Trends in
Ecology & Evolution

CellPress

Special issue: Symbiosis

Review

Symbiosis and host responses to heating

Tobias E. Hector,[1,2,@] Kim L. Hoang,[1,2] Jingdi Li,[1] and Kayla C. King[1,*,@]

Virtually all organisms are colonized by microbes. Average temperatures are rising because of global climate change – accompanied by increases in extreme climatic events and heat shock – and symbioses with microbes may determine species persistence in the 21st century. Although parasite infection typically reduces host upper thermal limits, interactions with beneficial microbes can facilitate host adaptation to warming. The effects of warming on the ecology and evolution of the microbial symbionts remain understudied but are important for understanding how climate change might affect host health and disease. We present a framework for untangling the contributions of symbiosis to predictions of host persistence in the face of global change.

Highlights

Organisms have evolved several ways to respond to heat stress. How symbionts mediate the ability of hosts to cope with warming temperatures and thermal extremes will be crucial in determining their responses in the face of global heating.

Through directly damaging hosts or by being energetically costly, parasites can substantially reduce the ability of their host to survive thermal stress.

Mutualistic symbionts conferring thermal tolerance impact on hosts from the molecular to the population-level scale, and can alter host evolutionary trajectories under stressful temperatures. Conversely, thermal stress can weaken host–symbiont interactions and communities and disrupt host microbiomes.

Symbiosis in a warming world

Parasitic and mutualistic **symbioses** (see Glossary) are widespread in nature. These interactions can occur when microbes (i.e., bacteria, fungi, and viruses) colonize host organisms and cause damage or confer advantages to the host. Symbioses between hosts and microbes can exist along a parasite–mutualist continuum [1]. **Mutualists** can increase host fitness by providing resources that are lacking in the environment [2], thereby influencing host immune development and responses [3], or by directly eliminating enemies [4,5]. These benefits can help hosts to occupy otherwise unsuitable niches [6] and can considerably impact host adaptation to stress [7–9]. Conversely, **parasites** (including pathogens) exploit host resources, and in doing so cause harm. The harm parasites inflict upon hosts, termed **virulence**, can be wide-ranging but commonly manifests via increases in host mortality or reductions in fecundity [10–12]. Parasites can also impact host responses to abiotic stress, but the magnitude and direction of these effects can depend on the system and type of stress [13,14]. Host thermal traits are similarly shaped by symbionts, and these outcomes are particularly pressing to tackle as temperatures escalate worldwide.

Managing the impacts of climate change is one of the biggest challenges of the 21st century. Average temperatures are rising, and an increase in environmental variability is predicted to escalate extreme climatic events such as heatwaves, causing thermal stress or even heat shock. Extreme heat has consequences at all levels of biology, including physiology [15], behavior [16], and evolution [17,18]. Organisms in turn have evolved several ways to respond to heat stress, from the expression of heat-shock proteins to DNA damage repair systems [19]. Epigenetic responses to warming can even be passed on to offspring [20,21] and influence the adaptive potential of subsequent generations.

A key aspect of an organism faced with warming is their **thermal safety margin** [22–24]. This margin is the difference between the **upper thermal limit** of an individual and the maximum environmental temperature they experience. Thermal safety margins therefore determine the capacity of an individual to cope with warming temperatures and thermal extremes. How symbionts mediate the thermal safety margins of individuals will therefore be crucial in determining how populations will respond in the face of global climate change [25].

[1]Department of Zoology, University of Oxford, 11a Mansfield Road, Oxford OX1 3SZ, UK
[2]Equal contributions and in alphabetical order

*Correspondence:
kayla.king@zoo.ox.ac.uk (K.C. King).
@Twitter: @kaylacking (K.C. King), @toby_hector (T.E. Hector).

We explore the influence of being in symbiosis with microbes, for better or worse, on host responses to heating stress (Figure 1) and on the persistence of host populations. We discuss all microbial symbionts (parasites and mutualists alike) from viruses to fungi in hosts ranging from microbes to animals and plants.

Symbioses can impair host responses to heat

Parasites can substantially impair the response of their host to heating (Box 1 and Table 1). Infection can reduce the thermal safety margin of the host [26,27], and reductions of over 2°C are not uncommon [25]. Indeed, infection can alter the thermal performance curve of the host [28]. However, these

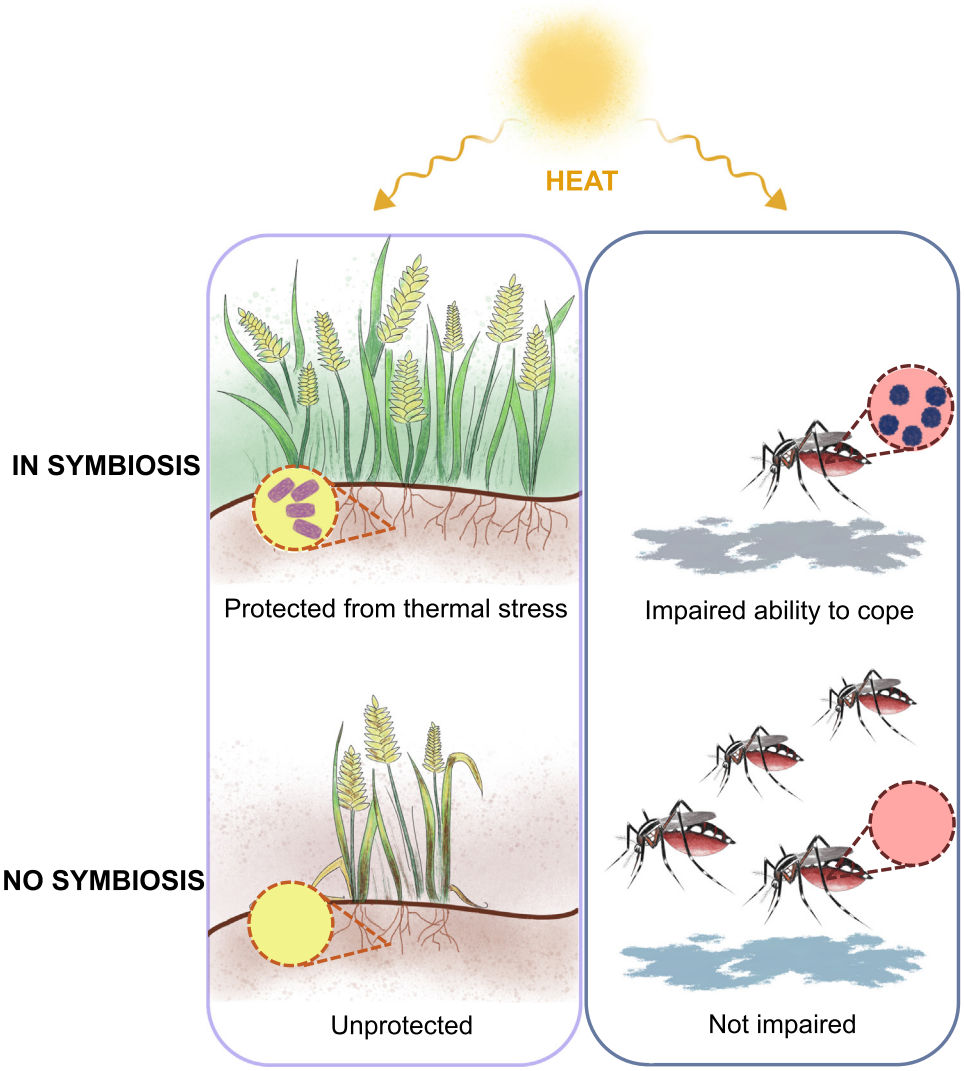

Figure 1. Symbiotic relationships with microbes and consequences for host fitness during heating. Hosts can be protected from thermal stress in their associations with microbes (outlined in purple) (e.g., *Enterobacter* spp. on wheat roots protects plant hosts from warmer temperatures [105]). Alternatively, colonization by microbes can reduce the thermal tolerance of hosts (outlined in blue) (e.g., dengue virus can impair mosquito vector thermal response [47]). These symbioses thus have the potential to impact host populations in the context of heating.

Glossary

Coevolution: reciprocal selection between interacting species leading to coadaptations.
Experimental evolution: experimental approach whereby populations are evolved under controlled conditions.
Holobiont: a host and its associated microbes.
Microbiome: the community of microorganisms residing in/on a host.
Mutualists: organisms that confer a reciprocal benefit to their host.
Parasites: organisms that exploit host resources and cause harm to the host.
Symbiosis: an association between two dissimilar organisms that have some degree of physical association, which is potentially long-lasting, regardless of the implications for the fitness of either organism.
Thermal mismatch hypothesis: a hypothesis which predicts that infection outcomes will depend on the degree of mismatch between the thermal performance curves of a host and a parasite.
Thermal safety margin: the difference between the upper thermal limit of an organism and the maximum environmental temperature.
Upper thermal limit: the maximum temperature at which an organism can remain physiologically active, often measured as CT_{max}.
Virulence: the reduction in host fitness caused by a parasite during infection.

responses are not straightforward. Parasites can differentially impact male and female responses to warming (Box 1) [29], and such sex-specific effects could have consequences for population growth and persistence. The response of a host to warming also will not depend solely on the direct damage caused by infection. Immune and heat-shock responses may allow infected hosts to extend their thermal safety margins or counteract some reduction in heat resistance caused by infection [30–32]. In addition, there may be tradeoffs between the ability of the host to tolerate

Box 1. *Daphnia*–parasite interactions under shifting temperatures: a model for studying the intersection between global change and disease

Daphnia crustaceans makes an ideal case study for answering these questions because (i) the impact of changes in average temperatures and warming on infection, disease outcomes, and pathogen transmission are well studied, (ii) there is natural variation in thermal limits across a vast geographic cline of populations, and (iii) data are available on the impact of infection on thermal limits (across both genotypes and the sexes).

Daphnia can be infected by various parasites (i.e., the bacterial parasite *Pasteuria ramosa* and the fungal parasite *Metschnikowia bicuspidata*; Figure I). Shifts in temperature are known to alter host susceptibility to infection, the virulence of parasites that establish an infection, and within-host parasite loads [106,107]. Warmer temperatures can lead to changes in the timing and size of disease epidemics within Daphnia populations [108,109]. Temperature is also key in determining the success of specific parasite genotypes, and this could have implications for coevolution in changing environments [106]. For *M. bicuspidata,* warming can increase spore infectivity, but can also increase host exposure via increases in foraging rate, leading to the potential for increased transmission [108,109]. Conversely, hot temperatures may also limit parasite transmission and dampen epidemics by decreasing the infectivity of parasite spores during subsequent transmission [110].

Although temperature is important for the outcome of infection and disease dynamics in *Daphnia*, recent work has shown that parasitism can fundamentally alter *Daphnia* thermal performance. Populations display considerable local adaptation in their thermal tolerance, and populations from warmer environments are more resistant to thermal stress than those from cool environments (Figure IIA) [86]. Infection with *P. ramosa* can reduce the thermal tolerance of female *Daphnia* (Figure IIB) [27]. Reductions are of equal magnitude to the variation seen across the entire geographic range of the species (Figure IIA,B) [25,27].

Finally, sexual dimorphism in thermal tolerance is common across species. However, in *Daphnia* infected with *P. ramosa*, female thermal tolerance is disproportionately impacted by infection (Figure IIC) [29]. This outcome could have serious implications for how host populations respond to changing environments if the sex that is most impacted by infection is also the one on which population growth is most dependent [25,29].

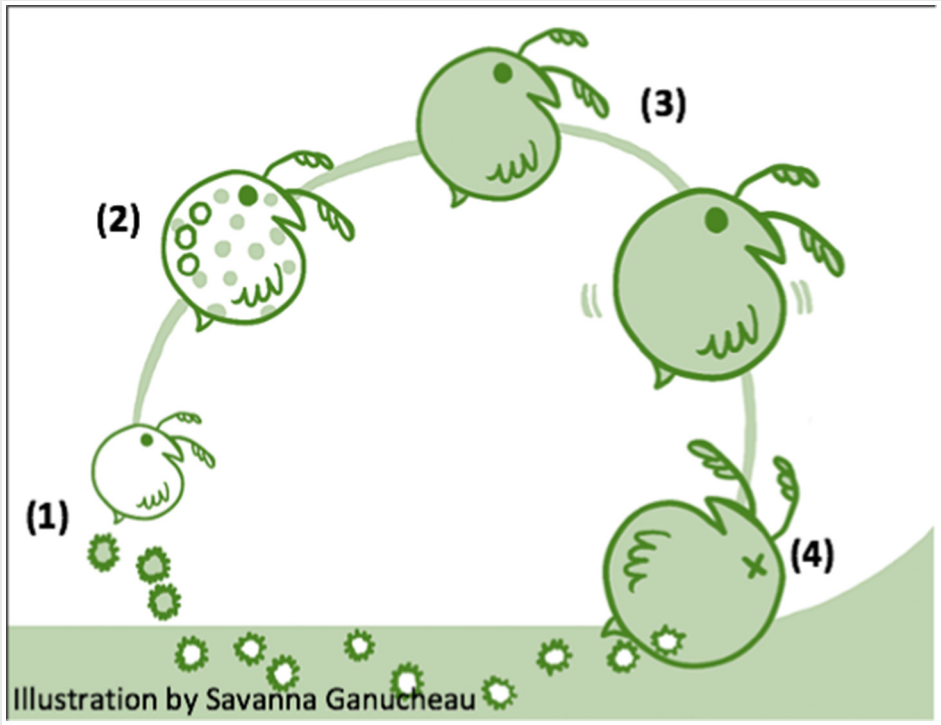

Figure I. *Daphnia* are cyclically parthenogenic crustaceans. Individuals reproduce clonal daughters, but also genetically identical males under stressful conditions, allowing sex to occur. Two parasites, *Pasteuria ramosa* and *Metschnikowia bicuspidate*, follow similar infection patterns: (1) *Daphnia* hosts pick up parasite transmission stages during feeding, (2) parasites able to traverse the esophagus or gut wall enter the body and replicate, (3) parasite replication leads to reduced fecundity and lifespan, (4) parasite-induced mortality occurs, at which point transmission stages are released into the environment to infect another host. Males and females are both impacted by infection, but females often represent a greater resource to parasites and experience greater virulence [29]. Except for the ability of these parasites to traverse host tissues, all stages are sensitive to temperature change.

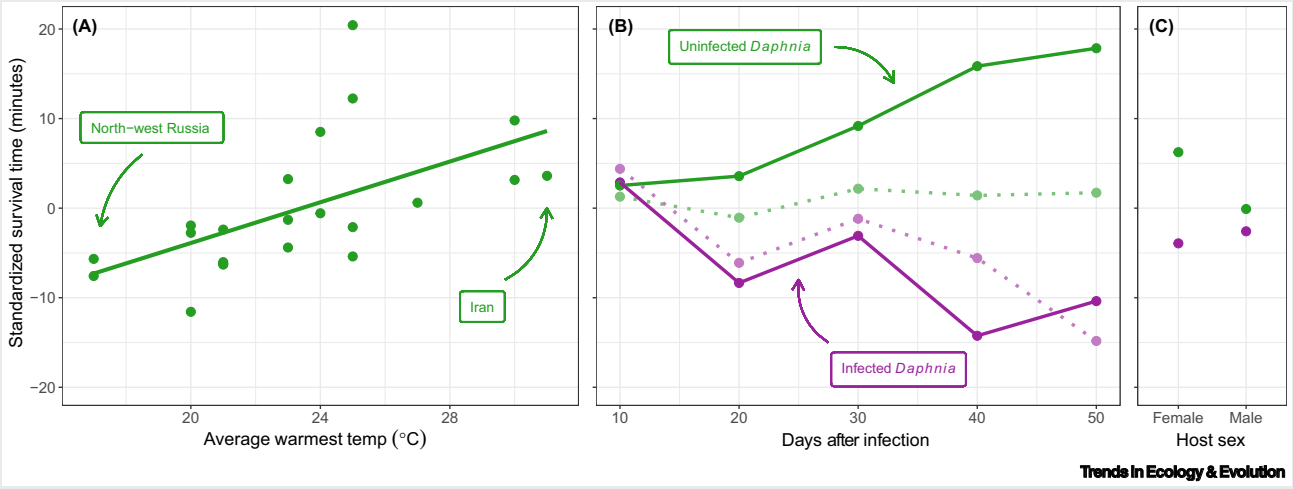

Figure II. *Daphnia* tolerance to heat stress and the impact of parasitism. All data are from measures of *Daphnia magna* thermal tolerance (survival time) under 37°C heat shock standardized to a mean of zero to aid comparison across studies. (A) Thermal tolerance of 22 female *Daphnia* genotypes from across a large geographic gradient, showing the intraspecific variation in heat tolerance across locally adapted populations (data from Yampolsky *et al*. [86]). (B) Infection with *Pasteuria ramosa* reduces female heat tolerance, which becomes more exaggerated as infection progresses. Shown are two *Daphnia* genotypes (unbroken and broken lines) either uninfected (green) or infected (purple) with *P. ramosa*, displaying genotype-specific variation (data from Hector *et al*. [27]). (C) Female *Daphnia* heat tolerance is more sensitive to *P. ramosa* infection compared to males, which erases sexual dimorphism (data from Laidlaw *et al*. [29]).

both thermal stress and infection [27]. Such trade-offs could lead to complex and unpredictable outcomes for host populations at ecological and evolutionary scales [30].

Parasites can impair host survival by reducing their upper thermal tolerance [25]. Infection may also interact with thermal stress to alter other important thermally dependent host traits. Recent work has shown that the thermal limits of fertility may be important for determining how host populations respond to heating [33,34]. Fertility is an important host trait because it is integral to population growth, but the thermal limits for fertility are likely much lower than thermal limits of survival [35]. It is therefore possible that species distributions are tightly regulated by the thermal limits of fertility, and, under scenarios of global change, many populations may be at greater risk of extinction than currently predicted by thermal limits of survival [33,34]. Importantly, however, parasite virulence often results in reductions in host fecundity or fertility [36]. Hotter temperatures may exaggerate this detrimental impact of infection on host reproductive ability ([37,38], but see [39]). If widespread, infected host populations may be at greater risk from warming.

The **thermal mismatch hypothesis** predicts that the degree of mismatch between the thermal limits or thermal performance of a host and parasite will determine the risk and outcome of infection [25,40,41]. Cool-adapted hosts faced with warm-adapted parasites are predicted to be at greater risk to succumbing to infection when their environment becomes warmer and vice versa. The thermal mismatch hypothesis can explain how susceptible hosts will fair when faced with parasites. However, by altering the response of the host to thermal stress and shifting the shape of their thermal performance curve, a parasite may also change the degree of thermal mismatch [25]. This could have substantial consequences: from mediating the outcome of infection to altering disease dynamics and the distributions of hosts and parasites as thermal environments change [25,30].

The dual stressors of infection and heating might also impact host evolutionary potential [25]. It is unclear to what extent many populations possess the genetic variation in thermal performance to

Table 1. Examples of parasitic symbionts and their effect on host thermal tolerance

Host	Parasite	Trait	Impact of infection	Refs
Mosquito (*Aedes aegypti*)	Dengue virus	Heat-shock survival	Decrease	[47]
Mosquito (*Aedes aegypti*)	*Wolbachia* symbiont	Heat-shock survival	Decrease	[47]
Daphnia	Bacteria (*Pasteuria ramosa*)	CT_{max}	Decrease	[27]
Daphnia	Bacteria (*Pasteuria ramosa*)	Heat-shock survival	Decrease	[27]
Frog (*Litoria spenceri*)	Fungus (*Batrachochytrium dendrobatidis*)	CT_{max}	Decrease	[26]
Crab (*Eurypanopeus depressus*)	Rhizocephala (*Loxothylacus panopaei*)	Survival	Decrease	[28]
Marine snail (*Zeacumantus subcarinatus*)	Trematode (*Maritrema*)	CT_{max}	Increase	[118]
Marine snail (*Zeacumantus subcarinatus*)	Trematode (*Philophthalmus*)	CT_{max}	Decrease	[118]
Newt (*Notophthalmus viridescens*)	Fungus (*Ichthyophonus*)	CT_{max}	Decrease	[119]

permit adaptation to further warming [42–44]. Most studies find that populations are largely constrained in their capacity to extend their thermal limits, although evidence for the mechanisms behind these constraints is mixed [42,45]. Stressful environments may hold the key for adaptation to heating if they promote the expression of cryptic genetic variation for thermal resistance traits [46]. Whether infection, as a source of host stress, further constrains or promotes genetic variation for host thermal limits could be crucial in determining whether host populations can adapt to heating [25].

An important question for human health is how infection with viruses impacts the thermal performance of vectors. Ware-Gilmore *et al.* [47] have shown that infection with dengue virus can reduce the thermal tolerance of its mosquito vector, *Aedes aegypti*. Huge effort is currently being focused on finding ways to control the transmission of mosquito-borne human diseases. One promising area has been to use the bacterial symbiont *Wolbachia pipientis* [48]. *Wolbachia*, although not a natural symbiont of mosquitoes, has been found to be effective at reducing viral titers within dengue-infected mosquitoes, hampering ongoing viral transmission [49]. *Wolbachia*-infected mosquitoes have been released into natural populations [50]. However, *Wolbachia* infection can reduce vector thermal tolerance, equal to the effect of dengue virus itself and of coinfection [47]. The sensitivity of mosquito thermal limits to these symbioses could affect the success of virus vector biocontrol programs under future heating.

Symbioses can protect hosts from heat

Impacts of single symbiont species

Host-associated microbes can protect their hosts from a variety of environmental stresses such as toxins, desiccation, salinity, and temperature [51–53]. Symbionts can increase host tolerance to high temperatures via different mechanisms, ranging from increasing the expression of host stress-response genes to producing protective metabolites (Table 2). By increasing host upper thermal limits, symbionts can improve host population growth and niche expansion. For example, 'fire-associated' fungi (*Morchella*) have been hypothesized to help cheatgrass (*Bromus tectorum*) invade western North America [54]. Such protection can also have an impact beyond the host

Table 2. Examples of symbiont-conferred heat-protection mechanisms

Host	Symbiont	Mechanism	Refs
Coral (*Acropora millepora*)	Algae (*Symbiodinium*)	Dominance by clade-specific thermotolerant algae	[120]
Caenorhabditis elegans nematode	Bacteria (*Lactobacillus gasseri*)	Upregulation of oxidative stress response genes (pathways also involved in lifespan extension and immunity)	[121]
Pea aphid (*Acyrthosiphon pisum*)	Bacteria (*Serratia symbiotica*)	Release of metabolites facilitated by bacterial cell lysis from heat shock	[74,92]
Tropical panic grass (*Dichanthelium lanuginosum*)	Fungus (*Curvularia protuberata*), *Curvularia* thermal tolerance virus	Host–fungus interaction confers thermotolerance to both partners, which is effectively eliminated in the absence of the viral symbiont of the fungus	[122]
Wheat (*Triticum durum*)	Bacteria (*Enterobacter*)	Upregulation of heat-shock memory genes	[105]
Whitefly (*Bemisia tabaci*)	Bacteria (*Rickettsia*)	Induction of stress-response genes at benign temperatures, priming hosts for heat stress (even though higher temperatures reduce symbiont titer)	[75]

and symbiont species. The barley yellow dwarf virus increases the thermal tolerance of its vector, the bird cherry-oat aphid (*Rhopalosiphum padi*), allowing the aphid to occupy warmer regions of the plant host and escape competition from a larger aphid species [31]. Association with thermal tolerance-conferring symbionts may mitigate declines in host performance from temperature increases.

Field experiments with pea aphids (*Acyrthosiphon pisum*) harboring heat-protecting symbionts have also shown that these hosts have higher population growth rates than hosts lacking these symbionts, suggesting that adaptation to heat stress may be facilitated by symbionts [55]. Similarly, *Caenorhabditis elegans* nematodes that harbor *Bacillus subtilis* bacteria produce more offspring under heat shock [56]. Ecological impacts can lead to evolutionary changes. Hosts associated with *B. subtilis* for 20 generations of heat-shock selection evolved to produce more offspring than those lacking the protective bacteria [57]. Beneficial symbionts can thus recover some of the fertility/fecundity damages caused by warming. Such **experimental evolution** approaches in general can provide a powerful strategy to directly address the role that protective symbionts have in host adaptation to heat stress, particularly when combined with ecological and molecular approaches (Box 2).

Impacts of the microbiome community

Hosts can harbor multiple symbiont species simultaneously, forming complex and dynamic communities that make up the host microbiome [58]. Microbiomes are involved in a wide range of host functions, from nutritional supplementation to stress resistance [59,60]. The complex ecosystem of the host, its microbiome, and their interactions has been referred to as a **holobiont** [61]. Hosts that develop without **microbiomes** may exhibit a slower development rate, stunted growth, reduced fecundity, or shorter lifespan [62,63].

Microbiome composition can correlate with host thermal tolerance. The transplantation of microbiomes from heat-tolerant *Drosophila melanogaster* improved the ability of recipient flies to cope with higher temperatures [64]. By contrast, experimentally depleting gut microbiome diversity was found to reduce tadpole thermal tolerance to both heat and cold, with impacts on survival under acute heat stress [65]. In coral-related systems, the abundance of particular

bacterial taxa relates to the host response in short-term heat-stress experiments [66]. These findings suggest that microbial communities are associated with improved host thermal tolerance, but there is no common indicator across diverse host species. Thus, in some systems, species interactions in microbial communities or the functions of the whole microbial community may play a more important role than individual symbionts in times of heat stress.

Impacts of warming on symbiont evolution and ecology

Parasite virulence evolution

Reduction of host tolerance to heating is an aspect of parasite virulence. The outcome of selection on virulence will generally depend on the balance between virulence and transmission [67], both of which is impacted by many (temperature-sensitive) host and parasite traits [68]. Gradual or mild heating may increase virulence alongside other epidemiological parameters (i.e., parasite replication, shedding, and host reproduction) which could promote transmission. Under gradual warming, increased virulence may be balanced by increased transmission, with no reason to expect selection for reduced virulence. Alternatively, this type of heating could allow hosts to counteract infection more effectively via increases in immune activity or thermal acclimation [24,28]. Hosts may also occupy thermal niches beyond the thermal limits of a pathogen [25,28]. Under rapidly increasing and severe heating, however, parasite virulence (in terms of reduction in host thermal tolerance) may increase [25], possibly without parallel changes in host or parasite traits that lead to increased transmission. Traits driving transmission may not increase under severe heating because of the brief nature of extreme temperature events or because extreme temperatures harm both host and parasite [69,70].

These scenarios are speculative. We currently do not have any models or clear predictions for how reductions in host thermal performance caused by infection will impact parasite virulence evolution. Incorporating parasite-induced alteration of host thermal performance into mechanistic

Box 2. Investigating symbiont-conferred heat-stress protection using a model system

The bacterium *Bacillus subtilis* can protect the model nematode *Caenorhabditis elegans* from heat stress. The properties of each organism are well characterized [111] and interest in the natural habitats of the nematode has increased in recent years [112]. *Caenorhabditis* species have also been the central focus of evolution studies from evolutionary genetics to experimental evolution [112,113]. Integrating model systems with established frameworks can thus illuminate how evolutionary processes and ecological conditions can drive changes at the molecular level and vice versa (Figure I A–C).

Mechanisms of *B. subtilis*-conferred heat protection

Bacillus subtilis protects *C. elegans* from heat stress through several processes (Figure IA). Nitric oxide (NO), a compound made by *B. subtilis*, can extend host lifespan and improve thermal tolerance when nematodes are heat-shocked at 34°C (standard *C. elegans* rearing temperatures are in the range 15–25°C) [114]. Similarly, biofilm-forming *B. subtilis* can increase host longevity and resistance to heat, osmotic, metal, oxidative, and pathogenic stresses [115,116]. Thermal tolerance is due to expression of heat-shock proteins induced by *B. subtilis* components, which improve host survival upon subsequent heat shock. However, this effect appears to be dependent on host age. The bacterium is less effective in conferring increased survival in young adult nematodes compared to older nematodes [56].

Nematodes, protective symbionts, and the microbiome

Nematodes colonized by *B. subtilis* gain a significant fitness advantage in terms of fecundity in response to heat stress [56]. Like many other beneficial symbioses, hosts exhibit a cost in the absence of the stressor [1], and produce fewer offspring on *B. subtilis* compared to the standard *C. elegans* laboratory diet, *E. coli* [56], demonstrating that the benefit is context-dependent. Although *B. subtilis* is not associated with *C. elegans* in nature, the nematodes do harbor a core microbiome acquired from their environments (Figure IB). One study demonstrated that temperature affected microbiome assembly differently in nematodes than in the soil in which the microbial community is found, illustrating that the host can have a direct influence on the composition of its microbiome [117]. Future research might expand on the functional roles of these bacteria to determine whether any are involved in host thermal tolerance, and, conversely, how heat stress affects microbiome community structure.

Bacillus subtilis facilitates host adaptation to heat

Drawing from the finding that *B. subtilis* protects nematodes by improving host reproduction following heat shock, a subsequent study addressed whether associating with *B. subtilis* promoted host adaptation to heat stress [57] (Figure IC). Nematodes produced significantly more offspring when exposed to non-evolving *B. subtilis* under heat stress for 20 generations, compared to in the absence of *B. subtilis* or heat. This result demonstrated that protective microbes can promote niche expansion and increase host thermal limits.

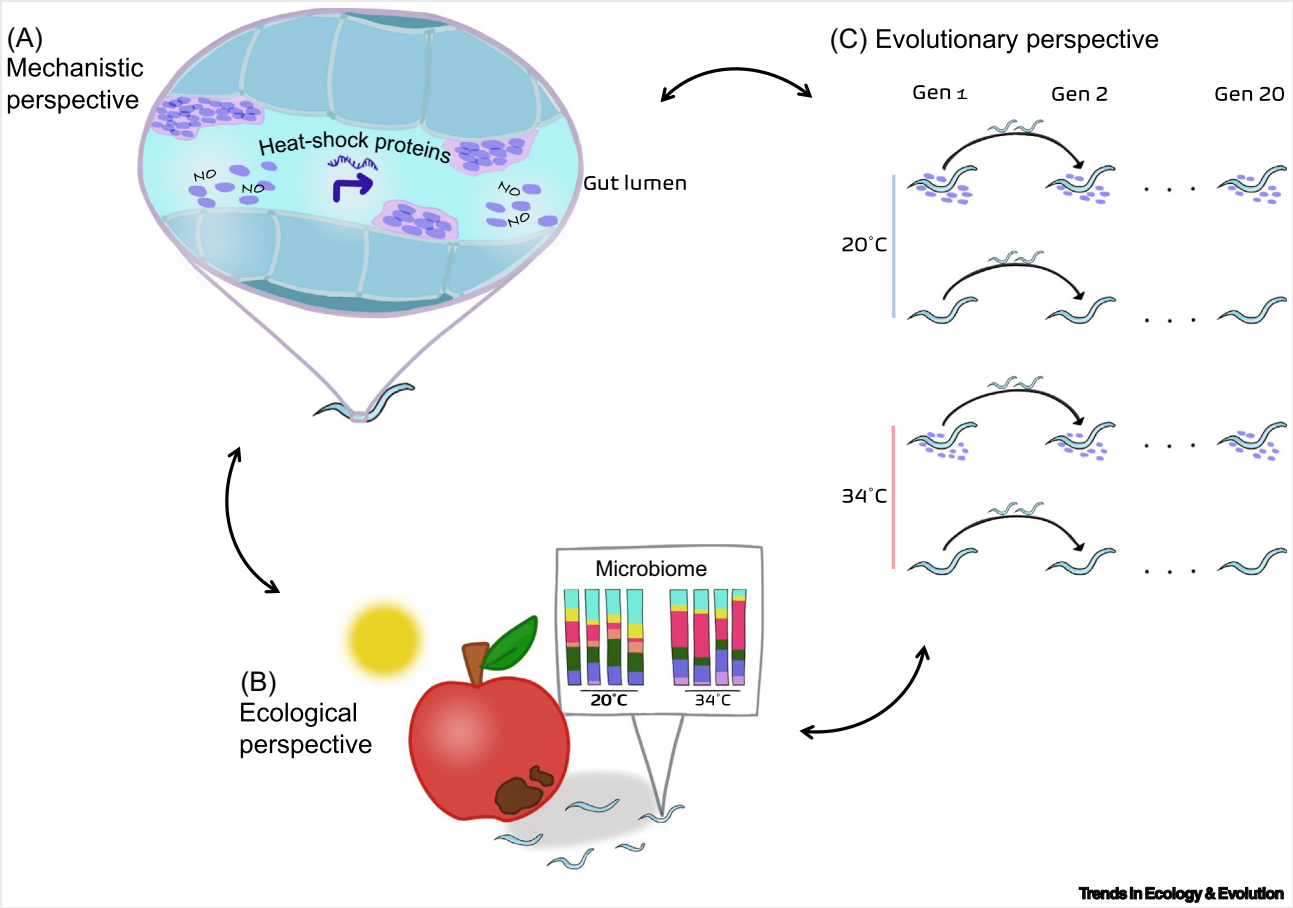

Figure I. Approaches for tackling protective symbiosis in a heated environment using *C. elegans* nematodes and *B. subtilis* bacteria. Findings from mechanistic perspectives (A) can inform subsequent ecological (B) and evolutionary (C) studies, which can then inform further mechanistic investigation. Abbreviation: Gen, generation.

and epidemiological evolutionary models would give us insight into how these processes feed back onto parasite evolution. Moreover, experimental evolution approaches are perfectly placed to answer these questions empirically. By passaging parasites through host populations exposed to warming temperatures and thermal extremes, one could directly test how different types of thermal variation affect parasite virulence evolution.

Symbiosis breakdown

Heat stress can lead to a breakdown of symbiosis between a host and its mutualistic symbiont, where the host no longer benefits from association. For example, bacteria that increase pea aphid survival from parasitoid wasps no longer provide the same level of protection under heat stress [71]. In cnidarian–algae symbioses, heat can affect symbiont uptake as well as prevent the symbiont from synthesizing proteins necessary for photosynthesis [72]. Many heritable symbionts are heat-sensitive, which can hinder their transmission to the next host generation, making symbioses unstable under warming [60].

When symbiont loss has devastating effects on host fitness – leading to sterilization or death – it becomes a thermal 'weak link' and limits host range expansion [60]. For example, planthoppers

(*Nilaparvata lugens*) harbor bacterial symbionts that help them to detoxify insecticides. Elevated temperatures cause declines in symbiont abundance, abolishing any tolerance to insecticides in the planthoppers [73]. These studies also suggest that the thermal tolerance of symbionts can have large impacts on host adaptation: symbionts that can thrive under heat stress may be better at facilitating host adaptation to high temperatures. Alternatively, heat-sensitive symbionts that decrease in abundance under heat stress may no longer confer hosts with any benefits. However, low symbiont titers can still be beneficial. This is the case when lysed symbionts provide metabolites necessary for host survival [74] or when exposure to the symbiont at benign temperatures is sufficient to prime hosts for heat stress [75].

Alterations in microbiome community structure and function

Host microbiomes are regulated by both host-related and environmental factors [76,77]. Host factors, such as immunity, can be affected by environmental stress, which in turn shapes host–microbiome interactions [78]. Although studies across host species (from plants to animals, ectotherms to endotherms, terrestrial to aquatic) have shown that microbiomes can be altered by temperature [79,80], it is unclear whether microbial alteration is the direct result of temperature, the physiological response of the host, or both.

Because microbiomes differ across host taxonomy and sampling locations (e.g., plant and animal microbiomes differ strongly, as well as microbiomes associated with body surface and the digestive tract), general patterns of microbiome diversity and compositional changes under warming are difficult to identify. Hartman *et al.* [66] found overall declines in bacterial alpha diversity in heat-stressed corals, whereas Ahmed *et al.* [79] found increased diversity and variation. Several studies, however, have shown parallel trends of microbiome change under warming. For example, warming destabilized the composition of the lizard (*Sceloporus occidentalis*) gut microbiome [81], and similar results were found in a sponge host (*Lendenfeldia chondrodes*) [80]. These findings support the hypothesis that unhealthy or dysbiotic hosts have more variable microbial composition than healthy hosts [82], and that microbiome instability is associated with host heat stress.

Although the taxonomic composition of microbiomes is distinct between diverse hosts, their functional capacity is broadly conserved. Multiple studies show that functional pathways that are altered by heat stress are mostly related to metabolism. For instance, Tian *et al.* [83] found that starch, sucrose, and energy metabolism were the most enriched functions in the intestinal microbiome of ducks (*Anas platyrhynchos*) after heat treatment. Ziegler *et al.* [84] found that several functions related to carbohydrate metabolism such as fructose transport proteins were enriched in microbiomes from heat-adapted corals (*Acropora hyacinthus*). Thus, microbiomes might alleviate the effects of warming in hosts through functional enrichment of metabolic pathways. Alternatively, beneficial microbial communities can increase thermotolerance by modulating host physiology. A selected consortium of bacteria induced upregulation of stress-protection proteins and lipid biosynthesis in the coral *Mussismilia hispida*, mitigating host cellular damage and mortality following long-term heat stress [85].

Implications for host species persistence

The implications for species persistence due to the impact of symbiosis on host thermal performance will be substantial. Tropical species and populations, for example, are often more resistant to thermal stress than those from temperature regions, suggesting adaptation to local conditions [30,48,86]. However, because tropical species and populations already live close to their upper thermal limits, and therefore have small thermal safety margins [24,26], they could be disproportionately harmed by infection [25]. In the absence of genetic and phenotypic variation in upper thermal limits, tropical populations might be under stronger selection to facilitate the colonization

of beneficial symbionts. The harm caused by infection may nevertheless be compounded by the likely greater parasite abundance in the tropics [87].

Alternatively, temperate species may instead be most vulnerable from infection and thermal stress. Models incorporating the thermal performance of parasites predict that warming will increase parasite prevalence in temperate regions, but decrease it in the tropics [88,89]. Any geographic shift in parasite prevalence due to global change may give tropical species a reprieve from the impacts of parasites on their thermal performance. Temperate species may not be so lucky. Alongside an increase in parasite prevalence, temperate hosts will frequently experience thermal stress due to an increase in thermal variability, alongside rising average temperatures [90]. Warmer temperatures may lengthen the season suitable for parasite growth and transmission in temperate regions [28]. Warmer average temperatures may therefore increase parasite abundance, prevalence and, potentially, the severity of disease outbreaks. Subsequent infections will dramatically impair the responses of these hosts to the increasing frequency of thermal stress.

Terrestrial animals may be able to access beneficial thermal niches via behavioral thermoregulation [91]. When infected hosts seek warmer microclimates, this could nevertheless result in very narrow thermal safety margins when infection also causes reductions in host thermal tolerance [25]. Aquatic organisms are unlikely to be able to access beneficial thermal niches and may experience body temperatures closer to their upper thermal limits during extreme heating [91]. The inability to behaviorally thermoregulate may put some hosts at particular risk from infection and heating.

Hosts that associate with heat-sensitive symbionts may be at increased risk during warming. However, species persistence will depend on the nature of the association – whether hosts are obligately dependent on their symbionts or benefit only under specific conditions. Furthermore, organisms in symbiosis will require more controlled experiments to disentangle the effects of each member that is present and their interactions with one another. More studies testing the response of microbiomes to experimental warming (see Outstanding questions) will be necessary to determine whether microbiomes can help to moderate the impacts of global heating and/or act as a warning of trouble ahead.

Many species do not currently possess sufficiently high thermal tolerances to cope with ongoing global change. Adaptation to ongoing heating requires populations to exhibit phenotypic variation in their thermal tolerance, alongside underlying genetic variation. Worryingly, it is unclear whether many species possess such variation, and there may be strong constraints because of complex genetic or physiological tradeoffs. Association with mutualists can impact variation in host thermal tolerance. For example, closely related symbiont isolates were found to contribute to differential host fitness in response to heat shock in pea aphids, and the isolate found in the warmest geographical location conferred the greatest protection [92]. Theoretical models have suggested that high symbiont variation (at the genetic and community levels) in thermal tolerance may allow long-term host persistence under warming [93]. However, experimental studies have challenged the paradigm that symbiotic flexibility enhances host resilience and suggest that symbiont fidelity rather than flexibility will be favored in future warming [94].

Symbionts are instrumental in shaping phenotypic variation, and the expression of genetic variation, in host populations. Symbionts likely represent a substantial source of variation for host thermal performance in natural populations. However, if the detrimental impact of infection on host thermal tolerance is too great, any promotion of the expression of genetic variation may simply be overpowered by the reduction in fitness caused by infection and thermal stress. Mutualists and microbiomes could enhance adaptation to thermal stress if they enable hosts to inhabit otherwise

unsuitable climates. Reliance on symbionts for thermal resistance could leave hosts maladapted when symbioses break down.

Concluding remarks and future perspectives

Understanding the impacts of symbioses across the mutualist–parasite continuum on the thermal performance of their hosts is challenging. It is often unclear how harm or benefit are conferred, and any mechanisms may be both host- and symbiont-specific (species and genotype-level) or community-specific (see Outstanding questions).

It is possible that heating shapes the relative benefits/harm conferred by symbionts over evolutionary time. Equally uncertain is the impact on host evolution. For host–parasite interactions, disrupted host responses to heating are likely the result of the interaction between the harm caused, the energy costs, and physiological responses to infection. The immune system presents us with one potentially generalizable mechanism behind how infected hosts respond to heating. In invertebrates, the immune system and the heat-shock response are part of a more general stress response which buffers against many biotic and abiotic stressors [30]. Such 'cross-tolerance' has been found for many sources of stress, reinforcing the idea of an important generalized stress response in invertebrates [95,96]. Plants also exhibit a large overlap in responses to heat and infection [97,98]. With shared underlying mechanisms, tradeoffs may occur. Hector *et al.* [30] found that tropical populations of *Drosophila*, which are adapted to be the most heat-resistant, experienced reductions in heat tolerance after immune system activation. Other environmental perturbations, such as anthropogenic disturbance [99] or those facilitating evolution of selfish mutualists [100], may also affect host adaptation to heating. Investment in responses to these other pressures might further divert resources from thermotolerance mechanisms. Tradeoffs between resistance to thermal stress and resistance to other environmental stressors could limit the capacity of populations to cope with heating at both the ecological and evolutionary scales.

Host responses to extreme temperatures could also feed back onto ongoing **coevolution** with parasites. In models of host–parasite coevolution, the fitness of a genotype is fixed across environments, although warming temperatures can increase host susceptibility and parasite virulence/growth rate [42,101]. Consequently, during warming, it has been predicted that there might be stronger selection for host resistance and counter-selection by parasites [60], with more rapid coevolution taking place. The rate of warming (e.g., heatwave vs. gradual warming), however, might influence host and parasite evolution differently. Because parasite generation times are often shorter than those of their hosts, parasite infectivity might evolve more rapidly than host resistance during heatwaves. Coevolution might break down [60]. Whether the degree of thermal stress alters the speed and stability of host–parasite coevolution, or indeed host–mutualist coevolution, remains untested. Measuring the temporal changes in symbiosis-related and thermal-related fitness traits, as well as the underlying molecular processes, will be key to predicting how coevolving relationships will change in a warming world.

Because mutualistic symbionts and microbiomes can help to improve host thermal performance, microbiome transplantation might be an effective way to help with faster host adaptation to warming [102,103]. Microbes have shorter generation times and are often more genetically tractable, and thus can potentially adapt faster than their hosts, making it feasible to evolve microbiomes in the laboratory and transplant them to susceptible hosts. This approach is highly applicable to coral-associated microbes, where selection for heat-tolerant algae and bacteria that can mitigate oxidative stress and metabolism disruption is part of ongoing efforts to restore bleached corals [104]. Release of heat resistance-conferring symbionts may be a viable option in general for species persistence, particularly for organisms such as plants and those with limited behavioral

Outstanding questions

What is the impact of alteration of host thermal performance on parasite evolution? By impairing host thermal performance, parasites may indirectly influence their own performance. Infection induced reductions in host thermal performance could become an increasingly important component of parasite virulence. However, we currently lack any clear predictions about how parasite effects on host thermal performance will feed back into the evolution of the parasites themselves.

What are the effects of heating on the ecology and evolution of host-protecting microbial symbionts? Heritable mutualistic symbionts are crucial for host fitness, but they are often unculturable and therefore less amenable to laboratory experiments. In addition, because of their complexity, little is known about how heat can impact on the persistence and function of microbiomes.

In what case are shifts in the microbiome a contributor to host thermal tolerance versus a consequence of host adaptation/maladaptation to warming? Although association studies have discovered links between microbiomes and host responses to heat, experimental studies will be necessary to disentangle cause and effect in microbiome research with respect to host health and temperature. Microbiome transplantation experiments have begun to fill these gaps.

Does thermal stress alter the stability of coevolving symbioses? It is unclear whether heat stress causes parasites to have a faster relative evolutionary rate than their hosts. If so, hosts may be more vulnerable to extinction from infection and thermal extremes. The degree to which heat stress can destabilize mutualist–host interactions is also unknown, and likely varies among systems. Symbionts in long-term coevolution with hosts tend to have reduced genomes, and therefore have limited capabilities to respond to heat [51].

modifications to avoid warmer niches. However, whether heat-tolerant mutualists can negatively affect other aspects of host physiology or cause disruptions to natural ecosystems is not well studied in many systems.

Going forward, we must integrate host–microbe interactions into our understanding of species persistence during global heating (see Outstanding questions). The symbiotic microbes colonizing species at risk may be useful in alleviating heat stress, or alternatively might accelerate species loss from habitats, with implications for their ecosystems. Models predicting future geographic range changes may wish to consider the effects that microbes can have on host survival. Ours is a warming world which is also dominated by microbial life.

Acknowledgments

K.L.H. is funded by a National Science Foundation Postdoctoral Research Fellowship in Biology (award number 1907076). J.L. is funded by a Pembroke College Oxford Graduate Scholarship. K.C.K is grateful for funding from a Philip Leverhulme Prize and a European Research Council (ERC) Starting Grant (COEVOPRO 802242).

Declaration of interests

The authors declare no conflicts of interest.

References

1. Drew, G.C. *et al.* (2021) Microbial evolution and transitions along the parasite–mutualist continuum. *Nat. Rev. Microbiol.* 19, 623–638
2. Douglas, A.E. (1998) Nutritional interactions in insect–microbial symbioses: aphids and their symbiotic bacteria *Buchnera*. *Annu. Rev. Entomol.* 43, 17–37
3. Gerardo, N.M. *et al.* (2020) Evolution of animal immunity in the light of beneficial symbioses. *Phil. Trans. R. Soc. Lond. B Biol. Sci.* 375, 20190601
4. Haine, E.R. (2008) Symbiont-mediated protection. *Proc. Biol. Sci.* 275, 353–361
5. Oliver, K.M. *et al.* (2013) Defensive symbiosis in the real world – advancing ecological studies of heritable, protective bacteria in aphids and beyond. *Funct. Ecol.* 28, 341–355
6. Fisher, R.M. *et al.* (2017) The evolution of host–symbiont dependence. *Nat. Commun.* 8, 15973
7. McFall-Ngai, M. *et al.* (2013) Animals in a bacterial world, a new imperative for the life sciences. *Proc. Natl. Acad. Sci. U. S. A.* 110, 3229–3236
8. Douglas, A.E. (2014) Symbiosis as a general principle in eukaryotic evolution. *Cold Spring Harb. Perspect. Biol.* 6, a016113
9. Ford, S.A. and King, K.C. (2016) Harnessing the power of defensive microbes: evolutionary implications in nature and disease control. *PLoS Pathog.* 12, e1005465
10. Day, T. (2002) On the evolution of virulence and the relationship between various measures of mortality. *Proc. Biol. Sci.* 269, 1317–1323
11. Ebert, D. *et al.* (2004) The evolution of virulence when parasites cause host castration and gigantism. *Am. Nat.* 164, S19–S32
12. Cressler, C.E. *et al.* (2016) The adaptive evolution of virulence: a review of theoretical predictions and empirical tests. *Parasitol* 143, 915–930
13. Hoang, A. (2001) Immune response to parasitism reduces resistance of *Drosophila melanogaster* to desiccation and starvation. *Evolution* 55, 2353–2358
14. Xu, P. *et al.* (2008) Virus infection improves drought tolerance. *New Phytol.* 180, 911–921
15. Guschina, I.A. and Harwood, J.L. (2006) Mechanisms of temperature adaptation in poikilotherms. *FEBS Lett.* 580, 5477–5483
16. Taylor, S.K.B. *et al.* (2021) *C. elegans* electrotaxis behavior is modulated by heat shock response and unfolded protein response signaling pathways. *Sci. Rep.* 11, 3115
17. Chakravarti, L.J. and van Oppen, M.J.H. (2018) Experimental evolution in coral photosymbionts as a tool to increase thermal tolerance. *Front. Mar. Sci.* 5, 227
18. Mesas, A. *et al.* (2021) Experimental evolution on heat tolerance and thermal performance curves under contrasting thermal selection in *Drosophila subobscura*. *J. Evol. Biol.* 34, 767–778
19. Richter, K. *et al.* (2010) The heat shock response: life on the verge of death. *Mol. Cell* 40, 253–266
20. Tedeschi, J.N. *et al.* (2016) Heritable variation in heat shock gene expression: a potential mechanism for adaptation to thermal stress in embryos of sea turtles. *Proc. Biol. Sci.* 283, 20152320
21. Klosin, A. *et al.* (2017) Transgenerational transmission of environmental information in *C. elegans*. *Science* 356, 320–323
22. Deutsch, C.A. *et al.* (2008) Impacts of climate warming on terrestrial ectotherms across latitude. *Proc. Natl. Acad. Sci. U. S. A.* 105, 6668–6672
23. Sunday, J.M. *et al.* (2014) Thermal-safety margins and the necessity of thermoregulatory behavior across latitude and elevation. *Proc. Natl. Acad. Sci. U. S. A.* 111, 5610–5615
24. Rohr, J.R. *et al.* (2018) The complex drivers of thermal acclimation and breadth in ectotherms. *Ecol. Lett.* 21, 1425–1439
25. Hector, T.E. *et al.* (2021) Thermal limits in the face of infectious disease: How important are pathogens? *Glob. Change Biol.* 27, 4469–4480
26. Greenspan, S.E. *et al.* (2017) Infection increases vulnerability to climate change via effects on host thermal tolerance. *Sci. Reports* 7, 9349
27. Hector, T.E. *et al.* (2019) Pathogen exposure disrupts an organism's ability to cope with thermal stress. *Glob. Change Biol.* 25, 3893–3905
28. Gehman, A.-L.M. *et al.* (2018) Host and parasite thermal ecology jointly determine the effect of climate warming on epidemic dynamics. *Proc. Natl. Acad. Sci. U. S. A.* 115, 744–749
29. Laidlaw, T. *et al.* (2020) Pathogen exposure reduces sexual dimorphism in a host's upper thermal limits. *Ecol. Evol.* 10, 12851–12859
30. Hector, T.E. *et al.* (2020) The influence of immune activation on thermal tolerance along a latitudinal cline. *J. Evol. Biol.* 99, e52613
31. Porras, M.F. *et al.* (2020) Enhanced heat tolerance of viral-infected aphids leads to niche expansion and reduced interspecific competition. *Nat. Commun.* 11, 1184
32. Desaint, H. *et al.* (2021) Fight hard or die trying: when plants face pathogens under heat stress. *New Phytol.* 229, 712–734
33. Parratt, S.R. *et al.* (2021) Temperatures that sterilize males better match global species distributions than lethal temperatures. *Nat. Climate Change* 11, 481–484

34. van Heerwaarden, B. and Sgrò, C.M. (2021) Male fertility thermal limits predict vulnerability to climate warming. *Nat. Comm.* 12, 2214
35. Walsh, B.S. *et al.* (2019) The impact of climate change on fertility. *Trends Ecol. Evol.* 34, 249–259
36. Perlmutter, J.I. and Bordenstein, S.R. (2020) Microorganisms in the reproductive tissues of arthropods. *Nat. Rev. Microbiol.* 18, 97–111
37. Lazzaro, B.P. *et al.* (2008) Genotype-by-environment interactions and adaptation to local temperature affect immunity and fecundity in *Drosophila melanogaster*. *PLoS Pathog.* 4, e1000025
38. Vale, P.F. *et al.* (2008) Temperature-dependent costs of parasitism and maintenance of polymorphism under genotype-by-environment interactions. *J. Evol. Biol.* 21, 1418–1427
39. Hector, T.E. *et al.* (2021) Temperature and pathogen exposure act independently to drive host phenotypic trajectories. *Biol. Lett.* 17, 20210072
40. Cohen, J.M. *et al.* (2017) The thermal mismatch hypothesis explains host susceptibility to an emerging infectious disease. *Ecol. Lett.* 20, 184–193
41. Rohr, J.R. and Cohen, J.M. (2020) Understanding how temperature shifts could impact infectious disease. *PLoS Biol.* 18, e3000938
42. Hoffmann, A.A. *et al.* (2012) Upper thermal limits in terrestrial ectotherms: how constrained are they? *Funct. Ecol.* 27, 934–949
43. Kelly, M.W. *et al.* (2012) Limited potential for adaptation to climate change in a broadly distributed marine crustacean. *Proc. Biol. Sci.* 279, 349–356
44. Hangartner, S. and Hoffmann, A.A. (2016) Evolutionary potential of multiple measures of upper thermal tolerance in *Drosophila melanogaster*. *Funct. Ecol.* 30, 442–452
45. Kellermann, V. *et al.* (2009) Fundamental evolutionary limits in ecological traits drive *Drosophila* species distributions. *Science* 325, 1244–1246
46. McGuigan, K. and Sgrò, C.M. (2009) Evolutionary consequences of cryptic genetic variation. *Trends Ecol. Evol.* 24, 305–311
47. Ware-Gilmore, F. *et al.* (2021) Microbes increase thermal sensitivity in the mosquito Aedes aegypti, with the potential to change disease distributions. *PLOS Negl. Trop. Diseases* 15, e0009548
48. Flores, H.A. and O'Neill, S.L. (2018) Controlling vector-borne diseases by releasing modified mosquitoes. *Nat. Rev. Microbiol.* 16, 508–518
49. Walker, T. *et al.* (2011) The wMel *Wolbachia* strain blocks dengue and invades caged *Aedes aegypti* populations. *Nature* 476, 450–453
50. Utarini, A. *et al.* (2021) Efficacy of *Wolbachia*-infected mosquito deployments for the control of dengue. *New Eng. J. Med.* 384, 2177–2186
51. Corbin, C. *et al.* (2017) Heritable symbionts in a world of varying temperature. *Heredity* 118, 10–20
52. Engl, T. *et al.* (2018) Ancient symbiosis confers desiccation resistance to stored grain pest beetles. *Mol. Ecol.* 27, 2095–2108
53. Wu, S. *et al.* (2018) Chromium detoxification in arbuscular mycorrhizal symbiosis mediated by sulfur uptake and metabolism. *Environ. Exp. Botany* 147, 43–52
54. Baynes, M. *et al.* (2012) A novel plant–fungal mutualism associated with fire. *Fungal. Biol.* 116, 133–144
55. Harmon, J.P. *et al.* (2009) Species response to environmental change: impacts of food web interactions and evolution. *Science* 323, 1347–1350
56. Hoang, K.L. *et al.* (2019) The effects of *Bacillus subtilis* on *Caenorhabditis elegans* fitness after heat stress. *Eco. Evol.* 9 34591–3499
57. Hoang, K.L. *et al.* (2021) Association with a novel protective microbe facilitates host adaptation to a stressful environment. *Evol. Lett.* 5, 118–129
58. Ferrari, J. and Vavre, F. (2011) Bacterial symbionts in insects or the story of communities affecting communities. *Phil. Trans. R. Soc. Lond. B. Biol. Sci.* 366, 1389–1400
59. Bahrndorff, S. *et al.* (2016) The microbiome of animals: implications for conservation biology. *Int. J. Genom.* 2016, 5304028
60. Hooper, L.V. *et al.* (2002) How host–microbial interactions shape the nutrient environment of the mammalian intestine. *Ann. Rev. Nutr.* 22, 283–307
61. Zilber-Rosenberg, I. and Rosenberg, E. (2008) Role of microorganisms in the evolution of animals and plants: the hologenome theory of evolution. *FEMS Microbiol. Rev.* 32, 723–735
62. Correa, M.A. *et al.* (2018) Generation of axenic *Aedes aegypti* demonstrate live bacteria are not required for mosquito development. *Nat. Comm.* 9, 4464
63. Rawls, J.F. *et al.* (2004) Gnotobiotic zebrafish reveal evolutionarily conserved responses to the gut microbiota. *Proc. Natl. Acad. Sci. U. S. A.* 101, 4596–4601
64. Moghadam, N.N. *et al.* (2018) Strong responses of *Drosophila melanogaster* microbiota to developmental temperature. *Fly* 12, 1–12
65. Fontaine, S.S. *et al.* (2022) Experimental manipulation of microbiota reduces host thermal tolerance and fitness under heat stress in a vertebrate ectotherm. *Nat. Ecol. Evol.* 6, 405–417
66. Hartman, L.M. *et al.* (2019) The effect of thermal stress on the bacterial microbiome of *Exaiptasia diaphana*. *Microorganisms* 8, 20
67. Alizon, S. *et al.* (2009) Virulence evolution and the trade-off hypothesis: history, current state of affairs and the future. *J. Evol. Biol.* 22, 245–259
68. Mordecai, E.A. *et al.* (2019) Thermal biology of mosquito-borne disease. *Ecol. Lett.* 22, 1690–1708
69. Shocket, M.S. *et al.* (2019) Can hot temperatures limit disease transmission? A test of mechanisms in a zooplankton–fungus system. *Funct. Ecol.* 9, 459
70. Claar, D.C. and Wood, C.L. (2020) Pulse heat stress and parasitism in a warming world. *Trends Ecol. Evol.* 35, 704–715
71. Doremus, M.R. *et al.* (2018) Breakdown of a defensive symbiosis, but not endogenous defences, at elevated temperatures. *Mol. Ecol.* 27, 2138–2151
72. Takahashi, S. *et al.* (2008) Heat stress causes inhibition of the de novo synthesis of antenna proteins and photobleaching in cultured *Symbiodinium*. *Proc. Natl. Acad. Sci. U. S. A.* 105, 4203–4208
73. Zhang, Y. *et al.* (2021) Decline in symbiont-dependent host detoxification metabolism contributes to increased insecticide susceptibility of insects under high temperature. *ISME J.* 15, 3693–3703
74. Burke, G. *et al.* (2010) Effects of facultative symbionts and heat stress on the metabolome of pea aphids. *ISME J.* 4, 242–252
75. Brumin, M. *et al.* (2011) *Rickettsia* influences thermotolerance in the whitefly *Bemisia tabaci* B biotype. *Insect. Sci.* 18, 57–66
76. Woodhams, D.C. *et al.* (2020) Hot-associated microbiomes are predicted by immune system complexity and climate. *Genome Biol.* 21, 23
77. Kers, J.G. *et al.* (2018) Host and environmental factors affecting the intestinal microbiota in chickens. *Front. Microbiol.* 9, 235
78. Posadas, N. *et al.* (2021) Microbiome diversity and host immune functions influence survivorship of sponge holobionts under future ocean conditions. *ISME J.* 16, 58–67
79. Ahmed, H.I. *et al.* (2019) Long-term temperature stress in the coral model *Aiptasia* supports the 'Anna Karenina Principle' for bacterial microbiomes. *Front. Microbiol.* 10, 975
80. Vargas, S. *et al.* (2021) Short-term exposure to high-temperature water causes a shift in the microbiome of the common aquarium sponge *Lendenfeldia chondrodes*. *Microb. Ecol.* 81, 213–222
81. Moeller, A.H. *et al.* (2020) The lizard gut microbiome changes with temperature and is associated with heat tolerance. *Appl. Environ. Microbiol.* 86, e01181-20
82. Zaneveld, J. *et al.* (2017) Stress and stability: applying the Anna Karenina principle to animal microbiomes. *Nat. Microbiol.* 2, 1712
83. Tian, Y. *et al.* (2020) High-temperature exposure alters the community structure and functional features of the intestinal microbiota in Shaoxing ducks (*Anas platyrhynchos*). *Poultry Sci.* 99, 2662–2674
84. Ziegler, M. *et al.* (2017) Bacterial community dynamics are linked to patterns of coral heat tolerance. *Nat. Comm.* 8, 14213

85. Santoro, E.P. *et al.* (2021) Coral microbiome manipulation elicits metabolic and genetic restructuring to mitigate heat stress and evade mortality. *Sci. Adv.* 7, eabg3088
86. Yampolsky, L.Y. *et al.* (2014) Adaptive phenotypic plasticity and local adaptation for temperature tolerance in freshwater zooplankton. *Proc. Biol. Sci.* 281, 20132744
87. Møller, A.P. (1998) Evidence of larger impact of parasites on hosts in the tropics: investment in immune function within and outside the tropics. *Oikos* 82, 265–270
88. Cohen, J.M. *et al.* (2020) Divergent impacts of warming weather on wildlife disease risk across climates. *Science* 370, eabb170
89. Ryan, S.J. *et al.* (2019) Global expansion and redistribution of *Aedes*-borne virus transmission risk with climate change. *PLOS Negl. Trop. Diseases* 13, e0007213
90. Kingsolver, J.G. *et al.* (2013) Heat stress and the fitness consequences of climate change for terrestrial ectotherms. *Funct. Ecol.* 27, 1415–1423
91. Pinsky, M.L. *et al.* (2019) Greater vulnerability to warming of marine versus terrestrial ectotherms. *Nature* 569, 108–111
92. Russell, J.A. and Moran, N.A. (2006) Costs and benefits of symbiont infection in aphids: variation among symbionts and across temperatures. *Proc. Biol. Sci.* 273, 603–610
93. Baskett, M.L. *et al.* (2009) Symbiont diversity may help coral reefs survive moderate climate change. *Ecol. App.* 19, 3–17
94. Howells, E.J. *et al.* (2020) Corals in the hottest reefs in the world exhibit symbiont fidelity not flexibility. *Mol. Ecol.* 29, 899–911
95. Sinclair, B.J. *et al.* (2013) Cross-tolerance and cross-talk in the cold: relating low temperatures to desiccation and immune stress in insects. *Int. Comp. Biol.* 53, 545–556
96. Gotcha, N. *et al.* (2018) Plasticity and cross-tolerance to heterogeneous environments: divergent stress responses co-evolved in an African fruit fly. *J. Evol. Biol.* 31, 98–110
97. Fujita, M. *et al.* (2006) Crosstalk between abiotic and biotic stress responses: a current view from the points of convergence in the stress signaling networks. *Curr. Op. Plant Biol.* 9, 436–442
98. Ben Rejeb, I. *et al.* (2014) Plant responses to simultaneous biotic and abiotic stress: molecular mechanisms. *Plants* 3, 458–475
99. Claar, D.C. *et al.* (2020) Dynamic symbioses reveal pathways to coral survival through prolonged heatwaves. *Nat. Commun.* 11, 6097
100. Sachs, J.L. and Simms, E.L. (2006) Pathways to mutualism breakdown. *Trends Ecol. Evol.* 21, 585–592
101. Wolinska, J. and King, K.C. (2009) Environment can alter selection in host–parasite interactions. *Trends Parasitol.* 25, 236–244
102. Doering, T. *et al.* (2021) Towards enhancing coral heat tolerance: a 'microbiome transplantation' treatment using inoculations of homogenized coral tissues. *Microbiome* 9, 102
103. Rodriguez, R.J. *et al.* (2008) Stress tolerance in plants via habitat-adapted symbiosis. *ISME J.* 2, 404–416
104. Maire, J. and van Oppen, M.J.H. (2021) A role for bacterial experimental evolution in coral bleach mitigation. *Trends Microbiol.* 30, P217–P228
105. Shekhawat, K. *et al.* (2021) Root endophyte induced plant thermotolerance by constitutive chromatin modification at heat stress memory gene loci. *EMBO Rep.* 22, e51049
106. Mitchell, S.E. *et al.* (2005) Host–parasite and genotype-by-environment interactions: temperature modifies potential for selection by a sterilizing pathogen. *Evolution* 59, 70–80
107. Vale, P.F. and Little, T.J. (2009) Measuring parasite fitness under genetic and thermal variation. *Heredity* 103, 102–109
108. Auld, S.K.J.R. and Brand, J. (2017) Simulated climate change, epidemic size, and host evolution across host–parasite populations. *Glob. Change Biol.* 23, 5045–5053
109. Shocket, M.S. *et al.* (2018) Temperature drives epidemics in a zooplankton–fungus disease system: a trait-driven approach points to transmission via host foraging. *Am. Nat.* 191, 435–451
110. Shocket, M.S. *et al.* (2018) Parasite rearing and infection temperatures jointly influence disease transmission and shape seasonality of epidemics. *Ecology* 99, 1975–1987
111. Belda, E. *et al.* (2013) An updated metabolic view of the *Bacillus subtilis* 168 genome. *Microbiol* 159, 757–770
112. Schulenburg, H. and Félix, M.-A. (2017) The natural biotic environment of *Caenorhabditis elegans*. *Genetics* 206, 55–86
113. Teotónio, H. *et al.* (2017) Experimental evolution with *Caenorhaditis nematodes*. *Genetics* 206, 691–716
114. Gusarov, I. *et al.* (2013) Bacterial nitric oxide extends the lifespan of *C. elegans*. *Cell* 152, 818–830
115. Donato, V. *et al.* (2017) *Bacillus subtilis* extends *Caenorhabditis elegans* longevity through downregulation of the insulin-like signaling pathway. *Nat. Commun.* 8, 14332
116. Smolentseva, O. *et al.* (2017) Mechanism of biofilm-mediated stress resistance and lifespan extension in *C. elegans*. *Sci. Rep.* 7, 7137
117. Dirksen, P. *et al.* (2016) The native microbiome of the nematode *Caenorhabditis elegans*: gateway to a new host–microbiome model. *BMC Biol.* 14, 38
118. Bates, A.E. *et al.* (2011) Parasitized snails take the heat: a case of host manipulation? *Oecologia* 167, 613–621
119. Sherman, E. (2008) Thermal biology of newts (*Notophthalmus viridescens*) chronically infected with a naturally occurring pathogen. *J. Thermal. Biol.* 33, 27–31
120. Berkelmans, R. and van Oppen, M.J.H. (2006) The role of zooxanthellae in the thermal tolerance of corals: a 'nugget of hope' for coral reefs in an era of climate change. *Proc. R. Soc. B* 273, 2305–2312
121. Nakagawa, H. *et al.* (2016) Effects and mechanisms of prolongevity induced by *Lactobacillus gasseri* SBT2055 in *Caenorhabditis elegans*. *Aging Cell* 15, 227–236
122. Marquez, L.M. *et al.* (2007) A virus in a fungus in a plant: three-way symbiosis required for thermal tolerance. *Science* 315, 513–516