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EFFECTS OF PARASITE EXCHANGE BETWEEN WILD AND FARMED SALMON

by

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Abstract

Human food production activities can dominate natural systems, altering ecological and evolutionary aspects of the environment. Disease-mediated interactions are of particular concern. For example, parasites may "spill-over" from farms to wildlife. Parasites isolated on farms can evolve resistance to treatment chemicals , but "spill-back" from wildlife to farms may alter evolutionary dynamics. Here, we consider exchange of parasites (*Lepeophtheirus salmonis*) between wild (*Oncorhynchus gorbuscha*) and farmed salmon. We derive and analyze discrete-time models that implicitly include wild salmon migrations. First, we extend a standard fisheries model to show parasite exchange affects "line-dominance" in the population ecology of salmon. Second, we extend a classic population genetics model to show that wild salmon can theoretically provide an "ecosystem service" by delaying the onset of chemical resistance in parasites on farms. This service, however is affected by a nonlinear feedback if farm parasites spill-back to affect wild salmon.

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Chapter 1

Introduction

As is increasingly recognized, human activities shape the ecological (Vitousek *et al.*, 1997) and evolutionary (Palumbi, 2001) environments of "natural" populations across terrestrial (Ellis & Ramankutty, 2008) and marine (Halpern *et al.*, 2008) systems. This has far reaching consequences, not only for conservation of wild populations (Vitousek *et al.*, 1997), but for the sustainability of the human population (Ehrlich, 2009). One concern gaining prominence is the potential for exchange of diseases and parasites between wild and domesticated animals (Daszak *et al.*, 2000). When wild and domestic animals are sympatric, pathogens can "spill-over" from domesticated to wild animals, which raises concerns for conservation and emergent diseases of wildlife (Daszak *et al.*, 2000; Costello, 2009*b*). Sympatry also permits "spill-back" of pathogens from wild to domestic hosts, which can hamper control efforts in animal production (Bengis *et al.*, 2002; Costello, 2009*b*).

Life histories of many wild animals involve migration (Dingle, 1996), and regular movements between habitats can give rise to alternating periods of sympatry and allopatry with domestic animals. These movements of wild hosts can play an important role in determining the effects of spill-over and spill-back on conservation (Morgan *et al.*, 2005; Krkošek *et al.*, 2007*b*) and disease spread (Kilpatrick *et al.*, 2006). Classical host-parasite and epidemiological models, however, do not include host movement or migration (Morgan *et al.*, 2004), and efforts to understand the role of host migration in parasite and disease systems have often employed predictive statistical models requiring large data sets (Kilpatrick *et al.*, 2006), and spatially-explicit simulation models requiring a large number of parameters (Morgan *et al.*,

2007). Spill-over and spill-back of disease with domestic animals occurs in a wide variety of migratory wild hosts, including terrestrial mammals like elk, bison and antelope (*Cervus canadensis*, *Bison bison*, *Saiga tatarica*; Cheville *et al.*, 1998; Morgan *et al.*, 2005), waterbirds (Anseriformes:Anatidae; Gilbert *et al.*, 2006; Muzaffar *et al.*, 2006), and fishes such as salmon (*Oncorhynchus gorbuscha*, *O. keta*; Krkošek *et al.*, 2006, 2007*b*). With the rise of aquaculture (FAO, 2007), these type of interactions may become more prevalent, particularly in the ocean (Krkošek *et al.*, 2007*b*; Krkošek, 2010)

To increase our understanding of the effects of these interactions there is a need to develop models for pathogen exchange between migratory wild hosts and domesticated hosts. These interactions occur in complex systems, often during disease emergence when knowledge is scarce, and may arise in systems that are poorly-understood in general. Thus, initial efforts at modelling must often proceed without highly-detailed understanding of host-parasite biology or detailed spatial information. Ideally, however, models can aid in understanding and eventually in management. Some types of models may be better suited to help developing understanding. One useful classification of models is into "strategic" models that describe important processes in a coarse way, and "tactical" models that include much detail and can aid to decision-making (Pielou, 1981). Here, we focus on developing strategic models that aim to include the important effects of space and migration, without introducing a large number of parameters or requiring spatially-explicit knowledge.

1.1 Mathematical modelling of parasites and hosts

Mathematical modelling has a long history in developing qualitative theories of host-parasite and disease ecology (Anderson & May, 1992) and population genetics (Crow & Kimura, 1970), and is increasingly important in management. Scientific understanding is ever-evolving, and phrasing scientific ideas in the language of mathematics permits rapid evaluation of the ideas inadequacies (Hastings, 1997). This owes to the observation that models in science are never *correct*, but some are useful in that they improve understanding (Box, 1979). In this thesis, to approach questions

of pathogen exchange and migration, we build on models that have proved useful in population ecology and population genetics.

Modelling is a valuable tool in investigating questions of population ecology, especially where species interactions are concerned (Turchin, 2003). Here, we focus on dynamics of the host species, a semelparous fish with dynamics that inspired the Ricker (1954) curve:

$$n_{t+2} = n_t e^{r-n_t}, \tag{1.1}$$

where n_t is population abundance in year $t$and r is the population growth rate. This equation, for over-compensating population growth, has become a classic in population ecology. In part, this is because the Ricker curve was used to demonstrate that simple mappings can exhibit a rich variety of complex dynamics. These include chaos (May & Oster, 1976), with increasing growth parameter r. Although we focus on the role of migration, a spatial process, we largely neglect the rich array of spatially-explicit modelling approaches (Tilman & Kareiva, 1997) in favour of a simple, spatially-implicit approach that captures the effect of migration.

Mathematics has also been fundamental to the development of population genetic theory[1] (Crow & Kimura, 1970). Many important models in genetics are mathematically simple, e.g. the Hardy-Weinberg law, but have been immensely successful in increasing knowledge and guiding enquiry (Hastings, 1997). Here, we employ a theory of genetic change under selection for discrete generations that dates back to Fisher, Haldane and Wright, specifically Fisher's fundamental theorem of natural selection:

$$\Delta p_i = \frac{p_i(1-p_i)}{2\bar{w}(p_i)} \frac{\partial \bar{w}(p_i)}{\partial p_i}, \tag{1.2}$$

where p_i is the frequency of an allele under selection in the ith generation, w is average fitness. The equation (1.2), defining change in the frequency of an allele as proportional to its effect on fitness, becomes quite simple under the assumptions of Hardy-Weinberg (Crow & Kimura, 1970). Although this model is simple, it has been used in a wide variety of efforts to model the evolution of insecticide resistance (Georghiou, 1977b,a; Comins, 1977a,b; Alstad & Andow, 1995).

[1] And *vice-versa*, at least for statistics.

1.2 System & Approach

Here, we develop theory motivated by the interactions between sea-cage salmon aquaculture and migratory wild salmon. Spill-over and spill-back of parasitic sea lice (*Lepeophtheirus salmonis*) occurs between wild salmonids (*Oncorhynchus* spp., *Salmo* spp.) and farm salmon (*Salmo* spp.) (Gargan *et al.*, 2003; Costello, 2006, 2009*b*; Krkošek, 2010). Sea lice are native copepod ectoparasites, transmitted primarily as planktonic larvae, common on both adult wild hosts and in sea-cage salmon aquaculture (Costello, 2006). Sea-cage salmon aquaculture production is associated with declines of wild salmon populations in Europe and North America (Ford & Myers, 2008). At the same time, sea lice cause economic losses through decreased production, and may serve as vectors for other diseases (Johnson *et al.*, 2004; Costello, 2009*a*). Although chemical treatments are used to control sea lice in aquaculture, the development of resistance to these treatments is a major concern (Denholm *et al.*, 2002; BCPSF, 2009), with resistance to the most commonly-used treatment, emamectin benzoate, apparently emerging in the Atlantic (Lees *et al.*, 2008). Migrations of wild salmon may play an important role both in explaining the observed declines in wild populations when spill-over infections from farms occur, and in determining the dynamics of spill-back infections of farms due to wild-origin parasites.

The interaction of spill-over infection from farm salmon and migrating wild salmon is one proposed mechanism for the observed declines in wild salmon associated with aquaculture (Krkošek *et al.*, 2006, 2007*a*; Costello, 2009*b*). Intensive infections of juveniles early in their marine life do not occur without farms, because the migratory behaviour of salmon results in a spatial separation of juveniles in early marine life from adults and their parasites, a characteristic termed "migratory allopatry"; host migration creates a barrier to adult-juvenile transmission during early marine entry (Krkošek *et al.*, 2007*b*). Aquaculture can break down this migratory barrier when farms containing adult fish are placed on migration corridors for juvenile salmonids (recent reviews: Krkošek, 2010; Costello, 2009*b*).

The migrations of wild salmon also influence the dynamics of spill-back infections of farms due to wild-origin parasites, potentially with implications for resistance management. On farms, treatment with chemicals selects parasites for resistance, while on wild hosts, which are not treated, selection

is neutral or against resistance (Denholm & Rowland, 1992). A sea lice population parasitic on both farm hosts and sympatric wild hosts thus experiences variable selection for resistance. Migration of wild salmon means that periods of between wild and farm hosts alternate in time with periods of allopatry. Further, migrations of wild salmon provide connections between sea lice subpopulations in farming regions and the population of sea lice at the scale of the ocean basin, which is panmictic (Todd *et al.*, 2006; Messmer *et al.*, 2010).

Models that are mathematically simple have been used to link salmon migration and parasite exchange with farms to observed declines in wild salmon populations in Europe and North America (Krkošek *et al.*, 2006, 2007*a*,*b*; Ford & Myers, 2008). These studies have focused on the consequences of infections (due to the interaction of host migration and aquaculture) of juveniles early in marine life for salmon population dynamics, primarily in pink salmon (*Oncorhynchus gorbuscha*), and avoid developing complex, spatially-explicit models of host-parasite population dynamics. Here, we extend that tradition in two ways. First, we couple a model for transmission to a model for pink salmon dynamics to obtain a host-parasite model for pink salmon and sea lice, permitting us to explore effects of spill-over and spill-back on wild host population dynamics. Second, we consider the potential effect of immigration of susceptible sea lice, mediated by wild salmon migrations, on emergence of resistance to chemical treatment in lice.

The focus of Chapter 2 is to understand the implications of parasite spill-over and spill-back with farm hosts for population dynamics. To do this, we introduce a discrete-time model for the host-parasite system of wild pink salmon (*Oncorhynchus gorbuscha*) and parasitic sea lice. In keeping with the approach of earlier work on this system (Krkošek *et al.*, 2007*a*,*b*), we use the classic Ricker (1954) model for pink salmon population dynamics. To this model, we couple a simple transmission model derived under the assumption of migratory allopatry. This results in a simple, spatially implicit, formulation for our host-parasite model of salmon and sea lice as a system of discrete-time equations.

The focus of Chapter 3 is to understand if chemical treatment decisions, interacting with wild salmon migrations, can delay emergence of resistance to chemicals in lice. To examine this question, we use a population genetics framework. We focus on time-to-resistance, the number of years for

the frequency of a resistance gene to reach a threshold from a low initial frequency. This extends a model based on Fisher's fundamental theorem that was introduced by Comins (1977*b*). We complement this analysis with numerical simulations. In these, we consider the possible effect of spill-over on abundance of migratory wild populations, examining what happens to the effects of treatment strategies on time-to-resistance if farm-origin lice reduce the abundance of salmon populations that migrate near farms.

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Chapter 2

Aquaculture-induced changes to dynamics of pink salmon and sea lice

2.1 Introduction

In recent decades, exchange of diseases and parasites between wild and domesticated animals has become a prominent concern for conservation and disease emergence (Daszak *et al.*, 2000), as well as management of pest species in food production (Bengis *et al.*, 2002; Costello, 2009). The occurrence of "spill-over" and "spill-back" of disease between wild and domestic animals has been demonstrated in a wide variety of taxa that have migratory life histories, including terrestrial mammals (*Cervus canadensis*, *Bison bison*, *Saiga tatarica*; Cheville *et al.*, 1998; Morgan *et al.*, 2005), birds (Anseriformes:Anatidae; Gilbert *et al.*, 2006; Muzaffar *et al.*, 2006), and fishes (*Oncorhynchus gorbuscha*, *O. keta*; Krkošek *et al.*, 2006, 2007*b*). Host migration plays an important role in determining the effects of spill-over and spill-back on conservation (Morgan *et al.*, 2005; Krkošek *et al.*, 2007*b*) and disease spread (Kilpatrick *et al.*, 2006). Foundational host-parasite and epidemiological models, however, do not include host movement or migration (Morgan *et al.*, 2004). Thus, efforts to understand the role of host migration in parasite and disease systems often employ complex tools, e.g., data-intensive statistical models (Kilpatrick *et al.*, 2006) or parameter-heavy, spatially-explicit simulation models (Morgan *et al.*, 2007).

One application where simple models are successful in understanding the effects of host migration and disease exchange is in linking the declines of wild salmon populations in Europe and North America to their association with sea-cage salmon aquaculture production (Ford & Myers, 2008). One proposed explanation for the declines, at least in the Pacific, is that spill-over and spill-back of parasitic sea lice (*Lepeophtheirus salmonis*) between wild salmonids and farm salmon leads to infections of juvenile wild salmon in early marine life (Krkošek *et al.*, 2006; Costello, 2006; Krkošek *et al.*, 2007*a*; Costello, 2009). Without farms, such infections do not occur because the migratory behaviour of salmon results in a spatial separation of juveniles in early marine life from adults and their parasites, a characteristic termed *migratory allopatry*; host migration creates a barrier to adult-juvenile transmission during early marine entry (Krkošek *et al.*, 2007*b*). Studies of sea lice and salmon have described how aquaculture can break down this migratory barrier when farms containing adult fish are placed on migration corridors for wild juvenile salmonids (recent reviews: Krkošek, 2010; Costello, 2009). Rather than develop complex, spatially-explicit models of host-parasite population dynamics, these studies have focused on the consequences of infections during early marine life (which are due to the interaction of host migration and aquaculture) for salmon population dynamics, primarily in pink salmon (*Oncorhynchus gorbuscha*). Using this approach, Krkošek *et al.* (2007*a*) demonstrated declines in pink salmon populations associated with epizootics in aquaculture regions. Another theoretical paper reports a probabilistic analysis of equilibrium infection levels to explain these declines (Frazer, 2009). The primary focus, however has been effects on *equilibrium* abundance of wild hosts. Salmon farming effectively augments host diversity, however, which according to epidemiological theory is expected to affect behaviour of population *dynamics* as well (Dobson, 2004).

Here, to understand the implications of parasite spill-over and spill-back with farm hosts for population dynamics, we introduce a model for the host-parasite system of wild pink salmon and parasitic sea lice. In keeping with the approach of earlier work, we use the classic Ricker (1954) model for pink salmon population dynamics, which we couple with a simple transmission model derived under the assumption of migratory allopatry. This permits a rather simple, spatially implicit, formulation of the model as a system of discrete-time equations. Because pink salmon have a two-year lifespan,

even- and odd-year lineages breed in alternate years in a given river. These lineages can have consistently different relative abundances of adults, a phenomenon termed "line dominance" in the salmon literature (Groot & Margolis, 1991). Mathematically, line dominance arises in our model through a period-doubling bifurcation, which links the degree of dominance with the strength of inter-lineage interactions. To understand the effects of introduced aquaculture hosts on wild host population dynamics, we focus on changes in this dominance relationship, demonstrating that a line dominance naturally maintained by negative density-dependent interactions between lineages can be altered by the introduction of farm hosts.

2.2 Models

Pink salmon, like many fish, display migratory allopatry in which juvenile fish are spatially separated from adult fish due to differences in habitat requirements, food supply, natural enemies, and migration. With a two-year generation time, a pink salmon population consists of two distinct lineages, or year-classes, that use river (breeding) and ocean (maturing) habitat sequentially in time. Without farms (Figure 2.1A), pink salmon of different lineages potentially interact through two means: (i) through effects on the environments (river and ocean habitat) that are sequentially used by the juvenile and adult age-classes in alternate years, and (ii) through transmission of a specialist parasite from adult hosts to juvenile hosts, i.e., between lineages.

Interactions of the first type occur through changes in the biotic or abiotic environment of the river or ocean habitat due to host density and include a variety of mechanisms proposed by Ricker (1962) to explain line dominance in pink salmon, including direct suppressive interactions between lineages, fouling of the rearing environment by large runs, and competition for food in ocean habitat (Groot & Margolis, 1991). Interactions of the second type occur due to parasite transmission, when the offspring of parasites associated with adults of one lineage infect juveniles of the other lineage as the two age-classes of host temporarily share space during migration. These "infection windows" are shown as shaded regions of Figure 2.1A between the river and ocean habitat. We assume that the density-dependent interactions of both types act to increase mortality.

Introduction of farmed hosts to migration routes between river and ocean habitats (Figure 2.1B) leads to infection of hosts earlier in life. Juveniles migrating out from the river are infected earlier in time and closer to the river in space by "spill-over" infection from farms than when farms are not present (Figure 2.1A). Farm infection status may, in turn, be influenced by "spill-back" infection from parasites of wild adult hosts. In this case, the farm provides a route of transmission *within* a lineage that is not present without farms (Figure 2.1A). This *intra*-lineage transmission mediated by the farm is shown in Figure 2.1B. When adult hosts migrate from ocean to river, they bring parasites that influence farm infections. These adult hosts breed to produce juveniles that out-migrate and receive infections from farms. For example, in Figure 2.1A adults of dash-dot lineage are migrating to the river at census time n. These adults breed, producing offspring that out-migrate and receive infections from farms just before census time $n + 1$.

We derive two models here, one for the case without farms (Figure 2.1A) and one for the case with farms (Figure 2.1B). In our models we census the salmon and parasite populations at the time period after summer sympatry of juveniles and adults. That is, after the period of transmission from adult to juvenile fish in coastal marine environments. We track numbers of wild adult (A) and juvenile (J) hosts, and average abundance of juvenile-associated parasites P_w. Because we are concerned with the parasite population attached to hosts, which provide a convenient sampling unit of the parasite population, we track parasites in terms of average abundance per host (Hudson & Dobson, 1995).

For transmission, both farm-wild and wild-wild, we use an approximation that applies when the number of juvenile hosts is low relative to the inverse probability of transmission. Sea lice are an ectoparasite with a direct life cycle: by "transmission" we refer to infection of juveniles by copepodid stage offspring of mature parasites on returning adult hosts. Developmental rates of sea lice are strongly dependent on temperature and salinity, with larvae becoming infective copepodids after surviving through a naupliar period that lasts from one to nine days (Johnson & Albright, 1991). In a well-mixed coastal environment, the probability that any one larva both survives to become infective *and* attaches to a host is low. Further, the number of juveniles at census is attenuated from the large numbers at initial out-migration. Our approximation assumes that the number of juvenile

hosts is low relative to the probability of any one infective larva becoming a mature parasite, and states that the average load of juvenile-associated parasites P_w following transmission increases with the *number* of mature parasites on returning adults at time of transmission. The full derivation is given in Appendix 2.A.

Importantly, our models substitute *temporal* heterogeneity in transmission for the *spatial* dynamics of migratory hosts. This captures the main effect of space and migration on host-parasite dynamics without farms: preventing adult-juvenile transmission during early marine life. Thus, our transmission function is derived by assuming that infection occurs only within "infection windows" that are brief relative to the yearly census time and defined by periods of sympatry between wild juveniles and adults: farm-wild transmission requires sympatry with farm adults (Figure 2.1B); wild-wild transmission requires sympatry with wild adults (Figure 2.1A).

2.2.1 Host-parasite system with migratory allopatry

To model the farm-free case (Figure 2.1A) we begin with the Ricker (1954) model, which for a species with a two-year life cycle like pink salmon is $A_{t+2} = A_t e^{r-bA_t}$. The parameter r is intrinsic growth rate of the host and the term $\exp(-bA(t))$ represents density-dependent mortality, such as competition for food among juvenile salmon or increased mortality of eggs at high spawner density. To this classic model, we introduce age-structure to track both adult and juvenile fish. We also add two forms of general negative density-dependent interactions between lineages. The first, $\exp(-c_0 J(t))$, represents reduced survival of juveniles due to lagged influences of prior-year populations on the nursery environment. Such an interaction could occur if detritus from large runs fouled river habitats (Groot & Margolis, 1991). The second, $\exp(-c_1 A(t))$, represents reduction in survival of juveniles to become adults due to lagged influence of prior-year adults on the marine environment. This type of interaction could be due to direct suppressive effects, e.g., cannibalism, or to competition for food at sea during summer sympatry (Groot & Margolis, 1991). We also add a term for parasite impacts on juveniles, $\exp(-aP_w(t))$, consistent with the parasite impact term used in empirical studies (Krkošek *et al.*, 2007*a*). Finally, we add a model for average parasite transmission between wild adults and juveniles. This function is a

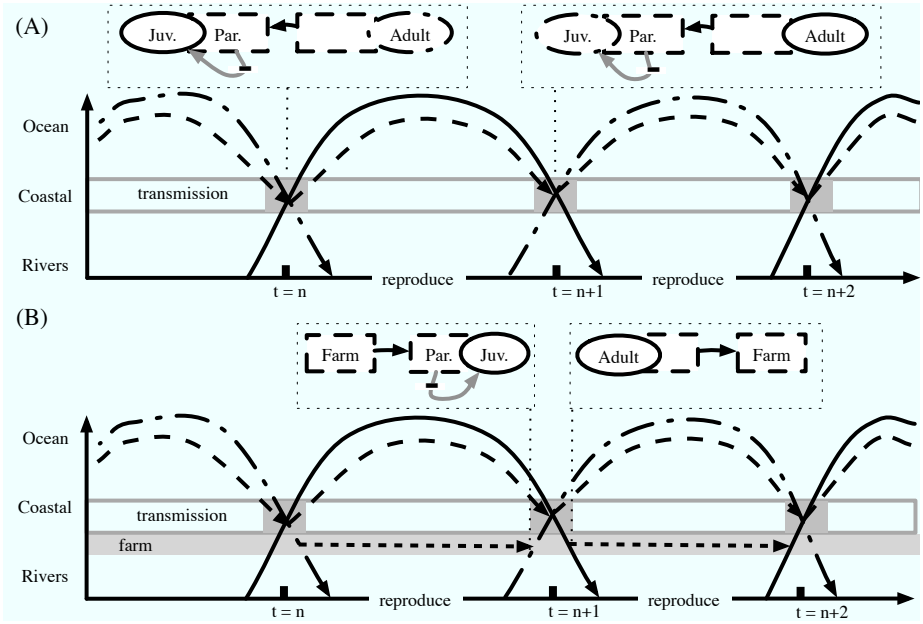

Figure 2.1: Schematic depiction of interactions between two lineages of wild host without (A) and with (B) farm hosts. The solid and dash-dot lines correspond to the two lineages, dashed lines correspond to the parasite population. The y axis depicts spatial extent of migration between breeding and maturing ranges, the x axis depicts time. Without farms, parasite transmission is only *inter*-lineage, from adults to juveniles, and occurs in space and time within the gray "infection windows" as adults of one lineage share space with juveniles of the other. Infection of juveniles by adult-origin parasites during inter-lineage transmission and subsequent parasite-induced mortality is depicted in the dotted boxes at each census time. With farms (light gray bar), static in space and acting as reservoir hosts, both inter- and *intra*-lineage transmission can occur, with the latter mediated by farm hosts. Intra-lineage transmission through the farm is shown as short dash lines within the light gray bar.

combination of transmission, during the period of summer sympatry (the infection window of length τ_w), and growth of the parasite population during the period of allopatry (the remainder of the year, of length $1-\tau_w$); see Appendix 2.A for derivation. This gives our full host-parasite model for pink salmon and lice without farms,

$$\underbrace{J(t+1) = s_0 s_2 A(t) \cdot e^{\log(f) - bA(t)}}_{\text{Reproduction of lineage}} \cdot \underbrace{e^{-c_0 J(t)}}_{\text{Negative effect of other lineage}} \tag{2.1a}$$

$$\underbrace{A(t+1) = s_1 J(t)}_{\text{Survival of lineage}} \cdot \underbrace{e^{-c_1 A(t)} \cdot e^{-a_w P_w(t)}}_{\text{Negative effects of other lineage, parasites}} \tag{2.1b}$$

$$P_w(t+1) = \underbrace{\beta_w \tau_w k}_{\text{Inter-lineage transmission}} \cdot \underbrace{\lambda(1-\tau_w) P_w(t)}_{\text{Parasites per adult}} \cdot \underbrace{s_1 J(t) e^{-c_1 A(t) - a P_w(t)}}_{\text{Wild adults } A(t+1)}, \tag{2.1c}$$

where s_0, s_1, and s_2 are survival probabilities, and f is the expected fecundity of salmon. Note that we assume inter-lineage negative density-dependent effects are *less strong* than the intra-lineage negative density dependence of the traditional Ricker model, i.e., $c_1 < b$. Table 2.1 summarizes our notation.

We introduce a scaling of (2.1) to obtain the nondimensional equations,

$$N_0(t+1) = N_1(t) e^{r - N_1(t) - \frac{s_1 c_0}{b} N_0(t)}, \tag{2.2a}$$

$$N_1(t+1) = N_0(t) e^{-\frac{c_1}{b} N_1(t) - P(t)}, \tag{2.2b}$$

$$P(t+1) = \eta P(t) N_0(t) e^{-\frac{c_1}{b} N_1(t) - P(t)}. \tag{2.2c}$$

Dynamical variables are $N_0 = b s_1 J$, $N_1 = bA$, and $P = a_w P_w$. Host growth rate is $e^r = s_0 s_1 s_2 f$. The nondimensional parameter for parasite-mediated density-dependence is

$$\eta = \frac{\beta_w \tau_w k \lambda (1-\tau_w)}{b s_1}. \tag{2.3}$$

2.2.2 Host-parasite system with farms

The parasites due to farm-origin infections affect the juveniles *prior* to census, which follows the period of summer sympatry between wild adults and juveniles in coastal marine waters (Figure 2.1B). Farm-origin infections occur during a period of sympatry between wild juveniles and farms of length τ_f. Including these infections in the model (2.1) decreases the juveniles at

Table 2.1: Summary of notation for salmon-sea lice model without farms

Symbol	Meaning	Units
$J(t)$	Juvenile hosts at time t	[host]
$A(t)$	Adult hosts at time t	[host]
$P_w(t)$	Mean mature parasites per *juvenile* at time t	[parasite][host]$^{-1}$
f	Fecundity of salmon	—
s_0	Density-independent survivorship of juveniles prior to transmission	—
s_1	Density-independent survivorship of juveniles during transmission	—
s_2	Density-independent survivorship of adults post-transmission	—
r	Intrinsic growth rate of host at low density $r = \log f s_0 s_1 s_2$	—
b	Density-dependent mortality of host associated with reproduction	[host]$^{-1}$
c_0	Negative density-dependent effect of prior-year juveniles on current-year juveniles	[host]$^{-1}$
c_1	Negative density-dependent effect of prior-year adults on current-year adults	[host]$^{-1}$
a_w	Average parasite virulence (wild-origin)	[host][parasite]$^{-1}$
k	Infective parasites produced per adult-associated parasite	—
β_w	Attachment rate of infective parasites per host (wild-wild)	[time·host]$^{-1}$
λ	Geometric growth rate in average parasite load	[parasite][host·time]$^{-1}$
τ_w	Infection window, wild adults and juveniles sympatric	[time]
$(1-\tau_w)$	Maturation period, wild adults and juveniles allopatric	[time]

census and increases their average parasite load. The resulting model has modified transmission (2.4c) and adult-to-juvenile (2.4a) maps,

$$J(t+1) = s_0 s_2 A(t) \cdot e^{\log(f) - bA(t)} \cdot e^{-c_0 J(t)} \cdot \underbrace{e^{-a_f \beta_f \tau_f k N P_f(t+1)}}_{\text{Parasites (farm-origin)}}, \tag{2.4a}$$

$$A(t+1) = s_1 J(t) \cdot e^{-c_1 A(t)} \cdot e^{-a_w P_w(t)} \tag{2.4b}$$

$$\begin{aligned} P_w(t+1) =& \beta_w \tau_w k \lambda (1-\tau_w) P_w(t) J(t) e^{-c_1 A(t) - a P_w(t)} \\ &+ \underbrace{\beta_f \tau_f k}_{\text{Farm-wild transmission}} \cdot \underbrace{N P_f(t+1)}_{\text{Total parasites on farm}} . \end{aligned} \tag{2.4c}$$

With the effect of farms, the number of parasites per juvenile, P_w, is the sum of contributions from parasites hosted by wild returning adults (first term) and the total *number* of parasites NP_f on farm hosts (second term). For consistency with our method of tracking parasites on wild hosts, we describe farm infections as average lice per farm fish P_f times the number of fish on the farm N. We assume throughout that the number of fish on the farm, N, is constant. Table 2.2 summarizes notation for the system with farms (2.4).

The number of parasites on the farm NP_f depends on several factors. Farm infections are influenced by the wild-associated parasite population. Perfect infection control, i.e., $NP_f = 0$ is not obtainable, and management of infections on farms can proceed in two broad ways: control infection to a constant level or control infection to some function of the number of parasites from wild hosts. The simplest mathematical expression of the first case is that the number of parasites on the farm is a constant each year $NP_f(t+1) = \gamma_1$. For the second case, the simplest assumption is that farm status depends linearly on prior-year wild infections, $NP_f(t+1) = \gamma_2 A(t) P_w(t-1)$, where the expression on the right hand side of the equation is the number of adult-associated parasites at time t. The index on variable P_w, the average number of parasites on *juveniles* tracked in model (2.1), is lagged one year relative to the index on variable A, the adults, to obtain the number of parasites on *adults* at time t. Combining these expressions, parasites on farm hosts are the sum of two terms, a contribution from constant management and a contribution dependent on wild-origin infection: $NP_f(t+1) = \gamma_1 + \gamma_2 A(t) P_w(t-1)$.

Table 2.2: Summary of notation for sea lice-salmon model with farms

Symbol	Meaning	Units
N	Fish on farm at time t	[fish]
$P_f(t)$	Parasites per fish on farm at time t	[parasites][fish]$^{-1}$
$N \cdot P_f(t)$	Parasites on farm at time t	[parasites]
β_f	Attachment rate (farm-wild)	[time·host]$^{-1}$
τ_f	Infection window (farm-wild), wild juveniles and farms sympatric	[time]
a_f	Average parasite virulence (farm-origin)	[host][parasite]$^{-1}$
γ_1	Farm input under constant management	[parasites]
γ_2	Farm-mediated transmission under proportional management	—

We also introduce a scaling of (2.4) to obtain nondimensional equations

$$N_0(t+1) = N_1(t) e^{r - N_1(t) - \frac{s_1 c_0}{b} N_0(t) - \phi - \frac{a_f}{a_w} \eta_f N_1(t) P(t-1)}, \tag{2.5a}$$

$$N_1(t+1) = N_0(t) e^{-\frac{c_1}{b} N_1(t) - P(t)}, \tag{2.5b}$$

$$P(t+1) = \eta P(t) N_0(t) e^{-\frac{c_1}{b} N_1(t) - P(t)} + \eta_f N_1(t) P(t-1) + \phi, \tag{2.5c}$$

where scaled dynamical variables are as in (2.2) This scaling introduces a nondimensional parameter that represents farm-mediated transmission,

$$\eta_f = \frac{\beta_f \tau_f k \gamma_2}{b}, \tag{2.6}$$

which incorporates the effect of prior year wild infections on farms. The scaling (2.5) also introduces a non-dimensional that represents constant input of infection from farms,

$$\phi = a_w \beta_f \tau_f k \gamma_1. \tag{2.7}$$

2.3 Methods

We analyzed the dynamical behaviour of systems without farms (equations 2.1) and with the effects of farm hosts (equations 2.4). Our focus was on

line dominance relationships between host lineages, specifically how farm hosts can change these relationships. Because model (2.1) includes both adult and juvenile hosts in each year, it represents both lineages. The adults, $A(t)$, in model (2.1) represent the odd-year lineage in odd years, and the even-year lineage in even years. The opposite holds for the juveniles $J(t)$. Mathematically, line dominance corresponds to a two-year periodic equilibrium of the system (2.1). The transition from a one-year periodic equilibrium, a fixed point of (2.1), to a two-year periodic equilibrium, a two-cycle of (2.1), occurs through a period-doubling bifurcation. Thus we use stability and bifurcation analysis, with a combination of analytical and numerical methods, to analyze changes to dominance induced by farm hosts.

In equations (2.1) density- and parasite- independent survivorship is partitioned among host-age classes according to terms s_0, s_1, and s_2. We show in Appendix 2.B that this partitioning does not affect equilibrium dynamics, which are governed by a combined host growth parameter r, where $r = \log(fs_0s_1s_2)$. The empirical estimate of host reproduction r for pink salmon is $r^* \approx 1.2$ (Myers *et al.*, 1999). Our interest is in the biological interpretation for pink salmon. Accordingly, we focus on behaviour for $r < 2$ because above 2, increases in r will drive a period-doubling cascade. When numerical analysis required fixing a value for r, we use the empirical estimate, which is consistent with the range of pink salmon population growth rates estimated for numerous stocks from Washington through Alaska (Dorner *et al.*, 2008).

Without farms, the behaviour of the model (2.1) depends on host population growth rate r, on negative density-dependent interactions between hosts, i.e c_0 and c_1, and on parasite-mediated interactions summarized by the nondimensional parameter η defined in equation (2.3). For systems with no nursery competition ($c_0 = 0$), the farm-free system (2.1) is amenable to standard analysis of qualitative behaviour from the theory of dynamical systems (Hale & Kocak, 1991). Because of our assumption that inter-lineage density dependence is less strong than intra-lineage density dependence, we require $c_1 < b$. Full details are in Appendix 2.B. When $c_0 > 0$, transcendental equations define the equilibria so we use numerical tools.

With farms, the dynamics are governed by model (2.4). Expressed

mathematically, our equation for farm status is

$$NP_f(t+1) = \eta_f P_w(t) A(t+1) + \phi = \eta_f P_w(t) \cdot \underbrace{s_1 J(t) e^{-c_1 A(t) - a_w P_w(t)}}_{A(t+1)} + \phi, \tag{2.8}$$

where ϕ the nondimensional parameter combination representing a constant farm input under constant management defined in (2.7) and η_f is the nondimensional parameter combination representing a farm-mediated transmission under proportional management defined in (2.6). Relative to (2.1), the first term when $\eta_f > 0$ modifies the dynamical structure of equations (2.2) because its effect depends on the values of dynamical variables. On the other hand, changes induced by $\phi > 0$ are independent of dynamical variable values and assumed constant at each time. We examined two cases: where parasites are managed to a constant level, i.e., $\eta_f = 0$ but $\phi > 0$, and where parasites depend on prior-year wild infections i.e., $\phi = 0$ but $\eta_f > 0$. For the first case, an analytical solution for the equilibria is impossible, and in the second case it is difficult. Therefore for both, we used the numerical continuation package cl_matcontM (Dhooge *et al.*, 2003) to compute stability diagrams for the location of the period-doubling bifurcation as a function of the farm parameters, η_f or ϕ.

Numerical computation of a period-doubling bifurcation also gives a quantitative prediction of how dominance varies as a function of the parameters with which we conducted bifurcation analysis. Dividing the equilibrium abundance of the non-dominant line by that of the dominant line yields an inverse measure of dominance, the "equivalence ratio." An equivalence ratio of unity means that both lineages have the same equilibrium abundance, i.e., there is a stable one-year periodic equilibrium.

2.4 Results

For a migratory allopatric host with a two-year lifespan and no farms, negative density-dependent inter-lineage interactions of sufficient strength can result line dominance. These interactions include both parasite-mediated and environment-mediated negative density-dependence, and a sufficiently strong level of either of these or a sufficiently strong combination of these is enough to produce line dominance. As shown below, introduction of farm

hosts can either decrease or increase the line dominance, depending on the manner in which farm management responds to wild-origin infections. If farm management controls infections to a constant level regardless of the intensity of wild infections, the presence of the farm increases line dominance. On the other hand, if farm control of infection is only proportional to the intensity of wild infections, then the farm's presence decreases line dominance.

2.4.1 Host-parasite dynamics without farms

Without farms, the model (2.1), has several distinct qualitative behaviours that depend on parameters governing host growth, r and on negative density-dependent interactions between hosts, i.e c_0 and c_1. Parasite-mediated interactions also influence system behaviour, and though (2.1) has many parameters governing parasites, these are summarized by the nondimensional parameter η defined in equation (2.3). Negative density-dependent inter-lineage interactions, both general, c_i, and parasite-mediated, η, have similar qualitative effects on dynamics. Stability diagrams for two pairings of parameters are in Figure 2.2. The dashed lines in Figure 2.2 separate regions labelled "stable," where both age-classes of the host has a constant abundance at every time step, from regions labelled "dominance," where age-class abundance alternates between relatively abundant and less abundant years. Two-year lifespans mean the hosts exist in lineages that breed independently, e.g., the odd- and even- year lineages in pink salmon, thus behaviour in the "dominance" region corresponds to constant abundance *within* a given lineage, but with abundance differing *between* lineages.

In the "stable" regions of parameter space shown in Figure 2.2, dynamics of the system (2.1) are a one-year periodic equilibrium. In the "dominance" regions, dynamics are a two-year periodic equilibrium. Transition between these regions in parameter space is through a period-doubling bifurcation. The bifurcation arises as negative density-dependent interactions between host lineages increase in strength. Dominance results from a sufficiently strong combination of general negative density-dependent interactions, c_i, between host lineages and inter-lineage transmission, η. In our model, inter-lineage transmission acts as a form of parasite-mediated negative density dependence. Parasites have a negative effect on juvenile hosts that increases with the average parasite abundance per juvenile P_w following transmission.

Parasites on juveniles arise through inter-lineage transmission from parasites of adult hosts, and P_w increase with the *absolute* abundance of parasites on adults. Because we track the average parasites per host, the absolute parasite population is larger when the abundance of adult hosts is greater. Thus, increased abundance of adult hosts in one lineage result in increased infections in juveniles of the other lineage, a negative density-dependent interaction between the lineages.

A sufficient combination of the two types of negative density dependence (general and parasite mediated) will induce line dominance. Figure 2.2A shows stable and dominance regions in parameters space of intra-lineage transmission and host growth. For moderate values of r, sufficiently strong intra-lineage transmission results in dominance. Increasing general negative-density dependence, e.g., c_1 in legend, reduces the strength of transmission needed for dominance. In the "host only" region there is no stable equilibrium with coexistence of the parasite and host at positive abundance. In the "cycles" region, equilibria with periods that exceed two years occur. Figure 2.2B shows the regions of qualitative dynamics in the parameter space of inter-lineage transmission (parameter η) and the negative density-dependent interactions that occur between lineages in the ocean habitat (parameter c_1), explicitly illustrating the trade-off along the dashed line. The regions of host-only dynamics, stable one-cycle dynamics and dominant lineage dynamics shift with changing c_1 but maintain their qualitative relationship. Numerical examination of behaviour for $c_0 > 0$ confirmed that the qualitative nature of the effect of c_0 is similar to that of c_1. See Appendix 2.B for analytical details.

Figure 2.3A shows a numerically-computed bifurcation diagram for adult hosts with inter-lineage transmission. The bifurcation branches in Figure 2.3A predict the equilibrium proportion of dominance as a function of η for $c_i = 0$. Dividing the equilibrium abundance of the non-dominant line by that of the dominant line yields the "equivalence ratio," which varies with η. Thus, viewed with line dominance in mind, the bifurcation branches give the equilibrium dominance relationship of the lineages as a function of the bifurcation parameter η. Figure 2.3B shows the equivalence ratio computed for adult hosts. Movement from the "stable" region into "dominance" in η rapidly increases dominance, shown by the decreasing equivalence ratio plotted in 2.3B.

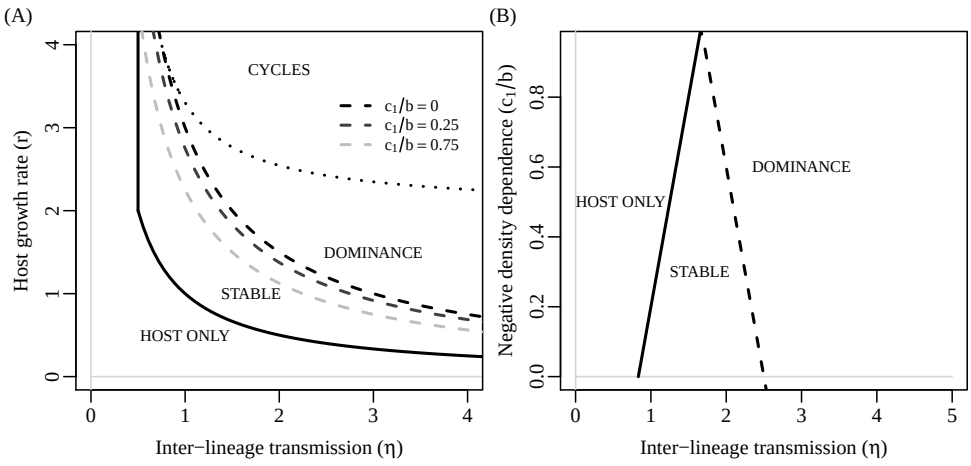

Figure 2.2: Behaviour of host-parasite system without farms in parameter space. In the "host only" regions, the parasite population cannot persist. In the "stable" regions, (2.1) has a stable one-year periodic equilibrium. Along the dashed lines, this equilibrium bifurcates through period-doubling to a two-year periodic equilibrium. Above the dotted line, which corresponds to a Niemark-Sacker bifurcation, cycles of period greater than two occur. The two-year periodic behaviour in the "dominance" regions corresponds to line dominance, see Figure 2.3. The panels show different parameter spaces: inter-lineage transmission η and host growth r (A) with changes due to various values of *scaled* inter-lineage negative density-dependence (coefficient $\frac{c_1}{b}$) given in legend; and inter-lineage transmission η and scaled negative density-dependence $\frac{c_1}{b}$ (B) for $r = r^*$. Note that within the "host only" region, for $r > 2$, increasing r drives host dynamics on a period-doubling cascade consistent with the Ricker equation. The period-doubling and Niemark-Sacker bifurcations were identified and curves computed by numerical continuation using Cl_matcontM (Dhooge *et al.*, 2003).

Further, the relationships between host density, parasite abundance and density dependence permit quantitative descriptions of how strong these interactions must be to induce line dominance in the nondimensionalized version of (2.1). When dominance does occur in host-parasite systems governed by (2.1), the more abundant lineage experiences proportionally less mortality due to inter-lineage negative density-dependence (whether mediated by parasites or not) than does the less abundant lineage. See Appendix 2.C for details.

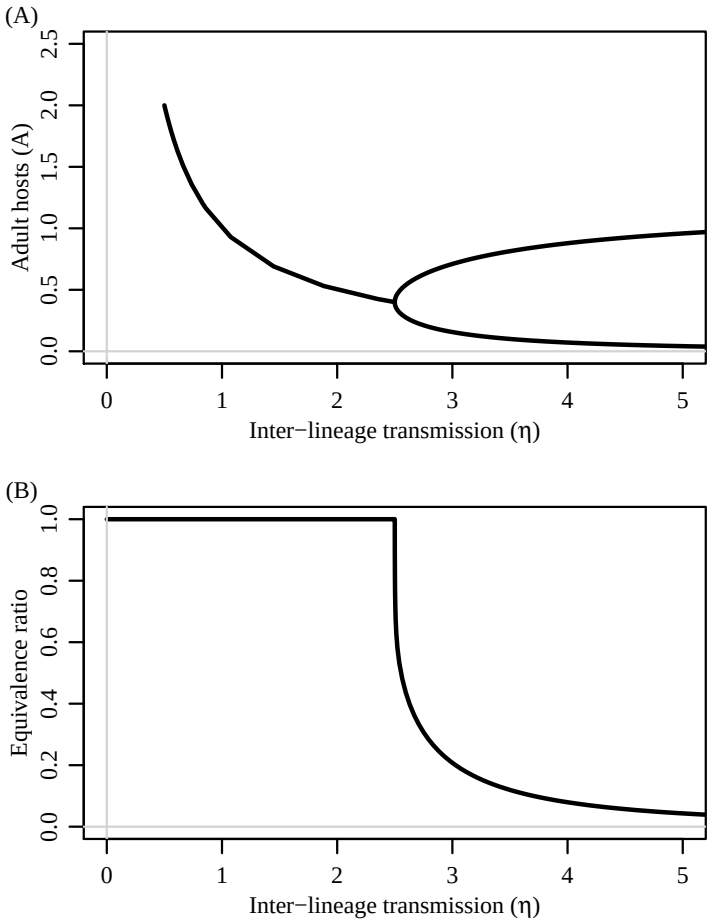

Figure 2.3: Line dominance arises through a period-doubling bifurcation. Bifurcation of adult hosts in η for $r \approx 1.2$ (A) shows single period doubling with increasing η, ($\eta = 2.5$ for this value of r), and period-two dynamics for a large range of $\eta > 2.5$. The period doubling occurs in the ηr plane for $\eta = 2.5$ along the black dashed line of Figure 2.2A. Model-predicted equivalence ratio as a function of η (B), computed by dividing lower branch by upper branch. The ratio is 1.0 for $\eta < 2.5$; intermediate equivalence ratios occur only for a small range of η.

2.4.2 Host-parasite dynamics with farms

The introduction of farm hosts, acting as reservoirs, causes changes in system dynamics from the model given in equations (2.1) to that given by equations (2.4) and (2.8). The qualitative nature of the change depends on the relationship of farm infections P_f to wild hosts and their parasites, i.e., dynamical variables J, A, and P_w. Farm infections are influenced by prior-year infections of wild adults. Infection status the next year, however, is dependent on management of infections on farms that arise from parasites of wild salmon. Using equation (2.8), we examined two cases: where infection in the farm is controlled to a constant level $\phi > 0, \eta_f = 0$, and where infection is linearly proportional to previous-year wild infections $\phi = 0, \eta_f > 0$. Through numerical bifurcation analysis we examined the changes induced by farm hosts in terms of shifts in the boundary between the stable and dominance regions, i.e., the onset of period-doubling, which without farms corresponds to the dashed line in Figure 2.2A.

Figure 2.4 summarizes the effect of constant and proportional management of infection on the location of the onset of period-doubling and resulting line dominance relationships relative to the transmission parameter η. Figure 2.4A gives the numerically-computed continuation of the period-doubling curve in the $\phi\eta$ plane with constant farm input ϕ. For fixed η, farm input moves the system further into the period-doubling region, increasing line dominance. Numerically computed bifurcations and resulting line dominance profiles shown in Figure 2.4B confirms the suggestion of Figure 2.4A that constant input from farms increases dominance at equilibrium.

Under proportional management a farm acts as a transmission route within a lineage. This has an effect opposite of constant farm input. Figure 2.4C shows the numerically-calculated continuation of the period-doubling point in $\eta_f\eta$ plane with farm-mediated transmission η_f. For fixed η, increased farm-mediated transmission moves dynamics away from the period-doubling region, decreasing line dominance. By recomputing bifurcations in adult numbers for various values of η_f we numerically computed the effect of farm-mediated transmission on the relationship between η and dominance, as shown in Figure 2.4D for values of η_f given in legend. This computation confirms the suggestion of Figure 2.4C that a farm under proportional management decreases dominance at equilibrium.

Intuition suggests that the negative effect of increased parasite load

on juvenile hosts means that increases in ϕ will decrease equilibrium host abundance. Structural stability of (2.1) permits analysis with ϕ as a bifurcation parameter. Numerical bifurcations in ϕ for values of $r < 2$ revealed that increased ϕ drives down equilibrium host abundance. Above a critical level, constant farm input ($\phi > .5$) results in host extirpation (equilibrium abundance of 0) for the deterministic model analyzed.

2.5 Discussion

The effect of salmon aquaculture sites as reservoirs for sea lice have long been recognized (Tully & Whelan, 1993; Costelloe *et al.*, 1996). Empirical studies have demonstrated that declines in wild salmon populations are associated with aquaculture (Krkošek *et al.*, 2007*a*; Ford & Myers, 2008). Recently, Frazer (2009) introduced an equilibrium theory for effects of a farmed hosts on sympatric wild hosts via a directly-transmitted parasite, demonstrating that increased farm host density and infections of wild juveniles can combine to explain observed declines. Such infections of juveniles arise when farms act as reservoirs and break the allopatric barrier to parasite transmission that is formed by the migratory life history of pink salmon under natural conditions (Krkošek *et al.*, 2007*b*). Though these infections are a consequence of migration, the analysis of Frazer (2009) did not include salmon population dynamics, so the inferred effect of reservoirs was limited to a decline in equilibrium abundance. Other analyses *have* coupled lice infections to models of population dynamics (Krkošek *et al.*, 2007*a*,*b*; Krkošek, 2010), but have not combined these with models for louse transmission. Here, we developed a host-parasite model that couples population dynamics of pink salmon with a simple transmission model incorporating temporal heterogeneity in transmission driven by migratory allopatry. We found that, in addition to declines in equilibrium population abundance, spill-over and spill-back with farms can alter qualitative patterns in population dynamics, either increasing or decreasing line dominance.

The direction of the change in line dominance depends on how farms respond to wild-origin infections. When infections on farms are independent of wild infections, farms provide a constant input of infection to the wild hosts that increases dominance; on the other hand, when infections on farms depend on wild-origin infection, farms provide an intra-lineage

transmission route that decreases dominance. These situations correspond to two management scenarios: in the first, infection on farms is managed to a constant abundance, and in the second, infection of farms is managed to a

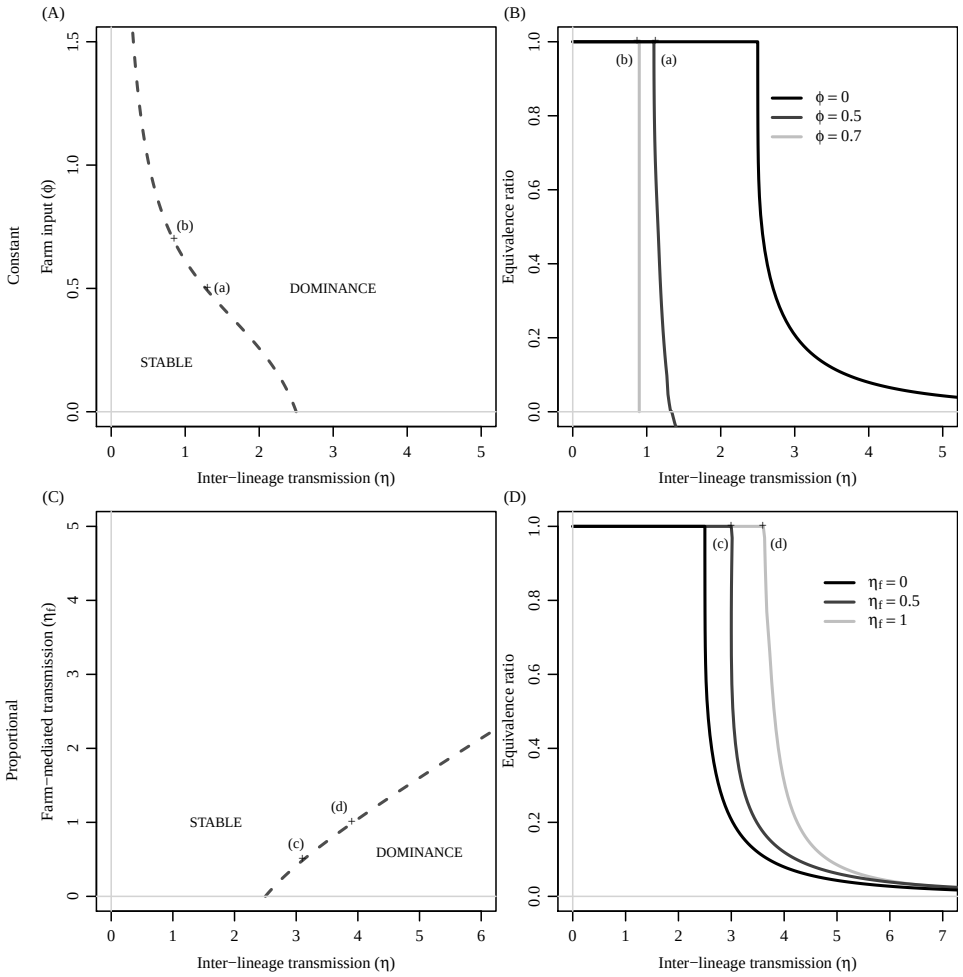

Figure 2.4: Constant (row 1) and proportional (row 2) management of infection of farms have opposite effects on dominance. Stability planes giving changes in the onset of period-doubling (dashed lines) in η-space for constant management (A), i.e., changing farm input ϕ and proportional management (C), i.e., changing farm-mediated transmission η_f. Equivalence ratio as function of η computed for $r = r^* \approx 1.2$ with constant management (B) for various values given in legend of constant input ϕ, and proportional management and (D) for various values given in legend of farm-mediated transmission η_f. For constant management (A,B), the locations in parameter space where period-doubling in η causes line dominance for different ϕ are labelled (a) and (b). For proportional management (C,D), locations where period-doubling in η causes line dominance for different η_f are labelled (c) and (d).

level proportional to prior-year wild infection.

The mechanism by which the first scenario ("constant" management) increases dominance is that the constant farm input has a proportionally larger effect on the less-abundant line. This is a depensatory effect and is thus similar to a number of additional hypotheses proposed by Ricker (1962) that related dominance to other mechanisms that can have depensatory effects, including fishing and predation.

The second scenario ("proportional" management) decreases dominance because the abundant parasites of the dominant lineage have a negative affect on juvenile survival *within that lineage*. This result demonstrates the potential, when wild hosts display migratory allopatry, of introduced farm hosts to change the *structure of density-dependence* governing wild host population dynamics. This farm-mediated intra-lineage transmission alters the "process order" of density-dependence in the population. Turchin (2003) defines process order as the number of population densities at earlier times needed to adequately describe fluctuations in the focal population. Populations governed by different structures of density dependence generally display different patterns of population fluctuations, e.g., period and amplitude (Turchin, 2003), thus changes to density-dependent interactions of the type demonstrated here are, in a more general context, expected to alter patterns of population fluctuations.

Under either management scenario (constant versus proportional response to wild-origin infection), equilibrium wild host abundance, averaged over both lineages, decreases. This result is consistent with empirical observations in wild salmon populations potentially affected by disease spillover from aquaculture (Gargan *et al.*, 2003; Krkošek *et al.*, 2007*a*; Ford & Myers, 2008; Costello, 2009). In the case of constant input, when dominance increases the abundance of the non-dominant lineage goes to zero while the dominant lineage increases slightly in abundance. In the second case, when dominance decreases both lineages decrease in abundance but the dominant lineage decreases more than the non-dominant lineage.

2.5.1 Connections to epidemiological theory

The reservoir effects of farms studied here have parallels in epidemiological theory. Under the management scenario of constant input, farm-origin

infection can be viewed as a deterministic, periodic forcing of the host-parasite system. Forcing affects behaviour of a variety of dynamical disease models (Hastings *et al.*, 1993). Perhaps the most common epidemiological application of forced models is to express seasonality, which has broad importance across human and wildlife disease systems (Altizer *et al.*, 2006). In the context of seasonally-forced disease models, the *shape* of continuous-time forcing has a strong influence on observed dynamics (Earn *et al.*, 2000). Though our study examined only one type of constant forcing, based on management of parasites to a constant threshold, future studies might benefit from considering a variety of forcing functions based on different management scenarios.

On the other hand, the scenario of proportional management results in farm-mediated transmission. This situation has conceptual connections to epidemiology of multi-host parasites and indirect transmission. Farm hosts can be viewed as a new introduced species that increases the number of parasites in coastal waters. This accords with the theory of multi-species epidemics for pathogens transmitted by free-living infective stages, where host species diversity can amplify epidemic outbreaks (Dobson, 2004). Because parasites on farm hosts are managed, however, farm hosts could also be viewed as a type of indirect or environmental transmission with the functional form of transmission depending on management actions. Different functions representing a variety of management response to infections could result in different dynamics. Rohani *et al.* (2009) showed that for a stochastic model of disease outbreaks in migratory hosts, neglecting the role of environmental transmission can underestimate the probability of outbreak. Though we did not include stochastic effects in the deterministic system studied here, transmission through farms plays a similar role, increasing the average intensity of infection in wild juveniles in the coastal region of the farm. In the case we treat, the regular migrations of wild hosts and the static location of the farm mean that the farm primarily mediates intra-lineage transmission.

2.5.2 Assumptions and implications

The analysis presented here rests on a great many assumptions that should be kept in mind when interpreting our results. Transmission poses a difficult

modelling problem (McCallum *et al.*, 2001). We assumed that transmission occurs through mass action between well-mixed infective parasites and wild juvenile hosts. We applied this assumption to infection both from wild adult hosts and from farm hosts. In British Columbia, farm-to-wild infections occur in fjords (Morton *et al.*, 2004), while wild-to-wild infections occur during a period of summer sympatry in neritic waters (Beamish *et al.*, 2007). Because these two types of transmission occur in different hydrodynamic environments, our approximate transmission function may not apply equally to both processes. The mass action assumption, however, is perhaps better justified in these marine environments than in many places where it has been applied. The difference between the transmission environments for farm-to-wild and wild-to-wild infections would be expected to result in lower transmission probability in the more dispersive neritic environment. This, however, does not address the potential for a *qualitative* difference in transmission between the fjord and the neritic zone. To address this possibility, one could build approximations based on more detailed models of transmission developed by Krkošek *et al.* (2005) for farm-to-wild transmission.

In addition, we focused on larvae in our transmission derivation. For sea lice, however, some evidence indicates that motile adult stages can play a role in transmission (Ritchie, 1997; Krkošek *et al.*, 2007*b*; Connors *et al.*, 2008, 2010). In general, very little is known about motile transmission (Costello, 2009). Despite this, our mass action transmission function could be adapted to describe motile transmission. The "infective parasites" attaching to juvenile hosts (Appendix 2.A) would then be motile adults, this would reduce the proportionality k between infective parasites and adults, but could increase the attachment probability β_w. Because motile adults swim actively unlike naupliar stages, the assumption that fish and infective parasites are well-mixed may be less justified for motile transmission. In addition, spatial scale for motile transmission may also differ from that of larval transmission. The differences in transmission between larval and motile transmission indicate that a single equation of the simple single mass action type used here may be inadequate to describe both processes. To consider multiple modes of transmission using mass action, an extended model using multiple transmission equations could be developed. Alternatively, a single equation that is spatially explicit might capture both types of transmission.

When farm hosts are present, our transmission function assumes that parasites from farms and wild additively contribute to total parasites on juveniles. Contributions may be additive when parasite abundance is low, but when there are very many lice attaching to juveniles this likely breaks down. Thus, during high intensity infections observed in salmon farming regions (Morton & Williams, 2003; Morton *et al.*, 2004; Krkošek *et al.*, 2006), the equations used here may overestimate the role of wild-wild transmission in host-parasite dynamics.

Additionally, our transmission function uses an approximation that is best when the number of juvenile hosts is small relative to the inverse probability of transmission. Thus, the approximation is better when the probability of transmission is lower. As discussed above, the probability of transmission is possibly higher in farm-to-wild transmission than in wild-to-wild transmission. Further, farm-to-wild transmission occurs earlier in time and space (Krkošek *et al.*, 2005), when populations of juvenile hosts are larger (Groot & Margolis, 1991). These two facts mean that the transmission function is likely less valid for farm-to-wild transmission than for wild-to-wild transmission. This is an additional reason that future work should look to bridge between the simple transmission model used here and more detailed models for farm-to-wild transmission (Krkošek *et al.*, 2005).

Another consequence of our transmission function is that more lice on a farm result in more lice on juvenile hosts, proportionally. This linearity is the reason that a constant farm input acts in a depensatory manner where the less abundant line suffers higher average infections from the farm. The increase in line dominance seen when farm status is constant is due to this depensatory effect. Because this theoretical increase in line dominance is clearly sensitive to assumptions on transmission, further work is needed to better understand whether management of farms to constant infection levels would be expected to increase line dominance.

Environmental stochasticity is thought to play an important role in pink salmon population dynamics (Myers *et al.*, 1999). Here, we focused solely on deterministic results, but future studies should examine the role of reservoirs in host-parasite systems in the presence of stochasticity. When noise is considered, the transient behaviour of the system is likely to be more important than the asymptotic equilibria (Hastings, 2004). The particular values of parameters pointed out here as resulting in dominance are based on asymptotic

analysis of equations (2.1). When transient behaviour of equations (2.1) is considered, the region of parameter space in which transient two-cycles, and thus line dominance, occurs may expand. Preliminary analysis and simulation of a related model (Krkošek *et al.*, 2010) indicates that when noise is included and statistical two-cycles are considered, dominance occurs over a large region of parameter space.

2.5.3 Significance and Future Directions

Our results suggest that when spill-over and spill-back occur with wild migratory hosts, the way in which managers of farms respond to wild-origin infections will determine the effect on wild host population dynamics. We were able to study interaction of wild host migration, farm hosts, and parasites by substituting temporal heterogeneity in transmission for an explicit spatial model. Temporal heterogeneity is common in epidemiological interactions and has been a focus of intensive study (Anderson & May, 1992; Altizer *et al.*, 2006). The importance of space and host movement have been studied extensively in human disease systems (see, e.g., Grenfell *et al.*, 2001), and recognized in wildlife-farm interactions (Morgan *et al.*, 2004). The model we formulate here combines these ideas, permitting us to study the effect of host movement through its connection to temporal changes in transmission processes. Though this type of space-time substitution may prove fruitful in other contexts, there are also reasons to develop explicit models of the spatial and continuous-time processes at work in the salmon-sea lice system. The difference between constant farm status and farm-mediated transmission is essentially one of forcing a dynamical system versus altering its dynamical structure. Future efforts to understand how infection management in farms, and other reservoirs, can interact with spill-over and spill-back to alter wildlife disease dynamics could examine a number of different functions defining either management response to wild infection or changing farm status over the time infections occur. Such research, however, might benefit from modelling in continuous time. Further, as discussed above, the spatial dynamics of lice transmission may differ between farm-wild and wild-wild transmission, and between motile and larval transmission. Considering the full richness of dynamics involved in these processes may require a spatially-explicit host-parasite model.

More broadly, we expect the processes of wild host migration, spill-over, spill-back, and management of farms to result in changes to wild host population dynamics in the large variety of avian, aquatic and terrestrial systems where wild hosts display migratory behaviour and potentially interact with domesticated animals. Our model is specific to the system of sea lice and pink salmon, however, and the interaction of these processes should be explored in other system-specific models, as well as more generally, e.g., in the setting of theoretical epidemiological models.

Appendix 2.A Derivation of the parasite map

In this Appendix we suppress the w subscripts. The map governing average parasite per juvenile dynamics, $P(t+1) = \beta\tau k\lambda(1-\tau)P(t)J(t)e^{-aP(t)}$, represents two processes, growth and transmission. For sea lice, problems of transmission (Krkošek *et al.*, 2005; Frazer, 2008) and growth (Stien *et al.*, 2005; Revie *et al.*, 2005; Krkošek, 2010; Frazer, 2009) have been studied in detail; however, the transmission models are spatially explicit descriptions of dynamics occurring in fjordic habitats over small time scales, and the growth models consider details of parasite age structure. We neglect the details of these formulations in favour of generality, assuming only that transmission results from low-probability infection events occurring in a well-mixed environment. Here, we derive the map used above to approximate a mass action process in a well-mixed environment that is valid when transmission is based on low-probability attachment events. Additionally, we assume that parasites grow without density dependence and have no age-structure.

Each year includes a short infection window τ, the period of wild adult and juvenile summer sympatry. During the remainder of the year, the maturation period, $(1-\tau)$, juveniles $J(t)$ become adults $A(t+1)$ and parasite population growth occurs. The total number of adult-associated parasites at the end of the maturation period, which we denote $\mathcal{P}_{adult}$ using a calligraphic "P" to differentiate from the variables for average parasite abundance used elsewhere, is reduced by host death due to parasitism and other factors, and increased by parasite reproduction and growth. Assuming the parasites are *uniformly* distributed on hosts, decline in host population from juvenile to adults due to parasites $(1-e^{-P_w})$ affects the parasite

population proportionally. Parasite population increase is expressed as a geometric growth in the *average* parasites per host at rate λ over the time $(1-\tau)$. Then, the number of adult-associated parasites at the end of maturation and the onset of transmission is given by

$$\mathcal{P}_{adult}(t+(1-\tau)) = \lambda(1-\tau)P_w(t)\cdot A(t+1), \tag{2.A.1a}$$
$$= \lambda(1-\tau)P_w(t)J(t)e^{-aP(t)-c_1A(t)}. \tag{2.A.1b}$$

We consider transmission during the infection window τ in continuous time. Specifically, we consider the process of infective parasites ψ, attaching to juvenile fish F, during an infection window of length τ. Because τ is short, we treat number of juveniles F as constant and ignore production or immigration of new infective parasites ψ, of which we assume there are an initial quantity proportional to the number of adult-associated parasites at the beginning of transmission,

$$\psi_0 = k\mathcal{P}_{adult}, \tag{2.A.2}$$

which relates back to model (2.1) through the definition of P_{adult} in equation (2.A.1). We further assume that infective parasites ψ become attached parasites $\mathcal{P}$ independently from one another at a constant rate β. Finally, for consistency with (2.1), where the units of P are motile parasites *per fish*, we track $P = \mathcal{P}/F$ the average attached parasites per fish. This gives the following equations for $t \in (0,\tau)$,

$$\begin{aligned} \dot{\psi} &= -\beta\psi F \\ \dot{\mathcal{P}} &= \beta\tfrac{\psi}{F} \\ \dot{P} &= \tfrac{\dot{\mathcal{P}}}{F} = \beta\psi, \end{aligned} \tag{2.A.3}$$

The equation for the change in parasites per fish, $\dot{P}$, comes from dividing the equation for total attached parasites $\dot{\mathcal{P}}$ by F. Note that attachment rate β implicitly includes mortality of infective parasites. This is similar to equations underlying the macroparasite model of Anderson & May (1978), but here considered only over a short time-scale.

With a constant number of juveniles F, we have $L(t) = \psi_0 e^{-\beta F t}$ and $P(t) = \beta\psi_0 \int_0^t e^{-\beta F s}\mathrm{d}s$ on $t \in (0,\tau)$. This expresses average parasites per fish at the end of the infection window as a function of juveniles, initial

infective parasites, the transmission rate, and the length of the window: $P(\tau) = \frac{\psi_0}{F}[1 - e^{-\beta\tau F}]$. If $\beta\tau F \ll 1$ a first-order Taylor approximation yields $\mathcal{P}(\tau) \approx \beta\tau\psi_0$. For $F < \frac{1}{\beta\tau}$, the error in this approximation is bounded by $\frac{\psi_0\beta\tau}{e}$ (where e is Euler's constant). Using equations (2.A.1) and (2.A.2) to relate this approximation back to the variables in (2.1),

$$P(t+1) = \beta\tau k\lambda(1-\tau)P(t)J(t)e^{-aP(t)-c_1A(t)}, \tag{2.A.4}$$

we also note that the relevant quantity of juveniles is $J(t+1)$. We use this equation under the assumption that the number of juveniles falls below a threshold $J(t+1) < \frac{1}{\beta\tau}$, which is an inverse measure of the strength of inter-lineage transmission. When inter-lineage transmission is very weak, β is very low and $\frac{1}{\beta\tau}$ is very large.

Appendix 2.B Analysis of farm-free system

Using both analytical techniques from dynamical systems and numerical bifurcation analysis we find regions where line dominance occurs in the two-dimensional space of parameters governing (i) negative density-dependent interactions between host lineages and (ii) host productivity. Line dominance corresponds to mathematical two-cycles and arises from stable equilibria through period-doubling so we focus on defining boundaries of the region where period-doubling occurs in parameter space. In the results of the main text we report how these boundaries shift with the introduction of farm hosts.

Recall that we treat the low-juvenile case, where $N_0 \leq \frac{1}{\beta_w\tau_w}$. We introduce a scaling of (2.1) to obtain the nondimensional equations,

$$N_0(t+1) = N_1(t)e^{r-N_1(t)-\tilde{c}_0N_0(t)}, \tag{2.B.1a}$$

$$N_1(t+1) = N_0(t)e^{-\tilde{c}_1N_1(t)-P(t)}, \tag{2.B.1b}$$

$$P(t+1) = \eta P(t)N_0(t)e^{-\tilde{c}_1N_1(t)-P(t)}, \tag{2.B.1c}$$

where nondimensional parameters $\tilde{c}_0 = \frac{s_1c_0}{b}$, $\tilde{c}_1 = \frac{c_1}{b}$ relate to inter-cohort density dependence. Dynamical variables are $N_0 = bs_1J$, $N_1 = bA$, and $P = a_wP_w$. Host growth rate is $e^r = s_0s_1s_2f$. The nondimensional parameter for parasite-mediated density-dependence is $\eta = \frac{\beta_w\tau_wk\lambda(1-\tau_w)}{bs_1}$. For the remainder

of the appendix we suppress tildes on $\tilde{c}_i$. The model (2.B.1) exhibits positive invariance to $\mathbb{R}^3_+$. To see this, define $\mathbf{N}(t)$ as $(N_0(t), N_1(t), P(t))$ then take $\mathbf{N}(t_0) > 0$ as initial data at time t_0. Applying (2.B.1) once, $\mathbf{N}(t_0 + 1) > 0$ and repeated application of (2.B.1) results in $\mathbf{N}(t) > 0$ for all $t > t_0$.

We assume that parameters r and η are positive thereby restricting attention to cases where wild adult-juvenile transmission occurs. Further, we focus attention on changes in parameters governing negative density-dependent inter-lineage interactions that result in two-cycles in (2.B.1). Mathematically, these are period-doubling bifurcations of stable equilibria.

Standard linearized stability analysis requires solving (2.B.1) for equilibria. The analytical tractability of (2.B.1) depends on the values of the parameters describing general negative density-dependent interactions c_i. We assume c_i are non-negative and treat several cases. In two of these, one parameter is zero and at least some analytical treatment is possible: (i) when $c_0 = 0$ but $c_1 > 0$ and maturation range inter-lineage interactions are possible, and (ii) when $c_0 > 0$ but $c_1 = 0$. In case (iii) where both maturation range and nursery range inter-lineage interactions are possible, i.e., $c_i > 0$, but the fixed points of (2.B.1) are not expressible in terms of elementary functions. We do not consider this case further. Biologically, this means that we treat cases where negative density dependent interactions occur between lineages either in ocean habitat (c_1) or in breeding habitat (c_0), but not in both.

2.B.1 Equilibria

Bifurcations of equilibria from fixed points to two cycles through period-doubling occur from both parasite-free $\mathbf{N}_{PFE}$ and coexistence $\mathbf{N}_*$ equilibria. The cases treated here differ in their potential for period-doubling bifurcations from these two types of equilibria. For cases (i), (ii) parasite-free equilibria are given in Table 2.3. Only for case (i) can the coexistence equilibria be obtained analytically in terms of elementary functions; given in Table 2.3.

In case (ii), when $c_0 > 0$ and $c_1 = 0$, the coexistence equilibria of (2.B.1) are defined by transcendental equations. Specifically, let $\mathbf{N}_*^{(ii)} := (N_0^*, N_1^*, P^*)$ denote the equilibrium in this case. Dividing (2.B.1c) through

Table 2.3: Fixed points of model for analytically tractable cases.

	Case (i)	Case (ii)
	$c_0 = 0, c_1 > 0$	$c_0 > 0, c_1 = 0$
$\mathbf{N}_{PFE}$	$\left(\frac{re^{r\frac{c_1}{1+c_1}}}{1+c_1}, \frac{r}{1+c_1}, 0\right)$	$\left(\frac{r}{1+c_0}, \frac{r}{1+c_0}, 0\right)$
$\mathbf{N}_*$	$\left(\frac{e^{r-\frac{1}{\eta}}}{\eta}, \frac{1}{\eta}, r-\frac{(1+c_1)}{\eta}\right)$	$\left(\frac{\text{LambertW}\left(\frac{c_0 e^{r-\frac{1}{\eta}}}{\eta}\right)}{c_0}, \frac{1}{\eta}, \log\left(\frac{\eta}{c_0}\text{LambertW}\left(\frac{c_0 e^{r-\frac{1}{\eta}}}{\eta}\right)\right)\right)$

by P^*, we see $1 = \eta N_0^* e^{-P^*}$. Substituting this relation into (2.B.1b),

$$N_1^* = \frac{1}{\eta}.$$

By substituting into (2.B.1a), we see that

$$N_0^* = \frac{1}{\eta} e^{r - c_0 N_0^* - \frac{1}{\eta}},$$

a transcendental equation for N_0^*. This equation does have a unique solution, which expressible in terms of the Lambert W function (see, e.g., Corless *et al.*, 1996), and is given in Table 2.3.

2.B.2 Stability

Standard linearized stability also requires linearizing the system (2.B.1). The linearization is expressed through the Jacobian matrix of the system:

$$\mathbf{D}(t) = \begin{pmatrix} -N_1 c_0 e^{r-N_1-N_0 c_0} & (1-N_1)e^{r-N_1-N_0 c_0} & 0 \\ e^{-P-N_1 c_1} & -N_0 c_1 e^{-P-N_1 c_1} & -N_0 e^{-P-N_1 c_1} \\ P\eta e^{-P-N_1 c_1} & -N_0 P\eta c_1 e^{-P-N_1 c_1} & (1-P)N_0\eta e^{-P-N_1 c_1} \end{pmatrix}. \qquad (2.B.2)$$

We use standard local stability analysis of dynamical systems. For discrete time systems, linear stability requires that each eigenvalue of the Jacobian matrix (2.B.2) evaluated at an equilibrium lies within the unit circle in the complex plane. If the linearized system at a particular equilibria satisfies this requirement, then it is stable. For analysis of the parasite-free equilibrium, $\mathbf{N}_{PFE}$ we are able to analytically compute the eigenvalues of (2.B.2) evaluated at the equilibrium and thus verify stability. For the coexistence equilibrium, $\mathbf{N}_*$, we use Jury's criteria, which provide necessary

and sufficient conditions on the characteristic polynomial of the Jacobian for stability. We do not focus on the stability of equilibria *per se*, but instead on the location in parameter space where stability is lost, through bifurcation. Thus, results of our stability analysis are described below in our bifurcation analysis.

2.B.3 Bifurcations

Throughout we focus on behaviour for moderate values of host reproduction, i.e. $r < 2$, that correspond to the situation of biological interest. This eliminates possible period-doubling bifucations due to the host reproduction parameter r. Such bifurcations occur in the classical Ricker model, as part of a period doubling cascade to chaos as outlined in (May & Oster, 1976). Because our concern is line dominance, we focus on period-doubling bifurcations that occur with changes in parameters governing negative density-dependent inter-lineage interactions, including general interactions c_i and parasite mediated interactions governed by the inter-lineage transmission term η.

Period-doubling (PD) bifurcations of maps must satisfy two criteria (Iooss, 1979, pp. 12):

Theorem 2.1 *Consider the map* $(\mu, X_i) \mapsto f_\mu(X_i) : \mathbb{R}^4 \to \mathbb{R}^3$ *where* $X_i \in \mathbb{R}^3$ *are dynamical variables and* $\mu \in \mathbb{R}$ *is a parameter. If* f_μ *is of class* C^k *for* $k \geq 2$ *near a fixed point* X^**, then a* period doubling *bifurcation exists at* $\mu = \mu^*$ *if the following conditions are satisfied:*

(PD1) Eigenvalue location *The Jacobian* $Df_\mu(X^*)$ *has an eigenvalue* $\lambda_0(\mu)$ *with* $\lambda_0(\mu^*) = -1$ *and* $|\lambda_i(\mu^*)| < 1$ *for* $i = 1, 2$*; and*

(PD2) transversal $\frac{d|\lambda(\mu^*)|}{d\mu} < 0$.

Specifically, there exists a unique one-sided bifurcated branch of fixed points of order 2, $(\mu(s), X_j(s), j = 1, 2)$ *for* f_μ *such that* $\mu(X^*) = X^*$, $\mu(-s) = \mu(s)$, $X_1(-s) = X_2(s)$, $\frac{d_{X_1}}{ds}(0) = 1$, $X_j(0) = X^*$, $f_\mu(X_j) = X_{j'}, \quad j \neq j'$. *The functions* μ *and* X_j *are* C^{k-1}.

Bifurcation from parasite-free equilibrium

For the parasite-free equilibria $\mathbf{N}_{PFE}$ we characterized period-doubling bifurcations for both case (i) and case (ii).

In case (i), $c_0 = 0$ the Jacobian (2.B.2) evaluated at N_{PFE} from Table 2.3 is given by

$$\begin{pmatrix} 0 & -\frac{re^{r-\frac{r}{1+c_1}}}{1+c_1}+e^{r-\frac{r}{1+c_1}} & 0 \\ e^{-\frac{c_1 r}{1+c_1}} & -\frac{c_1 r}{1+c_1} & -\frac{r}{1+c_1} \\ 0 & 0 & \frac{\eta r}{1+c_1} \end{pmatrix}. \tag{2.B.3}$$

The characteristic equation of (2.B.3) is

$$\begin{aligned} \lambda^3 + \lambda^2\left(\frac{c_1 r}{1+c_1} - \frac{\eta r}{1+c_1}\right) - \lambda\left(1 - \frac{r}{1+c_1} + \frac{\eta c_1 r^2}{(1+c_1)^2}\right) \\ + \frac{\eta r}{1+c_1} - \frac{\eta r^2}{(1+c_1)^2} = 0. \end{aligned} \tag{2.B.4}$$

The polynomial on the right hand side of (2.B.4) can be factored,

$$\begin{aligned} \left(\lambda - \frac{\eta r}{1+c_1}\right) \cdot \left(\lambda + \frac{c_1 r}{2+2c_1} - \frac{1}{2}\sqrt{4 - 4\frac{r}{1+c_1} + \frac{c_1^2 r^2}{(1+c_1)^2}}\right) \\ \cdot \left(\lambda + \frac{c_1 r}{2+2c_1} + \frac{1}{2}\sqrt{4 - 4\frac{r}{1+c_1} + \frac{c_1^2 r^2}{(1+c_1)^2}}\right). \end{aligned}$$

To find potential curves in parameter space where period-doubling occurs, we set one root of the characteristic equation (2.B.4) to negative unity. The resulting curve is $c_1 = 1$. Along this curve, one eigenvalue of (2.B.3), i.e. root of (2.B.4), is negative unity. The eigenvalue of (2.B.3)

$$\lambda_{PD(i)} = -\frac{c_1 r}{2+2c_1} - \frac{1}{2}\sqrt{4 - 4\frac{r}{1+c_1} + \frac{c_1^2 r^2}{(1+c_1)^2}} \tag{2.B.5}$$

evaluates to negative unity when $c_1 = 1$. The other roots of (2.B.4) have absolute value less than unity when conditions on η and r are satisfied: the root $\frac{\eta r}{1+c_0}$, has absolute value less than unity when η is sufficiently small, i.e., $\eta < \frac{2}{r} = \frac{1+c_1}{r}$; the other root is the complex conjugate of (2.B.5), and has absolute value less than unity for values of r considered here, i.e., $r < 2$. Thus the Eigenvalue location (PD1) criterion is satisfied for $r < 2$ and sufficiently small values of η. For this eigenvalue,

$$\frac{\partial \lambda_{PD(i)}(c_1)}{\partial c_1}\Big|_{c_1=1} = -\frac{1}{8}r - \frac{1}{8}\frac{4r + r^2}{r-4},$$

thus satisfying the transversal (PD2) criterion for values of r considered

here, i.e. $r < 2$.

In case (ii), $c_1 = 0$, the Jacobian (2.B.2) evaluated at N_{PFE} from Table 2.3 is given by

$$\begin{pmatrix} -\frac{c_0 r e^{r-\frac{r}{1+c_0}-\frac{c_0 r}{1+c_0}}}{1+c_0} & -\frac{r e^{r-\frac{r}{1+c_0}-\frac{c_0 r}{1+c_0}}}{1+c_0}+e^{r-\frac{r}{1+c_0}-\frac{c_0 r}{1+c_0}} & 0 \\ 1 & 0 & -\frac{r}{1+c_0} \\ 0 & 0 & \frac{\eta r}{1+c_0} \end{pmatrix}. \tag{2.B.6}$$

The characteristic equation of (2.B.6) is

$$\begin{aligned} \lambda^3 + \lambda^2\left(\frac{c_0 r}{1+c_0} - \frac{\eta r}{1+c_0}\right) - \lambda\left(1 - \frac{r}{1+c_0} + \frac{\eta c_0 r^2}{(1+c_0)^2}\right) \\ + \frac{\eta r}{1+c_0} - \frac{\eta r^2}{(1+c_0)^2} = 0. \end{aligned} \tag{2.B.7}$$

The polynomial on the right hand side of (2.B.6) can be factored,

$$\begin{aligned} \left(\lambda - \frac{\eta r}{1+c_0}\right) \cdot \left(\lambda + \frac{c_0 r}{2+2c_0} - \frac{1}{2}\sqrt{4 - 4\frac{r}{1+c_0} + \frac{c_0^2 r^2}{(1+c_0)^2}}\right) \\ \cdot \left(\lambda + \frac{c_0 r}{2+2c_0} + \frac{1}{2}\sqrt{4 - 4\frac{r}{1+c_0} + \frac{c_0^2 r^2}{(1+c_0)^2}}\right). \end{aligned}$$

To find potential curves in parameter space where period-doubling occurs, we set one root of the characteristic equation (2.B.7) to negative unity. The resulting curve is $c_0 = 1$. Along this curve, one eigenvalue of (2.B.6), i.e. root of (2.B.7), is negative unity. The eigenvalue of (2.B.6)

$$\lambda_{PD(ii)} = -\frac{c_0 r}{2+2c_0} - \frac{1}{2}\sqrt{4 - 4\frac{r}{1+c_0} + \frac{c_0^2 r^2}{(1+c_0)^2}} \tag{2.B.8}$$

evaluates to negative unity when $c_0 = 1$. The other roots of (2.B.7) have absolute value less than unity when conditions on η and r are satisfied: the root $\frac{\eta r}{1+c_0}$, has absolute value less than unity when η is sufficiently small, i.e., $\eta < \frac{2}{r} = \frac{1+c_0}{r}$; the other root is the complex conjugate of (2.B.8), and has absolute value less than unity for values of r considered here, i.e., $r < 2$. Thus the Eigenvalue location (PD1) criterion is satisfied for $r < 2$ and sufficiently small values of η.

For this eigenvalue,

$$\frac{\partial \lambda_{PD(ii)}(c_0)}{\partial c_0}\Big|_{c_0=1} = -\frac{1}{8}r - \frac{1}{8}\frac{4r+r^2}{r-4},$$

thus satisfying the transversal (PD2) criterion for values of r considered here, i.e. $r < 2$.

Bifurcation from coexistence equilibrium

For the coexistence equilibrium, $\mathbf{N}_*$, in case (i), the Jacobian (2.B.2) evaluated at N_* from Table 2.3 is given by

$$\begin{pmatrix} 0 & -\frac{e^{r-\frac{1}{\eta}}}{\eta}+e^{r-\frac{1}{\eta}} & 0 \\ e^{-r+\frac{1}{\eta}} & -\frac{c_1}{\eta} & -\frac{1}{\eta} \\ \eta\left(r-\frac{1}{\eta}-\frac{c_1}{\eta}\right)e^{-r+\frac{1}{\eta}} & -c_1\left(r-\frac{1}{\eta}-\frac{c_1}{\eta}\right) & 1-r+\frac{1}{\eta}+\frac{c_1}{\eta} \end{pmatrix} \tag{2.B.9}$$

The characteristic equation of (2.B.9) is

$$\lambda^3 + \lambda^2\left(r-1-\frac{1}{\eta}\right) + \lambda\left(\frac{1-c_1}{\eta}-1\right) + 1 - \frac{1}{\eta} = 0 \tag{2.B.10}$$

To find potential curves in parameter space where period-doubling occurs, we set one root of the characteristic polynomial (2.B.10) to negative unity. The resulting curve is $r = \frac{3-c_1}{\eta}$. Along this curve, one eigenvalue of (2.B.9) is negative unity and thus part of the Eigenvalue location (PD1) criterion is satisfied. The roots of (2.B.10) are obtainable through the formula for the roots of a cubic. The formulae that result from these roots, however, are very long and would be tedious to treat analytically. We use Jury's criteria, which provide necessary and sufficient conditions on the characteristic polynomial of the Jacobian for stability, to verify that the remaining eigenvalues fall within the unit circle. We state Jury's stability criteria from (Cain, 2007):

Theorem 2.2 *(Jury stability test) All roots of the polynomial*

$$q(x) = a_m x^m + a_{m-1} + \cdots + a_1 x + a_0 \tag{2.B.11}$$

lie in the open disc in the complex plane if and only if

— *(J1):* $a_m q(1) > 0$,
— *(J2):* $(-1)^m a_m q(-1) > 0$, *and*

— *(J3.j):* $|\mathrm{r}_j| < 1$ *for* $j = 1, 2, \ldots m$*, where* r_j *are given by the following iterative procedure. First, set* $b_j = a_{m-j}$ *for* $j = 0, 1, \ldots m$ *and define* $\mathrm{r}_m = b_m/a_m$*. Then, define* $a_{j-1}^{\mathrm{new}} = a_j - \mathrm{r}_m b_j$ *for* $j = 1, 2, \ldots m$*. This gives the coefficients* $a_{m-1}, a_{m-2} \ldots a_0$ *for the next iteration.*

The characteristic polynomial of (2.B.9) is given by the left-hand side of the characteristic equation (2.B.10). To apply Theorem 2.2 to the linearization (2.B.9), we identify coefficients of the polynomial from (2.B.10) with coefficients a_j of (2.B.11):

$$\begin{aligned} a_3 &= 1, \\ a_2 &= r - 1 - \frac{1}{\eta}, \\ a_1 &= \frac{1 - c_1}{\eta} - 1, \\ a_0 &= 1 - \frac{1}{\eta}. \end{aligned}$$

The full set of Jury's criteria from Theorem 2.2 for $\mathbf{N}_*$ in case (i) are given in Table 2.4. Equality in condition J2 of Table 2.4 corresponds to the curve $r = \frac{3-c_1}{\eta}$. Condition J1 is satisfied along this curve for $c_1 < 1$, and condition J3.1 is satisfied for $\eta > \frac{1}{2}$. Thus, along the curve $r = \frac{3-c_1}{\eta}$, for $r < 2$, $\eta > \frac{1}{2}$, and $c_1 < 1$, when criteria J3.2 and J3.2 are also met, the full Eigenvalue location criterion (PD1) is satisfied.

Because we did not explicitly compute the eigenvalues of (2.B.10), we could not verify the transversal condition analytically. Using the numerical continuation tool Cl_matcontM (Dhooge *et al.*, 2003), however, we verified that the system undergoes a period-doubling bifurcation along the dashed line of Figure 2.2A. This tool, like many software packages for numerical analysis of bifurcations, solves equations that define a bifurcation type, e.g. period-doubling, and computes corresponding normal forms to identify the bifurcation (Dhooge *et al.*, 2003; Kuznetsov, 2004).

Thus, equality in the conditions of Table 2.5 defines boundaries between regions in which the coexistence and parasite-free equilibria are stable and those in which two-cycles occur. For $c_i < 1$ period-doubling bifurcations from a stable coexistence equilibrium are possible. The dashed lines in Figure 2.2 represent curves where the eigenvalue location (PD1) criterion is satisfied for the coexistence equilibrium $\mathbf{N}_*$. Numerical computations

Table 2.4: Conditions for existence and stability of $\mathbf{N}_*$ in case (i). The term r_3 is defined in line J3.1. The terms $\mathrm{r}_{2\mathrm{n}}$ and $\mathrm{r}_{2\mathrm{d}}$ are defined in line J3.2.

J1.	$0 < r - \frac{(1+c_1)}{\eta}$
J2.	$0 < \frac{3-c_1}{\eta} - r$
J3.1.	$\lvert \mathrm{r}_3 \rvert := \lvert 1 - \frac{1}{\eta} \rvert < 1$
J3.2.	$\lvert \mathrm{r}_{2\mathrm{n}} \rvert := \lvert \frac{1-c_1}{\eta} - 1 - \mathrm{r}_3 \left(r - 1 - \frac{1}{\eta} \right) \rvert < \lvert 1 - \mathrm{r}_3 \left(1 - \frac{1}{\eta} \right) \rvert =: \lvert \mathrm{r}_{2\mathrm{d}} \rvert$
J3.3	$\left\lvert \left(r - 1 - \frac{1}{\eta} - \left(1 - \frac{1}{\eta} \right) \left(\frac{1-c_1}{\eta} - 1 \right) \right) \left(1 + \frac{\mathrm{r}_{2\mathrm{n}}}{\mathrm{r}_{2\mathrm{d}}} \right) \right\rvert < \left\lvert \mathrm{r}_{2\mathrm{d}} - \left(\frac{\mathrm{r}_{2\mathrm{n}}}{\mathrm{r}_{2\mathrm{d}}} \right) \mathrm{r}_{2\mathrm{n}} \right\rvert$

Table 2.5: Conditions that, if violated, result in loss of stability through period-doubling of parasite-free $\mathbf{N}_{PFE}$ and coexistence $\mathbf{N}_*$ fixed points; for analytically tractable cases.

	Case (i)	Case (ii)
$\mathbf{N}_{PFE}$	$c_1 < 1$	$c_0 < 1$
$\mathbf{N}_*$	$r < \frac{3-c_1}{\eta}$	—

using Cl_matcontM (Dhooge *et al.*, 2003) confirm these curves represent the location of period-doubling bifurcations with increasing η. In this case the dynamics undergo a qualitative transition from stable endemic equilibrium to dominance through period doubling with increase in either η or c_1.

The ηr stability plane, i.e. Figure 2.2A in the main text, shows curves based on the applying Jury's criteria to $\mathbf{N}_*$ for case (i), i.e., Table 2.4, and results from numerical continuation. The structure shown in this figure indicate that the governing of dynamics by r is also typical for $\eta > 0$. For fixed r, e.g. $r = r^* = 1.2$ the empirical estimate for pink salmon (Myers *et al.*, 1999), as η becomes very large, a bifurcation across the dotted line of Figure 2.2A to higher-order cycles is possible. This line corresponds to Niemark-Sacker bifurcation, i.e. a Hopf bifurcation for maps (Hale & Kocak, 1991). Bifurcation in η is shown in Figure 2.3A. The character of the bifurcation in η is a single period doubling. In contrast to the "cascade to chaos" familiar from the Ricker model (May & Oster, 1976), the period-two regime is present for a large range, $\eta \approx 2.5$ to $\eta \geq 100$ (not shown).

Appendix 2.C Differential mortality between lines when dominance occurs

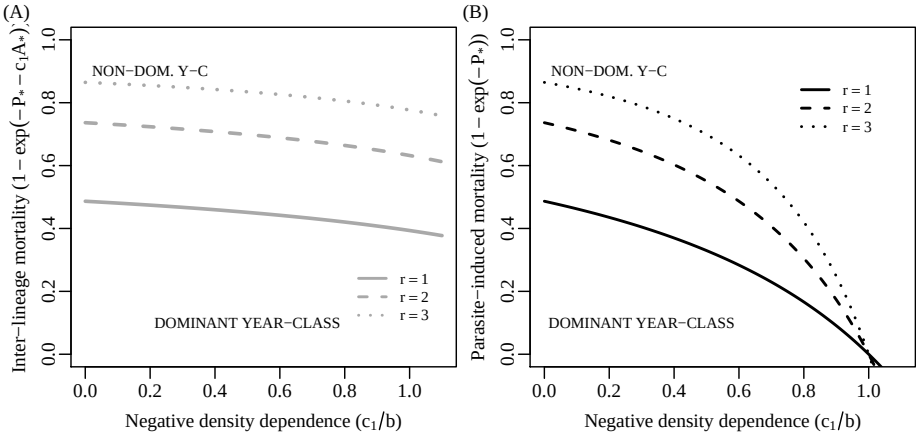

Figure 2.5: Bounds on mortality of "dominant" and "non-dominant" lineage juveniles at equilibrium for (A) parasite-mediated *and* general negative density-dependence between lineages, and (B) parasite-mediated interactions only. The curves are computed for various values of r, given in legend, at the boundary of the dominance region, i.e., at onset of period-doubling induced by parameter c_1. For a given value of r, mortality of the dominant lineage has a value *below* the curve while mortality of the non-dominant lineage has a value *above* the curve.

If dominance occurs in (2.1), the less abundant lineage experiences 40% mortality (or greater) due to negative density-dependent inter-lineage interactions, while the dominant lineage experiences less mortality. Figure 2.5A shows the equilibrium mortality of juvenile hosts due to general negative density-dependence and parasitism at the edge of the dominance region, i.e., dashed lines in Figure 2.2. The degree of overall mortality due to both factors decreases slightly as the general negative density-dependent, c_1/b, interaction strength is increased. The figure was computed for a system with where negative density-dependent effects occur between lineages only based on adult abundance ($c_1 > 0, c_0 = 0$). In the "dominance" region of Figure 2.2A, mortality for the more-abundant lineage falls below the curves given, while mortality for the less-abundant lineage is above the curve.

As the strength of general negative density-dependent interactions is increased, the amount of parasite-mediated negative density-dependent mortality needed to maintain dominance decreases. Figure 2.5B shows this

effect, plotting the mortality due to parasite-mediated effects alone that is needed to maintain line dominance plotted against the strength of general negative density-dependent inter-lineage interactions c_1/b.

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Chapter 3

Evolution of chemical resistance in parasites of aquaculture

3.1 Introduction

Sea lice, notably *Lepeophtheirus salmonis* in Scotland, Ireland, Norway and Canada, and *Caligus rogercresseyi* in Chile, pose problems for salmon aquaculture, particularly economic losses due to decreased production (Johnson *et al.*, 2004). Salmon aquaculture managers have implemented sea lice control programs to mitigate these economic losses (Costello, 2009*b*). Salmon aquaculture is also associated with declines in wild abundance, potentially due to sea lice (Krkošek *et al.*, 2007; Ford & Myers, 2008). As concerns over the impacts of salmon aquaculture on wild stocks grow, lice control programs also aim to reduce farm impacts on wild populations (Heuch *et al.*, 2005; Krkošek, 2010). Chemical treatment of lice on farms is a central tool to achieve both conservation and economic goals (BCPSF, 2009; Costello, 2009*b*; Krkošek, 2010). Sea lice have developed resistance, or demonstrated potential for resistance, to chemical treatments including organophosphates (Fallang *et al.*, 2004), pyrethroids (Sevatdal & Horsberg, 2003; Fallang *et al.*, 2005), and avermectins (Bravo, 2003; Lees *et al.*, 2008). Resistance development threatens the continued efficacy of management plans that rely on chemical treatment.

The history of resistance development in sea lice differs between the

North Atlantic and North Pacific basins. In the Atlantic, resistance has occurred multiple times to multiple different compounds, while in the Pacific resistance has not been observed. The two ocean basins differ in their history of chemical use (Denholm *et al.*, 2002). However, in the most recent episode of resistance emergence, to emamectin benzoate, the chemical was used for a similar time period in both basins (Lees *et al.*, 2008). An alternative explanation for the apparent difference in propensity for resistance is that the basins may differ in the amount of immigration of susceptible parasites from wild-origin parasite populations.

Wild salmonids are migratory in both Atlantic and Pacific basins. In both basins, migrations of hosts may provide connectivity between parasite populations, likely explaining panmixis of lice observed at the basin scale (Todd *et al.*, 2006; Messmer *et al.*, 2010). The basins differ greatly, however, in the abundance of wild salmonids relative to salmon in farms: in the Atlantic, wild salmonids are greatly outnumbered by salmon in farms, while in the Pacific this situation is reversed (Costello, 2009*b*; Krkošek, 2010). Because the basins differ in the ratio of non-selective to selective habitat, aquaculture sites in the Atlantic may receive lower immigration of susceptible parasites from wild populations relative to the Pacific.

The amount of susceptible immigration can influence resistance evolution (Comins, 1977*a*). On domesticated hosts, chemical treatment selects parasites for resistance. On wild hosts, no treatment occurs and resistance is neutral, or selected against (Denholm & Rowland, 1992). Sea-cage aquaculture results in "spill-over" and "spill-back" of parasites between sympatric domesticated and wild hosts (Costello, 2009*b*). This means that a lineage of sea lice can experience variable selection for resistance as infestations spread back and forth between farms and wild populations.

This situation echoes a strategy employed in terrestrial agriculture to slow resistance emergence: planting but not treating areas, termed "evolutionary refuges," adjacent to treated fields (Figure 1A; Alstad & Andow, 1995; Gould, 2000). If wild migrating salmon mediate immigration of susceptible lice (Figure 3.1B), they could help fulfil a human need for increased time to resistance. Thus, salmon could provide an *ecosystem service*, where a natural population serves a human demand (de Groot *et al.*, 2002). This also raises the question: can management of parasites on farms can maximize the benefit potentially provided by salmon migrations? To address this

question, we use analytical approximations and numerical simulations within a population genetics framework. We focus on "time-to-resistance," the generation in which the frequency of chemical resistance in a farm population of parasites reaches a predetermined threshold from a low initial value. First, we ask how a chemical treatment strategy can maximize time-to-resistance. Second, we consider whether a decline in migratory wild populations due to sea lice spill-over from the farm changes the strategy that maximizes time-to-resistance.

3.2 Models

We model the genetic and demographic dynamics of parasite populations on salmon farms that receive immigration from parasite populations on wild hosts. Because sea lice are sexually-reproducing macroparasites, we begin with the classical equations for selection of single-locus two-allele gene in a randomly-mating, sexually-reproducing population with discrete generations to describe the process of resistance evolution (Crow & Kimura, 1970). We assume (i) major-gene control of a resistance trait, which (ii) has no cost in a parasite population that (iii) reproduces without density-dependence. Further, we assume that (iv) only one generation of the parasite is treated per year, and (v) immigration to the parasite population takes place once per year.

There are several reasons why we use a simple population genetic model. First, there is a strong theoretical context for single locus models in resistance management, based on the equations of population genetics describing changes in gene frequency under selection (Comins, 1977*b*,*a*; Mangel & Plant, 1983; Plant *et al.*, 1985; Alstad & Andow, 1995; Lenormand & Raymond, 1998). Second, field-origin resistance to pesticides is often single-locus (Denholm & Rowland, 1992). Third, lice have physiological potential for resistance to chemical treatments currently in widespread use against sea lice, such as emamectin benzoate (Lees *et al.*, 2008; Westcott *et al.*, 2008). Although the genetic and physiological bases of resistance in lice remain a topic of ongoing research, potential single-locus mechanisms of resistance have been identified in lice (Burridge *et al.*, 2010).

Because we deal with resistance, we assume that the resistance allele is beneficial during treatment and has no effect in the absence of treatment.

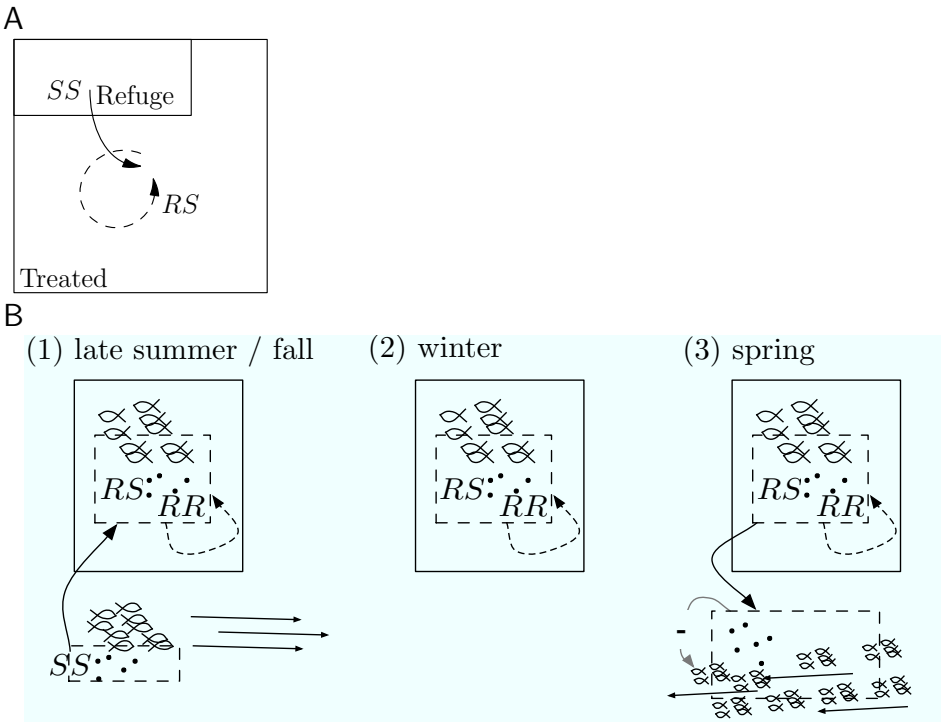

Figure 3.1: A refuge strategy to delay chemical resistance in pests as employed in transgenic crops (A), and as embodied by seasonal immigration of lice brought to farms by wild salmon migrations (B). We assume single-locus, two-allele control of resistance. Under the refuge strategy in agriculture, treated and untreated refuge habitats are planted. Pests with susceptible genotype SS migrate (solid arrows) from refuge habitat (A) to reproduce (dashed arrows) with heterozygote RS or resistant RR pests in treated habitat (A). When wild adult salmon (B1) migrate past salmon farms (solid boxes in B) in fall or late summer they bring immigrant susceptible SS lice (dash boxes) to farms. Migrating wild juveniles (B3) move past farms in spring, receiving spill-over infection from farms that may cause population declines (note that we do not consider the genetics of these spill-over lice). In winter, and perhaps early summer, (B2) the farm population of lice is isolated.

Some studies in resistance management (Comins, 1977*a*; Lenormand & Raymond, 1998; Vacher *et al.*, 2003) make a further assumption that resistance has a cost and is selected against without treatment. That resistance has a cost, however, is not universally true (Denholm & Rowland, 1992). In lice, the tools to investigate whether resistance mechanisms have fitness implications are just being developed. Further, the assumption of a cost is less conservative because it increases time to resistance (REX Consortium, 2010). For these reasons, we assume no cost to resistance.

To derive an analytical formula for time-to-resistance, we assume that numbers of immigration events and treatment events are constant from year-to-year and that immigration and treatment overlap the same number of times per year. For numerical simulations, we relax this assumption. We assume that treatment occurs often enough to ignore any intrinsic density-dependence in the parasite. Thus, we assume the population grows or shrinks geometrically depending on treatment. We assume also that the environment is constant except for changes due to treatment. We assume treatment selects on survivorship, not fecundity, and precedes mating. Under these conditions relative genotypic fitness acts as differential survivorship (Bourguet *et al.*, 2000).

We use approximations to classical population genetic models based on the low initial frequency of resistance to describe emerging chemical resistance. Using approximate models permits analytical results that would not be possible when considering the full nonlinear dynamics of population genetic change under selection.

We begin with an approximation for time-to-resistance based on Taylor expansion of the classical Fisher-Haldane-Wright equations, originally due to Comins (1977*b*), which we re-derive in Appendix 3.B using our notation and assumptions. Under the assumptions of classical population genetics, the change in resistance frequency p during the ith generation follows Fisher's fundamental theorem (Appendix 3.A; Crow & Kimura, 1970). The change is proportional to the product of the genetic variability under selection and the gradient of selection. We consider a resistance trait following these dynamics with resistant allele R and susceptible allele S. Following Comins (1977*b*), we parametrize the relative genotypic fitness according to the dominance of resistance and strength of selection given in Table 3.1. To first order in p, frequency of resistance during the ith generation changes according to the

ratio of heterozygote fitness to susceptible homozygote fitness, $p_{i+1} \approx \frac{w_{RS}}{w_{SS}} p_i$; this is equation (3.B.1) in Appendix 3.B. This ratio, which we refer to as "heterozygote advantage," depends on treatment status, as well as the strength and dominance of selection due to treatment.

We parameterize genotypic fitness using parameters $s \in (0,1)$ for the strength of treatment and $\beta \in (0,1)$ for the dominance of resistance. When s is closer to 1, selection due to treatment is more intense, i.e. treatment strength is higher. When β is closer to 1, the resistance trait is more dominant. Under this parameterzation, during treatment fitness of the RS heterozygote is $(1-s)^{1-\beta}$, which is intermediate between fitness of the susceptible SS homozygote, $1-s$, and fitness of the resistant RR homozygote, 1. Then, the heterozygote advantage as a function of treatment and the genetics of resistance is $\frac{w_{SR}}{w_{SS}} = \left(\frac{1}{1-g_i \cdot s}\right)^{\beta}$, where s is selection strength due to treatment, β is dominance of resistance, and g_i indicates treatment ($g_i = 1$) or non-treatment ($g_i = 0$). During treatment, the ratio exceeds unity so resistance will increase in frequency, while without treatment the ratio is unity. Dynamics are according to

$$p_{i+1} = \underbrace{\left(\frac{1}{1-g_i \cdot s}\right)^{\beta}}_{\text{Selection}} \cdot p_i. \tag{3.1}$$

When the number of treated generations is the same each year, the emergence threshold frequency p_e is the initial frequency of resistance p_0 multiplied by the product of heterozygote advantages to the power of T_R, the number of *years* until resistance is detected. We perform this computation in Appendix 3.B. With our assumption of one treatment per year, we set $g_i = 1$ for the one treated generation each year, time-to-resistance in years is

$$T_R = \underbrace{T_g \frac{\log \frac{p_e}{p_0}}{\beta}}_{\text{Biological}} \cdot \underbrace{\frac{1}{\log \frac{1}{1-s}}}_{\text{Treatment}}, \tag{3.2}$$

where T_g is the generation time. This equation, which we rederive in Appendix 3.B as equation (3.B.3), is equivalent to equation (6) of Comins (1977*b*) or equation (4) of May & Dobson (1986). The time to resistance is affected by factors relating to parasite biology, e.g., generation time and initial frequency of resistance, and to the strength of treatment. Note that

this approximation only applies when resistance is not completely recessive; however, even in this case, $\lim_{\beta \to 0} T_R = \infty$, the equation gives the correct intuition: time-to-resistance is very long (May & Dobson, 1986).

3.2.1 Approximate dynamics of resistance emergence with migration from a purely susceptible pool

To understand the effect of immigration on approximate time-to-resistance (3.2), we extend the approximation of Comins (1977*b*). To model the situation in the Pacific, where there are a large number of hosts and lice, we assume that lice immigrating to farms via wild hosts come from a very large pool. For qualitative insight into how immigration of susceptible genes and treatment interact to affect time-to-resistance, we assume that immigrants all have homozygous susceptible genotype SS. Therefore the frequency of resistance in the immigrants is zero, $\bar{p} = 0$.

The resistance frequency in the farm after selection and immigration is obtained by averaging the resistance frequency p in the resident population with that of the immigrants, assumed to be zero. This average is weighted according to the abundance of the farm population n and of the immigrants $\bar{n}$,

$$p_{i+1} = \left(\underbrace{\left(\frac{1}{1 - g_i \cdot s} \right)^{\beta}}_{\text{Selection}} \cdot \underbrace{\frac{1}{\frac{\bar{n} \cdot m_i}{n_i} + 1}}_{\text{Immigration}} \right) p_i. \tag{3.3}$$

The effect of immigration enters through the ratio of immigrants to residents $\frac{\bar{n}}{n_i}$. Equation (3.3) is derived in Appendix 3.C (as equation (3.C.2)). This formulation assumes that if immigration and treatment occur within the same generation, immigrants are incorporated into the population before treatment. The value of the ratio depends on demographic changes in the parasite population, models of which are described in Section 3.2.2.

To first order in p_i, the change over one year in the resistance frequency is given by the term in the parenthesis on the right hand side of (3.3). When the magnitude of this term is the same each year, the equation can be

Table 3.1: Summary of notation

Symbol	Meaning	Units
w_{RR}	Resistant homozygote fitness $= 1$	—
w_{RS}	Heterozygote fitness $= (1 - g \cdot s)^{1-\beta}$	—
w_{SS}	Susceptible homozygote fitness $= 1 - g \cdot s$	—
$\bar{w}_i$	Average genotypic fitness in ith generation	—
λ	Geometric growth rate of parasite	[parasite][time]$^{-1}$
g_i	Indicator of treatment ($g_i = 1$), non-treatment ($g_i = 0$)	—
β	Dominance of resistance ($\beta = 1$ implies dominant resistance gene)	—
s	Selection strength of treatment	—
$\left(\frac{1}{1-g_i \cdot s}\right)^{\beta}$	Heterozygote advantage under treatment	—
p_i	Frequency of resistance in farm in ith generation	—
n_i	Farm parasite population in ith generation	[parasite]
m_i	Indicator of immigration ($m_i = 1$), no immigration ($m_i = 0$)	—
$\bar{p}$	Frequency of resistance in immigrant parasite population	—
$\bar{n}_t$	Immigrant parasite population in year t	[parasite]
$\frac{\bar{n}}{n_i}$	Ratio of immigrants to residents in ith generation	—
p_e	Emergence threshold for resistance frequency	—
T_R	Time-to-resistance	[years]
T_g	Generation time, $\frac{1}{T_g}$ assumed an integer	[years]
i	Time scale for parasite	[generations]
t	Time unit for migratory wild salmon ($t \cdot \frac{1}{T_g} = i$ parasite generations)	[years]
Δ	Number of generations between wild host breeding and wild host juvenile migration	[generations]
e^r	Geometric population growth rate for migratory wild salmon	[host][time]$^{-1}$
b	Inverse carrying capacity for parasites on migratory wild salmon	[parasite]$^{-1}$
a	Parasite-induced mortality of juvenile wild salmon	[host][parasite]$^{-1}$
k	Proportionality between parasites on farm and on juvenile wild salmon	[host]$^{-1}$

rearranged for time-to-resistance with immigration,

$$T_R = \underbrace{\frac{T_g \log \frac{p_e}{p_0}}{\beta}}_{\text{Biological}} \cdot \frac{1}{\underbrace{\log\left(\frac{1}{1-s}\right)}_{\text{Treatment}} - \underbrace{\log\left(\frac{\bar{n}}{n_i}+1\right)^{\frac{1}{\beta}}}_{\text{Immigration}}}. \tag{3.4}$$

Equation (3.4) is derived in Appendix 3.C (as equation (3.C.6)). The approximate effect of immigration enters via the term labelled "Immigration" in the denominator. When this term, which grows with the ratio of immigrants to residents $\frac{\bar{n}}{n_i}$, approaches the term labelled "Treatment," the time-to-resistance becomes very long (theoretically infinite). Other terms are as in (3.2).

3.2.2 Demography of farm parasites under treatment and immigration

To simulate time-to-resistance, we require a model for the demographics of the parasite population on farms. We employ the demographic model underlying the standard population genetic model from which our approximation (3.4) is derived. The discrete-time geometric growth of the population is the product of the maximum growth rate λ and average relative fitness $\bar{w}_i$ which depends on generation (Crow & Kimura, 1970). The equation for geometric growth is $n_{i+1} = \lambda \bar{w}(p_i) n_i$, see Appendix 3.A for the full form of average fitness. Average fitness is a function of the resistance frequency p_i and whether treatment occurs g_i, as parametrized by the strength of selection s and dominance of resistance β. Whenever immigration occurs ($m_i = 1$), the immigrants $\bar{n}$ increase the size of the population. The demographic dynamics are

$$n_{i+1} = \underbrace{\lambda(1 - g_i \cdot s)}_{\text{Susceptible growth}} \cdot \left(1 + \underbrace{2p_i\left(\left(\frac{1}{1-g_i \cdot s}\right)^{\beta} - 1\right)}_{\text{Resistant growth}}\right) \cdot (n_i + \underbrace{m_i \cdot \bar{n}}_{\text{immigration}}). \tag{3.5}$$

This approximation states that the population grows at a rate determined by the more-prevalent SS genotype with a correction term for demographic growth under treatment in the fraction of the population that is resistant.

The correction, labelled "Resistant growth," is proportional to the resistance frequency and governed by the strength and dominance of selection on heterozygotes under treatment. This is equation (3.C.7), derived in Appendix 3.C.1.

3.2.3 Immigration when parasites on farms affect wild host abundance

To explore the implications for time-to-resistance if wild-origin infections cause declines in abundance of wild hosts, we couple a model for salmon population dynamics with the genetic (3.3) and demographic (3.5) models for the farm population of parasites. The association between infections of juvenile pink salmon in farming regions and declines in pink salmon abundance was shown in an empirical study of Krkošek *et al.* (2007). To incorporate the potential effect of parasites on farms on wild salmon populations, we assume that lice immigrating to farms are proportional to the number of wild salmon migrating near the farm. Then, equations for population dynamics of *salmon* can be used to describe the number of *lice* immigrants. For this, we use a extension to the Ricker model for pink salmon population dynamics that accounts for the effect of spill-over infections. This extension, introduced by Krkošek *et al.* (2007), states that salmon decline in abundance exponentially with the average number of parasites per juvenile. We also use the transmission function developed in Chapter 2, which assumes that the average number of lice on juveniles during out-migration is proportional to the number of lice on farms. In turn, the lice on juveniles result in declines in the number of adults returning and thus the number of lice immigrating to the farm. This yields an equation for the number of wild-origin sea lice immigrating to the farm from year-to-year,

$$\bar{n}_{t+2} = \underbrace{\bar{n}_t \cdot e^{r-b\bar{n}_t}}_{\text{Ricker production}} \cdot \underbrace{e^{-akn_{t\cdot(\frac{1\text{year}}{T_g})+\Delta}}}_{\text{Lice-induced mortality}} . \tag{3.6}$$

In this equation, we use time units of *years* t appropriate to salmon population dynamics, but we must convert the index on resident lice, n_i, to to lice generations. The term Δ represents the time difference, less than a year and measured in lice generations, between when wild host adults migrate in to rivers and when wild host juveniles migrate out past farms. Equation (3.6)

states that the number of immigrants in a given year $(2+t)$ is a function of the number of immigrants two years in the past (t), but is also affected by the population of lice on the farm at the time in the previous year when wild host juveniles were migrating past the farm. Measured in lice generations, this time is $(t \cdot (\frac{1\text{year}}{T_g}) + \Delta)$, where the conversion from units of years to units of lice generations is through the generation time T_g of lice. Although this is a modified version of the Ricker (1954) equation, the dynamical variable is *parasites* and not fish. This reflects our assumption that the number of immigrant lice is proportional to the number of wild salmon returning to the region of the farm. These units are connected to parasite generation i by the relation $\frac{1\text{year}}{T_g} \cdot t = i$. Parameter b reflects density-dependence in salmon reproduction, and r is the growth rate of salmon. Note that b has units $[\text{parasites}]^{-1}$, while r is governed purely by host productivity. This equation also assumes that infections on juveniles are proportional (k) to the number of lice in the farm.

3.3 Methods

We analyzed the interaction of immigration and treatment using equation (3.4) for time-to-resistance, as well as the underlying genetic (3.3) and demographic (3.5) dynamics of the parasite. These dynamical equations also served as the basis for numerical simulations of time-to-resistance, which we used to examine the effect of treatment strategy. We also used numerical simulations to examine the effect of farm-wild interactions on time-to-resistance under varying treatment strategy. These simulations employed genetic (3.3) and demographic (3.5) dynamics of the parasite coupled with wild host populations through (3.6). We define time-to-resistance in simulations as the generation in which resident gene frequency reaches emergence threshold p_e, divided by the number of generations per year. Simulation of time-to-resistance was based on the following recipe: (1) set the farm parasite population to an initial abundance n_0 and frequency of resistance p_0 (assumed to be low), (2) allow the resident population to vary from initial values according to genetic (3.3) and demographic (3.5) dynamics, (3) when p_e is reached, stop the simulation.

3.3.1 Interaction of treatment strategies and immigration

To assess how different treatment strategies interact with a constant yearly immigration to affect time-to-resistance, we used numerical simulations of two basic strategies: treatment based on timing relative to immigration, and treatment based on a threshold. The strategy of treatment based on timing relative to immigration that we considered is to treat only once per year at a predetermined time (generation). To simulate this strategy, we fixed a within-year time of immigration, a number of immigrants per year $\bar{n}$, and a timing of treatment relative to immigration. Then, for each possible timing of treatment, we simulated time-to-resistance under genetic (3.3) and demographic (3.5) dynamics as described above. The strategy of threshold-based treatment that we considered is to treat when the mean abundance of parasites per farm host, n_i/N for N farm hosts, exceeds a threshold. To simulate treatment based on thresholds, we fixed a number of fish in a farm N and a treatment threshold. Then, we then simulated time-to-resistance under genetic (3.3) and demographic (3.5) dynamics as described above, treating whenever n_i/N exceeded the threshold. We also considered a combined strategy, with treatment *both* at a time relative to immigration and based on a threshold.

3.3.2 Changes when farm infections cause declines in wild abundance

To understand how the influence of immigration changes if we relaxed the constant immigration assumption, we also employed numerical simulations of time-to-resistance. We focused on the possible negative effect of farm infections on wild host abundance, modelling the year-to-year changes in the number of immigrants to the farm using (3.6). This model, in addition to the genetic (3.3) and demographic (3.3) models for the parasite, forms a system of equations that describe farm demographics and genetics, and immigrant input. Model (3.6) assumes that impact on wild hosts occur only during one generation per year during outmigration when wild juvenile hosts migrate past and are sympatric with farms. In the model, the generation of outmigration is defined relative to the time of wild host immigration by parameter Δ. Accordingly, we examined several strategies:

(1) treatment based on a threshold but only during this period of sympatry, (2) treatment based on a threshold year-round, (3) treatment based on timing of immigration only, and (4) treatment that combines treating based on a threshold during out-migration *and* treating based on immigration timing. The strategies of treating only during out-migration (1) or timed treatment (3) treat a maximum of one generation per year. With threshold-based treatment all year (2), treatment is possible in every generation. Under the combined strategy of timing and threshold-based treatment during out-migration, a maximum of two generations per year are treated. We simulated time-to-resistance under the threshold-based strategies for a variety of farm population densities, i.e., number of fish stocked, N.

3.3.3 Parameter values

For numerical simulations we fixed parameter values, listed in Table 3.2. Parameters for genetics of resistance, i.e., β, s, p_0, p_e, were chosen to agree with those used in general theoretical studies of chemical resistance (Comins, 1977*b*; May & Dobson, 1986). Lice life-history parameters, i.e., λ, T_g, were based on louse biology (Johnson & Albright, 1991). The parameter for wild salmon growth r, was drawn from a study of pink salmon (Myers *et al.*, 1999). Other parameters were chosen heuristically, i.e., b was set so that the equilibrium of (3.6) was near n_0, and $a \cdot k$ was set very small to reflect a low probability of transmission for an individual larva.

3.4 Results

According to equation (3.4), the effect of immigration on time-to-resistance is strong and positive. Mathematically, the effect is governed by term $(1 + \frac{\bar{n}}{n_i})$: the larger this term, the longer the time-to-resistance T_R. At the zero-immigration limit (3.4) corresponds to (3.2). When the ratio of immigrants to residents $\frac{\bar{n}}{n_i}$ is increased from zero, time-to-resistance increases as well, strongly at first, then less strongly and finally very strongly, diverging to infinity when the denominator of (3.4) approaches zero. Maximizing the ratio of immigrant to resident populations at immigration, $\frac{\bar{n}}{n_i}$, thus maximizes time-to-resistance.

Table 3.2: Summary of parameters employed in simulations

Parameter	Value
λ	1.5
β	0.6
s	0.99
$\left(\frac{1}{1-g_i \cdot s}\right)^{\beta}$	15.85 (treated), 1 (untreated)
p_0	1×10^{-3}
p_e	0.5
n_0	1×10^5 [lice]
$\bar{n}$	$0.3 \times n_0$ [lice]
$\bar{p}$	0
T_g	$\frac{1}{6}$ [year]
Δ	2 [generations]
e^r	3.32, i.e., $(r = 1.2)$ [fish][two years]$^{-1}$
b	$\frac{1}{n_0}$ [immigrant lice]$^{-1}$
$a \cdot k$	1×10^{-7} [farm lice]$^{-1}$

3.4.1 Interaction of treatment strategies and immigration

With immigration however, timing of treatment relative to immigration is important. Strategies that treat based on timing of immigrations take advantage of the potentially strong increase in time-to-resistance with immigration, while strategies where treatment is based only on a threshold do not.

Altering timing of treatment within a year corresponds to changing the generation in which the heterozygote advantage term, $\left(\frac{1}{1-g_i \cdot s}\right)^{\beta}$, is greater than unity (in all untreated generations the magnitude of the heterozygote advantage is unity). Without immigration, in model (3.2), the term labelled "Treatment" governs time-to-resistance. Changing treatment timing within the year does not change the value of any of the parameters within (3.2). Thus, without immigration, treatment timing within the year does not affect time-to-resistance.

Timing

Strictly, our equation (3.4) for time-to-resistance applies only when $\frac{\bar{n}}{n_i}$ is the same each year. Even if we assume constant immigration, however,

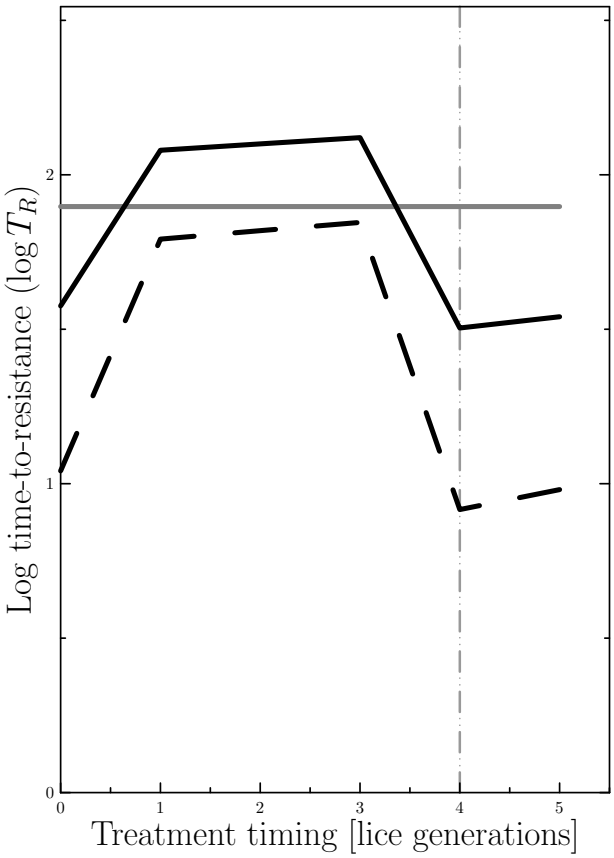

Figure 3.2: Results of simulations of T_R on log scale with different timing of treatment (x-coordinate) relative to immigration. The vertical line represents the timing of immigration within each year. The black lines represent timed treatment, for full non-linear (solid) and approximate (dashed) genetic dynamics. The gray line represents treatment that is *not* timed, but based on a threshold of 3.5 lice per fish. The maximum in time-to-resistance occurs with treatment during the generation just prior to immigration.

the farm population changes dynamically as given by equations (3.3) and (3.5). Numerical results indicate that even when the resident population fluctuates in abundance, time-to-resistance increases with the ratio of *initial* farm population to immigrants $\frac{\bar{n}}{n_0}$.

Analysis of the demographic equation (3.5) indicates that treating immediately before immigration each year maximizes time-to-resistance, if there is a periodic, yearly immigration event and one treatment per year. The strategy tunes the relative timing of immigration and treatment to minimize the number of lice in the resident population at immigration. This is possible because the approximate demographic model for residents describes log-linear changes in population of lice. Because the number of immigrants is the same each year, minimizing the number of residents at immigration maximizes the ratio of immigrants to residents $\frac{\bar{n}}{n_i}$, and in turn maximizes time-to-resistance T_R. Mathematically, altering timing corresponds to altering the ordering of the heterozygote advantage terms, all of which are unity except the during the one treatment event. The first term in the denominator of equation (3.4), is the product of these terms. The magnitude of this term is $\left(\frac{1}{1-g_i \cdot s}\right)^{\beta}$ regardless of the ordering of the product. This implies the timing of treatment affects time-to-resistance only through the immigrant-to-resident ratio $\frac{\bar{n}}{n_i}$.

Numerical results support this simple analysis, indicating that, when treatment strength s is the same each year, treating immediately before immigration yields the longest (or equally longest) time-to-resistance. Figure 3.2 illustrates time-to-resistance T_R on log scale versus immigration timing of one treatment relative to an immigration event indicated by the vertical dashed line. The maximum in time-to-resistance occurs when treatment is the generation just prior to immigration. Simulations of the full nonlinear model for change in gene frequency (solid lines) show that under these dynamics, relative timing of treatment and immigration has a similar qualitative effect. Note however, that time-to-resistance is systematically shorter under the approximate dynamics, indicating that the approximation underestimates the benefits of timing. Under both approximate and full dynamics, the effect of varying within-year timing of one treatment timed relative to immigration is up to one order of magnitude. Threshold-based treatment strategies are insensitive to within-year timing of immigration.

3.4.2 Farm-origin infections and declines in wild abundance

When parasites on farms affect wild abundance according to model (3.6), timing of treatment relative to immigration to minimize the farm population at immigration can still extend time-to-resistance. The largest potential increase in time-to-resistance, however is given by a treatment strategy that combines treatment timed relative to immigration with a threshold-based treatment during out-migration to minimize spill-over infections of wild juveniles. Figure 3.3 shows results of simulations using equations (3.3) and (3.5) for parasite genetic and demographic dynamics and model (3.6) for the effect of farm parasites on the abundance of wild hosts. When used alone, the strategy of timing treatment relative to immigration (dashed lines) results in relatively modest gains in time-to-resistance, with the best gains in time-to-resistance occurring with treatment is immediately prior to immigration. Threshold based treatment used alone (dotted lines) is insensitive to the timing of immigration. The best gains occur with a combined strategy that times treatment the generation prior to immigration and also treats during out-migration (solid lines). The effect of changing treatment timing on time-to-resistance under this strategy is shown in Figure 3.3.

The increase in time-to-resistance under the best strategy, however, is sensitive to the number of fish stocked in the farm, decreasing as the number of fish stocked in the farm N increases. As the number of fish in the farm increases relative to the average abundance of lice immigrating to the farm (Figure 3.3 A-C), the gains in time-to-resistance under optimally-timed treatment disappear and the effect of changing treatment timing becomes negligible. Note that in Figure 3.3C the lowest solid curve is qualitatively the same as without out-migration treatment. The range of fish stocking densities N over which gains are seen depends on the treatment threshold used during out-migration. When this threshold is relatively lower (darker lines) gains are seen at relatively higher stocking densities, i.e., the solid black line still reaches a peak in Figure 3.3C. In contrast, a relatively higher threshold (lighter lines) means gains in time-to-resistance are seen only at lower stocking densities.

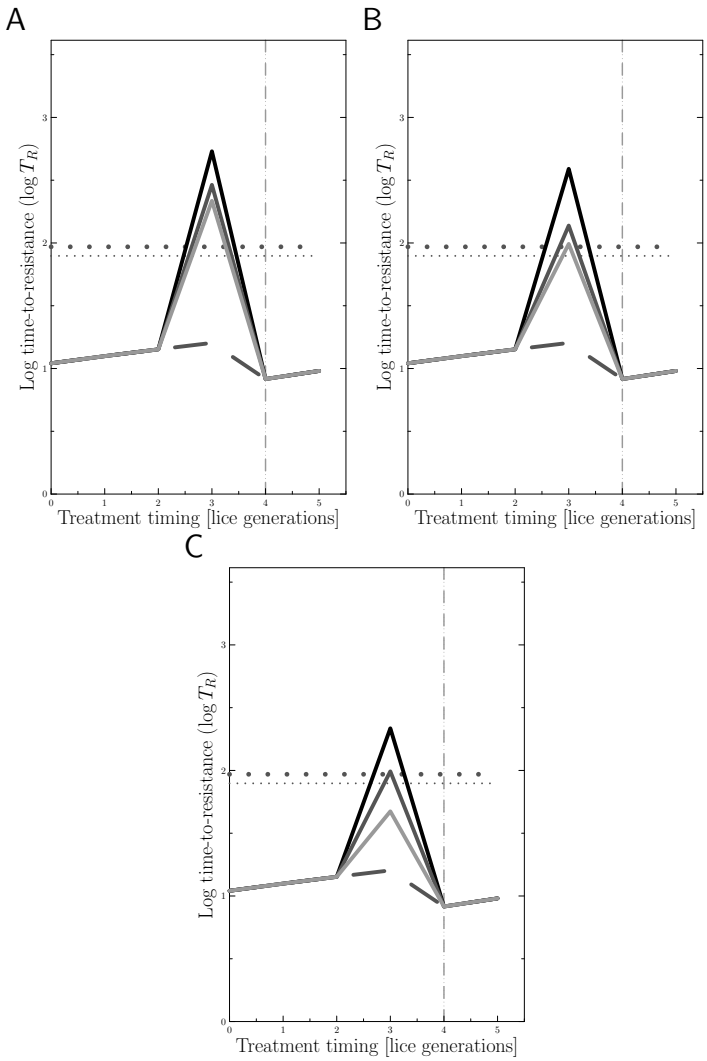

Figure 3.3: Effect of treatment timing relative to immigration on log time-to-resistance when farms affect wild abundance according to model (3.6). The x axis shows the timing of treatment relative to the immigration event (vertical line). Several treatment strategies are shown, including (1) threshold-based during out-migration only (large dotted), (2) threshold-based year-round (small dotted) , (3) timed only (dashed), and (4) timed *and* threshold-based treatment during out-migration only (solid lines). For threshold-only strategies (1) and (2), the threshold is 2.5. For the mixed strategy (4), out-migration is fixed at time 4 louse generations, and several thresholds are shown: 1.0 (black), 2.5 (dark gray), and 4.0 (light gray). The panels represent different values for the ratio of number of fish stocked N to the average number of immigrants $\bar{n}$ over the time-to-resistance: (A) 0.5, (B) 1.0, and (C) 2.0.

3.5 Discussion

Our results show that when spill-over and spill-back between farms and migratory wild salmon results in immigration of susceptible parasites to a farm, managers of farms can use this as an ecosystem service to extend the time-to-resistance on the farm.

These results lead to a strategy for maximizing time-to-resistance that has several key aspects:

- treatment must be timed based on wild migrations: treating the generation prior to immigration of parasites to the farm maximizes the effect of susceptible immigrants,
- maintaining viable populations of migratory salmon near farms is required, meaning
  - if parasites on farms affect wild salmon abundance a combination of treatment timed just prior to fall return and protection during out-migration provides the best benefit in terms of extending time-to-resistance,
  - a combination of decreased intensity of production and threshold-based treatment can provide protection during out-migration,
  - there is a trade-off where increases in the intensity of production on farms make delays in time-to-resistance harder to achieve.

3.5.1 Treatment timing relative to immigration

The importance of timing in mediating the ability of immigration to delay resistance has been recognized since theoretical work on multi-year treatment strategies by Mangel & Plant (1983). That study was inspired by cotton-spider mites (Aracina: Tetranychidae), where seasonal infestations receive continuous immigration from a "pool." In that system, treating earlier in the season delays resistance by permitting a longer period of interbreeding with susceptible immigrants following treatment (Plant *et al.*, 1985). Here, we found that treating the generation prior to immigration delays resistance. This result was based on analysis of the demographic equation (3.5) and the formula (3.4) that we derived for time-to-resistance with immigration. Our result is analogous to that of (Plant *et al.*, 1985) for our system, which

involves a single, discrete immigration event per year. Note that this result contrasts with the situation without immigration, i.e., the formula (3.2) of Comins (1977*b*), where altering treatment timing within the year does not affect the time-to-resistance.

Operational and biological factors other than immigration also affect time-to-resistance. Time-to-resistance is long when heterozygote advantage is close to one during treatment, which corresponds to weak selection or near-recessive advantage. This agrees with the original results of Comins (1977*b*), discussed by May & Dobson (1986), because model (3.4) includes several terms that appear in the approximation derived by Comins (1977*b*): the ratio of emergence threshold to initial resistance frequency p_e/p_0 (in the numerator) and the heterozygote advantage (in the denominator). The magnitudes of these terms are fixed by the underlying biology and the number of treatments per year (May & Dobson, 1986). Note also that if treatment intensity affects dominance, then operational and biological factors interact (Denholm & Rowland, 1992).

The link between intensity of treatment and dominance is part of the "high-dose refuge" (HDR) strategy used in terrestrial agriculture (Alstad & Andow, 1995). The observation that managers could create refuges to facilitate such immigration, combined with the observation that recessive resistance traits emerge much more slowly, led to the development of the HDR strategy (Georghiou, 1977; Denholm & Rowland, 1992). This strategy, shown schematically in Figure 3.1A, combines a refuge with a treatment strength that is high enough to render resistance effectively recessive (Denholm & Rowland, 1992). HDR was developed based on population genetic models similar to those we employ (Comins, 1977*a*; Alstad & Andow, 1995; Tabashnik, 2008). The primary focus in developing HDR has been genetically-modified plants, e.g., Bt corn and cotton, which continually express toxins. Thus, *timing* has not often been considered as a component of HDR, with studies focusing on other factors like dose strength (Denholm & Rowland, 1992), and spatial configuration of refuges (Lenormand & Raymond, 1998; Vacher *et al.*, 2003). Timing is critically important in the situation we treat here, but otherwise there is some similarity to HDR. Because a recessive resistance trait is slow to emerge in our situation as well, if treatment strength can be used to influence dominance then the strategy described in this paper will likely be more effective.

Compared with treatment based on timing relative to immigration, strategies that use thresholds to determine treatment provide less benefit from immigration, in terms of extending time to resistance. For threshold-based treatment, analytically determining the magnitude of the impact of host migration on time-to-resistance is complicated because immigration of wild-origin lice has two potentially-opposite effects: to increase time-to-resistance T_R by introducing susceptible alleles into the parasite population and to decrease T_R by increasing the number of treatments. Combined strategies are likely to be required in practice, as some upper threshold is needed to prevent economic losses to parasites (Costello, 2009*a*). Combining thresholds and timing relative to immigration appears to preserve much of the benefit of timing-based treatment, which is encouraging.

3.5.2 Maintaining viable populations of salmon near farms

Simulations based on model (3.6) suggest that the benefits in terms of decreased time-to-resistance provided by wild host migrations decrease as the number of fish stocked in the farm, i.e., the intensity of production, increases. When production is high, there are very many fish in farms near where out-migration occurs. Threshold-based treatment means the absolute number of parasites in the region scales with the number of fish in the farm. Because of our assumptions on transmission, more parasites in a region means more effects on wild out-migrant juveniles. This echoes a finding of Frazer (2009), that stocking density influences the effectiveness of treatment in conserving wild populations. Our result, however, suggests that stocking density also influences ability of farms to use immigration from wild stocks in resistance management. These results suggest that a combination of decreased intensity of production and threshold-based treatment during out-migration *and* treatment timed just before fall return may provide the best benefit in terms of extending time-to-resistance.

Under the hypothesized link between farm parasites and wild abundances, farm managers do have some degree of control over the refuge effect provided by wild migrations. There are, however, critical differences between this situation and HDR in terrestrial systems due to lack of direct control over refuge habitat (wild fish) that is dynamic in space and time. In the case that

we study here, the susceptible immigrants brought by migrating salmon are the cause of the refuge effect. Because of salmon migrations, these susceptible immigrants may come from a larger population of immigrants geographically separated from the farm. Thus, wild host populations that migrate near farms do not simply provide "habitat" for parasites proportional to their area but form a link between a large panmictic population of parasites at the scale of the ocean basin and the coastal regions where farming occurs. As highlighted here, the effect of farm-origin infections on wild salmon abundance (Krkošek *et al.*, 2007) means that farms must manage infections to maintain the ecosystem service provided by migrating salmon.

Because wild host migrations mediate immigration of susceptible individuals they provide for a human demand, and are thus an ecosystem service (de Groot *et al.*, 2002). Though the term "ecosystem service" has often been applied to benefits related to pest control, particularly in agriculture, discussion has focused on biological control and provision of *hosts* that are resistant to pests (Pimentel *et al.*, 1997). In the marine context, discussion of ecosystem services has focused on resilience, food provision, and water quality (Holmlund & Hammer, 1999; Worm *et al.*, 2006). Similarly, discussion of ecosystem services provided by salmon populations has focused on salmon as a food resource, or source of enjoyment from recreational fishing or ecotourism (Pimentel *et al.*, 1997; Holmlund & Hammer, 1999). In our study, the migratory hosts provide a service by delaying resistance, which relies on spill-back of parasites from wild hosts to farms. So long as managers of the farm are able to minimize the effects of spill-over in reducing wild host abundance, this effect can be maintained. This points out a potential upside of spill-over and spill-back with migratory hosts. However, the potential for emerging disease threats to travel via the same routes and impact wild populations means that caution should be taken employing the type of "service" discussed here.

3.5.3 Assumptions and Implications

We assumed major-gene control of resistance. Though this is a very common assumption in studies of chemical and antibiotic resistance (REX Consortium, 2010). The genetics of resistance in sea lice are a topic of current research, and incorporating knowledge gained from these studies into future modelling

efforts is critical (Burridge *et al.*, 2010). In the meantime, theoretical investigations of the interactions studied here when resistance is governed by other genetic mechanisms, e.g. a quantitative trait, could be fruitful. Our analysis neglects the production cycle of the farm, which in practice will influence treatment timing (Heuch *et al.*, 2005). It would be beneficial to reconsider the strategies discussed here within a broader framework of optimization, for example along the lines of (Plant *et al.*, 1985). In this case, economic losses to parasites would also need to be considered.

We have not thoroughly investigated the sensitivity of our results to uncertainty in parameters used. For the parameters governing genetics of resistance our models and simulations behave similarly to the early studies of insecticide resistance (Comins, 1977*b*; Alstad & Andow, 1995). Strong treatment, i.e., higher s, and more-dominant resistance, i.e. higher β, result in fast emergence of resistance. Though uncertainty in these parameters may change the quantitative output of our model, it is unlikely to alter our qualitative conclusions. For the parameters involving salmon productivity, and the effects of lice on salmon, however, the effects of uncertainty are much less clear. Future studies should more thoroughly examine behaviour of the system derived here relative to these parameters. Both mathematical analysis and numerical simulations could be useful in assessing sensitivity.

The assumption of model (3.6) is that farm-origin parasites affect abundance of migratory wild hosts and thus the magnitude of immigration of parasites to the farm. The notion that wild salmon abundance is affected by sea-cage salmon aquaculture salmon is supported by many recent studies (Gargan *et al.*, 2003; Krkošek *et al.*, 2007; Ford & Myers, 2008). By using model (3.6) for effects of lice on host populations, we also make several assumptions about how parasites on farms affect wild hosts. First, we assume that the average number of lice on juveniles during out-migration is proportional to the number of lice on farms. This assumption is supported by the basic physics of lice transmission (Frazer, 2009), at least at low density. In Chapter 2 we showed that this assumption follows from an approximation to mass-action transmission that is most valid when the probability of transmission is low. Second, we assume that lice infections from farms have a negative impact on juvenile survival to adulthood of the form $\exp(-a \cdot \text{lice/juvenile})$. This assumption has been employed in the empirical studies demonstrating associations between salmon aquaculture

and wild salmon declines (Krkošek *et al.*, 2007; Ford & Myers, 2008). We use parameter values for pink salmon (*Oncorhynchus gorbuscha*) productivity. These salmon, along with chum salmon (*Oncorhynchus keta*), form the dominant biomass of migrations to farming regions in the Eastern Pacific.

Our assumption that lice from returning wild salmon are all homozygous susceptible is not critical; however, the frequency of resistance in the immigrants must be low relative to emerging resistance in farms for immigration to provide any break on evolution. Because of this, the results developed here apply primarily to the North Pacific. Low resistance frequency in immigrants is supported by ecology in Pacific where lice associated with returning wild adults are (i) a major factor governing lice-infection dynamics in Pacific farms (Saksida *et al.*, 2007; Krkošek, 2010), and (ii) from a population, mostly not selected for resistance, that is panmictic at the scale of the Eastern Pacific (Messmer *et al.*, 2010). Salmon farming, however, occurs in many regions, including the Atlantic and South Pacific, where the assumption of susceptible immigrants may not be justified because the number of farmed hosts rivals or exceeds the number of wild hosts (Costello, 2009*b*).

3.5.4 Future directions

To truly accommodate panmixis and migratory connections when the abundance of wild and farmed salmon is comparable, models should be posed at the scale of an ocean basin. This issue of scale is pervasive in ecology (Levin, 1992), and it is unsurprising that it arises here. For example, at the scale of a farming region gene flow can lead to spread of resistance genes among farms (Denholm *et al.*, 2002). The result of panmixis at the Atlantic basin scale, combined with the high intensity of farming in that basin, means spread of resistance may occur among farming regions at the basin scale as well. To accommodate a situation where the selected and non-selected habitat are of a similar size, the assumption of immigration from an infinite pool would need to be relaxed. Cues could be taken from Comins (1977*a*), who modelled resistance evolution with a regular migration between selected and unselected populations. This model would need to be modified to account for the feedback when farm-origin infections affect wild salmon. Plant *et al.* (1985) also considered migration to a treated area from a finite pool, with a

continuous-time model. This model assumed that the pool was depleted, i.e., all residents moved from the pool to the treated field, by the season's end, which may not be justified in the case of salmon and sea lice because of some salmonids inhabit the North Pacific year-round (Groot & Margolis, 1991).

Our study highlights the importance of including wild host ecology in analysis of pest population biology. Here, the migration of hosts, combined with parasite exchange and treatment, can delay evolution of resistance on farms. Although our results appeal to evolutionary and ecological intuition, it should be noted that our models are very simple, and "strategic" (Pielou, 1981). We aim only to give a *qualitative* idea of how immigration, wild host migration, and treatment decisions might interact. For management, "tactical" models will be required (Pielou, 1981). These models should assess the *quantitative* benefits of the strategy proposed here for management of resistance, conservation, and economic goals. Such models may need to incorporate details of parasite biology, e.g., stage-structure, farm operation, e.g., production cycle, and ecology of wild salmon, e.g., migration timing.

Appendix 3.A Population genetic model

We focus on the resistance frequency p_i and abundance n_i of parasites in the farm during the i-th generation. We denote the vector of fitnesses as $\mathbf{w} = (w_{RR}, w_{RS}, w_{SS})$. We assume selection due to treatment causes differential survivorship or viability. Therefore the fitnesses will depend on the environment of the parasites; as given by treatment ($g = 1$) or no treatment ($g = 0$), so that fitness is a function of treatment $\mathbf{w}(g)$. When treatment varies over time then g_i will be either zero or one and $\mathbf{w}_i = \mathbf{w}(g_i)$.

Census time matters for population genetic models (Crow & Kimura, 1970). Without fecundity selection, however average fitness at adult census and zygote census are equivalent. We assume adult census, constant environmental conditions, and no differential fecundity; i.e., that selection is on survivorship of chemical treatment. Under these assumptions, the average fitness $\bar{w}(p_i; \mathbf{w}_i)$ is given by the sum of the second row of Table 3.3.

Under random mating, the resistance frequency follows Fisher's fundamental theorem (Crow & Kimura, 1970): the change in the i-th generation is proportional to the product of the genetic variability under selection and

Table 3.3: Change in genotype frequencies during a generation assuming selection-reproduction order. The average fitness, $\bar{w}(p_i; \mathbf{w}_i)$, used in the third row is given by the sum of the second row.

Zygote	RR	RS	SS
Before selection	p_i^2	$2p_i(1-p_i)$	$(1-p_i)^2$
Fitness-weighted	$p_i^2 w_{RR}$	$2p_i(1-p_i)w_{RS}$	$(1-p_i)^2 w_{SS}$
After selection	$p_i^2 \frac{w_{RR}}{\bar{w}(p_i;\mathbf{w}_i)}$	$2p_i(1-p_i)\frac{w_{RS}}{\bar{w}(p_i;\mathbf{w}_i)}$	$(1-p_i)^2\frac{w_{SS}}{\bar{w}(p_i;\mathbf{w}_i)}$

the gradient of selection,

$$\Delta p_i = \frac{p_i(1-p_i)}{2\bar{w}(p_i)} \frac{\partial \bar{w}(p_i; \mathbf{w}_i)}{\partial p_i}.$$

Explicitly, the dynamics of p_i follow the classical population genetics equations of Fisher, Haldane, and Wright (see e.g., Crow & Kimura, 1970):

$$p_{i+1} = \frac{(w_{RR}p_i + (1-p_i)w_{RS})p_i}{p_i^2 w_{RR} + 2p_i(1-p_i)w_{RS} + (1-p_i)^2 w_{SS}} =: F(p_i; \mathbf{w}_i). \qquad (3.A.1)$$

Assuming $N = \frac{1}{T_g}$ generations occur per year and that each generation can have differing relative fitness due to the variable environment arising from treatment, these equations can be extended to cover a year. We denote the change in frequency during the ith generation as $F^i(p_i) := F(p_i, \mathbf{w}_i)$, where the effect of treatment g_i on fitness $\mathbf{w}$ is included as $\mathbf{w}_i = \mathbf{w}(g_i)$. The change over the N generations during a year is $p_N = F^{N-1} \circ F^{N-2} \circ \cdots \circ F^1 \circ F(p_0)$. More compactly,

$$p_N = \left(\bigcirc_{i=0}^{N-1} F(\cdot; \mathbf{w}_i)\right)(p_0), \qquad (3.A.2)$$

where (3.A.2) specifies functional composition using F defined in (3.A.1) and the generation-indexed genotypic fitness $\mathbf{w}_i$. The right-hand side of (3.A.2) is a repeated composition of the nonlinear function $F(p_i; \mathbf{w}_i)$.

Appendix 3.B Approximate population genetics without immigration

In this section we rederive the approximation of Comins (equation (6), 1977*b*) for time-to-resistance using our notation and assumptions. Though analysis of (3.A.2) for time-to-resistance is impractical or impossible, a series

approximation for small p yields insight (Comins, 1977*b*; May & Dobson, 1986). Following these authors we begin with (3.A.1), which is analogous to equation (2) of Comins (1977*b*) or equation (1) of May & Dobson (1986). The small p approximation to (3.A.1) states that resistance frequency p in the next generation is linearly proportional to prior-generation frequency,

$$p_{i+1} = F(0;\mathbf{w}) + \frac{\partial}{\partial p_i}F(0;\mathbf{w})p_i + O(p_i^2) = p_i\frac{w_{RS}}{w_{SS}} + O(p_i^2), \qquad (3.B.1)$$

where we suppress the dependence of w on generation. This equation (3) of Comins (1977*b*) or equation (2) of May & Dobson (1986) expressed in our notation. Thus, the change in frequency is proportional to the ratio of the genotypic fitnesses of the heterozygote and the susceptible homozygote. Expressed in our parametrization this ratio is $\frac{w_{RS}}{w_{SS}} = \left(\frac{1}{1-g_i\cdot s}\right)^{\beta}$, see Table 3.1 and main text for details and discussion of this parameterization. The heterozygote advantage exceeds unity in treated generations and *is* unity in untreated generations (because we assume resistance has no cost). Figure 3.4 shows cobwebbing diagrams of the full nonlinear map. The gray line illustrates the linear approximation based on heterozygote advantage. The cobwebbing indicates that with treatment resistance becomes fixed ($p = 1$ eventually). Note also that as p grows the linear approximation diverges from the nonlinear map.

Over a year, N generations, the change in the frequency of the resistance allele is given to first order in p_i by the product of the heterozygote advantage terms for each generation,

$$p_N = p_0\prod_{i=0}^{N-1}\left(\frac{1}{1-g_i\cdot s}\right)^{\beta}. \qquad (3.B.2)$$

This is equation (3) of May & Dobson (1986) expressed in our notation.

Because we assume one treatment per year and no cost to resistance (recall without treatment $g = 0$), over one year the product in equation (3.B.2) is equal to $\left(\frac{1}{1-s}\right)^{\beta}$. Then, over the emergence threshold p_e is related to the initial resistance frequency p_0 as

$$p_e = p_0\left(\frac{1}{1-s}\right)^{\beta\frac{T_R}{T_g}},$$

where T_R is time-to-resistance in years and T_g is the generation time. Taking logarithms and rearranging yields

$$T_R = \underbrace{T_g \frac{\log \frac{p_e}{p_0}}{\beta}}_{\text{Biological}} \cdot \underbrace{\frac{1}{\log \frac{1}{1-s}}}_{\text{Treatment}}, \tag{3.B.3}$$

which is analogous to equation (6) of Comins (1977*b*) or equation (4) of May & Dobson (1986).

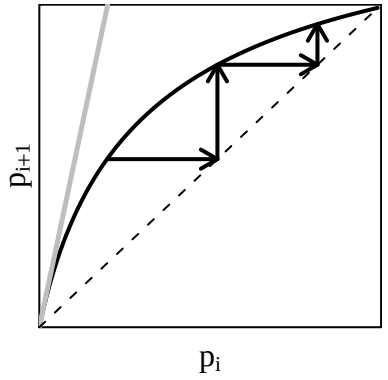

Figure 3.4: Dynamics of gene frequencies $p_{i+1} = \frac{w_{rs}}{w_{ss}} p_i$ with treatment where $w_{RS} > w_{SS}$

Appendix 3.C Genetic and demographic model with immigration

To consider the effect of immigration mediated by wild host migration, we focus on the dynamics of the resident population of parasites on the farm only, considering immigration from a source population, e.g., the lice population at the scale of the Eastern Pacific. This neglects the bidirectional nature of the coupling between farm and source through host migration, but reflects the concept of a very large source population. As size of the source population tends to infinity, the genetics and demographics of the source population become independent of any coupling to the finite population of residents. We assume only one immigration event each year, and further that this number is the same each year. We use $\bar{n}$ and $\bar{p}$ to denote the abundance and resistance frequency of the immigrant population.

Accounting for changes in gene frequency due to both immigration

and population processes on the farm requires tracking both genetics and demographics in the farm. Both the *number* of migrants and the resistance frequency in the source population determine the effect on the resident population:

$$p_{i+1} = F(\hat{p}_i; \mathbf{w}_i)\Big|_{\hat{p}_i=\frac{p_i\cdot n_i+m_i\cdot\bar{n}\cdot\bar{p}}{n_i+m_i\cdot\bar{n}}} \approx \left(\frac{1}{1-g_i\cdot s}\right)^{\beta} \frac{p_i\cdot n_i + m_i\cdot\bar{n}\cdot\bar{p}}{n_i+m_i\cdot\bar{n}}. \quad (3.C.1)$$

Equation (3.C.1) is an extended version of (3.A.1), and reuses the function F defined there. The input to the function F, however, is $\hat{p}_i$, the population weighted-average of the resident frequency p and the frequency in immigrants $\bar{p}$. Because we assume that if immigration occurs within a generation, then immigrants are included in the population that undergoes selection and then reproduces, the gene frequency dynamics with immigration operate on an abundance-weighted average *prior to reproduction* of the resistance frequency p_i in the resident population and $\bar{p}$ the resistance frequency in the immigrants. Equation (3.C.1) uses the approximation (3.B.1) of F developed in Appendix 3.B.

To obtain simple analytical results that capture the qualitative effect of immigration from a susceptible pool, we treat the case where $\bar{p} = 0$. Then, the abundance-weighted average is taken on the resistance frequency p_i in the resident population with zero, the assumed resistance frequency in the immigrants. Setting $\bar{p} = 0$ and rearranging, we see that the effect of immigration enters through the ratio between residents and immigrants,

$$p_{i+1} = \frac{\left(\frac{1}{1-g_i\cdot s}\right)^{\beta}}{\frac{m_i\cdot\bar{n}}{n_i}+1} p_i. \quad (3.C.2)$$

In contrast to the situation without immigration, now the change in gene frequency is coupled to demographic changes in population size.

If we denote the gene frequency dynamics of equation (3.C.2) as $p_{i+1} := G_i(p_i)$, then a series of functional compositions gives the change in gene frequency with immigration over a year,

$$p_{i+N} = G_N \circ G_{N-1} \circ G_{N-2} \cdots \circ G_1(p_i).$$

Thus to first order in p_i, the change over the N generations in a year is

given by

$$p_N = p_0 \prod_{i=0}^{N-1} \left(\frac{1}{1 - g_i \cdot s} \right)^{\beta} \prod_{i=0}^{N-1} \frac{1}{\frac{m_i \cdot \bar{n}}{n_i} + 1}. \tag{3.C.3}$$

Because we assume one treatment per year, no cost to resistance, and one immigration per year, we can drop the products in equation (3.C.3). Recall that $\left(\frac{1}{1-g_i \cdot s}\right)^{\beta}$ is the heterozygote advantage, which is greater than one with treatment and equal to unity without treatment. Also note that in generations without immigration, $m_i = 0$ and the term $\frac{1}{\frac{m_i \cdot \bar{n}}{n_i}+1}$ is unity. Then, the change over a year is

$$p_N = p_0 \left(\frac{1}{1 - s} \right)^{\beta} \frac{1}{\frac{\bar{n}}{n_i} + 1}. \tag{3.C.4}$$

Note however, that $\frac{\bar{n}}{n_i}$ depends on demographics, which in turn depend on the frequency of resistance when treatment occurs. Because of this, (3.C.4) does not give a closed-form map from one year to the next and thus cannot be used to derive a formula for time-to-resistance in *general*. If, however, the ratio of immigrants to residents ($\bar{n}/n$), the strength of treatment (s), and dominance of resistance (β) are the same every year, then (3.C.4) can be used to relate the initial frequency of resistance p_0 and the emergence threshold p_e,

$$p_e = p_0 \left(\left(\frac{1}{1 - s} \right)^{\beta} \frac{1}{\frac{\bar{n}}{n_i} + 1} \right)^{\frac{T_R}{T_g}}, \tag{3.C.5}$$

where T_R is time-to-resistance in years and T_g is the generation time. Taking logarithms and rearranging yields

$$T_R = \underbrace{\frac{T_g \log \frac{p_e}{p_0}}{\beta}}_{\text{Biological}} \cdot \frac{1}{\underbrace{\log\left(\frac{1}{1-s}\right)}_{\text{Treatment}} - \underbrace{\log\left(\frac{\bar{n}}{n_i} + 1\right)^{\frac{1}{\beta}}}_{\text{Immigration}}}. \tag{3.C.6}$$

3.C.1 Demographic model

We use a standard model from classical population genetics that states that the population grows geometrically at a rate determined by the average fitness (Crow & Kimura, 1970). The average fitness depends on whether treatment occurs, and on the frequency of allele R and the values of relative

genotypic fitness, i.e., the vector $\mathbf{w}$, so $\bar{w}(i) = \bar{w}(p_i; \mathbf{w}_i)$. The equation for geometric growth is, $n_{i+1} = \lambda \bar{w}(p_i; \mathbf{w}_i) n_i$. Suppressing for now dependence on generation i, average fitness is second order in p, explicitly $\bar{w} = w_{SS} + p(2w_{RS} - 2w_{SS}) + p^2(w_{RR} + w_{SS} - 2w_{RS})$. We also apply a first-order approximation, valid for small resistance frequency p, to the demographic equation and rewrite average first order, $\bar{w}(p_i; \mathbf{w}_i) \approx w_{SS} + 2p(w_{RS} - w_{SS})$. Rewriting with our parametrization of genotypic fitness, $\bar{w}(p_i; \mathbf{w}_i) \approx (1 - g_i \cdot s)\left(1 + 2p_i\left(\left(\frac{1}{1-g_i \cdot s}\right)^{\beta} - 1\right)\right)$. Then, using indicator m_i for immigration, the demographic model is

$$n_{i+1} = \lambda(1-s)\left(1 + 2p_i\left(\left(\frac{1}{1-s}\right)^{\beta} - 1\right)\right)(n_i + m_i \cdot \bar{n}). \qquad (3.C.7)$$

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Chapter 4

Conclusion & General Discussion

In this thesis, we developed simple models to address the interactions of host migration and disease exchange with farms in a system of migratory wild salmon (*Oncorhynchus gorbuscha*), parasitic sea lice (*Lepeophtheirus salmonis*), and aquaculture. Our models implicitly include the effect of wild salmon migrations on exchange of parasites between wild and farm salmon. In Chapter 2, we explored implications of parasite exchange for population ecology of wild pink salmon. We developed a model that couples population dynamics of pink salmon with a simple model for transmission of parasitic sea lice. We were able to make predictions for the effect of parasite exchange on dynamics by focusing on "line dominance," consistent difference in abundance between two lineages (Groot & Margolis, 1991). In Chapter 3, we explored implications of parasite exchange for population genetics of chemical resistance in parasitic sea lice on farms. We used a standard population genetic model for selection of resistance on farms. The effect of parasite exchange entered this model through our assumption that wild salmon migrations mediate yearly immigration of susceptible sea lice to lice populations on farms. We included the potential effect of farms on salmon abundance by using the model of Chapter 2.

Our work in Chapter 2 shows that, in addition to declines in equilibrium population abundance, exchange of parasites with farms can alter qualitative patterns in host population dynamics, either increasing or decreasing line dominance. The direction of the change in line dominance depends on the relationship between infections on farms and infections of wild salmon. When

infections on farms are constant regardless of wild infections, farms provide a constant input of infection to the wild hosts that increases dominance. On the other hand, when infections on farms are proportional to wild infections, farms provide an intra-lineage transmission route that decreases dominance.

The results of Chapter 3 show that with constant yearly migrations, treatments that minimize the parasite population on farms when migration occurs maximizes expected time-to-resistance. If parasites on farms affect wild populations, a combination of protection during out-migration and treatment timed just before fall return may provide the best benefit in terms of extending time-to-resistance.

4.1 Key conclusions

The main outcome of Chapter 2 is the prediction that line dominance in pink salmon can be affected by parasite exchange with salmon farms. The direction of the effect on line dominance is tied to the way salmon farms respond to infections originating from wild hosts. Thus, this prediction could be tested hierarchically, first by examining the relationship between infections on farms and those of wild adult salmon returning in the fall, then by examining patterns of line dominance in pink salmon populations in farming regions.

The main outcome of Chapter 3 is the idea that if wild salmon immigrations bring susceptible parasites to farms, strategies for chemical use against parasites on farms can be developed to use these immigrations to delay evolution of chemical resistance. The potential effect of farm infections on wild salmon abundance lends a subtlety to this idea, where protection of juvenile wild salmon from intense infections during out-migration is required to obtain the maximum benefit in terms of extending time-to-resistance.

4.2 Salmon population dynamics

In Chapter 2, we used line dominance relationships that naturally occur in pink salmon to study the effects of farms on dynamics. In our model, dominance occurs due to negative density-dependent interactions, both general and parasite-mediated, between lineages. Ricker (1962) explored a number of possible mechanisms for line dominance in pink salmon. These

include mechanisms that operate in rearing habitat, such as fouling of the river by large runs of salmon, and mechanisms that operate in the marine habitat, such as direct suppression or food competition during sympatry. Our model includes both types of mechanisms (parameters c_i), and also includes disease-mediated interactions (parameter η), which Ricker did not explicitly consider, but which have similar dynamical effects. Through either general or parasite-mediated means, adults of an abundant lineage cause proportionally large negative effects on a relatively less abundant lineage. These negative effects do not affect the offspring of the abundant line and this results in line dominance. Introducing farms changes this scenario by either increasing line dominance if farms provide a constant input of parasites, or decreasing line dominance if farms provide a parasite transmission route within a lineage. The scenario of constant input of parasites increases dominance because it has a proportionally larger effect on the less-abundant line. This is a depensatory effect and is thus similar to a number of additional hypotheses proposed by Ricker (1962) that relates dominance to other depensatory mechanisms, including fishing and predation.

4.3 Understanding farm-wild interactions

The results of Chapter 2 extend our understanding of farm-wild interactions in salmon and sea lice to effects on the patterns in fluctuations of wild salmon populations. This is in contrast to previous studies, which focused on the effects on equilibrium population abundance or productivity (Frazer, 2009; Krkošek *et al.*, 2007*a*,*b*). Though our approach involves simple, discrete-time maps and a spatially-implicit treatment of the effects of migration, we were able to disentangle some effects of a complicated interaction that involves space, migration, and disease exchange. This simple approach contrasts with the often-complex tools used to understand the effects of wildlife migrations and disease, which include detailed simulation studies (e.g. Morgan *et al.*, 2005) and highly-parametrized statistical models (e.g. Kilpatrick *et al.*, 2006). There is probably opportunity to use a spatially-implicit treatments of the effects of migration along the lines of Chapter 2 within the context of standard epidemiological models, e.g. an SIR-type (Anderson & May, 1992). This would shed light on the generality of the effects seen here.

The results of Chapter 2 also provide a prediction that links the response

of farms to infections originating from wild hosts to effects on pink salmon line dominance. Though this prediction might be testable, doing so requires collaboration between salmon farming operations and researchers of juvenile salmon ecology. The link between farm status and wild infections has been controversial in Canada (Costello, 2009; Krkošek, 2010). In part because of this controversy, independent scientists have had little access to data on farm infection status in Canada (Krkošek, 2010). In contrast, workers in Europe have access to more detailed farm data, where management of infections on farms and impacts on wild fishes has been coordinated for several years (Heuch *et al.*, 2005; Krkošek, 2010). Fortunately, collaborations between industry, government, and independent researchers have increased in Canada, due in part to activities of the Pacific Salmon Forum (PSF; www.pacificsalmonforum.ca). Thus there is hope for future testing of our model's qualitative predictions.

4.4 Management of resistance & ecosystem services

If wild salmon migrations bring susceptible parasites to farms, they provide a service that can be used to manage chemical resistance on the farm. This is perhaps a novel example of an ecosystem service (de Groot *et al.*, 2002) that relates conservation of wild animals to management of chemical resistance in pests. In our study, the migratory salmon provide a service by bringing susceptible parasites from wild hosts to farms, possibly permitting managers to delay resistance. Our results suggest that for farms to take advantage of this service, managers should time chemical treatment based on wild salmon migrations. Further farm managers must minimize the effects of spill-over in reducing wild host abundance to maintain the populations of salmon that migrate near farms. Though this theory highlights a potential benefit that arises for farm operations when migratory wild hosts and farms exchange parasites, the exchange of other, more pathogenic, diseases is still a concern for conservation and farm operations.

4.5 Future work

In Chapter 2, we were able to study interaction of wild host migration, farm hosts, and parasites without an explicit spatial model by substituting temporal heterogeneity in transmission for explicit tracking of the wild host movements that cause this heterogeneity. Though this type of time-for-space substitution may prove fruitful in other contexts, there are also reasons to develop models that include details of space, time, stochasticity, or abiotic forcing. Spatial models could account for multiple modes of parasite transmission, and potentially incorporate physical differences in processes of transmission from wild-to-wild versus farm-to-wild. Continuous-time models might incorporate various exogenous forcing functions based on different management scenarios, rather than just constant forcing as examined here, or alternatively various dynamical functions defining management *response* to wild infection. Stochastic models could incorporate environmental noise in host population dynamics, and in transmission. For lice in particular, abiotic factors including oceanography, salinity, and temperature are important in governing distribution and abundance (Krkošek, 2010). More detailed models that account for some of these factors, but still capture important processes of host population dynamics, could be useful for management.

Implications of disease exchange with stationary farms for population dynamics could also be explored for other salmonids, including chum (*O. keta*) and sockeye (*O. nerka*). These species have longer life cycles than pink salmon (3-5 years for chum and 1-4 years for sockeye versus 2 years for pink; Groot & Margolis, 1991). Their population dynamics also can involve cycles of order higher than two (e.g. 4 year patterns of dominance for Fraser sockeye; Groot & Margolis, 1991). Because of these facts, models of chum and sockeye dynamics are more complex, and mathematical analysis more difficult. Despite these facts, the type of analysis we applied here (bifurcations theory) for two-cycles in pink salmon can in principle be used to delineate and understand higher-order cycles in more complex models.

In Chapter 3, we show that, in theory, wild salmon can provide an ecosystem service that permits managers of farms to delay evolution of chemical resistance in lice. We derived a model that links population genetics and demographics of parasites on farms, and immigration of susceptible parasites that is mediated by wild salmon. Some of our results derive

from numerical simulations of this system; however, analytical treatment of this system using the tools of dynamical systems might yield deeper understanding. Such analysis would be a good next step to understand the implications of parasite exchange for resistance.

To derive the models of Chapter 3, we also assumed that the immigrants to farms are purely susceptible. This may be an accurate approximation for the Pacific, where populations are connected at the scale of the basin by salmon migrations and most hosts are wild. In the Atlantic, however, the high intensity of farming means wild host migrations may spread resistance among farming regions. To reconcile these possibilities, models must include both wild host migration and the relative sizes of selected and non-selected hosts, i.e. farm and wild hosts. Such models could be posed in discrete time, as we did in Chapter 3, or in continuous time. For discrete time, a good starting point is the model of Comins (1977), which accounted for migration between finitely-sized habitats. A continuous time approach might follow Plant *et al.* (1985), who treated influx of parasites within a season and linked seasons using discrete-time mappings. These models would need to be modified to account for the fact that wild salmon migrations provide links between selected and non-selected regions, and that farm-origin infections may affect wild salmon abundance.

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