Conceptualizing Evolutionary Novelty: Moving Beyond Definitional Debates

Ingo Brigandt[1*] and Alan C. Love[2]

[1]Department of Philosophy, University of Alberta, Edmonton, Alberta, Canada

[2]Department of Philosophy and Minnesota Center for Philosophy of Science, University of Minnesota, Minneapolis, Minnesota

[*]Correspondence to: Ingo Brigandt, 2-40 Assiniboia Hall, University of Alberta, Edmonton, AB T6G 2E7, Canada. Email: brigandt@ualberta.ca

Abstract

According to many biologists, explaining the evolution of morphological novelty and behavioral innovation are central endeavors in contemporary evolutionary biology. These endeavors are inherently multidisciplinary but also have involved a high degree of controversy. One key source of controversy is the definitional diversity associated with the concept of evolutionary novelty, which can lead to contradictory claims (a novel trait according to one definition is not a novel trait according to another). We argue that this diversity should be interpreted in light of a different epistemic role played by the concept of evolutionary novelty—the structuring of a problem space or setting of an explanatory agenda—rather than the concept's capacity to categorize traits as novel. This distinctive role is consistent with the definitional diversity and shows that the concept of novelty benefits ongoing investigation by focusing attention on answering different questions related to comprehending the origins of novelty. A review of recent theoretical and empirical work on evolutionary novelty confirms this interpretation.

Explaining the evolutionary origins of morphological novelty and behavioral innovation are central endeavors in contemporary evolutionary biology (Müller and Newman, 2005; Reader and Laland, 2003; West-Eberhard, 2003). These endeavors are not confined to a single methodological approach as a variety of biological disciplines contribute to ongoing empirical and theoretical efforts to shed light on various instances of novelty in different taxa. The evolution of several conspicuous novelties have been investigated for many decades, such as the origin of paired fins in fish and their transformation into limbs (Hall, 2006). Increasing attention is being devoted to less studied examples in diverse clades, such as the suction discs of ectoparasitic crustaceans (Kaji et al., 2011), the helmet morphology of treehoppers (Prud'homme et al., 2011), or the venom delivery system of centipedes (Dugon and Arthur, 2012). One reason for this broader array of examples is the growing potential for developmental biology to make crucial contributions to these explanatory endeavors. For example, developmental genetic experiments purport to show that the treehopper ‘helmet’ is a modified wing appendage on the first thoracic segment because appendage formation regulatory genes, such as *nubbin*, are no longer repressed by *Hox* genes—in this case, *Sex combs reduced* (Prud'homme et al., 2011; but see Mikó et al., 2012 for a critical review).

Despite this rapidly advancing body of research, the idea that ‘novelty’ and ‘innovation’ constitute core concepts related to a central explanatory agenda for evolutionary biology can be contested in at least two ways (Brigandt and Love, 2010). First, the claims that explanations of novelty represent a challenge to traditional evolutionary biology (Erwin, this issue; Laubichler, 2010), or that an enlarged conceptual framework that includes development is required (Müller and Pigliucci, 2010; Müller and Wagner, 2003; Wagner, 2000), are disputed by a number of biologists. For example, some hold that an evolutionary theory centered on population genetics is able to explain the origin of novelty just as it does the evolution of any other phenotype (Hoekstra and Coyne, 2007; Lynch, 2007), even if there are still open questions concerning how developmental biology or evo-devo relate to more traditional approaches within evolutionary biology (Minelli, 2010; Rice, this issue; Wagner, 2007).

Second, even among those who agree that explaining the origin of novelty is a distinctive and major aim of contemporary evolutionary research, there is little consensus about how exactly to define novelty or innovation. These differences in definition can be stark: a trait may qualify as a novelty on one definition, but not on another. Thus, there is disagreement over which traits should count as evolutionary novelties in the first place and thereby receive distinct explanatory attention. Although the emphasis has been on novelty as a qualitative departure from the ancestral condition, the existence of a continuum between a qualitative difference and a mere quantitative variant will always make it difficult to distinguish novelty from non-novelty in absolute terms; different biologists draw the line where they see fit (Brigandt and Love, 2010; Palmer, this issue). One common definition, due to Müller and Wagner ('91), asserts that a novelty is "a new feature in a group of organisms that is not homologous to a feature in an ancestral taxon" (Hall, 2005, p.549). Despite being fruitful in many contexts (e.g., agnathans versus jawed vertebrates), the identification of novelty with non-homology may not eliminate the conceptual continuum between novelty and non-novelty, especially if homology can come in degrees, as advocates of 'partial homology' argue (Minelli, '98, 2003; West-Eberhard, 2003). Empirically, even for those structures that appear to be qualitatively novel, there are always precursors or homologous features at lower levels, such as tissues, cells, or gene expression patterns (Hall and Kerney, this issue; Shubin et al., 2009).

In response to these difficulties, one might opt to replace a criterion derived from considerations about pattern (novelty as non-homology) with a criterion derived from considerations about mechanisms (novelty as brought about by new developmental processes or new gene functions). But this strategy would simply shift the burden to another hierarchical level of traits. For developmental processes, gene functions, and other mechanisms, the question remains—how much change qualifies as genuinely novel (Palmer, this issue)? Many novelties may have been created by rather minor rearrangements of developmental features: "we may be surprised by how much new is possible through modifications of the familiar" (Moczek, 2008, p.443). This vantage point seems to rob novelties of their privileged status in evolution, or at least suggests that once their origin has been explained they may not appear novel any longer: "the apparently novel evolutionary transitions … are reduced to a set of steps that appear more tractable" (Davis, this issue).

Thus, there are a variety of conceptual questions relevant to understanding the import of these vigorous and diverse empirical investigations of evolutionary novelties and innovations. How should we conceptualize evolutionary novelty? To what degree are diverse definitions of 'evolutionary novelty' the result of disciplinary differences or heterogeneous methodological and theoretical approaches? Is there a way to reconcile these differences and generate a consensus view? Does this impinge on different visions of how evo-devo is related to other areas of evolutionary biology? In the second half of the paper we will argue that this diversity should be interpreted in light of a different epistemic role played by the concept of evolutionary novelty—the structuring of a problem space or setting of an explanatory agenda—rather than the concept's capacity to categorize traits as novel or not. This distinctive role is consistent with the definitional diversity and shows that it benefits ongoing investigation by focusing attention on answering different questions related to comprehending the origins of novelty. Additionally, it helps to make explicit the different visions of how evo-devo is related to more traditional perspectives in evolutionary biology.

A Workshop Project on Novelty and Evo-Devo

The papers in this special issue (‘Perspectives on Evolutionary Novelty and Evo-Devo’) deal with how to construe novelty, what the nature of evo-devo is, and other associated questions from a variety of empirical, theoretical, and conceptual angles. They are the result of a workshop project that brought together biologists and philosophers from Canada and the US. The project was initiated from the perspective of philosophy of science because the issues that arise in the context of accounting for the origin of novelties make contact with more general questions about how integrative explanations using epistemic resources from different biological disciplines are developed. Philosophers have tended to conceptualize the relation among different disciplines primarily in terms of ‘theory reduction,’ which assumes that the knowledge of one or more areas of science can be logically deduced from a more fundamental theory, such as deriving the principles of classical genetics from molecular genetics or biochemistry (Brigandt and Love, 2012). Theory reduction proved to be an inadequate philosophical model for a variety of reasons, but one of the most significant was its inability to handle the complex relations among various aspects of biological disciplines, which have resisted the monolithic characterization of reducing one discipline to another. As a result, recent discussions have highlighted this complexity with a special emphasis on the integrative relations in the domains of cell biology and neuroscience (Bechtel, 2006; Craver, 2007; Darden, 2005).

Developmental evolution is another domain where the integration of disciplines and approaches can be studied philosophically (Brigandt, 2010; Brigandt and Love, 2010; Love, 2008a). Accounting for the evolutionary origin of novelty is a complex problem because intellectual resources—data, methods, and models (among other things)—from different biological fields have to be coordinated and synthesized to arrive at robust explanations for any single case, whether it be crustacean suction discs, treehopper helmets, or centipede venom delivery systems. One advantage of scrutinizing ongoing biological investigation is the possibility of obtaining insight by observing how the *process* of disciplinary integration works, rather than only examining integrative theories as the final *product* (a bias in many philosophical analyses of the sciences). Examining the scientific process of unraveling the origin of particular novelties, including the associated conceptual maneuvering involved in developing an explanatory framework, permits philosophers to identify intellectual and institutional factors that promote or hinder interdisciplinarity (Gerson, 2009). It also carves out a potential role for philosophers to contribute to the ongoing integrative endeavors of biologists through the avenue of conceptual clarifications or models for understanding the patterns of reasoning involved (one of which we will offer in the second part of the paper). At a minimum, interactions among philosophers and biologists can make the latter more reflective about their explanatory aims, the integrative strategies they rely on, and the presuppositions embedded in their conceptualizations.

Although accounting for the origin of novelty is just one endeavor that manifests the integrative potential of evo-devo to develop complex explanatory frameworks using different intellectual resources, the nature and future of this multidisciplinary configuration is still contested and undetermined. Evo-devo is often understood to be a synthesis of developmental biology and evolutionary biology—a “marriage between developmental biology and Darwinian theory” (De Robertis, 2008, p.194)—with developmental genetics providing the link between the two traditional fields (Carroll, 2005; Wilkins, 2002). From this perspective evolutionary change is understood in terms of gene regulation processes, with a special emphasis on *cis*-regulatory elements (Carroll, 2008; Davidson, 2006). Other evo-devo practitioners, however, do not focus exclusively on developmental genetics, and view other mechanisms as pertinent to explanations of the developmental generation of variation, including processes on several levels of organization (Hallgrímsson and Hall, 2011; Kirschner and Gerhart, 2005; Müller and Newman, 2003; Newman and Müller, 2000; Palmer, this issue; West-Eberhard, 2003). If the successful explanation of the evolution of a novelty requires contributions from several fields beyond population biology and developmental genetics (such as phylogeny, paleontology, morphology, and ecology), then evo-devo can be understood as a broader synthesis of many biological fields (Müller, 2007; Müller and Newman, 2005).

A major difficulty with the conception of evo-devo as a nascent 'synthesis' of several biological fields is the implication that the different disciplines and approaches *are* a single field or *should* merge to form a unified evo-devo. But key barriers remain, making this vision of a complete synthesis descriptively inaccurate: "we think devo-evo is still in a stage where the contributing disciplines are in conceptual discontinuity" (Wagner and Larsson, 2003, p.3; see also Larsson and Wagner, this issue). And even the prescriptive version—that different disciplines should merge into a whole—may be problematic. Wallace Arthur has argued for unifying evo-devo and allied disciplines in evolutionary biology: "If evo-devo is to come of age, its different component approaches need to become more closely intertwined, both with each other and with relevant strands of other disciplines" (Arthur, 2004, p.288; Rice, this issue, envisions a unification of evolution and development within an overarching mathematical framework). However, if evo-devo is construed as an *autonomous* discipline with its own questions, explanations, and methods (Hendrikse et al., 2007; Raff, 2000), then evolutionary biology appears to consist of several fields that should retain a significant degree of independence—a cohesively structured evo-devo and relatively disunified evolutionary biology. But views of how evo-devo can be internally unified may involve questionable presumptions about particular concepts being more central than others, such as evolvability (Hendrikse et al., 2007; Minelli, 2010) or gene regulatory networks (Laubichler, 2009; Linksvayer et al., 2012), which suggests that less restrictive characterizations that depict evo-devo as a constellation of evolutionary problems neglected by neo-Darwinism may be warranted (Love, 2010; Love and Raff, 2003).

Devoting effort to sorting out these questions about how to understand evo-devo is important because making progress on explaining evolutionary novelty may be connected with a particular perspective on evo-devo. For example, if a new or separate discipline focuses on the problem, then it may increase the likelihood that appropriate empirical methods and theoretical approaches are taught to the next generation, which could facilitate long-term research on evolutionary novelty. But the formation of a full-blown discipline with all of its social and institutional structures is a lengthy process. Evo-devo appears to be constituted in such a way as to resist this consolidation, which may be a part of its vitality and dynamic nature (Gerson, forthcoming).

The workshop project on novelty and evo-devo consisted of two meetings, the first one held in November 2009 at the University of Alberta in Edmonton (Brigandt and Love, 2010), followed by a second meeting in November 2010 at McGill University. Funded by the Social Sciences and Humanities Research Council of Canada, both workshops brought together biologists and philosophers of different stripes, with an eye to having diverse disciplines and heterogeneous approaches germane to explanations of novelty represented. The interactions at the workshops provided ample time for fruitful discussions on such topics as the nature of evo-devo and its relation to other biological fields, controversies about how to define ‘novelty,’ and the kinds of integrative explanatory frameworks that are needed to account for evolutionary novelty. The papers in this special issue that stem from these workshop interactions exhibit diversity with respect to the taxon studied, kinds of characters addressed, disciplinary approaches taken, theoretical concerns pursued, and definition of novelty favored. This diversity demonstrates that rich conceptual resources are available and being used, but at the same time it raises worries about whether a consensus definition of novelty is forthcoming, or even possible. In fact, a consensus definition may not be desirable (see below, ‘A Fruitful Role for the Concept of Novelty’).

Showcasing Diverse Perspectives on Novelty

As noted above, many evo-devo studies have focused on longstanding conundrums about novelties in vertebrates, such as the tetrapod limb. Nowadays there are also a variety of studies in invertebrate taxa that fall outside of the standard experimental models used in developmental biology, including the origin of mesoderm (Martindale et al., 2004) and epithelia (Fahey and Degnan, 2010), or teeth-like denticles in nematodes (Bento et al., 2010). The empirical papers in this special issue scrutinize novelties in aphids and sponges (Davis, this issue; Leys and Riesgo, this issue), and nearly all of the more conceptual contributions address several different metazoan cases, including traits found in lobsters, molluscs, earthworms, earwigs, and tubeworms (Hall and Kerney, this issue; Hallgrímsson et al., this issue; Larsson and Wagner, this issue; Palmer, this issue; Rice, this issue). Botanical examples are rare (but see the botanical literature, e.g., Niklas and Kutschera, 2009; Specht and Bartlett, 2009; Townsley and Sinha, 2012), though they are central to Erwin's discussion of ecology and macroevolution (Erwin, this issue). The thematic focus differs dramatically across the papers despite the common concern of evolutionary novelty: from phenotypic plasticity (Palmer) to offspring-parent phenotype covariation (Rice); from gene duplication and lateral gene transfer (Hall and Kerney) to use and disuse of organs (Palmer); from morphological and developmental considerations (Davis; Larsson and Wagner; Hall and Kerney) to the importance of functional integrity (Leys and Riesgo), behavior (Palmer), adaptation (Hallgrímsson et al.), or ecological role (Erwin).

The diversity of views in these discussions derives from at least two sources, and sometimes a mixture of both: (1) the distinctive aspects of different biological cases; and, (2) different theoretical or disciplinary perspectives. Empirical cases such as epithelia in sponges and life history traits in aphids guide the discussions of Leys and Riesgo (this issue) and Davis (this issue). Larsson and Wagner (this issue) address the theoretical question of how to make sound inferences via hypothesis testing about ancestral changes in development by probing a case where paleontological and embryological evidence appear to support conflicting evolutionary scenarios. Hallgrímsson et al. (this issue) develop a theoretical framework with four empirical examples that shows how novelty is a concern for evolutionary biology more generally (not just evo-devo) because it combines questions of developmental generation and adaptive benefit. Although Hall and Kerney (this issue) discuss more standard cases, such as the vertebrate fin-limb transition and the origin of neural crest cells, they also wrestle with cases that go beyond the scope of traditional evo-devo discussions, such as novelties due to lateral gene transfer. Common to all of these cases are conceptual issues about the nature and explanatory significance of hierarchy and levels of organization (Love, 2006). Palmer (this issue) offers a model for the evolution of novelty via phenotypic plasticity and behavior, which are conspicuous in the cases of morphological and functional asymmetry that he considers. The distinctiveness of macroevolutionary dynamics related to innovation motivate the paleontologist Erwin (this issue), who focuses on the long-term ecological success of taxa harboring certain novel traits. Rice (this issue), writing from the vantage point of mathematical evolutionary theory, departs from traditional evolutionary models (e.g., in rejecting the assumption of a single heritability parameter) and elegantly shows how developmental factors are essential to an adequate mathematical representation of population-level evolution based on drift and selection.

Most evo-devo studies dealing with novelty concentrate on structure; the definition in terms of non-homology encourages this (Müller and Wagner, ’91), as does evo-devo’s disposition to investigate morphological evolution (Raff, 2000). Although a functional orientation in evo-devo is rare (Breuker et al., 2006), it is noteworthy how many of the special issue contributions touch upon function. The notion of ‘function’ is used in different ways throughout the life sciences (Wouters, 2003), and two different (though not mutually exclusive) conceptions figure in the special issue. First, a function can be understood as an *activity* performed by one or several structures and is often referred to as the ability to perform this activity. An anatomical function is the activity performed by the coordinated interaction and movement of several anatomical structures, such as the movement of the jaw that might support the mastication of food in digestion or differentiate vocalizations in communication. A gene function is the expression pattern or regulatory activity of a gene, such as the metabolic enzymes that also serve as lens crystallins in different cellular contexts in vertebrates (Piatigorsky, 2007).

Functions in the sense of activities are bodily *components*, which as characters can be homologous to a function in other organisms and species (Amundson and Lauder, ’94; Love, 2007). Conversely, a function character is novel if it is not homologous to ancestral functions.

Leys and Riesgo (this issue) argue that the epithelium is a metazoan novelty based on their definition that the possession of an epithelium is the ability to seal and control the ionic composition of the internal milieu—a function or activity. This functional trait was already present in sponges, before the advent of eumetazoans, even though the same (homologous) basic function can be performed by a different set of specific structures in more derived eumetazoans. Hall and Kerney (this issue) touch upon the cotton root-knot nematode's ability to digest plant products, a physiological function, which arose from multiple lateral gene transfers. Davis (this issue) discusses cyclical parthenogenesis as an innovation of aphids, and the evolution of viviparity in a large aphid subtaxon. Cyclical parthenogenesis and viviparity are life history traits, and, as such, complex functions or abilities to perform specific activities.

A second notion of 'function' involves how a trait contributes to an organism's survival and reproduction, and thus which traits are favored by natural selection ('biological role' *sensu* Bock and von Wahlert '65). While a function understood as an activity is a trait internal to an organism, this second conception of function depends on relations to the external environment. Many evo-devo investigations concentrate on the developmental generation of variation that leads to novelty, often without explicit invocation of the fitness effects of a new trait. But several papers in this special issue address how novelties can evolve in the face of selection. Hallgrímsson et al. (this issue) combine development with the tenet that the evolution of novelty always involves a transition between adaptive peaks on a fitness landscape. Their discussion of the decrease in covariation between forelimb and hindlimb development during the origin of hominoids includes aspects of the adaptive benefit of this developmental change. Adaptive benefit is also central for Erwin (this issue), who argues that novelties which increase an ecosystem's carrying capacity have a significant long-term impact by creating positive feedback loops that generate self-propagating radiations. Selective dynamics are central to Palmer's (this issue) argument that the use and disuse of behaviorally plastic traits (during an organism's lifetime) is a way in which phenotypic innovation increases the probability of highly adaptive phenotypes. From the vantage point of mathematical representation, Rice (this issue) uses a population-based theoretical framework to capture how novel traits can become subject to selection, such as through changes in a trait's heritability.

Different Legitimate Definitions of Novelty?

Even among those who deem the explanation of evolutionary novelty and innovation to be a distinctive task for contemporary evolutionary biology, different definitions of novelty have been put forward and are on display in the contributions to this special issue. These diverging definitions not only differ on which particular traits are classified as novel, but also arise from different but legitimate explanatory concerns. This makes it unlikely that a single, consensus definition of novelty will be able to encompass the various conceptual aspects that make each definition fruitful, both theoretically and empirically.

By stipulating that a novelty is a trait "not homologous to a feature in an ancestral taxon," Sally Leys and Ana Riesgo (this issue) endorse a common perspective on novelty (Müller and Wagner, '91, 2003), which Brian Hall and Ryan Kerney (this issue) echo when asserting that "a novelty is a new feature (structure, or behavior) in a group of organisms (taxon) that is not homologous to any feature in any taxon in the ancestral lineage." Greg Davis (this issue) adds a related emphasis—qualitative versus quantitative patterns of variation: "novelties are qualitatively new structures that lack homologous counterparts in related taxa." There is a clear theoretical motivation for such a definition, as it highlights the special burden of explaining the origin of a structure that is not just a modification of an ancestral homologue: “quantitative change is only part of the story of evolution, for it does not address the question of the origin of discrete (qualitatively different) novelties” (West-Eberhard, 2003, p.6; see also Müller and Wagner, 2003). Despite the above-mentioned difficulty of unambiguously identifying non-homology apart from precursors (which there will always be), these authors succeed in using this construal of novelty to shed light on their concrete empirical cases.

The criterion of non-homology makes a trait’s novelty a matter of what traits were historically present in a lineage. There are also forward-looking definitions that characterize novelty in terms of what can happen to the trait or what the trait can make happen in the future. For example, a trait is a novelty if it provides potential for future morphological variation and diversification (‘evolvability’) that did not previously exist (Brigandt, 2007; Müller and Wagner, 2003; Wagner and Larsson, 2006; Wagner and Stadler, 2003). The notion of a key innovation is typically applied to new structures or functions that permit future adaptive radiations (Bock and von Wahlert, ’65; Galis, 2001; Liem, ’73). Doug Erwin (this issue) expands this perspective significantly. Beyond the mere enlargement of species diversity, Erwin stresses how novelties can increase an ecosystem’s carrying capacity. As a result, they have a significant *ecological* impact on a macroevolutionary scale via niche construction and ecosystem engineering through the creation of positive feedback loops.

More formally, Sean Rice (this issue) offers a definition that emphasizes a trait’s future evolutionary potential by stipulating that a “novel evolutionary trait appears when there is a change in the expected offspring–parent distribution for some character of an organism, such that there is sufficient heritable variation in that character for it to evolve under selection or drift.” Since a trait’s heritability is a function of the trait’s environment, a paradoxical implication emerges: a trait can become a novelty without any change in its phenotypic characteristics (as long as the trait's heritability—and thus its ability to be propagated by natural selection—changes from negligible to significant). This is at odds with definitions of novelty in terms of qualitative structural change. But Rice defends this approach in terms of its fruitfulness for explaining phenotypic change on the population level. He offers an analogy with species definitions whose explanatory impact is tied to accounts of speciation via underlying mechanisms, such as the presence or disruption of interbreeding and gene flow. Just as Rice's definition of novelty does not require phenotypic change, so also these species definitions do not require phenotypic (dis)similarity (a different criterion used by other species definitions).

Definitions of novelty as non-homology do not mention natural selection and are often intended to explicitly exclude issues surrounding adaptation (Müller and Newman, 2005; Müller and Wagner, '91, 2003). In addition to Rice's (this issue) conceptualization, a definition that makes selection a key part of the criteria for novelty is advanced by Benedikt Hallgrímsson and collaborators (this issue): "for a feature to be novel it must have evolved both by a transition between adaptive peaks on the fitness landscape and … overcome a previous developmental constraint." The second part of this two-sided account (significant changes in development) is a proxy for the more common idea of non-homology and qualitative departure from the ancestral condition, while the first part involves fitness and adaptive peaks. Hallgrímsson et al. argue that the theoretical virtue of integrating developmental and adaptive factors into the definition of novelty is to span two dimensions of inquiry—the generation of variation and the large-scale transitions observed in the fossil record. The distinctive inclusion of changes in adaptive regimes also shows how novelty is a core issue not just for evo-devo but also for evolutionary biology.

All of these definitions are allied with theoretically significant issues but may differ on which traits are classified as novel. What should be done about this conflict? Can one simply eliminate the definitional diversity that has surrounded studies of evolutionary novelty, perhaps by isolating the most appropriate definition or unifying all of them? Our alternative suggestion is to move away from the conceptual role of *definitions*—classifying and delineating the set of entities a term applies to ('categorization')—and to focus on the structuring of a problem space or setting of an explanatory agenda. This brings to the fore questions about what counts as an *adequate explanatory framework*, a clear motivator in all of these discussions, whether in terms of developmental mechanisms, the adaptive advantage of anatomical functions, or ecological interactions. Focusing on the nature and structure of questions addressed by research on evolutionary novelty and articulating criteria of explanatory adequacy may reveal common ground among different researchers in the midst of definitional disagreements about which traits are novelties (Brigandt and Love, 2010; Palmer, this issue), and thereby highlight the fecundity of this perspective for ongoing theoretical and empirical inquiry.

How Problem Agendas Structure Integration

The preceding discussion makes clear that the concepts of evolutionary novelty and innovation do more than categorize phenomena. Their animating conceptual role is the setting out of an explanatory agenda for scientific investigation with respect to questions neglected by neo-Darwinism surrounding the evolution of development and the causal impact of ontogenetic processes on evolutionary trajectories. How does this work? What does it mean to say that the concept of novelty plays a role in structuring a problem space or agenda? The first item to unpack is the idea of a *problem agenda*. We can begin with some overlooked observations made by Karl Popper that have nothing to do with falsification.

In *Conjectures and Refutations*, Popper argued that as scientists, “we are not students of some subject matter but students of problems” (Popper, 2002 [’63], p.88). This by itself is unsurprising and commonly noted, but Popper combined it with another observation from the history of science about the architecture of progress: “from problems to problems—to problems of ever increasing depth” (p.301). For a problem to have ‘increasing depth,’ it cannot be equated with a standard interrogative; biological problems—such as how cells differentiate or how evolutionary novelties originate—are not single questions similar to interrogatives like “who won the World Cup?” Biological problems constitute an agenda, a list of things that need to be addressed or multiple, interrelated questions, which have grown up over time and one sense of problem depth is captured by the structure visible through extended *historical* debate (Hattiangadi, ’78, ’79). Another sense of problem depth is in terms of epistemic *heterogeneity* (Laudan, ’77), such as the difference between an empirical question (e.g., the extent of cryptic variation) and a theoretical question concerning complex relationships among concepts (e.g., how do we understand the relationship between genetic variation and phenotypic variation in evolutionary theory?). Finally, depth also can be understood in terms of nested *hierarchies*, with problems containing sub-problems or definable arrays of questions that can be thought of as parts to the whole (Nickles, ’81).

Although history, heterogeneity, and hierarchy are abstract labels, we can translate this perspective into a more concrete description with an explicit analogy to anatomy. A hand, as an anatomical unit, is composed of a variety of parts (heterogeneity) at different levels of spatial organization (hierarchy) that are the result of evolutionary processes (history). Heterogeneity is manifested at different hierarchical levels: anatomical parts (digits, palm), organ systems (skin, nervous, circulatory), tissue types (epidermis, bone, blood vessels, collagen), cell types (nerve, muscle, skin, blood), and biochemical components (DNA, proteins, sugars). The history of selection pressures and inheritance structure from common ancestors accounts for arrangements of these parts at different levels. The analogy to anatomy underwrites our linguistic choice for an epistemology of the sciences: there is *an anatomy of problems* in biology.

What constitutes the epistemic history, heterogeneity, and hierarchy of a problem agenda like the origin of evolutionary novelty? We have already observed that the recent *history* of evo-devo explicates some of what is central to thinking about explanations of evolutionary novelty, and is visible in how researchers have discussed it: "evolutionary innovations are outside the scope of any current research program. Through its contribution to the solution of that question, [evo-devo] genuinely expands the explanatory range of evolutionary theory" (Wagner et al., 2000, p.822). To the extent that 20th century neo-Darwinian theory recognized the evolution of novelty as a problem at all, it assumed that population genetic processes were explanatorily sufficient. Only more recently has the developmental generation of structure been added as an explicitly recognized criterion for any adequate explanatory framework: "it is essential to include developmental mechanisms in the explanation of evolutionary innovations. … this is also the reason why developmental evolution makes an indispensable contribution to evolutionary biology" (Wagner, 2000, p.97). This historical controversy shapes the problem agenda of evolutionary novelty through debate about the need for different disciplinary contributors to answer distinct and previously neglected or downplayed questions, including phylogeny and paleontology (to reconstruct character polarity, ancestral character states, and transitional stages) and morphology (to determine the compositional identity of a feature and performance conditions for activities). The articles in this special issue display this historical aspect of problem structure in that they rely on disciplinary approaches and methods that are not typically associated with population-based evolutionary explanations, and when they do (Rice, this issue) it involves a departure from the standard theoretical apparatus. Historical debate indicates part of the problem agenda structure, such as the agenda's component questions and the currently recognized criteria of explanatory adequacy.

The *heterogeneity* aspect of problem agenda anatomy can be understood in terms of the different types of questions found in the agenda and the various necessary intellectual contributions for answering them. Empirical questions ('what regulatory genes control appendage formation?') are answered differently than theoretical questions ('how is pleiotropy represented in a mathematical model?'); pattern questions ('what is the phylogenetic juncture for understanding jaw origins?') are answered differently from process questions ('how can changes in *cis*-regulatory binding sites contribute to heterotopy?'). Questions about the cellular level of organization differ from questions about the anatomical level of organization; questions about the origin of features early in ontogeny (e.g., asynchronous cleavage) differ from questions about the origin of features that occur later in ontogeny (e.g., metamorphosis). This list is not exhaustive but it makes clear that different disciplinary approaches and methods will be required to address this heterogeneous set of questions in the problem agenda. The focus of one discipline on some questions rather than others creates a fruitful division of labor and organizes different lines of investigation in terms of the kinds of questions they tackle.

The final structural aspect of problems, *hierarchy*, highlights that the different components of a problem agenda stand in systematic relations. This systematic structure provides a template that indicates how the various explanatory contributions are to be coordinated and integrated, so that reflecting on the structure of the problem agenda makes clear how an overall explanatory framework can be generated (Brigandt, 2010; Love, 2008a). Some aspects of hierarchy can be cashed out in terms of two standard epistemological dimensions: abstraction and generalization (Love, 2008b). Questions that are more abstract (‘how is variation generated?’ or ‘how can complex traits overcome developmental constraints?’) can be seen as higher up in the hierarchy of the problem structure than others (‘how is gene regulatory network variation generated?’ or ‘how can post-cranial skeletal traits overcome developmental constraints due to pleiotropy?’). But since more concrete questions involve distinct biological processes (‘how is gene regulatory network variation generated?’ versus ‘how is epigenetic variation generated?’), the ability to offer an explanatory framework at the desired level of abstraction requires diverse methodological approaches. Questions that are more general (‘how do novelties originate in metazoans?’) can be seen as higher in the hierarchy of problem structure than others (how do novelties originate in mammals?). But since more specific questions involve clade-level differences, appropriately diverse taxa must be studied and the results judiciously compared. Otherwise, any explanatory framework will be fragmentary and therefore less illuminating of how novelties originate.

Even when the investigative focus is on the origin of a particular novelty in one taxon, the necessity of coordinating diverse epistemic components to address multiple related questions remains. Because a morphological structure develops based on prior changes in lower level traits (e.g., gene transcription, cell migration), an account explaining the generation of this structure is in terms of these mechanistic interactions among lower and higher level features. Because an anatomical function (e.g., tetrapod limb movement) involves various structures that articulate and interact in specific ways, an explanation of the innovation’s evolution is guided by the relation among the anatomical function’s components. And, because the precise phylogenetic pattern leading up to a novelty (character transformations at particular junctures) has to be settled prior to assessing which developmental mechanisms contributed to the evolutionary transition, the architecture of the problem agenda not only requires different approaches (paleontology, phylogeny, developmental biology) but also shows *how* contributions from different approaches are to be integrated. Thus, the hierarchical structure of a problem agenda provides a scaffold upon which to insert the relevant disciplinary contributions.

Another way to understand the structure of a problem agenda is in terms of the agenda's associated *criteria of explanatory adequacy*, which organize research because ongoing inquiry is directed at fulfilling these criteria. For example, the emphasis on the adaptive modification of traits in much neo-Darwinian population biology led to a neglect of questions about the origin of structure. The stress on the need to explain the origin of new morphological units in the problem agenda of novelty corresponds to an attempted correction of this functional bias. And the emphasis in the special issue papers on functional aspects surrounding the origin of new characters serves as a corrective to an overly structural conception of explaining novelty. This historical dialectic corresponds to a criterion of adequacy: any adequate explanatory framework for the origin of new characters *must address both morphology (form) and function*. Since different disciplinary approaches engage form and function with a variety of theoretical and empirical methods, this criterion of adequacy prompts an integrated explanatory account of novelty and innovation.

Similarly, we can derive at least two other criteria of adequacy for the problem agenda from heterogeneity and hierarchy considerations. The first is that any adequate explanatory framework for the origin of new characters *must be sufficiently abstract and general.* The demand of abstraction requires that the necessary disciplinary contributions have been made, such as the developmental generation of variation being investigated using methods from quantitative genetics, developmental genetics, epigenetics (broadly construed), and phenotypic plasticity. An important part of the needed integration is an explicit articulation of the relations among the levels these methods concentrate on: “An understanding of complex evolutionary transitions thus requires integration at the genetic, developmental, and morphological levels” (Davis, this issue). The demand of generality requires that diverse characters in different clades are investigated using many methods (as evidenced in the special issue papers), and that appropriate proxies for extinct taxa are utilized in experimental research with full knowledge of their epistemic limitations (Metscher and Ahlberg, ’99). Investigations of model systems raise issues about the inference from contemporary experimental contexts to distant events in the past (Larsson and Wagner, this issue). It also requires that successful explanatory proposals for particular novelties (e.g., tetrapod limbs) be evaluated with respect to their applicability to other characters (e.g., suction discs in crustacean ectoparasites). Are discussions of cryptic variation derived from studies of yeast relevant to morphological asymmetry in metazoans (Palmer, this issue)?

The other criterion of adequacy we can derive is that any adequate explanatory framework for the origin of new characters *must exhibit sufficient complexity and balance*. Although this might seem counterintuitive (shouldn’t explanatory frameworks be governed by a principle of parsimony?), the *complexity* invoked is about matching the heterogeneous questions in the problem agenda with corresponding answers. It goes hand in hand with the *balance* of the explanatory framework, which should handle empirical and theoretical questions, not neglect pattern questions for process questions, deal with lower levels of organization as well as higher levels, and address later moments in ontogeny in addition to earlier ones. Here also we can see an interactive effect among the criteria of explanatory adequacy because complexity and balance will be secured through attending to both form and function, and through achieving a framework that is sufficiently abstract and general.

These criteria of explanatory adequacy for the problem agenda describe a role for the concept of evolutionary novelty that goes far beyond the categorization of traits into novel or non-novel. We now have a clear-cut rationale for the multi-disciplinary prerequisites involved in explaining novelty, something Popper glimpsed for scientific problems more generally: “problems may cut right across the borders of any subject matter or discipline” (Popper, 2002 [’63], p.88). Convincing explanations require substantive natural historical knowledge of a species (Davis, this issue), combine histology, morphology, physiology, molecular genetics, and phylogeny (Leys and Riesgo, this issue), and address the relation of characters at different levels of organization (Larsson and Wagner, this issue) to generate substantive conclusions.

Significant procedural lessons can be drawn about explanatory integration across disciplines from this model of problem agendas. For example, productive explanatory integration occurs more readily by starting in the context of a specific question (avian digit homology), rather than at a global level (the developmental basis of evolution). The concreteness and specificity of these more ‘local’ research problems facilitate a more transparent picture of what actual intellectual contributions are needed for an adequate explanation; different novelties at different levels of organization may require different explanatory ingredients in different combinations and thus the complexity and balance criterion can be approached through a piecemeal synthesis of local explanatory integrations of distinct disciplinary approaches. This suggests that successful multidisciplinary coordination with respect to different problems may involve different integrative relations across fields (Brigandt, 2010). As a consequence, we can relinquish the aim of securing a single set of theoretical relations between evolutionary biology and developmental biology (as well as other fields). Not only is this an unproductive strategy for evo-devo inquiry;

it also may be wholly unnecessary.

A Fruitful Role for the Concept of Novelty

In conclusion, it is worth returning to the question of how our discussion of problem agendas can clarify the debate about different definitions of novelty and helps us move beyond it. Scientific concepts can have many different epistemic functions: concepts can classify objects, explain phenomena, and structure explanatory agendas. Some of these functions involve providing definitions, as a definition specifies which entities fall under a concept (a reason why a precise definition is preferable). However, a concept that primarily sets a problem agenda does not earn its keep through categorizing objects in the natural world, but by structuring ongoing investigation. It guides explanatory endeavors and provides standards for seeking an adequate explanatory framework. These standards or criteria of explanatory adequacy appear in historical debates, the heterogeneity of component questions, and the hierarchical structure of a problem agenda. As a result, discussions on how to explain evolutionary novelty should not be conducted in terms of which definition to choose. Rival proposals about how to define ‘evolutionary novelty’ tend to obscure the issue of how the problem agenda of novelty structures inquiry—something on which there is more agreement than on the question of which particular features are novelties. By separating issues that tend to be conflated and highlighting features that tend to be neglected, these philosophical considerations can play a therapeutic role for science (Wimsatt, 2007).

For example, overreliance on single definitions can be a sign of bias in the methodologies utilized or questions asked in a problem agenda, and thus we can reinterpret the definitional diversity with respect to novelty positively, as an indicator of fruitful research. This achievement requires that we shift our attention away from the definitional role of concepts to their role in setting a problem agenda in scientific investigation. The status of explanatory proposals as complementary or competing can be evaluated because answers to questions about the evolutionary origin of a new trait in terms of developmental genetic mechanisms and changes in organismal development (including epigenetic mechanisms; see Müller and Newman, 2005; Newman and Müller, 2000) need not be in conflict with answers to questions about its subsequent spread and adaptive improvement, even when dealing with functions rather than structures. Leys and Riesgo (this issue) construe the epithelium as a function-feature (the ability of tissues to seal) and argue that the epithelium is a novelty of metazoans because this cellular function is not present in the ancestor (i.e., non-homology). This functional definition of a character does not exclude the problem of accounting for its evolutionary origin in terms of changes in cellular-developmental mechanisms.

Conversely, even a structural definition of novelty (e.g., novelties as structures non-homologous to any ancestral structures) does not mandate an explanation purely in terms of developmental-structural changes. Gerd Müller ('90) endorsed a definition that counted only structures as novelties (apparently with the intent of focusing on explanation in terms of development rather than adaptation), yet it is still possible to ask how such a novel structure evolved based on the operation of natural selection. A case in point is the approach of Benedikt Hallgrímsson and collaborators (this issue), who persuasively argue that evolutionary novelty is not just an issue for evo-devo, but a core concern for evolutionary biology more generally, because accounting for novelty requires attention to both developmental generation and adaptive benefit. But this does not require that we adopt their stated *definition* of novelty (a trait is novel only if it has "evolved both by a transition between adaptive peaks on the fitness landscape and

… overcome a previous developmental constraint”) because “it applies broadly to the kinds of transitions that are commonly classified as novel.” The concept of evolutionary novelty sets a structured explanatory agenda that is scientifically fruitful apart from our intuitive notions of which traits count as evolutionary novelties.

None of this precludes serious disagreements about what the problem agenda of novelty and innovation involves. For example, does it include considerations about natural selection, and if so, in what way? But these issues are best addressed in terms of *the structure of the problem agenda*, not the separate issue of how best to define ‘novelty’ and determine which traits are genuinely novel. Philosophers of science can make a contribution in this context by emphasizing that an initially implicit or vague problem agenda needs to be made more explicit and clear (Love, 2008b). Our discussion of historical, heterogeneous, and hierarchical problem agenda structure and the criteria of explanatory adequacy is one such attempt at this kind of a contribution. Consensus among biologists and progressive engagement with the problem agenda is most likely to occur when explanatory aim(s) are articulated precisely, their scientific significance is widely comprehended, and the standards that determine the elements and structure of an adequate and integrated explanatory framework are as explicit as possible. The problem agenda of novelty and innovation is not preformed by the mere existence of the term ‘evolutionary novelty’, but takes on shape and internal order by deliberate and discursive problem explication (Love, 2008b).

We have emphasized that a scientific concept can fulfill a variety of epistemic functions. Classifying objects and picking out phenomena by means of a definition is one of them; setting a problem agenda is another. Agreement about the structure of the problem agenda of evolutionary novelty and innovation is possible, even if it is not settled which traits ought to count as novel, and thus accounts of the evolutionary origin of a trait that fulfill the criteria of explanatory adequacy are genuine achievements, regardless of whether the trait is labeled a ‘novelty’ by a certain definition (Brigandt and Love, 2010). By setting a problem agenda that structures ongoing inquiry, the concept of evolutionary novelty plays a fruitful epistemic role in evolutionary biology that is fully consistent with, if not supported by, the diversity of definitions for which characters count as evolutionary novelties.

Acknowledgements

We thank an anonymous referee for useful suggestions on an earlier draft of this essay. Ingo Brigandt's work was supported by the Social Sciences and Humanities Research Council of Canada (Standard Research Grant 410-2008-0400). Alan Love's work is supported in part by a grant from the John Templeton Foundation ("Complexity, emergence and reductionism: toward a multilevel integrative analysis of the brain and cognition"; ID 24426).

Literature Cited

Amundson R, Lauder G. 1994. Function without purpose: the uses of causal role functions in evolutionary biology. Biology and Philosophy 9:443-469.

Arthur W. 2004. The effect of development on the direction of evolution: toward a twenty-first century consensus. Evolution & Development 6:282-288.

Bechtel W. 2006. Discovering Cell Mechanisms: The Creation of Modern Cell Biology. Cambridge: Cambridge University Press.

Bento G, Ogawa A, Sommer RJ. 2010. Co-option of the hormone-signalling module dafachronic acid-DAF-12 in nematode evolution. Nature 466:494-497.

Bock WJ, von Wahlert G. 1965. Adaptation and the form-function complex. Evolution 19:269-299.

Breuker CJ, Debat V, Klingenberg CP. 2006. Functional evo-devo. Trends in Ecology and Evolution 21:488-492.

Brigandt I. 2007. Typology now: homology and developmental constraints explain evolvability. Biology and Philosophy 22:709-725.

Brigandt I. 2010. Beyond reduction and pluralism: toward an epistemology of explanatory integration in biology. Erkenntnis 73:295-311.

Brigandt I, Love AC. 2010. Evolutionary novelty and the evo-devo synthesis: field notes. Evolutionary Biology 37:93-99.

Brigandt I, Love AC. 2012. Reductionism in biology. In: Zalta EN, editor. The Stanford Encyclopedia of Philosophy. http://plato.stanford.edu/entries/reduction-biology

Carroll SB. 2005. Endless Forms Most Beautiful: The New Science of Evo-Devo. New York: W.W. Norton.

Carroll SB. 2008. Evo-devo and an expanding evolutionary synthesis: a genetic theory of morphological evolution. Cell 134:25-36.

Craver CF. 2007. Explaining the Brain: Mechanisms and the Mosaic Unity of Neuroscience. Oxford: Oxford University Press.

Darden L. 2005. Relations among fields: Mendelian, cytological and molecular mechanisms. Studies in History and Philosophy of Biological and Biomedical Sciences 36:349-371.

Davidson EH. 2006. The Regulatory Genome: Gene Regulatory Networks in Development and Evolution. San Diego: Academic Press.

Davis GK. this issue. Cyclical parthenogenesis and viviparity in aphids as evolutionary novelties. Journal of Experimental Zoology (Molecular and Developmental Evolution) DOI:10.1002/jez.b.22441.

De Robertis EM. 2008. Evo-devo: variations on ancestral themes. Cell 132:185-195.

Dugon MM, Arthur W. 2012. Comparative studies on the structure and development of the venom-delivery system of centipedes, and a hypothesis on the origin of this evolutionary novelty. Evolution & Development 14:128-137.

Erwin DH. this issue. Novelties that change carrying capacity. Journal of Experimental Zoology (Molecular and Developmental Evolution) DOI:10.1002/jez.b.21429.

Fahey B, Degnan BM. 2010. Origin of animal epithelia: insights from the sponge genome. Evolution & Development 12:601-617.

Galis F. 2001. Key innovations and radiations. In: Wagner GP, editor. The Character Concept in Evolutionary Biology. San Diego: Academic Press. p. 581-605.

Gerson EH. 2009. Specialty boundaries, compound problems, and collaborative complexity. Biological Theory 4:247-252.

Gerson EM. forthcoming. The interaction of research systems in the evo-devo juncture. In: Love

AC, editor. Conceptual Change in Biology: Scientific and Philosophical Perspectives on Evolution and Development. Berlin: Springer.

Hall BK. 2005. Consideration of the neural crest and its skeletal derivatives in the context of novelty/innovation. Journal of Experimental Zoology (Molecular and Developmental Evolution) 304B:548-557.

Hall BK, editor. 2006. Fins into Limbs: Evolution, Development and Transformation. Chicago: University of Chicago Press.

Hall BK, Kerney R. this issue. Levels of biological organization and the origin of novelty. Journal of Experimental Zoology (Molecular and Developmental Evolution) DOI:10.1002/jez.b.21425.

Hallgrímsson B, Hall BK, editors. 2011. Epigenetics: Linking Genotype and Phenotype in Development and Evolution. Berkeley: University of California Press.

Hallgrímsson B, Jamniczky HA, Young NM, Rolian C, Schmidt-Ott U, Marcucio RS. this issue. The generation of variation and the developmental basis for evolutionary novelty. Journal of Experimental Zoology (Molecular and Developmental Evolution) DOI:10.1002/jez.b.22448.

Hattiangadi JN. 1978. The structure of problems, part I. Philosophy of the Social Sciences 8:345-365.

Hattiangadi JN. 1979. The structure of problems, part II. Philosophy of the Social Sciences 9:49-76.

Hendrikse JL, Parsons TE, Hallgrímmson B. 2007. Evolvability as the proper focus of evolutionary developmental biology. Evolution & Development 9:393-401.

Hoekstra HE, Coyne JA. 2007. The locus of evolution: evo devo and the genetics of adaptation. Evolution 61:995-1016.

Kaji T, Møller OS, Tsukagoshi A. 2011. A bridge between original and novel states: ontogeny and function of "suction discs" in the Branchiura (Crustacea). Evolution & Development 13:119-126.

Kirschner MW, Gerhart JC. 2005. The Plausibility of Life: Resolving Darwin's Dilemma. New Haven: Yale University Press.

Larsson HCE, Wagner GP. this issue. Testing inferences in developmental evolution: the forensic evidence principle. Journal of Experimental Zoology (Molecular and Developmental Evolution) DOI:10.1002/jez.b.22458.

Laubichler MD. 2009. Form and function in Evo Devo: historical and conceptual reflections. In: Laubichler MD, Maienschein J, editors. Form and Function in Developmental Evolution. New York: Cambridge University Press. p. 10-46.

Laubichler MD. 2010. Evolutionary developmental biology offers a significant challenge to the neo-Darwinian paradigm. In: Ayala F, Arp R, editors. Contemporary Debates in the Philosophy of Biology. Malden: Wiley-Blackwell. p. 199-212.

Laudan L. 1977. Progress and its Problems: Towards a Theory of Scientific Growth. Berkeley and Los Angeles: University of California Press.

Leys SP, Riesgo A. this issue. Epithelia, an evolutionary novelty of metazoans. Journal of Experimental Zoology (Molecular and Developmental Evolution) DOI:10.1002/jez.b.21442.

Liem KF. 1973. Evolutionary strategies and morphological innovations: cichlid pharyngeal jaws. Systematic Zoology 22:425-441.

Linksvayer TA, Fewell JH, Gadau J, Laubichler MD. 2012. Developmental evolution in social insects: regulatory networks from genes to societies. Journal of Experimental Zoology (Molecular and Developmental Evolution) 318:159-169.

Love AC. 2006. Evolutionary morphology and evo-devo: hierarchy and novelty. Theory in Biosciences 124:317-333.

Love AC. 2007. Functional homology and homology of function: biological concepts and philosophical consequences. Biology and Philosophy 22:691-708.

Love AC. 2008a. Explaining evolutionary innovations and novelties: criteria of explanatory adequacy and epistemological prerequisites. Philosophy of Science 75:874-886.

Love AC. 2008b. From philosophy to science (to natural philosophy): evolutionary developmental perspectives. The Quarterly Review of Biology 83:65-76.

Love AC. 2010. Rethinking the structure of evolutionary theory for an extended synthesis. In: Müller G, Pigliucci M, editors. Evolution: The Extended Synthesis. Cambridge, MA: MIT Press. p. 403-441.

Love AC, Raff RA. 2003. Knowing your ancestors: themes in the history of evo-devo. Evolution & Development 5:327-330.

Lynch M. 2007. The frailty of adaptive hypotheses for the origins of organismal complexity. Proceedings of the National Academy of Sciences USA 104:8597-8604.

Martindale MQ, Pang K, Finnerty JR. 2004. Investigating the origins of triploblasty: 'mesodermal' gene expression in a diploblastic animal, the sea anemone *Nematostella vectensis* (phylum, Cnidaria; class, Anthozoa). Development 131:2463-2474.

Metscher BD, Ahlberg PE. 1999. Zebrafish in context: uses of a laboratory model in comparative studies. Developmental Biology 210:1-14.

Mikó I, Friedrich F, Yoder MJ, Hines HM, Deitz LL, Bertone MA, Seltmann KC, Wallace MS, Deans AR. 2012. On dorsal prothoracic appendages in treehoppers (Hemiptera: Membracidae) and the nature of morphological evidence. PLoS ONE 7:e30137.

Minelli A. 1998. Molecules, developmental modules, and phenotypes: a combinatorial approach to homology. Molecular Phylogenetics and Evolution 9:340-347.

Minelli A. 2003. The Development of Animal Form: Ontogeny, Morphology, and Evolution.

Cambridge: Cambridge University Press.

Minelli A. 2010. Evolutionary developmental biology does not offer a significant challenge to the neo-Darwinian paradigm. In: Ayala F, Arp R, editors. Contemporary Debates in the Philosophy of Biology. Malden: Wiley-Blackwell. p. 213-226.

Moczek AP. 2008. On the origins of novelty in development and evolution. BioEssays 30:432-447.

Müller G, Pigliucci M, editors. 2010. Evolution: The Extended Synthesis. Cambridge, MA: MIT Press.

Müller GB. 1990. Developmental mechanisms at the origin of morphological novelty: a side-effect hypothesis. In: Nitecki MH, editor. Evolutionary Innovations. Chicago: University of Chicago Press. p. 99-130.

Müller GB. 2007. Six memos for evo-devo. In: Laubichler MD, Maienschein J, editors. From Embryology to Evo-Devo: A History of Developmental Evolution. Cambridge, MA: MIT Press. p. 499-524.

Müller GB, Newman SA, editors. 2003. Origination of Organismal Form: Beyond the Gene in Developmental and Evolutionary Biology. Cambridge, MA: MIT Press.

Müller GB, Newman SA. 2005. The innovation triad: an EvoDevo agenda. Journal of Experimental Zoology (Molecular and Developmental Evolution) 304B:487-503.

Müller GB, Wagner GP. 1991. Novelty in evolution: restructuring the concept. Annual Review of Ecology and Systematics 22:229-256.

Müller GB, Wagner GP. 2003. Innovation. In: Hall BK, Olson WM, editors. Keywords and Concepts in Evolutionary Developmental Biology. Cambridge, MA: Harvard University Press. p. 218-227.

Newman SA, Müller GB. 2000. Epigenetic mechanisms of character origination. Journal of

Experimental Zoology (Molecular and Developmental Evolution) 288:304-317.

Nickles T. 1981. What is a problem that we may solve it? Synthese 47:85-118.

Niklas KJ, Kutschera U. 2009. The evolutionary development of plant body plans. Functional Plant Biology 36:682-695.

Palmer AR. this issue. Developmental plasticity and the origin of novel forms: unveiling of cryptic genetic variation via "use and disuse". Journal of Experimental Zoology (Molecular and Developmental Evolution) DOI:10.1002/jez.b.21447.

Piatigorsky J. 2007. Gene Sharing and Evolution: The Diversity of Protein Functions. Cambridge, MA: Harvard University Press.

Popper K. 2002 [1963]. Conjectures and Refutations: The Growth of Scientific Knowledge. London: Routledge.

Prud'homme B, Minervino C, Hocine M, Cande JD, Aouane A, Dufour HD, Kassner VA, Gompel N. 2011. Body plan innovation in treehoppers through the evolution of an extra wing-like appendage. Nature 473:83-86.

Raff RA. 2000. Evo-Devo: the evolution of a new discipline. Nature Reviews Genetics 1:74-79.

Reader SM, Laland KN, editors. 2003. Animal Innovation. New York: Oxford University Press.

Rice SH. this issue. The place of development in mathematical evolutionary theory. Journal of Experimental Zoology (Molecular and Developmental Evolution) DOI:10.1002/jez.b.21435.

Shubin N, Tabin C, Carroll S. 2009. Deep homology and the origins of evolutionary novelty. Nature 457:818-823.

Specht CD, Bartlett ME. 2009. Flower evolution: the origin and subsequent diversification of the angiosperm flower. Annual Review of Ecology, Evolution, and Systematics 40:217-243.

Townsley BT, Sinha NR. 2012. A new development: evolving concepts in leaf ontogeny. Annual Review of Plant Biology 63:535-562.

Wagner GP. 2000. What is the promise of developmental evolution? Part I: Why is developmental biology necessary to explain evolutionary innovations? Journal of Experimental Zoology (Molecular and Developmental Evolution) 288:95-98.

Wagner GP. 2007. How wide and how deep is the divide between population genetics and developmental evolution? Biology and Philosophy 22:145-153.

Wagner GP, Chiu C-H, Laubichler MD. 2000. Developmental evolution as a mechanistic science: the inference from developmental mechanisms to evolutionary processes. American Zoologist 40:819-831.

Wagner GP, Larsson HCE. 2003. What is the promise of developmental evolution? Part III: The crucible of developmental evolution. Journal of Experimental Zoology (Molecular and Developmental Evolution) 300B:1-4.

Wagner GP, Larsson HCE. 2006. Fins and limbs in the study of evolutionary novelties. In: Hall BK, editor. Fins into Limbs: Evolution, Development, and Transformation. Chicago: University of Chicago Press. p. 49-61.

Wagner GP, Stadler PF. 2003. Quasi-independence, homology and the unity of type: a topological theory of characters. Journal of Theoretical Biology 220:505-527.

West-Eberhard MJ. 2003. Developmental Plasticity and Evolution. Oxford: Oxford University Press.

Wilkins AS. 2002. The Evolution of Developmental Pathways. Sunderland: Sinauer Associates.

Wimsatt WC. 2007. Re-Engineering Philosophy for Limited Beings: Piecewise Approximations to Reality. Cambridge, MA: Harvard University Press.

Wouters A. 2003. Four notions of biological function. Studies in History and Philosophy of Biological and Biomedical Sciences 34:633-668.