

AT THE ROOT OF ANIMAL DIVERSITY: EVOLVABILITY, MODULARITY, AND HOMOLOGY

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We cannot satisfactorily explain the origin of biological diversity without considering that natural selection can only test the phenotypes that the developmental system is able to produce. In other terms, we must consider its evolvability, the scenario of possible, likely and (apparently at least) forbidden changes that a species' developmental system can accept. Evolvability is sometimes systemic, but more frequently modular, in terms of morphological organization but also of the temporal articulation of developmental processes, as shown by heterochrony. This has important consequences on our possible approach to homology. The traditional "all-or-nothing" notion of homology must be replaced by a combinatorial approach that abandons the Owenian requirement of conservation of sameness. Conservation of homology across evolutionary transitions between environmentally controlled and genetically encoded traits encourages approaching the issue of homology from the perspective of evolutionary developmental biology, including the appreciation of the multiplicity of paths along which inheritance of traits is carried across generations.

У ИСТОКОВ РАЗНООБРАЗИЯ ЖИВОТНЫХ: ЭВОЛЮИРУЕМОСТЬ*, МОДУЛЬНОСТЬ И ГОМОЛОГИЯ

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Мы не можем удовлетворительно объяснить происхождение биологического разнообразия без учёта того, что естественный отбор может только «испытывать» фенотипы, которые способна производить онтогенетическая система. Другими словами, мы должны рассматривать её эволюируемость, а именно совокупность возможных, вероятных

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**Прим. ред.* В рунете нам не удалось найти русскоязычный эквивалент термина «evolvability», означающего способность (склонность) эволюировать. Калька «эволюбельность», аналогичная прижившимся «вариабельности» или «мутабельности», не слишком благозвучна. Термин «эволюируемость» здесь использован по аналогии с принятыми «мутируемостью» и «растворимостью», означающими способность мутировать и растворяться, соответственно.

и (по крайней мере явно) запрещённых изменений, которые может включать онтогенетическая система вида. Рассматриваемая с точки зрения морфологической организации, а также различных временных членений процессов онтогенеза, эволюируемость может быть системной (затрагивает весь организм), чаще же она модульная, иллюстрацией чего служит гетерохрония. Это имеет важное значение для разработки возможных подходов к трактовке гомологии. Традиционное понимание гомологии по принципу «всё или ничего» должно быть заменено комбинаторным подходом, подразумевающим отказ от оуэновского требования сохранения тождественности. Сохранение гомологии между контролируемой средой и генетически кодируемыми признаками при их эволюционных изменениях побуждает исследовать гомологию с точки зрения эволюционной биологии развития, включая признание множественности путей, по которым осуществляется наследование признаков в цепочке поколений.

1. Introducing evo-devo into comparative biology

Our approach to biodiversity necessarily includes comparisons. Comparisons of morphological features, of genes and perhaps of genomes, of life cycle characteristics, of behavioural schedules. Comparisons targeted to the identification of traits shared by different species, or suggesting their phylogenetic relationships, as well as to diagnostic traits differentiating them. Comparisons leading to the untangling of the alpha-diversity in a biological community or an ecosystem, but also to an appreciation, albeit necessarily a subjective one, of disparity, i. e. of the extent of morphospace occupied by the representatives of a taxonomic group within that community or ecosystem. With a further step, the analysis of biodiversity proceeds in the direction of functional ecology, or towards a historical and causal analysis of biodiversity, perhaps in the traditional terms of Neodarwinian evolutionary biology, that is, looking for processes of adaptation and speciation.

Not necessarily these two aspects of evolution — adaptation and speciation — are tightly coupled together. Prolonged interruption of gene flow caused by external (es-

pecially geographical) barriers is very often the cause of the origin of new species, but the latter is not necessarily associated with the evolution of new adaptations. For example, many genera of terrestrial animals with poor dispersal ability, such as flightless ground-living insects or land snails, include large or very large numbers of allopatric species confined either to individual islands or to individual mountaintops or to isolated calcareous outcrops surrounded by substrates of different nature. In terms of adaptation, rapid and richly ramified patterns of speciation are often explained (tentatively at least) in terms of adaptations made possible by the presence, in a megadiverse clade, of some “key” trait the emergence of which would have opened the possibility to undergo abundant speciation. Globally, this explanation of biological diversity is looked for in the usual terms of evolution as *the survival of the fittest*.

However, this is only one side of the coin: the other side is *the arrival of the fittest*. Natural selection can only test the fitness of the phenotypes that the developmental system is able to produce (de Vries, 1905). Investigating the arrival of the fittest is one of the qualifying targets of evolutionary develop-

mental biology, or evo-devo (e. g., Gilbert et al., 1996; Alonso, 2008; Wagner, 2011).

2. Evolutionary transitions

Remarkably, the landscape of the possible morphological transitions from an existing to a novel phenotype is neither isotropic nor necessarily continuous (e. g. Theißen, 2006, 2009; Minelli et al., 2009). Evolution offers examples of discontinuities (Frazzetta, 2012) that cannot be explained as the long-term result of a prolonged accumulation of small adaptive changes.

Morphological discontinuities that do not appear to be bridgeable by a series of micro-mutations are, for example, the torsion of the visceral sac that distinguishes the gastropods from all other molluscs, or the sudden transition from bilateral symmetry to directional asymmetry in the flatfishes. In the evo-devo literature, the most popular case is the pectoral girdle of turtles, which is encased within the ribs, rather than external to them as in all other tetrapods, a change that Gilbert et al. (2001) and Rieppel (2001) did not hesitate to describe as saltational.

Many phenotypes, often very similar to existing and even successful ones, are not present in nature, not because of a very low fitness, but because the existing developmental systems cannot be modified easily, or at all, in such a way as to produce them. For example, there is no reason to expect that a scolopendromorph centipede with 22 pairs of legs would be functionally impaired, compared to those possessing either 21 or 23 pairs of legs, nevertheless not a single specimen (not to say, a species) of scolopendromorph with 22 pairs of legs has ever been recorded, whereas the “neighbouring” phenotypes with either 21 or 23 pairs of legs are characteristic of hundreds of species each (Minelli, 2009). But this is not the whole story. Within the clade Scolopendromorpha, all representa-

tives of which were until recently thought to have either 21 or 23 pairs of legs, a species with 39 or 43 pairs of legs, *Scolopendropsis duplicata*, has evolved, probably derived in a single step from an ancestor very similar to *Sc. bahiensis*, a species with either 21 or 23 pairs of legs (Minelli et al., 2009). Back in the evolutionary history of the Chilopoda, a transition from 15 pairs of legs, the plesiomorphic number of leg pairs within centipedes, to 21 pairs was an innovation of the lineage leading to the extant Scolopendromorpha. Within the latter, a further increase in the number of leg-bearing segments occurred repeatedly, always with discontinuous transitions: from 21 to 23 in the Scolopocryptopidae (Vahtera et al., 2013), from 21 to 23 and again to 39 and 43 in *Scolopendropsis* (Minelli et al., 2009). From an ancestor belonging to the stem-group Scolopendromorpha (that is, likely provided with 21 or 23 pairs of legs) evolved also the lineage leading to the extant Geophilomorpha, within which the leg pair number was first in the order of 41, 43 or 45, but subsequently diverged between 27 and 191 leg pairs. Besides the obvious saltations, the whole evolutionary radiation of centipedes is characterized by a remarkable constraint: the number of leg pairs is always limited to odd values (Minelli, Bortoletto, 1988).

These examples suggest that phenotypic evolution is shaped in part by the constraints under which developmental systems operate (Arthur, 2004). We are therefore prompted to investigate *evolvability*, that is, the scenario of possible, more probable, less probable and (apparently, at least) forbidden changes that a species’ developmental system can accept, thus imposing a bias on the production of new phenotypes. Discussing evolvability will bring us to discuss briefly the *modularity* of animal organization as well as the complexity of the relationships that may link an

organism's genotype to the phenotypes it is eventually able to express. Modularity is not limited to the morphological organization of the animal, but extends to the temporal sequence of individual developmental processes or stages along an animal's ontogeny, and this brings us to *heterochrony* and its consequences for the notion of *homology*.

The two concepts of homology and evolvability are interrelated. Brigandt (2007, p. 710) defines a homologue "as a unit of morphological evolvability, i. e., as a part of an organism that can exhibit heritable phenotypic variation independently of the variation that the organism's other homologues can undergo," or as "a unit of heritable phenotypic variability — a structural unit being able to phenotypically vary in response to genetic variation". Similar concepts, but framed in more comprehensive terms, that is, in respect both to ontogeny and evolution, have been proposed e. g. by Laubichler (2000), Newman and Müller (2000), Müller (2003, 2007), and Jamniczky (2008) (cf. Pavlinov, 2012).

3. Evolvability

Some architectural aspects are very stable throughout the animal kingdom, or a sizeable part of it, well beyond any reasonable explanation in terms of adaptation. In many such instances, it is not natural selection that must be regarded as responsible for evolutionary stasis, but the lack of selectable variation. Constraints must be searched for at the level of developmental systems.

This approach can be expressed in terms of evolvability, a term that has unfortunately been applied by different authors to a plurality of different concepts (e. g., Dawkins, 1988; Alberch, 1991; Hansen, 2003, 2006; Schlichting, Murren, 2004; Klingenberg, 2005; Wagner, 2005; Colegrave, Collins, 2008; Pigliucci, 2008; Brookfield, 2009). I will follow here Hendrikse et al.'s (2007, p.

394) definition of evolvability as "the capacity of a developmental system to evolve [...] largely [as] a function of the developmental system's ability to generate variation".

Potentially adaptive phenotypes do not show up because their production is very difficult, think of mammals with a number of cervical vertebrae other than seven: this number is conserved between animals with so differently elongated necks as hippo and giraffe. Yet, as soon as variation appears in the system, alternative phenotypes evolve rapidly, often departing amazingly from the original phenotype. Here are two examples.

The axoneme of cilia and flagella of eukaryotic cells is generally composed of two central microtubules surrounded by a circle of nine doublets (the usual 9+2 arrangement). This structure is remarkably stable among the vast majority of eukaryotes provided with cilia or flagella, but it is far from being universal. Exceptions to the rule, however, are not limited to the phenetically closest arrangements such as 9+1, 9+0 or 9+9+2. Departures from 9+2 have occasionally opened the way towards the evolution of an extraordinary diversity of arrangements, most conspicuous being those in the sperm flagellum of gall midges (Diptera: Cecidomyiidae), with up to 2500 doublets in *Asphondylia ruebsaameni* (Lanzavecchia et al., 1991; Mencarelli et al., 2000).

Another example of diversity obtained by abandoning a previously very stable phenotype is provided by the antennal articles of the Coleoptera. Here, the plesiomorphic number is 11, widely conserved throughout the order, despite very conspicuous variation in the relative size and shape of the individual articles and thus in the overall shape of the appendage. Nevertheless, this number has been repeatedly reduced, e. g. to ten articles in 46 families, to nine in 31, to eight in 22, and even to three articles in five

families and to two articles in two families (Minelli, 2004). However, variation in the opposite direction has been rare and mostly limited to one extra article and very rarely extended to numbers higher than 20 (only in some Lampyridae, Cerambycidae and Rhipiceridae).

With the advent of evolutionary developmental biology, evolvability has taken a central role in explanations of evolutionary change and its study is even regarded as the core feature of evolutionary developmental biology (Hendrikse et al., 2007). Studying evolvability has caused an increasing appreciation of the complex relationships linking the genotype to the phenotype (the so-called “genotype→phenotype map”), which are now largely acknowledged to be mostly non-linear and far from uniform (e. g. Alberch, 1991; Wagner, Altenberg, 1996; West-Eberhard, 2003; Draghi, Wagner, 2008; Pigliucci, 2010). In simple terms, rarely, if ever, does one gene correspond to one phenotypic trait, and vice versa. As a rule, the expression of one gene affects a diversity of phenotypic traits (pleiotropy), and indistinguishable phenotypes can be under the control of different genes, or genetic cascades (convergence and/or redundancy).

To some extent, what we register as pleiotropy is nothing but a consequence of the way we describe a phenotype as a sum of characters: this articulation into units is perhaps reasonable in terms of morphology, but does not necessarily correspond to distinct developmental processes responsible for the individual characters, or to the expression patterns and the functions of as many genes. Strictly speaking, the only uniquely controlled phenotype corresponding to a given gene is perhaps its primary mRNA transcript, previous to any post-transcriptional editing.

4. Genes and homology

Are there genes individually “responsible for” a given feature, as we have possibly learned from schoolbooks introducing elementary Mendelian genetics? A one-to-one correspondence between genes and phenotypic features would help consolidating our appreciation of homology relationships, but this path of enquiry would bring us nowhere. Two problems must be acknowledged.

First, there is abundant evidence of homologous morphological features controlled, in different species, by nonhomologous genes or networks of genes, and vice versa, i.e. nonhomologous morphological features controlled by homologous genes (discussed e. g. in Wray, Abouheif, 1998). It is remarkable that this mismatch between genotype and phenotype has eventually caused one of the 19th century scientists who most contributed to the conceptual development of comparative biology to eventually take distance from the very notion of homology (de Beer, 1971; Pavlinov, 2012).

Evidence from developmental genetics can assist in identifying homologous morphological structures but does not provide necessary nor sufficient conditions for determining structural homology (Galis, 1999; Bolker, Raff, 2003; Minelli, 2003a; Pavlinov, 2012).

Acknowledging this frequent mismatch between genes and morphology, Nielsen and Martinez (2003) recognized, under the new term of *homocracy*, the correspondence between organs or structures organized through the expression of the same patterning genes, irrespective of whether these structures can be regarded or not as homologous in terms of comparative morphology. A related concept stressing the conservation throughout phylogeny of genetic networks underlying the production of eventually diverging organs

has been suggested by Shubin et al. (2009) under the evocative but controversial name of *deep homology* (briefly discussed in: Minelli, Fusco, 2013a).

Second, hundreds and hundreds of genes are differentially expressed in each body parts. For example, in the mouse, many genes involved in limb initiation and patterning are part of regulatory networks common to both forelimbs and hindlimbs: many of them are differentially expressed between the growing and differentiating anterior vs. posterior appendages, and contribute to the specification of limb-type identity (Logan et al., 1998; Logan, 2003).

Admittedly, the extent to which a given body feature is controlled by any one of the genes whose expression in the Anlage of that body part is somehow different from its expression elsewhere in the organism will not be the same for all genes. One might argue that the molecular (genotypic) unit corresponding to a morphological homologue is not a gene whatsoever, but a *master control gene*, that is, a gene responsible for a major switch in the expression of a large number of downstream genes. This fashionable concept was first introduced by Lewis (1992) for the homeotic genes of the *Bithorax* complex in *Drosophila*, but was mostly championed by Gehring (for an historical perspective, see: Gehring, 1998). Again in *Drosophila*, targeted expression of the *eyeless* (*ey*) gene can result in the production of ectopic eyes (e. g., on a tibia) and this result has been regarded as an experimental proof that *ey* is the master control gene for eye morphogenesis. Homologues of the *Drosophila ey* gene (generally known as the *Pax6* genes) are involved in the production of eyes in metazoans as different as a squid and a vertebrate; as a consequence, *Pax6* genes have been interpreted as master control genes in the production of eyes throughout the Metazoa (Halder et al., 1995).

However, the very existence of master control genes is questionable. Davidson (2001, p. 27), for example, disposed of the idea of a linear hierarchical control sequence beginning with a hypothetical master gene describing it as just a “fantasy of earlier days”. Evidence suggests instead that morphogenesis is controlled by complex networks of signal systems and transcriptional regulators (Davidson, 1993). This revised interpretation of the molecular circuitry controlling morphogenesis is certainly more realistic than the older one, based on the putative existence of master control genes. However, compared to the morphological features they presumably control, even Davidson’s *gene regulative networks* are not conservative enough to represent the genetic or mechanistic counterparts of homologues. The evolvability of regulatory cascades is shown by examples where the same molecule is regulated by different genes in different species or even within the same organism (Larsen, 2003). For example, the gene *hedgehog*, which is involved in establishing the antero-posterior axis of the embryonic segments and in patterning the larval imaginal discs, is controlled by *bicoid* in *Drosophila* and by *caudal* in the beetle *Tribolium* (Dearden, Akam, 1999), whereas *engrailed*, whose expression is critically important in fixing segmental boundaries in *Drosophila*, is regulated by *paired* in some cells but by *fushi tarazu* in others, a few cell diameters apart (Manoukian, Krause, 1992).

5. Parallelism and convergence

Lack of selectable variation is sometimes responsible for discontinuities in the occupancy of the morphospace, but biased evolvability is also involved in the opposite phenomenon, that is, in the occurrence of “privileged” phenotypes evolved in multiple lineages as the effect of parallel or convergent evolution. In those instances, selective

advantage is likely involved, but a bias in the landscape of evolvable forms is probably much more frequent than generally acknowledged. In recent times, strict focus on phylogeny reconstruction has caused homoplastic features to be simply regarded as noise contrasting the phylogenetic signal provided by synapomorphies, but parallelism and convergence deserve to be studied as important evolutionary phenomena. Towards the turn of the century, Moore and Willmer (1997) provided a detailed overview of the occurrence of convergent evolution in invertebrates; soon thereafter, Conway Morris (e.g. 2003a, b, 2006) went so far as to regard convergence as a major feature of evolution and to acknowledge that it allows some predictions of long-term evolutionary trends.

It is by now nearly one century since Vavilov (1922) proposed a *law of homologous variation*, according to which the similarity of developmental pathways in related species causes the appearance of similar variants. Translated into the current language of evo-devo, this means that the recurrent evolution of similar phenotypes among closely related species is suggestive of positively biased evolvability of some *developmental modules* (Inge-Vechtomov, 2004).

6. Modularity

To address evolutionary change in terms of evolvability, we must identify operationally sensible units of change. Functional integration of the phenotype must be preserved for the change to have a chance of success over evolutionary time. According to Kemp (2016), three categories of mechanisms can account for the maintenance of phenetic integration during the course of extensive evolutionary transition: developmental homeostasis, modularity and correlated progression. I will not discuss here developmental homeostasis, a topic that pertains to developmental

biology, whereas modularity and correlated progression are briefly discussed below.

In many rapid radiations, the explosion of phenotypes is essentially restricted to large variation in a well circumscribed *module*. According to Klingenberg (2005, p. 6), “Modules are assemblages of parts that are tightly integrated internally by relatively many and strong interactions but relatively independent of one another because there are only relatively few or weak interactions between modules”.

Examples of extensive radiations based on rapid and diversified change in a single module are those based on the copulatory structures, especially the male ones, of many insect groups, and those of the helminthomorph millipedes (Minelli, 2015a).

The latter case is a unique example of modularity in which a tiny fraction of a long, apparently homogeneous series of modular units undergoes a dramatic metamorphosis, whereas all remaining, initially identical units do not undergo ontogenetic modifications other than growing. Adult helminthomorph millipedes (a clade to which the majority of the Diplopoda belong) have between 32 and 375 pairs of legs, according to species. In the females, and also in male juveniles, all leg pairs are morphologically identical except for the smaller size of the first pair, or the first few pairs. New pairs of legs are added, with a number of post-embryonic moults, to those already present in the previous stage. Eventually, however, the eighth pair of legs, and often also the ninth, regress totally, to be finally replaced in the adult male by gonopods, specialized and generally very complex sexual appendages used as claspers or to transfer sperm. To stress the strict localization of the ontogenetic changes these appendages undergo, the term “non-systemic metamorphosis” has been introduced (Drago et al., 2008). In all but a few genera, the go-

nopods of helminthomorph millipedes are by far the most diversified module of these arthropods' architecture and are therefore the main morphological resource for millipede taxonomy.

Much of the species-level diversity within *Onthophagus*, a huge genus of dung beetles with close to 2000 described species, is also concentrated in a couple of modules, the cephalic and prothoracic horns. These horns are a conspicuous morphological novelty in the evolution of which phenotypic plasticity is also involved (e. g. Wasik, Moczek, 2011), as discussed in the section 13.

7. Correlated progression

Is evolvability always dependent on modularity? A number of conceptual arguments and empirical examples suggests that this is not the case. According to Kemp (2016, p. 177), "Despite the popularity of modularity as an explanation of evolvability, its role [...] is necessarily limited to relatively short-term evolution. In principle this is because much of the phenotype is not modular but consists of functional processes integrated with the rest of the organism. Empirically, modules are demonstrably transient, with their components changing over evolutionary time, so they cannot be long-term evolutionary units".

There is also another reason not to expect that a developmental module can maintain its autonomy for long. In principle at least, natural selection operates on organisms as wholes (Kemp, 2007). If so, it is reasonable to accept that the evolution of the different parts of the body is subjected to *correlated progression* (Lee, 1996; Budd, 1998; Kemp, 1999, 2007).

Kemp (2016, p. 177) defines correlated progression as "the mechanism of change by which small modifications to single parts of the phenotype are acceptable because there is enough functional flexibility between

them to prevent loss of adequate integration and therefore of fitness. But no part can change unless and until appropriate compensatory change in the functionally linked parts have accumulated over evolutionary time [...] Unlike [...] modularity, correlated progression as a process sets no limit to how much evolution can occur in a lineage, that is to say how far through morphospace it can travel".

8. Permissive and generative apomorphies

In cladistic reconstructions of phylogenetic relationships, clades are defined by apomorphies shared by their members (synapomorphies), but it is not granted if and how those characters may have contributed to the clade's diversity.

In this respect it is sensible to distinguish between permissive and generative apomorphies (Minelli, 2015b).

Permissive apomorphies have only an indirect effect on the rate of speciation, the latter being mainly dependent on the specific geographic and ecological context in which the clade is evolving. For example, many birds and insects of oceanic islands have reduced wings, a trait positively adaptive in that geographic context, where stormy winds would severely affect the chance of survival of winged animals (e. g. Carlquist, 1965, 1974). However, the effects of flightlessness on speciation are clearly indirect. Flightlessness involves reduced vagility, thus reduced gene flow between populations and their eventual divergence in a classic allopatric scenario. Only in this very indirect sense is wing reduction or loss responsible for the remarkable species diversity of many genera, e. g. of rails (Rallidae) among the birds and ground beetles (Carabidae) and weevils (Curculionoidea) among the beetles, all well represented on oceanic islands.

In contrast, a *generative apomorphy* provides a clade with the access to an environmental resource positively involved in speciation, e. g. the access to a new exclusive food source such as in many parasites or parasitoids.

9. Systemic change

The evolutionary effects of change in the developmental schedule can be either modular or systemic.

A first group of systemic changes occur *by reduction*, often as the effect of progenesis (Westheide, 1987): reproductive maturity is reached at a stage corresponding in morphology to an embryonic or larval stage of their relatives. These animals lack many of the parts or organs usually found in the members of the group to which they belong. Reduction, however, is sometimes accompanied by the expression of novel traits. Examples are offered by *Buddenbrockia* and *Polypodium*, two miniaturized and morphologically very unusual representatives of the Hydrozoa. These small cnidarians do not exhibit any trait characteristic of a polyp or a medusa. *Buddenbrockia*, a parasite of freshwater bryozoans, is worm-like, without tentacles or other appendages (Jiménez-Guri et al., 2007), whereas *Polypodium*, a parasite of sturgeon's eggs, is an irregular mass of jelly with finger-like projections (Raikova et al., 1994).

Other systemic morphological transitions are based on evolutionary changes in the structure of the cells of which the whole animal is formed. This is the case of the Loricifera, minuscule but anatomically complex metazoans formed by a high number of cells of extremely small size: these are the only animal cells known not to possess mitochondria (Danovaro et al., 2010). Not less dramatic, but modular rather than systemic, is the case of the minuscule trichogrammatid wasps of

the genus *Megaphragma*, where 95% of the ca. 4,600 neurons forming the brain are anucleate (Polilov, 2012).

A different kind of systemic change is *paramorphism* (Minelli, 2000, 2003b), i. e. the evolution of new axes initiated and patterned by the iteration of existing developmental dynamics previously responsible for the production of the main body axis — possibly followed by divergence and specialization further ahead in evolution. The existence of a systemic coupling between the different body axes is suggested by a large number of examples (Minelli, 2000), e.g. the presence of segmented appendages in segmented animals, whereas unsegmented animals have (if any) unsegmented appendages. In this case, the systemic nature of segmentation is additionally suggested by the fact that segmentation has very likely evolved independently in arthropods, annelids and vertebrates, nevertheless all three lineages have eventually evolved segmented, rather than unsegmented, appendages.

Systemic phenotypic changes do not necessarily depend on large genetic differences, as shown by the change from left-handed to right-handed shell, or vice versa, in some gastropod taxa. In the only gastropod species in which this phenomenon (enantiomorphism) has been studied, i. e. in *Lymnaea stagnalis*, shell's chirality depends on a single maternally inherited factor (reviewed in: Asami et al., 2008). Yet, according to Gittenberger (1988), inversion of chirality has contributed to speciation e. g. in *Partula*, a genus including numerous (about 150 species) and showy snails from the islands between New Guinea and French Polynesia.

10. Modular vs. systemic evolvability along the life cycle

Along the animal's life cycle, some stages, or some periods, are more conservative

than others. A high degree of conservation has been often claimed to extend to the majority of the members of a given phylum, to such extent that a *phylotypic stage* can be recognized, in arthropods and vertebrates at least (Sander, 1983; Slack et al., 1993; Raff, 1994; Galis and Metz, 2001). Richardson (1995), however, rightly claimed that individual stages, per se, are actually less conservative than the phylotypic concept would imply, and therefore suggested to speak of a *phylotypic period*, rather than phylotypic stage, at least in the case of vertebrates.

The existence of a phylotypic stage (but also, to some extent, the existence of a phylotypic period) suggests a degree of temporal modularity of evolvability. In other instances, however, evolvability is ontogenetically systemic, that is, it affects most of the life cycle. For example, in the Cycliophora, minuscule animals that live on the appendages of the Norwegian lobster (*Nephrops norvegicus*), the whole life cycle is represented by an unusual sequence of unusually shaped stages for some of which no term was available in zoology, previous to the recent discovery of this phylum; as a consequence, new terms such as the Pandora larva and the Prometheus larva were introduced (Obst, Funch, 2003).

11. Heterochrony

The modularity of developmental processes legitimates searching for homology between modules. Indeed, acknowledging a degree of individuality of developmental processes is the ontological background of Wagner's biological concept of homology. In Wagner's (1989a, p. 62) original formulation, "[s]tructures from two individuals or from the same individual are homologous if they share a set of developmental constraints, caused by locally acting self-regulatory mechanisms of organ differentiation. These structures are thus developmentally individu-

alized parts of the phenotype". The legitimacy of a *homology of process* is quite largely acknowledged (e. g., Laubichler, 2000; Gilbert, Bolker, 2001; Scholtz, 2005; Pavlinov, 2012) although these authors' statements of principle are seldom accompanied by actual examples, not to say by demonstrations of the heuristic importance of process homology. More or less explicitly, however, process homology is implied in the identification of heterochronies. This can be seen even in the crudest form of heterochrony, the traditional *growth heterochrony* (e. g., de Beer, 1930, 1940; Gould, 1977) where the temporal deployment of somatic development was contrasted with the temporal course of development towards sexual maturity. However, it must be acknowledged that somatic development and sexual maturation are both far too complex to legitimately qualify as developmental modules.

Very different, and actually cognate to our discussion of developmental modularity, is the more recent approach to heterochrony, currently known as *sequence heterochrony* (e. g., Smith, 1997, 2001, 2002, 2003; Velhagen, 1997; Bininda-Emonds et al., 2007). Here, a number of developmental processes are singled out and the temporal schedule according to which these processes begin or end is compared between two or more animal species. Basic condition to this kind of comparison is the identity (operational at least) of individual developmental processes among the species compared.

Quite different from homology of developmental processes is the *homology of developmental stages* that Scholtz (2005, 2008) recognizes as morphologically constrained and independently evolving units and thus as legitimate units of comparison, but this perspective is questionable. Bininda-Emonds et al. (2003) presented quantitative evidence against the existence of a strictly defined

phylotypic stage in vertebrate development and a comparative review on the periodization of arthropod post-embryonic development (Minelli et al., 2006a) suggested that developmental stages are not necessarily conserved in evolution, especially when distantly related taxa are compared, but sometimes even between species classified in the same genus.

The individuality of post-embryonic developmental stages is often blurred in decapods crustaceans (Minelli and Fusco, 2013b). For example, the very short larval stage of *Upogebia savignyi* is a kind of “advanced zoea” with several pairs of appendages like those of the adult (Gurney, 1937). The reasons for classifying a developmental stage (or phase) as larval (e. g., megalopa) or post-larval (e. g., zoea) are sometimes completely arbitrary. For example, in the shrimp of the genus *Macrobrachium*, Shokita (1977) distinguished a “megalopal phase” from a second “zoeal phase” despite the fact that the “megalopa” exhibits some zoeal characters combined with many more postlarval ones.

12. Character individuality and the emergence of novelties

Sixteen years before the publication of Darwin’s *Origin*, Owen (1843, p. 379) defined homologue as “the same organ in different animals under every variety of form and function”. Nowadays, in a scientific context dominated by an evolutionary perspective on life, it seems difficult that we can still be satisfied with the ill-defined and subjective criterion of “sameness” to which Owen appealed. Nevertheless, the notion that homologous features can be recognized as “the same” survives, in different ways, in many current approaches to the problem of homology. The assumption of “sameness” is mainly implicit, although arguably oblige, so long as homology is conceived as

an “all-or-nothing” relationship, as traditionally accepted. Sometimes, however, the “sameness” of homologues is explicitly mentioned: “There are numerous examples of corresponding characters between species for which it is hard to escape the conclusion that organisms from different species are clearly composed of the same building blocks, such as heads, limbs and brains” (Wagner, 2014, p. 40). These are the body parts we can trace as homologous in comparing one species to another: “Any character that can be homologized is assumed to have continuity in terms of its existence in a lineage of descent, as well as persistence of differences from other parts of the body (individuality)” (Wagner, 2014, p. 42–43). There are problems also with the appeal to a specific “lineage of descent” because continuity through descent is, in Darwin’s words, “common descent with modification”. The idea that characters can “remain themselves” throughout an indefinite number of evolutionary modification suggests an idealistic interpretation of how organisms evolve (Minelli et al., 2006b; Minelli, Fusco, 2013a).

The problem becomes more critical when the so-called evolutionary novelties are involved. Müller and Wagner (1991, p. 243) defined a morphological novelty as “a structure that is neither homologous to any structure in the ancestral species nor homonomous to any other structure of the same organism”. The same authors (Müller, Wagner 2003, p. 218–219) redefined evolutionary innovation as “a specific class of phenotypic change that is different from adaptive modification [such as] the origin of new body parts [or] major organizational transitions” and distinguished as novelties those innovations that “introduce new entities, units, or elements into phenotypic organization”.

Eventually, the line of arguments apparently follows this path. First, there are body

parts, or features, among which there is homology; in other terms, homology, despite all difficulties to recognize it in practice, is accepted as given. If homology can be predicated of structures, or features, then there must be a way in which these structures, or features, can be predicated to be “the same”. The problem then is, on which foundation this sameness can be predicated. Eventually, this question has been answered in three different ways: (i) in terms of “universal laws” of form, (ii) as the product of common ancestry, or (iii) in terms of proximal causes responsible for the emergence of conserved developmental modules.

A search for universal laws of form has surfaced several times in the history of biology, at least since the time of Wilhelm Roux’s developmental mechanics (*Entwicklungsmechanik*) (cf. Goodwin, 1977). In the last decades, it has shown up again, in two different forms at least. On the one side, in the abstract, formalized terms of process structuralism (Resnik, 1994; Webster, Goodwin, 1996); on the other, in terms of the physico-chemical properties of living matter. The latter perspective has been championed by Stuart Newman, who has suggested that in early stages of the evolution of metazoans the shapes of the emerging multicellulars were essentially determined by mechano-elastic properties, arguably sufficient to produce a set of generic forms, e. g. hollow spheres and segmented beads (Newman, Comper, 1990; Forgacs, Newman, 2005; Newman et al., 2006).

Unfortunately, these physicalist and structuralist approaches only apply to the simple geometric structure of early embryos, but the whole range of shapes studied by comparative morphology remain beyond reach. This may explain the limited audience these approaches have found among anatomists, embryologists and especially systematists

working on complex animal structures. The mainstream attitude towards the issue of homology still rotates around the *historical concept of homology*: “homologous features (or states of features) in two or more organisms are those that can be traced back to the same feature (or state) in the common ancestor of those organisms” (Mayr, 1969, p. 85). This was reformulated by Bock (1974, p. 881) in the following terms: “Features (or conditions of a feature) in two or more organisms are homologous if they stem phylogenetically from the same feature (or the same condition of the feature) in the immediate common ancestor of these organisms”, a definition that opens the door to a revisit of the historical concept of homology in consequent phylogenetic terms (Hennig, 1966).

Other researchers have been searching instead for a *proximal-cause concept of homology* (this term was introduced by: Minelli, Fusco, 2013a), perhaps in terms of continuity or commonality of information (e. g., Osche, 1973, 1982; van Valen, 1982; Roth, 1984, 1988; Minelli, Peruffo, 1991; Minelli, 1996). Eventually, Wagner (1989a,b) introduced the so-called biological concept of homology, with the definition quoted above. The underlying concept of developmental individualization has been revisited in subsequent papers (Wagner, Misof, 1993; Wagner, 1994), and eventually rephrased in terms of independent units of developmental control, due to either morphogenetic or morphostatic constraints, although, in a later revisit of the problem, Müller and Wagner (1996, p. 4) adopted a less deterministic approach, suggesting “some degree of independence of structural homology from its genetic and developmental makeup”.

Of course, one may argue that homology is not an “all-or-nothing” correspondence: in this case, no sameness is implied, and

an explanation of homology in terms of either common ancestry or common proximal causes can be advocated. But this requires abandoning the Owenian requirement of sameness, to follow instead the path of reasoning suggested in the next section.

13. Towards a combinatorial approach to homology

“Nirgends ist Neubildung, sondern nur Umbildung“ — “nowhere is there new formation [= origin of fully new parts], there is only transformation”. This iconic characterization (von Baer, 1828, p. 156) of ontogenetic change could be used also to describe evolution, including the “origin” of evolutionary novelties. According to West-Eberhard (2008, p. 198), a novelty is indeed a “phenotypic trait that is new *in composition or context of expression* relative to established ancestral traits” (italics mine, — A.M.). Indeed, even the best characterized feature is a mosaic, or a mixture, of a multiplicity of traits, some of which can be traced to homologous traits of remote ancestors, others are more recent one, while total novelty cannot be predicated of any feature as a whole (Minelli, Fusco, 2005; see also Moczek, 2008; Hall, Kerney, 2012). It is therefore difficult to establish where homology ends and novelty begins, if and when establishing that boundary makes sense at all.

A fine dissection of the old and new aspects of an evolutionary novelty has been carried on by Armin Moczek and colleagues. Target of their studies were the head and prothoracic horns of the scarab beetles of the genus *Onthophagus*, already mentioned in section 6 above. During pre-pupal and pupal stages, the development of these horns is regulated through the expression of *Distal-less* (*Dll*), *dachshund* (*dac*) and *homothorax*

(*hth*), three genes otherwise involved in the specification of the proximal-distal axis of insect legs (Moczek, Nagy, 2005; Moczek, Rose, 2009). Thus, the horns of these beetles, while representing an evolutionary novelty, in the sense that similar structures were not present in their (even quite recent) ancestors and have no equivalent in many of their close relatives, are not totally new. The legs and the horns of these beetles are historically non homologous despite the involvement in their development of similar (“serial”) patterns of expression of homologous genes.

Evolutionary change is a continuous process based on the never ending remodeling of pre-existing features or, to adopt Jacob’s (1977) well-known metaphor, of the never ending tinkering with the genetic networks that regulate and control their development. This has induced several authors (e. g., Van Valen, 1982; Gans, 1985; Roth, 1984; Sattler, 1992, 1994; Haszprunar, 1992; Shubin, Wake, 1996; Meyer, 1998; Minelli, 1998, 2003a; Abouheif, 1999; Wake, 1999; Pigliucci, 2001; Minelli, Fusco, 2013) to abandon the traditional “all-or-nothing” notion of homology in favour of a different one, described as either partial or relative. An important distinction is in order. As remarked by Endress (2011, p. 122), “a sensible evolutionary question in the detailed comparison of two parts is not by what percentage they are homologous, but in which respects they are homologous”. This corresponds to my suggestion (Minelli, 1998, p. 344) that “we must proceed, in every assessment of homology, by specifying first the structural layer, or the developmental control, or the gene (or complex of genes), which identifies the morphological or developmental unit on which we are focusing [...] that amounts to adopting a combinatorial approach to homology (Bachmann, 1989; Minelli, 1992, 1996; Haszprunar, 1992)”.

14. Homology in the context of phenotypic plasticity

Phenotypic plasticity (reviewed, e. g., in Schlichting, Pigliucci, 1998; Pigliucci, 2001; West-Eberhard, 2003; Fusco, Minelli, 2010) is “a property of individual genotypes to produce different phenotypes when exposed to different environmental conditions” (Pigliucci et al., 2006, p. 2363). It is through phenotypic plasticity that the different castes are generally produced among social insects, but this applies also to the environmental determination of sex in reptiles such as the alligator and the origination of predator-induced morphs in water fleas and frogs.

It has been suggested (Nijhout, 2003) that non-adaptive or just incidentally adaptive phenotypic plasticity is likely the primitive character state for most if not all traits. Eventual fixation can result either by progressive reduction of plasticity, thus ensuring the production of a stable phenotype irrespective of environmental variation, or by evolution of a genetic polymorphism by genetic assimilation of multiple phenotypes. However, evolution likely occurs through repeated cycles along which plasticity and genetic fixation alternate. There is arguably no evidence that genes — to use the terminology of Schwander and Leimar (2011) — must necessarily be leaders or followers in respect to environmentally directed change.

In addition, there is also evidence of stochastic production of alternative phenotypes (without intermediates) even in the absence of genotypic differences and in strictly uniform, standardized environmental conditions. Within the diplogastrid nematodes, a conspicuous example of stochastic polymorphism appears to be a condition secondarily evolved in a line previously showing polyphenism (environmentally induced polymorphism). Many members of this family (for

example, 23 out of the 54 species discussed by Susoy et al., 2015) are dimorphic for the armature of the mouth: the two phenotypes, the stenostome and the euryostome one, are differentially successful in exploiting different kinds of prey. In the vast majority of the dimorphic species, this trait is phenotypically (and adaptively) plastic, the alternative phenotypes being preferentially expressed in the presence (the stenostomous one) or in the absence (the euryostomous one) of bacteria. Starvation and population density also affect the relative proportions in which the two phenotypes are produced. But in isogenic lines of the genus *Pristionchus* both phenotypes are also expressed in the absence of any environmental stimulus, a stochastic developmental property that phylogeny shows to be a derived, genus-specific trait.

A comparative zoologist may ask if, in what sense or to what extent the stenostomous (or the euryostomous) phenotypes of a *Pristionchus* species can be regarded as homologous to the morphologically equivalent phenotype expressed by a nematode where the trait's expression is not subject to stochasticity. The same comparative zoologist may also ask if, in what sense or to what extent a trait expressed under strict genetic control is to be considered homologous to a morphologically equivalent trait expressed under environmental control by a related species exhibiting plasticity for the same trait. Once more, to answer these questions we need to specify the perspective (e. g., strictly morphological, or developmental, or genetic-mechanistic) from which we want to address them.

Evolutionary developmental biology offers some useful suggestions, encouraging to scrutinize

— the evolvability of morphological traits, of developmental processes and also of inheritance systems, which are not limited

to the conventional, DNA-encoded information carried by chromosomes (Helanterä, Uller, 2010),

— the modularity of developmental processes, which nevertheless is never total and exclusive, and itself evolves,

— the mosaic nature of virtually all morphological traits we are able to isolate within the phenotype, and of the developmental stages through which the ontogeny proceeds.

This articulated perspective requires a combinatorial approach to homology and the rejection of the traditional “all-or-nothing” perspective. The latter would be suitable if the object we need to compare were natural kinds, but the contingent, historical nature of living organisms does not fit into this philosophical category.

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