Review

Genes as leaders and followers in evolution

Tanja Schwander[1,3] **and Olof Leimar**[2,3]

[1] Evolutionary Genetics, Centre for Ecological and Evolutionary Studies, University of Groningen, 9700 CC Groningen, The Netherlands
[2] Department of Zoology, Stockholm University, 10691 Stockholm, Sweden
[3] Wissenschaftskolleg zu Berlin, Wallotstrasse 19, 14193 Berlin, Germany

A major question for the study of phenotypic evolution is whether intra- and interspecific diversity originates directly from genetic variation, or instead, as plastic responses to environmental influences initially, followed later by genetic change. In species with discrete alternative phenotypes, evolutionary sequences can be inferred from transitions between environmental and genetic phenotype control, and from losses of phenotypic alternatives. From the available evidence, sequences appear equally probable to start with genetic polymorphism as with polyphenism, with a possible dominance of one or the other for specific trait types. We argue in this review that to evaluate the prevalence of each route, an investigation of both genetic and environmental cues for phenotype determination in several related rather than in isolated species is required.

Environmental and genetic cues for alternative phenotypes

Within virtually all species, individuals differ in behaviour, physiology, or form. These differences can be striking and discrete (e.g. male vs female) or subtle and continuous (e.g. ecotypic variation). Such phenotypic variation can stem from genetic differences between individuals (genetic polymorphism), from environment-dependent developmental plasticity (polyphenism), or some combination of the two. The existence of these different control systems for phenotype differentiation raises a fundamental question: which system precedes which evolutionarily? For instance, environmentally cued plasticity could dominate initially. Phenotypic variants might later become controlled genetically, as a consequence of selection on standing genetic variation or subsequent mutations in reaction norms [1–4]. Alternatively, variants could be genetically controlled from the start. They could later be fixed in different environments or the genetic cue for phenotype control might be replaced by an environmental one. We use the labels 'plasticity first' or 'genes as followers' [3,4] for evolutionary sequences where plasticity dominates initially and 'genetic polymorphism first' or 'genes as leaders' for sequences where genetic polymorphism is more important at the start. The prevalence of these alternative sequences has been a topic of interest and controversy in recent years [1–10]. In particular, the suggestion that 'plasticity first' sequences are more common than traditionally believed [1,3,11] has attracted much attention.

Here we use a phylogenetic perspective to assess the prevalence of the two kinds of sequences. We focus exclusively on discrete polymorphism and polyphenism, because their categorical nature greatly simplifies empirical study. Discrete alternative phenotypes occur for many traits, so a predominance of either 'plasticity first' or 'polymorphism first' sequences is unlikely to emerge simply as a consequence of constraints imposed by a specific developmental pathway or gene network.

We surveyed species groups traditionally used in the study of alternative phenotypes [3,12–14], including groups studied in the context of mimicry and other colour polymorphisms, dispersal phenotypes, resource polymorphisms, predator-induced phenotypes, alternative mating strategies, and sex determination. We identify examples where experimental studies allow us to classify the mode of phenotype control as predominantly genetic or environmental, and where established phylogenetic relations among species can be used to infer transitions between modes, or from alternative phenotypes to monomorphism (Box 1). In addition, we summarize available information on species groups for which a certain evolutionary path is probable but needs to be corroborated with additional evidence (Table S1 in the

Glossary

The terms defined here have been used historically with different meanings in various contexts (sometimes indicated in brackets after the definition), the indicated definitions refer to how they are used in the text.

Alternative phenotypes: phenotypic variation, independent of the underlying architecture (often used to refer to discrete as opposed to continuous variation).

Genetic assimilation: the classic genes-as-followers scenario where environmentally induced phenotypic variation becomes fixed by secondary genetic control.

Genetic polymorphism: genetically determined phenotypic variation (sometimes just referred to as polymorphism; often used to indicate any type of genotypic variation).

Monomorphism: a relatively uniform phenotype; note that except for discrete phenotypic variation, there is no clear-cut distinction between monomorphism and alternative phenotypes.

Polyphenism: environmentally-cued alternative phenotypes (sometimes limited to indicate discrete phenotypes).

Stochastic polyphenism: random environmental influences, either external or internal to an organism, serve as cues for development; characteristic of left–right asymmetries [11,48].

Corresponding authors: Schwander, T. (tanja.schwander@gmail.com); Leimar, O. (olof.leimar@zoologi.su.se)

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Box 1. Evolutionary transitions between modes of phenotype control

When following a lineage over time, modes of phenotype control can change repeatedly. For a given trait, genes could be followers or leaders depending on the time window considered. Figure I shows transitions between environmental and genetic control of alternative phenotypes, and between each of these and monomorphism. For transitions away from polyphenism, (F_1 and F_2 in Figure I), genes appear as followers in evolution. This is because environmental control of alternative phenotypes is either replaced by genetic control (F_1) or mutations appear that fix a subset of the initial phenotypes (F_2). Similarly, for transitions away from genetic polymorphism, genes appear as leaders because genetic control of alternative phenotypes is either replaced by environmental control (L_1) or there is fixation of one of the phenotypes (L_2).

The direction of a transition between polyphenism and genetic polymorphism could be inferred in clades of related species where alternative phenotypes are genetically controlled in some species and environmentally induced in others. Using ancestral state reconstruction methods [20] one can infer the modes of phenotype control for the extant species' ancestors and thus the transitions between them. Because of uncertainties associated with such reconstructions, an ideal scenario for diagnosing whether genes appear as leaders or followers would be a minority of species with one system embedded in a clade characterized by the alternative system. In any case, an inference requires available phylogenies and many experimental studies on phenotype determination.

Alternative phenotypes, either in the form of polyphenism or genetic polymorphism, can also emerge from a monomorphism (A_1 or A_2), after which one of the phenotypes might be fixed. In these transitions between monomorphisms, genes would be followers or leaders depending on whether the intermediate stage is polyphenism (A_1 followed by F_2) or genetic polymorphism (A_2 followed by L_2). Although the emergence of alternative phenotypes followed by a rapid return to monomorphism might be common, these events will be hard, or even impossible, to diagnose, depending on how long the polymorphism or polyphenism persists.

In addition to the modes of phenotype control depicted in Figure I, with evolutionary transitions between them, it is worth noting that there can be intermediate situations. For instance, environmental and genetic cues could jointly influence phenotypic variability over appreciable stretches of evolutionary time.

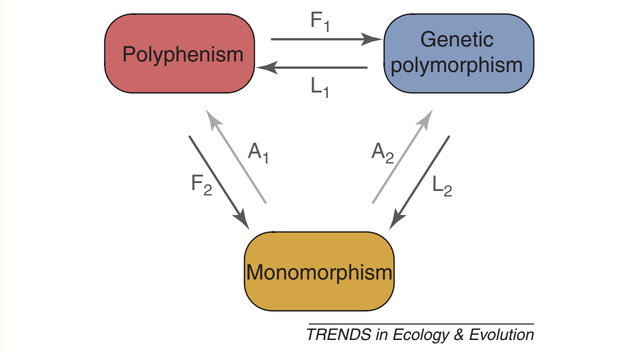

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Figure I. Transitions between environmental and genetic control of phenotypes.

supplementary material online). We illustrate the 'plasticity first' and 'genetic polymorphism first' routes and suggest factors influencing their likelihood. We also recommend research directions that can provide additional information about the relative roles of developmental plasticity and genetic polymorphism in generating and transforming variability.

Evolutionary transitions between modes of phenotype control

With gene–environment interchangeability, the same trait, and the same developmental cascade, can be controlled either by a genetic or an environmental cue [2,3,11,15,16]. Artificial selection experiments support interchangeability by showing that the same alternative phenotypes can represent either genetic differences or developmental plasticity, for instance for a wing-vein trait in *Drosophila melanogaster* [17,18] and for larval coloration in the tobacco hornworm *Manduca sexta* [19]. Interchangeability is sometimes used in arguments for the role of plasticity in evolution [3]. It also underpins the idea that there can be evolutionary transitions between genetic polymorphism and polyphenism (Box 1, Box 2). If there is information on the control mode of the same alternative phenotypes for several related species, it is possible to infer the direction of transitions between genetic and environmental phenotype control using standard phylogenetic methods [20], and so identify whether genes are followers or leaders in such transitions (Box 1).

Even if all species with alternative phenotypes in a clade have the same phenotype control system (either genetic or environmental), it is possible to discover whether genes are leaders or followers (Box 1). Genes would be followers if populations characterized by polyphenism give rise to populations expressing only some of the ancestral phenotypes, provided that genetic change is the reason for the phenotype loss. This corresponds to the process of 'genetic assimilation,' where an environmentally induced phenotype becomes fixed through secondary genetic change [3,21,22]. Conversely, genes would be leaders if populations with genetically controlled alternative phenotypes give rise to populations comprising only some of the ancestral phenotypes (Box 1, Box 2).

Transitions between genetic polymorphism and polyphenism

The best evidence for genes as leaders and followers in the evolution of alternative phenotypes comes from sex determination in tetrapods, alternative wing-morphs in insects, conspicuous left-right asymmetries, and social insect castes (Table S1 in the supplementary material online). In each of these systems, the phenotypic alternatives are present over long evolutionary time scales, and the selective forces maintaining them have attracted much interest. The mode of phenotype control has been studied most intensively for vertebrate sex determination. Phylogenetic analyses indicate that genetic sex determination is ancestral for all vertebrates and that environmental (generally temperature-dependent) sex determination repeatedly emerged from a genetic system [23]. Theoretical models show that selection often favours genetic systems, because they generate 50:50 sex ratios, but will favour environmental over genotypic sex determination if the developmental environment differentially influences male and female fitness [24,25]. At least six independent transitions from environmental to genetic sex determination have been reported in turtles and at least three transitions in the opposite direction in lizards [26]. A phylogenetic analysis in teleost fishes [27] also revealed substantial evolutionary lability of sex-determination modes, with numerous transitions

Box 2. Proximate mechanisms underlying shifts in phenotype control

Transitions between modes of phenotype control are mediated by proximate processes. In the simplest case, the same developmental cascades produce the alternative phenotypes, independent of the mode of phenotype control. Transitions can occur if elements of the cascades are modified in how they respond to environmental or genetic input, or if the inputs themselves change. Alternatively, transitions might occur through addition of new regulatory elements to established developmental programs. Such additions typically occur upstream of established programs [79].

From the perspective of developmental cascades, transitions from genetic polymorphism to monomorphism can simply be a loss of alleles required to cue a subset of the ancestral phenotypes. Transitions from polyphenism to monomorphism are instead changes in response thresholds, i.e. changes in the strength of environmental stimulus required to induce a phenotype. Populations of polyphenic species often harbour genetic variation in thresholds [1]. A transition to monomorphism occurs if thresholds shift outside the range of environmental cues [1,80,81]. Specifically, a transition could involve mutations that change the activity or expression level of an enzyme, such that the mutational effect exceeds or outweighs the one previously induced by environmental stimuli. Transitions could also occur through mutations that change hormone secretion or receptor sensitivity [82]. For instance, some mutants of the seasonally polyphenic butterfly *Precis coenia* express only one of the phenotypic alternatives, the *rosa* phenotype, because the mutant wing tissue is insensitive to the hormonal stimulus that otherwise would induce the alternative, *linea*, phenotype [83].

Transitions from polyphenism to genetic polymorphism are similar to transitions to monomorphism, in that the distribution of response thresholds in a population changes. The difference is that at least two thresholds remain in the population, positioned on each side of the range of environmental input. Apart from this, the proximate processes responsible for threshold shifts can be the same for either type of transition.

Finally, for transitions from genetic polymorphism to polyphenism, one genotype might become polyphenic and the other genotypes might be lost. To achieve polyphenism, processes at any of the steps of a developmental cascade might become sensitive to environmental stimuli. Temperature, for example, directly affects the activity of certain enzymes [36] and expression levels of genes [37]. Other environmental stimuli, especially photoperiod, can influence development by affecting hormone secretion via the central nervous system. Indeed, many alternative phenotypes are controlled by hormones whose secretion is regulated by the central nervous system [82].

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from genetic to environmental systems and possibly also transitions in the reverse direction ([27], but see [28]).

The relative ease of transitions between genetic and environmental sex determination is illustrated by sex reversal from exposure to extreme temperatures in species that normally have genetic sex determination [29,30], by the presence of sex-chromosomes in species with documented environmental sex determination [31], and by *Caenorhabditis elegans* nematode and housefly laboratory strains exhibiting novel genetic and temperature-dependent sex determination systems [32,33]. Furthermore, a rapid replacement of an environmental sex determination system by a genetic one has been demonstrated in experimental silverside populations (*Menidia menidia*) by exposing them to temperature conditions that generate extremely biased sex ratios [34]. The molecular changes underlying this transition have not been characterized.

The gonadal developmental pathways of vertebrates show extraordinary evolutionary conservatism [35], indicating that genetic and environmental sex determination share developmental cascades to a large extent. At several points along the developmental pathway, temperature might affect sex differentiation by altering the molecular processes involved, and this can mediate shifts between modes of phenotype control (Box 2). Temperature can directly affect the activity of enzymes involved in sex determination (as shown for an aromatase that transforms testosterone into estradiol [36]), as well as alter the expression level of genes. DMRT1 [37], for example, is a temperature-sensitive gene encoding a transcription factor required for the male differentiation cascade throughout the vertebrates [38]. Generally, in environmental sex determination, temperature seems to act on steroidogenic enzymes or steroid hormone receptors, altering the hormone environment of the developing embryo and thus shunting it into either the male or female pathway [36,39].

Unidirectional transitions from genetic to environmental determination of alternative phenotypes are well illustrated by wing dimorphism in insects, *viz.* the presence of winged and wingless (or short-winged) individuals in the same species. The two morphs represent dispersal alternatives, encompassing a suite of morphological, behavioural, physiological, and life history traits, such that the long-winged morph expresses a ‘migratory syndrome’ [40]. This dimorphism has independently evolved many times in insects and its maintenance is supposed to depend on spatial and temporal heterogeneity in the environment. Within a local patch, the wingless morph usually has a higher fitness than the winged morph, because trade-offs in resource allocation and genetic correlations result in a younger age at first reproduction and higher fecundity in the wingless compared to the winged morph [41,42]. Reduced wing development is therefore often favoured in the short term, whereas the winged morph can be favoured in the long term, given a certain risk of local patch extinction [41,42]. The wing morph can be cued genetically, sometimes with a simple architecture [42], indicating that a single mutation can be enough to generate a new wingless morph from a winged ancestor. In species where wing morph is cued environmentally, typical stimuli include temperature and photoperiod [43].

A transition from a single-locus wing polymorphism to a nutrition and temperature-dependent wing polyphenism has occurred in a group of carabid beetles (Figure 1). The developmental cascades underlying such transitions from genetic polymorphism to polyphenism (Box 2) could derive from polarized stress-response pathways, because wingless forms can often be induced artificially by different stress factors [44,45]. The pattern of wing polyphenism in the carabid beetle is consistent with this idea. Individuals with a long-winged genotype express the long-winged phenotype under favourable environmental conditions only, and differentiate into the wingless morph under low rearing temperatures and with restricted nutrition [46].

Possibly the clearest illustrations of unidirectional transitions from polyphenism to genetic polymorphism are found among conspicuous left–right asymmetries [11,47,48]. When asymmetries vary within populations, with right-handed and left-handed individuals about equally common, the direction of handedness is typically

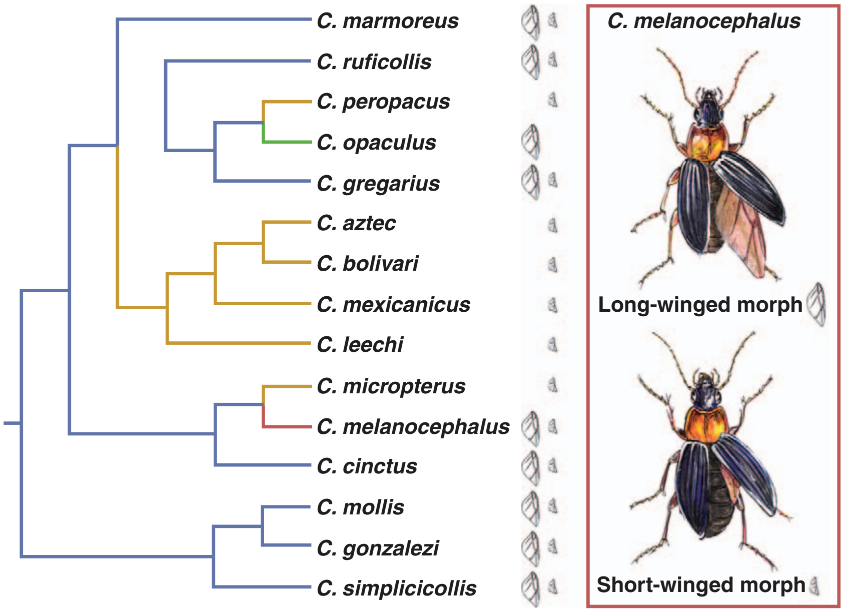

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Figure 1. Transitions from genetic polymorphism to polyphenism and monomorphism in carabid beetles. The phylogenetic distribution of winged and wingless species in the genus *Calathus* illustrates the pattern expected for a transition from genetic polymorphism (blue branches) to polyphenism (red). In the majority of species, wing morph is a genetic polymorphism. In cases where the detailed genetic architecture has been inferred by mating crosses, the phenotype is determined by a one-locus two-allele system, with short wings dominant [46,84,85]. In the species *Calathus melanocephalus*, however, long winged morph development further depends on temperature and food conditions, whereby individuals with a long wing genotype only develop the long wing phenotype under favourable environmental conditions. Thus, the genetic polymorphism has been modified into an environment-dependent expression of the phenotype, illustrating a probable first step in the transition to a fully polyphenic trait. Phylogeny simplified from [86] with morph-determination data added from [46,84,85,87]. Several transitions from a genetic polymorphism to monomorphism have also occurred in this group; the species in green has lost the short-winged morph, whereas species in yellow have lost the long-winged morph.

not inherited [11], indicating random phenotype determination [49]. The latter is sometimes recognized as a separate mode of phenotype control, but has also been referred to as stochastic polyphenism [49]. This is reasonable if random environmental influences, either external or internal to an organism, serve as cues for development. Such stochastic polyphenism is found among flowers in plants of the genus *Heteranthera* and the family Haemodoraceae, where styles can bend either to the left or right of the anther (Figure 2). In a small subset of species in each

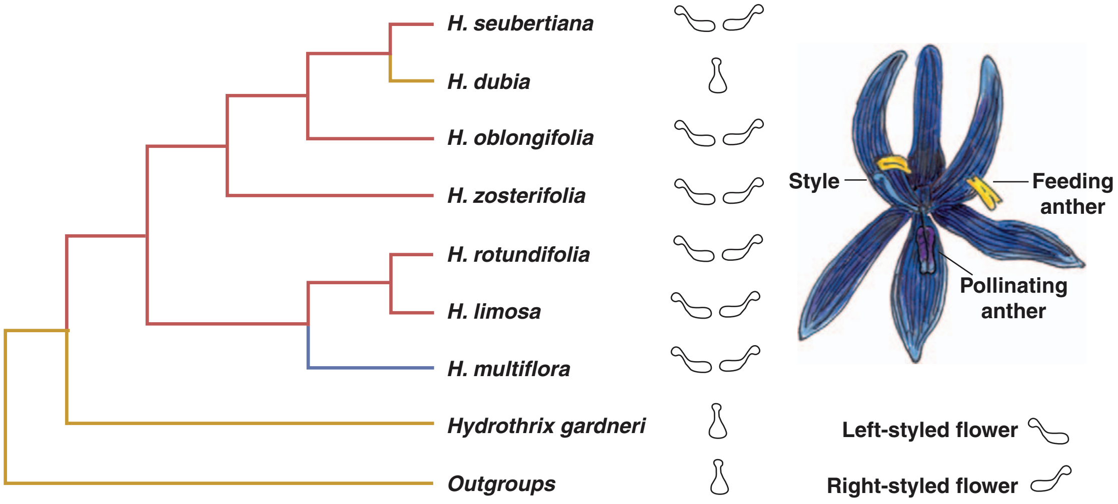

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Figure 2. Transitions from polyphenism to genetic polymorphism and monomorphism in *Heteranthera* plants. The phylogeny illustrates the transition from a stochastic polyphenism (red branches) to genetic polymorphism (blue; phylogeny adapted from [11,50,51]). In plants of the genus *Heteranthera*, flowers are asymmetrical with respect to the relative position of the anther and the style (see illustration). In the majority of species, each individual plant has both types of flowers, revealing that handedness is a stochastically polyphenic trait [11,50,51]. In the species *Heteranthera multiflora*, however, each individual plant has only one type of flower, and crossing experiments have shown that handedness is determined by a two-allele locus, with the right-styled allele dominant to the left-styled allele [88]. Thus, the stochastic polyphenism was probably secondarily replaced by a genetic polymorphism [11,50,51]. A transition to monomorphic straight-styled flowers has also occurred in the species *Heteranthera dubia* (yellow). Note that the available molecular phylogeny for *Heteranthera* includes only a small subset of the extant species and does not include *H. multiflora* [51], which was added as a sister group to the species pair *Heteranthera rotundifolia* and *Heteranthera limosa* as suggested by a morphology-based cladogram [89]. Given that, with the exception of *H. multiflora*, all *Heteranthera* species with asymmetric flowers display stochastic polyphenism; the exact position of *H. multiflora* within the *Heteranthera* clade is not important for the inference of the direction of the transition, as long as this species does not have a basal position in the clade.

group, the stochastic polyphenism was most likely secondarily replaced by genetic polymorphism [11,50,51], indicating a genes as followers route (Figure 2). This transition has been explained by selection against selfing, because selfing rates are lower in entirely left- or entirely right-styled plants than in those possessing both floral forms [52]. In *Heteranthera* species with stochastic polyphenism, individual plants have a mixture of left- and right-handed flowers, whereas with the genetic polymorphism, each individual has only one type of flowers. Similar to other conspicuous left-right asymmetry traits [11], the genetic cue is presumed to direct the positional information consistently to either the right or left side within the developing tissue [53] without otherwise affecting the developmental cascade.

Transitions from genetic polymorphism to monomorphism

In species with genetically determined alternative phenotypes, drift and habitat-specific selection, combined with low levels of gene flow among populations, often result in the local loss of one or several phenotypes. The probability of losing specific phenotypes by drift can also depend on the genetic architecture [54,55]. Many examples of phenotype loss occur in insects with genetically determined wing polymorphism and in taxa with colour morphs (Table S1 in the supplementary material online). The loss of colour morphs is nicely illustrated by female-limited polymorphism in damselflies of the genera *Ischnura* and *Enallagma* and throat colour morphs in males of side-blotched lizards. In these cases, polymorphism is ancestral and different morphs have been lost in different species or subspecies [56,57] (Figure 3). Morph losses probably correspond to a loss of alleles (Box 2), but it is also conceivable that mutant modifiers have repressed the expression of morphs [56]. Although the ultimate processes driving female morph losses in the damselflies remain controversial (Figure 3, [56,58]), at least one throat-colour morph in the lizard example is hypothesized to be disfavoured during colonization of new habitats [57]. The throat colour patterns of male side-blotched lizards signal different mating tactics; orange-throated males control large territories with many females, blue-throated males mate-guard females by cooperative territory defence, and yellow-throated males (female-mimics) sneak into other males' territories to obtain mates [59,60]. Although conditional changes between strategies can occur [61], these phenotypes are largely genetically determined [59,60]. In most populations the male mating types are maintained by negative frequency-dependent selection, with orange being most fit when blue is common, yellow being most fit when orange is common, and blue being most fit when yellow is common [59]. Phylogenetic reconstruction revealed that the polymorphism, in particular the yellow sneaker morph, was independently lost eight times, often in distinct subspecies [57].

Many more such losses must have occurred in transitions from genetically controlled wing polymorphism to monomorphism in insects [41,42], but the exact number of independent transitions cannot be inferred because the phylogenetic and experimental data are too scattered across orders (Table S1 in the supplementary material online). The transitions can result in fully wingless or fully winged species and subspecies. Four convincing examples of such polymorphism loss have occurred in the carabid beetle genus *Calathus* (Figure 1).

Transitions from polyphenism to monomorphism

Transitions from polyphenism to monomorphism provide the best examples for the role of plasticity in evolution [8]. Monomorphism can be adaptive if the maintenance of alternative phenotypes is costly and only some phenotypes are favoured in a given environment [14]. Alternatively, if environmental conditions are such that certain phenotypes are never expressed, these phenotypes might be lost as a consequence of drift [14,62].

Random conspicuous asymmetries provide many examples of transitions from polyphenism to monomorphism

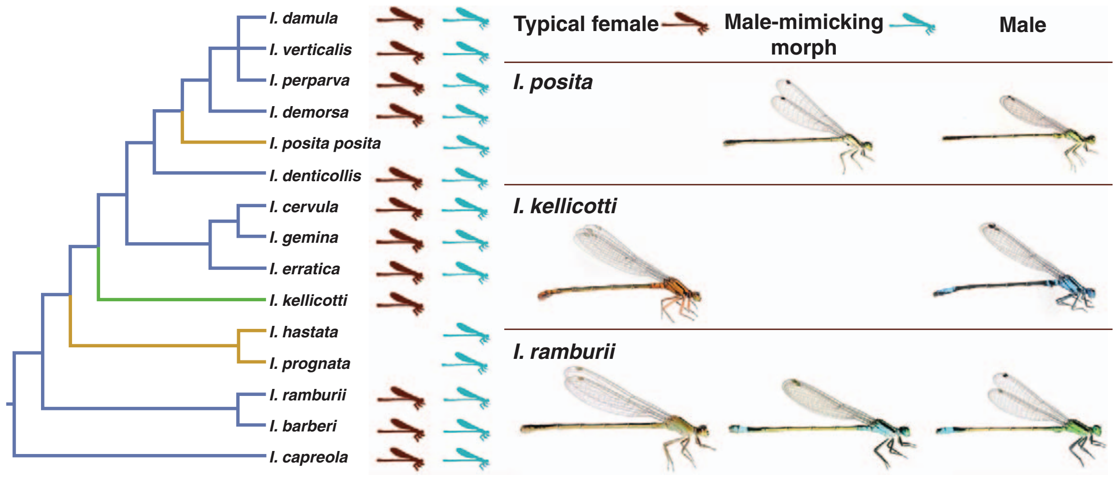

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Figure 3. Transitions from genetic polymorphism to monomorphism in damselflies of the genus *Ischnura*. Females in this genus have different genetically determined colour morphs, some of which are typical female morphs whereas others are male mimics [58,90]. The male mimics are supposed to reduce costs associated with harassment from males [58]. In different species, either the male-mimicking morph (green branches) or the typical female morphs (yellow) have been lost. The ultimate processes driving these morph losses remain poorly understood. Several mutually non-exclusive explanations are possible, including mate limitation because of low population densities, morph-specific predation risks or genetic drift [56]. Phylogeny simplified from [56], photographs courtesy of Gayle and Jeanell Strickland.

(see [11] for a detailed review). The relative ease with which such transitions occur suggests that canalization of developmental noise into a defined 'left' versus 'right' axis requires only minor molecular changes. The evolution of canalized switches can be illustrated by phallostethid fish [11]. The species in this group are characterized by the presence in males of a complex, bilaterally asymmetric copulatory organ ('priapium'), as well as other traits associated with internal fertilization [63]. Phylogenetic patterns suggest that the priapium asymmetry was random in the ancestor, and that four species independently evolved directional asymmetry with individuals either only right-sided or only left-sided. These species might thus represent up to four independent transitions from polyphenism to monomorphism [11], the uncertainty mainly stemming from some species being known from a small number of specimens only [64].

Transitions from polyphenism to monomorphism can also readily occur by a large shift in the threshold for switching between alternative phenotypes, such that the threshold is moved outside the variation range of the environmental input (Box 2). For example, tadpoles of *Spea* spadefoot toads can develop either into omnivorous or carnivorous morphs, depending on the amount of freshwater shrimp in their diet [65]. The tadpoles in some populations seem to have lost the sensitivity to the environmental cue, and thus the ability to differentiate into the carnivorous morph, possibly as a consequence of character displacement through interspecific competition [66]. Similarly, genetic variation in the tendency of *Aquarius remigis* water striders to develop short instead of long wings has resulted in the near fixation of the short-winged morph in some populations, and of the long-winged morph in others [67]. Habitat instability and the need for upstream migration are suggested to favour the long-winged morph over the more fecund short-winged morph.

Strong evidence for repeated losses of conditional alternative phenotypes is found for male mating strategies in *Cardiocondyla* ants and *Onthophagus* horned beetles. *Cardiocondyla* males gain access to females either by defending local harems or by dispersing. Coexistence of both strategies is ancestral for the genus. However, several species have lost the disperser morph (Figure 4), presumably because of very low post-dispersal mating chances. In horned beetles, alternative reproductive tactics are associated with the presence or absence of horns, and many species exhibit conditional horn expression [68]. Horn tissue differentiation starts during the prepupal stage, and the tissue can either be transient and resorbed during pupal development or give rise to horns of various shapes and sizes [69]. Horns appear to have originated only a few times, perhaps only once, during early *Onthophagus* evo-

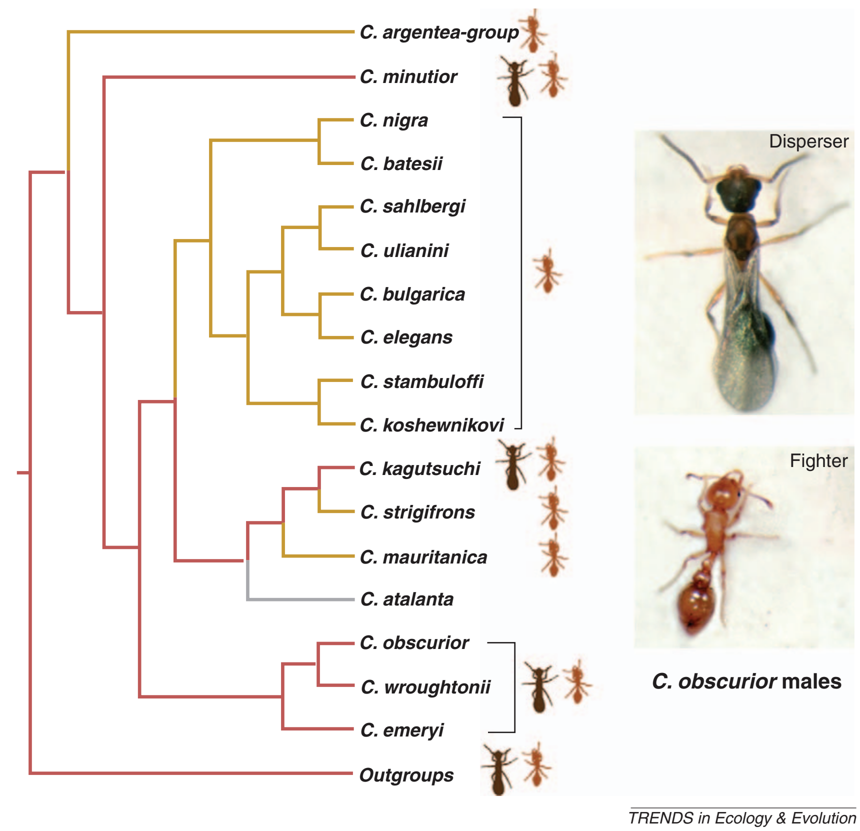

Figure 4. Transitions from polyphenism to monomorphism in *Cardiocondyla* ants. Males in several species in the genus *Cardiocondyla* have different mating strategies [91] associated with striking differences in morphology and physiology. The fighter morph has saber- or shear-shaped mandibles, small eyes, no wings, and continuous spermatogenesis. To monopolize the matings in their natal colonies, these males are aggressive and engage in lethal fighting with other males. By contrast, the disperser male morph has large eyes, wings, and a limited sperm supply. These males are docile and usually leave their natal nests a few days after eclosion to mate with females from other nests. Male morph development depends on environmental conditions: fighter males are reared year-round, whereas winged males are induced by sudden changes in temperature or colony fragmentation [92,93]. The presence of both male types (red branches) appears to be ancestral in the genus, and the disperser morph has been lost several times [94] (yellow). Male morphs for *Cardiocondyla atalanta* (grey) are not known. Phylogeny simplified from [94], pictures copyright Sylvia Cremer, University of Regensburg.

lution, but have been lost independently many times [69]. These losses have been explained by variation in the intensity of sexual selection and by the energetic costs associated with horn production [70].

Which factors favour 'genetic polymorphism first' versus 'plasticity first'?

Based on the case studies (Table S1 in the supplementary material online), the debate on genes as leaders and followers in the evolution of phenotypic variation cannot be resolved in favour of one route or the other. Transitions between genetic polymorphism and polyphenism are rare. However, there is ample evidence for species with alternative phenotypes generating populations, subspecies or derived species with only a subset of the ancestral phenotypes, and this process occurs as frequently via genetic polymorphism as via polyphenism, at least among the available examples.

Although we find no clear tendency for genes to be followers or leaders overall, trends appear in certain trait categories. Reciprocal transitions between genetic polymorphism and polyphenism have only been documented for sex determination; for the other systems, the thus far inferred transitions are unidirectional. Genes appear typically as leaders in colour polymorphisms, even though these traits can be associated with very different adaptations, including mimicry systems and alternative mating strategies (Table S1 in the supplementary material online). However, colour polymorphisms occurring with seasonality in butterflies are plastic traits [71]. We do not yet know whether such seasonal polyphenism frequently arose secondarily from genetic polymorphism because the environment-dependent regulation of the phenotypes was favoured over a genetic determination.

In contrast to colour polymorphisms, genes often appear as followers in conspicuous asymmetry traits [11,48]; a large proportion of the genetically determined asymmetries appear to have arisen from ancestors where the asymmetry direction was not inherited [11,50]. The reason might be that asymmetry traits entail a developmentally simple left-versus-right axis definition, which is independent of the function of the asymmetric trait [11,50]. In addition, asymmetric mating structures, which represent an abundant asymmetry trait category, often prevent individuals of opposite handedness from mating with each other, in which case within-population genetic polymorphism could not be maintained [72]. A notable exception occurs in some *Amphidromus* snails, where coexisting dextral and sinistral shell morphs are genetic polymorphisms rather than stochastic polyphenisms, and where matings are more successful between morphs than within [73,74].

An important explanation for the distribution of phenotype control systems is most likely that polyphenism and genetic polymorphism are beneficial under different conditions, so that the frequency and direction of transitions between them depends not only on how often either system emerges but also on how often one system is more beneficial than the other. Polyphenism should be favoured when a phenotype-determining environmental cue accurately predicts the selective condition for which the corresponding morph is suited [14,75], whereas genetic polymorphism should be favoured when such environmental cues are lacking and there is local frequency dependence or spatial variation in conditions, combined with limited gene flow [76,77]. Photoperiod and temperature as cues for seasonal polyphenism versus spatial variation in the frequency of different model species in genetically polymorphic mimicry nicely illustrate these alternatives [77].

Genetic and environmental cues for phenotype determination representing different adaptations might also explain the rarity of examples of transitions between polymorphism and polyphenism. Because a transition to the more advantageous system can completely replace the ancestral one, many ephemeral transitions might not be detected. The only cases where one can infer the direction of a transition might be those where both systems are roughly equally adaptive. Alternatively, transitions between polyphenism and polymorphism might simply not occur very often and both systems might evolve directly and independently.

To objectively quantify how much genetic polymorphism and polyphenism contribute to the generation and transformation of variation, one needs a representative sample, which is not available at present. Species groups that are currently sufficiently well studied to make inferences on transitions are not random selections of species with alternative phenotypes, but represent systems suited for specific research programs. In addition, the most often studied instances of alternative phenotypes have an adaptive background [14], whereas there are many examples of partly or wholly non-adaptive phenotypic variation [78]. An even greater uncertainty might lie in the potentially large number of transitions leading from one monomorphism to another, via evolutionarily short-lived genetic polymorphism or polyphenism (Box 1). Such ephemeral transitions are difficult to assess and it remains to be studied whether they are more likely to be associated with genetic or environmental phenotype control.

Even so, experimental investigation of the mode of phenotype control in additional species groups is feasible and could significantly increase knowledge about how much genetic polymorphism and polyphenism contribute to the generation and transformation of variation. Often the mode of phenotype control in a focal species is simply assumed to be representative of an entire clade, which precludes inferences on possible transitions between modes. Another potentially fruitful approach could be to identify intermediate steps in transitions from continuous to discrete variation. This might require studying clades related to species with alternative phenotypes, but in which species display continuous instead of discrete variation for the trait of interest. In general, more information on phenotype determination in groups of related species, together with comparative developmental and endocrinological data, could elucidate the relative importance of genes and plasticity in the generation of variation.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tree.2010.12.010.

References

1 Schlichting, C.D. and Pigliucci, M. (1998) *Phenotypic Evolution: A Reaction Norm Perspective*, Sinauer Associates
2 Nijhout, H.F. (1999) Control mechanisms of polyphenic development in insects. *Bioscience* 49, 181–192
3 West-Eberhard, M.J. (2003) *Developmental Plasticity and Evolution*, Oxford University Press
4 West-Eberhard, M.J. (2005) Developmental plasticity and the origin of species differences. *Proc. Natl. Acad. Sci. U.S.A.* 102, 6543–6549
5 Orr, H.A. (1999) An evolutionary dead end? *Science* 285, 343–344
6 de Jong, G. (2005) Evolution of phenotypic plasticity: patterns of plasticity and the emergence of ecotypes. *New Phytol.* 166, 101–118
7 de Jong, G. and Crozier, R.H. (2003) Developmental plasticity and evolution. *Nature* 424, 16–17
8 Pfennig, D.W. *et al.* (2010) Phenotypic plasticity's impacts on diversification and speciation. *Trends Ecol. Evol.* 25, 459–467
9 Lande, R. (2009) Adaptation to an extraordinary environment by evolution of phenotypic plasticity and genetic assimilation. *J. Evol. Biol.* 22, 1435–1446
10 Fusco, G. and Minelli, A. (2010) Phenotypic plasticity in development and evolution: facts and concepts. *Philos. Trans R. Soc. B* 365, 547–556
11 Palmer, A.R. (2004) Symmetry breaking and the evolution of development. *Science* 306, 828–833
12 Roff, D.A. (1996) The evolution of threshold traits in animals. *Q. Rev. Biol.* 71, 3–35
13 Whitman, D. and Ananthakrishnan, T.N. (2009) *Phenotypic Plasticity of Insects: Mechanisms and Consequences*, CRC Press
14 Moran, N.A. (1992) The evolutionary maintenance of alternative phenotypes. *Am. Nat.* 139, 971–989
15 Braendle, C. *et al.* (2005) Genetic variation for an aphid wing polyphenism is genetically linked to a naturally occurring wing polymorphism. *Proc. R. Soc. B* 272, 657–664
16 Evans, J.D. and Wheeler, D.E. (2001) Gene expression and the evolution of insect polyphenisms. *BioEssays* 23, 62–68
17 Scharloo, W. (1970) Stabilizing and disruptive selection on a mutant character in *Drosophila.* 2. Polymorphism caused by a genetical switch mechanism. *Genetics* 65, 681
18 Scharloo, W. (1970) Stabilizing and disruptive selection on a mutant character in *Drosophila*. 3. Polymorphism caused by a developmental switch mechanism. *Genetics* 65, 693
19 Suzuki, Y. and Nijhout, H.F. (2006) Evolution of a polyphenism by genetic accommodation. *Science* 311, 650–652
20 Harvey, P.H. and Pagel, M.D. (1991) *The Comparative Method in Evolutionary Biology*, Oxford University Press
21 Pigliucci, M. *et al.* (2006) Phenotypic plasticity and evolution by genetic assimilation. *J. Exp. Biol.* 209, 2362–2367
22 Price, T.D. *et al.* (2003) The role of phenotypic plasticity in driving genetic evolution. *Proc. R. Soc. B* 270, 1433–1440
23 Janzen, F.J. and Phillips, P.C. (2006) Exploring the evolution of environmental sex determination, especially in reptiles. *J. Evol. Biol.* 19, 1775–1784
24 Charnov, E.L. and Bull, J. (1977) When is sex environmentally determined? *Nature* 266, 829–830
25 Pen, I. *et al.* (2010) Climate-driven population divergence in sex-determining systems. *Nature* 468, 436–438
26 Pokorna, M. and Kratochvil, L. (2009) Phylogeny of sex-determining mechanisms in squamate reptiles: are sex chromosomes an evolutionary trap? *Zool. J. Linn. Soc.* 156, 168–183
27 Mank, J.E. *et al.* (2006) Evolution of alternative sex-determining mechanisms in teleost fishes. *Biol. J. Linn. Soc.* 87, 83–93
28 Ospina-Álvarez, N. and Piferrer, F. (2008) Temperature-dependent sex determination in fish revisited: prevalence, a single sex ratio response pattern, and possible effects of climate change. *PLOS ONE* 3, e2837
29 Quinn, A.E. *et al.* (2007) Temperature sex reversal implies sex gene dosage in a reptile. *Science* 316, 411
30 Radder, R.S. *et al.* (2008) Genetic evidence for co-occurrence of chromosomal and thermal sex-determining systems in a lizard. *Biol. Lett.* 4, 176–178
31 Shine, R. *et al.* (2002) Co-occurrence of multiple, supposedly incompatible modes of sex determination in a lizard population. *Ecol. Lett.* 5, 486–489
32 Hodgkin, J. (2002) Exploring the envelope: systematic alteration in the sex-determination system of the nematode *Caenorhabditis elegans*. *Genetics* 162, 767–780
33 Schmidt, R. *et al.* (1997) The Y-chromosomal and autosomal male-determining M factors of *Musca domestica* are equivalent. *Genetics* 147, 271–280
34 Conover, D.O. *et al.* (1992) Sex-ratio selection and the evolution of environmental sex determination in laboratory populations of *Menidia menidia*. *Evolution* 46, 1722–1730
35 Sarre, S.D. *et al.* (2004) The ends of a continuum: genetic and temperature-dependent sex determination in reptiles. *BioEssays* 26, 639–645
36 Lance, V.A. (2009) Is regulation of aromatase expression in reptiles the key to understanding temperature-dependent sex determination? *J. Exp. Zool. Part a: Ecol. Genet. Physiol.* 311A, 314–322
37 Hattori, R.S. *et al.* (2007) Temperature-dependent sex determination in Hd-rR medaka *Oryzias latipes*: gender sensitivity, thermal threshold, critical period, and DMRT1 expression profile. *Sex Dev.* 1, 138–146
38 Hodgkin, J. (2002) The remarkable ubiquity of DM domain factors as regulators of sexual phenotype: ancestry or aptitude? *Genes Dev.* 16, 2322–2326
39 D'Cotta, H. *et al.* (2001) Aromatase plays a key role during normal and temperature-induced sex differentiation of tilapia *Oreochromis niloticus*. *Mol. Reprod. Dev.* 59, 265–276
40 Dingle, H. (1985) Migration and life histories. In *Migration: Mechanisms and Adaptive Significance.* (Rankin, M.A., ed.), pp. 27–44, Contributions to Marine Science
41 Roff, D.A. (1994) The evolution of flightlessness - is history important? *Evol. Ecol.* 8, 639–657
42 Roff, D.A. and Fairbairn, D.J. (2007) The evolution and genetics of migration in insects. *Bioscience* 57, 155–164
43 Harrison, R.G. (1980) Dispersal polymorphisms in insects. *Annu. Rev. Ecol. Syst.* 11, 95–118
44 Zera, A.J. and Tanaka, S. (1996) The role of juvenile hormone and juvenile hormone esterase in wing morph determination in *Modicogryllus confirmatus*. *J. Insect. Physiol.* 42, 909–915
45 Lees, A.D. (1966) The control of polymorphism in aphids. *Adv. Insect. Physiol.* 3, 207–277
46 Aukema, B. (1990) Wing-length determination in 2 wing-dimorphic *Calathus* species (Coleoptera Carabidae). *Hereditas* 113, 189–202
47 Palmer, A.R. (1996) From symmetry to asymmetry: phylogenetic patterns of asymmetry variation in animals and their evolutionary significance. *Proc. Natl. Acad. Sci. U.S.A.* 93, 14279–14286
48 Palmer, A.R. (2009) Animal asymmetry. *Curr. Biol.* 19, R473–R477
49 Walker, T.J. (1986) Stochastic polyphenism – coping with uncertainty. *Fla. Entomol.* 69, 46–62
50 Levin, M. and Palmer, A.R. (2007) Left-right patterning from the inside out: widespread evidence for intracellular control. *BioEssays* 29, 271–287
51 Jesson, L.K. and Barrett, S.C.H. (2003) The comparative biology of mirror-image flowers. *Int. J. Plant. Sci.* 164, S237–S249
52 Jesson, L.K. and Barrett, S.C.H. (2002) Enantiostyly: solving the puzzle of mirror-image flowers. *Nature* 417, 707–707
53 Barrett, S.C.H. *et al.* (2000) The evolution and function of stylar polymorphisms in flowering plants. *Ann. Bot.* 85, 253–265
54 Pannell, J.R. *et al.* (2005) 'Haldane's Sieve' in a metapopulation: sifting through plant reproductive polymorphisms. *Trends Ecol. Evol.* 20, 374–379
55 Craze, P.G. (2009) The fate of balanced, phenotypic polymorphisms in fragmented metapopulations. *J. Evol. Biol.* 22, 1556–1561
56 Van Gossum, H. and Mattern, M.Y. (2008) A phylogenetic perspective on absence and presence of a sex-limited polymorphism. *Anim. Biol.* 58, 257–273
57 Corl, A. *et al.* (2010) Selective loss of polymorphic mating types is associated with rapid phenotypic evolution during morphic speciation. *Proc. Natl. Acad. Sci. U.S.A.* 107, 4254–4259

58 Fincke, O.M. *et al.* (2005) The evolution and frequency of female colour morphs in Holartic Odonata: why are male-like females typically the minority? *Int. J. Odonatol.* 8, 183–212
59 Sinervo, B. and Lively, C.M. (1996) The rock-paper-scissors game and the evolution of alternative male strategies. *Nature* 380, 240–243
60 Zamudio, K.R. and Sinervo, E. (2000) Polygyny, mate-guarding, and posthumous fertilization as alternative male mating strategies. *Proc. Natl. Acad. Sci. U.S.A.* 97, 14427–14432
61 Sinervo, B. *et al.* (2000) Testosterone, endurance, and darwinian fitness: natural and sexual selection on the physiological bases of alternative male behaviors in side-blotched lizards. *Horm. Behav.* 38, 222–233
62 Masel, J. *et al.* (2007) The loss of adaptive plasticity during long periods of environmental stasis. *Am. Nat.* 169, 38–46
63 Parenti, L.R. (1989) A phylogenetic revision of the phallostethid fishes (Atherinomorpha Phallostethidae). *Proc. Calif. Acad. Sci.* 46, 243–277
64 Parenti, L.R. (1996) Phylogenetic systematics and biogeography of phallostethid fishes (Atherinomorpha Phallostethidae) of northwestern Borneo, with description of a new species. *Copeia* 703–712
65 Pfennig, D.W. (1992) Proximate and functional causes of polyphenism in an anuran tadpole. *Funct. Ecol.* 6, 167–174
66 Pfennig, D.W. and Murphy, P.J. (2002) How fluctuating competition and phenotypic plasticity mediate species divergence. *Evolution* 56, 1217–1228
67 Fairbairn, D.J. and King, E. (2009) Why do Californian striders fly? *J. Evol. Biol.* 22, 36–49
68 Emlen, D.J. (2000) Integrating development with evolution: a case study with beetle horns. *Bioscience* 50, 403–418
69 Moczek, A.P. *et al.* (2006) When ontogeny reveals what phylogeny hides: gain and loss of horns during development and evolution of horned beetles. *Evolution* 60, 2329–2341
70 Emlen, D.J. *et al.* (2005) Diversity in the weapons of sexual selection: horn evolution in the beetle genus *Onthophagus* (Coleoptera: Scarabaeidae). *Evolution* 59, 1060–1084
71 Shapiro, A.M. (1976) Seasonal polyphenism. *Evol. Biol.* 9, 259–333
72 Huber, B.A. *et al.* (2007) The evolution of asymmetric genitalia in spiders and insects. *Biol. Rev.* 82, 647–698
73 Schilthuizen, M. *et al.* (2007) Sexual selection maintains whole-body chiral dimorphism in snails. *J. Evol. Biol.* 20, 1941–1949
74 Sutcharit, C. *et al.* (2007) Evolution of whole-body enantiomorphy in the tree snail genus *Amphidromus*. *J. Evol. Biol.* 20, 661–672
75 Sultan, S.E. and Spencer, H.G. (2002) Metapopulation structure favors plasticity over local adaptation. *Am. Nat.* 160, 271–283
76 Leimar, O. *et al.* (2006) A new perspective on developmental plasticity and the principles of adaptive morph determination. *Am. Nat.* 167, 367–376
77 Leimar, O. (2009) Environmental and genetic cues in the evolution of phenotypic polymorphism. *Evol. Ecol.* 23, 125–135
78 Ghalambor, C.K. *et al.* (2007) Adaptive versus non-adaptive phenotypic plasticity and the potential for contemporary adaptation in new environments. *Funct. Ecol.* 21, 394–407
79 Wilkins, A.S. (2002) *The Evolution of Developmental Pathways*, Sinauer Associates
80 Hazel, W.N. *et al.* (1990) A polygenic model for the evolution and maintenance of conditional strategies. *Proc. R. Soc. Lond. B* 242, 181–187
81 Roff, D.A. (1998) Evolution of threshold traits: the balance between directional selection, drift and mutation. *Heredity* 80, 25–32
82 Nijhout, H.F. (1994) *Insect Hormones*, Princeton University Press
83 Rountree, D.B. and Nijhout, H.F. (1995) Genetic-control of a seasonal morph in *Precis coenia* (Lepidoptera Nymphalidae). *J. Insect. Physiol.* 41, 1141–1145
84 Aukema, B. *et al.* (1986) Winglength determination in relation to dispersal by flight in two wing dimorphic species of *Calathus* Bonelli (Coleoptera, Carabidae), In *Carabid Beetles. Their Adaptations and Dynamics. 17th International Congress of Entomology*, Hamburg, 1984. pp. 91–99
85 Ball, G.E. and Negre, J. (1972) The taxonomy of the nearctic species of the genus *Calathus* Coleoptera Carabidae Agonini. *Trans Am. Entomol. Soc. (Phila)* 98, 413–533
86 Ruiz, C. (2010) Molecular phylogeny and Holarctic diversification of the subtribe Calathina (Coleoptera: Carabidae: Sphodrini). *Mol. Phylogenet. Evol.* 55, 358–371
87 Aukema, B. *et al.* (1996) Wing dimorphism and development in *Pterostichus melanarius* (Coleoptera: Carabidae). *Entomol. Ber. (Amst.)* 56, 93–100
88 Jesson, L.K. and Barrett, S.C.H. (2002) The genetics of mirror-image flowers. *Proc. R. Soc. Lond. B* 269, 1835–1839
89 Eckenwalder, J.E. and Barrett, S.C.H. (1986) Phylogenetic systematics of Pontederiaceae. *Syst. Bot.* 11, 373–391
90 Andres, J.A. and Cordero, A. (1999) The inheritance of female colour morphs in the damselfly *Ceriagrion tenellum* (Odonata Coenagrionidae). *Heredity* 82, 328–335
91 Seifert, B. (2003) The genus *Cardiocondyla* (Insects: Hymenoptera: Formicidae)—a taxonomic revision of the *C. elegans*, *C. bulgarica*, *C. batesii*, *C. shuckardi*, *C. stambuloyi*, *C. wroughtonii*, *C. emeryi*, and *C. minutior* species groups. *Ann. Naturhist. Mus. Wien* 104B, 203–338
92 Cremer, S. and Heinze, J. (2003) Stress grows wings: environmental induction of winged dispersal males in *Cardiocondyla* ants. *Curr. Biol.* 13, 219–223
93 Heinze, J. *et al.* (2004) Production of winged and wingless males in the ant, *Cardiocondyla minutior*. *Insectes Soc.* 51, 275–278
94 Heinze, J. *et al.* (2005) Evolution of male morphology in the ant genus *Cardiocondyla*. *Mol. Phylogenet. Evol.* 37, 278–288