Biological Journal of the Linnean Society, 2022, **XX**, 1–8. With 0 figures.

When the end modifies its means: the origins of novelty and the evolution of innovation

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Received 15 February 2022; revised 29 April 2022; accepted for publication 3 May 2022

The origin of novel complex traits constitutes a central yet largely unresolved challenge in evolutionary biology. Intriguingly, many of the most promising breakthroughs in understanding the genesis of evolutionary novelty in recent years have occurred not in evolutionary biology itself, but through the comparative study of development and, more recently, the interface of developmental biology and ecology. Here, I discuss how these insights are changing our understanding of what matters in the origin of novel, complex traits in ontogeny and evolution. Specifically, my essay has two major objectives. First, I discuss how the nature of developmental systems biases the production of phenotypic variation in the face of novel or stressful environments toward functional, integrated and, possibly, adaptive variants. This, in turn, allows the production of novel phenotypes to precede (rather than follow) changes in genotype and allows developmental processes that are the product of past evolution to shape evolutionary change that has yet to occur. Second, I explore how this nature of developmental systems has itself evolved over time, increasing the repertoire of ontogenies to pursue a wider range of objectives across an expanding range of conditions, thereby creating an increasingly extensive affordance landscape in development and developmental evolution. Developmental systems and their evolution can thus be viewed as dynamic processes that modify their own means across ontogeny and phylogeny. The study of these dynamics necessitates more than the strict reductionist approach that currently dominates the fields of developmental and evolutionary developmental biology.

ADDITIONAL KEYWORDS: agency – affordance landscape – evolutionary developmental biology – ecological developmental biology – evolvability – niche construction – symbiosis.

INTRODUCTION

The origin of novel complex traits constitutes a central yet largely unresolved challenge in evolutionary biology (Müller & Wagner, 1991; Moczek, 2008; Wagner, 2014), mostly for two overarching reasons. First, we continue to struggle to define novelty in evolution in unambiguous ways. Ernst Mayr defined novelty in evolution as 'any newly acquired structure or property that permits the assumption of a new function' (Mayr, 1960: 351), which holds intuitive appeal but leaves *how* such a new function may be acquired to the imagination. Likewise, Müller (1990: 101) defined novelty as 'a qualitatively new structure with a discontinuous origin, marking a relatively abrupt deviation from the ancestral condition', yet it was again left unclear by exactly what qualities a structure could be judged as new and deviating from ancestral conditions. Lastly, aiming to address some of these shortcomings Müller & Wagner (1991: 243) proposed a two-part requirement, defining a structure as a novelty if it is '… neither homologous to any structure in the ancestral species nor homonomous to any other structure in the same organism'. Although, on the surface, this definition captures clear cut-offs by equating novelty to the absence of (serial) homology, it was quickly challenged by changes in the conceptualization of homology. Up to the 1980s, two traits either were or were not homologous (e.g. Remane, 1952), but this black or white dichotomy eventually had to give way to shades of grey and a much more nuanced and layered understanding of homologous relationships in evolution: two traits could now be homologous on the level of gene regulatory network components but not the morphological structures instructed by them in their development (Shubin *et al.*, 2009). Conversely, structures unambiguously homologous on the level of morphology could, nevertheless, diverge in their underlying developmental mechanisms though the action of developmental systems drift (Weiss &

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Fullerton, 2000; True & Haag, 2001). Exactly where homology ends and novelty begins thus became increasingly difficult to articulate. Perhaps most importantly, all these definitions not only failed to define evolutionary novelty in unambiguous terms, they most of all failed to provide a framework for formulating research programs into *how* evolutionary novelties may first originate.

The second major reason why the origins of novel complex traits have remained unresolved in evolutionary biology lies in how we conceptualize the evolutionary process itself. Of the four evolutionary processes conventionally recognized (natural selection, genetic drift, migration and mutation), the first three can only affect existing variants and their distribution within and among populations, but by themselves cannot bring about novel features (Moczek, 2012; Sultan *et al.*, 2022). This privilege is instead restricted to mutation, yet attempts to explain the evolution of novel complex traits solely via the coincident origin, spread and fixation of one beneficial mutation at a time have proved largely unsuccessful. Not that mutational variation is irrelevant, but in the words of Fox Keller (2010), genes and genetic variants have emerged primarily as difference makers, factors that contribute to variation in traits, but by themselves do not suffice to make traits. Thus, exactly why and how evolutionary innovations occur when they occur has mostly eluded conventional approaches in evolutionary biology, to the point that fields such as population genetics have long stopped asking the question how evolution innovates, not because it is not a foundational question in evolutionary biology, but because population genetics lacks the ability to even frame the question (Wagner, 2014).

Instead, many of the most promising breakthroughs in understanding the genesis of novel complex traits have occurred not in evolutionary biology itself, but through the comparative study of development (Carroll *et al.*, 2004) and the interactions between development and ecology (Gilbert & Epel, 2015; Sultan, 2015). In this essay, I discuss how these insights are changing our understanding of what matters in the origin of novel, complex traits in ontogeny and evolution. Specifically, my presentation has two major objectives. First, I discuss how the nature of developmental systems biases the production of phenotypic variation in the face of novel or stressful environments toward functional, integrated and, possibly, adaptive variants. This, in turn, allows the production of novel phenotypes to precede (rather than follow) changes in genotype and allows developmental processes that are the product of past evolution to bias and facilitate evolutionary change that has yet to occur. Second, I explore how the nature of developmental systems itself has evolved over time, increasing the repertoire of ontogenies to pursue a wider range of objectives across an expanding range of conditions, thereby creating an increasingly extensive affordance landscape in development and developmental evolution.

INNOVATION BECAUSE, NOT IN SPITE, OF CONSERVATION

Before the 1980s, the developmental biology of mice, chicken, frogs, flies, nematodes or sea stars seemed to have little in common. Each came with its own ontogenetic phenomena and nomenclatures, and how the study of one could inform understanding of the other was entirely unclear. Evolutionary developmental biology changed all that (Raff & Kaufman, 1983; Carroll *et al.*, 2004; Gilbert, 2013). Armed, for the first time, with the ability to sequence genes across phyla and, eventually, to assess their expression and then function in at least some taxa, it became clear that the extraordinary diversity that exists on the level of morphology was not paralleled by a corresponding diversity of genes and developmental pathways. Instead, across phyla, diverse organisms emerged as modified re-assemblages instructed by the same and seemingly very limited pool of genes, cellular transduction pathways, cell types and morphogenetic processes (Shubin *et al.*, 2009). Put another way, the same genes, cellular transduction pathways, cell types and morphogenetic processes could be used to help build a wide range of both very similar and very different types of traits in distantly related organisms. Nowhere did this become more obvious than in complex yet convergently evolved, non-homologous traits. For instance, the eyes of vertebrates, insects, molluscs and jellyfish constitute independently evolved, non-homologous structures, yet each relies in ontogeny on the same set of homologous transcription factors, opsin proteins, cell types and neural circuits (Oakley, 2003; Erclik *et al.*, 2008; Shubin *et al.*, 2009). The hearts of vertebrates and arthropods constitute independently evolved contractile pumps, yet the gene regulatory network instructing their respective formation uses many of the same, homologous transcription factors (Bodmer & Venkatesh, 1998; Tanaka *et al.*, 1998; Souidi & Jagla, 2021). And appendages and outgrowths as diverse as the arthropod leg, beetle horns, the mouse tail, the siphons of ascidians or the tube feet of echinoderms all rely on the same set of patterning genes to instruct the establishment of their proximodistal orientation during ontogeny (Panganiban *et al.*, 1997; Mercader *et al.*, 1999; Moczek *et al.*, 2006; Moczek & Rose, 2009). Suddenly, the study of eye, heart or appendage formation in one phylum could inform understanding of the complementary process in another.

At the same time, the extraordinary degree of conservation observed in developmental genetic

underpinnings across phyla seemed paradoxical (Pfennig *et al.*, 2010; Schwab *et al.*, 2016). How could a limited pool of developmental properties not serve as a major constraint on diversification? The resolution emerged through the realization that development is also highly modular across levels of biological organization, allowing key developmental properties, no matter how conserved, to be redeployed in evolution independently of each other. For example, evolutionary changes in the location (heterotopy), timing (heterochrony), amount of developmental product (heterometry) or governance (heterocyberny) of otherwise conserved developmental events are now recognized as ubiquitous mechanisms, able to fuel massive diversification in developmental evolution with modest genetic change (reviewed by Moczek, 2019; see also Truman & Riddiford, 1999; Smith, 2003; Abzhanov *et al.*, 2004, 2006). Acting individually or in combination, evolutionary changes in developmental space, time, downstream output and/or upstream regulation all allow old and deeply conserved developmental processes to facilitate diverse and novel developmental outcomes, yet without necessitating the evolution of new genes, pathways, cell types or morphogenetic processes, only changes in regulation. Diversity is thus made possible not despite, but because of the deep conservation of developmental processes, facilitated by the modular and combinatorial nature of development.

What allows developmental properties to be so modular in developmental space, time, upstream regulation and downstream output? The explanation lies predominantly in the fact that the underlying regulatory mechanisms are themselves highly modular and on a variety of levels (reviewed by Carroll *et al.*, 2004; Gerhart & Kirschner, 2010; Gilbert, 2013). For example, cellular transduction pathways convert signals external to a cell into signals that enter the nucleus and affect gene expression, function predominantly as on/off switches, are ultra-conserved across phyla, but are flexible with respect to the cues to which they respond and the outputs that they facilitate. Consequently, a very modest number of transduction pathways is sufficient to modulate an extraordinary diversity of regulatory decisions (Gerhart & Kirschner, 2010). Transcription factors and *cis*-regulatory elements (CREs; e.g. promotors, enhancers, silencers), too, contribute modularity through their highly combinatorial action in regulating gene expression, whereby subtle changes in the timing or location of a single transcription (co) factor, or evolved changes in the presence/absence or precise location of a CRE might suffice to generate heterochronic/topic/metric developmental changes, yet without resulting in negative developmental consequences in other aspects of phenotype formation or necessitating the need to evolve new factors for new developmental decisions (Carroll *et al.*, 2004; Prud'homme *et al.*, 2007). Once again, by relying on pre-existing and clearly finite regulatory mechanisms, developmental systems are able to generate diverse and novel regulatory settings without having to generate novel regulatory component parts.

PHENOTYPE CONSTRUCTION, INTEGRATION, ROBUSTNESS AND PLASTICITY

In addition to being deeply conserved and highly modular, organismal development also revealed itself as a highly constructive process, whereby a given aspect of phenotype formation builds upon a pre-existing phenotype created during previous stages of phenotype construction. Cells differentiate and proliferate into tissues, establish boundaries and coordination systems; some form lumens into which others grow to create supply routes for oxygen and nutrients, setting the stage for other cell types to initiate the location-specific formation of the organs they will eventually help to build, and so forth (Gilbert, 2013). As such, developmental processes are highly responsive to context. Although this insight is, of course, not new from the perspective of developmental biologists, more recently it has permitted an interesting integration with the field of developmental plasticity in ways previously not recognized. Developmental (also known as phenotypic) plasticity has a long and rich history in evolutionary biology, where it is conceptualized traditionally as the ability of a genotype to produce different phenotypes in response to changes in environmental conditions (e.g. Pfennig *et al.*, 2010; Scheiner, 1993; Via *et al.*, 1995). The resulting changes in the expression of phenotypes can be gradual, discrete, reversible or not, but what they all share was that through the 1980s and 1990s such plastic responses were juxtaposed to non-plastic, environment-insensitive, canalized forms of development, where genotypes output the same phenotype during development despite environmental changes (reviewed by Schwab *et al.*, 2019).

The above conceptualization of plasticity persists in evolutionary biology to this day, but it has also run into significant challenges, one of which constitutes the largely unsuccessful search for developmental or physiological costs of plasticity (DeWitt *et al.*, 1998; Murren *et al.*, 2015). Such costs had to exist to explain the major differences in the degree of plasticity found across taxa and why plasticity is not limitless. Yet standard means of estimating the hypothesized costs of, for instance, environmental sensing or the production of tissues, receptors or hormonal cascades that orchestrate plastic responses mostly came back empty. Here, developmental biology was able to provide a partial resolution by emphasizing that

to develop is to interact with the environment and to be responsive to context, and whether this results in an altered or canalized trait is simply a function of the level of biological organization considered by the experimenter. Organisms adjust growth plastically in complex, dynamic ways to ensure that relative trait sizes are kept constant; blood sugar levels are maintained within specific boundaries in the face of major fluctuations in nutrient input by an endocrine system that is highly responsive to nutritional conditions, and so on (reviewed by Schwab *et al.*, 2019; see also Mirth & Shingleton, 2012; Nijhout *et al.*, 2014; Casasa & Moczek, 2018). Thus, dividing traits into those whose development is responsive to the environment or not generates a false dichotomy. Instead, much of what we perceive as robust, canalized development in undergirded by plastic, context-responsive development at other levels of biological organization. The reverse is, of course, equally correct. Complex plastic responses to environmental changes are underlain by canalized developmental properties able to sense conditions reliably and robustly adjust responses accordingly (Schwab *et al.*, 2019).

In combination, the modular, constructive and context-responsive nature inherent in all of development has critical implications for our understanding of how novel, complex traits might originate in ontogeny and evolution. Collectively, these developmental properties facilitate trait integration. For example, during vertebrate development muscle precursors migrate at random throughout the embryo, but stabilize in positions relative to where bones are forming at the same time (Herring, 2011). Likewise, motor neurons proliferate abundantly during early development, yet are maintained only if they find themselves close to developing muscle tissue (Kovach *et al.*, 2011). The vascular system expands randomly into empty space during early embryogenesis, but subsequently biases its differentiation through its attraction to hypoxic conditions, such as those where musculoskeletal growth is occurring (Marti, 2005). In each instance, discrete developmental processes integrate with each other through reciprocal, context-responsive interactions (Gerhart & Kirschner, 2010).

The reciprocally constructive and context-responsive nature of development also facilitates robustness and resilience in the face of environmental perturbations. To continue our example above, if perturbations to bone growth were to occur (e.g. though changes in environmental conditions or newly introduced mutational variation), these would be accommodated through subsequent rounds of phenotype construction by adjusting the attachment of ligaments and muscles, the placement of motor neurons and the balancing of mechanical load across the entire musculoskeletal system (Uller *et al.*, 2018). Importantly, these adjustments would not necessitate the evolution of new regulatory settings; instead, they come for free as products of the self-constructing and self-adjusting nature of musculoskeletal growth. Even profound experimental perturbations well outside the range of what most organisms might encounter in nature can be compensated, depending on the complexity of the developmental system already in place. For instance, experimental knockdown of *orthodenticle*, which encodes a transcription factor involved in patterning anterior head formation across bilaterian phyla, is invariably lethal in embryonic development (Blanco *et al.*, 2009). Yet in later developmental stages, the same perturbation can be accommodated developmentally, causing heads to reorganize dramatically but retain functionality (Zattara *et al.*, 2016, 2017). These and now many other examples illustrate that development generally does not fall apart in response to perturbations; instead, it adjusts subsequent rounds of phenotype construction to maintain functional integration. Most importantly, this resilience in phenotype construction can manifest even in response to conditions never encountered before.

This raises the possibility that innovation in evolution might be shaped by the self-constructing and self-adjusting nature of development in ways that might initially not require (but might subsequently be stabilized by) genotypic changes (West-Eberhard, 2003). A growing body of evidence also supports this perspective. For example, *Polypterus* fish that are reared in a low-water, terrestrialized environment, which forces fish to walk on their pectoral fins rather than swim, adjust during ontogeny not only their behaviour, gait and posture, but also their skeletal features in ways that parallel, in part, the fossil record of tetrapod transition from water onto land (Standen *et al.*, 2014). Similarly, anuran tadpoles of species that reflect the ancestral detritivorous lifestyle and associated gut morphology will adjust components of gut formation, if forced to assume a carnivorous diet, in ways that parallel some of the evolved changes in specialized carnivorous lineages (Ledón-Rettig *et al.*, 2010; Bloom *et al.*, 2013). Examples such as these suggest that, when confronted with novel or stressful environments, the self-constructing and self-adjusting nature of development has significant potential to bias the production of phenotypic variation toward functional, well-integrated and, potentially, novel variants, even in the absence of mutational variation (Sultan *et al.*, 2022). The resulting developmental bias then channels phenotypic evolution along developmentally privileged routes, while vetoing others. Developmental bias in evolvability is, of course, an evolved property itself; one that did not come into being all at once, and one whose evolution is probably far from over, a subject area I will turn to next.

THE EVOLUTION OF EVOLVABILITY

In the preceding sections, I aimed to emphasize the role of development in scaffolding the production of phenotypic variation toward developmental outcomes that are well integrated and functional even in the face of altered, stressful or novel environmental conditions. In the following, I would like to expand this perspective to highlight two additional dimensions, the first of which is that this scaffolding itself evolves over time. Put another way, what we now refer to as the nature of developmental systems, with all its biases on phenotypic variation highlighted above, did not come into being all at once, but instead was added to over time to generate the developmental repertoire of living systems we observe today (e.g. Abedin & King, 2010; Richter & King, 2013; Brunet & King, 2017). That is, the developmental processes necessary to generate complex traits, from cell division and adhesion to epithelium formation, the differentiation into different cell types, cellular migration and tissue folding, the production and sensing of morphogens, compartment formation and individuation, lumen formation, contractibility, etc., all emerged sequentially over hundreds of millions of years (Newman, in press; Erwin, 2020). While operating on diverse levels of biological organization, all share that even though they were all products of evolution, once in existence each of them fed back in unique ways to influence subsequent evolution by contributing unique degrees of freedom with respect to what development could build, how it could respond to perturbations, and what selectable variation it could produce for evolutionary processes to act upon (Newman, in press). Therefore, in the same way that developmental systems can be thought of as entities that modify their own means through ontogeny as increasingly complex phenotypes add degrees of freedom to subsequent routes of phenotype construction, so can the evolution of development be understood as a process that has consistently increased the repertoires of ontogenies to pursue an ever wider range of objectives across an ever expanding range of conditions, creating an increasingly extensive affordance landscape in development and developmental evolution. In short, evolution and development emerge as both cause and effect of each other.

The second point I would like to make is that it is worth considering that these interactions between developmental systems and the affordances they have added over time, on one side, and the shaping of selectable phenotypic variation and commensurate biases in phenotype evolution, on the other, are likely to be ongoing. That is, developmental systems continue to acquire new degrees of freedom, simultaneously accessing but also shaping newly available phenotype space. For instance, colonies of related individuals or symbioses between unrelated taxa allow teams to execute functions, modify environments and respond in a resilient manner to modified environments in ways that single individuals or component taxa cannot (e.g. McFall-Ngai *et al.*, 2013; Gilbert *et al.*, 2015). Although colonies or symbioses have been formed ever since life originated, novel associations continue to be formed all the time as organisms migrate, invade and/or confront altered environmental conditions (e.g. Parker *et al.*, 2020; Szabó *et al.*, 2022). Likewise, niche construction (the non-random modification of environmental conditions through the actions, behaviours, physiology, etc. of organisms that often feeds back to influence selective conditions experienced by themselves and/or their descendants) has been an important part of the evolution and diversification of life on this planet (Odling-Smee *et al.*, 2003; Laland *et al.*, 2016; Schwab *et al.*, 2016; Schwab *et al.*, 2017; Schwab & Moczek, 2017). Yet it is also a process that is ongoing; for instance, as invasive species modify newly invaded habitats, or as culture and technology change the nutritional, social and immunological environments that surrounded us (e.g. Dassonville *et al.*, 2011; Boivin *et al.*, 2016; Jeong *et al.*, 2018). Once again, although these processes operate on different levels of biological organization, all share the potential to bias and to create novel phenotypic variation available for evolutionary processes to act upon.

CONCLUSIONS AND OUTLOOK

As developmental systems construct phenotypes, they change their own abilities to build future phenotypes, to respond to internal and external inputs and to exhibit resilience in the face of perturbation. Likewise, the evolution of developmental systems emerges as a process that has consistently modified its own repertoire and reachable phenotype space. Development and developmental evolution can thus both be viewed as dynamic processes that modify their own means, dynamics whose study necessitates more than the strict reductionist approach that currently dominates the fields of developmental and evolutionary developmental biology. Specifically, advancing our understanding of the self-organizing and self-adjusting nature of development and its evolution will require approaches that integrate the roles of component parts (e.g. genes or cells) in the functioning of larger wholes (e.g. tissues, organs and organisms) with how those larger wholes then instruct the actions of their component parts (Sultan *et al.*, 2022). Moreover, it will require more explicit recognition of the active role played by living systems in not only responding to a set of circumstances that surrounds them, but

actively modifying this set of circumstances. As such, it will require a more nuanced understanding of what constitutes environment, away from a view of the environment as passive, external to and separable from the organisms and towards a perspective of the environment as, at least in part, constructed by developmental systems, as existing both outside and inside the conventional boundaries of the organism, as potentially heritable, and thus, as able to evolve alongside conventional organismal traits (Moczek, 2012, 2015). Although such conceptual extensions might, at times, feel uncomfortable because they unsettle familiar categorizations, they are likely to be key to overcoming current limitations to our understanding of the nature of innovation in development and evolution.

ACKNOWLEDGEMENTS

This article forms part of the special issue *Teleonomy in Living Systems*, guest edited by Richard I. Vane-Wright and Peter A. Corning and based on the Linnean Society meeting held on 28 and 29 June 2021. I would like to thank Peter and Dick for their invitations to contribute to the meeting and to this special issue. I also thank four anonymous reviewers for their constructive feedback on an earlier draft. The empirical work that motivates much of the topics discussed in this essay is currently funded by National Science Foundation grants IOS 1256689 and 1901680 and by grant 61369 from the John Templeton Foundation. The opinions, interpretations, conclusions and recommendations are, of course, my own and are not necessarily endorsed by the National Science Foundation or the John Templeton Foundation. I have no conflicts of interest to declare.

DATA AVAILABILITY

This article is based on data available in the published literature.

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