Homology in Development and the Development of the Homology Concept1

Article *in* Integrative and Comparative Biology · October 2000

DOI: 10.1668/0003-1569(2000)040[0777:HIDATD]2.0.CO;2

1 author:

Manfred Laubichler
Arizona State University
211 PUBLICATIONS **2,895** CITATIONS

SEE PROFILE

AMER. ZOOL., 40:777–788 (2000)

Homology in Development and the Development of the Homology Concept[1]

MANFRED D. LAUBICHLER[2]

Program in History of Science, Princeton University, Princeton, New Jersey 08544

SYNOPSIS. Homology is a central concept for Developmental Evolution. Here I argue that homology should be explained within the reference processes of development and evolution; development because it is the proximate cause of morphological characters and evolution because it deals with organic transformations and stability. This was already recognized by Hans Spemann in 1915. In a seminal essay "A history and critique of the homology concept" Spemann analyzed the history and present problems of the homology concept. Here I will continue Spemann's project and analyze some of the 20th century contributions to homology. I will end with a few reflections about the connections between developmental processes and homology and conclude that developmental processes are inherent in (i) the assessment of homology, (ii) the explanation of homology, (iii) the origin of evolutionary innovations (incipient homologues), and (iv) can be considered homologous themselves.

INTRODUCTION

Seventy-five years ago Hans Spemann concluded his essay *Zur Geschichte und Kritik des Begriffs der Homologie* (A history and critique of the homology concept) with the following, in hindsight rather prophetic, words. ''We no longer believe, that we first can establish the phylogenetic relations between animals in order to subsequently derive developmental laws. Rather we begin to realize, that we first have to determine these laws, before we can understand or even establish the morphological series that we use to classify organisms (Spemann, 1915, p. 84).'' In this passage Spemann argues for the central role of developmental processes for any understanding of morphological transformations, *i.e.*, of phenotypic evolution, that we now pursue under the heading of *Developmental Evolution* or of *Evolution and Development.* (To refer to the titles of the two new journals that serve the field, but see also (Hall, 1992; Gilbert *et al.*, 1996; Raff, 1996; Gerhart and Kirschner, 1997).) In stressing the role of development even for systematics, Spemann was reacting against the then widespread fashion of deriving phylogenies based on comparative anatomical and embryological data that relied heavily on what he defined as the historical concept of homology (phylogenetic and ontogenetic continuity.) In the decades after Spemann wrote his essay both developmental and evolutionary biologists continued to be interested in the relationship between developmental processes and phenotypic evolution and, more specifically, also in the problem of homology. And in recent years, fueled by the availability of new technologies and data, questions related to the role of developmental processes in evolution have received unprecedented attention (for a good overview see the papers in this volume [Hox gene and Evo-Devo Symposium].)

In all these discussions homology has been recognized as ''the central concept for all of biology'' (Wake, 1994) as well as ''an unsolved problem in biology'' (De Beer, 1971). Furthermore, there has been no shortage of new and not so new interpretations of homology (see *e.g.*, Hall, 1994; Bock and Cardew, 1999).

In this paper I will focus on the problem of homology in development. I will divide my essay into two parts. The first part will be historical. Here I will continue Spemann's project of a history and critique of

[1] From the Symposium *Evolutionary Developmental Biology: Paradigms, Problems, and Prospects* presented at the Annual Meeting of the Society for Integrative and Comparative Biology, 4–8 January 2000, at Atlanta, Georgia.

[2] E-mail: manfredl@princeton.edu

the homology concept. I will briefly sketch some of the contributions to the problem of homology during the last 75 yr and emphasize the rather remarkable continuities in the ways biologists have thought about homology. Spemann identified three basic approaches to homology during the 19th century: idealistic, historical, and causal–analytical. Here I will argue that all 20th century definitions of homology fall within one of these categories as well (sometimes including combinations of categories.) However, the further differentiations within these approaches are of considerable interest when one wants to understand the role of the homology concept in the new discipline of developmental evolution.

In the second part of this essay I will present an analysis of the different dimensions of ''homology in development.'' The homology concept, like all other biological concepts, has multiple interpretations depending on the relevant theoretical context. In the context of developmental evolution the homology concept is on the one hand a problem in search of an answer and on the other hand a conceptual tool that allows us to bring together different data (genetic, embryological, and comparative). I will argue that it is through the lens of development that we can hope to arrive at a mechanistic or biological understanding of homology. Developmental processes mediate between different levels of historical homology, such as between the homology of genes and of morphological traits. In each case the homology relationship is established by independent criteria of comparison. And it is the non-trivial mapping between genes and phenotypes that calls for a mechanistic understanding of morphological transformations, of evolution, and, finally, also of homology.

A HISTORY AND CRITIQUE OF THE HOMOLOGY CONCEPT, 1915–1999

Several papers already deal with specific aspects of the history of the homology concept (*e.g.*, Spemann, 1915; Panchen, 1994, 1999; Rieppel, 1994). Most of these authors, however, focus on 19th century developments (but see Donoghue, 1992). Here I will discuss a few of the 20th century milestones that have led to our present conception of homology. Because I will have to be selective I will focus on contributions that are in some way connected to the question of homology in development.

Hans Spemann and the causal–analytical conception of homology

By his own admission Hans Spemann was not a friend of theoretical speculation. He preferred detailed experimental work in order to establish secure facts that would eventually lead to a comprehensive understanding of development. His method was that of an archeologist who ''recreates the image of a god from fragments that only he holds in his hands. He has to believe in the existence of the whole, even though he does not know it; but he also cannot just recreate it according to his own ideas. . . . Foremost he is obliged to honor the fractures (*Bruchflächen.*) Only then can he hope to fit new findings at their right place (Spemann, 1936, p. 275).'' Spemann employed the same archeological sensibility when he wrote his ''History and Critique of the Homology Concept'' in 1915. In this paper he traced the origins of the modern conception of homology. Spemann distinguished between a period of idealistic morphology (Camper, Goethe, Geoffroy de St. Hilaire, and Owen), a historical period of comparative anatomy and phylogeny (Darwin, Haeckel, Gegenbaur, Müller), and finally the causal–analytical period of causal morphology and *Entwicklungsmechanik.*

Spemann argued that the basic tenets of the homology concept were already established during the idealistic period of morphology. Homology was based on a geometric conception of an ideal archetype and entailed the comparison between similar parts of different animals irrespective of their function. This version of the homology concept found its canonical expression in Owen's definition of homology: ''HOMOLOGUE: The same organ in different animals under every variety of form and function (Owen, 1843).'' Owen further distinguished general homology, the similarity between a morphological character and its representation in the archetype, from special homology, the similarity between the

same character in two species (Owen, 1848). This distinction that identified ''general'' with ''ideal'' was especially characteristic of the idealistic period of morphology.

The following historical period of comparative anatomy adds two temporal dimensions to discussions about homology, one ontogenetic and the other phylogenetic. In the decades after Darwin comparative anatomists (especially in Germany) were mainly concerned with the derivation of phylogenetic trees. Homology played an important role in this endeavor. The sameness of morphological structures could be explained by common descent, and, correspondingly, the identification of homologues could then become an important tool for deriving phylogenetic relationships. This, however, required independent criteria for the identification of homologies. While previously the ideal archetype served as the reference frame for establishing homologies, now many researchers looked to embryology to do the job. Evolutionary morphologists such as Haeckel and Gegenbaur argued that true homology can only exist between two parts that have developed from the same *anlage* (Haeckel, 1866; Gegenbaur, 1878). Interpreting individual development (ontogeny) as a recapitulation of phylogeny then led Haeckel to further distinguish between palingenesis and caenogenesis in order to account for shortened or otherwise altered ontogenetic sequences (Haeckel, 1866). However, attempts to find an explanation for homology between adult characters in the early embryonic stages (*anlagen*) soon encountered difficulties.

The flexibility of development, and especially also the phenomenon of regeneration, were the main empirical challenges to this preformistic approach to homology. Among the best known of these examples are the phenomena of vertebrate lens induction and regeneration. In the normal course of development the lens is formed out of the head ectoderm at the point of contact with the optic vesicle of the forebrain. After surgically removing the lens, or even larger parts of the eye, the lens is regenerated in certain amphibian species. But it is no longer formed out of the original tissue (the head ectoderm), but rather out of a different source, the dorsal margin of the iris. Furthermore, Spemann himself found that in certain amphibian species transplanted pieces of epidermis that were not part of the *anlage* of the lens also could be induced to produce a lens.

To counter these problems Spemann reintroduced Lankester's original distinction between *homogeny* and *homoplasy* (Lankester, 1870, p. 39). In Lankester's definition homogeny refers to those aspects of homology that can be traced directly to the common ancestor. This is a more restricted definition insofar as it requires the continuous presence of all features of a particular character between ancestor and descendant species. Therefore only the more general aspects of organismal design will be homogenous between species, while further differentiations or independent developments would not fall under this category. In Lankester's definition homoplasy, on the other hand, refers to the similarity that is produced ''when identical or nearly similar forces, or environments, act on two or more parts of an organism which are exactly or nearly alike.'' Then ''the resulting modifications of the various parts will be exactly or nearly alike'' (Lankester, 1870, p. 39). For Spemann this distinction is operational in the sense that it focuses our attention on those ''forces or environments'' that are the mechanistic cause for organic similarity. When seen this way, lenses that originate in different ways and from different materials could still be seen as homologous, as could the characters of two embryos/adults that develop from cells separated after the first divisions in which case the reduction of homology to common *anlagen* reaches its limit. The homology concept of the historical period (homogeny *sensu* Lankester) with its emphasis on historical continuity (both ontogenetically and phylogenetically) disintegrates because it cannot account for the peculiar features of development. Therefore, Spemann argued, homology has to be approached from within the causal–analytical analysis of development as captured by Lankester's original definition of homoplasy.

Adolf Remane: Systematic account of homology criteria

During the decades between the two world wars a discourse of ''theoretical biology'' emerged, mainly in Germany, Russia, the Netherlands and England. Issues related to the conceptual foundation of biology, and here especially of morphology, and questions related to new directions in developmental physiology and genetics were at the center of these debates. The homology concept was also discussed at several occasions; however, these treatments of homology mostly involved conceptual analysis and matters of definition. Both Ludwig von Bertalanffy and Adolf Meyer attempted to distinguish between different forms of homology, such as typological, ontogenetic-typological, phylogenetic, and developmental–physiological homology (Meyer, 1926; Bertalanffy, 1934). But in general, while there was a lot of progress in analyzing the conceptual problems associated with homology during these years, little was accomplished in terms of developing operational research programs.

The situation changed when in 1952 Adolf Remane published his treatise *Die Grundlagen des natürlichen Systems, der vergleichenden Anatomie und der Phylogenetik* (The principles of the natural system, comparative anatomy, and phylogenetics) (Remane, 1952). Here Remane discussed homology in the context of phylogeny and systematics. He gives the following rationale for his theoretical analysis. At the time he was working on a comprehensive overview of all animal phyla that would later become the basis for his successful textbook in systematic zoology (Remane, 1975). Therefore it was important to clarify the theoretical foundations of both phylogeny and systematics. For Remane this was only possible through a thorough understanding of the principles of comparative anatomy which, in turn, entailed an operational account of homology.

As we have seen earlier, natural systems of classification were always based on some notion of similarity. In the context of phylogeny a natural system implies that systematic groups are distinguished by the shared characters they inherited from their last common ancestor, *i.e.*, by historical homologues. The problem is how these shared characters can be identified within the practice of comparative anatomy. For this purpose Remane developed a set of criteria that provided the morphologist with a checklist for establishing sameness, *i.e.*, homology.

Remane's criteria (three main and three auxiliary criteria) lead to a probabilistic argument for homology. If these criteria are fulfilled, then it is more likely that two characters are homologous than that they are completely independent. Homology is likely when there is similarity between relative positions of characters within a common structural plan, similarity in the structural details between these characters, and when transitional forms exist. In those cases where the characters under consideration are too simple and do not have enough structural details to be compared directly according to the three main criteria they can still be considered homologous, if they are present in a large number of related species and if there are other such characters that have a similar distribution. The likelihood of homology is, however, diminished, if such characters are also present in non-related species.

As might be expected from someone who attempts to produce a phylogenetic system Remane's approach to homology is historical. The distribution of homologues among different taxa is seen as a consequence of their phylogenetic relationship. But this leaves one with the epistemological problem of how one can identify those homologues that are used to establish phylogenetic relationships between taxa independently of a pre-existing phylogeny. Remane's homology criteria are intended to overcome this problem. But Remane does not stop there. In the second part of his book, which is nowadays mostly ignored, he discusses various ''phylogenetic laws,'' such as the biogenetic law, the principle of conserved earlier stages of development, and various principles of differentiation and specialization that could account for the remarkably ordered transformations observable in phylogeny. All these ideas place him squarely within the historical tradition of

comparative anatomy as described by Spemann.

Willi Hennig: Homology in phylogenetic systematics

In the 1950s Willi Hennig also began to develop his method of phylogenetic systematics (cladistics) (Hennig, 1950; Hennig, 1966). Drawing heavily from the rich German tradition of systematics and also from the conceptual discussions in theoretical biology Hennig developed an operational definition of homology in the context of phylogenetic systematics. Hennig started with the assumption that ''evolution is the transformation of organismal form and behavior (Zimmermann, 1953).'' This process of organic transformation includes anagenesis as well as cladogenesis. Hennig assumed that it is possible to reconstruct this process, *i.e.*, phylogeny, by following the sequence of transformations of specific characters. Hennig's main insight was to characterize each new lineage by one or more transformed characters, the so-called synapomorphies. These have to be distinguished from those character states that are shared between different lineages, the symplesiomorphies. Whether a particular character or character state is a synapomorphy or a symplesiomorphy therefore depends on the rank of the taxa one is analyzing. But in any case, both synapomorphies and symplesiomorphies refer to the sameness between characters. They are, however, more inclusive than traditional homology because the absence of a character is also a legitimate character state in phylogenetic analysis.

Hennig's methods eventually transformed systematics, especially after the English translation of his book on phylogenetic systematics was published in 1966 (Hennig, 1966). But while his methods are operational in the sense that they allow for a logically consistent reconstruction of phylogeny, they still depend on a prior assessment of the sameness of characters, *i.e.*, of homology. Henning defined homology to include all the transformed states of a character. This definition, however, still requires independent criteria for the assessment of homology. Hennig employed a variety of methods to identify homologues, such as palaeontological evidence, but he also heavily relied on Remane, whose homology criteria then become auxiliary criteria in the context of Hennig's definition.

I have described both Remane's and Hennig's contributions to homology in some detail, even though they do not make many references to development, because their insights have become the basis for modern phylogenetic systematics. And as Paula Mabee (2000) and others (such as Wagner, 1999) have pointed out, a proper phylogeny is still the basis for all further work in developmental evolution.

Gavin de Beer: The return of development

In the early 1970s Gavin de Beer reconnected the question of homology with the old problems of embryology (De Beer, 1971). In a widely read primer written for students de Beer discussed several of the still unsolved problems of homology. Not surprisingly, most of these problems were connected with questions of development. De Beer realized that the principle of common descent does not solve all the difficulties that are associated with the homology of morphological characters. While common descent can at least suggest a reason for some apparent oddities in development, such as the location of the laryngeal nerve in mammals, which runs backwards, loops around the ductus arteriosus and then runs forward to innervate the larynx, by pointing out the homology of the mammalian ductus arteriosus with the 6th arterial arch of the fish and the homology of the laryngal nerve with the 4th branchial branch of the vagus, it cannot give a mechanistic explanation for this conservatism of evolution. And for many other features, common descent does not even provide such an explanation.

De Beer, in analyzing the contributions of embryology and genetics for understanding the problem of homology, raised several important issues. For instance he pointed out that a correspondence between early stages of development is not necessary for adult characters to be homologous, that different organizer-induction processes can lead to homologous adult structures, and that the identity of genes does not guarantee

the homology between characters. De Beer essentially restated Spemann's positions of 1915. In doing so he brought development back to the discussions about homology.

Rupert Riedl: The order of homology and the systems theory of evolution

A few years after de Beer identified homology as the great unsolved problem in biology Rupert Riedl presented his ''systems theory of evolution'' (Riedl, 1975; Riedl, 1978). Riedl attempted to explain, as the title of his book already suggests, the often astonishing manifestations of ''order'' in the living world. Animal morphologies are clustered and the morphospace of all possible life forms is mostly empty (Gould, 1977, 1989). These facts cannot easily be reconciled with the idea of gradual evolution that was at the core of models in population and quantitative genetics at that time. In the early seventies many theorists challenged the canonical Neo-Darwinian picture of evolution that was an outgrowth of the Modern Synthesis of the 1930s and 1940s (*e.g.*, Eldredge and Gould, 1972; Gould and Vrba, 1982; Margulis, 1982; Maynard-Smith, *et al*., 1985). Indeed, a newly emerging focus on the role of developmental processes in evolution, the romatic phase of ''evo-devo'' also blossomed in those years (Wagner *et al*., 2000).

Homology is central to Riedl's theory, probably more so than to most other proposals of that time. For Riedl homology is the most visible expression of natural order. In one sense homology is simply a consequence of common descent. However, phylogenetic relationships only explain the distribution of homologues but not their mechanistic cause. But neither could the models of quantitative and population genetics account for the remarkable expression of biological order as evidenced by the distribution of homologues. In Riedl's opinion the answer to the problem of homology could only be found in the systemic conditions of development. These could be seen as an expression of a fourfold order of norm, hierarchy, interdependency and tradition. In Riedl's theoretical system all four expressions of order—norm, hierarchy, interdependency and tradition—are part of the explanation of homology. Homologues are seen as identical, that is normative parts, whose identity is maintained by systemic (functional) interdependencies within the developmental processes that produce them, and that form a hierarchical system that is a consequence of tradition (*i.e*., inheritance and common descent). Another concept that Riedl introduced to describe the mechanistic causes for the identity of homologues is the notion of burden. Burden is a measure of the degree of systemic integration of specific characters within the developmental process. The more integrated a character is within development, the higher its burden and the more stable the character. The idea of burden is closely related to the notion of developmental constraints that was proposed around the same time. Both concepts acknowledge the intrinsic limitations that the developmental system imposes on the degrees of variation of a specific character. They differ in that developmental constraints focus more on the limitations imposed on variation, whereas burden is defined as a quantitative measurement of the cost of changing a character that is functionally embedded in a complex developmental system of interdependencies. But, insofar as homology can be seen as a statement about the limitations of variation of specific characters (Wagner, 1999), the notions of burden and developmental constraint stand at the beginning of the recent interest in a mechanistic explanation of homology that is the core of the biological homology concept (see below).

Riedl's approach to the problem of homology contains many elements of earlier conceptions. His distinction between different forms of homology and his reliance on Remane's homology criteria puts him right into the traditions of comparative anatomy and theoretical biology. However, his emphasis on a causal mechanism for the explanation of homology makes him also an heir to Spemann's causal–analytical approach to homology.

The last decades: The biological homology concept, hierarchical homology, and partial homology

In recent years the problem of homology has received more attention than ever be-

fore in this century. Here I cannot discuss all the different proposals in any detail (but see Donoghue, 1992; Hall, 1994; Bock and Cardew, 1999 for excellent reviews of the current state of the discussions). Many of the new proposals deal with development. Development plays an important role especially in the biological homology concept (Roth, 1984, 1988; Wagner, 1989, 1994, 1995, 1996; Donoghue, 1992). Here I follow Wagner's (1999) outline of the basic principles of the biological homology concept. The core assumption of the biological homology concept is that homologues are the units of phenotypic evolution. As such they are individuated quasi-autonomous parts of an organism that share certain elements and variational properties. Therefore, if two characters are to be homologous, they can only differ in those aspects of their structure that are not subject to shared developmental constraints. The role of developmental mechanisms is to guarantee the identity of two structures since they limit the variational properties of quasi-autonomous units. Below I will further explore the connections between developmental mechanisms and the problem of homology. Here I just want to mention two additional dimensions of homology, which have recently received some attention, hierarchical and partial homology.

Homology can occur between objects at different levels of the biological hierarchy (Riedl, 1975; Abouheif, 1997). Homology at these different levels is generally recognized by independent criteria of comparison at each level, such as Remane's criteria or sequence comparisons (see also Laubichler, 1999). It is an open question to what extent these different forms of homology coincide, *i.e.*, whether we can deduce morphological homology based on established genetic homologues (see also below). Developmental processes figure prominently in this context. They mediate between the different levels of homologues (genetic and morphological). It is the goal of the causal–analytic approach to homology to find an explanation for the existence of morphological homologues in the developmental processes that produce them. So far all studies that have explicitly considered this question, rather than just assumed that the developmentally prior objects determine the status of the derived characters, have cautioned against this form of preformism (see *e.g.*, Wagner, 1989; Dickinson, 1995; Abouheif, 1997).

Related to the question of hierarchical homology is the problem of partial homology (Wake, 1999). Partial homology assumes that in the case of certain complex characters not all elements need to be homologous, but that it is possible to identify certain parts that are. There are, for instance, cases, such as the paired appendages of gnathostomes, that share certain developmental mechanisms (anteroposterior patterning), but differ in others (skeletogenesis) (Wagner, 1999). These cases usually represent a hierarchy of shared derived characters (Hennig, 1966) that can be interpreted as an increasingly inclusive set of partial homologues (see also Lankester, 1870).

In conclusion, what this brief history of the homology concept in the 20th century tells us is that homology is indeed ''the central concept of biology.'' We have also seen that all contributions to homology fall within the three categories discussed by Spemann in 1915. Even though Spemann already formulated the basic principles of the causal–analytical approach to homology, his program did not really become realized until about 25 yr ago, when new conceptual insights began to challenge the dominance of the Modern Synthesis in evolutionary biology. This challenge coincided with breakthroughs in developmental genetics and has led to the present program of developmental evolution. We have, in a sense, come full circle. Fortunately, we can also draw on the insights gained in the context of other approaches to homology, especially within phylogenetic systematics.

HOMOLOGY IN DEVELOPMENT

In the previous sections we have seen that different notions of homology have emphasized either a historical or a causal explanation of organic sameness. Furthermore, it has become clear that we have to distinguish between a historical or causal (or a combination of the two) explanation

of organic similarity and various criteria for establishing this similarity (see also Bolker and Raff, 1996). As with most biological concepts the interpretation of homology depends on a specific reference process (Laubichler, 1999; Wagner and Laubichler, 2000). In the case of homology the relevant reference processes are evolution and development. Both are complex, hierarchical processes that are linked in various ways. It is therefore not surprising that, depending on which aspect of evolution or development one is studying, different interpretations of homology will be relevant. Attempts to eliminate this inherent multi-dimensionality of the homology concept and to develop increasingly ''sharper'' definitions of homology are therefore rather fruitless. David Wake recently suggested that we stop worrying about what homology ''is'' and that we begin to address the interesting empirical questions that are connected with the notion of homology, such as stasis, modularity, the preservation of design, or latent homology (Wake, 1999). But the multi-dimensionality of the homology concept is also one of the main reasons why it is indeed ''the central concept of all biology (Wake, 1994).'' Homology is no longer tied exclusively to morphological characters; rather it is a notion that applies to everything from genes to behaviors (see Bock and Cardew, 1999 for a recent overview). The ubiquitous presence of the homology concept in different areas of biology makes it all the more pressing that we are clear about the relevant reference process in each case. In the case of sequence homology the reference process of molecular evolution encompasses the mechanisms of base pair substitution, the translocation of chromosomal elements, the duplication of genes etc. On the other hand, the reference process of phenotypic evolution that is the basis for the homology of morphological characters includes a different set of evolutionary mechanisms, such as allometric growth, changes in the timing of developmental events, developmental constraints, canalization, modularity, etc.

Here I cannot explore all dimensions of homology; rather I will limit my analysis to the different connections that exist between the homology of morphological characters and developmental processes.

There are at least four different connections between morphological homology and development. Developmental processes can be used to establish the homology between morphological characters, developmental processes can provide an explanation for the homology between morphological characters, developmental pathways can themselves be homologues, and developmental processes are part of the explanation of evolutionary innovations that can also be interpreted as incipient homologues. Below I will briefly sketch the assumptions and problems associated with these four dimensions of homology in development. One cautionary note, however, applies to all four cases. None of these cases is ''clear-cut'' in the sense that we can establish *a priori* a general set of rules how developmental processes are connected to homology. Rather, as new evidence suggests, the homology is a systemic property of evolving developmental systems. Only when we understand the properties of these systems can we hope to come any closer to unraveling this ''unsolved problem of biology (De Beer, 1971).''

Developmental processes and the assessment of homology

Establishing homology between morphological characters is central for understanding evolutionary transformations and innovations. Consequently, in the course of the last 150 yr various criteria for identifying homology have been proposed. However, in recent years many researchers tend to assume that sequence and gene expression data overrule all other forms of evidence when considering homology between morphological characters (*e.g.*, Quiring *et al.*, 1994; Halder *et al.*, 1995). This attitude is reminiscent of earlier attempts to establish homology between morphological characters by comparing their embryological origins (*anlagen*). But while the earlier focus on the similarity of embryological origins generally limited the number of possible homologues, the present focus on expression patterns is more likely to increase the reach of homology relations thereby ren-

dering them uninformative. The recent discussion about a possible homology between vertebrate and insect eyes due to a shared master control gene (*Pax-6*) is just one example of this trend (Quiring *et al*., 1994; Halder *et al*., 1995; Dahl *et al*., 1997).

Both the genetic and the embryological approach tie morphological homology to the presence of specific elements in the ontogenetic sequence that leads to these characters. This is an inherently preformistic notion. The problem with such an approach to homology is that while it is appealing to reduce the problem of establishing homology on the morphological level to the simpler question of the presence or absence of certain identifiable elements, it does not, in most cases, adequately represent the complexities of the developmental processes that create the shared similarities between homologues. The same developmental role of orthologous genes does not guarantee the identity of morphological characters, nor are the same developmental pathways required to create homologous characters. As our data on the multiple roles of many transcription factors such as *distalless* demonstrate, the same regulatory module can be employed in different developmental pathways (Panganiban *et al*., 1997). Similarly, a regenerated lens develops through a different developmental pathway (see above).

All these problems do not imply that sequence and gene expression data are useless for assessing homology relations between morphological characters. On the contrary, they provide us with additional information that needs to be weighted together with all other forms of evidence, not unlike in systematics where it is increasingly common to use both molecular and morphological data to resolve questions of phylogeny. We can, however, conclude that morphological identity is a systemic property that needs to be understood in the context of the reference process of morphological and developmental evolution, rather than a preformistic concept.

Developmental processes and the explanation of homology

It is the goal of the causal–analytical (biological) approach to homology to provide a mechanistic explanation for the phenomenon of organic sameness. The relevant reference process for morphological homology is developmental evolution; development because it is the proximate cause of morphological characters and evolution because it deals with organic transformations and stability. Recently Günter Wagner (1999) outlined a research program to test the biological homology concept empirically. Its basic steps involve identifying putative homologues, determining a proper phylogeny, describing intra- and interspecific patterns of variation, analyzing the modes of development for each putative homologue, and testing whether differences in the modes of development affect differences in variational properties (Wagner, 1999).

The assumption behind this approach is that an explanation for the stability of homologues can be found in the properties of the developmental processes that create them. Stability of morphological characters implies that the potential variation of these characters is limited or at least constrained in particular ways. This can be accomplished by constraints acting on morphogenetic mechanisms as well as by morphostatic mechanisms that maintain or stabilize character identity (Wagner and Misof, 1993). The question of homology is therefore connected to the related issues of modularity and canalization (Wagner, 1996; Wagner and Altenberg, 1996; Wake, 1999). We can therefore conclude that in the context of the biological homology concept a mechanistic explanation of the homology of morphological characters has to involve the systemic properties of developmental processes of both morphogenesis and morphostasis.

Developmental processes and evolutionary innovations

Developmental processes have also been implicated in the origin of evolutionary novelties or innovations (Müller and Wagner, 1991, 1996; Müller and Newmann, 1999). Evolutionary innovations are incipient homologues. They are the apomorphies that are the backbone of phylogenetic systematics (Hennig, 1966). In the context of the reference process of developmental evo-

lution novelties provide us with the biggest challenge but they are also a window through which we can study the role of developmental processes in shaping morphological transformations.

Recently Müller and Newman (1999) have suggested that there might be different phases in the origin and establishment of morphological novelties. They argued that epigenetic processes, such as interactions between cells, tissues, and the environment, as well as the basic biomechanical properties of these parts, play an important role in the generation and integration of new structures. In a second step these incipient homologues would then become integrated, both genetically and developmentally, to function as autonomous organizers of organismic design (Müller and Newmann, 1999). This hypothesis suggests an important role for developmental processes in the generation of organic diversity.

Developmental processes as homologues

Descriptions of developmental processes now routinely involve characterizations of regulatory gene networks. Recently, it has become clear that regulatory gene networks are modular structures (Wagner, 1996; Abouheif, 1999; Wake, 1999). As modular structures they have the potential to be recognized as a distinct level of homology within the biological hierarchy (Riedl, 1975; Abouheif, 1997). There are several important questions that are associated with the potential homology of regulatory gene networks. One the one hand we need to define criteria to assess the homology between different networks. This requires further detailed studies of the interactions between the elements of these networks (the structure of these characters). Complications are prone to arise due to genetic redundancy. Also, these networks acquire additional regulatory linkages and new developmental roles in the course of evolution (Abouheif, 1997; Gerhart and Kirschner, 1997). While this does not change the basic modular structure of networks, it makes it more difficult to delineate the exact boundaries of these characters. It is therefore to be expected that in many cases we will find partial homology between networks (and true homology between certain elements of these networks.) Many components are very old, as is evidenced by their remarkable conservation across different phyla (De Robertis, 1994) and the fact that they have often recombined with other modules to form new networks (Gerhart and Kirschner, 1997). We therefore need a good phylogeny before we can assess the homology between different networks. Focussing on the homology between regulatory networks also raises the question to what extent their homology implies the homology of morphological characters. As we have seen, this is an old problem. But, due to the modular organization of biological systems and the present evidence of multiple functions of many key elements as well as of recombination between the elements of these networks, unambiguous cases will be quite rare.

CONCLUSION

Homology is one of the central concepts in developmental evolution. The expected exponential growth of available gene-expression and sequence data only increases the need for an operational approach to homology (Wagner, 1999). It also highlights the fact that there is no single concept of homology that would capture all the interesting empirical questions that are associated with biological order (Riedl, 1975) or the phenomena of organic sameness (Wake, 1999). The causal–analytical approach to homology, *i.e.*, ''homology in development'' has a long tradition that goes back at least to Hans Spemann. A mechanistic, or biological, explanation of the causes for homology will be the key to understanding the transformations of organic forms, *i.e.*, of phenotypic evolution (*e.g.*, Müller and Wagner, 1996; Raff, 1996).

The success of the causal–analytical approach to homology depends on the availability of reliable phylogenies (Wagner, 1999; Paula Mabee, 2000). A historical approach to the problem of homology has been at the core of the development of modern phylogenetic systematics (cladistics). Therefore different approaches to the problem of homology converge in the context of developmental evolution.

We might thus conclude with Spemann (1915, p. 63): ''There are concepts of such centrality, that their origin, change and disintegration, in short, their history captures the development of the science they are part of. Homology is such a concept for comparative anatomy.'' (And, we might add, for developmental evolution.)

ACKNOWLEDGMENTS

I would like to thank the organizers for inviting me to participate in this symposium and Günter Wagner and Hans-Jörg Rheinberger for insightful discussions on the subject of this paper and two anonymous reviewers for their helpful comments.

REFERENCES

Abouheif, E. 1997. Developmental genetics and homology: A hierarchical approach. Trends in Ecology and Evolution 12:405–408.

Abouheif, E. 1999. Establishing homology criteria for regulatory gene networks: Prospects and challenges. *In* G. R. Bock and G. Cardew (eds.), pp. 207–222 *Homology. Novartis Foundation Symposium 222*, Wiley, Chichester.

Bertalanffy, L. v. 1934. Wesen und Geschichte des Homologiebegriffes. Unsere Welt 28.

Bock, G. R. and G. Cardew (eds.) 1999. Homology. Novartis Foundation Symposium 222. John Wiley & Sons, Chichester.

Bolker, J. A. and R. A. Raff. 1966. Developmental genetics and traditional homology. BioEssays 16: 489–494.

Dahl, E., H. Koseki, *et al*. 1997. Pax genes and organogenesis. BioEssays 19:755–765.

De Beer, G. 1971. *Homology, an unsolved problem*. Oxford University Press, Oxford.

De Robertis, E. M. 1994. The homeobox in cell differentiation and evolution. *In* D. Duboule (ed.), Guidebok to the homeobox genes. Oxford University Press, Oxford.

Dickinson, W. J. 1995. Molecules and morphology: Where's the homology? Trends in Genetics 11: 119–121.

Donoghue, M. J. 1992. Homology. *In* E. F. Keller and E. A. Lloyd (eds.), *Keywords in evolutionary biology*. Harvard University Press, Cambridge, MA.

Eldredge, N. and S. J. Gould 1972. Punctuated Equilibria: An alternative to phyletic gradualism. *In* T. J. M. Schopf (ed.), *Models in Paleobiology*. Freeman, San Francisco.

Gegenbaur. 1878. *Grundriß der vergleichenden Anatomie.* Engelmann, Leipzig.

Gerhart, J. and M. Kirschner 1997. *Cells, embryos, and evolution.* Blackwell, Malden, Massachusetts.

Gilbert, S. F., J. M. Opitz, *et al*. 1996. Resynthesizing Developmental Biology. Develop. Biol. 173:357–372.

Gould, S. J. 1977. *Ontogeny and phylogeny*. Harvard University Press, Cambridge, Massachusetts.

Gould, S. J. 1989. *Wonderful life*. W. W. Norton. New York.

Gould, S. J. and E. Vrba. 1982. Exaptation: A missing term in the science of form. Paleobiology 8:4–15.

Haeckel, E. 1866. *Generelle Morphologie der Organismen.* Reimer, Berlin.

Halder, G., P. Callaerts, *et al*. 1995. Induction of ectopic eyes by targeted expression of the *eyeless* gene in *Drosophila*. Science 267:1788–1792.

Hall, B. K. 1992. *Evolutionary developmental biology*. Chapman & Hall, London.

Hall, B. K. (ed.) 1994. *Homology. The hierarchical basis of comparative biology.* Academic Press, San Diego.

Hennig, W. 1950. *Grundzüge einer Theorie der Phylogenetischen Systematik.* Berlin, Deutscher Zentralverlag.

Hennig, W. 1966. *Phylogenetic systematics*. University of Illinois Press, Urbana.

Lankester, R. 1870. On the use of the term homology. The Annals and Magazine of Natural History, Zoology, Botany and Geology 6:34–43.

Laubichler, M. D. 1999. A semiotic perspective on biological objects and biological functions. Semiotica 127:415–431.

Mabee, P. M. 2000. Developmental data and phylogenetic systematic evolution of the vertebrate limb. Amer. Zool. 40:789–800.

Margulis, L. 1982. *Symbiosis in cell evolution.* Freeman, San Francisco.

Maynard-Smith, J., R. Burian, *et al*. 1985. Developmental constraints and evolution. Quart. Rev. Biol. 60:265–287.

Meyer, A. 1926. *Logik der Morphologie im Rahmen einer Logik der gesamten Biologie.* Julius Springer, Berlin.

Müller, G. B. and S. A. Newmann. 1999. Generation, integration, and autonomy: Three steps in the evolution of homology. *In* G. R. Bock and G. Cardew (eds.), *Homology. Novartis Foundation Symposium 222*, pp. 65–72. Wiley, Chichester.

Müller, G. B. and G. P. Wagner. 1991. Novelty in evolution: Restructuring the concept. Annu. Rev. Ecol. Syst. 22:229–256.

Müller, G. B. and G. P. Wagner. 1996. Homology, *Hox* genes, and developmental integration. Amer. Zool. 36:4–13.

Owen, R. 1843. *Lectures on the comparative anatomy and physiology of the invertebrate animals, delivered at the royal college of surgeons, in 1843.* Longman, Brown, Green, and Longmans, London.

Owen, R. 1848. *On the archetype and homologies of the vertebrate skeleton.* John van Voorst, London.

Panchen, A. L. 1994. Richard Owen and the concept of homology. *In* B. K. Hall. (ed.), *Homology. The hierarchical basis of comparative biology*, pp. 22–62. Academic Press, San Diego.

Panchen, A. L. 1999. Homology—history of a concept. *In* G. R. Bock and G. Cardew (eds), *Homology. Novartis Foundation Symposium 222*, pp. 5–17. John Wiley & Sons, Chichester.

Panganiban, G., S. M. Irvine, *et al*. 1997. The origin

and evolution of animal appendages. Proc. Natl. Acad. Sci. U.S.A. 94:5162–5166.
Quiring, R. and *et. al*. 1994. Homology of the eyeless gene of drosophila to the small eye gene in mice and aniridia in humans. Science 265:785–789.
Raff, R. A. 1996. The Shape of Life. Genes, Development, and the Evolution of Animal Form. University of Chicago Press, Chicago.
Remane, A. 1952. *Die Grundlagen des natürlichen Systems, der vergleichenden Anatomie und der Phylogenetik.* Akademische Verlagsgesellschaft, Leipzig.
Remane, A., V. Storch, *et al*. 1975. *Systematische Zoologie.* Gustav Fischer, Stuttgart.
Riedl, R. 1975. *Die Ordnung des Lebendigen.* Parey, Berlin und Hamburg.
Riedl, R. 1978. *Order in living organisms.* John Wiley & Sons, New York.
Rieppel, O. 1994. Homology, topology, and typology: The history of modern debates. *In* B. K. Hall (ed.), *Homology. The hierarchical basis of comparative biology*, pp. 63-100. Academic Press, San Diego.
Roth, V. L. 1984. On homology. Biol. J. Linn. Soc. 22:13–29.
Roth, V. L. 1988. The biological basis of homology. *In* C. J. Humphries (ed.), *Ontogeny and systematics*, pp. 1–26. Columbia University Press, New York.
Spemann, H. 1915. Zur Geschichte und Kritik des Begriffs der Homologie. *In* C. Chun and W. Johannsen (eds.), *Allgemeine Biologie.* B. G. Teubner, Leipzig und Berlin. 3.4.1:63–85.
Spemann, H. 1936. *Experimentelle Beiträge zu einer Theorie der Entwicklung.* Springer, Berlin.
Wagner, G. P. 1989. The biological homology concept. Ann. Rev. Ecol. Syst. 20:51–69.
Wagner, G. P. 1994. Homology and the Mechanisms of Development. *In* B. K. Hall (ed.), *Homology: The hierarchical basis of comparative biology*, pp. 273–299 Academic Press, San Diego.
Wagner, G. P. 1995. The biological role of homologues: A building block hypothesis. N. Jb. Geol. Paläont. Abh. 195:279–288.
Wagner, G. P. 1996. Homologues, natural kinds, and the evolution of modularity. Amer. Zool. 36:36–43.
Wagner, G. P. 1999. A research programme for testing the biological homology concept. *In* G. Bock and G. Cardew (eds.), *Homology (Novartis Foundations Symposium 222)*, pp. 125–134. Wiley, Chichester.
Wagner, G. P. and L. Altenberg. 1996. Complex adaptations and the evolution of evolvability. Evolution 50:967–976.
Wagner, G. P. and M. D. Laubichler. 2000. Character identification in evolutionary biology: The role of the organism. Theory in Biosciences 119:20–40.
Wagner, G. P. and B. Y. Misof. 1993. How can a character be developmentally constrained despite variation in developmental pathways? J. Evolutionary Biology 6:449–455.
Wagner, G. P., C-h. Chiu, and M. Laubichler. 2000. Developmental evolution as a mechanistic science: The inference from developmental mechanisms to evolutionary processes Amer. Zool. 40: 819–831.
Wake, D. 1999. Homoplasy, homology and the problem of 'sameness' in biology. *In* G. Bock and G. Cardew (eds.), *Homology (Novartis Foundations Symposium 222)*, pp. 24–33. Wiley, Chichester.
Wake, D. B. 1994. Comparative terminology. Science 265:268–269.
Zimmermann, W. 1953. *Evolution. Geschichte ihrer Probleme und Erkenntnisse.* Alber, Freiburg und München.