Homology

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1 Concept(s) of Homology

1.1 Common Usages of the Term Homology

Homology is one of the terms most widely employed in biology. Together with species, gene and a few others, it is likely to occur in texts devoted to the most diverse biological disciplines, from morphology to systematics to molecular genetics. However, the frequent occurrence of this term in such a diversity of contexts and the very long tradition of its recurrence in biology should not be construed as a proof that the scientific community agrees on a definition of homology. On the contrary, a less than critical attitude towards its variegated use is likely to cause dangerous misunderstandings.

Leaving aside a number of more technical contexts where homology and related terms take specific meanings, some of which will be explained in this chapter, there are three main contexts in which a reader is confronted with the term in a range of items ranging from elementary textbooks in biology to research articles in developmental genetics.

A first usage documents the survival, in educational texts especially, of the once fashionable contrast between *homology* and *analogy*, usually accompanied by traditional examples such as the foreleg of a quadruped and the wing of a bird as examples of homologous body parts, while the same bird wing compared to a butterfly wing exemplifies analogy.

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More recent or more updated texts usually ignore analogy and present homology with the terminology introduced in biological systematics by the phylogenetic school championed by Hennig (1966), which, for a given set of taxa, distinguishes between ancestral (*plesiomorphic*) shared traits (*symplesiomorphies*) from derived (*apomorphic*) shared traits (*synapomorphies*). This basic set of concepts and terms is completed by *homoplasy*, covering trait similarities due to convergence, parallelism or reversal to an ancestral condition.

Third, homology is sometimes used as equivalent to structural similarity. This is a grossly unfortunate usage, which should be ignored, were it not for its very frequent occurrence, especially as applied to nucleic acid and polypeptide sequences. In this chapter, when not specifically stated, we will not consider this meaning.

The vast modern literature on homology includes, among many others and in addition to the works cited elsewhere in this chapter the studies of Boyden (1943, 1947), A. Remane (1955), Inglis (1966), Jardine (1967, 1969), de Beer (1971), Osche (1973), Voigt (1973), Ghiselin (1976, 2005), Riedl (1980), Sudhaus (1980), Van Valen (1982), Roth (1984, 1988, 1991), Patterson (1988), Rieppel (1988, 1992, 2005), Bock (1989), Michaux (1989), J. Remane (1989), Schmitt (1989, 1995), Striedter and Northcutt (1991), Donoghue (1992), Haszprunar (1992), Panchen (1992), Goodwin (1993), Young (1993), Hall (1994, 1995, 2003), McKitrick (1994), Minelli and Schram (1994), Minelli (1996), Sluys (1996), Wray and Abouheif (1998), Müller and Newman (1999), Butler and Saidel (2000), Laubichler (2000), Mindell and Meyer (2001), Müller (2001, 2003), Brigandt (2002, 2003), Rutishauser and Moline (2005), Griffiths (2006), Brigandt and Griffiths (2007), Kleisner (2007), Szucsich and Wirkner (2007), Sommer (2008), Ereshefsky (2010, 2012), Scholtz (2010) and Ramsey and Peterson (2012).

The sometimes confusing terminology about homology and related concepts is summarized in Appendix 1.

1.2 *Historical Overview*

The concept of homology is a traditional pillar of comparative anatomy and, more generally, of comparative biology. However, this concept and those related to it have witnessed a deep transformation and diversification since their first introduction in the biological literature. We can distinguish four steps (Fig. 1) in this complex semantic evolution.

1.2.1 Non-historical Concept of Homology

The roots of the concept (cf. Peters 1922; Boyden 1943; Panchen 1994, 1999) are usually traced back to the great French school of comparative anatomy of the early nineteenth century although, in the writings of Etienne Geoffroy Saint-Hilaire and other authors, what later became known as homology was called instead analogy, while the term homology was often used (for example by Serres 1827) to connote what we now call serial homology (see Sect. 4.1).

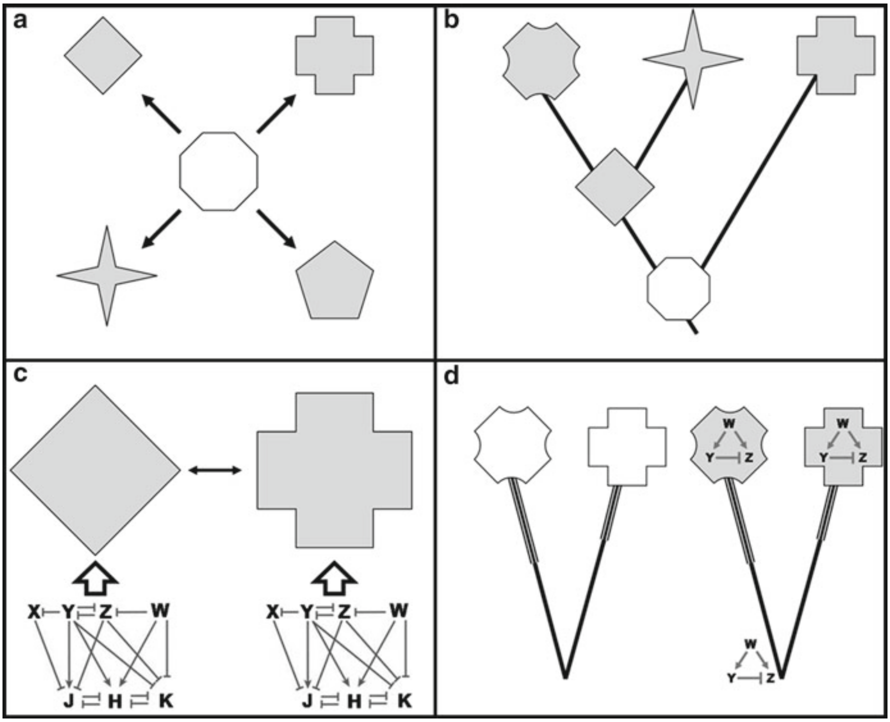

Fig. 1 Four concepts of homology. (**a**) Non-historical concept of homology. *Solid figures* are homologous because they are variants of the same archetype (*empty figure*). (**b**) Historical concept of homology. *Solid figures* are homologous because they stem phylogenetically from the same figure in the most recent common ancestor (*empty figure*) with which they are homologous too. (**c**) Proximal-cause concept of homology. The two *solid figures* are homologous because they share the same generative gene network module. (**d**) Factorial concept of homology. The two *empty figures* are structurally non-homologous (*left*) because they cannot be traced back to a structure present in the most recent common ancestor, having evolved independently from different ancestral structures (*striped lines*), but at the same time they are developmentally homologous (*solid figures, right*) because they have independently co-opted the same developmental module present in their most recent common ancestor

Circumscription of the terms ‘homology’ and ‘analogy’ that definitely opens to their modern use is due instead to Owen (1843), who defined as homologue “*the same organ in different animals under every variety of form and function*” (p. 379) and as analogue “*a part or organ in one animal which has the same function as another part or organ in a different animal*” (p. 374).

This is evidently a ***non-historical concept of homology*** (Fig. 1a), i.e. one not committed to evolutionary thinking. “Sameness” in this context is the result of an idealistic, or essentialistic concept of body plan (Ghiselin 2005; for “Essentialism in Biology” see Wilkins, this volume). This is the reason why, when Darwin (1859) used homology to support his theory of descent with modification, he did not beg the question. The specific examples he chose were merely cases of structural similarity not justified by functional necessity.

While the meaning of the term ‘homology’ has evolved through the subsequent biological literature, and has a long acknowledged status in evolutionary biology (see the next section), the term ‘analogy’ has remained associated to a pre-Darwinian concept of similarity between traits in organisms with broadly different, if not ‘incommensurable’ body-plans. Outside discussions in the domain of history and philosophy of biology, its use is thus strongly discouraged. Note that the term ‘homoplasy’ (see the next section) is not a modern synonym of ‘analogy’.

1.2.2 Historical Concept of Homology

With the advent of evolutionary thinking, it seemed quite obvious to reinterpret the “sameness” in Owen’s definition as similarity due to common ancestry. This is indeed the core of the so-called ***historical concept of homology*** (Fig. 1b), as exemplified by Mayr’s (1969, p. 85) definition: “homologous features (or states of features) in two or more organisms are those that can be traced back to the same feature (or states) in the common ancestor of those organisms” and reformulated by Bock (1974) 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.”

Conversely, a relation of similarity between two traits in two or more organisms that do not derive from the same trait in their most recent common ancestor is termed ***homoplasy***.

The historical concept of homology is further articulated into the notions of *apomorphy* and *plesiomorphy* developed by Hennig (1966). An ***apomorphy*** is a trait that is homologous among the members of a taxon and is also in a derived (*apomorphic*) condition with respect to that in a reference common ancestor. A ***plesiomorphy*** is a trait that is homologous among the members of a taxon and is in the same primitive (*plesiomorphic*) condition in which it is found in a reference common ancestor (Fig. 2). For instance, the feather, as an epidermis derivative, is a bird apomorphy within the clade Amniota, while the same character is a Passeriformes plesiomorphy within the clade of birds. This distinction, complemented by the notion that only apomorphies shared by more than one taxon (synapomorphies) are informative for phylogenetic inference, is the basis of the cladistic method of phylogenetic inference and cladistic taxonomy (see Sect. 5.1).

1.2.3 Proximal-Cause Concepts of Homology

Other researchers, however, especially those interested in developmental biology rather than in taxonomy or phylogenetic reconstructions, conceived homology as a relation between traits that share the same developmental causes, or generative mechanisms. An example is the notion that considers homologous those traits that share the same genetic basis or, more generally, the same basis of information, be it genetic or epigenetic (Osche 1973; Van Valen 1982; Roth 1984, 1988; Minelli 1996; Minelli and Peruffo 1991). We introduce here the umbrella term ***proximal-cause concepts of homology*** for this set of concepts (Fig. 1c).

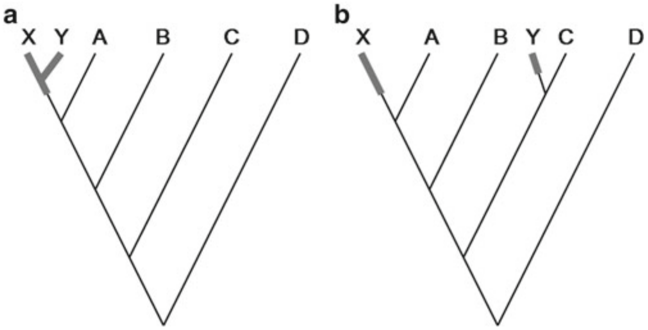

Fig. 2 The same distribution of character states (*gray* or *black*) in six terminal taxa under two different phylogenetic scenarios. (**a**) Homology. The states in taxa X and Y are homologous, because they are derived from the same condition in the most recent common ancestor of the two taxa. Since this is also a derived condition with respect to that at the root of the cladogram, the *gray* state is an apomorphy, while the *black* state in taxa A to D is a plesiomorphy because it represents the primitive condition. (**b**) Homoplasy. The derived states in X and Y are homoplastic, because they are obtained through independent transitions from the primitive state

Instances of proximal-cause homology do not necessarily overlap with cases of historical homology. Developmental genetics studies have shown how often 'obviously' homologous structures are under the control of different genes, or result from different ontogenetic processes. At the very least, a single gene is too weak a unit to provide unquestionable support to homology, and this seems true, as we shall see, even in those cases in which the expression of a single gene appears to be critically important for the entire construction of an eye or a heart. Wray (1999) did not hesitate to say that between homologous genes and homologous structures can exist all sorts of evolutionary dissociations (see also Wray and Abouheif 1998).

A less reductionist perspective than a notion of homology strictly based on gene expression leads to Wagner's *biological concept of homology* (Wagner 1989a, b, 1994, 1996, 1999): "*Structures 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*" (Wagner 1989a: 62). The greater inclusiveness of this definition stems from the fact that shared developmental constraints do not necessarily require shared developmental pathways or shared genes (Wagner 1989a).

Anticipated in this definition is the concept of *module* that Wagner and other authors developed in the following years (Wagner 1996; see also Wagner and Altenberg 1996; Schlosser 2002; Schlosser and Wagner 2004; Love and Raff 2006; Brigandt 2007). A module is intended as a unit, more or less extensive and complex, which boasts its own autonomy in ontogenetic terms, being under the control of a network of genes closely related by mutual epistatic relationships, but with very few connections to the gene networks that control other modules. It is important to note that in the general case these modules do not correspond to body parts with a distinct topographic and/or functional identity, like wings, fingers, and eyes, and do not coincide with the usual characters that the morphologist, or the systematist, typically uses as units of description and comparison (e.g., Minelli and Fusco 1995).

Despite their limits (further discussed in the following section), the proximal-cause concepts of homology are those that allow to compare different structures within the same individual organism (see Sect. 4.1).

1.2.4 Factorial Concept of Homology

It has become clear that units (modules) ascribed to different levels of biological organization (e.g., genes, mechanisms of development, morphological structures) evolve to an extent largely independent from each other, sometimes providing conflicting pictures of homology relationships (Müller and Wagner 1996; Abouheif 1997). Abouheif (1997) remarked that the mixed message that seems to stem from research on homology conducted at different levels must be understood as an indication of the relative nature of homology and the need to contextualize research.

At the basis of the proximal-cause concepts of homology there is the belief that one can explain homologous characters as the outcome of homologous causal mechanisms (Spemann 1915; Atz 1970; Hodos 1976; Roth 1984).

However, as noted by Striedter and Northcutt (1991), any character at any level of organization is subject to several kinds of change during evolution, including change in its causative (generative) mechanisms. The same authors suggests a *hierarchical view of homology*, whereby at any level of biological organization we can recognize homologies between characters, even if at a different level the two characters would cease to be homologous. For example, in terms of morphology, nobody would arguably dispute that the alimentary canal is homologous throughout the vertebrates. However, the ontogenetic precursors of this canal are very different in the different lineages. For example, it derives from the roof of the embryonic primitive gut (the archenteron) in the lampreys and salamanders, from yolk cells in the legless gymnophione amphibians, and from the lower layer of the blastoderm in the amniotes.

Striedter and Northcutt (1991) also recognized that the causal relationships between the various levels of biological organization are complex. The most obvious example of this complexity is *pleiotropy*. Or, as the authors note, the same morphological structure can be involved in a large number of different behaviors (Gans 1974; Liem and Wake 1985) and a same behavior can involve many different morphological structures. Consequently, there is no simple correspondence between characters recognizable at different levels of organization. We would arguably regard the songs produced by the different species of acridid grasshoppers as homologous, but not all of them produce these songs by rubbing the femur of the hindlegs against the forewings. When producing songs, a species known as *Calliptamus italicus* moves indeed its hindlegs with the same rhythmic pace as its relatives, but the femurs of these legs do not come in touch with the wings, and the song is produced instead by rubbing one mandible against the other.

A first conclusion we can draw from this first order of questions (more examples in Ereshefsky 2007 and Brigandt and Griffiths 2007) seems to be that the traditional notion of homology as a simple relationship between two structures, which exist or may simply not exist, depending on the characters and organisms involved in the comparison, is inadequate and must be replaced by a context-dependent notion, requiring case-after-case specification of the scope and level at which the comparison takes place.

In the spirit of the relatively recent field of studies of evolutionary developmental biology (see Love this volume), this leads us to the ***factorial*** (or ***combinatorial***) ***concept of homology*** (Minelli 1998) (Fig. 1d). The central issue here is that homology cannot be an all-or-nothing relation (two structures are either homologous or non-homologous; e.g., Striedter and Northcutt 1991; Bolker and Raff 1996). Because evolutionary change is a continuous process, based on the remolding of pre-existing features along with the underlying genetic networks that regulate and control their development, homology should rather be treated as relative, or partial (Roth 1984; Haszprunar 1992; Shubin and Wake 1996; Meyer 1998; Minelli 1998, 2003; Abouheif 1999; Wake 1999; Pigliucci 2001). The relation of homology becomes a 'matter of degree', although this is generally complex, i.e. multidimensional, or more easily expressed in terms of quality rather than quantity. For example, clearly homologous structures (in a historical sense), can differ radically from the point of view of the developmental paths that carry them out, for example, segments of different groups of arthropods (Abouheif 1997). Conversely, the development of apparently non-homologous structures (again in a historical sense), like the legs and horns of certain beetles, can be under homologous genetic control (Moczek and Rose 2009).

A second conclusion is that a factorial concept of homology goes beyond any hierarchical view of homology. It is true that for complex traits, describable as an assemblage of lower-lever traits, the latter may well be homologous, while this does not necessarily entail homology between the higher level structures. For instance, all the feathers of a bird are homologous, while not all the body parts covered with feathers are homologous. However, beyond this trivial meaning, the use of a hierarchical description of the factors contributing to the expression of a trait is misleading as it is at odds with the results of modern developmental genetics. For instance, for a regulatory gene network involved in the development of a given morphological trait, not only it cannot be described as sub-parts of the trait (hierarchical belonging), but it cannot even be described as a more basic level of its realization (hierarchical causation), because of the biunivocal relationship between gene expression and the material growth and patterning of the trait in question. A factorial description of homology relationships between different features contributing to the expression of a trait, that is not constrained by/committed to a description in terms of hierarchical relationships, seems to be superior.

An inescapable final conclusion is that the idea that characters can 'remain themselves', i.e. homologous throughout an indefinite number of possible alternative states that follow one another in the course of evolution, is probably based on an idealistic interpretation of how organisms evolve (Minelli et al. 2006b).

1.3 Logical Analysis

What would be an ontological characterization of homology? Is it a relation (of similarity/sameness)? A state (of similarity/sameness)? A qualifier (of similarity/sameness)? A quantifier (of similarity/sameness)? The answer depends on the definition adopted, which is not univocal, as it will be shown along this chapter. However, there is a possible core on which most readers would agree.

Homology is a biunivocal relation between two or more entities (like friendship). This can be expressed in different ways, e.g., *A is homologous to B*, or *A is a homologue of B*, or *A and B are homologues*. The relation is symmetric (if *A* is homologous, to some extent, to *B*, then *B* is homologous, to the same extent, to *A*) and reflexive (*A* is homologous to *A*). When homology is intended as an all-or-nothing relation (disregarding its factorial nature), this is also transitive (if *A* is homologous to *B* and *B* is homologous to *C*, then *A* is homologous to *C*) so that, in mathematical terms, it qualifies as an *equivalence relation*.

In some contexts the relation of homology needs to be semantically circumscribed before any analysis. Consider this classic example: bird and bat wings are historically homologous *as* tetrapod forelimbs, but are not homologous *as* tetrapod wings. Thus a proposition on the homology of bird and bat wing can be true or false depending on whether we are comparing them as appendages or as wings. Homology statements need to include a specification about what aspects of variation constitute a different state of the same thing, and what aspects identify different things.

As we will see soon, this is just one instance in which ‘sameness’, without further specifications, qualifies as a vague concept that can assume different meanings and can have different extensions and implications depending on the context where it is applied and the way is qualified by adjectives. The core of the problem is the meaning for a trait of remaining itself, thus preserving its identity, while at the same time changing across evolutionary or developmental time or body space (Wagner and Stadler 2003; Brigandt 2007; Wagner 2007).

The next three sections provide an analytical review of this fact, while some schematic classifications of different concepts of homology and similarity are presented in Appendixes 2 and 3.

2 Sameness Across Evolutionary Time

The classic comparative context where homology applies is comparisons of organism traits (or states of a trait) across different taxa that are interpreted in an evolutionary context.

2.1 Classic Criteria to Recognize Homology

The traditional views on homology were summarized by Adolf Remane (1952) who listed the following ***criteria for the identification of homology***:

Main criteria:

1. Position – homologous structures occupy equivalent positions

2. Special quality of the structures – two structures agreeing in a number of structural details are homologous and this can be said with much more confidence, the more complex and numerous details are coincident
3. Continuity of form – in spite of their dissimilarity, two structures can be considered equivalent if we know other structures that represent intermediate forms in a continuum between the two structures compared

Accessory criteria:

1. Even in the case of simple structures it is legitimate to suspect the existence of a relationship of homology, if these structures are present in a large number of species
2. The likelihood of a relationship of homology increases with the number of additional homologies found between the two organisms compared
3. The likelihood of a relationship of homology decreases with the number of distantly related species where the same character is present

At the time it was published, Remane's work appeared to many as a definitive crystallization of the results of a long process of study, application and rethinking of notions derived from the comparative method of the great comparative anatomists of the first half of the nineteenth century. However, since the late 1960s different approaches to the concept of homology emerged, which were only in part the result of a reformulation of older concepts. The topic has been discussed from a historical perspective by Breidbach (2003), Williams (2004), Hoßfeld and Olsson (2005), Brigandt (2006) and Ghiselin (2006).

2.2 *Development-Based Criteria to Recognize Homology*

That the study of development can provide an important and often decisive key in our attempts to establish homologies, is a notion we find already in the works of Geoffroy Saint-Hilaire (1807), who identified the centres of ossification as the modules, or structural units, of which the skull of vertebrates consists.

The homology of the germ layers can be arguably traced through the expression patterns of specific markers like the products of the genes *snail* and *twist* (see e.g. Sommer and Tautz 1994), whose expression is an early marker of the mesoderm, or *serpent*, a gene which specifies endoderm versus ectoderm in the gut of *Drosophila* (Reuter 1994). However, homologous structures in different animals are sometimes produced from different germ layers (Hall 1998).

There are several studies in which the study of ontogeny is used to reconstruct the homologies between e.g. the limbs of tetrapod vertebrates (Hinchliffe and Hecht 1984; Rieppel 1993a, b; Burke and Feduccia 1997; Hinchliffe and Vorobyeva 1999), the appendages of arthropods (Grygier 1994; Williams 1999), or the skeletal plates of echinoderms (Hendler 1978, 1988). It should also be noted, however, that since the late nineteenth century cases are known where morphological structures that appear to be homologous differ significantly in terms of ontogeny (see for example

Wilson 1894; Remane 1952; de Beer 1958, 1971; Sander 1983, 1989; Roth 1984; Hanken 1986; Henry and Raff 1990; Wray and Raff 1990; Striedter and Northcutt 1991). We must thus conclude that developmental biology is far from being an infallible guide in our search for homologies (Young and Wagner 2011).

However, processes (Sattler 1994; Gilbert and Bolker 2001) or behaviors (Wenzel 1992; Greene 1999), rather than structures, are reasonable candidates for homology, whereas the occasionally floated idea of *homology of function* (e.g., Love 2007) seems rather to point to what is currently understood as homoplasy by parallelism or convergence.

2.3 Molecules and Homology

Growing dissatisfaction with the often contradictory evidence offered by morphology has prompted many researchers to searching for homologies based on molecules. However, as soon as they began using molecules for comparative purposes, many of the problems that had long troubled the sleep of comparative morphologists were not slow to recur. Fitch (1970) was among the first to emphasize the need to distinguish between homologous and analogous proteins, but also to remark the problems of comparison due to the frequent presence, in the same individual, of two (or more) similar molecular sequences resulting from gene duplication – something comparable, in a sense, to structures in serial homology (see Sect. 4.1).

Whenever a structural component is liable to evolve by duplication, as it is the case for genes and their products, different kinds, or subtypes of homology can be recognized (Fig. 3). ***Orthologous*** genes are those homologues that are present in different organisms and have evolved from a common ancestral gene throughout speciation events. As, by definition, the phylogeny of orthologous genes coincides with the phylogeny of species, orthologous genes are of particular interest for phylogenetic inference. ***Paralogous*** genes instead have evolved from a common ancestral gene by a gene duplication event and are present now in the same organism or in different organisms. If this gene duplication event took place before a speciation event, paralogous genes are retained in the diverging genomes of the daughter species. ***Xenologous*** genes are homologues found in different species because of interspecies (horizontal) transfer of genetic material (Fitch 1970; Holland 1999). In general, phylogenies of paralogous and xenologous genes from different species do not match with species phylogeny.

But when can we say that two macromolecules are homologous? In molecular biology, the term homology has been very frequently used in the mere sense of similarity, and often expressed in percent value to record the amount of identical units (nucleotides, amino acids) in identical position between two strings. Reeck et al. (1987) reacted to this rampant abuse of the term, and strongly stressed the need to speak of homology only when there are enough clues to believe that two molecules are copies, however divergent, of the same molecule present in a common ancestor of the organisms in which the two molecules are found – that is, the notion

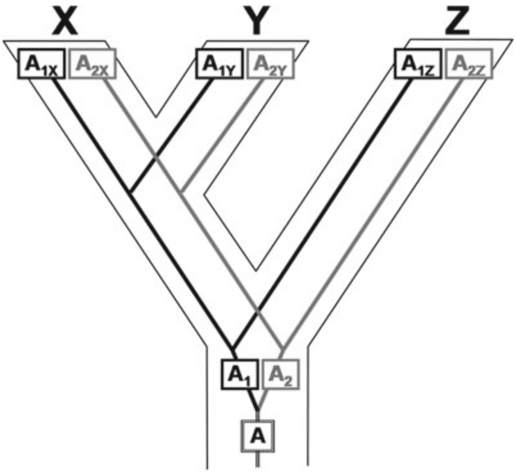

Fig. 3 Phylogeny of six genes (A_{1X}, A_{2X}, A_{1Y}, A_{2Y}, A_{1Z} and A_{2Z}) within the phylogeny of the three species that carry them (X, Y and Z). A duplication event of the ancestral gene A in the common ancestor of the three species produced two paralogous copies (A_1 and A_2). Subsequently, each of them diverged repeatedly within the whole lineage, according to the pattern of speciation events. Thus, in the three terminal taxa each gene can have either a orthology or a paralogy relationship with any of the other five genes. For instance, A_{1X} is orthologous to A_{1Y} and A_{1Z} and is paralogous to A_{2X}, A_{2Y} and A_{2Z}. Note that for a set of orthologous genes (e.g., A_{1X}, A_{1Y} and A_{1Z}) genes phylogeny coincides with the species phylogeny, while for a set of genes from different species that include paralogy relationships (e.g., A_{1X}, A_{2Y} and A_{1Z}) this relation may not hold (A_{1X} is more closely related to A_{1Z} than to A_{2Y}, while species X is more closely related to species Y than to species Z)

of homology must be applied in the historical, phylogenetic sense. A similar malpractice also transpires in morphometrics, despite Bookstein's (1994) remark that there is no legitimation to calling homologous the reference points (landmarks) arbitrarily used to compare biological forms with the techniques of geometric morphometrics.

Beyond the non trivial problem represented by the homology between genes as such, there is a second level of analysis, involving the possible homology of the temporal and spatial patterns of expression of these genes in the context of ontogenetic trajectories of the species involved in the comparison, which does not follow by logical implication from the homology at the level of gene sequence.

The first considerations about the genetic basis of homology, such as those of Boyden (1935) and Kosswig (1961), were steeped in the traditional naive notion according to which between genes and phenotypic traits there would be simple and direct causal relations, apart from the cases – long regarded in genetics as infrequent – of epistasis (the influence of a locus on the phenotypic effect of a separate locus) and pleiotropy (the influence of a locus on separate phenotypic characters). However, with the advancement of our understanding of the temporal and spatial patterns of expression of many genes and their actual mechanisms of action, this notion has been gradually abandoned for models where the focus is on complex interactions within networks of genes and their products.

One wonders what the specific role of these genes is in relation to the complex structures that are in some way under their control. More and more often it turns out that the mechanisms of action of genes that appear to play a key role in the morphogenesis of a complex structure are nothing more than generic control mechanisms responsible, for example, for the orientation of the mitotic spindle or for a process of dichotomous branching.

Dickinson (1995) and Wray (1999) admitted an evolutionary dissociation between homologous genes and homologous structures. Often, genes that appear to be involved in the morphogenesis of more or less equivalent structures in phylogenetically very distant organisms may actually perform very general jobs, so it can be very risky to use their role in these developmental processes as indicating homology of the structures eventually produced. Even more dramatically, Akam (1999) observed that it does not make any difference to organisms what this or that gene do: what matters is not whether a particular function is under the control of a specific gene or another, provided that the cell in which some of these genes are expressed is able to perform that particular function. Moreover, the genetic circuitry controlling the development of a trait is frequently redundant, and this circumstance can drastically reduce the liability of a particular gene for a particular function. Arendt (2005), discussing nervous system evolution, went on distinguishing between different levels of comparison involving, respectively, gene functions, expression patterns, and cell type molecular fingerprints.

Nielsen and Martinez (2003) proposed a new term, *homocracy*, to designate organs or structures which are organized through the expression of identical patterning genes, irrespective of whether these structures, as such, can be regarded as homologous. 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.

A virtually opposite concept of homology has been lately suggested by Wagner (2007), who regards the homology of morphological characters as rooted in the historical continuity of gene regulatory networks to which he refers as to ‘character identity networks’ that enable the execution of a character-specific developmental programme.

3 Sameness Across Developmental Time

In applying the concept of homology to the study of developmental processes we meet, indeed, new and perhaps unexpected problems. On which basis or under which perspective can we say that developmental stage X of animal A is homologous, and therefore directly comparable with stage Y of animal B? Of course, between X and Y, there may be large similarities that invite to call both of them a gastrula, a larva, or a pupa. But these terms have often a purely descriptive value and their current use does not necessarily express a reasonable hypothesis of homology between the ontogenetic stages of different animals.

This is the case, for example, of the term larva. Raff (1999) relied on a hypothesis of homology between the larvae of related species of sea urchins to discuss radical evolutionary changes in the early development of those animals. However, do we imply homology when we use this identical term for organisms as diverse as the trochophore of a polychaete, the caterpillar of a butterfly and the tadpole of a frog? According to Hanken (1999), even the homology between the tadpole of a frog and the tadpole of a newt is far from granted. On the other hand, if those are larvae anyway, why not to call a newly born kangaroo also a larva?

Of course, it is not easy to make a sensible periodization of development into objectively defined and meaningfully comparable stages (Minelli et al. 2006a). The main difficulty is caused perhaps by **heterochrony** (e.g., McNamara 1986; McKinney 1988; Raff and Wray 1989; McKinney et al. 1990; Raff et al. 1990; McKinney and McNamara 1991; Reilly et al. 1997; Slack and Ruvkun 1997; Hart and Wray 1999), that is, by the different times, or different speeds with which the different parts of the body are formed during the development of the two organisms under comparison.

In a sense, it is possible to argue that every organ (or, rather, every body part developing with a certain degree of autonomy from the rest of the animal) goes through its own succession of stages. If so, during its development the animal behaves like a mosaic of parts, which, compared to those of another animal, can have somewhat different ages – a situation that encourages the adoption of a factorial approach to homology, able to account for the composite nature of developmental processes.

It has been suggested (Sander 1983) that along the ontogeny of all metazoans there is a ‘phylotypic’ stage that is largely invariant within an entire phylum. This concept has evolved into the so-called hourglass model, proposed by Duboule (1994), whereby the phylotypic stage (e.g. the vertebrate pharyngula) is a necessary developmental stage (and a structural model) comparable to the bottleneck that separates the two halves of an hourglass. The animal can reach this stage through different ontogenetic pathways, mainly dependent on the amount of yolk in the egg. Downstream of the phylotypic stadium, ontogenetic trajectories diverge again, with a gradual accumulation of differences eventually culminating in the adults.

As a consequence, phylotypic stages would be privileged points of reference against which to study homologies. Even the phylotypic stages, however, are an idealization, as Richardson (1995; also Richardson et al. 1997) has shown convincingly, for the vertebrates at least.

In an attempt to dissect homology relationship through developmental time, Scholtz (2005, 2008) distinguishes between *homology of developmental stages* as morphologically constrained and independently evolving units and *homology of developmental processes* (as evolutionarily modifiable sequences of otherwise comparable developmental stages), regarding both of them as legitimate targets of enquiry and instruments of comparison. Expressing an opposite view, Minelli et al. (2006a) have argued that while a firm subdivision of arthropod development in stages delimited by the moulting cycle is useful for describing ontogeny, this is limiting as a starting point for studying its evolution. Evolutionary change affects the association between different developmental processes, only some of which are paced by the molting cycle. Events occurring but once in life (hatching; first achievement of sexual maturity) are traditionally used to establish boundaries between major units of arthropod developmental time, but these boundaries are quite labile. The presence of embryonic molts, the ‘gray zone’ of development accompanying hatching (with the frequent delivery of an immature whose qualification as ‘free embryo’ or ordinary postembryonic stage is arbitrary), and the frequent decoupling of growth and molting suggest a more complex reality, where homology of developmental events and developmental stages are not relations of the kind all-or-nothing, a fact more easily accounted for by a factorial concept of homology.

4 Sameness Across the Body Space

4.1 *Serial Homology*

The proximal-cause concepts of homology also apply to different structures within the same individual. Homology between repetitive structures of the same individual, like vertebrae, fingers, or petals is currently known as ***serial homology*** (Fig. 4a). The term is generally used irrespectively of the spatial distribution of the repetitive structures, which are not necessarily in a row, as in the case of the segments of an earthworm, but can also occur in a different regular pattern (i.e., radial, as the sectors of a sea urchin) or even be sparsely distributed as are the setae of a fruit fly.

According to Ax (1989) and Wake (1999), we should not apply the notion of homology to the relationships between members of the same series. In their view, homology can be predicated only of equivalent structures in two separate bodies. It is a curious fact, however, that in the days when homology was known as special similarity, the French anatomists of the early nineteenth century used this term just to indicate what would later be called serial homology. Of course, the issue at stake when we establish a comparison between different parts of the same organism is different from a comparison of structures belonging to individuals of different species.

Wake (1999) remarked anyway that the structural similarity between the front and hind legs of tetrapods, a similarity that often goes down to the smallest details, has challenged the interpretative efforts of comparative anatomists since the days of Owen. Shared developmental constraints between the two pairs of limbs remain very strong even in those tetrapods where fore and hind limbs are subjected to divergent selection, as in the case of apes and humans, with the two pairs of limbs eventually becoming the upper and the lower limbs. Rolian et al. (2010) have shown, in our own species as well as in the chimp, that fingers and toes evolve along highly parallel trajectories deceptively suggestive of parallel directional selection. However, this parallel evolution is possibly due to the fact that both pairs of appendages represent a sort of copies of a common model, that is, of the trunk of the same animal;

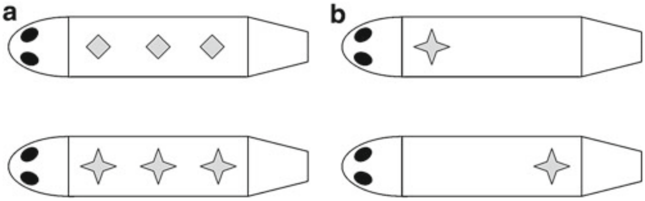

Fig. 4 (**a**) Positional homology. Different, non homologous structures are localized in homologous positions in the body of two species. This drawing also illustrates the concept of serial homology, as within each species there is a serial repetition of the same structure. (**b**) Special homology. The same homologous structure is localized in non-homologous positions within the body of the two species

this is the concept of *paramorphism* (Minelli 2000) according to which the appendages are a sort of duplicates of the main body axis. If so, the serial homology between the anterior and posterior limbs of a vertebrate would derive, by transitivity, from the fact that both are partial homologues of the main body axis.

4.2 Special Homology and Positional Homology

Another source of debate on homology is the distinction between ***positional homology*** and ***special homology*** (Minelli and Schram 1994; Minelli 1998, 2002) (Fig. 4). To illustrate this point, let's consider a homeotic mutant, in which a body part, well built to the finest details, develops at a 'wrong' site i.e., where one would expect to find a different structure. Famous examples are some *Drosophila* mutants, like the one with two pairs of wings, of which the 'wrong' one is the second, borne on the metathorax where wild-type flies carry a pair of halteres, or the one with a pair of legs replacing the antennae. In these cases, ectopic structures (the second pair of wings and the supernumerary feet, respectively) are the positional counterparts of very different structures (halteres and antennae, respectively), but from the standpoint of special homology, they are perfectly comparable to the structures (wings, legs) with the name of which we call them (Wagner 2007). The ability to dissociate the control over the position of a structure from the quality of the same structure was soundly confirmed by experiments that led to the production, in *Drosophila*, of ectopic compound eyes (Halder et al. 1995).

Fruitflies and mice exemplify two animal models of organization so different as to make it very difficult to find homologies between them. For example, *Drosophila* is a representative of the Gastroneuralia, those animals in which the main longitudinal axis of the central nervous system runs ventrally to the gut. The mouse belongs instead to the Notoneuralia, in which the main axis of the central nervous system runs dorsally to the gut. In a sense, we can say that arthropods become comparable to vertebrates as long as you turn them upside down. A pioneer in comparative anatomy as Etienne Geoffroy Saint-Hilaire (1822) did not hesitate to propose this formal exercise, in his attempt to demonstrate the fundamental organizational unit of all animals. No wonder, however, that his attempt was ridiculed (Appel 1987) and relegated to the dark corner of abstract speculation.

Yet the bold comparison of Geoffroy Saint-Hilaire has found support in recent discoveries in the molecular genetics of development. Following a tentative hypothesis formulated by Arendt and Nübler-Jung (1994), DeRobertis and Sasai (1996) explained in detail its possible molecular underpinnings. In vertebrates, the formation of dorsal mesoderm and central nervous system is induced by a region called the organizer. However, the way in which the organizer acts remained uncertain for a long time. Today we know that the *chordin* gene encodes a protein whose presence has the same effect as the organizer. Similar inductive effects are produced by the protein encoded by the *Drosophila* gene *short gastrulation* (*SOG*), which has significant similarities with the nucleotide sequence of *chordin*. However, the expression patterns of these two genes are mutually inverted along the dorsoventral axis. The comparison extends to another pair of genes, whose expression domains are opposite and complementary to *chordin/SOG*. These are *decapentaplegic* in *Drosophila*, which is expressed dorsally and promotes the development of dorsal structures, and its vertebrate counterpart *bone morphogenetic protein 4*, which is expressed on the ventral side and controls the formation of ventral mesoderm.

4.3 Anatomical Frames of Reference

Nineteenth-century comparative anatomists realized that some organs or organ systems are more conservative than others in position and special organization and could be therefore selected as topographical markers with reference to which to recognize homologies, while other organs undergo extensive and frequent changes in shape, development and possibly even position. Thus, insertion points of muscles, blood vessel patterns and, above all, nerve pathways (see Sect. 2.1, Remane's criterion 1; A. Remane 1952, 1963) became the main points of reference which the morphologist called for help, in the not rare cases where clues provided by other structures (for example, the bones in the vertebrates or the sclerites in the exoskeleton of arthropods) were uncertain or contradictory. It is unlikely that the early anatomists had arrived by chance at these guides to the comparative work. More likely, the initial choices had been probably tinged by a somewhat metaphysical and essentialist bias, in the belief that some organs or organ systems are more important than others and therefore more reliable in the search for homologies. No wonder, in particular, that the nervous system was granted a privileged role, since it is only for the brain, the most complex part of the nervous system, that humans can claim a indisputable anatomical superiority over all other animals. Of course, this anthropocentric bias does not detract from the likely interest that patterns of innervation may have in the identification of topographical relationships within a animal's body.

Breidbach and Kutsch (1990) used the neurons that innervate the dorsal longitudinal muscles of adult and juvenile stages of two locusts (*Schistocerca gregaria* and *Locusta migratoria*) and a beetle (*Zophobas morio*) to identify a set of homologies involving the three key dimensions of comparative morphology. These authors were in fact able to identify a set of 11 neurons that are common to all species studied (special homology or historical (= phylogenetic) dimension of the comparison), are repeated in each animal from one segment to another (serial homology) and are also recognizable in the later stages of the insect, regardless of whether it will face (beetle) or not (grasshoppers) a dramatic metamorphosis (ontogeny).

However, other studies have shown that innervation might be subject to change dependent on use and age, changes ranging from simple addition or elimination of synapses up to a whole reorganization of the nervous system during metamorphosis (Hallam and Jin 1998). The question is, rather, what are the real reasons of this biological stability – certainly not absolute, but higher than that of many other systems – the nervous system seems to boast.

According to many indications, a large proportion of genes expressed at early stages of embryonic development, which are involved in defining the overall architecture of the most diverse Metazoa, and the different structures of their bodies, would have originally had a role in specifying the structure of the nervous system. Secondary, and more recent, would be their responsibility in other choices, including segmentation of the longitudinal axis of the animal. If so, in a historical sense the neural organization would be the first aspect of an animal's complex organization to whose service a network of genes would have evolved, capable of producing a highly ordered structure in a reliable way.

5 Homology at Work

Homology is not only a central concept that organizes biological knowledge. It is also a basic conceptual tool for a number of applications in biological research.

5.1 Homology in Phylogenetic Inference

Distinguishing between plesiomorphies and apomorphies was the first, critically important step in Hennig's program aimed at providing biological systematics with a solid foundation allowing a methodologically sound reconstruction of phylogenetic relationships, the central problem of what eventually emerged as the phylogenetic, or cladistic, systematics. In cladistic methods of phylogenetic inference, shared plesiomorphies (*symplesiomorphies*) among a set of taxa within a group of interest (*ingroup*) do not convey any information about their phylogenetic relationships, as these are interpreted as an homologous trait inherited (in its primitive form) from an ancestor of the whole ingroup, and are therefore neutral with respect to any phylogenetic hypothesis within it. On the contrary, shared apomorphies (*synapomorphies*) among a subset of taxa of the ingroup support all the phylogenetic hypotheses that see the taxa sharing the character in its innovative form as more closely related to each other than to any other taxa of the ingroup. In other terms, the reconstruction of phylogenetic relationships can only be based on synapomorphies. Methods have been thus developed for distinguishing plesiomorphies from apomorphies, a problem to which phylogeneticists technically refer as to the problem of identifying character polarity. This analysis is independent from the specific natures of the characters to be analyzed, whether e.g. morphological or molecular, but only depends on the distribution of their alternative states among the taxa to be compared. An accessible illustration of these concepts and methods, well suitable as a reference work for educational purposes, is provided by the introductory chapter of Lecointre and Le Guyader (2006), while a classic reference book is Felsenstein (2004). A classic reference to the role of homology in the context of cladistics is Patterson (1982), while more recent discussions of homology in the wider context of phylogenetic inference are found in Sober (1988, 2008), Brower (2000), Stevens (2000), Reif (2004), Williams and Humphries (2004), Richter (2005), Williams and Ebach (2008), Nixon and Carpenter (2011).

In the context of phylogenetic analysis, de Pinna (1991) distinguished between ***primary homology***, i.e., the assumption of a hypothesis of homology, and ***secondary homology***, i.e. the legitimation of such a statement. Primary homologies are the characters that we code in the data matrices for phylogenetic reconstruction. These are characters that have passed the most severe observational tests of similarity and topological correspondence. When the matrix of putative homologues is analyzed and a cladogram is obtained, the primary homologies that survived the test, i.e. the characters that have a single origin on the cladogram, are then elevated to secondary homologies, while the primary homologies that have multiple origins are declassed to homoplasies (Edgecombe 2008).

5.2 Homology and Evolutionary Novelties

A classic problem in evolutionary biology is the origin of evolutionary novelties (Müller and Wagner 2003). As a first approximation, we can define an evolutionary novelty as a trait suddenly emerging in the course of the evolutionary history of a particular group of organisms, a trait that was not present, even in a different form, in earlier representatives of this group. Classic examples of evolutionary novelties are insect wings, the echolocation system (sonar) of bats, the lantern of fireflies, the flower of angiosperms and the digestive enzymes of insectivorous plants.

In the literature there is a degree of inaccuracy in the use of the term ‘evolutionary novelty’. This obtains slightly different meanings in different contexts, while alternative terms (evolutionary novelty, invention, or innovation) do sometimes refer to the same concept (Minelli and Fusco 2005; Brigandt and Love 2010). At the root of this confusion is the fact that some authors care for distinguishing between the emergence of a new trait during the evolution of a lineage and its possible evolutionary success through a species radiation, while other authors do not. Not all the novelties lead to a phyletic radiation, and an innovation may prove to be a key character in a radiation long after its first appearance, once other boundary conditions have changed (e.g., the appearance of feathers in theropod dinosaurs and the subsequent radiation of birds). In general, the success of an innovation depends on the environmental context in which this is actually tested. Beyond the problems of terminology, the two concepts are certainly independent, in principle at least.

With respect to the subject of this chapter, the most relevant aspect is the emergence of novelties, regardless of their potential contribution to a lineage's evolutionary success (Müller and Wagner 1991; Hall 2005), which is also a special focus of evolutionary developmental biology (see Love this volume). An evolutionary novelty is thus *a trait that has no obvious homology with any other trait in another organism or the same organism, and whose origin can not be easily traced back to a modification of a body structure existing in an ancestral species*.

However, evolution does not produce novelties from scratch. Evolution 'operates' on what already exists, and thus we expect that at a sufficiently accurate analysis, each novelty will reveal some evidence of these changes, thus appearing as a more or less complex mixture of conserved and novel elements (Moczek 2008; Hall and Kerney 2012). This applies to large-scale transformations that we can trace through evolutionary history, such as the emergence of a new body architecture, but also to changes at smaller scale, limited to the appearance of a new feature in the context of an unchanged body organization. Thus, no novelty is totally new and distinguishing what is new from what is preserved is not necessarily easy or straightforward. The new components (or those preserved) can be structural elements, metabolic pathways, properties of development, genetic regulatory factors, or other. It is therefore difficult to establish where homology ends and novelty begins, if establishing that boundary makes sense at all.

A nice example of the evolution of a new structure is offered by horned scarab beetles. Several thousand species of beetles have rigid, non-articulated 'horns' on the head and/or the prothorax. These are used as weapons in male-male competition to access to the females, the latter generally having less developed horns or no horns at all. Armin Moczek and his collaborators have studied the genetic basis of the development of these structures in a few species of *Onthophagus*, a scarab group which, with 2,400 species, is one of the largest genera in the animal kingdom. These researchers found (Moczek and Rose 2009) that the development of these horns shares many properties with the development of the 'true' insect appendages such as legs and antennae. During pre-pupal and pupal stages, groups of cells that will form the horns of the adult undergo significant proliferation followed by a more or less intense phase of modeling and (often) remodeling, depending on the species and sex. During these stages, horn development 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. Two of these genes (*Dll* and *hth*) are expressed in the horns in the same relative positions in which they are expressed in the legs of *Onthophagus*, as well as in those of all other insects studied thus far (Moczek and Nagy 2005), whereas *dac* is expressed all along the axis of the horns, overlapping with the domains of expression of two other genes, suggesting that it does not have a specific role in the development of these structures.

Thus, beetle horns, while representing an evolutionary novelty, are not totally new. And beetle legs and horns, while sharing the same underlying genetic networks, so to be qualified as homologous in terms of genetic control, are historically non-homologous. A factorial concept of homology finds in the study of evolutionary novelties its most obvious application.

5.3 Homology and Nomenclature

With the exclusion, perhaps, of biological terms that are common also in everyday language, like ‘head’ or ‘leg’, the use of the same name for two structures, or two features, in two different organisms is easily taken as an implicit declaration of homology (see Edgecombe 2008). Attempts to avoid this over-interpretation can generate an over-proliferation of morphological and anatomical terminology (Fusco 2008). For instance, as a heritage of a specific, and now surpassed, view of animal phylogeny and the evolution of segmented body architectures, there is a variety of names with which serially homologous elements of the trunk of different animals are indicated: ‘segments’ for annelids and arthropods, ‘somites’ for vertebrates, ‘rings’ for rotifers, ‘zonites’ for kinorhynchs, ‘proglottids’ for cestodes etc. (Minelli and Fusco 2004).

Undesirable interferences between name choice and homology investigation are found also in gene nomenclature. Ferrier (2008) has convincingly argued that a sensible labeling and classification of developmental control genes, on the basis of their phylogeny, are essential to any research program in evolutionary developmental biology and evolutionary genomics, since it is crucial that the structure, expression and function of orthologous genes are being correctly compared between taxa. This is particularly true for the homeobox genes, for which there are confusing and conflicting names and classifications that bias investigations and understanding of their evolution and their role in the evolution of animal development.

5.4 Homology and the Reconstruction of Ancestors

The genes that first arouse strong illusions of having finally found an objective basis of homology are the *Hox* genes. Based on the presence in many different animals of the same set of *Hox* genes, each of which, in all species studied, has a substantially equivalent expression domain along the anterior-posterior body axis, but different from that of other *Hox* genes, Slack et al. (1993) introduced the important concept of the *zootype*. According to these authors, the origin of the basic body architecture of the Metazoa (or at least the origin of the bilaterian animals) would be associated with the appearance of a first group of *Hox* genes able to specify the main axis of the body, with its “hot spots” at which the basic structures such as the brain, the genital openings etc. will be expressed in precise antero-posterior sequence.

However, following initial enthusiasm (e.g., Akam 1989; Holland et al. 1993; Sondergaard 1993; Tabin and Laufer 1993) more recent authors have become much more cautious about the possibility of using patterns of *Hox* genes expression as safe markers of positional homology, not to mention special homology (see for example Müller and Wagner 1996; Akam 1998a, b; Schierwater and Kuhn 1998; Galis 1999; Holland and Holland 1999). Indeed, when we compare insects to vertebrates, it is easier to find good examples of homeobox genes (including genes other than those of the *Hox* class) involved in the control of non-homologous rather than homologous structures (Galis 1996). For example, the gene *Brachyury (T)* is involved in forming the notochord in vertebrates, while its counterpart in *Drosophila* is involved in producing the terminal intestine.

The discovery that homologies at the level of developmental genes can be traced back to very old ancestors has fuelled an often indiscriminate use of these data to make inferences about the organization of the most recent common ancestor of distantly related groups, including very ancient lineages, for which the fossil record is generally poor or nonexistent. The inference is based on this simple inductive reasoning: since all the extant members of a certain group of organisms possess genes x, y, and z, involved in the development of organs X, Y and Z, respectively, then the most recent common ancestor of this group also had to possess traits X, Y and Z. For example, because all animals have homologous genes for the development of eyes (one for all, the gene *eyeless/Pax6*), then the most recent common ancestor of all Bilateria must have had at least some rudimentary form of photoreceptors, and animal groups without eyes (e.g., echinoderms) must have lost them secondarily (Gehring 2002).

Inferences of this kind are often in obvious conflict with assumptions based on other lines of reasoning. For example, on the basis of the expected distribution of homologous developmental genes in their living descendants, the most recent common ancestor of all Bilateria (often referred to as Urbilateria), probably a tiny inhabitant of the seabed in the Precambrian, would have presented an organizational plan that some have judged ‘illogical’. In addition to being equipped with antero-posterior and dorso-ventral polarity, two features on which there is the largest agreement among the students of animal evolution, it would also have had a segmental organization, photoreceptor organs, a heart (or a pulsating vessel), an haemocele, a skeleton, a brain and cephalic sensory appendages. Many of these features obviously would not sit well within the body architecture of a small benthic marine organism, as these traits prove to be useful only at larger body size (Minelli 2003).

Homologies, often at the level of genes, between distantly related organisms are sometimes labeled *deep homologies*, to express the idea of their coalescence in the far past, or ‘deep time’. However, the discovery of an homologous gene involved in the development of two traits in two very distantly related organisms does not automatically transform a supposed homoplasy into a homology. Rather, this invites to a ‘deeper analysis’ of the historical relationship between the two traits, once again, we suggest, through a factorial approach (Fig. 1d).

For instance, the simplistic inferences about Urbilateria briefly discussed above do not take adequately into account the phenomenon of gene co-option, i.e. the recruitment of an already existent gene into a different regulative gene network so that it acquires a novel function. The fact that the same gene, essential for photoreception, is involved in the development of the eyes in all the taxa that have these structures does not necessarily entail that eyes are structurally homologous, i.e., derived from the eye possessed by these animals' most recent common ancestor. The same gene might have been involved independently, over and over again, in different lineages where structurally non-homologous eyes are formed. In addition, genes may change function during evolution. This also explains the apparent paradox of finding genes whose products feature in a prominent role in a particular evolutionary transition to recur within the genome of the sister clade, which suggests that these genes were already present in an evolutionary stage prior to the transition itself. For example, the genome of the unicellular eukaryote *Monosiga brevicollis*, which belongs to a group, the choanoflagellates, believed to be the sister clade of animals, contains genes that encode cell adhesion proteins (cadherins, integrins and lectins) that are considered the key to the evolution of multicellularity in animals. In choanoflagellates the genes encoding these proteins are obviously not involved in the development of a multicellular soma, but in different, oldest functions, such as feeding or reproduction (King et al. 2008).

As emphasized by the developmental biologists Hejnol and Martindale (2008) "There are no such things as 'segmentation', 'eye', 'heart' or 'limb' genes. [...] There are just molecules that can bind to DNA or interact with receptors, phosphorylate other molecules, etc." The association between specific gene products and functions of the body is itself a product of evolution.

6 Educational Suggestions

As a central concept in comparative biology, homology is listed among the inescapable topics of most courses in biology, from basic to advanced levels. However, more often than not, the subject is presented through examples, while a deep analysis of the concept is considered of historical interest only. A closer examination of the notion complemented by practical or conceptual exercises is generally restricted to very specific classes on methods of phylogenetic inference, although a few papers with the character of a tutorial and accompanied by exercises on the more inclusive subject of 'tree thinking' have been recently published (e.g., Baum et al. 2005). Also, an analysis of the concept of homology is relevant in science education in any discussion about the challenge to evolution represented by creationism and intelligent design arguments (see Brigandt this volume).

However, homology can also offer an interesting subject of study per se, providing a special opportunity to inspect in depth the logic behind a fundamental concept in biology.

A first question is how an object can remain itself, preserving its identity, while at the same time changing across time or space. This is a classic problem of sameness in logic, as often exemplified by the *Theseus' ship paradox*, that raises the question of whether a ship which was repeatedly restored by replacing all its original parts one after the other nonetheless remained the same ship. It is interesting to note that among the solutions offered in modern logic there is the distinction between 'objects' and their 'properties', something that has a very strict analogy with the concept of 'character' and 'character state' in comparative biology. In natural language the same verb, to be, is used to express the properties of an object and its identity, but logicians distinguish a 'to be of predication' from a 'to be of identity' and these translate into different symbols in logic formalism (Priest 2000).

A second question relates to the vagueness of the homology concept. In classic logic, the problem of definition fuzziness is often exemplified by the *sorite's paradox*, where in a heap of sand, removing the grains of sand one at a time there is no defined point at which the heap changes from a heap to a non-heap, producing the paradoxical conclusion that also one grain of sand (or even no grains at all, or a negative number of grains) must also form a heap. The question is obviously amplified if one accepts a factorial concept of homology. Homology is a perfect test-bench for a deep reflection on a wide class of objects the student of biology will necessarily face, that is objects with a fuzzy definition. Homology is in good company with 'species', 'sexuality', 'heritability', 'novelty', 'evolvability' etc. Handling of objects with no clear-cut definition or with context-dependent definition requires special care and specific reasoning tools. Nonetheless, inference can be quite rigorous once fuzziness has been recognized and accounted for. Homology is obviously a good subject for class discussion on these matters.

Here we suggest a few exercises to be developed in class under the guidance of a teacher or autonomously tackled by the student:

- Given a set of definitions of homology, find a number of organism features that, depending on the definition, would qualify as cases of either homology or homoplasy (e.g., the historical and proximal-cause definitions of homology and the mouths of an annelid and of a sea urchin, which are historically homologous, as both derive from the mouth of their last common ancestor, but are non-homologous in terms of developmental origin).
- Given a set of structures in different organisms, lay out different meanings of sameness in order to produce different patterns of homologous and homoplastic relationships between the same structures (e.g., the legs of a fly, the legs of a bug, the chelicera of a spider, the tube feet of a sea urchin: all structures basically share the same genetic cassette, the first three historically derive from the appendages of an ancestral arthropod, the first two historically derive from the legs of an ancestral insect).
- Given a set of structures in different organisms that are credited of some degree of homology, carry out a factorial analysis, by identifying the different components of their sameness (e.g., segments in a centipede and in a polychete worm, evaluating their possible historical derivation from a common ancestor, developmental origin, genetic control).

- Find examples of failure for each of Remane's homology criteria taken individually (e.g., for 'position', the anal pore of leeches is historically homologous to the anal pore in the other clitellate annelids, however, in leeches it opens dorsally rather than posteriorly).
- Discuss the question of identity (sameness) in the light of Theseus' ship paradox.
- Discuss the question of partial homology in the light of the sorite's paradox.

Appendixes

Appendix 1

Grammatical tagging and cross-relations of key terms

analogy	Noun. A relation of non-sameness (see main text) between two or more similar traits or states of a trait (a pre-Darwinian concept)
analogous	Adjective. Of a (state of a) trait in analogy relationship with s.e.
analogue/analog	Noun. A (state of a) trait in analogy relationship with s.e.
apomorphic	Adjective. Of a (state of a) trait in a set of homologues that is derived, i.e. in different condition with respect to that in a reference ancestor
apomorphy	Noun. An apomorphic homologue
autapomorphy	Noun. An apomorphy exhibited by one terminal taxon
synapomorphy	Noun. An apomorphy shared by members of a taxon
homology	Noun. A relation of sameness (see main text) between two or more traits or states of a trait
homologous	Adjective. Of a (state of a) trait in homology relationship with s.e.
homologue/homolog	Noun. A (state of a) trait in homology relationship with s.e.
homoplasy	Noun. 1. A relation of non-sameness (see main text) between two or more similar traits or states of a trait. 2. A homoplastic (state of a) trait
homoplastic/ homoplasious	Adjective. Of a (state of a) trait in homoplasy relationship with s.e
orthology	Noun. A type of homology relation (see main text) between two or more traits or states of a trait
orthologous	Adjective. Of a (state of a) trait in orthology relationship with s.e
orthologue/ortholog	Noun. A (state of a) trait in orthology relationship with s.e.
paralogy	Noun. A type of homology relation (see main text) between two or more traits or states of a trait
paralogous	Adjective. Of a (state of a) trait in paralogy relationship with s.e.
paralogue/paralog	Noun. A (state of a) trait in paralogy relationship with s.e.
plesiomorphic	Adjective. Of a (state of a) trait in a set of homologues that is primitive, i.e. in the same condition of that in a reference ancestor
plesiomorphy	Noun. A plesiomorphic homologue
symplesiomorphy	Noun. A plesiomorphy shared by members of a taxon

(continued)

Appendixes (continued)

xenology	Noun. A type of homology relation (see main text) between two or more traits or states of a trait
xenologous	Adjective. Of a (state of a) trait in xenology relationship with s.e.
xenologue/xenolog	Noun. A (state of a) trait in xenology relationship with s.e.

Appendix 2

Non mutually exclusive classifications of homology

- Classification 1
  - historical (evolutionary)
  - non-historical
    - idealistic (pre-Darwinian)
    - proximal-cause (e.g., developmental)
- Classification 2
  - all-or-nothing
  - degree (partial)
    - quantitative
      - one-dimensional (a scalar, e.g., percentage)
      - multidimensional (a vector)
    - qualitative (factorial)
- Classification 3
  - structural similarity (e.g., DNA sequences)
  - sameness
    - in space (body)
      - serial (e.g., annelid segments)
      - radial (e.g., echinoderm sectors)
      - sparse (e.g., arthropod setae)
    - in time
      - developmental
      - evolutionary

Appendix 3

A classification of similarity

- similar (or somehow comparable)
  - homoplastic
    - by convergence
    - by parallelism
  - homologous
    - orthologous
      - apomorphic
      - plesiomorphic
    - paralogous
    - xenologous

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