Ann. N.Y. Acad. Sci. ISSN 0077-89



ANNALS OF THE NEW YORK ACADEMY OF SCIENCES
Special Issue: *The Year in Evolutionary Biology*
REVIEW

# Adaptation to environmental stress at different timescales

Torsten Nygaard Kristensen,[1,2] Tarmo Ketola,[3] and Ilkka Kronholm[3]

[1]Department of Chemistry and Bioscience, Aalborg University, Aalborg, Denmark. [2]Department of Bioscience, University of Aarhus, Aarhus, Denmark. [3]Department of Biology and Environmental Sciences, University of Jyväskylä, Jyväskylä, Finland

Address for correspondence: Torsten Nygaard Kristensen, Department of Chemistry and Bioscience, Aalborg University, Fredrik Bajers Vej 7H, DK-9220 Aalborg East, Denmark. tnk@bio.aau.dk

**Environments are changing rapidly, and to cope with these changes, organisms have to adapt. Adaptation can take many shapes and occur at different speeds, depending on the type of response, the trait, the population, and the environmental conditions. The biodiversity crisis that we are currently facing illustrates that numerous species and populations are not capable of adapting with sufficient speed to ongoing environmental changes. Here, we discuss current knowledge on the ability of animals and plants to adapt to environmental stress on different timescales, mainly focusing on thermal stress and ectotherms. We discuss within-generation responses that can be fast and induced within minutes or hours, evolutionary adaptations that are often slow and take several generations, and mechanisms that lay somewhere in between and that include epigenetic transgenerational effects. To understand and predict the impacts of environmental change and stress on biodiversity, we suggest that future studies should (1) have an increased focus on understanding the type and speed of responses to fast environmental changes; (2) focus on the importance of environmental fluctuations and the predictability of environmental conditions on adaptive capabilities, preferably in field studies encompassing several fitness components; and (3) look at ecosystem responses to environmental stress and their resilience when disturbed.**

**Keywords:** plasticity; evolution; trangenerational effects; environmental stress

## Coping with environmental stress—an overview

Stressful environmental conditions can be defined as those that lead to a sharp reduction in fitness.[1] Periods of environmental stress such as extreme temperatures, droughts, or food shortage may wipe out a population unless it is capable of coping with these conditions.[2] There is clear evidence that many habitats are becoming increasingly stressful and that anthropogenic global changes, including altered thermal conditions, are partly responsible for the increased rates of current and expected future extinctions.[3,4] As an example of the negative influence that changed environments may have on biodiversity, it is expected that 15–20% of all species will go extinct in the near future due to climate change.[3,5] There are pronounced geographical differences in climate change–driven extinction prognoses; for example, species extinction probabilities seem to be higher at lower latitudes.[3,6] The causes of extinctions are typically multifactorial and can include several environmental and genetic factors.[7,8] Environmental stress can reduce population sizes dramatically,[9,10] leading to population bottlenecks often associated with loss of additive genetic variance[2] and with increased inbreeding that typically has more severe negative effects in stressful environments.[11,12] Thus, the combined effects of multiple and interacting environmental and genetic factors are typically causative factors when a population or species goes extinct. Understanding the mechanisms behind adaptation and the speed with which adaptation occurs are therefore crucial for predicting the future abundance and distribution of species.

The type and predictability of environmental change will influence which mechanisms are important for coping with these changes.[13] In this discussion, we will emphasize future avenues of research and the importance of the duration and extent of

doi: 10.1111/nyas.13974

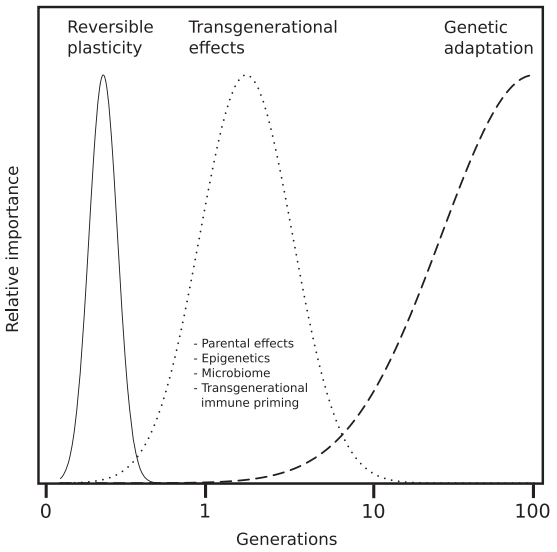


**Figure 1.** **Schematized population responses to environmental stress using different strategies on different timescales. The *x*-axis is the number of generations on a logarithmic scale, while the *y*-axis is the proposed relative importance of the different strategies. We hypothesize plastic responses to be most important for short-term exposure to environmental stress, transgenerational coping strategies to occur at intermediate intervals, and that populations respond to more permanent environmental changes primarily through evolutionary responses.**

environmental stress for response mechanisms and opportunities to adapt to changing and stressful environmental conditions. Populations will likely respond to environmental stresses by using multiple mechanisms that occur on different timescales (Fig. 1). In addition to evolutionary adaptation working on time spans of tens and hundreds of generations, we discuss how transgenerational effects and epigenetic changes may allow for faster adaptation (ca. 1–10 generations) to stressful environments. Finally, we discuss within-generation phenotypic plasticity and its role in coping with stress. All these mechanisms can operate simultaneously and contribute to coping with environmental stress. Therefore, we finally discuss how future research can address this complication and we map out the relative roles of the different mechanisms for coping with environmental stress.

Bet-hedging, the increase in fitness under stress that occurs at the expense of decreased fitness in benign environments, and migration, are two central topics in ecology and evolutionary biology that are not covered in this review. Both are surely central and important for the theme discussed, but the importance of bet-hedging and migration for coping with environmental stress and climate change has been recently discussed in several excellent papers.[14–17] Therefore, we refrain from discussing these topics in detail due to space limitations and instead refer to the published work. However, we would like to emphasize that both bet-hedging and migration constitute types of adaptation that occur through several mechanisms and at all timescales that are discussed in this review (Fig. 1). This is supported by evidence that evolutionary, plastic, and transgenerational/epigenetic components are important in relation to both phenomena.[18–20]

## Long-term responses to environmental stress

The classic view of evolution emphasizes that phenotypes can change across generations due to genetic changes caused by selection pressures induced by the environment. The magnitude of evolutionary change is recapitulated in the breeder's equation, which predicts that phenotypic change depends upon the strength of selection and the narrow sense heritability of the trait. Thus, the response to selection can be predicted from the expression $R = h^2 S$, where $R$ is the response to selection in one generation, $h^2$ is the narrow sense heritability of the trait considered, and $S$ is the selection differential, that is, the difference in mean trait value between the selected parents and all parents in the population. In order for a trait to respond to selection in a population, genetic variation in regions of the genome that influence phenotypic variation for the trait is a prerequisite. The literature on experimental studies of environmental stress adaptation provides numerous estimates of selection responses and heritability estimates.[21–23] Furthermore, genomic tools have enabled detailed insights into the genetic architecture of important stress tolerance traits in a rapidly increasing number of species.[24,25] Also, the field of conservation genetics provides estimates of environmental tolerance and evolutionary capacities for adapting to environmental challenges.[26,27] Generally, results show that environmental stress resistances are complex quantitative genetic traits that are influenced by the combined effect of multiple genes and environmental conditions. Narrow sense heritabilities are typically low to intermediate for stress resistance traits,[21] revealing that most

populations are able to respond to changing environmental conditions through evolutionary adaptation, but typically at a relatively slow pace, therefore increasing the risk of extinction.[2]

However, recent studies on ectotherms, including plant and insect species, have shown that some populations are evolutionarily constrained in important traits for the ability to cope with, for example, heat and drought stress.[22,28–32] Different mechanisms have been proposed to explain this pattern, including evolutionary trade-offs, phylogenetic constraints, and lack of adaptive variation in genomic regions relevant for heat and desiccation resistance.[2,28,33–35] The finding that several important stress resistance traits seem to be evolutionarily constrained is obviously worrying given the demand for evolutionary shifts caused by rapidly changing environmental conditions in many parts of the world, and may be a causative factor for expected future high extinction rates. Since heritability is a function of environmental ($V_E$) and additive genetic variation ($V_A$), it is important to note that low heritability due to lack of $V_A$ is of greater concern than a low $h^2$ caused by high levels of $V_E$. If the amount of $V_E$ is under genetic control, as suggested by recent literature (see, e.g., Ref. 36), it should be possible to mount an evolutionary response in performance traits by selection on genes controlling $V_E$.[37,38]

When discussing evolutionary responses to stressful environments, it is important to keep in mind that the narrow sense heritability is an imperfect metric for predicting the speed of evolutionary change. This is because population size has a disproportionate effect on the selection response. As formulated by Robertson,[39] the maximal selection response $R_{max}$ is dependent on the effective population size ($R_{max} = 2N_e i h^2 \sigma_p$), where $N_e$ is the effective population size, $i$ is the intensity of selection, $h^2$ is the narrow sense heritability, and $\sigma_p$ is the phenotypic standard deviation of trait values. This equation is illuminating as it shows that even with a relatively high heritability the response to selection can be low if $N_e$ is small. In contrast, very high effective population sizes will allow fast responses even if $h^2$ is low. Population size is especially important when populations adapt through new mutations, as mutational supply, which is proportional to population size, determines the speed at which new adaptive mutations appear in a population.[40] In summary, these concerns suggest that focusing on maintaining a high $N_e$ is of utmost importance for the ability of populations to adapt to stressful environmental conditions through evolutionary changes.

In conservation and evolutionary biology and in animal and plant breeding, there is often a strong focus on $h^2$. However, the $h^2$ of a particular trait might not always provide a good estimate of adaptation in varying and stressful environments for the reasons mentioned above and because estimates of $h^2$ can be environmentally dependent.[31,41] Furthermore, it can be hard to pinpoint which tolerance traits (e.g., upper or lower thermal limits, starvation and desiccation resistances) are most important for fitness and, thereby, the prospering of a given population.[42]

An important aspect of evolutionary adaptation to environmental stress or environmental change is that current environmental changes occur very rapidly.[33] Evidence suggests that some species will not be able to keep track with these shifts through evolution and will go extinct.[3,30,32,43] Part of the risk factors for extinction are the generation intervals of species. Species with short-generation intervals are likely to be better able to respond genetically to rapid environmental changes relative to species with longer generation intervals because evolution occurs in units of generations—not units of absolute time. At high altitudes, where climate changes are most extreme and resources often limited, development is typically slow for ectotherms due to low temperatures. In such habitats, evolutionary processes have been hypothesized to proceed at a slower pace,[44–47] and extinctions to be more prevalent.

### *Evolution of generalism and correlated traits*

It is often found that individuals that maintain high fitness in one environment and for one trait are superior in other environments and for other traits,[23,48] suggesting that genotypes that are robust across environmental gradients can evolve.[37,38] However, recent studies also emphasize that genetic correlations between performances in contrasting environments decrease with increasing environmental differences.[49] The finding of predominantly positive genetic correlations is by no means new,[50] and the discussion on how this is possible in life-history traits is very illuminating also with respect to stress tolerance traits. A model by Van Noordwijk and De Jong[51] on acquisition and allocation exemplifies one potential explanation for why

predominantly positive genetic correlations between traits and across environments are observed (see also Ref. 52). The model is based on relative amounts of genetic variation in acquisition and allocation between traits. If more genetic variation is found in acquisition than in allocation, it is inevitable that genetic correlations between traits remain positive, that is, individuals differ much more in their capabilities to acquire resources, or effectively process them,[43] than they differ in their allocation patterns between traits. This mechanism allows good quality individuals to have high robustness across environments, whereas low-quality individuals suffer from low tolerance in all environments.

Obviously, even in stressful environments, it is not only traits related to stress resistance that are under selection, but also those for the general quality of the individual. Depending on whether there is more genetic variation in the traits for overall quality than on stress resistance traits, selection can lead to elevated overall tolerance. For example, quantitative genetic studies typically show that there is more genetic variation in reaction norm elevation than the slope,[4,48,53] which could be explained by the relative roles of acquisition and allocation in the traits. This evoked the idea of "condition," where a pool of resources that is dependent on many genes dictates the amount of shared resources between traits.[54] This yields a prediction that whatever gene contributes positively to condition can be selected for in stressful environments, and will allow higher tolerance due to the increased amounts of resources that individuals can allocate to stress tolerance. In accordance with this idea, several traits associated with energy efficiency have been found to be important for fitness.[55–58]

The ideas about condition might explain experimental studies that suggest some shared genetic mechanisms among stress tolerance traits. In a classic study, Bubliy and Loeschcke[23] created replicate *Drosophila melanogaster* lines selected for different stress resistance traits, including heat, cold, desiccation, and starvation resistance. Correlated responses were observed for most traits; thus, lines selected for increased cold resistance were also more starvation-, desiccation-, heat-resistant, etc. This suggests some shared genetic mechanisms, in accordance with a general stress response hypothesis.[24,59] Similarly in bacteria, selection at fluctuating temperatures led to a higher overall performance also in other stressful environments.[60] It is noteworthy that while much of the evolutionary literature is about trade-offs, even negative genetic correlations allow traits to evolve independently, but the magnitude of the genetic correlation is predictive for the speed of independent evolution of the traits. Only highly unlikely scenarios of genetic correlations of –1 or 1 would constrain trait-independent evolution fully (eq. 20.5b in Refs. 61 and 62). Evolution of genotypes capable of tolerating several environments may also be hampered by the fact that when the number of selective environments increases, the time spent in each environment must decrease. This time limitation, which reduces the strength of selection for each particular environmental state, may be effective in preventing the evolution of "super genotypes" capable of performing well in all environments.[36] This is also in accordance with recent results from *Drosophila* that highlight that the quantitative genetics of stress resistance, such as tolerance to low temperatures, is environment-specific.[37,63,64] For example, Ørsted *et al.*[37] showed that candidate genes and levels of additive genetic variation affecting cold tolerance differed between flies that developed at low and high temperatures. This suggests reranking of genotypes across environments and that the evolutionary trajectories of certain traits are highly environment dependent (see also Ref. 49).

Detection of the evolution of apparent "super genotypes" can also be affected by the fact that not all of the possible traits, where trade-off can be manifested, are measured.[65] Moreover, reducing the expression of costly traits that are not used anymore can be a way to achieve higher fitness. Perhaps the best examples of this are obligate pathogens that have reduced genome sizes in comparison to their free-living relatives.[66,67] They might have increased their fitness in the host by losing genes essential for growing outside the host environments. Similar ideas have been suggested to explain evolutionary constraints in desiccation resistance in rainforest *Drosophila* species.[68] This kind of genome purging is one plausible mechanism for evolution of a general stress response and for the lack of evidence for trade-offs in adaptation.[35]

Genetic variation is not a guarantee for evolutionary changes and, similarly, predominantly positive correlations do not mean that evolutionary change is given. The opposite, namely little genetic variation

and unfavorable genetic correlations, does not necessarily imply evolutionary constraints. Work in the field of multivariate evolution suggests that instead of basing conclusions on single trait heritabilities or bivariate genetic correlations, an understanding of evolutionary trajectories and possible constraints must be sought from multivariate space. One should ask whether the alignment of genetic variation of several traits is parallel or perpendicular to the direction of selection. If the least amount of variation in traits is parallel to the direction of selection, then populations have little opportunity to evolve.[62] The opposite is true if selection leads toward the direction of largest genetic variation. In the framework of genetic correlations, one can also explore how traits in combination are able to explain genetic variation in fitness, and how much variation in fitness is left unexplained.[60,62] To give an example, instead of investigating the genetic architectures and evolutionary trajectories of proposed fitness components, such as heat and cold tolerance, and coping mechanisms, such as expression of heat shock proteins separately, these proxies should be considered at the same time, and the association of the traits with fitness should be verified experimentally.[42]

### *Take home messages—evolutionary adaptation*

On the basis of the topics covered in this first section of the paper, we emphasize that (1) the evolutionary capacity of several stress resistance traits in at least some ectotherms is limited/constrained; however, these constraints may be environment dependent, emphasizing the need to perform studies under ecologically relevant conditions; (2) when considering extinction risks of species and populations, the most important determinant of evolutionary speed is population size; this should be remembered in conservation efforts aiming to save populations and be an important consideration in conservation management; (3) single trait and bivariate correlation studies should preferably be replaced by multivariate studies that consider the role of several traits at the same time; by doing this, it is possible to reveal if genetic constraints occur in multivariate space; and (4) much experimental work on the evolutionary capacity of stress resistance is performed on traits and under environmental conditions that are proposed to be fitness relevant; it is important to verify these claims experimentally.

## Intermediate-term responses to environmental stress

In addition to traditional, genetically based adaptation, populations may also adjust their phenotype on a scale of one to a few generations by transgenerational effects. "Transgenerational effects" is often used as a broad term to describe all nongenetic effects that are transmitted from parent to offspring or from grandparents to grandoffspring.[69] Some transgenerational phenomena, such as maternal effects, were regarded for a time as a nuisance in experiments, but are now considered to be interesting in their own right.[70,71] Demonstrations that transgenerational effects can be adaptive in the wild do exist,[72] and it is often suggested that transgenerational effects may be important for how populations adapt to different types of stress and changing environments. Transgenerational effects can allow stress experienced by the parents to be minimized in the offspring. However, these transgenerational effects can have varied effects in populations,[73] and they can also be maladaptive.[74] Understanding transgenerational effects and the mechanisms behind them is therefore important for elucidating the effects of increasingly stressful environments on the population level and for biodiversity in general. Experiments and observations from nature are, however, needed to investigate and potentially verify the importance of transgenerational effects for coping with variable and stressful conditions. As with most new ideas, there is a lot of hyperbole and great expectations for their importance. In a recent review, it was concluded "... that evidence for 'widespread transgenerational epigenetic inheritance is lacking to date', and that 'the concept of transgenerational epigenetic inheritance in humans remains equivocal.'"[75] Thus, we should not overemphasize the importance of epigenetics and transgenerational effects, but be aware of methodological problems in many studies of transgenerational effects, such as those addressed by Engqvist and Reinhold,[76] and also remember that transgenerational effects can be incorporated into traditional evolutionary theory.[75]

While transgenerational phenomena have been known for a long time, many studies have lacked a clear mechanism by which they could be explained. The elucidation of molecular mechanisms for these effects, namely that information can also be passed

along epigenetically, has led to an increased interest in this topic and its role in adaptation.[77] It is noteworthy that in an ecological and evolutionary context, the causal mechanisms of transgenerational effects can be very different, but still lead to ecologically similar outcomes. These mechanisms can, for example, be maternal provisioning of nutrients to egg cells or seeds,[78] transfer of antibodies through the placenta in mammals,[79] or immune response priming in insects[80] and crustaceans,[81] or transgenerational epigenetic inheritance where information is transferred from one generation to the next without DNA sequence changes.[82–84] We use the term "epigenetic" here to refer to changes in gene expression caused by changes in chromatin in the absence of DNA sequence changes.[85] Epigenetic changes are therefore a subclass of nongenetic inheritance and they typically involve changes in chromatin structure via methylation of cytosine nucleotides or different modifications to histone proteins that are associated with DNA. The state of chromatin structure can influence the ability of transcription factors to bind DNA and, thus, transcription of particular genes. Furthermore, it is important to note that epigenetic changes are often involved in other processes than transgenerational epigenetic inheritance, such as development and within-generation phenotypic plasticity.[86]

### *Examples of transgenerational effects*

The older literature on transgenerational and in particular epigenetic inheritance has been reviewed in several recent papers.[87,88] Thus, here, we will focus on the recent literature. Transgenerational effects have been observed in animals and plants in a variety of taxonomic groups.[88] In plants, transgenerational responses are often associated with priming of defenses against pathogens and herbivores,[82,89,90] and effects on biomass[91] and drought resistance.[92] It has been proposed that transgenerational effects are more common in plants because they are sedentary organisms that have only passive migration of pollen and seeds. Moreover, the distinction between germline and soma is less clear in plants compared with animals, which may facilitate epigenetic inheritance as many epigenetic marks are reset during gametogenesis and many plants can reproduce clonally.[69] However, transgenerational effects in diverse animal groups also exist. In fish, for example, the environmental temperatures experienced by parents affect the growth and physiology of their offspring.[93–95] In some instances, reduced growth at high temperatures could be almost entirely compensated for in the next generation.[93,94] The zooplanktonic crustacean *Daphnia* also exhibits transgenerational responses for the induction of defense-related traits.[96] Population density experienced by fathers had transgenerational effects on the morphology of the migratory locust *Locusta migratoria*.[97] Transgenerational effects of nutrition have also been observed in the nematode *Caenorhabditis elegans*,[98] where the offspring of animals that had experienced starvation during early life were more resistant to starvation.

### *Epigenetic mechanisms and inheritance*

Transgenerational effects can be mediated via a variety of mechanisms, including DNA methylation,[99] histone modifications, and small RNAs. The mechanism of inheritance of DNA methylation is well established as cytosine methylation often occurs in symmetric sequence contexts of CG or CHG.[99] Semiconservative DNA replication leads to newly synthesized DNA strands that are hemimethylated, and maintenance DNA methyltransferase recognizes hemimethylated sites and methylates the unmethylated cytosines.[99] There is also some evidence for inheritance of histone modifications.[100–103] However, the mechanisms of inheritance for histone modifications remain poorly understood, and some studies have supported a model where the histone methyltransferases remain associated with the newly synthesized DNA strand instead of the modifications themselves and that these proteins then add the modifications to the histones.[104] In addition, there is evidence for the inheritance of small RNA molecules.[105–107] The stable inheritance of a small diffusible molecule through multiple cell divisions requires that there is a positive feedback loop where more RNA molecules are synthesized in each cell generation.

The demonstration that a transgenerational effect is truly based on epigenetic inheritance is not straightforward, particularly in mammals where the *in utero* exposure to a particular stress can potentially affect the epigenetic state of the developing offspring and its germ line, which will give rise to the F2 generation.[69,108] This is true to a lesser extent for developing seeds in plants as well.

However, from an ecological perspective, the exact mechanisms of transgenerational effects may be less important.

In plants, it has been shown that transgenerational responses often depend on the RNA-directed DNA methylation (RdDM) pathway.[109] In the canonical RdDM pathway, RNA polymerase IV and RNA-dependent polymerase 2 together transcribe double-stranded RNA that is cut by Dicer-like 3 into 24-nucleotide small interfering RNAs. These RNA molecules then are bound by Argonaute 4, resulting in direct DNA methylation of target sequences.[109] It has been shown that mutants for certain genes in the RdDM pathway are not able to produce transgenerational responses to pathogens.[83,110] In addition, transgenerational response to herbivory and leaf damage is dependent on the biogenesis of small RNAs in the RdDM pathway,[82] and the transgenerational response to osmotic stress is also abolished in RdDM pathway mutants.[84] These transgenerational responses seem to be mediated by DNA methylation of target genes,[82–84] where the silencing has been initiated by an environmental stress via the RdDM pathway. DNA methylation has also been implicated in other plant transgenerational responses, such as to nitrogen deficiency[111] and heavy metal exposure in rice,[112] drought stress in *Polygonum*,[113] and various stresses in dandelions.[114]

Animals do not possess the RdDM pathway, so the exact mechanisms for transgenerational effects mediated by epigenetic changes must be different. DNA methylation is absent or very low in certain groups of insects, such as *Drosophila*,[115] nematodes, and fungi. Indeed, it seems that in *Drosophila*, the function of DNA methylation has been replaced by the Polycomb repressive complex[99] responsible for the trimethylation of lysine 27 in histone 3 (H3K27me3). However, transgenerational effects transmitted through fathers have been observed in *Drosophila*.[116] In *Drosophila*, the diet of fathers has been shown to influence the triglyceride content of offspring, and this transgenerational response requires the histone modifications H3K27me3 and H3K9me3.[116] In nematodes, different mechanisms have been implicated in transgenerational effects; transgenerational inheritance of an antiviral and starvation responses are mediated by a small RNA molecule.[106,117] Histone modifications have also been implicated in the transgenerational responses to various environmental stresses, and this process seems to be dependent on H3K4me3.[118]

Mammals, however, do possess DNA methylation, and mice subjected to odor fear conditioning had a transgenerational response to the odor that was associated with DNA methylation changes in specific genes.[119] However, mammalian studies have the complication that exposure to stress in the intrauterine environment can influence, for example, DNA methylation patterns of the offspring directly, thus not constituting epigenetic inheritance per se.[108] However, maternal effects can still be mediated via epigenetic mechanisms even if they are not inherited via the germ line. For example, maternal care given by rat mothers influenced the DNA methylation patterns of their offspring.[120]

There is some evidence from bacteria that environmental stress can be mutagenic.[121,122] Furthermore, Aldrich and Maggert[123] have recently shown that dietary excess in *Drosophila* leads to genome rearrangements, where the copy number of ribosomal RNA genes is reduced. This occurs both in somatic and germline tissues, and it was shown that these genetic changes are transmitted to the offspring. Pathogens cause dramatic reductions in fitness and cause stress to host species. However, highly specific information on pathogens present in parents can be carried to the next generation by maternal antibodies in many organisms,[79] and in insects via immune elicitors maternally transmitted between generations by the egg-yolk protein vitellogenin.[80,124,125] Such transgenerationally transmitted information can be beneficial if the same pathogens stay prevalent for a long time.

### *Transmission of transgenerational effects*

Transgenerational effects have different durations. Some last only for a single generation, so that an exposed parent transmits the effect to its offspring, but with environmental signals being absent in subsequent generations. Priming by osmotic stress in *Arabidopsis*[84] is an example of such a response. Other effects can last for multiple generations, such as transgenerational temperature responses in sticklebacks[95] where grandparental effects transmitted through the male parent were observed. In *Arabidopsis,* the induction of defenses as a response to herbivory lasted for two generations.[82] Even longer lasting responses have been observed in

nematodes, where antiviral responses lasted for at least 10 generations.[106]

It is expected that for transgenerational effects to evolve in the first place, the environment the parents experience has to be similar to the environment of the offspring. Long-distance dispersal can break the environmental correlation between parents and offspring; thus, differences in transmission of transgenerational effects among the parents are expected if males and females disperse differently. For example, in many plant species, seed dispersal can be limited, while pollen can disperse much further. Interestingly, Wibowo *et al.*[84] noted that transmission of the osmotic stress response in *Arabidopsis* occurred only through seed and not by pollen, and this was due to DNA glycosylase activity in pollen. In pollen development, DNA methylation marks responsible for the osmotic stress response were reset. This makes sense from an ecological perspective as the correlation between parent and offspring environments is expected to diminish with increasing dispersal. Indeed, it has been observed that in plants, transgenerational effects are transmitted more often through seeds.[126]

In mammals, maternal transmission can occur via multiple mechanisms,[127] but paternal transmission has also been observed.[128] In particular, small RNAs in sperm have been shown to contribute to this phenomenon.[128]

The predictive ability of reaction norms is impaired if the environmental conditions at previous time steps (generations, across or within developmental stages) provided poor cues for upcoming environments, that is, environmental changes are characterized by random fluctuations between the generations. However, there are several issues to consider, as different modeling approaches have reached different conclusions about when transgenerational effects are adaptive or maladaptive. Earlier work suggested that short environmental fluctuations should favor transgenerational effects.[129,130] In contrast, more recent work has suggested that fluctuations on longer timescales favor transgenerational responses;[131–134] the differences can be traced back to different assumptions of the models. Nevertheless, the frequencies of environmental fluctuations in relation to generation time and the predictive power of environmental cues are crucial factors in determining when transgenerational effects evolve.[131]

### *Take home messages—transgenerational effects*

In summary, examples of transgenerational effects are found throughout the tree of life. Their duration varies, but there are examples where these effects persist for more than two generations. These effects can be mediated by a wide variety of mechanisms. While there are significant gaps in our knowledge regarding the exact mechanisms, DNA methylation in plants and histone modifications in animals seem to be involved, as well as small RNAs in both plants and animals. There is no doubt that transgenerational effects exist, but so far meta-analyses have shown that the effects are small.[135] A challenge for the future is to investigate if transgenerational effects also have small fitness effects in nature, how often transgenerational effects are adaptive, and under what circumstances we can expect them to occur. The importance of transgenerational effects for coping with environmental stress is so far poorly understood, and there is a strong need for properly designed experimental work so that the properties of transgenerational effects can be understood and subsequently incorporated into evolutionary theory.[75]

## Short-term responses to environmental stress

The fastest responses to changing and stressful environmental conditions are plastic responses such as altering the physiology of a genotype in response to a change in the environment. Phenotypic plasticity can be defined as the ability of a single genotype to produce different phenotypes in different environments.[136,137] However, this definition does not take into account if plasticity is fixed for lifetime or whether it is inducible and reversible (Fig. 2). In the following paragraphs, unless otherwise stated, we use plasticity to describe inducible and reversible plasticity.

Both empirical and theoretical work suggest that plastic adjustments contribute strongly to fitness in fluctuating environments; for example, plastic adjustments of the physiology are well described in the literature.[138] Thus, exposure to low or high temperatures can dramatically increase tolerance toward subsequent exposure to cold and heat stress, respectively,[1,139] emphasizing the potential benefits associated with plasticity.[140] Physiological adjustments, however, seem to affect upper

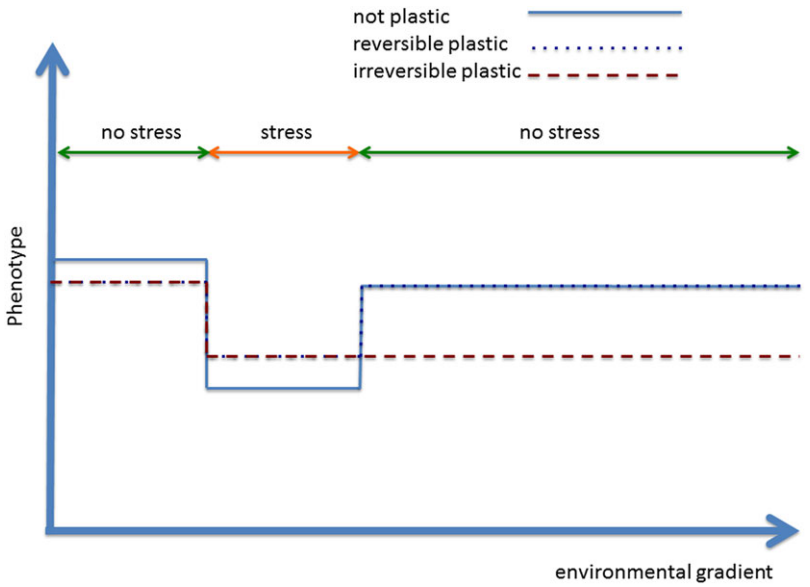


**Figure 2.** A plastic response can be reversible, irreversible, or nonexistent. Here, we schematize the effect on fitness of the three scenarios. In the figure, a favorable environment is replaced by a stressful environment that later becomes favorable again. In the "not plastic" scenario, fitness is highest before stress, relative to the two other scenarios, because the costs of plasticity are not present. Fitness decreases under exposure to stress and increases again after stress vanishes. However, fitness will likely not return to its level before stress because of the energy used to cope with stressful environmental conditions, energy not available for maintenance and reproduction, and because of irreversible cellular damage. In the "reversible plastic" scenario, fitness decreases with stress exposure but not to the same extent as in the "not plastic" case, and then increases after the environment becomes favorable again. As with the "not plastic" scenario, fitness does not reach the same level as before stress exposure because of the energy costs associated with plasticity. In the "irreversible plastic" scenario, fitness is high before stress exposure, decreases under stress, and does not increase again after stress disappears because the plastic response, which was beneficial under stressful conditions, now becomes costly. Depending on the frequency and intensity of environmental fluctuations over time, different strategies may be optimal. Evolution will favor genotypes in a given environment that, on average, maintain the highest level of fitness across the environments they are exposed to. The figure is not exhaustive of the possible fitness consequences associated with a plastic response. For example, fitness for a reversible plastic genotype under favorable conditions may well be higher than for a nonplastic genotype.

thermal limits much less than lower thermal limits.[138,139,141,142] Thus, effects of heat acclimation typically increase heat resistance much less than cold acclimation increases cold resistance. Among several *Drosophila* species, developmental temperatures altered cold limits by 2–4 °C, but heat limits by <1 °C.[139,143] Such a pattern has been generally noted for both ectotherms and endotherms[30,138,139] despite the fact that heat acclimation typically leaves a stronger signal than cold acclimation on, for example, transcript and protein levels.[144–146] Moreover, it seems that heat tolerance across kingdoms is far more similar between species than cold tolerance.[30,33,34] This could reflect different selective pressures or biochemical constraints for heat and cold resistance.[30,32,147]

### *Physiological responses to stressful environments*

Perhaps the best-described physiological response to sudden changes in temperature and other environmental stresses is the upregulation of heat shock proteins (Fig. 3). This is a common and highly conserved response to acute exposure to high temperatures and other abiotic as well as biotic stresses.[59,148] Upregulation can be induced within minutes and has multiple vital functions in cells exposed to stress.[59,148] However, the speed with which heat shock proteins and other stress response genes are upregulated differs between species. For example, Bahrndorff *et al.*[149] found that the gene and protein expression of an important heat shock protein (Hsp70) follow different dynamics in the

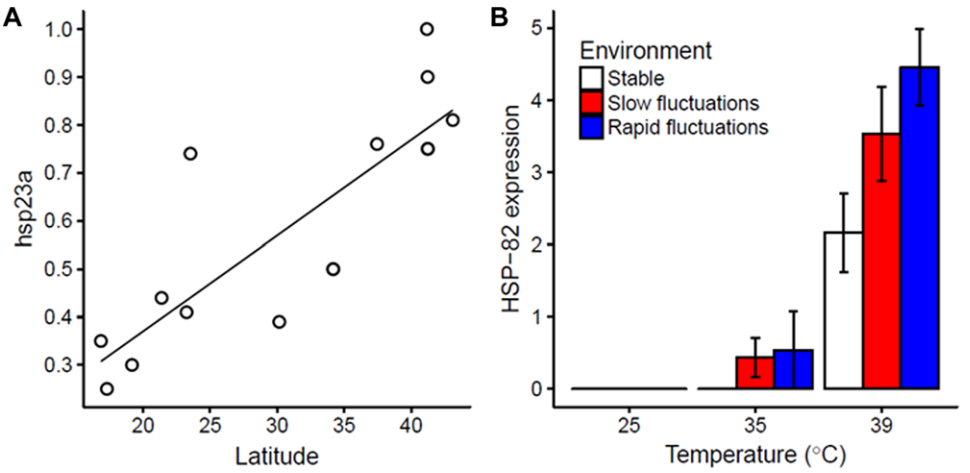


**Figure 3.** Examples of physiological adaptations to fluctuating environments. (A) Linear regression of the haplotype frequencies of heat shock protein 23a (hsp23a) in *D. melanogaster* populations collected along the east coast of Australian with the latitude (in degrees South) (data from Ref. 195). (B) Amount of inducible expression of heat shock protein 82 (Hsp82) in the ciliate protozoa *Tetrahymena thermophila* in response to experimental evolution in stable, slowly fluctuating, and rapidly fluctuating thermal environments (data from Ref. 196).

collembolan *Orchesella cincta* compared with observations from, for example, *Drosophila*.[150] These differences might be adaptations, respectively, to temperature-buffered soil habitats and highly fluctuating above-ground temperatures.

Conditions that induce upregulation of heat shock proteins are species-specific and best described for exposure to heat stress where upregulation is typically observed when organisms are suddenly exposed to abrupt heat waves.[151] However, expressing heat shock protein genes and many other stress response genes is costly in terms of energy, and long-term upregulation is not a beneficial evolutionary strategy.[59,152–154] Therefore, the adaptive benefits of these plastic responses are most pronounced in response to coping with sudden and transient changes in environmental conditions.

Although the heat shock response is perhaps the most recognized response to environmental fluctuations, it is obviously not the only one. With slow thermal fluctuations, the changes in lipid bilayer viscosity constitute another potential adaptation mechanism enabling organisms to cope with thermal fluctuations.[147] Interestingly, monthly fluctuations in temperature over 63 generations in *Drosophila* improved the ability of strains from fluctuating environments to regulate the number of double bonds in lipids, and hence lipid fluidity.[155] In the case of heat shock genes, these genes can be responsive over different periods of time. Small heat shock proteins appear to play an important role in the response to fast changes, whereas larger molecular mass chaperones, such as Hsp70 and Hsp90, respond more strongly to long-term exposure to stress, best illustrated with high temperatures.[156]

Another study has shown that the rate of temperature change in so-called ramping assays, used to assess upper critical temperatures, also influences Hsp expression.[157] Thus, flies ramped slowly to stressful temperatures induce a stronger heat shock protein response compared with flies ramped to the same temperature at a faster rate, likely because slow ramping induces more heat damage at the cellular level due to longer exposure time. The fact that different genes are involved in responses to sudden and more long-term exposure to stress is also nicely illustrated in the killifish *Fundulus heteroclitus*, in which an osmotic challenge triggers high expression of several genes that differs from the time window in which most genes were expressed.[158] This suggests that different within-generation fluctuations could target different genes, contributing to differently timed plasticity.

### *The importance of environmental cues for adaptive plastic responses*

Environmental cues and efficiently working sensory mechanisms may allow organisms to adjust the

phenotype through plastic responses quickly enough to respond to environmental changes. Physiological adjustments induced to cope with temperature changes are not only induced by shifts in temperature but also by changed photoperiods, changed food abundance, or any other environmental time series, that if positively autocorrelated, can provide cues about upcoming thermal changes. Daily fluctuations in temperature have been shown to induce changes in phototransduction genes, which have been linked with the ability to sense thermal changes or to prefer certain temperatures.[159,160] In addition to daily thermal changes, similar kinds of sensing mechanisms operate also on longer time scales, for example, in sensing annual changes in the environment when preparing to diapause.[161,162]

For plasticity to be adaptive, it requires correct cues about altered environmental conditions. Bradshaw and Holzapfel[163] have argued that evolutionary responses to environmental changes, such as climate alterations, are more about responding to seasonal cues, such as changes in day length, changes in temperatures, and changes in food availability, for example, than they are to changes in, for example, upper temperatures. This argument is supported by several studies showing genetic responses to earlier spring and, thereby, food supplies for bird species.[163,164] Evidence regarding whether such changes are due to genetic selection or due to phenotypic plasticity is very scarce.[164–166] However, at least in squirrels, the observed advancement of mating due to global change has been linked mostly to phenotypic plasticity rather than a genetic response.[167] In the long run, cue–response–environment mismatch could select for lessened reliance to a cue, or increase selection toward bet-hedging strategies.[168] Therefore, in coping with extreme temperatures, the ability to respond to cues is likely under selection.[163]

In experiments where plastic effects and mismatch can be controlled for, it was found that fruit flies (*D. melanogaster*) that had developed at a hot temperature will benefit at hotter temperatures as adults but pay a cost at cold temperatures, and vice versa.[169] The mismatch between cue and upcoming environments can act as a cost that hinders evolution of plasticity. The cost of plasticity could also be manifested if maintaining plastic reactions requires resources even if not in use.[48,137] For example, irreversible plasticity in the form of irreversible morphological changes constitutes examples where plasticity is maladaptive in the absence of, for example, predators, and selection may therefore act against such mechanisms in environments where predators are only transient visitors.[170] However, such costs of plasticity are commonly found to be low, suggesting that there must be other constraints than costs[171] (see Fig. 2 for a further presentation of the costs and benefits associated with different types of plasticity).

### *Take home messages—plasticity*

Plasticity is recognized to be an important adaptation mechanism, and research on this topic has progressed dramatically over the years.[137,172,173] Several distinct forms of plasticity can be defined, that is, reversible or irreversible plasticity, and each form can have adaptive or maladaptive effects on individuals. Where and when these different forms of plasticity are adaptive and can be selected for are critically different.[42,139,174] Future work should be on testing the relative roles of the different types of plasticity on fitness in naturally relevant, fluctuating environments, and manipulating the speed and predictability of fluctuations in environmental conditions to pinpoint the adaptive importance of plasticity for the ability to prosper in a rapidly changing environment. The different forms of plasticity, and where and when they are selected for, are critically different.[42,174]

## Conclusions and future tasks

In this paper, we have sketched how coping with environmental stress can occur through different mechanisms and on different timescales (see also Ref. 134). This is an important and timely research area given the fast environmental changes and increased rates of extinctions currently observed. Theoretical and experimental work has provided detailed insight into important mechanisms for coping with environmental stress. On the basis of this work, we are able to discuss and answer central questions related to coping with stressful conditions and suggest future research avenues.

### *Why is it important to consider how short and intermediate mechanisms of adaptation change subsequent evolutionary dynamics?*

Plasticity or transgenerational effects can move a population closer to the phenotypic optimum when the population has to adapt to drastic environmental

change; this is known as the Baldwin effect.[175] Moreover, phenotypic plasticity that occurs within a generation can influence evolutionary dynamics by keeping population size higher when a drastic environmental change occurs, relative to a situation without plasticity. This will allow faster subsequent evolutionary adaptation because of higher effective population size, increased mutational supply, and therefore more efficient natural selection.[176,177] Transgenerational effects can speed up adaptation for the same reasons.[178] Moreover, there is a theoretical argument that plastic genotypes can respond more effectively to selection.[179] Essentially, the idea is that a genotype that already has the ability to adjust a given phenotype may also have a larger mutational target should this phenotype need to be changed permanently during long-term adaptation.[179] Indeed, there is some experimental evidence that plastic genotypes can respond more efficiently to selection compared with less plastic genotypes.[180,181] In relation to coping with rapid temperature changes, for example, caused by climate change, this theory suggests that traits that are highly plastic should respond more effectively to selection compared with less plastic traits. For example, the ability to tolerate low temperatures is a highly plastic trait in ectotherms.[139] Traits associated with cold tolerance also seem to have large evolutionary potentials compared to traits related to heat resistance, which are typically less plastic and evolutionarily constrained in some species,[30–32,139] thus supporting this hypothesis.

### *Knowledge on genetic, transgenerational, and within-generation adaptation mechanisms is important, but it is even more important to disentangle when and in which situations they are in operation*

The rich literature in ecophysiology and adaptation research contains numerous heritability estimates, estimates of selection responses, and reports from omics studies pinpointing candidate genes, transcripts, proteins, and metabolites. These data are typically obtained from detailed and highly controlled laboratory experiments performed on a few model species. These excellent data and techniques have provided the foundation for performing more ecologically relevant studies, enabling, for example, testing hypotheses based on experimental laboratory work and theory. We propose that more work should also be done in the field to understand how organisms cope with variable and periodically stressful environmental conditions. We have numerous estimates of upper and lower thermal limits, and of desiccation and starvation resistance from laboratory studies, but we have little knowledge as to whether these estimates are good proxies for fitness in the field across species and natural environments. For example, a high $CT_{max}$ or a low $CT_{min}$ are not valid predictors of field fitness if these proxies have zero correlation with fitness in prevailing conditions in the wild.[42,58,182,183]

A future challenge will also be to disentangle differential evolutionary responses across generations, adaptive plasticity, and adaptive transgenerational effects. All have been convincingly shown to be important for coping with environmental challenges. However, it is challenging to dissect the relative importance of these mechanisms because they typically work simultaneously, as do bet-hedging and migration (which are not covered in depth here). Obtaining data on lifetime fitness across generations in field populations combined with detailed tracking of experimental conditions experienced by individuals throughout life will likely provide new knowledge on this in the near future.[184–186]

Another topic that has just recently begun to be investigated in the context of environmental stress research is the study of microbiomes. Microbiomes are currently receiving enormous attention in multiple disciplines. Evidence, which is typically of correlative nature, suggests that intestinal microbiome abundance and composition is important for the ability to cope with extreme temperatures and other types of environmental stress.[187–189] This opens up for new avenues of existing research questions, where the focus is not only on the particular species/population but also on the myriad of microorganisms in the microbiome and its resilience across environmental conditions. The microbiome is highly plastic and environment dependent; thus, this field of research adds a new dimension to the study of plasticity.

### *The effects of interacting species will be an important future research area in environmental stress research*

The ability of a system to recover its original function after a disturbance likely depends on complex interactions between partners of which we have

little knowledge. It is crucial to ask if environmental adaptation in multispecies systems differs from single-species studies and how much context dependencies different communities and competitors impose on adapting to new conditions.[34,190–193] Such species interactions are not only limited to typical trophic interactions. Moreover, it is of utmost importance to consider the relative roles of evolution and ecology; will species have the option of evolving to cope with new conditions or are they just replaced by others? Thus, while ecophysiological and evolutionary studies on stress tolerances have typically centered on single-species responses to environmental changes and environmental stress, future research encompassing several biological disciplines should also investigate ecosystem responses.[194]

## Acknowledgments

We thank Douglas Braaten and two anonymous reviewers for their thoughtful comments on an earlier version of this paper. The K. Viipale and Konnevesi Research Station is acknowledged for nourishment of soul and body. This research was financed by the Danish Natural Science Research Council through a Sapere aude stipend to T.N.K. (DFF—4002-00036), and by the Academy of Finland Grants to T.K. (278751) and to I.K. (274769).

## Competing interests

The authors declare no competing interests.

## References

1. Hoffmann, A.A. & P.A. Parsons. 1991. *Evolutionary Genetics and Environmental Stress.* Oxford, UK: Oxford University Press.
2. Hoffmann, A.A., C.M. Sgró & T.N. Kristensen. 2017. Revisiting adaptive potential, population size, and conservation. *Trends Ecol. Evol.* **32:** 506–517.
3. Urban, M.C. 2015. Accelerating extinction risk from climate change. *Science* **348:** 571–573.
4. Windig, J.J. 1994. Reaction norms and the genetic basis of phenotypic plasticity in the wing pattern of the butterfly *Bicyclus anynana. J. Evol. Biol.* **7:** 665–695.
5. La Marca, E., K.R. Lips, S. Lötters, *et al.* 2005. Catastrophic population declines and extinctions in neotropical harlequin frogs (Bufonidae: Atelopus). *Biotropica* **37:** 190–201.
6. Newman, J.A., M. Anand, H.L. Henry, *et al.* 2011. *Climate Change Biology*. Wallingford, CT: CABI.
7. Hanna, L. 2015. *Climate Change Biology*. London, UK: Academic Press.
8. Spielman, D., B.W. Brook & R. Frankham. 2004. Most species are not driven to extinction before genetic factors impact them. *Proc. Natl. Acad. Sci. USA* **101:** 15261–15264.
9. Glynn, P.W. 1988. El Niño-southern oscillation 1982–1983: nearshore population, community, and ecosystem responses. *Ann. Rev. Ecol. Syst.* **19:** 309–345.
10. Hoffmann, A.A. & M.J. Hercus. 2000. Environmental stress as an evolutionary force. *BioScience* **50:** 217–226.
11. Armbruster, P. & D.H. Reed. 2005. Inbreeding depression in benign and stressful environments. *Heredity* **95:** 235–242.
12. Reed, D.H., C.W. Fox, L.S. Enders, *et al.* 2012. Inbreeding–stress interactions: evolutionary and conservation consequences. *Ann. N.Y. Acad. Sci.* **1256:** 33–48.
13. Botero, C.A., F.J. Weissing, J. Wright, *et al.* 2015. Evolutionary tipping points in the capacity to adapt to environmental change. *Proc. Natl. Acad. Sci. USA* **112:** 184–189.
14. Simons, A.M. 2011. Modes of response to environmental change and the elusive empirical evidence for bet hedging. *Proc. R. Soc. B Biol. Sci.* **278:** 1601–1609.
15. Charmantier, A. & P. Gienapp. 2014. Climate change and timing of avian breeding and migration: evolutionary versus plastic changes. *Evol. Appl.* **7:** 15–28.
16. Shama, L.N.S. 2015. Bet hedging in a warming ocean: predictability of maternal environment shapes offspring size variation in marine sticklebacks. *Glob. Change Biol.* **21:** 4387–4400.
17. Donelson, J.M., S. Salinas, P.L. Munday, *et al.* 2018. Transgenerational plasticity and climate change experiments: where do we go from here? *Glob. Change Biol.* **24:** 13–34.
18. Veening, J.-W., W.K. Smits & O.P. Kuipers. 2008. Bistability, epigenetics, and bet-hedging in bacteria. *Ann. Rev. Microbiol.* **62:** 193–210.
19. van Buskirk, J., R.S. Mulvihill & R.C. Leberman. 2012. Phenotypic plasticity alone cannot explain climate-induced change in avian migration timing. *Ecol. Evol.* **2:** 2430–2437.
20. O'Dea, R.E., D.W.A. Noble, S.L. Johnson, *et al.* 2016. The role of non-genetic inheritance in evolutionary rescue: epigenetic buffering, heritable bet hedging and epigenetic traps. *Environ. Epigenet.* **2:** 1–12.
21. Mousseau, T.A. & D.A. Roff. 1987. Natural selection and the heritability of fitness components. *Heredity* **59:** 181–197.
22. Hoffmann, A.A., R.J. Hallas, J.A. Dean, *et al.* 2003. Low potential for climatic stress adaptation in a rainforest *Drosophila* species. *Science* **301:** 100–102.
23. Bubliy, O.A. & V. Loeschcke. 2005. Correlated responses to selection for stress resistance and longevity in a laboratory population of *Drosophila melanogaster. J. Evol. Biol.* **18:** 789–803.
24. Kultz, D. 2005. Molecular and evolutionary basis of the cellular stress response. *Ann. Rev. Physiol.* **67:** 225–257.
25. Shafer, A.B., J.B. Wolf, P.C. Alves, *et al.* 2015. Genomics and the challenging translation into conservation practice. *Trends Ecol. Evol.* **30:** 78–87.
26. Frankham, R., J. Ballou & D. Briscoe. 2010. *Introduction to Conservation Genetics.* Cambridge: Cambridge University Press.
27. Edwards, C.E. 2015. Looking to the future of conservation genetics: the case for using quantitative genetic experiments

to estimate the ability of rare plants to withstand climate change. *Am. J. Bot.* **102:** 1011–1013.
28. Kellermann, V., B. van Heerwaarden, C.M. Sgró, *et al.* 2009. Fundamental evolutionary limits in ecological traits drive *Drosophila* species distributions. *Science* **325:** 1244–1246.
29. Kelly, M.W., E. Sanford & R.K. Grosberg. 2012. Limited potential for adaptation to climate change in a broadly distributed marine crustacean. *Proc. R. Soc. B Biol. Sci.* **279:** 349–356.
30. Araújo, M.B., F. Ferri-Yanez, F. Bozinovic, *et al.* 2013. Heat freezes niche evolution. *Ecol. Lett.* **16:** 1206–1219.
31. Kristensen, T.N., J. Overgaard, J. Lassen, *et al.* 2015. Low evolutionary potential for egg-to-adult viability in *Drosophila melanogaster* at high temperatures. *Evolution* **69:** 803–814.
32. Hoffmann, A.A., S.L. Chown, S. Clusella-Trullas, *et al.* 2013. Upper thermal limits in terrestrial ectotherms: how constrained are they? *Funct. Ecol.* **27:** 934–949.
33. Kellermann, V., J. Overgaard, A.A. Hoffmann, *et al.* 2012. Upper thermal limits of *Drosophila* are linked to species distributions and strongly constrained phylogenetically. *Proc. Natl. Acad. Sci. USA* **109:** 16228–16233.
34. Kellermann, V., V. Loeschcke, A.A. Hoffmann, *et al.* 2012. Phylogenetic constraints in key functional traits behind species' climate niches: patterns of desiccation and cold resistance across 95 *Drosophila* species. *Evolution* **66:** 3377–3389.
35. Hoffmann, A.A. 2014. Evolutionary limits and constraints. In *Princeton Guide to Evolution.* J.B.E.A. Losos, Ed.: 247–252. Princeton University Press.
36. Whitlock, M.C. 1996. The red queen beats the jack-of-all-trades: the limitations on the evolution of phenotypic plasticity and niche breadth. *Am. Nat.* **148:** S65–S77.
37. Ørsted, M., D.R. Rohde, A.A. Hoffmann, *et al.* 2018. Environmental variation partitioned into separate heritable components. *Evolution* **72:** 136–152.
38. Blasco, A., M. Martínez-Álvaro, M.-L. García, *et al.* 2017. Selection for environmental variance of litter size in rabbits. *Genet. Select. Evol.* **49:** 48.
39. Robertson, A. 1960. A theory of limits in artificial selection. *Proc. R. Soc. B Biol. Sci.* **153:** 234–249.
40. Bell, G. & S. Collins. 2008. Adaptation, extinction and global change *Evol. Appl.* **1:** 3–16
41. Hoffmann, A.A. & J. Merilä. 1999. Heritable variation and evolution under favourable and unfavourable conditions. *Trends Ecol. Evol.* **14:** 96–101.
42. Ketola, T. & T.N. Kristensen. 2017. Experimental approaches for testing if tolerance curves are useful for predicting fitness in fluctuating environments. *Front. Ecol. Evol.* **5:** 129.
43. Ceballos, G., P.R. Ehrlich, A. Barnosky, *et al.* 2015. Accelerated modern human–induced species losses: entering the sixth mass extinction. *Sci. Adv.* **1:** e1400253.
44. Bleiweiss, R. 1998. Slow rate of molecular evolution in high-elevation hummingbirds. *Proc. Natl. Acad. Sci. USA* **95:** 612–616.
45. Dillon, M.E., M.R. Frazier & R. Dudley. 2006. Into thin air: physiology and evolution of alpine insects. *Integr. Comp. Biol.* **46:** 49–61.
46. Gillman, L.N., D.J. Keeling, H.A. Ross, *et al.* 2009. Latitude, elevation and the tempo of molecular evolution in mammals. *Proc. R. Soc. B Biol. Sci.* **276:** 3353–3359.
47. Puurtinen, M., M. Elo, M. Jalasvuori, *et al.* 2016. Temperature-dependent mutational robustness can explain faster molecular evolution at warm temperatures, affecting speciation rate and global patterns of species diversity. *Ecography* **39:** 1025–1033.
48. Scheiner, S.M. 1993. Genetics and evolution of phenotypic plasticity. *Ann. Rev. Ecol. Syst.* **24:** 35–68
49. Ørsted, M., A.A. Hoffmann, P.D. Rohde, *et al.* 2018. Strong impact of thermal environment on the quantitative genetic basis of a key stress tolerance trait. *Heredity* https://doi.org/10.1038/s41437-018-0117-7.
50. Roff, D.A. 1996. The evolution of genetic correlations: an analysis of patterns. *Evolution* **50:** 1392–1403.
51. van Noordwijk, A.J. & G. de Jong. 1986. Acquisition and allocation of resources: their influence on variation in life history tactics. *Am. Nat.* **128:** 137–142.
52. Riska, B. 1986. Some models for development, growth, and morphometric correlation. *Evolution* **40:** 1303.
53. Nussey, D.H., A.J. Wilson & J.E. Brommer. 2007. The evolutionary ecology of individual phenotypic plasticity in wild populations. *J. Evol. Biol.* **20:** 831–844.
54. Rowe, L. & D. Houle. 1996. The lek paradox and the capture of genetic variance by condition dependent traits. *Proc. R. Soc. B Biol. Sci.* **263:** 1415–1421.
55. Ketola, T. & J.S. Kotiaho. 2009. Inbreeding, energy use and condition. *J. Evol. Biol.* **22:** 770–781.
56. Kristensen, T.N., P. Sørensen, M. Kruhøffer, *et al.* 2005. Genome-wide analysis on inbreeding effects on gene expression in *Drosophila melanogaster*. *Genetics* **171:** 157–167.
57. Pedersen, K.S., T.N. Kristensen, V. Loeschcke, *et al.* 2008. Metabolomic signatures of inbreeding at benign and stressful temperatures in *Drosophila melanogaster*. *Genetics* **180:** 1233–1243.
58. Ketola, T., Z. Boratyński & J.S. Kotiaho. 2014. Manipulating genetic architecture to reveal fitness relationships. *ProcPoS* **1**:e1. https://www.peerageofscience.org/proceedings/2014_e1.
59. Sørensen, J.G., T.N. Kristensen & V. Loeschcke. 2003. The evolutionary and ecological role of heat shock proteins. *Ecol. Lett.* **6:** 1025–1037.
60. Ketola, T., L. Mikonranta, J. Zhang, *et al.* 2013. Fluctuating temperature leads to evolution of thermal generalism and preadaptation to novel environments. *Evolution* **67:** 2936–2944.
61. Falconer, D.S. & T.F.C. Mackay. 1996. *Introduction to Quantitative Genetics.* Harlow, UK: Longman Publishing Group.
62. Walsh, B. & M.W. Blows. 2009. Abundant genetic variation + strong selection = multivariate genetic constraints: a geometric view of adaptation. *Ann. Rev. Ecol. Evol. Syst.* **40:** 41–59.
63. Wilson, A.J., J.M. Pemberton, J.G. Pilkington, *et al.* 2006. Environmental coupling of selection and heritability limits evolution. *PLoS Biol.* **4:** 1270–1275.

64. Telonis-Scott, M., R. Hallas, S.W. McKechnie, *et al.* 2009. Selection for cold resistance alters gene transcript levels in *Drosophila melanogaster*. *J. Insect Physiol.* **55:** 549–555.
65. Huey, R.B. & P.E. Hertz. 1984. Is a jack-of-all-temperatures a master of none? *Evolution* **38:** 441–444.
66. Sundberg, L.-R. & K. Pulkkinen. 2015. Genome size evolution in macroparasites. *Int. J. Parasitol.* **45:** 285–288.
67. Weinert, L.A. & J.J. Welch. 2017. Why might bacterial pathogens have small genomes? *Trends Ecol. Evol.* **32:** 936–947.
68. Kellermann, V. & A.A. Hoffmann. 2006. Revisiting heritable variation and limits to species distribution: recent developments. *Israel J. Ecol. Evol.* **52:** 247–261.
69. Heard, E. & R.A. Martienssen. 2014. Transgenerational epigenetic inheritance: myths and mechanisms. *Cell* **157:** 95–109.
70. Wolf, J.B. & M.J. Wade. 2009. What are maternal effects (and what are they not)? *Philos. Trans. R. Soc. B Biol. Sci.* **364:** 1107–1115.
71. Pertoldi, C., D.H. Andersen, A. Røgilds, *et al.* 2005. Heat induced maternal effects in *Drosophila mercatorum* and its evolutionary consequences. *Evol. Ecol. Res.* **7:** 203–217.
72. Galloway, L.F. & J.R. Etterson. 2007. Transgenerational plasticity is adaptive in the wild. *Science* **318:** 1134–1136.
73. Dyer, A.R., C.S. Brown, E.K. Espeland, *et al.* 2010. The role of adaptive trans-generational plasticity in biological invasions of plants. *Evol. Appl.* **3:** 179–192.
74. Guillaume, A.S., K. Monro & D.J. Marshall. 2016. Transgenerational plasticity and environmental stress: do paternal effects act as a conduit or a buffer? *Funct. Ecol.* **30:** 1175–1184.
75. Charlesworth, D., N.H. Barton & B. Charlesworth. 2017. The sources of adaptive variation. *Proc. R. Soc. B Biol. Sci.* **284**. https://doi.org/10.1098/rspb.2016.2864.
76. Engqvist, L. & K. Reinhold. 2016. Adaptive transgenerational phenotypic plasticity and the lack of an experimental control in reciprocal match/mismatch experiments. *Methods Ecol. Evol.* **7:** 1482–1488.
77. Galloway, L.F. 2005. Maternal effects provide phenotypic adaptation to local environmental conditions. *New Phytol.* **166:** 93–100.
78. Mousseau, T.A. & C.W. Fox. 1999. Maternal effects as adaptations. *Q. Rev. Biol.* **74:** 468–469.
79. Grindstaff, J.L., E.D. Brodie & E.D. Ketterson. 2003. Immune function across generations: integrating mechanism and evolutionary process in maternal antibody transmission. *Proc. R. Soc. Lond. B Biol. Sci.* **270:** 2309–2319.
80. Sadd, B.M., Y. Kleinlogel, R. Schmid-Hempel, *et al.* 2005. Trans-generational immune priming in a social insect. *Biol. Lett.* **1:** 386–388.
81. Little, T.J., B. O'Connor, N. Colegrave, *et al.* 2003. Maternal transfer of strain-specific immunity in an invertebrate. *Curr. Biol.* **13:** 489–492.
82. Rasmann, S., M. De Vos, C.L. Casteel, *et al.* 2012. Herbivory in the previous generation primes plants for enhanced insect resistance. *Plant Physiol.* **158:** 854–863.
83. Luna, E. & J. Ton. 2012. The epigenetic machinery controlling transgenerational systemic acquired resistance. *Plant Signal. Behav.* **7:** 615–618.
84. Wibowo, A., C. Becker, G. Marconi, *et al.* 2016. Hyperosmotic stress memory in Arabidopsis is mediated by distinct epigenetically labile sites in the genome and is restricted in the male germline by DNA glycosylase activity. *eLife* **5:** e13546.
85. Allis, C.D., T. Jenuwein & D. Reinberg. 2007. Overview and concepts. In *Epigenetics.* C.D. Allis, T. Jenuwein & D. Reinberg & M-L. Caparros, Eds.: 23–62. Cold Spring Harbor: Cold Spring Harbor Laboratory Press.
86. Kronholm, I. & S. Collins. 2016. Epigenetic mutations can both help and hinder adaptive evolution. *Mol. Ecol.* **25:** 1856–1868.
87. Jablonka, E. & G. Raz. 2009. Transgenerational epigenetic inheritance: prevalence, mechanisms, and implications for the study of heredity and evolution. *Q. Rev. Biol.* **84:** 131–176.
88. Salinas, S., S.C. Brown, M. Mangel, *et al.* 2013. Non-genetic inheritance and changing environments. *Non-Genet. Inherit.* **1:** 38–50.
89. Slaughter, A., X. Daniel, V. Flors, *et al.* 2012. Descendants of primed Arabidopsis plants exhibit resistance to biotic stress. *Plant Physiol.* **158:** 835–843.
90. Colicchio, J. 2017. Transgenerational effects alter plant defense and resistance in nature. *J. Evol. Biol.* **30:** 664–680.
91. Latzel, V., Š. Janeček, J. Doležal, *et al.* 2014. Adaptive transgenerational plasticity in the perennial *Plantago lanceolata*. *Oikos* **123:** 41–46.
92. Herman, J.J., S.E. Sultan, T. Horgan-Kobelski, *et al.* 2012. Adaptive transgenerational plasticity in an annual plant: grandparental and parental drought stress enhance performance of seedlings in dry soil. *Integr. Comp. Biol.* **52:** 77–88.
93. Donelson, J.M., P.L. Munday, M.I. McCormick, *et al.* 2012. Rapid transgenerational acclimation of a tropical reef fish to climate change. *Nat. Clim. Change* **2:** 30–32.
94. Salinas, S. & S.B. Munch. 2012. Thermal legacies: transgenerational effects of temperature on growth in a vertebrate. *Ecol. Lett.* **15:** 159–163.
95. Shama, L.N.S. & K.M. Wegner. 2014. Grandparental effects in marine sticklebacks: transgenerational plasticity across multiple generations. *J. Evol. Biol.* **27:** 2297–2307.
96. Walsh, M.R., T. Castoe, J. Holmes, *et al.* 2016. Local adaptation in transgenerational responses to predators. *Proc. R. Soc. Lond. B Biol. Sci.* **283:** 1823.
97. Chen, B., S. Li, Q. Ren, *et al.* 2015. Paternal epigenetic effects of population density on locust phase-related characteristics associated with heat-shock protein expression. *Mol. Ecol.* **24:** 851–862.
98. Jobson, M.A., J.M. Jordan, M.A. Sandrof, *et al.* 2015. Transgenerational effects of early life starvation on growth, reproduction and stress resistance in *Caenorhabditis elegans*. *Genetics* **201:** 201–212.
99. Bird, A. 2002. DNA methylation patterns and epigenetic memory. *Genes Dev.* **16:** 6–21.
100. Gaydos, L.J., W. Wang & S. Strome. 2014. H3K27me and PRC2 transmit a memory of repression across generations and during development. *Science* **345:** 1515–1518.

101. Ragunathan, K., G. Jih & D. Moazed. 2014. Epigenetic inheritance uncoupled from sequence-specific recruitment. *Science* **348:** 1256899.
102. Audergon, P.N., S. Catania, A. Kagansky, *et al.* 2015. Epigenetics. Restricted epigenetic inheritance of H3K9 methylation. *Science* **348:** 132–135.
103. Siklenka, K., S. Erkek, M. Godmann, *et al.* 2015. Disruption of histone methylation in developing sperm impairs offspring health transgenerationally. *Science* **350:** aab2006.
104. Chen, T. & S.Y.R. Dent. 2014. Chromatin modifiers and remodellers: regulators of cellular differentiation. *Nat. Rev. Genet.* **15:** 93–106.
105. Rassoulzadegan, M., V. Grandjean, P. Gounon, *et al.* 2006. RNA-mediated non-mendelian inheritance of an epigenetic change in the mouse. *Nature* **441:** 469–474.
106. Rechavi, O., G. Minevich & O. Hobert. 2011. Transgenerational inheritance of an acquired small RNA-based antiviral response in *C. elegans. Cell* **147:** 1248–1256.
107. Ashe, A., A. Sapetschnig, E.-M. Weick, *et al.* 2012. piRNAs can trigger a multigenerational epigenetic memory in the germline of *C. elegans. Cell* **150:** 88–99.
108. van Otterdijk, S.D. & K.B. Michels. 2016. Transgenerational epigenetic inheritance in mammals: how good is the evidence? *FASEB J.* **30:** 2457–2465.
109. Matzke, M.A. & R.A. Mosher. 2014. RNA-directed DNA methylation: an epigenetic pathway of increasing complexity. *Nat. Rev. Genet.* **15:** 394–408.
110. Luna, E., T.J.A. Bruce, M.R. Roberts, *et al.* 2012. Next-generation systemic acquired resistance. *Plant Physiol.* **158:** 844–853.
111. Kou, H.P., Y. Li, X.X. Song, *et al.* 2011. Heritable alteration in DNA methylation induced by nitrogen-deficiency stress accompanies enhanced tolerance by progenies to the stress in rice (*Oryza sativa* L.). *J. Plant Physiol.* **168:** 1685–1693.
112. Ou, X., Y. Zhang, C. Xu, *et al.* 2012. Transgenerational inheritance of modified DNA methylation patterns and enhanced tolerance induced by heavy metal stress in rice (*Oryza sativa* L.). *PLoS One* **7:** e41143.
113. Herman, J.J. & S.E. Sultan. 2016. DNA methylation mediates genetic variation for adaptive transgenerational plasticity. *Proc. R. Soc. Lond. B Biol. Sci.* **283:** 20160988.
114. Verhoeven, K.J.F. & T.P. van Gurp. 2012. Transgenerational effects of stress exposure on offspring phenotypes in apomictic Dandelion. *PLoS One* **7:** e38605.
115. Krauss, V. & G. Reuter. 2011. DNA methylation in *Drosophila*—a critical evaluation. In *Modifications of Nuclear DNA and Its Regulatory Proteins.* Vol. 101. X. Cheng & R.M. Blumenthal, Eds.: 177–191. Academic Press.
116. Öst, A., A. Lempradl, E. Casas, *et al.* 2014. Paternal diet defines offspring chromatin state and intergenerational obesity. *Cell* **159:** 1352–1364.
117. Rechavi, O., L. Houri-Ze'evi, S. Anava, *et al.* 2014. Starvation-induced transgenerational inheritance of small RNAs in *C. elegans. Cell* **158:** 277–287.
118. Kishimoto, S., M. Uno, E. Okabe, *et al.* 2017. Environmental stresses induce transgenerationally inheritable survival advantages via germline-to-soma communication in *Caenorhabditis elegans. Nat. Commun.* **8:** 14031.
119. Dias, B.G. & K.J. Ressler. 2014. Parental olfactory experience influences behavior and neural structure in subsequent generations. *Nat. Neurosci.* **17:** 89–96.
120. Weaver, I.C.G., N. Cervoni, F.A. Champagne, *et al.* 2004. Epigenetic programming by maternal behavior. *Nat. Neurosci.* **7:** 847–854.
121. MacLean, R.C., C. Torres-Barcelo & R. Moxon. 2013. Evaluating evolutionary models of stress-induced mutagenesis in bacteria. *Nat. Rev. Genet.* **14:** 221–227.
122. Krašovec, R., R.V. Belavkin, J.A.D. Aston, *et al.* 2014. Mutation rate plasticity in rifampicin resistance depends on *Escherichia coli* cell–cell interactions. *Nat. Commun.* **5:** 3742.
123. Aldrich, J.C. & K.A. Maggert. 2015. Transgenerational inheritance of diet-induced genome rearrangements in *Drosophila. PLoS Genet.* **11:** e1005148.
124. Freitak, D., H. Schmidtberg, F. Dickel, *et al.* 2014. The maternal transfer of bacteria can mediate transgenerational immune priming in insects. *Virulence* **5:** 547–554.
125. Salmela, H., G.V. Amdam & D. Freitak. 2015. Transfer of immunity from mother to offspring is mediated via egg-yolk protein vitellogenin. *PLoS Pathog.* **11:** e1005015.
126. Herman, J.J., H.G. Spencer, K. Donohue, *et al.* 2014. How stable 'should' epigenetic modifications be? Insights from adaptive plasticity and bet-hedging. *Evolution* **68:** 632–643.
127. Sales, V.M., A.C. Ferguson-Smith & M.-E. Patti. 2017. Epigenetic mechanisms of transmission of metabolic disease across generations. *Cell Metab.* **25:** 559–571.
128. Chen, Q., M. Yan, Z. Cao, *et al.* 2016. Sperm tsRNAs contribute to intergenerational inheritance of an acquired metabolic disorder. *Science* **351:** 397–400.
129. Jablonka, E., B. Oborny, I. Molnár, *et al.* 1995. The adaptive advantage of phenotypic memory in changing environments. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **350:** 133–141.
130. Lachmann, M. & E. Jablonka. 1996. The inheritance of phenotypes: an adaptation to fluctuating environments. *J. Theor. Biol.* **181:** 1–9.
131. Ezard, T.H.G., R. Prizak & R.B. Hoyle. 2014. The fitness costs of adaptation via phenotypic plasticity and maternal effects. *Funct. Ecol.* **28:** 693–701.
132. Furrow, R.E. & M.W. Feldman. 2014. Genetic variation and the evolution of epigenetic regulation. *Evolution* **68:** 673–683.
133. Uller, T., S. English & I. Pen. 2015. When is incomplete epigenetic resetting in germ cells favoured by natural selection? *Proc. R. Soc. Lond. B Biol. Sci.* **282:** 1811.
134. Rando, O.J. & K.J. Verstrepen. 2007. Timescales of genetic and epigenetic inheritance. *Cell* **128:** 655–668.
135. Uller, T., S. Nakagawa & S. English. 2013. Weak evidence for anticipatory parental effects in plants and animals. *J. Evol. Biol.* **26:** 2161–2170.
136. West-Eberhard, M.J. 2003. *Developmental Plasticity and Evolution.* New York, NY: Oxford University Press.
137. DeWitt, T.J. & R.B. Langerhans. 2004. Integrated solutions to environmental heterogeneity: theory of multimoment reaction norms. In *Phenotypic Plasticity. Functional and*

*Conceptual Approaches*. T.J. DeWitt & S.M. Scheiner, Eds.: 98–111. New York: Oxford University Press.
138. Chown, S.L. & S. Nicolson. 2004. *Insect Physiological Ecology: Mechanisms and Patterns*. Oxford, UK: Oxford University Press.
139. Sørensen, J.G., T.N. Kristensen & J. Overgaard. 2016. Evolutionary and ecological patterns of thermal acclimation capacity in *Drosophila*: is it important for keeping up with climate change? *Curr. Opin. Insect Sci.* **17:** 98–104.
140. Levins, R. 1968. *Evolution in Changing Environments: Some Theoretical Explorations*. Princeton, NJ: Princeton University Press.
141. Overgaard, J., T.N. Kristensen, K.A. Mitchell, *et al.* 2011. Thermal tolerance in widespread and tropical *Drosophila* species: does phenotypic plasticity increase with latitude? *Am. Nat.* **178**(Suppl. 1): S80–S96.
142. Alford, L., T.M. Blackburn & J.S. Bale. 2012. Effect of latitude and acclimation on the lethal temperatures of the peach-potato aphid *Myzus persicae*. *Agric. Forest Entomol.* **14:** 69–79.
143. Schou, M.F., M.B. Mouridsen, J.G. Sørensen, *et al.* 2017. Linear reaction norms of thermal limits in *Drosophila*: predictable plasticity in cold but not in heat tolerance. *Funct. Ecol.* **31:** 934–945.
144. Swindell, W.R., M. Huebner & A.P. Weber. 2007. Plastic and adaptive gene expression patterns associated with temperature stress in *Arabidopsis thaliana*. *Heredity* **99:** 143–150.
145. Colinet, H., B.J. Sinclair, P. Vernon, *et al.* 2015. Insects in fluctuating thermal environments. *Ann. Rev. Entomol.* **60:** 123–140.
146. Kristensen, T.N., H. Kjeldal, M.F. Schou, *et al.* 2016. Proteomic data reveal a physiological basis for costs and benefits associated with thermal acclimation. *J. Exp. Biol.* **219:** 969–976.
147. Hochachka, P.W. & G.N. Somero. 2002. *Biochemical Adaptation*. Oxford, UK: Oxford University Press.
148. Feder, M.E. & G.E. Hofmann 1999. Heat-shock proteins, molecular chaperones, and the stress response: evolutionary and ecological physiology. *Ann. Rev. Physiol.* **61:** 243–282.
149. Bahrndorff, S., J. Mariën, V. Loeschcke, *et al.* 2009. Dynamics of heat-induced thermal stress resistance and hsp70 expression in the springtail, *Orchesella cincta*. *Funct. Ecol.* **23:** 233–239.
150. Dahlgaard, J., V. Loeschcke, P. Michalak, *et al.* 1998. Induced thermotolerance and associated expression of the heat-shock protein Hsp70 in adult *Drosophila melanogaster*. *Funct. Ecol.* **12:** 786–793.
151. Lindquist, S. 1986. The heat-shock response. *Ann. Rev. Biochem.* **55:** 1151–1191.
152. Krebs, R.A. & M.E. Feder. 1997. Tissue-specific variation in hsp70 expression and thermal damage in *Drosophila melanogaster* larvae. *J. Exp. Biol.* **200:** 2007–2015.
153. Silbermann, R. & M. Tatar. 2000. Reproductive costs of heat shock protein in transgenic *Drosophila melanogaster*. *Evolution* **54:** 2038–2045.
154. Hoekstra, L.A. & K.L. Montooth. 2013. Inducing extra copies of the Hsp70 gene in *Drosophila melanogaster* increases energetic demand. *BMC Evol. Biol.* **13:** 68.
155. Cooper, B.S., L.A. Hammad, N.P. Fisher, *et al.* 2012. In a variable thermal environment selection favors greater plasticity of cell membranes in *Drosophila melanogaster*. *Evolution* **66:** 1976–1984.
156. Podrabsky, J.E. 2004. Changes in gene expression associated with acclimation to constant temperatures and fluctuating daily temperatures in an annual killifish *Austrofundulus limnaeus*. *J. Exp. Biol.* **207:** 2237–2254.
157. Sørensen, J.G., V. Loeschcke & T.N. Kristensen. 2013. Cellular damage as induced by high temperature is dependent on rate of temperature change—investigating consequences of ramping rates on molecular and organismal phenotypes in *Drosophila melanogaster*. *J. Exp. Biol.* **216:** 809–814.
158. Whitehead, A., F. Galvez, S. Zhang, *et al.* 2011. Functional genomics of physiological plasticity and local adaptation in killifish. *J. Hered.* **102:** 499–511.
159. Nielsen, M.M., J.G. Sørensen, M. Kruhøffer, *et al.* 2006. Phototransduction genes are up-regulated in a global gene expression study of *Drosophila melanogaster* selected for heat resistance. *Cell Stress Chaperones* **11:** 325–333.
160. Sørensen, J.G., M.F. Schou, T.N. Kristensen, *et al.* 2016. Thermal fluctuations affect the transcriptome through mechanisms independent of average temperature. *Sci. Rep.* **6:** 30975.
161. Kankare, M., D.J. Parker, M. Merisalo, *et al.* 2016. Transcriptional differences between diapausing and non-diapausing *D. montana* females reared under the same photoperiod and temperature. *PLoS One* **11:** e0161852.
162. Parker, D.J., M.G. Ritchie & M. Kankare. 2016. Preparing for winter: the transcriptomic response associated with different day lengths in *Drosophila montana*. *G3* **6:** 1373–1381.
163. Bradshaw, W.E. & C.M. Holzapfel. 2006. Evolutionary response to rapid climate change. *Science* **312:** 1477–1478.
164. Gienapp, P., C. Teplitsky, J.S. Alho, *et al.* 2008. Climate change and evolution: disentangling environmental and genetic responses. *Mol. Ecol.* **17:** 167–178.
165. Merilä, J. 2012. Evolution in response to climate change: in pursuit of the missing evidence. *Bioessays* **34:** 811–818.
166. Merilä, J. & A.P. Hendry. 2014. Climate change, adaptation, and phenotypic plasticity: the problem and the evidence. *Evol. Appl.* **7:** 1–14.
167. Reale, D., D. Berteaux, A.G. Mcadam, *et al.* 2003. Lifetime selection on heritable life-history traits in a natural population of red squirrels. *Evolution* **57:** 2416–2423.
168. Starrfelt, J. & H. Kokko. 2012. Bet-hedging—a triple trade-off between means, variances and correlations. *Biol. Rev.* **87:** 742–755.
169. Kristensen, T.N., A.A. Hoffmann, J. Overgaard, *et al.* 2008. Costs and benefits of cold acclimation in field-released *Drosophila*. *Proc. Natl. Acad. Sci. USA* **105:** 216–221.
170. Forsman, A. 2015. Rethinking phenotypic plasticity and its consequences for individuals, populations and species. *Heredity* **115:** 276–284

171. Murren, C.J., J.R. Auld, H. Callahan, *et al.* 2015. Constraints on the evolution of phenotypic plasticity: limits and costs of phenotype and plasticity. *Heredity* **115:** 293–301.
172. Levins, R. 1969. Thermal acclimation and heat resistance in *Drosophila* species. *Am. Nat.* **103:** 483–499.
173. Scheiner, S.M. & T.J. DeWitt. 2004. Future research directions. In *Phenotypic Plasticity: Functional and Conceptual Approaches.* T.J. DeWitt & S.M. Scheiner, Eds.: 98–111. New York: Oxford University Press.
174. Schulte, P.M., T.M. Healy & N.A. Fangue. 2011. Thermal performance curves, phenotypic plasticity, and the time scales of temperature exposure. *Integr. Comp. Biol.* **51:** 691–702.
175. Simpson, G.G. 1953. The Baldwin effect. *Evolution* **7:** 110–117.
176. Lande, R. 2009. Adaptation to an extraordinary environment by evolution of phenotypic plasticity and genetic assimilation. *J. Evol. Biol.* **22:** 1435–1446.
177. Chevin, L.M., R. Lande & G.M. Mace. 2010. Adaptation, plasticity, and extinction in a changing environment: towards a predictive theory. *PLoS Biol.* **8:** e1000357.
178. Hoyle, R.B. & T.H.G. Ezard. 2012. The benefits of maternal effects in novel and in stable environments. *J. R. Soc. Interface* **9:** 2403–2413.
179. Draghi, J.A. & M.C. Whitlock. 2012. Phenotypic plasticity facilitates mutational variance, genetic variance and evolvability along the major axis of environmental variation. *Evolution* **66:** 2891–2902.
180. Schaum, C.E. & S. Collins. 2014. Plasticity predicts evolution in a marine alga. *Proc. R. Soc. B Biol. Sci.* **281**. https://doi.org/10.1098/rspb.2014.1486.
181. Lind, M.I., K. Yarlett, J. Reger, *et al.* 2015. The alignment between phenotypic plasticity, the major axis of genetic variation and the response to selection. *Proc. R. Soc. Lond. B Biol. Sci.* **282**. https://doi.org/10.1098/rspb.2015.1651.
182. Overgaard, J., J.G. Sørensen, L.T. Jensen, *et al.* 2010. Field tests reveal genetic variation for performance at low temperatures in *Drosophila melanogaster. Funct. Ecol.* **24:** 186–195.
183. Kristensen, T.N., V. Loeschcke & A.A. Hoffmann. 2007. Can artificially selected phenotypes influence a component of field fitness? Thermal selection and fly performance under thermal extremes. *Proc. R. Soc. B Biol. Sci.* **274:** 771–778.
184. Jeltsch, F., D. Bonte, G. Pe'er, *et al.* 2013. Integrating movement ecology with biodiversity research—exploring new avenues to address spatiotemporal biodiversity dynamics. *Mov. Ecol.* **1:** 6.
185. Kays, R., M.C. Crofoot, W. Jetz, *et al.* 2015. Terrestrial animal tracking as an eye on life and planet. *Science* **348:** aaa2478.
186. Hu, J., L. Lei & J. de Meaux. 2017. Temporal fitness fluctuations in experimental *Arabidopsis thaliana* populations. *PLoS One* **12:** e0178990.
187. Chevalier, C., O. Stojanovic, D.J. Colin, *et al.* 2015. Gut microbiota orchestrates energy homeostasis during cold. *Cell* **163:** 1360–1374.
188. Bahrndorff, S., T. Alemu, T. Alemneh, *et al.* 2016. The microbiome of animals: implications for conservation biology. *Int. J. Genomics* **2016:** 5304028.
189. Moghadam, N.N., P.M. Thorshauge, T.N. Kristensen, *et al.* 2018. Strong responses of *Drosophila melanogaster* microbiota to developmental temperature. *Fly* **12:** 11–12.
190. Fiegna, F., A. Moreno-Letelier, T. Bell, *et al.* 2015. Evolution of species interactions determines microbial community productivity in new environments. *ISME J.* **9:** 1235–1245.
191. Ketola, T., L. Mikonranta & J. Mappes. 2016. Evolution of bacterial life-history traits is sensitive to community structure. *Evolution* **70:** 1334–1341.
192. Ashrafi, R., M. Bruneaux, L.-R. Sundberg, *et al.* 2017. Application of high resolution melting assay (HRM) to study temperature-dependent intraspecific competition in a pathogenic bacterium. *Sci. Rep.* **7:** 980.
193. Trøjelsgaard, K., P. Jordano, D.W. Carstensen, *et al.* 2015. Geographical variation in mutualistic networks: similarity, turnover and partner fidelity. *Proc. R. Soc. B Biol. Sci.* **282:** 0142925.
194. Trøjelsgaard, K. & J.M. Olesen. 2016. Ecological networks in motion: micro- and macroscopic variability across scales. *Funct. Ecol.* **30:** 1926–1935.
195. Frydenberg, J., A.A. Hoffmann & V. Loeschcke. 2003. DNA sequence variation and latitudinal associations in hsp23, hsp26 and hsp27 from natural populations of *Drosophila melanogaster. Mol. Ecol.* **12:** 2025–2032.
196. Ketola, T., J. Laakso, V. Kaitala, *et al.* 2004. Evolution of hsp90 expression in *Tetrahymena thermophila* (protozoa, ciliata) populations exposed to thermally variable environments. *Evolution* **58:** 741–748.