The perturbation effect in wildlife systems: An emergent property of simple models

by

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Abstract

Population reduction is often used as a control strategy when managing infectious diseases in wildlife populations, however it disrupts existing social structures and increases movement of infectives due to the vacuum effect, which may lead to enhanced disease transmission. Using a generic non-spatial model, key characteristics of disease systems are identified for which such effects reduce or even reverse the disease control benefits of population reduction. If population reduction is not sufficiently severe, then enhanced transmission can lead to the perturbation effect, whereby disease levels increase or disease can be stabilised where it would otherwise be unstable. Perturbation effects are enhanced for systems with low levels of disease, e.g. low levels of endemicity or emerging disease.

Mechanisms observed in real systems are examined for their role in the perturbation effect. If population reduction is non-random and fails to target infected individuals, then vertical transmission (an important mechanism in many diseases including tuberculosis and paratuberculosis) can lead to the perturbation effect if horizontal transmission is low. The perturbation effect can also arise when population reduction preferentially targets resistant individuals, or mature individuals with low susceptibility, a factor implicated in wild boar and classical swine fever.

In a stochastic spatial model of demography and disease dynamics with density dependent dispersal (implicated in the spread of rabies in foxes, and tuberculosis in badgers and wild boar due to the vacuum effect), enhanced transmission is found to arise implicitly as an emergent property of the disease-system, even when population reduction is entirely random. Culling strategies are examined, and the spatial heterogeneity of distribution of culling resources and timing of culling intervals are shown to influence the perturbation effect. Whilst the perturbation effect may not always be apparent, the various effects modelled are likely present in many disease systems, mitigating the results of population reduction.

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Author's Declaration

I declare that the work contained in this thesis is my own, and has not been submitted for any other degree or award.

Chapter 1

Introduction

1.1 Animal health and wildlife disease

Maintaining animal health is essential to farming, and this includes treatment and prevention of infectious diseases. One source of infection is from sympatric wildlife, which can act as a reservoir for livestock diseases: this means that, even though an infection may be successfully removed from livestock, it can persist in the wildlife population, to be later reintroduced to the livestock. This is a consequence of the existence of multihost pathogens (e.g. bovine tuberculosis or rabies), which are capable of infecting a variety of species.

Around 61% of human infectious diseases are zoonotic, such as rabies, bovine tuberculosis, malaria, H1N1 influenza, cholera, and many others, and around 75% of zoonotic diseases have a wildlife origin (Cleaveland *et al.*, 2001; Taylor *et al.*, 2001; Jones *et al.*, 2008). Wildlife diseases are therefore an important problem for livestock production and welfare, and disease control must consider the threat of wildlife reservoirs, and make use of appropriate techniques to prevent reinfection.

1.2 Wildlife disease control

There are three basic approaches to disease control (Wobeser, 1994; Carter *et al.*, 2009): (*i*) reduce reproduction of the pathogen (e.g. via vaccination of susceptible hosts, or treatment of infected hosts), (*ii*) reduce host density (e.g. via dispersing, culling, or controlling reproduction), or (*iii*) reduce contact between susceptible and infected animals (e.g. via controlling the environment and restricting movement). Reducing host density is the most common approach to managing disease in wildlife, and essentially involves some form of

population reduction.

1.2.1 Population reduction

Population reduction has traditionally been used in disease control of wildlife populations (Wobeser, 1994), particularly when the wildlife species acts as a reservoir for livestock diseases (Artois *et al.*, 2001). Its use is inspired by traditional epidemic models, such as those by Anderson & May (1979), and the aim is twofold: to reduce the absolute number of infected animals, and to reduce contact between healthy and infected animals — and thus disease transmission rate — leading to a reduction in disease prevalence. An important consideration is the balance between animal health and conservation of the wildlife species, and it is usually not desired to eliminate the entire wildlife species, but merely to reduce numbers to the level where the disease can no longer persist. This is made possible due to the existence of a threshold susceptible population size N_T (Kermack & McKendrick, 1927), below which the disease is not spread fast enough to be maintained. This threshold is affected by specific host-pathogen combinations.

A useful way of comparing the various host-pathogen combinations is the basic reproduction ratio, R_0, which is the expected number of secondary infections produced in a completely susceptible population, when a single typical infective is introduced. If $R_0 > 1$, then a disease may invade a population and is expected to persist, otherwise it is expected to die out. When the disease is endemic, then another measure of R_0 is the ratio of the population size to the number of non-infectives (which therefore must be ≥ 1). Much work has been done to obtain R_0 for different diseases and disease systems (Diekmann *et al.*, 1991). When the rate of disease transmission depends on the number of infectives in the population (e.g. many airborne or waterborne diseases), then transmission is referred to as "density dependent", and one of the results of calculating R_0 leads to the concept of the threshold host density. Note that some diseases (e.g. sexually transmitted diseases) do not depend on number of infectives present, but rather the proportion of infectives (the prevalence), in which case they are referred to as "frequency dependent"; in these cases there is no threshold population size to aim for when culling (McCallum *et al.*, 2001), and frequency dependent transmission with high disease induced mortality may be associated with extinction in small populations (Beeton & McCallum, 2011). However, both R_0 and thresholds may be difficult to measure, be affected by features of demography such as seasonality, and be blurred by stochasticity such that a disease may still fail to invade even if $R_0 > 1$ (Diekmann & Heesterbeek, 2000; Lloyd-Smith *et al.*, 2005b).

Disease control methods to reduce R_0 to below 1 may take several forms, including vaccinating individuals (reducing the number of susceptibles), fertility control, and partitioning of groups into smaller sub-populations to prevent contact. It has, however, been observed that control measures featuring population reduction rarely include evaluation of the desired level of population decrease, and attempts are often offset by the compensatory effects of immigration and compensatory reproduction (Artois *et al.*, 2001).

1.2.2 Examples of population reduction: success and failure

Population reduction has had mixed success in controlling a variety of wildlife diseases. Complete host eradication from an area may be an option, however conservation is frequently an important issue, whence the goal is to reduce host density. The four main methods are hunting, trapping, gassing and poisoning (Carter *et al.*, 2009).

Gassing, which involves flooding host habitats with poisonous gas, has been used to successfully reduce numbers of red foxes (*Vulpes vulpes*) (Müller, 1971), striped skunks (*Mephitis mephitis*) (Gunson *et al.*, 1978), and vampire bats (*Desmodus rotundus*) (Fornes *et al.*, 1974) for rabies control (Carter *et al.*, 2009). However, gassing may be non target-specific, and difficult to deliver to extremities of complex burrow systems.

Poison, with toxic baits, can be an effective culling method for wild animals over large areas (Carter *et al.*, 2009). However, poison often has very low specificity, leading to high mortality rates in species other than the target, e.g. use of strychnine in rabies control to remove foxes in Alberta, Canada, also resulted heavy removal of coyotes (*Canis latrans*), wolves (*Canis lupus*), lynx (*Lynx* spp.), and bears (*Ursus* spp.) (Ballantyne & O'Donoghue, 1954). Also, prolonged exposure to poison may lead to either resistance or aversion to poison baits via selection for neophobia traits (e.g. trap shyness), reducing its effectiveness (Bomford & O'Brien, 1995; Leung & Clark, 2005).

Hunting (either by shooting or using trained dogs) is highly species-specific, and can be implemented selectively, targeting by age or gender classes, and even sometimes by infectious status (Carter *et al.*, 2009). It has been used to successfully remove brushtail possums (*Trichosurus vulpecular*), which severely damage native ecosystems (Payton, 2000) and are the primary wildlife reservoir of bTB in New Zealand. Use of hunting may be problematic when some hosts are not accessible to the hunters, but this can often be supported by use of dogs, which were used to successfully remove brushtail possums from many offshore islands, during the final stages of possum eradication when host density was low (Brown & Sherley, 2002). However, recreational or sports hunters may not wish

to significantly suppress a population size because they hope to maintain a viable population for future harvesting. Also, hunting with dogs has been associated with increased ranging behaviour (Maillard & Fournier, 1995; Artois *et al.*, 2001), which can promote the geographical spread of disease.

Trapping, with devices to either capture or kill the target, is one of the most important methods of disease management in wild carnivores (Carter *et al.*, 2009). When combined with lethal dispatch, it is very labour intensive, but also extremely target specific. The effectiveness of trapping may, however, be reduced by selection for trap-shy individuals, and trappability may vary greatly between different species, and age groups within species (Tuyttens *et al.*, 1999), which could lead to unintentionally selective culling.

Even when there are no such issues carrying out culling, it is not always successful. Tasmanian devils (*Sarcophilus harrisii*) are threatened with extinction by devil facial tumour disease (DFTD), an infectious cancer with a very high mortality rate. Despite being easily trappable, and infectives easily identifiable, culling has so far failed to remove the disease, mostly because of a lengthy latent period and frequency dependent transmission (as DFTD is spread by biting during mating). Disease models by Beeton & McCallum (2011) suggest that culling alone is unlikely to prevent extinction of the species.

Control of Classical Swine Fever (CSF) in wild boar (*Sus scrofa*) by shooting was attempted in Europe in the 1990s, but poorly documented, and no methods were used to assess the culled fraction of the population. Compensatory reproduction quickly allowed population levels to recover, and persistence of the disease was commonly observed (Artois *et al.*, 2001). Even when eradication was claimed, persistence of antibodies in juveniles suggested otherwise. Since recovery from CSF can lead to immunity, high numbers of recovered can deplete the susceptible population to below the threshold density required for disease persistence. Hunting of adults was more likely to remove such immune individuals, to be replaced with susceptible young due to compensatory reproduction, whereas without hunting, the disease was expected to die out within a year or two. Studies showed that the level of culling necessary to control disease was both greater than the level provided by existing hunting (Artois *et al.*, 2001), and should be targeted at the juveniles (aged 6–18 months). Following modelling of the infection by Guberti *et al.* (1998), control measures recommended that hunting should stop as soon as CSF is detected, in order to prevent dispersal from infectious herds, and limit the risk of transmission to neighbouring groups (Laddomada, 2000).

Following the identification of badgers (*Meles meles*) as a key wildlife host for bTB in

the 1970s, population reduction has been at the centre of bTB control to protect sympatric cattle populations. Since 1973, DEFRA (previously MAFF) have employed a number of population reduction strategies to reduce transmission of bTB from badgers to cattle. From 1975 to 1982, following detection of bTB in cattle attributed to badgers, badger populations up to 1 km from the farm boundary were sampled, and infected setts were gassed with hydrogen cyanide, with sites revisited for two years to prevent reintroduction from immigrant badgers; however, despite being one of the most effective methods of disease control (Smith *et al.*, 2001a) gassing ceased on welfare grounds, as low concentrations in sett extremities led to serious suffering in some animals (Dunnet *et al.*, 1986). From 1982 gassing was replaced by cage trapping due to these welfare concerns, and badger social groups surrounding infected farms were removed in increasing rings, until a ring of uninfected groups had been removed (the average size of the control areas was 7 km^2); from 1986 to 1993 an interim strategy was introduced, where badger removal was confined to land used by reactor cattle, or the whole farm if the origin of the infection could not be determined. During this time, there was no significant decline in the number of infected herds (MAFF, 1993).

In 1998 The Randomised Badger Culling Trial (RBCT) was launched, to investigate the effects of reactive and proactive population reduction on cattle herd breakdowns. They concluded that population reduction did not reduce disease incidence — in fact it led to its increase.

1.3 The perturbation effect

The RBCT was a huge ecological experiment; it focused on 30 areas, each measuring 100 km^2 and located in regions of high bTB risk to cattle. These areas were grouped into 10 triplets, and the areas within each triplet were randomly assigned to three different treatments: widespread proactive culling, aiming to maintain low badger densities; localised reactive culling; and an 'experimental control' with no culling (Woodroffe *et al.*, 2008)

Localised reactive removal of badgers in response to a bTB outbreak in cattle was found to be ineffective for control of bTB in cattle and indeed resulted in an increase in incidence (Donnelly *et al.*, 2003). In contrast, proactive badger population reduction reduced the incidence of bTB in cattle in the removal area; however, incidence increased in adjacent areas (Donnelly *et al.*, 2006), with an overall net increase in bTB incidence. As a result

it was concluded that badger population reduction could not contribute meaningfully to the control of cattle bTB in Britain (Independent Scientific Group, 2007; Woodroffe *et al.*, 2008).

Since this effect was considered a consequence of social perturbation, the increase in disease incidence following population reduction is known as the "perturbation effect" (Tuyttens *et al.*, 2000a; Macdonald *et al.*, 2006; Carter *et al.*, 2007; Vicente *et al.*, 2007). This is a convenient term to describe the enhanced disease transmission, and is used throughout this thesis.

1.3.1 Suggested mechanisms for the perturbation effect

Carter *et al.* (2007) reviewed several mechanisms believed to be responsible for the perturbation effect in badgers. Population reduction disrupts the population, leading to:

- The "vacuum effect". This is a tendency for neighbouring individuals to disperse into a culled area to seek new territory (Macdonald, 1995), which has been observed or suspected in many species including foxes (Macdonald, 1995), badgers (Tuyttens *et al.*, 2000a; Carter *et al.*, 2007; Woodroffe *et al.*, 2008), wild boar (Artois *et al.*, 2001), possums (Barlow, 1994), grizzly bears (*Ursus arctos horribilis*) (Mace & Waller, 1998), and lions (*Panthera leo*) (Woodroffe & Frank, 2005; Davidson *et al.*, 2011).

- Territorial disruption. This is the tendency for animals to ignore previously established territorial boundaries, and increase contact with neighbouring social groups.

- Increased ranging behaviour. This can lead to a greater chance of contact with neighbouring social groups and sympatric livestock populations.

Davidson *et al.* (2008) show that social structures may have a strong influence on disease persistence and prevalence. These behaviour changes may lead to increased contact between animals, and therefore higher than expected disease transmission rates, contrary to those predicted by traditional disease models.

This suggests that considering the ecology of a host-pathogen disease system, in particular behaviour that determines population mixing and structure, is a good starting point when trying to explain the perturbation effect. However, while these mechanisms have been implicated in the perturbation effect, little work has been done to properly understand it. In order to understand the perturbation effect, it is important to understand how

wildlife ecology is affected by population reduction, specifically demography and disease dynamics.

1.4 Wildlife population ecology

Population demography is the set of behaviours and rates that define the population dynamics, i.e. how a population changes through fertility, mortality, and movement. These processes are often highly dependent on the environment and the present state of the population, and play a considerable role in disease transmission thus making them important mechanisms to include when studying disease spread.

1.4.1 Reproduction and mortality

Population numbers change as individuals are born and die, and the patterns of birth and death can vary strongly between species. Reproduction generally takes place in the adult phase of an animal's lifecycle. In some species it occurs seasonally, while in others it may occur at any time. Fecundity may vary: some species give birth to large litters, while others only give birth to one offspring at a time. Reproduction is often limited by resources, and not all animals within a given population get the opportunity to reproduce, which can lead to density dependent growth, and population equilibria. Mortality can happen at any time due to senescence, predation, disease, accident or lack of resources. Mortality can remove infected animals from a population, reducing disease transmission rates.

Interaction of different reproduction / mortality combinations can lead to different growth patterns, with the extremes characterised by so called r and K species (MacArthur & Wilson, 1967). r species (e.g. bacteria, weeds and rodents) have fast reproduction rates, and tend to rapidly fill ecological niches, but just as rapidly can exhaust resources or face a hostile change in environment and decrease in numbers. This leads to boom and bust style population dynamics.

K species (e.g. elephants, trees, humans) on the other hand (so called because their numbers tend to remain close to the population equilibrium, K) tend to have low growth rates, and longer lives. K species may be better at sustaining a disease, provided the disease induced mortality rates are not too high. In most cases, species exist in a continuous spectrum between these two extremes, however it is useful to consider how different places in the spectrum react to population reduction, and how that in turn affects disease

transmission.

1.4.2 Social organisation and structure

While it is often convenient when modelling to assume that the host population is homogeneously mixed (Anderson & May, 1992), populations do not normally exist as a homogeneous group of identical individuals (Carter *et al.*, 2009). Individuals may be divided up socially in many different ways, such as by sex, age, dominance, or core risk groups (Cross *et al.*, 2009), and a mixing matrix can be used to incorporate data on contact rates within and between classes (Blower & McLean, 1991).

Populations may also be divided spatially, when individuals within groups aggregate to form smaller sub-groups; this can add considerable heterogeneity to a system, which can lead to processes (particularly density dependent processes) occurring at different rates within different sub-populations.

The infective population itself may not be homogeneous, as it is suggested that typically 20% of infectives may be responsible for 80% of transmission potential (Woolhouse *et al.*, 1997), which is sometimes referred to as the "20/80 rule". For example, when modelling badgers and bTB, infectives have been divided into excretors (of the bacterium) and super-excretors (Smith *et al.*, 1995b, 2001b), and the latter may also be subject to increased mortality rates (Wilkinson *et al.*, 2000).

1.4.3 Dispersal

While animals may aggregate to form social groups, they may also move between social groups via dispersal; this process is important for finding resources (e.g. food and mating opportunities), and for preventing inbreeding. When more food resources are desired, per capita dispersal rate may be greater into social groups with fewer members; prior to dispersal, individuals may sometimes "test the water" by examining nearby sites in order to check suitability (Cheeseman *et al.*, 1998; Rogers *et al.*, 1998; Bodin *et al.*, 2006). These processes can lead to density dependent dispersal (Johst & Brandl, 1997; Bowler & Benton, 2005), which can help to reduce heterogeneity in population densities, and is a potential driver of the vacuum effect. In addition, dispersal may be a stressful event, leading to increased susceptibility following movement (Carter *et al.*, 2009).

Hess (1996) discusses how increased movement in metapopulations (a set of populations connected by dispersal) can reduce the probability of metapopulation extinction, but

also increase the prevalence, incidence, and geographical spread of disease in the overall population.

1.4.4 Population reduction and wildlife ecology

Here lies the gap in our current knowledge leading to several questions, including:

- What is the effect of population reduction on wildlife disease dynamics?
- Can a behaviour change that is a natural formulation of demography and disease transmission lead to a perturbation effect? (i.e. can a perturbation effect occur without adding explicit mechanics not representative of any specific biological processes)?
- How can a behaviour change arise implicitly in epidemic models?
- How does population reduction interact with behaviour change mechanisms, and how can it contribute to the perturbation effect?
- How best to implement population reduction in order to avoid the perturbation effect?

1.5 Modelling wildlife ecology and disease dynamics

Disease transmission can occur when a susceptible individual comes into contact with infectious material, either directly from an infected animal (e.g. via a bite, or respiratory transmission), or indirectly via a vector or infected food and water etc. Transmission therefore depends on both contact rates and susceptibility, and both of these depend on the behaviour of the individuals; for example, avoidance behaviour may offer some protection, while close proximity may increase transmission.

1.5.1 Compartmental models and complexity

A powerful tool in epidemiology is the compartmental model, which has been frequently used to study disease dynamics (Kermack & McKendrick, 1927; Anderson & May, 1992). Compartmental models reduce population diversity to a few important categories, primarily disease status (e.g. susceptible, infected, vaccinated etc.), and then consider how different mechanisms affect the rate of change of those categories.

Some of the most common epidemiological models include SI, SIR, SIS, and $SEIR$, where S represents susceptible, E exposed, I infected, and R resistant or recovered. While

simple, these capture the fundamental features of many infection dynamics, and can be used to represent a wide range of different host-pathogen systems such as bTB, measles, rabies, and the common cold.

Most early models, e.g. Kermack & McKendrick (1927); Anderson & May (1978), measured variables at the population level, e.g. where $I(t)$ reflects the total number of infectives in the population at time t; these models are some of the simplest, and hence easiest to analyse algebraically, and solve numerically (Keeling & Danon, 2009). However, population structure often plays a significant role in disease dynamics (Davidson *et al.*, 2008), as populations may segregate into similar groups. Recent empirical studies have highlighted the role of this structure in disease transmission, e.g. in badgers (Shirley *et al.*, 2003; Vicente *et al.*, 2007), birds (Kulkarni & Heeb, 2007), and red deer (*Cervus elaphus*) (Blanchong *et al.*, 2007). By subdividing the population and considering each group as a separate variable (e.g. where $I_{f,1}(t)$ and $I_{m,3}(t)$ might reflect the number of female infectives of age 1–2, and the number of male infectives of age 3–4 respectively) the model can accommodate more complicated behaviour, and have better predictive power (e.g. testing the effects of vaccination on different age groups). In a similar manner, spatial structure is often added by dividing the population into discrete patches, and considering dispersal and inter-group infection between patches, e.g. White & Harris (1995a). By moving from modelling at the population level to the individual level, an even wider range of biological problems and realistic assumptions may be included (Keeling & Danon, 2009).

However, there are several drawbacks to increasing model complexity (Keeling & Danon, 2009): including multiple categories can lead to many category interactions (e.g. male-juvenile-susceptible etc.) which can result in considerable complexity, and it can be expensive and difficult to obtain the data required to parametrise such models, even in well studied species, and especially in wildlife populations (Artois *et al.*, 2001). Consequently, there is a trade off between better approximation of reality, and confidence in parameters. Next, algebraic complexity increases, and becomes less useful; numerical solutions become more important. Finally, where numeric solutions are required, computation time becomes an issue, although computational power is continually increasing, providing greater scope for model complexity.

Where data are insufficient, complex models with large numbers of parameters can be "tuned" to better account for observed behaviour; however a parsimonious approach may provide much of the required behaviour, with little loss in predictive power. Also, it is often easier in a simpler model to understand which mechanisms account for a given

pattern of behaviour, and thus improve biological understanding of the problem. For these reasons, and in an attempt to gain a thorough understanding of generic disease dynamics, the models used in this thesis start from the simplest possible, building up to include extra complexity only where necessary.

1.5.2 Mass action models and stochasticity

The law of mass action in Chemistry states that the rate of a chemical reaction containing only a single mechanical step is proportional to the product of the concentrations of the molecular species involved. When applied to disease transmission, densities of susceptible and infective animals are considerably smaller, and heterogeneity and stochasticity play a considerable role (Keeling, 1999; Marion *et al.*, 2002).

Disease models often assume that disease transmission occurs via mass action, i.e. if the density of susceptibles and infectives are S and I respectively, then the number of new infectives per unit area, per unit time is βSI, where β is the transmission coefficient (McCallum *et al.*, 2001), and this is referred to as "density dependent transmission"; however, this assumes that susceptibles and infectives are well mixed, and all such individuals are equally likely to contact one another. In the case of large populations (e.g. 10,000 individuals), or in small populations where the disease spread is severely limited (e.g. sexually transmitted) it is unlikely that all individuals are able to make contact, in which case only the proportion of infectives (the prevalence) is relevant. Here, the number of new infectives per unit area, per unit of time is $\beta SI/N$, where N is the population size, and this is referred to as "frequency dependent transmission". It should be noted that in a spatial model with a large population divided into multiple small sub-populations, each sub-group may be small enough to consider density dependent transmission, while transmission between neighbouring groups either via dispersal of infectives, or between group transmission, is intrinsically frequency dependent.

When modelling disease systems, the starting place is often a deterministic model, however these tend to overestimate transmission rates for low population densities, and it is therefore useful to consider stochastic models. Deterministic models assume completely mixed populations (or sub-populations), however this is frequently not the case, as infected animals tend to be highly aggregated, and do not provide the level of infection predicted by the mean field approximations given by the deterministic models (Marion *et al.*, 1998). Another advantage of stochasticity is that each realisation of a stochastic process is different, therefore taking the average of a large number of runs can capture the

variability of the epidemic profile (Keeling & Danon, 2009).

1.5.3 Comparison of deterministic and stochastic models

Both deterministic and stochastic models can be used to describe the dynamics of a host-disease system, and will give similar results, albeit with important differences. These are now compared and contrasted using a basic SI model as an example.

Both models share the same processes, with two time dependent parameters $S(t)$ and $I(t)$, which represent the number of susceptibles and infectives at time t. Density dependent birth occurs at intrinsic rate r and is limited by carrying capacity c, natural mortality occurs at per capita rate d, and infection is density dependent, and the coefficient of transmission is β. The deterministic model that describes these processes is

$$\dot{S} = rN(1 - N/c) - dS - \beta SI$$
$$\dot{I} = \beta SI - dI$$

where $N = S + I$, while the probabilities of each event over a small time interval δt, and the associated change in state space, are given for the stochastic model in Table 1.1. The stochastic model may be simulated using the Gillespie algorithm (Keeling & Rohani,

Event	**Rate**	δS	δI
Birth of S	$rN(1 - N/c)\delta t$	$+1$	0
Death of S	$dS\delta t$	-1	0
Death of I	$dI\delta t$	0	-1
Infection of S	$\beta SI\delta t$	-1	$+1$

Table 1.1: Event rates for the deterministic and stochastic SI model, and corresponding effects in the stochastic model.

2007), however this process is used throughout the thesis, and so is described in more detail here. The times between events are exponentially distributed according to the total event rate, which is the sum of the rates of each individual event in Table 1.1

$$R_{\text{tot}} = rN(1 - N/c) + dS + dI + \beta SI$$

The time until the next event is obtained by first choosing $y \sim \exp(R_{\text{tot}})$, and letting

$$\delta t = \min(y, \delta t_{\min})$$

(where $\delta t_{\min}$ may be convenient to ensure that time steps are not too great, e.g. when recording population values, or disrupting the population at specific times). The next event is then randomly chosen by generating $z \sim U(0, R_{\text{tot}}/\delta t)$, and letting the next event be

birth of S	if $z < rN(1 - N/c)$
death of S	if $z < rN(1 - N/c) + dS$
death of I	if $z < rN(1 - N/c) + dS + dI$
infection of S	if $z < rN(1 - N/c) + dS + dI + \beta SI$
no event	otherwise

This process is then repeated as necessary to obtain a realisation of the stochastic process given any set of initial conditions.

There are three equilibria, which can be found for the deterministic model by solving $\dot{S} = 0$, $\dot{I} = 0$ for S^* and I^*

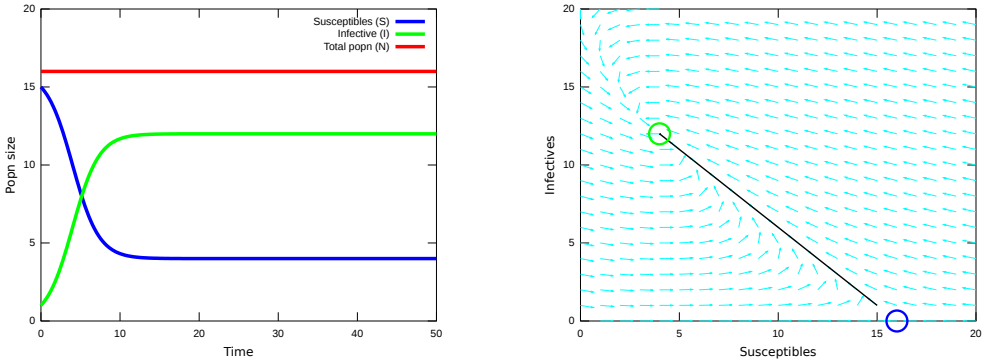
1. Population extinction $\{S_0^*, I_0^*\} = \{0, 0\}$
2. The disease free equilibrium $\{S_{\text{DF}}^*, I_{\text{DF}}^*\} = \{c(r-d)/r, 0\}$, and
3. The endemic equilibrium $\{S^*, I^*\} = \{d/\beta, c(r-d)/r - d/\beta\}$

Fig. 1.1 shows the results of solving the deterministic model numerically for $t \in [0, 50]$ years, and taking the mean and 95% confidence interval of 100 realisations of the stochastic model, using the parameters $r = 1$, $c = 20$, $d = 0.2$, and $\beta = 0.05$, starting from initial conditions $\{S(0), I(0)\} = \{15, 1\}$, which is near the disease free equilibrium. Phase portraits for both models are shown, overlaying a vector field for the deterministic model.

The main observation is that, while the general behaviour of both are similar, the endemic equilibrium of the stochastic model appears to contain fewer infectives than in the deterministic endemic equilibrium. In fact, in 22 out of the 100 realisations, the disease died out within the first 10 years. If these are removed, then the mean of the remaining realisations (see Fig. 1.2) is much closer to the deterministic model, however the phase portrait reveals that it is not identical, and still contains fewer infectives.

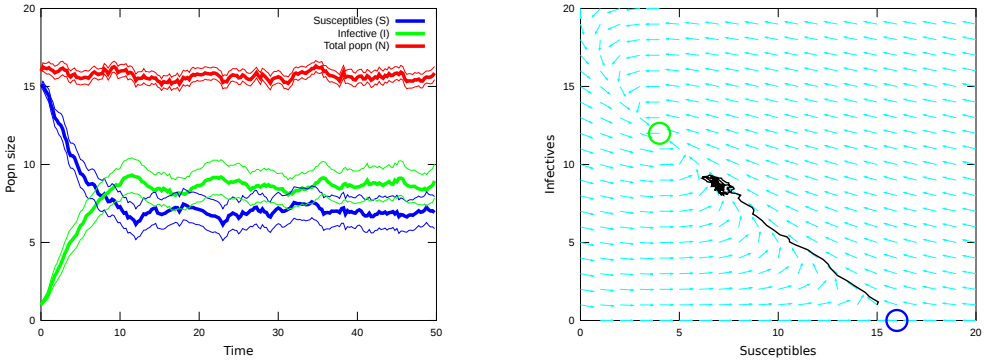
It is interesting to note that calculating $R_0 = S_{\text{DF}}^* \beta / d = 4$, and using the probability of stochastic fadeout of the disease (Lloyd-Smith *et al.*, 2005b) as $(1/R_0)^{I_0} = 0.25$, agrees with the number of realisations where the disease failed to invade.

The deterministic and stochastic models do give qualitatively similar results, although the deterministic model fails to account for the possibility of disease fadeout, and when this



(a) Deterministic trajectory

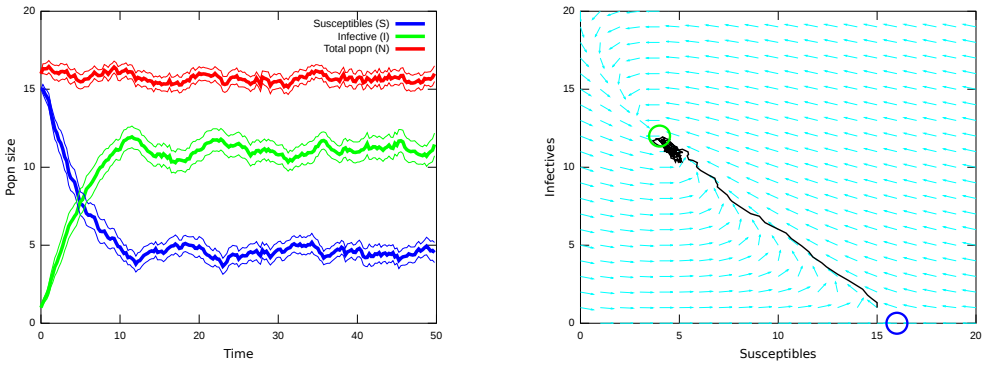
(b) Deterministic phase portrait



(c) Stochastic trajectory

(d) Stochastic phase portrait

Figure 1.1: Time trajectories and phase portraits of the deterministic and stochastic models (with 95% confidence intervals). The deterministic endemic and disease free equilibria are marked with green and blue circles.



(a) Stochastic trajectory, without extinctions

(b) Stochastic phase portrait, without extinctions

Figure 1.2: Time trajectories and phase portraits of the stochastic model with disease extinctions removed.

is corrected for by removing failed invasions, it still overestimates the number of infectives. In addition, the stochastic equilibrium does not remain fixed, but fluctuates continually, and the eventual fate of all stochastic realisations is for the disease — and indeed the entire population — to die out, although this may take a very long time if the population is large. In a spatial model, adjacent sub-populations may fluctuate differently, opening up population gradients that do not exist in the deterministic model, which may better account for the heterogeneities observed in wildlife populations.

This does not mean that the deterministic model should be rejected however, as it still predicted some of the dynamics correctly, and allowed for calculation of a point value of the endemic equilibrium to a reasonable degree, which would be considerably more difficult with the stochastic equations without solving the equations numerically (note that the endemic equilibrium is a probability distribution, not a point value). Techniques such as moment closure analysis can help to correct for the differences due to non-linearity between the deterministic and stochastic equations (Whittle, 1957; Krishnarajah *et al.*, 2005).

1.6 The thesis

1.6.1 Aims

The overall aim of this thesis is to increase our understanding of the perturbation effect, both generically and in specific host-disease systems, and to show how demographic factors may contribute to the perturbation effect. My aims are therefore to: (*i*) characterise and determine the dynamics of the perturbation effect; (*ii*) examine the role of population reduction, to find out what maximises or minimises the perturbation effect; and (*iii*) examine how demographic factors may contribute to the perturbation effect.

1.6.2 Thesis structure

Chapter 2 examines various properties of the perturbation effect. Using a generic non-spatial SI model, the effects of enhanced disease transmission subsequent to population reduction are investigated and characterised. Using a spatial stochastic model, density dependent dispersal is demonstrated to be a process that can account for the perturbation effect. The two models are compared and contrasted, and shown to be qualitatively similar.

Chapter 3 investigates how culling strategies may influence the perturbation effect. In particular, how different strategies, both spatially and temporally, using the same effort might give different results.

Chapter 4 investigates further mechanisms in a non-spatial context that may lead to the perturbation effect, especially when a population is subject to non-random population reduction. An SI model with vertical transmission, an SIR model, and an SI model with age structure are examined and found to be susceptible to the perturbation effect.

Chapter 5 provides a general discussion that places the research of each chapter and the thesis as a whole into context.

Chapter 2

Host behavioural responses reduce the efficacy of population reduction approaches to disease control

2.1 Background

The relevance of ecology to understanding the dynamics and persistence of infectious disease has long been recognised (Anderson, 1991), and ecological factors are critical to wildlife disease systems. Control of disease in wildlife is of considerable importance for managing risks to humans (Jones *et al.*, 2008; Daszak *et al.*, 2000) and livestock (Frölich *et al.*, 2002; Gortázar *et al.*, 2007), as well as for the conservation of wildlife species themselves (Cunningham, 1996; Daszak *et al.*, 2000, 2001; Evensen, 2008). Population reduction is a commonly employed strategy used to control disease in wildlife (Wobeser, 1994; Artois *et al.*, 2001) with the aim of reducing the number of infected animals and the overall size of key populations, leading to a reduction in rates of transmission, disease prevalence and risks to other populations. Application of this strategy is supported by theoretical evidence of a threshold for disease persistence below which disease becomes unstable and eventually dies out (Anderson & May, 1979; Wobeser, 1994; Carter *et al.*, 2009). However, there is growing evidence that population reduction may be less effective than standard analyses predict, and in some cases be counter-productive (see below). Such unexpected increases in disease prevalence following population reduction are often termed the "perturbation effect" (Carter *et al.*, 2007). Lloyd-Smith *et al.* (2005b) review the theoretical basis and empirical evidence for disease thresholds in wildlife concluding that important elements of wildlife ecology are neglected by current theories.

It is known that the social and spatial structure of host populations has significant implications for disease persistence and prevalence (Keeling, 1999; Davidson *et al.*, 2008). Population reduction disrupts existing social structures and this may lead to increased numbers of contacts (Tuyttens *et al.*, 2000a) and/or a greater proportion of agonistic encounters within or between groups (Swinton *et al.*, 1997; Tuyttens & Macdonald, 2000). Similarly, a change in susceptibility of individual hosts may also occur as a consequence of population reduction due to stress (Gallagher & Clifton-Hadley, 2000). Both effects will enhance disease transmission and are likely to be widespread and reduce or even reverse the efficacy of population reduction measures.

For example, management of rabies in foxes (*Vulpes vulpes*) has shown that vaccination is more suitable than culling, as the latter can destabilise social structure and lead to enhanced transmission rates (Macdonald, 1995; Artois *et al.*, 2001). Studies of the management of classical swine fever (CSF) in wild boar (*Sus scrofa*) recommend that hunting should cease following detection of the disease (Guberti *et al.*, 1998), in order

to discourage dispersal of infected individuals, and reduce risks to neighbouring groups (Artois *et al.*, 2001). The U.K. Randomised Badger Control Trial (RBCT) (Independent Scientific Group, 2007) showed that reactive culling of badgers (*Meles meles*) in response to a confirmed bovine tuberculosis (*Mycobacterium bovis*, bTB) herd breakdown in cattle, was associated with a 27% increase in the incidence of confirmed breakdowns, relative to survey-only trials (Donnelly *et al.*, 2003). Repeated reactive culling was also associated with increased bTB prevalence in badgers (Vial & Donnelly, 2012).

In this chapter, the potential for behavioural and demographic aspects of the ecology of wildlife species to reduce or reverse the efficacy of population reduction as a means of disease control is studied. The results are based on the analytical and numerical treatment of generic models of demography and disease dynamics in wildlife populations. In a non-spatial context, the potential that individual and collective behavioural responses to population reduction have on disease control is analysed. This framework is used to explore the demographic and epidemiological characteristics of wildlife disease systems that make them susceptible to such effects. It is then demonstrated that such impacts arise as an emergent property of spatial models of wildlife disease systems with density dependent dispersal. Finally, the significance of these results for disease control in wildlife is discussed.

2.2 Methods

2.2.1 A non-spatial model of demography and disease dynamics

Consider a generic single pathogen wildlife disease system with a fluctuating host population. The number of susceptible and infected individuals in the population at time t are $S(t)$ and $I(t)$ respectively, and the total population size is given by $N(t) = S(t) + I(t)$. Growth is assumed to be density dependent (logistic), with intrinsic reproduction rate r (the maximum rate that individuals can reproduce in optimal circumstances), limited by a carrying capacity c (the maximum number of individuals that the location being modelled can support). Natural mortality (from causes unrelated to disease or explicit population reduction measures) occurs at constant per-capita rate d, while disease induced mortality occurs at constant per-capita rate e. The rate of infection is a combination of susceptibility and contact rates between susceptible and infective individuals and here density dependent infection is considered (i.e. disease transmission depends on the density of infectives, I) with horizontal transmission rate β.

Population reduction is modelled as a constant per-capita death rate p which applies to all individuals regardless of disease status. As noted earlier such measures can alter host behaviour and hence contact rates. Therefore the horizontal disease transmission rate is modelled as $\beta + kp$. Here $k > 0$ represents any mechanism or combination of mechanisms that lead to increased contact rates or susceptibility in a host population subjected to population reduction at rate p. Note that this formulation represents a simplification in that the effect is linear in p, there is no lag as p changes and the effect is constant for the duration of the population reduction event.

In Appendix 2.A, it is shown how to formulate a simple non-spatial deterministic model that encapsulates the above assumptions. Also, this representation is simplified, removing the variables c and r by respectively scaling the variables S, I and N by $1/c$ to obtain values between 0 (empty) and 1 (at carrying capacity) and rescaling time by r. Analysis can then focus on the effects of population characteristics (parameters d and e), disease dynamics (β), population reduction (p), enhanced transmission (k) and the interactions between them. However, results for specific values of c and r can still be obtained by appropriate back scaling. The rescaled deterministic ordinary differential equations (ODEs) that combine the demography and disease dynamics described above with population reduction and a corresponding enhanced transmission resulting from explicit behavioural and implicit ecological (system) responses are given by:

$$\begin{aligned} \dot{S} &= N(1-N) - (d+p)S - (\beta + kp)SI \\ \dot{I} &= -(d+e+p)I + (\beta + kp)SI \end{aligned} \tag{2.1}$$

Three fixed points of this system of equations are derived in Appendix 2.A: population extinction, where $\{S, I\} = \{0, 0\}$; the disease free equilibrium, where $\{S, I\} = \{1-d-p, 0\}$; and the endemic equilibrium $\{S, I\} = \{S^*(p), I^*(p)\}$, where both the population and the disease persist. The stability properties of these equilibria are discussed in the Appendix. Note that the endemic equilibrium is written as a function of the reduction rate p, even though it also depends on other parameters, as this highlights the effect of population reduction.

2.2.2 A stochastic spatial model of demography and disease dynamics

In the stochastic spatial model, consider a set of sites on a lattice, where, at time t, the integer number of susceptibles and infectives in site i are $S_i(t)$ and $I_i(t)$ respectively. Since the stochastic model deals with numbers of individuals, these are not rescaled as

above. The demography and disease dynamics of each sub-population are governed by the same processes as for the non-spatial model, with the addition of dispersal and disease transmission within and between groups.

Dispersal is the movement of individuals between social groups, for the purposes of obtaining more resources such as food or reproductive opportunities (including inbreeding avoidance). In the model dispersal from any given site on the lattice occurs at constant per-capita rate m, into any of its nearest neighbouring sites. However, since this process may be mediated by the population levels in the destination site (Johst & Brandl, 1997; Bodin *et al.*, 2006) this is modified by a function $f(N_j)$, where N_j is the population at neighbouring site j. Consider a step function

$$f(N_j) = \begin{cases} 1 & \text{if } N_j < \alpha N^*_{\mathrm{DF}} \\ 0 & \text{if } N_j \geq \alpha N^*_{\mathrm{DF}} \end{cases} \tag{2.2}$$

where $N^*_{\mathrm{DF}} = c(r-d)/r$ is the population size in the disease free equilibrium, and α is the fraction of the disease free equilibrium at which the neighbouring site becomes accessible. Dispersal rates may also be affected by conditions in the source area, e.g. due to overpopulation, social exclusion, or lack of resources, lack of mating opportunities in small populations; however, these effects are not considered here.

Disease transmission rates within and between groups are denoted β_w and β_b respectively. The horizontal disease transmission rate in site j is therefore given by

$$H_i = \beta_w S_i I_i + \beta_b S_i \sum_j I_j$$

where the sum is over neighbouring sites of i. The total infection rate is given by $H = \sum_i H_i$ and the effective disease transmission rate is defined as

$$\beta_{\mathrm{eff}} = \frac{H}{(\sum_i S_i)(\sum_i I_i)}$$

The spatial model is implemented as a discrete state-space Markov process, to account for demographic stochasticity, with events and associated rates shown in Table 2.1, and simulated using the Gillespie algorithm (Keeling & Rohani, 2007). In the spatial model population reduction is parametrised by the probability that a site is targeted p_1 and the rate of removal of individuals within targeted sites p_2.

See Table 2.2 for a summary of parameters, symbols, and used in both the non-spatial and spatial models.

Event	**Rate**	δS_i	δI_i	δS_j	δI_j
Birth of S_i	$rN_i(1-N_i/c)\delta t$	$+1$	0	0	0
Death of S_i	$dS_i\delta t$	-1	0	0	0
Death of I_i	$(d+e)I_i\delta t$	0	-1	0	0
Infection of S_i	$H_i\delta t$	-1	$+1$	0	0
Dispersal of S_i to site j	$mzS_if(N_j)\delta t$	-1	0	$+1$	0
Dispersal of I_i to site j	$mzI_if(N_j)\delta t$	0	-1	0	$+1$

Table 2.1: Event rates and corresponding effects in the spatial stochastic model.

Parameter	**Symbol**	**Non-spatial**	**Spatial**	**Units**
Intrinsic reproduction rate	r	1	1	year^{-1}
Carrying capacity	c	1	20	—
Natural mortality rate	d	0.2	0.01	year^{-1}
Disease induced mortality rate	e	0.1	0.1	year^{-1}
Horizontal transmission rate	β	0.4	—	year^{-1}
background	β_e	—	0	year^{-1}
within group	β_w	—	0.5	year^{-1}
between groups	β_b	—	0	year^{-1}
Dispersal rate	m	—	0.1	year^{-1}
threshold value	α	—	0.7	—
Population reduction rate	p	0.1	—	year^{-1}
coverage	p_1	—	0.2	—
removal within sites	p_2	—	0.5	year^{-1}
Disease enhancement	k	5	—	—

Table 2.2: A summary of the parameters and their symbols used in the non-spatial and spatial models are described here. Values shown indicate both the parameters and their default values used in the spatial and non-spatial models.

2.2.3 Measuring the perturbation effect

The magnitude of the perturbation effect at time t after the application of population reduction at rate p is defined as

$$\Pi(t;p) = I(t;p) - I(t;0) \tag{2.3}$$

A population that is in equilibrium $I^*(0)$ prior to the application of population reduction at rate p, will reach a new equilibrium $I^*(p)$. The persistent perturbation effect is defined as

$$\Pi_{\text{eqm}} = \max\{I^*(p), 0\} - \max\{I^*(0), 0\} \tag{2.4}$$

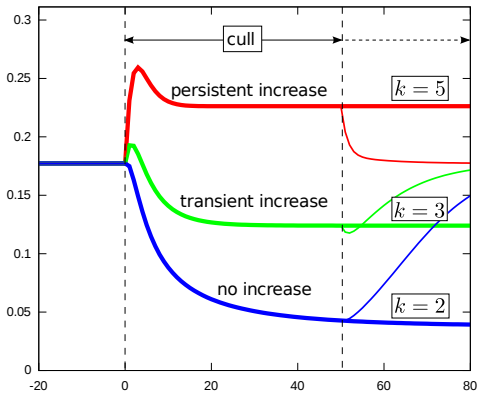
Note that while I^* may be negative, in this case the disease becomes unstable, and $I(t) \to 0$, hence the restrictions (see Appendix 2.A.3 for more details). In the results, both the persistent Π_{eqm} and transient $\Pi(t;p)$ perturbation effects are studied. In the spatial case the proportion of sites containing infectives, $P_I(t;p)$, are also examined as the basis for measuring the perturbation effect

$$\Pi_{\text{sites}}(t;p) = P_I(t;p) - P_I(t;0) \tag{2.5}$$

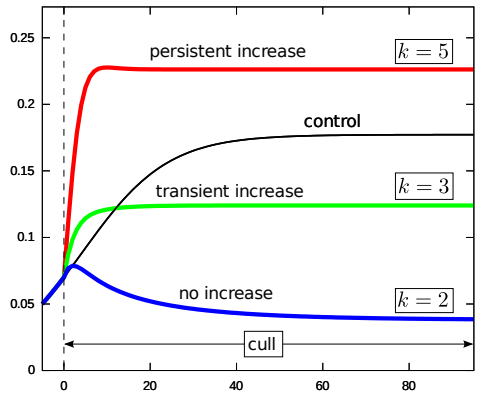
2.3 Results

2.3.1 Explicit enhancement of disease transmission induced by population reduction

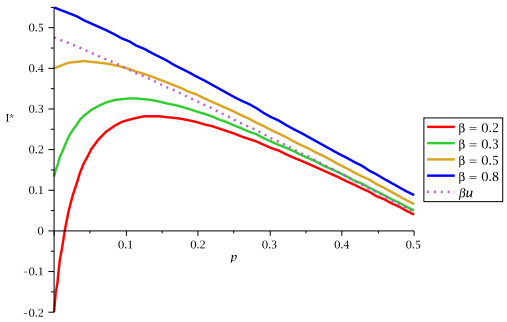
The perturbation effect in the deterministic non-spatial model is considered first. Several features of the perturbation effect caused by increased horizontal disease transmission in response to population reduction are demonstrated in Fig. 2.1. For different levels of transmission enhancement k, a range of outcomes are possible when a population in the endemic equilibrium $I^*(0)$ (disease endemic before intervention starts), is subjected to sustained population reduction at rate p (see Fig. 2.1a). The long term equilibrium $I^*(p)$ increases with k (i.e. the effectiveness of population reduction reduces) and when k is greater than some critical value k_p, $\Pi_{\text{eqm}} > 0$. However, another behaviour is also apparent: when k approaches a lower threshold k_t, there is a temporary increase in $I(t)$, which results in $\Pi(t;p) > 0$ for a short period, despite no perturbation effect in the long term ($\Pi_{\text{eqm}} < 0$). These two increases are called the persistent and the transient perturbation effect, and their properties are examined in the following sections. Both



(a) $I(t)$ for different values of disease enhancement k, starting in the endemic equilibrium



(b) $I(t)$ for different values of disease enhancement k, starting near the disease free equilibrium



(c) I^* vs population reduction rate p for different values of disease transmission rate β

Figure 2.1: Deterministic simulation of $I(t)$, and algebraic solution of $I^*(p)$ for different β, with parameters given in Table 2.2, except $p = 0.2$. Results are shown for population reduction ongoing, and also for between time $t \in (0, 50)$ in the endemic case. In Fig. 2.1c, β_u marks the upper bound for β that permits the perturbation effect, and crosses each line at the point where the increase no longer occurs for that value of β.

persistent and transient perturbation effects are also possible in the case of emerging disease (when starting from close to the disease free equilibrium) (see Fig. 2.1b).

Behaviour in the long-term equilibrium can be seen by plotting the endemic equilibrium $I^*(p)$ versus population reduction rate p, for several values of the horizontal transmission rate β, and three important points are evident (see Fig. 2.1c). First, persistent population reduction at a sufficiently intense rate does reduce the level of disease, leading to $I^*(p) < I^*(0)$. Second, the maximum size of the persistent perturbation effect reduces as the horizontal transmission rate increases, with no perturbation effect present in the deterministic model for β sufficiently high. Finally, increased horizontal transmission induced by population reduction can stabilise the disease when disease is unstable in the absence of culling.

Persistent perturbation effect with no disease induced mortality

The properties of the persistent perturbation effect Π_{eqm} are now explored in more detail. For clarity focus is on the algebraically simpler case where there is no disease induced mortality, $e = 0$, and technical details of the analysis are given in Appendix 2.A.4. Subsequently numerical analysis is applied in Eqn. 2.1 with disease induced mortality $e > 0$.

Case 1: Disease stable without population reduction, $I^*(0) > 0$

In this case there is a perturbation effect if

$$\Pi_1 = \Pi_{\text{eqm}} = -p - \frac{d+p}{\beta + kp} + \frac{d}{\beta} > 0$$

Minimum disease enhancement required to produce perturbation effect

Note that when $k = 0$, one obtains $\Pi_1 = -p(1 + 1/\beta)$, which is always negative, showing that culling reduces disease when there is no mechanism enhancing disease transmission. Rearranging gives a threshold value of k, above which a perturbation effect is possible

$$k > k_1 = \frac{\beta(1+\beta)}{d - p\beta}$$

There is a lower bound on this threshold, such that $k_1 > \beta(1+\beta)/d > (1+\beta) > 1$ (since the disease is stable, which requires that $\beta > d/(1-d) > d$, hence $\beta/d > 1$).

High disease prevalence precludes a perturbation effect

As $\beta \to \infty$, $\Pi_1 \to -p$, showing that for sufficiently high β, the perturbation effect cannot occur in the deterministic model. In fact in this case there is an upper bound, β_u, on the value of β for which $\Pi_1 > 0$,

$$\beta < \beta_u = \frac{1}{2}\sqrt{(1+pk)^2 + 4dk} - \frac{1}{2}(1+pk)$$

and $\Pi_1 > 0$ only when $\beta < \beta_u$ (see Fig. 2.2a for high β). Similarly, as $d \to 0$, $\Pi_1 \to -p(1 + 1/(\beta + kp)) < 0$, showing that the perturbation effect is possible only for higher mortality rates. There is a corresponding lower bound on d for which $\Pi_1 > 0$, at

$$d > d_l = \beta(1 + \beta + kp)/k$$

(see Fig. 2.2b, for low d). For low $d < d_l$, infectives are removed from the population slowly, and for high $\beta > \beta_u$, the disease spreads quickly; either situation leads to disease saturation, with insufficient susceptibles to allow for a perturbation effect.

High rates of population reduction will reduce disease levels

A simple observation is that a persistent perturbation effect is possible (for any model) only if the population size under persistent culling is greater than the equilibrium number of infected individuals without population reduction i.e. $N^*(p) > I^*(0)$ which implies that there is an upper bound on the culling rate, $p = d/\beta$, above which population reduction will reduce disease (see Appendix 2.A.4). This is also evident in k_1 (the lower bound for k) which diverges as $p \to d/\beta$ from below implying that, in order to see a perturbation effect, population reduction must produce ever greater enhanced transmission k as p approaches this critical level. Furthermore (see Appendix 2.A.4), it is shown that the range of p that permits the perturbation effect also depends on k and is given by

$$0 < p < \frac{d}{\beta} - \frac{1+\beta}{k}$$

which is illustrated in Fig. 2.1c.

Case 2: Disease unstable without population reduction, $I^*(0) < 0$

Population reduction can stabilise otherwise unstable disease

In this case there is a persistent perturbation effect if the disease is stable under persistent population reduction for a given p and k, i.e. when

$$\Pi_2 = \Pi_{\text{eqm}} = 1 - d - p - \frac{d+p}{\beta + kp} > 0$$

The conditions under which the disease is stable under population reduction are detailed in Appendix 2.A.3. The minimum k in order to stabilise disease following population reduction is

$$k > k_2 = \frac{d + p - \beta(1 - d - p)}{p(1 - d - p)}$$

and therefore sufficiently large k can lead to a perturbation effect under these conditions. For example, given $d = 0.2, p = 0$, $I^*(0) < 0$ for $\beta < 0.25$; however, given $d = 0.2, \beta = 0.2$, (thus unstable disease for $p = 0$), when population reduction is applied at rate $p = 0.1$, then the $I^*(p = 0.1) > 0$ for $k > k_2 = 2.286$, therefore the disease can persist as long as population reduction is sustained, leading to a perturbation effect (see Fig. 2.1c, for $\beta = 0.2$).

Persistent perturbation effect with disease induced mortality

Now the persistent perturbation effect is investigated in the more complex situation with disease induced mortality $e > 0$ by solving Eqn. 2.1 numerically to show how Π_{eqm} varies with e itself, and also with horizontal disease transmission β, background mortality d, and enhanced transmission k resulting from population reduction.

Numerical analysis of the role of transmission rate β is consistent with the analysis of the previous section (see Fig. 2.2a). Under case 1 (where $I^*(0) \geq 0$ and $\Pi = \Pi_1$), Π decreases with β and no perturbation is possible for $\beta > \beta_u$ because the disease has saturated the population, whereas in case 2 (where $I^*(0) < 0$ and $\Pi = \Pi_2$), Π increases with β, and there is a lower limit below which the disease becomes extinct despite enhanced disease transmission. This is in accordance with analysis of Π_1 and Π_2 (see Appendix 2.A.4, and above).

The role of natural mortality d is also consistent with the previous analysis (see Fig. 2.2b). In the region of case 1, there is a lower bound d_l, below which the perturbation effect is not possible due to disease saturation, and above which Π increases with d. In the region of case 2, Π decreases with d, and there is an upper limit on d above which the disease becomes unstable despite enhanced transmission. The role of disease induced mortality e, is broadly similar to that of d (see Fig. 2.2c).

The impact of the behaviour change parameter k on the perturbation effect is illustrated for case 1 in Fig. 2.2d. Π increases with k, tending to an asymptote as $k \to \infty$, while there is no perturbation effect below the threshold k_1. The behaviour under case 2 (not shown) is broadly similar with a different lower bound k_2 and lower asymptote.

Maximising the persistent perturbation effect

An important addendum to these results is related to the conditions that maximise the perturbation effect. For low mortality rates d or e, or high transmission rate β, the disease is stable before and during population reduction, the prevalence is very high and there is little room for further increase. As mortality increases or transmission decreases, the size of the perturbation effect Π_{eqm} increases until $\beta = (d+e)/(1-d)$, where the stability changes, and the disease becomes unstable for $p = 0$ (as in case 2). After this point, as mortality increases, or transmission decreases, Π_{eqm} decreases, until mortality is too high, or transmission is too low to maintain the disease either before or during population reduction. This implies that the maximum perturbation effect occurs when $I^*(0) \approx 0$ and $I^*(p) > 0$. Therefore in practice, the persistent perturbation effect is most likely in a disease with very low prevalence. These results can be seen graphically in Fig. 2.2.

Transient perturbation effect

The transient perturbation effect can be assessed by linearising the system and examining the rate of change of $\Pi(t;p)$ with respect to time, at time $t = 0$, which is positive (i.e. the disease increases faster under population reduction) only if $I \in (0, N - 1/k)$ (see Appendix 2.B.1). To obtain an initial increase in disease levels there must be some infectives, but similar to the results in the persistent case, too many infectives will prevent a transient perturbation effect; as k increases a transient perturbation effect is possible for ever larger numbers of infectives. The lower bound here is equivalent to $k > k_t = 1/S$ and since $S \in (0,1)$, this requires that $k_t > 1$; therefore, the transient perturbation effect does not occur in the absence of a change in behaviour. It is also possible to show that the transient perturbation effect increases fastest when $S = N/2 + 1/2k$ and $I = N/2 - 1/2k$ (i.e. roughly equal numbers of susceptibles and infectives) and that $\dot{\Pi}(0;p)$ increases with both p and k (see Appendix 2.B for details). Also, a temporary peak, where $I(t) > I^*(p)$ may occur, if the disease increases quickly before culling completely reduces the population size N; this can be observed in both endemic and emerging disease cases (see Fig. 2.1).

Starting from the endemic equilibrium

Consider the case where the disease is in the endemic equilibrium $\{S^*, I^*\}$ prior to disease intervention (as shown in Fig. 2.1a). In Appendix 2.B it is shown that $k_t = \beta/(d+e)$ so that the minimum disease enhancement required for a transient perturbation effect is reduced when the infection rate β is small and mortality rates d and e are large. In addition

$k_t < k_p$ (where k_p is the relevant k_1 or k_2) and the transient perturbation effect occurs for smaller k than the persistent perturbation effect. Consequently, for small $k < k_t$, there is no perturbation effect. For larger $k \in (k_t, k_p)$, $I(t;p) > I(t;0)$ for small t, i.e. the number of infectives is initially larger following disease intervention, however eventually $I(t) \to I^*(p)$ which is less than the initial level $I^*(0)$, and in this case the increase is temporary. However, for $k > k_p$, the number of infectives increases and remains higher than the control.

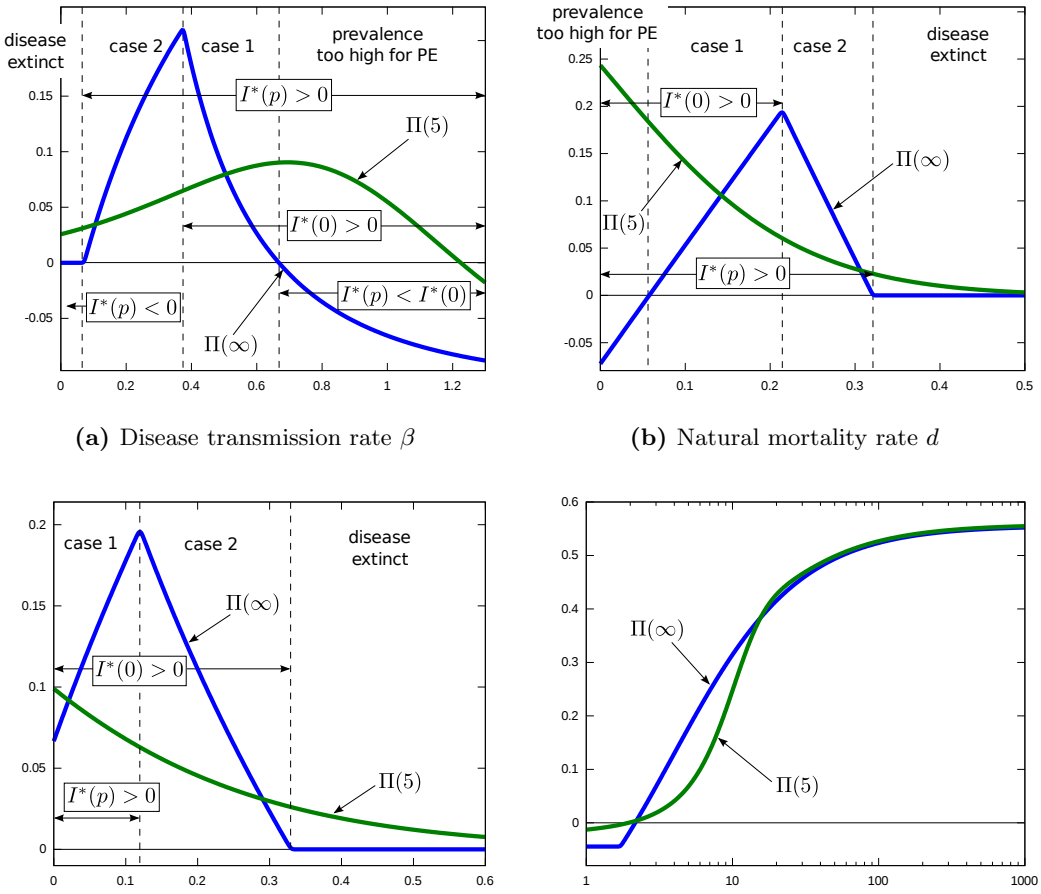
Starting from near the disease free equilibrium

The situation is somewhat different in the case of an emerging outbreak where $I(0) = \epsilon$ where $\epsilon > 0$ is small, and $S(0) = S^*_{\mathrm{DF}} - \epsilon$, as shown in Fig. 2.1b. Here, $k_t = 1/(1-d-\epsilon)$ (see Appendix 2.B.2), and so the minimum behaviour change required for a transient perturbation effect is reduced when the initial prevalence is low (although contrary to the persistent perturbation effect, when mortality rates are also low). Fig. 2.2 shows the impact of varying d, e, β and k on the transient perturbation effect for the case of an emerging outbreak where $I(0) = \epsilon$ where $\epsilon > 0$ is small, and $S(0) = S^*_{\mathrm{DF}} - \epsilon$. These numerical results show that the transient perturbation monotonically decreases with both natural and disease induced mortality, whilst it monotonically increases with enhanced transmission k. The disease transmission rate β affects the time disease takes to reach equilibrium, and therefore small β can result in a slow initial increase (and small transient perturbation effect), while very large β can saturate the population and prevent the transient perturbation effect from occurring at the time considered; the largest increase therefore occurs with an intermediate value of β, although this will vary depending on the time at which the transient perturbation effect is assessed.

These results contrast with those for the persistent perturbation effect (also shown in Fig. 2.2), demonstrating that conditions required for the transient and persistent perturbation effect are not necessarily the same for both emerging and endemic disease.

2.3.2 Implicit enhancement of disease transmission induced by population reduction

Now it is shown how the intrinsic dynamics of a natural spatial formulation of disease transmission and demography may give rise to an increased effective horizontal transmission when population reduction is applied, leading to an implicit perturbation effect. The non-spatial results of the previous section suggest that perturbation is strongest when



(a) Disease transmission rate β

(b) Natural mortality rate d

(c) Disease induced mortality rate e

(d) Disease enhancement k (with log scale)

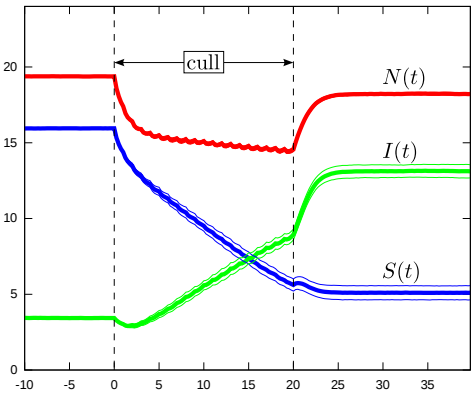
Figure 2.2: The size of the perturbation effect $\Pi(t)$, near the start of culling (at $t = 5$), and at equilibrium (here $t = 1{,}000$). Default parameters are given in Table 2.2, one parameter is varied at a time; initial conditions are $\{S_0, I_0\} = \{0.75, 0.05\}$. The stability of I^* changes at certain parameter values: cases 1 and 2 are bounded when the stability changes for $p = 0$, and case 1 and disease extinction are bounded when the stability changes for $p = 0.1$; the persistent perturbation effect is maximised near the point where I^* crosses 0 for $p = 0$. See also Fig. 2.4 for analogous results in the spatial case. Regions are indicated for case 1 ($I^*(0) \geq 0$) and case 2 ($I^*(0) < 0$).

disease prevalence is relatively low and where population reduction is intermediate, and gives rise to a sufficiently large increase in the horizontal transmission rate. Analysis of the horizontal infection rate in a simple two-site model (see Appendix 2.C.1) suggests that in the spatial model such an enhancement of the transmission rate will be strongest in situations where infection levels are most heterogeneous between groups.

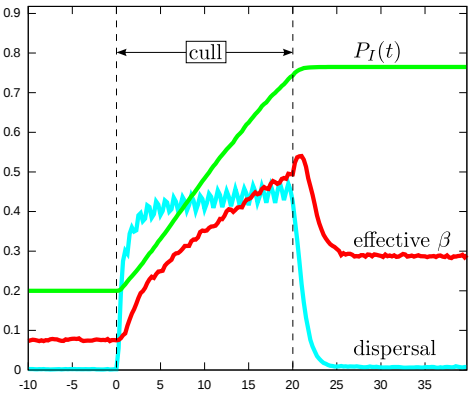
Therefore, in studying the spatial model focus is on cases where disease is heterogeneously distributed between groups and overall prevalence is low. This is most easily achieved when the system is close to the disease free equilibrium with: (i) disease stabilised in each site by high within-site transmission rate β_w and low mortality; (ii) low levels of disease transmission between sites; and (iii) relatively large and stable populations at each site leading to low levels of dispersal between sites. Under this scenario, even in the absence of population reduction, the number of sites infected, and thus overall prevalence, tends to slowly increase (from close to the disease free equilibrium) as rare dispersal or transmission events spread disease. Fig. 2.3 (discussed in detail below) shows how transient perturbation effects occur in such a system. In contrast, it is shown in Appendix 2.C.3 that by making both disease and population less stable within sites it is possible to achieve a dynamic quasi-equilibrium (quasi- because the ultimate fate of all simulations of this model is total extinction) where the spread of disease to uninfected sites is balanced by spontaneous recovery of infected sites, e.g. through death of infectives and birth of susceptible individuals. When the system is in such an endemic state population reduction leads to a persistent perturbation effect, as seen in the non-spatial model. However, this endemic state is very sensitive to the balance between site-level establishment and recovery of disease which makes it difficult to explore variation in the perturbation effect with respect to the value of key parameters. Attention is therefore focussed on the transient perturbation effect when starting close to the disease free state in the spatial model.

2.3.3 Transient perturbation effect in the spatial model

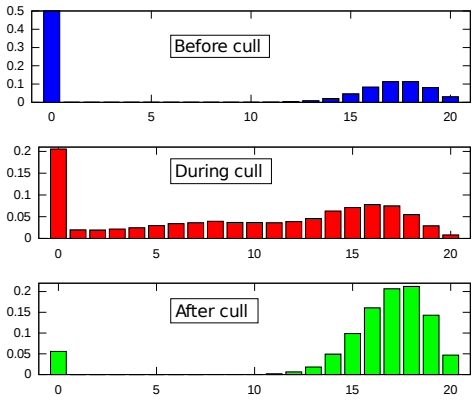
The behaviour during population reduction in the spatial model is shown for the population values $S(t)$, $I(t)$, and $N(t)$ (see Fig. 2.3a), and the proportion of infected sites $P_I(t)$, dispersal rates and effective transmission rate β_{eff} (see Fig. 2.3b). The distribution of infectives between sites is shown in Fig. 2.3c before, during, and after population reduction. Prior to population reduction, sites can be classified as disease-free or infected. During population reduction, the typical level of disease within sites decreases, but the number of



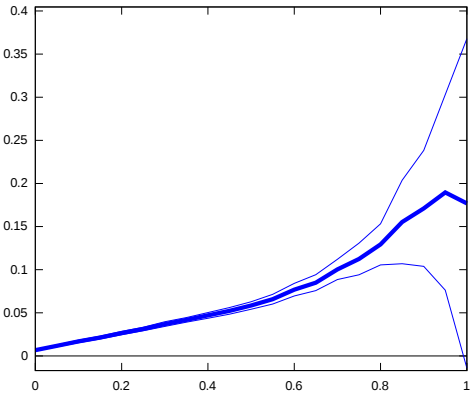
(a) Population numbers, $S(t)$, $I(t)$, and $N(t)$



(b) Proportion of sub-populations containing infectives, $P_I(t)$, effective transmission rate β, and dispersal rate



(c) Distribution of I across sites

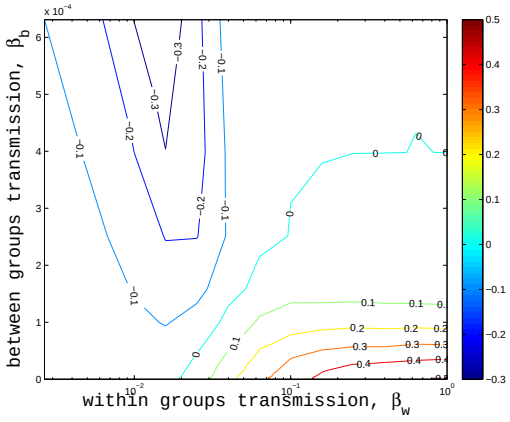


(d) Effective transmission rate β for disease transmission vs population reduction coverage p_1

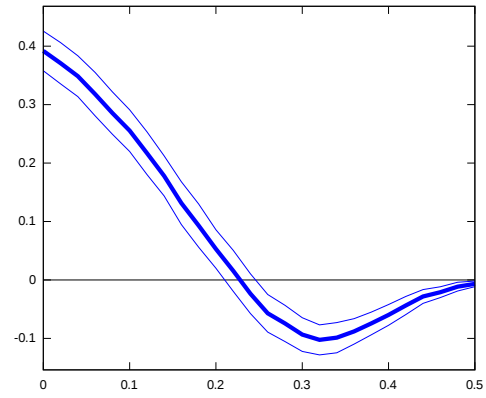
Figure 2.3: Stochastic simulation of the spatial SI model. Parameters are given in Table 2.2, and initial conditions are at the disease free equilibrium $\{S, I\} = \{20, 0\}$, while in 20% of sites randomly chosen, a single individual is infected, resulting in $\{S, I\} = \{19, 1\}$. Population reduction occurs annually from years 50–69, and in $p_1 = 20\%$ of sites (chosen randomly each year) the removal rate is set to $p_2 = 1.0$, without regard to disease status (equivalent to an overall culling rate of $p = 0.2$). An initial reduction in I is rapidly replaced by an increase, which is due to the increased chance of invasion of naïve groups by infectives due to the density dependent dispersal. The CI for the effective transmission rate increases for large p_1 due to the increasing number of simulations where the disease becomes extinct.

infected sites increases. When population reduction ceases, typical prevalence in infected sites returns to previous levels which, given that there are now more of them, leads to a rapid increase in global prevalence. Some light may be shed on the mechanisms behind such changes, as population reduction leads to a large increase in dispersal, followed by increasing rates of horizontal disease transmission, H (see Fig. 2.3b). Population reduction disrupts the stable demographic structure (shown in Fig. 2.3c) leading to an increase in the dispersal rate and movement of infectives to previously disease free sites. This *vacuum effect* (Macdonald, 1995; Carter *et al.*, 2007) emerges from the spatial model's density dependent dispersal and leads to increased transmission. The effective horizontal transmission rate parameter varies with population reduction effort p_1: for small p_1, there is an almost linear increase in β_{eff} (see Fig. 2.3d), which agrees well with the explicit increase assumed to be $\beta_{\text{eff}} = \beta + kp$ in the non-spatial model. However, one key difference (as shown in Fig. 2.3b), is that the increase is not immediate, but grows linearly with time — an effect not accounted for by earlier analysis.

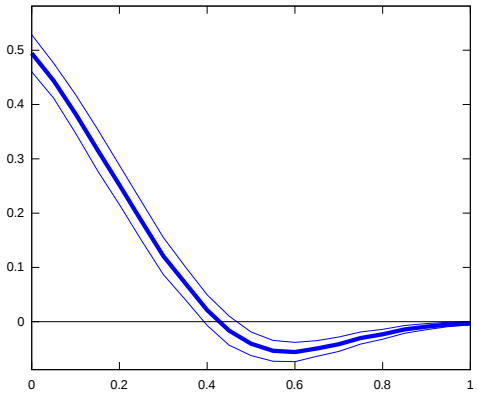
Now the sensitivity of this perturbation effect is explored with respect to key aspects of demography and disease dynamics. The results are broadly consistent with those obtained when starting close to the disease free equilibrium in the non-spatial model. Fig. 2.4 shows results for parameters analogous to those in Fig. 2.2, and that Π decreases with mortality rates d and e and increases with dispersal rate m (similar to k in the non-spatial case). The role of disease transmission is more complex. The perturbation effect decreases with between-group infection rate β_b which reduces the number of disease free sites and increases with β_w which increases within-site stability of disease. Thus for small β_b and sufficient β_w, population reduction is able to spread disease to uninfected sites where it is able to persist. The impact is also explored of varying the threshold parameter α, which determines how sensitive the rate of dispersal is to local reductions in the size of the population in the destination site (see Appendix 2.C). Results show that a perturbation effect occurs for a wide range of values, although the largest effects are seen for α around 0.9 (it is suspected that the largest increase would be observed for α near $1 - p_2$). Perturbation effects were also found for alternative forms of the density dependent dispersal function $f(N_k)$ (results not shown).



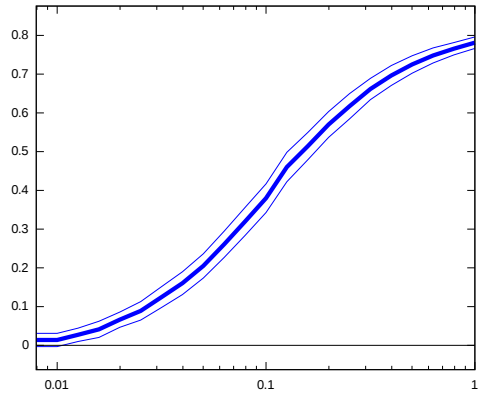
(a) Between and within-groups infection rates β_b and β_w (log scale)



(b) Natural mortality rate d



(c) Disease induced mortality rate e



(d) Dispersal rate m (log scale)

Figure 2.4: The size of the perturbation effect, Π_{sites}, at time $t = 20$ starting near the disease free equilibrium. Default parameters are given in Table 2.2, and one parameter is varied at a time. This is analogous to Fig. 2.2 for the non-spatial case. Initial conditions are such that 20% of sites are randomly chosen to start near the endemic equilibrium (with a minimum of 1 infective), while the remainder begin at the disease free equilibrium.

2.4 Discussion

In this chapter, the impact on disease control of enhanced transmission resulting from individual or demographic responses to population reduction was explored. Using a generic non-spatial and deterministic model of demography and disease dynamics the potential for such effects to reduce and reverse the disease control benefits of population reduction was explored. It was found that there was a threshold of enhanced transmission above which a perturbation effect occurred, whereby the number of infected individuals increases during the period when population reduction is applied. However, sufficient population reduction (the level rising with mortality rates d and e and behaviour change k, but decreasing with infection rate β) will always reduce numbers of infectives in the area it is applied. Disease systems with low levels of disease are more sensitive to the impacts of enhanced transmission. For systems with endemic disease, the perturbation effect increases with natural and disease induced mortality rates (due to reduced levels of endemic disease), with the opposite trend where disease is emerging, as higher mortality removes cases caused by enhanced transmission. Increasing horizontal transmission rate reduces the perturbation effect in the endemic case since it reduces the number of susceptibles, whereas for emerging disease the largest transient increase (at a particular point in time) occurs for intermediate β. With low β there is a large perturbation effect, but it takes much longer to occur, whereas with high β the disease quickly reaches equilibrium, so the perturbation occurs earlier, and is small (as in the persistent case). Enhanced transmission effects can also lead to disease being stabilised by population reduction in systems where it is otherwise unstable.

A spatially explicit model representing demographic fluctuations and disease transmission within locally well mixed populations, and dispersal and disease transmission between such groups was also considered. In this context it was found that enhanced transmission emerged implicitly as a demographic response to population reduction when dispersal was density dependent. This enhancement would be increased if individuals explicitly changed their behaviour, e.g. by dispersing more or by increasing agonistic interactions and therefore disease contacts between groups. However, the implicit dispersal mechanism alone was sufficient to give rise to a perturbation effect. It was found that the system was susceptible to enhanced transmission in both the case of endemic and emerging diseases when infection was heterogeneously distributed among groups and when overall levels of disease were low. For emerging disease it was shown that the impact of mortality rates was

qualitatively similar to the predictions of the non-spatial analysis. In the spatial model, dispersal rate played a similar role to the non-spatial enhancement parameter k, whereas the role of horizontal disease transmission is not directly comparable between the two cases. In the spatial context, higher within-group transmission increased the size of the perturbation effect, but even a small rate of between-group transmission reduced it. Analysis of the effective contact rate in the spatial model reveals that enhanced transmission varied in time and this could be incorporated in future analysis of the non-spatial system.

Many authors have noted problems related to disease control via population reduction in wildlife (Macdonald, 1995; Guberti *et al.*, 1998; Artois *et al.*, 2001; Donnelly *et al.*, 2003; Woodroffe *et al.*, 2006a), including situations were disease risks are increased rather than reduced (Carter *et al.*, 2007; Vial & Donnelly, 2012). Individual behavioural (Swinton *et al.*, 1997; Gallagher & Clifton-Hadley, 2000; Tuyttens & Macdonald, 2000) and demographic (Smith *et al.*, 2001b) responses to population reduction are thought to enhance disease transmission in wildlife. The results of this chapter suggest that a wide range of wildlife disease systems are sensitive to such effects. This is consistent with the marked inefficiencies of population reduction as a disease control strategy observed to date. However, the effects studied here are likely to be even more widespread than current empirical studies suggest as they undermine the efficacy of population reduction measures even in situations where they do not lead to a complete reversal of its effectiveness.

2.A Derivation and analysis of the deterministic non-spatial model

2.A.1 Formulation of non-spatial deterministic model

A deterministic ordinary differential equation (ODE) that includes only the demographic aspects and disease dynamics described for the non-spatial model in the text (see Methods) is given by:

$$\frac{dS}{dt} = rN(1 - N/c) - dS - \beta SI$$
$$\frac{dI}{dt} = -(d + e)I - \beta SI$$

The first equation represents the rate of change of the susceptible population in terms of three processes: birth of susceptibles at rate $rN(1 - N/c)$ (note all individuals are assumed susceptible at birth since vertical and pseudo-vertical transmission are ignored); death of susceptibles at rate dS and infection of susceptibles at rate βSI. Similarly, the second equation represents the dynamics of the infected population which increases as susceptibles become infected at rate βSI, and decreases as infectives die due to the effects of the disease at rate eI and due to other causes at rate dI.

As described in the main text the effect of simple population reduction is modelled by introducing an additional death rate p. Thus the death rates become $(d + p)S$ and $(d + e + p)I$ for susceptibles and infectives respectively. To account for the impact of changes in host susceptibility and behaviour induced by population reduction kp is added to the horizontal disease transmission rate which therefore becomes $(\beta + kp)SI$. The resulting equations,

$$\frac{dS}{dt} = rN(1 - N/c) - (d + p)S - (\beta + kp)SI$$
$$\frac{dI}{dt} = -(d + e + p)I - (\beta + kp)SI$$

can be simplified by rescaling, leading to Eqn. 2.1 in the main text.

2.A.2 Disease free and endemic equilibria

Solving Eqn. 2.1 for biologically realistic steady states, where $\dot{S} = \dot{I} = 0$, and $S, I \geq 0$, gives:

1. *Population extinction*, at $S_0^* = 0$, $I_0^* = 0$.

2. The *disease free equilibrium*, at $S^*_{\mathrm{DF}} = 1 - d - p$, $I^*_{\mathrm{DF}} = 0$. S^*_{DF} is often referred to as K.

3. The *endemic equilibrium*, at

$$S^* = \frac{d + e + p}{\beta + kp},$$
$$I^* = \frac{1}{2}(1 - d - e - p) - \frac{d + e + p}{\beta + kp} + \frac{1}{2}\sqrt{(1 - d - e - p)^2 + 4\frac{d + e + p}{\beta + kp}e}$$

When $e = 0$, provided that $d + p < 1$ (i.e. where the population persists because the birth rate, rescaled to 1, exceeds the combined mortality and removal rate), the endemic equilibrium becomes

$$S^* = \frac{d + p}{\beta + kp}, \quad I^* = 1 - d - p - \frac{d + p}{\beta + kp}$$

When $p = 0$, the endemic equilibrium simplifies further to

$$S^* = d/\beta, \quad I^* = 1 - d - d/\beta$$

2.A.3 Disease stability

Equilibria are stable when the eigenvalues are all negative, unstable when they are all positive, or a saddle node when some are positive and the rest are negative. The eigenvalues of Eqn. 2.1 with $e = 0$ are examined for tractability. These are:

$$\lambda_1 = 1 - d - p - 2N, \quad \lambda_2 = (\beta + kp)(S - I) - d - p$$

Evaluating the eigenvalues for the endemic equilibrium gives:

$$\lambda_1 = d + p - 1, \quad \lambda_2 = -(\beta + kp)(1 - d - p) + d + p$$

Evaluating the eigenvalues for the disease free equilibrium gives:

$$\lambda_1 = d + p - 1, \quad \lambda_2 = (\beta + kp)(1 - d - p) - d - p$$

$\lambda_1 < 0$ if $d + p < 1$ (required for non-extinction), therefore the endemic equilibrium is stable, and the disease free equilibrium is a saddle node if $\lambda_2 < 0$, which occurs when:

$$\beta > \frac{d + p}{1 - d - p} - kp$$

otherwise the stabilities are reversed. For $p = 0$, this becomes $\beta > d/(1 - d)$.

Assuming the disease is stable, it can only persist if $I^* > 0$. If $e \geq 0$, this is equivalent to $S^* < S^*_{\mathrm{DF}}$, which is an easier calculation. Therefore $I^* > 0$ if

$$\frac{d+e+p}{\beta+kp} < 1-d-p$$

Bounds under which the disease is stable can be obtained for each of the parameters by rearranging the above inequality as follows:

$$\begin{aligned} d &< \frac{(1-p)(\beta+kp)-e-p}{1+\beta+kp} \\ e &< (\beta+kp)(1-d-p)-d-p \\ \beta &> \frac{d+e+p}{1-d-p} - kp \\ k &> \frac{d+e+p}{p(1-d-p)} - \frac{\beta}{p} \\ p &< \frac{1}{2}\left(1-d-\frac{1+\beta}{k}\right) + \frac{1}{2}\sqrt{\left(1-d-\frac{1+\beta}{k}\right)^2 - 4\frac{d+e-(1-d)\beta}{k}} \end{aligned} \tag{2.6}$$

In the absence of population reduction, when $p = 0$ these become:

$$\begin{aligned} d &< \frac{\beta-e}{1+\beta} \\ e &< \beta-d-d\beta \\ \beta &> \frac{d+e}{1-d} \end{aligned}$$

2.A.4 Conditions for the deterministic perturbation effect $\Pi_{\mathbf{eqm}} > 0$

The size of the persistent PE is given by:

$$\Pi_{\mathrm{eqm}}(p) = \max\{I^*(p), 0\} - \max\{I^*(0), 0\}$$

Focussing on the algebraically tractable case without disease induced mortality, $e = 0$, and on situations where disease is still present with culling, $I^*(p) > 0$, two cases are examined:

Case 1: $I^*(0) \geq 0$, whence

$$\Pi_{\mathrm{eqm}} = \Pi_1 = -p - \frac{d+p}{\beta+kp} + \frac{d}{\beta}$$

Case 2: $I^*(0) \leq 0$, whence

$$\Pi_{\mathrm{eqm}} = \Pi_2 = 1-d-p-\frac{d+p}{\beta+kp}$$

Note that $\Pi_2 = S^*_{\mathrm{DF}} - S^*$, and so for case 2, the values are exactly the same as for Eqns. 2.6 in Section 2.A.3. Also note that $\Pi_1 = \Pi_2$ when the stability changes, i.e. when $I^*(0) = 0$.

Next, look for conditions on the perturbation effect under Case 1, by solving $\Pi_1 > 0$ for different parameters (conditions for Case 2 correspond to the bounds for stability given by Eqns. 2.6).

- Natural mortality rate d. Rearranging $\Pi_1 > 0$ for d obtains:

$$d > \beta(1 + \beta + kp)/k$$

- Infection rate β. Similarly:

$$\beta < -\frac{1}{2}(1 + kp) + \frac{1}{2}\sqrt{(1 + kp)^2 + 4dk}$$

- Population reduction rate p. First, observe that if the number of infectives prior to culling is greater than the total population size under persistent culling, then there is no room for I to increase. Therefore

$$I^*(0) < N^*(p) \tag{2.7}$$
$$\Rightarrow p < d/\beta$$

  However, rearranging $\Pi_1 > 0$ gives:

$$0 < p < \frac{d}{\beta} - \frac{1 + \beta}{k} \tag{2.8}$$

  For which Eqn. 2.7 is the limit as $k \to \infty$.

- Behaviour change k. Look for conditions on the perturbation effect under both cases:

  Case 1:

$$k > k_1 = \frac{\beta(1 - \beta)}{d - \beta p}$$

  Case 2:

$$k > k_2 = \frac{d + p - \beta(1 - d - p)}{p(1 - d - p)}$$

  Note that k_2 is the minimum k for which the disease is stable (i.e. population reduction stabilises the disease when $k > k_2$). Also note that $k_1 = k_2$ when $I^*(0) = 0$.

This demonstrates that β is bounded below in order for the disease to persist, $0 < I^*(p)$, however it also bounded above in order for the disease to increase with population reduction, $I^*(0) < I^*(p)$. If both of these bounds are satisfied, then $0 < I^*(0) < I^*(p)$ (which gives Case 1). Note that this interval increases with k.

2.B Transient perturbation effect

2.B.1 Analysis

While intermediate behaviour of $I(t)$ prior to the disease reaching a new equilibrium can only be solved numerically, both the long term and initial behaviour can be analysed algebraically. Here the initial behaviour of $\Pi(t;p)$ is examined by linearising the system, and measuring the difference between $\dot{I}(t;p)$ and $\dot{I}(t;0)$ at time $t=0$. Substituting $I(t)$ from Eqn. 2.1 into Eqn. 2.3, and differentiating with respect to time gives

$$\dot{\Pi} = \dot{I}(p) - \dot{I}(0) = pI(kS-1)$$

hence $\dot{\Pi} > 0$ if

$$k > k_t = 1/S$$

Note that since $S \in (0,1)$, this requires that $k_t > 1$, therefore the transient perturbation effect does not occur in the absence of a change in behaviour.

It is immediately clear that the transient perturbation effect depends directly on, and increases with, p and k, however it also depends on initial conditions $S(0)$ and $I(0)$, which in turn depend on the remaining parameters. Intermediate behaviour must be found numerically, but some further insight can be obtained by observing how $\dot{\Pi}(t)$ depends on $S(t)$ and $I(t)$.

Substituting $S = N - I$ into $\dot{\Pi}$ gives a quadratic in I, which can be solved to show that $\dot{\Pi}_0 > 0$ when $I \in (0, N-1/k)$, and is maximised when $S = N/2+1/2k$ and $I = N/2-1/2k$. Therefore the transient perturbation effect increases fastest when S and I are near these values (i.e. roughly equal), and larger k permits a greater range of I for which the transient perturbation effect is possible.

2.B.2 Initial conditions

Endemic disease

First the case is examined where the disease is in the endemic equilibrium, $\{S^*, I^*\}$ prior to disease intervention. Substitute $S(0) = S^*$ into k_t, to obtain $k_t = \beta/(d+e)$, therefore the minimum behaviour change required for the perturbation effect is reduced when the infection rate β is small and mortality rates d and e are large. Note that

$$k_p = \frac{\beta(1+\beta)}{d-p\beta} > \frac{\beta(1+\beta)}{d+e} > \frac{\beta}{d+e} = k_t$$

which leaves $k_t < k_p$, so the transient perturbation effect occurs for smaller k than the persistent perturbation effect.

Emergent disease

If the disease is not in equilibrium prior to disease intervention, then another sensible initial condition to examine is when the disease has been newly introduced, in which case $I(0) = \epsilon$ where $\epsilon > 0$ is small, and $S(0) = 1 - d - \epsilon$, in this case the transient perturbation effect occurs if $k > k_t = 1/(1 - d - \epsilon)$, and so the minimum behaviour change required is when $I(0)$ is smallest, which agrees with the concept that the perturbation effect occurs most readily in diseases with low prevalence (as it does in the persistent case).

2.B.3 Intermediate behaviour

Some insight into the intermediate behaviour can be obtained by noting that $\dot{\Pi}$ is a quadratic in I, maximal at $I = N/2 - 1/2k$, and negative for $I > N - 1/k$. This means that the perturbation effect will begin slowly when $I(0)$ is small, and then increase in rate as $I(t)$ passes through $N(t)/2 - 1/2k$. If $I > N - 1/k$, then $\dot{\Pi}$ becomes negative, and Π will decrease.

However, $N^*(p) < N^*(0)$ (since population reduction reduces the population size N), so the boundary $N - 1/k$ will decrease with time. This means that $\Pi(t)$ may increase for larger I near the start of the cull when N is larger than it can later on when N is smaller. If the boundary decreases below I, then $\dot{\Pi}$ becomes negative, forcing Π to decrease until it reaches the equilibrium value. Consequently it is possible for the disease to temporarily increase above $I^*(p)$, provided it happens early when the population has not yet been fully reduced in size (this explains the temporary peak seen near the start of the perturbation effect in Figs. 2.1b and 2.1a).

2.C Analysis and simulation of the perturbation effect in the stochastic spatial model

2.C.1 Heterogeneity and the perturbation effect in the spatial model

First the importance of heterogeneity in the model is demonstrated. Consider a simple two-site model, with density dependent dispersal between the two groups A and B. The global infection rate, H, is

$$H = H_A + H_B = \beta_w(S_A I_A + S_B I_B) + \beta_b(S_A I_B + S_B I_A)$$

Assuming disease induced mortality rate $e = 0$, then $N_A = N_B = N$, and the number of infectives is $I_A + I_B = I$, this can be simplified to

$$H = \text{constant} + 2(\beta_w - \beta_b)(I - I_A)I_A$$

so when between-group infection rate β_b is small, and $\beta_w > \beta_b$, H is maximised when the infection is distributed evenly between sub-populations, and $I_A = I_B$. Conversely, H is minimised when $I_A = 0$ or $I_A = I$ (i.e. all infectives are restricted to one of the groups).

Considering fluctuating I, and differentiating global infection rate H with respect to time obtains

$$\begin{aligned}\dot{H} =&\beta_e(\dot{S}_A + \dot{S}_B) + \beta_w(\dot{S}_A I_A + S_A \dot{I}_A + \dot{S}_B I_B + S_B \dot{I}_B) \\ &+ \beta_b(\dot{S}_A I_B + S_A \dot{I}_B + \dot{S}_B I_A + S_B \dot{I}_A)\end{aligned}$$

While $\dot{H}$ is affected by all processes, including birth, death, infection and dispersal, if only the effect of dispersal on $\dot{H}$ is examined by substituting only the relevant components ($\dot{S}_A = \ldots + mS_B f(N) - mS_A f(N)$ etc.) then one obtains

$$\dot{H}_{\text{dispersal}} = 2m(\beta_w - \beta_b)(I_A - I_B)^2 f(N)$$

Consequently, if $\beta_w > \beta_b$ and $I_A \neq I_B$, then the effect of dispersal is to increase $\dot{H}$, i.e. horizontal disease transmission decreases due to heterogeneity, but increases as dispersal equalises the population densities. This effect increases with m, but then the presence of the density dependence function $f(N)$ shows that it is greater for smaller N (e.g. as a consequence of population reduction).

This demonstrates the importance of heterogeneity, and also of the density dependence function $f(N_j)$. Note that a large β_b will lead to rapid spread between sites, quickly spreading to all sub-populations, and reducing the heterogeneity in I_i.

2.C.2 Robustness of transient perturbation effect in the spatial model

The impact of varying certain mechanisms on the transient perturbation effect is examined; in particular, the density dependent dispersal. In the main body the case was considered where $f(N_j) = 1$ when $N_j < \alpha N^*_{\text{DF}}$ (where N^*_{DF} is the disease free equilibrium), and 0 otherwise.

The threshold parameter $\alpha = 0.7$ was arbitrarily chosen, however Fig. 2.5 shows that the transient perturbation effect occurs for a range of α that determines how sensitive the rate of dispersal is to local reductions in the size of the population in the destination site.

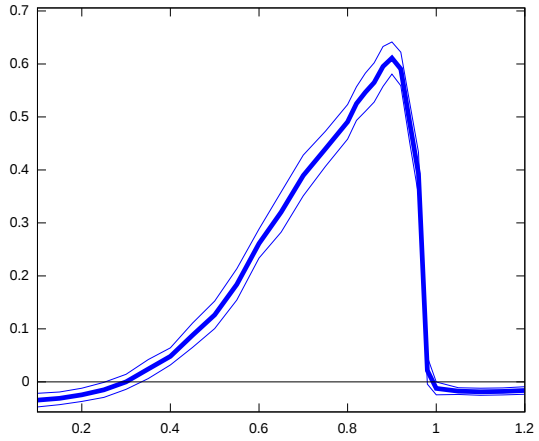


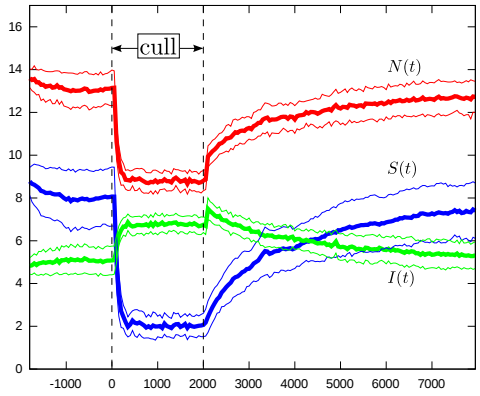
Figure 2.5: The difference in proportion of sub-populations containing infectives, Π_{sites}, at $t = 20$ starting near the disease free equilibrium. This is similar to Fig. 2.4, but for the parameter α.

Another, more linear, density dependent dispersal function, $f(N_j) = 1 - N_j/c$, was also explored. For this function, dispersal rates prior to population reduction tended to be much greater, and consequently the perturbation effect was much weaker (although still present); the strongest perturbation effect tended to occur when the disease free equilibrium, N^*_{DF}, was close to the carrying capacity c (i.e. when d is small), giving the greatest potential for increase in dispersal rates. Results (not shown), while weaker, were broadly similar to those found with the step function for density dependence function.

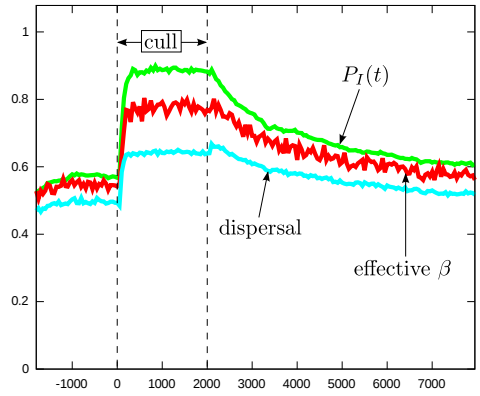
2.C.3 Persistent perturbation effect in the spatial model

It is important to demonstrate that the persistent perturbation effect still occurs in the spatial model, however this requires that the equilibrium value P^*_I remains between 0 and 1 (ideally near 0.5). In addition, $P_I(t)$ should be allowed to fluctuate freely, with an non-negligible chance of the disease becoming extinct within any individual sub-population, and of the disease transferring to neighbouring disease free groups; thus, from any set of initial conditions, the system should reach equilibrium within a reasonable time period. Only a very narrow parameter range allows for this situation, while still allowing the perturbation effect to occur.

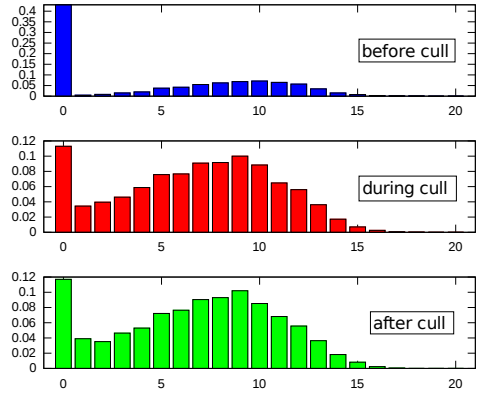
A set of parameters that allowed the perturbation effect to occur, while still allowing $P_I(t)$ to fluctuate freely and that $P_I(t) \to P^*_I \in (0, 1)$ in a reasonable time period are: $c = 20$, $r = 1$, $d = 0.08$, $e = 0.46$, $m = 0.1$, $\alpha = 0.7$, $\beta_w = 0.8$, $\beta_b = 0$. See Fig. 2.6 for results.



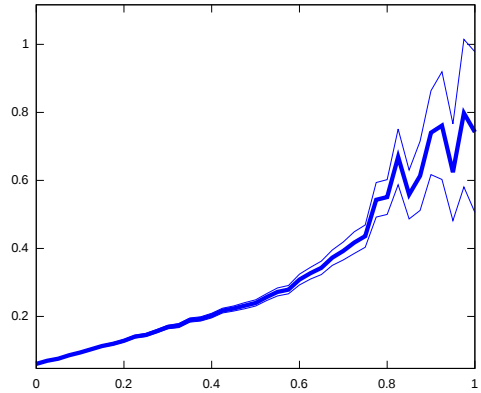
(a) Population numbers, $S(t)$, $I(t)$, and $N(t)$



(b) Proportion of sub-populations containing infectives, $P_I(t)$, effective disease transmission rate H_{eff}, and effective dispersal rate m_{eff}



(c) Distribution of I across sites at 3 different times



(d) Effective rates for disease transmission vs population reduction coverage p_1

Figure 2.6: The persistent case in the spatial model. Parameters are: $c = 20$, $r = 1$, $d = 0.08$, $e = 0.46$, $m = 0.1$, $\alpha = 0.7$, $\beta_w = 0.8$, $\beta_b = 0$, $p_1 = 0.2$, $p_2 = 1.0$. These parameters were chosen to provide a stable equilibrium, where $P_I(t)$ fluctuates, but remains between 0 and 1, and the perturbation effect still occurs. The system is given 2000 years to stabilise, then population reduction is applied for 2000 years, during which a new equilibrium appears to be reached. Afterwards, the system eventually returns to the original equilibrium.

Chapter 3

Accounting for behavioural responses to population reduction when planning disease control strategies

3.1 Background

Population reduction is often used to control disease in wildlife populations, especially when those populations act as a reservoir for livestock disease (Wobeser, 1994). However, in some disease systems, such as rabies and foxes (*Vulpes vulpes*), classical swine fever (CSF) and wild boar (*Sus scrofa*), or bovine tuberculosis (bTB) and badgers (*Meles meles*), it can be ineffective, or even detrimental to disease control (Blancou *et al.*, 1991; Guberti *et al.*, 1998; Artois *et al.*, 2001). Increases in disease levels following population reduction are often referred to as the "perturbation effect", since they are often a result of social perturbation (Carter *et al.*, 2007).

The perturbation effect occurs when increases in disease transmission are greater than the decrease expected due to a reduced number of susceptible or infective hosts. This may be due to changes in behaviour that increase contact rates or susceptibility levels, or because the population structure changes in such a way that disease transmission occurs more readily (e.g. due to increased movement in structured populations).

The most well documented case of the perturbation effect is the Randomised Badger Culling Trail (RBCT), which investigated the effects of culling on badgers to reduce bTB (Independent Scientific Group, 2007). In the RBCT, two different population reduction strategies — proactive and reactive culling — were implemented and compared to a survey-only experimental control. It was found that reactive culling increased disease incidence in cattle populations (Donnelly *et al.*, 2003) and increased disease prevalence in badgers Woodroffe *et al.* (2006b) in the target area, while proactive culling decreased disease in the target area, but increased disease in surrounding areas (Donnelly *et al.*, 2006). These influences of population reduction extended beyond the culling period, with increased disease prevalence in the following year (Donnelly *et al.*, 2007).

An important mechanism in disease transmission is dispersal, as it is at least partially responsible for geographic spread of disease. Dispersal is the movement of individuals between social groups, in search of new resources and mating opportunities. The rate of dispersal may typically depend on the density of the target population (Johst & Brandl, 1997; Bowler & Benton, 2005), in which case culling can lead to an increase in dispersal into targeted sites from neighbouring areas, a phenomenon called the "vacuum effect" (Carter *et al.*, 2007). The vacuum effect has been implicated in several disease systems where culling failed to control the disease, including the RBCT (Carter *et al.*, 2007), due to increased disease transmission as a result of movement of infectives.

In Chapter 2, it was demonstrated that dispersal can lead to a perturbation effect if disease prevalence is spatially heterogeneous, disease spread between groups is mainly by dispersal of infectives, and if dispersal is considerably limited by density dependence when the population is near equilibrium density. Under non-selective culling regimes, low levels of culling, sufficient to increase dispersal rates but not remove disease from targeted sites, led to increased disease prevalence as dispersal introduced the disease into previously naïve groups. More severe culling was necessary to reduce overall disease levels.

It is therefore important to consider the culling strategy used, in order to maximise disease control, and limit disease spread. Culling can be varied spatially, by choosing the number and location of sites to target and by choosing the intensity of culling within targeted sites. It can also be varied temporally, by choosing the duration of the culling period, and time between culling events, and the scheduling of which sites are targeted within a spatial design.

In this chapter, a spatial stochastic susceptible-infective SI model of demography and disease dynamics is used to explore various population reduction strategies, when the host-disease system is susceptible to the perturbation effect. Heterogeneity and intensity of culling are examined to show the influence of spatial design. The influence of culling outside the targeted areas is examined to explore results observed in the RBCT. Finally, scheduling and duration of culling is examined, to show the influence of temporal design.

3.2 Methods

3.2.1 Demography and epidemiology

Consider a disease system within an SI framework, prone to the perturbation effect as a result of density dependent dispersal (see Chapter 2). Hosts are either susceptible to the disease (S), or infected (I), without the possibility of recovery.

The population is divided into multiple sub-populations, each subject to logistic growth as a consequence of density dependent birth at intrinsic rate r, with carrying capacity c, and natural mortality at rate d (i.e mortality for any reason other than disease or as a consequence of population reduction). The total population size within each group is $N = S + I$, and the competing effects of birth and death give rise to an equilibrium population size in the non-spatial deterministic system of N_{DF}.

Each sub-population is connected with neighbouring groups via dispersal (e.g. for better resource or mating opportunities, or for inbreeding avoidance) at intrinsic rate m. The

population is assumed to be bordered in such a way that dispersal does not extend beyond the edges of the population, and all attempts automatically fail (hence movement is proportionately less at the boundaries, although this is not expected to significantly affect results).

Dispersal is dependent on the density of the target group, and entry is only possible into a group that is below a certain threshold proportion α of the disease free equilibrium size. The density dependence function that gives this behaviour is

$$f(N_j) = \begin{cases} 1 & \text{if } N_j < \alpha N^*_{\text{DF}} \\ 0 & \text{if } N_j \geq \alpha N^*_{\text{DF}} \end{cases}$$

where N_j is the size of the neighbouring group, and N^*_{DF} is the disease free equilibrium. If α is large (roughly $\alpha \geq 1$), then movement is effectively unlimited, and dispersal is not-density dependent, and so there is no mechanism leading to the perturbation effect as shown in Chapter 2. The results of density and non-density dependent dispersal will be compared by examining both, but adjusting the intrinsic dispersal rate m so that effective dispersal rates are similar in both cases.

Disease transmission is density dependent within groups, and occurs at rate $H = \beta SI$, where β is the horizontal transmission coefficient. The possibility of direct transmission between groups is ignored, as that is largely a barrier to the perturbation effect via dispersal (see Chapter 2). In Chapter 2 it was shown that the impact of disease induced mortality did not qualitatively change the properties of the perturbation effect, therefore it is not considered here, although it is acknowledged that it may be useful to consider it due to its influence on population size.

In Chapter 2, it was shown that the perturbation effect is more likely in an emerging disease when infection is spatially heterogeneous, with little to no direct between-group disease transmission, but high within-group transmission, low mortality rates, and high intrinsic dispersal severely limited by density dependence. This chapter examines design of population reduction strategies in a system that has such characteristics and is thus prone to the perturbation effect when subjected to culling.

Throughout this chapter, a set of parameters (see Table 3.2) are used such that the perturbation effect is likely to occur.

Event	**Rate**	δS_i	δI_i	δS_j	δI_j
Birth of S_i	$rN_i(1-N_i/c)\delta t$	$+1$	0	0	0
Death of S_i	$(d+p_2)S_i\delta t$	-1	0	0	0
Death of I_i	$(d+e+p_2)I_i\delta t$	0	-1	0	0
Infection of S_i	$H_i\delta t$	-1	$+1$	0	0
Dispersal of S_i to site j	$mzS_if(N_j)\delta t$	-1	0	$+1$	0
Dispersal of I_i to site j	$mzI_if(N_j)\delta t$	0	-1	0	$+1$

Table 3.1: Event rates during time interval $(t, \delta t)$ and corresponding effects in the spatial stochastic SI model. Sites are indexed by i, and neighbouring sites are indexed by j. z is the reciprocal of the number of neighbouring sites, and is used to normalise dispersal rates at boundaries.

3.2.2 Structure of the spatial stochastic model

The model is implemented within a spatial SI framework. Spatial structure is represented by a 20×20 lattice of sites, each indexed by i and containing time dependent integer variables $S_i(t)$ and $I_i(t)$, representing the number of susceptibles and infectives in each group. Each group is subject to demography and epidemiology described above.

Stochasticity can have important effects on disease spread, especially in small populations; it introduces heterogeneities, which can be significant when disease transmission is non-linear, and it increases the chance of disease extinction due to stochastic fade-out. A discrete Markov process with exponentially distributed waiting time between events is used to reflect stochasticity in the model, and is simulated using Gillespie's algorithm (Keeling & Rohani, 2007). Events and their corresponding rates are shown in Table 3.1.

3.2.3 Measuring the perturbation effect

The size of the perturbation effect is defined as

$$\Pi(t;p) = I(t;p) - I(t;0) \tag{3.1}$$

where p is the rate of population reduction, and t is the time. A similar measure, based on the proportion of sites containing infectives $P_I(t)$, is

$$\Pi_{\text{sites}}(t;p) = P_I(t;p) - P_I(t;0) \tag{3.2}$$

Parameter	Symbol	Value	Units
Intrinsic reproduction rate	r	1	year^{-1}
Carrying capacity	c	20	—
Natural mortality rate	d	0.01	year^{-1}
Horizontal transmission rate			
environmental	β_e	0	year^{-1}
within groups	β_w	0.5	year^{-1}
between groups	β_b	0	year^{-1}
Intrinsic dispersal rate	m	0.1	year^{-1}
threshold value	α	0.7	—
Population reduction rate	p	0.1	year^{-1}
coverage	p_1	0.2	—
within-site removal rate	p_2	1.0	year^{-1}
within-site removal probability	p_2	0.5	—

Table 3.2: Summary of parameters, symbols, and default values used.

Π_{sites} is useful because it reflects the geographical spread of disease, which fluctuates less rapidly than the number of individuals within sites during culling, especially following cessation of intervention: an increase in P_I is typically a precursor to an increase in the global number of infectives when the sub-populations return to equilibrium (see Chapter 2).

Analysis here focuses only on the transient perturbation effect, not the persistent case, as the long term equilibrium is $P_I = 1$ unless culling is sufficiently severe to remove the disease, and therefore the increase in disease associated with population reduction is only temporary. Culling begins 5 years after the model is started, giving sufficient time for sub-populations to stabilise, and the population is measured at time $t = 20$ following the start of culling.

Two other measurements that are useful are the effective dispersal and transmission rates, as these provide insight into the mechanisms leading to the perturbation effect (see Chapter 2). The effective dispersal rate is the average per-capita dispersal rate across all sites, and is indicative of the total level of dispersal occurring within the population. The effective transmission rate is given by

$$\beta_{\text{eff}} = \frac{\sum_i H_i}{\sum_i S_i \sum_j I_j}$$

which indicates the force of infection within the total population, or the average risk of

infection to each susceptible. It is also the effective contact rate if the disease dynamics were modelled assuming complete mixing. In Chapter 2, it was shown that while β_{eff} is expected to increase with P_I (since more susceptibles are exposed to infection), it was also elevated during population reduction and returned to expected values after culling stopped. A high β_{eff} during population reduction demonstrates higher than expected disease transmission, and is therefore indicative of the perturbation effect, which may not be obvious if $\Pi < 0$ or $\Pi_{\text{sites}} < 0$.

3.2.4 Implementation of population reduction strategies

There is considerable flexibility in the design of population reduction schemes within the spatially explicit model described above.

Spatial design

Since the population is arranged into a lattice of sub-populations, culling may be applied to any subset of the lattice, and at any level of intensity within those groups. Two main parameters describe population reduction:

1. Coverage $p_1 \in [0, 1]$, which is the proportion of groups in which culling takes place.
2. Within-site removal intensity p_2, which determines the rate or probability that individuals are removed from a group.

In the first designs explored here, the coverage is obtained by randomly selecting groups to target until the desired proportion is achieved. The within-site removal is the same throughout the targeted groups, and so the overall culling rate is $p = p_1 \times p_2$. Within such a design it is possible to obtain the same overall culling rate for different combinations of p_1 and p_2 by keeping p fixed and choosing $p_1 = p/p_2$ (e.g. culling is homogeneous when $p_1 = 1.0$, $p_2 = 0.2$, or more heterogeneous when $p_1 = 0.2$, $p_2 = 1.0$, but both strategies have the same overall rate of $p = 0.2$). Therefore, assuming the effort and cost required depends only on p, it is possible to evaluate the results of different strategies for any given level of resources (overall culling rate).

Temporal design

First it is assumed that individuals are removed continuously by increasing the natural mortality rate in targeted sites from $d \rightarrow d + p_2$. When the coverage is incomplete (i.e. $p_1 < 1$), and not a fixed area, then the targeted sites must be randomly chosen. After a

period of time, a switch event is triggered, the mortality rates in targeted sites are returned to normal, and a new set of sites are targeted. The time between such events is referred to here as the "switch time". By default the switch time is one year, but the effect of changing the switch time is also examined.

Instead of such continuous culling, it is possible that culling is a single discrete event, in which individuals are randomly removed with probability p_2 — thus the total number removed from site i is binomially distributed (with parameters N_i and p_2). For discrete culling, the switch time is the time between culling events, during which mortality rates remain at the normal level d.

It is important to note that rates and probabilities do not directly correspond, since a removal rate is $p_2 \in [0, \infty)$, while a removal probability is $p_2 \in [0, 1]$. In some circumstances it is possible to translate directly between probabilities P and rates R using $R = -\ln(1-P)/t$ and $P = 1 - \exp(-Rt)$. For example, an individual exposed to a removal rate of $p_2 = 1.0$/yr for one year would correspond to removal probability of $p_2 = 0.63$. Similarly, a removal probability of $p_2 = 1$ corresponds to instantaneous removal of all individuals, i.e. an infinite instantaneous rate of p_2.

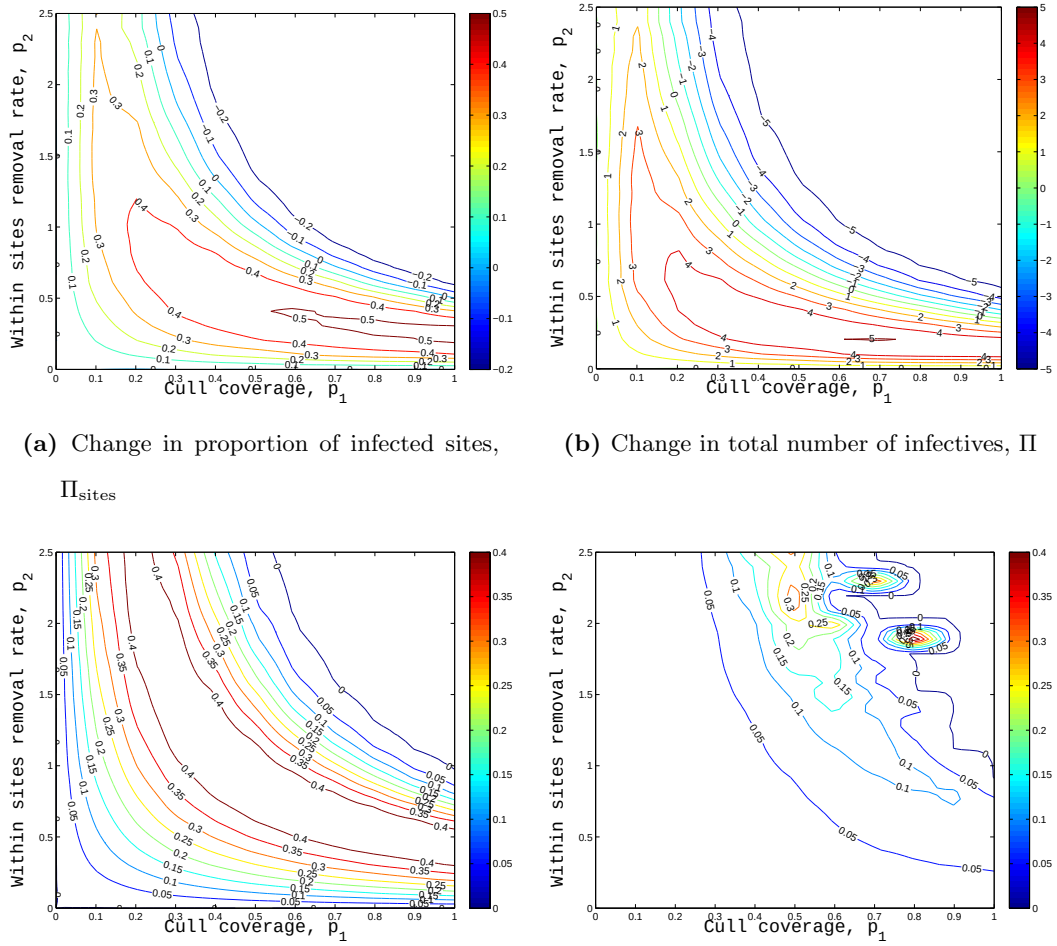
Non-selective culling

When disease status can be readily identified, it may be preferable to remove only diseased individuals, while leaving susceptible or resistant ones, however this is often difficult to achieve, and is not considered here. In this chapter, it is assumed that all culling is non-selective (i.e. each individual in a targeted site has the same increased mortality rate or chance of immediate removal, regardless of disease status), however the case of selective culling is discussed in more detail in Chapter 4.

3.3 Results

3.3.1 Coverage and within sites removal

The effects of varying coverage p_1 and within-site removal rate p_2 are shown in Figure 3.1. The proportion of infective sites, Π_{sites}, is maximised (reflecting the worst outcome from culling) for intermediate values of p_1 and p_2, and appears to roughly follow the contour $p = p_1 \times p_2$ such that p is constant (see Fig. 3.1a, and also below). Culling rates need to be quite high (around $p > 0.6$, and both p_1 and p_2 large) before Π_{sites} is reduced below zero, so intensive culling is necessary to reduce disease levels in the system studied here.



(a) Change in proportion of infected sites, Π_{sites}

(b) Change in total number of infectives, Π

(c) Change in effective dispersal

(d) Change in effective horizontal transmission, β_{eff}

Figure 3.1: Effect of coverage p_1 and within-site removal rate p_2, at time $t = 20$, starting near the disease free equilibrium. Fig. 3.1a shows Π_{sites}, Fig. 3.1b shows Π, Fig. 3.1c shows effective dispersal, and Fig. 3.1c shows effective horizontal transmission β_{eff}. All other parameters are as given in Table 3.2. The maximum increase in disease spread is strongly dependent on p_2, but tends to occur for intermediate values of $p_1 \times p_2$.

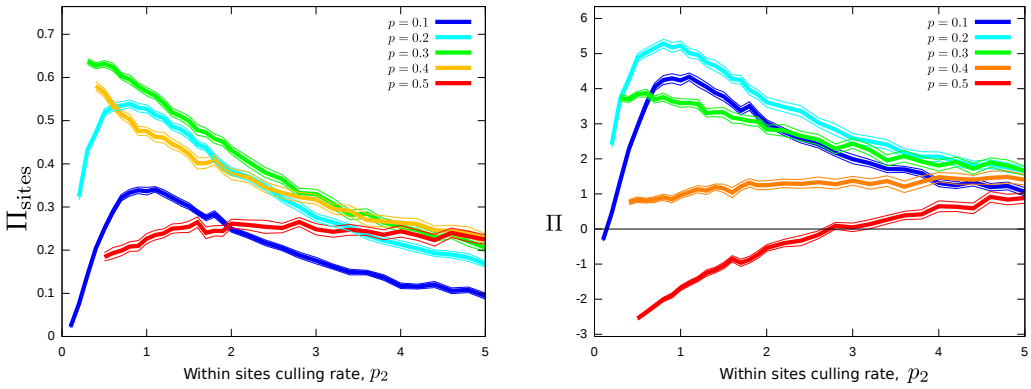
The change in the global number of infectives, Π, also appears to reflect the contour of constant p, however it becomes negative for smaller p than Π_{sites} (see Fig. 3.1b). This is potentially misleading, because this is a snapshot of one particular point in time during the cull, and the number of infectives is likely to increase when culling stops, reflecting the increase in P_I. Of note is that the effective horizontal transmission rate β_{eff} is maximised for high within-sites removal p_2, but intermediate coverage p_1, suggesting that the force of infection may be less affected than the other quantities, but more strongly affected by the culling heterogeneity.

3.3.2 Culling heterogeneity

In Fig. 3.1a, the increase in geographical spread of the disease Π_{sites} appears to follow the contour for constant $p_1 \times p_2$, suggesting that the overall culling rate p is more important than the culling heterogeneity, however this is examined in more detail now. In Fig. 3.2, Π_{sites} is shown for a range of overall efforts $p = 0.1$ to $p = 0.5$, while coverage p_1 and within-sites removal p_2 are varied simultaneously such that $p_1 \times p_2 = p$. Homogeneous culling is given by $p_1 = 1$, $p_2 = p$, while highly heterogeneous culling is given by $p_1 = p/5$, $p_2 = 5$.

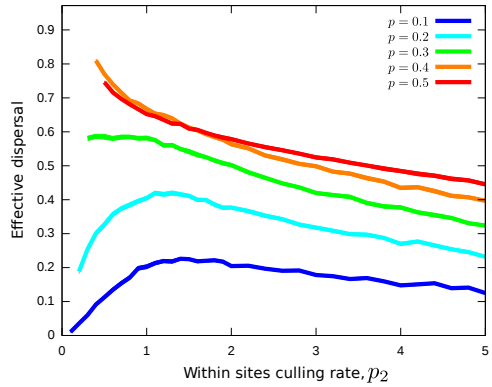
For small p, the perturbation effect is minimised when culling is homogeneous, but is maximised by a small level of heterogeneity (e.g. for $p = 0.2$, the perturbation effect is maximised when $p_1 = 0.2$, $p_2 = 1$). This intermediate maximum occurs because of the trade off induced by increasing p_2, which reduces the sub-population sizes, and increasing dispersal due to density dependence (increasing the perturbation effect around those sites), and the lower p_1, which results in fewer sites contributing to the perturbation effect.

Fig. 3.3 illustrates in more detail how the perturbation effect is influenced by heterogeneity in the culling regime. Four subfigures show the temporal evolution of quantities describing key processes involved in the perturbation effect. Effective dispersal rates increase soon after culling begins, leading to increased β_{eff} as the disease is introduced into new sites. Both fall rapidly after culling ceases, although effective β remains slightly elevated due to the greater number of sites containing infectives. For low heterogeneity ($p_1 = 0.5$, $p_2 = 0.4$) the dispersal rates are maximised, leading to the greatest disease spread. For high heterogeneity, dispersal rates remain low, as although targeted sites are more likely to allow movement, there are fewer of them, and so disease spreads much more slowly between groups. Note that following movement, there is an initial increase in disease transmission, as culling ceases suppressing disease transmission within groups,

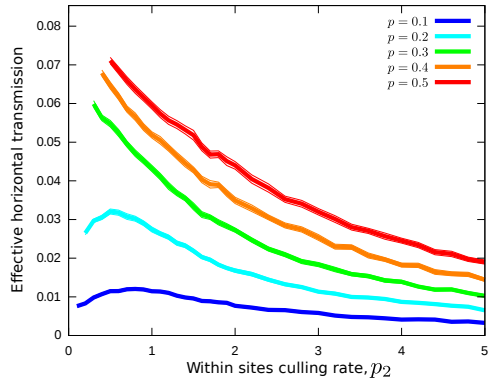


(a) Π_{sites}

(b) Π



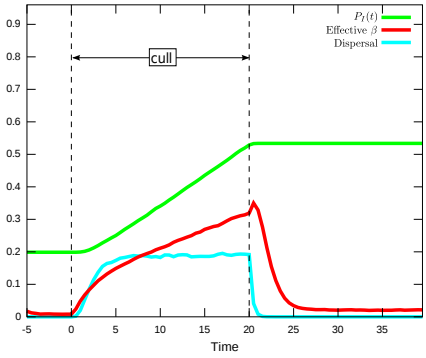
(c) Effective dispersal



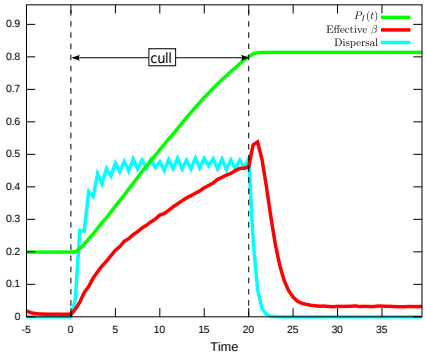
(d) Effective horizontal transmission, β_{eff}

Figure 3.2: Varying heterogeneity by varying within-site culling rate p_2, while simultaneously varying p_1 such that the total culling rate $p = p_1 \times p_2$ is constant. All other parameters are as given in Table 3.2. See Fig. 3.3 for further details for $p = 0.2$

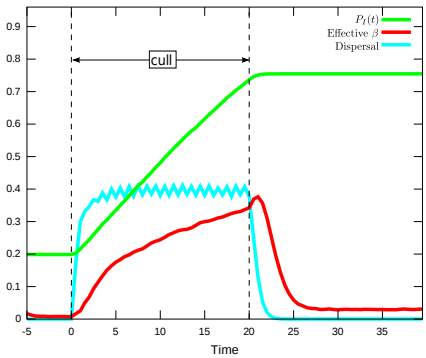
leading to a rapid increase in the number of infectives in infected sites.



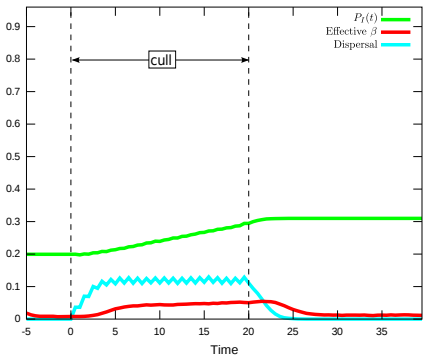
(a) Homogeneous culling: $p_1 = 1$, $p_2 = 0.2$



(b) Low levels of heterogeneity: $p_1 = 0.5$, $p_2 = 0.4$



(c) Intermediate heterogeneity: $p_1 = 0.2$, $p_2 = 1.0$



(d) Highly heterogeneous culling: $p_1 = 0.02$, $p_2 = 5.0$

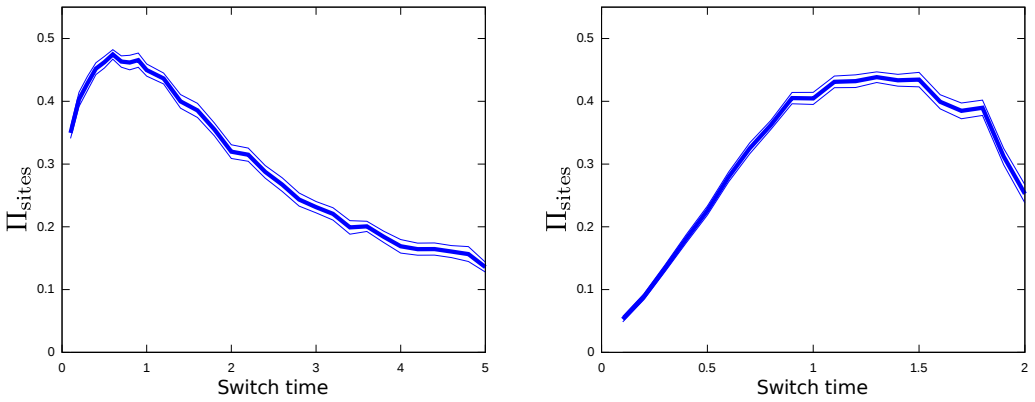
Figure 3.3: Time trajectories, showing how increasing levels of heterogeneity in culling (keeping $p_1 \times p_2$ fixed at $p = 0.2$) affects key processes that determine or govern the perturbation effect. Effective dispersal rate (cyan, scaled by 0.2), effective disease transmission rate β_{eff} (red), and proportion of infected sites P_I (green) are shown versus time for particular levels of heterogeneity. All other parameters are as given in Table 3.2.

When dispersal is not density dependent, then $\Pi_{\text{sites}} < 0$ for all values of $p > 0$, although its level is still dependent on the heterogeneity (see Appendix), suggesting that heterogeneity may still be an important factor in disease control even in the absence of the perturbation effect.

3.3.3 Switch time

Fig. 3.4 shows the effects of varying the time that a selected subset of groups are subjected to culling before a new subset are chosen. Figs. 3.4a and 3.4b show the results of continuous and discrete culling respectively. For discrete culling, the culling probability p_2 is varied

such that it is proportional to the switch interval (i.e. if the time between switches is halved, so is the culling intensity, so the average culling rate is effectively constant). Note that discrete culling is bounded by $p_2 \leq 1$, limiting the switch time possible. However, continuous culling is not bounded, and so higher switch times are shown.



(a) Continuous culling **(b)** Discrete culling

Figure 3.4: The size of the perturbation effect, Π_{sites}, at $t = 20$, for varying switch interval. In Fig. 3.4a, culling occurs continuously with within-site culling rate $p_2 = 1.0$. In Fig. 3.4b, culling occurs discretely with within-site culling probability $p_2 = 0.5\times$ switch interval. Coverage $p_1 = 0.2$ in both cases. All other parameters are as given in Table 3.2.

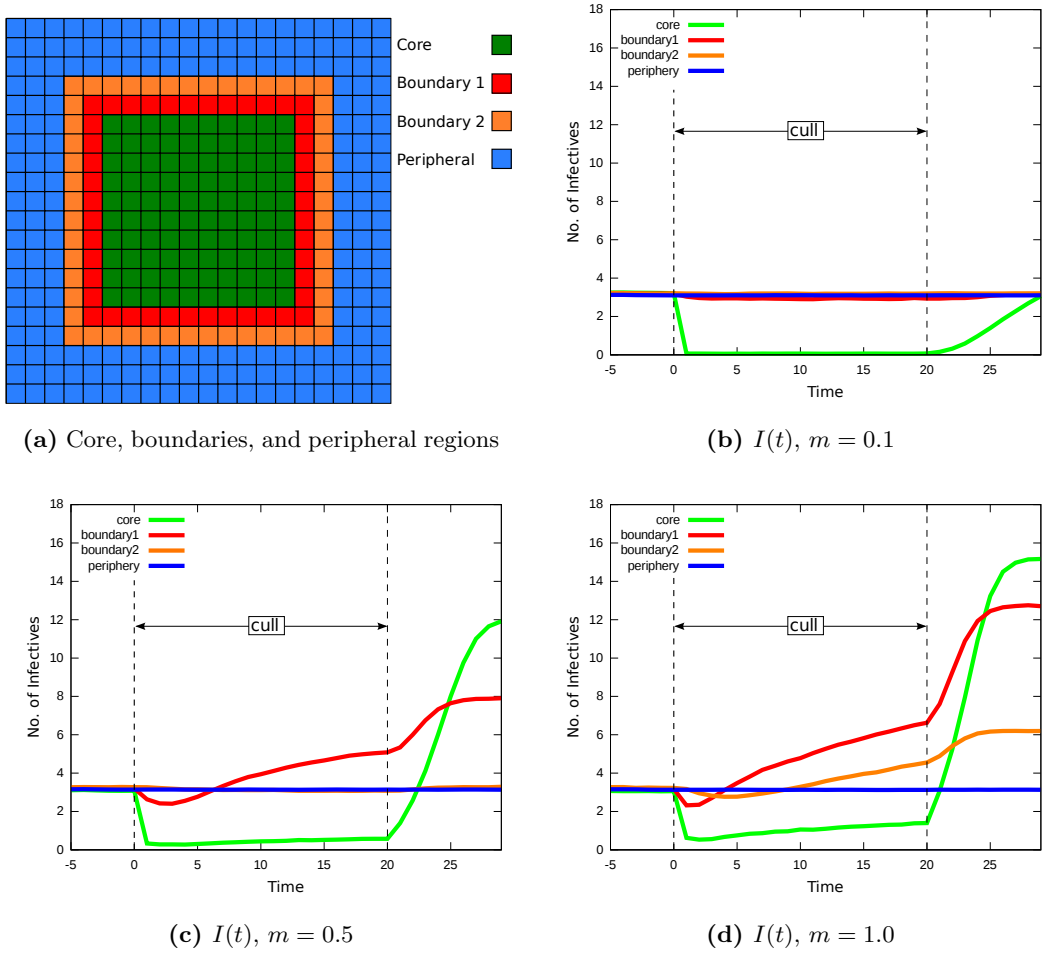
The maximum perturbation effect occurs when the interval is approximately 1 year in duration (0.6 for continuous, 1.3 for discrete culling), indicating that an annual cull may be the worst strategy for this parameter set. For shorter intervals, the perturbation effect reduces (more sharply for continuous culling) as sub-population sizes are not sufficiently reduced to permit increased dispersal; for longer intervals, after the peak increase the perturbation effect reduces more slowly as there are fewer sites available to encourage dispersal, despite targeted sites having smaller sub-population sizes. Of particular interest is that the minimum perturbation effect for continuous culling occurs when the switch time is high, but for discrete culling when the switch time is low.

3.3.4 The boundary of the cull

In the RBCT, proactive culling reduced bTB incidence within the target area, but this was more than matched by increased incidence in the surrounding areas (Donnelly *et al.*, 2007). To examine this effect, severe culling (matching proactive culling) is applied to a core area, and disease levels are examined in the core and surrounding areas.

In a 20×20 lattice, the middle 10×10 core was subjected to intensive culling ($p_1 = 1$, $p_2 = 0.8$). Fig. 3.5 shows the proportion of sites containing infectives P_I, in four areas:

the core, the boundary areas immediately surrounding the core, and the peripheral areas (see Fig. 3.5a).



(a) Core, boundaries, and peripheral regions

(b) $I(t)$, $m = 0.1$

(c) $I(t)$, $m = 0.5$

(d) $I(t)$, $m = 1.0$

Figure 3.5: Culling performed on a 10×10 core within the 20×20 lattice, and P_I is shown for sites in the core, sites in the boundaries surrounding the core, and the remaining peripheral sites. Culling is $p_1 = 1$, $p_2 = 0.8$ within core, whereas $p_1 = p_2 = 0$ outside. All other parameters are as given in Table 3.2.

For low intrinsic dispersal rate $m = 0.1$ (see Fig. 3.5b), there is very little movement across the border, as local compensatory population growth is a greater contributing factor in replacing individuals that dispersed into the low population density core. For larger $m = 0.5$ (see Fig. 3.5c), the dispersal rate is sufficiently high that it significantly surpasses rates of compensatory growth, allowing dispersal in from the outer sites; this increases the chance of introducing infectives into disease free boundary groups. However, there is still little movement across the outer boundary. When culling ceases in the core, the disease levels quickly increase due to the flow of infectives from the boundary. This flow continues for a few years until the population levels recover sufficiently to prevent further dispersal. For $m = 1$, dispersal leads to movement across both inner and outer boundaries, leading

to an increase in disease in both areas.

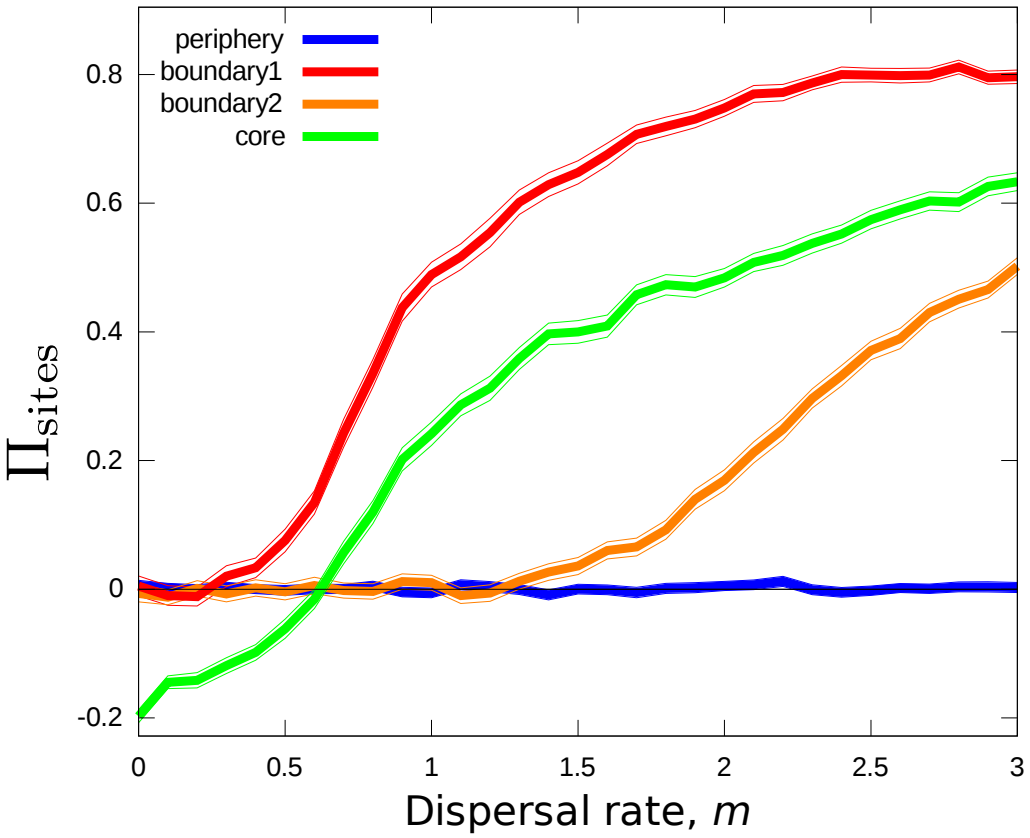


Figure 3.6: The size of the perturbation effect, Π_{sites}, at $t = 20$ in the core and surrounding regions, for varying intrinsic dispersal rate m. As m increases, regions further from the culled area become increasingly susceptible to the perturbation effect. Culling is $p_1 = 1$, $p_2 = 0.8$ within core, whereas $p_1 = p_2 = 0$ outside. All other parameters are as given in Table 3.2.

3.4 Discussion

3.4.1 Culling heterogeneity

It has been demonstrated that the perturbation effect can vary with the heterogeneity of the culling regime, and it is clear that such heterogeneity can have an impact on the perturbation effect whenever density dependent dispersal is a causative mechanism. Even in disease systems where the perturbation effect only partially interferes with population reduction (reducing culling efficacy but not leading to an increase in disease), culling strategies could usefully take the results into account. It is also important that any culling strategies are well coordinated across an entire area, and not left to individuals in charge of small areas to devise independently.

In comparing the results with density dependent dispersal (see Fig. 3.1) and without (see Fig. 3.7 in Appendix 3.A), it is interesting to note that homogeneous culling seems most effective at removing disease when there is a perturbation effect, but heterogeneous culling when there is not. This may be because heterogeneous culling reduces the total population size by a greater amount, as individual sub-populations may be completely removed and take time to recolonise and return to equilibrium, which is less likely with homogeneous culling. The reduced population size is expected to have greater impact on disease control when demographic responses do not lead to enhanced transmission.

When comparing the effect of varying the interval between selecting a new subset of groups in which to apply culling, the perturbation effect was maximised for a switch time of about 1 year when culling was applied continuously, and about 1.5 years when culling was applied discretely (see Fig. 3.4). With a longer switch time targeted sites are culled more intensively (increasing the chance of allowing immigration), but fewer sites receive treatment (thus fewer opportunities for the disease to spread to new sites). Also, the disease is less likely to persist in heavily culled sites. Hence, there is a trade-off, leading to a maximum perturbation effect. In contrast, the perturbation effect was minimised for continuous culling when the switch time was high, but for discrete culling when the switch time was low.

3.4.2 Effects in the boundary

Previous results assumed that culling took place across the entire population, and had no influence beyond the population boundaries. Limiting the cull to a core area entirely contained within the population allowed examination of the dynamics outside the culled area.

One of the results observed in the RBCT was increased badger ranging behaviour observed up to 2 km beyond the boundary of the target area in proactive culling (Donnelly *et al.*, 2006). Similar results are observed here: if the increase in movement is sufficiently high, then the perturbation effect occurs in the areas bordering the culled inner core (see Fig. 3.5). As the dispersal rate increases, so does the distance from the inner core where the perturbation effect occurs (see Fig. 3.6). Depending on how far the perturbation effect extends from the boundaries of the core, a very large area of proactive culling may be required in order to cause an overall reduction in disease, and it may not be desirable to conduct proactive culling in small areas.

The proportion of badgers captured close to the culling boundary increased on successive culls due to immigration from surrounding areas (Woodroffe *et al.*, 2008). When the dispersal rate was sufficiently high, disease levels within the core area increased, indicating immigration from outside the boundary since these levels were sufficiently severe to remove the disease if movement beyond the boundary was not possible (as in Fig. 3.1a). The entry of infectives from the border is sufficient not only to maintain the disease, but also to ensure that it spreads to more sites within the core.

This infers that without barriers preventing dispersal into an area, culling may be unable to remove the disease without removing the population entirely, which would be an obstruction to disease control if conservation of the host species is an important consideration.

In conclusion, this work demonstrates the importance of the role of heterogeneity in culling strategies, both spatially and temporally, which must be considered when density dependent processes lead to enhanced disease transmission. Effort may be better spent by re-examining the culling strategies. Also, it is important to remain aware that the effects of population reduction may extend beyond the culling area, causing undesired effects in neighbouring areas.

3.A Non-density dependent dispersal

No increase in disease was found for any set of parameters when dispersal did not include density dependence, however the perturbation effect is not limited to increases in disease, but also includes failure to achieve expected levels of decrease. Since density dependence considerably reduces realised dispersal rates, intrinsic dispersal rate m is set much lower for non-density dependent dispersal, in order to compare similar average realised dispersal rates.

Fig. 3.7 shows movement in the core, analogous to Fig. 3.1. The maximum values of Π_{sites}, Π, and effective dispersal rates occur when no culling takes place, indicating that culling does decrease disease. However, the effective horizontal transmission is maximised for intermediate coverage and high within-sites removal, as it is for density dependent dispersal.

Fig. 3.8 shows movement in the core, analogous to Fig. 3.6. The increase in dispersal has very little effect outside the core, as movement rates are not affected by the change in sub-population sizes.

Fig. 3.9 is analogous to Fig. 3.4. In both cases, the disease is most strongly reduced by a long switch time, but more so with discrete culling.

3.B Maintaining consistency between rates and probabilities

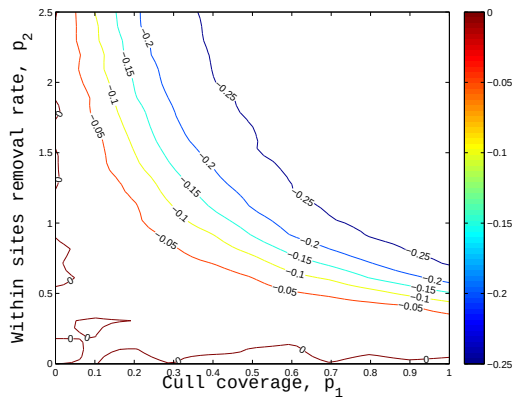
When single events remove multiple individuals, each individual is removed with a probability $p_2 \in [0, 1]$. However, when population reduction is implemented continuously, individuals are now removed at a rate $p_2 \in [0, \infty)$, and so the probability does not map simply into the rate. Discrete probabilities P over a time interval t can be converted into continuous rates R via

$$R = -\ln(1 - P)/t$$

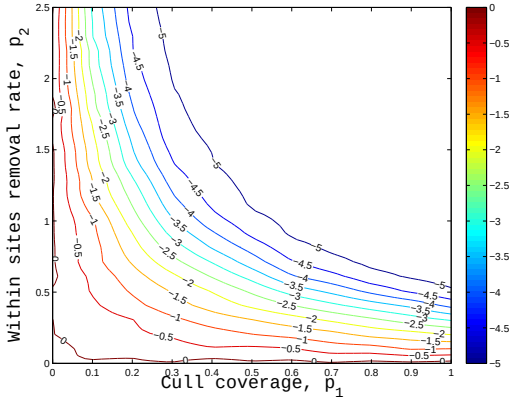
however with logistic growth this is more complex, and may require manual tuning.

Removal rates can be compared when the population reaches equilibrium during sustained culling, i.e. $N(t) \to N^*(p)$. Unfortunately, $N^*(p)$ is a static value for continuous culling, but a periodic value for discrete culling. A static value can be approximated by sampling the population at multiple times throughout the year, and using the mean, i.e.

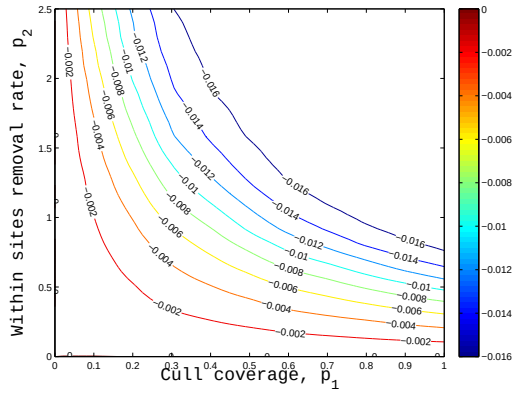
$$N^*(p) \approx \frac{1}{T} \int_0^T N(t; p) dt$$



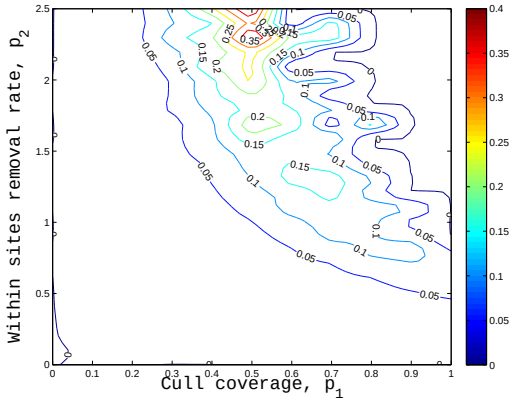
(a) Change in proportion of infected sites, Π_{sites}



(b) Change in total number of infectives, Π



(c) Change in effective dispersal



(d) Change in effective horizontal transmission rate

Figure 3.7: Coverage p_1 versus within-site removal rate p_2, at time $t = 20$, starting near the disease free equilibrium. All other parameters are as given in Table 3.2. Culling does not increase disease, however there is an increase in effective transmission rate for $p_1 \approx 0.5$ and large p_2.

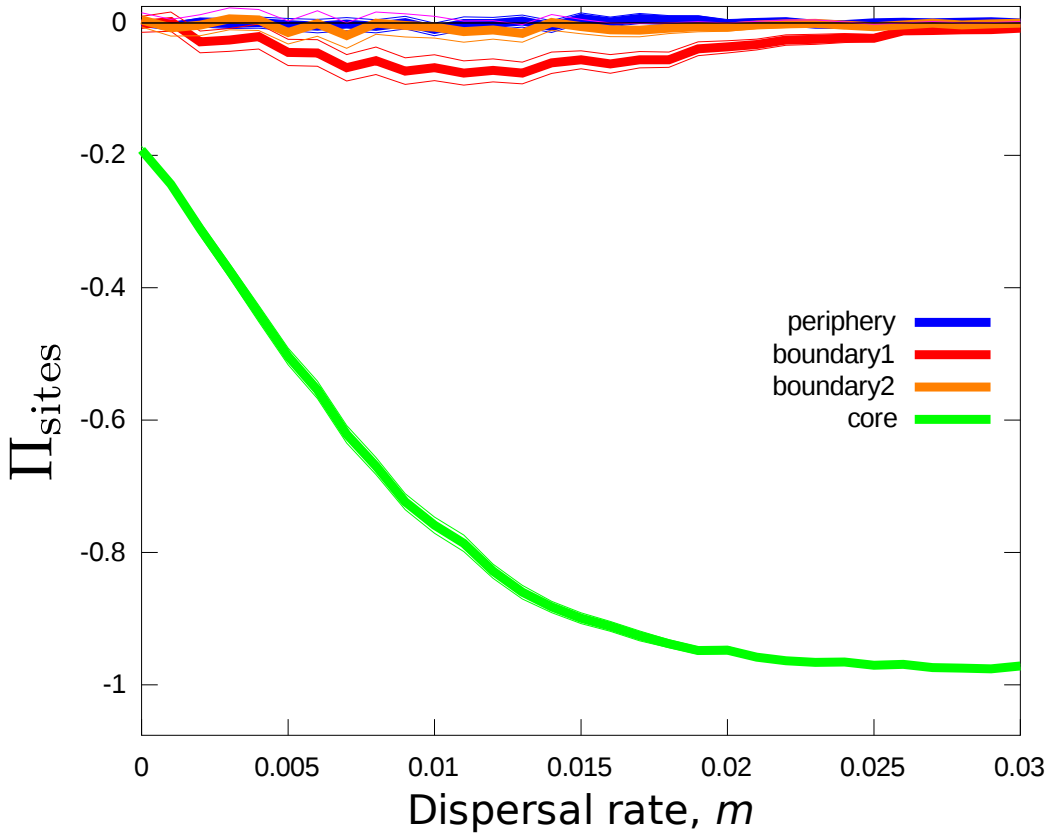
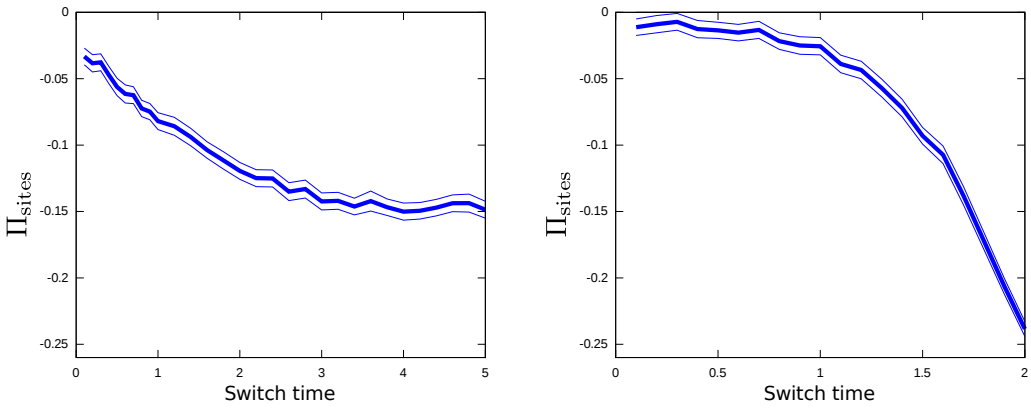


Figure 3.8: The size of the perturbation effect, Π_{sites}, at $t = 20$ in the core and surrounding regions, for varying intrinsic dispersal rate m. As m increases, regions further from the culled area become increasingly susceptible to the perturbation effect. Culling within core is: $p_1 = 1$, $p_2 = 0.8$, and outside: $p_1 = p_2 = 0$, all other parameters are as given in Table 3.2.



(a) Continuous culling **(b)** Discrete culling

Figure 3.9: The size of the perturbation effect, Π_{sites}, at $t = 20$, for varying switch interval, with non-density dependent dispersal. In Fig. 3.4a, culling occurs continuously with within-site culling rate $p_2 = 1.0$. In Fig. 3.4b, culling occurs discretely with within-site culling probability $p_2 = 0.5\times$ switch interval. Coverage $p_1 = 0.2$ in both cases. All other parameters are as given in Table 3.2.

With coverage $p_1 = 0.5$, removal probability of $p_2 = 0.5$ was most closely approximated by a removal rate $p_2 = 0.75$ for $r = 1$, and $p_2 = 1.0$ for $r = 5$. Table 3.3 provides a complete list of rates for both $r = 1$ and $r = 5$.

Discrete	**Predicted**	**Continuous** $r = 1$	**Continuous** $r = 5$
0.0	0.00	0.00	0.00
0.1	0.11	0.11	0.12
0.2	0.22	0.23	0.27
0.3	0.36	0.37	0.43
0.4	0.51	0.53	0.61
0.5	0.69	0.71	0.82
0.6	0.92	0.94	1.07
0.7	1.20	1.22	1.39
0.8	1.61	1.60	1.90
0.9	2.30	2.00	2.85
1.0	∞	5.00	5.30

Table 3.3: Conversion between discrete culling probability and continuous culling annual rate p_2. Given probability P, the predicted rate R is $R = -\ln(1 - P)$, which is very close for $r = 1$, but less so for $r = 5$.

Chapter 4

Non-spatial processes and the impact of unintentional selective population reduction

4.1 Background

4.1.1 Selective population reduction

Population reduction (e.g. culling) is often used as a disease control method, when dealing with wildlife diseases affecting livestock, however the aim is usually not eradication, but to maintain population numbers below a certain threshold where the disease can no longer spread fast enough to persist (Kermack & McKendrick, 1927; Wobeser, 1994). Where conservation of the host species is important, there is a clear benefit to being able to remove only individuals infected with the disease, and retain those that are susceptible or resistant (Carter *et al.*, 2009). This may be particularly useful when a small part of the population contributes disproportionately to disease transmission (Woolhouse *et al.*, 1997; Lloyd-Smith *et al.*, 2005a).

Selective culling methods (e.g. test and slaughter) have achieved some success in the control of chronic infections that spread slowly through populations such as bovine tuberculosis (bTB) and brucellosis, especially in ungulates that tend to form large aggregations (Tweddle & Livingstone, 1994; Cross, 2005; Carter *et al.*, 2009). A test and slaughter strategy was used to significantly reduce the prevalence of bTB in buffalo herds in Hluhluwe Umfolozi National Park, South Africa (Michel *et al.*, 2006), and has been used in the control of Foot and Mouth disease in cattle in the UK.

However, test and slaughter may be complicated by difficulty detecting infectives, e.g. the ELISA test for Bovine TB in cattle only has 41% sensitivity (Smith *et al.*, 2001b), which means a high chance of giving a false negative, and so repeated testing is necessary to ensure disease free status. Even in cases where the infectives can be readily identified however, population reduction does not guarantee successful removal of the disease, e.g. the Tasmanian Devil (*Sarcophilus harrisii*) and Tasmanian Devil facial tumour disease. Models suggest that despite being very trappable and infectives easily identified, culling alone is insufficient to prevent extinction of the species (Beeton & McCallum, 2011), as the lengthy latent period means that the disease may not have been removed from the population even if all individuals expressing symptoms are culled, and frequency dependent transmission prevents a population threshold for which the disease will not be able to spread fast enough to persist (McCallum *et al.*, 2001).

In some cases, it is possible that population reduction could fail to target certain groups (Clutton-Brock & Lonergan, 1994; Smith, 1995a). For example, trappability may vary between different age groups (Tuyttens *et al.*, 1999), infective individuals might display

non-standard behaviour, and thus avoid capture (Coltherd *et al.*, 2010), or poisoning may select for the stronger susceptible individuals who are able to control access to the food stores (Hammond & Anthony, 2006). Hunting may also preferentially target the larger, older animals, who are most resistant to a particular disease (Guberti *et al.*, 1998; Rossi *et al.*, 2005b; Choisy & Rohani, 2006). In these circumstances, population reduction that is unintentionally selective may produce unexpected and unwanted results, i.e. an increase in disease.

In a host-disease system, there are three ways that the number of infectives can increase:

1. An infective from a neighbouring sub-population enters a group via *dispersal*.
2. A susceptible individual is infected via *horizontal transmission* (either from another infective, possibly of a different species, or via some intermediate vector).
3. An infective individual gives birth to infective offspring via *vertical transmission*, or transmits the disease soon after birth (*pseudo-vertical transmission*).

The first case (discussed in detail in Chapter 2), results in a local increase in disease, with a corresponding decrease elsewhere. However, the rearrangement of infection can lead to an increase in the horizontal disease transmission rate due to increased contact rates between susceptibles and infectives (e.g. by introducing an infective into a group of susceptibles). Increasing the rate of dispersal (e.g. due to the vacuum effect) may be an important mechanic responsible for the perturbation effect.

In this chapter, the consequences are considered of unintentionally applying selective population reduction, and its interaction with other processes, in order to show how other mechanisms may cause the perturbation effect. In particular, the roles of compensatory reproduction, vertical or pseudo-vertical transmission, and disease resistance are examined.

4.1.2 Vertical or pseudo-vertical transmission

In some host-disease systems, the disease is able to transmit to offspring before or around birth, which can have a significant effect on the stability of a disease (Judge *et al.*, 2007). Vertical or pseudo-vertical transmission is a common feature of many wildlife diseases, including badgers (*Meles meles*) and bTB (Anderson *et al.*, 1981; Bentil & Murray, 1993), wild boar (*Sus scrofa*) and CSF (Artois *et al.*, 2002), and foxes (*Vulpes vulpes*) and rabies (Bacon, 1985).

In disease systems driven mostly by vertical transmission, this tends to result in relatively low virulence compared to diseases that are driven mostly by horizontal transmission, as host fitness and fecundity must be maintained in order to ensure transmission to the next generation (Stewart *et al.*, 2005). Consequently, if fecundity in infectives is not reduced, compensatory reproduction could lead to an increase in the infective birth rate, potentially leading to an overall increase in disease levels.

4.1.3 Disease resistance

Thus far, two categories of individual have been considered: *susceptible* and *infective*. However, in many disease systems individuals may recover and gain immunity to the disease; in this case a third category may also be considered: *resistant*. A large resistant population depletes the number of susceptible individuals without disrupting the social hierarchy, and reduces the horizontal transmission rate, thus reducing the infective population.

Vaccination is a frequently used technique to increase the number of resistant individuals, and apart from preventing new infections, sufficient coverage may help to provide herd immunity to the population (Fine, 1993). Given the basic reproduction ratio R_0, it can be shown that if a proportion $1 - 1/R_0$ of the population is resistant, then the disease should not be able to invade (Kermack & McKendrick, 1927).

However, if these resistant individuals are disproportionately removed by population reduction, then compensatory reproduction should increase the population size by recruiting new susceptible individuals, which can increase R_0, and allow disease levels to increase.

4.1.4 Age structure

Horizontal disease transmission depends on both contact rates and host susceptibility, and these may not be homogeneous throughout the population. A change in population structure may lead to an increase in the horizontal transmission rate. For example, if adults are less susceptible to a disease than juveniles (Cattadori *et al.*, 2005), or contain a higher prevalence of resistant individuals, then removing the adults will reduce the herd immunity and increase the average population susceptibility. Strong density dependence may further increase this problem, as the number of juveniles may temporarily increase as the population recovers.

4.2 Methods

Several different models containing key mechanisms observed in wildlife hosts are investigated. No process as described in Chapter 2 directly enhances disease transmission, so any perturbation effect is an emergent property of the underlying model. The disease systems are all described by non-spatial ordinary deterministic equations (ODEs), which describe the rates of change of the different categories of individual in the model.

See Table 4.1 for a list of parameters and default values used in each of the models.

Parameter	**Symbol**	**VT**	**SIR**	**Age**	**Units**
Intrinsic reproduction rate	r	1	1	1	year^{-1}
Carrying capacity	c	20	20	20	—
Natural mortality rate	d	0.2	0.2	0.2	year^{-1}
Disease induced mortality rate	e	0	0	0	year^{-1}
Maturation (ageing) rate	α	—	—	1	year^{-1}
Horizontal transmission rate	β	0.2	0.4	—	year^{-1}
in juveniles	β_j	—	—	2	year^{-1}
in adults	β_a	—	—	0	year^{-1}
Recovery rate	γ	–	1	—	year^{-1}
Vertical transmission probability	p_v	0.5	—	—	—
Population reduction rate for class X	p_X	0.2	0.2	0.2	year^{-1}

Table 4.1: A summary of the parameters and their symbols used in the models are described here. Class X represents any category of individual, e.g. culling rates for susceptibles S, or infective adults I_a are p_S and p_{Ia} respectively. With selective culling, $p_X = 0$ for non-targeted individuals. Parameter values are the default for each type of model considered.

4.2.1 Key mechanisms

Population growth

The longer the time interval over which the disease is studied, the more important the role of demography, as fluctuations in population size can significantly affect the disease dynamics, but for sufficiently short time scales, the population size can be considered to be fixed. Changes in population size occur when new individuals are born (or recruited) into the population, and are removed via mortality (whether due to disease or population

reduction, or causes unrelated to either). It is assumed that mortality occurs at constant per-capita rate d, and various forms of reproduction are considered.

The simplest form of growth can be considered by introducing new individuals at a constant rate. Here birth occurs at constant rate r, which gives

$$\dot{N} = r - dN \tag{4.1}$$

resulting in a disease free equilibrium $K = r/d$. However, since the birth rate is independent of the population size, this does not reflect compensatory reproduction, which may be a key mechanism related to the perturbation effect.

A common form of compensatory reproduction is logistic growth, where per capita birth is limited by a maximum population size (or carrying capacity) $N_{\max} = c$. Here birth occurs at rate $rN(1 - N/c)$, which gives

$$\dot{N} = rN(1 - N/c) - dN \tag{4.2}$$

resulting in a disease free equilibrium $K = c(r - d)/r$, and an extinction equilibrium $N = 0$.

Unfortunately, while population growth in the form of Eqn. 4.2 may be the most biologically "realistic", the non-linearity in the N^2 term can complicate algebraic analysis, although solutions can still be found numerically.

For this reason, it may be helpful to consider a simpler form of compensatory reproduction, birth at rate $r(1 - N/c)$, which gives

$$\dot{N} = r(1 - N/c) - dN \tag{4.3}$$

resulting in disease free equilibrium $K = cr/(r + dc)$, while there is no extinction equilibrium.

Note that Eqn. 4.3 is similar (and identical when $c = 1$) to the result of expanding Eqn. 4.2 around $N = 1 + \epsilon$, and allowing higher order terms $\epsilon^2 \to 0$. This provides a good approximation to behaviour near the disease free equilibrium, but may overestimate population growth for small N, and ignores the possibility of population extinction (however it may reflect density dependent dispersal into the population from a similar neighbouring population). For very small population size, Eqn. 4.2 can be expanded around $N = 0 + \epsilon$, obtaining birth at rate rN.

For this reason is is helpful to consider populations of the form Eqn. 4.3 during analysis where necessary; results should be broadly similar provided N is sufficiently close to the disease free equilibrium and not too small.

Disease dynamics

Horizontal disease transmission occurs at per capita rate H; transmission is normally assumed to be density dependent, in which case $H = \beta SI$, however sometimes diseases are frequency dependent, in which case $H = \beta SI/N$.

Since individuals are only exposed to vertical transmission once (at the time of introduction), vertical and pseudo-vertical transmission take place with probability p_v, which applies to the growth rate, e.g. for logistic growth, the birth rate is

$$\dot{S} = r(N - p_v I)(1 - N/c) + \dots$$
$$\dot{I} = r p_v I(1 - N/c) + \dots$$

Disease induced mortality removes infectives at per-capita rate e. However, it is often algebraically simpler to solve equations where $e = 0$, and therefore this is generally assumed to be the case, although the effect of disease induced mortality is considered in the sensitivity analysis where results are solved numerically.

Population reduction

Population reduction is performed by culling individuals from the population. The per-capita culling rate is represented by p_X, where X is the class of individual to which it is applied, non-selective culling is therefore the special case where $p_X = p$ for all classes.

Measuring the perturbation effect

The size of the perturbation effect, $\Pi(t; p)$, is measured by

$$\Pi(t; p) = I(t; p) - I(t; 0) \tag{4.4}$$

where $I(t; p)$ is the number of infectives at time t, where the population is subject to reduction at rate p (with applicable p for each group).

A useful special case to study, is when the disease is subject to persistent culling, and sufficient time passes for the system to reach equilibrium. This gives the persistent perturbation effect. It is important to note that I^* could be negative (and hence the disease would be unstable), and therefore these situations must be discounted. The persistent perturbation effect is given by

$$\Pi_{\text{eqm}} = \max\{I^*(p), 0\} - \max\{I^*(0), 0\}; \tag{4.5}$$

Another useful measure is the instantaneous change in the perturbation effect, $\dot{\Pi}$, given by

$$\dot{\Pi}(t;p) = \frac{d}{dt}I(t;p) - \frac{d}{dt}I(t;0) \tag{4.6}$$

Rescaling

By scaling the population by the reciprocal of the carrying capacity, it is possible to remove the parameter c from models e.g.

$$\dot{N} = N(1-N) - dN$$

which simplifies analysis (see Chapter 2). The population variables now represent fractions of the carrying capacity. Remaining equations have been rescaled to remove c as described, however r is retained in this chapter, as its role may be important to disease dynamics.

4.2.2 Disease models

Three different models are considered here.

First an SI disease model featuring vertical transmission with probability p_v is considered:

$$\begin{aligned} \dot{S} &= +r(N - p_v I)(1-N) - (d + p_S)S - \beta SI \\ \dot{I} &= +rp_v I(1-N) + \beta SI - (d + e + p_I)I \end{aligned} \tag{4.7}$$

Second, a classic disease system featuring susceptible, infective, and resistant individuals (S, I, and R respectively) is examined:

$$\begin{aligned} \dot{S} &= +rN(1-N) - (d + p_S) - \beta SI \\ \dot{I} &= +\beta SI - (d + e + \gamma + p_I)I \\ \dot{R} &= +\gamma I - (d + p_R)R \end{aligned} \tag{4.8}$$

where γ is the recovery rate.

Finally, an SI disease system with age structure is examined. Rather than having a separate resistant class, it is assumed that adults are less susceptible to the disease than juveniles. The relevant model is

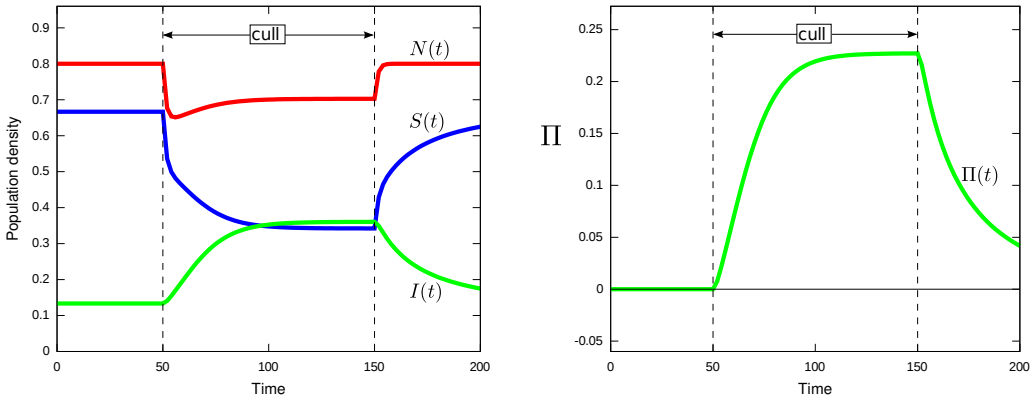
$$\begin{aligned} \dot{S}_j &= +rN(1-N) - (d + \alpha + p_{Sj})S_j - \beta_j S_j(I_j + I_a) \\ \dot{S}_a &= +\alpha S_j - (d + p_{Sa})S_a - \beta_a S_a(I_j + I_a) \\ \dot{I}_j &= +\beta_a S_a(I_j + Ia) - (d + \alpha + p_{I_j})I_j \\ \dot{I}_a &= +\alpha I_j + \beta_a S_a(I_j + I_a) - (d + p_{Ia})I_a \end{aligned} \tag{4.9}$$

where α is the maturity rate (i.e. $1/\alpha$ is the average time to adulthood), β_j is the infection rate for juveniles, β_a is the infection rate for adults, and $N = S_j + S_a + I_j + I_a$. Juveniles are considered to contribute towards density dependence for the purposes of reproduction, although this may differ from species to species.

4.3 Results

4.3.1 Vertical Transmission

An example of the perturbation effect for Eqn. 4.7 is shown in Fig. 4.1



(a) $S(t)$, $I(t)$, and $N(t)$ **(b)** $\Pi(t)$

Figure 4.1: Numerical solution of the SI model with vertical transmission, starting from the endemic equilibrium. Selective culling is applied to susceptibles only for $t \in [50, 150]$ (marked by the dashed lines) during which time the number of infectives $I(t)$ increases. Population values are shown in Fig. 4.1a, while $\Pi(t; p)$ is shown in Fig. 4.1b. Other parameters are as given in Table 4.1.

Equilibrium analysis

First the case $p_S = p_I = p$ is examined, and $e = 0$ is also assumed for algebraic simplicity. Solving for biologically realistic equilibria finds the endemic equilibrium

$$S^* = \frac{(d+p)(1-p_v)}{\beta}$$
$$I^* = 1 - \frac{(d+p)(r+\beta-rp_v)}{r\beta}$$

thus $p > 0$ serves only to reduce I^*, therefore non-selective culling does not produce a persistent perturbation effect, and some bias in culling is necessary in order to generate a perturbation effect in a system with only vertical transmission, compensatory reproduction, and density dependent horizontal disease transmission.

Next, the case $p_S \neq p_I$ is examined. The endemic equilibrium is algebraically complex, but some progress can be made by focusing on key values of p_v, in particular $p_v = 0$, $p_v = 1$, and $p_v = \beta/r$.

If $p_v = 0$ (reducing to the simple case of an SI model without vertical transmission), then the endemic equilibrium is

$$S^* = \frac{d + p_I}{\beta}$$
$$I^* = \frac{1}{2}\left(1 - \frac{d + p_I}{r}\right) - \frac{d + p_I}{\beta} + \frac{1}{2}\sqrt{\left(1 - \frac{d - p_I}{r}\right)^2 + 4(p_I - p_S)\frac{d + p_I}{r\beta}}$$

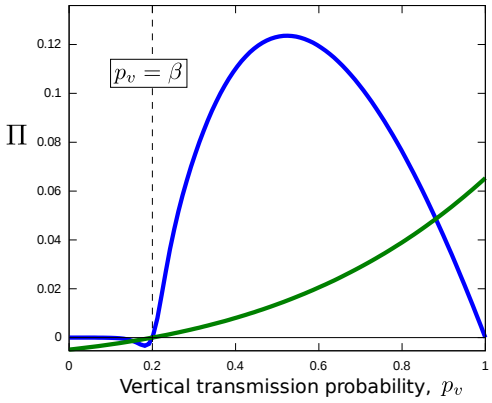
Here the only effect of $p_S > 0$ is to reduce I^*, hence the removal of susceptibles only leads to reduced I^*, and so there is no persistent perturbation effect. The effect of $p_I > 0$ is not so clear, but numerical solutions (see Fig. 4.4b) suggest that the only effect is to reduce I^*, again resulting in no persistent perturbation effect.

If $p_v = 1$, then the endemic equilibrium is $\{S^*, I^*\} = \{0, 1 - (d + p_I)/r\}$, which does not depend on p_S, but is reduced by p_I, and so there is no persistent perturbation effect.

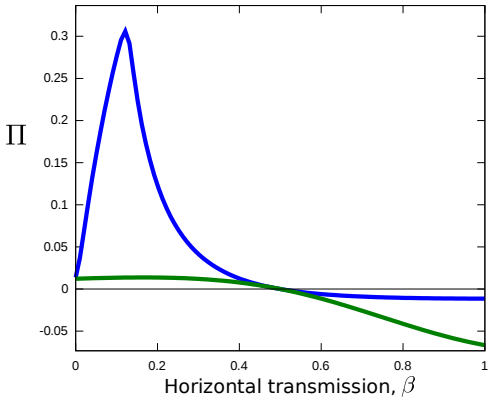
If $p_v = \beta/r$, then $\dot{I}$ does not depend on S, and the endemic equilibrium is $\{S^*, I^*\} = \{\ldots, 1 - (d + p_I)/\beta\}$, where I^* does not depend on p_S, but is reduced by p_I, and so there is no persistent perturbation effect.

The four special cases (non-selective culling, and selective culling with $p_v = 0, 1, \beta/r$) do not give rise to the persistent perturbation effect, while the general case does not provide a solution that is easy to solve algebraically. However, progress can be made by noting that horizontal transmission $H = \beta SI$ increases with S, while vertical transmission $V = p_v I(1 - N)$ decreases with S. Since $p_S > 0$ leads to decreased S, it is therefore expected to lead to increased V and decreased H. In the special case $rp_v = \beta$, the equilibrium no long depends on S and so culling of susceptibles does not affect I^*, since the reduction in H is exactly compensated for by the increase in V. Note also that the special case $p_v = 1$ does not depend on p_S either, since there are no susceptibles in the endemic equilibrium (or if $\beta = 0$ there may be disease present); as the disease is saturated, no increase in I^* due to compensatory reproduction is possible.

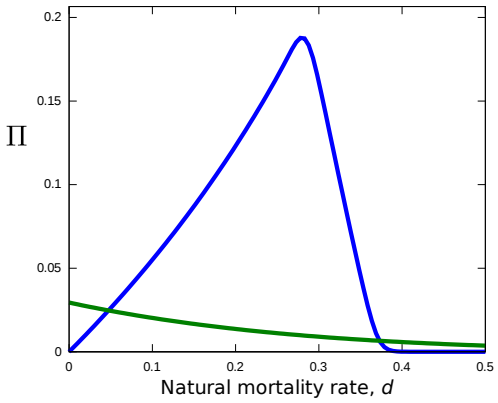
The bounds for p_v for which the persistent perturbation effect is possible are therefore $\beta/r < p_v < 1$. For $rp_v < \beta$, it is expected that $\Pi_{\text{eqm}} \leq 0$, although it also expected that $\Pi_{\text{eqm}} = 0$ if β and p_v are insufficient to maintain disease stability prior to culling.



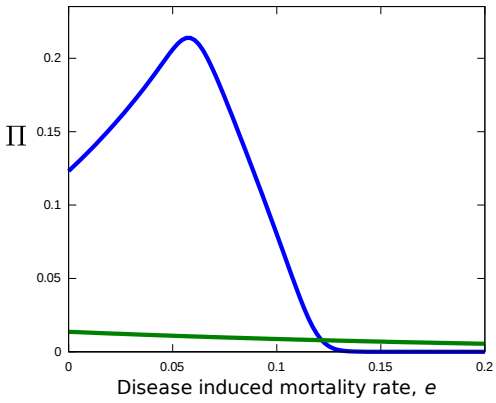
(a) Vertical transmission, p_v



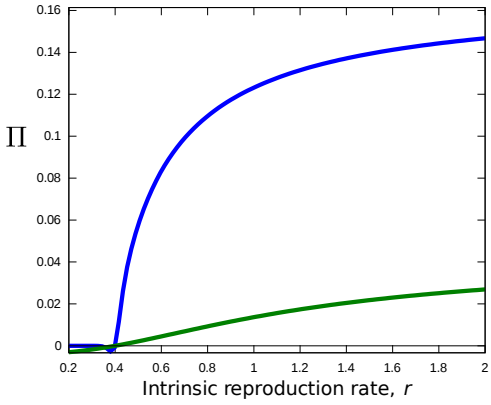
(b) Horizontal transmission, β



(c) Natural mortality rate, d



(d) Disease induced mortality rate, e



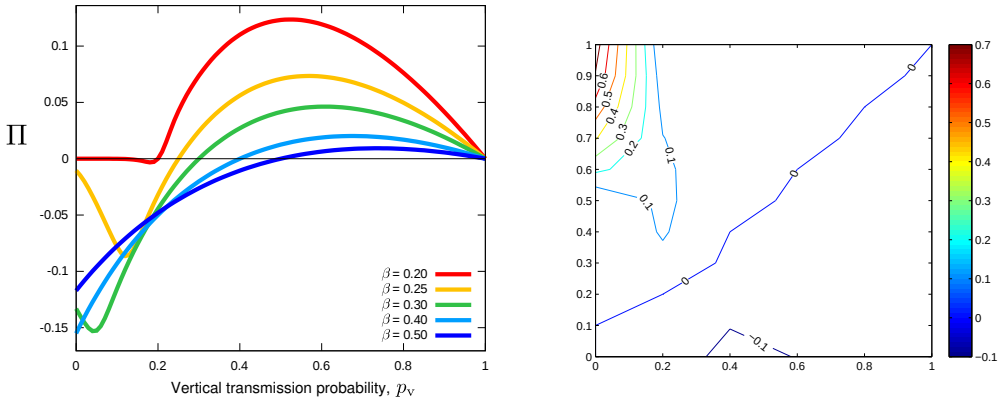
(e) Intrinsic reproduction rate, r

Figure 4.2: VT model: sensitivity analysis of $\Pi(t)$, near the start of culling (at $t = 5$, in green), and at equilibrium (at $t = 1000$, in blue). Other parameters are as given in Table 4.1, one parameter is varied at a time; initial conditions are $\{S_0, I_0\} = \{S^*_{\text{DF}} - 0.05, 0.05\}$.

Sensitivity analysis

The results are obtained by numerical analysis of p_v (see Fig. 4.2a), which shows a maximum persistent perturbation effect for intermediate p_v between β and 1. Differentiating $\dot{I}$ in Eqn. 4.7 with respect to S, obtains $\partial_S \dot{I} = (\beta - p_v)I$, which is positive if $p_v > \beta$, suggesting that a transient perturbation effect is possible even for very high p_v, which is confirmed in Fig. 4.2a, where both Π_{eqm} and $\Pi(5)$ become negative for $\beta > p_v$. The transient perturbation effect occurs for $p_v > \beta$ and increases with p_v, reaching its maximum at $p_v = 1$.

Numerical analysis of β (see Fig. 4.2b) shows a maximum persistent perturbation effect for intermediate β, where the disease changes stability, and no perturbation effect if $\beta > p_v$. Further examination of the interaction of p_v and β (see Fig. 4.3) confirms that $\Pi_{\text{eqm}} > 0$ for $p_v > \beta$, except for very small p_v and β due to disease instability. The perturbation effect is largest for small β, and $p_v \approx (1 + \beta)/2$ (see Fig. 4.3a).



(a) Π_{eqm} vs p_v, for varying β

(b) Contour of Π_{eqm} vs p_v, β

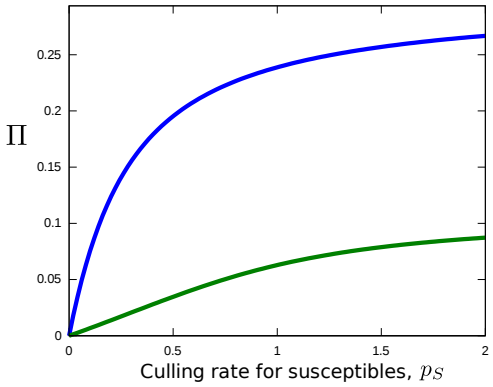
Figure 4.3: VT model: sensitivity analysis of Π_{eqm}, varying p_v and β. Other parameters are as given in Table 4.1. Note the zero contour along roughly $p_v = \beta$ (as predicted when $r = 1$).

Numerical analysis of mortality rates d and e (see Figs. 4.2c and 4.2d) shows a maximum persistent perturbation effect for intermediate values, similar to the maximum occurring when $I^*(0)$ changed stability in Chapter 2, and no perturbation effect for $d = 0$ (where the disease becomes saturated) or for large d and e (where the disease is not maintained within the population). Similarly, transient perturbation effects are greatest for low mortality rates, although e has very little influence. These results mirror the transient case described in Chapter 2.

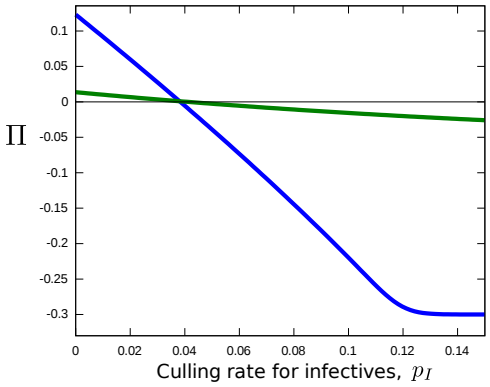
Numerical analysis of the intrinsic reproduction rate r (see Fig. 4.2e) shows that both

persistent and transient perturbation effects increase with r, but do not occur if r is too low, since one of the requirements for the perturbation effect is that $rp_v > \beta$. High compensatory reproduction can therefore reduce the degree of vertical transmission required for the perturbation effect to occur.

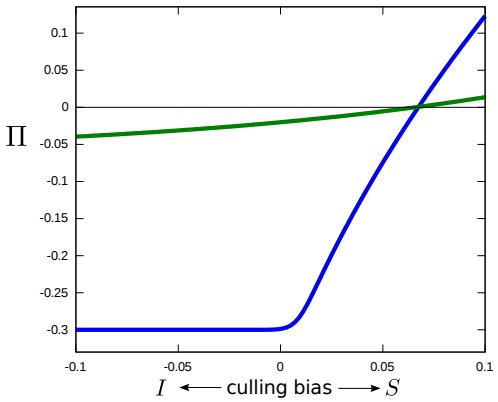
Numerical analysis of the culling rates (see Fig. 4.4) shows that both persistent and transient perturbation effects rise with the culling rate for susceptibles p_S, and decrease with with the culling rate for infectives p_I. Fig. 4.4c shows the effects of assuming that culling is non-selective, and introducing a bias towards S; this indicates that a perturbation effect is possible given sufficient bias towards S, but still with $p_I > 0$.



(a) Culling rate for susceptibles p_S ($p_I = 0$)



(b) Culling rate for infectives p_I ($p_S = 0.2$)

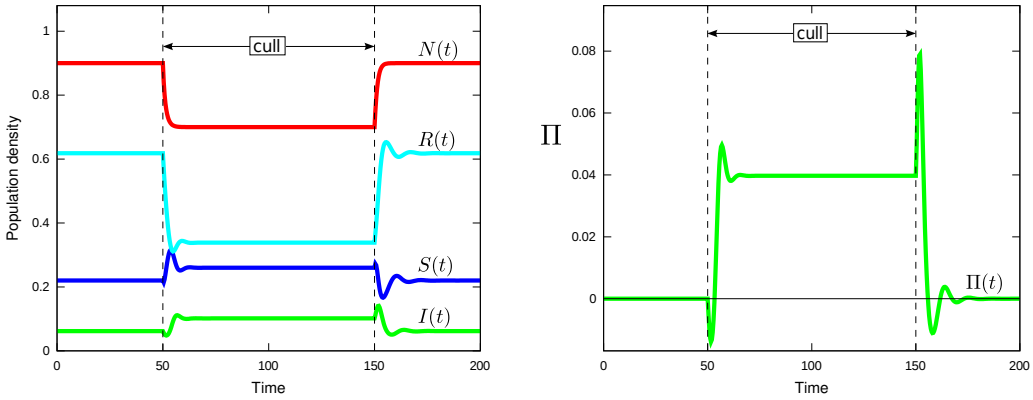


(c) Culling bias

Figure 4.4: VT model: sensitivity analysis of $\Pi(t)$, near the start of culling (at $t = 5$, in green), and at equilibrium (at $t = 1000$, in blue). In Fig. 4.4a, the culling rate for susceptibles p_S is varied, while the culling rate for infectives $p_I = 0$. In Fig. 4.4b, p_I is varied, while $p_S = 0.2$. In Fig. 4.4c, the culling rate is $p_S = 0.1 + b$, $p_I = 0.1 - b$, where b is the bias, so $b = 0$ represents non-selective culling, while $b = 0.1$ selects only S. One parameter is varied at a time, as shown for each graph above; initial conditions are $\{S_0, I_0\} = \{S^*_{\mathrm{DF}} - 0.05, 0.05\}$. Other parameters are as given in Table 4.1.

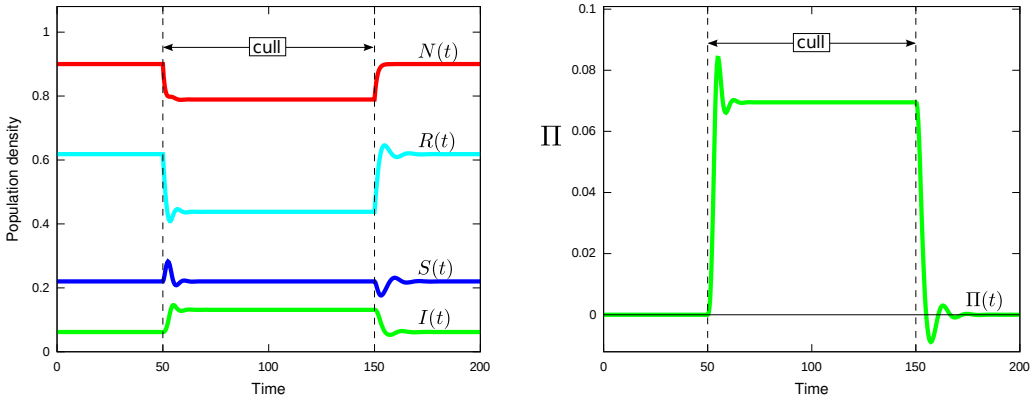
4.3.2 SIR model

An example of the perturbation effect is shown in Fig. 4.5 for non-selective culling, and in Fig. 4.6 for selective culling.



(a) $S(t)$, $I(t)$, $R(t)$, and $N(t)$ **(b)** $\Pi(t)$

Figure 4.5: Numerical solution of the SIR model with non-selective culling. Culling is applied equally to all classes of individual for $t \in [50, 150]$ (marked by the dashed lines) during which time the number of infectives $I(t)$ increases. $\Pi(t; p)$ is shown in Fig. 4.5b. Other parameters are as given in Table 4.1.



(a) $S(t)$, $I(t)$, $R(t)$, and $N(t)$ **(b)** $\Pi(t)$

Figure 4.6: Numerical solution of the SIR model with selective culling. Culling is applied only to resistant individuals for $t \in [50, 150]$ (marked by the dashed lines) during which time the number of infectives $I(t)$ increases. $\Pi(t; p)$ is shown in Fig. 4.6b. Other parameters are as given in Table 4.1.

Equilibrium analysis

First the case $p_S = p_I = p_R = p$ is examined. Solving Eqn. 4.8 for biologically realistic equilibria finds an endemic equilibrium

$$I^* = \frac{(d+p)(1-(d+p)/r)}{d+\gamma+p} - \frac{d+p}{\beta}$$

and so

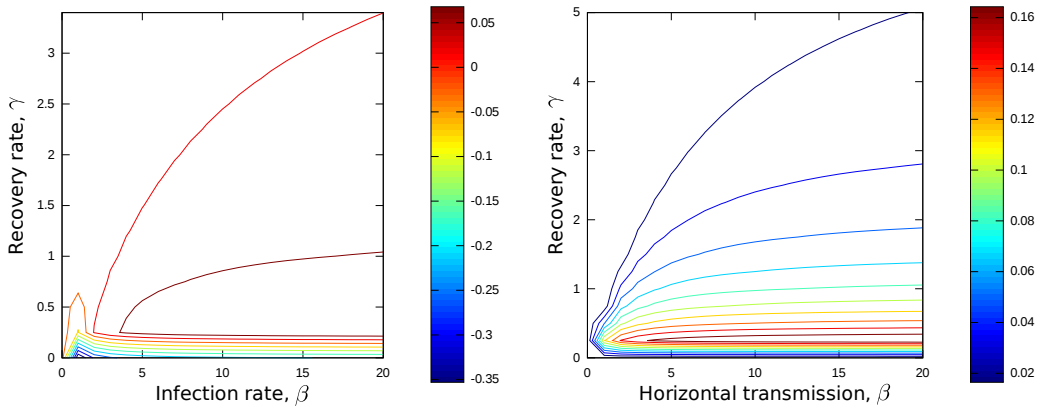
$$\Pi_{\text{eqm}} = \frac{(d+p)(1-(d+p)/r)}{d+\gamma+p} - \frac{p}{\beta} - \frac{d(1-d/r)}{d+\gamma}$$

which can be solved for boundaries for each parameter (results not shown).

Sensitivity analysis

Numerical analysis of horizontal transmission rate β (see Figs. 4.8a and 4.9a) shows that the perturbation effect increases with β, however non-selective culling can reduce infection when β is small.

Numerical analysis of recovery rate γ (see Figs. 4.8b and 4.9b) shows that the perturbation effect is maximised for small γ; non-selective culling can reduce infection when γ is small, but selective culling always results in the perturbation effect if $\gamma > 0$.



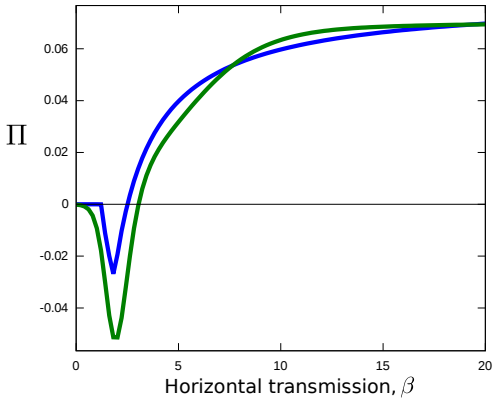
(a) Non-selective culling **(b)** Selective culling

Figure 4.7: *SIR* model: sensitivity analysis of Π_{eqm}, varying infection rate β and recovery rate γ. Non-selective is $p_S = p_I = p_R = 0.2$, selective culling is $p_S = p_I = 0$, $p_R = 0.2$ and other parameters are as given in Table 4.1.

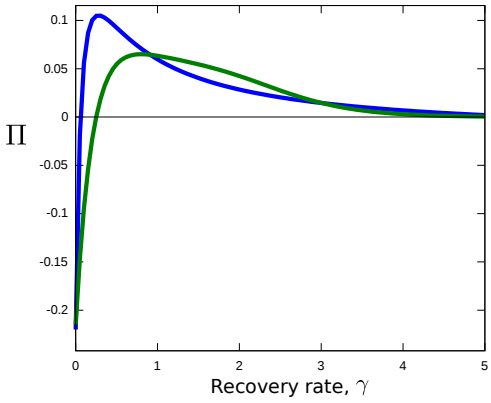
Simultaneous numerical analysis of both β and γ (see Fig. 4.7) shows that selective and non-selective culling are generally similar, except that selective culling gives a stronger perturbation effect, and prevents any reduction in infection.

Numerical analysis of mortality rates d and e (see Figs. 4.8c, 4.8d, 4.9c and 4.9d) shows that the perturbation effect occurs for smaller d and e, although high mortality reduces the perturbation effect more when culling is non-selective.

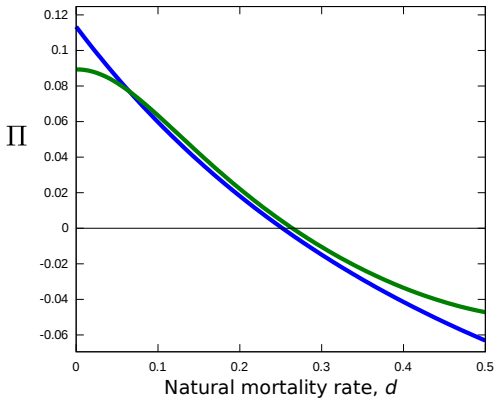
Numerical analysis of reproduction rate r (see Figs. 4.8e and 4.9e) shows that the perturbation effect increases with r, but does not occur for low r.



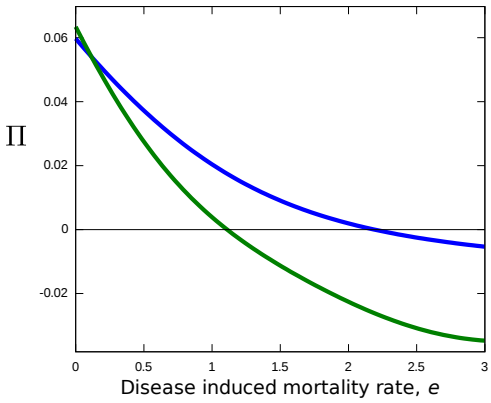
(a) Horizontal transmission, β



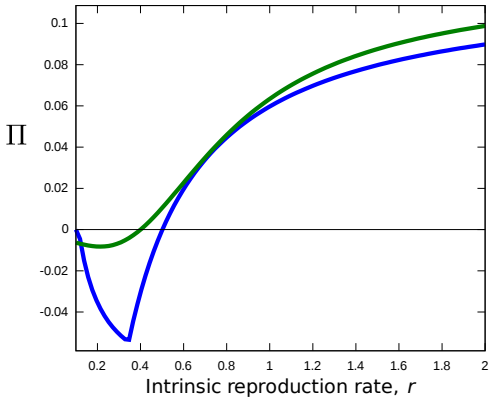
(b) Horizontal transmission, γ



(c) Natural mortality rate, d

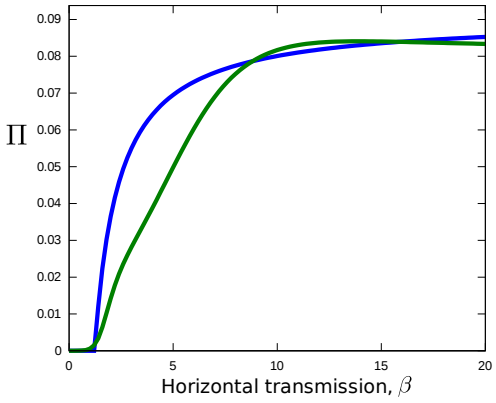


(d) Disease induced mortality rate, e

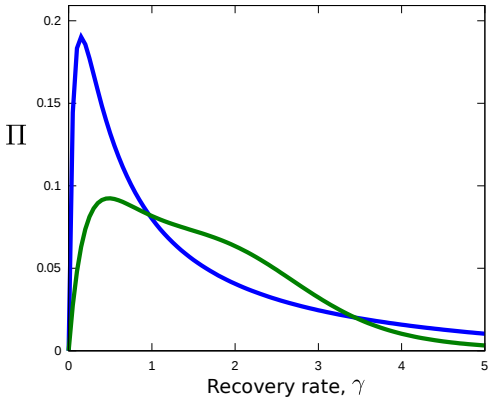


(e) Intrinsic reproduction rate, r

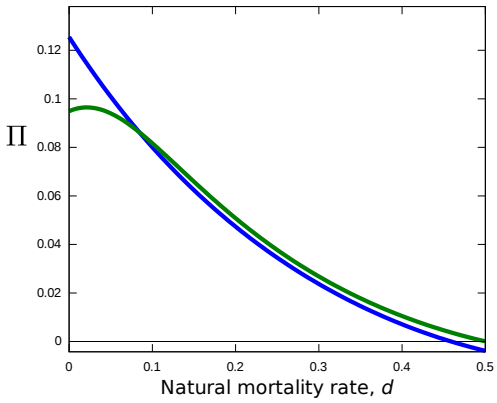
Figure 4.8: SIR model: sensitivity analysis of $\Pi(t)$, near the start of culling (at $t = 5$, in green), and at equilibrium (at $t = 1000$, in blue). Culling is non-selective: $p_S = p_I = p_R = 0.2$, and other parameters are as given in Table 4.1. One parameter is varied at a time; initial conditions are $\{S_0, I_0, R_0\} = \{S^*_{\mathrm{DF}} - 0.05, 0.05, 0\}$.



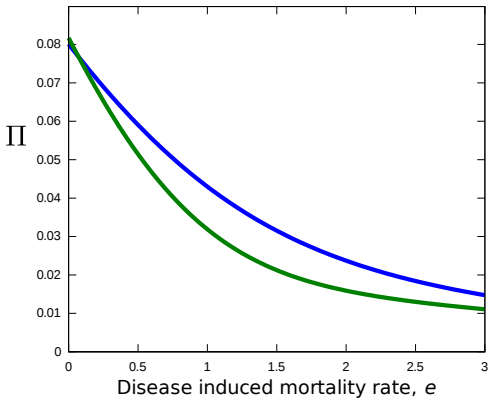
(a) Horizontal transmission, β



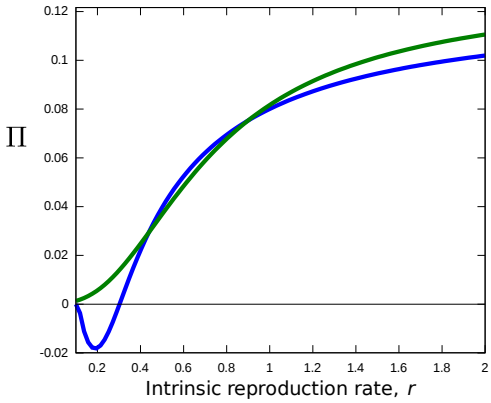
(b) Horizontal transmission, γ



(c) Natural mortality rate, d



(d) Disease induced mortality rate, e

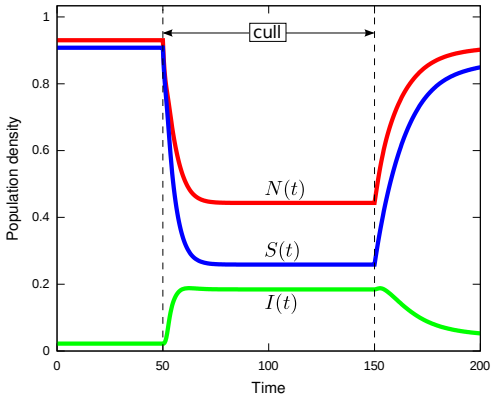


(e) Intrinsic reproduction rate, r

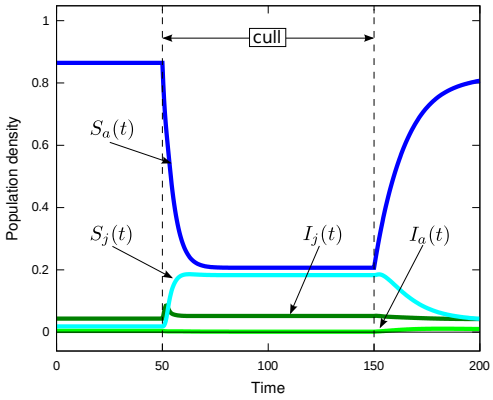
Figure 4.9: *SIR* model: sensitivity analysis of $\Pi(t)$, near the start of culling (at $t = 5$, in green), and at equilibrium (at $t = 1000$, in blue). Culling is selective: $p_S = p_I = 0$, $p_R = 0.2$, and other parameters are as given in Table 4.1. One parameter is varied at a time; initial conditions are $\{S_0, I_0, R_0\} = \{S^*_{\mathrm{DF}} - 0.05, 0.05, 0\}$.

4.3.3 Age structure

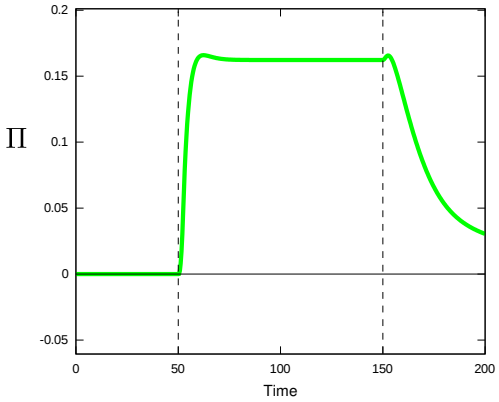
An example of the perturbation effect in the age model is shown in Fig. 4.10.



(a) $S(t)$ and $I(t)$



(b) $S_j(t)$, $S_a(t)$, $I_j(t)$, and $I_a(t)$



(c) $\Pi(t)$

Figure 4.10: Numerical solution of the age structured SI model with selective culling. Culling is applied only to susceptible adults for $t \in [50, 150]$ (marked by the dashed lines) during which time the total number of infectives $I(t) = I_j(t) + I_a(t)$ increases. The total density of susceptibles and infectives are shown in Fig. 4.10a, while the individual densities for adults and susceptibles are shown in Fig. 4.10b. $\Pi(t; p)$ is shown in Fig. 4.10c. Other parameters are as given in Table 4.1.

Even with simplifications, an algebraic solution for the endemic equilibrium in Eqn. 4.9 is too complex to examine directly, so instead equilibria are solved for numerically.

Sensitivity analysis

With four different categories of individual, there are many possible culling combinations. Analysis begins by showing the effects of culling each category individually (see Fig. 4.11). Culling of any group other than susceptible adults S_a reduces disease levels, showing that S_a is the most important group for the perturbation effect. Next, culling that targets all

susceptibles (i.e. $p_{Sj} = p_{Sa} = p_S$, and $p_{Ij} = p_{Ia} = 0$) shows that the perturbation effect may occur for small p_S, while culling that targets all adults does not give a perturbation effect. Some unusual behaviour is observed near $p_S \approx 0.375$, which may be a precision error, although the exact reason is unknown. Further sensitivity analysis assumes that culling selects only for susceptible adults.

Analysis of the natural mortality rate d (see Fig. 4.12c) shows that the perturbation effect is greatest for small d near 0, since this is associated with the greatest number of susceptible adults before culling. For the disease induced mortality rate e (see Fig. 4.12d), there is a maximum that occurs for small $e > 0$, near where the stability changes for I_a.

Analysis of the reproduction rate r (see Fig. 4.12e) shows that the perturbation effect is greatest for small d near 0, since this is associated with the greatest number of susceptible adults before culling. For the disease induced mortality rate e (see Fig. 4.12d), there is a maximum that occurs for small $e > 0$, near where the stability changes for I_a.

Analysis of the juvenile horizontal transmission rate β_j (see Fig. 4.12a) shows that the perturbation effect is maximised for small $\beta_j > 0$, around the point of stability change for the disease in adults, and then slowly decreases as the number of infective adults prior to culling increases. The transient perturbation effect increases with β_j, as this leads to the biggest increase in I_j.

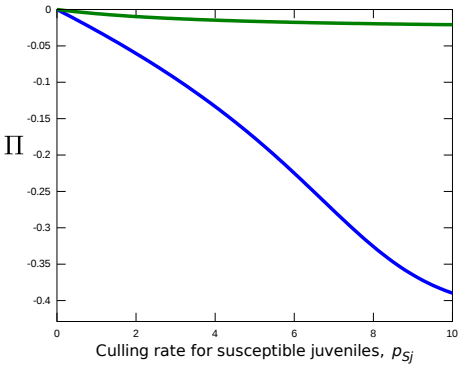
Analysis of the adult horizontal transmission rate β_a (see Fig. 4.12b) shows that the perturbation effect only occurs for very small β_a. As β_a increases, the population of susceptible adults rapidly decreases, depleting the number of adult susceptibles, which are needed for the perturbation effect to occur.

Analysis of the maturity rate α (see Fig. 4.12f) shows that with low α (i.e. maturity takes a long time and the proportion of adults is low), there is no perturbation effect. However, $\Pi_{\text{eqm}} > 0$ for intermediate α. For large α, the disease dies out as there are not enough juveniles for the disease to persist. The transient perturbation effect is maximised by a low $\alpha > 0$, as this provides the most juveniles for the disease to spread to.

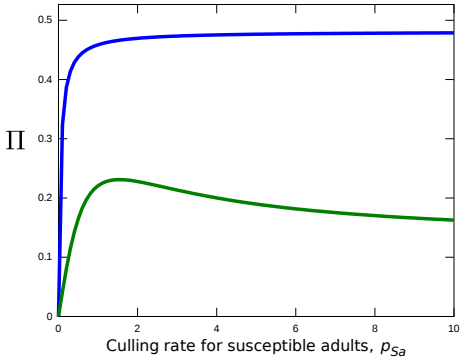
4.4 Discussion

This chapter explored the impact on disease control of unintentional selective culling, and how it interacts with compensatory reproduction, alternative disease transmission routes, disease resistance, and age structure.

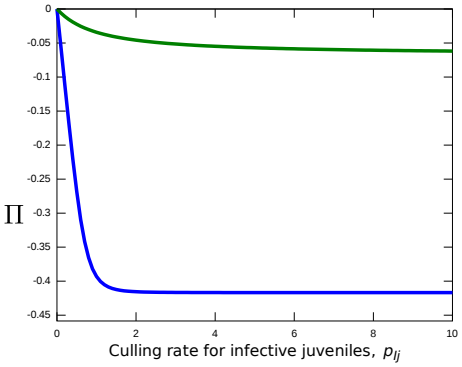
In an SI model with vertical transmission, the perturbation effect can occur when the



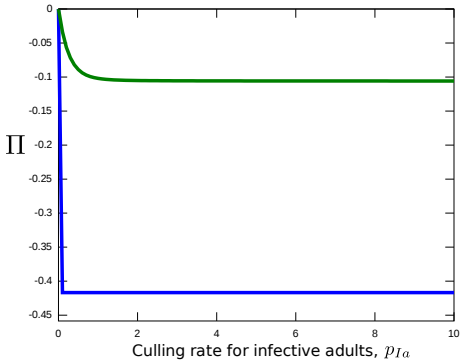
(a) Susceptible juveniles, p_{Sj}



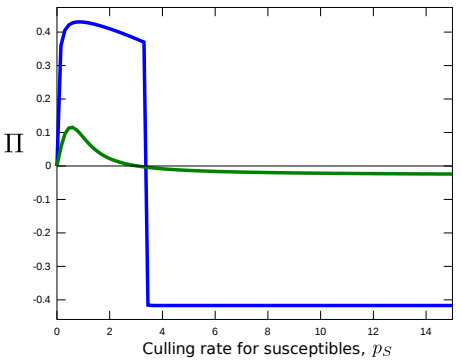
(b) Susceptible adults, p_{Sa}



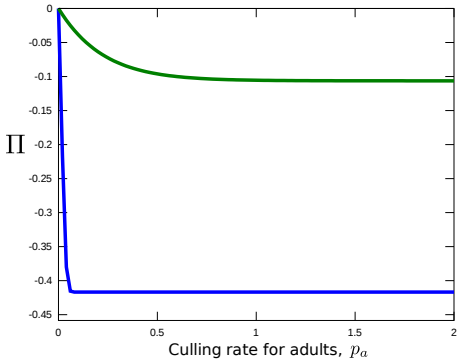
(c) Infective juveniles, p_{Ij}



(d) Infective adults, p_{Ia}

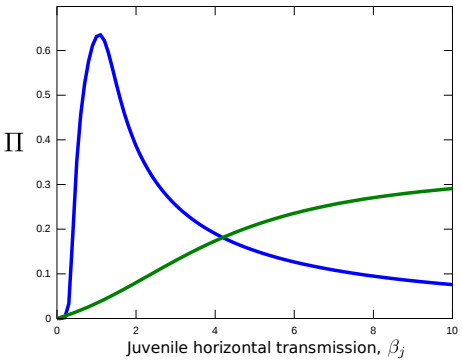


(e) Susceptibles, $p_{Sj} = p_{Sa} = p_S$

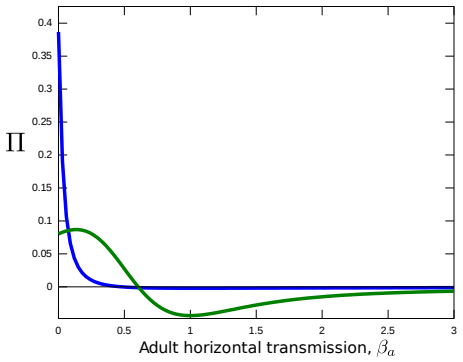


(f) Adults, $p_{Sa} = p_{Ia} = p_a$

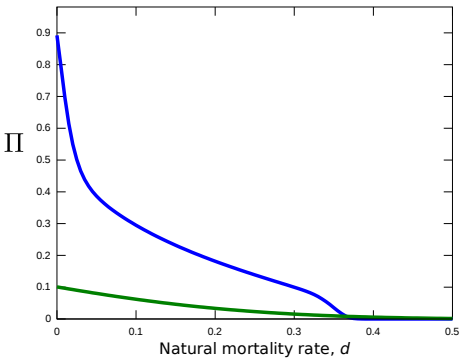
Figure 4.11: Age model: sensitivity analysis of $\Pi(t)$, targeting each group individually, near the start of culling (at $t = 5$, in green), and at equilibrium (at $t = 1000$, in blue). Other parameters are as given in Table 4.1, one parameter is varied at a time; initial conditions are $\{S_0, I_0\} = \{S^*_{\text{DF}} - 0.05, 0.05\}$ for both adults and juveniles.



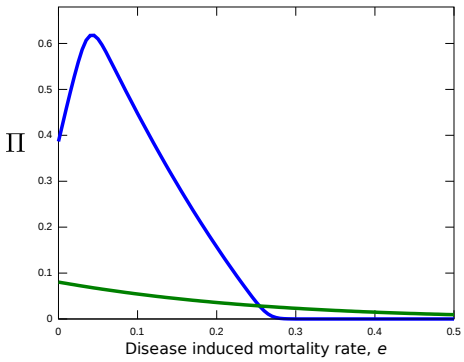
(a) Juvenile horizontal transmission, β_j



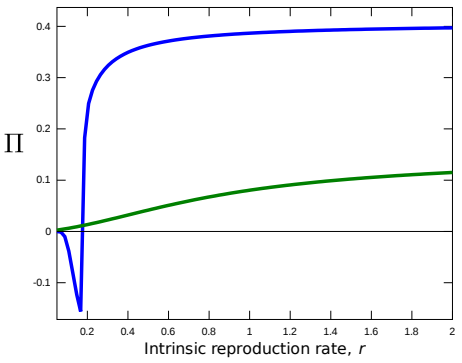
(b) Adult horizontal transmission, β_a



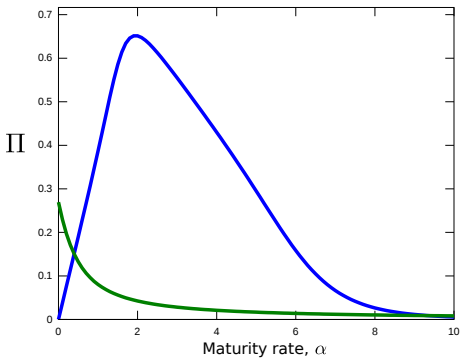
(c) Natural mortality rate, d



(d) Disease induced mortality rate, e



(e) Reproduction rate, r



(f) Maturity rate, α

Figure 4.12: Age model: sensitivity analysis of $\Pi(t)$, near the start of culling (at $t = 5$, in green), and at equilibrium (at $t = 1000$, in blue). Other parameters are as given in Table 4.1, one parameter is varied at a time; initial conditions are $\{S_0, I_0\} = \{S^*_{\mathrm{DF}} - 0.05, 0.05\}$.

rate of introduction of infectives due to vertical transmission is greater than the rate of introduction of infectives due to horizontal transmission, and population reduction fails to select for infectives. The increase in disease is a consequence of compensatory reproduction increasing the number of infectives recruited via vertical transmission.

In an SIR model, the perturbation effect can occur with non-selective population reduction, although this can be greatly strengthened by selecting only for resistant individuals. The increase in disease is a consequence of compensatory reproduction due to the loss of resistant individuals R, increasing the number of susceptibles S, resulting in an effective loss of herd immunity. With selective culling, this leads to an increase in S with no decrease in infectives I, which increases the horizontal transmission rate; with non-selective culling, there is a decrease in I, but that is offset by the increase in S, provided the recovery rate is sufficient to prevent a high prevalence.

In an SI model with age structure, where the adults are effectively resistant to the disease due to low susceptibility, the perturbation effect can occur when population reduction selects for susceptibles, although this can be increased when population reduction targets only susceptible adults. The increase in disease is a consequence of compensatory reproduction increasing the average susceptibility of the population, due to the higher susceptibility of juveniles.

As in Chapters 2 and 3, the maximum perturbation effect often occurs when the disease is near the point of stability change due to insufficient horizontal transmission for the disease to persist, or high mortality rates removing the disease from the population. In some cases, a process can work to both increase and reduce the rate of disease transmission, causing a maximum value of the relevant parameter. This is particularly true of the maturity rate α in Eqn. 4.9, which is necessary to provide resistant adults and allow for a reduction in the population during culling, when α is high however, individuals spend less time in the juvenile state, reducing the opportunity for infection.

One consistent factor in all the models was the reliance on the intrinsic reproduction rate r for disease increase. With high r, new susceptibles were quickly recruited to replace those culled, allowing the disease to persist and leading to a high infective population. Density dependence clearly plays an important role in the perturbation effect, as culling reduces the population size, increasing the rate of density dependent processes. Horizontal transmission itself may be a density dependent process, although one normally reduced by population reduction, and so the perturbation effect requires other processes to increase that compensate. In the SI model with vertical transmission, new infectives are recruited

directly, bypassing the requirement for horizontal transmission.

Compensatory reproduction is an important process that can complicate population reduction (Carter *et al.*, 2009), and interact with unintentional selective culling to further reduce the efficacy, even leading to increases in disease. As with the control of bTB in Britain, population reduction has been used to control CSF in wild boar (Artois *et al.*, 2001). However, the disease was shown to persist in the population, especially in young animals. The Perturbation effect in CSF and wild boar is due in part to an increase in the dispersal behaviour and thus levels of population mixing of herds following the population reduction event increasing the risk of transmission. The perturbation effect in wild boar and CSF is discussed by Bolzoni *et al.* (2007), who outline the role of heterogeneities in infection rates (due to different susceptibilities of different age groups) in disease increase, although using density dependent in mortality rather than birth. Strong seasonality and delay differential equations may interact with compensatory reproduction to also explain the perturbation effect (Choisy & Rohani, 2006; Keeling & Rohani, 2007). Disease control strategies for CSF now include removal only of the young more susceptible boar as the main virus target (Laddomada, 2000). Prior to the recommendation of targeted culling, control measures were much less effective, or even counterproductive (Guberti *et al.*, 1998; Ferrari *et al.*, 1998).

Stochasticity was not included in the models in this chapter, however the perturbation effect was observed in an extension to include vertical transmission in the model used in Chapters 2 and 3 (results not shown). One technique that may be used to account for the effects of stochasticity is moment closure analysis (Whittle, 1957; Krishnarajah *et al.*, 2005; Marion *et al.*, 2005), which provide analytic approximations to non-linear stochastic models. These techniques, combined with numerical sensitivity analysis, may be useful for improving prediction of the perturbation effect in real wildlife host species.

It is acknowledged that the outcome of the sensitivity analysis of other parameters varied significantly with different values of β_j in the SI model with age structure. Use of one-at-a-time sensitivity analysis may therefore give an incomplete picture of how the disease behaves; two parameter sensitivity analysis was performed for the SIR model and the SI model with vertical transmission, however the increasing parameter space can make analysis difficult and computationally expensive. While not used here, other techniques, such as Latin Hypercube sampling (LHS) (McKay *et al.*, 1979) can be used for models with a large parameter space.

While selective culling can be an effective tool in disease control, the possibility remains

of unintentionally selecting for individuals who provide herd immunity or whose presence reduces density dependent processes from increasing disease spread. It is important that population reduction strategies should consider this, and aim to select for the class of individuals most likely to reduce disease spread.

Chapter 5

General Discussion

5.1 Summary of thesis aims

The overall aims of this thesis were to: (*i*) characterise and determine the dynamics of the perturbation effect, examine the role of population reduction, (*ii*) to find out what maximises or minimises the perturbation effect, and (*iii*) examine how demographic factors may contribute to the perturbation effect.

The first aim was addressed in Chapter 2 by creating representative susceptible-infective SI disease models, and using algebraic analysis to understand the critical points of the system, and numeric analysis to investigate transient behaviour. The second aim was addressed by sensitivity analysis of the models throughout the thesis. The third aim was addressed by adding various extra demographic factors, and demonstrating how their presence was sufficient to allow the perturbation effect.

These results are now discussed in more detail.

5.1.1 Chapter 2

A generic non-spatial deterministic SI model was used to examine the effects of adding enhanced disease transmission consequent to population reduction, which identified both persistent and transient perturbation effects. Analysing their sensitivity to various demographic factors showed that the perturbation effect is more likely to occur in a disease system that has a very low prevalence prior to culling. When the disease is initially endemic, the perturbation effect is maximised when infection and mortality rates are near the values that cause the disease to change stability. When the disease has been newly introduced, then the perturbation effect is instead increased when the disease spreads

quickly (low mortality rates and high infection rate), although the duration of the perturbation effect is limited by high infection rates, and so maximised by intermediate infection rates. An important corollary is that population reduction can stabilise disease that would otherwise fade out naturally.

Next, a generic spatial stochastic SI model was used to show how density dependent dispersal can lead to a perturbation effect, which was shown to be qualitatively similar to the perturbation effect in the non-spatial model. This demonstrated the possibility of a perturbation effect despite no explicit disease enhancement mechanism. While both transient and persistent perturbation effects were identified, sensitivity to demographic factors meant that only the transient perturbation effect was examined in detail. The perturbation effect is found to be more likely in disease systems with low prevalence, heterogeneously distributed groups of sites containing infectives. As in the non-spatial model with emergent disease, the perturbation effect was increased by low natural and disease induced mortality rates, and high within-groups infection, but was extremely susceptible to between-groups infection, as the disease rapidly spread to all groups, eliminating the heterogeneity required for a perturbation effect.

Density dependent dispersal was shown to be a necessary process for the perturbation effect to occur in the absence of any behaviour change. A change in behaviour that directly enhanced disease transmission could also account for the perturbation effect, however significantly more so if the enhanced transmission is between groups, as even a small increase in between-group transmission (e.g. due to increased ranging behaviour) could rapidly account for an increase in geographical disease spread.

5.1.2 Chapter 3

A spatial stochastic SI model was used to examine various population reduction strategies, and to show how varying the approach can have varying influence on the perturbation effect, for any given level of effort. The effects of varying spatial coverage and culling intensity within sites, the effects on culling for brief periods of time at increased effort, and the effects of leaving gaps in culling regimes are shown to influence the response of the perturbation effect. In addition, the range of the perturbation effect outside areas subject to intensive culling are investigated for various dispersal rates. The perturbation effect is found to be influenced by how culling effort is spread between sub-populations, and by whether or not culling is sustained or applied intermittently.

Comparison between density and non-density dependent dispersal showed very different results when subject to culling, and therefore it is important to characterise host dispersal behaviour before planning culling strategies.

5.1.3 Chapter 4

Chapter 4 showed how other standard demographic factors and disease mechanisms can lead to the perturbation effect. Non-spatial mechanics associated with countering the effects of culling were investigated using a number of generic non-spatial models, including several different mechanics associated with the perturbation effect in particular disease systems, and also the role of selective culling.

Vertical transmission was examined in an SI model, and the perturbation effect is shown to occur if culling is targeted towards susceptibles. In an SIR model, non-selective culling is shown to result in a small perturbation effect given a large recovery rate, and the perturbation effect is increased if selective culling ignores infectives, or targets only resistant individuals. In an SI model with age structure, compensatory reproduction can lead to the perturbation effect if adults have a lower susceptibility to the disease than juveniles, and if culling avoids the juveniles.

5.2 Important processes in the perturbation effect

The perturbation effect is closely associated with interaction of population reduction and density dependent processes. Traditional models, such as those by Anderson & May (1979), suggest that when disease transmission is a density dependent process, then a reduction in host density should reduce disease transmission, potentially reducing the basic reproduction ratio R_0 to the point where the disease can no longer persist. However, when other density dependent processes counteract that reduction either directly or indirectly, then the predicted reduction in disease may be neutralised, or even reversed.

Horizontal disease transmission increases with the number of susceptibles, the number of infectives (with density dependent transmission) or the disease prevalence (with frequency dependent transmission), the average population susceptibility, and the contact rates between susceptibles and infectives. While population reduction may decrease disease transmission by reducing either the number of susceptibles or infectives, or the contact rates between them, it can simultaneously affect the rate of other processes, which might indirectly contribute to components necessary for new infections.

Density dependent processes can increase disease transmission indirectly: by rearranging host population structure, e.g. density dependent dispersal leads to increased mixing between neighbouring groups, or increases contact between susceptibles and infectives; or by density dependent growth that recruits susceptibles to replace disease resistant individuals, reducing herd immunity and increasing R_0. Alternatively, they can also increase disease transmission directly, e.g. compensatory reproduction can increase the recruitment of infectives via vertical transmission. When frequency dependent transmission occurs between two separate groups or species, then selectively targeting the susceptibles in one group can increase the prevalence and directly increase the disease transmission in the other.

Population structure can add new routes for the perturbation effect to occur. When individuals aggregate into separate groups with limited interaction between them (whether spatially, or by age or sex), disease transmission may be decreased due to the reduced contact between individuals (which is partly the basis of frequency dependent transmission). Heterogeneities due to stochasticity may lead to disease fade out in certain groups, in which case the average disease level may well be lower than that of a well mixed population. Heterogeneities in susceptibility between different classes of individual may lead to an increase in average susceptibility when proportions of those classes change.

Processes that are not density dependent, but instead occur in response to disruption of social structure, may also lead to enhanced disease transmission. This response may be temporary, until a new structure is established, but during that time changes in host behaviour may lead to increased contact rates and susceptibility (Carter *et al.*, 2009), which in turn may result in significant increases in disease transmission. In Chapter 2, the case of enhanced between-group transmission (without increased dispersal) was not examined, but the system was so sensitive to this mode of transmission that it seems clear that even a small increase would result in a significant perturbation effect.

5.3 Risk factors and species susceptible to the perturbation effect

In Chapters 2 and 4, it was shown that risk factors varied depending on whether the disease was endemic or emergent. In the case of endemic disease, the perturbation effect was most likely in a host-disease system with a low prevalence due to low disease transmission, or high mortality rates, as this tends to maximise the number of susceptibles for the disease

to spread to; in the case of emerging disease, this situation was often reversed. In all cases, strong compensatory reproduction was an important factor.

Highly structured populations can lead to heterogeneities, which reduce contact rates and disease transmission. Processes such as dispersal that counter this and break down the structure can increase contact rates and lead to the perturbation effect. It is important in structured populations to consider whether culling could be unintentionally targeting groups whose presence may be helping to reduce the increase in disease transmission. Where frequency dependent transmission is present, such as may be the case for transmission from badgers to cattle (Donnelly & Hone, 2010), failure to target infectives could lead to an increase in badger bTB prevalence, which would lead to an increase in transmission to cattle without further processes to enhance disease transmission necessary.

The perturbation effect in badgers should come as no surprise. As a host-pathogen system, it is prone to many of the risk factors previously discussed. Geographical bTB prevalence in badgers is low, but is slowly spreading in the southeast of England, and is clustered (Krebs *et al.*, 1997), which mirrors the spatially heterogeneous emergent case discussed in Chapter 2. Culled badger populations experience extensive social perturbation, and enhanced movement (Cheeseman *et al.*, 1993; Tuyttens *et al.*, 2000a), both from the vacuum effect and increased ranging behaviour.

There have, however, been conflicting results from the RBCT (Clifton-Hadley *et al.*, 1995b; Eves, 1999; Griffin *et al.*, 2005). In the Irish studies, no perturbation effects were observed, and proactive culling was shown to be more effective than reactive culling. The Irish trial attributed this to the presence of natural boundaries, limiting immigration from neighbouring areas (Fenwick, 2012). While this was also an important consideration in the RBCT (Donnelly *et al.*, 2006), and areas were chosen such that geographical boundaries formed the perimeter of a proportion of areas chosen, areas were generally considered permeable to badger movements.

While the results are not included here, some work was done to parametrise the spatial SI model from Chapter 2 using parameters converted from Smith *et al.* (2001a). While not occurring for the parameters as given, a 50% increase in the carrying capacity c from 12 to 18 was sufficient to demonstrate the perturbation effect.

Wild boar are another species at risk from the perturbation effect with CSF, and have many of the risk factors discussed in this thesis. They aggregate into stable herds, which are prone to increased dispersal following hunting (Laddomada, 2000); they show heterogeneous susceptibility among age groups (Bolzoni *et al.*, 2007); they have strong

compensatory reproduction (Bieber & Ruf, 2005); and sports hunting was known to target the less susceptible adults (Artois *et al.*, 2001). In addition, CSF is prone to vertical transmission, which plays an important role in CSF epidemiology, as piglets born infective remain immunotolerant and may survive for a long time, persistently shedding the disease (Ribbens *et al.*, 2004).

Foxes and rabies may also be prone to the perturbation effect as a consequence of the vacuum effect (Bacon, 1985). The rate of spread of rabies is limited by dispersal (Saunders *et al.*, 1997), and fox dispersal ranges are much higher in low density populations (Holmala & Kauhala, 2006). The disease is also more prevalent among juveniles, which may indicate heterogeneous susceptibility (Holmala & Kauhala, 2006). Despite frequent use, population reduction has had little success in control of rabies (Smith & Harris, 1989; Blancou *et al.*, 1991), and vaccination is seen as a much better technique.

In conclusion, there may be many wildlife species that are in some way affected by the perturbation effect. It is important that, when planning culling strategies, the mitigating effects of density dependent processes and enhanced transmission due to social disruption are considered. A number of mechanics in basic models are shown to lead to the perturbation effect. The scope for the perturbation effect increases with the complexity of the model, and there may be many other biological processes and demographic factors that reduce or reverse the effectiveness of population reduction when dealing with wildlife hosts.

Chapter 6

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