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CONTROL OF PHENOTYPIC PLASTICITY VIA REGULATORY GENES

What is the form of genetic control of phenotypic plasticity? Are there specific loci determining plastic responses (Bradshaw 1965; Schlichting 1986; Scheiner and Lyman 1989, 1991), or is plasticity simply an epiphenomenon of selection for different trait means in different environments (Via and Lande 1985; Via 1987)? This central issue in a long-standing dispute is of fundamental importance because the mechanism of genetic control of plasticity will determine the long-term dynamics, rates, and constraints on the evolution of reaction norms.

Via (1993) reiterates her view that there is no need to invoke separate loci controlling the shape of reaction norms: phenotypic plasticity is not a trait itself but merely a by-product of evolution at numerous loci to produce appropriate trait means in different environments. Without presenting new empirical evidence, she observes that "current models illustrate how phenotypic plasticity can evolve . . . without requiring the existence of separate 'genes for plasticity' " (pp. 352–353). To avoid semantic wrangling, we define plasticity genes as regulatory loci that exert environmentally dependent control over structural gene expression and thus produce a plastic response. Such loci represent a genetic mechanism for plastic response that is distinct from that assumed in quantitative genetic models of reaction norm evolution.

We have the following disagreements with Via's (1993) viewpoint. (1) There is a wealth of evidence for the existence of plasticity genes as defined above. (2) The evolution of adaptive plasticity involves two processes: (i) adjustment of the available quantitative genetic variation to approach the phenotypic optimum and (ii) development of new genetic machinery for controlling response to the environment. (3) The argument that current statistical models can explain the evolution of plasticity avoids the issue that similar statistical results may be produced by means of very different genetic mechanisms.

1. *The existence of plasticity genes.*—Two types of genetic control of phenotypic plasticity have been proposed (Schmalhausen 1949; Smith-Gill 1983; Dragavtsev and Aver'yanova 1984). (i) Allelic sensitivity is the case in which in different environments all loci are expressed, but individual alleles vary in their sensitivity, that is, there are direct effects of the environment on structural gene expression. With allelic sensitivity we expect gradual changes in phenotype, proportional to the environmental gradient. (ii) Regulatory control is the scenario in which not all gene loci are expressed in each environment, that is, gene expression is mediated through the action of regulatory loci that can control the expression of multiple structural genes. For the simplest case of regulatory control, distinct phenotypes will be produced on each side of an environmental threshold.

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With regulatory control, phenotypic plasticity is determined (at least in part) by different loci from those responsible for the expression of a trait in any particular environment (Bradshaw 1965; Schlichting 1986; Schlichting and Levin 1986; Jinks and Pooni 1988; Scheiner and Lyman 1991).

Regulatory genes that control phenotypic expression and are independent of trait means do exist. Evidence exists in the form of observations of threshold phenotypic responses to environmental change, including some extraordinarily complex ones involving coordinated plastic responses of many traits. For example, environmentally cued metamorphosis in amphibians (Semlitsch 1987; Newman 1988), seasonal polyphenisms of some insects (Moran 1992), the production of emergent versus submerged leaf forms (Cook and Johnson 1968), and the suite of changes accompanying leaf drop in deciduous plants are well-documented examples of adaptive phenotypic plasticity, and each is congruent with a model of regulatory control.

The direct molecular evidence for such environmentally controlled regulation of gene expression is overwhelming. In these systems, the environment determines the manner in which particular genes control the expression of other genes and thus control the plastic response. Such systems have been described in members of all five kingdoms: monerans (Goransson et al. 1989), protistans (Plumley and Schmidt 1989), fungi (Song et al. 1991), animals (Nagao et al. 1990; Liu and Ambros 1991), and plants (Dixon and Harrison 1990; Herrera-Estrella and Simpson 1990; Scandalios 1990). As an example, take the production of photosynthetic pigment proteins in the cyanobacterium *Calothrix*. Phycocyanin production is controlled by three genes: *cpc1*, an environmentally stable gene that encodes phycocyanin 1 subunits, *cpc2*, a red-light-triggered gene for phycocyanin 2 subunits, and *cpc3*, a locus similar to *cpc2* that lacks codons for sulfur-containing amino acids. Under low sulfur conditions, *cpc3* transcription is vastly increased and *cpc1*, *cpc2*, and *cpe* (phycoerythrin) are switched off, which results in a vast savings in the sulfur economy of these organisms (Mazel and Marliere 1989).

2. *Evolution of and selection for plasticity*.—We propose that there are two distinct processes in the evolution of adaptive plasticity in response to an environmental stimulus. In the first, selection exploits any available allelic variation, adjusting the traits toward the new joint optimum. This corresponds to the evolution of trait means envisioned by Via (1987, 1993). As pointed out by Via (1987) and Gomulkiewicz and Kirkpatrick (1992), this process will quickly lose momentum as selection attempts to optimize the responses of multiple traits. Further evolution toward the optimum can then be achieved only by circumventing these contraints. This is accomplished through a second process, with the creation or direct modification of the genetic system that controls plastic response of multiple traits. This system will consist of the receptors, transducers, and controllers present in the regulatory systems described above. Selection during this phase is directly on the mechanisms enabling response and thus is selection for plasticity per se.

Subsequent modifications of the reaction norm (e.g., to reflect changes in environmental frequency and predictability) may be accomplished by either of the processes. The advantage of modifying a regulatory system is that constraints

may be broken down by directly altering the across-environment genetic correlation structure among multiple traits. Current quantitative genetic models do not allow alteration of this across-environment correlation; that is, the regulatory machinery cannot evolve. Thus, these models describe evolution through the first process only—modification of the plastic response through allelic substitution.

3. *Statistical versus genetic models.*—We do not argue that the Via and Lande (1985) model could not provide a reasonable description of the short-term evolution of plasticity. It is, in fact, an important conceptual starting point for investigating the evolution of reaction norms. Our point of contention is that, as a purely statistical representation of evolutionary trajectories, it is not informative about the underlying genetic mechanisms. Despite claims that they can incorporate different forms of genetic control, quantitative genetic models (Via and Lande 1985; Via 1987; Gomulkiewicz and Kirkpatrick 1992) assume a very specific type of genetic architecture: an underlying distribution of many loci with small additive effects. Goodness-of-fit criteria provide little information about the reasonableness of this assumption in the absence of rigorous empirical data.

The phenotypic effects of both allelic sensitivity and the actions of regulatory switches may be roughly approximated by a quantitative genetic model over the short term (because both types of genetic systems contain statistically additive genetic variation [Falconer 1989]). Regulatory control of plasticity, however, is accomplished by the interaction of different genes; any nonadditive epistatic effects will not be incorporated into the matrices of additive genetic variances and covariances and will thus be invisible to the selection applied in these models. To take into account the evolution of such systems, we suggest that certain cases of plasticity evolution (e.g., process ii) would be better described by means of genotypic models. Whether the long-term evolutionary dynamics of a system with numerous additive loci versus one with loci of strong epistatic effect will be similar remains to be demonstrated and seems to us unlikely.

To attain a full understanding of the evolution of reaction norms (and therefore phenotypic evolution in general), we will need to incorporate the distinctive ways in which new phenotypes can be produced in response to environmental change. This becomes particularly important when we begin to extend our investigations of reaction norm evolution from the single trait to the whole-phenotype level: the plastic responses of many individual traits must be coordinated to produce an appropriate response to environmental change (Schlichting 1986, 1989*a*, 1989*b*; Lechowicz and Blais 1988). In this context, regulatory control that integrates the plastic responses of these varied traits represents a relatively simple means for accomplishing an apparently complex task: the production of an altered, yet still functional, phenotype.

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