DOI: 10.1111/ede.12309

PERSPECTIVE

WILEY

Plasticity-led evolution: A survey of developmental mechanisms and empirical tests

Nicholas A. Levis | **David W. Pfennig**

Department of Biology, University of North Carolina, Chapel Hill, North Carolina

Correspondence
Nicholas A. Levis, Department of Biology, CB#3280, University of North Carolina, Chapel Hill, NC 27599.
Email: nicholasalevis@gmail.com

Abstract

Recent years have witnessed increased interest in evaluating whether phenotypic plasticity can precede, facilitate, and possibly even bias adaptive evolution. Despite accumulating evidence for "plasticity-led evolution" (i.e., "PLE"), critical gaps remain, such as: how different developmental mechanisms influence PLE; whether some types of traits and taxa are especially prone to experience PLE; and what studies are needed to drive the field forward. Here, we begin to address these shortcomings by first speculating about how various features of development—modularity, flexible regulation, and exploratory mechanisms—might impact and/or bias whether and how PLE unfolds. We then review and categorize the traits and taxa used to investigate PLE. We do so both to identify systems that may be well-suited for studying developmental mechanisms in a PLE context and to highlight any mismatches between PLE theory and existing empirical tests of this theory. We conclude by providing additional suggestions for future research. Our overarching goal is to stimulate additional work on PLE and thereby evaluate plasticity's role in evolution.

1 | INTRODUCTION

The environment has long been viewed as crucial in both selecting on phenotypes and in creating those phenotypes in the first place (e.g., Baldwin, 1896, 1902; Morgan, 1896; Osborn, 1896; West-Eberhard, 1989, 2003). However, the notion that the environment can serve this dual role remains contentious (Futuyma, 2015; Sarkar, 2003; Wray et al., 2014). This debate has been reinvigorated with renewed interest in environmentally initiated phenotypic change (i.e., phenotypic or developmental "plasticity"; Forsman, 2014; West-Eberhard, 2003). Specifically, many researchers have begun asking whether and how such developmental flexibility can precede and facilitate the evolution of novel, complex, adaptive traits (e.g., Badyaev, 2005; Levis & Pfennig, 2016; Moczek et al., 2011; West-Eberhard, 2003). Under this view, novel traits start out evolutionarily as environmentally induced phenotypic variants. Later, they come under genetic control through selection on developmental processes. Taken together, these steps—environmental induction, subsequent refinement, and possible transition to genetic control—constitute the plasticity-led hypothesis of adaptive evolution (sensu Levis & Pfennig, 2019c; see also Schwander & Leimar, 2011; West-Eberhard, 1989, 2003).

The process of plasticity-led evolution (hereafter, "PLE") begins when individuals encounter a novel environment. Typically, exposure to a novel environment is stressful, and plastic responses to such environments may often be maladaptive. However, many organisms have also evolved phenotypic plasticity to mitigate such stress and potentially enhance

their fitness under the new conditions (Badyaev, 2005; Palmer, 2012). Following induction, this environmentally induced phenotype is often stabilized by the complex, interconnected, and contingent nature of developmental and physiological processes (i.e., "phenotypic accommodation" occurs; sensu Badyaev, 2005; Lande, 2019; West-Eberhard, 2003, 2005). Yet, if different genotypes stabilize the induced phenotype in different ways and/or they exhibit different reaction norms, then selection can act on this variation and improve the new phenotype's functionality by promoting the evolution of heritable changes (i.e., "genetic accommodation" occurs; Moczek, 2007; Moczek et al., 2011; Suzuki & Nijhout, 2006; West-Eberhard, 2003). Moreover, selection can favor either increased environmental sensitivity (Nijhout, 2003)—which might, in the extreme, lead to the evolution of a "polyphenism" (sensu Michener, 1961)—or decreased environmental sensitivity (Nijhout, 2003)—which might favor canalization of a particular variant and loss of plasticity (i.e., "genetic assimilation"; sensu Waddington, 1953). Ultimately, PLE results in an adaptive phenotype that began as an environmentally induced variant (e.g., see Figure 1).

Despite increasing support for PLE (e.g., Braendle & Flatt, 2006; Jones & Robinson, 2018; Levis & Pfennig, 2016, 2019b; Schlichting & Wund, 2014; Schneider & Meyer, 2017), at least three important gaps remain. First, phenotypic plasticity is inherently a developmental phenomenon. Yet, little is still known about how different developmental mechanisms influence how PLE unfolds. For example, some developmental systems might be biased in the types of variants that are produced under stressful conditions (Badyaev, 2005). That is, particular developmental features and responses might bias the types of phenotypes that are produced (Uller, Moczek, Watson, Brakefield, & Laland, 2018). Indeed, in some cases, environmentally induced phenotypes might be somewhat well-suited to novel conditions when they are initially expressed. Similarly, we also know relatively little about the types of traits and taxa that are likely to experience PLE. Ascertaining whether some traits and/or taxa are especially prone to undergo PLE is important because such traits/taxa may be particularly useful for studying PLE. Finally, and related to the previous point, it is unclear how best to study PLE. Indeed, as noted above, although recent reviews have concluded that PLE may have played an important role in the evolution of novelty and adaptation in both laboratory and natural systems (e.g., Braendle & Flatt, 2006; Jones & Robinson, 2018; Levis & Pfennig, 2016, 2019b; Schlichting & Wund, 2014; Schneider & Meyer, 2017; Figure 1), some researchers remain skeptical of PLE as a general and important route to evolutionary novelty (Futuyma, 2015; Orr, 1999; Wray et al., 2014). This ongoing skepticism suggests that more empirical testing of PLE theory is needed.

In this paper, we seek to help overcome these shortcomings. Our central premise is that the mechanisms that underlie plasticity must be identified if we are to fully appreciate plasticity's impacts on evolution. Moreover (and of relevance to this special issue), because different developmental mechanisms might bias PLE, these same mechanisms might ultimately bias plasticity's downstream evolutionary consequences.

We therefore begin our paper by briefly synthesizing the relationships among PLE and various developmental mechanisms. We especially focus on how different developmental mechanisms might make PLE more or less likely to occur and thereby bias PLE. We then shift our attention from discussing the theory of PLE to examining the empirical tests of PLE in light of this theory. Connecting theory to empirical research is important because it is vital to know whether or not empirical tests of PLE are following the prescribed theory. We conclude our paper by further integrating the theory and data to suggest future directions of inquiry. Through this approach, we hope to identify any underrepresented areas of investigation (e.g., developmental processes or types of traits or taxa) that may yield valuable insights into PLE.

2 | HOW DIFFERENT DEVELOPMENTAL MECHANISMS MIGHT BIAS PLE

As noted in the Introduction, PLE hinges on the dual ability of an organism's developmental systems to: (1) generate a viable phenotypic variant in the face of environmental perturbation, and (2) have this phenotypic variant undergo subsequent adaptive refinement. Here, we survey how various mechanisms of development can impact each stage of PLE. An important conclusion from this speculation is that some of the same developmental mechanisms that promote evolvability (the ability to generate adaptive genetic diversity and evolve through natural selection; sensu Kirschner & Gerhart, 1998) likely also promote PLE.

Indeed, many aspects of developmental systems allow for the flexible accommodation of disruptive stimuli (e.g., environmental stress or new mutation) and can even facilitate and bias the production of novel (and in some cases heritable and/or adaptive) phenotypic variation (Badyaev, 2005; Snell-Rood, Kobiela, Sikkink, & Shephard, 2018). A key feature of these processes is an ability to reduce constraints among other developmental

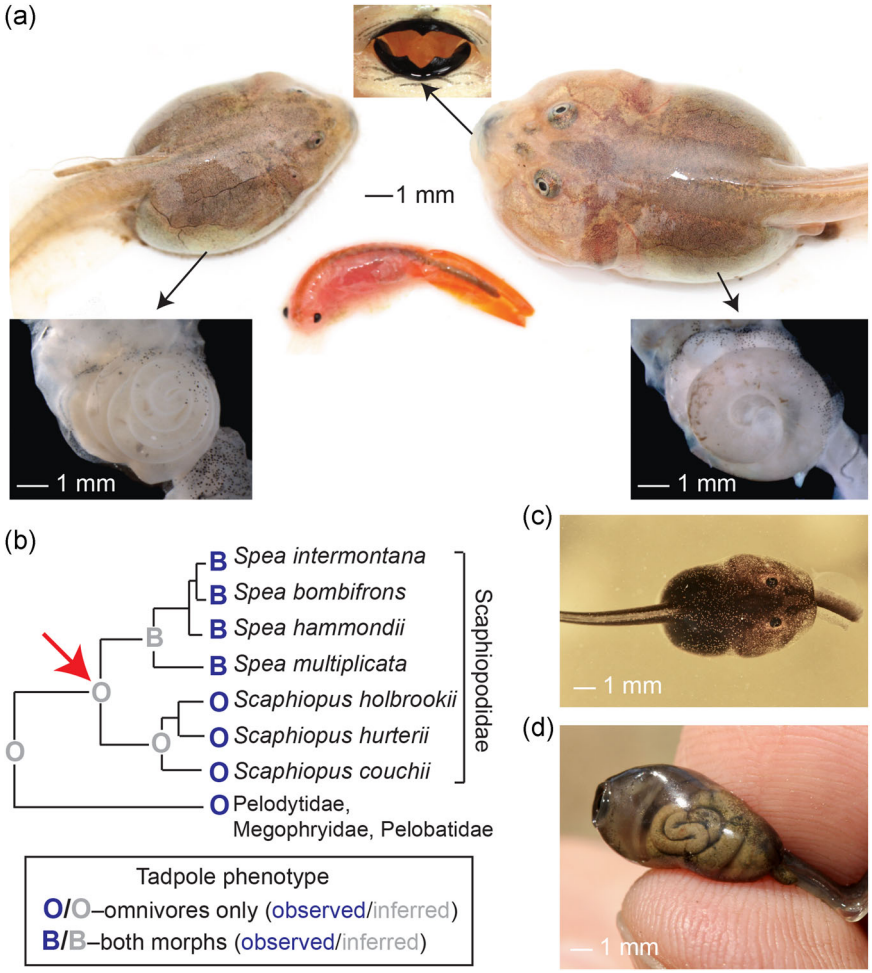

FIGURE 1 An example of a novel, complex phenotype that appears to have evolved via plasticity-led evolution. (a) Spadefoot toads (genus *Spea*) have evolved a unique polyphenism among their tadpoles. Normally, *Spea* tadpoles develop into an "omnivore" morph (left), but if they eat large animal prey, such as shrimp (middle), they produce a distinctive "carnivore" morph (right), which is characterized by large jaw muscles, notched mouthparts (upper inset) and a short gut (lower inset). (b) In contrast to *Spea*, most frogs produce omnivores only, and it is therefore likely that the ancestor of Scaphiopodidae also did so. To study the evolutionary origin of the carnivore morph, Levis et al. (2018) used an omnivore-only producer, *Sc. holbrookii*, as a proxy for the last common ancestor of *Scaphiopus* and *Spea* (red arrow). (c) When *Sc. holbrookii* tadpoles were fed large animal prey, the tadpoles of this species exhibited diet-induced plasticity—in gene expression and (d) in morphology (i.e., they produced a shorter gut)—suggesting that the ancestors of *Spea* likely possessed pre-existing plasticity in these features as well. Levis et al. (2018) hypothesized that when an ancestral population began consuming fairy shrimp and other tadpoles, this novel diet uncovered selectable variation in morphology and gene expression. Because some of this variation was adaptive (e.g., producing a shorter gut is adaptive when consuming a protein-rich diet), selection presumably favored further refinement of the carnivore morph. As a footnote to this story, many animals produce a short gut when they eat meat. Thus, a pre-existing developmental bias might have also played a role in the evolution of the distinctive carnivore morph [Color figure can be viewed at wileyonlinelibrary.com]

mechanisms and permit exploration or acquisition of alternative developmental and phenotypic states. Major categories of conserved developmental processes that promote such "deconstraint"—and that can thereby foster PLE—include: (1) flexible regulation; (2) modularity; and (3) exploratory mechanisms (for a detailed explanation of how these categories contribute to evolvability, see Gerhart & Kirschner, 1997; Kirschner & Gerhart, 1998). Below, we speculate on how each of these three developmental features might impact and possibly even bias PLE.

2.1 | Flexible regulation

Flexible regulation is widespread in developmental systems and likely important for PLE. As an example of flexible regulation, consider that many signaling molecules and signal transducers can modify, inhibit, or promote (i.e., regulate) activities performed by other molecules, and that these regulatory molecules typically have numerous targets (Aharoni et al., 2005; Gordon & Nusse, 2006; Payne & Wagner, 2019; Payne, Moore, & Wagner, 2014). This diversity of targets is important because it can both

reduce the number of mutational steps required to evolve new regulatory connections (Abouheif & Wray, 2002; Ehrenreich & Pfennig, 2016; Kirschner & Gerhart, 1998; Pfennig & Ehrenreich, 2014) and provide numerous opportunities for the environment to influence development.

Flexible versatile regulation might be relevant to both major stages of PLE by (1) generating a viable phenotypic variant in the face of environmental perturbation, and (2) allowing this phenotypic variant to undergo subsequent adaptive refinement. Regarding this first step, the number and diversity of connections that can be rewired to generate new phenotypic outcomes is often large and therefore offers ample opportunities for environmentally contingent changes to occur. For example, the diversity and abundance of trans regulatory variants (e.g., transcription factors, environmental sensors, noncoding RNAs, co-activating proteins, etc.) is large (Albert & Kruglyak, 2015; Yvert et al., 2003) and is often orders of magnitude larger than that of *cis* regulatory variants (Denver et al., 2005; Gruber, Vogel, Kalay, & WIttkopp, 2012; Landry, Lemos, Rifkin, Dickinson, & Hartl, 2007). This large mutational target space may increase the likelihood of a trait becoming decoupled from its environmental cue and/or experiencing various other modifications to its expression (Ehrenreich & Pfennig, 2016). Of course, most traits are governed by numerous genetic variants (Mackay, Stone, & Ayroles, 2009), and these variants often show nonadditive effects because of their network structure (Ehrenreich & Pfennig, 2016; Gjuvsland, Hayes, Omholt, & Carlborg, 2007; Nuzhdin, Friesen, & McIntyre, 2012; Omholt, Plahte, Oyehaug, & Xiang, 2000), which provide additional targets for changes to gene-by-environment (or gene-by-gene) interactions. When we also consider additional molecular processes, such as posttranslational regulation of proteins or changes in protein–protein interactions, then the target space for changes in environmental sensitivity and developmental trajectory becomes even greater. However, such flexible regulation can bias developmental and phenotypic possibilities insofar as any new developmental variants that arise are critically dependent on, and must be integrated with, existing variation, pathways, and networks (Payne & Wagner, 2019; Payne et al., 2014; Uller et al., 2018).

Flexible regulation is also relevant to the second step of PLE. Specifically, during the adaptive refinement phase of PLE, flexible versatile regulation can reduce the mutational steps needed to stabilize and refine a novel phenotypic variant. Such a reduction could, in turn, increase the likelihood and rate of genetic accommodation and/or genetic assimilation (Ehrenreich & Pfennig, 2016). Regulatory variants (such as those mentioned above) that cause signaling activity in conditionally active pathways, even in the absence of their inductive cues, could lead to genetic assimilation. One example of such an environmentally insensitive variant has been described in strains of *Saccharomyces cerevisiae* that possess an allele of *GPA1*, a component of the mating pheromone responsive mitogen activated protein kinase (MAPK) pathway. This variant shows high activity, even in the absence of the mating pheromone (Yvert et al., 2003). Similarly, a derived allele at the *ptch1* locus in Lake Malawi cichlids has contributed to reduced environmental sensitivity (i.e., reduced plasticity) in jaw functionality (Parsons et al., 2016). Finally, numerous studies have identified reductions in gene expression plasticity (Corl et al., 2018; Levis, Isdaner, & Pfennig, 2018; Levis, Serrato-Capuchina, & Pfennig, 2017; Scoville & Pfrender, 2010) or shifts in thresholds of induction in derived populations compared to ancestral ones (Moczek & Nijhout, 2003; Moczek, Hunt, Emlen, & Simmons, 2002; Sikkink, Reynolds, Ituarte, Cresko, & Phillips, 2014; Suzuki & Nijhout, 2006). Thus, changes in gene regulation are a common, if not required, route to genetic assimilation (we say "not required," because changes in gene regulation might alternatively be underlain by epigenetic changes, leading to "epigenetic assimilation"; sensu Pfennig & Pfennig, 2012).

2.2 | Modularity

Modularity refers to the correlation among various genetic, developmental, and/or functional components. Such a correlation determines the ease with which these components can be separated and recombined, thereby determining flexibility (Watson & Pollack, 2005; West-Eberhard, 2003). By permitting the semi-independent regulation and evolution of different developmental processes, modularity can reduce constraints (Kirschner & Gerhart, 1998; Montes-Cartas et al., 2017; West-Eberhard, 2003). Moreover, modularity can reduce pleiotropy caused by a new mutation or environmental input and thereby permit greater levels of genetic and phenotypic variation to arise (Wagner, 1996; West-Eberhard, 2003). Modularity can therefore play an important role in PLE.

Modularity is related to the concept of developmental switches. In particular, development can be viewed as a branching series of decision points ("switches"; John & Miklos, 1988; Raff, 1996; West-Eberhard, 2003), where each switch marks the expression or use of a trait (i.e., a modular set). Subordinate switches would mark lower level modules. Thus, this branching series of decision points creates a modular hierarchy of development. Because inputs from the environment can influence where, when, and how branching patterns develop

(potentially by altering regulatory interactions; see above), modular development helps make PLE possible by facilitating the production of new variation (Abouheif & Wray, 2002; Bento, Ogawa, & Sommer, 2010; Moczek, 2010; Moczek et al., 2011).

In addition to helping produce new developmental variants by rewiring modules, modularity may also be important during the adaptive refinement phase—especially toward canalization—of PLE. Once a new phenotypic variant arises in a population, modularity can allow the form and regulation of each variant to evolve and be refined by selection without necessarily affecting the refinement of other variants (Levis & Pfennig, 2019c; Moczek et al., 2011; Snell-Rood, Van Dyken, Cruickshank, Wade, & Moczek, 2010; West-Eberhard, 2003). Such semi-independent refinement could allow a population to undergo continuous adaptation to a variety of environments relatively simultaneously.

Modularity can impact PLE when relaxed selection and bias in accumulation of nonspecific modifiers lead to the fixation of a previously environmentally induced phenotypic variant. Specifically, when one phenotypic variant is expressed and exposed to selection, modules associated with the alternative variants are not expressed and exposed to selection (Van Dyken & Wade, 2010). These alternative variants may then be subject to relaxed selection and thereby accumulate variation that could reduce their phenotypic effects and functionality (e.g., Lahti et al., 2009; Masel, King, & Maughan, 2007; Moczek et al., 2011; Snell-Rood et al., 2010; Van Dyken & Wade, 2010). Such deterioration may inhibit alternative states from being produced altogether and result in phenotypic canalization (Levis & Pfennig, 2019a). This same process could also foster the accumulation of genetic variation that, under different environmental conditions, could restart the PLE sequence (Hunt et al., 2011; Levis & Pfennig, 2016; Moczek, 2007; Moczek et al., 2011). Even if PLE is not restarted, the above observations point to variation in the frequency of expression of alternative, plastically induced modules biasing what phenotypes are available to development and evolution.

A similar route through which modularity (more precisely, imperfect modularity) might contribute to canalization during PLE is if selection is acting on loci that show antagonistic pleiotropy among environmentally induced phenotypic variants. If such pleiotropy exists, then selection should favor regulatory changes (e.g., mutations) that modify and improve the most frequently expressed variant (Slatkin, 1979; West-Eberhard, 2003), even if this is at the detriment to other such variants. This bias in modifier accumulation should drive a pattern of frequency-dependent adaptation (Levis & Pfennig, 2019c), such that the more often a phenotype is produced, the greater its magnitude of adaptive refinement (Levis & Pfennig, 2016; West-Eberhard, 2003). In contrast to the first route above, in which relaxed selection passively erodes alternative variants, in this second route, selection favors mutations that improve a specific phenotypic variant, actively erodes alternative variants, and may thereby bias available phenotypic variation for future generations.

Although either passive or active erosion could produce a pattern of canalization (Levis & Pfennig, 2019a), active erosion is closer to West-Eberhard's (2003) original concept of genetic accommodation. This is because active erosion of alternative phenotypes involves selection favoring regulatory changes to a particular variant, and it may ultimately bring different developmental modules under common control (i.e., improve their integration; Cheverud, 1996). In addition, both active and passive erosion likely occur simultaneously, but active erosion may be a more important driver of canalization since loss of plasticity through passive forces could take a prohibitively long time (Masel et al., 2007). Regardless of the mechanism, when fixation of a single alternative phenotype occurs, it is expected to be accompanied by accelerated evolution of the fixed trait (Schneider & Meyer, 2017; Susoy, Ragsdale, Kanzaki, & Sommer, 2015; West-Eberhard, 2003). Thus, any factors (e.g., abundances of alternative resources) that bias which of any number of alternative phenotypes gets fixed can have far-reaching implications for subsequent bouts of evolutionary change.

2.3 | Exploratory mechanisms

Exploratory mechanisms (or mechanisms of developmental selection) comprise the final category of features we will discuss. These mechanisms, which include, but are not limited to, cytoskeleton formation (Kirschner & Gerhart, 1998), neuron growth and development (Oppenheim, 1991), neuronal connections (Sanes & Lichtman, 1999), tissue architecture (Snell-Rood et al., 2018), vertebrate adaptive immunity (Kirschner & Gerhart, 1998), plant growth and foraging (Hutchings & de Kroon, 1994), habitat choice (Levins, 1968) and trial-and-error learning (West-Eberhard, 2003), can provide high sensitivity to local conditions and thereby might produce adaptive outcomes. In general, these processes constitute some form of environmental sampling and reinforcement such that certain aspects of the phenotype are reinforced during development in response to feedback from the environment (Frank, 1996; Hull, Langman, & Glenn, 2001; West-Eberhard, 2003). That is, these mechanisms often begin with extreme levels of variation that are subsequently

reduced and refined to only include those responses that afford the greatest benefit (Kirschner & Gerhart, 1998; West-Eberhard, 2003). Depending on the exact mechanism under investigation, the environment being sampled can be either internal or external to the organism.

These mechanisms are relevant to evolution because they often yield functional outcomes, and because they reduce the number of mutations necessary to generate new functional interactions or morphologies (discussed in Kirschner & Gerhart, 1998 and West-Eberhard, 2003). Unlike the processes described above whose capacity to bias developmental and phenotypic outcomes largely stems from their interdependence with existing developmental processes, biases produced by exploratory mechanisms may be more likely to result from variation among environments (broadly defined) encountered during development. That is, any biases in the rate of environmental encounter and/or intensity of signals received from alternative environments could bias which phenotypes develop and ultimately evolve (Snell-Rood et al., 2010; Whitlock, 1996).

Exploratory mechanisms are likely a powerful force during both PLE's initial stages (particularly when a new phenotypic variant is first accommodated by developmental processes) and final stages (when selection may favor genetic assimilation). Through the use of fine-grained local responses generated by subunits of the larger phenotype, exploratory mechanisms can yield organized developmental configurations that are well-suited to the current environment (Kirschner, 1992; Snell-Rood, 2012; Snell-Rood et al., 2018). In this way, exploratory mechanisms can produce appropriate phenotypes even under novel conditions (Lande, 2014). However, the high costs typically associated with such mechanisms may make the phenotypes they produce more prone to genetic assimilation (Scheiner, Barfield, & Holt, 2017; Snell-Rood et al., 2018).

Learned traits might have an especially high evolutionary potential. Such traits can both produce close phenotype-environment matching and result in recurrent expression of behavioral traits. This recurrence exposes behavior and associated morphology and physiology to context-specific selection, which can result in fine-tuned responses (Ravigné, Dieckmann, & Olivieri, 2009; West-Eberhard, 2003). The ability of learning to expose a complex suite of behavioral, morphological, and/or physiological traits to context-specific selection may make the transition of a phenotype from environmentally induced to genetically determined particularly likely (Price, Qvarnström, & Irwin, 2003). Moreover, because learning has the characteristics of an exploratory mechanism, responses that are learned in a new environment may be well-calibrated to that environment and require minimal adaptive refinement (i.e., they potentially could become adaptive more rapidly than other traits).

More generally, *behavior* has long been recognized as playing a key role during PLE (e.g., Baldwin, 1896; Bateson, 2004; Duckworth, 2009; Lister, 2014; Wcislo, 1989). Indeed, behavior is often described as "hyperplastic" because of the wide array of behavioral changes organisms can perform depending on environmental context (external or internal environment). Behavioral responses are most likely to influence PLE during the initial transition to a novel environment by facilitating the accommodation of any new environmental stresses or inputs (Badyaev, 2005; West-Eberhard, 2003). Moreover, behavior (or any exploratory mechanism) may also be important for reducing the amount of environmental variation an organism experiences and help drive specialization to a particular environment (i.e., genetic accommodation; Ravigne et al., 2009) and potentially even canalization (i.e., genetic assimilation; Scheiner, 2016). We discuss the special role of behavior in more detail below (see Section 3.1).

2.4 | The plasticity mechanisms continuum

The developmental mechanisms underlying plastic responses have been categorized as occurring along a continuum from "deterministic" (or "one shot") to "exploratory" (or "labile") (Lande, 2014, 2015; SnSnell-Rood et al., 2018; ell-Rood, 2012). The ends of this continuum consist of such phenomena as discrete polyphenisms on the deterministic side and trial-and-error learning on the exploratory side. Here, we discuss attributes of these extremes and how they might affect PLE (Table 1). An important conclusion to emerge from our discussion is that the extreme ends of this plasticity mechanisms continuum can either facilitate or impede PLE (reviewed in Table 1). The balance among these mechanisms likely determines which outcome occurs.

We begin by discussing how deterministic processes can facilitate PLE in at least two ways and impede PLE in at least one way. First, to understand how deterministic processes can facilitate PLE, recall from above that regulation of transcription and signal transduction of external stimuli often have both switch-like properties and modular network-like structure. Any changes at higher levels of the regulatory network can therefore have dramatic consequences for downstream components of the network (Uller et al., 2018). For these processes, DNA sequence variation might be particularly important for generating phenotypic variation (Figure 2). This is because gene expression is often dependent on the

TABLE 1 How extremes along the continuum of plasticity mechanisms might affect different aspects of plasticity-led evolution

Mechanism	Characteristic	Effect	Outcome
Deterministic	Relatively high dependence on DNA sequence variation	Facilitate	Genetic assimilation
Deterministic	Noninstructive signals and emphasis on switches	Facilitate	Large variation in fitness and/or opportunity for refinement and/or phenotype production
Deterministic	Relatively weak costs of phenotype production	Impede	Genetic assimilation
Exploratory	Relatively high costs of phenotype production	Facilitate	Genetic assimilation
Exploratory	High capacity for phenotypic accommodation	Facilitate	Survival in new environment and/or genetic assimilation
Exploratory	Relatively high phenotype-environment matching	Facilitate	Higher fitness and/or evolution of greater plasticity
Exploratory	Relatively high phenotype-environment matching	Facilitate	Accumulation of genetic variation
Exploratory	Relatively high rate of response to local conditions	Facilitate	Potential bias in phenotype production
Exploratory	Relatively high phenotype-environment matching	Impede	Genetic assimilation

presence or absence of particular *cis* regulatory sequences, and any changes to such sequences that disrupt transcription factor binding or otherwise modify expression levels can cause dramatic changes to the resulting phenotypes (Carroll, 2008; Ehrenreich & Pfennig, 2016; Prud'Homme et al., 2006; Wray, 2007). In addition to *cis* regulatory changes, alterations to the coding sequences controlling formation of binding and effector sites of signal transduction molecules or transcription factors (i.e., *trans* regulatory changes) could also result in dramatic changes to development and phenotype production (Ehrenreich & Pfennig, 2016). If any such genetic changes (*cis* or *trans*) can supplant environmentally sensitive processes that govern the same phenotype, then selection might favor genetic assimilation (i.e., loss of environmental induction and fixation of the phenotype; e.g., Ehrenreich & Pfennig, 2016; Fanti, Piacentini, Cappucci, Casale, & Pimpinelli, 2017; Parsons et al., 2016; Suzuki & Nijhout, 2006; Waddington, 1953). In this way, deterministic processes can facilitate some aspects of PLE.

There is a second way that deterministic processes can facilitate PLE. Because signals only activate or inactivate a switch without directly guiding its downstream activity or interactions (Kirschner & Gerhart, 1998), the phenotypic variants produced by deterministic (switch-like) processes under novel conditions may have greater variation in their fitness effects than exploratory mechanisms. That is, by chance, any variants produced may be adaptive, maladaptive, or selectively neutral in the new environment. This might be expected, at least in part, because switch-like plasticity (e.g., polyphenisms) would have presumably evolved in coordination with cues that predict particular environmental conditions (Moran, 1992; Sultan & Spencer, 2002). Moreover, whether such plasticity is adaptive in a new environment depends on whether that particular environment is novel relative to those environments in which the plasticity evolved (Snell-Rood et al., 2018). For example, if the environment undergoes an extreme shift or changes in a discrete way (e.g., introduction of new resource or anthropogenic toxin), ancestral switches may not be able to produce a well-adapted phenotype (Snell-Rood et al., 2018). Yet, such environmental changes might uncover previously cryptic genetic variation and thereby reveal a range of developmental and phenotypic variation (Badyaev, 2005; Ghalambor, McKay, Carroll, & Reznick, 2007; Ledón-Rettig, Pfennig, Chunco, & Dworkin, 2014; Schlichting, 2008). Natural selection works most effectively when there is abundant variation, and recent work suggests that even maladaptive plastic responses could potentiate rapid evolution and adaptation (Ghalambor et al., 2007, 2015; Huang & Agrawal, 2016). Thus, the relatively broad distribution of potential phenotypic outcomes following a change in the environment could facilitate genetic accommodation (and PLE).

Alternatively, the relatively low cost with which deterministic processes generate variation can actually impede genetic assimilation (Snell-Rood, 2012) and thereby preclude PLE. Consider that, compared to

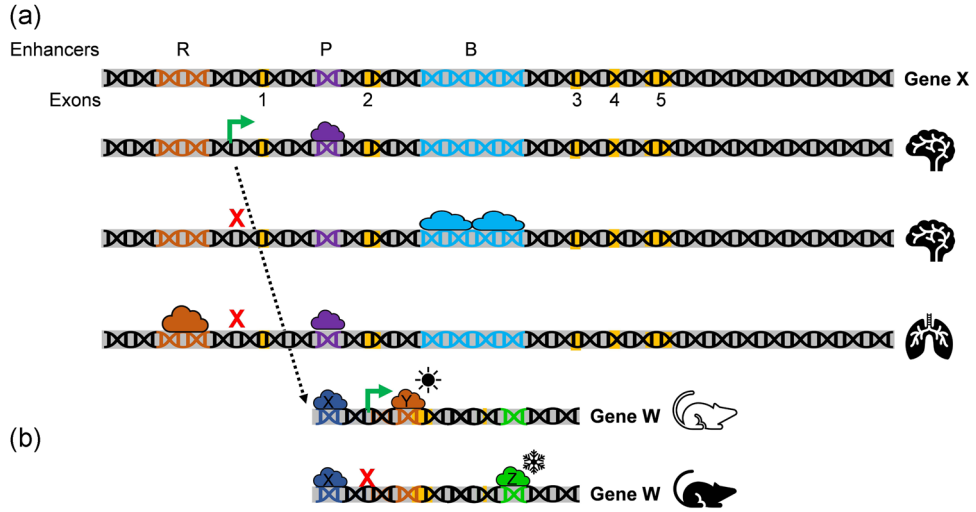

FIGURE 2 Deterministic processes and DNA sequence variation. (a) Gene X, which encodes a transcription factor, is expressed in the brain and in the lungs. Specific regions of DNA (enhancers; designated 'R', 'P', 'B') bind tissue-specific combinations of transcription factors (colored blobs) that promote (green arrow) or inhibit (red X) transcription of Gene X. (b) Since Gene X encodes a transcription factor, it helps govern expression of other genes in these tissues. In the brain, Gene X works with temperature-sensitive transcription factors Y (hot) or Z (cold) to regulate expression of Gene W. Expression of Gene W activates a developmental module leading to expression of a white phenotype, whereas lack of expression activates a module leading to expression of a black phenotype. In this simple example, any new mutations that affect the enhancer sequences of Genes W, X, Y, or Z, coding sequences of Genes W, X, Y, or Z, or the binding sites of transcription factors X, Y, or Z could cause heritable changes in the organism's ability to develop alternative phenotypes [Color figure can be viewed at wileyonlinelibrary.com]

exploratory mechanisms, deterministic processes generally require less time, energy, and resources to enact their effects (Kirschner & Gerhart, 1998; Snell-Rood, 2012; West-Eberhard, 2003). Yet, some theoretical models suggest that genetic assimilation will not occur unless plasticity is costly (Gomez-Mestre & Jovani, 2013; Scheiner et al., 2017). Thus, the lower costs of phenotype production associated with deterministic processes might ultimately impede genetic assimilation.

Exploratory mechanisms may facilitate PLE in at least three ways and impede some outcomes of PLE in at least one way. First, exploratory mechanisms typically require greater time, resources, and/or, energy to produce a phenotype than deterministic processes (i.e., they are more costly; Snell-Rood et al., 2018), and these greater costs might make genetic assimilation more likely for traits impacted by exploratory mechanisms (Lande, 2015; Snell-Rood, 2012). If an individual can produce the same phenotype with a deterministic process as with an exploratory mechanism—without wasting time, energy, and resources associated with the more-costly exploratory mechanism—then the deterministic process should be favored by selection. Furthermore, the relatively high costs of exploratory mechanisms may drive the selective loss of plasticity altogether (Scheiner et al., 2017; Snell-Rood, 2012). Second, the relatively tight phenotype-environment matching that can be attained through exploratory mechanisms can reduce the amount of environmental variation an organism experiences (e.g., via habitat choice). This, in turn, might favor the loss of plasticity and/or increased specialization toward that environment (i.e., genetic assimilation and/or accommodation; Ravigne et al., 2009; Scheiner, 2016). Moreover, exploratory mechanisms may be more likely to experience developmental bias than deterministic ones. Exploratory mechanisms continually attune phenotypic responses to prevailing environmental conditions rather than simply switch a process on or off without continual updating. Early rounds of sampling and phenotype updating during development might restrict which areas of phenotype space can be explored by later rounds of sampling during development. Finally, exploratory mechanisms such as plasticity in behavior and learning can shield genetic variation from selection and thereby allow genetic variation to accumulate and potentially be released if the environment changes (Lynch, 2010; Snell-Rood, Burger, Hutton, & Moczek, 2016). Thus, the relatively high costs, the ability to match prevailing environmental conditions, the continual sampling and updating during development, and the buffering capacity of exploratory mechanisms could allow exploratory mechanisms to drive, and potentially bias, parts of PLE.

Alternatively, exploratory mechanisms might impede genetic assimilation. Because these mechanisms often generate phenotypes that closely match current environmental conditions, they might generally shield populations from the effects of selection favoring genetic assimilation. Indeed, if the environment changes

frequently, selection might instead favor any exploratory mechanism—and the resulting enhanced plasticity—that enables phenotype-environment matching across diverse environments.

In sum, while PLE may be a general process by which adaptation and novelty arise, the diverse mechanisms governing developmental variation and responsiveness to external stimuli may yield different evolutionary outcomes. Thus, understanding the developmental basis of any given plastic response is essential for understanding its evolution.

Having examined the theoretical relationships among PLE and various developmental mechanisms, we now shift our attention to examining the empirical tests of PLE in light of the above theory.

3 | TRAITS AND TAXA USED TO STUDY PLE

As noted in the Introduction, recent reviews have confirmed that PLE likely plays an important role in the evolution of novelty and adaptation in both laboratory and natural systems. Here we ask: are some traits and taxa used more than others to test PLE theory? Answering this question is important, because it is essential to clarify whether empirical tests of PLE are following the theory. Our goal in this section is therefore to both highlight potential inconsistencies in which traits or taxa are used in the study of PLE and to identify potential study systems that may be useful for deeper explorations of development in the context of PLE.[1]

3.1 | Traits used in the study of PLE

We reviewed 150 papers that explored topics related to PLE (Figure 3; Table S1) and categorized the focal trait(s) as "morphological," "physiological," "behavioral," "life history," and/or "other." This approach yielded 202 traits. "Morphological" traits dominated the literature with 91 traits (45.1%). "Physiological," "behavioral," and "life history" traits occurred at similar levels (39, 34, and 32 traits, respectively; 19.3%, 16.8%, and 15.8%, respectively). There were few traits categorized as "other" (6 traits; 3.0%), and these were primarily performance-based traits

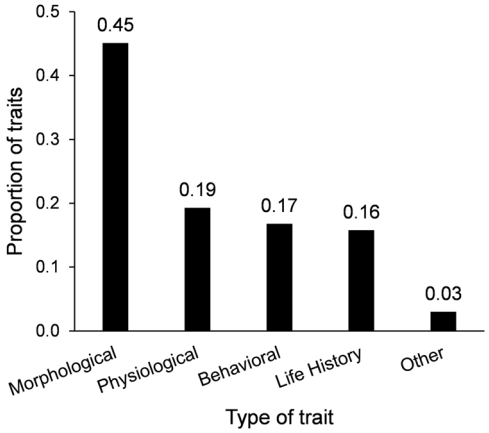

FIGURE 3 The proportion of various trait categories investigated by plasticity-led evolution studies. Values above each bar indicate the proportion of traits that fell in that category. Our exploration started with the list of studies provided by Schlichting and Wund (2014) and Levis and Pfennig (2016) and then surveyed the literature for more recent studies. To do so, we utilized Google Scholar to search for papers that were published after 2014 and included the key words "Baldwin effect," "genetic accommodation," "genetic assimilation," "phenotypic accommodation," "plasticity-first evolution," or "plasticity-led evolution." We then removed studies that explored the same trait(s) in the same system to minimize duplications. For each study, we categorized the focal trait(s) as "morphological," "physiological," "behavioral," "life history," and/or "other" (Table S1; note that although most traits have a physiological component, we categorized traits as "physiological" only if physiology was studied specifically). Occasionally, studies examined either multiple traits or a trait that did not clearly fall into only a single category. In these cases, we included all relevant categories

(e.g., biting force, locomotor performance, salinity tolerance), or measures of gene expression.

Most studies contained only a single trait category: 55 "morphological," 20 "physiological," 14 "behavioral," 12 "life history," and 3 "other." Of the 40 studies that contained two-trait categories (either two separate traits or a single trait composed of two categories), 11 studies did not contain a "morphological" trait, and 29 studies included "morphological" with one of the other four categories. Only five of the two-trait studies contained "behavioral" and "morphological" categories together. Finally, six studies had three-trait categories, and each of these studies contained both the "morphological" and "behavioral" categories.

The relative paucity of studies focusing on multiple traits is surprising, given that theory predicts that behavioral traits and complex traits may be particularly important during PLE (Lande, 2019; Price et al., 2003). For example, Price et al. (2003) proposed that moderate levels plasticity are most conducive to PLE. They further suggested that complex traits that include both a

[1]In our literature survey, we found that many terms have been used to describe PLE. For example, the "Baldwin effect" and "genetic assimilation" are both possible outcomes of genetic accommodation (the adaptive refinement step of PLE). Moreover, "plasticity-first evolution" is sometimes used synonymously with PLE. However, we do not use this phrase here, because it has caused confusion regarding the importance versus order of events during an evolutionary sequence. Although there are slight nuances among the above terms (e.g., Crispo, 2007), we consider them all under the umbrella of PLE for our purposes here.

behavioral component (which tends to be highly plastic) as well as either a morphological or physiological component (which tend to be less plastic) are most likely to constitute moderate levels of plasticity and to therefore undergo PLE. That most studies explored only a single trait category indicates that such complex traits (sensu Price et al., 2003) are not being explored at the rate that perhaps they should. However, we did find some evidence of empirical work aligning with these theoretical predictions: of the 46 studies that contained multiple trait categories, 43% contained a behavioral trait, and all three-trait category studies contained a behavioral and morphological trait. It is possible that the traits measured in these studies are "complex," but their constituent parts have not been identified or explored in detail.

More generally, the paucity of studies focusing on any behavioral traits (or complex traits with a behavioral component) is surprising. Indeed, behavioral traits have only been investigated roughly a third as often as morphological traits. Yet, many researchers have suggested that "exploratory plasticity" in general, and *behavioral* plasticity in particular, may be especially important in jump starting genetic evolution; i.e., PLE (e.g., Allf, Durst, & Pfennig, 2016; Baldwin, 1896; Bateson, 2004; Duckworth, 2009; Lister, 2014; Mayr, 1963; Price et al., 2003; Skúlason & Smith, 1995; Wcislo, 1989; West-Eberhard, 2003; Zuk, Bastiaans, Langkilde, & Swanger, 2014). Mayr (1963, p. 604), for example, wrote: "A shift into a new niche or adaptive zone is, almost without exception, initiated by a change in behavior. The other adaptations to the niche, particularly the structural ones, are acquired secondarily."

There are examples in which behavioral plasticity appears to have instigated morphological evolution. We highlight two such examples here. The first involves the evolution of eusociality in insects. Eusociality is a highly complex, derived trait that is characterized by overlapping adult generations, cooperative brood care, and a reproductive division of labor, which is often manifested as distinct behavioral categories or "castes" (Bourke, 2011). Recent studies have shown that rudimentary castes can be experimentally induced through forced association of typically nonassociating females, suggesting that ancestral behavioral plasticity for eusociality might have been present in solitary (or subsocial) forms (reviewed in Jones & Robinson, 2018).

A second example involves the evolution of the rattlesnake's rattle. The rattlesnake's rattle is one of nature's most spectacular signals, and it has evolved only once in rattlesnakes (Klauber, 1956). A recent study provided evidence suggesting that the rattle might have originated following the elaboration of a common form of behavioral plasticity in squamate reptiles: vibrating the tail when threatened (a). By reconstructing the ancestral state of defensive tail vibration, Allf et al. (2016) showed that this behavior is nearly ubiquitous in the Viperidae (the family that includes rattlesnakes) and widespread in the Colubridae (the largest snake family, nearly all of which are nonvenomous), suggesting a shared origin for the behavior between these families. After measuring tail vibration in dozens of species of Viperidae and Colubridae, they further showed that the more closely related a species was to rattlesnakes, the more similar it was to rattlesnakes in duration and rate of tail vibration. From these data, Allf et al. (2016) speculated that tail vibration by rattleless ancestors of rattlesnakes might have served as the signal precursor to rattlesnake rattling behavior. Moreover, they suggested that this environmentally induced behavior might have preceded—and even facilitated—the evolution of the rattle either by exposing existing morphological variants to novel selection pressures or following genetic assimilation of callus-type formation wrought by repeated tail vibration.

We hasten to add, however, that whether and how behaviors influence evolution—particularly, whether behavior often leads morphological evolution—remains the subject of intense debate (Duckworth, 2009). For example, many researchers have pointed out that, rather than facilitating morphological evolution, behavioral changes can also retard morphological evolution by hiding genetic variation from selection (Bogert, 1949; Huey, Hertz, & Sinervo, 2003; Losos, Schoener, & Spiller, 2004; Robinson & Dukas, 1999). Indeed, recall from above that Price et al. (2003) suggested that highly plastic traits alone, such as behavioral traits, tend to impede evolution. More generally, it is often hard to ascertain which type of traits—behavior, physiology, or morphology—truly evolved first and which evolved secondarily.

Despite our long discussion of the importance of behavior in PLE, we want to end this section by noting the important role that further study of morphology will play. Morphological changes in the context of PLE have been well-documented in many systems, possibly because morphology is generally easier to study than behavior. Thus, morphology may be the best candidate for initial forays into the developmental basis of PLE (e.g., Casasa & Moczek, 2018; Corl et al., 2018; Parsons et al., 2016; Scoville & Pfrender, 2010).

3.2 | Taxa used in the study of PLE

The study organism(s) in the 150 papers mentioned above were categorized as angiosperms, bacteria, invertebrates, prions, or vertebrates. If a study focused on multiple groups, each group was included. We then subdivided our categorization of vertebrates into

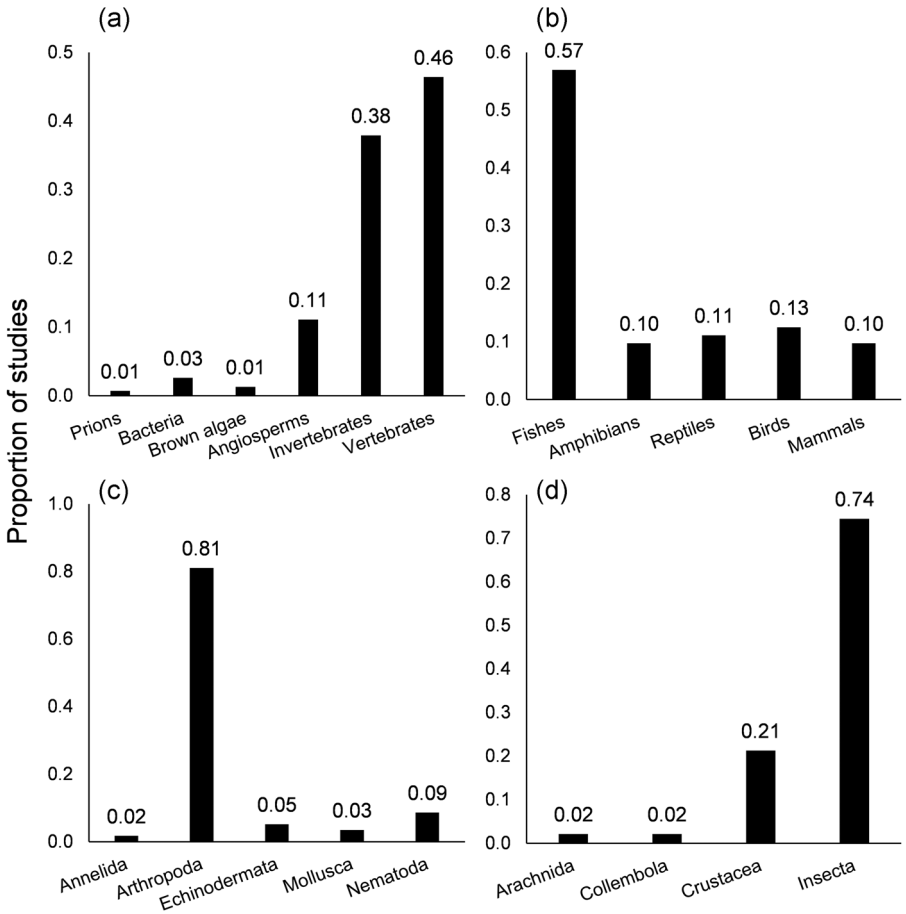

FIGURE 4 The taxonomic breadth at which plasticity-led evolution has been studied across (a) broad taxonomic groups; (b) vertebrates; (c) invertebrate phyla; and (d) arthropod classes. In all cases, values above each bar indicate the proportion of studies that fell in that category

amphibians, birds, fish, mammals, and nonavian reptiles. Likewise, we further sub-divided invertebrates into annelids, arthropods, echinoderms, mollusks, and nematodes. Because arthropods greatly outnumbered the other groups, we then divided this category further into arachnids, collembolans, crustaceans, and insects.

Although PLE has been studied at a wide taxonomic breadth, most studies focus on animals (Figure 4a), with vertebrates slightly outpacing invertebrates. Of the former (Figure 4b), fish were the most commonly used vertebrate. This focus on fish likely reflects their diversity and abundance (i.e., there are more species of fish than all other vertebrate groups; Reynolds, Dulvy, Goodwin, & Hutchings, 2005), the relative ease with which they can be studied in the laboratory, and their numerous adaptive radiations (e.g., Martin & Wainwright, 2011; Schluter, 1993; Seehausen, 2006). Furthermore, fish have well-developed genetic and genomic resources (e.g., Crawford & Oleksiak, 2016; Oleksiak, 2018; Valenzuela-Quinonez, 2016). These features make this group an obvious choice for investigating the significance of various developmental mechanisms during PLE (see Section 2). Perhaps even more powerfully, the fact that a diversity of traits (e.g., ecomorphology, parental care strategy, salinity tolerance, etc.) are often studied in a single species (e.g., three-spined stickleback; *Gasterosteus aculeatus*) means that new discoveries on development in one context (e.g., paternal care) may be directly compared to, or used to inform, developmental studies of the same organism in other contexts (e.g., salinity tolerance). Avoiding comparisons at high taxonomic levels (e.g., between species) should help uncover what is happening at the initial stages of PLE (Levis & Pfennig, 2016).

Not surprisingly, arthropods (especially, insects) are the most commonly studied invertebrates (Figure 4c,d), and, among insects, Diptera (10 studies) and Hymenoptera (6 studies) are the most commonly studied in PLE research. In the former, *Drosophila* spp. have been used to explore a variety of traits, and in the latter, various ants, bees, and wasps have been used to explore traits associated with castes and/or eusociality. The emphasis on *Drosophila* is unsurprising, given that they are used to study many evolutionary questions. What is surprising is the diversity of studies using Hymenoptera, where researchers have done a good job of breaking down the complexities of eusociality for evaluating PLE. As noted above, eusociality is a highly complex, derived trait that is characterized (in part) by the evolution of discrete castes, and recent work emphasizing inducibility of a caste system is consistent with a possible role of PLE in the

evolution of eusociality (Jones & Robinson, 2018). Both systems, will likely be among the most important for exploring the developmental underpinnings of PLE. In particular, the capacity for experimental evolution in *Drosophila* and its abundant genetic and genomic resources, make it a great candidate for studying various phases and the underlying mechanisms (especially the transition from plastic to nonplastic trait production) of PLE as it unfolds (e.g., Debat, Debelle, & Dworkin, 2009; Fanti et al., 2017; Wang & Althoff, 2019).

Overall, however, there is a strong preference toward the use of animals to study PLE, which could be preventing researchers from making even greater insights (Walbot, 1996). For example, plants offer excellent opportunities to investigate, among others, the consequences of late separation between the soma and germline, somatic selection, indeterminate body plans, niche construction, colonization of new habitats (e.g., invasions), and transgenerational plasticity (e.g., Bock, Kantar, Caseys, Matthey-Doret, & Rieseberg, 2018; Galloway & Etterson, 2007; Sultan, 2015; Walbot, 1996). Moreover, although behavior is expected to be important for PLE, what is considered behavior in plants may differ from what is considered behavior in animals (Silvertown & Gordon, 1989). For example, if exploration during shoot or canopy growth is considered a behavior, then plants may be a rich source for studying behavior-led evolution. Even if such exploration is not considered a behavior, this type of growth is still a form exploratory development and can have important implications for how development and PLE unfold (see Section 2). Moreover, the diversity of leaf forms within and among plants, and their inducibility, provides great opportunities to study plasticity-led evolution of morphology (Spriggs, Schmerler, Edwards, & Donoghue, 2018). Research on phenotypic plasticity in plants has a rich history (e.g., reviewed in Bradshaw, 1965; Schlichting, 1986; Sultan, 2015; Walbot, 1996), and additional focus on this taxonomic group should significantly enhance the PLE research program. More generally, research across a broader range of taxa will uncover whether the observed preference in research foci constitute actual variation in the taxa that experience PLE.

4 | SUGGESTIONS FOR FUTURE RESEARCH

Finally, we close with eight suggestions for future PLE research.

First, theoretical and empirical studies are needed to help identify the signature(s) of PLE to differentiate PLE from mutation-driven evolution (Kovaka, 2018). Finding a generalizable signature of PLE will likely prove difficult, however, because a trait that was initially generated by a new mutation might result in the same final product as one that begins as an environmentally induced phenotype (Levis & Pfennig, 2016). This difficulty arises because genetic and environmental inputs are often interchangeable during evolution (West-Eberhard, 2003). Getting around this difficulty will likely require sampling from multiple evolutionary (and potentially developmental) time points. In such a time series, samples during the early stages of an evolutionary sequence may be useful in distinguishing between PLE and mutation-driven evolution (Levis & Pfennig, 2019b). We speculate that a molecular signature of PLE will be similar to that for adaptation from standing genetic variation (Barrett & Schluter, 2008) and of conditional expression (Van Dyken & Wade, 2010), but may have additional features (e.g., concordance of timing between environmental change and increased genetic variation and/or conditional neutrality; Paaby & Rockman, 2014) that may help point toward PLE. These genetic tests would also require additional evidence that there was ancestral plasticity before fixation of a particular phenotype, and this evidence of ancestral plasticity might take many forms. For example, one could demonstrate greater environmental sensitivity of ancestral alleles compared to derived ones (e.g., Corl et al., 2018; Parsons et al., 2016) and/or use comparisons among outgroups or ancestors and descendants to evaluate divergence in environmental sensitivity in gene regulation or expression (e.g., Czypionka, Goedbloed, Steinfartz, & Nolte, 2018; Koch et al., 2017).

Second, additional theoretical and empirical studies are needed to clarify how different developmental processes and plasticity mechanisms influence PLE (e.g., see Table 1 and Section 2). These approaches should especially focus on how different developmental plasticity mechanisms (e.g., deterministic versus exploratory) influence the mode and tempo of PLE.

Third, future studies should assess whether particular traits or developmental processes are more or less interchangeable between genetic and environmental control than other such categories. Addressing this issue may help unravel the details of genetic assimilation and how environmental induction switches to constitutive production. Some studies have noted that changes in thresholds of responsiveness to external cues are important (e.g., Kulkarni, Denver, Gomez-Mestre, & Buchholz, 2017; Sikkink et al., 2014; Suzuki & Nijhout, 2006), and others have noted concomitant changes in gene expression (e.g., Levis et al., 2017; Schrader, Helanterä, & Oettler, 2017; Scoville & Pfrender, 2010). However, additional investigations that place

developmental processes such as hormonal regulation, epigenetic change, and gene expression in the context of gene regulatory networks (Pfennig & Ehrenreich, 2014) could elucidate the developmental changes that facilitate the transition from environmental induction to canalization (Debat & David, 2001; Debat et al., 2009).

Fourth, we need better information on development in a variety of ecologically relevant contexts (e.g., Abouheif et al., 2014; Gilbert & Epel, 2015; Gilbert, Bosch, & Ledón-Rettig, 2015; Sultan, 2015). While controlled laboratory studies have yielded much information about a myriad of developmental mechanisms, such work is incomplete. Some topics that should be explored include the type (e.g., random versus biased) and extent of variation produced by different developmental mechanisms and how effective different mechanisms are at accommodating novel inputs to development. Ideally, efforts to understand ecological development should be expanded to include non-model organisms in natural habitats.

Fifth, some authors have suggested that the adaptive evolution (more precisely, the process of natural selection) is like an active problem solver, seeking ingenious solutions to difficult environmental challenges (e.g., Kouvaris, Clune, Kounios, Brede, & Watson, 2017; Watson & Szathmary, 2016). If complex evolving systems are able to "learn" and generalize from past experiences and apply these learned rules to novel conditions, then it might be worth exploring if particular developmental mechanisms (switch-like vs. exploratory) and/or properties (modularity and flexible regulation) are more or less important for such generalization and application to novel environments.

Sixth, we need increased empirical work on complex traits—identifying their constituent parts, the plasticity of those parts, and how these parts evolve and shape the evolution of the complex trait itself. Like behavior, complex traits are expected to play an important role during PLE (see Section 3.1). The development and evolution of constituent traits and modules should be evaluated in a variety of ecological contexts separately from, and in addition to, the complex trait itself.

Seventh, despite theory implicating behavioral plasticity as being important in evolution, few studies have examined behavior in the context of PLE. More work is needed on behavior-led evolution and how behavioral changes may precipitate morphological and physiological change. In addition, a unified framework for studying behavioral plasticity in plants (and fungi and microorganisms) and animals would be useful. One difficulty is that many plant behaviors are focused on growth (Silvertown & Gordon, 1989) and could be described (as by us) as morphological or life history changes rather than true behaviors.

Finally, the taxonomic diversity of the PLE research program, while broad, could be improved (see Figure 4). In particular, fungi and microorganisms are underrepresented in PLE research (see Section 3.2). Research on these and other underrepresented taxa will likely generate new insights. For example, these groups could be used to study a potential role of plasticity in major evolutionary transitions (sensu Standen, Du, & Larsson, 2014) such as the evolution of multicellularity, origins of eukaryotes, and potentially the rise of metazoans. Such research will also help us determine if there is any real variation in the types of traits or organisms that experience PLE.

5 | CONCLUSIONS

Despite the growing evidence for PLE, further tests are needed. In general, the future of this study program hinges on more detailed investigations of developmental plasticity mechanisms; additional theoretical models illustrating the conditions that favor PLE; empirical work aimed at uncovering a developmental or genetic signature of PLE; and a broader taxonomic focus. By exploring these research avenues, we will have a better understanding of whether or not plasticity can, and actually does, "lead" evolution.

ACKNOWLEDGMENTS

We thank the organizers and participants of the "Developmental bias workshop" for providing the intellectual stimulus for this study, Armin Moczek for inviting us to participate in this special issue, and Emily Harmon, Andrew Isdaner, Patrick Kelly, and two anonymous referees for helpful comments.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

ORCID

Nicholas A. Levis http://orcid.org/0000-0001-7650-2371

REFERENCES

Abouheif, E., Favé, M.-J., Ibarrarán-Viniegra, A. S., Lesoway, M. P., Rafiqi, A. M., & Rajakumar, R. (2014). Eco-Evo-Devo: The time has come. In C. R. Landry, & N. Aubin-Horth (Eds.), *Ecological genomics: Ecology and the evolution of genes and genomes, advances in experimental medicine and biology* (pp. 107–125). Springer.

Abouheif, E., & Wray, G. A. (2002). Evolution of the gene network underlying wing polyphenism in ants. *Science*, *297*, 249–252.

Aharoni, A., Gaidukov, L., Khersonsky, O., Gould, S. M., Roodveldt, C., & Tawfik, D. S. (2005). The 'evolvability' of promiscuous protein functions. *Nature Genetics*, *37*, 73–76.

Albert, F. W., & Kruglyak, L. (2015). The role of regulatory variation in complex traits and disease. *Nature Reviews Genetics*, *16*, 197–212.

Allf, B. C., Durst, P. A. P., & Pfennig, D. W. (2016). Behavioral plasticity and the origins of novelty: The evolution of the rattlesnake rattle. *The American Naturalist*, *188*, 475–483.

Badyaev, A. V. (2005). Stress-induced variation in evolution: From behavioural plasticity to genetic assimilation. *Proceedings of the Royal Society B: Biological Sciences*, *272*, 877–886.

Baldwin, J. M. (1896). A new factor in evolution. *The American Naturalist*, *30*, 441–451.

Baldwin, J. M. (1902). *Development and evolution*. Oxford, UK: Macmillan Co.

Barrett, R., & Schluter, D. (2008). Adaptation from standing genetic variation. *Trends in Ecology & Evolution*, *23*, 38–44.

Bateson, P. (2004). The active role of behaviour in evolution. *Biology & Philosophy*, *19*, 283–298.

Bento, G., Ogawa, A., & Sommer, R. J. (2010). Co-option of the hormone-signalling module dafachronic acid-DAF-12 in nematode evolution. *Nature*, *466*, 494–497.

Bock, D. G., Kantar, M. B., Caseys, C., Matthey-Doret, R., & Rieseberg, L. H. (2018). Evolution of invasiveness by genetic accommodation. *Nature Ecology and Evolution* , *2*, 991–999.

Bogert, C. M. (1949). Thermoregulation in reptiles, a factor in evolution. *Evolution*, *3*, 195–211.

Bourke, A. F. G. (2011). *Principles of social evolution*. Oxford: Oxford University Press.

Bradshaw, A. D. (1965). Evolutionary significance of phenotypic plasticity in plants. *Advances in Genetics*, *13*, 115–155.

Braendle, C., & Flatt, T. (2006). A role for genetic accommodation in evolution? *BioEssays*, *28*, 868–873.

Carroll, S. B. (2008). Evo-devo and an expanding evolutionary synthesis: A genetic theory of morphological evolution. *Cell*, *134*, 25–36.

Casasa, S., & Moczek, A. P. (2018). Insulin signalling's role in mediating tissue-specific nutritional plasticity and robustness in the horn-polyphenic beetle *Onthophagus taurus*. *Proceedings of the Royal Society B: Biological Sciences*, *285*, 20181631.

Cheverud, J. M. (1996). Developmental integration and the evolution of pleiotropy. *American Zoologist*, *36*, 44–50.

Corl, A., Bi, K., Luke, C., Challa, A. S., Stern, A. J., Sinervo, B., & Nielsen, R. (2018). The genetic basis of adaptation following plastic changes in coloration in a novel environment. *Current Biology*, *28*, 2970–2977.

Crawford, D. L., & Oleksiak, M. F. (2016). Ecological population genomics in the marine environment. *Briefings in Functional Genomics*, *15*, 342–351.

Czypionka, T., Goedbloed, D. J., Steinfartz, S., & Nolte, A. W. (2018). Plasticity and evolutionary divergence in gene expression associated with alternative habitat use in larvae of the European Fire Salamander. *Molecular Ecology*, *27*, 2698–2713.

Debat, V., & David, P. (2001). Mapping phenotypes: Canalization, plasticity and developmental stability. *Trends in Ecology & Evolution*, *16*, 555–561.

Debat, V., Debelle, A., & Dworkin, I. (2009). Plasticity, canalization, and developmental stability of the Drosophila wing: Joint effects of mutations and developmental temperature. *Evolution*, *63*, 2864–2876.

Denver, D. R., Morris, K., Streelman, J. T., Kim, S. K., Lynch, M., & Thomas, W. K. (2005). The transcriptional consequences of mutation and natural selection in *Caenorhabditis elegans*. *Nature Genetics*, *37*, 544–548.

Duckworth, R. A. (2009). The role of behavior in evolution: A search for mechanism. *Evolutionary Ecology*, *23*, 513–531.

Ehrenreich, I. M., & Pfennig, D. W. (2016). Genetic assimilation: A review of its potential proximate causes and evolutionary consequences. *Annals of Botany*, *117*, 769–779.

Fanti, L., Piacentini, L., Cappucci, U., Casale, A. M., & Pimpinelli, S. (2017). Canalization by selection of de novo induced mutations. *Genetics*, *206*, 1995–2006.

Forsman, A. (2014). Rethinking phenotypic plasticity and its consequences for individuals, populations and species. *Heredity*, 1–9.

Frank, S. A. (1996). The design of natural and artificial adaptive systems. In M. R. Rose, & G. V. Lauder (Eds.), *Adaptation* (pp. 451–505). New York: Academic Press Inc.

Futuyma, D. J. (2015). Can modern evolutionary theory explain macroevolution? In E. Serrelli, & N. Gontier (Eds.), *Macroevolution: Explanation, interpretation and evidence* (pp. 29–85). New York: Springer.

Gabriela montes-Cartas, C., Padilla, P., Rosell, J. A., Domínguez, C. A., Fornoni, J., & Olson, M. E. (2017). Testing the hypothesis that biological modularity is shaped by adaptation: Xylem in the *Bursera simaruba* clade of tropical trees. *Evolution & Development*, *19*, 111–123.

Galloway, L. F., & Etterson, J. R. (2007). Transgenerational plasticity is adaptive in the wild. *Science*, *318*, 1134–1136.

Gerhart, J., & Kirschner, M. (1997). *Cells, embryos, and evolution: Toward a cellular and developmental understanding of phenotypic variation and evolutionary adaptability*. Malden, MA: Blackwell Science.

Ghalambor, C. K., Hoke, K. L., Ruell, E. W., Fischer, E. K., Reznick, D. N., & Hughes, K. a (2015). Non-adaptive plasticity potentiates rapid adaptive evolution of gene expression in nature. *Nature*, *525*, 372–375.

Ghalambor, C. K., McKay, J. K., Carroll, S. P., & Reznick, D. N. (2007). Adaptive versus non-adaptive phenotypic plasticity and the potential for contemporary adaptation in new environments. *Functional Ecology*, *21*, 394–407.

Gilbert, S. F., Bosch, T. C. G., & Ledón-Rettig, C. (2015). Eco-Evo-Devo: Developmental symbiosis and developmental plasticity as evolutionary agents. *Nature Reviews Genetics*, *16*, 611–622.

Gilbert, S. F., & Epel, D. (2015). Ecological developmental biology: Integrating epigenetics, *medicine, and evolution* (2nd ed.). Sunderland, MA: Sinauer.

Gjuvsland, A. B., Hayes, B. J., Omholt, S. W., & Carlborg, Ö. (2007). Statistical epistasis is a generic feature of gene regulatory networks. *Genetics*, *175*, 411–420.

Gomez-Mestre, I., & Jovani, R. (2013). A heuristic model on the role of plasticity in adaptive evolution: Plasticity increases adaptation, population viability and genetic variation. *Proceedings of the Royal Society B: Biological Sciences*, *280*, 20131869.

Gordon, M. D., & Nusse, R. (2006). Wnt signaling: Multiple pathways, multiple receptors, and multiple transcription factors. *Journal of Biological Chemistry*, *281*, 22429–22433.

Gruber, J. D., Vogel, K., Kalay, G., & WIttkopp, P. J. (2012). Contrasting properties of gene-specific regulatory, coding, and copy number mutations in *Saccharomyces cerevisiae*: Frequency, effects, and dominance. *PLOS Genetics*, *8*, e1002497.

Huang, Y., & Agrawal, A. F. (2016). Experimental evolution of gene expression and plasticity in alternative selective regimes. *PLOS Genetics*, *12*, 1–23.

Huey, R. B., Hertz, P. E., & Sinervo, B. (2003). Behavioral drive versus behavioral inertia in evolution: A null model approach. *American Naturalist*, *161*, 357–366.

Hull, D. L., Langman, R. E., & Glenn, S. S. (2001). A general account of selection: Biology, immunology, and behavior. *The Behavioral and Brain Sciences*, *24*, 511–573.

Hunt, B. G., Ometto, L., Wurm, Y., Shoemaker, D., Yi, S. V., Keller, L., & Goodisman, M. A. D. (2011). Relaxed selection is a precursor to the evolution of phenotypic plasticity. *Proceedings of the National Academy of Sciences*, *108*, 15936–15941.

Hutchings, M. J., & de Kroon, H. (1994). Foraging in plants—The role of morphological plasticity in resource acquisition. *Advances in Ecological Research*, *25*, 159–238.

John, B., & Miklos, G. (1988). *The eukaryote genome in development and evolution*. London: Allen and Unwin.

Jones, B. M., & Robinson, G. E. (2018). Genetic accommodation and the role of ancestral plasticity in the evolution of insect eusociality. *Journal of Experimental Biology*, *221*, jeb153163.

Kirschner, M., & Gerhart, J. (1998). Evolvability. *Proceedings of the National Academy of Sciences*, *95*, 8420–8427.

Kirschner, M. W. (1992). Evolution of the cell. In P. R. Grant, & H. S. Horn (Eds.), *Molds, molecules, and metazoa: Growing points in evolutionary biology* (pp. 99–126). Princeton, NJ: Princeton University Press.

Klauber, L. M. (1956). *Rattlesnakes*. Berkeley, CA: University of California Press.

Koch, R., Kupczok, A., Stucken, K., Ilhan, J., Hammerschmidt, K., & Dagan, T. (2017). Plasticity first: Molecular signatures of a complex morphological trait in filamentous cyanobacteria. *BMC Evolutionary Biology*, *17*, 209.

Kouvaris, K., Clune, J., Kounios, L., Brede, M., & Watson, R. A. (2017). How evolution learns to generalise: Using the principles of learning theory to understand the evolution of developmental organisation. *PLOS Computational Biology*, *13*, e1005358.

Kovaka, K. (2018). Underdetermination and evidence in the developmental plasticity debate. *The British Journal for the Philosophy of Science*, *70*(1), 127–152.

Kulkarni, S. S., Denver, R. J., Gomez-Mestre, I., & Buchholz, D. R. (2017). Genetic accommodation via modified endocrine signalling explains phenotypic divergence among spadefoot toad species. *Nature Communications*, *8*, 993.

Lahti, D. C., Johnson, N. A., Ajie, B. C., Otto, S. P., Hendry, A. P., Blumstein, D. T., ... Foster, S. A. (2009). Relaxed selection in the wild. *Trends in Ecology & Evolution*, *24*, 487–496.

Lande, R. (2014). Evolution of phenotypic plasticity and environmental tolerance of a labile quantitative character in a fluctuating environment. *Journal of Evolutionary Biology*, *27*, 866–875.

Lande, R. (2015). Evolution of phenotypic plasticity in colonizing species. *Molecular Ecology*, *24*, 2038–2045.

Lande, R. (2019). Developmental integration and evolution of labile plasticity in a complex quantitative character in a multiperiodic environment. *Proceedings of the National Academy of Sciences of the United States of America*, *116*, 11361–11369.

Landry, C. R., Lemos, B., Rifkin, S. A., Dickinson, W. J., & Hartl, D. L. (2007). Genetic properties influencing the evolvability of gene expression. *Science*, *317*, 118–121.

Ledón-Rettig, C. C., Pfennig, D. W., Chunco, A. J., & Dworkin, I. (2014). Cryptic genetic variation in natural populations: A predictive framework. *Integrative and Comparative Biology*, *54*, 783–793.

Levins, R. (1968). *Evolution in changing environments*. Princeton: Princeton University Press.

Levis, N. A., Isdaner, A. J., & Pfennig, D. W. (2018). Morphological novelty emerges from pre-existing phenotypic plasticity. *Nat Ecol Evol*, *2*, 1289–1297.

Levis, N. A., & Pfennig, D. W. (2016). Evaluating 'plasticity-first' evolution in nature: Key criteria and empirical approaches. *Trends in Ecology & Evolution*, *31*, 563–574.

Levis, N. A., & Pfennig, D. W. (2019a). How stabilizing selection and nongenetic inheritance combine to shape the evolution of phenotypic plasticity. *Journal of Evolutionary Biology*.

Levis, N. A., & Pfennig, D. W. (2019b). Phenotypic plasticity, canalization, and the origins of novelty: Evidence and mechanisms from amphibians. *Seminars in Cell & Developmental Biology*, *88*, 80–90.

Levis, N. A., & Pfennig, D. W. (2019c). Plasticity-led evolution: Evaluating the key prediction of frequency-dependent adaptation. *Proceedings of the Royal Society B: Biological Sciences*, *286*, 20182754.

Levis, N. A., Serrato-Capuchina, A., & Pfennig, D. W. (2017). Genetic accommodation in the wild: Evolution of gene expression plasticity during character displacement. *Journal of Evolutionary Biology*, *30*, 1712–1723.

Lister, A. M. (2014). Behavioural leads in evolution—Evidence from the fossil record: Behavioural Leads in the Fossil Record. *Biological Journal of the Linnean Society*, *112*, 315–331.

Losos, J. B., Schoener, T. W., & Spiller, D. A. (2004). Predator-induced behaviour shifts and natural selection in field-experimental lizard populations. *Nature*, *432*, 505–508.

Lynch, M. (2010). Rate, molecular spectrum, and consequences of human mutation. *Proceedings of the National Academy of Sciences*, *107*, 961–968.

Mackay, T. F. C., Stone, E. A., & Ayroles, J. F. (2009). The genetics of quantitative traits: Challenges and prospects. *Nature Reviews Genetics*, *10*, 565–577.

Martin, C. H., & Wainwright, P. C. (2011). Trophic novelty is linked to exceptional rates of morphological diversification in two adaptive radiations of Cyprinodon pupfish. *Evolution*, *65*, 2197–2212.

Masel, J., King, O. D., & Maughan, H. (2007). The loss of adaptive plasticity during long periods of environmental stasis. *The American Naturalist*, *169*, 38–46.

Mayr, E. (1963). *Animal species and evolution*. Cambridge, MA: Harvard University Press.

Michener, C. D. (1961). Social polymorphism in Hymenoptera. *Symposium of the Royal Entomological Society of London*, *1*, 43–56.

Moczek, A. P. (2007). Developmental capacitance, genetic accommodation, and adaptive evolution. *Evolution & Development*, *9*, 299–305.

Moczek, A. P. (2010). Phenotypic plasticity and diversity in insects. *Philosophical Transactions of the Royal Society, B: Biological Sciences*, *365*, 593–603.

Moczek, A. P., Hunt, J., Emlen, D. J., & Simmons, L. W. (2002). Threshold evolution in exotic populations of a polyphenic beetle. *Evolutionary Ecology Research*, *4*, 252–264.

Moczek, A. P., & Nijhout, H. F. (2003). Rapid evolution of a polyphenic threshold. *Evolution and Development*, *5*, 259–268.

Moczek, A. P., Sultan, S., Foster, S., Ledón-Rettig, C., Dworkin, I., Nijhout, H. F., … Pfennig, D. W. (2011). The role of developmental plasticity in evolutionary innovation. *Proceedings of the Royal Society B: Biological Sciences*, *278*, 2705–2713.

Moran, N. A. (1992). The evolutionary maintenance of alternative phenotypes. *The American Naturalist*, *139*, 971–989.

Morgan, C. L. (1896). On modification and variation. *Science*, *4*, 733–740.

Nijhout, H. F. (2003). Development and evolution of adaptive polyphenisms. *Evolution & Development*, *5*, 9–18.

Nuzhdin, S. V., Friesen, M. L., & McIntyre, L. M. (2012). Genotype-phenotype mapping in a post-GWAS world. *Trends in Genetics*, *28*, 421–426.

Oleksiak, M. F. (2018). Adaptation without boundaries: Population genomics in marine systems. In O. Rajora (Ed.), *Population genomics: Concepts, approaches, and applications* (pp. 587–612). Springer.

Omholt, S. W., Plahte, E., Oyehaug, L., & Xiang, K. (2000). Gene regulatory networks generating the phenomena of additivity, dominance, and epistasis. *Genetics*, *155*, 969–980.

Oppenheim, R. W. (1991). Cell death during development of the nervous system. *Annual Review of Neuroscience*, *14*, 453–501.

Orr, H. A. (1999). Evolutionary biology: An evolutionary dead end? *Science*, *285*, 343–344.

Osborn, H. F. (1896). Oytogenic and phylogenic variation. *Science*, *4*, 786–789.

Paaby, A. B., & Rockman, M. V. (2014). Cryptic genetic variation: Evolution's hidden substrate. *Nature Reviews Genetics*, *15*, 247–258.

Palmer, A. R. (2012). Developmental plasticity and the origin of novel forms: Unveiling cryptic genetic variation via"use and disuse": Developmental plasticity and novel forms. *Journal of Experimental Zoology Part B: Molecular and Developmental Evolution*, *318B*, 466–479.

Parsons, K. J., Concannon, M., Navon, D., Wang, J., Ea, I., Groveas, K., … Albertson, R. C. (2016). Foraging environment determines the genetic architecture and evolutionary potential of trophic morphology in cichlid fishes. *Molecular Ecology*, *25*, 6012–6023.

Payne, J. L., Moore, J. H., & Wagner, A. (2014). Robustness, evolvability, and the logic of genetic regulation. *Artificial Life*, *20*, 111–126.

Payne, J. L., & Wagner, A. (2019). The causes of evolvability and their evolution. *Nature Reviews Genetics*, *20*, 24–38.

Pfennig, D. W., & Ehrenreich, I. M. (2014). Towards a gene regulatory network perspective on phenotypic plasticity, genetic accommodation and genetic assimilation. *Molecular Ecology*, 1–3.

Pfennig, D. W., & Pfennig, K. S. (2012). *Evolution's wedge: Competition and the origins of diversity*. Berkeley, CA: University of California Press.

Price, T. D., Qvarnström, A., & Irwin, D. E. (2003). The role of phenotypic plasticity in driving genetic evolution. *Proceedings of the Royal Society of London. Series B: Biological Sciences*, *270*, 1433–1440.

Prud'Homme, B., Gompel, N., Rokas, A., Kassner, V. a, Williams, T. M., Yeh, S. D., … Carroll, S. B. (2006). Repeated morphological evolution through cis-regulatory changes in a pleiotropic gene. *Nature*, *440*, 1050–1053.

Raff, R. A. (1996). *The shape of life: Genes, development, and the evolution of animal form*. Chicago: University of Chicago Press.

Ravigné, V., Dieckmann, U., & Olivieri, I. (2009). Live where you thrive: Joint evolution of habitat choice and local adaptation facilitates specialization and promotes diversity. *The American Naturalist*, *174*, E141–E169.

Reynolds, J. D., Dulvy, N. K., Goodwin, N. B., & Hutchings, J. A. (2005). Biology of extinction risk in marine fishes. *Proceedings of the Royal Society B*, *272*, 2337–2344.

Robinson, B. W., & Dukas, R. (1999). The influence of phenotypic modifications on evolution: The Baldwin effect and modern perspectives. *Oikos*, *85*, 582–589.

Sanes, J. R., & Lichtman, J. W. (1999). Development of the vertebrate neuromuscular junction. *Annual Review of Neuroscience*, *22*, 389–442.

Sarkar, S. (2003). From the reaktionsnorm to the evolution of adaptive plasticity: A historical sketch, 1909–1999. In T. J. DeWitt, & S. M. Scheiner (Eds.), *Phenotypic plasticity: Functional and conceptual approaches*. Oxford: Oxford University Press.

Scheiner, S. M. (2016). Habitat choice and temporal variation alter the balance between adaptation by genetic differentiation, a jack-of-all-trades strategy, and phenotypic plasticity. *The American Naturalist*, *187*, 633–646.

Scheiner, S. M., Barfield, M., & Holt, R. D. (2017). The genetics of phenotypic plasticity. XV. Genetic assimilation, the Baldwin effect, and evolutionary rescue. *Ecology and Evolution*, *7*, 8788–8803.

Schlichting, C. D. (1986). The evolution of phenotypic plasticity in plants. *Annual Review of Ecology and Systematics*, *17*, 667–693.

Schlichting, C. D. (2008). Hidden reaction norms, cryptic genetic variation, and evolvability. *Annals of the New York Academy of Sciences*, *1133*, 187–203.

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

Schluter, D. (1993). Adaptive radiation in sticklebacks: Size, shape, and habitat use efficiency. *Ecology*, *74*, 699–709.

Schneider, R. F., & Meyer, A. (2017). How plasticity, genetic assimilation and cryptic genetic variation may contribute to adaptive radiations. *Molecular Ecology*, *26*, 330–350.

Schrader, L., Helanterä, H., & Oettler, J. (2017). Accelerated evolution of developmentally biased genes in the tetraphenic ant cardiocondyla obscurior. *Molecular Biology and Evolution*, *34*, 535–544.

Schwander, T., & Leimar, O. (2011). Genes as leaders and followers in evolution. *Trends in Ecology & Evolution*, *26*, 143–151.

Scoville, A. G., & Pfrender, M. E. (2010). Phenotypic plasticity facilitates recurrent rapid adaptation to introduced predators. *Proceedings of the National Academy of Sciences*, *107*, 4260–4263.

Seehausen, O. (2006). African cichlid fish: A model system in adaptive radiation research. *Proceedings of the Royal Society B: Biological Sciences*, *273*, 1987–1998.

Sikkink, K. L., Reynolds, R. M., Ituarte, C. M., Cresko, W. A., & Phillips, P. C. (2014). Rapid evolution of phenotypic plasticity and shifting thresholds of genetic assimilation in the nematode *Caenorhabditis remanei*. *G3: Genes, Genomes, Genetics*, *4*, 1103–1112.

Silvertown, J., & Gordon, D. M. (1989). A framework for plant behavior. *Annual Review of Ecology and Systematics*, *20*, 349–366.

Skúlason, S., & Smith, T. B. (1995). Resource polymorphisms in vertebrates. *Trends in Ecology & Evolution*, *10*, 366–370.

Slatkin, M. (1979). The evolutionary response to frequency- and density-dependent interactions. *The American Naturalist*, *114*, 384–398.

Snell-Rood, E. C. (2012). Selective processes in development: Implications for the costs and benefits of phenotypic plasticity. *Integrative and Comparative Biology*, *52*, 31–42.

Snell-Rood, E. C., Burger, M., Hutton, Q., & Moczek, A. P. (2016). Effects of parental care on the accumulation and release of cryptic genetic variation: Review of mechanisms and a case study of dung beetles. *Evolutionary Ecology*, *30*, 251–265.

Snell-Rood, E. C., Van Dyken, J. D., Cruickshank, T., Wade, M. J., & Moczek, A. P. (2010). Toward a population genetic framework of developmental evolution: The costs, limits, and consequences of phenotypic plasticity. *BioEssays*, *32*, 71–81.

Snell-Rood, E. C., Kobiela, M. E., Sikkink, K. L., & Shephard, A. M. (2018). Mechanisms of plastic rescue in novel environments. *Annual Review of Ecology, Evolution, and Systematics*, *49*, 331–354.

Spriggs, E. L., Schmerler, S. B., Edwards, E. J., & Donoghue, M. J. (2018). Leaf form evolution in viburnum parallels variation within individual plants. *The American Naturalist*, *191*, 235–249.

Standen, E. M., Du, T. Y., & Larsson, H. C. E. (2014). Developmental plasticity and the origin of tetrapods. *Nature*, *513*, 54–58.

Sultan, S. E. (2015). *Organisms and environment: Ecological development, niche construction, and adaptation*. Oxford, UK: Oxford University Press.

Sultan, S. E., & Spencer, H. G. (2002). Metapopulation structure favors plasticity over local adaptation. *The American Naturalist*, *160*, 271–283.

Susoy, V., Ragsdale, E. J., Kanzaki, N., & Sommer, R. J. (2015). Rapid diversification associated with a macroevolutionary pulse of developmental plasticity. *eLife*, *4*):e05463.

Suzuki, Y., & Nijhout, H. F. (2006). Evolution of a polyphenism by genetic accommodation. *Science*, *311*, 650–652.

Uller, T., Moczek, A. P., Watson, R. A., Brakefield, P. M., & Laland, K. N. (2018). Developmental bias and evolution: A regulatory network perspective. *Genetics*, *209*, 949–966.

Valenzuela-Quiñonez, F. (2016). How fisheries management can benefit from genomics? *Briefings in Functional Genomics*, *15*, 352–357.

Van Dyken, J. D., & Wade, M. J. (2010). The genetic signature of conditional expression. *Genetics*, *184*, 557–570.

Waddington, C. H. (1953). Genetic assimilation of an acquired character. *Evolution*, *7*, 118–126.

Wagner, G. P. (1996). Homologues, natural kinds and the evolution of modularity. *American Zoologist*, *36*, 36–43.

Walbot, V. (1996). Sources and consequences of phenotypic and genotypic plasticity in flowering plants. *Trends in Plant Science*, *1*, 27–32.

Wang, S. P., & Althoff, D. M. (2019). Phenotypic plasticity facilitates initial colonization of a novel environment. *Evolution*, *73*, 303–316.

Watson, R. A., & Pollack, J. B. (2005). Modular interdependency in complex dynamical systems. *Artificial Life*, *11*, 445–457.

Watson, R. A., & Szathmáry, E. (2016). How can evolution learn? *Trends in Ecology & Evolution*, *31*, 147–157.

Wcislo, W. T. (1989). Behavioral environments and evolutionary change. *Annual Review of Ecology and Systematics*, *20*, 137–169.

West-Eberhard, M. J. (1989). Phenotypic plasticity and the origins of diversity. *Annual Review of Ecology and Systematics*, *20*, 249–278.

West-Eberhard, M. J. (2003). *Developmental plasticity and evolution*. New York: Oxford University Press.

West-Eberhard, M. J. (2005). Phenotypic accommodation: Adaptive innovation due to developmental plasticity. *Journal of Experimental Zoology Part B: Molecular and Developmental Evolution*, *304B*, 610–618.

Whitlock, M. C. (1996). The red queen beats the jack-of-all-trades: The limitations on the evolution of phenotypic plasticity and niche breadth. *The American Naturalist*, *148*, S65–S77.

Wray, G. A. (2007). The evolutionary significance of cis-regulatory mutations. *Nature Reviews Genetics*, *8*, 206–216.

Wray, G. A., Hoekstra, H. E., Futuyma, D. J., Lenski, R. E., Mackay, T. F. C., Schluter, D., & Strassmann, J. E. (2014). Does evolutionary theory need a rethink? No, all is well *Nature*, *514*, 161–164.

Yvert, G., Brem, R. B., Whittle, J., Akey, J. M., Foss, E., Smith, E. N., … Kruglyak, L. (2003). Trans-acting regulatory variation in *Saccharomyces cerevisiae* and the role of transcription factors. *Nature Genetics*, *35*, 57–64.

Zuk, M., Bastiaans, E., Langkilde, T., & Swanger, E. (2014). The role of behaviour in the establishment of novel traits. *Animal Behaviour*, *92*, 333–344.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Levis NA, Pfennig DW. Plasticity-led evolution: A survey of developmental mechanisms and empirical tests. *Evolution & Development*. 2019;1–17.
https://doi.org/10.1111/ede.12309