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Phenotype-first hypotheses, spandrels and early metazoan evolution

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Abstract
Against the neo-Darwinian assumption that genetic factors are the principal source of variation upon which natural selection operates, a phenotype-first hypothesis strikes us as revolutionary because development would seem to constitute an independent source of variability. Richard Watson and his co-authors have argued that developmental memory constitutes one such variety of phenotypic variability. While this version of the phenotype-first hypothesis is especially well-suited for the late metazoan context, where animals have a sufficient history of selection from which to draw, appeals to developmental memory seem less plausible in the evolutionary context of the early metazoans. I provide an interpretation of Stuart Newman's account of deep metazoan phylogenesis that suggests that spandrels are, in addition to developmental memory, an important reservoir of phenotypic variability. I conclude by arguing that Gerd Müller's "side-effect hypothesis" is an illuminating generalization of the proposed non-Watsonian version of the phenotype-first hypothesis.

Keywords Variability · Novelty and Innovation · Plasticity-first hypothesis · Early metazoan evolution · Spandrels

1 Introduction

The view that the variation required for evolution is ultimately sourced in genetic factors (mutation, drift) has been called the "genotype-first hypothesis," and tends to be associated with phyletic gradualism (Eldredge & Gould, 1972, pp. 82–115; Futuyma, 2013) and the Modern Synthesis (Lewin, 1980, p. 883). The "phenotype-first perspective" (Wagner, 2011, p. 182) or "plasticity-first hypothesis" (West-Eberhard,

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2003, pp. 157–158; Watson et al., 2014; Levis & Pfennig, 2016, pp. 563–574; Pfennig, 2021) maintains that development constitutes an independent source of variation and, further, that these developmental variants can have greater evolutionary potential because they can be preadapted or biased.

What is the means by which developmental variation comes to be so productive? Richard Watson and his co-authors propose one such mechanism: "developmental processes, shaped by past selection, may constitute a 'memory' of phenotypes or phenotypic features that have been selected for in the past" (Watson et al., 2014, p. 208). Accordingly, and in contrast to mutational effects, at least some of the variability incipient in developmental processes is not neutral, undirected, or random, but consists in biased or preadapted "memories" of past evolutionary accomplishments that can be unleashed if a novel environment resembles a past environment. Along these lines, Alexander Badyaev argues that developmental memory constitutes an explanation for the rapidity with which finch beaks can evolve (Badyaev, 2010, pp. 1111-1126).

Watson's characterization of developmental memory is well-suited for the late metazoans, which have a sufficient history of selection from which to draw. However, how is a phenotype-first hypothesis applicable to the earliest metazoans, which, by definition, have no such history *qua* metazoans?

In this paper, I present an interpretation of Stuart Newman's account of early metazoan evolution that exemplifies the possibility of a non-Watsonian phenotype-first hypothesis. Cellular cohesion is a condition for multicellularity, and different lineages (animal, plant, fungi) evolved different cohesion mechanisms. If, as argued, it is the magnitudinal effects of these various mechanisms that drove selection, which allowed these creatures to exploit unoccupied ecological niches, then the other biomechanical properties of these mechanisms, including the capacity to support the liquid-like random perambulation that Newman identifies as the definitive pan-metazoan homology, would initially qualify as a spandrel (Gould & Lewontin, 1979, pp. 581–598). This suggests that spandrels, like developmental memory, are an important reservoir of phenotypic variability. I then appeal to Gerd Müller's "side-effect hypothesis" to suggest that this non-Watsonian model of the phenotype-first hypothesis is applicable outside the scope of early metazoan evolution.

An outline of the paper is as follows. In Sect. 2, I present and motivate Watson's account of the phenotype-first hypothesis. In Sect. 3, I argue that Newman's account of early metazoan evolution represents one instance of a phenotype-first explanation that could not appeal to the "memories" of past evolutionary accomplishments. I interpret Newman as claiming that if some developmental variability takes the form of spandrels, then this variability is not a selected effect of genetic factors, even if it is an effect of selection. The proposed hypothesis is presented as a complement to Watson's phenotype-first explanation. After addressing objections, I claim that Gerd Müller's "side-effect hypothesis" expresses the general explanatory pattern exemplified by Newman's account of early metazoan evolution. In Sect. 4, I review my findings.

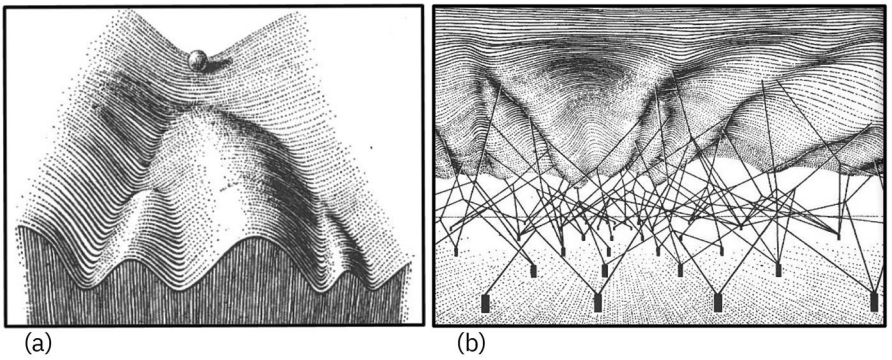

Fig. 1 (a) Waddington's epigenetic landscape, wherein bifurcating valleys represent developmental variation. (b) The genes (pegs) and the network of regulatory interactions (lines) which support the underside of the epigenetic landscape

2 Developmental memory as a reservoir of phenotypic variability

In this section I present and motivate Watson's account of how development can be a source of biased or preadapted variation. I do this by showing how Watson's account helps resolve two issues that arise with C. H. Waddington's account of developmental variability.

2.1 Waddington's epigenetic landscape

Waddington's "epigenetic landscape" (Waddington 1942; 1957) prefigures contemporary phenotype-first views. According to Waddington, the variation required for many evolutionary innovations can be sourced in an organism's capacity to facultatively respond to different environmental and internal inducers over the course of its development.

As shown in Fig. 1a, Waddington's epigenetic landscape visually illuminates key features of von Baer's laws (Waddington, 1956, p. 9), insofar as possible developmental pathways are represented by a series of bifurcating and, so, increasingly differentiated valleys or canals. The valleys through which the ball passes, as opposed to the superset of valleys through which the ball could pass, represent the actual developmental trajectory of a model organism or the average trajectory of a population of organisms. The bifurcated and/or shallow valleys depict the possibility of variability,[1] so that even if there remains a tendency for the ball to roll into one valley, the magnitude of perturbation required to change the ball's course at a point of bifurcation is significantly less as compared to what would be required in a non-bifurcated valley.

[1] The distinction between the differences actually present among the individuals in a population and potential or propensity to vary, represented by the possible routes the ball could have followed, corresponds to Wagner's and Altenberg's distinction between variation and variability (1996).

The bifurcating valleys of Waddington's epigenetic landscape vividly represent how, according to the phenotype-first hypothesis, developmental processes constitute a trove of environmentally and internally inducible variation (Saunders, 1993, pp. 43–44). While Waddington exemplified the epigenetic landscape by showing how shocks can induce a crossveinless or abnormal bithorax phenocopy in *Drosophila* (Williams, 1966, pp. 70–81; Sober, 2014, pp. 199–200), I will also make use of the following example of polyphenism: *Spea* spadefoot tadpoles default to a detritus-consuming omnivore ectomorph unless exposed to meat, in which case they tend to develop into a distinct carnivore morph, characterized by a larger head, serrated beak, and cannibalistic proclivities (Levis & Pfennig, 2016, pp. 563–574).

Since expressed phenotypes are represented by the ball's actual trajectory, the contours of the landscape explain the ball's movements. However, as shown in Fig. 1b, given Waddington's ancillary hypothesis that these contours are "controlled by the pull of these numerous guy-ropes which are ultimately controlled by genes" (Waddington, 1957, p. 36), these surface explanations are proxies for the possibility of a more detailed, mechanistic explanation in terms of the complex interactions of gene products (Fagan, 2012, pp. 186–188). "It is important to realise that the comparatively simple orderliness of the epigenetic landscape … is a property of a higher order dependent on an underlying network of interactions which is vastly more complicated" (Waddington, 1957, pp. 34–35). This network of interactions constitutes the genotype-phenotype map (G. Wagner & Altenberg, 1996).

The logic of Waddington's images is such that they imply two sources of hidden variation. Phenotypic variability is explicitly represented by the bifurcating valleys. However, because the landscape itself can change over time, revealing new valleys and passes, the underlying genes and networks of regulatory interactions that support the landscape constitute an unthematized storehouse of variation. This "cryptic variability" (e.g., Gibson & Dworkin, 2004) can nevertheless become thematized if we imagine a series of counterfactual landscapes that are within causal reach of the depicted landscape.

"Genetic assimilation" is a final theme of Waddington's that requires some explanation. While crossveinless characteristics in *Drosophila* and carnivorous characteristics in *Spea* are initially environmentally induced, these facultative responses can become transformed (by canalization or stabilizing selection) into obligate responses that manifest irrespective of environmental conditions. Thus, genetic assimilation is the selection-driven loss of plasticity (West-Eberhard, 2021, p. xvi). For example, some derived populations of *Spea* are carnivorous regardless of resource availability (Levis & Pfennig, 2016, pp. 563–574; Pfennig & Murphy, 2000). Genetic assimilation by, e.g., stabilizing or internal selection, can be represented as a tectonic shift of the epigenetic landscape, wherein one branch of a previously bifurcated valley becomes inaccessible or canalized (Smith et al., 1985; Loison, 2019).

2.2 Waddington's explanation of developmental variability

Wilkins (2008) argues that Waddington's concept of the epigenetic landscape remains a promising counterweight to the simplifying assumptions that animate some neo-Darwinist analytical procedures. Where neo-Darwinists would see genetic factors,

such as mutation and drift, as the principal sources of variation upon which natural selection operates, the epigenetic landscape suggests that development itself is an additional reservoir of variation. If a carnivore morph is among the accessible pathways in a spadefoot toad's epigenetic landscape, then we can easily explain how an environmental change might prompt a population of omnivores to, over the course of relatively few generations, become a population of large headed, beaked carnivores (or vice versa).

However, Wilkins also describes Waddington's criticism of Neo-Darwinism as incomplete. If these networks are, as discussed above, repositories of hidden variation, Wilkins criticizes Waddington for failing to even formulate the question of how such reserves evolved: "he never seems to have asked himself how these alternative capacities [for morphological trait development] might have themselves first arisen" (Wilkins, 2008, pp. 229–230).

Wilkins is not the first to complain about this omission. Because hidden variation is such that it is expressed under certain conditions, George Williams describes such variation as a modality of facultative response and claims that "Waddington gives very little attention to the origin of the facultative responses with which he starts his arguments" (1966, p. 82). This same criticism has been recently echoed by Laurent Loison: "Waddington's own synthesis was only sketchy and incomplete" insofar as the "evolutionary building of an epigenetic landscape must be explained in the first place" (2019, p. 12).

In fact, Wilkins' and Loison's claim that Waddington "seems *never to have raised* [the] set of questions" (Wilkins, 2008, p. 229) about the evolutionary origins of hidden variation is incorrect. Not only does the logic of Waddington's own imagery suggest that developmental variability can be ultimately explained in terms of the play of genes and guy-ropes that support the landscape, the passage quoted by Williams shows not only that Waddington raised the question, but sketched an answer to the question so raised: Waddington writes that "natural selection would favour those organisms which had a high capacity to become adapted to an abnormal situation … It would, in fact, build into the developmental system a tendency to be easily modified in directions which are useful in dealing with environmental stresses and to be more difficult to divert into useless or harmful paths" (Waddington, 1958, pp. 6–7 in Williams, 1966, p. 82). "It would appear," Williams summarizes, "that [Waddington] finds the theory of natural selection entirely adequate to explain facultative adaptations" (1966, p. 82).

2.3 Watson's explanation of preadapted or biased variability

What explains the origins of hidden variation (variability)? As discussed in the previous section, Waddington maintains that variability is itself an adaptation, insofar as the capacity to conditionally express a character allows a population to better cope with changing environments. Mary Jane West-Eberhard strikes the same chord when she claims that "plasticity itself is a trait subject to natural selection and evolutionary change" (West-Eberhard, 1989, p. 251). Stepping back, the picture seems to be as follows: just as a certain prey environment might select for a novel beak shape in a finch population, populations that are developmentally sensitive to rapidly changing

environments might have a fitness advantage over those that are not. More generally still, variability—the potential to vary in response to environmental and internal influences—is intimately related to the notion of evolvability, which is the adapted capacity for organisms to generate heritable phenotypic variation (Sterelny, 2007; Brigandt, 2007; Brown, 2014).[2]

Despite the prima facie attractiveness of the suggestion that developmental variability, like any other adaptation, is just another selected effect, I highlight two problems with this proposal.

First, Williams argues that the accumulation of *mere* or *neutral* variation is not likely to confer a fitness advantage onto a population (1966, 78; see also Dennett, 1995, p. 288). As shown in Waddington's own experiments, wherein heat shocks produced missing cross-veins and other anatomical and developmental anomalies, many of the propensities that manifest in response to external perturbations are likely to be maladaptive under most circumstances. By contrast, if an otherwise omnivorous population of *Spea* tadpoles becomes carnivorous in response to shrimp being in the water, this adaptation would seem biased or non-random. What is required is an account of how some phenotypic variation comes to be "enriched" (Eshel & Matessi, 1998, p. 2128), "facilitated" (Kirschner & Gerhart, 2006), "regulated" (Sharov, 2014), or "preadapted" to a new environment (Cuénot, 1914; Hayden et al., 2011, p. 92).

Second, since natural selection only operates on expressed traits or variation, and variability is a dispositional property, how could natural selection operate on variability itself (as opposed to any of its expressions)? Lee Altenberg writes, "because variation is not the phenotype of an organism, but a property of genetic transmission between organisms. How, therefore, can organismal selection get a 'handle' on the processes that produce variation?" (1995, p. 208).

A plausible response to both of these problems holds that developmental variability is incrementally accumulated over the history of a population's encounters with various environments. In this way, Watson and his coauthors claim that "developmental processes, shaped by past selection, may constitute a 'memory' of phenotypes or phenotypic features that have been selected for in the past" (2014, 208; see review and references in Watson & Szathmáry, 2016). This solves the first problem insofar as the accumulated mutations that are stored as developmental memory would be biased or preadapted, on the assumption that future selective environments are similar to past selective environments (Masel, 2006, p. 1989). The second problem is resolved because at least a subset of a population's hidden variation will have been expressed and exposed to selective processes before being committed to developmental memory.

The proposal that Watson and his co-authors advance is an enriched version of the phenotype-first hypothesis. The variability incipient in developmental processes is not neutral, undirected, or random, but biased or preadaptive because these forking valleys often constitute a memory of past evolutionary accomplishments:

[2] There is also the distinct, but related notion of evolvability as used in quantitative genetics, which focuses on the evolutionary potential of populations (Hansen & Pélabon, 2021).

> Whilst genetic variation might be undirected, the pattern of phenotypic variation is shaped and biased by the processes of development. Moreover, the organisation of developmental processes (from gene regulatory interactions to morphological body plans) is itself, in large part, a product of past evolution. This affords the possibility that random genetic changes might produce phenotypic changes that are 'informed' by past selection. (Watson & Szathmáry, 2016, p. 147)

While it remains unclear how the facultatively expressed cross-veinless trait in *Drosophila* might be the expression of a past evolutionary accomplishment, we can easily imagine a fossil record that supports the contention that, e.g., the carnivore traits facultatively expressed by *Spea* tadpoles are instances of Watsonian recollection. Similarly, Alexander Badyaev has argued that rapidly evolving and highly adaptive finch beaks "represent a historical record of the most recurrent developmental and functional interactions" (Badyaev, 2010, pp. 1111–1126).

2.4 Summary and outlook

In this section, I sought to articulate and motivate Watson's version of the phenotype-first hypothesis by considering limitations of Waddington's articulation of the hypothesis. In the next section I consider some limitations of Watson's account. While an appeal to developmental memory is well-suited for the late metazoans, which have a sufficient history of selection from which to draw, it struggles to illuminate how a phenotypic-first hypothesis might apply to the earliest metazoans, who lack a comparable history *qua* metazoans. I suggest an interpretation of Newman's account of deep metazoan evolution which makes room for a complementary variety of non-Watsonian phenotypic-first explanation. In particular, where Watson's appeals to previously selected effects as the basis for a phenotype-first hypothesis, Newman's account of early metazoan evolution vividly illustrates how spandrels can also serve as a reservoir of phenotypic variation. After responding to possible objections to the proposed account, I argue that Müller's "side-effect hypothesis" expresses the general explanatory pattern exemplified by Newman's account of early metazoan evolution.

3 Spandrels are a reservoir of phenotypic variability

3.1 Newman's account of deep metazoan evolution

In what follows, I review Newman's account of deep metazoan phylogenesis. I also occasionally draw from Wallace Arthur's and Iñaki Ruiz-Trillo's accounts of the same evolutionary era.

Newman follows Schmalhausen (1949) in positing a class of relatively unconstrained "primitive metazoans" from which the core animal phyla abruptly emerged. His "physio-genetic" account of early metazoan speciation sees such events as principally driven by the physical biases and constraints made possible by multicellularity itself, along with the effects the environment had on such mesoscale properties

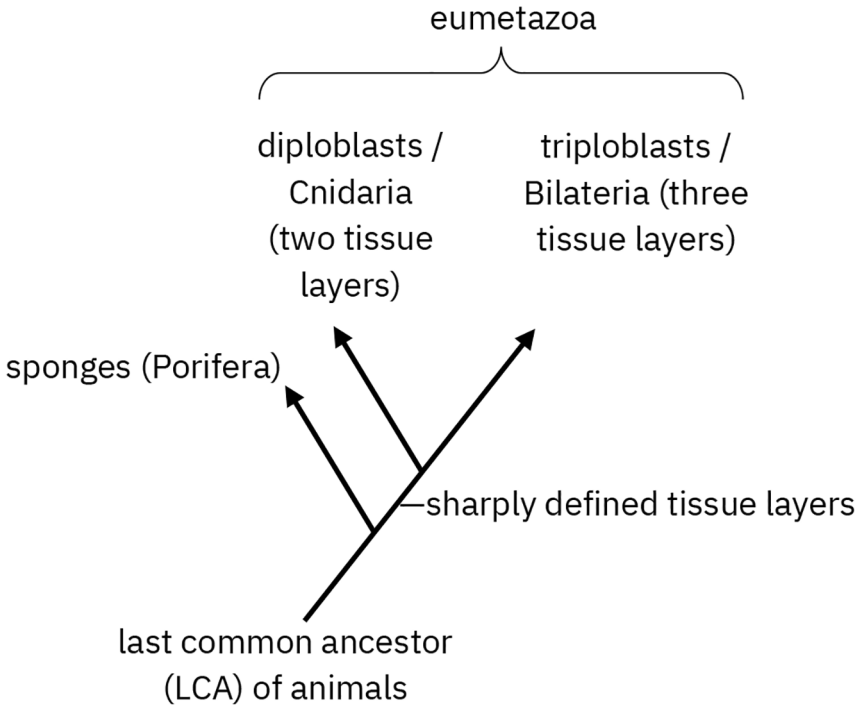

Fig. 2 A simplified cladogram of deep metazoan phylogeny

(Newman, 2004, p. 162). CAMs, or cadherin-based cell attachment molecules, allow animal cells to adhere to one another in a way that confers emergent, liquid-like properties to the structure as a whole. The cells that make up an early metazoan, like the constituents of any liquid, can cohere while permitting random perambulation. Newman's principal thesis is that this liquid-like property is the definitive pan-metazoan homology and that the major lineages of the metazoans are characterized by elaborations on or von Baerian differentiations of this basic form (Newman, 1995, p. 222; see Rust, 2021).

Of course, these mesoscale liquid properties are genetic products. Newman describes a set of shared "toolkit genes"—many of which were present in the metazoans' unicellular ancestors—employed by the early metazoans "to mobilize well-characterized physical effects and processes (cohesivity, phase separation and disaggregation, surface and shape polarization of cells, chemical oscillation, reaction-diffusion coupling) in the cell aggregates that eventually evolved into animal bodies and organs" Newman, 2016, p. 131).

In the following three paragraphs, and as shown in Fig. 2, I briefly describe the way in which this basic liquid tissue came to be uniquely expressed in three of the five main lineages of metazoa—the sponges (Porifera), the diploblasts (Cnidaria) and the triploblasts (Bilateria). These lineages are thought to have abruptly and consecu-

tively emerged via speciation events over a relatively short time period in the early history of the metazoans.

If this "living liquid" contains at least two kinds of cellular units, the uniquely protozoan Wnt protein enables this liquid tissue to both elongate and form interior spaces via the induction of asymmetries on cellular surfaces (Newman, 2019a, p. 4; 2019b, p. 333; 2020, pp. 130–131). The generic liquid-like properties promoted by CAMs and the Wnt protein are sufficient to account for the elongated and hollow forms of the sponges (Porifera) and Placozoans.

The eumetazoa are characterized by sharply defined tissue layers. The diploblasts (Cnidaria), such as jelly fish and corals, are characteristically elongated and tubular and have body walls that consist of two cell layers (*epithelia*). These liquid-like, mesolevel properties are realized by an eumetazoa-specific Wnt-activated pathway that causes cells to be polarized, not just over their surfaces, but in their overall shapes. This, in turn, allows cells to envelope a unique supporting structure (*basal lamina*) that enables the elongation of the body and the development of appendages (Newman, 2019a, p. 4; 2019b, p. 333; 2020, pp. 130–131).

Finally, the triploblasts (Bilateria) represent a further specification of the liquid tissue which characterizes all metazoans. Where both the diploblasts and triploblasts are able to form sharply layered tissue, only triploblasts are able to form a third, mesodermal tissue layer. The novel mesoderm can disaggregate into mesenchymal tissue, which forms the basis of the novel body plans, skeletal structures, and complex organs that are characteristic of most present-day animal phyla.

Stepping back, Newman locates these deep metazoan phylogenetic developments—each involving differentiation of the basic liquid tissue form—within a larger story wherein the "mutually transformable" activity of primitive, multicellular organisms become subject to what he calls the "intensification of uniqueness" in a way that gave rise to these core phyla.

> In the internalist [or plasticity-first] view … almost all overt biological diversification occurs early on, when primitive organisms, because of the physical contribution to the determination of their forms, are to a certain extent mutually transformable. Through subsequent evolution the disparate kinds of organisms, by accumulating mechanisms which promote their capacity to develop "true to type" despite genetic mutation ("morphological stasis") and to maintain their phenotypic character in the face of changing conditions ("physiological homeostasis"), turn more and more into "themselves." According to the internalist view, then, the intensification of uniqueness, rather than the open-ended production of overt difference, may thus be the hallmark of organismal evolution once it has left its early, "physical" stage. (Newman, 1995, pp. 119–220; see also 2004, pp. 161–163; 2020, p. 144)

There was an early, "physical" stage wherein "primitive organisms" or early metazoans exhibit a high degree of intergenerational, morphological plasticity ("the open-ended production of overt difference"). This malleability was due to the ontogenies of primitive animals being principally constrained by the liquid-tissue morphospace described above, as opposed to the genetically canalized constraints to which their

speciated descendants were subject: "these earliest prototypes of animal bodies and organs were still to be transformed by canalizing evolution into modern, stable organismal 'types'" (Moss & Newman, 2016, p. 108). Or again: "if the origin of organismal diversity was an epigenetic process, and if genetic evolution acted upon those dramatically divergent forms and consolidated them under various conditions of life, then after vast amounts of time you would have organisms that were no longer malleable or interconvertible" (Newman, 2004, p. 162). Genes are principally implicated as a canalizing or stabilizing mechanism—genetic accommodation—so that fitness-enhancing facultatively expressed traits can become more regularly expressed irrespective of environmental triggers ("physiological homeostasis").[3]

While environmentally conditioned or facultative responses have a genetic basis because they supervene on the capacity for cells to cohere while permitting random perambulation, as made possible by the "toolkit genes," it would be a mistake to follow Williams in construing these facultative responses as genetically programed responses. While toolkit genes enable an aggregate of cells to behave in a liquid-like fashion, the way in which this living liquid responds to environmental perturbations is not a programmed response, but more akin to the way in which liquid water might evaporate or freeze when exposed to different temperatures: "Physical and epigenetic determination may have been so important at these early periods of evolution that if the temperature, salinity, or some other aspect of the environment was changed, you would have got a very different looking organism" (Newman, 2004, p. 162). In short, Newman maintains "ancient metazoa were even more developmentally plastic than modern ones" (Newman et al., 2003, p. 290). Arthur affirms that the ontogenies of the primitive animals are "evolutionarily flexible," because "they had not been subject to a comparable history of selection for integration and canalization" (Arthur, 1997, p. 227). And along these lines, Ruiz-Tillo and his co-authors cite studies which suggest early- and pre-metazoan gene innovation was high, implying that these organisms were "probably relatively plastic" compared to the late metazoans (Ros-Rocher et al., 2021, pp. 9–11; see also Paps & Holland, 2018; Fernández & Gabaldón, 2020; Guijarro-Clarke, Holland, & Paps, 2020).[4]

It is important to be clear about the primitive metazoans' scope of variability. Newman's thought is not that some of the primitive metazoans might have responded to environmental cues by turning into the equivalents of, e.g., modern-day pigs or fruit flies. Primitive variability of this kind is always *shallow* in the sense that it can give rise to forms that would fall within the scope of a possible and proximal speciation event. Although actual speciation requires canalization, some of the basic speciated forms described above must have been transiently expressed prior to speciation by the proto-metazoans.

[3] But even here, Newman maintains that genetic accommodation may not have been in every case required. "Some [anatomical distinctions among metazoan body plans]—even the clade-defining ones—may not have initially been genetically determined, but relatively arbitrary 'frozen accidents,' alternative morphotypes within evolving populations of organisms for which body plans were still plastic" (Newman, 2016, p. 150).

[4] This said, Love and Lugar flag Mark Webster's argument to the effect that the fossil record does not unequivocally support the claim that greater initial variation is typically followed by less intraspecific variation in Cambrian lineages (Love & Lugar, 2013, p. 454; Webster, 2007).

Also implied by Newman's account of early metazoan phylogenesis is the claim that a primitive propensity for variability is not quashed upon speciation, but narrowed, so that individual sponges remain primitively variable within the scope of the constraints which typify the species. Thus, Newman writes that "[w]ithin the confines of phylotypic identity … subtypes (not all of them natural kinds) can be elaborated, consolidated, and intensified, down to the level of the individual organism" (Newman, 2020, p. 144).[5]

3.2 Spandrels are a reservoir of phenotypic variability in deep metazoan evolution

As discussed in the previous section, Watson and his colleagues maintain that to the extent that facultative responses are biased or pre-adaptive, such responses can be explained as the expression of a "memory" of past adaptations. However, how might the phenotype-first hypothesis apply to the earliest metazoans, which, presumably, do not have a comparable history of adaptations from which to draw? An answer to this question suggests a complementary, non-Watsonian version of the phenotype-first hypothesis.

Do the biased responses of the early metazoans require explanation in terms of a history of adaptive response to different environments? The question needs to be rejected on two grounds. First, in this context, there is no requirement that the variability exhibited by the primitive metazoans be especially biased or pre-adaptive. Because multicellularity opened up the empty ecological niches found at supercellular or intermediate scales, following Arthur, "[i]n such a situation, a badly coadapted but viable mutant animal may be *more* fit than its well-coadapted progenitor in the sense that on average it leaves more surviving progeny, simply because of the lack of competition for its new-found resource" (Arthur, 1997, p. 232). As Newman describes it, "[n]ovel combinations of intrinsically generated motifs may not be optimal for survival in the venue where they originated, but living organisms typically exhibit ingenuity and are not locked into preordained niches" (Newman, 2019a, p. 4; 2019b, p. 333; 2020, pp. 130–131). Second, not only does the gross variation facultatively expressed by the early metazoans not need to be pre-adaptive or biased, but, at least *prima facie*, there is little reason to think it could be—by definition, there is little history of selection upon which the earliest metazoans could draw.[6] In this way, Watson's explanation of biased variation in terms of developmental memory seems inapplicable to the earliest metazoans.

So, barring the possibility of Watsonian recollection, what might a phenotype-first explanation look like in the context of the earliest metazoans?

[5] In this way, just as the morphologies of the primitive metazoans were responsive to environmental stimuli in a relatively unconstrained way, Gould and Lewontin suggest that the "good design" of modern-day sponges and corals is a function of how their relatively contained liquid tissue form is tuned by the aquatic environments in which they find themselves. The fact that such marine organisms "are well adapted to the flow regimes in which they live" need not be explained by natural selection, but "may be purely phenotypic in origin, largely induced by the current itself" (Gould & Lewontin, 1979, p. 592).

[6] I return to this point in Sect. 3.3.

As mentioned, in the primitive metazoans, a set of toolkit genes were responsible for cellular coherence (by way of CAMs), in particular, and the pan-metazoan liquid tissue form, in general. Of the various properties that are indicative of the liquid tissue form, it is the magnitudinal properties made possible by the CAMs that might have been initially sufficient to propel these primitive animals into unexploited or protective "mesoscale" niches (Newman & Bhat 2009, p. 695; Newman, 2019a, p. 9). "Any major change in the ontogenetic trajectory and adult morphology of an animal is likely to alter its pattern of resource use and indeed its ecological characteristics generally. In a few cases, such changes will by chance result in utilization of a novel resource, and in Vendian times there was a reasonable probability that no other multicellular consumer was already using that resource" (Arthur, 1997, p. 232). The possibility that multicellularity might be partially explained by appeal to the way in which magnitudinal properties render new ecological niches accessible has also been entertained by Stanley (1973), Ruiz-Trillo & his co-authors (2021, pp. 12, 14; 2017, pp. 7–8), and others (Boraas et al., 1998; Alegado et al., 2012; Herron et al., 2019; but see Kumler et al., 2020).

As discussed in detail by Ruiz-Trillo and his collaborators, not only was the capacity for cellular adhesion present in the pre-metazoans, but they exhibited a variety of such mechanisms. This capacity was present in the unicellular ancestors of multicellular lineages (and remains present in modern unicellular relatives) because many of these ancestors had a "multicellular" life stage. And these unicellular progenitors exhibited dramatically different modes of cell adhesion, the nature of which helps explain the rise of different multicellular lineages (animals, plants, fungi) (Sebé-Pedrós, Degnan, & Ruiz-Trillo, 2017, p. 2; Ruiz-Trillo & de Mendoza, 2020, p. 1; Abedin & King, 2010, p. 734). For example, where the hard walls of plant cells are connected via extracellular "glues," adhesion between "naked" animal cells is mediated by proteins such as cadherins (CAMs).

Because these multicellular lineages evolved independently using different adhesion mechanisms, and because it was adhesion's magnitudinal effects that opened up empty mesoscale niches, it is not implausible to conclude that these magnitudinal properties were, at least initially, the selected effect of a given adhesion mechanism. However, magnitudinal effects are not the only consequences of such mechanisms. Where extracellular "glues" keep the cellular structures of plants in place, as we have seen, these cadherins also made possible the liquid tissue form which is the pan-metazoan homology. In this way, liquid tissue--anon-magnitudinal consequence of a given adhesion mechanism--may have initially been a spandrel (Gould & Lewontin, 1979, pp. 581–598) or, in other words, "after-the-fact" (Newman, 2019a, p. 12), "side-effect" (Müller, 1990), or a accidental by-product (Dennett, 1995, pp. 279–280) of selection on magnitudinal properties.[7] Given that all metazoans are characterized by a liquid tissue form, the fact that the solid-tissued plants (Abedin & King, 2010,

[7] Alasdair Houston documents a narrow and broad use of the term "spandrel" in biology (2009, p. 227). Where Gould and Lewontin characterize a spandrel as the "necessary byproduct" of an adaptation (Gould, 1997, p. 10, p. 754), George Williams adopts the less restricted view that a spandrel is a "structure arising as an incidental consequence of some evolutionary change" (1992, p. 78). This conception of spandrel as "accident" has also been endorsed by Dennett (1995, pp. 279–280). In the present case I employ the broad use of the term. Thus, in characterizing liquid tissue as a "spandrel," I am not implying

p. 734) were also able to exploit empty mesoscale niches suggests that it was the cadherins' magnitudinal properties that were the initial targets of selection and that liquidity was a spandrel.[8]

Along these lines, Newman writes that characters associated with multicellularity need not always be explained as an adaptation, even as they subsequently become implicated in selective processes:

> The characters' origination, whatever the source of the associated genes, can often only be understood on the basis of physico-genetic effects specific to the multicellular context. … If they enable organisms to survive in new ways in existing ecological niches, or to occupy new niches (Laland, Odling-Smee, & Endler, 2017), their roles in enhancing fitness will be "after-the-fact" (Gould & Lewontin 1979, pp. 581–598; Müller, 1990; West-Eberhard, 2003) and thus do not require elaborate or farfetched adaptationist narratives to account for their existence. (Newman, 2019a, p. 12)

Of course, the liquid-like properties enabled by a certain mode of cellular cohesion were soon subject to natural selection.

Spandrels, such as the non-magnitudinal properties of certain modes of cellular cohesion as enabled by the metazoan toolkit genes, are important because they constitute a non-recollective source of phenotypic variation, and so a non-Watsonian version of the phenotype-first hypothesis. The points of contrast are as follows. First, if a genetic mutation more or less directly gave rise to the capacity for cellular cohesion, then this is a straightforward example of a genotype-first hypothesis. Second, if, following Watson, a genetic mutation gave rise to a phenotype that conferred some fitness advantage onto a population and if this phenotype was subsequently repressed, then developmental memory is one source of phenotypic variability. However, as on the present account, if a mutation gives rise to a fitness-enhancing phenotype (e.g., the magnitudinal effects of cellular cohesion mechanisms) along with a number of "after-the fact" effects or spandrels (e.g., the liquid-like capacity to cohere while permitting random perambulation), then the latter is a source of variation that looks importantly different than either of the first two cases. Spandrels exemplify a non-Watsonian version of the phenotype-first hypothesis.

Whether or not this interpretation of Newman's account of the dynamics of deep metazoan evolution is factually correct (a counterexample need not be actualized), the account points to the possibility of a variety of phenotypic variability that (1) is not a selected effect but a spandrel or "after-the-fact" effect of selection and (2) is a source of variation upon which selection subsequently operates.

that it is a "necessary byproduct" of a certain mechanism of cellular cohesion, but merely an "accident" or "incidental consequence" of that mechanism relative to its selected effects.

[8] To be clear, while this interpretation is compatible with Newman's plasticity-first account of early metazoan evolution, he makes no appeal to a "spandrel" or "side-effect" to disentangle the adaptive and incidental products of the toolkit genes. Thus, I cannot be sure if this interpretation would ultimately be met with his endorsement.

3.3 Addressing objections

In what follows, I address two objections to the proposed non-Watsonian account of a phenotype-first hypothesis in the early metazoan context.

First, is the proposed account really tantamount to a "phenotype-first" hypothesis?

Whether a mutation (a) more or less directly gives rise to a selected effect (the genotype-first hypothesis), or (b) the mutation directly gives rise to a selected effect that is subsequently repressed in memory and eventually reexpressed under favorable conditions (Watson's phenotype-first hypothesis), or (c) the mutation directly gives rise both to a selected effect and a set of spandrels that are subsequently subject to selection (the proposed, non-Watsonian phenotype-first hypothesis), doesn't it remain the case that all such selections are ultimately sourced in genetic events? The only reason, the objection continues, we are tempted to describe the latter two cases as instances of the "phenotype-first" hypothesis is because the mutational cause is not sufficiently proximate to the selected effect, relative to the first, paradigm case, of genotype-first explanation.

Andres Wagner articulates a version of this objection as follows:

> Systems with clear genotype-phenotype relationships allow us to see that the "phenotype first-genotype first" dichotomy is a false dichotomy. To be sure, evolutionary innovations may first appear as (minor) phenotypes in a genotype's spectrum of plastic phenotypes. From this point of view, the phenotype-first view is correct. However, the spectrum of plastic phenotypes a system can assume is determined by its genotype in the first place. This holds regardless of whether one considers molecular noise or external environmental change as the source of plasticity. From this perspective, the genotype-first view is correct. Which of these perspectives to choose is a matter of taste. Neither of them is wrong—they are complementary views of the same phenomenon. (A. Wagner, 2011, p. 182)

In response, I want to begin by conceding that, in all three cases, the evolutionary innovation stands in a causal relation with the relevant mutation. This is because, on standard counterfactual and/or interventionist accounts of causation, we can be relatively sure that had the cause (the mutation) not occurred, the effect (the innovation) would not have occurred.

However, the concession that all three cases of selection are ultimately sourced in genetic events in no way entails that the choice of perspective is, as Wagner puts it, a "matter of taste." This is because, when causal relations are present, we can draw further distinctions between those causal relations, as reflected in judgments to the effect that some causal relationships are "stronger," more informative, or more salient than others (Woodward, 2021, p. 229). David Lewis vividly illustrates this difference by describing two cases in which a person's action causes the death of another (1986, p. 184). In the first case, a person murders another by shooting them. In the second case, a person writes a letter of recommendation for X which issues in a cascade of effects that wouldn't have otherwise happened: X gets a job which displaces another candidate who got a job elsewhere and married a colleague. They had a child who

eventually died. The murderer and the letter writer are both *causes* of another's death; had the letter not been written, the child wouldn't have been born and so couldn't have died. Lewis marks the distinction by describing the gunshot as *the* cause of a death whereas the letter writing is only *a* cause of a death.

What is the difference, then, between *the* cause of a death and *a* cause of a death? While letter writing can result in death, the firing of a gun much more reliably does so. In James Woodward's terms (2021, p. 228), the causal relation between the firing of a gun and the victim's death is relatively "invariant" (i.e., "stable" or "robust"), insofar as the effect would still occur under various sorts of changes or departures from the actual background conditions. By contrast, the letter writing is a relatively non-invariant (or, as Lewis puts it, "sensitive") cause of the death, insofar as minor changes or departures from the actual background conditions would issue in different effects (there are many ways in which the displaced candidate's child might not have been born and so couldn't have died).

Correspondingly, while a given evolutionary innovation might eventually be traced to a mutation in cases (a), (b), and (c), it doesn't follow that the choice of perspective is a "matter of taste." Scenario (a) describes a "classical Mendelian" genotype-phenotype relationship (Woodward, 2010, p. 294), where the link between the mutation and the resulting phenotype is relatively direct or invariant.[9] However, scenarios (b) and (c) introduce confounding factors between the mutation and the resulting innovation which render the causal relation, as in the letter writing case, less invariant or stable, thus rendering some other factor more salient or explanatorily interesting in virtue of the invariance relation. That is, in scenario (b) (Watson's phenotype-first hypothesis), a mutation directly gives rise to a selected effect that is subsequently repressed in memory and eventually reexpressed under favorable conditions. Because this reexpression is dependent, not only on the mutation, but a host of other factors (repression via stabilizing selection, a novel environment that is sufficiently akin to an ancestral environment, etc.), the relation between the mutation and reexpressed innovation is less invariant than the classical Mendelian case. Likewise for the proposed scenario (c), wherein a mutation doesn't directly give rise to an innovation, but to a spandrel which, given the right internal and external conditions, may become a target of selection. In scenarios (b) and (c), because of the confounding factors that mediate the causal relations between the mutation and the evolutionary innovation, phenotypical (e.g., spandrels) and/or environmental events have a better claim to the label, "*the* cause," than do the genotypical events that preceded them because the former are more invariantly related to the evolutionary innovations under investigation.

I take it that this is the force of the "phenotype first-genotype first" distinction, which adequately gestures to the fact that there can be sufficiently deviant causal chains between genetic events and selected effects (e.g., via developmental memory or a spandrel). That is, the dichotomy marks the difference, not between when one

[9] I'm speaking loosely here. While, as a general rule, spatially and temporally proximal causal relationships tend to be more invariant, as Woodward points out, proximal causal relationships can lack invariance or be "sensitive" to interference and distal relationships can be relatively invariant (Woodward, 2010, pp. 294–295).

or another cause is or is not present, but between different *kinds* of causes—as when the genotype is flagged as being a relatively invariant cause of an innovation (the genotype-first perspective) and when it is not (the phenotype-first perspective). And invariance, following the interventionist, tells us something about when a factor is reliably altered by natural selection (Woodward, 2010, p. 295); just as it would be a mistake to look to letter writing as a reliable means by which someone's death could be brought about, sometimes a phenotypical or environmental change is a better candidate as *the* cause of an evolutionary innovation.

The problem with Wagner's suggestion that the choice of perspective is a "matter of taste" is the same problem Woodward finds with analogous claims, advanced by P.E. Griffiths & R.D. Gray (1994) and Oyama (2000), to the effect that there is a "causal parity" between DNA sequences and "other cellular machinery" (Woodward, 2010, pp. 316–317). Causal factors do not have a claim to an equality of salience, and invariance marks one way of introducing the required explanatory asymmetry between such factors.

A second objection is as follows: is the Watsonian account really inapplicable to the earliest metazoans?

I motivated the proposed non-Watsonian account of the phenotype-first hypothesis by suggesting that an appeal to "memory" can't help us understand how such a hypothesis might be applicable to the earliest metazoans who, by definition, lack the required memory *qua* metazoans. The qualifier, "*qua* metazoans," is important because, of course, even the earliest metazoans appeared billions of years after life originated on earth. Thus, it is entirely plausible that phenotypic innovations which typify the metazoans, including, e.g., the capacity for cellular cohesion while permitting liquid-like random perambulation, are "remembered" expressions of unicellular capacities that predated the metazoans.

Indeed, this is a fair description of the important work coming out of Ruiz-Trillo's lab: "animal development evolved using morphogenetic processes already present in their ancestors and later recruited for animal development" (Ruiz-Trillo & de Mendoza, 2020, p. 1). And, as discussed above, these already-existing processes include not just the capacity to cohere into temporary colonies, but to cohere in ways that are already indicative of the liquid tissue form. For example, Ruiz-Tillo and Mendoza describe a species of choanoflagellate that can modify the colony shape in a way "reminiscent of that of animal gastrulation" (Ruiz-Trillo & de Mendoza, 2020, p. 4; Brunet et al., 2019, Fig. 2D). Thus, perhaps metazoan liquid tissue is an instance of Watsonian recollection after all.

This is ok. The point of this paper is not to make substantive claims about early metazoan evolution and, in this case, the explanation given might be transposed onto these earlier, pre-metazoan innovations. While I have relied on Newman's account to fashion a plausible story about the factors which drove deep metazoan selection (e.g., the importance of magnitudinal properties in being able to exploit empty mesoscale niches), this story was ultimately in the service of illustrating a relatively clear instance of the phenotype-first hypothesis that relies, not on Watsonian recollection, but on spandrels as a source of phenotypic variation. Despite the prima facie attractiveness of the deep metazoan context for those purposes, once the point about spandrels has been seen, we can look elsewhere for even more plausible instantiations.

This is, indeed, the task of the final section of the paper, where I connect the proposed account of a phenotype-first hypothesis to Müller's "side-effect hypothesis."

3.4 Generalization to Müller's "side-effect hypothesis"

What remains is to gesture to how the proposed phenotype-first explanation in the deep metazoan context might express itself in other evolutionary scenarios. Generalization might not only help clarify the proposed account of phenotype-first explanation but would also address a requirement, as articulated by Alan Love and Gary Lugar, that accounts of the origins of multicellularity should be sufficiently fecund. A "critical explanatory burden" of any explanation of early metazoan evolutionary innovation is that these investigations "generalize to other research on different innovations or novelties" (Love & Lugar, 2013, p. 541; see also Love, 2008).

I have claimed that spandrels are a source of phenotypic variability. While spandrels are genetic products, they are not adaptations. Thus, if this non-Watsonian version of a phenotype-first explanation is to be generalized to other evolutionary contexts, we should hunt for cases where phenotypic variability (1) is not a selected effect but a spandrel or mere effect of selection and (2) is a source of variation upon which selection subsequently operates.

Tim Peterson & Gerd Müller (2016, p. 323) provide a good example of a late metazoan evolutionary innovation that satisfies these two desiderata. Cichlidae and related fish species have internal pharyngeal jaws that process the prey secured by their outer oral jaws. However, the pharyngeal jaw apparatus of the Cichlidae has several features not found in other species with pharyngeal jaws.[10] These include, as shown in Fig. 3, a novel cartilage joint between the cranium and the upper pharyngeal jaw (in other species, these are fused) and an epibranchials 4 that is decoupled from the upper pharyngeal jaw (in other species, these are coupled).

The evolutionary innovation to be explained is the novel joint present in this population. Many developmental events are not directly programed by genes, but, as we have seen in the case of spadefoot tadpoles, are the result of internally and environmentally-induced context-dependent cues. In the case of these fish, the genetically encoded cue for cartilage joint formation is pressure on connective tissue. Peterson and Müller's explanation of this novel joint is a phenotype-first hypothesis insofar as they explain its formation by appeal to the "side effects" of the decoupling of the epibranchials 4 and upper pharyngeal jaw, which produce four times the pressure on the upper pharyngeal jaw as compared to otherwise similar species of fish whose structures are not decoupled. Let us imagine that the decoupling was the direct result of a mutation whose phenotypic effects were selected for reasons that made no reference to the formation of the joint.[11] Perhaps, for example, the decoupling increased the capacity to process prey by increasing the force of the lower pharyngeal jaw's crushing power, to which it remains connected (by way of the ceratobranchial 4). This increase in force was the selected effect and the cartilage formation is just a mere

[10] Except for the Labridae fish family.

[11] This posit is a simplifying assumption. In fact, the decoupling is likely just another biomechanical side-effect of a different selected effect of a mutation.

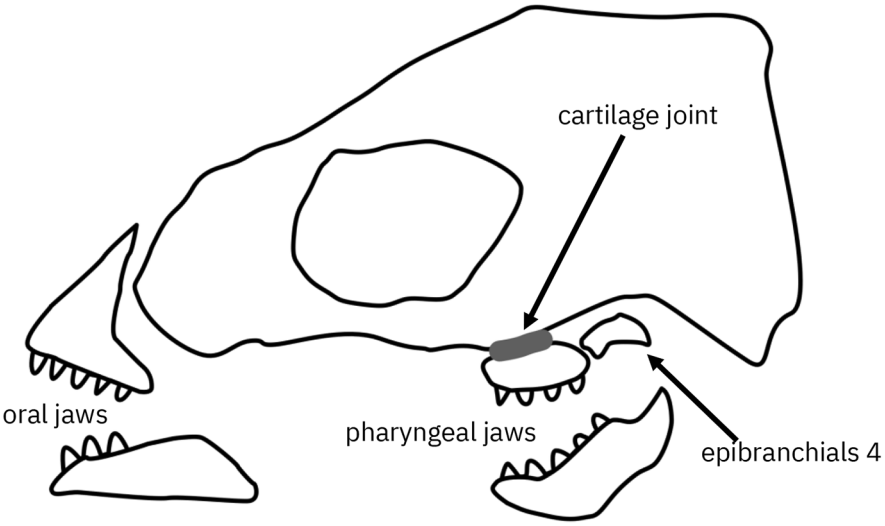

Fig. 3 Schematic of the pharyngeal jaw apparatus of Chichlidae, adapted from (Peterson & Müller, 2018, p. 3). The gray area is the location of the novel cartilage joint found only in Chichledae. The epibranchials 4 and the upper pharyngeal jaw is uniquely decoupled in Chichledae

side effect of selection. Because the fish also happens to be genetically disposed to form cartilage when sufficient pressure is applied to connective tissue, then this structural variation initially appears as a spandrel. However, to the extent that this spandrel results in a fitness advantage (perhaps the cartilage joint compounds the lower jaw's increased crushing power or buffers against damage), it becomes a target of selection and genetic accommodation (exaptation by way of secondary selection).

It is well understood that a tweak in one part of a complex system can issue in a cascade of unforeseen and normatively valenced effects. In this way, a sufficiently complex biomechanical system, such as the cichlid pharyngeal jaw apparatus, is, like the particular adhesion mechanism of the early metazoans, a repository of hidden variability. Just as, for the early metazoans, the magnitidinal properties of a given adhesion mechanism, rather than a capacity to support liquid-like random perambulation, might be the initial target of selection, Müller claims that the cartilage joint is an accidental consequence of selection on another part of the cichlid jaw system (namely, the decoupling of the epibranchials 4 and upper pharyngeal jaw). Such biomechanical consequences are an important source of phenotypic variability upon which selection might operate.

While Müller does not, to my knowledge, use the term "spandrel" to characterize the cascading consequences that result from a change in one part of a biomechanical system, he has long relied on the notion of a "side effect" to articulate what I understand to be an analogous idea:

> Novelty can … arise as a side effect of evolutionary changes of size and proportion, with the specific result depending on the reaction of the affected systems. In this scenario the emerging structure becomes only secondarily a target of

> selection which will determine its maintenance and persistence throughout the population; the disruption of a morphogenetic sequence lies at its origin. (Müller, 1990, p. 109)

4 Conclusion

Watson's version of the phenotype-first hypothesis sees developmental memory as a key reservoir of phenotypic variability. This memory also helps explain why some adaptations would appear to be preadapted to a novel environment, on the assumption that this environment is sufficiently analogous to an ancestrally encountered environment.

Because Watson's hypothesis depends on an accumulated history of environmental interactions, it is especially well-suited to explain preadapted late metazoan innovations. But what of the earliest metazoans?

I have argued that an interpretation of Newman's account of early metazoan evolution suggests that spandrels can, like Watson's developmental memory, serve as an important reservoir of phenotypic variability. In particular, a condition for multicellularity is the presence of an intercellular cohesion mechanism. Because plants, animals, and fungi independently evolved multicellularity, and because these lineages have importantly different cohesion mechanisms, this suggests that it was these mechanisms' magnitudinal effects that were the initial targets of selection, as they enabled these lineages to exploit unoccupied "mesoscale" niches. In the case of the early animals, their cadherin-based cohesion mechanism also facilitated the liquid-like random perambulation of cells. I argued that this metazoan-specific property was initially a spandrel that became a subsequent target of selection. In this way, spandrels represent a reservoir of phenotypic variability that makes no reference to the idea of developmental memory. I then argued that the proposed, non-Watsonian account of the phenotype-first hypothesis is closely related to Müller's "side-effect hypothesis."

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