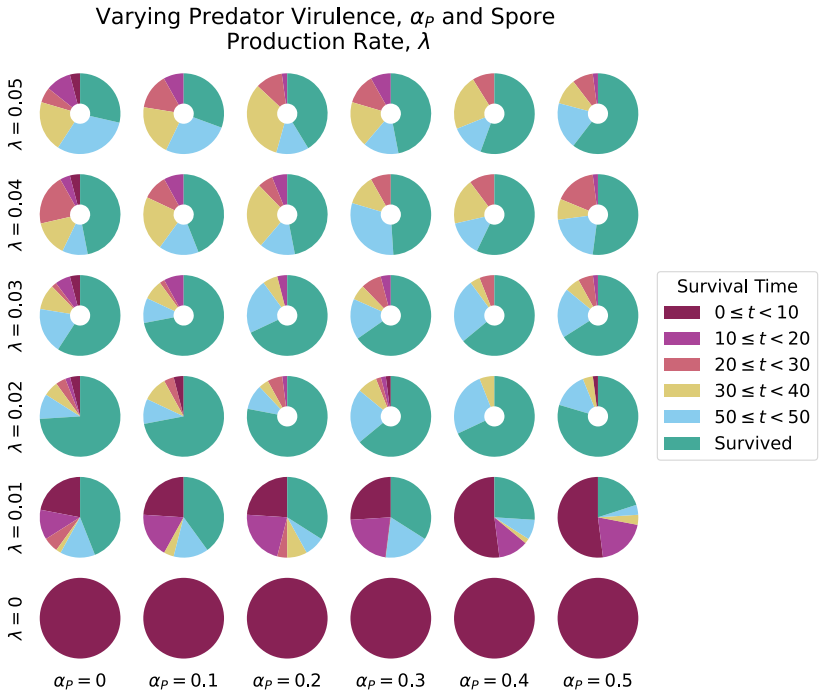

Figure 4.5: Pie charts showing infected prey survival times in 50 stochastic simulations when we vary predator virulence α_P and spore production rate λ. The white circles indicate pairs of parameter values that result in predator extinction in all stochastic simulations. Standard parameter values are as in figure 4.4.

in an increased number of infected predators that cannot reproduce. The infected predators will eventually die from the infection and the susceptible predator population is reduced by increased infection prevalence. A greater number of longer-lived spores will be released into the environment resulting in more infected prey. This cycle will continue until predators, and eventually parasites, are extinct. Increasing parasite mortality so that $\mu > 0.1$ prevents predator extinction, but large parameter values reduce infected prey survival. This is likely because spores will decay faster and are less likely to be picked up by prey from the environment, thus reducing infection prevalence amongst prey and parasite survival in the population. Increasing the spore consumption rate by prey β increases parasite survival since more prey will become infected if more spores are consumed. Intermediate values of parasite mortality with maximised spore consumption by prey maximise parasite survival success.

Our final result investigates the effect of altering prey death rate b and baseline predation rate c. Increasing the prey death rate shortens the lifespan of susceptible and infected prey, so clearly, infected prey survival is compromised. When baseline predation is small, predators cannot survive in the population, as marked by the white circles on the pie chart. If predators are not eating enough, processes necessary for survival and reproduction will be compromised due to lack of energy and will lead to predators dying out. Parasites cannot exist without predators since, as we have already discussed, there are no spores, and parasite transmission will stop. If the predation rate gets too large, then this may negatively impact parasite survival because the prey population may get too small. The susceptible and infected prey are affected by an increasing baseline predation rate. This means the pool of suitable hosts to infect will eventually get too small that the parasite will struggle to survive in the population. Hence, an intermediate predation rate will increase the parasite survival chance since the consumption rate is large enough to guarantee predator survival but not too big that the prey population is forced to too small numbers, and the prey death rate should be minimised.

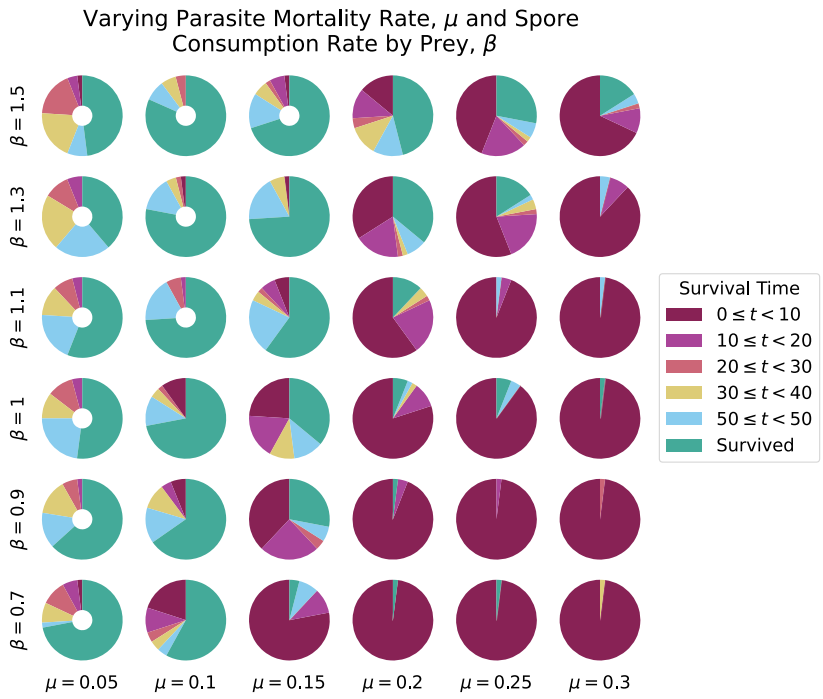

Figure 4.6: Pie charts showing infected prey survival times in 50 stochastic simulations when we vary parasite mortality rate μ and spore consumption rate by prey β. The white circles indicate pairs of parameter values that result in predator extinction in all stochastic simulations. Standard parameter values are as in figure 4.4.

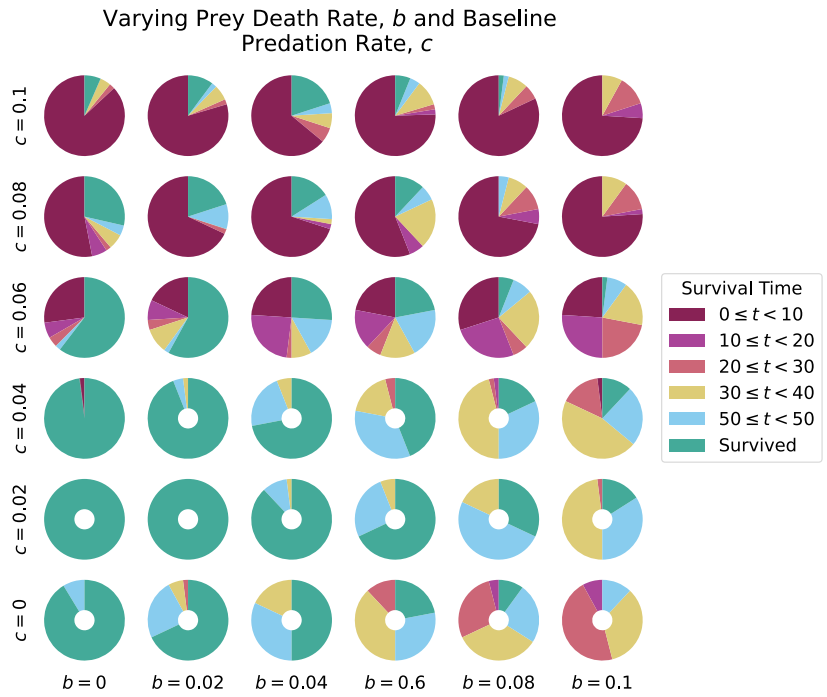

Figure 4.7: Pie charts showing infected prey survival times in 50 stochastic simulations when we vary prey mortality rate b and the baseline predation rate c. The white circles indicate pairs of parameter values that result in predator extinction in all stochastic simulations. Standard parameter values are as in figure 4.4.

Our results are focused on the conditions necessary to prevent parasite extinction. There are two main branches in which extinction can occur. The first is that infected prey and predators die out, leaving just susceptible prey and predators in the population (figure 4.8). This population should be able to survive in this state for a long period. Since both hosts in the parasite's life cycle are still present, if the infection were to be reintroduced theoretically, the parasite could still be successful in this population composition. Another outcome we often see in our results is predator extinction (figure 4.9) highlighted by the white circle marked on the pie charts. On first inspection, the parasite looks like it will be successful, but it will not survive for much longer because predators are not present. Since they are an important part of the parasite's life cycle, parasites cannot survive without this host to transmit to. This scenario will eventually lead to what we see in figure 4.10, where both predators and the parasite go extinct, and only susceptible prey survives. In this scenario, only the natural mortality rate reduces the susceptible prey population; hence, in each stochastic simulation, the susceptible prey population numbers go to the carrying capacity.

4.4.1 Summary of Results

In our results, we do show that there are possible parameter values that promote parasite survival. However, this set of parameter values is quite specific and not very large, meaning that stochastic extinction of the parasite is much more likely whether it arises because infected prey survival is compromised or from predator depletion that will also eventually lead to infected prey dying out because a host is removed from the parasite's life cycle. This means that despite this model exhibiting cyclic behaviour that influences evolution and leads to interesting results, we must be careful when interpreting them since, when populations are small, the parasite is unlikely to survive in these regions of fluctuating dynamics.

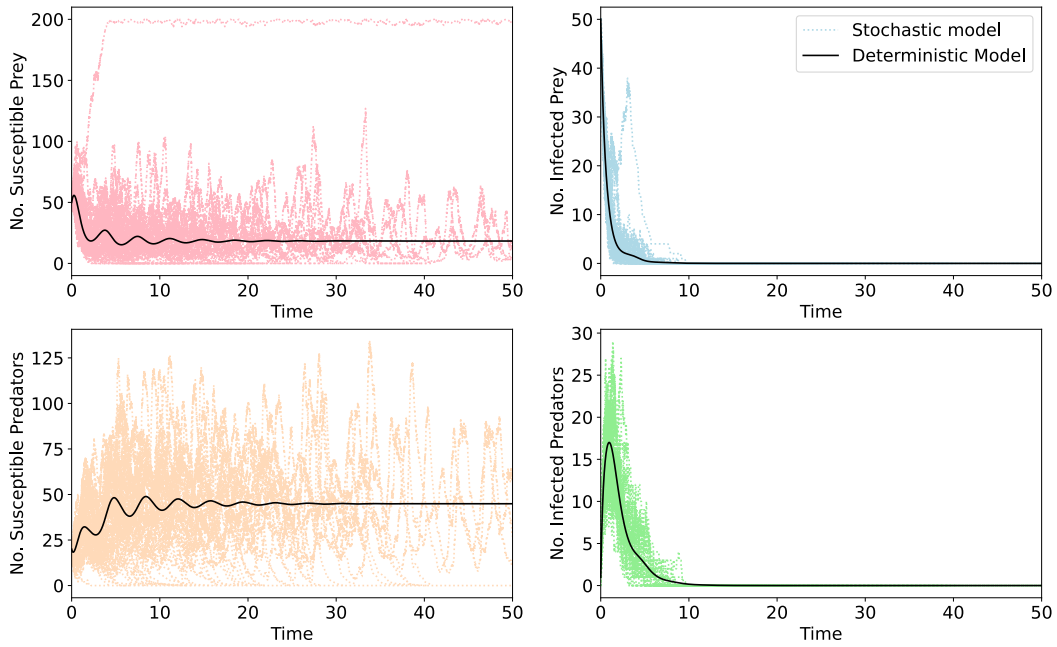

Figure 4.8: Time courses showing stochastic extinction of the parasite. Parameter values are as follows: $\alpha = 0.5$, $\alpha_P = 0.05$, $b = 0.03$, $d = 1.1$, $a = 3$, $c = 0.06$, $\theta = 1$, $\phi = 1$, $\beta = 1$, $\mu = 0.3$, $q = 0.005$, $\lambda = 0.01$.

4.5 Discussion

Previous theoretical work proposes that fluctuating dynamics may put the parasite at risk of stochastic extinction (Fenton & Rands 2006, Oliver & Best 2024). These studies have motivated our research to account for stochastic effects and look at how often the parasite can survive in these rapidly changing environments for these previous results to be relevant. While we do find some instances where the parasite can survive in regions of fluctuating dynamics, it is more likely that the parasite will go extinct. This is similar to the findings by Fenton & Rands (2006), who described how the oscillations can drive prey or predator densities very close to zero, while in the deterministic case, the host numbers can regroup and allow for parasite survival, in reality, the parasite is likely to go extinct. There are examples in wildlife populations, particularly the UK squirrel system, that demonstrate extinction by stochastic processes both empirically (Chantrey et al. 2014) and theoretically (White et al. 2014). In

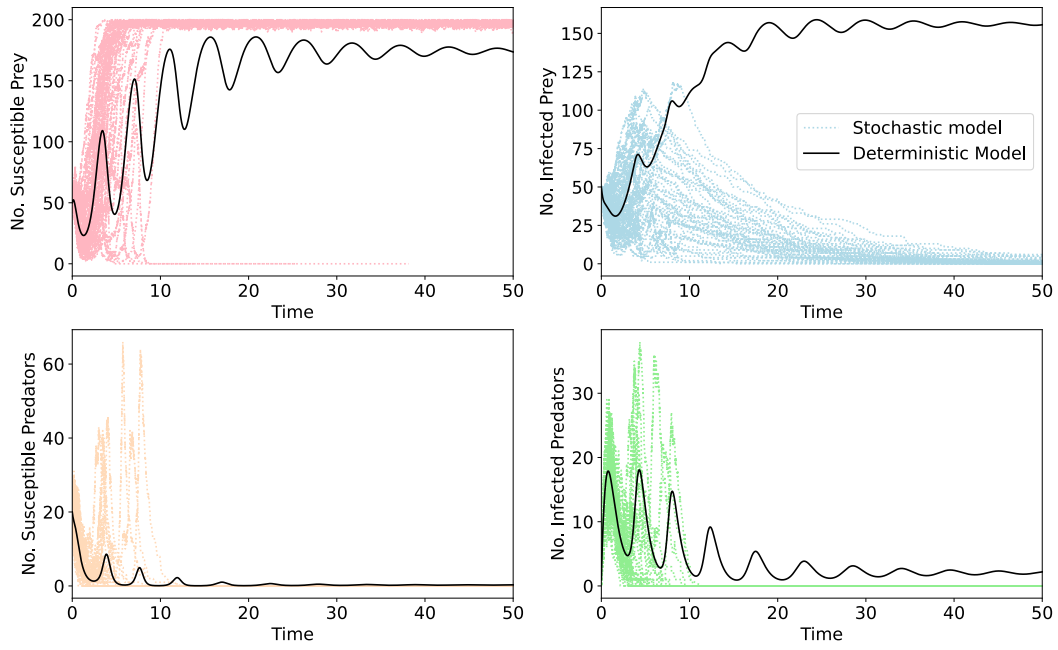

Figure 4.9: Time courses showing stochastic extinction of the predators as represented by a white circle marked on our pie charts in figures 4.5, 4.6, and 4.7. Parameter values are as follows: $\alpha = 0.05$, $\alpha_P = 0.1$, $b = 0.04$, $d = 1.1$, $a = 3$, $c = 0.06$, $\theta = 1$, $\phi = 1$, $\beta = 1$, $\mu = 0.1$, $q = 0.005$, $\lambda = 0.01$.

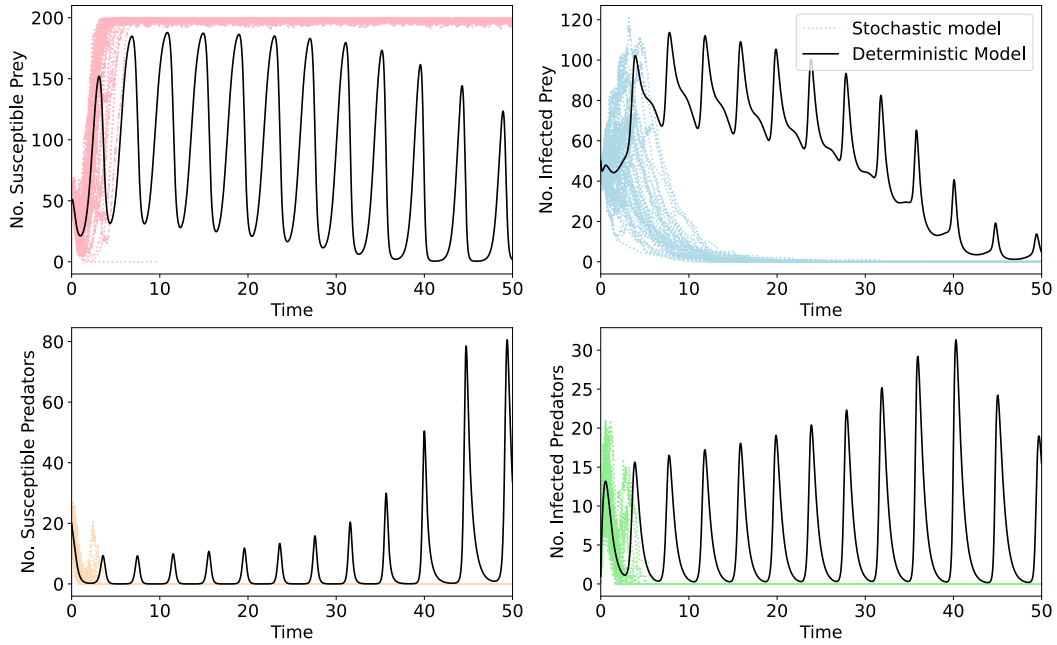

Figure 4.10: Time courses showing stochastic extinction of the parasite and predators and only the susceptible prey surviving. Parameter values are as follows: $\alpha = 0.3$, $\alpha_P = 0.2$, $b = 0.03$, $d = 1.5$, $a = 3$, $c = 0.06$, $\theta = 1$, $\phi = 1$, $\beta = 1$, $\mu = 0.05$, $q = 0.005$, $\lambda = 0.01$.

Victorian times grey squirrels *Sciurus carolinensis* were introduced into the UK and have since replaced the native red squirrel *Sciurus vulgaris* (Bryce 1997, Teangana et al. 2000, Gurnell et al. 2004, White et al. 2014, Chantrey et al. 2014). This is largely owing to red and grey squirrels both being susceptible to the virus squirrelpox (SQPV) and that while it is avirulent to grey squirrels, it is highly virulent to red squirrels (White et al. 2014, Chantrey et al. 2014). Hence we highlight that our results showing parasite extinction when stochastic effects are accounted for have been documented in real-world systems.

In our results using the stochastic model, we find that an intermediate level of manipulation may be optimal for parasite survival. This is similar to the findings by Fenton & Rands (2006) who, using a deterministic framework, documented that parasite extinction seemed more likely at higher degrees of manipulation when host densities reached low numbers during the cyclic dynamics. It appears that an intermediate level of manipulation will facilitate parasite transmission but will also mean that some predators will still eat susceptible prey instead of infected prey and that there is still a pool of susceptible predators left to reproduce to ensure that there will be new hosts to infect.

Evolutionary analysis by Oliver & Best (2024) found that the qualitative direction of selection for the degree of parasite manipulation altered across the boundary between equilibrium and cyclic dynamics, so there is evidence of the impact of these fluctuations on evolution. In light of our findings that when population sizes are small, these fluctuations are likely to cause parasite extinction, these results must be reconsidered carefully to ensure the parasite can survive for them to hold. This is just one model system that is known to exhibit fluctuating ecological dynamics, which could be attributed to the inclusion of a predator (Kisdi et al. 2013), free-living infective stages (Anderson & May 1981) or because the parasites harbour manipulation strategies (Fenton & Rands 2006). Other systems, however, can also show similar behaviour, and different factors can cause the cycles. For example, Donnelly et al. (2013) incorporate seasonality in the host birth rate. They find that this induces cyclic

behaviour and that parasites will invest more in infectivity as the amplitude of seasonality increases. Similarly, Ferris & Best (2018) documented that host defence increases with seasonal amplitude when seasonality is incorporated into the host birth rate. Many systems exhibit oscillatory ecological behaviour, and now that we have found the potential impact this has on parasite survival, it is important for models to include stochastic effects to explore parasite existence when cycles are observed.

Our findings utilising a stochastic model show that parasite extinction is very likely in regions of fluctuating dynamics when population sizes are small. The deterministic framework, despite showing host densities can drop to extremely small numbers, shows that the parasite can survive in these regions. These two cases could be at the extremes of a scale of what we might see in a real-world system, and actually, a more likely outcome could be some intermediate scenario between the two. An example of this may be repeated epidemics where the parasite could die out for some time before a resurgence. This would require both prey and predator hosts to remain in our system after the infection dies out, a scenario we presented in figure 4.8. Despite cholera being recorded as eradicated from Haiti in 2019, it resurfaced again in 2022 (Wenzel 2022). The *Vibrio cholerae* strain may have persisted in environmental reservoirs or been reintroduced from a nearby country if an infected individual, or another vector, travelled to Haiti (Rubin et al. 2022). Similarly, a repeat epidemic of phocine distemper virus (PDV) in harbour seals was observed in Anholt, a Danish island, in 1988 and again in 2002, resulting in over $23,000$ and $30,000$ deaths, respectively, with no reported cases between the two outbreaks (Härkönen et al. 2006). Harbour seals are known to be sedentary, whereas grey seals, also located in the same area, travel long distances. Hence, the study suggests that grey seals may have been reservoirs for PDV and reintroduced it amongst the harbour seal population to cause the resurgence of the virus. Modelling work could look at the potential for parasite reservoirs to see if repeat epidemics are possible in this system instead of complete eradication of the infection.

Overall this work has highlighted that results gained from deterministic models with small populations should be taken cautiously if fluctuating dynamics are observed. Future work may wish to utilise stochastic models to check the likelihood of parasite survival to test the relevancy of the results drawn. Experiments could utilise some of the known host-parasite systems where previous empirical work evidences that the parasite is known to harbour manipulation mechanisms to investigate how this may affect parasite survival.

Chapter 5

Discussion

5.1 Summary

Throughout this thesis, I utilise a modelling system with trophic parasites that transmit via an intermediate prey host to a definitive predator host. Hence, the predators are non-immune and thus form an important stage of the parasite's life cycle. The parasites in this system can evolve manipulation strategies whereby they alter prey host behaviour or appearance to increase predation on infected prey to facilitate parasite transmission. I have, therefore, studied a complex parasite transmission process and, by including a predator, investigated a host-parasite system in the context of wider community interactions. My three key research questions in this thesis are as follows:

- When are parasites most likely to evolve a higher degree of manipulation? (chapter 2)
- When will hosts evolve defence mechanisms against parasitic infection when faced with the threat of predation? (chapter 3)
- Do parasites go extinct in regions on cyclic dynamics when stochastic effects are accounted for? (chapter 4)

Parasite manipulation is the focus of chapter 2 but an underlying theme

throughout this thesis.

A key result arises that population densities are evolutionary drivers of both parasite (chapter 2) and host (chapter 3) evolution. For example, the size of the susceptible prey and predator population together determine whether selection will favour an increase in the degree of manipulation utilised by the parasite or an increase in the spore production rate depending on which transmission route (environment to prey or prey to predator) would benefit from facilitation. Vries & van Langevelde (2018), albeit they did not conduct an evolutionary invasion analysis, also found that population densities are important for determining when manipulation is most beneficial to the parasite. Given a significant level of infection in the population, host evolution of defence against the parasite is governed by the size of the predator population. When the predator population is large, selection is less likely to favour defence mechanisms against infection since prey are likely to be consumed anyway. In this instance, an increased birth rate is beneficial in replacing individuals lost to predation or infection. Although a different trade-off was used, Toor & Best (2016) found that the composition of the enemy population was key for determining whether infection or predation defence would evolve. Throughout this thesis, I emphasise that a feedback exists between ecological and evolutionary dynamics, so they should be considered in concert. Thus, my results add to the growing literature that draws attention to the importance of eco-evolutionary models (Gokhale et al. 2013, Song et al. 2015, Papkou et al. 2016, Best et al. 2017, MacPherson & Otto 2018, Ashby et al. 2019, Best & Ashby 2023).

Some predators selectively choose to consume infected prey. There are numerous reasons for this, but manipulative strategies that alter prey behaviour or appearance to promote predation is one of them. This adaptive parasite trait is a major focus of this thesis. As already discussed, population densities govern the degree to which this strategy evolves in parasites, but I have also shown that manipulation affects the host evolution of infection defence mechanisms (chapter 3). Defences are likely to evolve to higher levels when

parasites have a maximum level of manipulation than when manipulation is minimised, likely because infection also increases predation risk. Hence, parasite defences provide some protection from being consumed. I also suggest that parasite survival may be greatest at intermediate levels of manipulation (chapter 4). My results highlight the importance of exploring manipulation as a parasite adaptive trait because it has important repercussions on host-parasite evolution and parasite survival. Manipulation is also imperative to study because of its consequences on human health. For example, not only can malaria-causing parasites *Plasmodium falciparum* increase the attractiveness of humans to its mosquito vector (Lacroix et al. 2005), but they also manipulate mosquito blood-feeding behaviour to increase transmission to humans (Koella & Packer 1996, Koella et al. 1998, Koella 1999). Given the severity of malaria, theoretical models must include manipulative mechanisms to understand the transmission route and learn how to limit it. In addition to human health, manipulative parasites may impact livestock hosts since gastrointestinal parasites are a significant issue (Tiele et al. 2023) and, as the benefit of a parasite harbouring these strategies is to increase predation, they could be detrimental to the conservation efforts of prey or predators.

I find the shape of the trade-off function to have important effects on population dynamics and evolution. When considering host evolution (chapter 3), only CSS points were found for an accelerating trade-off, but our system was bistable when costs were decelerating. A second set of singular points that were repellers was discovered, though this is unsurprising as decelerating costs give rise to repellers in general (Hoyle et al. 2008). In this case, the host would either evolve some intermediate level of defence against infection or selection would favour maximum susceptibility, opting for a maximal birth rate instead. Depending on the direction of evolution, the population dynamics looked starkly different in the two cases: the first at equilibrium and the latter exhibiting cycles with great amplitudes. Other studies also find the shape of the trade-off function to be influential on the dynamics of host-parasite in-

teractions and the evolutionary outcomes (Boots & Haraguchi 1999, Rueffler et al. 2004, de Mazancourt & Dieckmann 2004, Bowers et al. 2005, Kisdi 2006, Hoyle et al. 2008, Best et al. 2015, Ashby & King 2017).

A significant outcome of this modelling system is that it readily exhibits fluctuating population dynamics (chapter 2, 3 & 4). These oscillations have a significant ecological effect since, in general, cycles cause low minimum host densities, and I observed this, as did Fenton & Rands (2006), in my results. An issue arises where the host densities get fleetingly close to zero, putting the parasite at risk of extinction. In chapter 2, I highlighted the effect of the fluctuations on parasite evolution. In some instances, the qualitative direction of selection would alter across the boundary between equilibrium and cyclic dynamics. Other theoretical models also document the evolutionary effects of cycles (Donnelly et al. 2013, Ferris & Best 2018, Best & Ashby 2023). Interestingly, when I instead considered host evolution, the host tended to evolve only within the equilibrium region and up to the boundary between equilibrium and cyclic dynamics. Singh & Best (2024) witnessed a similar occurrence in their coevolutionary model whereby fluctuating dynamics prevented coexisting dimorphic host and parasite strains from reaching their extremes, and so evolution takes both the parasite and host strain to a region where the population dynamics converge to equilibrium and lie close to the boundary between the regions of cyclic and equilibrium dynamics. Further analysis would be needed to determine why cycles stop the host from evolving to cyclic regions. Since these fluctuations put the parasite at risk of extinction, I considered how likely the parasite is to survive when stochastic effects are included. I discovered that survival is unlikely and results that depend on fluctuating dynamics should be re-evaluated to discover if and when they hold. My work emphasises the significant impact of cyclic dynamics on ecological and evolutionary dynamics in host-parasite systems, so careful analysis must be undertaken whenever they are observed.

Overall, I summarise my theoretical work into two key points. First, population

densities should not be ignored when considering host-parasite evolution since I have demonstrated their influence as evolutionary dynamics. Second, cyclic dynamics can have complex effects on ecological and evolutionary drivers that should be investigated thoroughly and carefully before presenting results from these regions.

5.2 Future Work

There are numerous avenues in which I could proceed to extend my theoretical research. A neat way to round off this body of work would be to now conduct a similar analysis to those in chapters 2 and 3 but consider how predators may evolve to defend themselves against infection, particularly when the parasites may harbour manipulative tendencies. I would utilise the same model framework but include a trade-off between predator reproduction and defence. Moore (2002) presented anecdotal evidence of predator response since oystercatchers were witnessed to reject clams infected by the trematode *Parvatremis affinis* even though parasitised clams are easier to find since they crawl beneath the surface of the sand, leaving tracks rather than burrowing as normal. It is not clear whether this was an adaptive trait by the predator, but Keymer et al. (1983) showed that hosts could learn to avoid parasitised food with a distinctive taste; therefore Lozano (1991) made the point that perhaps predators can also avoid prey with certain behaviour or appearance. Lafferty (1992) created a theoretical model looking at the balance between energy taken to find and eat prey and the cost of infection to the predator. While they found that there was no benefit of parasite avoidance by predators if they only caused minimal damage and facilitated prey capture, it would still be interesting to conduct an evolutionary invasion analysis to see if there are certain conditions under which predators will evolve to higher degrees of defence.

I could repeat my analysis but remove a simplifying assumption to allow infected hosts to reproduce and include host recovery to see what effect this

may have. Some theoretical studies have already looked, in general, at some of the possible effects that these inclusions may have. Donnelly et al. (2015) discovered that parasite-induced loss of fertility will alter the driving force of the evolutionary dynamics, which determines whether or not host resistance will be selected for. Best et al. (2017) concurred since they also found fertility to be the evolutionary driver but discovered that higher sterility by parasites led to higher host resistance but lower tolerance. These studies indicate that reproduction by infected individuals and host recovery can significantly impact selection. Fenton & Rands (2006) did utilise models that included reproduction by infected individuals but found no qualitative differences in the population dynamics compared to when infected individuals were rendered infertile. As my work has shown that population densities are key drivers of evolution (chapters 2 & 3), it may mean that evolution is not affected if the population dynamics are not significantly different given what Fenton & Rands (2006) found. Despite this, the effect of these assumptions on evolution should still be checked, particularly since Fenton & Rands (2006) did not investigate the inclusion of host recovery.

Increasing the complexity of my evolutionary analysis by looking at parasite evolution of manipulation strategies simultaneously with prey host evolution of defence mechanisms would be an interesting research question. Coevolution studies of host-parasite relationships that consider other species interactions are limited (Buckingham & Ashby 2022). However, Best (2018) did consider coevolution in the presence of a predator and found that lower host resistance and higher pathogen infectivity evolve compared to when no predator is present, and fluctuating selection dynamics are expected to occur in populations where predators are very selective about the prey they consume and have low handling times. This study highlights the significant effect of a predator and selective predation on coevolutionary dynamics but assumes the predator is immune; it is important now to consider what happens when the predator forms an important stage of the parasite's life cycle and the parasite can evolve

to use manipulation strategies to facilitate predation, like in our system.

Creating a model system with a wider community structure would increase model complexity but would improve biological realism. For example, other predators that may consume infected prey, other parasites that may co-infect the prey or other prey that may consume the free-living stages could be included to investigate how manipulation strategies may evolve when the parasite is at risk of transmitting to a dead-end host (Mouritsen & Poulin 2003, Seppälä et al. 2008, Vries & van Langevelde 2018), or competing for within-host resources. Some studies have discussed the possibility of modelling specific manipulation to target host predators (Seppälä & Jokela 2008, Parker et al. 2009), and other models have looked at parasites manipulating their hosts by switching between predation suppression and predation enhancement while they mature (Vries & van Langevelde 2018). Utilising this previous work, perhaps looking at the evolution of these complex manipulation traits would be useful to see if this would be a preventive measure for prey being consumed by non-host predators and whether there are conditions under which it would be selected for.

A final way in which I would extend my theoretical study would be to consider reservoir hosts that harbour parasites and can introduce infection to other host populations that are usually too small to support the maintenance of the parasite (Haydon et al. 2002, Ashford 2003). In chapter 4, using a stochastic model, I found that parasitic extinction when host populations are small due to fluctuating ecological dynamics is extremely likely. I would investigate the potential for infection resurgence in this system and what this would mean for parasite survival if there are nearby reservoir hosts that can cause infection by between-species transmission. Fenton & Pedersen (2005) created a framework that included these reservoir hosts, which we could utilise to adapt our system. Interestingly, parasites harboured by reservoir hosts can drive target hosts to extinction (de Castro & Bolker 2005, Fenton & Pedersen 2005), meaning that parasite survival in the target host may not increase when considering reservoir

hosts but would increase overall when you consider their long-term survival in reservoir populations. Parasite resurgence due to between-species transmission from reservoir hosts is important to study because it has important applications to conservation since infection can be introduced to struggling populations in zoological parks or breeding facilities despite their numbers being too small to maintain the parasite (Nunn & Altizer 2006). For example, in a baboon troop in Kruger National Park, the prevalence of bovine tuberculosis was 50% and was likely introduced to the primates because they fed on infected buffalo carcasses (Keet et al. 1996, 2000).

In addition to extending the theoretical model, it is important to work in synergy with experimental and empirical work to test model predictions. As my work has highlighted that population densities are evolutionary drivers for both parasite (chapter 2) and host (chapter 3), I stress the importance of keeping a record of host numbers throughout any experiments to see if the same results can be witnessed in real-world systems.

Helminths, parasitic flatworms (acanthocephalans, cestodes, nematodes, and trematodes) (Sepulveda & Kinsella 2013), are a leading cause of infectious disease in humans (Hotez et al. 2008). Helminths also induce alterations in host behaviour or appearance (Poulin et al. 1994); Moore (2002) tabulates many examples. For instance, the nematode *Myrmeconema neotrpicum* infects ants to turn their abdomen from black to red to induce fruit mimicry and make the ants vulnerable to predation by birds (Poinar & Yanoviak 2008, Yanoviak et al. 2008). An experimental system that involves a helminth parasite that has been documented to manipulate its intermediate host, like the *Myrmeconema neotrpicum* nematode, will be useful in testing model predictions to see if host behaviour or appearance is modified, whether any defence mechanisms by hosts are observed, and to investigate parasite survival. New knowledge about these systems, when parasites are trophically transmitted and able to evolve to manipulate their host to facilitate transmission, is vital to understanding how to control or decrease transmission since helminths are detrimental to human

health

As with humans, parasites can cause widespread disease in livestock. Gastrointestinal parasites in cattle are a major issue (Tiele et al. 2023). Manipulation strategies can facilitate parasite transmission to livestock since ants infected by *Dicrocoelium dendriticum* have been documented to move to a position of vulnerability from grazing sheep rather than return to their nest for safety when temperatures drop (Carney 1969, Wickler 1976, Poulin 2007). This may form another useful system to explore trophic transmission and manipulation strategies in real-world systems with extremely important applications in agriculture.

Bacteriophages (Phages) act as obligate bacterial predators (Chaturongakul & Ounjai 2014) and are also used in many coevolutionary studies in the laboratory and nature (Koskella & Brockhurst 2014). Phages are documented to manipulate host recombination functions (Bobay et al. 2013). Bacteria can also readily evolve defence mechanisms to protect against phage (Koskella & Brockhurst 2014). Other experimental setups we have discussed may be utilised more for observations of manipulation and collection of data for population numbers to help support or counter our model predictions surrounding densities being linked to manipulation evolution. A bacteria-phage system, however, may be useful to see parasite or host evolution in real-time since experiment conditions could be set up to either promote or prevent manipulation or defence evolution based on my theoretical work to see if it is correct.

An important area of research is the evolution of host-parasite relationships with other species interactions. I have focused on trophically transmitted parasites utilising, and often manipulating, an intermediate prey host to infect a predator host. The results I have presented build on previous theoretical work, and I have presented avenues for proceeding by extending the modelling system and suggesting suitable empirical work to test model predictions. Infectious diseases have many severe impacts on public health, agriculture, and conserva-

tion efforts, to name but a few. So, in improving knowledge about host-parasite relationships interacting with other species, how they evolve and, most importantly, understanding complex transmission processes, we can manage, control, reduce and prevent diseases caused by parasites.

Appendix A

Appendix: The Evolution of a Parasite to Manipulate the Host

A.1 Holling Type I Functional Responses

We include further plots that show what happens to the CSS investment in manipulation as model parameters are altered and the densities of the susceptible prey population and the total predator population at this CSS point.

In figure A.1, we vary the predator death rate d. As this parameter increases, the predator population is slightly reduced and then varies between quite small densities (figure A.1C). Consequently, the susceptible prey population is relatively quite large (figure A.1B), meaning that selection will favour investment in manipulation strategies (figure A.1A). The level of manipulation varies before plateauing at higher predator death rates. If we look at what happens to the susceptible prey and predator populations we can see that they also plateau at these values of higher values of d. This highlights how these population densities significantly influence where the parasite invests its limited energy resources.

In figure A.2 the colour map is different because the maximum period of the

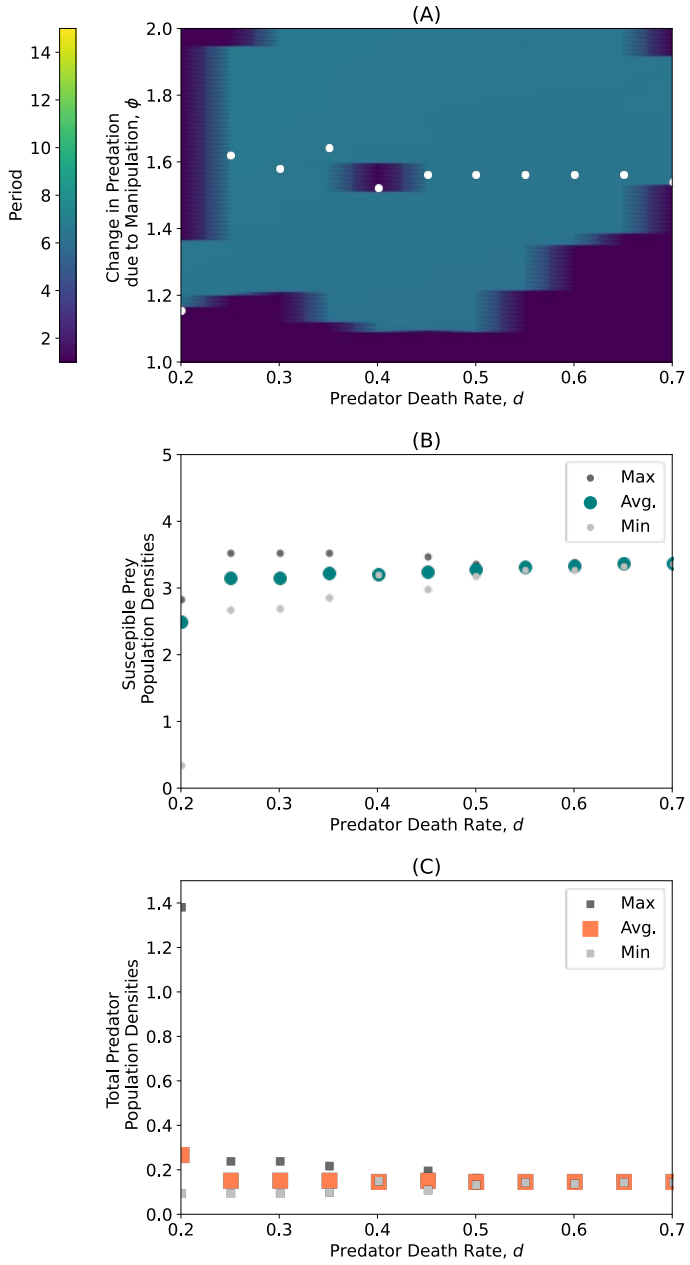

Figure A.1: The predator death rate, d is varied to see how it affects the singular strategy ϕ^* (A), the susceptible prey population densities (B) and the total predator population densities (C). The x-axis is limited since the parasite cannot persist in the population for values smaller than this. Standard parameter values are $\mu = 0.15$, $b = 0.2$, $d = 0.4$, $\beta = 0.95$, $\alpha = 0.8$, $\alpha_P = 0.7$, $a = 2$, $\theta = 0.5$, $q = 0.2$, and $c = 1.2$.

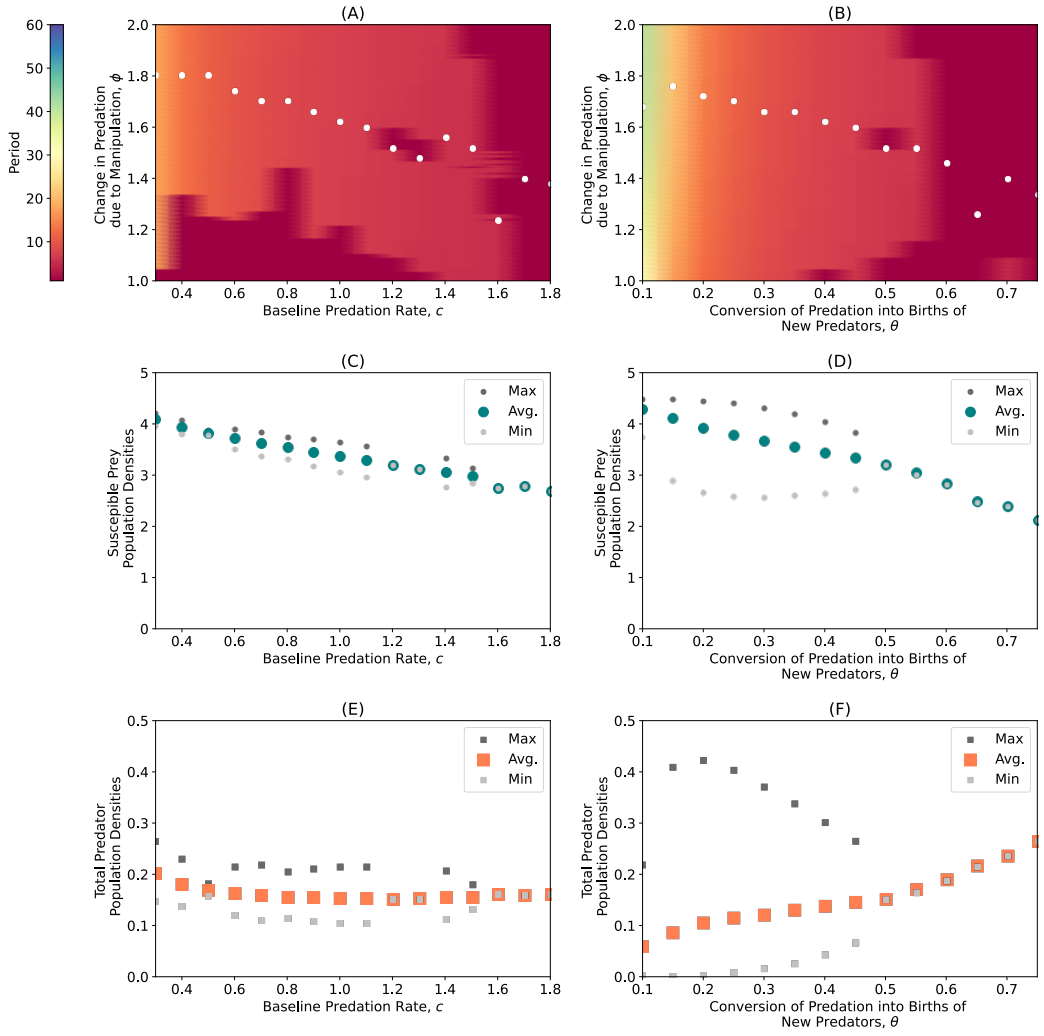

Figure A.2: The baseline predation rate, c and conversion rate of prey deaths into births of new predators, θ are each varied to see how it affects the singular strategy ϕ^* (A-B), the susceptible prey population densities (C-D) and the total predator population densities (E-F). The x-axis is limited in both cases since the parasite cannot persist in the population for values smaller than this. Standard parameter values are as in figure 2.4.

cycles is larger. We can increase the baseline predation rate c (figure A.2A) and we can increase the conversion of predation into births of new predators, θ (figure A.2B). This change to these parameters results in reduced investment in manipulation by the parasite and from our previous discussion we know that this is likely to be a result of the significant reduction in the susceptible prey

population (figures A.2C and A.2D). This trend continues across the boundary between equilibrium and cyclic dynamics since the trend in change to the population densities does not change. As we emphasised in our discussion for figure 2.6 these densities seem to govern manipulation evolution.

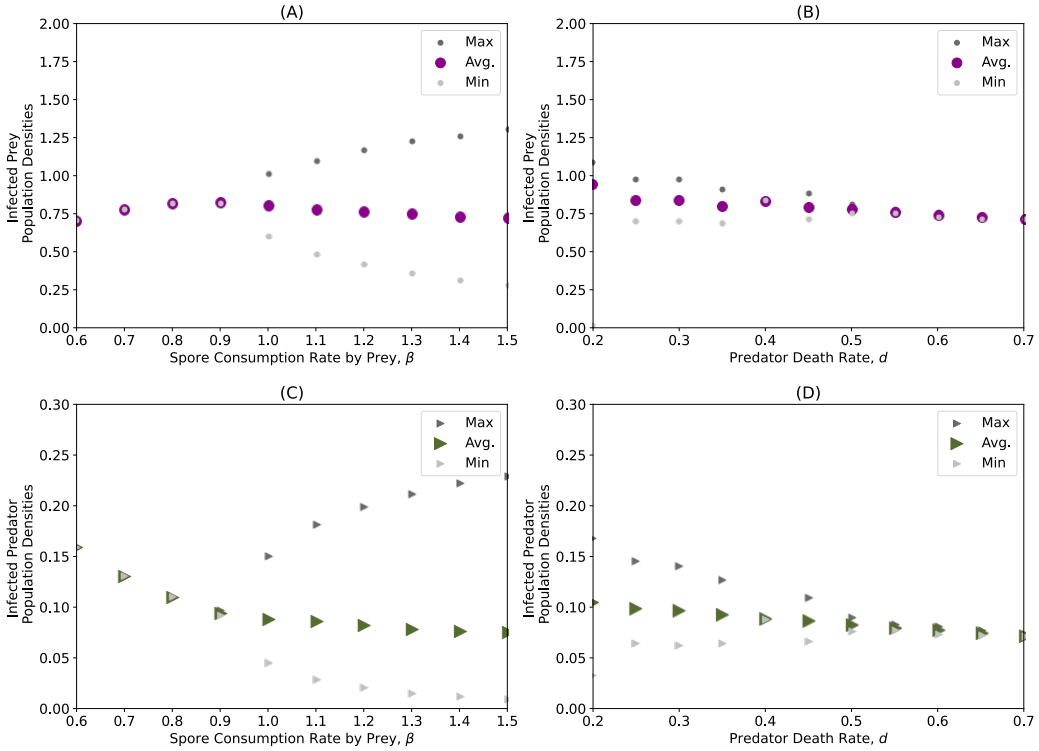

Figure A.3: The consumption rate of spores by prey β and predator death rate d are varied to see how it affects the population dynamics of the infected prey population (A-B) and the infected predator population (C-D). Standard parameter values are as in figure 2.4.

A.2 Holling Type II Functional Responses

We now consider what happens to the CSS investment in manipulation as model parameters are altered when we instead use the Holling Type II functional responses (Holling 1959). This response is different than the linear Type I case because there is now some limitation on predation so the predation rate is decelerating with prey density growth. We use the same parameter values

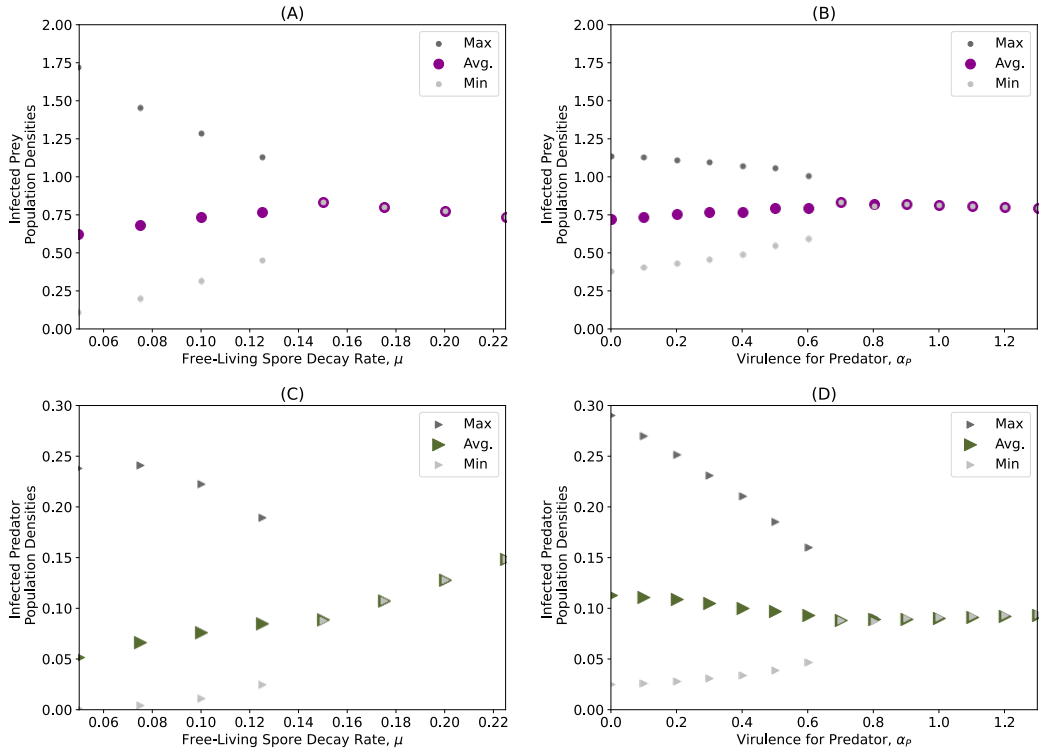

Figure A.4: The decay rate of parasite free-living spores, μ and predator virulence, α_P are varied to see how it affects the population dynamics of the infected prey population (A-B) and the infected predator population (C-D). Standard parameter values are as in figure 2.4.

and trade-off function (equation 2.3) as in the Type I case and we take the handling times h_S and h_I as 0.6 and 0.1 respectively.

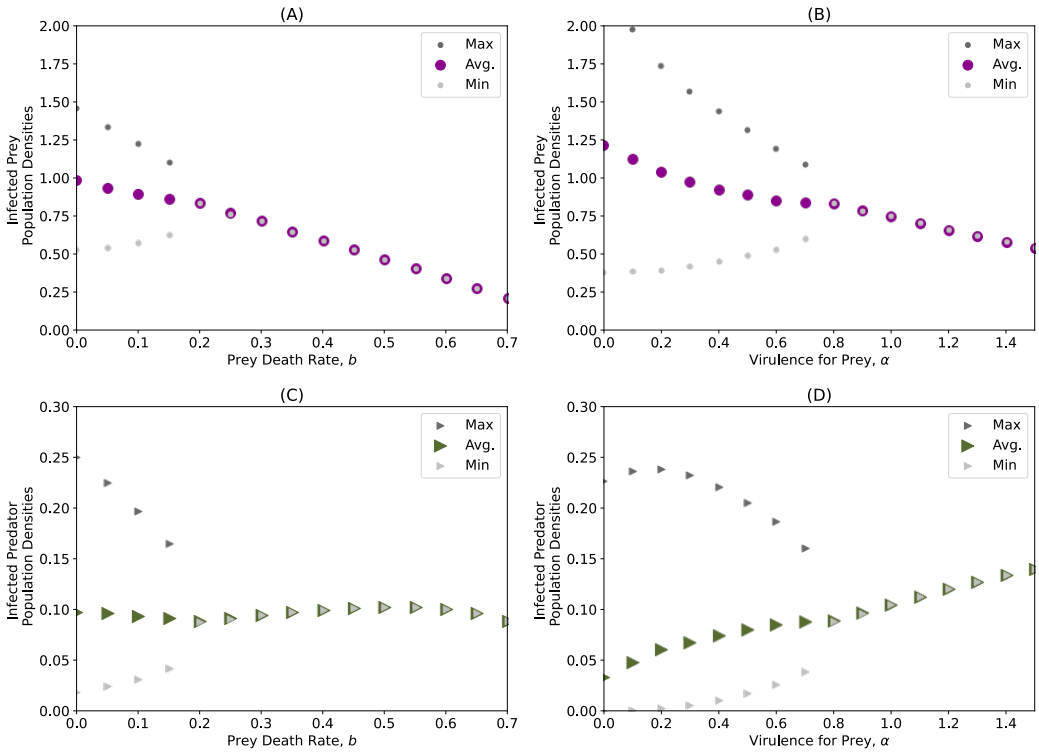

Figure A.5: The prey death rate b and prey virulence α are varied to see how it affects the population dynamics of the infected prey population (A-B) and the infected predator population (C-D). Standard parameter values are as in figure 2.4.

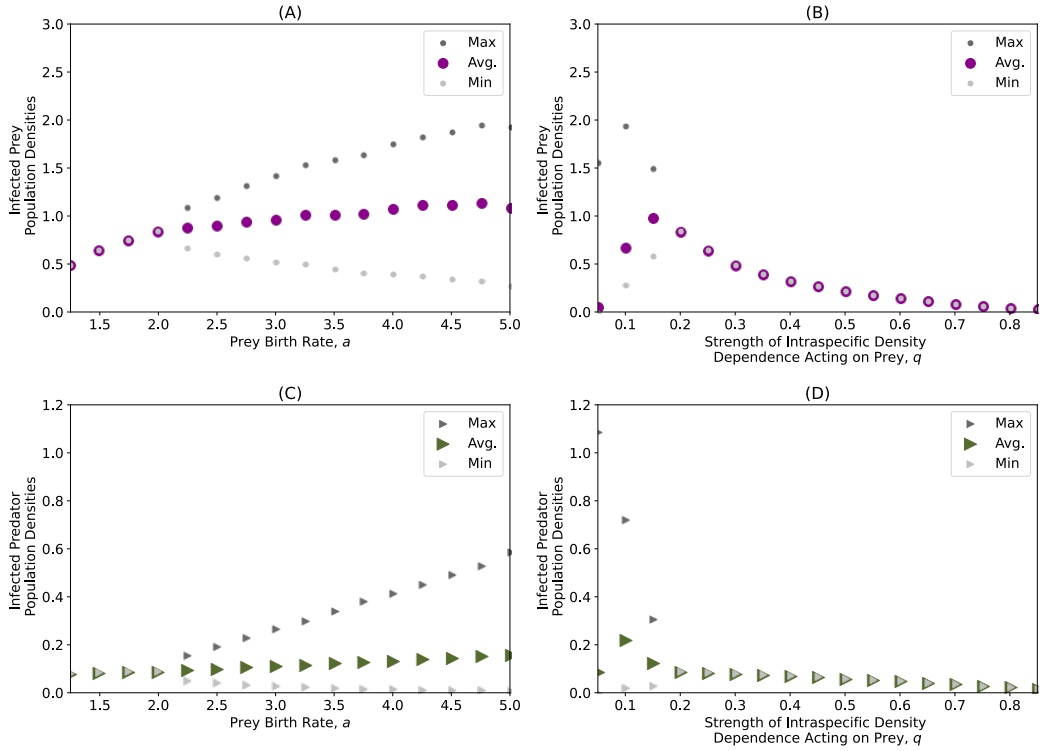

Figure A.6: The prey birth rate, a and strength of intraspecific density acting on on prey, q are varied to see how it affects the population dynamics of the infected prey population (A-B) and the infected predator population (C-D). Standard parameter values are as in figure 2.4. Note that the scale of the y-axis is larger for infected predators than in the previous figures for infected host densities.

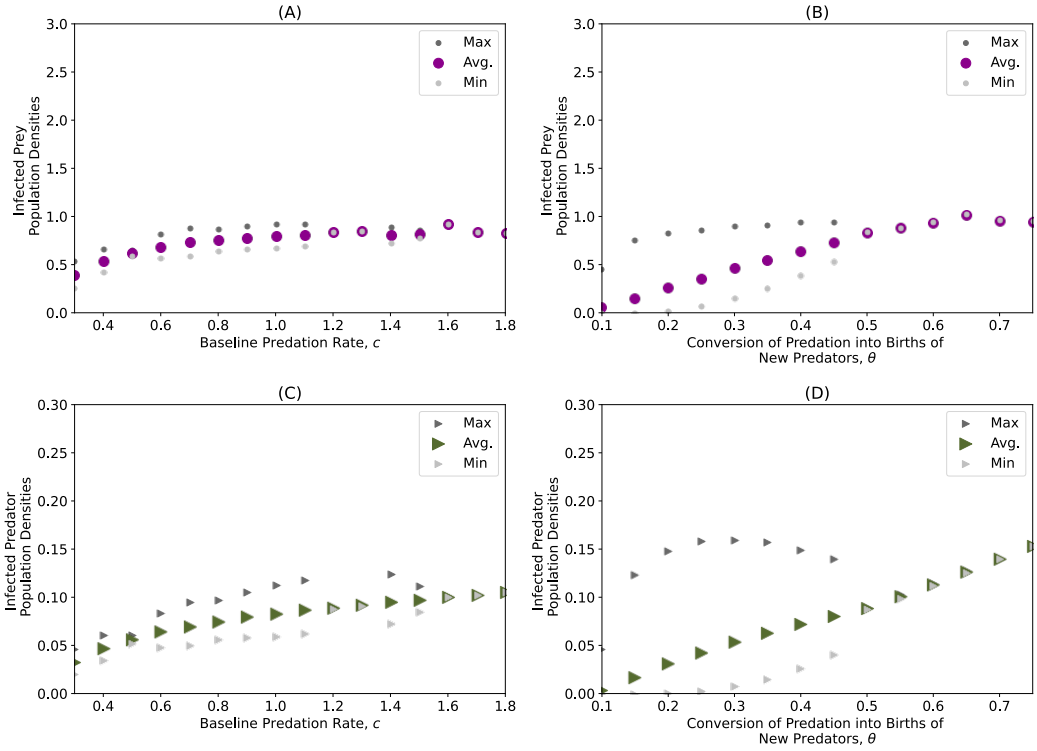

Figure A.7: The baseline predation rate, c and conversion rate of prey deaths into births of new predators, θ are varied to see how it affects the population dynamics of the infected prey population (A-B) and the infected predator population (C-D). Standard parameter values are as in figure 2.4.

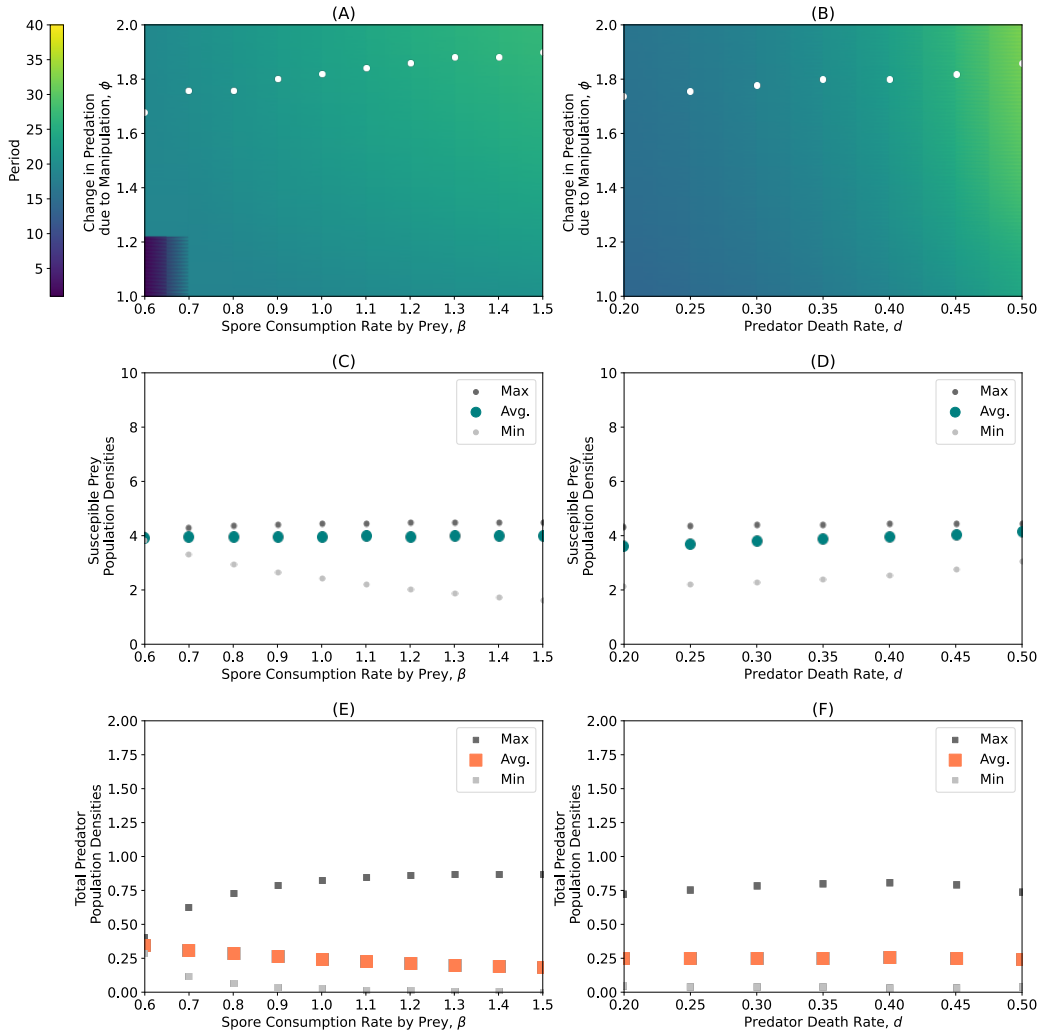

Figure A.8: The consumption rate of spores by prey β and predator death rate d are each varied to see how it affects the singular strategy ϕ^* (A-B), the susceptible prey population densities (C-D) and the total predator population densities (E-F). Standard parameter values are $\mu = 0.15$, $b = 0.2$, $d = 0.4$, $\beta = 0.95$, $\alpha = 0.8$, $\alpha_P = 0.7$, $a = 2$, $\theta = 0.5$, $q = 0.2$, and $c = 1.2$, $h_S = 0.6$, and $h_I = 0.1$.

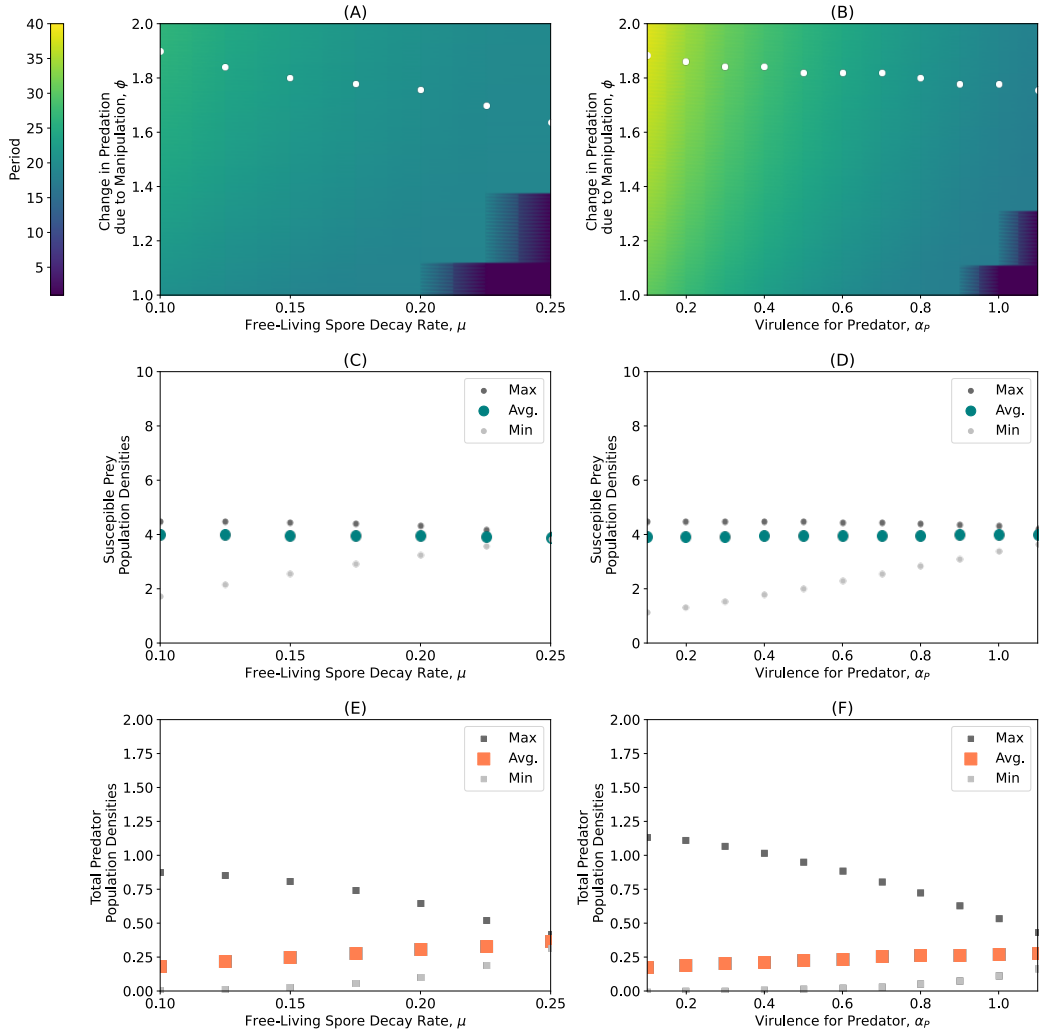

Figure A.9: The decay rate of parasite free-living spores, μ and predator virulence, α_P are each varied to see how it affects the singular strategy ϕ^* (A-B), the susceptible prey population densities (C-D) and the total predator population densities (E-F). Standard parameter values are as in figure A.8.

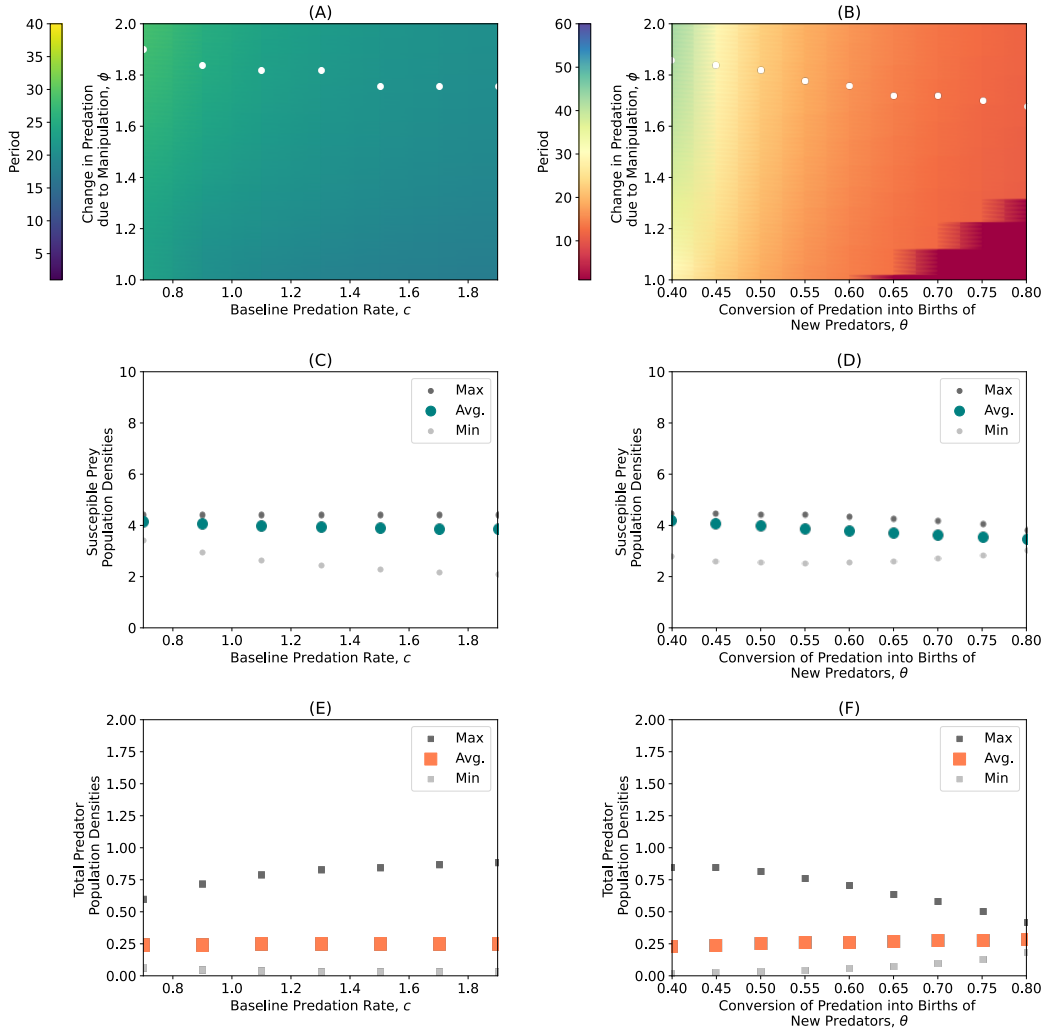

Figure A.10: The baseline predation rate, c and conversion rate of prey deaths into births of new predators, θ are each varied to see how it affects the singular strategy ϕ^* (A-B), the susceptible prey population densities (C-D) and the total predator population densities (E-F). Standard parameter values are as in figure A.8.

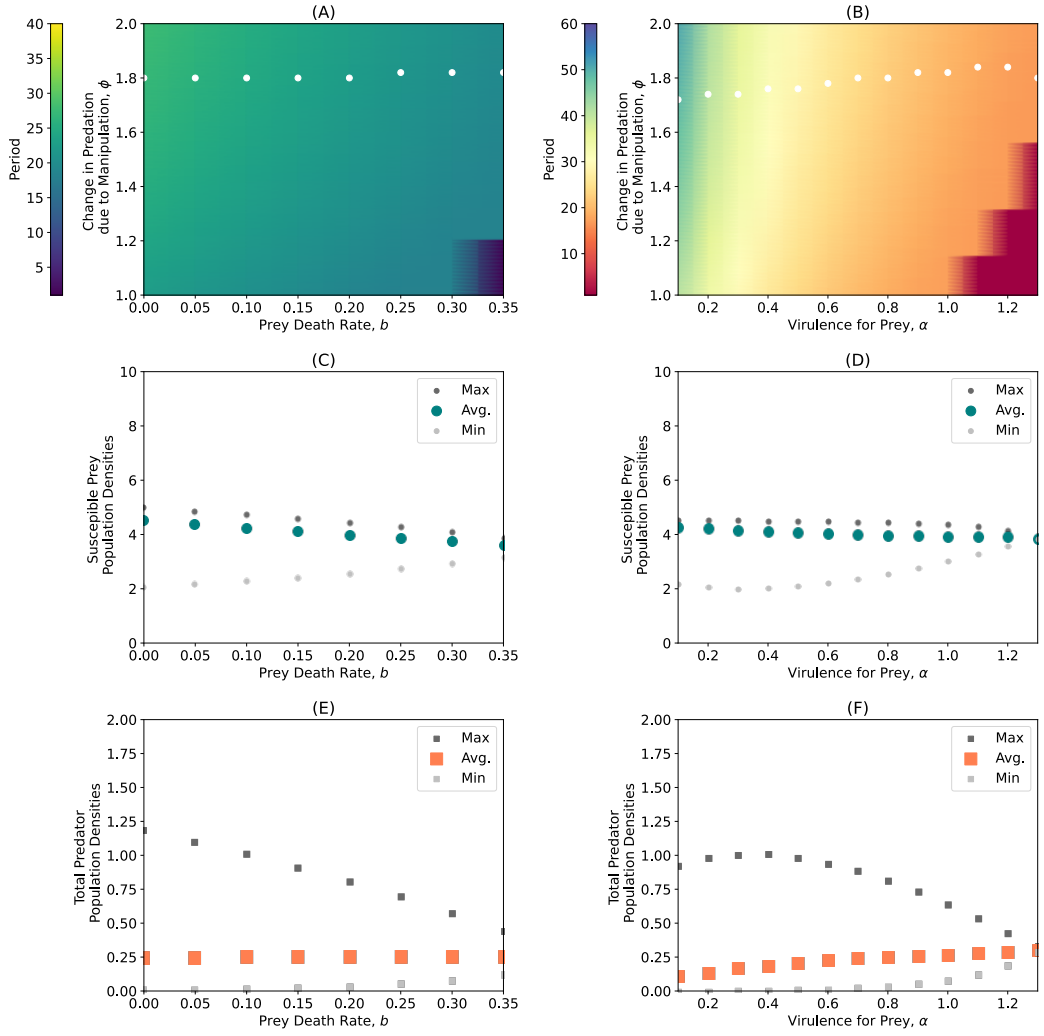

Figure A.11: The prey death rate b and prey virulence α are varied to see how it affects the singular strategy ϕ^* (A-B), the susceptible prey population densities (C-D) and the total predator population densities (E-F). Standard parameter values are as in figure A.8.

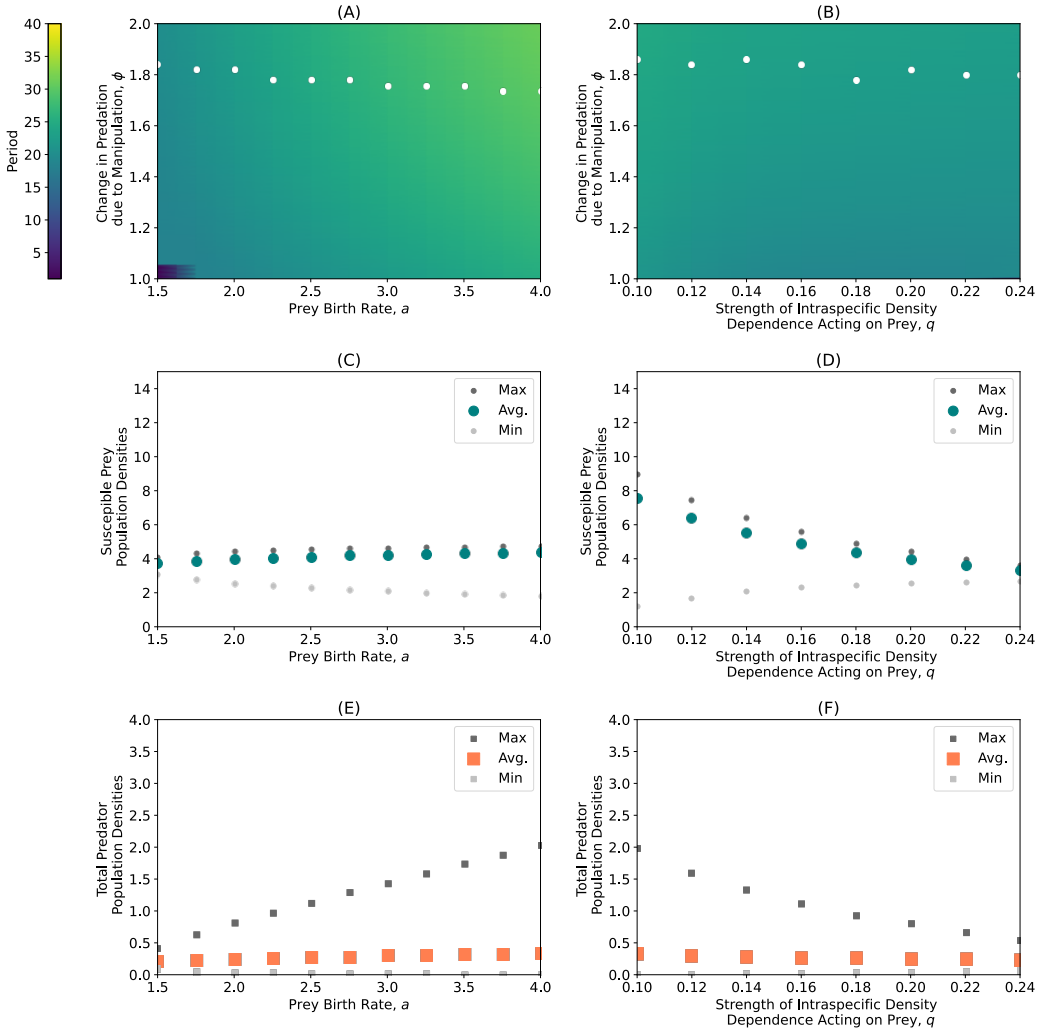

Figure A.12: The prey birth rate, a and strength of intraspecific density acting on on prey, q are each varied to see how it affects the singular strategy ϕ^* (A-B), the susceptible prey population densities (C-D) and the total predator population densities (E-F). Standard parameter values are as in figure A.8.

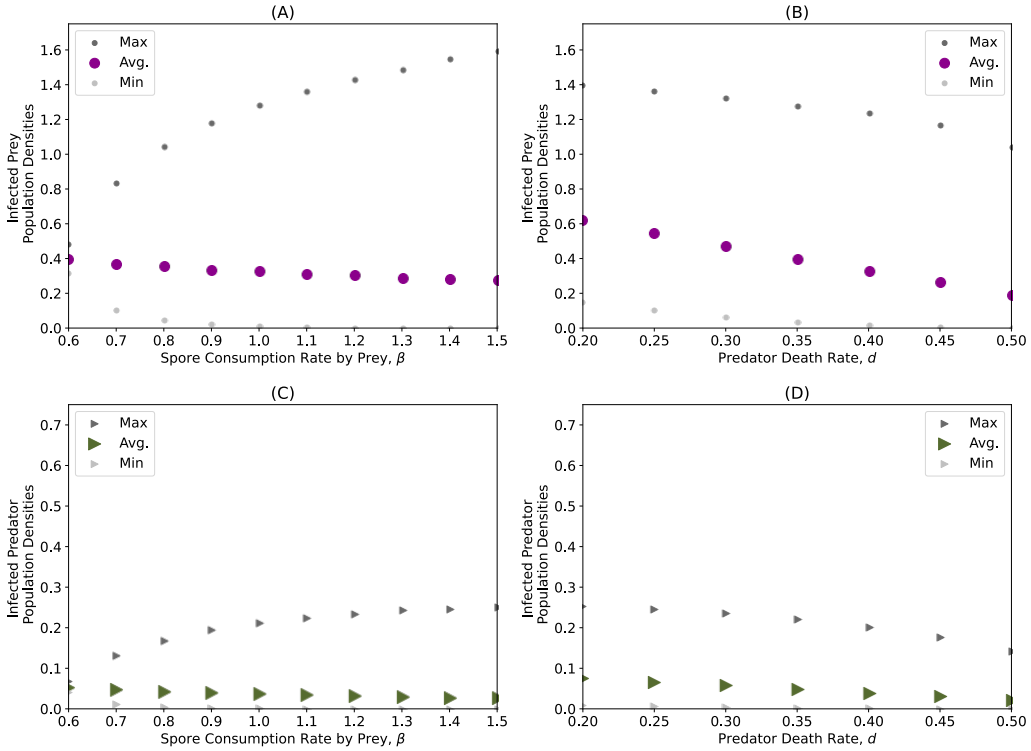

Figure A.13: The consumption rate of spores by prey β and predator death rate d are varied to see how it affects the population dynamics of the infected prey population (A-B) and the infected predator population (C-D). Standard parameter values are as in figure A.8

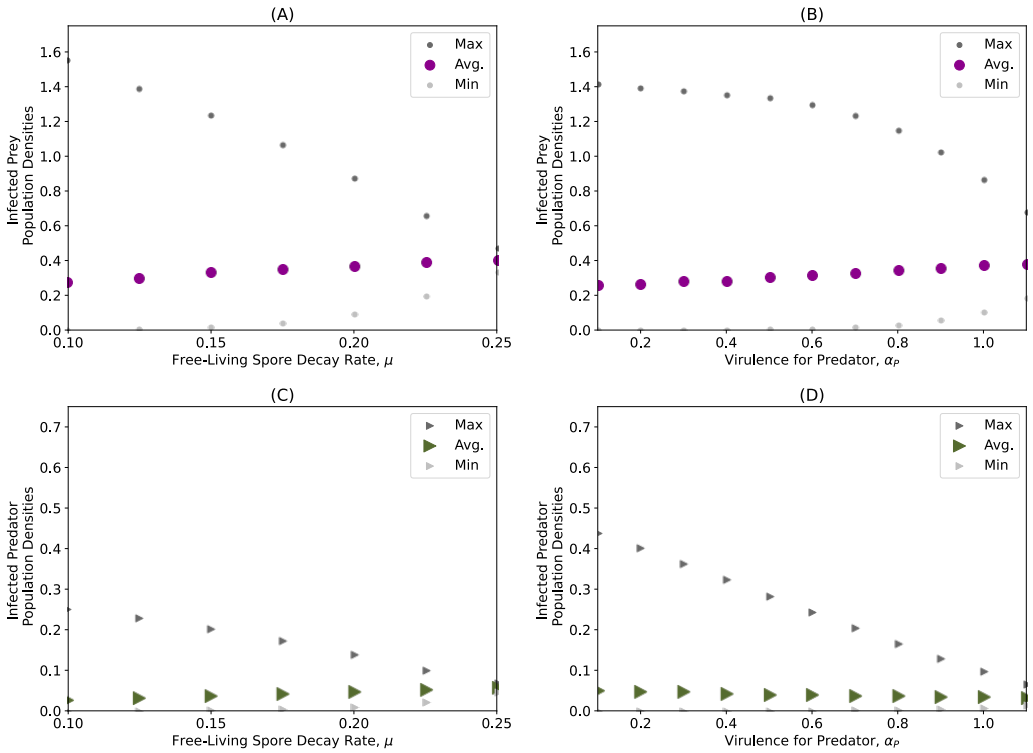

Figure A.14: The decay rate of parasite free-living spores, μ and predator virulence, α_P are varied to see how it affects the population dynamics of the infected prey population (A-B) and the infected predator population (C-D). Standard parameter values are as in figure A.8.

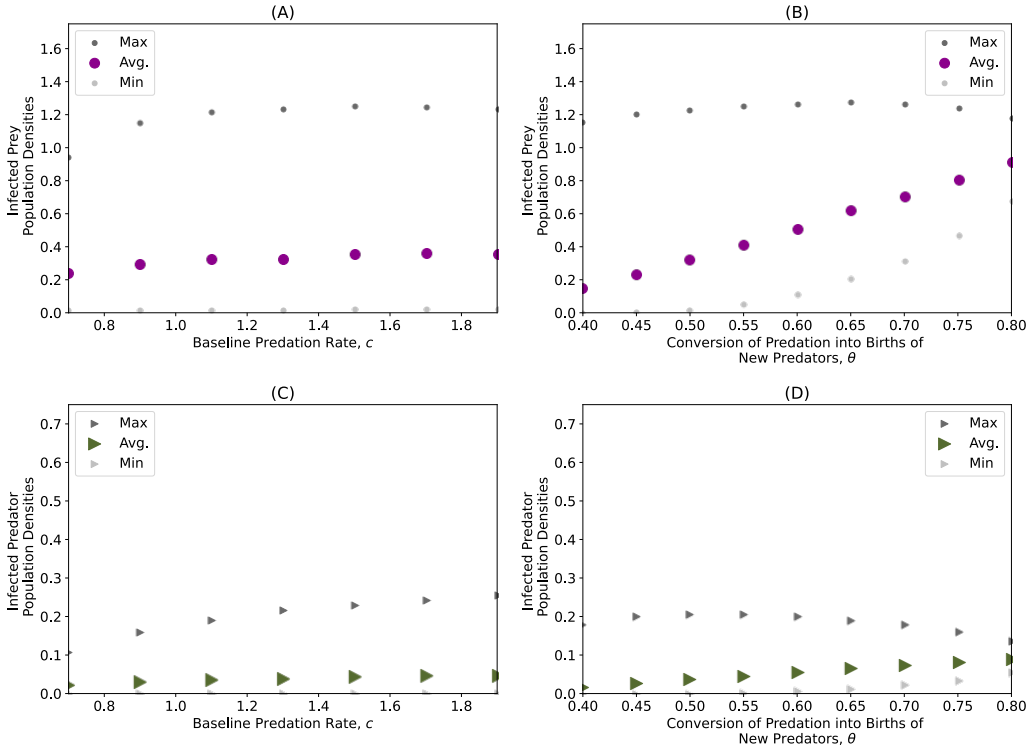

Figure A.15: The baseline predation rate, c and conversion rate of prey deaths into births of new predators, θ are varied to see how it affects the population dynamics of the infected prey population (A-B) and the infected predator population (C-D). Standard parameter values are as in figure A.8.

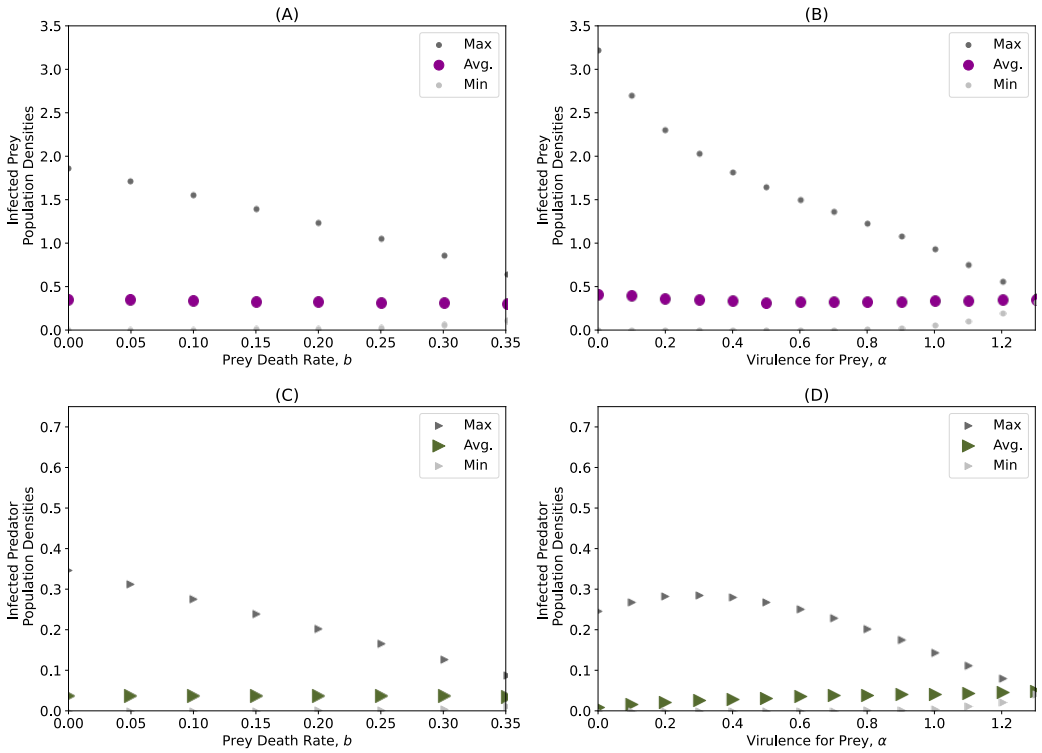

Figure A.16: The prey death rate b and prey virulence α are varied to see how it affects the population dynamics of the infected prey population (A-B) and the infected predator population (C-D). Standard parameter values are as in figure A.8.

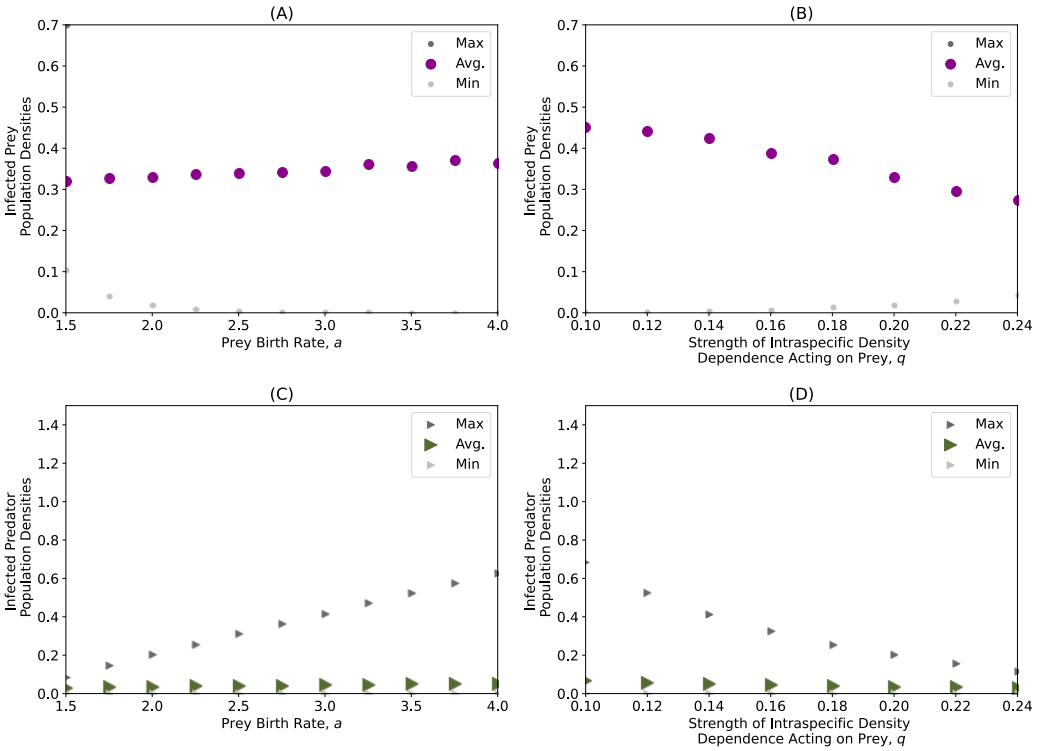

Figure A.17: The prey birth rate, a and strength of intraspecific density acting on on prey, q are varied to see how it affects the population dynamics of the infected prey population (A-B) and the infected predator population (C-D). Standard parameter values are as in figure A.8.

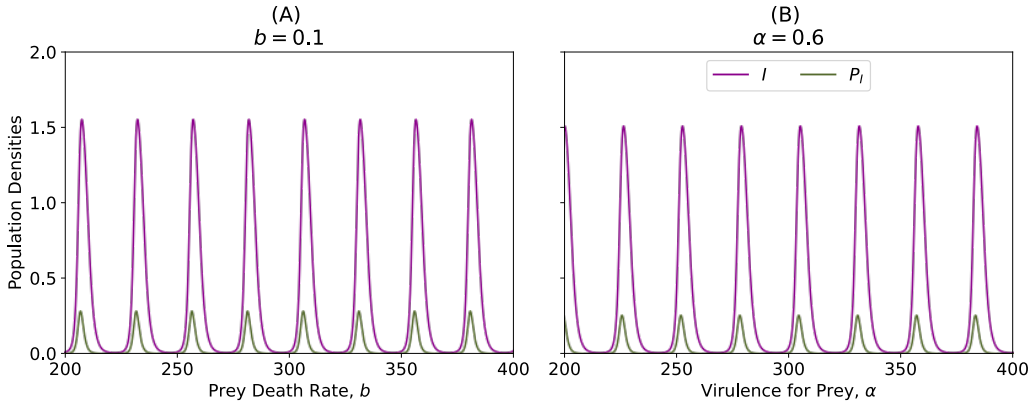

Figure A.18: A small subsection of the infected prey and infected predator population dynamics to show how the minimum densities coincide for two values of prey mortality rate b and prey virulence α.

Appendix B

Appendix: The Evolution of Host Defence Against Parasite Manipulation

B.1 Accelerating Costs

We include the ecological dynamics for a value of the parasite mortality rate μ at two different levels of host susceptibility to infection β.

In figure B.2 we present the population dynamics for two values of predator death rate d where prey evolve to a level of susceptibility to infection β that lies in the region of fluctuating dynamics. We include these plots to help illustrate why this might be the case.

B.2 Decelerating Costs

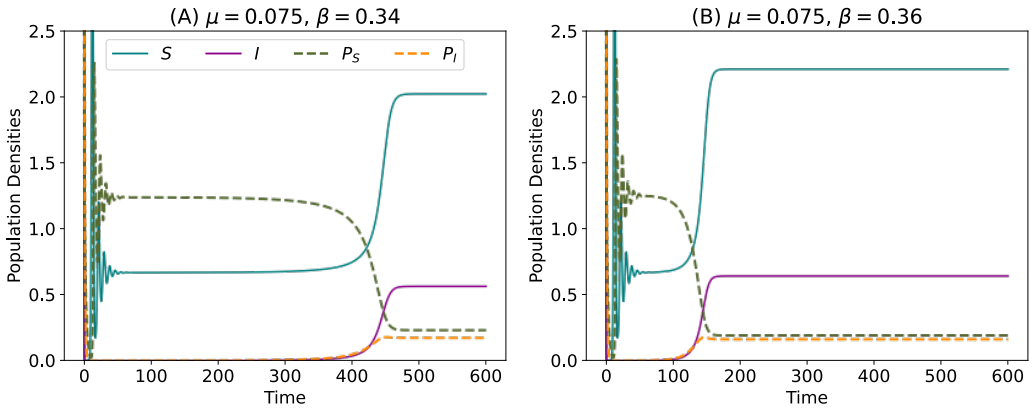

Figure B.1: Population dynamics for two values of parasite mortality rate μ as we vary host susceptibility to infection β.

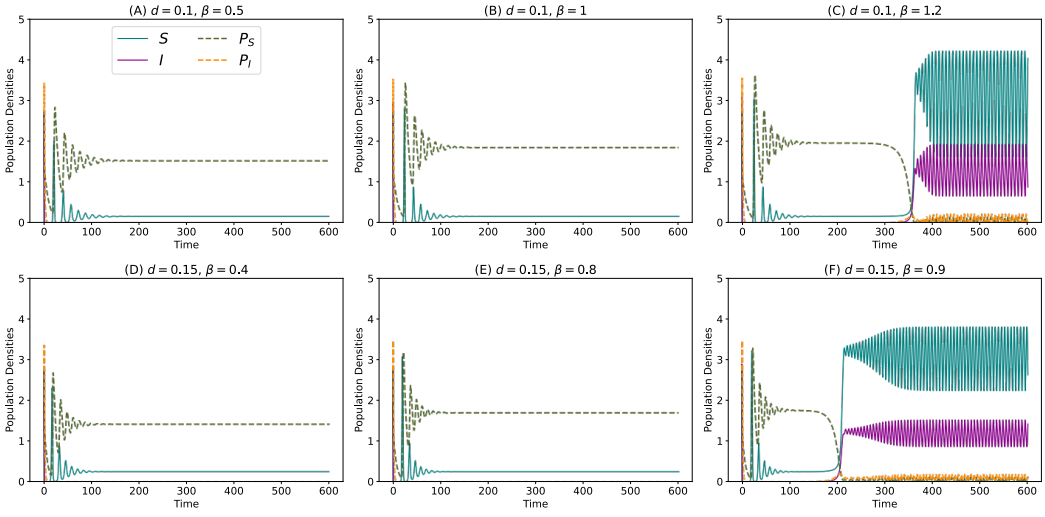

Figure B.2: Population dynamics for two values of predator death rate d as we vary host susceptibility to infection β.

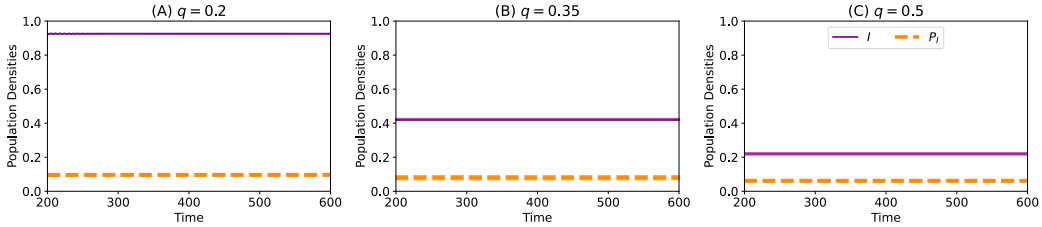

Figure B.3: Subsections of the infection population dynamics for increasing values of the strength of intraspecific density dependence acting on prey (competition) q showing that infection prevalence decreases as q increases.

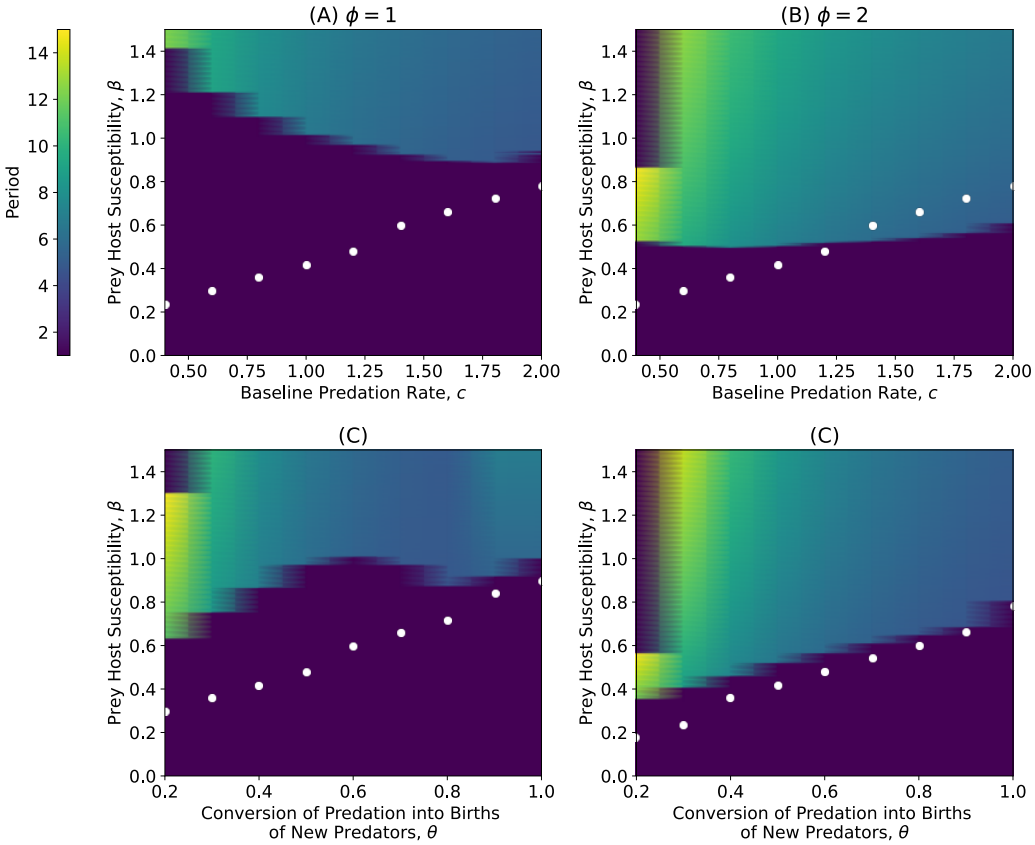

Figure B.4: Comparing prey host evolution of host susceptibility β when the parasite does not manipulate its host ($\phi = 1$) and when manipulation is maximised ($\phi = 2$) as we vary the baseline predation rate, c (A-B) and the rate of conversion of predation into the births of new predators, θ (C-D).

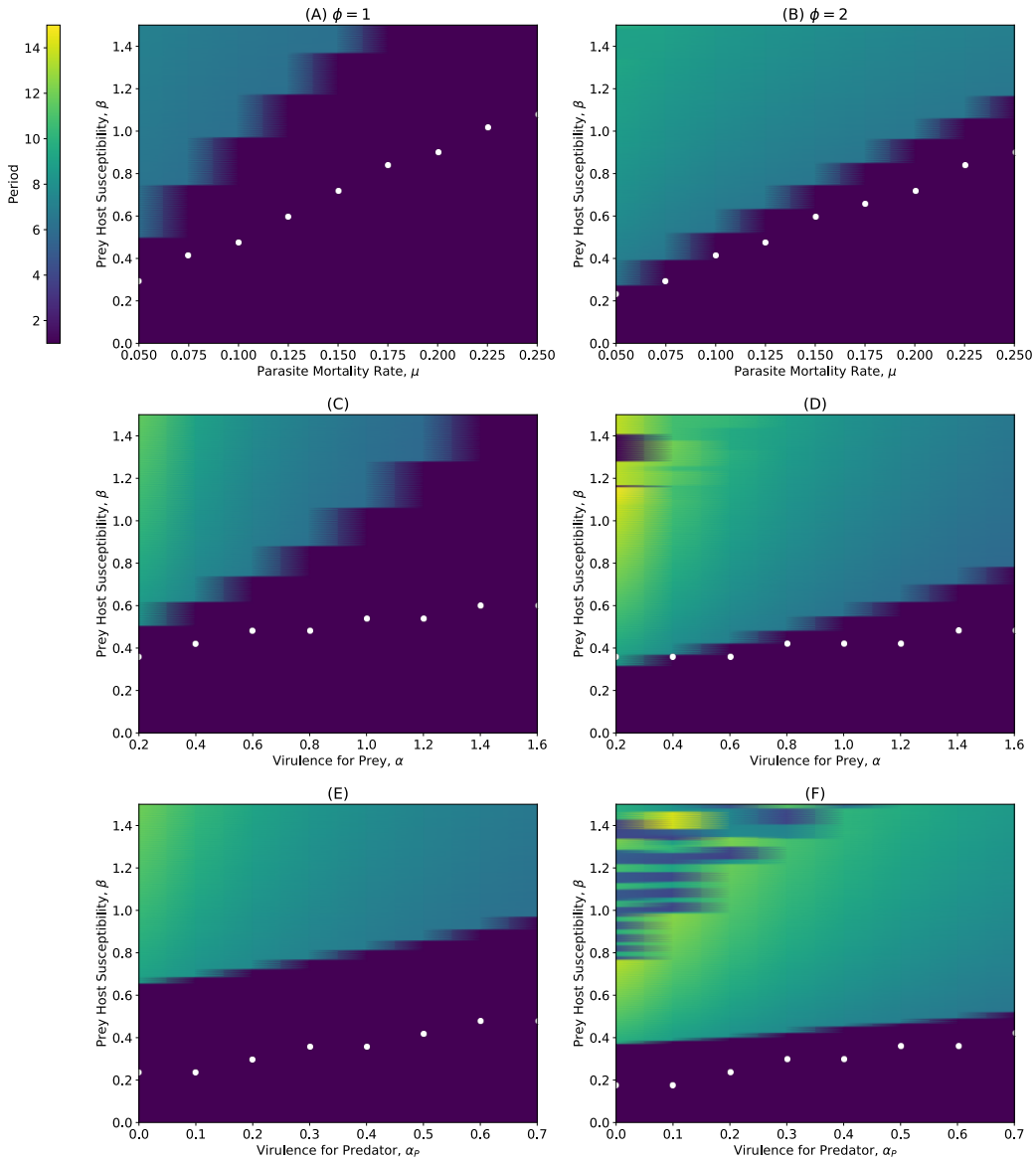

Figure B.5: Comparing prey host evolution of host susceptibility β when the parasite does not manipulate its host ($\phi = 1$) and when manipulation is maximised ($\phi = 2$) as we vary parasite mortality rate, μ (A-B), prey virulence, α (C-D), and predator virulence, α_P (E-F).

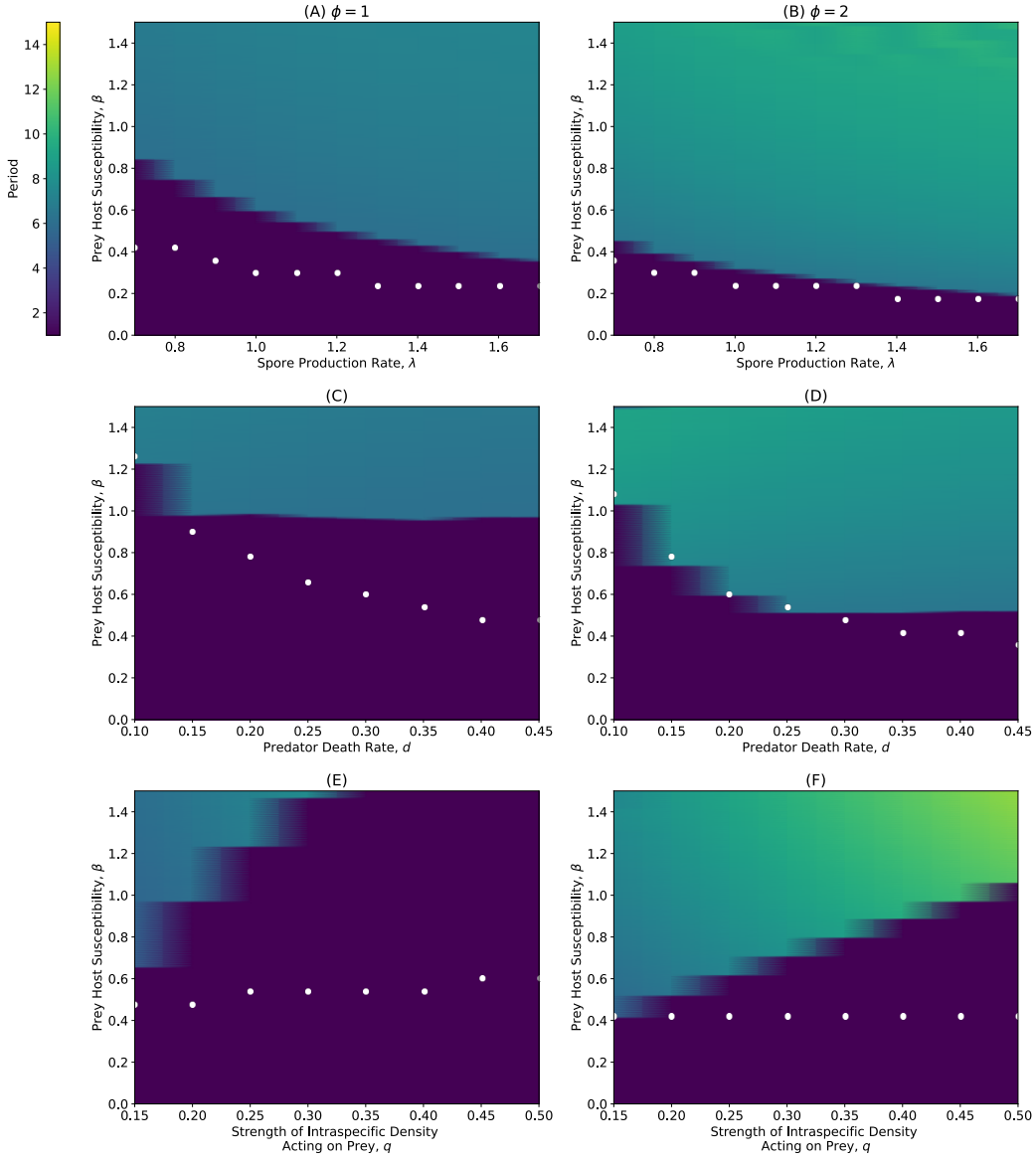

Figure B.6: Comparing prey host evolution of host susceptibility β when the parasite does not manipulate its host ($\phi = 1$) and when manipulation is maximised ($\phi = 2$) as we vary the spore production rate, λ (A-B), predator mortality rate, d (C-D), and the strength of the intraspecific density acting on prey, q (E-F).

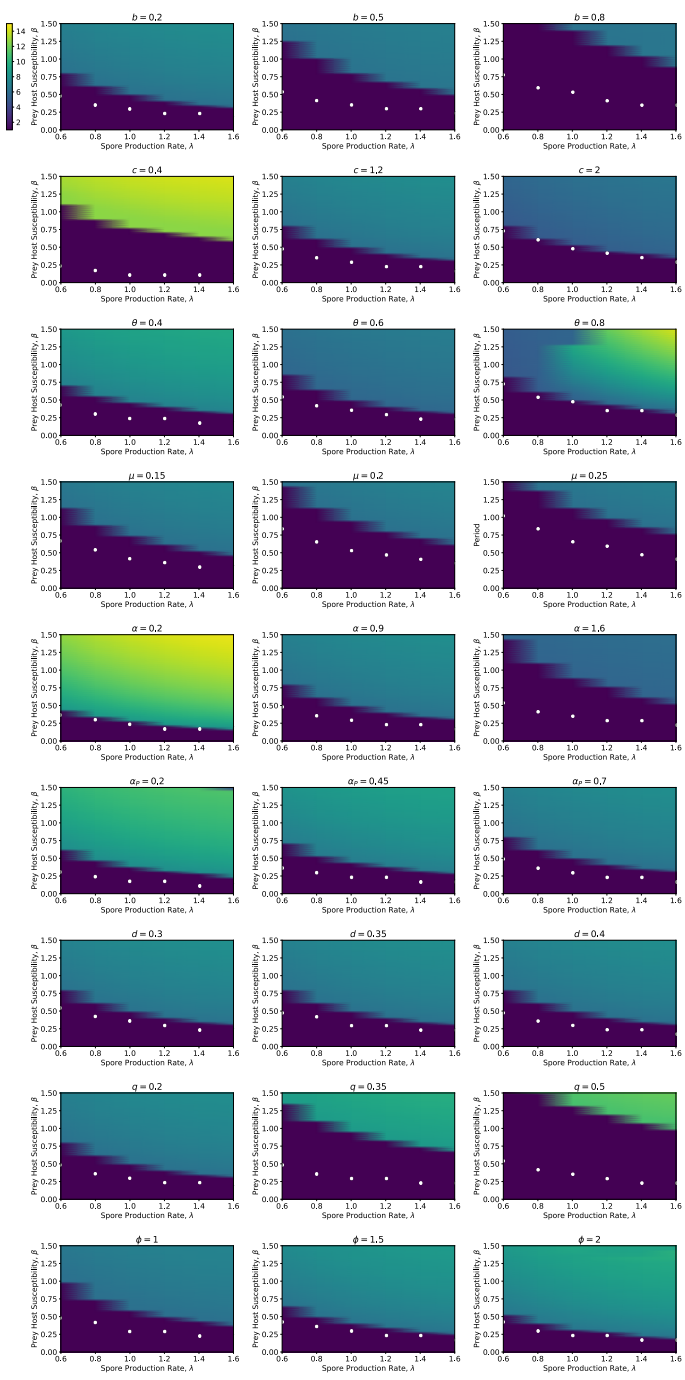

Figure B.7: Host susceptibility evolution as we vary spore production rate and another parameter simultaneously to show that the CSS points tend to stay in the equilibrium region.

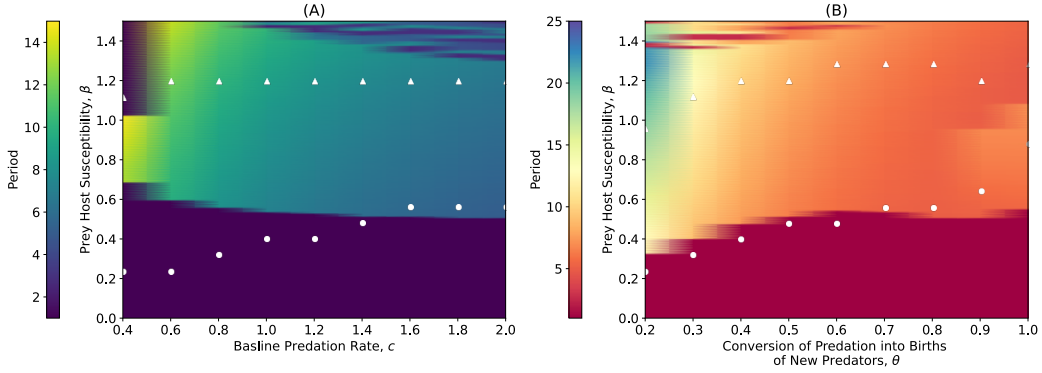

Figure B.8: Colour maps that display how host susceptibility β evolves against the period of the population dynamics when costs are decelerating as we vary the baseline predation rate, c (A) and the conversion rate of predation into the births of new predators, θ (B).

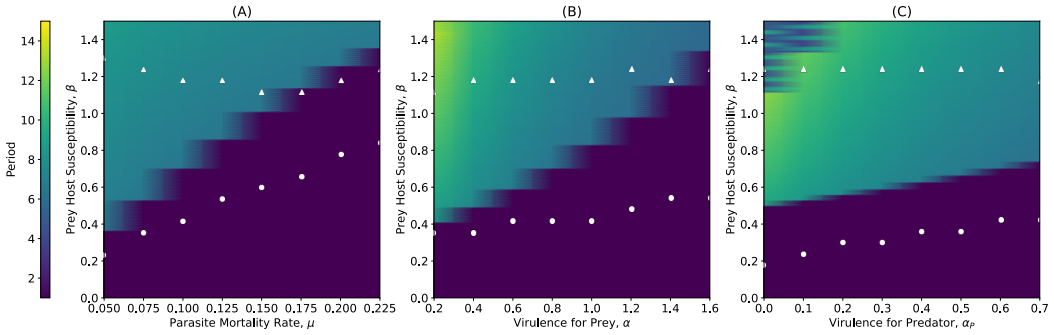

Figure B.9: Colour maps that display how host susceptibility β evolves against the period of the population dynamics when costs are decelerating as we vary parasite mortality rate, μ (A), prey virulence, α (B), and predator virulence, α_P (C).

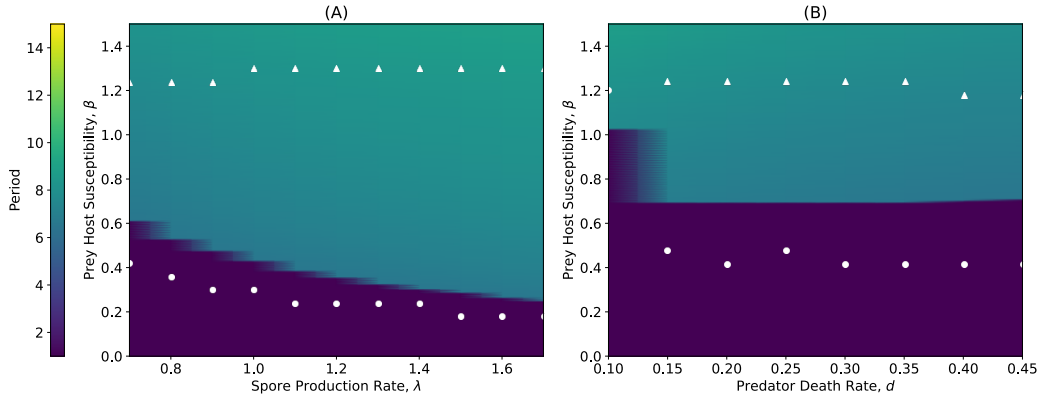

Figure B.10: Colour maps that display how host susceptibility β evolves against the period of the population dynamics when costs are decelerating as we vary the spore production rate, λ (A), and predator mortality rate, d (B).

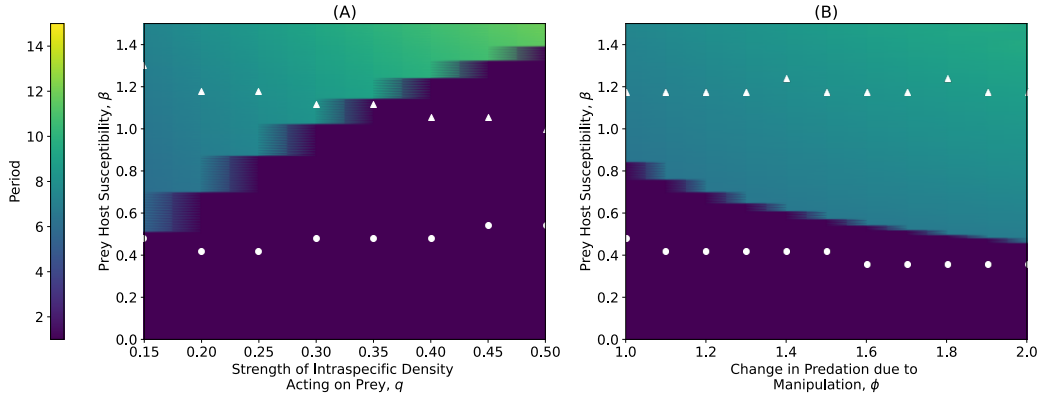

Figure B.11: Colour maps that display how host susceptibility β evolves against the period of the population dynamics when costs are decelerating as we vary the strength of intraspecific density dependence acting on prey, q (A), and the change in predation due to manipulation, ϕ (B).

Appendix C

Appendix: Do fluctuating ecological dynamics result in parasite extinction when stochastic effects are accounted for?

We include plots where only a single parameter is varied instead of two simultaneously. For each parameter value we run the stochastic model fifty times and display the survival times of the infected prey as a pie chart.

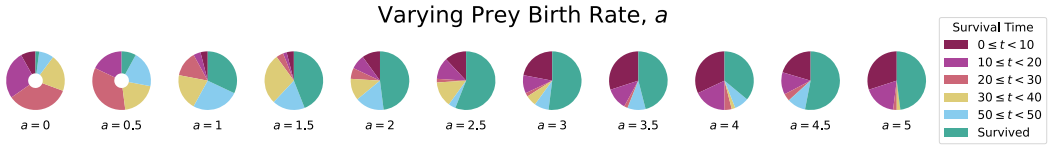

Figure C.1: Pie charts showing infected prey survival times in 50 stochastic simulations when we vary prey birth rate a. The white circles indicate predator extinction occurred in all of the stochastic simulations. Standard parameter values are $\alpha = 0.05$, $\alpha_P = 0.05$, $a = 3$, $b = 0.03$, $d = 1.1$, $\theta = 1$, $c = 0.06$, $q = 0.005$, $\phi = 1$, $\beta = 1$, $\lambda = 0.01$, and $\mu = 0.15$.

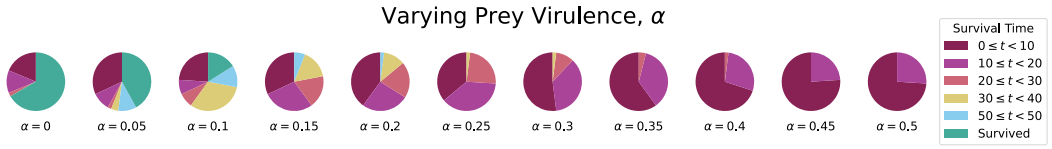

Figure C.2: Pie charts showing infected prey survival times in 50 stochastic simulations when we vary prey virulence α. Standard parameter values are as in figure C.1.

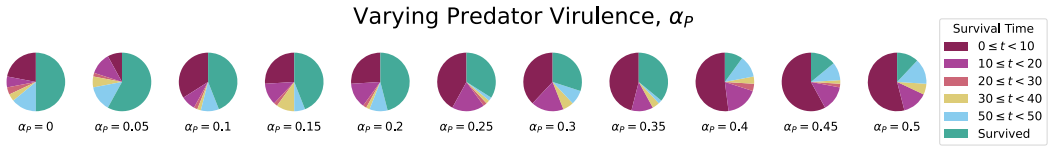

Figure C.3: Pie charts showing infected prey survival times in 50 stochastic simulations when we vary predator virulence α_P. Standard parameter values are as in figure C.1.

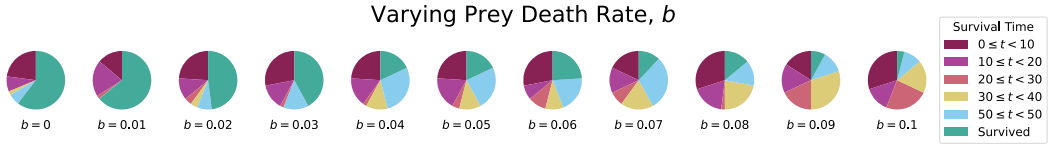

Figure C.4: Pie charts showing infected prey survival times in 50 stochastic simulations when we vary prey mortality rate b. Standard parameter values are as in figure C.1.

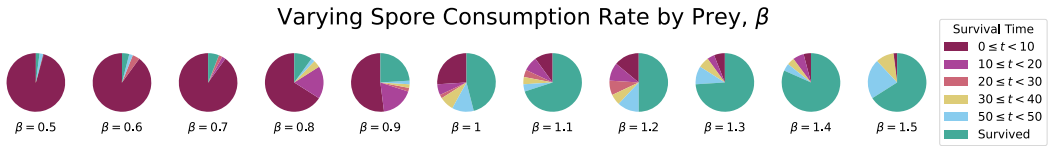

Figure C.5: Pie charts showing infected prey survival times in 50 stochastic simulations when we vary the spore consumption rate of spores by prey β. Standard parameter values are as in figure C.1.

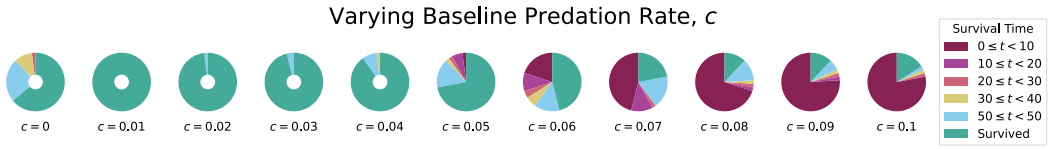

Figure C.6: Pie charts showing infected prey survival times in 50 stochastic simulations when we vary the baseline predation rate c. The white circles indicate predator extinction occurred in all of the stochastic simulations. Standard parameter values are as in figure C.1.

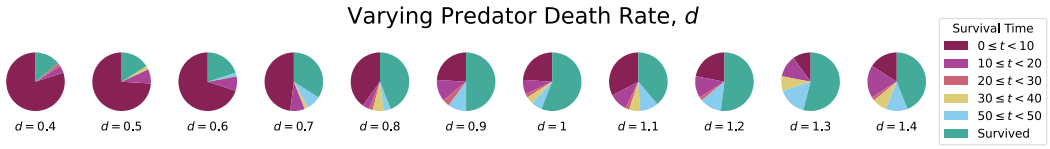

Figure C.7: Pie charts showing infected prey survival times in 50 stochastic simulations when we vary predator mortality rate d. Standard parameter values are as in figure C.1.

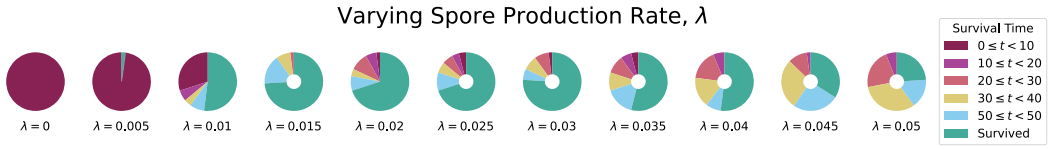

Figure C.8: Pie charts showing infected prey survival times in 50 stochastic simulations when we vary the spore production rate λ. The white circles indicate predator extinction occurred in all of the stochastic simulations. Standard parameter values are as in figure C.1.

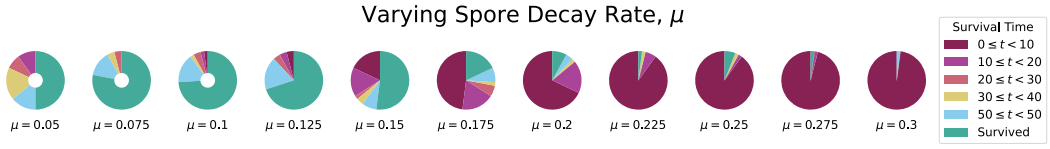

Figure C.9: Pie charts showing infected prey survival times in 50 stochastic simulations when we vary parasite mortality rate μ. The white circles indicate predator extinction occurred in all of the stochastic simulations. Standard parameter values are as in figure C.1.

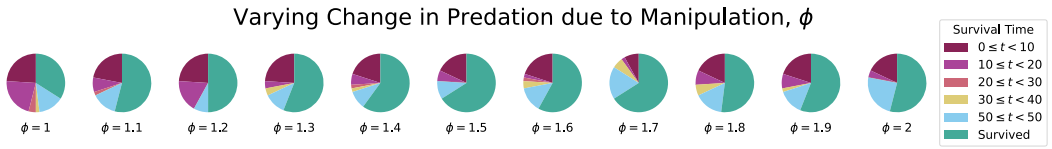

Figure C.10: Pie charts showing infected prey survival times in 50 stochastic simulations when we vary the change in predation due to manipulation ϕ. Standard parameter values are as in figure C.1.

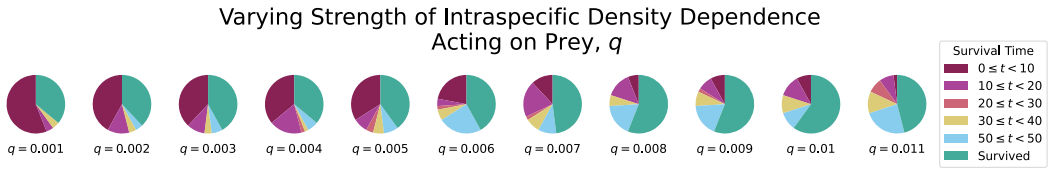

Figure C.11: Pie charts showing infected prey survival times in 50 stochastic simulations when we vary the strength of intraspecific density dependence acting on prey q. Standard parameter values are as in figure C.1.

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