# Developmental phenotypic plasticity: where internal programming meets the external environment

Massimo Pigliucci

Developmental plasticity has long been the focus of research in both evolutionary ecology and molecular genetics. Recently, the concept of ontogenetic contingency has been proposed to indicate the dependence of plastic responses on the timing and sequence of developmental events. Also, the idea of the developmental reaction norm has been put forward to indicate the complex interactions among development, phenotypic plasticity, and allometry of different structures. Finally, for the first time, studies ranging from the ecological to the molecular aspects of the same plastic response are available on insect and flowering plant model systems.

**Addresses**
Departments of Botany and of Ecology & Evolutionary Biology, University of Tennessee, Knoxville, TN 37996, USA;
e-mail: pigliucci@utk.edu
URL: http://fp.bio.utk.edu/pgl

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**Abbreviation**
**DRN** developmental reaction norm

## Introduction

Developmental plasticity is undergoing a renaissance due to a renewed interest in both evolutionary [1–3] and molecular biology [4,5]. The field is actually very old, tracing back to the first studies of genotype–environment interaction at the beginning of the 20th century [6••]. Before we proceed, let me summarize what is actually meant by the term developmental plasticity, since there has been considerable confusion about it. Phenotypic plasticity is a general attribute of genotypes, and it refers to the fact that the same set of genes can yield different phenotypic (or physiological, or behavioral) outcomes when exposed to distinct environmental conditions [7•]. When studied in a developmental context, plasticity refers to the fact that there are some windows of time during ontogeny when the organism is prone to alter its developmental trajectory in response to the external environment [5,8–11]. Both the degree of plasticity of a genotype and the location and duration of its developmental windows may vary considerably, depending on the species, the environmental factor under study, and the specific trait the researcher focuses on.

In this review, I will summarize recent research in this field, contrasting the molecular point of view with the more classical evolutionary and ecological perspective. I will then attempt to show that some interesting ideas emerge if one considers these two approaches as complementary and that we need their full integration in order to finally answer some of the longest-standing questions concerning how organisms develop and how they respond to their own environment.

## Evolutionary ecology of developmental plasticity

The same developmental phenomenon (for example flowering) may be independent of environmental influences, or may respond to specific conditions, depending on which species we are considering. A major goal of organismal biology is to determine what ecological framework favors one strategy over another. For example, heteroblasty, the production of two (or more) distinct types of leaves during the ontogeny of a plant, has historically been linked to fixed developmental sequences [12,13]. On the other hand, an identical phenomenon occurs in response to specific environmental conditions such as water or light levels, whence it takes the name of heterophylly [14]. Winn [15•] has studied a case involving the annual mint *Dicerandra linearifolia* in northern Florida, in which both phenomena co-occur in the same individual [15•]. She studied how leaf traits varied with the ontogenetic stage of the plant (in this case, the specific node producing the leaf) as well as with the level of external temperature experienced by the plant. For example, leaf thickness was different at different nodes, generally decreasing with age. Simultaneously, higher temperature also decreased leaf thickness. Furthermore, there was a statistically significant interaction between the two sources of variation for that trait, with late leaves responding differently (i.e., they were thicker in the switch treatment) depending on whether they were raised at a constantly high temperature or if they were switched during the experiment.

A second fundamental goal for evolutionary biologists is to determine the extent to which development constitutes a constraint limiting adaptive evolution of organisms. Several studies have adopted optimality models as a baseline against which to test the actual adaptation of living organisms, attributing deviations from the expectations to some sort of genetic or developmental constraint [16–18]. A good example is provided by Gedroc *et al*'s [19••] study on root/shoot partitioning in two annual plants, *Abutilon theophrasti* and *Chenopodium album*. They tested the theoretical expectation that the partitioning of resources between roots and shoots should vary in a simple fashion with the level of nutrients available. They did find results partially consistent with this null hypothesis; however, they also concluded that there are substantial developmental constraints involved in

root/shoot partitioning. These constraints take the form either of ontogenetic drift (i.e. the persistence of the 'wrong' resource allocation pattern for some time after a change in environmental conditions), or of plasticity windows outside which the developmental program is incapable of altering resource allocation in response to a change in the external environment.

The general scenario emerging from these studies is consistent with Diggle's idea of ontogenetic contingency [1,20,21]. Organisms can be plastic and respond to environmental challenges in a flexible way, but the extent of this plasticity depends on the sequence of developmental events. Either some developmental processes have to occur before the system can react to the external environment, or such reactions are limited or precluded once other developmental processes have taken place. Evolutionary biology can address two fundamental components of this problem: first, which ecological conditions should lead to what kind of adaptive response? Second, how well do real organisms match the theoretical expectations, and, therefore, how important are constraints in channeling organismal evolution? Addressing a third component of this puzzle necessarily requires molecular methods: how are constraints and developmental contingencies actually produced by the genetic machinery present in each organism?

## Molecular biology of developmental plasticity

Three levels of analysis have marked the search for the mechanistic basis of developmental plasticity: studies involving hormonal manipulation [22•,23–25] use of mutants [26–28]; and research on transgenic organisms [11,29–34].

Visser *et al.* [35] have investigated the role of the ubiquitous plant hormone auxin in the formation of adventitious roots in two species of *Rumex* which presumably evolved under different water regimes. *R. palustris* is a species colonizing areas frequently subjected to flooding, while *R. thyrsiflorus* hardly ever experiences waterlogging. *R. palustris* was able to produce a much more extensive system of adventitious roots in response to hypoxia, as predicted by the adaptive plasticity hypothesis. (See Sultan's critical review of what constitutes an adaptation in plants, in which she warns against some simplistic approaches commonly used in the literature and provides empirical examples illustrating the conceptual difficulties involved in this kind of research [36]). Both species also produced adventitious roots as a reaction to application of auxin to leaves, but *R. thyrsiflorus* did not produce levels of response comparable to those of the other species even under very high concentrations of the hormone. Therefore, there are species-specific differences in the sensitivity to hormones; these differences presumably evolved in response to specific ecological contexts. From a mechanistic standpoint, Visser *et al.* [35] suggested that hypoxia of the root system causes stagnation of auxin transport in the roots. This accumulation of auxin in turn stimulates the development of adventitious roots.

A very informative example of the power of mutagenesis studies to unveil the basis of developmental constraints on phenotypic plasticity is the one provided by Brakefield and colleagues in their studies of the formation of eyespot in butterflies [37,38,39••]. Members of the *Bicyclus anynana* species produce two morphs depending on the season. In the dry and cold season the butterflies display reduced eyespots, while during the warm and wet season the eyespots are prominent. From an ecological standpoint, large eyespots are produced when the cohort needs to be active (for foraging or mating) and there is a high abundance of predators: the eyespots attract the attention of the predator away from vital organs. When the level of activity of the cohort is low the butterflies spend most of their time stationary, only mating occasionally. In this case an inconspicuous morphology blends better with the background environment (helping to avoid predation). Brakefield and co-workers [39••] examined several mutants at four loci, characterized by different types of abnormalities in the location, size, and developmental sequence of the eyespots. They concluded that natural selection could catalyze very rapid evolution of different eyespot patterns because these can be modulated at different stages of the developmental pathway, and because one or a few changes in specific regulatory elements can exert major phenotypic alterations.

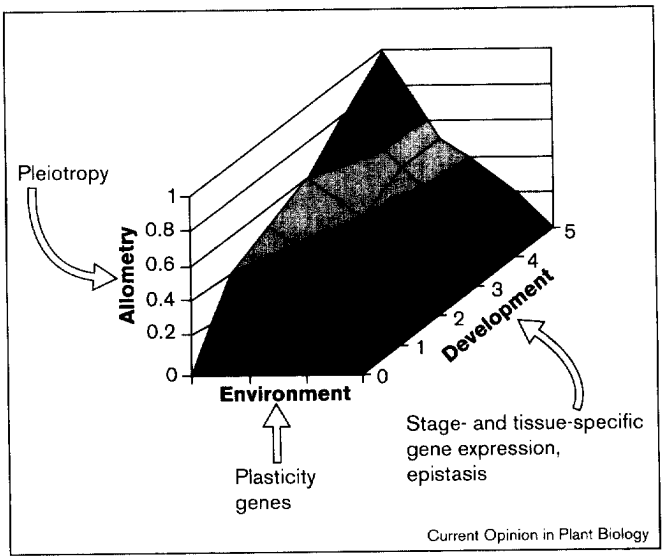
The use of transgenic organisms has allowed a relatively fine mapping of the developmental expression of genes involved in plastic responses. Prandl *et al.* [4], for example, tracked the tissue-specific expression of a heat-inducible gene (tagged with the reporter gene *gus*) in tobacco and *Arabidopsis*. Gus activity was found in leaves, roots, and flowers only after the plants were exposed to heat shock, and vascular tissues displayed the highest levels of activity. The two species differed in the level of activity when no heat shock was administered: while seeds of tobacco accumulated the protein, there was no developmental induction in *Arabidopsis*. This points to species-specific differences in the regulation of the same genetic and developmental machinery. Unfortunately, no ecological context was provided in this case, and it is therefore impossible to infer why the two taxa should behave so differently.

## Unraveling the 'developmental reaction norm'

Schlichting, Pigliucci and co-workers [2,40] recently proposed the concept of the developmental reaction norm (DRN) as a way of properly thinking about whole organism–environment interactions while also considering an ontogenetic perspective (Figure 1). The DRN simply depicts how a single genotype can alter the allometric relationships among a suite of characters through development, and in a fashion that depends on the particular environment to which the organism happens to be exposed. Thus the DRN can typically be divided into three components: allometry, environment,

and development. So, for example, if the genotype in Figure 1 is growing under conditions close to the left portion of the environmental axis, the characters under study will gradually develop a tight correlation through the five stages of development, until at the adult stage two given traits will exhibit perfect covariance. On the other hand, the same exact genotype will fare very differently at the other extreme of the environmental gradient, with the traits maintaining complete independence from each other throughout the ontogeny. This is a fairly common situation in evolutionary biology, a case in which the strength of the constraint of one character over another depends on the developmental stage and on the environment. But what does this mean from a mechanistic standpoint?

**Figure 1**




Schematic representation of the developmental reaction norm and of the genetic phenomena underlying its components. The scale on the allometry axis represents the correlation coefficient. The five stages of development are arbitary. Only one genotype is represented. Depending on the environment, the relationship between two traits (allometry) can change through development. Plasticity genes, pleiotropic effects, stage- and tissue-specific gene expression, as well as epistasis mediate the complex interaction between the organism and its environment.

Recent work has yielded some insight into the genetic machinery underlying such broad patterns of phenotypic variation. The emerging picture seems to contradict one of the oldest truisms of evolutionary biology: evolutionarily meaningful changes in phenotypic expression can be obtained by altering one or a few regulatory genes. For example, the extreme allele of the *Ultrabithorax* gene in *Drosophila* dramatically alters the phenotype of the insect, essentially creating a novel phenotype (a doubling of the thoracic segment). Natural allelic variation at the same locus, however, affects homeostasis, a fundamental property of the development system, without causing the abnormal phenotype [41]. In another example, studies of the natural genetic variation for heat-shock related proteins have now been published for *Drosophila* [42••]. These works represent the first experimental evidence that natural populations demonstrate variable expression of genes with major effects, contrary to the expectation of many evolutionary biologists, who cling to the old paradigm that all genetic variation available to natural selection comes from many loci with small effects (see [43]).

As for the three components of the DRN (allometry, environment, development), we have at least some ideas about which mechanisms may affect them from a genetic standpoint [44]. It is not difficult to see that the covariation of two or more characters (allometry) can be caused by pleiotropy, that is to say, by the action of a single gene on both traits [45,46••,47–49]. The response to environmental changes can be (although it does not have to be) very specific and mediated by genetic elements (plasticity genes) which directly sense the external conditions and then trigger the switch toward one of a series of alternative developmental pathways [7•,44]. Finally, the developmental component is probably marked by genes whose expression is stage- or tissue-specific, and in general by epistatic (gene–gene) interactions [50–52].

Although molecular and evolutionary biology seem to finally converge toward a truly complete synthesis of the biological sciences, a word of caution is necessary to counteract all of the hype that is accompanying the process. Even modern molecular techniques are only scratching the surface of what used to be referred to as the black box of development. We are learning a lot about what one or a few genes can do, but we also know from basic biochemistry that the genetic machinery is highly integrated and complex. We have been unsuccessful in producing organisms with combinations of more than two or three mutations at regulatory loci, because they are not viable. Furthermore, it seems that many interesting genes will be forever beyond the direct manipulative approach, because they are so vital that any change in their pattern of expression or in their sequence will simply kill the organism [53]. Similarly, it is often not possible to get transgenes permanently integrated into the genome. They are either excised or methylated, and therefore not expressed. Perhaps new technology and new theoretical insight will eventually overcome these problems. It is also possible, however, that the complexity of living beings is truly irreducible to the sum of their parts [52,54] and that we will have to content ourselves with an appreciation for their general characteristics. It is still far too early to bet one way or the other.

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