Annu. Rev. Ecol. Syst. 1989. 20:51–69

THE BIOLOGICAL HOMOLOGY CONCEPT

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INTRODUCTION

Two structures are called homologous if they represent corresponding parts of organisms which are built according to the same body plan (23, 33). The existence of corresponding structures in different species is explained by derivation from a common ancestor that had the same structure as the two species compared (25, 35). The eye of a cow is homologous to the eye of a fish but not to the eye of a squid. Homology is assessed regardless of shape or function. Only morphological equivalence in terms of relative position, structure, and connections with nerves and blood vessels counts.

Among evolutionary biologists, homology has a firm reputation as an elusive concept (27, 44). Nevertheless, homology is still the basic concept of comparative anatomy and has been used successfully in reconstructions of phylogenetic history. A large number of characters are certainly derived from the same structure in a common ancestor and are therefore undoubtedly homologous. One simply cannot escape the conclusion that the brain of a rat and a human are actually the "same" in spite of their obvious differences.

However, there are also quite problematic aspects of the current homology concept, which has been in use since the time of Darwin. This is here called the *historical homology* concept, since it is defined by historical continuity of descent from a common ancestor. The historical homology concept explicitly ignores iterative homology (12, 25), i.e. the correspondence between parts of the same organism, (e.g. the correspondence between two segments of an annelid). More importantly a large body of developmental data seems to contradict certain implications of the current homology concept (see below).

This chapter reviews the open biological questions associated with the homology concept. In addition, the different attempts to establish a biological

0066-4162/89/1120-0051$02.00

homology concept are compared, and a preliminary definition of biological homology is proposed.

THREE HOMOLOGY CONCEPTS

In the present context it is important to distinguish between types of homology on the one hand and homology concepts on the other. Different types of homology refer to different kinds of comparisons, e.g. whether the comparison is between the characters of different species or between the parts of the same organism (23, 33, 35, 37, 41). In the first case phylogenetic or evolutionary homology is concerned, provided the organisms are members of different species (25, 33). This type of homology is the one commonly used in systematics and phylogenetics. The second basic type of homology is iterative homology, i.e. homology between parts of the same organism, like the homology between foliage leaves and petals on flowering plants. Iterative homology is sometimes also called *homonomy,* or *serial homology,* if the structures are arranged along the main body axis (33, 35, 41).

Concepts differ in their explanations of homology (25, 35, 41). For instance, the commonly used historical concept explains homology by the supposition that an organ has been inherited from a common ancestor.

Before the three homology concepts are discussed below, it is useful to remember the common empirical denominator of all homology concepts. Each homology concept has to accommodate extraordinarily conservative morphological patterns that are maintained in spite of variation in function and position within the body (12, 34, 35, 46, 47). A prime example of a homolog is the tetrapod limb. The basic osteological pattern remains the same despite variation in position along the anterior posterior axis of the body, the function (swimming, running, flying . . .), and changes in the proportions of elements and loss of distal elements (19). "The realization that homologous organs conform to a pattern is valuable," said de Beer in his otherwise resigned monograph, "Homology, an Unsolved Problem" (12).

The empirical basis of all homology concepts is the recognition of conservative features in some parts of the body that are used to identify other structures as "the same" in different organisms or in different regions of the same body (12, 34, 35, 46).

The Idealistic Homology Concept

The characteristic feature of the idealistic homology concept is its appeal to nonhistoric causes (23, 41). Two characters are thought to be homologous because they are built according to the same plan or archetype. An "archetype" was considered to be something like a law of nature according to which the bodies of animals and plants are made. This concept is older than the

term *homology,* which was defined in a more or less modern way by Owen (23, 25, 41). A fairly well-developed understanding of this concept can already be found in Goethe's *Morphology*(15a), and in other publications even earlier (23). Nowadays the proper evaluation of this concept is hindered because of the idealistic terminology in which it was framed and the erroneous conclusions reached by early anatomists. But at a second glance this concept is not as absurd as it may appear to a Darwinist of this century. One should remember that there are other classification schemes of natural kinds that are actually justified by nonhistoric causes, i.e. by "laws of nature." Examples are the periodic system of chemical elements and the system of crystallographic classification. The regularities of the chemical properties of elements are explained by the quantum mechanical principles governing the electron arrangement in the atomic shell. Why not expect the same for the living world, as long as evolution was not an established fact? At least it could be said that the idealistic homology concept had some heuristic value since it stimulated progress in comparative anatomy and systematics; for example, it motivated the detection of the premaxillary bone in humans (23). That the concept was finally not viable in the light of Darwinism is another matter.

The Historical Homology Concept

After Darwin the homology concept was subjected to a radical reinterpretation (25). Supplemented by a historical perspective, it was redefined as a relationship between those parts of different organisms that correspond to an equivalent organ in a common ancestor. In other words homology is explained by historical continuity of inheritance from a common ancestor. This is the now commonly accepted meaning of the historical homology concept (25). However, it is important to go a little further and see what was implied by the founding fathers of this concept. Otherwise one cannot understand why certain facts of developmental biology are considered as "anomalies" in its context.

The early proponents of the historical homology concept (Haeckel, Gegenbaur) inferred that homologous structures have to be derived from the same anlage (primordium, precursor) (41). Homology is defined by Gegenbaur as "the relationship between two organs of common descent, which therefore have been derived from the same anlage" (cited after Spemann (41), p. 71, transl. by the author).

Such a definition of homology has strong preformistic connotations. It was expected that each organ could be traced back in ontogeny to an equivalent part of the zygote. Furthermore, the ontogenetic transmission of this hypothetical part of the zygote was thought to be the cause for the inheritance of the character. Experimental embryology and developmental genetics clearly have undermined the meaning of this concept of homology. The problems

come from the fact that morphological characters are not directly inherited but are built anew in each generation (11). (Exceptions are perhaps the morphological characters of the cortex of ciliates, 14.) Hence, in most cases there is no continuity of descent in the strict sense, as it actually exists in gene lineages or lineages of genetically autonomous organelles like mitochondria. Already in the year 1915 Spemann wrote: "The causal approach (to development) also has implications for the core of morphology, the homology concept, and has affected it in a destructive and transforming way" [Spemann (41), p. 78, transl. by the author].

But remember, only the preformistic implications of the historical homology concept are affected by Spemann's dictum, not the common empirical basis of all homology concepts—the conservation of morphological patterns.

Another implication of a strictly historical definition of homology is that any form of iterative homology has to be excluded (25), in part because of contradictions between interative and phylogenetic homology in the case of tooth evolution (44). Iterative homology is "a misnomer," according to the proponents of the historical homology concept, "because it is not concerned with tracing organs in different organisms to their representatives in a common ancestor" (deBeer (12), p 9). This seems to imply that the similarity of two hairs on the same animal has a different cause than the similarity of two hairs from two mammalian species (35). This is hard to believe.

A cladistic reformulation of the historical homology concept has been proposed recently (31). This cladistic concept is a deviation from the original meaning of homology, where homology was assessed between parts of the phenotype. Patterson applies it to any synapomorpic character state or feature. Though this is a necessary correction of the homology concept for systematic purposes, it seems to be counterproductive for a biological homology concept (46, 47). Therefore the original meaning, i.e. homology as a relation between parts of the body, is retained here.

The subsequent discussion applies only to multicellular structures. This does not mean that the homology concept cannot be applied to subcellular structures as well (36). However, the developmental biology of subcellular organelles is sufficiently different from the morphogenesis of multicellular organs that it is sensible to exclude subcellular characters from this discussion of the biological basis of homology (see below).

The Biological Homology Concept

There is no generally accepted definition of biological homology. However, a number of authors have argued for redefining homology on a mechanistic rather than a genealogical basis. Roth used the term "biological homology" in her 1984 paper (37). Other authors have redefined homology in de-

velopmental terms, e.g. Kroeger (22) and Van Valen (44), without mentioning that this leads to a completely new concept. Riedl gave an explanation of the conservativion of morphological patterns on the basis of functional and developmental constraints but did not redefine homology explicitly (34, 35).

It is more significant that most of these authors share a host of arguments which call for a new concept of homology. This may be called the "biological homology concept," because it refers to biological mechanisms rather than to genealogical connections alone.

Two lines of thought lead from the historical to a more inclusive (biological) homology concept. One is put forward by morphologists and originates from questions about the individuality of morphological characters, and from considerations of the relationship between phylogenetic and iterative homology (5, 34, 35, 37, 38, 44). The other line of thought goes back to Spemann (41) and other experimental embryologists (4, 16, 22, 40, 47) who have discussed the homology concept from a developmental point of view.

A further indication that all these authors are contributing to a common conceptual goal is that the consequences seen by different authors are very similar. Most such authors consider developmental mechanisms as essential for the definition of homology (4, 22, 34, 35, 37, 38, 40, 41, 44). Consequently, some authors allow an ambiguity between homology and parallelism (37, 44). Finally, it seems necessary to consider homology as a matter of degree rather than an all-or-nothing relation (15, 37, 44).

The rest of the chapter is devoted to an explanation of the biological homology concept as it emerges in the biological literature of this century. The next section describes the empirical evidence that undermines the historical homology concept. In the following section the different approaches to redefining homology in a biological way are discussed, and a preliminary definition of biological homology is given.

THE DEFICIENCIES OF THE HISTORICAL HOMOLOGY CONCEPT

Three topics emerge again and again in discussions about the biological implications of the homology concept: questions about what continuity of descent really means; the question of whether one can identify single structures in the case of variation in the number of repeated organs; and the variability of developmental sequences of undoubtedly homologous structures.

Lack of Continuity

Only replicators like genes pass on their own structure to their descendants directly. Morphological structures are not replicators, however (11). The

notion of continuity of descent is not problematic for genes but is less clear for organs (40a).

Heritability of morphological variation certainly exists, but morphological structures are inherited via intervening stages. In the germ cells the morphological adult characters are not represented, not even in the form of tiny primordia (anlagen). Even though adult organs can be traced back to certain parts of the zygote (3, 48), those prospective regions cannot be identified with the organs themselves (41). This was shown by nineteenth century experiments which altered the material from which the definitive organs are derived. These experiments often led to perfectly organized structures (28, 41, 48). All examples of regulatory development are in place here. Most of the adult structures are built anew and cannot be identified with particular features of the germ cells.

A reasonable suggestion is that the continuity of descent is an epiphenomenon of the continuity of gene lineages (37). To some degree this is true, since genetic variation is the predominant cause of heritable phenotypic variation, and thus the basis of evolutionary change (25). Even if empirical evidence is thus far inadequate, it seems implausible that continuity of gene lineages alone could account for the homology of morphological features (12, 38, 47). This was first noted by de Beer (12) who considered this possibility as "the worst shock of all" (12, p. 15).

Recently Roth brought the problem to the fore by introducing the concept of "genetic piracy" (38). It is the principle that "genes, previously unassociated with the development of a particular structure, can be deputized in evolution, that is, brought in to control a previously unrelated developmental process, so that entirely different suits of genes may be responsible for the appearance of the structure in different contexts" (38, p. 7). Although a direct verification of genetic piracy has to wait for the comparison of molecular data of distantly related species, there is indirect evidence in favor of genetic piracy.

Transdetermination between nonhomologous organs without any phylogenetic relationship such as legs, wings, and eyes suggests that these structures share certain genetic switch mechanisms. It is argued that these genetic relations have to be the result of genome reorganization in a way that brought about a common genetic control. This is an intriguing possibility and should stimulate the comparison of highly derived animals like *Drosophila* with presumably more ancestral species like orthopterans, which may have retained an independent genetic control of wings and legs.

In insects, genetic piracy may be a consequence of the evolution of the holometabolous life cycle, where the adult structures are derived from imaginal discs (40, 48). All cases of radical reorganizations of early development, found in many phyla, suggest a reorganization of the genome that might involve "genetic piracy."

Similarly, certain anatomical observations can be counted as preliminary evidence for genetic piracy (38). For instance, features of a certain organ can be found in other organs later in phylogeny. The most interesting case is the convergent evolution of the tetrapod pattern in the fore- and hindlimb. The fore- and hindlimbs are derived from pectoral and pelvic fins. The origin of the tetrapod pattern common to the fore- and hindlimb is thus a striking example of intraindividual convergence.

A closely related argument was raised by de Beer (12), citing a paper by Morgan where modifiers of the *eyeless* allele of *Drosophila* are able to restore the original phenotype in the absence of a wild type allele at the *eyeless* locus. "Homologous structures need not be controlled by identical genes, and homology does not imply similarity of genotypes" (12, p. 15).

Hence, the question whether the homology of morphological characters can be reduced to the continuity of gene lineages is not self-evident. Certain answers have to wait for comparative molecular data on developmental genes.

Lack of Individuality

In the simplest case phylogenetic homology is a one-to-one mapping from the characters of one species onto the characters of another species. A one-to-one mapping implies that in each species all characters can be recognized individually. Often such an individual one-to-one mapping is possible, as shown by the success of comparative anatomy in identifying two of the ear ossicles of mammals as corresponding to the elements of the jaw hinge of reptiles (12).

Whether such a one-to-one mapping is possible in all cases is an open question, to be empirically answered. This was first claimed by Bateson (5) in the year 1892, when he published his study on numerical variation of teeth in mammals. In particular he was interested in whether the identity of each element remains detectable in the case of variation in the number of repeated organs. In other words, Bateson asked whether it is possible to tell which tooth got lost or which one is new if the number of teeth has changed?

Bateson concluded that this is possible in some cases but not in all. He found a monkey skull with three premolars in the right upper jaw and four in the left. It was not possible to identify the new one in the left jaw.

Riedl introduced the concept of a "homonomy limit" below which morphological characters cannot be identified individually (35). This limit is evident in the case of identical repeated characters like serial segments or just blood cells. Where this limit is found depends on the degree of organization and differentiation of the respective species. But there are some indications that even anatomically different structures, i.e. structures with apparently different shapes or positions, may not be developmentally individualized.

Recently Goodwin & Trainor (16) pointed out that carpal and tarsal elements are essentially parts of a common pattern, and none of them can

disappear without affecting the whole pattern. In the case of reduction in the number of elements, there are no certain individual elements missing. It is just a new pattern, and there is no way to tell which element of the new pattern corresponds to which element in the old one. This suggestion is supported by the fact that already the prechondrogenic condensations show the class-specific features of the respective Tetrapod class (18). Hence, lack of developmental individuality of parts may render the identification of structures meaningless (46, 47).

A lack of individuality can be assumed if different criteria of homology (e.g. shape or position) lead persistently to conflicting results. For instance, digital reduction in amphibians can be caused by a size-related repatterning of chondrogenic condensations (2). If one asks which phalanx got lost we come to a paradoxical situation (20). If we compare the shape of the terminal elements in two hands with different numbers of phalanges we see identity of shape. But the proximo-distal position of the new terminal element is identical to that of a former preterminal element. Without further evidence it cannot be decided whether a terminal or a preterminal element got lost (20). This question may be meaningless anyway, as long as the elements have not acquired developmental individuality in some respect, so that they could autonomously express their own characteristic features (47).

A one-to-one mapping of single characters in two species is only meaningful if each of the two elements compared is developmentally individualized. Only individualized characters can exhibit specific features that would allow identification (46). The possible mechanistic basis of developmental individuality is discussed in the section on the biological homology concept.

Variability of Development

Phylogenetically homologous characters need not share common pathways of ontogenetic development. This fact has been established by three types of observations: (*a*) The origin of cellular material for a character can vary between species and even experimentally (6, 28, 33, 39); (*b*) the embryological sequences leading to homologous characters can be very different (12, 32, 39, 40, 41, 43); and (*c*) the same organs can be induced by different blastemata in different species (17).

ORIGIN OF MATERIAL The amount of evidence showing the variability of cell material for homologous characters is tremendous. Only a few examples can be mentioned here.

Primary mesenchyme and neural crest both contribute to the formation of cartilages (43). The relative contributions from these cell populations can vary dramatically between species, as for instance in the case of the reptilian orbitosphenoid (6, 15). Under a variety of experimental conditions a normal

avian columella can be formed by different proportions of cells derived from the neural crest and mesenchyme (28). Similarly the contribution of germ layers to various body parts can vary to an extent that undermines the germ layer concept (39).

Obviously the source of cells that make up a particular organ is irrelevant as long as the cells are competent to express the relevant genetic information.

MODE OF DEVELOPMENT The process of development is in itself an ecologically relevant phenotypic character (42). For instance, developmental time can be a major component of fitness, especially in ephemeral or expanding populations (9). In species with high intrinsic growth rates, the developmental process becomes modified to meet two goals at once (40): (*a*) to generate the complex of all the necessary adult characters inherited from the ancestor, and (*b*) to reduce the time required for development. The latter goal is often met by completely deviant patterns of development as exemplified by the comparison of short-germ and long-germ development of insects (40). In short-germ development, most of the body segments are laid down one after the other, while in the quickly developing dipterans the totality of the body segments is produced more or less at once. The main body regions of short-germ and long-germ developers are undoubtedly homologous, but the way they are made is not.

VARIABILITY OF INDUCTION Even on the mechanistic level, the development of homologous organs is not invariable. This has been most convincingly demonstrated in the case of Meckel's cartilage.

The inductive stimuli for Meckel's cartilage can come from the pharyngeal endoderm (amphibians), the cranial ectoderm (birds), or the mandibular epithelium (mammals) (17). This variability in the inductive blastemata is not in itself evidence that the inductive stimulus is actually different, since the same inducer substance may be produced by different cell populations (C. Gans, personal communication). However, even a difference in the physicochemical nature of the stimulus would not be a surprise, because it is known that the effect of "specific" inducer substances can be mimicked by simple changes in pH and Li-ion concentration (48).

Different

If one looks at homologous structures from a mechanistic or developmental point of view, one recognizes different types of characters. They differ in the mechanistic reasons, in why they can be regarded as "the same" in different species or in different parts of an individuum. On the one hand there are structures that are either replicators themselves (e. g. DNA or RNA) or are homomorphic to a replicator, like polypeptides. Replicators are directly

copied from their ancestors; for instance, the similarity of two homologous genes is easily explained by direct descent. On the other hand there are parts of the phenotype, undoubtedly homologous, that are not directly copied from an ancestral structure but are built anew in each generation. In addition their structure seems to be only indirectly related to the nucleotide sequence of genomic DNA. Those are the problematic cases (12, 38, 40a, 47). Among them are some which result from the cooperation between individual cells. Most of developmental biology deals with them. Then there are morphological structures that are either sub- or non-cellular, like cuticular scales of insects or cilia and microvilli. However, little is known about their development. Only this lack of insight leads me to exclude them in the present discussion.

OUTLINE OF A BIOLOGICAL HOMOLOGY CONCEPT

Bits and Pieces

CONTINUITY OF INFORMATION The most inclusive definition of biological homology was given by Van Valen (44): "Homology is resemblance caused by a continuity of information." (See also 28a, p. 21.) This definition embraces phylogenetic as well as iterative homology because it does not rely on genealogical derivation. Its charm as well as its weakness lies in the term "information," which does not imply a particular mechanism. Specifically, Van Valen does not identify information with DNA-structure. This is because DNA is not the only way to store and transmit information, and because the correlation between phenotypic changes and DNA-modification can be very loose in some cases (1, 2, 7, 14, 16, 20, 24, 26, 30, 32, 50).

The term "information" is also a weak point of the definition, because it is as elusive as homology itself. The precise information concept from mathematical communication theory is not very useful here, mainly because it requires the existence of a decoding rule independent of the signal to be decoded (45). But in embryonic development, the genotype is both, the signal as well as a part of the decoding device (30). Products of gene activity (cells, hormones, extracellular matrix, morphogens, . . .) expressed earlier in development take part in the expression (decoding) of genes active later in development. The term "information" is undefined in developmental biology because of the self-referential nature of gene expression during development.

THE SYSTEMS APPROACH The first systematically elaborated and mechanistic theory of homology is due to Riedl (34, 35). His theory consists essentially of two parts: (*a*) the origin of individualized parts of the phenotype is explained as adaptation to special functional demands. Also the maintenance of morphological features is explained by functional constraints, or

"functional burden." (*b*) The second part of his theory postulates the internalization of functional constraints into the epigenetic system. The process of internalization is thought to be caused by selection for adaptation rate and is assumed to lead to an "imitation" of the pattern of functional constraints by a system of developmental constraints. Developmental constraints are required to explain the maintenance of the morphological pattern in spite of changes in function.

To assess the plausibility of the internalization mechanism is difficult today, mainly because the population genetic models required to simulate imitation include many loci and require high levels of linkage disequilibrium for which no analytical approximations are available so far (G. P. Wagner, unpublished ms.). Also the question whether imitation occurs at all is unsettled because the relevant type of data is not thus far available.

COMMON DEVELOPMENTAL PATHWAYS A strictly developmental approach was taken by Roth (37). Her first definition of biological homology was "sharing of pathways of development, (. . .) controlled by genealogically related genes" (37, p. 13). This definition has to be qualified in two respects. The first was done by Roth in her 1988 paper (38), by introducing the concept of "genetic piracy" discussed above. It acknowledges that strict identity of loci responsible for a certain feature is not required.

This definition must be qualified further because of the variability of development, reviewed above. It has been argued that only those aspects of development are relevant for a biological homology concept that cause developmental constraints on the further adaptive modification of the structure (46). Developmental constraints are required to explain the maintenance of morphological patterns characteristic for a homolog (34, 35). Hence the source of cell material, inductive stimuli, and the mode of development (e.g. aggregation of migratory cells, or folding from an epithelial sheet) are all irrelevant, since none of them determines the structure of the feature or even constrains its evolutionary modification.

SELF-REGULATORY NATURE OF DIFFERENTIATION Important steps towards the identification of the presumably relevant developmental mechanisms were taken by Spemann (41) and Baltzer (4). They noted that the development of many features (skeletal elements, central nervous system of vertebrates) have a considerable degree of independence from their context and are homeostatic against experimental perturbations in certain stages of development. According to Baltzer and Spemann, this self-regulatory ability of developing organ rudiments explains the conservation of morphological patterns, in spite of variation of function and position of the anlage. The implicit assumption in this conclusion is that developmental homeostasis also

canalizes the expression of genetic variation, an assumption closely related to the concept of developmental constraints (1, 24, 29, 30, 46).

The decisive feature of Spemann's and Baltzer's propositions is that the relevant developmental factors are assumed to be the mechanisms of self-differentiation acting within the blastema. This approach resolves the seeming paradox of conservative morphological patterns and diverse developmental pathways for homologous structures. Not all developmental factors are relevant for the actual morphogenesis of the rudiments; only the internal factors governing pattern formation and differentiation are.

PREPATTERNS A further proposition was introduced by Kroeger in a paper reviewing the results of his recombination experiments with imaginal discs of *Ephestia* larvae (22). He concluded that iteratively homologous characters in the fore- and hindwing are derived from identical parts of the prepattern. He therefore defined homologous parts as features derived from the same part of the prepattern.

However, the extent to which this definition can be applied to other systems, e.g. vertebrates, is not clear. The fact that the nonhomologous larval characters of newts and frogs (balancers and suckers) appear to be responses to the same "prepattern" in the mesoderm (48) leads to serious doubts regarding the generality of this definition.

A Preliminary Definition of Biological Homology

Based on the attempts to find and express the biological homology concept reviewed above, a preliminary definition of biological homology is discussed in this section.

DEFINITION 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. These structures are thus developmentally individualized parts of the phenotype.

This definition is both more inclusive and more restrictive than the historical homology concept. It is more inclusive because it allows homology between parts of the same organism, i.e. iterative homology, and between individuals of the same species. The latter (between two individuals) is important to include for homology between sexually differentiated parts (e.g. penis and clitoris, or testis and ovary), or between different generations in a complex life cycle (e.g. parthenogenetic and sexual generations of parasitic insects).

INDIVIDUALIZATION The proposed homology concept is also more restrictive than the historical one because it is restricted to individualized parts of the

phenotype. In principle the historical homology concept is applicable to any discernable structure, regardless of its developmental organization.

To narrow the homology concept to developmentally individualized parts seems necessary to avoid the problems reviewed above in "Lack of Individuality." To require individuality for the application of the homology concept has consequences in two directions: for tracing a structure back to its ontogenetic precurser and for the comparison of repeated structures among species.

In earlier stages of ontogeny a particular morphological structure is represented only if there is a cell population that is determined to generate the structure or that exhibits somehow a norm of reaction specific for this structure. Hence, the definition proposed above identifies a structure with the self-regulatory epigenetic interactions responsible for the generation and maintenance of its visible morphological aspects.

The same principle applies to the phylogenetic origin of a morphological trait. Structures are homologous in two species only if the necessary epigenetic requirements for their individuality are met in both species. Hence, the origin of a new morphological feature is identified with the acquisition of individuality and the associated developmental constraints. The acquisition of individual structural features is considered to be of secondary importance to the acquisition of developmental individuality.

An example of a structure that arose by the acquisition of individuality among repeated parts is the thorax of insects. There is little doubt that insects have evolved from annelid-like ancestors possessing a number of identical segments plus nonsegmental anterior and posterior appendages. The ancestor of modern day insects most probably had segments in historical continuity with segments 7, 8, and 9, which constitute the insect thorax. There is no indication that these segments became intercalated at the origin of insects. The thorax originated from a gradual differentiation and individualization of the respective segments. Nevertheless there is little credit to the assumption that the "thorax" as such is homologous to the corresponding segments in centipeds and annelids. Only the single segments of the thorax are homologous to any other arthropod segment in general. The thorax is the unit differentiated from the rest of the body in terms of appendages and internal anatomy, a condition not found in centipedes. The homolog "thorax" is an entity that originated from certain segments by synorganization and differentiation and is not identical with the segments it comprises.

Mechanistic Models of Individualization

In the proposed definition of biological homology the term "individuality" plays a central role. To make this term operational it is necessary to specify what individualization means in developmental terms.

All parts of the phenotype have multiple connections to each other. Their function, growth, and differentiation are influenced by systemic factors like the distribution of nutrients, hormones, and other signal substances or mechanical clues. However, differentiated parts of the body react to systemic or environmental stimuli according to their own norms of reaction. The fact that different tissues have different norms of reaction is the very basis of developmental individualization.

The development of complex multicellular organisms includes several steps in which parts of the embryo individualize with regard to the rest of the body. Steps towards individualization of parts are, for instance, structural decoupling of blastema from the rest of the germ layer, or cell determination. Cell determination is defined as an irreversible change in the reaction norm of cell populations (3). After neurulation the cells within the neural anlage react to perturbations in a way specific to the nervous system, e.g. by growth or regression of cell processes and synaptic contacts or the secretion of transmitters (21, 50), while connective tissue cells react by secretion of extracellular matrix material (3, 43, 48).

Even organs composed of several tissue types of different origin can form ensembles reacting as an individualized whole. The best known example is the vertebrate eye, composed of neural, ectodermal, and mesenchymal components (10). As shown by transplantation experiments between the large and fast-growing *Ambystoma tigrinum* and the small and slow-growing *A. punctatum,* growth of the eye is autonomous. Autonomy emerges at the level of the organ but not at the level of the parts (8). This has been shown by recombination of the optic vesicles of one species with the lens of the other species. These chimeric eyes grow to intermediate size (8).

The mechanistic basis of this emergent autonomy appears to be a closed cycle of epigenetic interactions. The central piece of this system appears to be a feedback between the neural retina (precursor) and the lens (anlage) (10). Lens formation is induced by the prospective neural retina and the differentiation of the neural retina is induced by the lens placode. Without a lens the prospective neural retina would develop into pigmented epithelium. The retina in turn stimulates the differentiation and growth of the lens which then causes the vitrious body to grow. The growth of the vitrious body finally is necessary to cause a coordinated growth of bulbus and retina. Without a lens the retina shows disproportional growth and finally degenerates.

In this case the individualization of a complex organ appears to be due to a cyclically closed epigenetic interaction leading to partial automony of differentiation and growth regulation of this organ (47).

Developmental Constraints and Epigenetic Traps

To invoke epigenetic mechanisms as a causal factor in evolutionary change leads to a conceptual difficulty. Heritable variation is in almost all cases

caused by genetic variation. In addition, all components of the epigenetic system (cells, extracellular material, signal substances) are the consequence of gene activity. How can the epigenetic system be of consequence for morphological evolution if everything can somehow be traced back to gene activity and gene substitutions? To clarify this problem the concept of epigenetic traps has been introduced (47).

The following explanation of this concept is phrased in the form of definite statements, although the mechanism proposed is hypothetical and calls for rigorous experimental test.

Developmentally individualized parts of the phenotype are not only autonomous with respect to their reaction to epigenetic and environmental stimuli; they also constrain the possible phenotypic effects of genetic variation. A blastema is autonomous if the relevant epigenetic interactions are realized within the primordium. If genes are expressed after the cell population becomes determined, the possible phenotypic effects of alleles at these loci are defined by the norm of reaction of this blastema. The best example for this principle is the etiology of the congenital neurologic disorders of Siamese cats (21). Of course the epigenetic organization at a stage of development is also a consequence of gene activity earlier in development. But a particular gene, expressed at a particular stage of development, can only interact with what is sensitive to its products at this stage of development. The same holds true for the consequences of allelic variation at a particular locus.

This principle is best exemplified with regard to a cyclically coupled ensemble of characters that constitutes a semi-autonomous part of the phenotype. The best example is the vertebrate eye. As explained above, growth regulation of the eye is autonomous on the level of the organ, because all the parts are coupled by cyclical interactions, leading to a mutual adjustment of the components of the eye. In such an organ genetic variation can have only two consequences. Either the modification of a part has no consequences for the interaction with the rest, e.g. different amounts of pigment in the retina. Or the allelic variation interferes with the feedback between the components. Then the allelic variation is of consequence for all features regardless of the tissue in which the gene is expressed. In the most extreme case the whole eye is lost, but in mild cases only the size of all parts is affected. It is not possible to reduce only one of the parts, e.g. the lens, without affecting the whole organ.

This last suggestion is supported by data on the genetics of eye reduction in cave populations of *Astyanax mexicanus*. Hybrids between surface and cave populations of *Astyanax* show that many genes influence eye size, but loci with effects only on the lens or only the retina were impossible to isolate. All genes were essentially "eye genes" (49).

Hence, self-regulatory parts of the phenotype are "epigenetic traps" because they constrain the possible phenotypic effects of genetic variation, even

though they became established by genetic variation and gene substitution in the first place.

Biological Homology Concept and Phylogenetic Inference

According to the definition of biological homology, the homology relation should be applied only to developmentally constrained morphological patterns. Hence, not all features can be meaningfully homologized. For instance, it is inherently difficult to homologize phenotypic differences caused by simple Mendelian factors, like color variants. Many color variants can be produced and destroyed simply by genetic recombination. There is no acquired constraint that maintains this feature and no basis to apply the biological homology concept.

On the other hand morphological patterns maintained by developmental constraints do not originate as easily as a Mendelian character. This is suggested by an in depth developmental analysis of the syndesmosis tibiofibularis (26). This structure links the weak fibula of birds to the tibia in order to transmit the force of the ileo-fibularis muscle to the tibia. It is synapomorphic for birds and theropod dinosaurs. In other groups the same functional problem is solved by other anatomical means. The analysis of Müller & Streicher suggests that the origin of this feature required a delicate coincidence of epigenetic conditions to allow the growth of a fibular crest (for details see 26).

This suggests that most of the homologs that fit the definition of biological homology in a comparison between species will be unique and that means they are also homologous in the sense of historical homology (47). Multiple independent origins of developmental constraints that fix a particular morphological pattern are highly improbable, because of the special requirements for establishment of a constrained morphological pattern.

The ambiguity between phylogenetic homology and homoplasy, which the proponents of a biological homology concept are willing to accept (37, 44), may not lead to contradictions with the historical homology concept in the most cases. The success of comparative anatomy in reconstructing phylogenetic history is remarkable. Parallelism can not be a very common phenomenon, since with a high frequency of homoplasy this would be impossible.

CONCLUSIONS

The common basis of all homology concepts is the recognition of highly conservative morphological patterns found in a wide variety of species. The discussion about the biological validity of the homology concept revolves around the following topics: the relationship between phylogenetic and iterative homology, the question of individuality of repeated organs, the nature of continuity, and the variability of development.

Several attempts have been made to formulate a more inclusive concept that might be called *biological homology*. Common to all these attempts is their reference to some kind of developmental mechanism to explain the conservation of morphological patterns (34, 35, 37, 38, 44, 46, 47). Variability of developmental pathways forces us to be more specific in defining the relevant developmental factors. The most probable candidates are developmental constraints caused by self-regulatory mechanisms of morphogenesis acting within the organ primordium (4, 41, 46, 47). Other developmental factors, like the origin of cells and inductive stimuli appear to be irrelevant. These mechanisms explain also the individualization of the organs. Only individualized parts of the phenotype deserve individual names that permit them to be called homologs.

There is a host of open questions—conceptual, theoretical, and empirical ones. The most pressing are whether the homology concept should be applied to features (37), parts (47), or developmental transformations (13), and whether homology is an all-or-nothing relation (15, 37, 40a, 44). The most important empirical questions are how individuality of characters is realized developmentally and how it emerges during phylogeny. Both questions require a combined experimental and comparative approach to the evolution of morphological characters. From the population genetic point of view it would be necessary to understand how natural selection on phenotypic characters influences the evolution of underlying developmental parameters. In summary, even though biological homology seems feasible from what is known today, its mechanistic explanation is still a challenge.

ACKNOWLEDGMENTS

The author is indebted to R. Bürger, B. Misof, R. Riedl, J. Rienesl, Ch. Pázmandi, and C. Vogl for stimulating discussions on the subject of this paper, and for reading an earlier version of the manuscript. The financial support by the Austrian Fonds zur Förderung der wissenschaftlichen Forschung (Project No. P6298-B) is gratefully acknowledged.

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