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Homoplasy, homology and the problem of 'sameness' in biology

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Abstract. The reality of evolution requires some concept of 'sameness'. That which evolves changes its state to some degree, however minute or grand, although parts remain 'the same'. Yet homology, our word for sameness, while universal in the sense of being necessarily true, can only ever be partial with respect to features that change. Determining what is equivalent to what among taxa, and from what something has evolved, remain real problems, but the word homology is not helpful in these problematic contexts. Hennig saw this clearly when he coined new terms with technical meanings for phylogenetic studies. Analysis in phylogenetic systematics remains contentious and relatively subjective, especially as new information accumulates or as one changes one's mind about characters. This pragmatic decision making should not be called homology assessment. Homology as a concept anticipated evolution. Homology dates to pre-evolutionary times and represents late 18th and early 19th century idealism. Our attempts to recycle words in science leads to difficulty, and we should eschew giving precise modern definitions to terms that originally arose in entirely different contexts. Rather than continue to refine our homology concept we should focus on issues that have high relevance to modern evolutionary biology, in particular homoplasy—derived similarity—whose biological bases require elucidation.

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Why are we still talking about homology?

I will grant that someone might be able to generate an original thought concerning homology, but I doubt it. When Hall (1994) appeared, I thought we were at the end of the line. Homology is important. Indeed, I argued that the general concept of 'sameness' was fundamental to the entire modern science of biology, which relies so heavily on model organisms (Wake 1994). Now we know about homology; we understand its importance as a general, even baseline, concept. Isn't it time to move on?

[1]Due to illness, David B. Wake was unable to attend the symposium, and Adam Wilkins presented this chapter in his stead.

There are several reasons for my stance. First, homology is seen by some to constitute the most fundamental kind of evidence of the existence of evolution, and this has led critics to raise challenges to specific instances of homology and even to challenge the basic idea on the grounds that biologists cannot agree on a definition of homology. If practitioners can fight about homology after all these years, the argument goes, perhaps there is nothing to it after all. Second, I detect a kind of modern-day essentialism creeping into the debates about homology. I, too, once sought the 'biological basis of homology' (Wagner 1989), and I remain fascinated by the general phenomenon of stasis in evolution (Wake et al 1983). There are genuine biological questions involved in these issues. But the risk is increasing that we will make homology something that it is not, as for example when we explore ideas such as the latent homology of organs (insect wings and tetrapod limbs) that might share elements of a developmental programme but are phylogenetically independent in origin (Shubin et al 1997). Finally, specialized fields of biology, such as phylogenetics, have seized the concept of homology for their own, even though the wise founder of cladistic methodology (Hennig 1966) saw well the intellectual quagmire in front of him and opted for a technical approach and specialized terms.

I wonder if we have made any progress in dealing with homology since the late 19th century, when the German morphologists accepted Darwinian principles. Gegenbaur (1870) recognized that the proper discrimination of homologies from analogies required the study of genealogical relationships. Berg (1926), in contrast, believed that genealogical matters could only be resolved on the basis of character data and that character analysis was necessarily prior to establishing hypotheses of relationship. Thus, we see the two main perspectives on homology that are with us today. On the one hand, systematists, and in particular cladists, focus on common ancestry and taxa (the systematic concept of homology, Sluys 1996), while morphologists focus on similarity and the developmental individuality of putative homologous structures (the biological concept of homology, Sluys 1996, Wagner 1989). This is close to a true dichotomy, with one group viewing homology of any given structure to be strictly dependent on the outcome of a formal cladistic analysis (i.e. there is a test of homology), while the other group views its task as the explanation of the maintenance of structural identity during the course of evolution. Often the terms taxic and transformational homology distinguish the two approaches (Rieppel 1988); one group focuses mainly on pattern while the other is concerned with process. While some authors (e.g. Sluys 1996) envision a complementarity in these two approaches, with one group (the biological homology approach) emphasizing the causes of what the other (the systematic homology approach) views as symplesiomorphies and homoplasies—features irrelevant to its search for a robust phylogeny which would reveal the synapomorphies, the true homologues—I have a different view. I think it is time

we focus on scientific research programmes and specific questions and avoid the fruitless quest for a compromise, or an accommodation, when none is likely to be forthcoming that will be stable through time.

Why the homology debate is a distraction

From time to time I have engaged in discussions with individuals who question aspects of evolutionary theory. These are usually professionals in other disciplines, but occasionally they are biologists who are not convinced that the modern synthetic theory of evolution is well established. It is interesting to determine what these often intelligent and even well-informed individuals see as the weak points in evolutionary theory. Often ancient words and concepts are the problem, such as adaptation, species and, of course, homology. These are pre-Darwinian concepts that we have recycled and massaged, attempting to save vague old concepts by clothing them in modern perspective. A molecular biological colleague once asked me, in frustration: 'how can we take you evolutionists seriously when you can't even agree on what a species is?' Evolutionary theory demands that there be entities, species, and the fact that there has been both branching and extinction means that the biological continuum is broken up into fragments of the genealogical nexus, and we continue to find it convenient to term these species. It is a separate, specialized task to determine the bounds of species. Adaptation was a term that served reasonably well as a general concept until we started trying to be precise and exact (e.g. Williams 1966). Then we came to understand that we wanted the term to be multifunctional (e.g. adaptation as a state of being, adaptation as a process, adaptation as an outcome). We tried to reify the concept by introducing new terms (e.g. exaptation, Gould & Vrba 1982), and finally, as happened with homology, it became clear that adaptation was only understandable in any exact sense in a phylogenetic context (e.g. Greene 1986). But scientific progress is related mainly to the development of specific research programmes not targeting adaptation but rather processes and patterns of evolution in general (many examples in Rose & Lauder 1996). When doubters, including creationists, raise questions about adaptation they are concerned with origins of novelties, not with the inner workings of evolutionary processes and the patterns that result.

Homology is subject to these same problems. We have taken an ancient term, accepted it as real, and then reified it to serve our present purposes. Doubters point out that if homology is so important, we all should agree as to what it is. One main criticism is that, like species and adaptation, there is no 'naturalistic' mechanism to determine what species, adaptations or homologues really are. Where is the empirically demonstrated naturalistic mechanism of homology? This is exactly the kind of question that we cannot answer, but more to the point, it is an

irrelevant question. The clear implication is that if there is no answer evolutionary theory is in trouble. But the central issue is overlooked—homology is the anticipated and expected consequence of evolution. Homology is not evidence of evolution nor is it necessary to understand homology in order to accept or understand evolution. That there is a genealogy of life on this planet necessitates that there be homology. Every component of an organism is involved, from nucleic acid base pairs to behaviours and even interactions between two or more genealogical entities (such as between host and parasite). Two organisms have the same organ because their common ancestor had the organ. It is a genealogical necessity, and no naturalistic mechanism is necessary to account for the phenomenon other than inheritance. Darwin knew this, and Gegenbaur accepted it, but we are still stuck somewhere between Darwin and Owen, knowing that homology is about evolution, but still wanting a naturalistic explanation. The only way out of this dilemma is to stop talking about homology and instead deal with the real questions that interest us. Systematists should adopt the terminology of Hennig (1966), who recognized that exact science requires precise, technical terminology. So-called homology assessment, however, is an essentially *post hoc* process in systematics, and there is no need to use the word homology. Besides, who wants homologues that can become homoplasies simply with the addition of another character to a matrix, or even in an alternative, equally parsimonious tree? Those interested in so-called biological homology should shift their attention to what I consider to be the real questions relating to similarity in form during the evolution of life.

Some futile exercises

Is homology absolute? That is, can homology be seen as being independent of a theory of phylogenetic relationships? No! As de Pinna (1996) has appropriately observed, absolute homology lacks any kind of theoretical foundation.

Can homologues be partial? Of course they can (Hillis 1994)! Consider the *Hox* gene system as a vivid example. In fact, one can argue that all homology among genealogical entities is likely to be partial at some level, except between the closest relatives. Homology is absolute only when we make it so methodologically, as when we identify characters and states, assume their homology and even 'verify' it with phylogenetic analysis. We forget that we have created the intellectual framework.

Are iterative structures homologues? Of course not! This is a 'levels of analysis' problem, a hierarchical issue (Lauder 1994). What causes iteration might well be homologous in different taxa, but the iterated parts are simply that.

Can homology ever be definitively demonstrated? I think not. I view homology as something that follows from the fact of evolution. There is a continuity, as

Darwin perceived, and branching and extinction have produced genealogical entities whose phylogenetic relationships are inferred largely on perceived degree of overall homology, especially that portion of overall homology that is uniquely shared. Depending on our outlook we may posit that organs are homologous on some biological grounds and be happy when the proposition passes a phylogenetic test (as with the transition from bones forming a lower jaw articulation in some amniotes to forming inner ear ossicles in others), but all that we have done really is identified a pathway of phylogenetic continuity. All proximal attempts to explain homology in terms of structure, connectivity, topography or morphogenesis, for example, can fail. Is homology any more than phylogenetic continuity? Maybe we need to turn Van Valen's (1982) definition ('correspondence caused by continuity of information') around: the continuity of information necessitates correspondence.

Some real questions

Stasis

That which Darwin termed unity of type and what Eldredge & Gould (1972) revived as a modern problem remains unexplained. At one level it is simple enough—inheritance mechanisms assure that descendant taxa continue to resemble ancestors, often in nearly every detail of structure. But natural selection theory tells us that local adaptation should be taking place, and so there must be some mechanistic explanation for the resistance of organisms to evolve (Wake et al 1983). Do any of the many suggested causes offer a general explanation for morphostatic mechanisms (those which maintain structure in evolution, contrasted to morphogenetic mechanisms which generate structure, Wagner 1994)?

Modularity

This leads to what has been termed iterative or serial homology. Some truly exciting research is taking place dealing with this large topic (see Raff 1996 for a general review). Modularity occurs at many levels of biological organization (like most issues relating to homology, hierarchical thinking is necessary), and the proximal (genetic and developmental) foundations for it are slowly being unravelled. The *Hox* gene system and its relation to brainstem organization, the formation and iteration of vertebrae, and limb development in vertebrates is an excellent example of how we are coming to understand one intricate system. We can construct gene trees, follow paralogous and orthologous changes, and come to understand how iteration and evolution have produced a genetic signalling system that appears to be central to vertebrate design. In turn, parts of the system are

deployed during morphogenesis to signal and perhaps direct events taking place in diverse black boxes that are beginning to be opened. Modularity occurs in this system at levels from gene sequences to discrete organs such as vertebrae.

How modules form and get organized is still largely unknown. My current favourite is a 5 kb fragment of DNA related to known retrotransposons of fungi that is repeated about 10^6 times in the genome of the plethodontid salamander *Hydromantes* (Marracci et al 1996). What is especially mysterious about this case is that the large genome of this salamander has severe developmental and morphological consequences, leading to extensive homoplasy in the form of simplification of brain tissue-level organization, for example (Roth et al 1997). Modularity at one level of organization frequently has consequences at other levels, and study of such systems will be enlightening for understanding how form evolves.

The similarity of structure, often down to fine details, of the fore- and hindlimbs of tetrapods has been a challenge since the time of Owen. This is a classic case of iterative homology. The parallel evolution of the two limbs can be stunning, and is nearly the same degree of similarity as bilateral symmetry (another morphological topic worthy of much more attention than it has received). For example, in the evolution of the Caudata two distal mesopodial elements (distal carpals 1 and 2 in the forelimb and distal tarsals 1 and 2 in the hindlimb) fused to form the basale commune, a structure universal in living salamanders and found nowhere else (a synapomorphy of Caudata, Shubin et al 1995). There are two views of how this event occurred. Either a caenogenetic (adaptive) event associated with precocial use of developing digits occurred, in which case a fused element provides a more substantive base for the first two digits, which function to some degree as sense organs in larvae (Marks et al 1998), or this is a neomorph, a secondary formation of the first two digits from an unknown ancestor which had undergone digital reduction and had only two or three digits (Wagner et al 1998). Whatever the evolutionary pathway to fusion, the fact remains that the same fusion occurred in both fore- and hindlimb. The adaptive explanation would apply only to the forelimb, so the hindlimb would have co-opted the forelimb developmental change. Alternatively, all living salamanders that have undergone limb or digital reduction follow different pathways in the fore- and hindlimbs (for example, having different numbers of digits on fore- and hindlimbs, or reducing the number of digits on one set but not the other) so it seems likely that if digits were re-evolved they probably arose from different patterns. Why they should be the same is unclear, but this is a repeated story in vertebrate limb evolution.

Progress has been great in understanding gene expression patterns in relation to structure and evolution of the vertebrate limb (e.g. Sordino & Duboule 1996) and the mechanics of limb development (Marks et al 1998). Limb development is a

research topic where we have moved beyond questions of homology to approach an understanding of how form has evolved.

Preservation of design

Lineages evolve distinctive designs that persist in the face of genetic and developmental change. One of the first clear examples was highlighted by Berg (1926)—Spemann's discovery that the lens of salamanders, which forms from the ectoderm at the spot where the optic vesicle adjoins the head, when removed and allowed to regenerate forms not from cornea but from the upper margin of the iris, an entirely different kind of tissue. Are the two lenses, in the same organism, homologous? There are many such puzzles in experimental embryology (recall the oft-cited example that the dorsal hollow nerve cord forms by infolding in most taxa but by cavitation in several). In salamanders the notochord plays a critical role in the formation of vertebrae, which will not form in its absence. However, in the regenerating salamander tail everything is present, including fully formed, individuated vertebrae, except the notochord!

Some persistent puzzles relate to the numbers of digits in vertebrates and their identities. This is especially the case in comparing early tetrapods with more than five digits with subsequent tetrapods, which virtually never have more than five (Coates 1993), and in comparing living birds with their presumptive theropod dinosaur ancestors (Burke & Feduccia 1997 and subsequent commentary). What is the mechanistic basis for determination of digital identity? I have studied this problem in salamanders, from two perspectives: first, an unusually large member of a four-toed lineage that produced five toes in an unusual manner; and second, an unusual member of a five-toed species that produced four external toes, but which had two skeletons in the last toe of one foot and one in the last toe of the other (Wake 1991). To attempt to homologize such digits and say which is which would be futile, whereas it would be illuminating to understand the morphogenetic processes responsible for longitudinally splitting a digital primordium. I suspect that basic developmental mechanics is involved and that in these large-celled organisms the numbers of cells available to form a condensation and then available to form a bifurcation is critical. In the four-toed example, it seems clear that the digit present is neither number 4 nor number 5, but both.

Latent homology and homoplasy

The condition of permanent larvae in salamanders has arisen many times independently, and there are species-level taxa that never metamorphose. We do not know if a non-metamorphic species has given rise to a species that

metamorphoses but it is certainly conceivable. Some bones never form in larvae, but even should a permanently larval species reproduce, the bones remain as latent elements. Imagine that maxillary, septomaxillary and prefrontal bones, all absent in plethodontid salamander larvae, reappear in a derivative species. These would be identified as homoplasies (in this case, reversals) in phylogenetic analysis, but a morphologist would insist that the tooth-bearing maxillary bone is the same bone as in distantly related salamanders. It must be a homologue! It is in the same place, it has the same form, it develops in the same way and in the same sequence, and it has the same relationship to neighbouring elements. What has been retained is the entire morphogenetic system. In contrast, one can imagine that only one or a few genes were involved in failure to metamorphose, and the time involved in the shutdown of the morphogenetic system may have been too short for the system to have undergone random mutational decay. This is, in short, a levels of analysis problem. The maxillary bone both is and is not a homologue. It does not need to be renamed. This is a simple example of a phenomenon that is extraordinarily important in evolutionary morphology.

Homoplasy is derived similarity that is not the result of common ancestry. The biologist who had an early clear vision of homoplasy and its significance in evolution was Berg (1926), who argued that the same 'laws' of development governed ontogeny and phylogeny. If we replace 'laws' with rules or regularities, and admit a fuller role for natural selection than Berg was willing to do, we approach a modern conception. We are interested in homoplasy because of what the phenomenon can teach us about the evolution of form. The topic has received a recent book-length treatment (Sanderson & Hufford 1996) and I have given my own perspective on the issue (Wake 1991) so I will not belabour the point here. I simply note that while investigating homoplasy we have an opportunity to study the persistence of morphogenetic pathways and ontogenetic trajectories, with related organisms progressing to differing extents along these and thus expressing variations on essentially the same theme. I see roles for functionalist (that is, selectionist or externalist) and structuralist (that is, mechanistic, developmental–genetical or internalist) approaches to the general problem, which always must have historical (phylogenetic) rooting.

Directionality in evolution?

Lineages do appear to have evolutionary directionality. There is a kind of evolutionary canalization that arises from the shared morphogenetic–morphostatic mechanisms that characterize lineages, so that lineages tend to travel in evolutionary pathways of least resistance. This, again, is a topic of great interest to Berg (1926), but one that has received far too little attention in recent years. It is time to return to this important issue.

Conclusions

We have a job before us. As students of form we must not be distracted by sterile debates over matters of interest mainly to students of the history of biology. Rather, we need to keep our eyes on the target—how does form evolve? Why do some structures evolve again and again and again, even iteratively in the same organism? Why do some structures, even entire phenotypes, persist in the face of ever-changing environments and great molecular change? What are the hierarchical interactions in biological systems that produce form and why is form so limited in its expression? Never has there been so much reason for optimism that we will finally come to understand how form evolves. Let us maintain focus and ask answerable questions.

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DISCUSSION

Hall: Did David Wake give any examples of partial homology?

Wilkins: No, he just asserts that it's true. One example, however, may be when genes have different exons from different sources.

Wagner: Another may be that, for example, paired appendages of vertebrates, or at least gnathostomes, share certain developmental mechanisms, such as those which determine anteroposterior patterning, but they differ with respect to skeletogenesis (see Wagner 1999, this volume). Therefore, at the paired appendage level, there is some degree of homology, but less so than the homology between the pectoral fins of two fish species or the limbs of two salamander species, for example. In that sense, there is a hierarchy of shared, derived characters that could be interpreted as levels of homology.

Hall: But David Wake referred to partial homology at a particular level, which is different to the situation you have described.

Wagner: It is still at the level of the structure of the paired appendage, but paired appendages from different groups of species (taxa) have different degrees of shared characters, and this leads to a higher degree of homology among fins than between fins and limbs.

Wilkins: When you say a higher degree of homology, do you mean greater similarity?

Wagner: Yes, but not in the sense of simple resemblance. As I have argued elsewhere (e.g. Wagner 1996), the homology concept captures the fact that most closely related characters share developmental constraints. For instance, the pectoral fin of a lion fish is not similar to the pectoral fin of a zebrafish, but they are still the same character because both evolve under the same set of developmental constraints. If we compare them to the pectoral fins of a lungfish, the number of developmental constraints is smaller. There can be dissimilarities that evolve within a constant framework of developmental constraints (one could call them 'variations on a theme') or more fundamental dissimilarities that lead to different developmental constraints on evolution (one could call them 'different themes'). Partial homology is partial overlap in developmental constraints, not just a lower degree of similarity in appearance.

Wray: Is this so different from simply stating that in two different lineages structures have diverged from their initial similar state?

Wagner: No, but it matters in what respect the characters have diverged. Only if the variational properties of the character have changed (i.e. developmental constraints and developmental degrees of freedom) is it useful to talk about partial homology. It is not sufficient that a character changes its size or colour if these differences are easily reversible and they do not change the constraints for further evolution.

Aboubeif: The comparison of fish with tetrapod limbs may be a good example of partial homology. Some of the proximal elements, such as the radius and the ulna, are conserved. However, in the tetrapod limb, although the proximal elements are conserved, the distal elements, such as the digits, are morphological novelties. Therefore, there is partial homology in that some of the elements are homologous, whereas others are not.

Roth: Some would argue that the idea of partial homology is an issue of character delineation, i.e. if you subdivide the character in a precise enough fashion you will find an entire component that is homologous and another that isn't. However, Rolf Sattler (1994) has argued that some characters, especially botanical ones, are so continuously melded together that is difficult to do a one-to-one comparison. Rather, it is necessary to talk in terms of percentages or continuous numerical differences and similarities.

I also have a question. You seemed to suggest that David Wake said that the debates about homology have been fruitless and we should move on to address more useful questions. Yet before moving away from those questions, in his introduction he seems to suggest answers to them himself. Do you take him to be saying 'these are the answers' or simply 'here are some definitions that we can work from'?

Wilkins: I was confused as to what elements of his critique he felt were the most important. On the one hand, he says the idea of homology is so simple that we needn't bother with it because it's a direct consequence of relationship through descent. But on the other hand, he says that it is a muddied concept because it has been used in different ways, and we should therefore leave it behind and not reify it. It seems to me that he gives two reasons for abandoning it or, at least, debates about it: (1) it's too simple to bother with; and (2) it's too confused to bother with.

Müller: I'm sure that it is not his intention to abandon the concept of homology. He probably means that the ongoing discussion of homology is becoming futile, and that we should accept homology as a biological fact.

Wilkins: It is important as a concept because we still need to determine whether certain characters are homologous, but he apparently feels that there has been too much emphasis on it. Instead of spending a lot of time debating whether certain characters are homologous or not, and trying to be specific about what that means, we should concentrate on looking into the processes that generate characters.

Striedter: It is interesting to distinguish between futile exercises and real questions, and I would like to suggest that latent homology be moved into the 'futile exercise' class because, in my opinion, the admission of latent homology into the general category of phylogenetic homology inevitably creates terrible confusion when one tries to use homologies to infer phylogenetic relationships. However, I would like to know other people's opinion on this, as it may depend on whether people have systematic or developmental perspectives on biology.

Meyer: I would like to address this not from a systematic but from a developmental point of view. Latent homology is an interesting concept. It is not futile because all one needs to do is keep separate the homology of the product produced by the developmental process and the homology of the process itself, or the underlying genes that produce molecules which carry out these processes. It is possible to recognize dissociations between homologies at different levels of biological organization, and as long as you're willing to agree that it is possible, it is no longer a futile exercise.

Lacalli: But suppose you have a lineage of organisms where the same gene expression patterns occur in the same part of the body, associated with a particular structure in some instances, but no structure in others. Then, in my view, you have a practical way of mapping the absence of that structure, which is a useful thing to be able to do. In addition to molecular homology and structural homology, you have something in-between, which I like to call regional homology: a tissue domain or region of the body that has certain identifiable characteristics, usually defined in molecular terms, but not always, which cannot otherwise be identified by reliable structural landmarks.

Maynard Smith: What interests me about this is that if the adult structures were present a million years ago, for example, but are now absent, what has been maintaining the machinery for making them?

Meyer: This is also of interest to David Wake. He's interested in homology as a concept that explains biological diversity, and if we use homology as a piece of evidence for evolution we also need to ask what the other pieces of evidence are. Homoplasy is an important piece of evidence that evolution occurs, but the question is, what is more important and more prevalent? Latent homology as a measure of retention of genetic potentiality, i.e. the capability to switch back on X or Y, is an important evolutionary concept. This is a mechanistic process-oriented issue, and in some ways the distinction between homology and homoplasy is futile.

Maynard Smith: Does David Wake discuss examples of homoplasy at the morphological level?

Wilkins: No, he refers to it but doesn't give any examples. One of the classic examples, however, is the development of the carnivorous habit in certain marsupials versus 'proper' carnivores.

Greene: The issue here is not marsupials versus carnivores. This is an ancient split and almost everything involved is homoplasic. What fascinates David Wake, and what fascinates me in behavioural studies, is that when you become familiar with a particular clade—such that you know the morphology, or in my case the defensive behaviour, of every species—and you do a cladistic analysis, you find that there is a lot of homoplasy, but what is bothersome is that homoplasy is hierarchically arranged, so that only above a certain node do you find these recurrent structures or behaviours.

Maynard Smith: What they have in common is the capability of evolving a particular structure.

Greene: In the case of defensive displays in snakes there is even evidence, admittedly slight, that all that is changing is the thresholds for expression.

Wagner: It could be that the problem is not having a proper definition of what the character is, i.e. the homoplasic characters could just be states of a character that were acquired at a particular node. Pre-digits in amphibians (prepollex, prehallex) can be present or absent—e.g. they are prevalent in anurans but do not usually occur in urodeles—and they are always a product of a pre-axial column of developing skeletal elements independent of the digital arch. We have a specimen in *Triturus* which has a pre-digit with three phalanges. It is possible that what is happening is that this is just a character state of this pre-axial series of skeletal elements that can have these terminal elements, but it always has the radiale or tibiale and element Y. Therefore, the actual unit may be the pre-axial series of skeletal elements that can exist with or without a pre-digit. There is a deeper character (the pre-axial series)

which may have different character states, i.e. presence or absence of the predigit.

Galis: There is also the work of Michael Bell (1988) on sticklebacks. Their predatory armour has been lost in the absence of predators independently many times, but the order in which these elements disappear is usually the same.

Tautz: John Brookfield (1992) and Martin Nowak et al (1997) have calculated that it takes millions of years to lose a gene. Therefore, following speciation events, which occur within a few hundred thousand years, the species will retain the same sets of genes. If the species then hybridize later on the genes will be muddled. Therefore, it is important to know the age of the species you are studying.

Rudolf Raff: We have shown that apparently silenced genes can be maintained over long periods if the gene is functioning in some other process. If not being so used, silenced genes can persist for up to 6×10^6 years, depending on gene size and base distribution and deletion rates within a lineage. Given that the rate of speciation is more rapid than this, characters should be able to switch on and off following speciation events in ways that are alarming for most people doing systematics, i.e. a potent source of homoplasy.

Wray: It is clear that many developmental regulatory genes have multiple functions at different times in the life cycle of the organism. Therefore, the genes are not going to disappear. What changes are the connections they make with other genes and the processes they regulate.

Wagner: It is also possible that our biochemical classifications of gene products and enzymes are not entirely meaningful. For example, the apparent absence of chitin synthetase in vertebrates might be a perceptual problem because the hyaluronic acid synthases are closely related to chitin synthetases. Therefore, we need to be prepared to redefine the boundaries of characters and the definitions of genes once we learn more about their functions.

Roth: We've been talking about the preservation of genes, and their switching on and off, but one could also imagine characters that are apparent at an epigenetic level, requiring tissue interactions or gene product interactions in an entire constellation or network. During evolution such characters could turn on and off with substitution or activation of different sets of genes. It is more difficult to think about the inheritance and dynamics of that kind of evolution, but latent homology at this level also requires some thought.

Hall: It is surprising how few of these regulatory switching genes there are.

Tautz: There may be relatively few regulatory switching genes, but these can act in different combinations. Thus, evolution can probably play around with any number of possible regulatory switches.

Akam: For the purposes of this discussion, the 'genes' we are talking about are really the modules of enhancers. For example, proteins encoded by the *achaete/scute* gene complex are needed to position each bristle on the surface of a fly, but for each

bristle or group of bristles these genes are regulated independently by a different regulatory module within the complex, which spans more than 100 kb. The number of such regulatory genes may be small, but each may have many independent regulatory inputs acting through different modules.

Wray: Sir Gavin de Beer (1971) described latent homology as independent appearances in cases where there is an underlying propensity for the appearance of that structure, but the structure itself was not in the ancestor. This relates to Harry Greene's point about structures only appearing above a certain node, because that would be the point at which the propensity appeared.

Striedter: Once you bring up the issue of potentialities, then you have to do experiments to find out what those potentialities are. In the case of behavioural homology, the ability to respond to a certain stimulus can be the character that has been maintained. The organisms may not normally encounter the stimuli necessary to exhibit the behaviour, but if you put them in a situation where they encounter the stimuli that their ancestors encountered, then the behaviour can be manifested. Similarly, the threshold to trigger a behaviour in response to a stimulus might be raised or lowered during evolution, leading to the disappearance or sudden appearance of specific behaviours.

Wilkins: I would like to stress this point with something from George Gaylord Simpson's last book, *Fossils and the history of life* (Simpson 1983). Simpson illustrated the difference between parallel evolution and convergent evolution. He said that we can think of parallel evolution as involving a common pool of genetic potential and then a subsequent divergence of lineages. The evocation of that genetic potential would be similar in those different lineages to give parallel evolution. Convergent evolution, in contrast, involves lineages that did not share any recent common ancestry but in which the genetic changes yield similar phenotypic outcomes under the influence of natural selection. And he gave an interesting example of parallel evolution in the true wolf *Canis lupus*, the Tasmanian wolf *Thylacinus cynocephalus*, which is a marsupial, and the borhyaenid *Prothylacinus patogonicus*, which is also a marsupial. He points out that the jaw and tooth structures of these animals are similar at a certain level, yet the estimate he gives for the divergence between the marsupial and placental lines is 100 million years, whereas that for the divergence between the South American borhyaenid and the Tasmanian wolf is about 60 million years. The interesting point is that these latter two animals evolved from a primitive marsupial that was not carnivorous and did not have jaw structures and teeth like either of these. This is therefore an example of genetic potential that has been evoked in two separate lineages that shared a common ancestry. Perhaps one doesn't want to go quite so far in explaining resemblance of the jaw and tooth structure in the true wolf to the marsupial carnivores, but it is valid for these two marsupial

lineages, and it illustrates over what sort of time potential it can be maintained and then evoked in similar ways.

Greene: With respect to marsupials there are cases within a lineage where the same structure is made more than once in the same way because the starting contingencies/constraints were the same. There is a difference between this and something that is literally the same but is re-expressed over and over again. I suspect that these marsupial carnivores are an example of the former, but there are many examples of the latter, and it is the latter that is making us talk about latent homology rather than the former.

Wray: There may be a continuum between these two situations, so rather than trying to worry too much about whether something is convergent or parallel evolution, perhaps we should recognize that in some cases genetic systems will be only a single mutation away from evoking a latent trait, whereas other cases will require quite a lot of reshuffling of machinery.

Greene: It would be exciting to understand how this array of possibilities is produced.

Meyer: The distinction between parallel evolution and convergent evolution is blurred because it involves determining how recent the recent common ancestry is and how similar the similar developmental mechanisms are. One could call it convergent evolution in the case of eutherians/marsupials, but what about different orders of mammals? For example, are the incisors of guinea-pigs and rodents the result of parallel or convergent evolution?

Wray: I don't think you can draw a line between them, it's just a matter of degree.

Hall: One can say the same for homology and homoplasy. If you go far enough back you will find a common ancestor that is homoplasic.

Rudolf Raff: It is possible to have them both together. For example, consider a developmental field of a certain size that produces a certain structure, if the size of that field is increased then duplicated structures are formed as a consequence of the way the field was built. However, if two related organisms independently increase the size of the field by two different mechanisms to produce the 'same' duplication, is it parallelism or convergence?

Roth: It's a matter of character delineation. The *potential* of the field can be homologously the *same* in two organisms, while the size of the field is a distinct characteristic, which in this example changes independently.

Wagner: The danger is that we won't recognize true innovations and that we will lose sight of important biological phenomena.

Hall: Exactly. The problem is where do we set the boundary?

Akam: We recently stumbled on a case that illuminates how characters may appear and disappear repeatedly. The legs of flies sometimes carry a large bristle at the tip of the tibia—the apical bristle. This bristle can appear on any of the legs, and is a useful taxonomic character, both within and between different

Dipteran families. Its formation has clearly been switched on and off repeatedly in the evolution of flies. My colleague Marion Rozowski has been studying the control of this bristle in *Drosophila*, where it appears on the second but not the third leg. She has found that the cell which will make the apical bristle is specified in both the second and the third leg, and begins to differentiate in both. Then the precursor cells in the third leg disappear—we do not know whether they die, or revert to an epidermal fate. Why is this bristle specified and then repressed? Probably because the same genetic routine is being used for the early steps in both legs. Because the bristle is still being specified in both legs, it is easy to see why it might reappear on the third leg in many independent lineages. When it does, is this homoplasy or homology?

Wagner: Gerd Müller pointed out a few years ago that in all cases of experimentally inducible atavisms there are developmental rudiments that are homologous to developmental rudiments in ancestors that had the structure (Müller 1991). The retention of this embryological rudiment is the basis of the continuity between the plesiomorphic character and the atavistic character.

Striedter: I would also like to mention iterative homology. People often argue that this is left out of the phylogenetic concept of homology. The machinery for making a bristle may have evolved at one point in phylogeny and may then be expressed in multiple places on the body of organisms that possess this machinery. Individual bristles in different places would be an instance of iterative homology. However, the developmental machinery for making bristles has a single phylogenetic origin and has been maintained continuously. Therefore, in my opinion, iterative homology is the phylogenetic homology of a developmental machinery that can be expressed in multiple places.

Wilkins: On the other hand, much of the molecular machinery of insect wings and tetrapod limbs is the same, yet we can be quite sure that they evolved quite separately. There was no common ancestral limb structure.

Hall: But are they homologous as appendages?

Wagner: One has to be clear which unit one is studying. Secondary axes of appendages are modules that appear at a certain stage of development and at a certain stage of evolution, so it is a matter of character delineation.

Hall: So the answer of whether they are homologous as appendages might be different to whether they are homologous at the level of similar, homologous genes.

Akam: The only characteristic I'm aware of that specifically unites appendages and does not include any other patterning systems is the expression of *distalless*.

Wray: Like all of these regulatory genes, *distalless* has multiple roles. An additional molecular similarity between insect wings and tetrapod limbs is the expression of *fringe*, which is an edge marker of dorsoventral patterning.

Akam: Are you suggesting that molecular mechanism is seen predominantly in limbs?

Wray: It has been suggested.

Akam: And *wingless* has also been suggested to be a significant shared characteristic of limbs, but many if not all organs are made with *wingless*.

Wagner: One way to look at this is that insect wings and tetrapod limbs not only share genes, but also mechanisms that bind together the capability for proximodistal outgrowth, and anteroposterior and dorsoventral polarization. This machinery characterizes many secondary axes but not all of them.

Müller: I agree, but it's useless to speak of homology at that level because then everything is homologous with everything.

Wagner: No, because there are appendages that don't have this property.

Galis: But what about the primary axis?

Wagner: The patterning there is completely different.

Tautz: At the moment we cannot make any statements because we don't yet have a systematic screen for limb mutants; we are currently relying only on chance observations. In the meantime we should keep an open mind.

Rudolf Raff: I agree. Some of these studies on developmental genetics are still at an early stage, and we don't have the full story. Once someone discovers a new gene they look for it everywhere, so it's not surprising that we find genes such as *wingless* doing jobs that we expect it might be doing in other organisms, based on what it is doing in, say, *Drosophila*, but we don't know all the genes involved in development.

Abouheif: Many members of the *wnt* gene family and *wingless* have different roles in specifying structures in *Drosophila*, mice and chicks.

Akam: If the entire network of anteroposterior and dorsoventral patterning interactions is conserved between vertebrate and insect limbs, I would be happy to say that they are homologous entities, but this is not the case.

Wray: Another important point is that if genes such as *wingless* are expressed at many places and times during development, we have to consider the possibility of chance association. The only way to work this out is not to focus our attention on trying to prove that the genes we know about are expressed everywhere, but rather to find out whether there are so many differences that we have to reject the hypothesis of similarity due to common descent and similarity to convergence.

Meyer: Another problem is that some organisms have several members of the *wingless* gene family, so which one is being compared to the single copy in *Drosophila*?

Hall: And the genes can have different roles in different systems. For example, *dpp* in *Drosophila* is involved in dorsoventral patterning in the nervous system, limb development and mesoderm induction. Clearly, this is a molecule that organisms have found useful, and they have therefore used it over and over again in completely different contexts.

Akam: Eric Davidson might argue that the homology in this case is the invention of mechanisms to pattern fields of cells, as opposed to single-cell interactions. This is a synapomorphy of large metazoa because you can't make a big metazoan unless you can pattern large fields of cells. All of these diffusible signals and gradient morphogens may have been essential at that basal stage.

Carroll: You said that large metazoans would have had these field molecules, and yet before the Cambrian explosion there were presumably a large number of small metazoan lineages that lacked them. They would have had to develop or make use of these molecules, and if they all did this separately what is the point of calling this a homologous situation?

Akam: It's clear that the signalling molecules themselves originated before the diversification of the phyla.

Carroll: The molecules are homologous but what they do is not, and the lineages they do it in are different.

Wray: The signalling molecules are a good example because there are many inductive interactions during development. In fact, there are many more inductive interactions during development than there are signalling molecules, although we can't yet put any numbers on these. This means that these signals have to be used over and over again.

Meyer: Evolution is going to work that way; it's going to be lazy, and it's going reuse the same genes, the same networks and the same genetic potentialities over and over again in different contexts.

Akam: I would like to challenge that. Clearly, the same cellular machinery is being used, i.e. the Wnt signal transduction system, but it is still an open question as to how often an entire genetic network is recruited. The genetic network for the immune response has been recruited for dorsoventral patterning in the *Drosophila* embryo, but that is probably a rare case. It is more likely that when a new structure is being built, cell identity molecules are recruited piecemeal. The link between transcription factors and target genes may be quite labile in evolution.

Lacalli: You refer to Eric Davidson's idea about the problem of controlling development in large tissue domains, but in the pre-Cambrian there were animals as big as doormats. I find it difficult to see why we should restrict our thinking about ancestral metazoans to tiny animals, when some of our earliest fossils are enormous.

Wray: We're not sure that Ediacaran organisms like *Dickinsonia* and *Pteridinium* were animals.

Lacalli: I agree there is a problem interpreting these fossils; what is the current consensus in your view?

Rudolf Raff: They are peculiar creatures. They have fractal structures, so it is not clear that they are metazoans at all.

Lacalli: But it is still possible that *Dickinsonia*, for example, is some sort of giant polychaete, though it looks like it has been flattened by a steamroller. You also have organisms like *Spriggina*, which look more like a modern metazoan, and yet are still several centimetres in length. This is considerably larger than the tiniest of modern flatworms, which are the usual models for ancestral bilateral metazoans.

Rudolf Raff: Animals that are only a few millimetres in length are still large in terms of setting up mechanisms for signalling between cells and tissues.

Lacalli: I agree that there could be a big difference between a fauna of tiny animals, no more than 200 μm, or of small animals 2 mm or even 2 cm long. Achieving the great size of 2 cm could have been major event in metazoan evolution.

Akam: Put in a slightly different way, there are mechanisms that allow cells to be specified as different from one another based purely on the segregation of determinants within cells and cells physically touching one another. Eric Davidson thinks these are the key mechanisms operating in what he thinks of as ancestral development. Signals operating at a distance to generate pattern across many cell diameters would be bolted onto to the ancestral mechanism.

Lacalli: I question whether this is a convincing argument.

Hall: Organisms do compartmentalize so that signals are passed within a compartmentalized population of cells and to other populations of cells. Those are the two ways to generate diversity.

Lacalli: We haven't yet discussed what some of these unknown common ancestors may have been like. In some evolutionary circles this is a bad thing to do, but in terms of looking at developmental phenomena and trying to rationalize how they may have evolved I would argue that it is necessary to use one's imagination to think about what sort of organisms they might have been.

Wagner: This is the step from phylogeny construction to character evolution. At the molecular level it is possible to reconstruct the ancestral molecules, synthesize them and test them, as for instance in the case of lysozymes, so with better technology we may be able to do this in the future at the developmental level.

Hall: The embryos of many vertebrates that have lost their limbs, e.g. whales which have lost their hindlimbs, and some snakes and legless lizards, have limb buds. They all carry these limb buds through to more or less the same stage of development, and then they regress. Therefore, there has clearly been a conservation of some basic patterning information that is used in other parts of the organism as well.

Akam: Is there an explanation for why they have kept the limb buds?

Hall: The traditional explanation is that the loss of the entire limb bud would entail the concomitant loss of much of the information specifying the basic patterning of the body axis, so that large areas of the embryo would be disrupted. But I'm not sure if this is a satisfactory explanation.

Müller: It cannot be fully satisfactory because there are also instances where the limb buds have been lost completely, such as in caecilians. And the axial patterning of these organisms seems quite ok.

Galis: The gene activity involved in specifying the limb is not necessarily involved in the patterning of the vertebrate body axis. The regulation of the genes during the development of these different structures appears to be independent of each other (Cohn et al 1997, Zakany et al 1997)

Peter Holland: When a structure is lost in evolution why does the defect in a pathway often occur late in development?

Akam: The changes do not have to be late. There are other examples where the defect occurs early. In the case of one bristle that Marion Rozowski looked at, she found that the bristle primordium is missing, suggesting that it is repressed at an early developmental stage. Evolution seems to have taken different routes in different cases; some routes may be amenable to reversion and some may not. I'm sure that the patterns of character change are consistent with this.

Tautz: In *Drosophila* we know that the position of the limbs is determined early in development by the crossing of *wingless* and *dpp* signals, and this is before the *Hox* genes become active. It seems almost impossible that a defect at this stage would result in a limb not being formed.

Müller: This discussion seems to have reached a point that reflects the general confusion in the literature on homology. And the confusion arises because we are constantly mixing up levels, such as defining homologies of the anatomical level by shared developmental or genetic programmes. We also cannot say something is homologous at the phenotypic level only because it is used for the same behaviour. We can homologize anatomical characters at the level of anatomical construction. We can also homologize behaviour, but only at the level of behaviour. We can homologize genes, and maybe even gene regulatory networks, but only at the level of the genome. And we can homologize developmental pathways, but only at the developmental level. However, we must not define homology at one level via mechanisms that belong to a different level of analysis.

Peter Holland: I would like to defend the opposing point of view. It is not really that we 'mix up' levels of homology, and we are not jumping out of control between them. These various levels of homology are not independently shifting planes. There may be a dependence between levels. That dependence may not always go in both directions, but clearly there is communication between the levels.

Response by David Wake

My omission of a precise definition of partial homology led to discussion that suggests that I should make my perspective clear. Because evolution is a

continuous process, I believe that homology can only ever be partial, in any real sense. A particular *Hox* gene is identified as such by some general criterion, but when the gene is examined in detail in two taxa, even closely related taxa, there will doubtless be found to be some small differences in base pair composition, for example. By the general criterion, the two genes are exact homologues, but at the next hierarchical level they are only partial homologues. Vertebrae are homologous as vertebrae, defined again by some general criterion (e.g. those bones forming the axial skeletons of osteichthyans), but they are not identical in structure even when comparing rather close relatives. Then there is the issue of strict partial homology, as occurs in cases of exon shuffling, as discussed by Hillis (1994).

There is also some question as to what elements of my critique were the most important. I will clarify my view. I certainly do not want to abandon the concept of homology; rather, I want to stop the fruitless discussion of what it is! Modern developmental genetics has given us the tools to create a new kind of evolutionary biology, one that is focused on the production of phenotypes and on the factors and processes that enable biological diversification to proceed. I want to get on with it and to leave behind debates that started when biologists really did not have sufficient biological knowledge to appreciate the causes of biological similarity and when they did not yet understand that Darwin was right in his view that there is one genealogy for all of life. Common ancestry is all there is to homology. Accordingly, a central theme of my chapter is that homology has necessarily become an abstract concept. When I say that the concept of homology has become reified I mean that the abstraction is being converted into a concrete material object by those who continue to debate what the essence of homology might be.

Axel Meyer has correctly expressed my view that homology is fundamental to questions of biological diversity. Homoplasy is an alternative perspective on homology, and when we can identify a phenomenon as latent homology we begin to approach an understanding of how homoplasy relates to homology on the one hand and to the production of diversity on the other. As Jacob (1977) so clearly enunciated, evolution works with materials on hand. The fact that genes, gene products, cellular and developmental processes, and even parts of organisms that we call homologues hang around to be used again and again bears testimony to homology, but especially to the endless possibilities that appear to us as homoplasies. It is understanding these processes that will lead to full appreciation of what I called the real problems of modern biology (for a useful perspective on these issues see Kirschner & Gerhart 1998).

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