# On the origins of morphological disparity and its diverse developmental bases

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**Summary**

**It has been repeatedly claimed that morphological novelties are an unresolved problem in evolutionary theory. Several definitions of novelty exist but most emphasize that novelties imply qualitative changes on the phenotype and not the quantitative gradual changes favored in the neo-Darwinian approach to evolutionary theory. This article discusses how the concept of novelty is used to describe aspects of morphological evolution that are not satisfactorily explained under the modern synthesis. In this article, it is suggested that there is a repertoire of morphological changes rather than two discrete qualitatively different types of morphological change. How these different types of morphological changes can be understood from the diversity of developmental mechanisms existing in animal development is explored. Specifically, it is proposed that animal morphology and its variation can be understood from the spatial patterns produced by a set of basic developmental mechanisms and their combination. Some specific examples of these kinds of morphologic changes are explained.** ***BioEssays*** **28:1112–1122, 2006.**


## Introduction

According to some authors,[1] a novelty is a novel trait based on a qualitatively distinct developmental variant. Others have proposed that novelty should be understood as a change in homology. Homology implies, for these authors, the sharing of historically acquired and genetically regulated developmental constraints or variational properties.[2] These definitions use relative concepts as ''new'', ''homologous'' or ''qualitatively different'' but there is no general agreement about how qualitatively different or new, or in which way, changes must be to be considered a novelty. There is a rich body of literature identifying novelties,[3–9] although the lack of a consensus definition of novelty that this research produces is not always focused on comparable phenomena.

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Most definitions of novelty consider that there are two kinds of morphological changes in evolution. Changes can occur according to the classical gradual neo-Darwinian view in which there is genetic additive variation for most traits and this variation is small (meaning that offspring is very similar to parents). This way variation and evolution can be seen as quantitative gradual changes in the values of morphologic traits. From this perspective, the mechanisms by which morphologic variation is produced during development do not play a major role in evolution because, eventually, most morphological changes can be achieved by accumulating small gradual morphological variation.[10,11] In addition, there are other kinds of changes that do not fit this schema of genetic gradual variation for most traits. These changes cannot be described as quantitative changes in trait's values but as qualitative changes in the nature of traits themselves. These can be the appearance of a new trait or the disappearance or change of the context of existing traits.[2] In other words, changes that do not affect the quantitative values of a morphological trait but the number of dimensions by which a morphology is properly described.[12] In some cases, these special changes are expected to involve special changes in development[2,13] while, in others, this is not supposed to be the case.[14] Researchers in novelties consider that development is an important factor in morphological evolution because it determines the nature of these special changes.[12] In fact, some research in novelties reflects an interest in the nature itself of the morphological variation arising in evolution. Thus, this research not only proposes a different perception of how morphological evolution works but also asks a different set of questions.

The neo-Darwinian approach to evolution describes morphological change in a simple but well-defined way: quantitative changes in traits values. In contrast, what is a ''qualitative'' change is not so easy to define and, in fact, it is a poor description of the diversity of morphological changes known to occur in animal evolution. This article does not propose a new definition or clarification of the concept of novelty. Instead, the goal is to describe the basic kind of morphological changes that are possible in animal evolution and their developmental bases. This article considers morphological change by itself irrespective of the nature or magnitude of their functional or adaptive consequences. This description is incomplete, as is the current understanding of

the relationship between developmental mechanisms and morphological variation, but it naturally includes insights from classical neo-Darwinism, research in novelties and recent advances in developmental biology. Here it is proposed that variation occurs (and should be understood) in different qualitative classes or patterns (due to development) in which a large but finite set of quantitative changes are possible. An attempt to identity these classes and their patterns of variation is provided. While doing that it will be explained how some of these changes fit into some definitions of novelty and the neo-Darwinian views. However, the main aim is to start to explain how morphological changes can be described by their nature (in terms of morphology itself) and not by whether they fit or not to the idealized conceptualization of morphological change present in the neo-Darwinian approach (as is the case in novelties research).

## Developmental patterns and developmental mechanisms

Before continuing further, we should present some definitions that will be used later on. One of the more important phenomena in development is pattern formation or transformation: the transformation of a previous pattern, i.e. the spatial distribution of cell types and extracellular components, into another pattern or resulting pattern, over time. A developmental pattern can be a pattern of gene expression or any other spatial distribution of cell properties. A territory is, in this paper, a group of contiguous cells that share the expression of a gene or another property. From that definition, the morphology of an organism is made of a set of patterns and these are made of territories with different morphologies. From this perspective, the ensemble of possible morphological changes can be described as the ensemble of possible territory forms. A gene network is a set of genes and the set of possible specific direct interactions between them (this is determined by the structure of these proteins while the dynamics of outgoing development determines which of these possible interactions does physically occur). A developmental mechanism is, in this article, any gene network that can produce some pattern transformation. For that purpose, at least one gene in the network must be able to regulate some basic cell behavior (adhesion, differentiation, apoptosis, mitosis, secretion and reception of extracellular signals).[15] Other authors have used a different definition of network and a different approach in describing their role in development and evolution.[16–18] A developmental mechanism has a developmental pattern (that includes at least a pattern of gene expression in one or more of its constituent genes) as input and, through changes in gene action and cell properties, it gives as a result, or output, another developmental pattern. Even if a developmental mechanism is defined simply as a gene network, it has to be taken into account that proper pattern formation would require a proper previous pattern, epigenetic context and environment (see later). In fact, all these other factors can be equally important to understand a specific pattern transformation and then it would be equally adequate to describe developmental mechanisms as comprising the gene networks, cell behaviors, previous patterns and epigenetic and environmental contexts. From these definitions, development can be seen as a set of *previous pattern/resulting pattern* transformations each performed by a developmental mechanism. Networks can be made of subnetworks and development can be arbitrarily partitioned into sequences of pattern transformations. Basic developmental mechanisms are the simplest gene networks that, by using only one cell behavior (as mitosis, apoptosis, adhesion, differentiation and secretion and reception of molecular signals), can produce pattern (Fig. 1). In inductive mechanisms pattern formation occurs because cells interchange molecular signals and in morphogenetic mechanisms because of changes in cells spatial location.[15]

The variational properties of a developmental mechanism are defined as the ensemble of patterns that it produces under all possible previous patterns, environmental conditions and genetic mutations that do not alter the topology of the network. These mutations are called here interaction strength mutations (IS-mutations). They can be changes in the sequence of protein–protein, protein–nucleic acid or nucleic acid–nucleic acid binding sites that affect binding affinities or other sequence changes that affect other biochemical properties of gene products (like for example the diffusion or reaction rates of a gene product). In contrast, mutations that alter the topology of a network (called in here T-mutations) involve changes in binding sites (of nucleic acids, proteins or other) that affect the identity of their specific targets.

The distinction between T-mutations and IS-mutations is not totally clear cut since it depends on the size of the gene networks into which development is arbitrarily partitioned. For example, a IS-mutation affecting the diffusivity of an extracellular molecule A may, as an indirect consequence, prevent this signal binding to its receptor R (for example a tyrosine kinase), which, in turn, prevents the activation of its immediate target C (for example by phosphorylation). If development is arbitrarily partitioned into the developmental mechanism that produces the spatial distribution of A and the developmental mechanism that is downstream of A, then the effect of the IS-mutation is to simply change the previous pattern in which the second mechanism acts. If a single developmental mechanisms is defined that includes A, R and C then the IS-mutation may have the effect of a T-mutation precluding that R binds to C (notice however that R and C have not changed as regards what they can bind and they could still bind in other stages of development). In addition, IS-mutations reducing the binding affinity of a binding site may prevent the binding of the molecule to all or part of its targets. The larger and more complex the developmental mechanism that is being

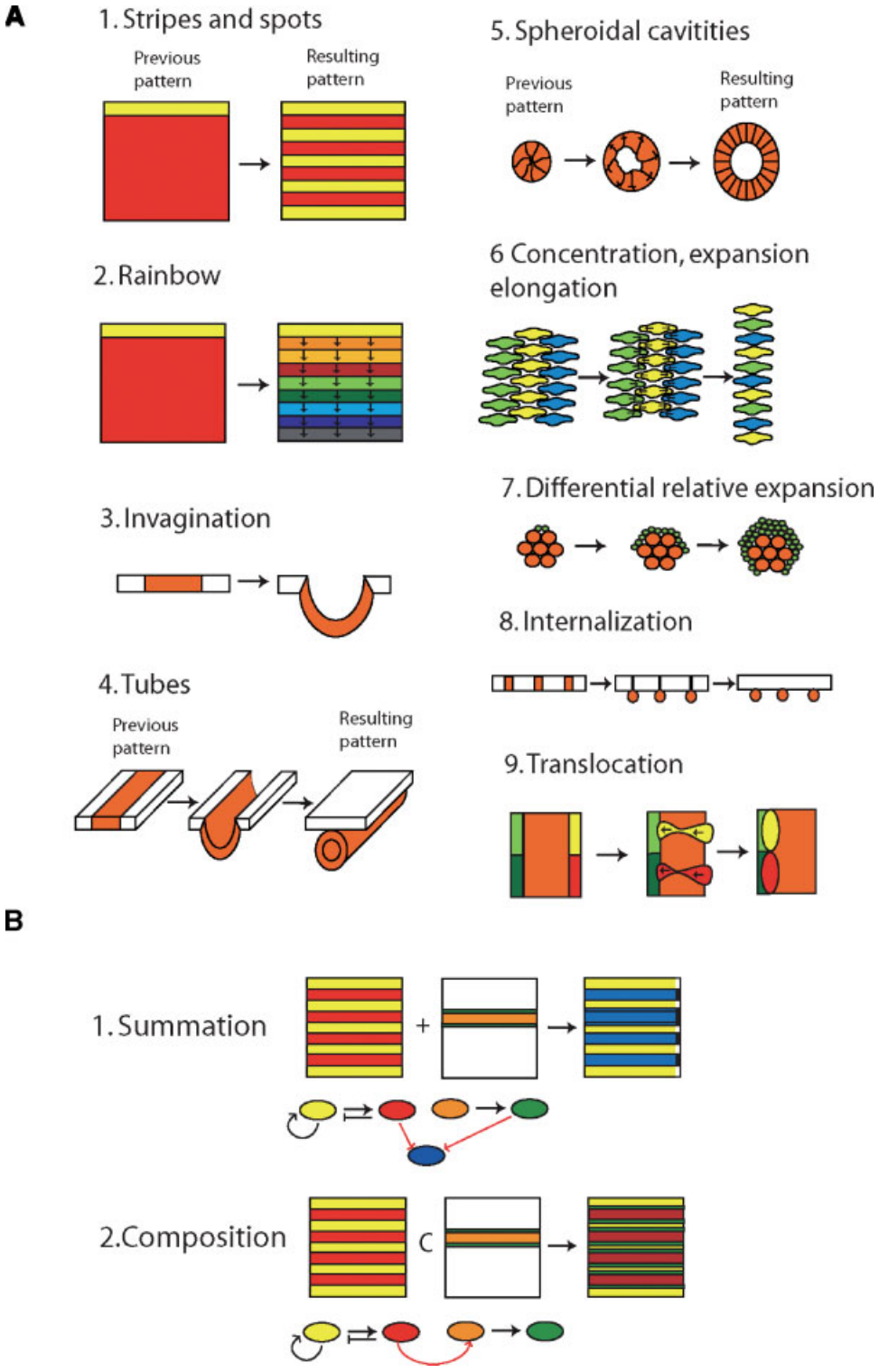


**Figure 1.** Schema of the different kinds of pattern transformations explained in the text. **A:** The basic pattern transformations and **B:** pattern transformations arising by summation of an emergent mechanism and a hierarchic mechanism (1) by composing an emergent mechanism and a hierarchic inductive mechanism. Colors represent territories of cells expressing a set of genes in common. Small arrows in **A** *1* represent signaling and in *9* direction cell migration. In **B** colored ellipsoids represent genes. The arrows in between ellipsoids represent genetic interactions. Under each pattern in **B**, the figure shows the topology of example gene networks that can produce that pattern. Red arrows are the gene interactions that mediate the summation or composition.

considered, the less useful is the distinction between these types of mutations. For development as a whole they may be of no use. In fact, these definitions are only useful to partition development into parts that are easy to study and are a mere question of convenience. Specifically, if most of the types of developmental mechanisms that are possible in development are known, and their variational properties are also known, then the pattern variation possible in animal development can be described as the variational properties of these mechanisms and the patterns arising by combining these developmental mechanisms (these are T-mutations by definition). Thus mutations are partitioned between those that affect which part of the variational properties of a mechanism are realized and those that transform developmental mechanisms into others (for example by combination). This does not imply or require that T-mutations, in general, produce different or larger pattern changes than IS-mutations (although some theoretical studies suggest that this is the case for some types of developmental mechanisms[19]) or that large changes are not possible by IS-mutations (although we will discuss some cases in which that may be the case). These distinctions simply provide an easy way to explain which morphological variation is possible in development from the developmental mechanisms that are currently known (see Ref. 20 for further discussion of this point). A similar attempt would be possible by partitioning development by different criteria but this one is useful because it allows incorporation into the discussion studies that explore possible morphological variation from non-changing gene topologies (see later). In this article, the patterns and variational properties of basic developmental mechanisms are explained. Later, how these can be combined in development and how that may provide an estimation of the types of morphological variation possible by development will be explained.

## Changes in developmental patterns and its developmental basis

### *Pattern changes due to changes in cell state or fate*

There are two kinds of patterns that have been repeatedly suggested in the literature to arise from inductive mechanisms. The same two kinds result from theoretical studies exploring the patterns possible from gene networks in cells that interchange molecular signals.[19]

### *Stripes and spots*

Patterns in which groups of equivalent cells are arranged on a more or less regular grid of spots or stripes can be found in the adult and embryonic phenotypes of many animals (Fig. 1A1). They are found, for example, in the coating skin patterns of many vertebrates,[21] in the patterns of expression of some genes during the segmentation of insects,[22] crustaceans,[23] chelicerates,[24] annelids[25] and some mollusks[26] and in the somites of chick and mouse.[27] There is evidence that some of these patterns are produced by emergent mechanisms[28–32] while others are produced by hierarchic mechanisms.[33–35] In hierarchic mechanisms, cells send signals to each other but the signaling of a molecule by a cell is not affected directly or indirectly by the response to it by neighboring cells. In these mechanisms, there is thus a strict lineal sequence of upstream to downstream genes. Inductive emergent mechanisms include a Turing-type reaction–diffusion mechanism for diffusible molecular signals and lateral-inhibition-type mechanisms for membrane-bound signals. In these mechanisms, there is no upstream–downstream hierarchy between genes and the signals sent by a cell are affected by the response to that signal by neighbor cells.[19]

In those cases in which the stripes and spots patterns are produced by an emergent mechanism, theoretical studies indicate[19,35,36] that IS-mutations would produce morphological variation that include: changes in the spacing between repeated elements (either spots or stripes territories), changes in the number of elements and changes in the sharpness of the borders of each element. The patterns produced do not easily change when the previous pattern changes. These changes will always happen for the ensemble of repeated elements in the pattern: parts cannot change independently. In addition, these changes often occur together (e.g. the spacing between elements easily changes the number of elements). These theoretical considerations are consistent with the mutationally induced changes in patterns that appear to arise by emergent mechanisms.[30,37] The new repeated elements in such patterns should not be considered in principle real novelties, in the form of a breakdown of homology, because they are formed by the same developmental mechanism and cannot change independently.

### *Rainbow or French flag patterns*

Another very common kind of pattern consists in territories of similar form arranged in parallel to each other (Fig. 1A2). The developmental mechanisms proposed to explain some of these patterns are of the inductive hierarchic type[38] and thus involve a hierarchic chain of consecutive inductions between territories. Each induced territory has the form of a band surrounding the inducing territory. Theoretical studies suggest[19,39] that the width of each territory depends on the diffusivity of the inducing signal and the form of all territories is ultimately dependent on the territory of the most upstream gene (except for border effects). Often these patterns are described as linear patterns in the anterior–posterior axis. This kind of pattern includes the expression patterns of Hox genes in the *Drosophila* blastoderm,[40] in the pharyngula of chick and mouse,[41] and in parts of the developing chick limb bud,[42] and gene expression in the cell tiers of regular echinoid blastula.[43]

Theoretical studies suggest that,[19,39] through IS-mutations these patterns can easily change the width of individual

territories and their levels of expression but not the form or number of territories. Consistent with that, it has been found the patterns of hox gene expression change between the species, more often in the width of the territory of expression than in its shape.[44] This does not explain how often they change (because this depends also on selective pressures) but only the direction that it can change when selective pressure allow it. These patterns can respond in a rather gradual way to IS-mutations giving a relatively simple relationship between phenotype and genotype.[35,36] In fact, the variation produced by basic inductive hierarchic mechanisms fits, to some extent, the neo-Darwinian view about morphological variation. If each territory width (Fig. 1A) is considered as a trait, then each trait can have a large and gradual range of variation that is relatively independent of the rest of the pattern elements. Then each trait value combination becomes possible and it can be said that there are no developmental constraints. At the same time, the variation is very restricted since no new territories appear (no new traits appear) and their shape is not significantly altered by IS-mutations. Hence variation is quantitatively unrestricted inside the qualitative class of rainbow patterns.

### *Pattern changes due to changes in cell location*

See Table 1.

### *Variational properties of morphogenetic mechanisms*

Many morphogenetic mechanisms function through the collective behaviour of large groups of cells that mechanically interact. The dynamics and outcomes of such mechanisms are highly dependent on the epigenetic context of the developing embryo.[51] This context includes the mechanical material properties of intervening tissues and surrounding territories[71–74] and the relative distances and shapes of surrounding territories because these factors affect the mechanical response and resistance of any given territories to stresses and stretches in different directions.[72] The variational properties of these mechanisms have rarely been studied[71–74] but many studies point out that this epigenetic dependence produces a complex relationship between genetic and morphological variation.[71–74] In other words, even when these mechanisms are highly regulated, small IS-mutations can produce important changes in the form of territories.

## Combining patterns by summation, subtraction and composition

Patterns arising from inductive mechanisms can be combined by summation or subtraction of gene activities that are downstream of two such independent developmental mechanisms (Fig. 1B). Combinations by composition occur when a gene is downstream of one developmental mechanism and upstream of another. Then the pattern produced by one mechanism is the previous pattern on which the other acts (Fig. 1B). In that way, new pattern combinations can arise by T-mutations connecting existing developmental mechanisms into new composite developmental mechanisms. This constitutes novelty in the sense that these new patterns and developmental mechanisms have new variational properties and, as a result, are not directly homologous to their ancestors.

### *Rainbow pattern combinations*

Such combined patterns have been found in comparing wing coloration patterns between *Drosophila melanogaster* and a closely related species.[75] In *Drosophila biarmipes*, males have a dark spot in the anterior part of the wing tip that spatially correlates with the expression of the gene *yellow*. In *Drosophila melanogaster*, the whole wing has a mild homogeneous pattern of *yellow* (and pigment). Genetic analyses have shown that *D. biarmipes yellow* gene has in its promoter two binding sites for the gene *engrailed*. In both species, *Engrailed* is expressed in the posterior part of wing primordia (as a one bar rainbow pattern) and the binding of engrailed protein to the promoter region of *yellow* has been shown to be responsible for the restriction of yellow to the anterior part of the wing. Why *yellow* is restricted to the distal tip of the anterior part of the wing is not known but clearly part of the pattern arises from subtracting the *engrailed* pattern from a previous homogeneous pattern of *yellow*. The variational properties of these combinations have been suggested to be similar to those of basic hierarchic developmental mechanisms.[15]

### *Spots and stripes pattern combinations*

Stripes and spot patterns can also be combined by summation, subtraction and composition (see Fig. 1B). These patterns often consist of several kinds of repeated elements distributed in a regular and complex symmetric grid. These kinds of combinations have been proposed for the pattern of skin appendages in several animals.[76]

### *Rainbow and stripes and spot combinations*

Stripes or spots and rainbow patterns can also be combined by summation, subtraction or composition (see Fig. 1B). If an emergent and a hierarchic inductive mechanism are involved, special mixed variational properties may occur. These patterns can comprise several repeated elements (produced by the emergent part) and at the same time have some polarity or asymmetry in some axis (produced by the hierarchic part). This also permits the characteristics of the repeated elements to be changed independently between parts of the pattern. These kinds of combinations have been suggested to be common in evolution. The reason is that emergent networks can readily appear in evolution (because they involve networks relatively simpler than hierarchic networks for patterns of the same complexity) but cannot fine-tune their patterns to small changes in selective pressures (although later hierarchic networks would allow independent variation of parts).[35] This kind of combination has been suggested to occur in limb

**Table 1.** Table describing the main types of patterns that are due to changes in cell location

| Name | Description | Mechanism | Variational properties | Examples |
|---|---|---|---|---|
| Invaginations | Blind tubes or pouches of epithelia | Absortion of water,[45–47] apical contraction,[48–51] differential proliferation of epithelia and mesenchymer[52] | Invagination size, deepness and relative concavity? | Echinoid archenteron[46,47] neurulation,[48] *Drosphila* gastrulation,[49] the salivary glands of Drosophila,[50] *Xenopus* blastopore formation. Vertebrate lens[52] |
| Tubes | Tubes | As invaginations, also by condensation into rods and later cavitation of dispersed mesenchymal cells[53] | Tube length and diameter? | Neurulation[53] and elongation of archenteron[54] |
| Spheroidal cavities | Spheroidal cavities | Tight junctions formation (Fig. 1A5) and active transport of ions produces forms the inner cavity. Also as in the cases of invagination | Changes in size? | Blastulation in Stronglyocentrotus[55] and in *Xenopus*.[56] Otic saccule.[57] |
| Concentration, elongation and expansion | Epithelial or mesenchymal reducing one of their dimensions to elongate in one or two other dimensions (Fig. 1A6) | Intercalation of groups of polarized cells[62] | Changes in the degree of contraction and elongation in different directions? | Notochord of ascidians,[58] germ band extension and hindgut formation in *Drosophila*,[59] ectoderm dorsal closure in *Caenorhabditis*.[60] Chick neural tube closure.[61] |
| Internalization | Non-epithelial groups of cells underlying epithelia or mesenchymes (Fig. 1A8) | Ingression of individual cells[63] by changes in adhesion. Also assymetric directed mitosis[66] | ? | Echinoid blastula micromere formation.[63] Mammalian and bird mesoderm formation[64] and neural crest delamination.[65] Nervous system precursors formation in *Drosophila*.[66] |
| Differential relative expansion of territories | Relative changes in size and shape of territories due to differential growth | Pattern changes occur because the cells (or extrecellular matrix) in different territories proliferate or die at different rates (Fig. 1A7) | See section Variational properties of morphogenetic mechanisms: | Different rates of proliferation among territories determine wing shape in *Drosophila*.[67] Gastrulation in some organisms[68] occurs by rapidly dividing cells covering large slowly dividing cells |
| Translocation | Individual migration of cells so that territories do not retain their neighbors (Fig. 1A9) | Migration towards a source of a diffusible molecule[69] or migration following gradient of adhesive non-soluble molecule[70] | See section Variational properties of morphogenetic mechanisms: | Neural crest, germinal cells in insects and Mammals |

development, where an inductive emergent mechanism has been suggested on experimental and theoretical grounds,[77] to be responsible for the spatial pattern of chondrogenic condensation that form the bone elements, while a rainbow pattern of hox genes (formed by an as yet unknown mechanism) may determine its polarity in the anterior–posterior axis by affecting adhesive properties.[78] A similar situation occurs in feathers where the pattern of feather distribution in the skin has been suggested to come from a reaction–diffusion mechanism[29] and the regional differences of this pattern have been suggested to come from a rainbow pattern of Hox genes affecting the spot pattern.[37]

### Combining patterns by translation and rotation

Animal phenotypes are made of patterns that often are much more complex than the ones just presented. Precise spatiotemporal regulation of where and when these basic patterns are combined may be the basis for the production of complex morphologies. Such combinations can occur when different territories express different transcriptional factors, leading to different regulation or activation of morphogenetic or inductive mechanisms. This process would involve supplying morphogenetic mechanisms with previous patterns that have more genetic territories and thus combine inductive and morphogenetic mechanisms. Inductive and morphogenetic mechanisms can be combined in a morphostatic way if inductive mechanisms act first and morphogenetic mechanisms act later or in a morphodynamic way if both mechanisms act at the same time or intercalate with each other over time (Fig. 2). A developmental mechanism is more, or less, morphodynamic depending on how long, or how often, morphogenetic and morphodynamic mechanisms act at the same time. Examples of morphostatic mechanisms would be those proposed for leg imaginal discs[79] and early *Drosophila* segmentation.[33] For examples of both kinds of mechanisms see Ref. 15.

In morphostatic mechanisms, the spatiotemporal coordination of cell behavior changes is attained by the autonomous execution of a specific genetic program in each cell. Which cell program is followed in each cell depends on the pattern previously established by the inductive mechanism.[80] In morphodynamic mechanisms, the coordination of cell behaviors is attained, in principle, by a simple but sequential set of responses to a set of constantly arriving signals. The place from which signals are sent (and consequently the places where they can be effectively received) changes constantly because the response of cells to received signals involves not only sending signals but also changing the regulation of cell behaviors that affect cell spatial location. Thus, instead of rigid deterministic genetic programs, there is a complex temporal sequence of complex spatially localized epigenetic influences (in the form of spatial distribution of signals and cell movements) that constantly guide cell behavior. In both mechanisms, cells follow a complex temporal ordered sequence of cellular changes but the dynamics behind these are dramatically different.

Theoretical studies indicate that morphodynamic mechanisms produce, relative to morphostatic mechanisms, patterns that are much more distinct (so there is not always a gradual transition between patterns) and a complex relationship between genetic and morphological variation.[81] The morphodynamic and morphostatic dichotomy is about relative temporal order and does not imply a significantly different genetic architecture. These different variational properties can be understood by considering which territorial forms can be attained by each kind of mechanism. Morphostatic mechanisms can produce the territorial forms possible from basic inductive and morphogenetic mechanisms (see Fig. 1A). Additional territory forms can be attained by molding the bars, stripes and spots territories produced by inductive mechanisms into the forms that mophogenetic mechanisms can produce. Morphodynamic mechanisms can produce, in addition to these same forms, the forms arising by signal diffusion from territories produced by morphogenetic mechanisms. In this way, the patterns produced from morphogenetic mechanisms can feedback into inductive mechanisms and a larger repertoire of pattern transformations can be used to construct the phenotype during development. Because the epigenetic dependencies of morphogenetic mechanisms are also feedback, the more often morphogenetic mechanisms act together the more complex is the relationship between genotype and phenotype.

In addition, in morphodynamic mechanisms, signals diffuse in a spatially complex embryonic context distorting the forms of the territories in which a signal is received with enough concentration., This allows an even larger repertoire of pattern transformations (if signaling occurs only before the overall form changes, the spatial context is simpler; Fig. 2). Complex intermediate phenotypes can signify that small IS-mutations in the morphogenetic or inductive part have produced sudden changes, such as the formation of new territories (see Fig. 3). These territories are serial homologues of each other because they are produced by the same developmental mechanisms and cannot change independently. However, they do not necessarily change in the same way (for example the central green territory in Fig. 3C does not change in the same way as the lateral green territories because the proximity of the target territory gives less space for the dilution of the signal).

In general, morphodynamic mechanisms can readily produce pattern variation that includes changes in the number and forms of territories. Morphostatic mechanisms produce, instead, variation in the relative sizes of territories. In other words, if any morphology can be described by a set of metric traits, morphodynamic variation is found in more traits but with fewer value combinations in these traits. In comparison, morphostatic variation is found in relatively fewer traits but allows many more trait value combinations.

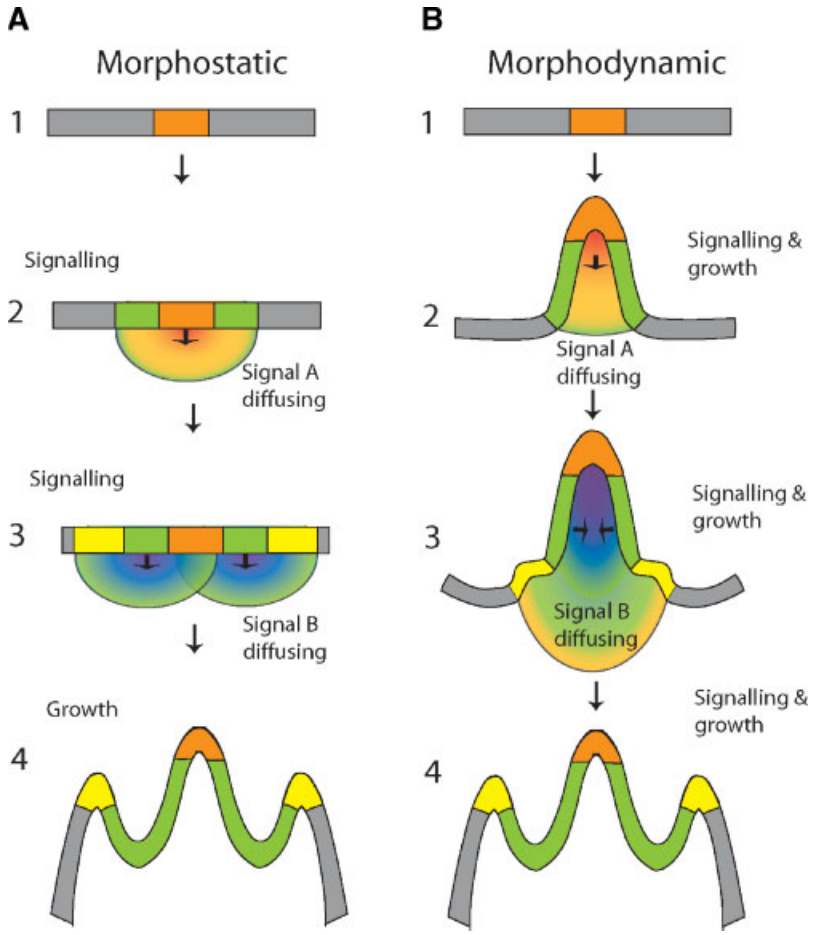


**Figure 2.** Schema of the different dynamics defining morphostatic and morphodynamic mechanisms. As before, shapes with different colors indicate territories of cells expressing a set of genes in common. In *2* the orange territory secretes a signal (in the form of a red–yellow gradient of concentration of the signal). The cells in the grey territory express a receptor of that signal and then differentiate to green cells if they receive enough signal. In the morphodynamic case, cells proliferate from the moment that they become green. This results in the red signal diffusing in a smaller space and the attaining of a higher concentration at larger distances from the orange territory. Then more green territory is induced in the morphodynamic mechanism. In *3* green cells start to secrete a blue signal (shown by a blue-to-green gradient of concentration in the figure) for which grey cells also express a receptor. Cells receiving enough blue signal become yellow and decrease their proliferation rate in the morphodynamic mechanism. In *4* in the morphostatic case cells start to proliferate with a rate established by their color. Orange cells do not proliferate, yellow proliferate a little and green and grey cells proliferate a lot. These two mechanisms do not necessarily produce the same morphologies (in fact the green territory may be larger).

The use of the spatial clues existing in the developing epigenetic context of the embryo by morphodynamic mechanisms can be seen as tinkering that allow complex and disparate spatial patterns to be produced without the requirement of a complex genetic structure.[81] Inevitably, however, as morphodynamic mechanisms can produce more morphologically distinct variations for the same genetic complexity than morphostatic mechanisms, morphological variation is related to genetic variation in a more complex fashion.

Tooth evolution and development offers some instructive examples of novelties in morphodynamic mechanisms. In developing teeth, the epithelia that will form the surface of the teeth and the underlying mesenchyme are sending and receiving signals while they proliferate. A morphodynamic mathematical model that implements the experimentally inferred gene network (and its effect on cell behavior) of tooth development can reproduce the three-dimensional morphology, patterns of gene expression and correct timing of mouse and vole (*Microtus rossameridionalis*) second molar development.[82] This model indicates that small changes in the interaction strengths between genes, or of their effects in proliferation (IS-mutations), can reproduce the recent evolutionary transition between vole and mouse morphology. These two morphologies differ in the relative positions of all

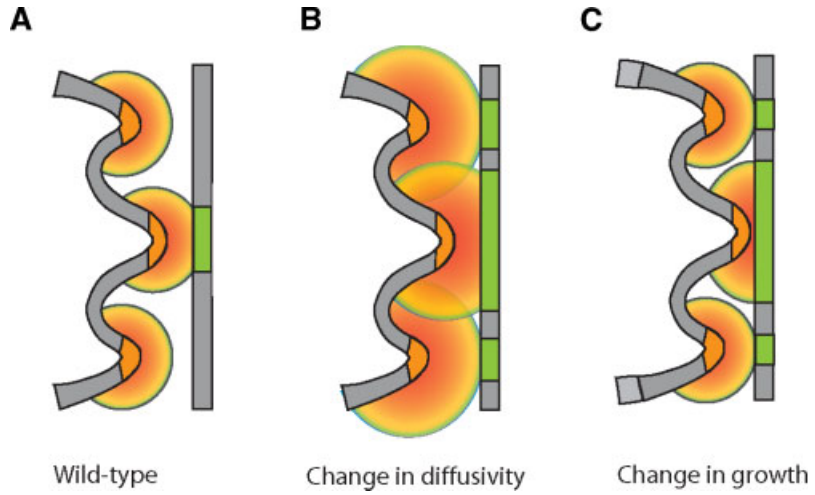


**Figure 3.** Hypothetical example of how the intermediate phenotype of the embryo in morphodynamic mechanisms can mean that IS-mutations produce sudden changes in the resulting patterns. **A:** A wild-type situation in which a clear grey territory and orange territories are embedded in a curved epithelia. The orange territories secrete a red signal as before. The dark grey territory expresses a receptor for the red signal and then if cells receive enough concentration of the signal they become green. **B:** In the wild type, only one green territory is found but changes in the diffusivity of the signal (for example due to sequence changes in the signal protein) can produce two extra territories. **C:** A similar effect arises when extra proliferation occurs in the dark-grey territory and inducing and target territories get closer. Notice that the large green territory growth is proportionally more when the distance between territories decreases. This is because, as the central tip of the inducing territory gets closer to the target territory, the space available for diffusion of the signal decreases. This is marked in the figure by a change in the shape of the red signal diffusion spectrum from the central tip. Notice also that the same situation would be found if the whole grey territory expressed the red signal.

their cusps and do not obviously resemble each other. The same can be done for the qualitative morphological transition between triconodont and tribosphenic teeth and the appearance of the hypocone (both appeared several times, independently, in the fossil record). It has also been experimentally shown that simple changes in the levels of expression of a single gene can give rise to dramatic changes in the overall morphology of mouse teeth (the changes are so apparent that they would lead to the classification of the mutant as a different species or genus[83]). These changes involve the number and relative position of cusps and teeth and different levels of expression affect different parts of the teeth differently. The position and number of homologous cusps are commonly used for the taxonomy of rodents and other mammals. However, as cusps are produced from the same developmental mechanism and have no unique genetically specified identity,[84] a cusp cannot be considered homologous to any other cusp in any other tooth. Then, according to the definition of novelty of Müller and Wagner,[2] these changes in tooth morphology are not novelties because they do not have genetic individualization.[85–87] However, they can be seen as obvious qualitative changes. In fact, the variation possible in different parts of a pattern (for example cusps in a tooth) can be different without requiring any kind of genetic individualization of parts (at least not in the sense of some differential gene expression in these parts). Different variation between parts can be due to epigenetic differences (as illustrated in Fig. 3A or is found in teeth) that can arise from genetic differences in other parts of the embryo or from environmental differences.

## On the origin of novelties: conclusions

Animal morphologies are always characterized by more than one metric measurement. To describe their variation as generically quantitative is not very informative unless all traits can change independently or, alternatively, the co-variation between traits is known and does not change often in evolution. Hierarchic inductive mechanisms are the only developmental mechanisms that produce only gradual and independent variation between traits but they will only produce patterns of the rainbow type. This later case is quantitative but multivariate. It is also qualitative in the sense that it includes the arbitrary choice of some metric traits. Since traits are often chosen to be measurable, there is a bias against traits that appear or disappear in evolution. These are exactly the traits that may be considered novelties. Thus, it is unlikely that morphological evolution can be seen as the accumulation of small morphological variation of trait values as described by some neo-Darwinian research.[10,11]

Among the variations discussed in this article, the one that would be more often characterized as a qualitative change or novelty is the one that includes the appearance of new

territories or territory forms. Since these territories do not necessarily appear, as we have seen, from previous territories their homology may be difficult to identify. As we have seen, these can occur from T-mutations combining different developmental mechanisms or by IS-mutations in morphogenetic and morphodynamic mechanisms. It has been argued that IS-mutations probably occur more often than T-mutations[20] and, in this light, this form of novelty may appear more often by morphodynamic mechanisms than by morphostatic mechanisms. It has also been suggested, however, that morphostatic mechanisms may often replace, or be co-opted with, morphodynamic mechanisms once a novelty is established.[78] This idea is consistent with studies suggesting that epigenetic changes are often at the origin of novelties.[2,88–91]

This article provides a characterization of the ensemble of possible morphological variation in evolution that can occur. This approach tries to be more based in development than the neo-Darwinian one. Morphological variation occurs as: (1) rainbow patterns, (2) stripes and spots patterns, (3) patterns generated by morphogenetic mechanisms, (4) summation, subtraction and composition of rainbow, stripes and spots patterns, and (5) combinations of all these patterns in a morphodynamic or morphostatic way. Thus, this article does not conceptualize morphological variation either as involving purely quantitative changes in trait values or as qualitative changes (as in novelty). Instead, morphology and its variation are seen as made of basic developmental patterns, their combination in several different ways and some specific ways of change for each basic pattern.

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