Evolutionary Ecology, 1995, **9**, 154–168

Gene regulation, quantitative genetics and the evolution of reaction norms

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Summary

The ideas of phenotypic plasticity and of reaction norm are gaining prominence as important components of theories of phenotypic evolution. Our understanding of the role of phenotypic plasticity as an adaptation of organisms to variable environments will depend on (1) the form(s) of genetic and developmental control exerted on the shape of the reaction norm and (2) the nature of the constraints on the possible evolutionary trajectories in multiple environments. In this paper we identify two categories of genetic control of plasticity: allelic sensitivity and gene regulation. These correspond generally to two classes of response by the developmental system to environmental change: phenotypic modulation, in which plastic responses are a continuous and proportional function of environmental stimuli and developmental conversion, where responses tend to be not simply proportional to the stimuli. We propose that control of plasticity by regulatory actions has distinct advantages over simple allelic sensitivity: stability of phenotypic expression, capacity for anticipatory response and relaxation of constraints due to genetic correlations. We cite examples of the extensive molecular evidence for the existence of environmentally-cued gene regulation leading to developmental conversion. The results of quantitative genetic investigations on the genetics and evolution of plasticity, as well as the limits of current approaches are discussed. We suggest that evolution of reaction norms would be affected by the ecological context (i.e. spatial versus temporal variation, hard versus soft selection, and fine versus coarse environmental grain). We conclude by discussing some empirical approaches to address fundamental questions about plasticity evolution.

Keywords: phenotypic plasticity; gene regulation; allelic sensitivity; genetic correlation

Introduction

Although much of the effort exerted in the study of the evolutionary process has focused on empirical and theoretical systems under constant conditions, interest has increased in understanding the evolution of organisms faced with spatial and temporal heterogeneity. Schmalhausen (1949) proposed that the concept of the reaction norm should be the centrepiece for a more general theory of phenotypic evolution for organisms occupying such environments. The reaction norm of an individual genotype includes not only information on trait values in particular environments, but on the form of the plastic responses of the trait across environments as well. Schmalhausen (1949) clearly perceived the reaction norm itself as the focus of selection – genotypes and their environments are inextricably intertwined in the production of the phenotype (Waddington, 1961; Lewontin, 1974). Unfortunately, this view was not integrated into the modern synthesis that was then taking shape. Consequently, this synthesis did not put enough emphasis on ecological genetics in variable environments or on the genetic bases of developmental processes.

The increased interest in the idea of reaction norms (Bradshaw, 1965; Via and Lande, 1985; Schlichting, 1986; Sultan, 1987; West-Eberhard, 1989) has led to a debate focused on two major issues: (1) the genetic and developmental bases of phenotypic plasticity and (2) how reaction

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norms evolve (Scheiner, 1993; Schlichting and Pigliucci, 1993; Via, 1993; Via *et al.*, 1994). Adaptive evolution of any aspect of the phenotype is ultimately a function of selective pressures imposed by the environment and of possible responses by the genotype; consequently, the two aspects of the debate are entangled.

The search for the genetic and developmental bases of plasticity requires the elucidation of both the genetic architecture and how this architecture is translated into observable phenotypes through developmental processes. Understanding how reaction norms evolve requires an estimation of how much genetic variation is present in natural populations, as well as characterization of what ecological conditions favour evolutionary changes in reaction norms. Accordingly, the aims of this paper are (1) to discuss the importance of understanding the genetic and developmental bases of plasticity, (2) to examine the assumptions and predictions of genetic and ecological models of plasticity evolution and (3) to survey empirical approaches aimed at the study of both the genetics and evolution of reaction norms.

Genetic and developmental bases of phenotypic plasticity

In this section we address two issues: (1) the genetic basis of phenotypic plasticity and (2) the developmental processes producing plastic phenotypes.

(1) A basic question to be addressed in studying the genetic bases of reaction norm evolution is: are there genes controlling the patterns and amounts of plasticity, as distinct from genes governing within-environment phenotypic expression? Via (1993) suggested that there are no 'plasticity genes', because phenotypic plasticity is a by-product of selection within environments: in other words, an apparent plastic response across two environments is simply due to the fact that selection favoured different character means in each. On the other hand, Schlichting and Pigliucci (1993) defined plasticity genes as '*loci that exert environmentally dependent control over structural gene expression*'. However, regardless of the specific genetic basis for plasticity, plasticity is clearly under genetic control and can therefore evolve (Westerman, 1970; Wu, 1975; Jain, 1978; Falconer, 1990; Hillesheim and Stearns, 1991; Huey *et al.*, 1991; Scheiner and Lyman, 1991; Scheiner, 1993). Furthermore, Waddington (1960) demonstrated that plasticity can respond to selection in cases in which the within-environment character means do not, a strong argument in favour of the existence of plasticity genes.

(2) There are two generally recognized classes of developmental response to environmental change (terminology of Smith-Gill, 1983): *phenotypic modulation*, where the plasticity is a continuous and proportional function of the environmental stimulus and *developmental conversion*, where responses are of a threshold type and are not proportional to the stimulus. Schmalhausen (1949, pp. 6–7 and following) made a clear distinction between these two forms of plasticity and Smith–Gill (1983) later comprehensively described the differences between them (see also Bradshaw, 1965; Levins, 1968; Scheiner and Lyman, 1989; West-Eberhard, 1989). These two phenotypic outcomes may have specific genetic controls and may be favoured under different ecological conditions (Fig. 1).

Allelic sensitivity versus regulatory plasticity: the genetic basis of phenotypic plasticity

We recognize two distinct forms of genetic control of plasticity.

(1) Allelic sensitivity, in which the expression of individual genes is altered by changes in external conditions (e.g. genes whose products are directly responsive to changes in temperature, pH, humidity, etc.); there is no controversy regarding their existence.

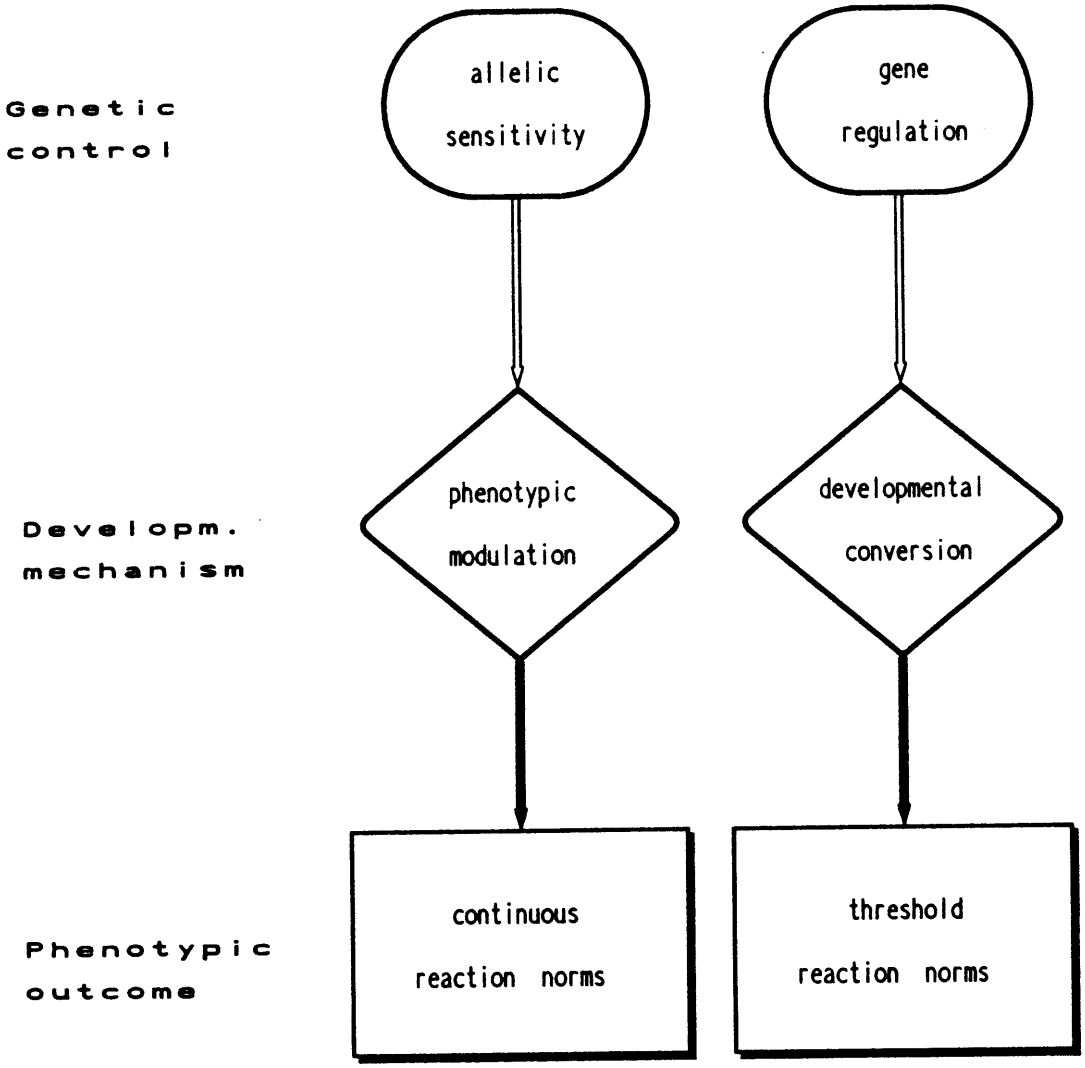

Figure 1. Diagram of the possible relationships between the genetic control and developmental basis of the two fundamental types of phenotypic plasticity. Allelic sensitivity/phenotypic modulation can also be a step in the origin of the more sophisticated gene regulation/developmental conversion system. Furthermore, nearly continuous reaction norms can result from developmental conversion when this is further affected by modifier genes.

(2) Regulatory plasticity, in which genes detect the change in external conditions (through appropriate receptors) and alter the expression of other genes (an indirect response). Such alterations can include changes in the rates of transcription or translation or switching genes on or off.

The distinction between these two forms is of fundamental importance because identical selective pressures operating on allelic sensitivity or regulatory plasticity could produce very different trajectories of reaction norm evolution.

We propose that there are several advantages for a regulatory system of control of plasticity and suggest that a substantial fraction of cases of adaptive plasticity are based on this form of genetic control. First, regulatory plasticity can produce discrete phenotypes that are stable across

a range of environmental conditions (Schmalhausen, 1949, p. 232), which is advantageous if such stability is adaptive. The typically continuous and proportional responses generated by allelic sensitivity would produce variable phenotypes in the presence of fluctuating environmental conditions.

Second, an environmentally cued regulatory system has the potential to *anticipate* the actual environmental change. This can be accomplished either by initiating the phenotypic response at a lower environmental threshold or by uncoupling the response from the stimulus, e.g. by responding to another environmental factor that is a reliable predictor of future conditions (Levins, 1968). Anticipatory responses such as the production of emergent or submerged leaf forms (Cook and Johnson, 1968), the suite of changes accompanying leaf drop in deciduous plants, the accelerated metamorphosis of amphibians in drying ponds (Newman, 1988) and the seasonal polyphenisms of some insects (Moran, 1992), offer the clearest examples of adaptive phenotypic plasticity that we have and in each case it is difficult to envision a mechanism of control not based on gene regulation.

Third, a regulatory control of reaction norms would relax the stringent constraints on evolution of plasticity predicted by Via and Lande (1985) and Gomulkiewicz and Kirkpatrick (1992). From a quantitative genetic perspective, genetic correlations between two traits (or between the same trait expressed in two environments) measure constraints on further evolution. These constraints can eventually completely halt evolutionary change if the mean genetic correlation is $\geq |1/n|$, where n is the number of traits (or environments) considered (Dickerson, 1955). With regulatory control however, the approach to these predicted constraints on the evolution of adaptive plasticity is slowed considerably: both regulatory and non-additive genetic effects on plastic responses tend to reduce the magnitude of genetic correlations across environments (r_{ae}) (see below).

Finally, with the acquisition of regulatory systems of control, the genetic and phenotypic correlations among traits *within* environments can be easily altered. The benefits of such flexibility lie in the ability of the organism to alter allometric relationships in response to environmental conditions. For example, *Phlox* plants in a benign environment produce more flowers with lower root production, whereas with leaf removal, flower production is highest for plants with greater root mass (Schlichting, 1986). There have been reports of both environment-dependent genetic (Service and Rose, 1985; Schlichting, 1986; Mazer and Schick, 1991a,b; Stearns *et al.*, 1991; Thomas and Bazzaz, 1993) and phenotypic (Schlichting, 1989a,b; Pigliucci *et al.*, 1991) correlations – such observations can be satisfactorily explained within a regulatory framework (note that a similar explanation obtains for changes in correlations among traits during development: Birot and Christophe, 1983; Cheverud *et al.*, 1983; Atchley, 1984; Ebert *et al.*, 1993).

There is a large and steadily growing literature on environmentally controlled expression of regulatory genes (at both the transcriptional and the translational levels). In these systems the environment determines the manner in which particular genes control the expression of other genes and, thus, control the plastic response. For example, Mazel and Marliere (1989) report the environmental regulation of different cyanobacterial photosythetic pigment proteins – under low sulphur conditions, a pigment protein lacking sulphur-containing amino acids is the only one produced. In the nematode *Caenorhabditis*, normally direct developing larvae may be arrested at the second larval stage by nutrient deprivation. This causes a switch in the genetic control of later development: the resumption of ontogeny is controlled by different genes than those controlling continuous development (Liu and Ambros, 1991).

Much attention in plant biology has been focused on the triggering of gene action by light (reviews by Kuhlemeier *et al.*, 1987; Herrera-Estrella and Simpson, 1990; Schmitt and Wulff, 1993).

Another extraordinarily well-studied, environmentally controlled system of regulation is the heat-shock protein response, in which these proteins are produced only when an individual crosses a temperature threshold. The threshold varies among species and is correlated with ambient conditions: some Arctic fish produce 'heat'-shock proteins at 5°C (Maresca *et al.*, 1988).

A more effective regulatory control can be achieved with the presence of multiple regulatory elements (evolving via gene duplication: Smith, 1990; Bustos and Golden, 1992) and partial overlap in the control of particular structural genes. Evidence from molecular studies lends support to both the ideas of multiple controlling elements and redundancy. Gralla (1991), in a review of the control of transcription in *Escherichia coli*, states 'Regulatory elements are duplicated or used in combination to provide additional flexibility and quantitative assistance in regulation.' In *Arabidopsis*, an acclimation polypeptide usually associated with cold tolerance is produced following three different stresses, each inducing a separate pathway to regulate its synthesis (Nordin *et al.* 1991).

Phenotypic modulation versus developmental conversion: the developmental basis of phenotypic plasticity

Schmalhausen (1949) proposed that many instances of *phenotypic modulation* (proportional responses) are due to direct environmental influences on gene activity and developmental phenomena. This view was shared by Smith-Gill (1983) who described phenotypic modulation as arising from direct environmental effects on developmental rates leading to non-specific variation in developmental phenotypes and lacking a distinctive genetic basis. In a sense, phenotypic modulation is a type of 'passive' plasticity. Both authors agree that phenotypic modulations may be non-adaptive or even maladaptive. However, genetically based modulations have the potential for adaptive evolution, if allelic variation for a selectively advantageous response is available.

Typical examples of phenotypic modulation are the influences of changes in nutrient availability, water or light on plant size. A well-known example is the case in *Drosophila* of the two alleles *pennant and vestigial* at a locus affecting the reaction norm of wing length to temperature (Schmalhausen, 1949). Phenotypic modulation may have reduced effectiveness as an adaptation because of a lag time between perception of the signal and the completion of the phenotypic alterations. The production of complex phenotypic alternatives requires highly coordinated control to integrate the responses of the multiple loci involved. The likelihood that such fine control could be accomplished by allelic sensitivity is low: the sensitivities of alleles at many loci would need to be adjusted through selection to produce appropriate proportions of gene products in each of the multiple environments.

Despite these limitations, phenotypic modulation undoubtedly plays an important role in the evolution of reaction norms. First, lacking more sophisticated responses, modulation may enable a population to persist during a period of environmental change. Second, it seems likely that phenotypic modulation is an intermediate step in the evolution of a more integrated system of plastic responses.

Developmental conversion due to regulation of the developmental program is considerably more likely to be adaptive (Schmalhausen, 1949; Smith-Gill, 1983). It operates by switching at some threshold between two or more alternative ontogenetic trajectories, producing more discrete phenotypes. Examples of threshold reactions of this type include some of the most complex plastic responses known, involving coordination of many traits. Compared to phenotypic modulation, developmental conversion therefore represents 'active' plasticity.

A particularly well-documented example of developmental conversion is that of the response of flowering time to light spectral quality. Under normal light conditions, i.e. high red : far red

ratio (R:FR), plants branch more and flower late; under low R:FR (typical of shaded conditions) plants branch less and flower early. This has the potential to be an important case of adaptive plasticity, as plants with this response can avoid competitive shading by their neighbours. In addition, the genetic basis is known: a particular class of phytochrome pigment molecules act as regulatory elements initiating (or inhibiting) a cascade of photomorphogenetic responses (Schmitt and Wulff, 1993).

How do reaction norms evolve?

In order to address the problem of the likely evolutionary trajectories of reaction norms, we need to discuss two distinct but interrelated questions.

(1) What amounts and types of genetic variation for reaction norms are available in natural populations and how can we use this knowledge to predict responses to selection? This has so far been the realm of quantitative genetics, which provides estimates of genetic variances and covariances, used in models of phenotypic evolution.

(2) What ecological conditions are more likely to favour changes in the existing reaction norms of a population and in which direction?

The following section will summarize the results of quantitative genetic studies and simulations on phenotypic plasticity and point to the limits intrinsic to this approach. Then, we will discuss reaction norm evolution under different ecologically relevant scenaria: spatial variation (hard or soft selection) and temporal variation (fine or coarse grained). These points will be examined in light of our distinction between the two genetic/developmental modes of plasticity (Fig. 2).

The quantitative genetic approach to the study of plasticity: results and limitations

Quantitative genetics has gained general acceptance as a tool for describing genetic variation of phenotypic characters in natural populations and predicting their response to selection. These methods have been extended for use in the analysis of evolution in multiple environments and to the prediction of long-term evolutionary trajectories. The experimental study of reaction norms from a quantitative genetic perspective typically involves rearing genetically distinct families of individuals in two or more environments and employs either a particular breeding design or a selection experiment. In models of the evolution of reaction norms, the focus is on a projection of phenotypic change based on the structure of the genetic variance–covariance matrix (**G**).

Several important points have emerged from experimental studies of reaction norm evolution.

(1) Both selection experiments and controlled breeding designs have ascertained the existence of a genetic basis to plasticity (Westerman, 1970; Wu, 1975; Jain, 1978).

(2) A few estimates of the number and type of genes involved in plastic responses are available (Westerman, 1970; Wu, 1975).

(3) The dynamics of the response of plasticity to selection have been investigated in a few cases (Falconer, 1990; Hillesheim and Stearns, 1991; Huey *et al.*, 1991; Scheiner and Lyman, 1991), suggesting that plasticity responds in some cases to artificial selection in a fashion similar to the previously known responses of trait means.

Theoretical investigations have produced a number of interesting results.

(1) Negative genetic correlations between the expression of the same character in two environments lead to constraints on reaction norm evolution (Via and Lande, 1985; Via, 1987).

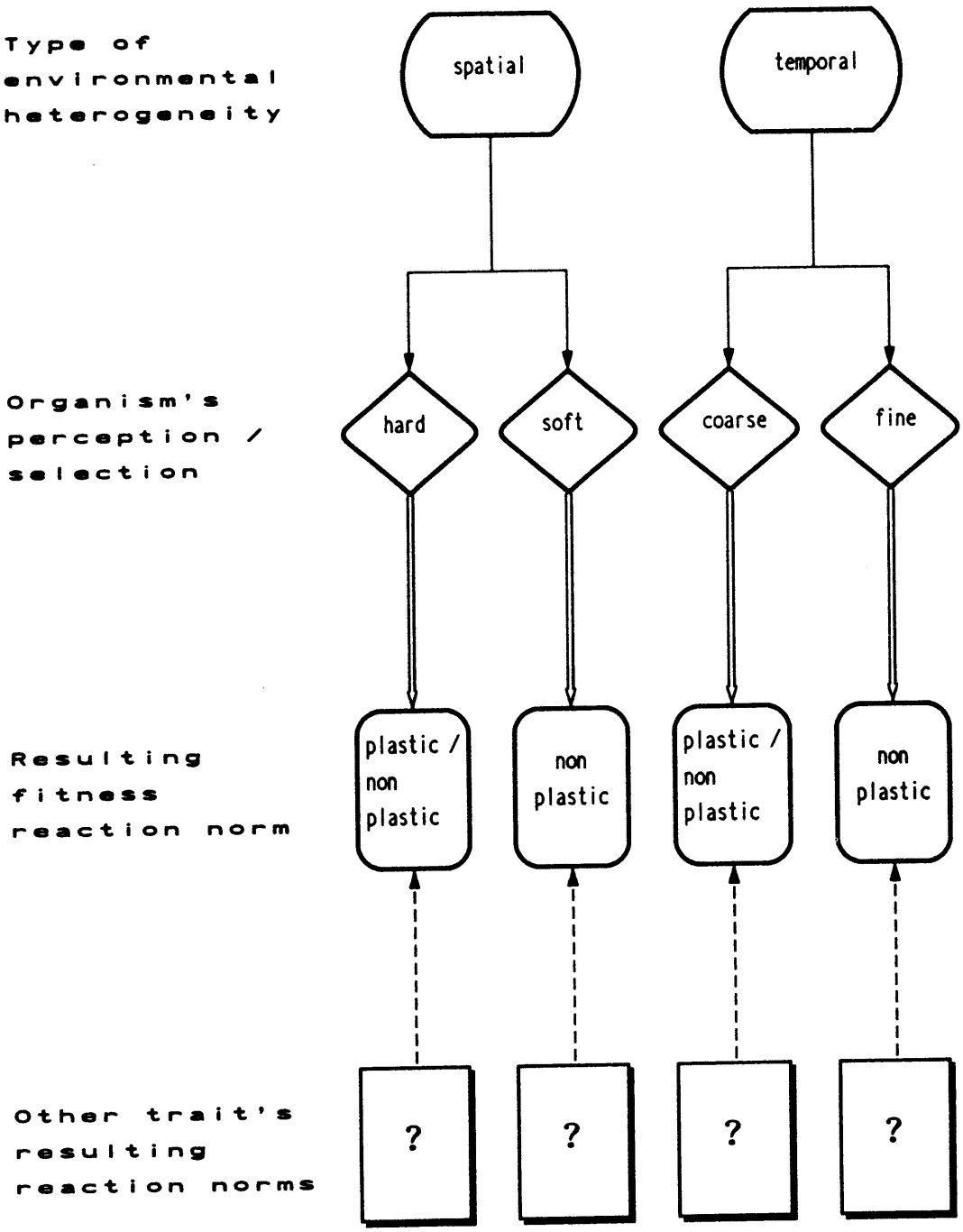

Figure 2. Concept map tracing the complex relationships between the type of environmental heterogeneity that an organism can experience, the associated selective pressures and the kind of fitness reaction norm that might result. A non-plastic fitness reaction norm means that the organism tends to be a generalist (i.e. it performs at the same level in all environments), while a plastic fitness reaction norm can be typical of a specialist (good performance in some environments, bad in others). The question marks indicating the shape of reaction norms of traits connected to fitness indicate that these will be plastic or homeostatic, depending on the exact functional relationship between each trait and fitness.

(2) Costs to plasticity can constrain reaction norm evolution (van Tienderen, 1990) and its dynamics are quite different under soft and hard selection. Notably, with soft selection the evolutionary outcome depends on the initial conditions (i.e. on the population's history).

(3) de Jong (1990) discussed the possibility of changes in the genetic variance–covariance matrix from one environment to another, describing the relationship between developmental constraints and pleiotropy.

(4) Gomulkiewicz and Kirkpatrick (1992) have extended the general quantitative genetic approach from the consideration of a set of discrete environments to evolution in continuous environmental variation (by application of the so-called infinite dimensional models).

(5) de Jong (1990) and Roff (1994) proposed describing reaction norms using polynomials (or mathematically equivalent methods). This allows the estimation of separate genetic variances for the height and shape of the reaction norm.

There are several problems inherent in the quantitative genetic approach because its major tools are estimates of genetic variances, covariances and correlations.

(1) One characteristic limitation derives from their statistical representation of the population (they therefore do not address the critical issue of the type of genetic control of plasticity).

(2) The genetic correlation between two traits (within an environment), r_g, is often interpreted as a measure of the degree of shared genetic control or genetic independence of the traits (Falconer, 1981). A correlation $< |1|$ suggests that different loci affect the character states and that the traits may be able to evolve at least partially independently. The genetic correlation of the values of a single trait in two environments (r_{ae}) has been used in a similar fashion to represent variation in phenotypic plasticity (Falconer, 1952; Via and Lande, 1985) and as a surrogate for r_g in evolutionary models. Is r_{ae} directly analogous to r_g? Recall the two mechanisms of genetic control of plasticity. With allelic sensitivity, the same loci are expressed in each environment (i.e. no genetic independence): we expect $r_{ae}=1$ in this case. With regulatory control, different loci can be expressed in the two environments (i.e. genetic independence): the logical expectation is that $r_{ae} < 1$ in such circumstances. However, such expectations are irrelevant for practical purposes, because calculation of the genetic correlation does not assess the presence or absence of shared genetic control. The actual correlation in the case of regulatory control can range from 1 to -1 depending entirely on the number and identity of loci affected by the regulatory switch. Conversely, organisms with the same genes expressed in both environments, but with alleles that differ in their sensitivity, can quite easily produce non-parallel reaction norms and $r_{ae} < 1$, suggesting some degree of independence. This, however, is not genetic independence as envisioned for r_g. The genetic correlation produced by allelic sensitivity is unique to the cross-environment context: the correlation arises from the similarities or differences of sensitivities and does not inform us at all about shared genetic control in the two environments. Both allelic sensitivity and differential gene expression can contribute to plastic responses; thus the genetic correlation of the same trait in two environments can include the combined effects of independence of loci and independence of sensitivities. This mixing effect may not be a problem when the goal is to provide a statistical description of plasticity; however, it is a major impediment if the objective is understanding long-term reaction norm evolution. Houle (1991) also pointed out the dependence of r_g on the interaction of different types of loci.

(3) It has been suggested that the use of r_{ae} in plasticity studies is appropriate because it is equivalent to the $G \times E$ term in an analysis of variance (Via, 1987; based on Yamada, 1962). As Fry (1992) points out, such an equivalence relies on the assumption of equal heritabilities in the two (or more) environments, a requirement not frequently met by real data and in fact unlikely given regulatory control. Furthermore, we note that r_{ae} will underestimate the amount of $G \times E$

interaction whenever there are non-linear genetic effects (i.e. epistasis, dominance) and if these show interactions with the environment.

(4) Another troubling feature of quantitative genetic models of reaction norm evolution is the assumption that r_{ae} (or r_g) remains constant through time. Given that the correlation matrix is used in projections of long-term phenotypic evolution, if the correlations change through time, then its long-term predictions, estimations of the rate of evolution and of equilibria become questionable (Turelli, 1988). There are at least five ways in which r_{ae} can be altered; (i) change in relationships among loci (epistasis), (ii) mutation, (iii) change in the genotypic frequencies (selection, migration, drift, etc.), (iv) dominance and linkage. We suggest that its use as a statistical descriptor should be restricted to local analyses (Lewontin, 1974). An argument could be made that only qualitative changes in **G** (e.g. changes in the sign of the correlations) would dramatically affect evolutionary trajectories, while simple changes in magnitudes should only affect rates of evolution. Although true in the simple case of the correlation between two traits, things become more complex if we consider the multivariate phenotype. In this instance, alterations in the magnitude of coupled correlations can change the ranks within **G**, therefore deflecting the evolutionary trajectory toward unpredictable equilibria.

Ecological conditions affecting the evolution of plasticity

Although admittedly a simplification, there are two basic types of environmental heterogeneity that a population can encounter; spatial (existence of different patches) or temporal (within or between generations). Classical ecological theory recognizes two distinct types of regimes under each of these situations (Levins, 1968).

(1) Spatial heterogeneity can lead to soft (or rank-order) selection or to hard (threshold) selection.
(2) Temporal heterogeneity can be fine grained (environments change within the same generation) or coarse grained (environments change between generations).

A major goal of evolutionary theory is to determine which of the above circumstances leads to the evolution of generalist versus specialist genotypes (Futuyma and Moreno, 1988). From a plasticity standpoint, it should be noted that a generalist genotype has a relatively good performance in all environments and therefore a *fitness reaction norm* with reduced plasticity. A specialist, on the other hand, has a good performance in one set of environments, but a poor one in another; its fitness reaction norm is plastic. However, the evolution of a generalist or specialist does not mean that all facets of the phenotype will have low or high plasticity. In fact, it is easy to imagine a case in which a non-plastic fitness reaction norm is made possible by the extreme plasticity of characters that are related to fitness (e.g. for heterophyllous plants, the high plasticity for leaf shape increases survivorship under both aerial and submerged conditions).

Models of phenotypic evolution predict the evolution of generalists (1) under soft selection in spatially heterogenous environments (van Tienderen, 1991) and (2) in fine-grained, temporally variable environments (Gomulkiewicz and Kirkpatrick, 1992). In the other two cases (spatial variation with hard selection or coarse-grained temporal variation), the outcome (generalist versus specialist) depends on initial conditions and on the cost of appropriate plasticity for being a generalist. From a genetic perspective, an important question in all these cases is whether selection acts directly on the reaction norm. Via (1993) argued that there is no need to invoke a specific genetic control for plasticity because reaction norms are the result of within-environment selection: if an individual experiences only one environment, then the change in allele frequency

will be in direct response to that environment, not to the potential range of situations. We suggest that there are two conditions that would result in selection on the reaction norm *per se*.

(1) Individual selection under temporally fine-grained heterogeneity, because a single individual would experience more than one environment (e.g. heterophylly, metamorphosis in amphibians).

(2) Any situation where the individuals from a progeny will encounter different environments (i.e. hard or soft spatial selection). In this case, a family of closely related genotypes encounters a range of environments, which would cause specific reaction norms to be selected.

The empirical questions

Genetics of phenotypic plasticity

There are five empirical approaches to the elucidation of the genetic bases of plastic responses: (1) the measurement of the genetic correlation between plasticity and within-environment character means, (2) experiments measuring the response of plasticity to selection, (3) classical crossing experiments, aimed at characterizing the number of genes affecting plastic responses and the type of inheritance of plasticity, (4) studies using quantitative trait loci (QTL) mapping, (5) isolation of mutants altering plastic responses.

(1) If plasticity is controlled by the same genes determining within-environment trait values, then the trait values and their plasticity should be perfectly genetically correlated. Several reports of correlations between plasticities and trait values for experiments with two environments suggest some degree of independence between the two (Falconer, 1990; Scheiner and Lyman, 1991). However when using only two environments, there is a direct mathematical relationship between the genetic correlation of plasticity and one within-environment mean (r_{pm}) and the genetic correlation of trait means across environments (r_{ae}) (the correlation between two means and their differences; Sokal and Rohlf, 1981). This makes the hypothesis of shared genetic control of trait means and plasticities untestable in fewer than three environments.

(2) Selection for an increase or decrease in plasticity and determination of its heritability has been done by Falconer (1990), Hillesheim and Stearns (1991), Huey *et al.* (1991) and Scheiner and Lyman (1989, 1991), among others. Future attempts using response to selection, however, need to determine the genetic basis for plasticity using more than two environments because of the problem cited in (1).

(3) Few studies have used controlled crossing experiments to characterize the genetic bases of plasticity (Westerman, 1970; Wu, 1975; Jain, 1978), but all conclude that plasticity and trait means are at least partially determined by different sets of genes and that the ability to display a plastic response can be dominant or recessive. This approach is valuable, but is limited in that further characterization of the type of genetic control is both labour intensive and of limited power. It is possible to describe dominance and epistasis, but it is very difficult to reliably estimate the number of genes or to determine the nature of the interactions among them.

(4) Mapping of quantitative trait loci is quite old in principle (Sax, 1923), but has been widely applied only very recently, due to the availability of enough molecular markers and of maximum likelihood techniques to detect the significance of the association between markers and phenotypes (Hartl and Clark, 1989). The environment-specific action of QTLs has been detected by Paterson *et al.* (1991). At least one gene controlling flowering time in *Arabidopsis thaliana* (a very plastic attribute of the phenotype) has been mapped close to the location of a regulatory gene involved in hormonal actions (L. Dorn, personal communication). This approach, although

statistically-based, holds more promise than classical quantitative genetics for identifying particular genes and understanding their mode of genetic control of plasticity.

(5) Isolation of mutant genotypes with different reaction norms to gain insights into the mechanistic details of the genetics of plasticity would allow estimation of how many genes are involved, study of the effects of different alleles at the same locus, characterization of the interactions among loci, determining how many pathways are involved in a specific plastic response, and mapping of the genes responsible for the plasticity, eventually leading to their molecular characterization. To our knowledge, no such attempt has been performed to date, possibly because of the technical difficulties involved: a potential plasticity mutant needs to be screened over several environments, considerably increasing the complexity and length of the experiments. However, data on the plasticity of mutants isolated during classical mutagenesis experiments have been collected (Markwell and Osterman, 1992; Schultz and Haughn, 1993). For example, mutants affecting the photomorphogenetic response in angiosperms indicate alterations in genes directly responsible for sensing environmental conditions and appropriately cueing a developmental cascade (Deng *et al.*, 1991).

Evolution of phenotypic plasticity

Three basic empirical approaches can yield information about the evolution and ecology of reaction norms: (1) descriptive studies of patterns of plasticity under controlled conditions, (2) comparative studies based on phylogenetic reconstructions and (3) 'cage' selection experiments.

(1) The majority of published studies on plasticity are descriptive experiments in which genotypes are reared under several controlled conditions (or by means of reciprocal transplants). These studies show variability for plasticity and suggest the presence of substantial genetic variation. The major limitation of this approach is that it rarely yields insights beyond the observation of variation. The ecological meaning or evolutionary relevance of the observed responses remain unaddressed. The controlled conditions should reflect natural values of environmental parameters (e.g. Weis and Gorman, 1990; Sultan and Bazzaz, 1993). This would allow a more meaningful interpretation of the reaction norms in relation to fitness. It is also possible to use environmental conditions for which the ecological context is particularly clear. For example, plastic responses to different aspects of light availability by plants, to water in heterophyllous species or to different host plants by insects, simplify the explicit formulation of ecological hypotheses.

(2) Comparative studies, in which a series of characters is mapped onto a known phylogeny (based on an independent character set), can yield information about evolutionary trends, convergence and phylogenetic constraints. No comparative studies of the evolution of plasticity have been published, aside from limited explorations by Schlichting and Levin (1984, 1988, 1990) on *Phlox*. Ideally, we would need closely related taxa, for which the same traits can be measured under similar environments. If the phylogenetic relationships among these taxa are known, descriptors of plasticity can be mapped onto the phylogram and ancestral states can be inferred. This would allow evaluation of the extent of phylogenetic inertia (i.e. the resistance to evolutionary change due to common ancestry), estimation of the frequency of convergence toward the same plastic response and study of the relationship between the plastic response of each species and its general ecology and life history.

(3) Another approach to the study of the evolutionary ecology of plasticity is based on 'cage' experiments, in which an initial population of known genotypes is allowed to evolve under controlled conditions. The genetic constitution of the population and the phenotypic means can be followed through time, leading to information on the dynamics of evolutionary change. The

difference from an artificial selection experiment is that there is no specific optimum that is selected by the experimenter and no *a priori* mating designs are used. To our knowledge, no such experiments on the evolution of plasticity have been completed so far.

Conclusions

We propose that the importance of regulatory systems for phenotypic plasticity represents just a specific example of a more general feature of phenotypic evolution – the acquisition of increased control over complex processes through evolution of epigenetic (regulatory) systems. The process of building or revamping epigenetic systems necessarily results in a concomitant alteration of genetic correlations among traits. The breakdown or build-up of patterns of character correlation is arguably the goal of such evolution in the first place. Indeed, theoretical studies already exist that point to the necessity for localized regulatory systems as the best option for evolution in rugged adaptive landscapes and for the appearance of emergent properties such as epigenetic effects (Kauffman and Levin, 1987). A comprehensive model of the evolution of reaction norms or of phenotypic evolution in general must include both forms of genetic control. The structural gene systems envisioned in the allelic substitution models of classical quantitative genetics and the regulatory (epigenetic) systems postulated for developmental conversion are both integral parts of such a model.

Acknowledgements

We thank Y. Carriere, B. Devlin, P. di Iorio, K. Holsinger, C. Jones, G. LeBuhn, P. Neal, D. Roff, S. Scheiner, J. Schmitt and S. Via for discussions or comments on previous versions of this manuscript. This work was supported by an NSF Dissertation Improvement grant (DEB-9122762) (C.D.S./M.P) and by an NSF grant (DEB-9220593) (C.D.S.).

References

Atchley, W.R. (1984) Ontogeny, timing of development, and genetic variance–covariance structure. *Am. Nat.* **123**, 519–40.

Birot, Y. and Christophe, C. (1983) Genetic structures and expected genetic gains from multitrait selection in wild populations of Douglas fir and Sitka spruce. *Silvae Genetica* **32**, 141–51.

Bradshaw, A.D. (1965) Evolutionary significance of phenotypic plasticity in plants. *Adv. Genet.* **13**, 115–55.

Bustos, S.A. and Golden, S.S. (1992) Light-regulated expression of the *psbD* gene family in *Synecoccus* sp. strain PCC7942: evidence for the role of duplicated *psbD* genes in cyanobacteria. *Mol. Gen. Genet.* **232**, 221–30.

Cheverud, J.M., Rutledge, J.J. and Atchley, W.R. (1983) Quantitative genetics of development: genetic correlations among age-specific trait values and the evolution of ontogeny. *Evolution* **37**, 895–905.

Cook, S.A. and Johnson, M.P. (1968) Adaptation to heterogenous environments. I. Variation in heterophylly in *Ranunculus flammula* L. *Evolution* **22**, 496–516.

de Jong, G. (1990) Quantitative genetics of reaction norms. *J. Evol. Biol.* **3**, 447–68.

Deng, X.W., Caspar, T. and Quail, P.H. (1991) *cop1*: a regulatory locus involved in light-controlled development and gene expression in *Arabidopsis*. *Genes Devel.* **5**, 1172–82.

Dickerson, G.E. (1955) Genetic slippage in response to selection for multiple objectives. *Cold Spring Harbor Symp. Quant. Biol.* **20**, 25–32.

Ebert, D., Yampolsky, L. and van Noordwijk, A.J. (1993) Genetics of life history in *Daphnia magna*. II. Phenotypic plasticity. *Heredity*, **70**, 344–52.

Falconer, D.S. (1952) The problem of environment and selection. *Am. Nat.* **86**, 293–8.

Falconer, D.S. (1981) *Introduction to Quantitative Genetics*. Longman, London.
Falconer, D.S. (1990) Selection in different environments: effects on environmental sensitivity (reaction norm) and on mean performance. *Genet. Res.* **56**, 57–90.
Fry, J.D. (1992) The mixed-model analysis of variance applied to quantitative genetics: biological meaning of the parameters. *Evolution* **46**, 540–50.
Futuyma, D.J. and Moreno, G. (1988) The evolution of ecological specialization. *Annu. Rev. Ecol. Syst.* **19**, 207–34.
Gomulkiewicz, R. and Kirkpatrick, M. (1992) Quantitative genetics and the evolution of reaction norms. *Evolution* **46**, 390–411.
Gralla, J.D. (1991) Transcriptional control – lessons from an *E. coli* promoter data base. *Cell* **66**, 415–18.
Hartl, D.L. and Clark, A.G. (1989) *Principles of Population Genetics*. Sinauer, Sunderland, MA.
Herrera-Estrella, L. and Simpson, J. (1990) Influence of environmental factors on photosynthetic genes. *Adv. Genet.* **28**, 133–64.
Hillesheim, E. and Stearns, S.C. (1991) The responses of *Drosophila melanogaster* to artificial selection on body weight and its phenotypic plasticity in two larval food environments. *Evolution* **45**, 1909–23.
Houle, D. (1991) Genetic covariance of fitness correlates: what genetic correlations are made of and why it matters. *Evolution* **45**, 630–48.
Huey, R.B., Partridge, L. and Fowler, K. (1991) Thermal sensitivity of *Drosophila melanogaster* responds rapidly to laboratory natural selection. *Evolution* **45**, 751–6.
Jain, S.K. (1978) Inheritance of phenotypic plasticity in soft chess, *Bromus mollis* L. (Gramineae). *Experientia* **34**, 835–6.
Kauffman, S. and Levin, S. (1987) Towards a general theory of adaptive walks on rugged landscapes. *J. Theor. Biol.* **128**, 11–45.
Kuhlemeier, C., Green, P.J. and Chua, N.-H. (1987) Regulation of gene expression in higher plants. *Annu. Rev. Plant Physiol.* **38**, 221–57.
Levins, R. (1968) *Evolution in Changing Environments*. Princeton University Press, Princeton.
Lewontin, R.C. (1974) The analysis of variance and the analysis of causes. *Am. J. Human Genet.* **26**, 400–11.
Liu, Z. and Ambros, V. (1991) Alternative temporal control systems for hypodermal cell differentiation in *Caenorhabditis elegans*. *Nature* **350**, 162–5.
Maresca, B., Patriarca, E., Goldenberg, C. and Sacco, M. (1988) Heat shock and cold adaptation in Antarctic fishes: a molecular approach. *Comp. Biochem. Phys.* **90B**, 623–9.
Markwell, J. and Osterman, J.C. (1992) Occurrence of temperature sensitive phenotypic plasticity in chlorophyll-deficient mutants of *Arabidopsis thaliana*. *Plant Physiol.* **98**, 392–4.
Mazel, D. and Marliere, P. (1989) Adaptive eradication of methionine and cysteine from cyanobacterial light-harvesting proteins. *Nature* **341**, 245–8.
Mazer, S.J. and Schick, C.T. (1991a) Constancy of population parameters for life history and floral traits in *Raphanus sativus* L. I. Norms of reaction and the nature of genotype by environment interactions. *Heredity* **67**, 143–56.
Mazer, S.J. and Schick, C.T. (1991b) Constancy of population parameters for life history and floral traits in *Raphanus sativus* L. II. Effects of planting density on phenotype and heritability estimates. *Evolution* **45**, 1888–907.
Moran, N. A. (1992) Phenotype fixation and genotypic diversity in the complex life cycle of the aphid *Pemphigus betae*. *Evolution* **45**, 957–70.
Newman, R.A. (1988) Adaptive plasticity in development of *Scaphiopus couchii* tadpoles in desert ponds. *Evolution* **42**, 774–83.
Nordin, K., Heino, P. and Palva, E.T. (1991) Separate signal pathways regulate the expression of a low-temperature-induced gene in *Arabidopsis thaliana* (L.) Heynh. *Plant Mol. Biol.* **16**, 1061–71.
Paterson, A.H., Damon, S., Hewitt, J.D., Zamir, D., Rabinowitch, H.D., Lincoln, S.E., Lander, E.S. and Tanksley, S.D. (1991) Mendelian factors underlying quantitative traits in tomato: comparison across species, generations, and environments. *Genetics* **127**, 181–97.

Pigliucci, M., Politi, M.G. and Bellincampi, D. (1991) Implications of phenotypic plasticity for numerical taxonomy of *Ornithogalum montanum* (Liliaceae). *Can. J. Bot.* **69**, 34–8.

Roff, D.A. (1994) The evolution of dimorphic traits: predicting the genetic correlation between environments. *Genetics* **136**, 395–401.

Sax, K. (1923) The associations of size differences with seed coat pattern and pigmentation in *Phaseolus vulgaris*. *Genetics*, **8**, 552–60.

Scheiner, S.M. (1993) Genetics and evolution of phenotypic plasticity. *Annu. Rev. Ecol. Syst.* **24**, 35–68.

Scheiner, S.M. and Lyman, R.F. (1989) The genetics of phenotypic plasticity. I. Heritability. *J. Evol. Biol.* **2**, 95–107.

Scheiner, S.M. and Lyman, R.F. (1991) The genetics of phenotypic plasticity. II. Response to selection. *J. Evol. Biol.* **4**, 23–50.

Schlichting, C.D. (1986) The evolution of phenotypic plasticity in plants. *Annu. Rev. Ecol. Syst.* **17**, 667–93.

Schlichting, C.D. (1989a) Phenotypic integration and environmental change. *BioScience* **39**, 460–4.

Schlichting, C.D. (1989b). Phenotypic plasticity in *Phlox*. II. Plasticity of character correlations. *Oecologia* **78**, 496–501.

Schlichting, C.D. and Levin, D.A. (1984) Phenotypic plasticity of annual *Phlox*: tests of some hypotheses. *Am. J. Bot.* **71**, 252–60.

Schlichting, C.D. and Levin, D.A. (1988) Phenotypic plasticity in *Phlox*. I. Wild and cultivated populations of *P. drummondii*. *Am. J. Bot.* **75**, 161–9.

Schlichting, C.D. and Levin, D.A. (1990) Phenotypic plasticity in *Phlox*. III. Variation among natural populations of *P. drummondii*. *J. Evol. Biol.* **3**, 411–28.

Schlichting, C.D. and Pigliucci, M. (1993) Evolution of phenotypic plasticity via regulatory genes. *Am. Nat.* **142**, 366–70.

Schmalhausen, I.I. (1949) *Factors of Evolution*. University of Chicago Press, Chicago.

Schmitt, J. and Wulff, R.D. (1993) Light spectral quality, phytochrome and plant competition. *TREE* **8**, 47–50.

Schultz, E.A. and Haughn, G.W. (1993) Genetic analysis of the floral initiation process (FLIP) in *Arabidopsis*. *Development* **119**, 745–65.

Service, P.M. and Rose, M.R. (1985) Genetic covariation among life history components: the effect of novel environments. *Evolution* **39**, 943–5.

Smith, H. (1990) Signal perception, differential expression within multigene families and the molecular basis of phenotypic plasticity. *Plant, Cell Environ* **13**, 585–94.

Smith-Gill, S.J. (1983) Developmental plasticity: developmental conversion versus phenotypic modulation. *Am. Zool.* **23**, 47–55.

Sokal, R.R. and Rohlf, F.J. (1981) *Biometry*. W.H. Freeman, San Francisco.

Song, O., Dolan, J.W., Yuan, Y.O. and Fields, S. (1991) Pheromone-dependent phosphorylation of the yeast STE12 protein correlates with transcriptional activation. *Genes Devel.* **5**, 741–50.

Stearns, S.G., de Jong, G. and Newman, B. (1991) The effects of phenotypic plasticity on genetic correlations. *TREE* **6**, 122–6.

Sultan, S.E. (1987) Evolutionary implications of phenotypic plasticity in plants. *Evol. Biol.* **21**, 127–78.

Sultan, S.E. and Bazzaz, F.A. (1993) Phenotypic plasticity in *Polygonum persicaria*. I. Diversity and uniformity in genotypic norms of reaction to light. *Evolution* **47**, 1009–31.

Thomas, S.C. and Bazzaz, F.A. (1993) The genetic component in plant size hierarchies: norms of reaction to density in a *Polygonum* species. *Ecol. Monogr.* **63**, 231–49.

Turelli, M. (1988) Phenotypic evolution, constant covariances, and the maintenance of additive variance. *Evolution* **42**, 1342–7.

Via, S. (1987) Genetic constraints on the evolution of phenotypic plasticity. In *Genetic constraints on adaptive evolution* (V. Loeschcke, ed.), pp. 47–71. Springer-Verlag, Berlin.

Via, S. (1993) Adaptive phenotypic plasticity: target or byproduct of selection in a variable environment? *Am. Nat.* **142**, 352–65.

Via, S. and Lande, R. (1985) Genotype–environment interaction and the evolution of phenotypic plasticity. *Evolution* **39**, 505–22.

Via, S., Gomulkiewicz, R., Scheiner, S.M., Schlichting, C.D. and van Tienderen, P. (1994) Adaptive phenotypic plasticity: consensus and controversy. *TREE* (in press).

Waddington, C.H. (1960) Experiments on canalizing selection. *Genet. Res.* **1**, 140–50.

Waddington, C.H. (1961) Genetic assimilation. *Adv. Genet.* **10**, 257–90.

Weis, A.E. and Gorman, W.L. (1990) Measuring selection on reaction norms: an exploration of the *Eurosta–Solidago* system. *Evolution* **44**, 820–31.

West-Eberhard, M.J. (1989) Phenotypic plasticity and the origins of diversity. *Annu. Rev. Ecol. Syst.* **20**, 249–78.

Westerman, C.H. (1970) Genotype–environment interaction and developmental regulation in *Arabidopsis thaliana*. II. Inbred lines; analysis. *Heredity* **26**, 93–106.

Wu, H.P. (1975) The genetic basis of adaptation in *Arabidopsis*. In *Adaptability in plants* (T. Matsuo, ed.), pp. 159–71. University of Tokyo Press, Tokyo.

Yamada, Y. (1962) Genotype × environment interaction and genetic correlation of the same trait under different environments. *Jpn J. Genet.* **37**, 498–509.