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 (e.g. 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...
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 I). 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 Ia). 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 Ib). 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 I). A comparison of Figures Ia and Ib 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 I. 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).
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...
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 polymorphism 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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References
3 Hall, B.K. (1992) Evolutionary Developmental Biology, Chapman & Hall
15 Kassai, Y. et al. (2005) Regulation of mammalian tooth cusp patterning by ectodin. Science 309, 2067–2070