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Mechanisms of Plastic Rescue in Novel Environments

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Abstract

Adaptive phenotypic plasticity provides a mechanism of developmental rescue in novel and rapidly changing environments. Understanding the underlying mechanism of plasticity is important for predicting both the likelihood that a developmental response is adaptive and associated life-history trade-offs that could influence patterns of subsequent evolutionary rescue. Although evolved developmental switches may move organisms toward a new adaptive peak in a novel environment, such mechanisms often result in maladaptive responses. The induction of generalized physiological mechanisms in new environments is relatively more likely to result in adaptive responses to factors such as novel toxins, heat stress, or pathogens. Developmental selection forms of plasticity, which rely on within-individual selective processes, such as shaping of tissue architecture, trial-and-error learning, or acquired immunity, are particularly likely to result in adaptive plasticity in a novel environment. However, both the induction of plastic responses and the ability to be plastic through developmental selection come with significant costs, resulting in delays in reproduction, increased individual investment, and reduced fecundity. Thus, we might expect complex interactions between plastic responses that allow survival in novel environments and subsequent evolutionary responses at the population level.

INTRODUCTION

Organisms today are faced with a diverse range of novel environments, which are often dramatically different from those they experienced in their evolutionary history. Urban and agricultural development in once-pristine habitats, the introduction of new toxins or highly competitive invasive species, and increasingly severe climatic shifts all pose unique challenges for native populations (Aitken et al. 2008, Ellis & Ramankutty 2008, Marzluff et al. 2008). In many cases, such drastic environmental change can cause immediate population collapse, preventing or limiting adaptation and ultimately leading to extinction (Butchart et al. 2010). Understanding how organisms respond and adapt to novel environments is critical to our efforts to conserve biodiversity and maintain ecosystem function. In addition, studying population responses to environmental challenges in the present day provides an opportunity to understand analogous responses to similarly dramatic changes in the past, such as the transition from water to land or postglacial climate change (Hoffmann & Parsons 1997). Here we consider environmental change that falls on continuous axes, such as temperature or precipitation frequency, but focus particularly on axes of change that are discrete, such as novel toxins, resources, or habitats, because many forms of anthropogenic environmental change compose this category.

The induction of novel phenotypes via phenotypic plasticity provides one means by which populations may survive in novel and changing environments (Beever et al. 2017, Langkilde et al. 2017, Sih et al. 2011, West-Eberhard 2003). Plasticity, broadly defined, is the ability of a genotype to develop different phenotypes in response to environmental conditions and encompasses a wide range of organismal processes, including morphological development, regulation of gene expression, and behavior (Snell-Rood 2013, West-Eberhard 2003). Importantly, plasticity facilitates rapid phenotypic change—within a single generation—in response to environmental conditions. Plasticity can thus provide a first stage of developmental rescue, prior to subsequent adaptation and evolutionary rescue of a population (Bell & Collins 2008, Carlson et al. 2014, Chevin & Lande 2010, Chevin et al. 2010). However, initial plastic responses to novel environments are likely to be maladaptive in many cases, as little to no selection has occurred on responses to completely new conditions. Here we concentrate on types of plasticity that are relatively more likely to result in adaptive developmental responses to new conditions, producing phenotypes that are matched to local conditions and thus maintaining performance across environments. We focus on shifts into novel, but constant, environments, similar to some evolutionary rescue models.

Although phenotypic plasticity affects a range of disparate organismal functions, we argue that the developmental mechanisms, or causes, of plasticity can be classified into three broad categories: evolved developmental switches, generalized physiological responses to stressors, and developmental selection. In this article, we review how these three mechanisms of plasticity each affect the degree to which the phenotype can be optimized for local conditions as well as the associated costs and life-history trade-offs, characteristics that are key to predicting the efficacy of developmental rescue and the progression of adaptation in novel environments. Indeed, the mechanism of plasticity may influence the proportion of the population that survives in a novel environment, the fecundity of those individuals, and the time between generations, which will in turn affect the rate of population growth and how evolution plays out in the novel environment. Overall, we argue that the mechanisms of plasticity likely to produce a highly adaptive response to a novel environment are also the most costly, resulting in shifts to relatively slower life histories and less pronounced evolutionary responses at the population level.

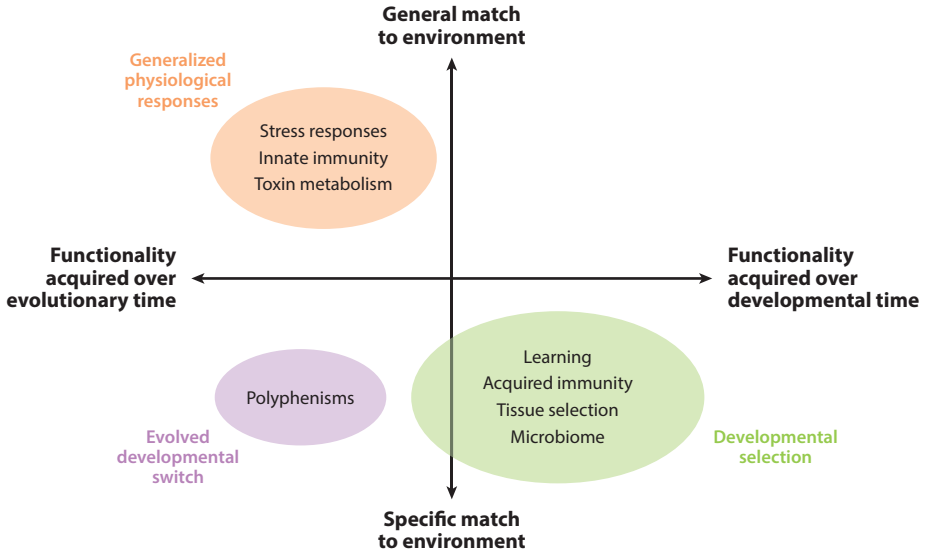

Figure 1

Classification of mechanisms of plasticity. Mechanisms of plasticity acquire their functionality over both evolutionary and developmental time. Evolved developmental switches are least likely to result in an adaptive phenotype in a novel environment because they are specific to historically relevant environments. Generalized physiological responses are relatively more likely to enable survival in novel conditions because the plastic responses are general to a range of environments. Developmental selection forms of plasticity are most likely to result in adaptive phenotype match to new conditions because individuals sample phenotypes over developmental time, adopting those that specifically match novel conditions.

MECHANISMS OF ADAPTIVE PLASTIC RESPONSES TO NOVEL ENVIRONMENTS

The mechanisms regulating phenotypic plasticity can be broadly categorized as developmental switches, generalized responses, or developmental selection. The developmental processes contributing to each mechanism are distinguished by their capacity to match the environment. Further distinguishing these processes is whether the plastic response can be optimized within an individual's life span or whether it evolves a match to the environment over subsequent generations (**Figure 1**). These mechanisms are not mutually exclusive—indeed, the development of many traits contains components of different mechanisms, such as innate and plastic responses to photoperiod in response to climate change (Charmantier & Gienapp 2014). However, we argue this classification is useful for predicting the probability that a plastic response will be adaptive in a novel environment, the degree and type of associated fitness costs, and subsequent implications for evolutionary rescue. We predict that plastic mechanisms that are general or that develop through selective processes within an individual are more likely to result in survival in novel environments, especially when conditions exceed the typical range of the ancestral environment in extreme ways (e.g., drastic temperature shifts) or offer fundamentally different environmental states (e.g., entirely new resources).

Evolved Developmental Switches May Shift Populations Toward New Adaptive Peaks

Evolved developmental switches that are "tailored" to different environments may be the most frequently cited examples of plasticity (West-Eberhard 2003). A particular case of such evolved developmental switches is polyphenism, in which one of several discrete alternate phenotypes are induced in different conditions, such as defenses in *Daphnia* (Black & Dodson 1990), nutrition-dependent mating tactics in beetles (Moczek & Emlen 2000), worker castes in social insects (Wheeler 1991), differing leaf morphologies in aquatic environments (Cook & Johnson 1968), or seasonal morphs in butterflies (Brakefield & Reitsma 1991). In these examples, cues such as predator chemicals, photoperiod, or temperature induce a developmental regulatory program that results in the expression of discrete phenotypes tailored to different environments (Nijhout 1999; e.g., Ragsdale et al. 2013, Snell-Rood et al. 2011a). This developmental program has presumably evolved in concert with cues that predict certain environmental conditions that an organism experiences (Moran 1992, Sultan & Spencer 2002). Similarly, many graded developmental responses, such as UV-induced melanization (Gilchrest et al. 1996) or phytochrome-mediated shade-avoidance responses in plants (Franklin 2008), represent evolved developmental mechanisms responsive to specific, predictive environmental cues.

Given that such pathways evolved in response to a particular set of environments, the extent to which they are adaptive may depend on the nature of the "novel" environment relative to ancestral environments. If novel conditions represent an extension of ancestral conditions along a continuous axis, it is possible that a preexisting plastic response will be somewhat adaptive in the new conditions, for instance, with shifting UV exposure or rising temperatures (Nielsen 2017, Rautio & Korhola 2002). However, if the environment is shifting to an extreme degree, or in a more discrete manner (e.g., resources, toxins), it is unclear to what extent these tailored switches will contribute to adaptive plastic responses in novel environments. Novel conditions—those not previously experienced during the evolution of a particular developmental switch—may result in the inability to respond adaptively (**Figure 2*a***). Alternatively, new environments may induce a range of maladaptive and potentially adaptive responses through the "spreading" of reaction norms and release of cryptic genetic variation (**Figure 2*b***) (sensu Ghalambor et al. 2007; Badyaev 2005, Schlichting 2008). For instance, extreme novel temperatures or pHs, pronounced diet shifts, or shifts in predation can expose previously cryptic variation in reaction norms in a wide range of directions (Fischer et al. 2016, Ledon-Rettig et al. 2010, Purchase & Moreau 2012). With such extreme environmental change, it is likely that plastic responses to novel environments are adaptive only by chance, resulting in survival of only a subset of genotypes in the population. For instance, many plastic responses of plants in phenology to shifting temperature are not adaptive (Duputie et al. 2015). Similarly, plastic responses of some lizards to rising temperatures are not adaptive, presumably because past selection has been stronger with respect to low temperatures (Telemeco et al. 2017). The question then becomes, what mechanisms of plasticity could potentially allow an adaptive response to an environment not previously experienced in an organism's evolutionary history? We predict that developmental switches may move organisms toward a new optimum for some forms of environmental change, but they are the least likely to result in an adaptive plastic response in novel conditions when environmental change is extreme or discrete. Instead, generalized physiological mechanisms and developmental selection represent forms of plasticity that may "preadapt" organisms to novel conditions.

Generalized Physiological Mechanisms May Allow Survival in Novel Conditions

Induction of generalized physiological responses can lead to tolerance of a wide range of novel stressors. Like developmental switches, generalized physiological mechanisms such as stress

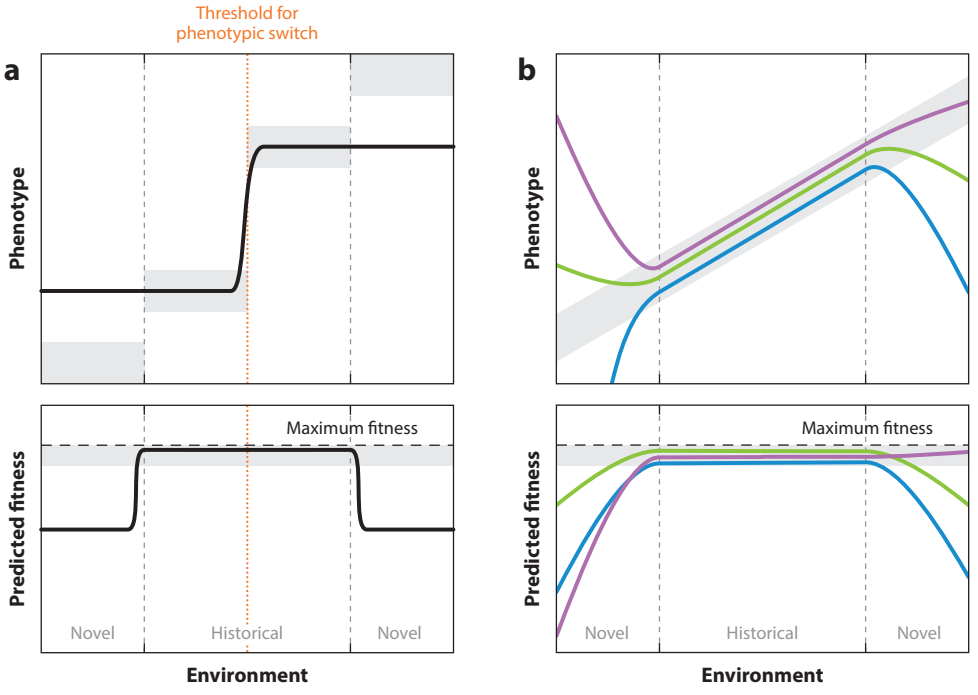

Figure 2

Responses of evolved developmental switches in novel environments. The shaded gray area indicates the optimal phenotype in a given environment. (*a*) Forms of plasticity that develop through a threshold-based developmental switch are unlikely to result in adaptive phenotypes in a novel environment. (*b*) A reaction norm that has evolved to produce phenotypes tailored to a historical range of environments is likely to reveal cryptic genetic variation in novel environments that have not yet shaped the reaction norm (*different genotypes indicated by different colors*). This "spreading of reaction norms" (sensu Ghalambor et al. 2007) should result in only a subset of genotypes matching the new optimal phenotype in novel conditions.

response pathways, toxin metabolism, and innate immunity have been optimized over evolutionary time. However, because such mechanisms can facilitate responses to a suite of potential environmental challenges, we predict that they are substantially more likely than tailored developmental switches to lead to an adaptive response to novel environments when the environmental change is extreme or discrete, such as encountering an entirely novel resource, toxin, or habitat (e.g., cities).

Generalized responses to stressors such as heat often confer resistance to other stressors as well, enabling partial plastic rescue in many novel environments. For instance, higher expression of heat shock proteins confers resistance not only to temperature stress, but also to oxidative damage, toxin exposure, and osmotic stress (Feder & Hofmann 1999, Kregel 2002, Wang et al. 2004). Induction of antioxidant pathways can have correlated positive effects on tolerating irradiation, toxins, pathogens, and dehydration (Deak et al. 1999, Gerschman et al. 1954, Kensler et al. 2007, Singh et al. 2013). Upregulating general responses when challenged with low levels of stress can serve as one of several mechanisms of hormesis, a phenomenon in which sublethal stress can have beneficial effects on performance (Costantini et al. 2010). For instance, given upregulation of such general stress responses, exposure to plant toxins in animal diets can reduce the risk of neural disorders, heart disease, and cancer (Mattson 2008). Plastic induction of these responses likely plays a role in survival in novel and changing environments (Costantini 2014); for instance,

upregulation of antioxidant pathways seems to have played a role in the survival of wild bird populations in irradiated areas near Chernobyl (Galvan et al. 2014).

Induction of enzymes with broad substrate reactivity serves as another mechanism by which organisms cope with entirely novel inputs. For instance, cytochrome P450s (CYPs) play an important role in the first phase of toxin metabolism and modify a broad range of toxins (Li et al. 2007, Schuler 2011). Secondary toxin metabolism employs similar enzymes with broad reactivity such as glutathione-S-transferases (GSTs) and UDP-glycosyltransferases to further conjugate modified toxins prior to export (Bock 2016, Gloss et al. 2014, Schramm et al. 2012). Plastic upregulation of broad-spectrum transporters, such as P-glycoproteins, in the third phase of toxin metabolism aids survival in polluted environments (Keppler & Ringwood 2001) and bolsters resistance to novel toxins, such as multidrug resistance of tumors in chemotherapy (Efferth & Volm 2017). Induction of CYPs and GSTs confers tolerance to some herbicides in plants (Riechers et al. 2010), and evolutionary increases in CYP and GST expression play an important role in recently acquired pesticide resistance in insects (Despres et al. 2007, Li et al. 2007), suggesting that evolutionary arms races may preadapt some species to tolerate novel toxins (Bock 2016).

Certain aspects of innate immunity are also "generalized," in that upregulation may have beneficial effects in novel contexts. For instance, insects upregulate antimicrobial peptides that recognize broad classes of pathogens from fungi to bacteria through conserved regions specific to those groups (Yi et al. 2014). Encapsulation defenses in insects can be upregulated in response to conditions that promote the spread of disease, such as high population densities, and increase resistance of individuals to a range of pathogens (Ruiz-Gonzalez et al. 2009, Wilson & Reeson 1998). Fever is another generalized immune response across vertebrates and some invertebrates. It may have initially evolved as a heat stressor against pathogens, but it also coordinates many other immune processes and is effective against many pathogens and even some cancers (Shephard et al. 2016).

Induction of physiological mechanisms that are general or cross-reactive is a powerful method of surviving novel stressors. However, these systems are not a silver bullet—a nonspecific response is likely not as effective as a more tailored response to a large or persistent stressor. For instance, studies contrasting specialists and generalists suggest that CYPs with broader active sites are less efficient (Li et al. 2004). Furthermore, as discussed in more detail below, constant upregulation of general mechanisms is costly; for example, the action of CYPs generates substantial oxidative stress (Gonzalez 2005). Such costs could favor plastic processes specialized to a given stressor or novel environment.

Developmental Selection Is Likely to Produce an Adaptive Phenotype in Novel Conditions

Developmental selection refers to forms of plasticity where aspects of a phenotype within an individual are reinforced over developmental time in response to feedback from the environment (Frank 1996, Hull et al. 2001, West-Eberhard 2003). Developmental selection is a particularly powerful mechanism of producing adaptive plasticity in novel environments because it requires no prior evolutionary history with an environment for a potential phenotype match, and complex functional phenotypes can emerge from relatively simple developmental rules (Frank 1996, Hull et al. 2001, Kirschner & Gerhart 1998). Developmental selection mechanisms of plasticity allow adaptive responses to a wide range of environments without suffering the costs of relaxed selection on developmental programs specific to different environments (e.g., Snell-Rood et al. 2010, Whitlock 1996). Selection within an individual may occur within or between cells, over space and time, or on the basis of the identity or location of a trait. In addition, developmental selection may occur over specific windows of development or across an individual's lifetime. Here we review

forms of development that include at least some within-individual selection. These feedbacks over developmental time result in a much greater likelihood of such mechanisms of plasticity producing adaptive responses to novel conditions.

Tissue architecture. Selective processes during organismal development often modify or reinforce patterns of cellular or tissue architecture on the basis of interactions with the environment. In other words, there is selection on the location of cells. For instance, the structure and composition of muscle and bone are responsive to mechanical load such that cell size, number, and composition are reinforced or atrophied on the basis of patterns of use (Duncan & Turner 1995, Moore 2003, Pette & Staron 2000). This is particularly well illustrated in the development of differences in jaw and skull morphology based on diet in fish (Meyer 1987, Wainwright et al. 1991) and mammals (Menegaz et al. 2010) as well as variation in locomotor abilities based on experience in athletes (Ducher et al. 2004, Sanchis-Moysi et al. 2011) and animals reared in different conditions (Congdon et al. 2012, Hammond et al. 2010). In another example, the sensitivity of cardiac cells to mechanical forces plays an important part in the developing architecture of the heart and circulatory system (Davies 1995, Hove et al. 2003). Similar to animal tissue, plant cells are responsive to mechanical stress (Niklas 2009, Speck & Burgert 2011), resulting in plasticity in growth form with environment, for instance, due to the mechanical stressors of dwelling in water versus air (Hamann & Puijalon 2013).

Developmental selection at the cellular network level is responsible for incredibly complex, functional networks of interacting cells that are robust to many developmental perturbations. In the developing nervous system, initial patterns of innervation are broad and then refined through activation of the networks and interaction with the environment (Katz & Shatz 1996, Luo & O'Leary 2005, Purves & Lichtman 1980). For instance, the precise wiring of neuromuscular junctions and the visual cortex develops through neural activity and synaptic competition that refines initially broad neural projections (Buffelli et al. 2003, Gordon & Stryker 1996). Similar network-level selective processes occur in the circulatory and respiratory systems, where early exploratory branches are refined as the network begins to function (Guillemin et al. 1996, Risau 1997). In plants, individual modules respond to local environmental conditions (de Kroon et al. 2005). Root systems explore soil space while "foraging" and proliferate in resource-rich areas (Doust 1981, Hodge 2004, Sachs et al. 1993), whereas branches explore the light environment resulting in plasticity in plant architecture (Sachs 2004, Van de Peer et al. 2017). Morphological plasticity is seen in modular colonial animals like corals, which alter branching arrangement with light levels and water flow (Bruno & Edmunds 1997). Developmental selection mechanisms of tissue reorganization are responsible for extreme examples of plasticity in novel conditions such as the well-known "two-legged goat," where massive plastic changes in the skeletal, muscular, and nervous systems accommodate extreme phenotypic changes like the loss of a pair of legs (West-Eberhard 2003).

Learning and acquired immunity. Learning and acquired immunity represent forms of developmental selection where individuals "sample" phenotype space over developmental time, reinforcing traits that match local conditions and atrophying those that do not. With respect to behavior, different behavioral phenotypes, consisting of a motor response to a sensory input, can be "sampled" by either attending to a range of cues or varying motor patterns in response to a given cue. In this way, animals can learn to use a variety of different resources and food types (Dukas 1998, Papaj & Prokopy 1989, Shettleworth 1998), increasing the likelihood of surviving in novel environments. For example, birds with larger forebrain size are more likely to learn novel foraging techniques and consequently survive in new regions following introductions or in urban

environments (Sol 2009, Sol et al. 2005). Similarly, human children will explore a wider range of cognitive hypotheses that explain observations, and this sampling range and resulting behavioral flexibility decline with age (Gopnik et al. 2017).

Analogous phenotype sampling occurs in the development of acquired immunity in jawed vertebrates, where somatic recombination results in the production of a wide range of B cells that interact with potential pathogens through antibody secretion. Within-individual diversity in B cells is generated through rearrangement of gene segments, nucleotide deletions and insertions, hyper-point mutation, and shifts in recombination locations, depending on the species (Honjo & Habu 1985, Litman et al. 1993, Rajewsky 1996). Matches to a pathogen are further refined through somatic hypermutation and continual clonal selection, and immune memory is maintained through memory B cells (Rajewsky 1996). This form of plasticity is powerful. Through selection within an individual, it can generate remarkable specificity in matching antibodies to a seemingly infinite array of antigens, thus generating complexity from a relatively simple underlying mechanism. Although distinct from mechanisms in vertebrates, many developmental mechanisms across invertebrates also create highly diverse molecules that interact with pathogens (Cerenius & Soderhall 2013). In insects, alternative splicing of the pattern-recognition gene *Dscam* creates more than 30,000 variant forms that function in specific protection against bacteria and parasites (Kurtz & Armitage 2006, Watson et al. 2005). Thus, specific forms of immunity develop through high degrees of within-individual variability—a sampling and selection process that occurs over developmental time.

The next frontier of developmental selection: the microbiome and patterns of gene expression. Recent discussions have considered how aspects of developmental selection also occur in populations of microbes within multicellular organisms. The microbiome represents selectable epigenetic variation within an individual (Gilbert et al. 2010), yielding both evolutionary changes within strains and competitive sorting between strains over the lifetime of an individual (Garud et al. 2017, Ley et al. 2006) that can allow survival in novel and changing environments (Alberdi et al. 2016, Pillai et al. 2017). For instance, shuffling of different strains or species of symbionts may allow corals to cope with increasing temperature such that harboring a diverse microbiome allows a greater range of acclimation responses (Baker 2003, Berkelmans & van Oppen 2006). Similarly, plastic changes in the gut microbiome of cold-exposed mice cause physiological changes that acclimate them to cold temperatures (Chevalier et al. 2015). Aspects of the microbiome are selected not only through interactions with the external environment, but also through active mechanisms of the host. For instance, plants can selectively reward the most cooperative fungal symbionts (Kiers et al. 2011). Similarly, nutrient secretion by intestinal epithelial cells may promote the growth of beneficial gut microbes (Schluter & Foster 2012).

Developmental selection may even play out at the level of gene expression, which is variable within individuals and changes over developmental time through epigenetic processes that respond to the environment. Stochastic variation in gene expression across a population of cells (McAdams & Arkin 1997) is thought to be beneficial in variable environments because cells sample a broad phenotypic space (Eldar & Elowitz 2010, Raj & van Oudenaarden 2008). Both empirical (Acar et al. 2008, Beaumont et al. 2009) and theoretical work (Kussell & Leibler 2005, Thattai & van Oudenaarden 2004) have intensively explored this idea in single-celled organisms. However, stochastic gene expression also occurs in multicellular organisms (Boettiger & Levine 2009, Raj et al. 2006) where variable gene expression across time or space may serve as a novel level of variation selected during development (Miller-Jensen et al. 2011). Epigenetic mechanisms could focus patterns of gene expression that lead to high performance, through selectable epigenetic differences between cells (Feinberg & Irizarry 2010), small RNA-mediated mechanisms (Ebert &

Sharp 2012), or chromatin modifications (Di Croce & Helin 2013). Thus, competition between gene expression patterns early in development, either over time or across cells (Johnston 2009, Tamori & Deng 2011), would allow a population of cells in a multicellular organism to select a higher performing pattern of gene expression, analogous to a learning process. Overall, this process would result in a transcriptional memory of past developmental experiences (Francis & Kingston 2001), similar to the priming effects of stress on gene expression (Ding et al. 2012) or age-dependent induction of flowering in plants (Bergonzi et al. 2013). Although the basic components of developmental selection are present at the level of gene expression, whether these processes serve more broadly as a mechanism of plasticity remains to be determined.

In developmental selection, the resulting phenotype is an emergent property of developmental programs interacting with the environment across a population of cells. Such processes can explain how functional, integrated, and complex individuals can develop from relatively simple genomes—for example, how a brain of 3 trillion synapses can develop from a genome of 25,000 genes. Developmental selection processes offer an answer to the challenges of reductionist approaches to development: Complex organisms cannot, by necessity, have completely deterministic development (Mazzocchi 2008). By employing such processes, functional, complex, and integrated individuals can develop in extremely novel conditions, whether resulting from external environmental change or large internal anomalies. The development of many traits is no doubt a combination of evolved cellular responses, such as the induction of certain proteins in the face of mechanical stress, and selective processes within individuals. For instance, many plants and animals have shown plastic adjustments in phenology in response to climate change (Charmantier & Gienapp 2014, Franks et al. 2014). Such plastic responses are likely a combination of evolved developmental switches that match temperature cues with physiological and behavioral responses and of learning as individuals gain information on whether new climate conditions match the best breeding conditions (Visser 2008). The degree to which a plastic response consists of evolved switches, generalized responses, and developmental selection may determine the chance that the resulting phenotype is adaptive in novel conditions as well as the associated costs and trade-offs, as discussed below.

INTEGRATING MECHANISMS OF PLASTIC RESCUE INTO A LIFE-HISTORY FRAMEWORK: COSTS OF PLASTICITY

To understand how plasticity may interact with evolutionary rescue in a novel or rapidly changing environment, we must understand the extent to which plasticity trades off with life-history variables that may influence demographic and evolutionary processes. Costs and trade-offs associated with plasticity, and generalist strategies more broadly, have been studied and debated for decades (DeWitt et al. 1998, Futuyma & Moreno 1988, Murren et al. 2015). Much of the existing literature stresses the costs of the ability to be plastic rather than the costs of a particular plastic phenotype: Only such global costs of plasticity can explain the coexistence of specialists and generalists because phenotype- or environment-specific costs are felt only in environments where the benefits of plasticity are also experienced (Van Tienderen 1991). Such global costs of plasticity also show up in models of plastic rescue (Chevin et al. 2013). A range of studies have documented fitness trade-offs associated with the ability to be plastic (e.g., Agrawal et al. 2002, van Kleunen et al. 2000, Weinig et al. 2006), and studies seeking to measure the costs of plasticity document such costs more often than expected by chance (Van Buskirk & Steiner 2009). However, in many cases, the costs of plasticity and generalist strategies appear weak or negligible (e.g., Callahan et al. 2005, Caruso et al. 2006, Turner & Elena 2000); indeed, a meta-analysis suggested that the costs of adaptive plasticity were documented in only 28% of corresponding tests (Van Buskirk & Steiner

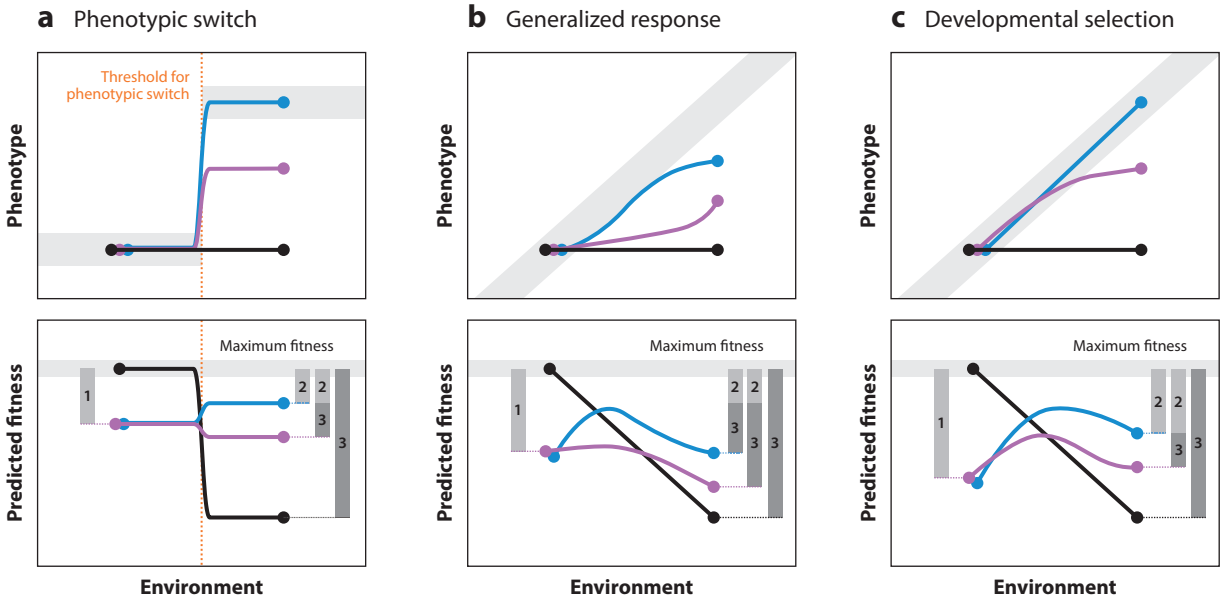

Figure 3

Costs of plasticity in novel environments vary with the mechanism of plasticity. Each line represents a genotype reaction norm of varying degrees of plasticity for each of the three mechanisms of plasticity: highly plastic genotype (*blue*), genotype with some level of suboptimal plasticity (*purple*), and unresponsive genotype (*black*). As discussed in the text, the probability of matching novel environments (*top row*) and the associated costs (*bottom row*) is expected to vary with the type of plasticity. The bottom row shows predicted changes in relative fitness for each genotype across the environmental gradient. The vertical bar labeled 1 indicates the fitness cost of the ability to be plastic (e.g., the cost of maintaining a system to detect environmental changes), and thus fitness trade-offs are more likely to be seen in a historical, or less stressful, environment. The vertical bar labeled 2 indicates that, in novel environments, the energetic cost to creating or inducing a particular plastic response, while the vertical bar labeled 3 indicates the cost of not matching the environment, assuming that the optimal phenotype is represented by the light shaded bar. Developmental selection forms of plasticity (*c*) are most likely to match novel conditions, but the cost of the ability to be plastic (*1*) is high for this mechanism relative to developmental switches (*a*) and generalized responses (*b*). In addition, for most forms of plasticity, an induced response in novel conditions is inherently costly regardless of the mechanism (*2*).

2009). Costs of plasticity are difficult to detect, in part because there is strong selection over time for mechanisms that reduce costs (Murren et al. 2015).

Despite challenges and mixed success in detection, here we argue that two generalizations about the costs of plasticity are particularly relevant for plastic rescue in novel environments. First, whereas the costs of the ability to be plastic are often less than we might expect, the costs of an induced plastic response in a novel or stressful environment are often measurable and significant (elsewhere referred to as the cost of phenotype) (e.g., Murren et al. 2015). Second, developmental selection is particularly costly in terms of the ability to be plastic as well as the plastic response (**Figure 3**).

Induced Plastic Responses in Novel Environments Are Costly Regardless of Mechanism

Induced plastic responses in novel or stressful environments often have clear energetic costs and life-history trade-offs, although the costs may depend somewhat on the phenotype induced. For

instance, induced antipredator defenses in *Daphnia* and tadpoles (i.e., tailored switches) come with trade-offs with growth as energy is reallocated toward the induced phenotype (Black & Dodson 1990, Van Buskirk 2000). In plants, induction of chemical and physical defenses comes with reproductive trade-offs in the absence of herbivores (Agrawal et al. 1999, Baldwin 1998). Induction of the immune system is also energetically costly (e.g., Boots 2011; reviewed in Schmid-Hempel 2003, Zuk & Stoehr 2002), increasing metabolic activity by 10–50% (Demas et al. 2012, Lochmiller & Deerenberg 2000). Similarly, the process (versus the ability) of learning also results in trade-offs with fecundity (Mery & Kawecki 2004). Thus, across all three mechanisms of plasticity reviewed here (**Figure 3**), induction of a plastic response in novel or stressful conditions is costly.

The finding that the costs of plasticity are significantly more pronounced in stressful environments reinforces the general observation that these costs are specific to certain induced phenotypes (in animals, see Van Buskirk & Steiner 2009; in plants, Steinger et al. 2003). Patterns may be amplified in nutrient- or resource-poor environments, as with life-history trade-offs more generally (Murren et al. 2015, Reznick et al. 2000, van Noordwijk & De Jong 1986). For instance, the costs of an induced immune response depend on resource availability (Moret & Schmid-Hempel 2000); thus, such responses are more likely to evolve in high-resource conditions (Boots 2011). Interestingly, given that humans are drastically increasing nutrient availability in some environments, the nutritional demands of an induced plastic response in a novel environment could be immediately ameliorated (Snell-Rood et al. 2015a).

The cost of an induced plastic response has important implications for shifts in life-history traits in novel and changing environments, by resulting in decreased growth rate and fecundity; other shifts toward a relatively slower life history might also occur. For example, upregulation of general stress mechanisms such as antioxidant pathways and heat shock proteins is linked to longer life spans but with trade-offs in fecundity (Gruber et al. 2007, Marshall & Sinclair 2010; A. Shephard, V. Aksenov, J. Tran, C. Nelson, D. Boreham & C.D. Rollo, manuscript in review). In novel environments, induction of immune responses, whether innate or acquired, may result in similar reductions in growth and fecundity (Demas et al. 2012). Thus, we might expect adaptive plastic responses in novel environments to result in slower growth (and thus longer generation times) and lower fecundity, shifting a population to relatively slower life histories.

Developmental Selection Mechanisms of Plasticity Are Particularly Costly

Developmental selection is the most costly mechanism of plasticity. The breadth of possible phenotypes an organism can develop scales with the range of phenotypes sampled across development, but this sampling process is incredibly demanding (Frank 1996). Costs are associated with producing the phenotypes, in addition to the time and energy related to sampling. Species that rely on learning, relative to more innate behavior, experience delays in performance (e.g., in the functionality of foraging behavior, Laverty & Plowright 1988), referred to as the cost of being naive or the exploration-exploitation trade-off (Cohen et al. 2007, Dukas 1998, Kaelbling et al. 1996). To sample and process a range of sensory inputs and motor outputs, animals must invest in larger or more connected networks of neurons (Huerta et al. 2004, Sporns et al. 2000), and neural tissue is particularly metabolically expensive (Laughlin et al. 1998). These costs of the learning process result in major shifts in life-history strategies toward slower life histories because offspring require greater investment to survive longer, more energy-demanding developmental periods (Snell-Rood 2012). Increased investment into learning delays reproduction, increases investment in offspring, and reduces fecundity, a pattern found in a wide range of taxa (Barrickman et al. 2008, Isler & van Schaik 2009, Iwaniuk & Nelson 2003, Kotrschal et al. 2013, Snell-Rood

et al. 2011b). Furthermore, the benefits of exploration are more likely to pay off with longer life spans (Eliassen et al. 2007, Kaplan et al. 2000).

Analogous costs and life-history shifts are seen in other forms of developmental selection. In acquired immunity, there are large upfront developmental costs (Best & Hoyle 2013), for instance, the time and energy required to develop specific immunological memory (e.g., Martin et al. 2007). Individuals must produce a wide range of cells to sample immune space. Fine-scaled sequencing has revealed that individuals sample 50–86% of their possible antibody space (Weinstein et al. 2009); in humans, more than 10 billion B cells are possible (Glanville et al. 2009). Significant useless or ineffective sampling of the phenotype space occurs in this process; in mammals, more than 70% of neurons undergo apoptosis during development (Oppenheim 1991). In the developing immune system, as much as 50% of somatic rearrangements in B cells result in pseudogenes with incorrect reading frames (Litman et al. 1993), and additional cells must be deleted through apoptosis because they are self-reactive (Krammer 2000). These costs could explain why some studies suggest limits to the benefits of increased diversity of immune cells; for instance, individuals with intermediate, versus very high, levels of major histocompatibility complex diversity tend to have relatively higher performance (Kubinak et al. 2012). More specifically, we might expect the sampling space to increase as immune cell diversity rises, resulting in a relative increase in the development time of a particular immune response—a cost that may pay off only in environments with particularly high pathogen diversity (Borghans et al. 2004). Because individuals vary in antibody repertoire (e.g., Weinstein et al. 2009), we may be able to test such predictions more precisely. High developmental costs of acquired immunity should translate into shifts toward slower life histories, with longer development times, and increased investment in each offspring. Models that incorporate the costs of immunity suggest that acquired immunity is particularly likely to evolve in long-lived species where the benefits of immunological memory are more likely to pay off (Best & Hoyle 2013, Boots & Bowers 2004).

Outside of learning and acquired immunity, there are hints that similar trade-offs occur any time we see developmental selection. Plant species that are more responsive to soil heterogeneity, through exploration by thin roots and reinforcement in nutrient-rich areas, tend to be relatively longer lived and slower growing (e.g., oaks, Chen et al. 2016), consistent with costs related to root foraging as a developmental selection mechanism of plasticity (van Kleunen et al. 2000). Similarly, there is some evidence that slower-growing species of plants are more likely to invest in thorough exploration and precise root placement (Kembel & Cahill 2005). Nematode species with less deterministic tissue organization have longer development times (Houthoofd et al. 2003). With respect to the microbiome, increases in microbe diversity within a host may increase the potential niche breadth of the host but could come with costs such as an increased chance of competitive microbial interactions that negatively affect the host (Koga et al. 2003). Similar to other examples of developmental selection, an increase in the diversity of the microbiome is expected to correspond to longer development times and increased investment in offspring as individuals "sort out" the microbiome community that matches their local environment. Species with varied diversity of symbionts with which they associate, such as corals (Cumbo et al. 2013), offer excellent opportunities to further test such ideas.

Across examples of developmental selection mechanisms of plasticity, we see time and energy costs associated with the sampling process. Thus, we might expect the sampling process to evolve over time to maximize the benefits of a wide sampling range, while minimizing costs. For instance, priors in Bayesian search algorithms may shift over evolutionary time to focus a learning or exploratory process in particularly promising areas of phenotype or information space (Dall et al. 2005, Stamps & Frankenhuis 2016). Additionally, the sampling process can be plastic, for instance being expressed only in conditions that are complex or unexpected, such as increases in neural

investment and learning in enriched and complex environments (van Praag et al. 2000). Similarly, facultative shifts in phenotype sampling space can allow individuals to avoid being caught on local optima (Mladenovic & Hansen 1997).

In many ways, developmental selection may be conceptualized as the "investment in self" that we refer to when discussing life-history strategies (Roff 2001, Stearns 2000). We often assume that increasing investment in offspring and development increases survival—the commonalities of developmental selection across levels and types of development offer a broad underlying mechanism supporting this assumption. By investing time, energy, and resources into within-individual selective processes, an individual can better match their phenotype to local conditions, thus increasing survival.

INTERACTIONS BETWEEN PLASTICITY AND EVOLUTION IN NOVEL ENVIRONMENTS

Understanding the costs and resulting life-history trade-offs associated with plasticity allows us to predict how plastic responses in novel environments will affect subsequent evolutionary processes (**Figure 3**). If a plastic response operates through generalized responses or developmental selection, it is more likely to be adaptive, leading to a higher probability of survival and thus maintenance of standing genetic variation in a population. However, as discussed above, induction of these mechanisms is costly and should result in an induced shift in life-history traits in the new environment, leading to relatively longer development times, increased investment in fewer offspring, and potentially longer life spans. Additionally, given the high costs of developmental selection mechanisms of plasticity, variation in the ability to be plastic across genotypes or species will result in selection on phenotypic plasticity such that the species or genotypes that survive in the novel environment will have relatively slower life histories associated with developmental selection. Such life-history variation is key for predictions of evolutionary rescue models, in terms of both potential population growth rate (r) and generation time (Boulding & Hay 2001, Chevin et al. 2010, Gomulkiewicz & Holt 1995, Lande 1998). Models of evolutionary rescue that integrate plastic and evolutionary responses show that critical variables include the costs of plasticity, generation time, population growth rate, and the degree the population is shifted toward a new optimal phenotype (Chevin & Lande 2010; Chevin et al. 2010, 2013), all factors influenced by the developmental mechanism of plasticity. For instance, increasing investment in developmental selection forms of plasticity is particularly tied to longer development and delayed reproduction, leading to increased generation times (e.g., Barrickman et al. 2008, Iwaniuk & Nelson 2003). Thus, increased investment in learning or acquired immunity may increase the chance of developing the optimal phenotype in a novel environment, but it would decrease the rate of environmental change a population could track evolutionarily (Chevin et al. 2010). Thus, although most models assume plasticity and evolution act synergistically with respect to population survival in novel environments, scaling life-history costs of developmental selection with benefits, in terms of hitting a new adaptive peak, suggests possible lineage-level trade-offs between adaptive plastic responses and the speed of a population-level evolutionary response.

By contrast, plasticity may positively affect standing genetic variation on which selection acts in new environments. As discussed above, investment in developmental selection forms of plasticity will likely increase the proportion of a population that survives in novel conditions, reducing loss of genetic variation in the new environment. In addition, plasticity is a well-known genetic capacitor, fostering cryptic genetic variation that is revealed in novel environments (Levy & Siegal 2008, Rutherford & Lindquist 1998, Schlichting 2008). Developmental selection forms of plasticity, which are responsive to immediate conditions, may be particularly likely to shelter novel genetic

variants. For instance, as has long been recognized, behavioral plasticity and learning can buffer selection on genetic variation, allowing genetic variation to accumulate (Lynch 2010, Snell-Rood et al. 2016). Thus, whereas short-lived fecund species are more genetically variable (Romiguier et al. 2014), species or genotypes that rely on developmental selection mechanisms of plasticity may harbor more genetic variation than expected from basic population genetic predictions. The environment also affects genetic architecture in more subtle ways that further alter evolutionary dynamics in novel environments (Sikkink et al. 2015, Wood & Brodie 2015). Because the developmental mechanism of plasticity not only influences life-history trade-offs, but may also impact levels of standing genetic variation in a new environment, modeling approaches that incorporate the mechanism of plasticity and interactions among these various factors would be particularly informative.

Interactions among plasticity, life history, and evolution will continue across generations in a new environment. Transgenerational induction of a plastic response has been observed for immunity (Barribeau et al. 2016), temperature stress (Donelson et al. 2012), learning (Arai & Feig 2011), and cross-resistance due to a generalized stress response (Mitchell & Read 2005). Costs associated with transgenerational induction of plasticity may be relatively less, owing to early life "preparation" for the plastic response based on parental cues or because not all developmental pathways for a plastic response have to be induced. For example, passive immunological memory in offspring through the passage of antibodies from the mother is significantly less costly to develop (Grindstaff 2008). If the costs of a plastic response are tempered across generations, population growth rate may rebound, making evolutionary rescue more likely. Transgenerational plasticity may also result in a broader range of potential phenotypic outcomes because cues about the state of the environment are received earlier in development (the epiphenotype hypothesis) (Herman & Sultan 2011, Snell-Rood et al. 2015b), setting up the potential for further complex interactions over time. However, transgenerational plasticity could increase the chance of costs associated with environmental mismatch if the environment is changing quickly (Costantini et al. 2014).

Once a population or species has survived a shift into a new environment, what are the consequences for diversification? Genetic assimilation is the mechanism by which an initial plastic response may lead to phenotypic diversification through genetic changes that stabilize the expression of the induced phenotype (Crispo 2007, Ehrenreich & Pfennig 2016, Pigliucci & Murren 2003). Genetic assimilation is more likely if plasticity is costly (Crispo 2007), such as with developmental selection mechanisms of plasticity. Thus, developmental selection may rapidly shift a population to a new adaptive peak (Price et al. 2003), but the continued costs of this plasticity result in selection to reduce plasticity and genetically assimilate the new phenotype (Lande 2009). Behavioral processes such as resource or habitat preferences (Davis & Stamps 2004, Edelaar & Bolnick 2012) may further reinforce this process by reducing environmental variation, favoring specialization, and losing plasticity (Ravigne et al. 2009, Scheiner 2016).

We close by returning to the question of how organisms respond to novel and rapidly changing environments. Plastic responses increase the ability of individuals and populations to survive in novel conditions, whether through mitigating new toxins, learning innovative foraging behaviors, or developing immune responses to novel pathogens. The importance of plasticity can explain why variation across species in neural investment is sometimes linked to success in novel and changing environments (Abelson 2016, Maklakov et al. 2011). However, the life-history trade-offs associated with both induced plasticity and the ability to be plastic underscore the fact that multiple mechanisms of population persistence in novel environments likely interact. For instance, the life-history trade-offs associated with neural investment put many large-brained species at risk of extinction in the face of environmental change (Gonzalez-Voyer, et al. 2016). Future modeling and empirical

approaches might consider exploring interactions between the type of plastic response and subsequent population-level evolutionary responses. In addition, although much of this review has focused on novel environments that are also relatively constant, it is important to consider how plastic rescue may operate in novel environments that are becoming more variable (e.g., climate change) or are rapidly and continuously changing. These more complicated forms of environmental change might favor greater repertoires of plastic responses that individuals can activate throughout their lives (Snell-Rood 2013) or even a bet-hedging or fixed strategy (Schlichting & Pigliucci 1998).

FUTURE ISSUES

1. How do models of evolutionary rescue change when developmental selection mechanisms of plasticity are integrated? When the costs and benefits of plasticity both scale with the degree of developmental variation, do lineage-level trade-offs emerge between plastic and evolutionary responses to environmental change?
2. To what extent do life-history trade-offs associated with learning and acquired immunity extend to analogous forms of developmental selection, ranging from microbiome selection to variability and epigenetic feedbacks in gene expression? Variations in the degree of developmental selection (e.g., differences in antibody repertoire, variability in gene expression, or microbiome diversity) create exciting opportunities for testing associated costs and life-history trade-offs.
3. Are evolved developmental switches more likely to be adaptive for environmental change on continuous axes? By contrast, are developmental selection or generalized mechanisms more likely to be adaptive for discrete changes, such as novel resources or toxins? To what extent does the degree of environmental change affect the expression of genetic variation in plasticity in novel environments, i.e., the spreading of reaction norms? Will ongoing and variable environmental changes favor different types of plasticity compared with shifts to novel, but constant or predictable, environments?

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LITERATURE CITED

Abelson ES. 2016. Brain size is correlated with endangerment status in mammals. *Proc. R. Soc. B* 283:20152772

Acar M, Mettetal JT, van Oudenaarden A. 2008. Stochastic switching as a survival strategy in fluctuating environments. *Nat. Genet.* 40:471–75

Agrawal AA, Conner JK, Johnson MTJ, Wallsgrove R. 2002. Ecological genetics of an induced plant defense against herbivores: additive genetic variance and costs of phenotypic plasticity. *Evolution* 56:2206–13

Agrawal AA, Strauss SY, Stout MJ. 1999. Costs of induced responses and tolerance to herbivory in male and female fitness components of wild radish. *Evolution* 53:1093–104

Aitken SN, Yeaman S, Holliday JA, Wang TL, Curtis-McLane S. 2008. Adaptation, migration or extirpation: climate change outcomes for tree populations. *Evol. Appl.* 1:95–111

Alberdi A, Aizpurua O, Bohmann K, Zepeda-Mendoza ML, Gilbert MTP. 2016. Do vertebrate gut metagenomes confer rapid ecological adaptation? *Trends Ecol. Evol.* 31:689–99

Arai JA, Feig LA. 2011. Long-lasting and transgenerational effects of an environmental enrichment on memory formation. *Brain Res. Bull.* 85:30–35

Badyaev AV. 2005. Stress-induced variation in evolution: from behavioural plasticity to genetic assimilation. *Proc. R. Soc. B* 72:877–86

Baker AC. 2003. Flexibility and specificity in coral-algal symbiosis: diversity, ecology, and biogeography of *Symbiodinium*. *Annu. Rev. Ecol. Evol. Syst.* 34:661–89

Baldwin IT. 1998. Jasmonate-induced responses are costly but benefit plants under attack in native populations. *PNAS* 95:8113–18

Barribeau SM, Schmid-Hempel P, Sadd BM. 2016. Royal decree: gene expression in trans-generationally immune primed bumblebee workers mimics a primary immune response. *PLOS ONE* 11:e1059635

Barrickman NL, Bastian ML, Isler K, van Schaik CP. 2008. Life history costs and benefits of encephalization: a comparative test using data from long-term studies of primates in the wild. *J. Hum. Evol.* 54:568–90

Beaumont HJE, Gallie J, Kost C, Ferguson GC, Rainey PB. 2009. Experimental evolution of bet hedging. *Nature* 462:90–97

Beever EA, Hall LE, Varner J, Loosen AE, Dunham JB, et al. 2017. Behavioral flexibility as a mechanism for coping with climate change. *Front. Ecol. Environ.* 15:299–308

Bell G, Collins S. 2008. Adaptation, extinction and global change. *Evol. Appl.* 1:3–16

Bergonzi S, Albani MC, van Themaat EVL, Nordstrom KJV, Wang RH, et al. 2013. Mechanisms of age-dependent response to winter temperature in perennial flowering of *Arabis alpina*. *Science* 340:1094–97

Berkelmans R, van Oppen MJH. 2006. The role of zooxanthellae in the thermal tolerance of corals: a 'nugget of hope' for coral reefs in an era of climate change. *Proc. R. Soc. B* 273:2305–12

Best A, Hoyle A. 2013. The evolution of costly acquired immune memory. *Ecol. Evol.* 3:2223–32

Black AR, Dodson SI. 1990. Demographic costs of *Chaoborus*-induced phenotypic plasticity in *Daphnia pulex*. *Oecologia* 83:117–22

Bock KW. 2016. The UDP-glycosyltransferase (UGT) superfamily expressed in humans, insects and plants: animal-plant arms-race and co-evolution. *Biochem. Pharmacol.* 99:11–17

Boettiger AN, Levine M. 2009. Synchronous and stochastic patterns of gene activation in the *Drosophila* embryo. *Science* 325:471–73

Boots M. 2011. The evolution of resistance to a parasite is determined by resources. *Am. Nat.* 178:214–20

Boots M, Bowers RG. 2004. The evolution of resistance through costly acquired immunity. *Proc. R. Soc. B* 271:715–23

Borghans JAM, Beltman JB, De Boer RJ. 2004. MHC polymorphism under host-pathogen coevolution. *Immunogenetics* 55:732–39

Boulding EG, Hay T. 2001. Genetic and demographic parameters determining population persistence after a discrete change in the environment. *Heredity* 86:313–24

Brakefield PM, Reitsma N. 1991. Phenotypic plasticity, seasonal climate and the population biology of *Bicyclus* butterflies (Satyridae) in Malawi. *Ecol. Entomol.* 16:291–303

Bruno JF, Edmunds PJ. 1997. Clonal variation for phenotypic plasticity in the coral *Madracis mirabilis*. *Ecology* 78:2177–90

Buffelli M, Burgess RW, Feng GP, Lobe CG, Lichtman JW, Sanes JR. 2003. Genetic evidence that relative synaptic efficacy biases the outcome of synaptic competition. *Nature* 424:430–34

Butchart SHM, Walpole M, Collen B, van Strien A, Scharlemann JPW, et al. 2010. Global biodiversity: indicators of recent declines. *Science* 328:1164–68

Callahan HS, Dhanoolal N, Ungerer MC. 2005. Plasticity genes and plasticity costs: a new approach using an *Arabidopsis* recombinant inbred population. *New Phytol.* 166:129–39

Carlson SM, Cunningham CJ, Westley PAH. 2014. Evolutionary rescue in a changing world. *Trends Ecol. Evol.* 29:521–30

Caruso CM, Maherali H, Sherrard M. 2006. Plasticity of physiology in *Lobelia*: testing for adaptation and constraint. *Evolution* 60:980–90

Cerenius L, Soderhall K. 2013. Variable immune molecules in invertebrates. *J. Exp. Biol.* 216:4313–19

Charmantier A, Gienapp P. 2014. Climate change and timing of avian breeding and migration: evolutionary versus plastic changes. *Evol. Appl.* 7:15–28

Chen WL, Koide RT, Adams TS, DeForest JL, Cheng L, Eissenstat DM. 2016. Root morphology and mycorrhizal symbioses together shape nutrient foraging strategies of temperate trees. *PNAS* 113:8741–46

Chevalier C, Stojanovic O, Colin DJ, Suarez-Zamorano N, Tarallo V, et al. 2015. Gut microbiota orchestrates energy homeostasis during cold. *Cell* 163:1360–74

Chevin L-M, Gallet R, Gomulkiewicz R, Holt RD, Fellous S. 2013. Phenotypic plasticity in evolutionary rescue experiments. *Philos. Trans. R. Soc. B* 368:20120089

Chevin L-M, Lande R. 2010. When do adaptive plasticity and genetic evolution prevent extinction of a density regulated population? *Evolution* 64:1143–50

Chevin L-M, Lande R, Mace GM. 2010. Adaptation, plasticity, and extinction in a changing environment: towards a predictive theory. *PLOS Biol.* 8:8

Cohen JD, McClure SM, Yu AJ. 2007. Should I stay or should I go? How the human brain manages the trade-off between exploitation and exploration. *Philos. Trans. R. Soc. B* 362:933–42

Congdon KA, Hammond AS, Ravosa MJ. 2012. Differential limb loading in miniature pigs (*Sus scrofa domesticus*): a test of chondral modeling theory. *J. Exp. Biol.* 215:1472–83

Cook SA, Johnson MP. 1968. Adaptation to heterogeneous environments. I. Variation in heterophylly in *Ranunculus flammula* L. *Evolution* 22:496–516

Costantini D. 2014. Does hormesis foster organism resistance to extreme events? *Front. Ecol. Environ.* 12:209–10

Costantini D, Metcalfe NB, Monaghan P. 2010. Ecological processes in a hormetic framework. *Ecol. Lett.* 13:1435–47

Costantini D, Monaghan P, Metcalfe NB. 2014. Prior hormetic priming is costly under environmental mismatch. *Biol. Lett.* 10:20131010

Crispo E. 2007. The Baldwin effect and genetic assimilation: revisiting two mechanisms of evolutionary change mediated by phenotypic plasticity. *Evolution* 61:2469–79

Cumbo VR, Baird AH, van Oppen MJH. 2013. The promiscuous larvae: flexibility in the establishment of symbiosis in corals. *Coral Reefs* 32:111–20

Dall SRX, Giraldeau LA, Olsson O, McNamara JM, Stephens DW. 2005. Information and its use by animals in evolutionary ecology. *Trends Ecol. Evol.* 20:187–93

Davies PF. 1995. Flow mediated endothelial mechanotransduction. *Physiol. Rev.* 75:519–60

Davis JM, Stamps JA. 2004. The effect of natal experience on habitat preferences. *Trends Ecol. Evol.* 19:411–16

de Kroon H, Huber H, Stuefer JF, van Groenendael JM. 2005. A modular concept of phenotypic plasticity in plants. *New Phytol.* 166:73–82

Deak M, Horvath GV, Davletova S, Torok K, Sass L, et al. 1999. Plants ectopically expressing the iron-binding protein, ferritin, are tolerant to oxidative damage and pathogens. *Nat. Biotechnol.* 17:192–96

Demas G, Greives T, Chester E, French S. 2012. The energetics of immunity. See Demas & Nelson 2012, pp. 259–96

Demas G, Nelson R, eds. 2012. *Ecoimmunology*. Oxford, UK: Oxford Univ. Press

Despres L, David JP, Gallet C. 2007. The evolutionary ecology of insect resistance to plant chemicals. *Trends Ecol. Evol.* 22:298–307

DeWitt TJ, Sih A, Wilson DS. 1998. Costs and limits of phenotypic plasticity. *Trends Ecol. Evol.* 13:77–81

Di Croce L, Helin K. 2013. Transcriptional regulation by Polycomb group proteins. *Nat. Struct. Mol. Biol.* 20:1147–55

Ding Y, Fromm M, Avramova Z. 2012. Multiple exposures to drought 'train' transcriptional responses in *Arabidopsis*. *Nat. Commun*. 3:9

Donelson JM, Munday PL, McCormick MI, Pitcher CR. 2012. Rapid transgenerational acclimation of a tropical reef fish to climate change. *Nat. Clim. Change* 2:30–32

Doust LL. 1981. Population dynamics and local specialization in a clonal perennial (*Ranunculus repens*). 1. The dynamics of ramets in contrasting habitats. *J. Ecol.* 69:743–55

Ducher G, Prouteau S, Courteix D, Benhamou CL. 2004. Cortical and trabecular bone at the forearm show different adaptation patterns in response to tennis playing. *J. Clin. Densitom.* 7:399–405

Dukas R. 1998. Evolutionary ecology of learning. In *Cognitive Ecology: The Evolutionary Ecology of Information Processing and Decision Making*, ed. R Dukas, pp. 129–74. Chicago: Univ. Chicago Press

Duncan RL, Turner CH. 1995. Mechanitransduction and the functional response of bone to mechanical strain. *Calcif. Tissue Int.* 57:344–58

Duputie A, Rutschmann A, Ronce O, Chuine I. 2015. Phenological plasticity will not help all species adapt to climate change. *Glob. Change Biol.* 21:3062–73

Ebert MS, Sharp PA. 2012. Roles for microRNAs in conferring robustness to biological processes. *Cell* 149:515–24

Edelaar P, Bolnick DI. 2012. Non-random gene flow: an underappreciated force in evolution and ecology. *Trends Ecol. Evol.* 27:659–65

Efferth T, Volm M. 2017. Multiple resistance to carcinogens and xenobiotics: P-glycoproteins as universal detoxifiers. *Arch. Toxicol.* 91:2515–38

Ehrenreich IM, Pfennig DW. 2016. Genetic assimilation: a review of its potential proximate causes and evolutionary consequences. *Ann. Bot.* 117:769–79

Eldar A, Elowitz MB. 2010. Functional roles for noise in genetic circuits. *Nature* 467:167–73

Eliassen S, Jorgensen C, Mangel M, Giske J. 2007. Exploration or exploitation: Life expectancy changes the value of learning in foraging strategies. *Oikos* 116:513–23

Ellis EC, Ramankutty N. 2008. Putting people in the map: anthropogenic biomes of the world. *Front. Ecol. Environ.* 6:439–47

Feder ME, Hofmann GE. 1999. Heat-shock proteins, molecular chaperones, and the stress response: evolutionary and ecological physiology. *Annu. Rev. Physiol.* 61:243–82

Feinberg AP, Irizarry RA. 2010. Stochastic epigenetic variation as a driving force of development, evolutionary adaptation, and disease. *PNAS* 107:1757–64

Fischer EK, Ghalambor CK, Hoke KL. 2016. Plasticity and evolution in correlated suites of traits. *J. Evol. Biol.* 29:991–1002

Francis NJ, Kingston RE. 2001. Mechanisms of transcriptional memory. *Nat. Rev. Mol. Cell Biol.* 2:409–21

Frank S. 1996. The design of natural and artificial adaptive systems. In *Adaptation*, ed. M Rose, G Lauder, pp. 451–505. New York: Academic

Franklin KA. 2008. Shade avoidance. *New Phytol.* 179:930–44

Franks SJ, Weber JJ, Aitken SN. 2014. Evolutionary and plastic responses to climate change in terrestrial plant populations. *Evol. Appl.* 7:123–39

Futuyma DJ, Moreno G. 1988. The evolution of ecological specialization. *Annu. Rev. Ecol. Syst.* 19:207–33

Galvan I, Bonisoli-Alquati A, Jenkinson S, Ghanem G, Wakamatsu K, et al. 2014. Chronic exposure to low-dose radiation at Chernobyl favours adaptation to oxidative stress in birds. *Funct. Ecol.* 28:1387–403

Garud N, Good B, Hallatschek O, Pollard K. 2017. Evolutionary dynamics of bacteria in the gut microbiome within and across hosts. bioRxiv 210955. **https://doi.org/10.1101/210955**

Gerschman R, Gilbert DL, Nye SW, Dwyer P, Fenn WO. 1954. Oxygen poisoning and X-irradiation: a mechanism in common. *Science* 119:623–26

Ghalambor CK, McKay JK, Carrol SP, Reznick DN. 2007. Adaptive versus non-adaptive phenotypic plasticity and the potential for contemporary adaptation in new environments. *Funct. Ecol.* 21:394–407

Gilbert SF, McDonald E, Boyle N, Buttino N, Gyi L, et al. 2010. Symbiosis as a source of selectable epigenetic variation: taking the heat for the big guy. *Philos. Trans. R. Soc. B* 365:671–78

Gilchrest BA, Park HY, Eller MS, Yaar M. 1996. Mechanisms of ultraviolet light-induced pigmentation. *Photochem. Photobiol.* 63:1–10
Glanville J, Zhai WW, Berka J, Telman D, Huerta G, et al. 2009. Precise determination of the diversity of a combinatorial antibody library gives insight into the human immunoglobulin repertoire. *PNAS* 106:20216–21
Gloss AD, Vassao DG, Hailey AL, Dittrich ACN, Schramm K, et al. 2014. Evolution in an ancient detoxification pathway is coupled with a transition to herbivory in the Drosophilidae. *Mol. Biol. Evol.* 31:2441–56
Gomulkiewicz R, Holt RD. 1995. When does evolution by natural selection prevent extinction? *Evolution* 49:201–7
Gonzalez-Voyer A, Gonzalez-Suarez M, Vila C, Revilla E. 2016. Larger brain size indirectly increases vulnerability to extinction in mammals. *Evolution* 70:1364–75
Gonzalez FJ. 2005. Role of cytochromes P450 in chemical toxicity and oxidative stress: studies with CYP2E1. *Mutat. Res.* 569:101–10
Gopnik A, O'Grady S, Lucas CG, Griffiths TL, Wente A, et al. 2017. Changes in cognitive flexibility and hypothesis search across human life history from childhood to adolescence to adulthood. *PNAS* 114:7892–99
Gordon JA, Stryker MP. 1996. Experience-dependent plasticity of binocular responses in the primary visual cortex of the mouse. *J. Neurosci.* 16:3274–86
Grindstaff JL. 2008. Maternal antibodies reduce costs of an immune response during development. *J. Exp. Biol.* 211:654–60
Gruber J, Tang SY, Halliwell B. 2007. Evidence for a trade-off between survival and fitness caused by resveratrol treatment of *Caenorhabditis elegans*. *Biogerontology* 1100:530–42
Guillemin K, Groppe J, Ducker K, Treisman R, Hafen E, et al. 1996. The pruned gene encodes the *Drosophila* serum response factor and regulates cytoplasmic outgrowth during terminal branching of the tracheal system. *Development* 122:1353–62
Hamann E, Puijalon S. 2013. Biomechanical responses of aquatic plants to aerial conditions. *Ann. Bot.* 112:1869–78
Hammond AS, Ning J, Ward CV, Ravosa MJ. 2010. Mammalian limb loading and chondral modeling during ontogeny. *Anat. Rec.* 293:658–70
Herman JJ, Sultan SE. 2011. Adaptive transgenerational plasticity in plants: case studies, mechanisms, and implications for natural populations. *Front. Plant Sci.* 2:102
Hodge A. 2004. The plastic plant: root responses to heterogeneous supplies of nutrients. *New Phytol.* 162:9–24
Hoffmann A, Parsons P. 1997. *Extreme Environmental Change and Evolution*. Cambridge, UK: Cambridge Univ. Press
Honjo T, Habu S. 1985. Origin of immune diversity: genetic variation and selection. *Annu. Rev. Biochem.* 54:803–30
Houthoofd W, Jacobsen K, Mertens C, Vangestel S, Coomans A, Borgonie G. 2003. Embryonic cell lineage of the marine nematode *Pellioditis marina*. *Dev. Biol.* 258:57–69
Hove JR, Koster RW, Forouhar AS, Acevedo-Bolton G, Fraser SE, Gharib M. 2003. Intracardiac fluid forces are an essential epigenetic factor for embryonic cardiogenesis. *Nature* 421:172–77
Huerta R, Nowotny T, Garcia-Sanchez M, Abarbanel HDI, Rabinovich MI. 2004. Learning classification in the olfactory system of insects. *Neural Comput.* 16:1601–40
Hull DL, Langman RE, Glenn SS. 2001. A general account of selection: biology, immunology, and behavior. *Behav. Brain Sci.* 24:511–73
Isler K, van Schaik CP. 2009. The expensive brain: a framework for explaining evolutionary changes in brain size. *J. Hum. Evol.* 57:392–400
Iwaniuk AN, Nelson JE. 2003. Developmental differences are correlated with relative brain size in birds: a comparative analysis. *Can. J. Zool.* 81:1913–28
Johnston LA. 2009. Competitive interactions between cells: death, growth, and geography. *Science* 324:1679–82
Kaelbling LP, Littman ML, Moore AW. 1996. Reinforcement learning: a survey. *J. Artif. Intell. Res.* 4:237–85
Kaplan H, Hill K, Lancaster J, Hurtado AM. 2000. A theory of human life history evolution: diet, intelligence, and longevity. *Evol. Anthropol.* 9:156–85

Katz LC, Shatz CJ. 1996. Synaptic activity and the construction of cortical circuits. *Science* 274:1133–38
Kembel SW, Cahill JF. 2005. Plant phenotypic plasticity belowground: a phylogenetic perspective on root foraging trade-offs. *Am. Nat.* 166:216–30
Kensler TW, Wakabayash N, Biswal S. 2007. Cell survival responses to environmental stresses via the Keap1-Nrf2-ARE pathway. *Annu. Rev. Pharmacol. Toxicol.* 47:89–116
Keppler C, Ringwood AH. 2001. Expression of P-glycoprotein in the gills of oysters, *Crassostrea virginica*: seasonal and pollutant related effects. *Aquat. Toxicol.* 54:195–204
Kiers ET, Duhamel M, Beesetty Y, Mensah JA, Franken O, et al. 2011. Reciprocal rewards stabilize cooperation in the mycorrhizal symbiosis. *Science* 333:880–82
Kirschner M, Gerhart J. 1998. Evolvability. *PNAS* 95:8420–27
Koga R, Tsuchida T, Fukatsu T. 2003. Changing partners in an obligate symbiosis: a facultative endosymbiont can compensate for loss of the essential endosymbiont *Buchnera* in an aphid. *Proc. R. Soc. B* 270:2543–50
Kotrschal A, Rogell B, Bundsen A, Svensson B, Zajitschek S, et al. 2013. Artificial selection on relative brain size in the guppy reveals costs and benefits of evolving a larger brain. *Curr. Biol.* 23:168–71
Krammer PH. 2000. CD95's deadly mission in the immune system. *Nature* 407:789–95
Kregel KC. 2002. Heat shock proteins: modifying factors in physiological stress responses and acquired thermotolerance. *J. Appl. Physiol.* 92:2177–86
Kubinak J, Nelson A, Ruff J, Potts W. 2012. Trade-offs limiting MHC heterozygosity. See Demas & Nelson 2012, pp. 225–58
Kurtz J, Armitage SAO. 2006. Alternative adaptive immunity in invertebrates. *Trends Immunol.* 27:493–96
Kussell E, Leibler S. 2005. Phenotypic diversity, population growth, and information in fluctuating environments. *Science* 309:2075–78
Lande R. 1998. Anthropogenic, ecological and genetic factors in extinction and conservation. *Res. Popul. Ecol.* 40:259–69
Lande R. 2009. Adaptation to an extraordinary environment by evolution of phenotypic plasticity and genetic assimilation. *J. Evol. Biol.* 22:1435–46
Langkilde T, Thawley CJ, Robbins TR. 2017. Behavioral adaptations to invasive species: benefits, costs, and mechanisms of change. *Adv. Study Behav.* 49:199–235
Laughlin SB, van Steveninck RRD, Anderson JC. 1998. The metabolic cost of neural information. *Nat. Neurosci.* 1:36–41
Laverty TM, Plowright RC. 1988. Flower handling by bumblebees: a comparison of specialists and generalists. *Anim. Behav.* 36:733–40
Ledon-Rettig CC, Pfennig DW, Crespi EJ. 2010. Diet and hormonal manipulation reveal cryptic genetic variation: implications for the evolution of novel feeding strategies. *Proc. R. Soc. B* 277:3569–78
Levy SF, Siegal ML. 2008. Network hubs buffer environmental variation in *Saccharomyces cerevisiae*. *PLOS Biol.* 6:2588–604
Ley RE, Peterson DA, Gordon JI. 2006. Ecological and evolutionary forces shaping microbial diversity in the human intestine. *Cell* 124:837–48
Li XC, Baudry J, Berenbaum MR, Schuler MA. 2004. Structural and functional divergence of insect CYP6B proteins: from specialist to generalist cytochrome P450. *PNAS* 101:2939–44
Li XC, Schuler MA, Berenbaum MR. 2007. Molecular mechanisms of metabolic resistance to synthetic and natural xenobiotics. *Annu. Rev. Entomol.* 52:231–53
Litman GW, Rast JP, Shamblott MJ, Haire RN, Hulst M, et al. 1993. Phylogenetic diversification of immunoglobulin genes and the antibody repertoire. *Mol. Biol. Evol.* 10:60–72
Lochmiller RL, Deerenberg C. 2000. Trade-offs in evolutionary immunology: Just what is the cost of immunity? *Oikos* 88:87–98
Luo LQ, O'Leary DDM. 2005. Axon retraction and degeneration in development and disease. *Annu. Rev. Neurosci.* 28:127–56
Lynch M. 2010. Rate, molecular spectrum, and consequences of human mutation. *PNAS* 107:961–68
Maklakov AA, Immler S, Gonzalez-Voyer A, Ronn J, Kolm N. 2011. Brains and the city: Big-brained passerine birds succeed in urban environments. *Biol. Lett.* 7:730–32
Marshall KE, Sinclair BJ. 2010. Repeated stress exposure results in a survival-reproduction trade-off in *Drosophila melanogaster*. *Proc. R. Soc. B* 277:963–69

Martin LB, Navara KJ, Weil ZM, Nelson RJ. 2007. Immunological memory is compromised by food restriction in deer mice *Peromyscus maniculatus*. *Am. J. Physiol*. 292:R316–20
Marzluff J, Shulenberger E, Endlicher W, Alberti M, Bradley G, et al, eds. 2008. *Urban Ecology: An International Perspective on the Interaction Between Humans and Nature*. New York: Springer
Mattson MP. 2008. Hormesis and disease resistance: activation of cellular stress response pathways. *Hum. Exp. Toxicol.* 27:155–62
Mazzocchi F. 2008. Complexity in biology: exceeding the limits of reductionism and determinism using complexity theory. *EMBO Rep*. 9:10–14
McAdams HH, Arkin A. 1997. Stochastic mechanisms in gene expression. *PNAS* 94:814–19
Menegaz RA, Sublett SV, Figueroa SD, Hoffman TJ, Ravosa MJ, Aldridge K. 2010. Evidence for the influence of diet on cranial form and robusticity. *Anat. Rec.* 293:630–41
Mery F, Kawecki TJ. 2004. An operating cost of learning in *Drosophila melanogaster*. *Anim. Behav*. 68:589–98
Meyer A. 1987. Phenotypic plasticity and heterochrony in *Cichlasoma managuense* (Pisces, Chichlidae) and their implications for speciation in cichlid fishes. *Evolution* 41:1357–69
Miller-Jensen K, Dey SS, Schaffer DV, Arkin AP. 2011. Varying virulence: epigenetic control of expression noise and disease processes. *Trends Biotechnol*. 29:517–25
Mitchell SE, Read AF. 2005. Poor maternal environment enhances offspring disease resistance in an invertebrate. *Proc. R. Soc. B* 272:2601–7
Mladenovic N, Hansen P. 1997. Variable neighborhood search. *Comput. Oper. Res.* 24:1097–100
Moczek AP, Emlen DJ. 2000. Male horn dimorphism in the scarab beetle, *Onthophagus taurus*: Do alternative reproductive tactics favor alternative phenotypes? *Anim. Behav.* 59:459–66
Moore SW. 2003. Scrambled eggs: mechanical forces as ecological factors in early development. *Evol. Dev*. 5:61–66
Moran NA. 1992. The evolutionary maintenance of alternative phenotypes. *Am. Nat.* 139:971–89
Moret Y, Schmid-Hempel P. 2000. Survival for immunity: the price of immune system activation for bumblebee workers. *Science* 290:1166–68
Murren CJ, Auld JR, Callahan H, Ghalambor CK, Handelsman CA, et al. 2015. Constraints on the evolution of phenotypic plasticity: limits and costs of phenotype and plasticity. *Heredity* 115:293–301
Nielsen ME. 2017. No geographic variation in thermoregulatory colour plasticity and limited variation in heat-avoidance behaviour in *Battus philenor* caterpillars. *J. Evol. Biol.* 30:1919–28
Nijhout HF. 1999. Control mechanisms of polyphenic development in insects: In polyphenic development, environmental factors alter same aspects of development in an orderly and predictable way. *Bioscience* 49:181–92
Niklas KJ. 2009. Functional adaptation and phenotypic plasticity at the cellular and whole plant level. *J. Biosci.* 34:613–20
Oppenheim RW. 1991. Cell death during development of the nervous system. *Annu. Rev. Neurosci.* 14:453–501
Papaj DR, Prokopy RJ. 1989. Ecological and evolutionary aspects of learning in phytophagous insects. *Annu. Rev. Entomol.* 34:315–50
Pette D, Staron RS. 2000. Myosin isoforms, muscle fiber types, and transitions. *Microsc. Res. Tech.* 50:500–9
Pigliucci M, Murren CJ. 2003. Genetic assimilation and a possible evolutionary paradox: Can macroevolution sometimes be so fast as to pass us by? *Evolution* 57:1455–64
Pillai P, Gouhier TC, Vollmer SV. 2017. Ecological rescue of host-microbial systems under environmental change. *Theor. Ecol.* 10:51–63
Price TD, Qvarnström A, Irwin DE. 2003. The role of phenotypic plasticity in driving genetic evolution. *Proc. R. Soc. B* 270:1433–40
Purchase CF, Moreau DTR. 2012. Stressful environments induce novel phenotypic variation: hierarchical reaction norms for sperm performance of a pervasive invader. *Ecol. Evol.* 2:2562–71
Purves D, Lichtman JW. 1980. Elimination of synapses in the developing nervous system. *Science* 210:153–57
Ragsdale EJ, Muller MR, Rodelsperger C, Sommer RJ. 2013. A developmental switch coupled to the evolution of plasticity acts through a sulfatase. *Cell* 155:922–33
Raj A, Peskin CS, Tranchina D, Vargas DY, Tyagi S. 2006. Stochastic mRNA synthesis in mammalian cells. *PLOS Biol*. 4:1707–19

Raj A, van Oudenaarden A. 2008. Nature, nurture, or chance: stochastic gene expression and its consequences. *Cell* 135:216–26
Rajewsky K. 1996. Clonal selection and learning in the antibody system. *Nature* 381:751–58
Rautio M, Korhola A. 2002. UV-induced pigmentation in subarctic *Daphnia*. *Limnol. Oceanogr*. 47:295–99
Ravigne V, Dieckmann U, Olivieri I. 2009. Live where you thrive: Joint evolution of habitat choice and local adaptation facilitates specialization and promotes diversity. *Am. Nat.* 174:E141–69
Reznick D, Nunney L, Tessier A. 2000. Big houses, big cars, superfleas and the costs of reproduction. *Trends Ecol. Evol.* 15:421–25
Riechers DE, Kreuz K, Zhang Q. 2010. Detoxification without intoxication: Herbicide safeners activate plant defense gene expression. *Plant Physiol*. 153:3–13
Risau W. 1997. Mechanisms of angiogenesis. *Nature* 386:671–74
Roff D. 2001. *Life History Evolution*. Sunderland, MA: Sinauer
Romiguier J, Gayral P, Ballenghien M, Bernard A, Cahais V, et al. 2014. Comparative population genomics in animals uncovers the determinants of genetic diversity. *Nature* 515:261–43
Ruiz-Gonzalez MX, Moret Y, Brown MJF. 2009. Rapid induction of immune density-dependent prophylaxis in adult social insects. *Biol. Lett.* 5:781–83
Rutherford SL, Lindquist S. 1998. Hsp90 as a capacitor for morphological evolution. *Nature* 396:336–42
Sachs T. 2004. Self-organization of tree form: a model for complex social systems. *J. Theor. Biol.* 230:197–202
Sachs T, Novoplansky A, Cohen D. 1993. Plants as competing populations of redundant organs. *Plant Cell Environ*. 16:765–70
Sanchis-Moysi J, Idoate F, Izquierdo M, Calbet JAL, Dorado C. 2011. Iliopsoas and gluteal muscles are asymmetric in tennis players but not in soccer players. *PLOS ONE* 6:10
Scheiner SM. 2016. Habitat choice and temporal variation alter the balance between adaptation by genetic differentiation, a jack-of-all-trades strategy, and phenotypic plasticity. *Am. Nat.* 187:633–46
Schlichting CD. 2008. Hidden reaction norms, cryptic genetic variation, and evolvability. In *Year in Evolutionary Biology 2008*, pp. 187–203. Oxford, UK: Blackwell
Schlichting CD, Pigliucci M. 1998. *Phenotypic Evolution: A Reaction Norm Perspective*. Sunderland, MA: Sinauer
Schluter J, Foster KR. 2012. The evolution of mutualism in gut microbiota via host epithelial selection. *PLOS Biol.* 10:e1001424
Schmid-Hempel P. 2003. Variation in immune defence as a question of evolutionary ecology. *Proc. R. Soc. B* 270:357–66
Schramm K, Vassao DG, Reichelt M, Gershenzon J, Wittstock U. 2012. Metabolism of glucosinolate-derived isothiocyanates to glutathione conjugates in generalist lepidopteran herbivores. *Insect Biochem. Mol. Biol.* 42:174–82
Schuler MA. 2011. P450s in plant-insect interactions. *Biochim. Biophys. Acta* 1814:36–45
Shephard AM, Bharwani A, Durisko Z, Andrews PW. 2016. Reverse engineering the febrile system. *Q. Rev. Biol.* 91:419–57
Shettleworth S. 1998. *Cognition, Evolution and Behavior*. Oxford, UK: Oxford Univ. Press
Sih A, Ferrari MCO, Harris DJ. 2011. Evolution and behavioural responses to human-induced rapid environmental change. *Evol. Appl.* 4:367–87
Sikkink KL, Reynolds RM, Cresko WA, Phillips PC. 2015. Environmentally induced changes in correlated responses to selection reveal variable pleiotropy across a complex genetic network. *Evolution* 69:1128–42
Singh S, Brocker C, Koppaka V, Chen Y, Jackson BC, et al. 2013. Aldehyde dehydrogenases in cellular responses to oxidative/electrophilic stress. *Free Radic. Biol. Med.* 56:89–101
Snell-Rood EC. 2012. Selective processes in development: implications for the costs and benefits of phenotypic plasticity. *Integr. Comp. Biol.* 52:31–42
Snell-Rood EC. 2013. An overview of the evolutionary causes and consequences of behavioural plasticity. *Anim. Behav.* 85:1004–11
Snell-Rood EC, Burger M, Hutton Q, Moczek AP. 2016. Effects of parental care on the accumulation and release of cryptic genetic variation: review of mechanisms and a case study of dung beetles. *Evol. Ecol.* 30:251–65
Snell-Rood EC, Cash A, Han MV, Kijimoto T, Andrews J, Moczek AP. 2011a. Developmental decoupling of alternative phenotypes: insights from the transcriptomes of horn polyphenic beetles. *Evolution* 65:231–45

Snell-Rood EC, Cothran R, Espeset A, Jeyasingh P, Hobbie S, Morehouse N. 2015a. Life-history evolution in the anthropocene: effects of increasing nutrients on traits and trade-offs. *Evol. Appl.* 8:635–49
Snell-Rood EC, Davidowitz G, Papaj DR. 2011b. Reproductive trade-offs of learning in a butterfly. *Behav. Ecol.* 22:291–302
Snell-Rood EC, Swanson EM, Young RL. 2015b. Life history as a constraint on plasticity: Developmental timing is correlated with phenotypic variation in birds. *Heredity* 115:379–88
Snell-Rood EC, Van Dyken JD, Cruickshank T, Wade M, Moczek A. 2010. Toward a population genetic framework of developmental evolution: costs, limits, and consequences of phenotypic plasticity. *BioEssays* 32:71–81
Sol D. 2009. Revisiting the cognitive buffer hypothesis for the evolution of large brains. *Biol. Lett.* 5:130–33
Sol D, Duncan RP, Blackburn TM, Cassey P, Lefebvre L. 2005. Big brains, enhanced cognition, and response of birds to novel environments. *PNAS* 102:5460–65
Speck T, Burgert I. 2011. Plant stems: functional design and mechanics. *Annu. Rev. Mater. Res.* 41:169–93
Sporns O, Tononi G, Edelman GM. 2000. Connectivity and complexity: the relationship between neuroanatomy and brain dynamics. *Neural Netw.* 13:909–22
Stamps JA, Frankenhuis WE. 2016. Bayesian models of development. *Trends Ecol. Evol.* 31:260–68
Stearns SC. 2000. Life history evolution: successes, limitations, and prospects. *Naturwissenschaften* 87:476–86
Steinger T, Roy BA, Stanton ML. 2003. Evolution in stressful environments II: adaptive value and costs of plasticity in response to low light in *Sinapis arvensis*. *J. Evol. Biol.* 16:313–23
Sultan SE, Spencer HG. 2002. Metapopulation structure favors plasticity over local adaptation. *Am. Nat.* 160:271–83
Tamori Y, Deng WM. 2011. Cell competition and its implications for development and cancer. *J. Genet. Genom.* 38:483–95
Telemeco RS, Fletcher B, Levy O, Riley A, Rodriguez-Sanchez Y, et al. 2017. Lizards fail to plastically adjust nesting behavior or thermal tolerance as needed to buffer populations from climate warming. *Glob. Change Biol.* 23:1075–84
Thattai M, van Oudenaarden A. 2004. Stochastic gene expression in fluctuating environments. *Genetics* 167:523–30
Turner PE, Elena SF. 2000. Cost of host radiation in an RNA virus. *Genetics* 156:1465–70
Van Buskirk J. 2000. The costs of an inducible defense in anuran larvae. *Ecology* 81:2813–21
Van Buskirk J, Steiner UK. 2009. The fitness costs of developmental canalization and plasticity. *J. Evol. Biol.* 22:852–60
Van de Peer T, Verheyen K, Kint V, Van Cleemput E, Muys B. 2017. Plasticity of tree architecture through interspecific and intraspecific competition in a young experimental plantation. *For. Ecol. Manag.* 385:1–9
van Kleunen M, Fischer M, Schmid B. 2000. Costs of plasticity in foraging characteristics of the clonal plant *Ranunculus reptans*. *Evolution* 54:1947–55
van Noordwijk AJ, de Jong G. 1986. Acquisition and allocation of resources: their influence on variation in life history tactics. *Am. Nat.* 128:137–42
van Praag H, Kempermann G, Gage FH. 2000. Neural consequences of environmental enrichment. *Nat. Rev. Neurosci.* 1:191–98
Van Tienderen PH. 1991. Evolution of generalists and specialists in spatially heterogeneous environments. *Evolution* 45:1317–31
Visser ME. 2008. Keeping up with a warming world; assessing the rate of adaptation to climate change. *Proc. R. Soc. B* 275:649–59
Wainwright PC, Osenberg CW, Mittelbach GG. 1991. Trophic polymorphism in the pumpkinseed sunfish (*Lepomis gibbosus* Linnaeus): effects of environment on ontogeny. *Funct. Ecol.* 5:40–55
Wang WX, Vinocur B, Shoseyov O, Altman A. 2004. Role of plant heat-shock proteins and molecular chaperones in the abiotic stress response. *Trends Plant Sci.* 9:244–52
Watson FL, Puttmann-Holgado R, Thomas F, Lamar DL, Hughes M, et al. 2005. Extensive diversity of Ig-superfamily proteins in the immune system of insects. *Science* 309:1874–78
Weinig C, Johnston J, German ZM, Demink LM. 2006. Local and global costs of adaptive plasticity to density in *Arabidopsis thaliana*. *Am. Nat.* 167:826–36

Weinstein JA, Jiang N, White RA, Fisher DS, Quake SR. 2009. High-throughput sequencing of the zebrafish antibody repertoire. *Science* 324:807–10

West-Eberhard MJ. 2003. *Developmental Plasticity and Evolution*. New York: Oxford Univ. Press

Wheeler DE. 1991. The developmental basis of worker caste polymorphism in ants. *Am. Nat.* 138:1218–38

Whitlock MC. 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

Wilson K, Reeson AF. 1998. Density-dependent prophylaxis: evidence from Lepidoptera-baculovirus interactions? *Ecol. Entomol.* 23:100–1

Wood CW, Brodie ED. 2015. Environmental effects on the structure of the G-matrix. *Evolution* 69:2927–40

Yi HY, Chowdhury M, Huang YD, Yu XQ. 2014. Insect antimicrobial peptides and their applications. *Appl. Microbiol. Biotechnol.* 98:5807–22

Zuk M, Stoehr AM. 2002. Immune defense and host life history. *Am. Nat.* 160:S9–22

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