Homologues, Natural Kinds and the Evolution of Modularity[1]

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SYNOPSIS. The fact that phenotypic evolution can be studied on a character by character basis suggests that the body is composed of locally integrated units. These units can be considered as modular parts of the body which integrate functionally related characters into units of evolutionary transformation. These units may either emerge spontaneously by self-organization, or may be the product of natural selection. A selection scenario that could explain the origin of modular units needs to explain the differential suppression of pleiotropic effects between different modules and the augmentation of pleiotropic effects among the elements within the module. Four scenarios are discussed: selection for adaptation rate, constructional selection, stabilizing selection and a combination of directional and stabilizing selection. It is concluded that a combination of directional and stabilizing selection is a prevalent mode of selection and a likely explanation for the evolution of modularity.

INTRODUCTION

Any phylogenetic investigation starts with a mental decomposition of the organisms into units of description or characters. Only then can the techniques to evaluate the historical relationships among character states be applied and genealogical continuity inferred. Character definition is expected to be non-arbitrary, such that the union of a hoof and the cerebellum is not acceptable as a character. Instead describing the shape of a claw, or the location of the nasal opening are acceptable units of description. It is implicitly expected that characters and then homologues are natural units, but no agreement has been reached about of what kind these natural units shall be. This is the main reason why the homology concept is so elusive (Wagner, 1995). To overcome this elusiveness it is necessary to find out how natural kinds or natural units are recognized.

An interesting answer to this question was provided by Willard V. Quine (1969) in his seminal essay on Natural Kinds. Paradigms of natural kinds are atoms, genes and species. Quine compared various approaches to define natural kinds, using similarity or statistical approaches but concluded that neither of them is suitable. He finally suggested that natural kinds can only be defined in the context of a process or a theory of a process in which these entities act as a unit. For instance atoms act as units in chemical reactions, genes are the units of genetic transmission, and species are the most inclusive units of evolutionary transformation. But there is no agreement on what the biological context is in which characters or homologues act as units. Homologues, if they are natural kinds, do not exist in order to serve the needs of comparative anatomists. There has to be a biological reason why the bodies of higher organisms are so obviously built in a modular way such that apparently natural units are often easy to recognize. In this paper it is argued that homologues can be understood as modular units of evolutionary transformation. In addition, the selection forces are discussed which may be responsible for the evolution of modularity. A way to test the suggested scenario is shortly outlined.

HOMOLOGUES AS UNITS OF EVOLUTIONARY TRANSFORMATION

The root of the homology concept is the fact that individuals from different species
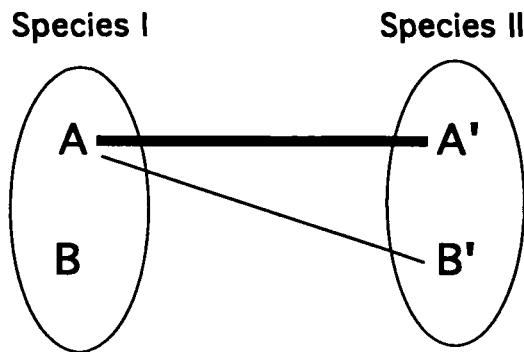
Species I   # Species II

FIG. 1. The parsimony principle of character identification after McKitrick (1994) states that the character A in species I corresponds to character A' in species II rather than B' if it takes "fewer steps to transform A into A' than it takes to transform A into B'."

often are composed of the same kind of building blocks, also called organs or characters. Therefore the starting point of any discussion of the homology concept has to be the idea of structurally identical parts. But what do we mean by structural identity?

For the present context the clearest concept of structural identity has been proposed recently by Mary McKitrick (1994), in a paper on the homology of bird hindlimb muscles. Consider two species with, say, characters A and B in species one and A' and B' in species two (Fig. 1). How do we decide whether A corresponds to A' or B'? McKitrick suggests a parsimony approach to this problem: character A corresponds to A' rather then to B' if it takes fewer steps to "transform" A into A' than it takes to transform A into B'. This is indeed a very good explanation of what we do as biologists comparing two species. We consider the wing of a bat to correspond to the foreleg of a cow because it would presumably take fewer steps to (mentally) transform the one into the other than it would take to transform the wing of the bat into the sternum of the cow. So we reject the possibility that the wing of the bat corresponds to the sternum of the cow but rather is comparable to the foreleg of the cow.

The reason why this approach of recognizing structurally identical parts is so well suited to a discussion of the biological role

of homologues is that it contains an implicit mechanistic assumption. If we recognize structurally identical parts between two species by "counting the number of steps" it takes to transform the one into the other, we implicitly make the assumption that these "transformation steps" are more likely to occur as natural variations than others. The parsimony principle of character identification is an implicit statement about the constraints and opportunities of evolutionary transformation. Furthermore, it assumes that the structures compared are modular units of evolutionary transformation and not just a dependent feature of some other parts of the phenotype.

This approach is naturally linked with another attempt to understand the biological significance of the homology concept. In a recent paper Louise Roth (1991) compared the formal properties of the units of selection, as defined by Lewontin (1970), with the recognized properties of homologues, such as conservation of the basic pattern with variation and individuality. A similar comparison between the gene concept and the character concept also recognized strong similarities between them (Stearns, 1992, pp. 14–16). Both comparisons lead to the suggestion that characters and homologues are modular units of phenotypic evolution and should be understood in the context of the mechanistic processes causing the evolution of phenotypic traits (Wagner, 1995). In the taxonomic context a recent attempt to identify the units of transformation based on species comparison has been proposed by Mary Mickevich (in preparation).

It is thus suggested that morphological characters may be understood as the phenotypic units of evolutionary transformation. This suggestion also naturally relates to the origin of the homology concept in comparative anatomy and taxonomy. The heuristic purpose served by the homology concept is to make the description of variation easier by identifying units that can be compared more or less independently of the rest of the body. The fact that texts of comparative anatomy can be organized either taxonomically or around organ systems illustrates the point. One can explain the
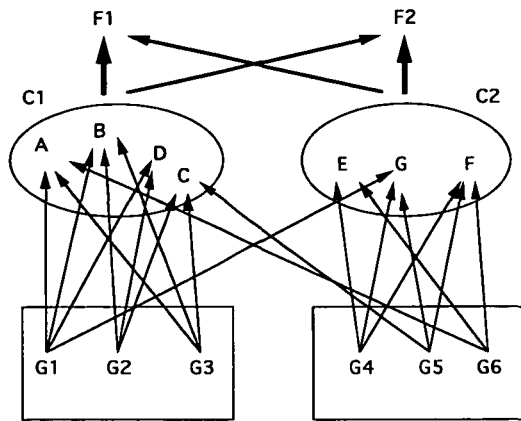
FIG. 2. The characters {A, B, C, D} and {E, F, G} form two modular character complexes C1 and C2, if each character complex serves different primary functions F1 and F2, and if the characters are more tightly integrated within a character complex than between them. This implies that there are more pleiotropic effects from genes {G1, G2, G3} connecting the elements of C1 than there are connecting elements of C1 with elements of C2 and vice versa.

FIG. 3. There are two ways that a modular organization may emerge: Parcellation consists in the differential elimination of pleiotropic effects between members of different complexes and the maintenance and/or augmentation of pleiotropic effects within a character complex. Integration consists in the creation of pleiotropic effects among primarily independent characters.

comparative anatomy of the kidney to a large extent independently of the comparative anatomy of limbs and fins. This is possible only if the described units are also units of interspecific variation, which is the same as a modular unit of evolutionary transformation.

EVOLUTIONARY BIOLOGY OF MODULARITY

In the context of evolutionary biology a modular unit of the phenotype has to fulfill three criteria (see Fig. 2 for a diagrammatic example): it is a complex of characters that 1) collectively serve a primary functional role, 2) are tightly integrated by strong pleiotropic effects of genetic variation and 3) are relatively independent from other such units (Wagner, 1995; Raff, 1995).

The evolutionary implications of modular organization of development were most clearly described by John Bonner in his book on the evolution of complexity (Bonner, 1988). Modularity allows the adaptation of different functions with little or no interference with other functions. Bonner considers modularity, or "gene nets" as he called it, a prerequisite for the adaptation of complex organisms. Related to this concept of "gene nets" is the idea of the dissocia-
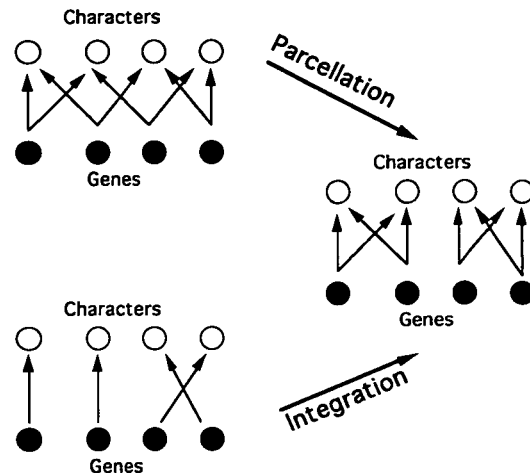
bility of developmental processes described by Needham (1933). Development is a well integrated process but it can be decomposed experimentally into dissociable processes. Gould (1977) pointed out that dissociability of developmental processes is necessary for heterochrony: only those developmental processes that can be dissociated can change their relative timing in development, i.e., can undergo heterochrony (Raff and Kauffman, 1983; Raff, 1995).

Modularity can be of two sorts: it may be a primary property of the way organisms are built, for instance due to organizational principles of self-maintaining systems (Fontana and Buss, 1994) or it may be an evolved property. Below I will only consider the second possibility, namely the origin of modular organizations by natural selection. Modularity, as the word is used here, can arise in two ways: by parcellation or by integration (Fig. 3). Parcellation consists of the differential elimination of pleiotropic effects among characters belonging to different character complexes. This mode is applicable if the phylogenetically primitive state is one with higher overall integration. In contrast, if the primitive state is one

with many independent characters it is conceivable that modularity arises by differential integration of those independent characters serving a common functional role.

Both parcellation and integration are possible, and the relative frequency of them is an empirical question (see Fink and Zelditch, 1996). One example of parcellation may be the evolution of metazoan animals from protozoan colonies, where all the cells are from the same species (Buss, 1987). Primarily each cell in such a colony is expressing the same genetic program and each mutation is thus affecting each cell in the individuum. The so-called higher organisms are characterized by a much stronger specialization of their parts; this specialization is associated with differential gene expression. I argue that this can be taken as a bona fide argument in favor of the view that higher metazoans are more modular than primitive ones. Recent work on molecular markers of heritable quantitative variation supports the notion that the mutational effects are in fact organized in a modular fashion (Cheverud, 1996). However, modularity may get lost secondarily, as suggested by the well known dedifferentiation events in evolution. Examples are, for instance, the evolution of homonomous vertebrae of snakes from the differentiated vertebral column general in tetrapods or the evolution of homodont teeth of whales from their heterodont ancestors. It shall be noted, however, that in both cases genetic evidence for loss of modularity is not yet available. Another pattern that suggests parcellation as a mode of evolution is the tendency of repeated elements to become differentiated. Examples are the differentiation of teeth with the origin of mammals or the differentiation of body segments with the origin of insects (for a review see Weiss, 1990).

SELECTION FORCES CAUSING THE EVOLUTION OF MODULARITY

Both modes of evolving modularity, parcellation and integration, consist of a formally equivalent "sorting" of gene effects. Genetic effects not "in line" with the directional selection on a set of functionally coupled characters become "aligned." For instance parcellation consists of the differential suppression of pleiotropic effects among characters from different character complexes and the maintenance of pleiotropic effects on characters within each complex. Integration results in correlations between characters which prevent non adaptive independent variation of the individual characters (Riedl, 1975). The challenge is to find a class of selection forces that have these differential effects on the structure of the genotype-phenotype map. Four possible candidates are found in the literature: 1) selection based on the rate of adaptation (Riedl, 1975; Rechenberg, 1972); 2) constructional selection (Altenberg, 1994); 3) stabilizing selection (Cheverud, 1984); and 4) a combination of stabilizing and directional selection.

Selection for adaptation rate is based on the fact that modularity can enhance the rate of evolution, because it avoids interference between different functional systems. If there are genotypes in a population that differ in their rate of adaptation to an environmental challenge then the faster class of genotypes will reach higher fitness values more quickly and thereby gain a selective advantage over the "slower" class of genotypes. This mode of selection works particularly well in the absence of recombination (Wagner, 1981). It is in principle also possible in sexually reproducing populations, but requires strong linkage disequilibrium (Wagner and Bürger, 1985). However, this mode of selection is only of limited importance in multilocus systems since it becomes more and more difficult to maintain the necessary level of linkage disequilibrium (Wagner, in preparation, and see below).

The model of constructional selection assumes that modularity evolves by preferential duplication of genes with fewer pleiotropic effects (Altenberg, 1994). This mode of evolution is indeed feasible as shown by simulation studies. It assumes that the effects of a gene are inherited by the duplicate copies of the gene, and that the spectrum of pleiotropic effects determines the probability of a gene duplication becoming fixed in the population. This is a highly interesting proposal that needs to be

followed up to assess its biological plausi-
bility.

The third mode of selection that needs to
be discussed here is stabilizing selection. It
is the mode of selection that a population
is likely to experience most of the time (En-
dler, 1986). Stabilizing selection in itself is
unlikely to produce modularity since it se-
lects against the total mutational variance of
all characters. Since modularity is the *dif-
ferential* elimination of some but not all
mutational effects on a group of characters,
stabilizing selection is not a candidate for
explaining the evolution of modularity
(Wagner, in preparation). It is nevertheless
important to consider stabilizing selection
since it may be a counter force against the
maintenance of modularity. However, si-
multaneous stabilizing selection against a
number of characters favors the reduction
of the overall mutational effects on these
characters irrespective of the strength of
stabilizing selection (Wagner, in prepara-
tion). Stabilizing selection is thus "blind"
to the modular structure of the genotype
phenotype mapping function and does not
"wash out" any modular structure that may
have evolved before. Modularity is stable
against simultaneous stabilizing selection
on all characters.

Adaptive evolution is most likely taking
place by a combination of directional and
stabilizing selection forces (Wagner, 1988).
This conclusion can be inferred from the
observation that during most adaptive pro-
cesses only a limited number of characters
actually change. For instance, the evolu-
tionary increase in body size during the
evolution of modern horses occurred under
the preservation of most of the shape char-
acters. Body size evolution generally occurs
under preservation of the relative brain size,
a trend that is not explainable as a corre-
lated selection response (Lande, 1979), but
is perhaps caused by stabilizing selection.
Darwin's finches are mostly adapting with
their beak shape but conserving other body
proportions (Grant, 1986). At a more ab-
stract level one can argue that any model
assuming a fitness optimum for more than
one character leads to a combination of di-
rectional and stabilizing selection on a pop-
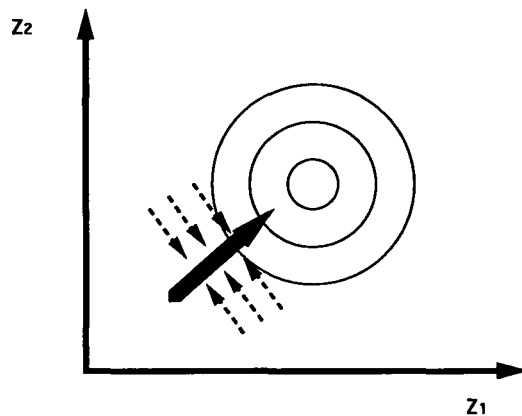ulation that is approaching the optimum

FIG. 4. This diagram illustrates that a population
which approaches an optimum in an at least two di-
mensional phenotype space is necessarily experiencing
a combination of directional (dark arrow) and stabiliz-
ing selection (dashed arrows). The concentric circles
are contour lines of fitness.

(Fig. 4). It is thus suggested that a combi-
nation of directional and stabilizing selec-
tion is a common mode of selection.

A simple fitness landscape that combines
directional and stabilizing selection is the
corridor model (Wagner, 1984, 1988; Bür-
ger, 1986). It assumes that one direction of
the phenotype space is under sustained di-
rectional selection while all the others are
under stabilizing selection. Taken literally
this model is highly unrealistic, since it as-
sumes that fitness increases indefinitely in
one direction. However, this is not an im-
portant part of the interpretation. What
counts is the fact that the corridor model
can be seen as a local approximation of the
fitness landscape far from the optimum,
such that the peak of the fitness landscape
is not yet in the reach of the population.
One can also think of the corridor as a sur-
rogate for a moving optimum model, where
the optimum is shifting in one direction and
the population has to evolve to keep up
with the optimum.

A simulation study on the rate of evolu-
tion in the corridor with pleiotropic effects
has shown that the rate of evolution along
a corridor is strongly influenced by the
strength of stabilizing selection on the
pleiotropic effects, confirming Bonner's in-
tuition that pleiotropic effects interfere with
adaptation (Baatz and Wagner, in prepara-

TABLE 1. *The selection coefficient s(b) of an allele which suppresses the pleiotropic effects of 50 genes while the populations evolve along a ridge of fitness (corridor model).* *

s(b)	k = 0.5	k = 0.1
s = 0.1	0.08	0.08
s = 0.2	0.17	0.15
s = 0.4	0.35	0.26

* The selection coefficient was estimated from the average time to fixation. The estimates are based on 100 simulations per parameter combination. The size of the parental population was 100. The parameter s measures the intensity of directional selection on the first character and k measures the strength of stabilizing selection on the second character. Stabilizing selection on the second character induces selection against the pleiotropic effects. Note that the selection coefficient is mainly influenced by the intensity of directional selection s.

tion). The question now is whether genetic variation that decreases the magnitude of pleiotropic effects will become selected. This question was considered in another simulation study (Wagner, in preparation) in which a "modifier gene" was introduced to suppress pleiotropic effects. Table 1 lists the selection coefficients estimated from the average fixation time. It can be seen that the selection coefficient of the modifier is mainly determined by the strength of directional selection and not so much by the intensity of stabilizing selection. The selection coefficients range from 0.08 to 0.35, which is quite high (note that the selection coefficient is a dimensionless value).

The magnitude of the selection coefficients is primarily determined by stabilizing selection against the variance caused by pleiotropic effects. Since it is assumed that each gene with an effect on the adaptive character (i.e., the one under directional selection) also has pleiotropic effects on the character under stabilizing selection, each gene substitution is associated with a transient peak of genetic variance in the character under stabilizing selection. This transient signal of genetic variance is under direct stabilizing selection and any decrease of this signal will be favored by selection. A study in which the causal components of the selection coefficient were measured shows that about 90 to 95% of the selection coefficient is caused by this direct stabiliz-

ing selection on the variance caused by pleiotropic effects. The rest is due to selection for adaptation rate, or, more technically, by linkage disequilibrium among genotypes with different genotype phenotype mapping (Wagner, in preparation).

These results suggest that a combination of directional and stabilizing selection induces a strong selection force differentially eliminating pleiotropic effects and maintaining the mutational effects on the other characters. It is effective under fairly general conditions and is thus likely to shape the structure of the genotype-phenotype mapping function.

A SCENARIO FOR THE EVOLUTION OF MODULARITY

The above simulation models were, perhaps, unrealistic in assuming sustained directional selection over long periods of time. This assumption was made to obtain a simple model to study the selection forces acting on pleiotropic effects. However, the analysis suggests that the unrealistic assumptions are not critical for the result. Here I want to suggest a biologically more realistic scenario that can lead to the evolution of modularity through the selection forces described above.

While sustained directional selection is unlikely to be realistic for natural selection, frequent episodes of strong directional selection seem to be quite common (Boag and Grant, 1981; Endler, 1986; Grant and Grant, 1989). A likely cause of these episodes of directional selection are climatic fluctuations, for instance those caused by El Niño events (Grant and Grant, 1987). A simple way to model fluctuations in climate is to assume that the selective optimum shifts in phenotype space. The population then responds with adaptation to the new optimum. Let us assume that these climatic fluctuations come in different kinds, one requiring the adaptation of beak size, the other the adaptation of the wings. The population experiences episodes of directional selection for either the beak size or wing shape. In each of these episodes the directional selection on one character, say the beak, will be accompanied by stabilizing selection on the other, the wings, or the oth-

er way round. Each episode will provide selection in favor of suppressing the pleiotropic effects between these two character complexes, because they rarely are simultaneously under directional selection in any given generation. Over time the cumulative selection against pleiotropic effects is expected to lead to a parcellation of the beak from the wings in terms of the structure of the genotype-phenotype mapping.

In this scenario the pattern of modularity in the genotype-phenotype mapping function would reflect the statistical pattern of selection episodes, such that characters that tend to be under simultaneous directional selection get integrated into a module of phenotypic change, while the characters that rarely adapt to environmental changes at the same time will be represented by genes that have no or only limited pleiotropic effects among them. Of course reality will be more complicated, since modules and selection forces may be hierarchically structured, such that modules at a lower level may be integrated into complexes at a higher level.

That character complexes which serve a common function tend to evolve together has been demonstrated in the bird skeleton (Nemeschkal et al., 1992). This pattern of coevolution is clade specific and correlates well with clade specific patterns of character use. The history of coevolution of characters can be reconstructed with the aid of the comparative method (Felsenstein, 1988; Maddison, 1990; Martins and Garland, 1991). The prediction from the present scenario is that the derived pattern of integration should reflect the pattern of character coevolution. To be more precise: the differences between the ancestral and derived patterns of integration are expected to reflect the pattern of character coevolution that occurred during the evolution of the clade.

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