

Functional evo-devo

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Functional factors such as optimal design and adaptive value have been the central concern of evolutionary biology since the advent of the New Synthesis. By contrast, evolutionary developmental biology (evo-devo) has concentrated primarily on structural factors such as the ways in which body parts can be built. These different emphases have stood in the way of an integrated understanding of the role of development in evolution. Here, we try to bridge this gap by outlining the relevance of functional factors in evo-devo. We use modularity and the view of development as a flexible evolutionary system to outline a unified perspective that includes both structural and functional aspects.

Development as a factor in evolution

Whereas development has long been recognized as being important in evolution, its role as an evolutionary factor has only begun to be investigated relatively recently with the study of heterochrony [1] and developmental quantitative genetics [2]. The rise of evolutionary developmental biology (evo-devo) as a biological discipline has brought about several changes in perspective [3,4]. In addition to a new focus on the developmental mechanisms that generate new variation, the discovery of the widespread evolutionary conservation of genes with prominent roles in development (e.g. *Hox* genes [5]) has revived an interest in comparative studies at a large phylogenetic scale.

This shift of interest and emphasis has drawn attention away from the traditional focus of evolutionary studies, namely the adaptive value and functional significance of phenotypic traits. Here, we attempt to integrate functional considerations with the central concepts emerging from evo-devo. We hope that this will contribute to a more unified understanding of the role of development in adaptive evolution.

Structural and functional factors in evolution

The debate about the relative importance of intrinsic structural factors and external adaptation in biological evolution has a long history [6,7]. By the mid-20th century, the neo-darwinian New Synthesis had established adaptation as the central theme of evolutionary biology, such that the primary research emphasis was on the external factors that shaped organisms through natural selection. The discovery of ample genetic variation in natural populations suggested that the raw material for natural selection is plentiful. It was therefore expected that selection would

produce optimal solutions in an engineering sense [8], where each organ is optimised for performing certain functions that confer maximum fitness jointly to the organism. The evolution of a trait could therefore be explained by its function.

Neo-darwinian theory has emphasized function at the expense of structural and historical concerns. When cladistics, the study of relationships among organisms through the branching of evolutionary lineages, became the dominant direction of systematics in the 1980s, historical considerations entered mainstream evolutionary biology under the headings of phylogenetics and the comparative method [9].

The discovery of the pervasive conservation of *Hox* genes [5] and their expression patterns across animal phyla was surprising because it was at odds with the expectation that genetic and developmental systems would evolve just as much as the morphological traits they generate [7]. This discovery of conserved developmental genes, along with similar findings for other families of genes involved in key developmental processes, provided an important impetus for the emergence of evo-devo as a discipline. Evo-devo also awakened a renewed interest in phylotypic stages [4], developmental stages shared by the species across entire phyla in spite of vast differences in the development and morphology before and after that stage, and coined the new concept of the zootype [10], a hypothetical ground plan for all bilaterian animals. These ideas were tied explicitly to the concept of the archetype, the idea of a common body plan that underlies the variation in a group (such as the vertebrates) that had been rejected vehemently by the main exponents of the New Synthesis [7]. Altogether, these discoveries have attracted new attention to structural factors.

Evo-devo has also revived structuralist arguments that emphasized the importance of generic physical factors [11,12], such as the forces driving morphogenetic movements, in the development and evolution of organismal forms. The combination of such factors with findings from developmental genetics has made it possible to formulate general models of pattern formation [13]. Models of this kind have been applied to the variation and morphological innovation in the patterns of mammalian tooth cusps [14] and have subsequently been confirmed experimentally [15].

Given its primary focus on large-scale phylogenetic comparison and developmental mechanisms generating variation, evo-devo has emphasized a structural and partly historical perspective on evolution, but has not concerned

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Box 1. Explanations in evolutionary biology

What counts as an explanation in evolutionary biology depends on the specific context. Explanations offered by studies of adaptation are different from those derived from phylogenetic analyses. Gould [6] has developed a graphical framework that is useful for thinking about evolutionary causation and constraints. He distinguished three primary kinds of causation in evolution—functional, historical and structural—and arranged them in a triangular diagram (Figure 1). Different types of study put the emphasis more or less on one of the corners of the diagram or between them.

The main emphasis in neo-Darwinian evolutionary biology is on functional aspects (Figure 1a). The goal is to understand how traits evolved by natural selection and how they contribute to fitness. Historical and structural factors act as constraints by setting boundary conditions in these explanations. In areas such as life-history studies, these factors have a relatively minor role by comparison, with the main aim being to document the adaptedness of different life-history strategies. By contrast, structural and historical factors have a prominent role in biomechanics or in studies using the phylogenetic comparative method for setting the context for functional explanations.

In evo-devo, the primary emphasis is on structural explanations (Figure 1b). The main goal of evo-devo is to understand how developmental mechanisms influence evolution and how these mechanisms themselves have evolved. Structural considerations about embryos and developmental processes have a central role in this endeavour. Studies such as the reconstruction of the zootype [10] clearly have a strong historical component, whereas comparisons of gene expression in more or less closely related species involve functional and historical components to some degree.

Unifying evo-devo and functional studies puts new emphasis on the lower side of the triangle (Figure 1). A comparison of Figures 1a and 1b shows that functional evo-devo is placed closely to biomechanics and related disciplines such as functional morphology. These specialties all combine structural and functional considerations, and the link between them therefore provides a promising new perspective to bring functional aspects into evo-devo. Biomechanics and functional morphology have clear criteria for establishing the functional performance of morphological traits. The challenge will be to apply those criteria to a context that explicitly considers the developmental origin of the traits.

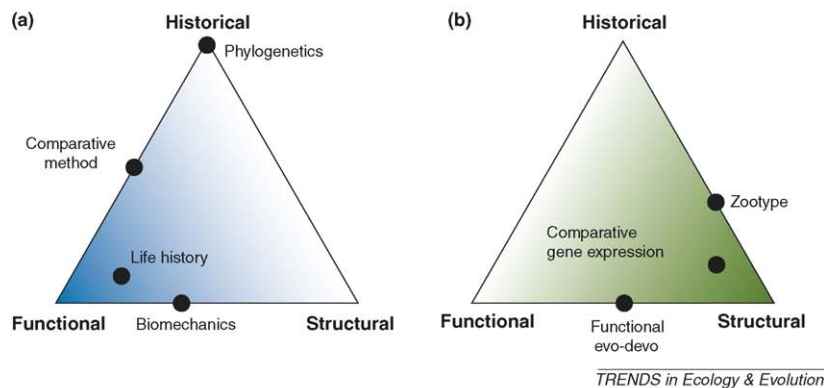


Figure 1. Differences in emphasis of explanatory factors (bold print) in different fields of evolutionary biology (dots). (a) Some of the traditional disciplines in evolutionary biology. (b) Some areas that have emerged as parts of evo-devo. The shading indicates the overall emphasis in neo-darwinian evolutionary biology (a) and in evo-devo (b).

itself with functional aspects. However, if the goal is to gain an integrated view of the role of development in evolution, the link to function is essential (Box 1).

Evo-devo researchers have begun to study the developmental basis of evolutionary changes with immediate adaptive significance such as the reduction of pelvic structures [16] and bony armour [17] in sticklebacks, the differences in beak shape among species of Darwin's finches [18], and divergence in jaw shape of cichlid fishes [19]. These are all examples of adaptive evolutionary change driven by natural selection, and therefore relate directly to the functions of the respective traits. A key challenge will be to make this relation more explicit.

Box 1 singles out biomechanics and functional morphology as disciplines where this kind of relation has been investigated already. These areas have a well established emphasis on performance as a measurable intermediate between morphology (or other phenotypic traits) and fitness [20]. Performance is an attribute of the organism and results from the function of a trait in a specific task. Performance can be measured in the laboratory or in the field, and established procedures exist for relating it to fitness [21]. The daunting challenge of relating development to function can therefore be rephrased as the more

tractable task of relating development to performance. This approach has only been adopted recently in a study linking the biomechanics of jaw movement in cichlid fishes explicitly to the quantitative and developmental genetics of mandibular shape [19].

There are alternatives to this way to bring functional considerations into evo-devo. Here, we outline work on developmental modularity and flexibility that also address function, albeit in a less direct manner.

Modularity

Biological systems consist of parts that are recognizable because they are integrated internally and are relatively distinct from other such parts [22,23]. In general, the concept of modularity refers to this property of integration within, and relative autonomy among, the parts or modules. Modularity is studied most often in a structural context, where it refers to the spatial arrangement of physical parts at different organizational levels from molecules to entire organisms. However, modularity also exists in contexts that are based on different kinds of interactions, such as pathways in metabolic networks, gene regulatory interactions, developmental and functional interactions among traits, and even behavioural interactions among individuals [24].

Box 2. Functional versus developmental modularity

It is difficult to evaluate empirically the hypothesis that developmental modules evolve adaptively to match functional modules [28,29] (here called the 'matching hypothesis') against the alternative that developmental modules are evolutionarily conserved features acting primarily as constraints [4]. The test has to rely on evidence provided by the comparison of multiple case histories.

The matching hypothesis predicts that functional and developmental modules evolve to coincide. It will therefore be necessary to compile lists of cases with matches and mismatches between functional and developmental modules. Developmental modularity can be inferred from information about the developmental organization of or from the covariation of the parts [23,26]. Functional modularity has to be inferred from other sources of information such as biomechanical analyses or studies of selection.

In many cases, developmental and functional modules will match. For instance, the forewing of a butterfly is a single developmental module that serves as a unit for functions such as flight and signalling (Figure 1a). This case is the one predicted by the matching hypothesis, but it is not informative by itself because it does not reveal the sequence of evolutionary changes that led to this state. Many other cases will also be problematic because the function is unclear or the developmental modularity is ambiguous (e.g. in the example of the hemelytra of a true bug; Figure 1b).

Informative cases involve a clear mismatch between functional and developmental modularity. Different parts of a single ancestral developmental module can have distinct functions. An example is the pitcher plant *Nepenthes*, where the tip of the leaf is transformed into the 'pitcher' for trapping insects (Figure 1c). If developmental modularity (e.g. as revealed by morphometric covariation) also follows this derived two-part modular structure, then the matching hypothesis is supported.

Another informative case is where several distinct ancestral developmental modules perform a single function. An example is the blossom of *Dalechampia*, which is an inflorescence consisting of several separate flowers and bracts that function together in pollination (Figure 1d). Integration among the parts of the blossoms is found, providing some support for the matching hypothesis [46]. Similarly, the scutellum and the basal part of the forewings of true bugs function together for protection (Figure 1b).

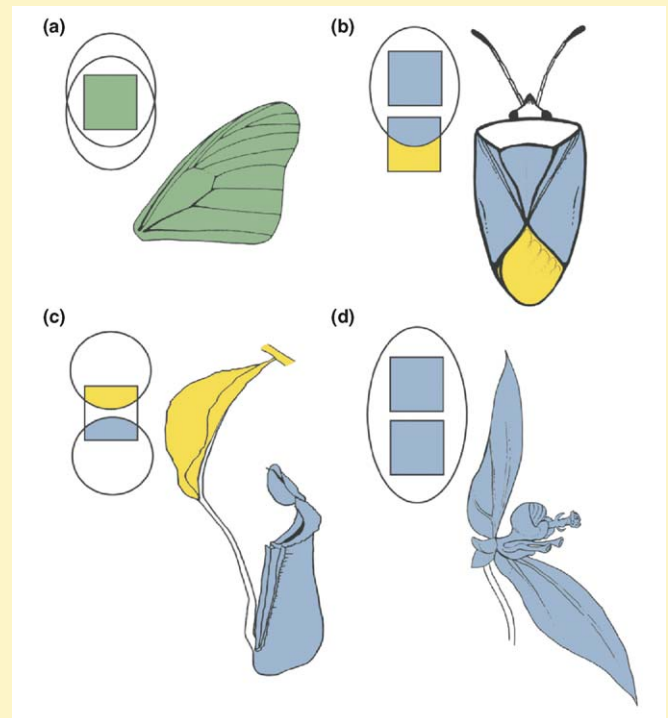


Figure 1. Comparison of the matching (a) or mismatching (b–d) of developmental modules (squares) and functional modules (ellipses). The putative different functions are indicated by different colours. (a) The butterfly forewing is involved as a whole in several functions (green). (b) The hemelytra and scutellum of a true bug. The scutellum and basal part of the forewing are involved in protection (blue), whereas the tip of the forewing is involved less clearly in this function (yellow). (c) Leaf of a *Nepenthes* pitcher plant. The basal part has retained the typical leaf-like structure and serves for photosynthesis (yellow), whereas the distal part is modified into the 'pitcher' functioning as an insect trap (blue). (d) A blossom of *Dalechampia*. The blossom is an inflorescence composed of different flowers and bracts that jointly function in pollination (blue). Drawing of *Dalechampia* blossom based on pictures generously supplied by C. Pélabon.

Developmental modules are integrated internally by developmental interactions between the components of the module, and the developmental processes within each module are relatively unaffected by the module's surroundings. In response to a developmental perturbation, component parts are therefore expected to covary only within a developmental module; the covariation among the resulting traits can therefore be used to infer developmental integration in various biological systems. This reasoning is used in studies inferring developmental modularity through the study of developmental mutants [25] or through the analysis of correlated asymmetry [26]. Because these developmental interactions also are involved in the expression of genetic variation, they are key determinants of patterns of pleiotropy [23].

A functional module is an integrated unit of traits serving a common function and is separable from other such units, which are associated with different functions. The interactions between traits that provide the coherence of modules are therefore of a functional nature, and usually are evolved by selection for optimal performance in that functional context. Functional interactions can be understood, for example, through biomechanical methods or by studying the arrangement of muscle insertions [19,27].

How functional and developmental modules relate to each other has been discussed extensively. One view is that developmental modules and the genetic architecture they determine are derived features that have been moulded by selection to match functional modularity [28,29]. Alternatively, developmental modules can be considered to be ancestral features that act potentially as developmental constraints influencing subsequent evolutionary changes [4,30]. These are not mutually exclusive alternatives, but the opposite ends of a spectrum of explanations. To distinguish between the possibilities, it is therefore important to compare developmental and functional modules (Box 2).

Modularity has often been used to illustrate the existence of developmental constraints, yet it can be argued just as easily that modularity in itself can be adaptive. The fact that developmental modules are independent developmentally and that functional modules are independent from surrounding traits in their fitness effects would enable rapid and specific adaptation to changing environmental conditions [28,31]. Modularity therefore contributes to the great flexibility of developmental processes and facilitates adaptive variation in developmental and functional units. The modular structure of butterfly wing patterns, for example, is often thought to have enabled not only the great diversity of

Box 3. Flexibility in eye development and evolution

The camera eyes of vertebrates and some cephalopod mollusks provide an example of the flexibility of development in arriving at a functional solution by transforming existing structures in different ways. Dibranchiate cephalopods, such as squid and octopus, have a camera-type eye that is similar to the vertebrate eye in its overall structure and function. But because the cephalopod eye develops differently from the vertebrate eye, it differs in one key aspect, namely the orientation of the photoreceptor cells [47,48] (Figure 1). The vertebrate eye develops from the neural plate as an evagination from the brain, whereas the cephalopod eye forms as an invagination of the ectoderm. This causes the photoreceptor cells in cephalopods to be directed towards the light source and those of vertebrate eyes to be facing in the opposite direction [47,48]. As a consequence of this arrangement in vertebrate eyes, the optic nerve passes through the retina and creates the 'blind spot', a suboptimal design that necessitated neurosensory and behavioral compensation [49]. This need for behavioural compensation of what appears to be a design flaw illustrates yet another form of flexibility associated with a functional structure: co-evolution of the eye and the associated neurosensory system.

A key feature of a camera eye is its lens, which is an example of a remarkable convergence by evolutionary tinkering. The lenses of both cephalopods and vertebrates consist of cells filled with soluble crystallin proteins, and that are packed together to form a concentration gradient from the periphery to the centre of the lens that produces the refractive index gradient necessary for a lens to be functional [48]. Although crystallins were long thought to be unique to lens tissue and to have evolved for this special function, more recent research suggests that they are co-opted proteins that are not specialized structurally for this function and are used in various other functional contexts as well [48]. Cephalopod lens tissue consists nearly entirely of the enzyme glutathione S-transferase, whereas 11 different vertebrate lens proteins have been identified and found to correspond to molecular chaperone proteins and various enzymes [48]. It appears, therefore, that the proteins destined to be used as lens crystallins were co-opted opportunistically from the available range of existing proteins.

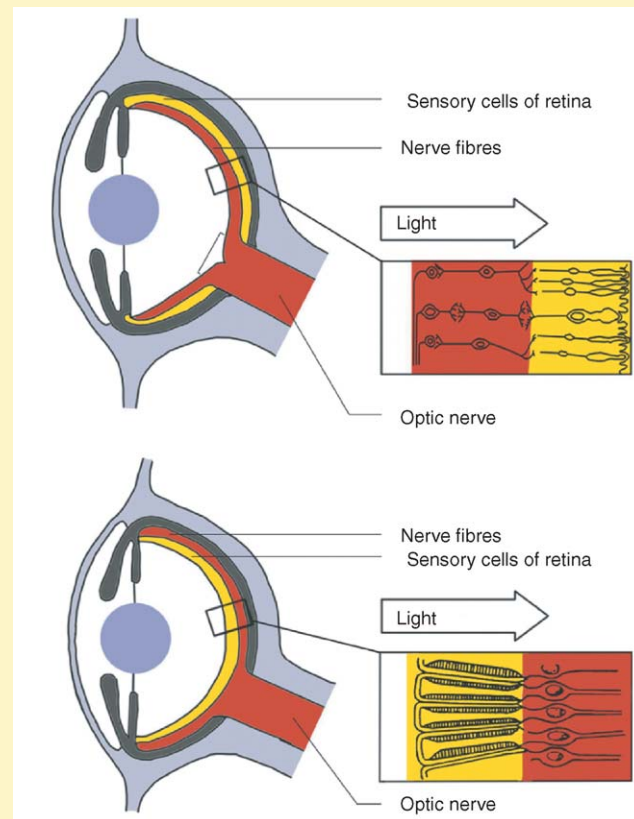


Figure 1. Diagrammatic cross-sections of a vertebrate and cephalopod camera-type eye. Modified with permission from [50].

colour patterns, but also the evolution of various adaptive features such as mimicry, mate selection, camouflage and seasonally polyphenic patterns [32].

Organisms as flexible functional systems

A common theme that has emerged from analyses in evo-devo and other areas of evolutionary biology is that organisms are flexible systems. If the surroundings of an organism change, its developmental systems provide the ability to adapt to achieve and maintain some function. This can be adaptation in either the physiological or evolutionary sense, and encompasses timescales from almost instantaneous physiological responses through reaction norms on an ecological timescale (the lifecycle of an individual) to adaptive responses of lineages over macroevolutionary timescales.

In evo-devo, the aspect of this flexibility that has received the most attention is 'evolutionary tinkering' [33,34]. To produce a new trait, natural selection does not start from scratch, but from what is already available: existing organs, tissues and cells, as well as existing genes and gene networks. This raw material often leads to surprising and sometimes suboptimal solutions to engineering problems. The inverted structure of the vertebrate retina (Box 3) or the evolution of the mammalian middle-ear ossicles from the jaw bones [35] are two examples. Evo-devo has provided these case studies not only with developmental genetic details, but has also shown that a similar

tinkering is occurring at the molecular level because genes can be co-opted in new contexts.

A gene (or a genetic network) can be co-opted independently in the formation of analogous traits in phylogenetically distant taxa. Among the most famous examples are the roles of *engrailed* in segmentation [36] and *distal-less* in the patterning of appendages [37,38]. In these cases, selection appears to have co-opted an already existing genetic network to perform a similar function [39] in a novel context (i.e. developmental exaptation [40]). One of the consequences of this process is that non-homologous structures can share developmental features, thereby complicating the detection of homology [41].

Another aspect of developmental flexibility that is just starting to be investigated in evo-devo is the maintenance of functionality under varying environmental conditions on an ecological timescale. Phenotypic plasticity, reaction norms and genotype-by-environment interactions are the labels under which this phenomenon has been studied so far. The developmental component of environmental reactions has begun to be fully integrated only recently [42], leading to the first cases of adaptive phenotypic plasticity that are well documented even at the molecular level. Examples of such integrations of developmental genetics and traditional evolutionary biology are the seasonal polyphenism in the butterfly *Bicyclus* [43] and the shade-avoidance syndrome in *Arabidopsis* [44].

Flexibility is a fundamental property of developmental and physiological systems that enables them to adapt to achieve new functions and to maintain them when the environment changes. Interestingly, these two aspects are not disconnected from each other; some authors have even argued that phenotypic plasticity, far from counteracting the effects of natural selection, provides selection with a wider spectrum of phenotypes to act upon, thereby facilitating adaptive evolution [45].

The way ahead for functional evo-devo

Combining structuralist and functionalist perspectives will facilitate a fuller understanding of evolutionary processes. To date, evo-devo has taken a mostly structuralist approach, whereas Neo-Darwinian evolutionary biology has taken the functionalist viewpoint. A full understanding of evolution requires the use of the entire conceptual space (see Box 1), and a fusion of functional aspects with evo-devo is therefore to be welcomed.

We have outlined two subjects, modularity and flexibility, in which the union of evo-devo with functional considerations is particularly straightforward. We do not imply that these two areas are the only ones in which a synthesis is possible, and we anticipate a wide range of research programmes exploring the interface between structural and functional aspects of evolution.

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