

Host Phenology Can Select for Multiple Stable Parasite Virulence Strategies in Obligate Killer Parasites

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ABSTRACT: The timing of seasonal host activity, or host phenology, is an important driver of parasite transmission dynamics and evolution. Despite the vast diversity of parasites in seasonal environments, the impact of phenology on parasite diversity remains relatively understudied. For example, little is known about the selective pressures and environmental conditions that favor a monocyclic strategy (complete a single cycle of infection per season) or a polycyclic strategy (complete multiple cycles). Here, we present a mathematical model that demonstrates that seasonal host activity patterns can generate evolutionary bistability in which two evolutionarily stable strategies (ESSs) are possible. The ESS that a particular system reaches is a function of the virulence strategy initially introduced into the system. The results demonstrate that host phenology can, in theory, maintain diverse parasite strategies among isolated geographic locations.

Keywords: parasite, phenology, evolution, adaptation.

Introduction

Seasonal environments are expected to have more available niche space, and thus greater biotic diversity, than constant environments (Tilman 1982). The impact of seasonality on parasite diversity, however, remains equivocal and relatively understudied (Sorrell et al. 2009; van den Berg et al. 2010; Hamelin et al. 2011; Donnelly et al. 2013). Parasites in seasonal environments have evolved one of two main strategies: monocyclic parasites complete a single cycle of infection per season, while polycyclic parasites complete multiple cycles of infection each season (Agrios 2005). For example, parasitic species such as ichneumonid wasps, which infect caterpillars, are found with monocyclic or polycyclic strategies in nature (Sugonyaev 2006; Sniegula et al. 2016; Prev y et al. 2017; Qiu et al. 2018). However, little is known about the selective pressures and environmental conditions that favor each of the diverse parasite strategies observed in nature.

Some studies have found evidence that seasonality generates diversity for certain parasite traits, while other

studies have been inconclusive. For example, an explicit trade-off between within-season transmission and between-season survival can select for both a polycyclic parasite strategy specialized on within-season infection initiation and a monocyclic parasite strategy specialized on between-season survival (Hamelin et al. 2011). A similar model incorporating the same trade-off did not find evidence that seasonality can drive evolutionary branching (van den Berg et al. 2010), suggesting that additional environmental conditions are important drivers. Seasonal host reproduction can also select for two divergent strategies, including a latent strategy that can be reactivated later and an immediately transmissible strategy (Sorrell et al. 2009). While these studies show that seasonality can drive diversity in some specific situations, other studies have shown that seasonality does not impact the diversity of other important parasite traits, such as virulence (Donnelly et al. 2013).

Monocyclic and polycyclic parasites are subject to different life history constraints and selection pressures. For example, the time required to assemble parasite progeny constrains virulence evolution so that infected hosts are not killed before progeny are fully developed. Thus, parasites may be monocyclic in seasonal environments because there is time to complete only one infectious cycle. Parasites may also be constrained by mechanistic trade-offs where the number of progeny produced is mechanistically correlated with infection duration. Longer latency periods, the equivalent of lower virulence in obligate killer parasites, can also be selectively advantageous in the absence of an explicit trade-off as low-virulence, monocyclic, obligate host-killer parasites remain in infected hosts to limit the decay of their progeny in the environment (MacDonald et al. 2022). However, parasites that are not constrained to a monocyclic lifestyle experience different selective pressures and may evolve alternate virulence strategies. Prior investigations of obligate killer parasites in nonseasonal environments suggest that high-virulence traits are adaptive, as they allow for exponential population growth (Levin and Lenski 1983;

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Ebert and Weisser 1997; Sasaki and Godfray 1999; Caraco and Wang 2008). How host seasonal activity impacts the strength and direction of selection pressures on polycyclic parasite strategies remains an open question in obligate killers.

Here, we investigate the impact of seasonal host activity on the virulence evolution of an obligate killer parasite that is not constrained to the monocyclic lifestyle. Furthermore, we examine how the timing and duration of host emergence (components of host phenology) impact parasite virulence evolution. We demonstrate that host seasonal patterns can drive the evolution of both stable monocyclic and polycyclic strategies, although these strategies do not coexist. The evolutionarily stable strategy (ESS) in each system is a function of the virulence trait of the starting parasite population. Low-virulence parasites evolve to a monocyclic ESS with a lower virulence trait or a long latency period between infection and host death, as seen previously (MacDonald et al. 2022), while high-virulence parasites evolve to a polycyclic ESS with higher virulence to

sequentially infect susceptible hosts within seasons. The population of high-virulence parasites at the polycyclic ESS have relatively low equilibrium densities, as they often reduce the number of susceptible hosts available to parasites late in the season, a process termed self-shading (Boots and Sasaki 1999; Kerr et al. 2006). These results demonstrate that there are multiple evolutionarily stable solutions for parasites in seasonal environments, which provides clues for the evolutionary origins of monocyclic and polycyclic parasites.

Model Description

The model describes the transmission dynamics of a free-living obligate killer parasite that infects a seasonally available host (fig. 1). The susceptible host cohort, $\hat{s}(n)$, enters the system at the beginning of the season; $\hat{s}(n)$ is either constant each season or a function of the number of uninfected hosts at $t = T$ in season $n - 1$. The timing of host emergence during the season (i.e., host phenology) is given by

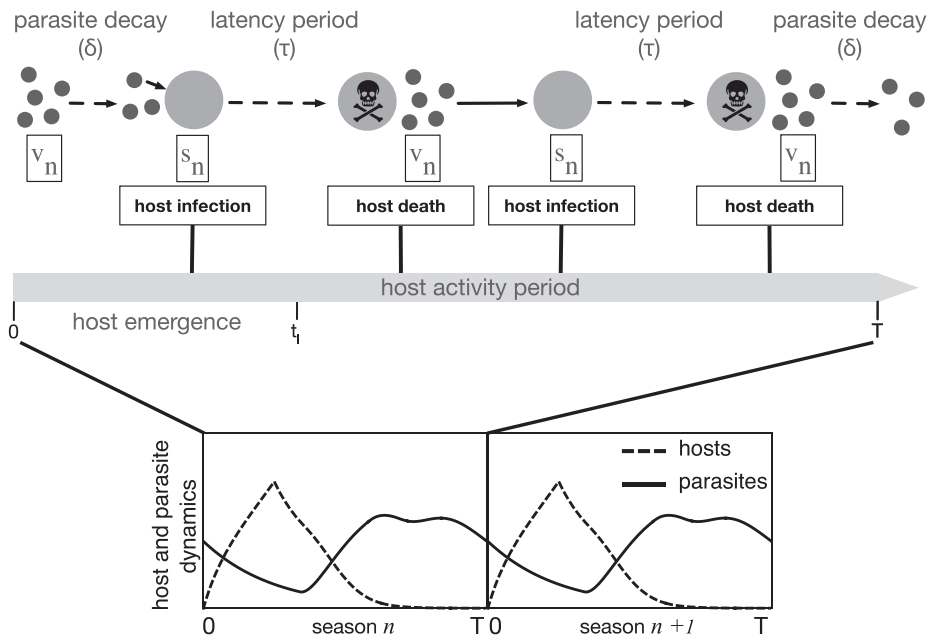


Figure 1: Diagrammatic representation of a polycyclic infectious cycle within and across seasons. All parasites (v_n) emerge at the beginning of season n ($t = 0$), while all hosts (s_n) emerge at a constant rate between time $t = 0$ and $t = t_i$ (where t_i is the length of the host emergence period). Parasites decay in the environment from exposure at rate δ throughout the season. The rate of infection is density dependent such that the majority of infections occur near the beginning of the season, when susceptible host and free parasite densities are high. Parasite-induced host death at time τ after infection releases parasite progeny (v_n) into the environment. This diagram depicts an example where τ is short enough such that two cycles of infections can occur within the season (polycyclic), although parasites with longer latency periods complete only one infectious cycle within each season. The host (dashed) and parasite (solid) population dynamics across two seasons when the end-of-season densities reach stable equilibria are portrayed in the lower panel. Parasite progeny surviving to the end of the season constitute the parasite population emerging the following season ($v_{n+1}(T) = \hat{v}(n)$). The density of hosts emerging each season were constant in some analyses and a function of the number of uninfected hosts surviving to the end of the season in other analyses. Host densities determined by the densities in the prior season can generate a quasiperiodic discrete-time attractor such that end-of-season densities for hosts and parasites vary among seasons (see fig. 6A and fig. B1.)

the function $g(t, t_i)$, where t_i is the length of time over which susceptible hosts ($\hat{s}(n)$) emerge. Hosts in season n , s_n , have nonoverlapping generations and are alive for one season. Parasites in season n , v_n , must infect and kill the host to release new infectious progeny. The number of cycles of infection the parasite completes within a season depends on the parasite latency period length (τ): the parasite is monocyclic (completes one cycle of infection within a season) when it has a long period between infection and progeny release, while the parasite is polycyclic (completing multiple infectious cycles within a season) when it has a short period between infection and progeny release (see fig. 1).

The duration of each season extends from $t = 0$ to $t = T$. Time units are not specified in order to maintain the generality of the model across disease systems. It is expected that the relevant time unit will be in months for many disease systems, corresponding to spring and summer (Baltensweiler et al. 1977; Grant and Shepard 1984; Donovan 1991; Danks 2006; Takasuka and Tanaka 2013), and weeks for other disease systems (Danks 2006; Cummins et al. 2011; Dalen 2013). The initial conditions in the beginning of the season are $s_n(0) = 0$, $v_n(0) = \hat{v}(n) = v_{n-1}(T)$, where $\hat{v}(n)$ is the size of the starting parasite population introduced at the beginning of season n determined by the number of parasite progeny remaining at the end of season ($t = T$) in season $n - 1$. The transmission dynamics in season n are given by the following system of delay differential equations (all parameter values are positive and described in table 1):

$$\frac{ds_n}{dt} = \hat{s}(n)g(t, t_i) - ds_n(t) - \alpha s_n(t)v_n(t), \quad (1a)$$

$$\frac{dv_n}{dt} = \alpha\beta(\tau)e^{-d\tau}s_n(t - \tau)v_n(t - \tau) - \delta v_n(t), \quad (1b)$$

where d is the host death rate, δ is the decay rate of parasites in the environment, α is the transmission rate, and τ is the delay between host infection and host death. The term τ is equivalent to virulence where low-virulence parasites have long τ and high-virulence parasites have short τ ; β is the number of parasites produced on host death. In most cases we assume β is a function of τ ($\beta(\tau)$), but we also investigate the impact of a constant, trade-off-free β . Parasites that have not killed their host by the end of the season do not release progeny. Background mortality arises from predation and other natural causes. Infected hosts that die from background mortality do not release parasites because the parasites are either consumed or the viable progeny have not had sufficient time to develop (Wang 2006; White 2011).

The function $g(t, t_i)$ is a probability density that describes host emergence phenology by capturing the per capita host emergence rate through the timing and length of host emergence. We use a uniform distribution for simplicity, although other distributions are expected to have qualitatively similar results (MacDonald et al. 2020):

$$g(t, t_i) = \begin{cases} \frac{1}{t_i}, & 0 \leq t \leq t_i; \\ 0, & t_i < t \leq T. \end{cases}$$

The term t_i denotes the length of the host emergence period, and T denotes the season length. The season begins ($t_0 = 0$) with the emergence of the susceptible host cohort ($\hat{s}(n)$) over the duration of $0 \leq t \leq t_i$.

Between-Season Dynamics

To study the impact of the feedback between host demography and parasite fitness on parasite evolution, we let the size

Table 1: Model parameters and their respective values

Parameter	Description	Value
s_n	Susceptible hosts in season n	State variable
v_n	Parasites in season n	State variable
$\hat{v}(n)$	Starting parasite population in season n	State variable
$\hat{s}(n)$	Host cohort in season n	State variable, 10^7 when constant
t_i	Length of host emergence period	Time (varies)
T	Season length	Time (varies)
α	Transmission rate	$10^{-8}/(\text{parasite} \times \text{time})$
β	Number of parasites produced on host death	200 parasites when constant
δ	Parasite decay rate in the environment	2 per unit time
d	Host death rate	.25 per unit time
τ	Latency period (1/virulence)	Time (evolves)
σ	Host fecundity	200 hosts
ρ	Density-dependent parameter	.0001
b	Trade-off parameter	100

of the emerging host cohort be a function of the number of uninfected hosts remaining at the end of the prior season,

$$\hat{s}(n+1) = \frac{\sigma s_n(T)}{1 + \rho s_n(T)},$$

which corresponds to Beverton-Holt growth, the discrete-time analogue of logistic growth in continuous time. The term $s_n(T)$ is the density of susceptible hosts at $t = T$ in season n , σ is host reproduction, and ρ is the density-dependent parameter.

We have shown previously that host carryover generates a feedback between parasite fitness and host demography that can drive quasiperiodic dynamics for some parameter ranges (MacDonald and Brisson 2022b).

Parasite Evolution

To study how parasite traits adapt given different seasonal host activity patterns, we use evolutionary invasion analysis (Geritz et al. 1998; Metz et al. 1992). We first extend system (1) to follow the invasion dynamics of a rare mutant parasite ($v_{n,m}$) in season n :

$$\begin{aligned} \frac{ds_n}{dt} = & \hat{s}(n)g(t, t_1) - ds_n(t) - \alpha s_n(t)v_n(t) \\ & - \alpha_m s_n(t)v_{n,m}(t), \end{aligned} \quad (2a)$$

$$\frac{dv_n}{dt} = \alpha\beta(\tau)e^{-d\tau}s_n(t-\tau)v_n(t-\tau) - \delta v_n(t), \quad (2b)$$

$$\begin{aligned} \frac{dv_{n,m}}{dt} = & \alpha_m\beta_m(\tau_m)e^{-d\tau_m}s_n(t-\tau_m)v_{n,m}(t-\tau_m) \\ & - \delta_m v_{n,m}(t), \end{aligned} \quad (2c)$$

where m subscripts refer to the invading mutant parasite and its corresponding traits.

In previous work on similar models that only considered monocyclic parasites, we were able to derive an analytical expression for mutant invasion fitness (MacDonald and Brisson 2022b; MacDonald et al. 2022). We are unable to solve the current model with polycyclic parasites analytically because of the nonlinear $\alpha s_n(t)v_n(t)$ terms and instead determine parasite evolutionary end points numerically. As in previous analyses (MacDonald and Brisson 2022b; MacDonald et al. 2022), the invasion fitness of a rare mutant parasite depends on the density of $v_{n,m}$ produced by the end of the season ($v_{n,m}(T)$) in the environment set by the resident parasite at equilibrium density \hat{v}^* .

To estimate the invasion fitness of a rare mutant numerically, we calculate the density of $v_{n,m}$ produced by the end of the season ($v_{n,m}(T)$) in the environment set by the resident parasite at equilibrium density \hat{v}^* . The mutant parasite is assumed to invade in a given host phenological scenario

if the density of $v_{n,m}$ produced by time T is greater than or equal to the initial $v_{n,m}(0) = 1$ introduced at the start of the season ($v_{n,m}(T) \geq 1$).

To study the evolution of virulence traits (τ), we first assume that all other resident and mutant traits are identical (e.g., $\alpha = \alpha_m$). When β is a function of τ , we assume that the number of new progeny released increases as the latency period increases: $\beta(\tau) = b(\tau + 0.5)^{0.8}$. Note that when there is no trade-off between β and τ , the parasite growth rate in the host is essentially the trait under selection. That is, β is constant regardless of τ ; thus, the trait that is effectively evolving is the rate that new parasites are assembled in between infection and host death (e.g., long τ corresponds to slow assembly of new parasites.)

Virulence traits (τ) determine whether parasites are monocyclic or polycyclic by setting the latency period length. Highly virulent parasites have short latency periods that facilitate the completion of multiple rounds of infection per season. By contrast, low-virulence parasites have long latency periods that have time to complete only one round of infection per season.

The simulation analysis was done by first numerically simulating system (1) with a monomorphic parasite population. A single mutant parasite is introduced at the beginning of the season after 100 seasons have passed. The mutant's virulence strategy is drawn from a normal distribution whose mean is the value of τ from the resident strain. System (2) is then numerically simulated with the resident and mutant parasite. New mutants arise randomly after 1,000 seasons have passed since the last mutant was introduced, at which point system (2) expands to follow the dynamics of the new parasites strain. This new mutant has a virulence strategy drawn from a normal distribution whose mean is the value of τ from whichever parasite strain has the highest density. System (2) continues to expand for each new mutant randomly introduced after at least 1,000 seasons have passed. Any parasite whose density falls below 1 is considered extinct and is eliminated. Virulence evolves as the population of parasites with the adaptive strategy eventually invade and rise in density. Note that our simulations deviate from the adaptive dynamics literature in that new mutants can be introduced before earlier mutants have replaced the previous resident. Previous studies have shown that this approach is well suited to predicting evolutionary outcomes (Kisdi 1999; White and Bowers 2005; White et al. 2006; MacDonald and Brisson 2022b).

When hosts that survive to the end of the season ($s_n(T)$) reproduce to determine next season's host cohort ($\hat{s}(n+1)$), simulations are conducted to determine the outcome of parasite adaptation. Simulations are necessary because host carryover creates a feedback between parasite fitness and host demography that can drive cycling for some parameter ranges. When parasite-host

dynamics are cycling, the density of $v_{n,m}(T)$ in the season the mutant was introduced does not reliably predict the outcome of parasite evolution, as mutants with a selective advantage do not always invade (MacDonald and Brisson 2022b). Simulations thus verify that the evolutionarily stable level of virulence is qualitatively the same as results when the emerging host cohort is constant across seasons and cycling cannot occur.

Results

Both monocyclic and polycyclic parasite strategies can be evolutionarily stable in environments with seasonal host activity (fig. 2). However, monocyclic and polycyclic parasite subpopulations do not coexist in the same host population. The evolutionary attractor that a population of parasites evolves toward is determined by their initial level of virulence, regardless of which strategy would be selected if both ESSs were initially present (fig. 3). We compared simulations with large versus small mutation steps to demonstrate that both strategies can outcompete the other depending on the parameters (fig. 3). Parasite populations always approach the nearest evolutionarily stable virulence strategy

(local ESS) when mutation step sizes are small. However, parasite populations eventually evolve to one or the other virulence strategy (depending on parameters; figs. 4, 5) when mutation step sizes are large. Moderate virulence strategies, which are evolutionary repellers, have virulence traits that kill hosts too quickly to limit progeny decay in the environment but do not kill hosts quickly enough to complete multiple infection cycles during the season.

The progeny decay rate in the environment impacts both monocyclic and polycyclic parasites. The evolutionarily stable virulence trait (latency period, τ) for both parasite strategies times the release of progeny from the final cycle of infected hosts to occur just prior to the end of the season (fig. 2B). Parasites employing the monocyclic strategy evolve long latency periods to reach high densities at the end of each season by losing few progeny to environmental decay, as has been shown previously (MacDonald et al. 2022). The monocyclic strategy outcompetes the polycyclic strategy when (1) host death rates (d) are low, such that infected hosts are unlikely to die prior to releasing progeny; (2) the variance in the timing that hosts become active during the season (t_i) is small, which results in a similarly small variance in the timing of infections near the start of the season;

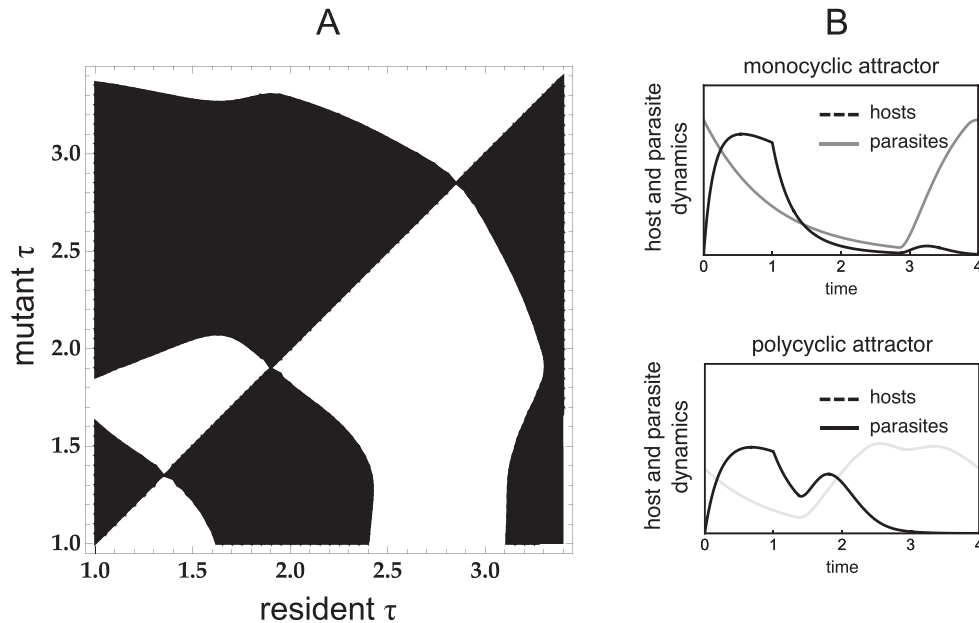


Figure 2: Seasonal host activity generates multiple parasite virulence attractors. *A*, Pairwise invasibility plot (PIP) showing the outcome of invasion by mutant parasite strains into resident parasite populations with virulence trait τ . Mutants possess an adaptive virulence trait and invade in black regions, while they possess a maladaptive virulence trait and become extinct in white regions. The PIP shows two evolutionarily stable strategies (ESSs) at $\tau \approx 2.85$ and $\tau \approx 1.35$ that are attractive and uninvadable. An evolutionary repeller lies between the two ESSs at $\tau \approx 1.9$. *B*, Parasites with the low-virulence phenotype (gray line; $\tau \approx 2.85$) release new parasites just prior to the end of the season and is thus monocyclic. Parasites with the high-virulence phenotype (black line; $\tau \approx 1.35$) complete two generations of infections during the season for the parameter values shown here and is thus polycyclic. The black line shows new host infections over time host. $T = 4$, $t_i = 1$, and $\beta(\tau) = b(\tau + 0.5)^{0.8}$; all other parameters are as in table 1. See appendix A for an explanation of how the PIP was produced.

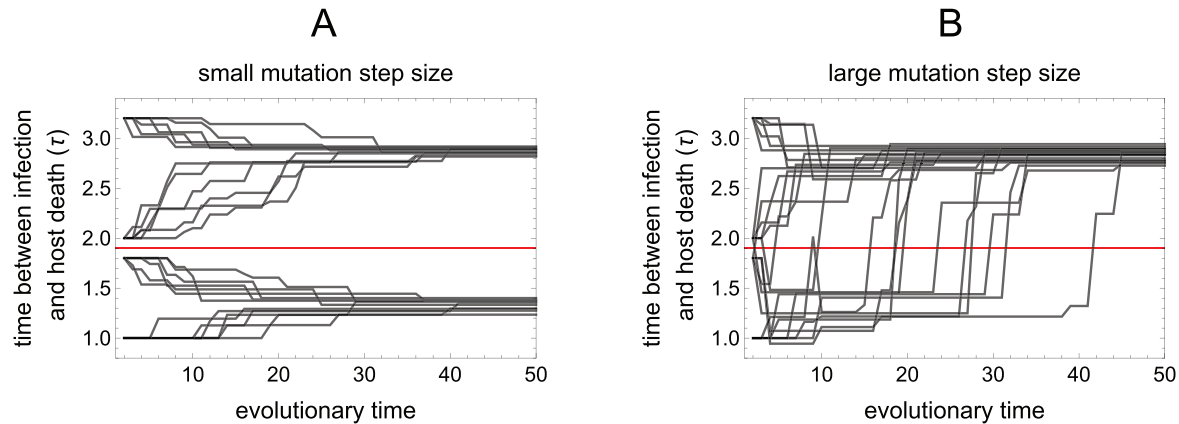


Figure 3: Initial conditions determine which virulence attractor parasite populations will evolve toward. A repeller exists between the two attractors at moderate virulence around $\tau = 1.9$. *A*, If mutation step sizes are small, parasite populations with $\tau > 1.9$ evolve toward the low-virulence monocyclic attractor at $\tau \approx 2.85$, while parasite populations with $\tau < 1.9$ evolve toward the high-virulence polycyclic attractor at $\tau \approx 1.35$. *B*, If mutation step sizes are large, all parasite populations eventually reach the low-virulence monocyclic attractor, as this strategy outcompetes the polycyclic attractor for these parameters. Plots show 24 independent simulation analyses with high or low mutation step sizes. Six runs start at $\tau = 3.2$, $\tau = 2$, $\tau = 1.8$, and $\tau = 1$. Evolutionary time represents the number of mutants introduced into each system. In a random season after at least 1,000 seasons have passed since the last mutant was introduced, the parasite population with the highest density is set as the “resident” population, and a new mutant is introduced with a virulence phenotype drawn from a normal distribution whose mean is the virulence phenotype of the “resident” parasite population. When the mutation step size is small, $\tau_m = \tau_r + \mathcal{N}(0, 0.1)$. When the mutation step size is large, $\tau_m = \tau_r + \mathcal{N}(0, 0.5)$. Parameter values in this figure are identical to those in figure 1.

and (3) transmission rates (α) are greater, which also reduces the timing of infection variance.

The polycyclic strategies use higher virulence to complete multiple rounds of infection within a season. The polycyclic strategy results in larger parasite population sizes than the monocyclic strategy when (1) host death rates (d) are high; (2) the host emergence period (t_i) is longer; and (3) the transmission rates (α) are lower, all of which result in greater numbers of susceptible hosts later in the season that can be infected by progeny generated within the same season. Polycyclic parasites are particularly susceptible to self-shading, a process where the first cycle of infections reduces the number of susceptible hosts to the point where many of the first-cycle progeny fail to find a host within the season and are subject to decay in the environment.

The end of season density is not equivalent to invasion fitness for polycyclic parasites because of self-shading. That is, high-virulence polycyclic parasites invade and replace endemic lower-virulence polycyclic parasites that achieve higher end-of-season densities. The higher-virulence polycyclic parasites quickly kill infected hosts and progeny that infect many of the remaining susceptible hosts before the lower-virulence parasite progeny have completed their first cycle. The progeny of the lower-virulence parasites fail to find a susceptible host and decay in the environment even when their virulence trait would result in greater equilibrium densities in the absence of competition. Including a mechanistic trade-off between transmission and latency period length reduces the advantage of high-virulence traits,

which produce few progeny per infection with this trade-off, such that a moderately virulent polycyclic strategy is an ESS (fig. 2). In the absence of any trade-off, bistability is maintained but the polycyclic ESS occurs at maximal virulence (fig. B2).

Shorter seasons and longer host emergence periods drive both the polycyclic ESS and the monocyclic ESS toward higher virulence, similar to results observed previously (van den Berg et al. 2011; MacDonald et al. 2022). More virulent monocyclic parasites successfully kill infected hosts and release progeny prior to the end of short seasons, while more virulent polycyclic parasites can complete multiple infection cycles (fig. 4). Short host emergence periods result in simultaneously high host and parasite densities—and thus high density-dependent infection rates—near the start of the season, which favors less virulent parasites that kill hosts closer to the end of the season (fig. 4). However, the impact of host emergence periods on virulence evolution differs for the monocyclic ESS and the polycyclic ESS. Small increases in the emergence period result in large virulence increases for the monocyclic parasite but only minor increases in polycyclic parasite virulence when the host emergence period length is short. This trend is reversed for long host emergence periods: short emergence period length increases cause negligible increases in monocyclic parasite virulence and large increases in polycyclic parasite virulence.

Some environmental parameter states support only one parasite ESS (fig. 5). For example, monocyclic parasite fitness is limited in environments with high host

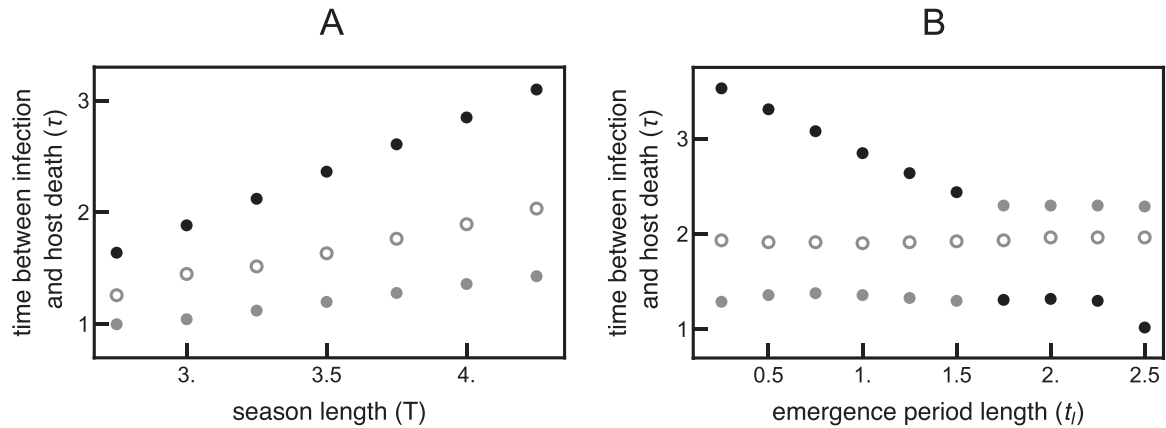


Figure 4: Host phenology impacts evolutionarily stable virulence strategies. *A*, Longer seasons select for lower virulence for both the monocyclic attractor and the polycyclic attractor. *B*, Higher emergence variability selects for higher virulence for both the monocyclic attractor and the polycyclic attractor; however, the impact of changing emergence period length is nonlinear. The strength t_i has on the respective attractors varies: increases in t_i when $t_i < 1.75$ result in a large increase in virulence for the low-virulence attractor but a small increase in virulence for the high-virulence attractor, while the opposite is true for $t_i > 1.75$. Black points indicate the attractor that outcompetes the other, gray points indicate local attractors, and hollow points indicate repellers. All other parameters are identical to those in figure 1. See appendix A for an explanation of how evolutionarily stable virulence was found.

mortality (d), as many infected individuals die prior to releasing parasites. Natural host mortality has little impact on the higher-virulence polycyclic ESSs that rapidly kill their hosts and infect subsequent hosts within a season. By contrast, the higher monocyclic parasite densities that result from lower host mortality increase early-season incidence and leave few susceptible hosts for a second generation of polycyclic parasite infections. Thus, the low-virulence monocyclic ESS is the only viable evolutionary end point when host mortality is low.

A feedback between host demography and parasite fitness can generate quasiperiodic host-parasite dynamics across seasons such that end-of-season host and parasite densities vary between seasons (fig. 6). This qualitative change in dynamical behavior does not impact the direction of virulence evolution. That is, the virulence level of the parasite originally introduced into the system will determine whether a polycyclic or monocyclic strategy evolves. However, the evolutionary rate proceeds much more slowly in dynamically cycling environments. Furthermore, cyclic host-parasite dynamics routinely drive the polycyclic parasite population to extremely low densities, while the monocyclic parasite population maintains densities well above extinction levels.

Discussion

Host phenological patterns can drive the evolution of multiple ESSs. These phenological patterns support both a higher-virulence strategy that completes multiple infection

cycles within each season (polycyclic) and a lower-virulence strategy that completes one infectious cycle each season (monocyclic). The monocyclic and polycyclic strategies are both evolutionarily stable attractors and are separated by an evolutionary repeller (fig. 4). Parasite populations that are more virulent than the repeller will evolve toward the polycyclic attractor, while parasites that are less virulent than the repeller evolve toward the monocyclic attractor. Seasonal host environments are not predicted to permit the coexistence of diverse parasite strategies within the same host population but could drive diversity across geography.

The majority of prior studies suggest that obligate killer parasites maximize their fitness by rapidly killing and infecting new susceptible hosts, akin to the polycyclic strategy observed in the present model (Levin and Lenski 1983; Ebert and Weisser 1997; Sasaki and Godfray 1999; Caraco and Wang 2008). This strategy relies on a constant supply of susceptible hosts, which are temporally rare in seasonal environments. Parasites can limit the impact of the seasonal absence of susceptible hosts by employing a less virulent monocyclic strategy that coordinates the release of parasite progeny with the influx of susceptible hosts. In the current model, both strategies are locally evolutionarily stable in many phenological environments. Host seasonality is also predicted to maintain multiple ESSs through mechanistic trade-offs between within-season transmission and between-season survival (Hamelin et al. 2011). In both cases, the monocyclic strategy evolves to decrease the impact of progeny decay in the environment during periods of host absence, while the polycyclic strategy evolves to

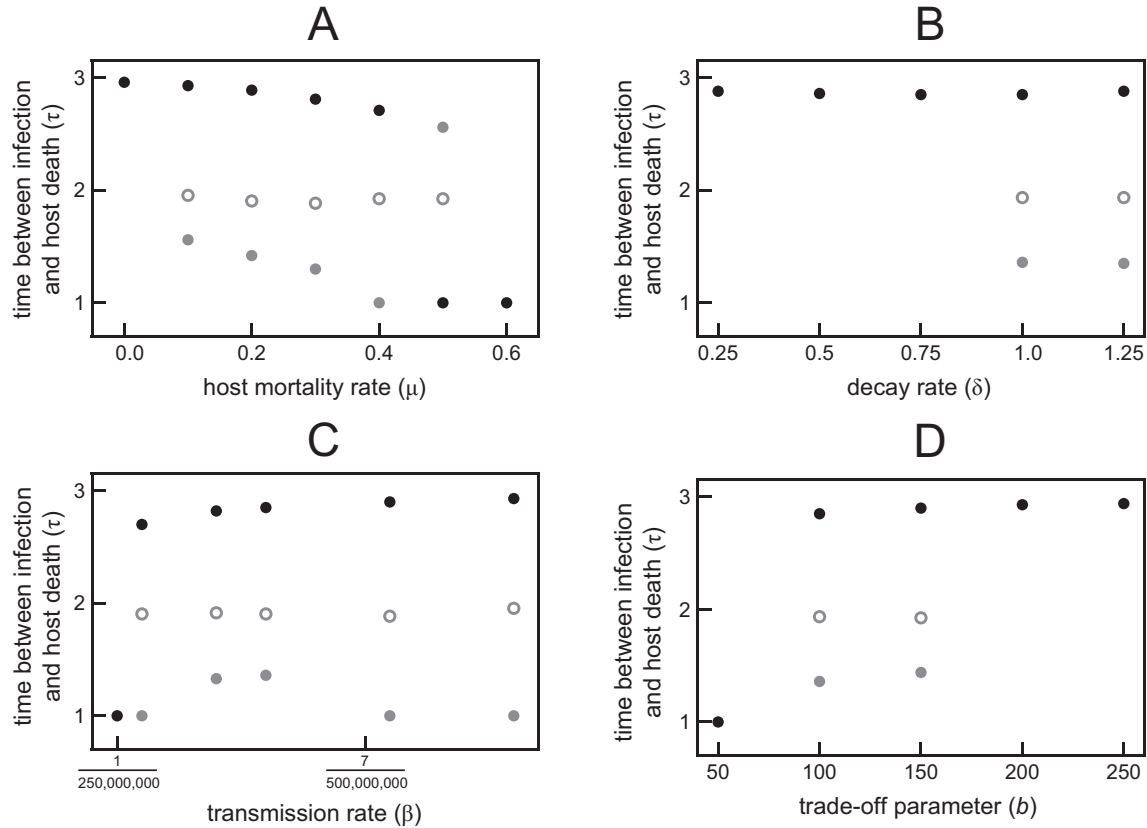


Figure 5: Certain conditions can destroy bistability or alter which evolutionarily stable strategy outcompetes the other. Shown are parasite virulence attractors and repellers for changing the host death rate, μ (A); the parasite decay rate, δ (B); the transmission rate, β (C); and the trade-off parameter, b (D). A, Low natural host mortality (μ) drives high host densities and thus high early-season incidence. High incidence early in the season selects for the low-virulence monocyclic strategy. High μ allows the high-virulence polycyclic attractor to generate larger parasite population sizes than the monocyclic attractor, as remaining in a host for long periods is risky. B, A low decay rate (δ) drives high parasite densities and thus high early-season incidence. High incidence early in the season selects for the low-virulence monocyclic attractor. C, A low transmission rate (β) pushes the timing of infections to later in the season. Late infections select for the high-virulence polycyclic strategy, as there is less time between infection and the end of the season. Higher β results in high early-season incidence and thus drives both attractors toward lower virulence. D, Low values of the trade-off parameter (b) result in low parasite density and thus slow incidence. High virulence is adaptive when incidence is slow, as parasites have less time to release progeny before the end of the season. High values of b result in high parasite density and thus high incidence early in the season. High early-season incidence selects for the low-virulence monocyclic strategy. $T = 4$, $t_i = 1$. When a parameter is not changing, its value is the same as in table 1. See appendix A for an explanation of how evolutionarily stable virulence was found.

exponentially increase population sizes by rapidly exploiting hosts when they are abundant (MacDonald et al. 2022).

The average fitness of high-virulence parasite populations is often depressed by self-shading (Boots and Sasaki 1999) in seasonal host environments. Self-shading occurs when many hosts are infected early in the season, leaving few susceptible hosts for the parasite progeny derived from early infections. Thus, self-shading can decrease the number of parasites that survive to the next season and the population densities of high-virulence parasites. These results resemble the effects of self-shading suffered by high-virulence parasites in environments with low migration that quickly exhaust their limited local

pool of hosts (Kerr et al. 2006). The results presented here suggest that temporal constraints on transmission can result in similar negative fitness impacts on high-virulence parasites, as seen in spatially constrained environments. These results suggest that longer seasons are analogous to lower migration rates in that both favor lower virulence by increasing the time between transmission opportunities.

The parameter space that supports multiple evolutionarily stable parasite strategies in this model is broad but not universal. For example, the monocyclic strategy is the only evolutionary attractor in environments with low parasite decay rates. Low decay rates increase parasite

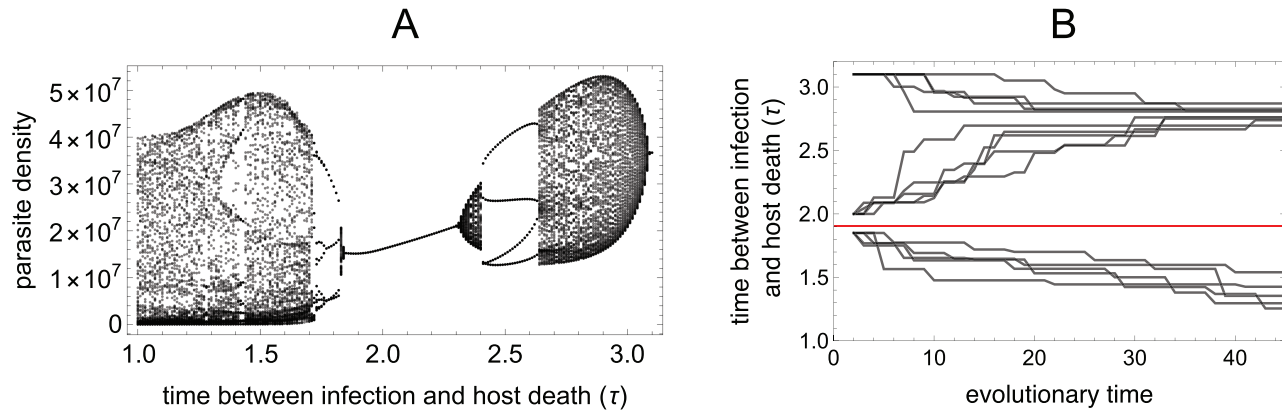


Figure 6: Virulence evolution generates periodic dynamics when host populations carry over from one season to the next. *A*, Parasite populations can reach sufficiently high densities in some host phenological patterns to destabilize demographic dynamics resulting in a bifurcation that drives quasiperiodic parasite-host dynamics. The bifurcation diagram shows end-of-season parasite densities for parasites with different virulence phenotypes (τ) for seasons 800–900 in a system where the host season is short ($T = 4$) and hosts emerge synchronously ($t_i = 1$). Moderate-virulence parasites ($1.85 < \tau < 2.3$) reach a stable equilibrium. *B*, Periodic host-parasite dynamics do not qualitatively impact the evolutionary end points, that is, high- and low-virulence attractors are separated by a repeller despite periodic dynamics. The same simulation analysis with a small mutation step size was used as in figure 2. $\alpha = 10^{-7}$ and $b = 75$ to prevent polycyclic parasite extinction; all other parameters are the same as table 1.

densities, which synchronizes early-season incidence and decreases the number of susceptible hosts later in the season (self-shading), limiting reproductive success for polycyclic parasites. By contrast, high early-season incidence increases monocyclic parasite fitness by synchronizing progeny release near the end of the season. This result deviates from the curse of the pharaoh hypothesis, which predicts that low parasite decay rates select for high virulence by decreasing the risk of leaving hosts early (Ewald 1983; Bonhoeffer et al. 1996; Day 2002). The results presented here are similar to prior theoretical results showing that environments with slow fluctuations in host availability can favor parasites with low virulence (Lion and Gandon 2021), further supporting season length as an important factor explaining the deviations between the evolution of virulence in constant and seasonal environments.

Monocyclic and polycyclic parasites in some host phenological environments can achieve densities that are sufficient to destabilize host-parasite dynamics and instigate population cycles, as observed previously with strictly monocyclic parasites (MacDonald and Brisson 2022*b*). Population cycles occur when parasites overexploit host populations, which results in few susceptible hosts in subsequent years and leads to a parasite population crash that allows host populations to recover (Hilker et al. 2020). While the current model could not be solved analytically, similar models have suggested that cycles are driven by a Neimark-Sacker bifurcation (Hilker et al. 2020; MacDonald and Brisson 2022*b*). Cycling does not qualitatively alter the

number of ESSs supported by an environment or the direction of parasite evolution within that system. However, population cycles can drive polycyclic parasites toward extremely low densities that could be at high risk for stochastic extinction (fig. 6). Polycyclic parasites exploit a greater number of susceptible hosts throughout the season than do monocyclic parasites, resulting in very small host populations and few infections in subsequent seasons. Thus, population cycles may drive polycyclic parasites extinct while maintaining monocyclic parasites in natural conditions.

The primary conclusions of this model correspond with empirical data from some host-parasite study systems. For example, parasitic wasp species are more likely to employ a monocyclic strategy at high latitudes, where seasons are shorter and host emergence is more synchronous, while the same species are dicyclic at low latitudes (Sugonyaev 2006; Sniegula et al. 2016; Prev y et al. 2017; Qiu et al. 2018). Similarly, the monocyclic attractor is predicted to outcompete the polycyclic attractor in short seasons and synchronous host emergence periods (fig. 4). However, experimental data are necessary to support host phenology as a driver of the evolution of monocyclic or polycyclic strategies across geography in this and other systems.

Several features of the current model can be altered to investigate more complex impacts of phenology on parasite diversity and virulence evolution. For example, relaxing the assumption that host populations reproduce once per season would likely favor higher virulence strategies, as within-season host reproduction would reduce or eliminate

the impact of self-shading for polycyclic parasites (van den Berg et al. 2011). The limited cost of self-shading in models with continuous host reproduction may explain why prior studies have not detected multiple evolutionarily stable parasite strategies for obligate killer parasites. Furthermore, relaxing the assumption that parasites evolve a fixed phenotype would likely select for plastic traits in some seasonal environments (Choisy and de Roodé 2010; Brown et al. 2012; Cornet et al. 2014). Finally, this model could be extended to investigate the impact of between-season dynamics on virulence evolution. This extension would likely reach the conclusion that high between-season parasite survival rates favors long periods between infection and host death (low virulence), similar to results in a prior study (Rozins and Day 2017).

The strict obligate killer assumption can likely be relaxed without altering the result that many host phenological patterns support evolutionarily stable monocyclic or polycyclic strategies. For example, parasites that reduce host fecundity or increase host death rates on progeny release likely experience similar evolutionary pressures on latency period duration as the obligate killer parasites modeled here. That is, releasing parasite progeny quickly (short latency period and polycyclic) and releasing progeny near the end of the season (long latency period and monocyclic) are both likely ESSs. Many parasite-host systems conform to the assumptions of this model extension, such as blackleg disease of *Brassica napus* and many diseases systems infecting univoltine insects (Crowell 1934; Zehr 1982; Gaulin et al. 2007; Li et al. 2007; Holuša and Lukášová 2017; Zhang and Fernando 2017).

Host phenology drives the timing and prevalence of transmission opportunities for parasites (Biere and Honders 1996; Altizer et al. 2006; Hamer et al. 2012; Gethings et al. 2015; Martinez 2018; Ogden et al. 2018; MacDonald et al. 2020; McDevitt-Galles et al. 2020), which impacts parasite life cycle strategies and virulence evolution (King et al. 2009; Sorrell et al. 2009; van den Berg et al. 2011; Donnelly et al. 2013; MacDonald et al. 2022). We add to this body of work by demonstrating that host phenology can also drive multiple evolutionarily stable parasite strategies. These results show that many host seasonal patterns impart selection pressures on parasites that can drive the evolution of parasite populations toward monocyclic and polycyclic life cycle strategies.

Statement of Authorship

H.M. conceived of the presented idea and developed the theoretical framework; H.M. conducted the mathematical analysis and performed numerical simulations; and both authors wrote the manuscript, gave final approval for publication, and agree to be held accountable for the work performed herein.

Data and Code Availability

Code is available on Zenodo (<https://zenodo.org/badge/latestdoi/454605949>; MacDonald and Brisson 2022a).

APPENDIX A

Here, we describe the numerical methods used to generate pairwise invasibility plots (PIPs) and to find evolutionary attractors and repellers. Code written for the numerical analysis is available on request.

We follow the same approach as previous work (MacDonald and Brisson 2022b; MacDonald et al. 2022) and define mutant invasion fitness as the density of mutant parasites produced by the end of the season ($v_{n,m}(T)$) in the environment set by the resident parasite at equilibrium density \hat{v}^* . The mutant parasite invades if the density of $v_{n,m}$ produced by time T is greater than or equal to the initial $v_{n,m}(0) = 1$ introduced at the start of the season ($v_{n,m}(T) \geq 1$). Note that the mutant will not coexist with the resident strain when $v_{n,m}(T) > 1$, given that there is an evolutionary repeller in between the two ESSs instead of an evolutionary branching point (Geritz et al. 1998; Metz et al. 1992; Waxman and Gavrilets 2005).

It is not possible to derive an algebraic expression for mutant invasion fitness in this study as it was in previous studies. To generate PIPs for pairs of residents with virulence (τ_r) and mutant's with virulence (τ_m), we instead numerically find the density of $v_{n,m}(T)$ after one season in an environment set by the resident parasite, v_r . As in the previous analytical approach (MacDonald and Brisson 2022b; MacDonald et al. 2022), $v_{n,m}(T) = 1$ corresponds to a neutral mutant, $v_{n,m}(T) > 1$ corresponds to a mutant-resident pair in which the mutant parasite can invade and replace the resident, and $v_{n,m}(T) \leq 1$ corresponds to a mutant-resident pair that drives the mutant parasite extinct.

We use a similar approach to locate virulence trait values (τ) that correspond to evolutionary attractors and repellers. We again numerically find $v_{n,m}(T)$ after one season in an environment set by the resident v_r . Values of τ corresponding to attractors and repellers prevent small-effect mutants with higher and lower virulence from invading. That is, when resident virulence is τ_r , mutants with $\tau_m = \tau_r + 0.01$ and $\tau_m = \tau_r - 0.01$ cannot invade. We determine which points are attractors and repellers if there is more than one virulence trait value that prevents mutant invasion. Repellers are always found in between two attractors. To determine their location, we find the value of τ in between the two attractors that corresponds to a minimum for $v_{n,m}(T)$.

To determine which attractor is the global attractor, we find the attractor that competitively excludes all others. Mutant parasites with the value of τ corresponding to the global attractor can invade a population of resident parasites with the value of τ corresponding to nonglobal local attractors. Resident parasites with the value of τ corresponding to the

global attractor also prevent invasion of a mutant parasite with the value of τ corresponding to nonglobal local attractors.

APPENDIX B

Here, we present a plot (fig. B1) that shows the infection diagram for the case when host densities are determined

by the densities in the prior season. This case can generate a quasiperiodic discrete-time attractor such that end-of-season densities for hosts and parasites vary among seasons. We also present a plot (fig. B2) that demonstrates that the high-virulence ESS occurs at maximal virulence when virulence evolution is not constrained by a trade-off between transmission and virulence.

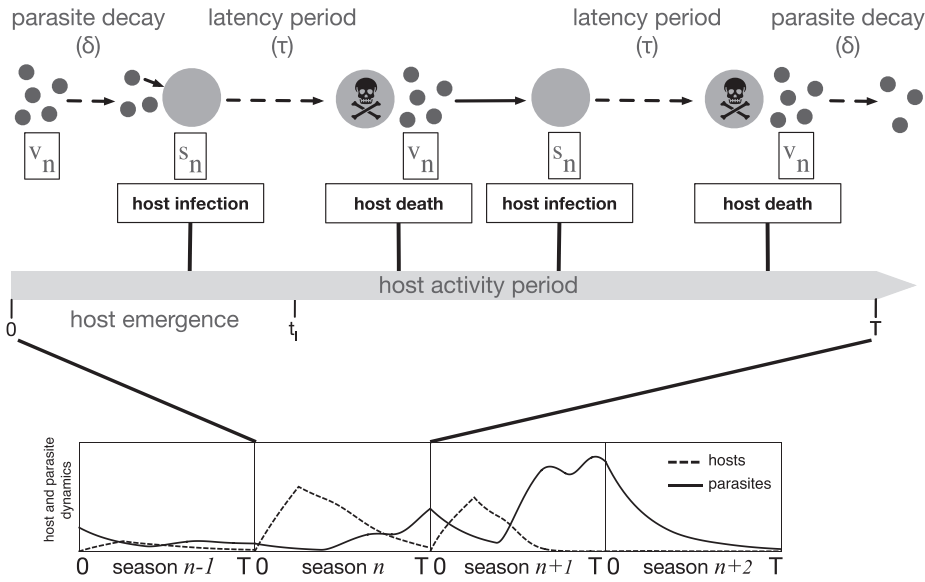


Figure B1: Diagrammatic representation of a polycyclic infectious cycle within and across seasons. All parasites (v_n) emerge at the beginning of season n ($t = 0$), while all hosts (s_n) emerge at a constant rate between time $t = 0$ and $t = t_i$ (where t_i is the length of the host emergence period). Parasites decay in the environment from exposure at rate δ throughout the season. The rate of infection is density dependent such that the majority infections occur near the beginning of the season, when susceptible host and free parasite densities are high. Parasite-induced host death at time τ after infection releases parasite progeny (v_n) into the environment. This diagram depicts an example where τ is short enough such that two cycles of infections can occur within the season (polycyclic), although parasites with longer latency periods complete only one infectious cycle within each season. The host (dashed) and parasite (solid) population dynamics across four seasons when the end-of-season densities reach a quasiperiodic attractor are portrayed in the lower panel. Parasite progeny surviving to the end of the season constitute the parasite population emerging the following season ($v_{n+1}(T) = \hat{v}(n)$), while hosts surviving to the end of the season give rise to next season's host cohort ($s_{n+1}(0) = \sigma s_n(T)/(1 + \rho s_n(T))$).

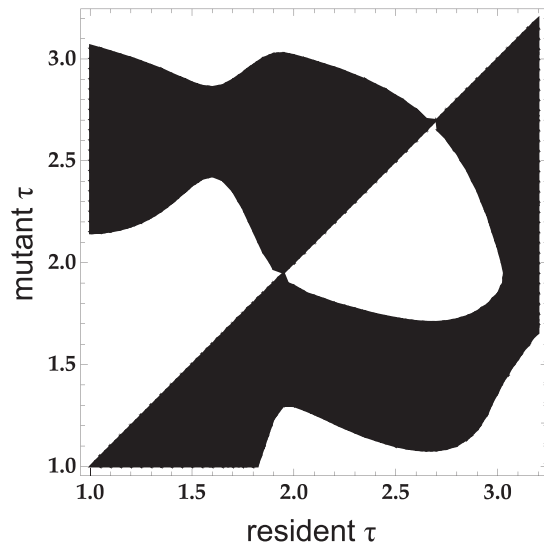


Figure B2: Pairwise invasibility plot showing the outcome of invasion by mutant parasite strains into resident parasite populations with virulence trait τ when $\beta = 200$ (i.e., β is not a function of τ). Notice that the high-virulence evolutionary attractor occurs at maximal virulence (set to $\tau = 1$).

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