Host phenology can select for multiple stable parasite virulence strategies

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Abstract

Host phenology is an important driver of parasite transmission and evolution. In a seasonal environment, monocyclic, obligate-killer parasites evolve optimal virulence strategies such that all parasite progeny are released near the end of the host season to limit parasite progeny death in the environment. It is unclear whether host seasonality imposes different constraints on polycyclic parasites such that both polycyclic and monocyclic parasites are maintained. We develop a mathematical model of a disease system with seasonal host activity to study the evolutionary consequences of host phenology on polycyclic, obligate-killer parasite virulence strategies. Seasonal host activity patterns create both monocyclic and polycyclic parasite evolutionarily stable strategies (ESS) separated by less-fit strategies (evolutionary repellors). The ESS that evolves in each system is a function of the virulence strategy of the parasite introduced into the system. The trait value for both monocyclic and polycyclic strategies is determined by two aspects of host phenology: the duration of the host activity period and the distribution in the time at which hosts first become active within each season. Longer host activity periods and more synchronous host emergence drive both the monocyclic and polycyclic strategies towards lower virulence. The results demonstrate that host phenology can, in theory, maintain diverse parasite strategies among isolated geographic locations.

Introduction

Classic ecological theory predicts that seasonality can create niche space for species competing for a shared resource. In an equilibrial environment, k-selected species mature slowly but are efficient at collecting resources as adults and outcompete r-selected species who mature quickly but are poor competitors for resources.[1] Fluctuating resources in seasonal environments can create niche space for the r-selected species who reproduces quickly when resources are temporarily abundant while the k-selected species persists as they are better competitors when resources are scarce.[2–5] Evidence for whether seasonality impacts the vast diversity of parasite strategies observed in nature remains equivocal.

Some studies have found that seasonality generates parasite diversity for certain traits while others have been inconclusive. One of the best examples of seasonality driving parasite diversity comes from theoretical work that considered a trade-off between within-season transmission and between-season survival.[6] This study showed that seasonal host absence allows polycyclic parasites specialized on initiating new infections

within the season to coexist with monocyclic parasites specialized on between-season survival. Seasonal host reproduction has also been shown to drive covert and overt parasite infection strategies towards multiple evolutionary attractors.[7] In this study, seasonality was shown to either select for parasites with a covert infection strategy that can be reactivated later in time or an overt infection strategy that is transmissible immediately. Other studies have shown that seasonality does not impact the diversity of other important parasite traits, such as virulence.[8]

Different selection pressures likely impact the virulence evolution of seasonal monocyclic and polycyclic parasites, which could impact diversity. Polycyclic parasites complete multiple rounds of infection within the season while monocyclic parasites complete one round of infection within the season. One potential driver of the monocyclic strategy is that parasites only have time to complete one generation of infections per season due to constraints on the minimum time required to assemble new parasites. That is, low virulence, *i.e.* a long latency period between infection and new parasite release, increases parasite fitness by increasing the number of progeny produced. Recent theoretical work puts forth another explanation by demonstrating that the optimal strategy for a monocyclic, obligate host-killer parasite is low virulence so that new parasites are released just before the short-lived host species perishes at the end of the season. This study demonstrated that low virulence is adaptive for parasites in a seasonal environment to minimize progeny decay in the environment. However, if there is no explicit constraint that the parasite must be monocyclic, its unclear whether this low virulence, monocyclic strategy would remain adaptive. Intuitively, high virulence should be adaptive for polycyclic parasites to increase the number of infections within the season. The question is thus whether different selection pressures on monocyclic and polycyclic strategies are sufficient to make both strategies adaptive.

Here we investigate the impact of host phenology on the virulence evolution of an obligate-killer parasite with no constraints on the number of infection cycles it can complete per season. We extend a mathematical model that tracks the dynamics of an exclusively monocyclic parasite that infects a seasonally available host species to study the impacts of seasonal host activity on parasites that can evolve monocyclic or polycyclic strategies. We demonstrate that seasonality drives either evolutionarily stable monocyclic or polycyclic strategies to evolve depending on the generation time of the starting parasite population. These two strategies are determined by parasite virulence as the monocyclic strategy has long periods between infection and host death (low virulence) while the polycyclic strategy has short periods between infection and host death (high virulence). Further, host season length and the synchronicity at which hosts first become active during the season impact the optimal virulence level for both monocyclic and polycyclic parasites. These results demonstrate that there are multiple evolutionary solutions for parasites in seasonal environments which provides clues for the evolutionary origins of monocyclic and polycyclic parasites.

1 Model description

The model describes the transmission dynamics of a free-living, obligate-killer parasite that infects a seasonally available host (Figure 1). $\hat{s}(n)$ enter the system at the beginning of the season over a period given by the function $g(t, t_l)$. Hosts, s, have non-overlapping generations and are alive for one season. The parasite, v, must infect and kill the host to release new infectious progeny. The number of rounds of infection the parasite completes within a season depends on how quickly the parasite kills its host after infection. If there is a long period between infection and progeny release, the parasite is monocyclic and completes one round of infection per season. If there is a short period between infection and progeny release, the parasite is polycyclic

and can complete multiple rounds of infection per season.

The initial conditions in the beginning of the season are $s(0) = 0, v(0^+) = v(0^-) = \hat{v}(n)$ where $\hat{v}(n)$ is the size of the starting parasite population introduced at the beginning of season n determined by the number of parasites produced in season $n-1$. In some cases, the size of the emerging host cohort in season n, $\hat{s}(n)$, is constant. We also explore the impact of host carryover between seasons by assuming that $\hat{s}(n)$ is determined by the number of hosts that reproduced in season $n-1$. The transmission dynamics in season n are given by the following system of delay differential equations (all parameters are described in Table 1):

$$\frac{ds}{dt} = \hat{s}(n)g(t, t_l) - ds(t) - \alpha s(t)v(t), \tag{1a}$$

$$\frac{dv}{dt} = \alpha\beta e^{-d\tau} s(t-\tau)v(t-\tau) - \delta v(t). \tag{1b}$$

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. 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 upon host death. In some cases we assume that β is constant and in other cases we assume it is a function of τ, $\beta(\tau)$.

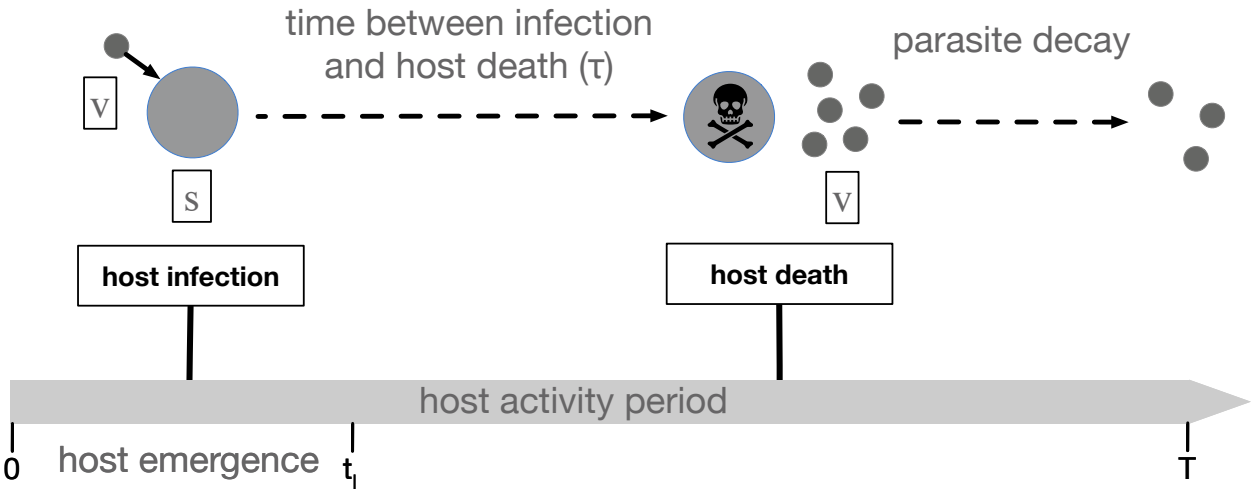

Figure 1: **Diagrammatic representation of the infectious cycle within each season.** All parasites (v) emerge at at the beginning of the season $(t = 0)$ while all hosts (s) emerge at a constant rate between time $t = 0$ and $t = t_l$. The rate of infection is density dependent such that the majority 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 post-infection releases parasite progeny (v) into the environment where they decay in the environment from exposure at rate δ. If τ is short enough, more than one generation of infections can occur within the season. Parasite progeny that survive in the environment to the end of the season comprise the parasite population that emerge in the following season $(v(T) = \hat{v}(n+1))$.

The function $g(t, t_l)$ is a probability density function that captures the per-capita host emergence rate by specifying the timing and length of host emergence. We use a uniform distribution $(U(\bullet))$ for analytical tractability, but other distributions can be used.

Parameter	Description	Value
s	susceptible hosts	state variable
v	parasites	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_l	length of host emergence period	time (varies)
T	season length	time (varies)
α	transmission rate	10^-8/(parasite $\times$ time)
β	number of parasites produced upon host death	200 parasites when constant
δ	parasite decay rate in the environment	2 parasites/parasite/time
d	host death rate	0.25 hosts/host/time
b	trade-off parameter	100
τ	time between host infection and host death (1/virulence)	time (evolves)
σ	host fecundity	500 hosts
ρ	density dependent parameter	0.0001

Table 1: Model parameters and their respective values.

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

t_l 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, $\hat{s}$. The host cohort emerges from $0 \leq t \leq t_l$. $\hat{s}(n)$ is either constant or a function of the number of uninfected hosts remaining in the system at $t = T$. v parasites remaining in the system at $t = T$ give rise to next season's initial parasite population ($\hat{v}(n) = v(0)$). Parasites that have not killed their host by the end of the season do not release progeny. Background mortality arises from predation or some other natural cause. We assume that infected hosts that die from background mortality do not release parasites because the parasites are either consumed or the latency period corresponds to the time necessary to develop viable progeny.[9,10]

In previous work on a similar model we derived an analytical expression for parasite fitness as the density of parasites at the end of the season, $v(T)$.[11] However we cannot solve system (1) in the current framework analytically, thus all results were found by performing numerical computations.

1.0.1 Between-season dynamics

To study the impact of the feedback between host demography and parasite fitness on parasite evolution we let the size of the emerging host cohort be a function of the number of uninfected hosts remaining at the end of the prior season

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

where 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.

1.0.2 Parasite evolution

To study how parasite traits adapt given different seasonal host activity patterns, we use evolutionary invasion analysis.[12,13] We first extend system (1) to follow the invasion dynamics a rare mutant parasite

$$\frac{ds}{dt} = \hat{s}g(t, t_l) - ds(t) - \alpha s(t)v(t) - \alpha_m s(t)v_m(t), \tag{2a}$$
$$\frac{dv}{dt} = \alpha\beta e^{-d\tau} s(t-\tau)v(t-\tau) - \delta v(t), \tag{2b}$$
$$\frac{dv_m}{dt} = \alpha_m\beta_m e^{-d\tau_m} s(t-\tau_m)v_m(t-\tau_m) - \delta_m v_m(t). \tag{2c}$$

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

The invasion fitness of a rare mutant parasite depends on the density of v_m produced by the end of the season ($v_m(T)$) in the environment set by the resident parasite at equilibrium density $\hat{v}^*$. The mutant parasite invades in a given host phenological scenario if the density of v_m produced by time T is greater than or equal to the initial $v_m(0) = 1$ introduced at the start of the season ($v_m(T) \geq 1$).

To study the evolution of virulence traits, we first assume all other resident and mutant traits are identical (*e.g.* $\alpha = \alpha_m$). 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 time between infection and when the parasite kills the host and releases new parasites is the rate that β new parasites are assembled.

In previous work on a similar model we also derived an analytical expression for mutant invasion fitness.[11] The invasion fitness of a rare mutant parasite depends on the density of v_m produced by the end of the season ($v_m(T)$) in the environment set by the resident parasite at equilibrium density $\hat{v}^*$. The mutant parasite invades in a given host phenological scenario if the density of v_m produced by time T is greater than or equal to the initial $v_m(0) = 1$ introduced at the start of the season ($v_m(T) \geq 1$). To find optimal virulence (τ^*) for a given host phenological scenario, we find the uninvadable trait value numerically that satisfies

$$\frac{\partial v_{2m}(T)}{\partial \tau_m}\Big|_{\tau_m=\tau_r} = 0$$
$$\frac{\partial^2 v_{2m}(T)}{\partial \tau_m^2}\Big|_{\tau_m=\tau_r} < 0$$

When we let $s(T)$ reproduce to determine next season's host cohort $\hat{s}$, we need to conduct simulations to determine the outcome of parasite adaptation. 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 $v_m(T)$ 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. We thus conduct simulations to verify that the evolutionary stable level of virulence is qualitatively the same as results when the emerging host cohort is constant each season and cycling cannot occur.

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 1000 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 1000 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.[14–16]

Results

Seasonal host activity drives both a monocyclic evolutionary optima and a polycyclic evolutionary optima separated by a repellor when parasites can complete multiple rounds of infection within a season (Figure 1). The monocylic strategy completes one round of infection per season by possessing a low virulence strategy that results in new parasite release close to the end of the season. The monocyclic strategy is adaptive because it minimizes environmental exposure of new progeny. The polycyclic strategy completes at least two rounds of infection per season by possessing a high virulence strategy. High virulence results in short periods between infection and new parasite release such that subsequent parasite generations have time to infect and release progeny before the end of the season. The optimal polycyclic strategy possesses a virulence level that releases the final generation of new parasites slightly before the end of the season. Parasites at the evolutionary repellor posses a moderate virulence level that falls between the virulence levels of the monocyclic and polycyclic optima. Moderate virulence parasites kill their host too quickly to minimize progeny decay in the environment but also do not kill hosts quickly enough to complete more than one round of infection during the season. The higher virulence, polycyclic strategy invade and replace populations of moderate virulence parasites by infecting remaining susceptible hosts before the second generation of moderate virulence parasites are released. Moderate virulence is thus a fitness minimum and an evolutionary repellor. The attractor that a population of parasites evolves towards is determined by their initial level of virulence, assuming mutation step sizes are small (Figure 2). The presence of an evolutionary repellor precludes evolutionary branching, *i.e.* parasite populations will not evolve towards moderate virulence and branch into strains with distinct virulence strategies.

A polycyclic parasite's fitness (end of season equilibrium density) is not equivalent to its invasion fitness when rare. Polycyclic parasites with high virulence invade and replace lower virulence polycyclic parasites despite the fact that the lower virulence strain reaches a higher equilibrium density. High virulence polycyclic parasites invade by quickly killing hosts and releasing new parasites after infection. The second generation of the high virulence polycyclic parasites then infect remaining susceptible hosts before the lower virulence polycyclic strain with a higher equilibrium density. Polycyclic parasites evolve the maximum biologically possible level of virulence by invading and replacing lower virulence parasites when there is no trade-off between transmission and virulence (in this model we arbitrarily set maximum virulence to $\tau = 1$). If there is a trade-off between transmission and virulence, the optimal virulence strategy balances the benefit of a competitive edge granted by high virulence with the cost of producing fewer new parasites per infection (see Figure 1).

Short seasons drive both the polycyclic and monocyclic optimums toward higher virulence (Figure 3). When seasons are short, there is less time between when parasites infect hosts at the beginning of the season

and the end of the season. Thus short seasons select for higher virulence so that new monocyclic parasites are released shortly before the end of the season. Similarly, higher virulence ensures enough time for multiple generations of infections for high virulence, polycyclic parasites. Short seasons thus drive the high virulence optimum towards higher virulence.

Short host emergence periods drive both the polycyclic and monocyclic optimums toward lower virulence (Figure 3). When the host emergence period is short, infections occur early in the season which drives both the polycyclic and monocyclic optimums towards lower virulence to position parasite-induced host death close to the end of the season. The strength of the impact of host emergence period length on parasite virulence for the two optima varies. When the host emergence period length is short, small increases in the emergence period drive large increases in virulence for the monocyclic optimum but only minor increases in virulence for the polycyclic optimum. In contrast, when the host emergence period is long, this trend is reversed: small increases in the emergence period drive negligible increases in virulence for the monocyclic optimum and large increases in virulence for the polycyclic optimum.

Environmental conditions, such as the length of the host emergence period, determine whether the monocyclic or polycyclic strategy is the global optimum (Figure 3). For example, the monocyclic strategy is the global optimum when the host emergence period is short. The fitness of the monocyclic strategy hinges on tight infection synchronization early in the season so that most new parasites are released near the end of the season. Monocyclic parasites thus reach high densities when the host emergence period is short. When the host emergence period is long, the polycyclic optimum is the global optimum instead. Infections are more spread out over time when the host emergence period is long. For the monocyclic strategy, asynchronous infections disrupt the ideally synchronous release of new parasites near the end of the season and instead results in many new parasites being released too early or not at all. By contrast, the polycyclic strategy is less reliant on perfect timing of early season infections. The progeny of polycyclic parasites that infect hosts early have time to complete another round of infection while the progeny of polycyclic parasites that infect hosts late are released close enough to the end of the season that not all decay in the environment. The polycyclic strategy is thus adaptive in environments with long host emergence periods.

Certain conditions destroy the bistability of evolutionary optima and instead preserve only one optimum (Figure 4). For example, there is no cost to remaining in the host for most of the season when host mortality is low. Few infections end from natural host mortality when host mortality is low which results in high parasite density. Incidence is high early in the season and there are few susceptible hosts available for a second generation of infections for high virulence parasites. Low virulence is thus the only viable evolutionary endpoint when host mortality is low. By contrast, when host mortality is high, it is beneficial to leave a host early who has a short life span. High virulence is thus the only viable evolutionary endpoint when host mortality is high.

A feedback between host demography and parasite fitness can generate periodic host-parasite dynamics as parasite virulence evolves (Figure 5). This qualitative change in dynamical behavior does not impact the result that either a polycyclic or monocyclic strategy evolves depending on the starting virulence level. However adaptation does proceed much more slowly when the dynamics are cycling.

variable ↑	impact on τ	global optimum	conditions for bistability
season length (T)	$\uparrow T, \uparrow \tau$	$\uparrow \tau$	probably only $\uparrow \tau$ for high T
emergence period length (t_l)	$\uparrow t_l, \downarrow \tau$	$\uparrow \tau$ for small t_l, $\downarrow \tau$ for large t_l	$\downarrow \tau$ only for large t_l
host mortality (μ)	$\uparrow \mu, \downarrow \tau$	$\uparrow \tau$ for small μ, $\downarrow \tau$ for large μ	$\uparrow \tau$ only for small μ, $\downarrow \tau$ only for large μ
decay rate (δ)	$\uparrow \delta, \downarrow \tau$	$\uparrow \tau$	$\uparrow \tau$ only for small δ
transmission rate (β)	$\uparrow \beta, \uparrow \tau$	$\uparrow \tau$	1 optimum for small β
trade-off parameter (b)	$\uparrow b, \uparrow \tau$	$\uparrow \tau$	1 optimum for small b

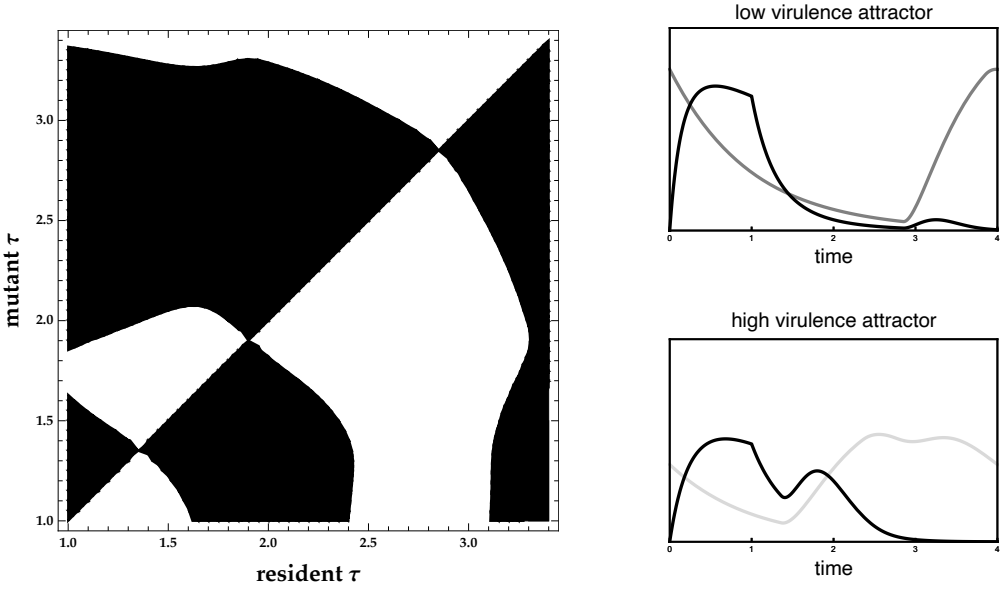

Figure 2: **Seasonal host activity generates multiple parasite virulence attractors.** Left panel: Pairwise invasibility plot (PIP) shows the outcome of mutant invasion. Mutants possess an adaptive virulence (τ) phenotype and invade in black regions while they possess a maladaptive virulence (τ) phenotype and go extinct in white regions. The PIP shows two evolutionarily stable strategy (ESS) at $\tau \approx 2.85$ and $\tau \approx 1.35$ that are attractive and uninvasible. A repelloing and invasible evolutionary repellor lies between the two ESS at $\tau \approx 1.9$. Right panel: The low virulence attractor ($\tau \approx 2.85$) releases new parasites just prior to the end of the season and is thus monocyclic. The high virulence attractor ($\tau \approx 1.35$) is polycyclic and completes at least two generations of infections during the season (two generations of infection for the parameter values shown here). $T = 4, t_l = 1, \beta(\tau) = b(\tau + 0.5)^{0.8}$, all other parameters in Table 1.

Discussion

Host phenological patterns govern parasite virulence and drive the evolution of diverse strategies. Host phenology drives parasites either towards a high virulence strategy that completes multiple rounds of infection within the season (polycyclic) or towards a low virulence strategy that completes one round of infection within the season (monocyclic). Both the monocyclic and polycyclic strategies are evolutionarily stable attractors across a range of phenological patterns. Between the two attractors is an evolutionary repellor. Parasite populations thus evolve towards the polycyclic attractor if they start out more virulent than the evolutionary repellor or towards the monocyclic attractor if they start out less virulent than the repellor. The exact host phenological pattern also drives a diverse range of parasite strategies due to its control of optimal virulence for both the monocyclic and polycyclic attractors. While host seasonality did not drive

the coexistence of diverse parasite strategies, these results predict that host seasonality could drive parasite diversity over geography.

The result that host seasonality drives parasites towards polycyclic or monocyclic evolutionary attractors provides clues on the evolutionary drivers of both strategies. The polycyclic strategy is adaptive as it allows parasites to complete multiple generations in a season. However the polycyclic strategy is potentially risky

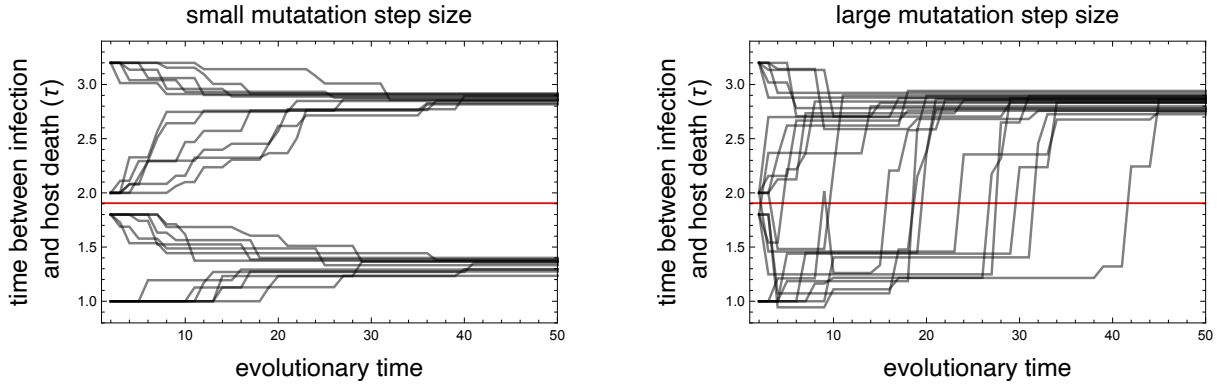

Figure 3: **Initial conditions determine which virulence attractor parasite populations evolve towards.** A repellor exists between the two attractors at moderate virulence around $\tau = 1.9$. If mutation step sizes are small, parasite populations with $\tau > 1.9$ evolve towards the low virulence, monocyclic attractor at $\tau \approx 2.85$ while parasite populations with $\tau < 1.9$ evolve towards the high virulence, polycyclic attractor at $\tau \approx 1.35$. If mutation step sizes are large, all parasite populations eventually reach the low virulence, monocyclic attractor as this is the global optimum 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 $\tau = 1$, respectively. Evolutionary time represents the number of mutants introduced into each system. In a random season after at least 1000 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.

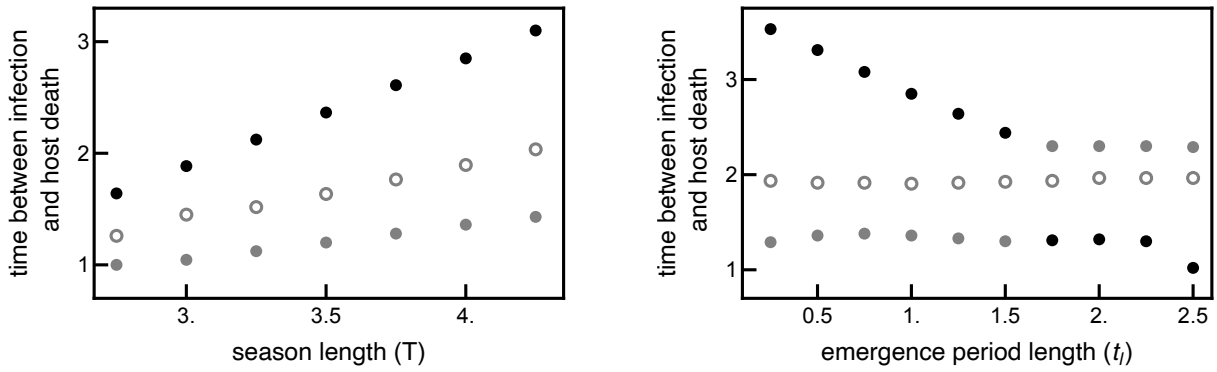

Figure 4: **Host phenology impacts parasite virulence optimums. A.** Longer seasons select for lower virulence. **B.** Higher emergence variability selects for higher virulence for both high and low virulence attractor impact of changing emergence period length is nonlinear. The strength t_l has on the respective attractors varies - increases in t_l when $t_l < 1.75$ results 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 $t_l > 1.75$. Black points mark global attractors, gray points mark local attractors and hollow points mark repellors. All other parameters are identical to those in Figure 1.

as it relies on there being enough susceptible hosts when later generations of parasites are released. The monocyclic strategy is adaptive because it it minimizes decay of new progeny in the environment by releasing new parasites slightly before hosts die at the end of the season. The monocyclic strategy is thus the safer strategy as long as the natural host mortality rate is low. Work by Hamelin et al. showed that host seasonality can drive coexistence between monocylic and polycyclic strategies if parasite evolution is constrained by a trade-off between within-season transmission and between-season survival.[6] In their study the monocyclic strategy has high between-season survival but low within-season transmission while the polycyclic strategy has high within-season transmission but low between-season survival. In our study, the timing of parasite release rather than an explicit trade-off drives the result that seasonality leads to bistability rather than the coexistence of polycyclic and monocyclic strategies. Nevertheless, our results and Hamelin et al. have some

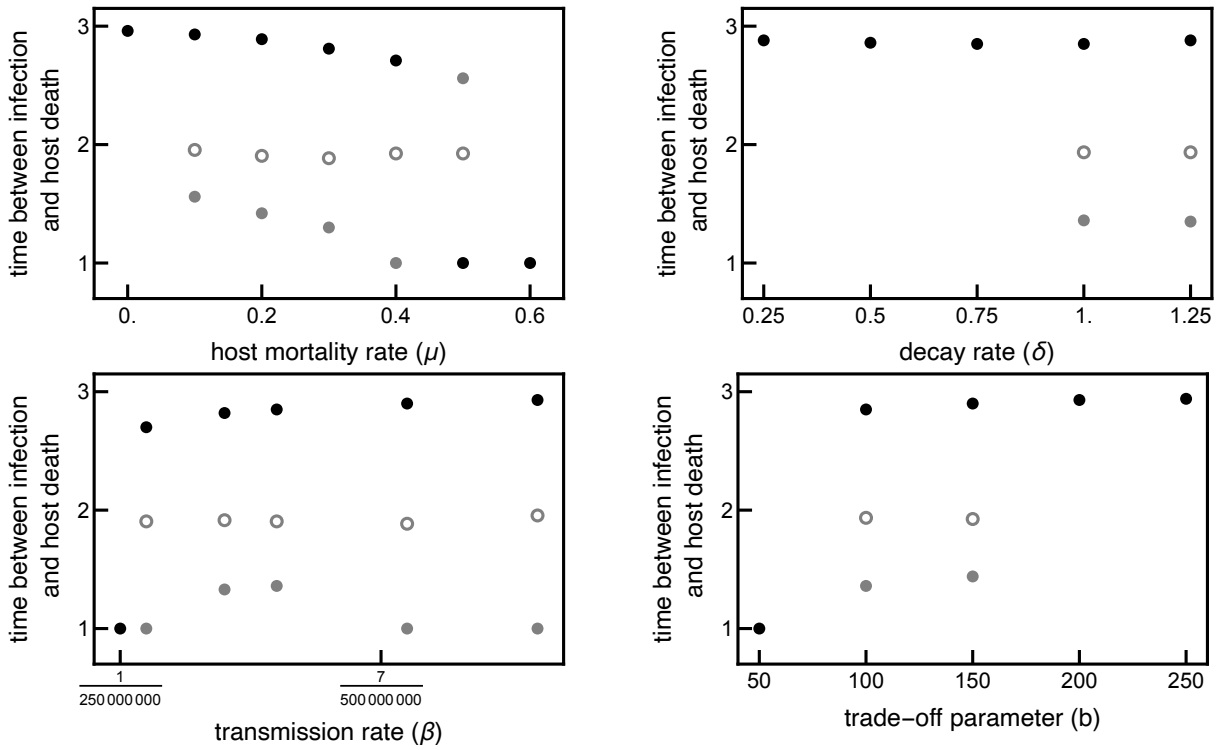

Figure 5: **Certain conditions can destroy bistability or switch the global optimum.** Parasite virulence attractors and repellors for changing: **A.** Host death rate, μ **B.** parasite decay rate, δ **C.** transmission rate, β **D.** trade-off parameter, b. **A.** Low natural host mortality, μ, drives high host densities and thus high early season incidence. High incidence early in the season selects for the low virulence, monocyclic strategy. High μ makes the high virulence, polycyclic attractor the global optimum as remaining in the 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 result in high early season incidence and thus drives both attractors towards 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. $T = 4, t_l = 1$. When a parameter is not changing, its value is the same as in Table 1.

similarities in that the monocyclic strategy evolves to decrease the impact of environmental exposure while the polycyclic strategy evolves to increase new infections.

Environmental conditions aside from host phenology can determine whether both polycyclic and monocyclic attractors exist. For example, the monocyclic strategy is the only evolutionary attractor in environments with low parasite decay rates. Low decay rates allow parasites to reach high densities. When parasite densities are high, infection incidence is high early in the season which drives the synchronous release of new parasites. Environments where new parasite release is tightly synchronized favors the monocyclic strategy as most parasites with this strategy are released slightly before the end of the season. In contrast, the negative impact of self-shading is high for polycyclic parasites when infection incidence is high early in the season. High early season incidence leaves few susceptible hosts for a second generation of parasites to infect which decreases the fitness of polycyclic parasites. Environments with low decay rates thus make the monocyclic strategy the only attractor which implies that these environments favors low virulence. This result deviates from the "Curse of the Pharoah" hypothesis which predicts that low parasite decay rates decrease the risk of leaving the host early which drives the evolution of high virulence.[18–20] In the current framework, seasonal host absence makes it advantageous for parasites to release new parasites near the end of the season. Low decay rates favor the low virulence monocyclic strategy over a high virulence polycyclic strategy.

Environmental conditions can also determine whether the polycyclic or monocyclic strategy has a competitive edge when both attractors exist. For example, the polycyclic strategy is the global optimum in environments where remaining in the host is risky, such as when hosts have a high natural mortality rate. Environments where host life expectancy is short are thus predicted to drive the evolution of high virulence polycyclic parasites. This result is in line with previous theory that predicts that high host mortality drives the evolution of high virulence.[21–24]

High parasite densities can drive cyclic host-parasite dynamics when the host population at the end of a

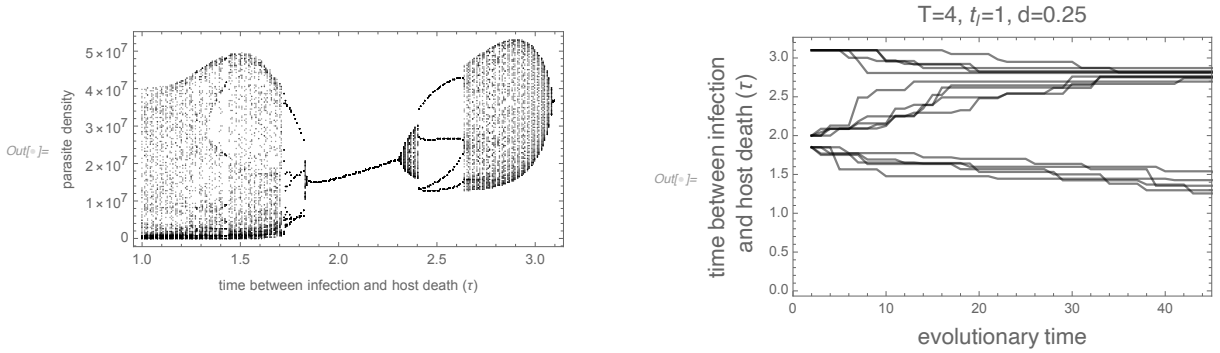

Figure 6: **Virulence evolution generates periodic dynamics when host populations carryover from one season to the next A.** Parasite density increases as the virulence phenotype approaches the time between infection and host death (τ) that maximizes parasite fitness.[17] Parasite populations can reach 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 ($t_l = 1$). Moderate virulence parasites ($1.85 < \tau < 2.3$) reach a stable equilibrium. The most fit parasites at high virulence ($\tau < 1.85$) and low virulence ($\tau > 2.3$) achieve densities that can disrupt dynamics and cause cycling. **B.** Periodic host-parasite dynamics do not qualitatively impact the evolutionary endpoints, *i.e.* high and low virulence attractors are separated by a repellor despite periodic dynamics. The same simulation analysis with small mutation step size was used as described in Figure 2. All other parameters are the same as Table 1.

given season produces the emerging host cohort the following season. Cycling does not qualitatively alter the result that either monocyclic or polycyclic parasite strategies evolve. These results are in line with previous work on a strictly monocyclic parasite where high parasite density drives cycling and cycling does not alter evolutionary endpoints when compared to a model without cycling.[11,17] While its not possible to solve the current model analytically, previous work on the similar model suggested that cycles are driven by a Neimark-Sacker bifurcation which is likely the case in the current model. In this study, cycling host-parasite dynamics could drive high virulence parasites extinct while maintaining low virulence parasite populations. Polycyclic parasites periodically have extremely low densities after reaching densities that drive cycling (Figure 6). Polycyclic strategies complete more rounds of infection within the season and are thus more exploitative of host populations. After the polycyclic strategy has driven dramatic decreases in host populations, there are not enough hosts to infect which drives parasite density to low levels. In nature, these polycyclic parasite populations would be at high risk for stochastic extinction. In contrast, when parasite populations evolve towards low virulence and drive cycling, their densities never approach extinction throughout the cycle. Thus in nature, high virulence parasites may be more likely to die out when cycling while low virulence parasites maintain safe densities that persist when cycling.

Several features of the current model can be altered to investigate more complex impacts of phenology on virulence evolution and parasite diversity. For example, relaxing the assumption that host populations reproduce once per season would likely favor the high virulence strategy. In the current model, the first generation of high virulence parasites in a season self-shades by killing too many hosts which results in few hosts remaining for the next generation of parasites to infect. Host reproduction throughout the season may reduce or eliminate the cost of self-shading and thus select for higher virulence. We will extend the current model to address this question in a future study.

The strict assumption that the parasites is an obligate host-killer can likely be relaxed without altering the result that phenology can drive the evolution of stable monocyclic or polycyclic strategies. For example, many parasites reduce host fecundity or increase the host death rate upon progeny release. Longer latency periods are equivalent to lower virulence in this type of system as infected hosts have more time to reproduce and thus higher fitness. Relaxing the obligate-killer assumption would not likely alter our results qualitatively as the same evolutionary pressures would act on the timing of parasite release. That is, releasing new parasites quickly (high virulence) or releasing parasites near the end of the season (low virulence) would likely both be viable strategies. Many parasite-host systems conform to the assumptions of this model extension such as soil-borne plant pathogens, demicyclic rusts, post-harvest diseases, and many diseases systems infecting univoltine insects.[25–28]

Host phenology drives the timing and prevalence of transmission opportunities for parasites[29–36] which further impacts parasite virulence evolution.[7,8,11,37,38] We add to this body of work by demonstrating that host phenology can also drive bistability in evolutionarily stable parasite strategies. These results show that seasonality can alter selection pressures on parasites and drive them either towards a monocyclic or polycyclic life cycle.

References

[1] David Tilman. Resource Competition and Community Structure.(MPB-17), Volume 17. Princeton university press, 2020.

[2] Arthur L Koch. Competitive coexistence of two predators utilizing the same prey under constant environmental conditions. Journal of Theoretical Biology, 44(2):387–395, 1974.

[3] Robert A Armstrong and Richard McGehee. Competitive exclusion. The American Naturalist, 115(2):151–170, 1980.

[4] Elena Litchman and Christopher A Klausmeier. Competition of phytoplankton under fluctuating light. The American Naturalist, 157(2):170–187, 2001.

[5] Christopher A Klausmeier. Floquet theory: a useful tool for understanding nonequilibrium dynamics. Theoretical Ecology, 1(3):153–161, 2008.

[6] Frédéric M Hamelin, Magda Castel, Sylvain Poggi, Didier Andrivon, and Ludovic Mailleret. Seasonality and the evolutionary divergence of plant parasites. Ecology, 92(12):2159–2166, 2011.

[7] Ian Sorrell, Andrew White, Amy B Pedersen, Rosemary S Hails, and Mike Boots. The evolution of covert, silent infection as a parasite strategy. Proceedings of the Royal Society B: Biological Sciences, 276(1665):2217–2226, 2009.

[8] Ruairi Donnelly, Alex Best, Andrew White, and Mike Boots. Seasonality selects for more acutely virulent parasites when virulence is density dependent. Proceedings of the Royal Society B: Biological Sciences, 280(1751):20122464, 2013.

[9] Ing-Nang Wang. Lysis timing and bacteriophage fitness. Genetics, 172(1):17–26, 2006.

[10] Nicholas J White. Determinants of relapse periodicity in plasmodium vivax malaria. Malaria journal, 10(1):1–36, 2011.

[11] Hannelore MacDonald, Erol Akçay, and Dustin Brisson. Host phenology can drive the evolution of intermediate parasite virulence in some parasites. bioRxiv, 2021.

[12] Johan AJ Metz, Roger M Nisbet, and Stefan AH Geritz. How should we define 'fitness' for general ecological scenarios? Trends in ecology & evolution, 7(6):198–202, 1992.

[13] Stefan AH Geritz, Géza Mesze, Johan AJ Metz, et al. Evolutionarily singular strategies and the adaptive growth and branching of the evolutionary tree. Evolutionary ecology, 12(1):35–57, 1998.

[14] Eva Kisdi. Evolutionary branching under asymmetric competition. Journal of Theoretical Biology, 197(2):149–162, 1999.

[15] Andrew White and Roger G Bowers. Adaptive dynamics of lotka–volterra systems with trade-offs: the role of interspecific parameter dependence in branching. Mathematical biosciences, 193(1):101–117, 2005.

[16] A White, JV Greenman, TG Benton, and M Boots. Evolutionary behaviour in ecological systems with trade-offs and non-equilibrium population dynamics. Evolutionary Ecology Research, 8(3):387–398, 2006.

[17] Hannelore MacDonald and Dustin Brisson. Host phenology regulates ecological and eco-evolutionary feedbacks underlying parasite-host demographic cycles. bioRxiv, 2021.

[18] Paul W Ewald. Host-parasite relations, vectors, and the evolution of disease severity. Annual Review of Ecology and Systematics, 14(1):465–485, 1983.

[19] Sebastian Bonhoeffer, Richard E Lenski, and Dieter Ebert. The curse of the pharaoh: the evolution of virulence in pathogens with long living propagules. Proceedings of the Royal Society of London. Series B: Biological Sciences, 263(1371):715–721, 1996.

[20] Troy Day. Virulence evolution via host exploitation and toxin production in spore-producing pathogens. Ecology letters, 5(4):471–476, 2002.

[21] R M Anderson and R M May. Coevolution of hosts and parasites. Parasitology, 85(Pt 2):411–426, 1982.

[22] Richard E Lenski and Robert M May. The evolution of virulence in parasites and pathogens: Reconciliation between two competing hypootheses. Journal of Theoretical Biology, 169:253–265, 1994.

[23] S Gandon, V A Jansen, and M Van Baalen. Host life history and the evolution of parasite virulence. Evolution, 55(5):1056–1062, 2001.

[24] VS Cooper, MH Reiskind, JA Miller, KA Shelton, BA Walther, JS Elkinton, and PW Ewald. Timing of transmission and the evolution of virulence of an insect virus. Proc Biol Sci, 269(1496):1161–1165, 2002.

[25] Elodie Gaulin, Christophe Jacquet, Arnaud Bottin, and Bernard Dumas. Root rot disease of legumes caused by aphanomyces euteiches. Molecular Plant Pathology, 8(5):539–548, 2007.

[26] Eldon I Zehr et al. Control of brown rot in peach orchards. Plant disease, 66(12):1101–1105, 1982.

[27] Ivan H Crowell. The hosts, life history and control of the cedar-apple rust fungus gymnosporangium juniperi-virginianae schw. Journal of the Arnold Arboretum, 15(3):163–232, 1934.

[28] J Holuša and K Lukášová. Pathogen's level and parasitism rate in ips typographus at high population densities: importance of time. Journal of Applied Entomology, 141(9):768–779, 2017.

[29] Arjen Biere and Sonja J. Honders. Impact of flowering phenology of silene alba and s. dioica on susceptibility to fungal infection and seed predation. Oikos, 77(3):467–480, 1996.

[30] Sonia Altizer, Andrew Dobson, Parviez Hosseini, Peter Hudson, Mercedes Pascual, and Pejman Rohani. Seasonality and the dynamics of infectious diseases. Ecology Letters, 9(4):467–484, 2006.

[31] Sarah A. Hamer, Graham J. Hickling, Jennifer L. Sidge, Edward D. Walker, and Jean I. Tsao. Synchronous phenology of juvenile ixodes scapularis, vertebrate host relationships, and associated patterns of borrelia burgdorferi ribotypes in the midwestern united states. Ticks and Tick-borne Diseases, 3(2):65–74, 2012.

[32] OJ Gethings, H Rose, S Mitchell, J Van Dijk, and ER Morgan. Asynchrony in host and parasite phenology may decrease disease risk in livestock under climate warming: Nematodirus battus in lambs as a case study. Parasitology, 142(10):1306–1317, 2015.

[33] Nicholas H Ogden, Genevieve Pang, Howard S Ginsberg, Graham J Hickling, Russell L Burke, Lorenza Beati, and Jean I Tsao. Evidence for geographic variation in life-cycle processes affecting phenology of the lyme disease vector ixodes scapularis (acari: Ixodidae) in the united states. Journal of Medical Entomology, 55(6):1386–1401, 2018.

[34] Micaela Elvira Martinez. The calendar of epidemics: Seasonal cycles of infectious diseases. PLOS Pathogens, 14(11):e1007327–15, 2018.

[35] Travis McDevitt-Galles, Wynne E Moss, Dana M Calhoun, and Pieter TJ Johnson. Phenological synchrony shapes pathology in host–parasite systems. Proceedings of the Royal Society B, 287(1919):20192597, 2020.

[36] Hannelore MacDonald, Erol Akçay, and Dustin Brisson. The role of host phenology for parasite transmission. Theoretical Ecology, 2020.

[37] Aaron A King, Sourya Shrestha, Eric T Harvill, and Ottar N Bjørnstad. Evolution of acute infections and the invasion-persistence trade-off. The American Naturalist, 173(4):446–455, 2009.

[38] Femke van den Berg, Nicolas Bacaer, Johan AJ Metz, Christian Lannou, and Frank van den Bosch. Periodic host absence can select for higher or lower parasite transmission rates. Evolutionary Ecology, 25(1):121–137, 2011.