Transgenerational plasticity and bet-hedging: a framework for reaction norm evolution in a rapidly changing climate.

Jens Joschinski[1*†], Dries Bonte[1‡]

[1] Terrestrial Ecology Unit (TEREC), Department of Biology, Ghent University, Ghent, Belgium.

* jens.joschinski@ugent.be

† Twitter: @jensjoschi

‡ Twitter: @bontedries

Abstract

Organisms are typically assumed to respond to environmental change by genetic adaptation or by phenotypic plasticity. While genetic tracking is potentially too slow to keep up with climate change, plasticity allows rapid responses to fluctuation and may moreover accelerate adaptation by genetic accommodation. However, phenotypic plasticity relies on environmental cues, and especially in the case of trans-generational plasticity these cues are imperfect indicators of future change. Decision-making under uncertain conditions favors diversified bet-hedging, a strategy of spreading risks by investing in a range of offspring phenotypes rather than a single optimal phenotype. Despite their close similarity, trans-generational plasticity and bet-hedging remain poorly connected, and the role of bet-hedging in adapting to climate change is rarely considered. We here develop a unifying framework: based on traits with binary outcomes (e.g. seed germination; wing polyphenism; diapause incidence) we clarify that diversified bet-hedging and trans-generational plasticity are mutually exclusive strategies, arising from opposing changes in reaction norms (allocating phenotypic variance among or within environments). Since these two strategies have in common that they shape phenotypic variance within populations, both may determine evolutionary dynamics and hence resilience to climate change. We advocate that a paradigm shift is required to accommodate the role of bet-hedging in evolution.

Keywords: Phenotypic plasticity, Trans-generational plasticity, Bet-hedging, Coin-flipping, GxE, Canalization, Adaptation, Climate change

Climate change: coping with variance

Global CO_2 concentrations are acceleratingly rising since at least 100 years (IPCC, 2014). Associated changes in abiotic conditions such as temperatures (Sinervo et al., 2010; Frölicher et al., 2018), precipitation patterns (McLaughlin et al., 2002; Trenberth, 2011) and drought occurrences (Harrison, 2000; Samaniego et al., 2018) may drive species to extinction (Urban, 2015), either directly or by disrupting trophic or intraspecific interactions (Shlesinger and Loya, 2019; Visser and Gienapp, 2019). To prevent further biodiversity loss we require accurate information about species' responses to change. The current rates of change are, however, unprecedented, so climate change predictions represent an interpolation beyond currently available data, and hence are inherently uncertain (Stainforth et al., 2007; Urban et al., 2016). Moreover, patterns of climate variability and predictability are themselves changing (Easterling et al., 2000; Lenton et al., 2017; Bathiany et al., 2018), which not only affects our ability to derive informed decisions, but also imposes further threats to species survival (IPCC, 2014; Bolt et al., 2018). For example, extreme events may cause environmental changes that force species beyond their fundamental niches and directly cause local extinction (Sinervo et al., 2010; Tinsley et al., 2015). More subtle effects include longer bouts of extreme conditions, which, for example, shift the sex ratio in species with environment-dependent sex determination (Janzen, 1994; Easterling et al., 2000). Changes in the temporal autocorrelation of environmental conditions can impact interactions among species, affect network stability (Yang et al., 2019) and contribute to ecological tipping points (Bolt et al., 2018). The twofold challenge of changing means and changing variability is therefore key to understanding extinction.

Responses to environmental change depend on the timescale of fluctuation (Rando and Verstrepen, 2007; Stomp et al., 2008). Fluctuations over very short terms can be addressed by physiological or behavioral buffering (Kearney et al., 2009), i.e. short-term responses that leave no lasting effects on the phenotype. Environmental change that occurs over the lifetime of an organism can be tackled by within-generational plasticity, i.e. by plastic adjustment of developmental pathways that lead to alternative phenotypes (Krueger and Dodson, 1981). Long-term changes that occur gradually over many generations, on the other hand, impose selection pressure and cause genetic adaptation (Gorter et al., 2015). Intergenerational and transgenerational plasticity, the induction of phenotypic change in the offspring generation (Donelson et al., 2018) or succeeding generations (Herman et al., 2014; Shama and Wegner, 2014), lies between those extremes. Thus, trans-generational plasticity is mostly expected when environmental conditions are only partially predictable across generations.

In view of recent climatic change and decreasing short-and long-term predictability, the role of phenotypic plasticity has been aptly discussed: multiple timely reviews have highlighted the importance of phenotypic plasticity not only in coping with changing environments, but also in steering the evolvability of traits in a changing climate (Fox et al., 2019). Trans-generational plasticity is also increasingly recognised as key player under predictable environments (Shama and Wegner, 2014; Baker et al., 2019), especially as the molecular basis is being uncovered (Rando and Verstrepen, 2007; Jablonka and Raz, 2009; Heard and Martienssen, 2014). Nevertheless, there is a lack of studies under only partially predictable conditions (Donelson et al., 2018; Burgess and Marshall, 2014; but see 2011). Unpredictable conditions generally favour bet-hedging strategies, i.e. strategies that reduce long-term fitness variance (Starrfelt and Kokko, 2012), and partially predictable conditions are expected to favour a mix of plastic and bet-hedging strategies (Donaldson-Matasci et al., 2013). Especially diversified bet-hedging, or the strategy to ‘not put all eggs into one basket’ by increasing the variance among offspring phenotypes, is closely related to transgenerational plasticity. Nevertheless, bet-hedging and transgenerational plasticity are surprisingly rarely discussed in unison, and the role of bet-hedging in adapting to climate change and possibly in accelerating trait evolvability remains obscure. A lack of clarity in the definition of both bet-hedging and phenotypic plasticity did neither promote an integrated view: plasticity refers typically to reaction norm shapes and their evolutionary outcome, while bet-hedging is defined only as an evolutionary risk spreading strategy. We here unify the two strategies in a common framework. We first provide a short review of (transgenerational) plasticity, bet-hedging, and their joint action as is envisioned to date, subsequently provide our own interpretation, and end with outstanding question in terms of understanding and predicting species’ adaptation to climate change.

(Transgenerational) plasticity: adapting to changing environments

Phenotypic plasticity is a cornerstone of ecological and evolutionary theory (West-Eberhard, 2003; Pigliucci, 2005; Laland et al., 2015). It refers to changes of the phenotype in response to an environmental cue, usually over the course of development. Alternatively, phenotypic expression may be influenced by its parents’ environmental conditions via parental effects (intergenerational plasticity), or via transmission of epigenetic information through the germ line (trans-generational plasticity). In any case, phenotypic plasticity often carries a connotation of being adaptive, as it allows matching the phenotype with the environment (Debat and David, 2001). Our modern view of plasticity (Bradshaw, 1965) is based on the combination of phenotypic variation with Woltereck`s (1913) concept of a reaction norm (Nicoglou, 2015). Trans-generational plasticity (and intergenerational plasticity) are obviously more difficult to visualize as there are multiple environments involved, but they can also be depicted as reaction norms of parental environment and offspring phenotype (Agrawal, 2001; Shama and Wegner, 2014). This explicit focus on a reaction norm makes plasticity an ecological *process* with which organisms cope with environmental change. In contrast to the above definition, one can also regard plasticity by its *outcome* on evolution: Nongenetic variation (or environmental variance, σ_E^2) reduces the heritability of a trait, $h^2 = \frac{\sigma_G^2}{\sigma_G^2 + \sigma_E^2}$ (Wright, 1920) and hence the response to selection via the breeder’s equation, $R = h^2 * S$. A great deal of the phenotypic variance is due to phenotypic plasticity; it is hence not a surprise that plasticity has been considered a nuisance parameter in evolutionary biology (Falconer, 1952). Since the 1980s it has, however, become apparent that plasticity itself is a trait that can evolve (Via and Lande, 1985; Schlichting, 1986; Nicoglou, 2015). For example, plasticity in egg laying dates of *Parus major* has increased in response to an increasing mismatch with food peak abundance, and this plasticity included a significant heritable component (Nussey et al., 2005). It is this focus on evolutionary outcomes that received most attention in light of recent climate change (Hollander et al., 2015; Fox et al., 2019).

There is an ongoing debate whether plasticity and parental effects are sufficiently incorporated in the modern synthesis, which predominantly focusses on the role of genetic variation in driving evolutionary change (Laland et al., 2014). On the one hand, the evolution of plasticity can be explained by standard evolutionary theory, just like any other trait under selection (De Jong, 2005). On the other hand, plasticity can create novel eco-evolutionary feedbacks that may alter the course and speed of evolution (West-Eberhard, 2003; Levis and Pfennig, 2016; Kelly, 2019). In short, typical environmental conditions do not exert selection pressure on extreme plasticity, giving rise to cryptic genetic variation in phenotypic plasticity (Paaby and Rockman, 2014). When the environment changes, the more plastic genotypes are favoured by selection. This may lead to the evolution of mechanisms that make the phenotypic change heritable (genetic accommodation), and stabilizing selection may then canalise the phenotype, so that the plasticity is lost and the genotype shifted to a new mean (genetic assimilation) (Crispo, 2007; Moczek, 2007). Regardless of whether this form of "plasticity-first" evolution becomes incorporated into a novel evolutionary theory (Laland et al., 2014), it plays an important role in adapting to rapid environmental change (Kelly, 2019).

In summary, the term phenotypic plasticity originally referred to reaction norm shapes, but is currently often used when a holistic view on phenotypic variance (which includes plasticity) would be better suited. Trans-generational plasticity, in particular, receives special attention as presumably adaptive responses to climate change, while non-plastic modes of transgenerational variation remain less studied.

Bet-hedging: surviving in unpredictable environments

Bet-hedging theory has historically been described from a fundamentally different perspective, as the focus was mostly on its outcome on evolution. Bet-hedging is, in short, the reduction of fitness variance at the cost of arithmetic mean fitness (Cohen, 1966; Seger and Brockmann, 1987; Starrfelt and Kokko, 2012). Population growth (and by extension, fitness) is a multiplicative process, and the loss due to negative variation can be higher than the gain due to positive variation (Jensen's inequality). In the extreme case a population may die out in a year with unsuitable conditions, despite high arithmetic mean growth rate. This sensitivity to variance can make a lower, but less fluctuating reproductive output pay off (Cohen, 1966). Long-term fitness variance may be reduced by avoiding risky investments (conservative bet-hedging), or by spreading the risk among one's offspring (diversified bet-hedging), i.e. producing offspring with varying phenotypes (Seger and Brockmann, 1987; Starrfelt and Kokko, 2012). Consider, for example, the extension of a species' phenology (seasonal timing) with climate change (see box 1 for a numerical example): extending the growth season into autumn might provide higher arithmetic mean fitness, but also increases the risk of damage by occasional early frosts. Hence it may pay off to hibernate early as a conservative bet-hedging strategy (Hopper, 1999). Diversified bet-hedging, on the other hand, would be the continued production of both hibernating and non-hibernating phenotypes, such that the genotype benefits to some extent from good years, but also is not driven to extinction in bad years (Halkett et al., 2004). Thus it is immediately obvious that bet-hedging strategies are an important component of adapting to climate change. Other examples of bet-hedging are seed banks of desert annuals

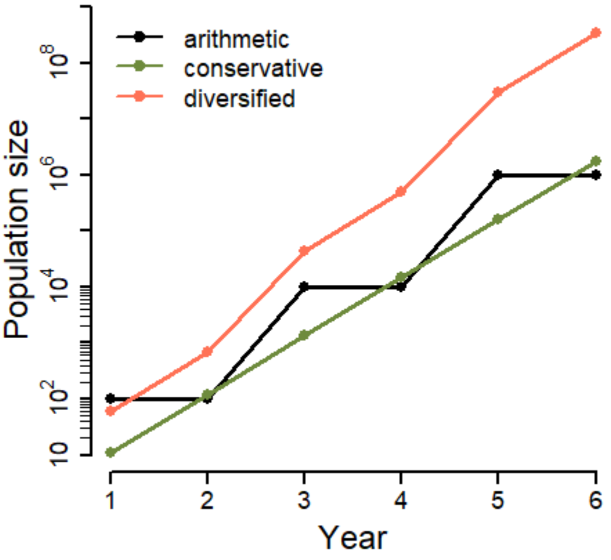
(Cohen, 1966); diapausing strategies of annual killifish (Furness et al., 2015); dispersal polyphenisms (Grantham et al., 2016); and the evolution of facultative sexual reproduction (Gerber and Kokko, 2018). All of those bet-hedging strategies have in common that they maximize geometric mean fitness by decreasing fitness variance, at the cost of the arithmetic mean.

While phenotypic plasticity was first developed from a reaction norm perspective and later assessed for its role in adaptation, bet-hedging lacks a firm physiological and developmental basis. The processes that generate random noise were not considered in early studies of bet-hedging (Cohen, 1966; Seger and Brockmann, 1987); at that time developmental variation was assumed to be maladaptive, and to be actively avoided (Waddington, 1942). The idea that developmental instability may also serve as bet-hedging trait followed only later (e.g. Simons and Johnston, 1997; Veening et al., 2008). In short, low copy numbers e.g. of transcriptional regulators may cause sampling errors which get amplified in the protein regulatory network (Kærn et al., 2005). This results in phenotypic variance, either of single cells (Volfson et al., 2006) or among cells of the same organism (Woods, 2014; Dueck et al., 2016). In the extreme case the "noise" affects developmental pathways and causes random determination of alternative phenotypes (Perrin, 2016). Selection for low copy numbers or slow regulator kinetics may thus provide a way to generate bet-hedging strategies (Simons and Johnston, 1997; Kærn et al., 2005).

A second theory regarding the creation of adaptive phenotypic variance is that it can be achieved by overly relying on cues with little predictive power ("microplasticity", Simons and Johnston, 2006; "hyperplasticity", Scheiner and Holt, 2012). For example (Maxwell and Magwene, 2017) engineered a yeast model that evolved a response to estradiol, a compound that was entirely unrelated to fitness but ensured phenotypic variance in a fluctuating environment. This idea has the advantage that variance does not require a *de novo* evolution of a separate system, but is achieved by repurposing existing phenotypic plasticity. On the other hand, developmental instability may reduce the costs of keeping the phenotype canalized (Tucić et al., 2005). Either way, one may argue that developmental instability is not an alternative to, but a special case of plasticity (Bradshaw, 1965) – the only difference is that the plastic reaction is on the cellular level rather than a reaction to the macroscopic environment. Thus, no matter how phenotypic variance is achieved, it can be described by reaction norm slopes, establishing a firm relationship to transgenerational plasticity. Importantly, the theories require the presence of two separate systems (two reaction norms, or one reaction norm and one noise generator), a condition that we will challenge later.

Box 1: A bet-hedging example

Aphids reproduce by parthenogenesis during summer, which enables quick population growth; in winter frost kills the soft-bodied insects and only diapausing eggs survive (Simon et al. 2002). The struggle to keep the growing season long on one hand and to avoid death on the other hand puts diapause timing under intense selection pressure. In the following we will consider three strategies to cope with unpredictable conditions. First, a genotype may time diapause such that it coincides with mean winter onset (arithmetic mean optimization); this is the strategy that may be intuitively expected. This genotype profits from high offspring numbers (say, 100 offspring) in half of the years, i.e. when winter is later than in an average year, but high mortality (1 surviving offspring) in the other half. A second genotype, the conservative bet-hedger, may diapause earlier in the year and may have 11 offspring regardless of winter onset. Thirdly, a genotype may reproduce with a mixed strategy(diversified bet-hedging), in which half of the offspring follow the first strategy and the other half follow the second strategy. The arithmetic mean offspring numbers are thus 50.5 ($\frac{100+1}{2}$) for the first genotype, but only 11 for the second and 30.75 ($\frac{50.5+11}{2}$) for the third genotype. Nevertheless, the bet-hedging strategies already pay off after four years, because the high between-years variance stalls the exponential growth of genotype 1 (see figure). This shows that the arithmetic mean does not adequately describe fitness (Seger and Brockmann 1987; Simons 2011; Starrfelt and Kokko 2012).



Bet-hedging and transgenerational plasticity: complementary or related?

Our short review of plasticity and bet-hedging should have made clear that there is large conceptual overlap not only in the *processes* of establishing transgenerational plasticity (determining offspring traits) and diversified bet-hedging (variance in offspring traits), but also in their *evolutionary outcomes* (coping with variability vs. coping with unpredictability). While some models considered the evolution of bet-hedging of a plastic trait with no evolution of plasticity (Venable and Brown, 1988; Halkett et al., 2004; Kivela et al., 2016), others have explicitly modelled their joint evolution. Consistent with the two ideas of generating trait variance, bet-hedging was either modelled as a reaction norm to random noise (e.g. Tufto, 2015), or as instability locus (Scheiner, 2014) or error probability (Sasaki and Jong, 1999; Donaldson-Matasci et al., 2013), though one notable exception modelled bet-hedging as a random decision between two reaction norms (Botero et al., 2015). It was then tested under which conditions plasticity or bet-hedging dominate. Plasticity is generally favoured when environmental change is predictable, while bet-hedging is favoured under unpredictable conditions (Scheiner, 2014; Tufto, 2015), such as those imposed by climate change. The balance depends, however, also on how environmental uncertainty is timed (within vs. between generations) and structured (shared uncertainty vs microenvironmental variation) (Donaldson-Matasci et al., 2013); on dispersal modes and environmental autocorrelation (Scheiner, 2014; Marshall and Burgess, 2015); and on physiological costs (Zhang and Hill, 2005) and limits (Tufto, 2015) of phenotypic plasticity and bet-hedging (Starrfelt and Kokko, 2012). We wish to reiterate that all of those models build on the premise that bet-hedging and plasticity are separate traits. As we will reason below, this condition may not be true for some of the most archetypical bet-hedging examples.

Bet-hedging and transgenerational plasticity: a problem of variance partitioning

For our own description of transgenerational plasticity and diversified bet-hedging we find it crucial to make a distinction between processes and emerging strategies. To avoid confusion, we will therefore not refer to plasticity or bet-hedging strategies in our description of processes, but rather introduce a set of terms that describes reaction norm shapes independently of their expected evolutionary outcome. Similarly, when describing evolutionary outcomes, we wish to refrain from terms like “canalization” or “robustness”, as we find them better suited to describe reaction norm properties.

The canonical bet-hedging example is the germination strategy of annual desert plants, in which seeds may either germinate or stay dormant in a given year (Cohen, 1966). Many other examples of bet-hedging share the basic concept that the mother decides among two phenotypes of its offspring (e.g. diapause, facultative sex). The probability of each state – or, from the mother’s perspective, the proportion of offspring – in response to an environmental cue can be described by a polyphenic reaction norm (Fig. 1A). We assume that the shape of the reaction norm is logistic, though our concepts are valid for any reaction norm that is bounded between 0 and 100%. The phenotypic distribution depends in this case on range, mean and slope of the curve: first, a phenotype may exhibit a steep slope and high range, such that the phenotype changes radically in response to the environment (see upper right in Fig. 1B). This shape maximizes the variance among environments, which we will refer to as σ^2_{among}. Secondly, the reaction norm may be flat (upper left). In this case, there is no variance among environments, but within each environment phenotypes may take one of two forms in probabilistic fashion. The variance of these phenotypes within each environment (σ^2_{within}) is calculated as p * (1-p), since the trait choice is a Bernoulli draw, and hence maximized with a flat reaction norm at the 50% level. The two variance components complement each other, i.e. it is not possible to maximize both σ^2_{among} (steep slope, high range) and σ^2_{within} (minimal departure from 50%). Combinations of the two components are however possible (middle column), and the ratio of the variances is determined by the range and slope of the reaction norm. Alternatively, a reaction norm may contain neither variance component, which can be achieved by moving the elevation of the reaction norm to 0 or 100% (lower row). Such a reaction norm represents a highly canalized phenotype, and we express the degree of total phenotypic variance as the sum of the variance components. Lastly, the curve may shift on the x-axis, which influences the mean phenotype rather than phenotypic variance (Fig. 1C). Reaction norms can therefore vary along three axes: in their mean, in the phenotypic variance, and in the variance composition (σ^2_{among} : σ^2_{within}).

Our description only defines the parameter space of transgenerational reaction norms, free of any assumptions about their adaptive value. To conclude that these reaction norm shapes represent adaptive plasticity or adaptive bet-hedging requires correlating them with the properties of the environment. The selection pressures imposed by the environment are, of course, manifold and complex and thus beyond this review. Instead we wish to propose three fundamental axes in which environments may vary, hoping that future research will advance this concept with a more nuanced view on environmental variation. First, we posit that environments vary in the amplitude of environmental change, such as seasonality in temperatures and rainfall probabilities. We expect that stable environments select for canalized reaction norms, while canalization is maladaptive if environments are cyclically changing. Reaction norms that adapted to environmental amplitude are said to follow an evolutionary strategy, and we name this strategy “responsiveness” (Fig. 1B, y-axis). The extremes on the responsiveness axis are “fixed” and “flexible”, and the according reaction norm shapes are characterized by high canalization and high phenotypic variance, respectively. Secondly, the mean environment may vary. One may expect that the reaction norm mean (inflection point in a logistic curve) evolves such that it optimizes arithmetic mean fitness, but unpredictable environments may also select for conservative bet-hedging (e.g. early diapause). We call this axis of adaptive strategies variance avoidance (Fig. 1C). Lastly, environmental predictability should affect the variance composition (among versus within environments) of the reaction norm, leading to phenotypic plasticity or diversified bet-hedging as extremes on an axis of information reliance (Fig. 1B, x-axis). We thus do not define plasticity and bet-hedging as physiological processes (reaction norm shapes), but as evolutionary strategies.

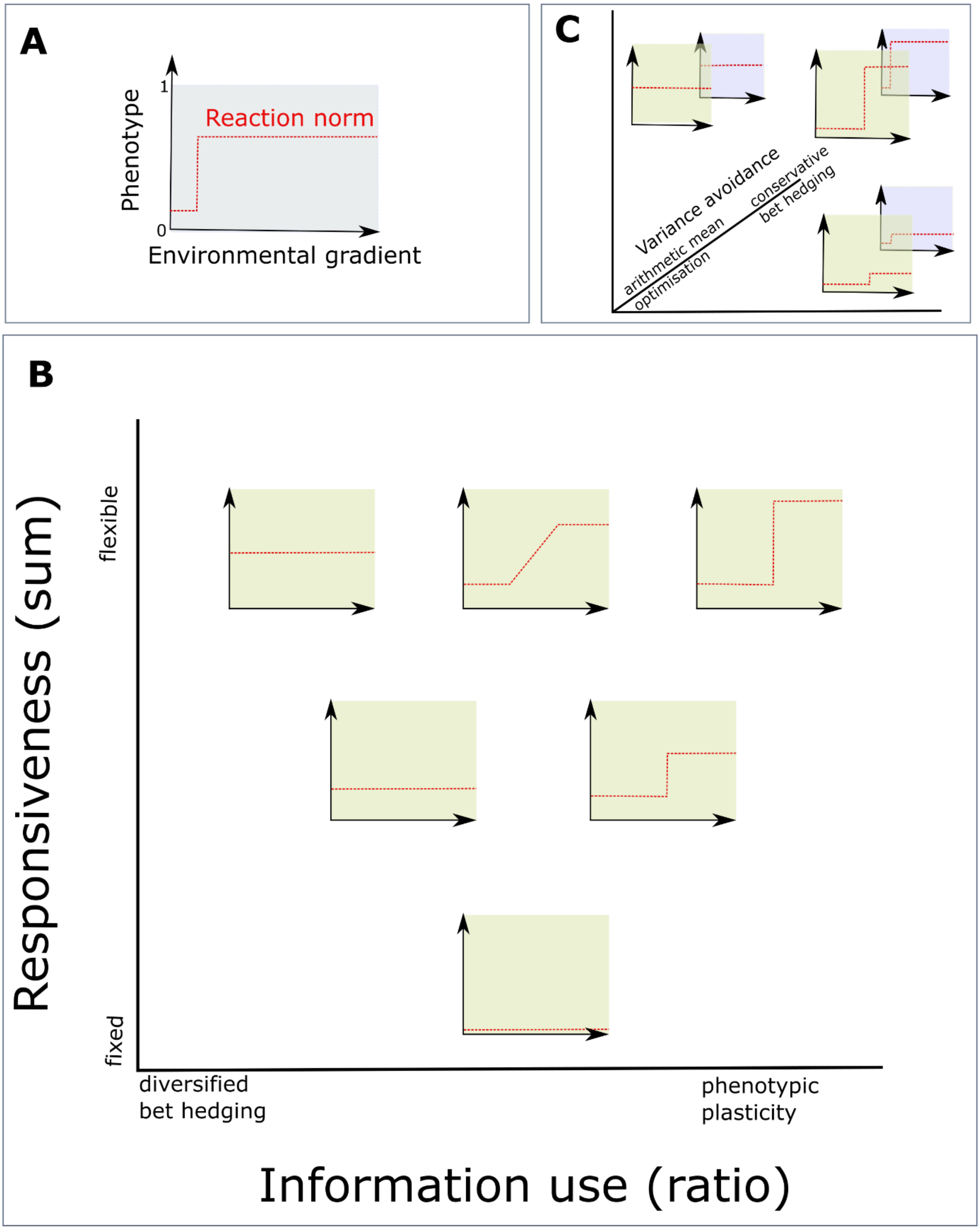


Fig. 1. Relationship of evolutionary strategies with reaction norm properties. Panel A shows a dichotomous reaction norm. The decision to switch phenotypes can be expressed by a steep logistic curve. Reaction norms can divert in various ways from this step function: By changes in the ratio (x-axis) and sum (y-axis) of the variance components σ^2_{among} and σ^2_{within}(Panel B), and by changes in the mean (Panel C). Axes describe the resulting evolutionary strategies.

Novel perspectives for climate change research

Our verbal model provides a three-dimensional concept of reaction norm shapes, which reflects the evolution of strategies along three dimensions. We believe that sorting the evolutionary strategies along these three dimensions has important implications for future studies.

First, our definition extends classical concepts of bet-hedging and transgenerational plasticity. Even though it has been acknowledged that developmental noise requires a plastic reaction norm (Simons and Johnston, 2006; Maxwell and Magwene, 2017), the two strategies were seen as alternative modes to respond to environmental fluctuation (Cooper and Kaplan, 1982; Seger and Brockmann, 1987; Tufto, 2015). We resolve the confusion around these terms by distinguishing reaction norm shapes and emerging strategies, and show that transgenerational plasticity and diversified bet-hedging mark the two extremes on a continuum of strategies. In a climate of decreased predictability (IPCC, 2014; Lenton et al., 2017; Bathiany et al., 2018) purely plastic strategies become increasingly unlikely, while pure bet-hedging strategies lack strong empirical support (Simons, 2011). By removing the dichotomy of bet-hedging versus transgenerational plasticity, we instead stimulate research on their *joint* eco-evolutionary consequences.

Secondly, we clearly separate conservative bet-hedging from diversified bet-hedging by placing the strategies on different axes of reaction norm evolution. The two strategies have been separated early on (Seger and Brockmann, 1987), yet are often discussed in conjunction (e.g. Simons, 2011). In our framework conservative and diversified bet-hedging have as little, or as much, in common as arithmetic mean optimization and transgenerational plasticity (Fig. 1 B/C). It is the joint evolution of conservative and diversified bet-hedging that needs to be studied in the context of a changing climate, just like the evolution of mean phenology and phenological plasticity need to be studied jointly (e.g. Lane et al., 2018),

Thirdly, we redefine canalization, i.e. the ability to produce a consistent phenotype. The current use of the term is ambiguous, as it is not consistently separated from the concepts of developmental stability and fluctuating asymmetry (Debat and David, 2001), hence canalization may be considered either the opposite of plasticity (Waddington, 1942; Van Buskirk and Steiner, 2009) or of developmental noise (Gibson and Wagner, 2000; Zhang and Hill, 2005). We take an integrative view and see environmental canalization as the opposite of phenotypic variance, including both variance components. This view raises the question what role developmental noise may play in adapting to novel environments. We think it is worth reconsidering the theory of phenotypic accommodation, which describes a way by which phenotypic variation becomes hardcoded into the genes (Crispo, 2007; Moczek, 2007; Levis and Pfennig, 2016). The sources of variation that have traditionally been considered for phenotypic accommodation are developmental plasticity (West-Eberhard, 2003), trans-generational plasticity (Schlichting and Wund, 2014; Vogt, 2017; Jones and Robinson, 2018), and learning (Baldwin, 1896). By framing noise as reaction norm property (Fig. 1), it becomes conceivable that the random determination of offspring phenotypes can also be rapidly canalized when environmental conditions change, so diversified bet-hedging may provide an alternative route to phenotypic accomodation. We argue that relating canalization only to phenotypic plasticity (rather than phenotypic variance) is precisely what prevented diversified bet-hedging from being acknowledged as major force in evolution, and we urge for further studies on the role of developmental noise in accelerating evolution to climate change.

The world is simultaneously changing in climate means, variability and predictability (IPCC, 2014; Lenton et al., 2017; Bathiany et al., 2018), and we argue that a model on reaction norm evolution should reflect this three-dimensional relationship. We think that the use of information, which is not commonly considered in plasticity research (Burgess and Marshall, 2014; Donelson et al., 2018), is central to our framework, and hope that it will lead to a better understanding of climate change adaptation. Currently there are many phenomenological studies on responses to climate change (Parmesan and Yohe, 2003, e.g.; Badeck et al., 2004; Cohen et al., 2018), but only few detailed case-studies on the mechanisms of adaptation (Nussey et al., 2005; Gienapp et al., 2013; Lane et al., 2018), and such correlative findings cannot be readily interpolated to novel conditions imposed by accelerated climate change (Stainforth et al., 2007). Ultimately mechanistic models are needed, but such model require fine-scaled data (Urban et al., 2016). We think that our reaction norm perspective is a good compromise that deals with specific processes but does not lose its generality.

Concluding remarks and future perspectives

In this review we rephrased reaction norm evolution as a complex trade-off among three axes of strategies. It is increasingly recognized that changes in climate extremes and in predictability are as important as changes in means (IPCC, 2014; Donelson et al., 2018) – focusing only on strategies to match the mean is hence not fruitful. For example, failure to shift mean phenology with climate change (Gienapp et al., 2013) is not problematic per se – it could be mitigated by concurrent changes in responsiveness. Similarly, the lack of both phenotypic plasticity and mean change may not have severe fitness consequences, if the lack of plasticity is mitigated by diversified bet-hedging. It is the combination along all three axes that defines fitness in a given environment.

Central to our arguments is the unification of transgenerational plasticity and diversified bet-hedging along a continuous axis of information use strategies. We are, of course, aware that empirical measurements beyond mean effects are difficult. Studies will need to go beyond the slope and consider reaction norms under more than three environmental conditions. Such high-resolution data across environments with varying predictability is obviously difficult to obtain – nevertheless there are valuable exceptions (Murren et al., 2014; Joschinski and Bonte, 2019), and the gaining momentum of open data principles and meta-analytic techniques offers exciting novel opportunities.

There is ample room to extend our framework. We have restricted our arguments to binary transgenerationally inherited traits, as this is the most commonly found mode of diversified bet-hedging (Cohen, 1966; Venable and Brown, 1988; Halkett et al., 2004; Gerber and Kokko, 2018). We argue that ultimately, all bet-hedging traits are binary, as bet-hedging is the solution to an information theoretical problem (Donaldson-Matasci et al., 2013), and hence inherently dichotomous (Cooper and Kaplan, 1982), so a unification with more continuous traits, e.g. clutch sizes of birds, seems possible. Another possible extension of our theory would include plastic responses that take place within an indivdual's life time (West-Eberhard, 2003), as well as risk-prone and risk-aversive behavioural strategies (Haaland et al., 2019). Lastly, there are also bet-hedging strategies that are not related to transgenerational plasticity at all. These include, for example, an iteroparous life history (Garcia-Gonzalez et al., 2015), hotspots for genetic mutations ("contingency loci", Rando and Verstrepen, 2007), and sexual reproduction in general (Li et al., 2017). A unification with these alternative strategies might lead to a better understanding of adaptation to rapid climate change.

Acknowledgments

JJ was financially supported by a DFG research fellowship. DB is funded by FWO project G018017N.

Conflict of interest disclosure

The authors of this article declare that they have no financial conflict of interest with the content of this article.

References

Agrawal, A. A. (2001). Transgenerational consequences of plant responses to herbivory: an adaptive maternal effect? *Am Nat* 157, 555–569. doi:10.1086/319932.

Badeck, F. W., Bondeau, A., Bottcher, K., Doktor, D., Lucht, W., Schaber, J., et al. (2004). Responses of spring phenology to climate change. *New Phytol* 162, 295–309. doi:10.1111/j.1469-8137.2004.01059.x.

Baker, B. H., Sultan, S. E., Lopez-Ichikawa, M., and Waterman, R. (2019). Transgenerational effects of parental light environment on progeny competitive performance and lifetime fitness. *Phil Trans R Soc B* 374, 20180182. doi:10.1098/rstb.2018.0182.

Baldwin, J. M. (1896). A New Factor in Evolution. *Am Nat* 30, 441–451.

Bathiany, S., Dakos, V., Scheffer, M., and Lenton, T. M. (2018). Climate models predict increasing temperature variability in poor countries. *Sci Adv* 4, eaar5809. doi:10.1126/sciadv.aar5809.

Bolt, B. van der, Nes, E. H. van, Bathiany, S., Vollebregt, M. E., and Scheffer, M. (2018). Climate reddening increases the chance of critical transitions. *Nature Clim Change* 8, 478–484. doi:10.1038/s41558-018-0160-7.

Botero, C. A., Weissing, F. J., Wright, J., and Rubenstein, D. R. (2015). Evolutionary tipping points in the capacity to adapt to environmental change. *PNAS* 112, 184–189. doi:10.1073/pnas.1408589111.

Bradshaw, A. D. (1965). Evolutionary significance of phenotypic plasticity in plants. *Adv Gen* 13, 115–155. doi:10.1016/S0065-2660(08)60048-6.

Burgess, S. C., and Marshall, D. J. (2011). Temperature-induced maternal effects and environmental predictability. *J Exp Bio* 214, 2329–2336. doi:10.1242/jeb.054718.

Burgess, S. C., and Marshall, D. J. (2014). Adaptive parental effects: the importance of estimating environmental predictability and offspring fitness appropriately. *Oikos* 123, 769–776. doi:10.1111/oik.01235.

Cohen, D. (1966). Optimizing reproduction in a randomly varying environment. *J Theor Biol* 12, 119–129. doi:10.1016/0022-5193(66)90188-3.

Cohen, J. M., Lajeunesse, M. J., and Rohr, J. R. (2018). A global synthesis of animal phenological responses to climate change. *Nature Clim Change* 8, 224–228. doi:10.1038/s41558-018-0067-3.

Cooper, W. S., and Kaplan, R. H. (1982). Adaptive “coin-flipping”: a decision-theoretic examination of natural selection for random individual variation. *J Theor Biol* 94, 135–151. doi:10.1016/0022-5193(82)90336-8.

Crispo, E. (2007). The Baldwin effect and genetic assimilation: revisiting two mechanisms of evolutionary change mediated by phenotypic plasticity. *Evolution* 61, 2469–2479. doi:10.1111/j.1558-5646.2007.00203.x.

De Jong, G. (2005). Evolution of phenotypic plasticity: patterns of plasticity and the emergence of ecotypes. *New Phytol* 166, 101–118. doi:10.1111/j.1469-8137.2005.01322.x.

Debat, V., and David, P. (2001). Mapping phenotypes: canalization, plasticity and developmental stability. *Trends Ecol Evol* 16, 555–561. doi:10.1016/S0169-5347(01)02266-2.

Donaldson-Matasci, M. C., Bergstrom, C. T., and Lachmann, M. (2013). When unreliable cues are good enough. *Am Nat* 182, 313–327. doi:10.1086/671161.

Donelson, J. M., Salinas, S., Munday, P. L., and Shama, L. N. S. (2018). Transgenerational plasticity and climate change experiments: Where do we go from here? *Glob Change Biol* 24, 13–34. doi:10.1111/gcb.13903.

Dueck, H., Eberwine, J., and Kim, J. (2016). Variation is function: Are single cell differences functionally important? *BioEssays* 38, 172–180. doi:10.1002/bies.201500124.

Easterling, D. R., Meehl, G. A., Parmesan, C., Changnon, S. A., Karl, T. R., and Mearns, L. O. (2000). Climate extremes: observations, modeling, and impacts. *Science* 289, 2068–2074. doi:10.1126/science.289.5487.2068.

Falconer, D. S. (1952). The problem of environment and selection. *Am Nat* 86, 293–298.

Fox, R. J., Donelson, J. M., Schunter, C., Ravasi, T. C., and Gaitán-Espitia, J. D. (2019). Beyond buying time: the role of plasticity in phenotypic adaptation to rapid environmental change. *Phil Trans R Soc B* 374, 20180174. doi:10.1098/rstb.2018.0174.

Frölicher, T. L., Fischer, E. M., and Gruber, N. (2018). Marine heatwaves under global warming. *Nature* 560, 360–364. doi:10.1038/s41586-018-0383-9.

Furness, A. I., Lee, K., and Reznick, D. N. (2015). Adaptation in a variable environment: Phenotypic plasticity and bet-hedging during egg diapause and hatching in an annual killifish. *Evolution* 69, 1461–1475. doi:10.1111/evo.12669.

Garcia-Gonzalez, F., Yasui, Y., and Evans, J. P. (2015). Mating portfolios: bet-hedging, sexual selection and female multiple mating. *Proc R Soc B* 282, 20141525. doi:10.1098/rspb.2014.1525.

Gerber, N., and Kokko, H. (2018). Abandoning the ship using sex, dispersal or dormancy: multiple escape routes from challenging conditions. *Phil Trans R Soc B* 373, 20170424. doi:10.1098/rstb.2017.0424.

Gibson, G., and Wagner, G. (2000). Canalization in evolutionary genetics: a stabilizing theory? *BioEssays* 22, 372–380. doi:10.1002/(SICI)1521-1878(200004)22:4<372::AID-BIES7>3.0.CO;2-J.

Gienapp, P., Lof, M., Reed, T. E., McNamara, J., Verhulst, S., and Visser, M. E. (2013). Predicting demographically sustainable rates of adaptation: can great tit breeding time keep pace with climate change? *Phil Trans R Soc B* 368, 20120289. doi:10.1098/rstb.2012.0289.

Gorter, F. A., Aarts, M. M. G., Zwaan, B. J., and de Visser, J. A. G. M. (2015). Dynamics of adaptation in experimental yeast populations exposed to gradual and abrupt change in heavy metal concentration. *Am Nat* 187, 110–119. doi:10.1086/684104.

Grantham, M. E., Antonio, C. J., O'Neil, B. R., Zhan, Y. X., and Brisson, J. A. (2016). A case for a joint strategy of diversified bet hedging and plasticity in the pea aphid wing polyphenism. *Biol Lett* 12, 20160654. doi:10.1098/rsbl.2016.0654.

Haaland, T. R., Wright, J., and Ratikainen, I. I. (2019). Bet-hedging across generations can affect the evolution of variance-sensitive strategies within generations. *Proc R Soc B* 286, 20192070. doi:10.1098/rspb.2019.2070.

Halkett, F., Harrington, R., Hullé, M., Kindlmann, P., Menu, F., Rispe, C., et al. (2004). Dynamics of production of sexual forms in aphids: theoretical and experimental evidence for adaptive "coin-flipping" plasticity. *Am Nat* 163, E112–E125. doi:10.1086/383618.

Harrison, R. D. (2000). Repercussions of El Niño: drought causes extinction and the breakdown of mutualism in Borneo. *Proc R Soc B* 267, 911–915. doi:10.1098/rspb.2000.1089.

Heard, E., and Martienssen, R. A. (2014). Transgenerational epigenetic inheritance: myths and mechanisms. *Cell* 157, 95–109. doi:10.1016/j.cell.2014.02.045.

Herman, J. J., Spencer, H. G., Donohue, K., and Sultan, S. E. (2014). How stable ‘should’ epigenetic modifications be? Insights from adaptive plasticity and bet hedging. *Evolution* 68, 632–643. doi:10.1111/evo.12324.

Hollander, J., Snell-Rood, E., and Foster, S. (2015). New frontiers in phenotypic plasticity and evolution. *Heredity* 115, 273–275. doi:10.1038/hdy.2015.64.

Hopper, K. R. (1999). Risk-spreading and bet-hedging in insect population biology. *Annu Rev Entomol* 44, 535–560. doi:10.1146/annurev.ento.44.1.535.

IPCC (2014). *Climate Change 2014: Synthesis report. Contribution of Working Groups I, II and III to the fifth assessment report of the Intergovernmental Panel on Climate Change.* Geneva, Switzerland.

Jablonka, E., and Raz, G. (2009). Transgenerational epigenetic inheritance: prevalence, mechanisms, and implications for the study of heredity and evolution. *Q Rev Biol* 84, 131–176. doi:10.1086/598822.

Janzen, F. J. (1994). Climate change and temperature-dependent sex determination in reptiles. *PNAS* 91, 7487–7490. doi:10.1073/pnas.91.16.7487.

Jones, B. M., and Robinson, G. E. (2018). Genetic accommodation and the role of ancestral plasticity in the evolution of insect eusociality. *J Exp Bio* 221, jeb153163. doi:10.1242/jeb.153163.

Joschinski, J., and Bonte, D. (2019). Diapause is not selected as a bet-hedging strategy in insects: a meta-analysis of reaction norm shapes [preprint]. *bioRxiv*, 752881. doi:10.1101/752881.

Kærn, M., Elston, T. C., Blake, W. J., and Collins, J. J. (2005). Stochasticity in gene expression: from theories to phenotypes. *Nat Rev Genet* 6, 451–464. doi:10.1038/nrg1615.

Kearney, M., Shine, R., and Porter, W. P. (2009). The potential for behavioral thermoregulation to buffer “cold-blooded” animals against climate warming. *PNAS* 106, 3835–3840. doi:10.1073/pnas.0808913106.

Kelly, M. (2019). Adaptation to climate change through genetic accommodation and assimilation of plastic phenotypes. *Phil Trans R Soc B* 374, 20180176. doi:10.1098/rstb.2018.0176.

Kivela, S. M., Valimaki, P., and Gotthard, K. (2016). Evolution of alternative insect life histories in stochastic seasonal environments. *Ecol Evol* 6, 5596–5613. doi:10.1002/ece3.2310.

Krueger, D. A., and Dodson, S. I. (1981). Embryological induction and predation ecology in Daphnia pulex. *Limnol Oceanogr* 26, 219–223. doi:10.4319/lo.1981.26.2.0219.

Laland, K. N., Uller, T., Feldman, M. W., Sterelny, K., Mülle, Moczek, A., et al. (2015). The extended evolutionary synthesis: its structure, assumptions and predictions. *Proc R Soc B* 282, 20151019. doi:10.1098/rspb.2015.1019.

Laland, K., Uller, T., Feldman, M., Sterelny, K., Müller, G. B., Moczek, A., et al. (2014). Does evolutionary theory need a rethink? *Nature News* 514, 161. doi:10.1038/514161a.

Lane, J. E., McAdam, A. G., McFarlane, S. E., Williams, C. T., Humphries, M. M., Coltman, D. W., et al. (2018). Phenological shifts in North American red squirrels: disentangling the roles of phenotypic plasticity and microevolution. *J Evol Biol* 31, 810–821. doi:10.1111/jeb.13263.

Lenton, T. M., Dakos, V., Bathiany, S., and Scheffer, M. (2017). Observed trends in the magnitude and persistence of monthly temperature variability. *Sci Rep* 7, 5940. doi:10.1038/s41598-017-06382-x.

Levis, N. A., and Pfennig, D. W. (2016). Evaluating 'Plasticity-First' Evolution in Nature: Key Criteria and Empirical Approaches. *Trends Ecol Evol* 31, 563–574. doi:10.1016/j.tree.2016.03.012.

Li, X.-Y., Lehtonen, J., and Kokko, H. (2017). Sexual reproduction as bet-hedging [preprint]. *bioRxiv*, 103390. doi:10.1101/103390.

Marshall, D. J., and Burgess, S. C. (2015). Deconstructing environmental predictability: seasonality, environmental colour and the biogeography of marine life histories. *Ecol Lett* 18, 174–181. doi:10.1111/ele.12402.

Maxwell, C. S., and Magwene, P. M. (2017). When sensing is gambling: An experimental system reveals how plasticity can generate tunable bet-hedging strategies. *Evolution* 71, 859–871. doi:10.1111/evo.13199.

McLaughlin, J. F., Hellmann, J. J., Boggs, C. L., and Ehrlich, P. R. (2002). Climate change hastens population extinctions. *PNAS* 99, 6070–6074. doi:10.1073/pnas.052131199.

Moczek, A. P. (2007). Developmental capacitance, genetic accommodation, and adaptive evolution. *Evol Dev* 9, 299–305. doi:10.1111/j.1525-142X.2007.00162.x.

Murren, C. J., Maclean, H. J., Diamond, S. E., Steiner, U. K., Heskel, M. A., Handelsman, C. A., et al. (2014). Evolutionary change in continuous reaction norms. *Am Nat* 183, 453–467. doi:10.1086/675302.

Nicoglou, A. (2015). The evolution of phenotypic plasticity: Genealogy of a debate in genetics. *Stud Hist Philos Sci C* 50, 67–76. doi:10.1016/j.shpsc.2015.01.003.

Nussey, D. H., Postma, E., Gienapp, P., and Visser, M. E. (2005). Selection on heritable phenotypic plasticity in a wild bird population. *Science* 310, 304–306. doi:10.1126/science.1117004.

Paaby, A. B., and Rockman, M. V. (2014). Cryptic genetic variation: evolution's hidden substrate. *Nat Rev Genet* 15, 247–258. doi:10.1038/nrg3688.

Parmesan, C., and Yohe, G. (2003). A globally coherent fingerprint of climate change impacts across natural systems. *Nature* 421, 37. doi:10.1038/nature01286.

Perrin, N. (2016). Random sex determination: When developmental noise tips the sex balance. *BioEssays* 38, 1218–1226. doi:10.1002/bies.201600093.

Pigliucci, M. (2005). Evolution of phenotypic plasticity: where are we going now? *Trends Ecol Evol* 20, 481–486. doi:10.1016/j.tree.2005.06.001.

Rando, O. J., and Verstrepen, K. J. (2007). Timescales of genetic and epigenetic inheritance. *Cell* 128, 655–668. doi:10.1016/j.cell.2007.01.023.

Samaniego, L., Thober, S., Kumar, R., Wanders, N., Rakovec, O., Pan, M., et al. (2018). Anthropogenic warming exacerbates European soil moisture droughts. *Nat Clim Change* 8, 421. doi:10.1038/s41558-018-0138-5.

Sasaki, A., and Jong, G. de (1999). Density dependence and unpredictable selection in a heterogeneous environment: compromise and polymorphism in the ESS reaction norm. *Evolution* 53, 1329–1342. doi:10.1111/j.1558-5646.1999.tb05398.x.

Scheiner, S. M. (2014). The genetics of phenotypic plasticity. XIII. Interactions with developmental instability. *Ecol Evol* 4, 1347–1360. doi:10.1002/ece3.1039.

Scheiner, S. M., and Holt, R. D. (2012). The genetics of phenotypic plasticity. X. Variation versus uncertainty. *Ecol Evol* 2, 751–767. doi:10.1002/ece3.217.

Schlichting, C. D. (1986). The evolution of phenotypic plasticity in plants. *Annu Rev Ecol Syst* 17, 667–693. doi:10.1146/annurev.es.17.110186.003315.

Schlichting, C. D., and Wund, M. A. (2014). Phenotypic plasticity and epigenetic marking: an assessment of evidence for genetic accommodation. *Evolution* 68, 656–672.

Seger, J., and Brockmann, H. J. (1987). "What is bet-hedging?," in *Oxford surveys in evolutionary biology (4)* (Oxford, UK: Oxford University Press), 182–211.

Shama, L. N. S., and Wegner, K. M. (2014). Grandparental effects in marine sticklebacks: transgenerational plasticity across multiple generations. *J Evol Biol* 27, 2297–2307. doi:10.1111/jeb.12490.

Shlesinger, T., and Loya, Y. (2019). Breakdown in spawning synchrony: A silent threat to coral persistence. *Science* 365, 1002–1007. doi:10.1126/science.aax0110.

Simons, A. M. (2011). Modes of response to environmental change and the elusive empirical evidence for bet hedging. *Proc Biol Sci* 278, 1601–1609. doi:10.1098/rspb.2011.0176.

Simons, A. M., and Johnston, M. O. (1997). Developmental instability as a bet-hedging strategy. *Oikos* 80, 401–406. doi:10.2307/3546608.

Simons, A. M., and Johnston, M. O. (2006). Environmental and genetic sources of diversification in the timing of seed germination: implications for the evolution of bet hedging. *Evolution* 60, 2280–2292. doi:10.1111/j.0014-3820.2006.tb01865.x.

Sinervo, B., Méndez-de-la-Cruz, F., Miles, D. B., Heulin, B., Bastiaans, E., Cruz, M. V.-S., et al. (2010). Erosion of lizard diversity by climate change and altered thermal niches. *Science* 328, 894–899. doi:10.1126/science.1184695.

Stainforth, D. A., Allen, M. R., Tredger, E. R., and Smith, L. A. (2007). Confidence, uncertainty and decision-support relevance in climate predictions. *Phil Trans R Soc A* 365, 2145–2161. doi:10.1098/rsta.2007.2074.

Starrfelt, J., and Kokko, H. (2012). Bet-hedging--a triple trade-off between means, variances and correlations. *Biol Rev* 87, 742–755. doi:10.1111/j.1469-185X.2012.00225.x.

Stomp, M., van Dijk, M. A., van Overzee, H. M. J., Wortel, M. T., Sigon, C. A. M., Egas, M., et al. (2008). The timescale of phenotypic plasticity and its impact on competition in fluctuating environments. *Am Nat* 172, E169–E185. doi:10.1086/591680.

Tinsley, R. C., Stott, L. C., Viney, M. E., Mable, B. K., and Tinsley, M. C. (2015). Extinction of an introduced warm-climate alien species, Xenopus laevis, by extreme weather events. *Biol Invasions* 17, 3183–3195. doi:10.1007/s10530-015-0944-x.

Trenberth, K. E. (2011). Changes in precipitation with climate change. *Climate Research* 47, 123–138. doi:10.3354/cr00953.

Tucić, B., Pemac, D., and Dučić, J. (2005). Life history responses to irradiance at the early seedling stage of Picea omorika (Pančić) Purkyňe: adaptiveness and evolutionary limits. *Acta Oecol* 27, 185–195. doi:10.1016/j.actao.2004.12.004.

Tufto, J. (2015). Genetic evolution, plasticity, and bet-hedging as adaptive responses to temporally autocorrelated fluctuating selection: A quantitative genetic model. *Evolution* 69, 2034–2049. doi:10.1111/evo.12716.

Urban, M. C. (2015). Accelerating extinction risk from climate change. *Science* 348, 571–573. doi:10.1126/science.aaa4984.

Urban, M. C., Bocedi, G., Hendry, A. P., Mihoub, J.-B., Pe'er, G., Singer, A., et al. (2016). Improving the forecast for biodiversity under climate change. *Science* 353. doi:10.1126/science.aad8466.

Van Buskirk, J., and Steiner, U. K. (2009). The fitness costs of developmental canalization and plasticity. *J Evol Biol* 22, 852–860. doi:10.1111/j.1420-9101.2009.01685.x.

Veening, J.-W., Smits, W. K., and Kuipers, O. P. (2008). Bistability, epigenetics, and bet-hedging in bacteria. *Annu Rev Microbiol* 62, 193–210. doi:10.1146/annurev.micro.62.081307.163002.

Venable, D. L., and Brown, J. S. (1988). The selective interactions of dispersal, dormancy, and seed size as adaptations for reducing risk in variable environments. *Am Nat* 131, 360–384. doi:10.1086/284795.

Via, S., and Lande, R. (1985). Genotype-environment interaction and the evolution of phenotypic plasticity. *Evolution* 39, 505–522. doi:10.2307/2408649.

Visser, M. E., and Gienapp, P. (2019). Evolutionary and demographic consequences of phenological mismatches. *Nat Ecol Evol* 3, 879. doi:10.1038/s41559-019-0880-8.

Vogt, G. (2017). Facilitation of environmental adaptation and evolution by epigenetic phenotype variation: insights from clonal, invasive, polyploid, and domesticated animals. *Environ Epigenet* 3. doi:10.1093/eep/dvx002.

Volfson, D., Marciniak, J., Blake, W. J., Ostroff, N., Tsimring, L. S., and Hasty, J. (2006). Origins of extrinsic variability in eukaryotic gene expression. *Nature* 439, 861–864. doi:10.1038/nature04281.

Waddington, C. H. (1942). Canalization of development and the inheritance of acquired characters. *Nature* 150, 563–565. doi:10.1038/150563a0.

West-Eberhard, M. J. (2003). *Developmental Plasticity and Evolution*. Oxford University Press.

Woltereck, R. (1913). Weitere experimentelle untersuchungen über Artänderung, speziell über das Wesen quantitativer Artunterschiede bei Daphniden. *Mol Gen Genet* 9, 146–146. doi:10.1007/BF01876686.

Woods, H. A. (2014). Mosaic physiology from developmental noise: within-organism physiological diversity as an alternative to phenotypic plasticity and phenotypic flexibility. *J Exp Bio* 217, 35–45. doi:10.1242/jeb.089698.

Wright, S. (1920). The relative importance of heredity and environment in determining the piebald pattern of guinea-pigs. *PNAS* 6, 320–332. doi:10.1073/pnas.6.6.320.

Yang, Q., Fowler, M. S., Jackson, A. L., and Donohue, I. (2019). The predictability of ecological stability in a noisy world. *Nat Ecol Evol* 3, 251. doi:10.1038/s41559-018-0794-x.

Zhang, X.-S., and Hill, W. G. (2005). Evolution of the environmental component of the phenotypic variance: stabilizing selection in changing environments and the cost of homogeneity. *Evolution* 59, 1237–1244. doi:10.1111/j.0014-3820.2005.tb01774.x.