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Research article

The impact of intrinsic and extrinsic factors on the epidemiology of male-killing bacteria

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Many arthropod species are vulnerable to infection by bacteria that kill the male offspring of their female hosts. These male-killing bacteria (MKB) can greatly impact the ecology and evolution of their hosts, particularly when MKB prevalence is high and persistent through time. However, we still do not have a holistic understanding of the key determinants of MKB ecological epidemiology, particularly regarding the interplay between host-MKB traits and environmental conditions. Here, we derived a mathematical model to analyse the role that several intrinsic and extrinsic factors play in determining MKB epidemiology, and how these factors interact with one another. We found that the invasion threshold and prevalence of MKB is determined by transmission rate and the rate at which female hosts recover from MKB infections. The invasion and prevalence of MKB is also highly sensitive to the extent that MKB can reduce intra-brood competition by killing male offspring. Environmentally-induced periodic changes to the epidemiological characteristics of MKB caused a sharp decline and a slow recovery of MKB prevalence and, in some cases, environmental disturbance can drive MKB extinct. Furthermore, the magnitude of the impact that environmental disturbance had on the dynamics of MKB prevalence was heavily modulated by intrinsic factors, particularly intra-brood competition. This is the first study to explore how both intrinsic and extrinsic factors interact to influence the dynamics of MKB infections over large timescales; our findings are central to predicting the current and future impacts of MKB on host populations.

Keywords: arthropod infections, bacteria, epidemiology, male killers, Spiroplasma, Wolbachia

Introduction

Infections caused by maternally inherited bacteria occur in at least 50% of arthropod species (Weinert et al. 2015, Sanaei et al. 2021). As these bacteria cannot be transmitted by males, males represent evolutionary 'dead ends' with the potential to hinder the fitness of their female siblings via costly competitive interactions (Engelstädter and Hurst 2009, Fea et al. 2014, Fisher et al. 2021). Thus, many maternally inherited

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bacterial species have evolved to kill the male embryos of their hosts, which is expected to increase female survival, presumably via reduced intra-brood competition (Werren et al. 1986, Jaenike et al. 2003, Engelstädter and Hurst 2009). These are known as male-killing bacteria (MKB).

The altered sex ratios caused by this removal of males can have wider effects on host populations. The evolutionary trajectory of host populations can be altered by the disruption of fundamental evolutionary processes such as sexual selection (Jiggins et al. 2000, Charlat et al. 2003). In addition, some studies propose that certain types of MKB infection can facilitate the evolution of haplodiploid reproductive systems (Normark 2004, Engelstädter and Hurst 2006). Sex ratio distortion driven by MKB infections can also lower adaptation rates in host populations by restricting genetic diversity and gene flow (Engelstädter and Hurst 2007). Although it's worth noting that in systems where individuals are already selected to produce female-biased sex ratios, as is often the case under local mate competition, the evolutionary impact of MKB may be weak (Hamilton 1967, Werren 1980). This is because the optimal sex ratio for the host and the MKB are likely to be more closely aligned than in panmictic systems where females are typically selected to produce even sex ratios (Macke et al. 2011). Moreover, in some heavily affected populations, MKB infections can create mate-finding Allee effects by reducing the availability of reproductive males in a population. While these Allee effects may have a negative impact on arthropod populations that are important for ecosystem functioning (Berec et al. 2007), the Allee effects created by MKB infections can also be used to control dangerous pest populations (Berec et al. 2016, Blackwood et al. 2018, Beebe et al. 2021). As well as the population-level impacts of male-killing, infection with MKB can directly affect a range of individual host fitness traits, from the ability to fight viruses to protection against parasitoids (Hedges et al. 2008, Oliver et al. 2014, Corbin et al. 2021).

The ability of MKB to infect hosts and persist within host populations varies greatly between different arthropod-MKB systems (Engelstädter and Hurst 2009). Understanding what drives this variation is crucial for predicting the long-term distribution of MKB and their future impact on host populations. Previous theoretical studies have found that MKB can only invade and persist in host populations when they confer a fitness benefit to their hosts, allowing them to outcompete uninfected individuals (Hurst 1991, Groenenboom and Hogeweg 2002, Jaenike et al. 2003, Berec et al. 2016). Several of these studies also found that a high vertical transmission rate (greater than ~60%) is required for MKB to invade a host population, and that the prevalence of MKB is positively associated with transmission rate. Consistent with this theoretical prediction, lab and field studies have revealed that natural MKB transmission rates vary between 72 and 100%, and transmission rates of 100% have been frequently observed (Majerus et al. 1998, Jiggins et al. 2000). Hence both theoretical and empirical studies suggest that high transmission rates are necessary if MKB infections are to spread through host populations.

The ability of MKB to infect host populations is also affected by temperature. Being poikilotherms, arthropods have limited ability to directly regulate their internal body temperature. Thus, the temperature variation experienced by microbes that reside within arthropods is heavily influenced by external conditions. As microbes, like all organisms, survive and reproduce within a certain temperature range, microbial infections in arthropods can be highly sensitive to environmental temperature fluctuations (Thomas and Blanford 2003). Indeed, many empirical studies have shown that MKB infections can be thermally-sensitive, such that both high and low temperatures can reduce vertical transmission rates leading to reduced MKB prevalence (Hurst and Jiggins 2000, Anbutsu et al. 2008, Corbin et al. 2021). As fluctuations in temperature are predicted to become more frequent and severe in the near future (Nijsse et al. 2019), a precise understanding of the link between temperature and MKB population dynamics is of particular importance.

Despite all we know about the drivers of MKB epidemiology, several important gaps remain in the literature. For example, while it is known that females are able to recover (i.e. transition from an infected to an uninfected state) from MKB infections (Li et al. 2014, Gunderson et al. 2020), it is not known how variation in recovery rate affects MKB population dynamics. Second, although MKB infections are known to be thermally sensitive, the impact of temperature on the long-term dynamics of MKB populations is not known. Finally, the potential interactive effects between temperature and the intrinsic determinants of MKB ecology have not been explored. In this study, we derive a mathematical model to predict the invasion and long-term persistence of MKB infections in host populations. We also use our model to examine the population dynamics of MKB in response to chronic and acute thermal disturbances.

Methods

The model

We derived a discrete-time deterministic population model with non-overlapping generations, representative of general seasonal invertebrates or tropical invertebrates with synchronised generations (Wolda 1988). Both infected (I) and uninfected (F) females have a maximum number of broods they can produce (a). We set a to a constant value of 10, which falls within the range of lifetime brood production observed across empirical arthropod studies (Ridley 1990, Arnqvist and Nilsson 2000). The proportion of females that produce a broods (P_a) is relative to the abundance of males (M) in the population such that (Eq.1):

$$P_a = \frac{M}{M + \varphi} \quad (1)$$

where φ scales the relationship between male abundance and female fecundity. Thus, when the value of φ is high, female fecundity is proportional to male abundance, as is the case in monogamous mating systems. Conversely, when φ is low, female fecundity is largely robust to changes in male abundance, as is often the case in polygynous mating systems with highly dispersive males. In this study, the value of φ, remained constant at five such that female fecundity was only sensitive to male abundance when there were relatively few males. As P_a is calculated independently of female abundance, the model assumes there is no female–female competition for males. Both infected and uninfected females produce β offspring per mating. Estimates of brood size vary wildly across arthropod species, with values ranging from 15 to > 1000 (Ridley 1988). Currently, there is not enough empirical evidence to calculate a reliable average brood size for arthropods. Thus, in this model, we set β at a constant value of 100, which represents an intermediate value based on the available arthropod fecundity data (Ridley 1988).

Infected females recover and join the uninfected population at rate θ. Infections are transmitted from infected females to their offspring at rate γ, and all infected male offspring die. Uninfected offspring produced by infected females join the uninfected population prior to mating. Broods produced by uninfected females have an even sex ratio.

Intrinsic offspring survival rate (r) is determined solely by intra-brood competition, such that when r is low intra-brood competition is high, and vice-versa. Thus, to simulate the release of resources that would otherwise be allocated to male offspring (Hurst 1991, Engelstädter and Hurst 2009, Berec et al. 2016), the intrinsic survival rate of broods produced by infected females (r_I) increases in proportion to the reduction of male siblings that occurs as a result of infection, giving (Eq. 2):

$$r_I = r + \left(1 - r\right)\frac{\gamma}{2} \tag{2}$$

To allow simulations of our model through time to be computationally manageable, it was necessary to prevent populations increasing to infinity. To limit population growth, offspring survival was made density-dependent and therefore decreases as the total population size increases. The full equations are therefore defined as (Eq. 3):

$$\begin{aligned} I_{t+1} &= aP_aI_t\left(1-\theta\right)\beta\gamma\frac{1}{2}\frac{r_I}{1+I_t+F_t+M_t} \\ F_{t+1} &= aP_a\left(F_t+I_t\theta\right)\beta\frac{1}{2}\frac{r}{1+I_t+F_t+M_t} \\ &\quad + aP_aI_t\left(1-\theta\right)\left(1-\gamma\right)\beta\frac{1}{2}\frac{r_I}{1+I_t+F_t+M_t} \\ M_{t+1} &= F_{t+1} \end{aligned} \tag{3}$$

Equilibria and stability

To simplify our mathematical analysis and obtain biologically meaningful solutions to our model, we transformed our original model by writing our equations in terms of the proportion of the female population that are infected with male-killing bacteria (μ), where $\mu = I/(I+F)$. Thus, the proportion of non-infected females is 1 − μ. As the abundance of males is assumed to be equal to that of non-infected females, the proportion of males relative to infected females is also defined as 1 − μ. By writing the model in this way, we were able to capture the relative dynamics of both the infected and non-infected population with a single variable (μ). Also, the density-dependent terms were removed from the model, as these only make sense when written in-terms of the absolute number of individuals, not proportions. The resulting transformed model can be written as the following single equation (Eq. 4),

$$\begin{aligned} \mu_{t+1} = \frac{a\frac{1-\mu_t}{\left(1-\mu_t\right)+\varphi}\mu_t\left(1-\theta\right)\beta\gamma\frac{1}{2}r_I}{a\frac{1-\mu_t}{\left(1-\mu_t\right)+\varphi}\mu_t\left(1-\theta\right)\beta\gamma\frac{1}{2}r_I} \\ + a\frac{1-\mu_t}{\left(1-\mu_t\right)+\varphi}\left(\left(1-\mu\right)+\mu\theta\right)\beta\frac{1}{2}r \\ + a\frac{1-\mu_t}{\left(1-\mu_t\right)+\varphi}\mu_t\left(1-\theta\right)\beta\left(1-\gamma\right)\frac{1}{2}r_I \end{aligned} \tag{4}$$

We calculated the equilibrium values (or 'fixed points') by solving the model for μ_t when $\mu_{t+1} = \mu_t$ before performing a Taylor expansion to analyse the stability of the equilibria. Specifically, to determine whether the equilibrium values of μ ($\hat{\mu}$) were locally stable, we calculated eigenvalues by differentiating the model with respect to μ_t and substituting the equilibrium value(s) for μ_t. These expressions for the eigenvalues were then set to one and simplified to find conditions under which the system was stable/unstable. For reliability and to check that our model transformations were biologically justified, our analytical solutions were compared to simulation output obtained from the original population equations (Eq. 3).

The sensitivity of $\hat{\mu}$

To determine how $\hat{\mu}$ varied, we plotted the non-trivial value of $\hat{\mu}$ with respect to the model parameters. To check that the results of our mathematical analysis were true to our original population equations (Eq. 3), we also ran simulations of our model over 100 generations. By running simulations under different parameter values, we graphically analysed how the absolute value of $\hat{\mu}$ varied with respect to γ, θ and r.

Simulating thermal† disturbance

Many arthropod infections are temperature sensitive (Thomas and Blanford 2003). Moreover, there is substantial evidence showing that infections caused by male-killing bacteria (MKB) are temperature sensitive, particularly regarding MKB transmission rate (Montenegro et al. 2005, Anbutsu et al. 2008, Corbin et al. 2021). To examine the impact of thermal disturbances on the population dynamics of MKB, we ran simulations in which after 50 generations γ was reduced and/or θ was increased. We compared the impact of chronic and acute thermal disturbance by altering the length of disturbance regime. To simulate a chronic disturbance, disturbances persisted for 500 generations or until the infected population went extinct, whichever came first. Note that throughout the paper, extinction refers to the death of all MKB infections, and not necessarily the hosts carrying those infections (as hosts can recover when $\theta > 0$). To simulate an acute disturbance, disturbance periods lasted for one or five generations, after which values of γ and θ returned to their original values. The most recent study investigating temperature sensitivity in MKB observed a ~40% reduction in transmission following a 3°C temperature change (Corbin et al. 2021). So that our main results follow the most up-to-date empirical findings, only the results of simulations in which the value of γ and/or θ changed by 0.4 in response to disturbance are displayed in the main text. However, we are aware that the effect of temperature is likely to vary across host and bacterial species (Anbutsu et al. 2008, Ross et al. 2020, Corbin et al. 2021). In addition, to the best of our knowledge there has been no formal quantification of how temperature affects the intra-generational recovery rate from MKB infections; thus, a narrow parametrisation of theta would be highly presumptuous. As such, to capture a broad range of possible scenarios, further simulation output in which the impact of disturbance caused the value of γ or θ to change by 0.2 or 0.6 are displayed in the Supporting information. It's also worth noting our model assumes that only MKB, and not hosts, are directly affected by thermal disturbance.

The impact of disturbance on the infected population was quantified in two ways depending on whether the disturbance was chronic or acute. The impact of chronic disturbances was quantified using the number of generations taken for the disturbance to drive the infected population to extinction. As a single acute disturbance is less likely to drive population to extinction than a chronic disturbance, the impact of acute disturbances was measured as the length of the post-disturbance recovery period of the infected population. Specifically, the recovery period is defined as the number of generations taken for μ to reach 90% of its value immediately prior to disturbance. To examine the extent to which the intensity of intra-brood competition (r) modulated the impact of disturbance on the dynamics of μ, the value of r varied between simulations.

Mathematical analyses were carried out using Maple (2021) (Maplesoft, a division of Waterloo Maple Inc., n.d.), simulations and graphical analyses were run in R (ver. 3.6.1) (<www.r-project.org>).

†We are aware that the impacts imposed on MKB infections by the disturbances simulated in this study may not be exclusive to thermal disturbances. However, we have defined our disturbances as thermal because temperature is the most commonly reported environmental driver of variation in the epidemiology of MKB infections.

Results

Invasion and long-term persistence

Our analysis showed that the following two solutions to the equilibrium $\mu_{t+1} = \mu_t$ are possible (Eq. 5):

$$\hat{\mu}\begin{cases} 0 \\ -\dfrac{\gamma r_I\left(\theta-1\right)+r}{\theta\left(r-r_I\right)-r+r_I} \end{cases} \quad (5)$$

As such, we can conclude that, in our model, infected females can go extinct or co-exist with uninfected females. However, as 1 is not a solution, it is impossible for infected females to reach fixation. This is intuitive given that infected females cannot produce infected males, and thus cannot reproduce in the absence of uninfected individuals. Further to this, we can conclude that the entire population will eventually go extinct due to a lack of males when females never recover from infection ($\theta = 0$), vertical transmission is 100% ($\gamma = 1$) and survival is greater in infected than uninfected offspring ($r_I > r$). In addition, we can see that the non-trivial equilibrium point is only dependent on θ, γ, r and r_I, meaning all other model parameters play no role in determining $\hat{\mu}$.

After simplifying the eigenvalue expressions (see Supporting information for the model derivative and full eigenvalue expressions), we found that the equilibrium at 0 is stable (i.e. male-killing bacteria cannot invade the host population) only when $r > r_I\gamma(1-\theta)$. Moreover, co-existence of infected and uninfected females is stable when $r > r_I\gamma(\theta - 1)$; thus, because r is always positive and $\theta - 1$ is always negative, co-existence is always stable. Stable co-existence of females infected with male-killing bacteria and uninfected females has also been found in previous studies (Hurst 1991, Engelstädter and Hurst 2007).

The results of our mathematical analysis matched those of our simulations (Fig. 1). We can therefore conclude that our transformed model (Eq. 4) is true to the assumptions of our original model (Eq. 3). The parameter space under which the invasion of infected females can occur is sensitive to female recovery rate (θ), vertical transmission rate (γ) and offspring survival rate (r). Furthermore, invasion can only occur when θ is low and γ is high; however, the extent to which θ and γ have to be low and high respectively is reduced as r decreases (Fig. 1).

Infection prevalence

The proportion of the female population infected with male-killing bacteria at the non-trivial equilibrium point (μ^*) was only dependent on recovery rate (θ), vertical transmission

rate (γ) and offspring survival rate (*r*). Thus, only model output in which we varied θ, γ and/or *r* is displayed.

Both our mathematical findings and simulation output confirmed that $\hat{\mu}$ was highly sensitive to variation in θ, γ and *r* (Fig. 2, Supporting information). Specifically, $\hat{\mu}$ was negatively related to θ and *r*, and positively related to γ (Fig. 2). $\hat{\mu}$ was slightly more sensitive to changes in γ than θ, so when values of γ are very high ($\gamma \approx 1$), the value of $\hat{\mu}$ is greater than when the value of theta is very low ($\theta \approx 0$) (Fig. 2). This also meant that μ more rapidly reached 0 as γ decreased compared to when θ increased (Fig. 1 and 2).

In addition to reducing the parameter space under which infected females could invade (Fig. 1), increasing *r* also had a strong negative effect on the value of $\hat{\mu}$ when μ was at nontrivial equilibrium (Supporting information). Variation in *r* modulated the relationship between θ, γ and $\hat{\mu}$ such that as *r* increased, the range of values for θ and γ for which $\hat{\mu} > 0$ shrunk; this effect was greater in θ than γ (visible as variation in the x-intercept in Fig. 2). Moreover, as *r* increased, the maximum of value of $\hat{\mu}$ that could be achieved by varying γ and θ was reduced (visible as variation in the y-intercept in Fig. 2). There was a subtle difference in how changes to *r* affected the maximum value of $\hat{\mu}$ with respect to γ and θ, with *r* having less of an effect on the value of $\hat{\mu}$ when γ was 1 compared to when θ was 0 (visible as variation in the y-intercept both within and between panels in Fig. 2).

The impact of thermal disturbance

The speed at which chronic temperature disturbances drove infected populations to extinction was positively related to the extent to which thermal disturbance reduced vertical transmission rate (γ) and increased female recovery rate (θ). In other words, extinction occurred more rapidly when thermal disturbances reduced γ and increased θ (Fig. 3). However, when disturbance-induced changes to γ and θ were very small, populations did not go extinct. Moreover, the parameter space under which extinction did not occur was heavily modulated by the survival rate of uninfected offspring (*r*). Specifically, as *r* increased, the range of parameters under which the infected population went extinct increased (Fig. 3).

Acute thermal disturbances caused the proportion of infected females in the population to decrease rapidly (Fig. 4). Unsurprisingly, disturbances that lasted five generations caused μ to decrease to a greater extent than those lasting only a single generation (Fig. 4). The impact of disturbance on the dynamics of μ was similar for disturbances that affected γ and disturbances that affected θ (Fig. 4), although the recovery period relative to the disturbance period was slightly higher for disturbances affecting γ (Fig. 5). When disturbances affected γ and θ, the length of the recovery period relative to the length of disturbance was far greater than when disturbances affected γ or θ (Fig. 3). Regardless of how disturbance affected γ and/or θ, the sensitivity of the relationship between the length of the disturbance period and that of the recovery period was heavily modulated by the value of *r* (Fig. 5). Specifically, as *r* increased, the positive relationship between disturbance and recovery period became more sensitive; this effect was particularly obvious when *r* increased from 0.3 to 0.5.

Discussion

In this study, we provide a robust theoretical analysis of how several intrinsic and environmental variables affect the ability of male-killing bacteria (MKB) to invade and persist within

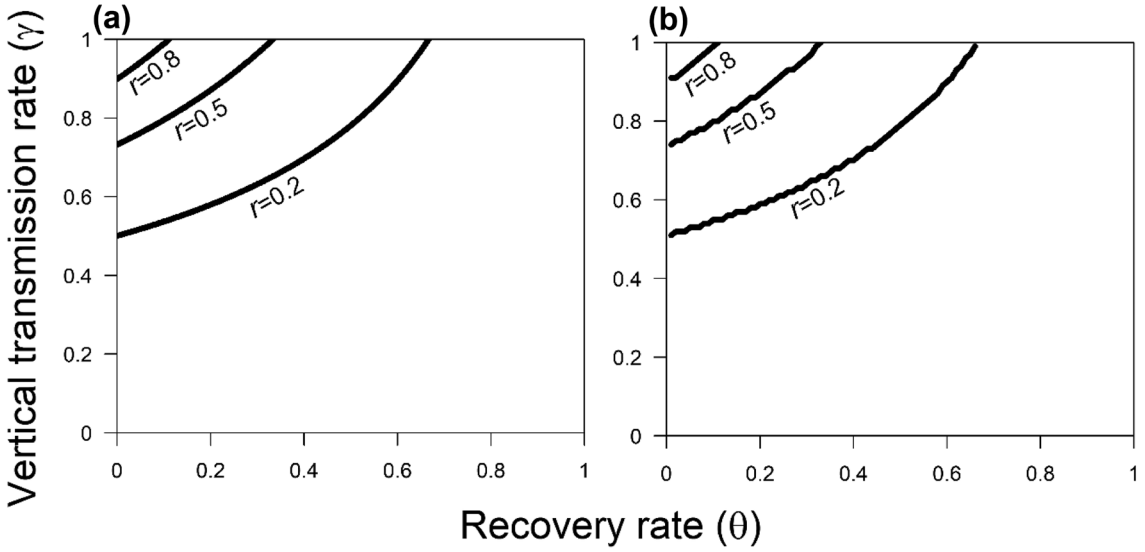

Figure 1. Thresholds for the invasion of females infected with male-killing bacteria into an uninfected population; areas above the curves represent the parameter space in which infected females can invade. For panel a, curves were generated by numerically calculating the parameter space in which the mathematical condition for invasion was satisfied. In panel b, curves were generated by running the original population equations (Eq. 3) for a range of θ and γ values for 1000 generations and identifying the parameter space under which infected females invaded. See Table 1 for other fixed parameter values.

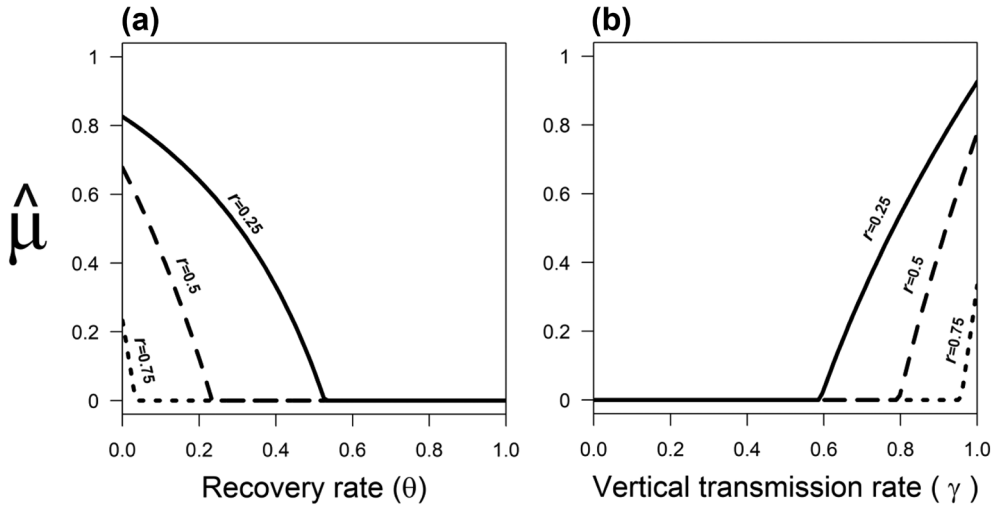

Figure 2. Variation in the non-trivial equilibrium point ($\hat{\mu}$) in response to variation in parameters θ, γ and *r*. (a) displays variation in $\hat{\mu}$ with respect to θ. (b) displays variation in $\hat{\mu}$ with respect to γ. In both panels, the solid, dashed and dotted lines refer to values of $\hat{\mu}$ when *r* was set to 0.25, 0.5 and 0.75 respectively. Default values for θ and γ are 0.1 and 0.9 respectively.

host populations. Consistent with previous theoretical work (Hurst 1991, Engelstädter and Hurst 2007) we found that MKB infections were always stable over time. Moreover, invasion success and MKB prevalence were both positively associated with vertical transmission rate and the extent to which MKB infections can increase host fitness. We also provide new insights by demonstrating that the rate at which hosts recover from MKB infection also has a strong positive effect on the invasion success and prevalence of MKB (Fig. 1 and 2). In addition, we provide the first theoretical insights into how the population dynamics of MKB are affected by environmental disturbances such as rapid temperature change. Specifically, we show that MKB infections can be eradicated from host populations under chronic thermal stress (Fig. 3), and that MKB prevalence can be slow to recover following acute thermal stress (Fig. 4). The survival rate of infected females relative to uninfected individuals is an important modulator of both the speed at which MKB is eradicated under chronic thermal stress, and the rate at which MKB prevalence recovers following acute thermal stress.

Our model contains multiple parameters that are known to influence host population dynamics in many species. We found, however, that whether or not MKB could invade a host population depended on three key parameters only:

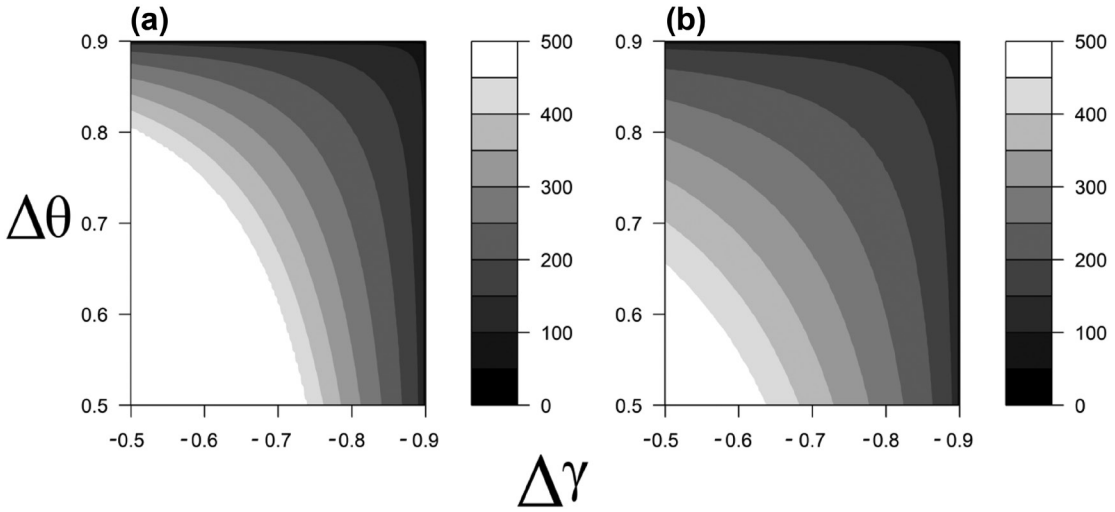

Figure 3. The impact of a chronic disturbance-induced change (Δ) in vertical transmission rate (γ) and recovery rate (θ) on the time taken for the infected female population to go extinct. Changes in γ correspond to a decrease, and changes in θ correspond to an increase. Simulations were run for 500 generations or until the infected population went extinct (μ = 0), whichever came first. As such, infected populations that did not go extinct within 500 generations were assumed to survive indefinitely. Levels of shading correspond to the number of generations taken for the infected population to go extinct after the disturbance is imposed. In each panel, the survival rate of uninfected offspring (*r*) varies between 0.1 and 0.5 in (a) and (b) respectively. Pre-disturbance values of γ and θ were 0.9 and 0.1 respectively.

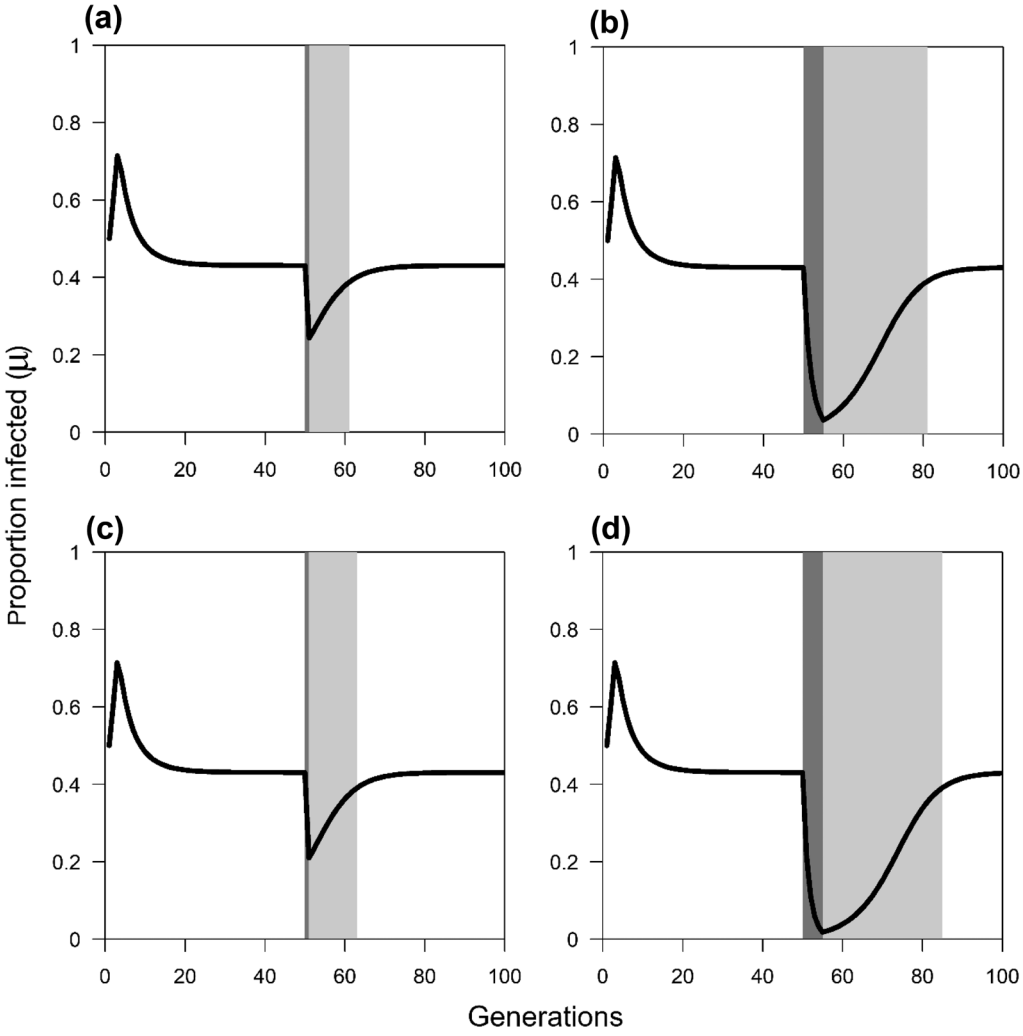

Figure 4. Simulation output illustrating how periods of disturbance affect the temporal dynamics of μ. In all panels, dark grey shading is used to highlight the duration of the disturbance and light grey shading is used to highlight the time taken for μ to recover to 90% of its value immediately prior to disturbance. Disturbance is defined as an increase in θ of 0.4 that lasts for a single (a) or 5 generations (b) or as a reduction in γ of 0.4 that lasts a single (c) or 5 generations (d). Default values of θ, γ and *r* are 0.1, 0.9 and 0.5 respectively.

1) vertical transmission rate of MKB, 2) the recovery rate of females with MKB infections and 3) the severity of intra-brood competition (Eq. 5, Fig. 1). As such, we can conclude that the invasion success of MKB is robust to variation in our other model parameters, i.e. the relative and absolute abundance of males and females, the number and size of broods produced by females, and the frequency at which reproductive individuals encounter one another. Given that the dynamics of MKB populations were only dependent on MKB traits or host traits directly affected by the presence of MKB, our results suggest that the success of MKB in host populations is largely independent of host population dynamics. This finding may help explain why MKB infections are found naturally across a range of arthropod hosts that differ vastly in their ecology (Weinert et al. 2015). Also, in clarifying the drivers of MKB ecology, our findings can inform the design of assessments used to determine whether or not a particular species of MKB will successfully infect a target host species; this may be particularly useful when MKB are to be artificially introduced to host populations, as is often the case when MKB are used for pest control (Berec et al. 2016, Ross et al. 2019).

Although our formal model analysis showed that the invasion and persistence of MKB was only determined by three parameters, the extent to which these parameters affected MKB ecology varied. Graphical analysis of our model showed that vertical transmission and recovery rate were similar in terms of the extent to which they affected MKB invasion success and prevalence. This is unsurprising, as although recovery and transmission affected the MKB prevalence in different age cohorts (i.e. recovery affects prevalence within a generation and transmission affects prevalence across generations), their impact on MKB prevalence within a given cohort is identical. By contrast, the offspring survival rate of infected broods was a much stronger determinant of the invasion success and prevalence of MKB than transmission rate or host recovery

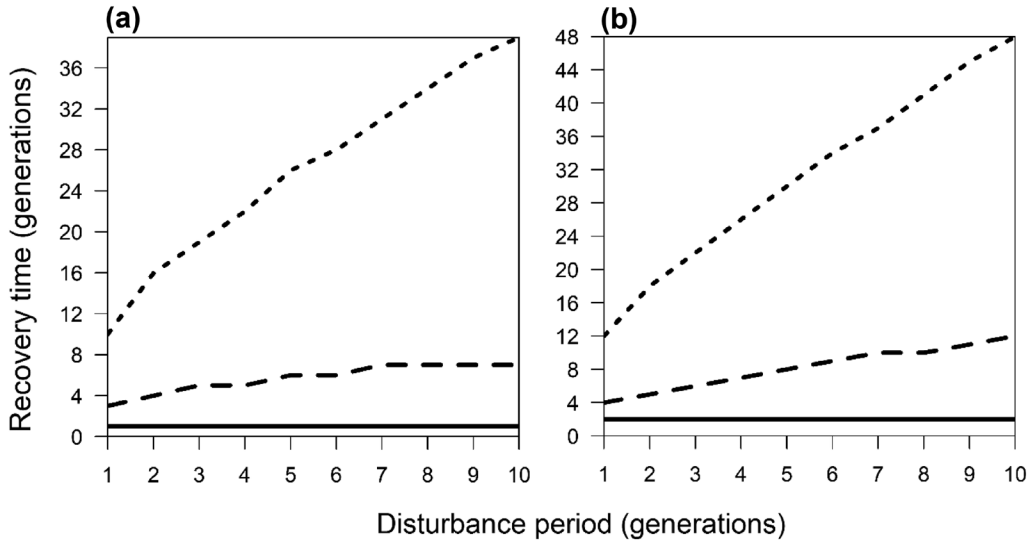

Figure 5. Simulation output illustrating the relationship between length of disturbance period and the time taken for the infected population (μ) to recover to 90% of it's pre-disturbance size. Solid, dashed and dotted lines show simulation output when $r = 0.1$, 0.3 and 0.5 respectively. (a) – disturbance is defined as an increase in θ of 0.4. (b) – disturbance is defined as a decrease in γ of 0.4. The default values for θ and γ are 0.1 and 0.9 respectively.

rate (Fig. 1, 2, Supporting information). This is likely due to the fact that our model assumed that offspring survival was determined solely by intra-brood competition, and that the survival of infected and uninfected offspring were intrinsically linked (Eq. 2). Therefore, reduced brood size caused by MKB infection directly improved the survival of infected broods relative to uninfected broods, and this relative survival benefit increased as intra-brood competition increased. As a result, infected females gained a competitive advantage over uninfected females. It is of course true that offspring survival in natural systems is almost certainly determined by more than just intra-brood competition. Nevertheless, while our model may overestimate the magnitude of the impact of intra-brood competition, our findings still suggest that MKB infections are much more likely to invade and persist at high prevalence in populations where intra-brood competition is intense. More importantly, this result is supported by previous work that experimentally demonstrated a positive association between intra-brood competition and *Wolbachia* prevalence (Jaenike et al. 2003). Our study builds on this finding by illustrating the importance of intra-brood competition for determining the long-term epidemiology of MKB, and how the effect of intra-brood competition co-varies with transmission and host recovery rate.

Numerous empirical studies have shown that microbial infections in arthropods can be temperature sensitive, both in terms of microbe transmission and host recovery (Blanford et al. 2000, Olsen and Hoy 2002, Thomas and Blanford 2003). However, the long-term population-level effects of temperature-induced changes to transmission rate and host recovery have not been explored. In this study, we found that both chronic and acute changes in vertical transmission and host recovery rate can reduce the long-term viability of MKB populations. Specifically, chronic reductions in vertical transmission and chronic increases in female recovery could drive MKB populations to extinction. Moreover, MKB populations were driven to extinction rapidly following large changes to transmission and/or recovery rate (Fig. 3). This is an important finding, as the time taken for an environmental stressor to drive a population extinct is an important predictor of natural extinction rates (O'Grady et al. 2004). In addition, MKB prevalence was slow to recover following acute changes in transmission rate or host recovery rate, and the length of the recovery period was dependent on the magnitude and duration of the disturbance (Fig. 4). When populations are slow to recover from an environmental disturbance, they are more likely to go extinct as a result of stepwise decline following repeated disturbances (Scheffer et al. 1995, Hörnfeldt 2004). Furthermore, as the population of infected individuals decreases in size, it will be more prone to extinction via stochastic events (Minayev and Ferguson 2009, Fisher 2021). As such, population recovery rate is likely to be an important predictor of long-term viability of MKB infections. Overall, these results illustrate the vulnerability of MKB infections to decline in the face global temperature change.

The impact that chronic and acute disturbances had on the viability of MKB populations was heavily modulated by intra-brood competition. Specifically, chronic disturbances were much more likely to cause the extinction of the infected population when intra-brood competition was high compared to when intra-brood competition was low (Fig. 3). Similarly, the length of time taken for MKB prevalence to return to normal following an acute disturbance was highly sensitive to changes in intra-brood competition (Fig. 5). In other words, in systems where offspring mortality is high due to intra-brood competition, MKB infections are much more likely to persist in the face of thermal disturbance. As mentioned earlier, these were driven by differences in the relative mortality rates of infected

Table 1. Model parameters and variables; definitions and canonical values.

Parameter	Definition	Value
a	The maximum number of broods a female can have	10
M	Number of reproductive males	0–∞
F	Number of uninfected reproductive females	0–∞
I	Number of reproductive females infected with male-killing bacteria	0–∞
μ	Proportion of females infected with male-killing bacteria	0–1
θ	Proportion of infected females per generation that recover from male-killer infection prior to mating	0–1
β	Number of offspring produced per brood	100
γ	Proportion of offspring per generation that inherit male-killing bacteria from their infected mother	0–1
r	Proportion of offspring per generation surviving intra-brood competition	0–1
φ	Scalar for the relationship between male abundance and female reproductive output	5

and uninfected offspring increasing as intra-brood competition increased (Eq. 2). Intra-brood competition over common resources is known to be a significant source of mortality for juveniles across a range of arthropod species, including fruit flies (Fisher et al. 2021), dragonflies (Hopper et al. 1996), earwigs (Dobler and Kölliker 2010), mantids (Fea et al. 2014) and spiders (de Tranaltes et al. 2022) to name but a few. Thus, our results may well be biologically plausible in suggesting that the extent to which MKB infections can provide relief from intra-brood competition is an important determinant of their long-term viability in response to temperature change. Future empirical work quantifying mortality driven by intra-brood competition in MKB hosts would be valuable for testing these model predictions.

As is the case with all theoretical modelling studies, our conclusions are not without caveats. For example, our model does not allow for evolution, and therefore cannot be used to predict potential evolutionary and co-evolutionary processes of MKB and hosts. Such processes could contribute to mitigating the increase in MKB extinction risk that occurs in response to chronic thermal stress. In addition, although our model allowed infected offspring to benefit from reduced intra-brood competition, it assumes that MKB infection does not incur any direct fitness benefits to the host by enhancing host traits. Laboratory studies have shown that some MKB infections have the potential to increase host fitness by boosting certain beneficial host traits such as immune function (Hedges et al. 2008, Cogni et al. 2021). These direct fitness benefits are likely to affect MKB ecology by providing infected hosts with a competitive advantage over uninfected individuals. Thus, our model may underestimate the fitness of infected individuals in some arthropod-MKB systems. Finally, two previous models (Groenenboom and Hogeweg 2002, Bonte et al. 2008) have shown that spatial structuring and host dispersal rates affect the long-term persistence of MKB populations. Local mate competition, which can occur in highly spatially-structured populations, may also affect the epidemiology of MKB infections. Our model is not spatially explicit and therefore cannot account for the potential impact of these processes.

Our model has shown the extent to which both intrinsic and extrinsic factors determine MKB ecology. Perhaps intuitively, vertical transmission and host recovery were important determinants of MKB ecology. However, perhaps less intuitively, our model showed that intra-brood competition was arguably the most fundamental determinant of MKB ecology. While previous models and an experimental study have shown that intra-brood competition is important for the initial invasion of MKB in host populations (Hurst 1991, Jaenike et al. 2003, Berec et al. 2016), ours is the first to demonstrate the relative importance of intra-brood competition for the long-term viability of MKB infections. Moreover, our study is unique in showing the long-term impact of temperature on MKB epidemiology, and how this impact is modulated by the intrinsic characteristics (particularly intra-brood competition) of hosts and MKB. Future empirical work quantifying how the interaction between temperature and host ecology affects MKB population dynamics would provide a valuable test of the predictions made by this model. Finally, it is worth noting that our results, particularly those regarding the persistence of infections in response to thermal disturbance, are not necessarily specific to MKB, and may have implications for other arthropod–bacteria systems.

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Author contributions

Adam M. Fisher: Conceptualization (equal); Formal analysis (lead); Methodology (lead); Writing – original draft (lead); Writing – review and editing (equal). **Robert J. Knell**: Conceptualization (equal); Methodology (supporting); Supervision (lead); Writing – review and editing (lead). **Thomas A. R. Price**: Conceptualization (equal); Writing – review and editing (equal). **Michael B. Bonsall**: Conceptualization (equal); Formal analysis (equal); Methodology (equal); Supervision (lead); Writing – review and editing (equal).

Data availability statement

There is no empirical data associated with this study, but the model analysis code (written and executed in Maple) can be found in the Supporting information.

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