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DEVELOPMENTAL CONSTRAINTS AND EVOLUTION

A Perspective from the Mountain Lake Conference on Development and Evolution

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ABSTRACT

Developmental constraints (defined as biases on the production of variant phenotypes or limitations on phenotypic variability caused by the structure, character, composition, or dynamics of the developmental system) undoubtedly play a significant role in evolution. Yet there is little agreement on their importance as compared with selection, drift, and other such factors in shaping evolutionary history. This review distinguishes between "universal" and "local" constraints; it deals primarily with the latter, which apply to a limited range of taxa. Such constraints, typically, can be broken even within the taxa to which they apply, though with varying degrees of difficulty. The origin of constraints *is discussed, five distinctive sources of constraint being explicitly considered. Three* means of identifying constraints *are set forth, as well as four* means of distinguishing developmental from selective constraints. *None of the latter (use of a priori adaptive predictions, direct measurement of selection, direct measurement of heritable variation, and use of the comparative method) is foolproof. In the final section, three larger issues regarding* the role of developmental constraints in evolution *are discussed: the extent to which evolutionary stasis can be explained in developmental terms, the extent to which evolutionary trends and patterns might be a consequence of developmental constraints, and the extent to which various genetic and developmental mechanisms have evolved in virtue of the need of lineages to manifest evolutionary plasticity (or adaptability) if they are to survive. Although no definitive conclusions are reached on these larger issues, we bring recent advances in developmental biology, evolutionary theory, and (to a limited extent) molecular biology to bear on them.*

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1. INTRODUCTION

A DEVELOPMENTAL constraint is a bias on the production of variant phenotypes or a limitation on phenotypic variability caused by the structure, character, composition, or dynamics of the developmental system. Developmental constraints may arise from a great variety of sources. Among these are properties of the materials out of which organisms are built, requirements governing storage and retrieval of information employed during development, particular features of the evolutionarily determined pathways of development examplified by a group of organisms, and mathematical structure pertaining to the class of complex systems within which a given developmental system falls. Whatever their sources, developmental constraints may influence the course of evolution. This idea is not new. T. H. Huxley, for example, wrote as follows in a letter to Romanes (quoted by Spurway, 1949): "It is quite conceivable that every species tends to produce varieties of a limited number and kind, and that the effect of natural selection is to favor the development of some of these, while it opposes the development of others, along their predetermined lines of modification." Vavilov (1922) proposed a "law of homologous variation," according to which the similarity of developmental pathways in related species causes the appearance of similar variants. The matter was taken further by Spurway (1949), who held that each species has its own characteristic potential for variation. From this she concluded that speciation "thus modifies, not only the anatomy and physiology of a species, but its evolutionary future" (p. 7).

Recent interest in the subject has been stimulated by the emphasis on evolutionary stasis by Gould and Eldredge (1977). When the morphology of a species remains virtually unchanged for millions of years, we would like to know whether this reflects developmental constraints limiting the possibility of change or, conversely, the maintenance of uniformity by stabilizing selection (Charlesworth, Lande, and Slatkin, 1982), and whether the genetic and developmental underpinnings of the morphology have remained as stable as the adult morphology. The problem of the interrelation between the adult phenotype and the developmental system has been approached from a different direction by numerous developmental biologists, some of whom have emphasized that the structure of a developmental process may be such as to give rise to a series of bounded discrete morphologies, without intermediates (Alberch, 1982; Oster and Alberch, 1982).

The present review discusses how developmental constraints might originate in evolution, how one might recognize them, how their effects can be distinguished from the action of natural selection, and what impact they may have on future evolution. Let us first, however, consider some properties that developmental processes must have in order that certain aspects of evolution should be possible. It is a general characteristic of populations that adaptations, i.e., genetically programmed features and behaviors that promote survival and reproduction, emerge in their constituent individuals. Where the acquisition of a complex adaptation by natural selection requires a number of genetic changes, this will be possible only if there exists a series of intermediate stages, each an improvement on, or not significantly worse than, the preceding one. As Lewontin (1980) has pointed out, this requirement of adaptive evolution implies something about the relation between genotype and phenotype. In such processes it must often be the case that small changes in genotype often cause small changes in phenotype and that genetic changes altering one trait do not always result in excessively maladaptive changes in others. If complex adaptations involving many genes are to evolve by natural selection, it must be possible to change single traits without disturbing others in a way that reduces overall fitness. In brief, since genotypes correlate with phenotypes through the dynamics of the developmental process, developmental constraints must not make it wholly impossible to alter one trait adaptively without producing excessive maladaptation in others.

However, there is more to evolution than an increase of adaptation, and various types of developmental constraints, linking diverse traits, do exist. Granted that many develop-

mental processes are relatively independent of one another (and thus allow stepwise evolution to occur), there remain many correlations, often strong ones, among traits in nature. Indeed, all organisms are subject to constraints. The specific character of the constraints varies from case to case; different developmental processes are coupled in different cases. Genetic change can alter the covariance among traits of the organism, and that covariance may itself be subject to selection. But there *is* covariance, and we can use its strength as a rough local measure of the strength of constraint.

2. LOCAL AND UNIVERSAL CONSTRAINTS

Some constraints are direct consequences of the laws of physics, whereas others arise from invariant properties of certain materials or of complex systems. An example of the first sort (discussed by Maynard Smith and Savage, 1956) is a simple consequence of the law of the lever: any uncompensated change in the shape of a skeleton that increases the speed with which some member can be moved will reduce the force which that member can exert. Such examples do not depend on any distinctive features of organisms. Constraints of these sorts are universal in the sense that they apply, respectively, to all physical systems (and hence to all organisms), to all things built out of the materials in question (including organisms), and to all physical systems of the requisite complexity (including organisms). Accordingly, we call these "universal constraints." "Local constraints," in contrast, are confined to particular taxa. They arise in consequence of some particular feature of the organisms of those taxa. Palms provide an example: unlike dicotyledons, which have branched and tapering trunks, nearly all palms (and other trunked monocotyledons) have trunks that do not branch and that are roughly uniform in diameter. The difference exists because most monocotyledons have not evolved the process of secondary thickening. To the extent that secondary thickening is not available, the ways in which monocotyledons can grow and the structures that they can achieve are constrained. Such constraints are taxon-specific.

The distinction between universal and local constraints is neither entirely clear nor entirely rigid. For one thing, two logically independent issues are considered in judging universality: the scope of a constraint (does it cover all cases?), and its "bindingness" or inescapability. For example, consider the apparent fact that, in all species, all amino acids incorporated into proteins are L-isomers (levorotatory) rather than D-isomers (dextrorotatory). Supposing that this generalization is universal, we can still ask how binding it is. It is certainly not grounded in physical law nor in the distribution of dextrorotatory and levorotatory molecules in the universe at large. (It should be noted that biological sugars are *dextro*rotatory.) Indeed, the degree of bindingness in question is probably historically contingent, having changed during the course of evolution. At a very early stage in the evolution of life, presumably, L- and D-isomers of amino acids were found in roughly equal proportions among proto-organisms. By some sort of random walk phenomenon, presumably, levorotatory amino acids came to be more prevalent. Once this happened, there was a clear advantage for those (proto-) organisms that happened to utilize the dominant molecular type most efficiently. Thus chirality, in this scenario, illustrates a change in the binding power of a constraint: the chirality of the constituent molecules of proto-organisms was once an accidental and indifferent matter, but it now constitutes a very strong constraint, playing an ill-understood role in the development of all terrestrial organisms.

There is a similar ambiguity regarding the universal vs. local character of the constraints arising from features of the materials out of which organisms are built. There are, presumably, universal physicochemical truths about, say DNA and chitin. As a matter of logic, these yield universal truths about organisms composed in part of these substances. Yet, arguably, all terrestrial organisms exemplify the truths about DNA (except RNA viruses?), whereas those about chitin are exemplified only in particular taxa. Thus, although the effective scope of a constraint stemming from the physicochemical features of DNA is greater than that stemming from those of chitin, *to the extent that a particular group of organisms is locked into employ-*

ing either of the two sorts of materials, the constraints stemming from one are as binding and inescapable as those stemming from the other.

For reasons such as these, "universal" and "local" are not logical contraries, but mark the extremes on a crude continuum. We often find ourselves able to agree about roughly where to place examples of constraint even though we have different reasons for classifying the examples as we do, and even though we cannot provide an exact account or classification of the kinds of constraint that are present.

All organisms are complex systems. Among the most interesting group of potentially universal constraints are those that stem from certain general, mathematically derivable features of complex systems. A surprising number of the features of complex dynamical systems, and hence of organisms, can be predicted on general grounds, even in the absence of much specific information about the particular system in question. Such predictions concern intrinsic stabilities, discontinuities, and nonrandom probabilities of transition from one state to another. Nonrandom transitions (i.e., constraints), may have evolutionary implications; some of these have been explored by Alberch (1982) and Oster and Alberch (1982). For example, many systems, living and nonliving, display *limit cycle behavior*, with its characteristic phase-setting and phase-locking properties (Glass and Winfree, 1984; Winfree, 1980). One interesting class of such systems is that of systems exhibiting the properties of "excitable media," whether animate or inanimate. Their temporal and spatial properties include point stability, limit cycles, and propagating waves. These capture the dynamical essence of a number of biological properties such as homeostasis, excitability, oscillations (with phase-resetting, phase-locking, and annihilation properties), such as circadian rhythms and heartbeat (Winfree and Strogatz, in press), and wave propagation (such as occurs in nerve impulse conduction and in such morphogenetic movements as gastrulation and neurulation; Odell, Oster, Burnside, and Alberch, 1981).

A further example is more speculative. Multicellular organisms are composed of at most several hundred different cell types. These types do not all arise, each in a single step, from a common ancestral cell or cell type. Instead, a single cell type can give rise directly to a small number of others, typically one or two. In this respect, development follows a branching pathway. The same is true of networks intended to simulate genetic control and differentiation: such networks may have several hundred stable behavioral states (corresponding to different cell types), but from each such state it is possible to pass directly to only a small number of others (Kauffman, 1983a). Now this is by no means a necessary feature of all such networks, but it is a feature of precisely those that have the properties (discussed above) necessary for adaptive evolution to occur. That is, it is true of those networks in which the connections of one control element (or "gene") can be changed without altering the nature of all, or most, of the stable behavioral states. Thus the observed branching nature of pathways of cellular differentiation may be a necessary and hence universal feature of systems capable of adaptive evolutionary change (Kauffman, 1983b).

A more mathematical example exhibiting features of both "universal" and "local" constraints is to be found in the fact that cacti, pine cones, pineapples, sunflowers, and various other plants exhibit the famous Fibonacci series in phyllotactic patterns of leaf or scale primordia. Thus the number of ascending lefthand or righthand spirals on a pine cone are typically adjacent members of the series 1, 1, 2, 3, 5, 8, 13, 21, 34, 55, . . . in which the last term is the sum of the previous two. There are two important aspects of these patterns. (1) There is a discontinuity between neighboring patterns: the left and right spirals of pine cones are 21:34 or 34:55, and so on. (2) The golden angle between adjacent scale or leaf primordia on the apical meristem is preserved. Although phyllotaxis is not fully understood, an attractive account (Mitcheson, 1977) suggests that close packing of the relevant units—e.g., of primordia on a conical meristem—suffices to explain the particular patterns in question. If this account is right, phyllotaxis will be a universal feature of those systems that are built to conform to the rules of close packing. And the widespread presence of phyllotaxis suggests

that the constraint involved, though not universal, is a strong one, perhaps in part because close packing is a common requirement of plant morphogenesis. What is needed to complete the case is independent evidence of the role and importance of close packing in at least some of the relevant instances.

It will be apparent from the preceding discussion that it is easier to identify and to understand taxonomically local constraints than global ones. The rest of this paper consequently concerns the former. As should now be clear, however, the distinction is by no means absolute. There are constraints confined to single species, and others that are common to all members of a class or phylum. Within a taxon, a constraint may apply universally or it may be breakable: thus, there *are* palm trees that branch. And even universal constraints may bind more or less tightly. Thus, it is important to distinguish between features, such as heredity, that are shared by all living organisms because without them life would be impossible, and other features, such as the assignment of codons to particular amino acids, that may have arisen in the first place largely by accident but that are universal because, once they have arisen and mutual adjustments among codons have taken place, they cannot be readily changed.

As our many examples show, even local constraints may exert considerable influence on the pathways followed by evolution. Organisms are capable of an enormous range of adaptive responses to environmental challenge. One factor influencing the pathway actually taken is the relative ease of achieving the available alternatives. By biasing the likelihood of entering onto one pathway rather than another, a developmental constraint can affect the evolutionary outcome even when it does not strictly preclude an alternative outcome. Indeed, such biasing (comparable with some degree of "loading" in dice) is more consistent with the diversity and unpredictability of evolution than is the setting of absolute prohibitions. Local constraints (and also weak universal constraints) are fully capable of having a significant effect on evolutionary pathways; for this reason they deserve increased attention in evolutionary studies.

3. THE ORIGIN OF CONSTRAINTS

Given that there are constraints on the morphological changes that can occur in a given taxon, how do they arise? The best we can do is to offer a list of possible reasons.

A. Phenotypes Accessible or Inaccessible, Given a Particular Developmental Mechanism

The patterns of homologous variation discussed by Vavilov and by Spurway, among others, are presemably to be explained by the fact that the developmental mechanisms of a given taxon render certain phenotypes more readily accessible than others. Since each developmental mechanism must bias the accessibility of novel phenotypes in some way or other, it is reasonable to expect every taxon to exhibit local constraints derived from this source. Furthermore, there is usually no reason to suppose that the developmental mechanisms in question evolved because of the particular phenotypes that they make readily accessible. In general, therefore, the direction of the resulting constraints (biases on the production of variant phenotypes) is "accidental" or "random" with respect to the demands of adaptive evolution.

B. Phenotypes Accessible or Inaccessible, Given Any Developmental Mechanism

A similar account may apply to more universal constraints. Ermentrout, Campbell, and Oster (in prep.) have described a series of banding patterns on gastropod shells that can readily be interpreted as the results of standing or travelling waves of pigment formation in the mantle. Geometrically similar pigment patterns occur on feathers and on the coats of mammals. Turing (1952) described one mechanism whereby such waves could arise, and it is known that there are many other such mechanisms. Looking at such patterns, it is easy to conclude that we are seeing the solution of a wave equation, even if it is hard to say what was waving. This exemplifies the point: certain patterns may arise repeatedly because they are easily generated by physicochemical processes or by certain classes of complex systems, even though the details of the process may be entirely different in different cases. The widespread phase-resetting and phase-locking properties of oscillatory systems mentioned

above provide a second example. The existence of smooth two-dimensional "positional information maps" (Wolpert, 1981) may be a third.

C. *Phenotypes Accessible or Inaccessible, for Selective Reasons*

Some constraints arise from the hill-climbing nature of the evolutionary processes underlying adaptation. Kangaroos, for example, travel in a series of leaps. Morphological changes that make them better at this mode of locomotion will be favored by selection. In contrast, it is unlikely that kangaroos will evolve adaptations to bipedal running, because the initial changes in that direction would be maladaptive. (Unlikely, but not impossible: tree kangaroos and, in a parallel case, arctic hares have broken this constraint.) Most populations, most of the time, are thus committed to particular ways of life. Although such commitments are not absolute, it should be recognized that one effect of selection is to limit the morphological and behavioral variations adequate to the tasks of living. By interacting with the developmental system, such effects of selection bias the variants available for subsequent selection to act upon.

D. *Constraints Resulting from Canalizing Selection*

Canalizing selection may best be conceived as a special case of the preceding type. Many natural populations are rather uniform in morphology, whereas populations carrying a mutant that disrupts significant features of that morphology are highly variable. Waddington (1957) suggested that the reason for this difference is that the typical "wild-type" pattern has been exposed to many generations of stabilizing selection, whereas the mutant pattern has not. According to this view, some developmental constraints are themselves the result of selection, and are not the automatic consequences of the structure of the developmental system. Various experiments support Waddington's view by showing that stabilizing selection can reduce the variability of mutant phenotypes (Maynard Smith and Sondhi, 1960; Rendel, 1959; Waddington, 1960). Since stabilizing selection is widespread in natural populations (Haldane, 1954), direct support for the claim that it reduces the phenotypic plasticity of natural populations would be obtained by showing that recently evolved phenotypes are more variable than long-established ones. One possible example concerns a novel secondary sexual character in one of two races of *Drosophila silvestris* from the island of Hawaii. The character consists of an extra row of elongated bristles on the tarsus of the male's forelegs, used in courtship. The number of bristles in the newly evolved row is conspicuously more variable than that in adjacent bristle rows with an older evolutionary history (Carson, Val, Simon, and Archie, 1982). An analysis of crosses between the races revealed that at least one X-linked gene and two unlinked autosomal genes were involved in the evolution of the new trait (Carson and Lande, 1984).

E. *Genotypes Accessible or Inaccessible, Given the Present Genetic System*

Evolutionary transitions from one (adult) phenotype to another are mediated by genetic change. Suppose that a utopian analysis of the selective regime faced by a given lineage in a particular environment were to reveal that a certain evolutionary transition would be likely if a particular sequence of phenotypes, each selectively preferable to its predecessor, were available. Even in this ideal case, it would not follow that the lineage would make the transition in question—for the requisite variation to produce the desired sequence of phenotypes (and to do so in the proper order) might not be available. There must be a *genetic* pathway, i.e., a series of mutations, accessible to the lineage for it to produce the phenotypes of the sequence in the proper order. But the accessibility of such a pathway is not guaranteed.

The work of Hall and his colleagues on the acquisition of new functions in bacteria (e.g., Hall, 1982) illustrate this point. *E. coli* can acquire novel metabolic functions (e.g., a novel pathway for regulated digestion of lactose in bacteria that have a defective *lac* operon) by an appropriate sequence of mutations in structural and regulatory genes. Early mutations in such a sequence are often "neutral" (i.e., they do not detectably alter current gene function or yield new functions) or even

slightly deleterious. Many such mutations are "dead ends" with respect to the novel function in the sense that they not only do not enter the bacterium on a pathway toward that function, but that they also must be reversed in order to enter onto such a pathway. Other mutations, fortuituously, allow some further mutation in the sequence to yield an incremental step toward the acquisition of the new function. There is a clear sense in which the bacteria that happen to acquire these latter mutations have easier access to the novel phenotype, say lactose digestion, than do either the "wild type" lineages or those with the mutations that interfere with acquisition of the new function. Most situations of concern to us are far more complicated and require a far mor sophisticated analysis—but the point remains that various features of the current genetic system affect the likelihood of a lineage producing "favorable" novel genotypes, and hence phenotypes. Such biases on the production of variant phenotypes fit our definition of developmental constraints and may play a significant role in evolution.

4. THE IDENTIFICATION OF DEVELOPMENTAL CONSTRAINTS

There are three methods for recognizing developmental constraints: from a study of morphology, usually of the adult; from genetic analysis; and from a knowledge of developmental mechanisms.

A. The Study of Morphology

(i) Distribution in Morphological Space

The recognition that winding number in phyllotaxy follows the Fibronacci series preceded any developmental theory of why this should be so. If adult phenotypes lie within a restricted range of phenotypic space, it is natural to seek a developmental explanation. There are, however, two other possible reasons for such a restriction. It may be that the chance wanderings of actual evolutionary lineages have not yet reached the unoccupied region although there are no reasons, selective or developmental, why the relevant phenotypes are ruled out (Raup and Gould, 1974). Alternatively, the adult phenotypes may be selectively constrained. The problem of distinguishing developmental from selective constraints will be discussed in the next section. Until that problem is solved, a restricted range of adult morphology can only suggest, but cannot by itself demonstrate, the existence of a developmental constraint.

(ii) Comparison across Species and Higher Taxa

A more promising way of identifying developmental constraints is from the repeated occurrence of a given variant in a given taxon. Vavilov (1922) and Spurway (1949) argued in this way. Spurway's examples included the occurrence of naked areas of skin on the neck and head of some birds and of horns in mammals (present as specific characters in 7 of 25 orders of placental mammals). At a lower taxonomic level, she cited phenotypes that have arisen repeatedly by mutation in *Drosophila subobscura*, but which have not been observed in *D. melanogaster*. Mutants at three different loci, for example, yield white hairs growing between the ommatidia coupled with longitudinally crumpled wings.

Alberch (1983) has studied the apportionment of osteological variation in the skull and limbs of the various species of bolitoglossid salamanders. He specifically compared the patterns of intraspecific and interspecific variability in the characters traditionally used by systematists working on the group. Unlike the characters employed in quantitative analyses, which are typically metric and highly variable, the characters employed in systematics are usually discrete and supposedly invariant. Alberch found surprisingly high levels of variation in these characters. The results indicate that (1) variation is definitively bounded (i.e., only certain bones are variably present, whereas the other elements are either always present or are never found); (2) traits observed as variants in a population of a given species are found fixed in other species (i.e., population polymorphisms parallel interspecific diversity); and (3) there is a tendency towards the appearance of atavistic forms.

Such nonuniformities in morphological variation suggest that the developmental system can be modified rather easily to give rise to certain variants, whereas others can be reached only with considerable difficulty.

The same conclusion is suggested by the existence of phenocopies. If a given variant can arise either from a genetic or an environmental cause, the developmental process must cause some sort of differential accessibility of that variant, making it easily available in the course of evolution.

It must be admitted that we do not yet have a firm understanding (or a good measure) of the relative accessibility of different variants (R. Lewontin, pers. commun.). Should the number of mutational steps count? The gradient of the selective surface? The number of organs that must be significantly altered? In spite of these difficulties, the evidence just cited reinforces the common conviction that genetic influence and environmental stimuli have the same causal status in developmental transformations. Specifically, both play the role of evocators rather than that of sufficient causes; in both cases, the relevant trigger calls forth one of a limited pre-existing or predetermined set of possible developmental pathways (Goodwin, 1984).

Garcia-Bellido (1983) has recently presented a similar argument with greater documentation. He pointed out that a number of qualitative changes in the pattern of bristles crop up irregularly at widely scattered locations in the phylogenetic tree of *Drosophila* and related genera. This conclusion is not an artifact of phylogeny—it would be forced on us whatever phylogeny we adopted. The implication is that at least some of these changes have occurred repeatedly during evolution. Whether these changes are the products of selection or are called forth by the internal dynamics of the developmental system is a matter calling for further investigation.

B. Genetic Analysis

Some constraints are made evident by the inability of a population to respond to repeated and powerful selection. For example, after eleven generations of breeding from mutant *Drosophila* possessing the left but not the right ocellus, the frequencies of lefthanded and righthanded individuals remained equal, as they had been all along (Maynard Smith and Sondhi, 1960). Hence, although individual flies were asymmetric, there was no heritable variance for handedness. This contrasted with the ease with which the relative frequencies of flies with the anterior and posterior ocelli could be altered. The explanation of this difference in response is, presumably, that no left-right asymmetry usable in determining handedness preexists in the head of a developing fly. The absence of heritable variation may account for the bar to selective modification in the present instance, but it leaves unanswered the important developmental question of why bilaterally symmetric structures seem, typically, not to exhibit heritable variation. If, indeed, the requisite variation is not available, then many cases of bilateral symmetry may be consequences of a developmental constraint rather than selection. The bias in favor of symmetry should be taken seriously even though this constraint is not universal, as is shown by the fact that many asymmetrical forms are known, from fiddler crabs to caribou. And handedness may sometimes be altered by single gene differences, as in gastropods.

One further consideration impinges on this issue. If one selects for asymmetric individuals in each generation irrespective of whether they are lefthanded or righthanded, one can obtain populations with a high proportion of asymmetrical individuals (Maynard Smith and Sondhi, 1960, Van Valen, 1962). Thus "fluctuating asymmetry"—asymmetry in which handedness cannot be predicted from generation to generation—*is*, in some instances, heritable. It would be most useful to learn more about the interaction between selection favoring symmetrical over asymmetrical forms and developmental processes that tend to generate symmetry automatically.

A similar (if more controversial) case can be made for the absence of genetic variance for the sex ratio in diploids with an X-Y sex-determining mechanism (Maynard Smith, 1978). The constraint is again not universal. Females in haplo-diploid species can choose the sex of each individual offspring.

In the cases just discussed, the presence of a developmental constraint is deduced from the absence of heritable variation. An addi-

tional series of cases, which may have broader evolutionary relevance, concerns situations in which there is plenty of heritable variation, but in which genetic change can take place more readily in some directions than others. These cases are usually analyzed in terms of the genetic correlation between traits. Such correlations typically reflect causal interrelations during development and may, in fact, depend primarily on the dynamics of the developmental system. We can picture the situation by supposing that there exist, in some population, a set of underlying variables—say a, b, and c—each of which can vary independently of the others, but which, collectively, determine the form of the adult. If two traits, X and Y, are each influenced by a, b, and c, then selection on X will alter a, b, and c, and hence will produce correlated changes in Y. If, however, it were possible to select directly on a, then, among the underlying variables, only a would change.

If such underlying variables exist, they can be discovered by appropriate genetic analysis. In particular, additive genetic variances and covariances of quantitative characters, including age-specific and growth-related traits, can be estimated from breeding and selection experiments (Cheverud, Rutledge, and Atchley, 1983; Falconer, 1981; Lande, 1979; Riska, Atchley, and Rutledge, 1984). Principal components of heritable variation that are uncorrelated with each other can be calculated. Their independence implies that they may evolve separately. They thus form a natural coordinate system for the description of phenotypic evolution, at least on a microevolutionary scale. Since the dimensionality of this natural system is often lower than that of a space whose coordinates are all the traits measured (e.g., Atchley, Rutledge, and Cowley, 1981; Bailey, 1956; Cheverud, 1982; Leamy, 1977; Wagner, 1984), then the new description will be simpler as well as more natural. Some of these points are illustrated by the example of gastropod morphology in Section 6.

The power of this method turns on its ability to yield a simpler coordinate system for the description of morphological variation, for it is the variables of that coordinate system that may shed some light on the character of particular developmental constraints and their effects on evolution. Of special interest are:

(i) Dimensionality

The example of handedness discussed above, in which there is no heritable variation, is merely a degenerate case in which the dimensionality of the natural system is zero. That is, no genetic component can be altered so as to determine handedness. An example of an unexpectedly one-dimensional system is afforded by Sinnott's (1935) analysis of the inheritance of fruit shape in squashes. Crosses between varieties that differed greatly in fruit shape, length, and diameter of the mature fruit displayed a complex polygenic pattern of inheritance. By plotting bivariate distributions of mature fruit length and diameter, Sinnott found evidence for segregation of a major gene influencing the slope of the resulting "allometric growth curve," and hence the mature fruit shape as measured by the ratio of length to diameter (reviewed in Wright, 1968: 117–118, 327–328, 388–389). (It is by no means necessary that the genetic component involved in cases of dimensionality one be a single major gene. Various sorts of gene complexes can play such a role.)

(ii) Threshold Characters

The mapping of the underlying variables a, b, and c onto phenotypes may not be continuous. A threshold character, X, may be present if a is greater than some value, but otherwise absent. The work of Rendel (1959) and his colleagues on scutellar bristles in *Drosophila* illustrates one way in which a discontinuously varying phenotype can be mapped onto a continuous underlying genetic variable.

(iii) Limitation of Genetic Analysis

If every gene in a species affected every trait directly and independently, then no underlying variables a, b, and c could be discovered by genetic analysis, for the simple reason that they would not exist. Again, it may be difficult to discriminate among alternative causes of genetic correlation. Correlations between characters may arise through pleio-

tropic effects of genes expressed through common developmental pathways, but they may also occur because of linkage disequilibrium (nonrandom combination) between alleles at loci affecting different characters. Tight linkage between genes affecting different traits, or a high level of inbreeding in a large population combined with a mutual selective constraint, can maintain a substantial genetic correlation between characters that are developmentally independent. Analyses of the kind considered above will work, therefore, only when development has the properties that, as we have already argued, are necessary for adaptive evolution to occur. We should not be surprised if the method sometimes breaks down.

C. A Knowledge of Developmental Mechanisms

If we fully understood the mechanisms responsible for the development of a structure and the ways in which gene changes could modify those processes, we could predict the possible range of phenotypes. There is no immediate prospect of such understanding. There are cases, however, in which our incomplete knowledge of development can be used to interpret, or better still to predict, possible morphological changes. One such interpretation is found in Lande's (1978) analysis of limb loss in tetrapods. Tetrapod limbs generally develop in a proximal to distal sequence under the influence of an apical ectodermal ridge. In the numerous lineages of amphibians, reptiles, birds, and mammals that have lost or greatly reduced their limbs, the evolutionary loss of limb bones always occurs in a distal to proximal sequence.

In contrast, other homologous parts—e.g., preaxial vs. postaxial digits and front vs. hind limbs—are lost in different orders in different, but related, lineages (Lande, 1978). Alberch and Gale (1983, 1985) have studied evolutionary parallels in digit reduction in amphibians. Their study, which integrates comparative and experimental data on limb development, found that several species of frogs and salamanders have lost digits independently. Despite the fact that the species are remotely related phylogenetically, there is a striking congruence in the sequence of digit reduction: some elements are always lost before others. They interpret this invariance as a developmental constraint. The constraints involved must be historically contingent (i.e., local), for frogs exhibit different trends than salamanders. In particular, frogs lost their pre-axial toes while salamanders always lost the post-axial ones.

Treatment of the limbs with reversible inhibitors of mitosis caused limbs to develop normally but with fewer cells. This reduction in cells caused a loss of phalanges and toes. The resultant experimental morphologies were highly ordered, i.e., there were well-defined sequences of skeletal reductions. Furthermore, they paralleled the trends observed in phylogeny. That is, the same experimental perturbation that caused *Xenopus* (a frog) to lose its first digit (the thumb) caused axolotls to lose a post-axial digit. This suggests that there are qualitative differences in the process of limb morphogenesis between anurans and urodeles (see also Maden, 1981). On the basis of these features of the developmental system, Alberch and Gale (1983, 1985) concluded that the observed patterns of diversity are essentially a reflection of the developmental properties of the system.

From a genetic point of view one of the best-understood developmental processes is the formation of segments in *Drosophila*. Genetic analysis reveals two fundamental, but separable, processes: (1) proper spacing of segments along the embryonic axis, and (2) proper specification of the character of each segment (e.g., prothoracic, mesothoracic, eighth abdominal). It is important that a surprisingly limited number of mutant phenotypic classes have been found in both processes. With respect to spacing, saturation mutagenesis for two of the four chromosomes (Nüsslein-Volhard, 1979; Nüsslein-Volhard and Wieschaus, 1980) reveals mutants that cause groups of missing adjacent segments, "pair rule" mutants that delete parts of all even-numbered or all odd-numbered segments, and intrasegmental deletion mutants, which also cause mirror symmetrical duplications within each segment. These fascinating but restricted classes have suggested several models of segment spacing, and directly demonstrate a restricted family of neighboring morphologies available to selection (Kauffman, Shymko, and Trabert,

1978; Meinhardt, 1977; Russell, in prep.; Sander 1975; Slack, 1980). Mutants affecting segment identity include the famous homeotic mutants, such as the *bithorax* cluster (Lewis, 1978), the *antennapedia* cluster (Wakimoto and Kaufman, 1981), and a number of others (Garcia-Bellido, 1975; Kauffman, Shymko, and Trabert, 1978; Ouweneel, 1976) which transform one segment's identity to another. Students of homeotic mutations have put forward several alternative models of segment specification in *Drosophila* (Garcia-Bellido, 1975; Kauffman, Shymko, and Trabert, 1978; Lewis, 1978; Meinhardt, 1977; Russell, in prep.; Sander, 1975; Slack, 1980), none of which has yet been clearly established.

For present purposes, it is striking that the set of homeotic transformations is so limited, and that most can be phenocopied in wild-type organisms. The parallels between phenocopies and homeotic mutants strongly suggest that mutations convert segments from one identity to another only when those identities are, in some sense, developmental neighbors in the wild-type organism. Just as different members of the phyllotactic series in pine cones are neighbors, so wing and eye, but not wing and genitalia are neighbors. Interestingly enough, this "neighborliness" seems to mirror evolutionary history, for homeotic "neighbors" reflect the apparent order of divergence among segments in the evolution of insects from myriapod worms.

In spite of this interesting conclusion, the presently available models of segment spacing and segment identity appear to have limited value in predicting evolutionary trends or directions. Models of segment spacing *do* suggest limited directions of pattern deformation, typically toward specific incomplete forms. Models of segment identity are difficult to apply to evolutionary questions because evolutionary changes in morphology predominantly alter segment-specific characters rather than segment identities. Thus halteres apparently evolved through step-by-step alteration of the size, shape, and other features of wings rather than by homeotic switching of segment identity. The present models of segment character specification are all silent about such alterations.

Such instances as these illustrate the difficulty of making a sharp distinction between "developmental" and "genetic" constraints. Our knowledge of the constraints in a particular case may come from genetic analysis or from a study of development, but the character of the constraint is not determined or affected by the way in which we happen to have studied it.

5. DISTINGUISHING DEVELOPMENTAL FROM SELECTIVE CONSTRAINTS

Like the distinction between local and universal constraints, that between developmental and selective constraints is rough and ready. Although there are clear cases in which one label is preferable to the other, many constraints involve an interacting mixture of developmental and selective factors. The most broadly applicable method for distinguishing the clear cases is probably the comparative one, but first we consider three other approaches.

A. By Use of a Priori Adaptive Predictions

In some cases, it is possible to make rather precise quantitative predictions about the structures or behaviors to be expected on selective grounds. A fit with such predictions indicates an absence of relevant developmental constraints strong enough to counteract selection, whereas departure from prediction indicates their presence at least locally. For example, in a large, random-mating population, we expect a parent to allocate resources equally to producing offspring of the two sexes (Fisher, 1930); if there is local competition for mates we expect a departure of a known degree from equal allocation (Hamilton, 1967). Haplo-diploid organisms meet these predictions rather well (Charnov, 1982). A detailed study of diploid organisms with similar life histories has not been undertaken, but might reveal a constraint arising from the nature of meiosis.

Quantitative predictions can sometimes be made concerning structures serving locomotion (Pedley, 1977); these allow a similar test for constraint. Because of the complexity of the mechanics of animal movement, however, the best evidence of the degree to which selection can mold form despite constraint comes from the convergence between lineages with similar modes of locomotion

(swifts and swallows; jerboas, kangaroos, and cape jumping hares; tunafish, icthyosaurs, and porpoises). Such convergence is independent of the a priori predictions pertaining to any single case, and thus a more reliable source of evidence.

We have an unambiguous idea of the "optimal" structure in cases of Batesian mimicry. The accuracy of Batesian mimicry, even across widely separated taxa, shows that developmental constraints do not prevent effective (even if morphologically superficial) convergence. In fact, shared developmental constraints may contribute significantly to the evolution of mimicry, since the emergence of a complex mimetic pattern would be facilitated by ready access to similar developmental pathways in model and mimic. Nijhout's (1978) analysis of lepidopteran wing patterns encourages this interpretation, as argued by Saunders and Ho (1984), although the orthodox view (e.g., Sheppard, 1959) holds that most instances of mimicry involve different developmental pathways. In some cases, such developmental pathways as are shared by two organisms play no particular role in forging mimetic patterns—e.g., in insect mimicry of twigs and dead leaves.

Genetic analysis of mimicry (Clarke and Sheppard, 1963; Turner, 1977) has shown that major mutatons are often involved. There are also some theoretical reasons for expecting mimicry to involve one or two mutations of large effect, as well as many modifiers. A small change in an initially cryptic species is likely to make it less cryptic without giving sufficient similarity to a distasteful model to afford any protection. Even when the mimic was not initially cryptic, the costs of small steps toward mimicry in disruption of mate recognition and courtship behaviors may be sufficiently high to require a considerable degree of protection as a first step. In both cases, therefore, the first step toward mimicry may have to be rather large.

Only some palatable species become mimics. Since the first step may well be a major mutation of an improbable kind, the occurrence of such mutations may be important in determining which species evolve as mimics. If so, the developmental system, because of its influence on what such mutations can accomplish, may be important in determining the path of evolution. One way of obtaining evidence bearing on this issue would be to make a three-way comparison of the developmental systems of (1) a group of mimetic models, (2) organisms in a group that mimicked those models relatively frequently, and (3) organisms in a similar or related group that mimicked those models relatively rarely.

B. By Direct Measurement of Selection

The measurement of selective differences within populations has been critical in the study of evolution at the species level, and in testing hypotheses about the selective significance of particular traits. It is not, however, a particularly effective way of identifying developmental constraints. One possibility is as follows. The occurrence of evolutionary stasis in traits that show intraspecific variability in existing populations has been explained in two ways. Population geneticists (e.g., Charlesworth, Lande, and Slatkin, 1982) have argued that stasis is a consequence of stabilizing selection, whereas others have argued that developmental constraints are the relevant factor. Where there is evolutionary stasis, but there is little or no stabilizing selection in contemporary populations, one might argue for the role of development in maintaining stasis. Conversely, the operation of stabilizing selection on a character with heritable variation, or of fluctuating directional selection on that character in an appropriate succession of environments, suggests that developmental constraints are not required to explain evolutionary stasis. Assessment of the selective regime on an appropriate time scale is extremely difficult, the more so since the measurement of natural selection on a particular character should account, insofar as possible, for the effects of selection on correlated characters (Lande and Arnold, 1983).

C. By Direct Measurement of Heritable Variation

If there is no heritable variation in a trait, selection cannot alter that trait. The result is constraint: whenever variants of a certain sort are wholly lacking, a lineage cannot evolve in the direction of the missing variants. Whenever those variants are (relatively speaking) extremely rare, there is a bias

(which selection can still overcome) against evolution of the lineage toward the phenotype in question. True, the absence of heritable variation may itself be the consequence of canalizing selection. Nonetheless, once heritable variation has been eliminated or become unavailable, features of the relevant phenotype are not maintained by selection, but are the product of constraint. If, as suggested above, variants breaking certain bilateral symmetries are not available, then constraint provides a sufficient explanation for the preservation of those symmetries.

D. By the Comparative Method

The comparative method can provide straightforward demonstrations that selection rather than developmental constraint governs certain suites of characters. A useful, if somewhat controversial, example concerns allometry. It has frequently been held that the presence of an allometric relation across adults demonstrates the operation of a developmental rather than a selective constraint. For example: "Whenever we find [such allometric relationships], we are justified in concluding that the *relative size* of horn, mandible, or other . . . organ is automatically determined as a secondary result of a single common growth-mechanism, and *therefore is not of adaptive significance*. This provides us with a large new list of non-adaptive specific and generic characters" (Huxley, 1932, p. 214). More recently Lewontin, following Huxley's line of argument and noting that tooth size increases more slowly than body size in adult primates, has concluded that " . . . it would be erroneous to argue that for some special adaptive reason gorillas have been selected for relatively small teeth" (Lewontin, 1980, p. 248).

Recent comparative studies raise serious doubts about such an interpretation. For example, Kay (1975) has found a close adaptive fit between tooth structure and diet in primates; frugivores, for instance, have small teeth relative to their size, and leaf-eaters have large ones. Indeed, far from there being some overall developmental constraint on tooth size, a particular tooth can vary independently of others in the tooth row, and can do so in a sex-limited manner. Thus Harvey, Kavanagh, and Clutton-Brock (1978) found that the extent of sexual dimorphism in canine size in primates was small in monogamous species, and large in harem-holding species and in those composed of social groups with several adult males.

Such studies, reviewed in Levinton (in press), suggest that allometric growth, the classic example of the importance of developmental constraints in evolution, has been wrongly interpreted. Allometric relations may themselves be the result of selection—they need not imply the existence of strong constraints. What requires further examination is the ease with which allometry can be broken. Only then will we understand the degree to which it is properly interpreted as a constraint.

Use of the comparative method to demonstrate the importance of developmental constraint (rather than selection) in determining a suite of characters is rather more difficult. As discussed, the mere existence of allometry based on adult characters is insufficient for the purpose. Stronger (but still only suggestive) evidence would be provided by an allometric relation among adults of different species which resembled that between the growth stages of a single species. More promising yet are comparative studies of two different taxa whose members have been exposed to a similar range of ecological conditions. Should one taxon show variants of a kind not shown by the other, it would be likely that the latter taxon was subject to some degree of developmental constraint.

A convincing example of this approach is afforded by flowers of monocotyledonous and dicotyledonous plants. In the former, a morphology based on sets of three elements is almost universal. (The grasses are the main exception to this rule.) Nevertheless, some monocotyledonous flowers adapted for pollination by animals have evolved bilateral symmetry. In orchids, the apparent bilateral symmetry is superimposed on a fundamentally three-rayed flower, whereas in cannas the flower retains its tri-radial symmetry, but presents three bilaterally symmetric faces to approaching insects. It is hard to imagine that the maintenance of a fundamentally three-rayed structure is imposed by selection, since the dicotyledons have been exposed to similar selective agents and have

also repeatedly evolved bilaterally symmetrical flowers to attract animals, but do seem to be rather labile in the number of parts of which they are composed. Further examples are discussed briefly by Hilu (1983). Similar instances are common in animals. For example, the irregular echinoids (e.g., sand dollars and heart urchins) evolved rather pronounced bilateral symmetry, presumably as an adaptation to highly directional movement and burrowing. Yet these echinoids retain the fundamental radial symmetry of their sea-urchin ancestors.

We close this section by citing a different way of using the comparative method to reveal developmental constraint. This traces back at least to Bateson's (1894) classical study of meristic variation in teeth, which revealed an important constraint on the response of such linear series to either an increase or a decrease in number. As Bateson showed, the characteristics of individual members of the series are not preserved under such variation; the whole set undergoes coordinated change. This observation applies also to other meristic series, such as vertebrae and digits. Kurtén (1953) has studied correlated variation in quantitative characters of repeated parts and Frankel, Jenkins, Bakowska, and Nelson (1984) and Frankel, Nelson, Bakowska, and Jenkins (1984) have recently found similar phenomena in variation of membranelle number in the oral apparatus of *Tetrahymena*. Because such observations suggest that global constraints affect meristic characters, they may have important implications concerning the mechanisms that generate periodic structures in organisms. It is of particular interest to explore the possibility that some of the correlations in question arise from spatial periodicities established over defined domains (fields) that conform to such constraints as integral wave numbers. It may not prove easy to determine the importance of such a mechanism since secondary modifications, acting before the adult form is achieved, may mask the operation of global constraints upon primary generating mechanisms.

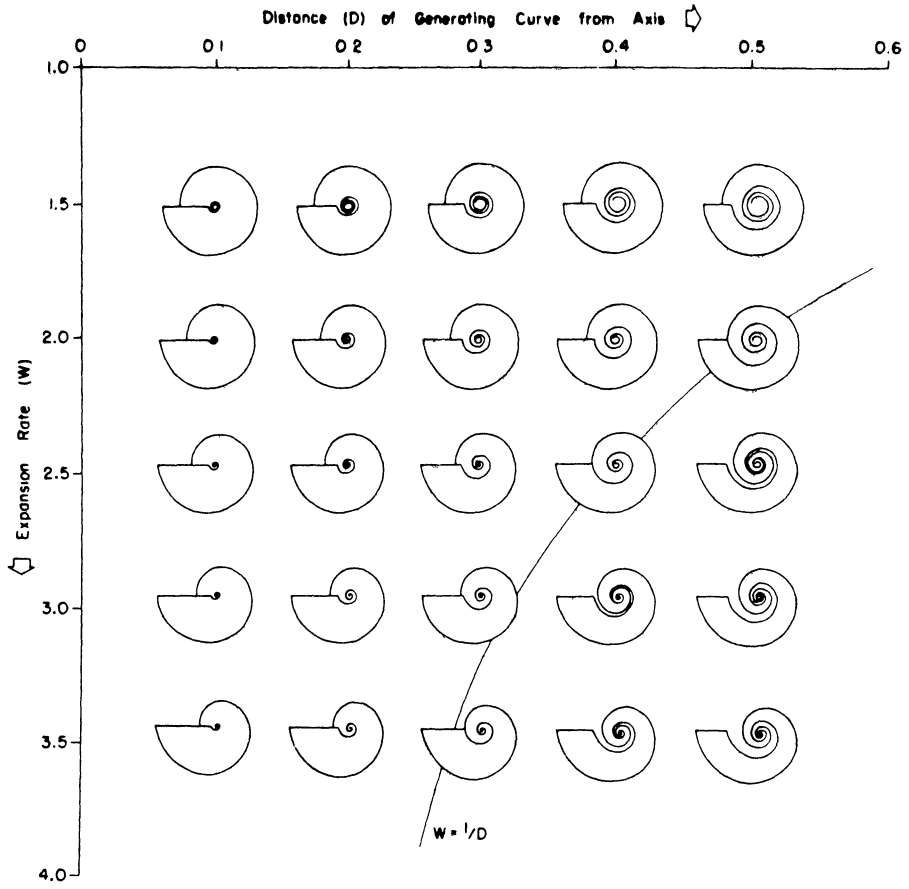
6. AN EXTENDED EXAMPLE: SHELL COILING

Several of the problems and approaches described above can be illustrated by the case of the logarithmically coiled shell common in molluscs, brachiopods, and some foraminifera. The vast majority of these shells grow by following a rather simple logarithmic spiral (Thompson, 1942; Raup, 1966). Bivalved molluscs and brachiopods have two shells, coiling in opposite directions. The path followed by any point on the growing edge of the shell can be described by the simultaneous solution of two linear differential equations, which has made computer simulation of all possible variants straightforward (Raup and Michelson, 1965). Several standard metric characters applicable throughout postlarval development have been defined, and these are closely related to the constants in the fundamental differential equations. When these characters are used to define coordinates of a multidimensional space, it is possible to map the distribution of actually occurring morphotypes (living or fossil). If the coiling parameters change during development, a not uncommon phenomenon, the change may be plotted as a line or trajectory in morphospace.

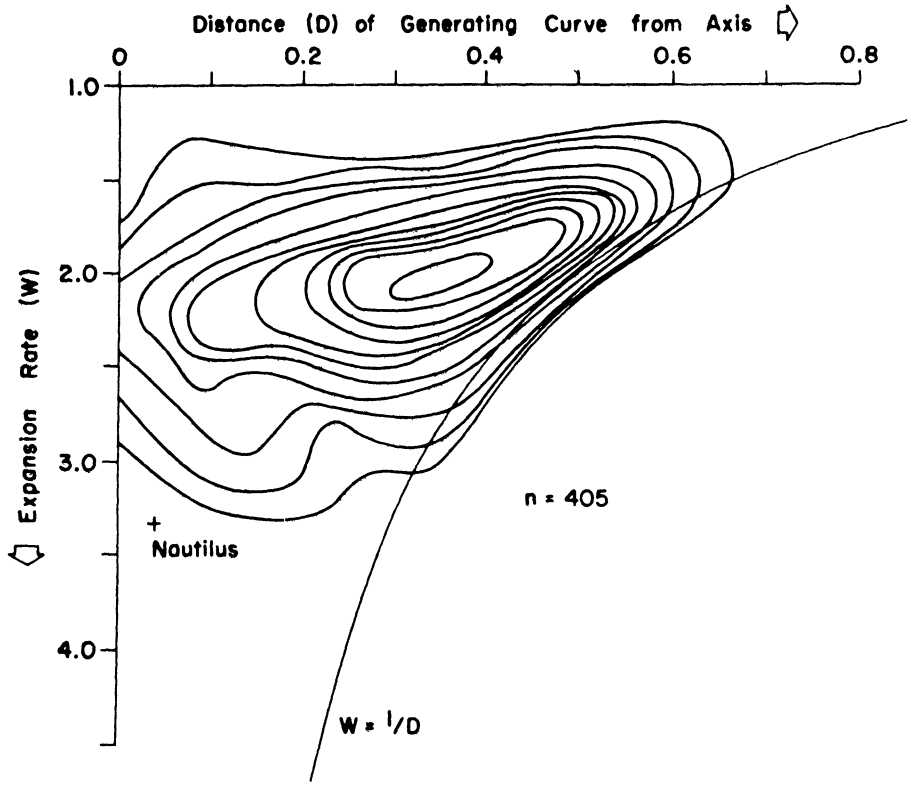
Maps of species occurrence in morphospace provide an ideal tool for tackling questions of developmental constraints, hill-climbing, and the like. An example is given in Fig. 1. Fig. 1A shows a plane surface through the theoretical morphospace. Sketches of the coiled shapes at arbitrary points on this plane are shown. The sketches may be seen as snails in apical view or as planispiral cephalopods (such as *Nautilus*) in lateral view. An important problem with such maps is that it is rarely known whether the coordinates (the metric characters) are truly natural in a genetic sense. That is, it is rarely known whether the organism is coding explicitly for these characters or whether the

FIG. 1. A PORTION OF ONE SURFACE THROUGH THE MORPHOSPACE OF SPIRALLY COILED SHELLS

A, sketches of ideal shells shown at arbitrary points on the surface. B, the occurrence of about 400 extinct ammonoid genera contoured in the same format. The W = 1/D line segregates open coiling from overlapping coiling. From Raup, 1967.



A



B

characters are complex transformations of the fundamental genetic information. Although much is known about the genetics of a number of coiled organisms, especially some pulmonate snails, the genetic reality of the characters used in Fig. 1 has never been tested. Studies of this sort are urgently needed.

Of interest in Fig. 1 is the curved line passing through the lower right portion of the diagrams. To the left of this line, successive coils (whorls) overlap one another whereas to the right of the line, the shell is "open" because successive coils are not in contact. Fig. 1B is a contoured map of the distribution of about 400 genera of extinct ammonoids (cephalopod molluscs). The position of the living cephalopod *Nautilus* is given for reference.

As can be seen in Fig. 1B, nearly all ammonoids fall on the left side of the curved line and thus display overlap between successive whorls. This is clearly a constraint in the evolution of the group but what kind of constraint? In this particular case, the answer is apparently straightforward (Raup, 1967). Evolving lineages can and occasionally do cross the line so there is no reason to believe that open coiling violates any strict genetic or developmental constraint. Rather, the reasons for not crossing the line appear to be biomechanical. Other things being equal, an open coiled shell is much weaker than its involute counterpart. Also, open coiling requires more shell material because the animal cannot use the outer surface of the previous whorl as the inner surface of the new whorl. So there is every reason to conclude that the constraint against open coiling is an adaptive one brought about by simple directional selection. This conclusion is strengthened when one considers the occasional exceptions. For example, the shell of the living pelagic cephalopod *Spirula* has a shape that places it in the lower right corner of Fig. 1 A, B. This shell not only has open coiling but it is also thin-walled and extremely fragile. The explanation lies in the anatomical position of the *Spirula* shell: it is internal, surrounded by a much larger animal, and only provides the animal with buoyancy. As an internal structure, the relative lack of strength is of negligible importance.

The general problem of open coiling among living gastropods has been explored by Rex and Boss (1976). Out of a total of 37,500 species, they found only fifteen species that display open coiling throughout development in an otherwise normal shell. The fifteen are all in the Prosobranchia and are distributed among marine, freshwater, and terresterial forms.

Pulmonate gastropods, which dominate fresh water and terrestrial snail faunas, never show open coiling consistently at the species level. It has been shown, however, that open coiling appears occasionally as a heritable sublethal genetic trait (Richards, 1970) and even as a fairly common genetic variant in some populations (Clark, 1973). For most of the fifteen, consistently open-coiled prosobranch species, Rex and Boss (1976) found reasonable adaptive explanations comparable to that noted above for *Spirula*.

The foregoing examples suggest that the relative paucity of open coiling in molluscs is not the result of a developmental constraint. In some other aspects of the coiled shell, however, a case for developmental or genetic constraints can be made with some confidence. Examples are found among the pholad bivalves, particularly *Teredo* and other boring clams (the so-called shipworms). Most pholads are rock or wood borers and have fairly typical clam shells that grow as two logarithmic spirals in mirror image of each other (H. Roder, pers. commun.). Their shape is well outside the limits of Fig. 1. They bore by a rotary motion which produces a perfectly cylindrical hole. But the boring behavior presents a problem because there is nothing inherently cylindrical about the bivalve shell. The problem has been "solved" in pholad evolution by selecting coiling growth parameters and an orientation of the animal during the boring process which combine in such a way that an approximately circular section of the whole shell is presented to the rock or wood surface to be bored. It is by no means an optimal design from an engineering standpoint but it works quite well. It can be considered optimal *only* if one accepts the idea that the animal is constrained to maintain the basic logarithmic spiral. If this general line of interpretation is correct, we conclude that the functional morphology of the pholad bivalve has evolved within strict

limits of a developmental constraint that favors the maintenance of the logarithmic spiral as the fundamental developmental program.

7. DEVELOPMENT AND EVOLUTION

To conclude, we address three of the larger themes implicit throughout this paper. The first is the extent to which evolutionary stasis can be explained in developmental terms. Developmental considerations of the sorts we have explored do not seem to help in the most paradoxical and interesting cases of evolutionary stasis, namely, those concerning traits for which there is considerable heritable variation in contemporary populations. It is only when stasis results from the absence of the relevant kind of heritable variation that the developmental system comes into question. Even then, one must disentangle cases in which drift or powerful selective forces have consumed the variation (recall our discussion of canalizing selection) from those in which certain features of the developmental system are the primary cause of the stasis. Traits in which heritable variation is (or appears to be) absent, such as the bilateral symmetries discussed above, are therefore of particular interest. An exploration of the role of the developmental system in such cases may well prove to shed light on evolutionary processes.

Second, we turn to the question of the extent to which developmental constraints play a role in accounting for trends and patterns in evolutionary history. Does development merely prevent evolution from following particular paths or does it also serve as a directing force, accounting in part for oriented features of various trends and patterns? We are fully aware that any attempt to account for long-continued evolution in a given direction in terms of some sort of inner drive arouses well-justified suspicions. Historically, the arguments for orthogenesis have often been shoddy. Nonetheless, it should be asked whether developmental systems can play an orienting role.

The difficulty with ascribing trends—or the direction of evolutionary change—to developmental constraints is the possibility that other agencies may cause the phenomena. Mutation pressure and subtle forms of selection may, in fact, underlie evolutionary trends that seem, superficially, to result from constraints of development. We will approach these matters by reference to some concrete examples. A variety of mechanisms at the level of genes or cells (perhaps favored by selection at levels below that of the organism) can have extremely important effects. Since it is now known that parts of the genome can multiply horizontally, out of phase with the rest of the genome (for example, by transposition or by gene conversion), the possibility arises that genetic elements may evolve characteristics that favor their own survival and replication. These characteristics may favor or hinder the survival of the organism, so that we can speak of symbiotic or parasitic DNA. As yet too little is known of the rates of these processes, or of their phenotypic effects, for us to speak with any confidence about their evolutionary relevance. One example of a trend that may have been caused by selection at the genic level is the increase in DNA content in some lineages of plethodontid salamanders (McGregor, 1982). Other examples of similar trends, driven by cellular mechanisms, include the tendency of chromosome number in certain ferns to increase because a doubling of chromosome number can occur rather readily, whereas a subsequent halving is virtually impossible. A similar instance concerns the tendency of B-chromosomes to accumulate in a variety of organisms.

A more extended example, in which selection at the level of cells has significant evolutionary consequences, occurs in the rapid restoration of the wild phenotype in cultures of *Drosophila melanogaster* with the *bobbed* mutation, a phenomenon known as "magnification" (Tartoff, 1975). The *bobbed* mutant, recognized by its shortened bristles, is caused by a deficiency in the number of ribosomal-RNA gene copies that are tandemly duplicated on the X-chromosome. An extreme deficiency of rRNA can restrict the rate of protein synthesis and cell-division during development. In the development of the germ line of an individual, variation between cells in the number of rRNA gene copies can be generated by unequal recombination during sister-chromatid exchange in mitosis. Increased proliferation rates of germ cells with

more rRNA genes tends to reconstitute the normal genotype, a process that can be detected even during the reproductive lifetime of individual males (R. Frankham, pers. commun.). In this case, natural selection against the more extreme mutant individuals would also act to restore the number of rDNA gene copies to their normal range.

Two separate issues are raised by these examples. The first is whether biases on the production of variant phenotypes (i.e., developmental constraints) such as those just illustrated cause evolutionary trends or patterns. Since the classic work of Fisher (1930) and Haldane (1932) established the weakness of directional mutation as compared to selection, it has been generally held that directional bias in variation will not produce evolutionary change in the face of opposing selection. This position deserves reexamination. For one thing, our examples (like many discussed during the last twenty years—e.g., White, 1965; Cox and Yanofsky, 1967) concern biased variation *in the genetic mechanism itself.* If such directed variation accumulates —as the results regarding DNA quantity and chromosome numbers suggest—one obtains a very effective evolutionary ratchet. For another, such directional biases may not stand in contradiction to the Fisher-Haldane point of view: within reasonable limits, neither the increase in cellular DNA content nor that in chromosome number is known to have deleterious effects at the organismic level. The interplay with selection may be complex: increased DNA content in plethodontid salamanders correlates with increased cell size and with lower average ambient temperature (G. L. Stebbins, pers. commun.). Still, these may both be significant cases of directional change in which the direction of change owes more to the mechanisms of development and mutation than to directional selection.

Some biologists (e.g., R. Lewontin, pers. commun.) argue that evolution is best viewed as a history of organisms finding devious routes for getting around constraints. Even a universal constraint, like the one (discussed briefly in Section 2) arising from the law of the lever, can be evaded, in a sense, by switching to another mode of locomotion, altering the overall skeletal configuration, or increasing the muscle mass. To evade such constraints—e.g., to increase both the load which a member can bear and the speed with which it can be moved—requires extraordinary reconstruction of the organism. But such reconstruction, although rare, does occur, and it may be of considerable evolutionary importance.

These considerations demonstrate the need for extreme caution in claiming that such constraints are responsible for evolutionary trends. Even when the evidence is strongest—for example, when the trend in question favors apparently less fit forms—selection may play the dominant role. The fact that selection is a multi-level process, capable of acting at the levels of genes, cells, individuals, demes, species, and so on, means that extremely subtle mechanisms for generating trends and patterns must be taken into account. Among these are intraspecific competition in the form of sexual selection (Lande, 1981) or of competition for other resources, both of which can cause continued change in a single direction despite a lowering of adaptedness for interspecific competition (see also Burian, 1983). Given the power and subtlety of selection and our current ignorance of the mechanisms of development, it will often prove impossible to resolve questions regarding the precise sources of evolutionary patterns.

The second issue raised by the preceding examples is whether constraints like those favoring high chromosome number or high copy number of rRNA genes should be ascribed to the developmental system. As the discussion of the *bobbed* mutant shows, the relevant constraints may be caused by selection acting at the genic, cellular, or other levels. And yet, since the cells of eukaryotes will operate efficiently only if they contain enough ribosomes, the developmental systems of all multicellular organisms will be biased toward the production of a sufficient number of copies of rRNA genes. Whatever mechanisms occur in different cases, this bias will remain. In consequence, it is at best difficult and at worst impossible to tease apart the separate contributions of developmental and selective factors in the etiology of this constraint, with its influence on evolutionary pattern. This sort of difficulty is quite common and must be taken into account in any

analysis of the interplay of selection and development.

Our final question concerns the extent to which genetic mechanisms themselves have evolved so as to serve an evolutionary function. There is no doubt that the nature of the genetic mechanisms in a taxon affect its evolutionary trajectory. For example, although prokaryotes can acquire drug resistances and new metabolic abilities by modifying their own genes step by step (Mortlock, 1984), they typically do so by acquiring the relevant genes on a plasmid from other bacteria. Such a capacity to sidestep the long process of mutation and selection enormously increases their potential for adaptive evolution. The point has considerable practical importance: failure to appreciate the degree to which bacteria are specifically organized so as to meet novel environmental challenges with extremely rapid evolution has led to serious mistakes in medicine and agriculture.

If even the lowly prokaryotes have developed special mechanisms that facilitate their evolution, one should not be surprised to find that higher organisms employ even more effective strategies for evolution. To be sure, eukaryotic processes differ from those of bacteria. For example, lateral transfer of genes is far rarer, and probably far less consequential, in eukaryotes than in prokaryotes. Nonetheless, higher organisms do possess their own distinctive specializations promoting the evolution of particular genes in some cases, that of the whole genome in others. Indeed, diploid sexuality may be seen in this light: it sorts the genes of a lineage into a gene pool in a way that allows transfer of advantageous gene combinations into sublineages without the transfer of plasmids. Turning to molecular mechanisms, geneticists are now in the process of describing a vast array of sophisticated enzymes to cut, splice, digest, rearrange, mutate, reiterate, edit, correct, translocate, invert, and truncate particular gene sequences (Campbell, 1983). Direct enzymatic intervention into the structure of the DNA turns out to be indispensable for the evolution of many significant sorts of eukaryotic genes, such as multigene families (Hood, Campbell and Elgin, 1975). DNA-processing enzymes also bring about highly particular and nonrandom changes in ordinary genes. Indeed, some enzyme pathways are capable of modifying the structure of a gene in direct response to specific relevant stimuli from the environment (Campbell, 1982), so permitting what Echols (1981) calls "inducible evolution."

This responsiveness of the genome is, at least in part, a product of selection acting at lower levels: transposons almost certainly evolved initially as selfish DNA and not because they could be coopted into mechanisms that speed up bacterial responses to drugs or to new metabolites. Nonetheless, it is worth inquiring whether mechanisms fostering genetic responsiveness to environmental challenge have evolved because of the speed with which they enable lineages to adapt to changing environments. Such a process of adaptation would resemble that by which the long legs of antelopes evolved because of their effects on the speed of running. Put differently, is it the "function" of certain genetic and developmental mechanisms to facilitate evolution or to increase its rate? If so, selection has presumably operated between *populations* and so has enabled those populations whose genetic mechanisms allowed rapid or favorable evolution to proliferate or survive in competition with others. This does happen at least occasionally. In the chemostat, mutable strains replace less mutable ones. Again, taxonomic distributions of higher organisms suggest that populations that wholly abandon sexual for asexual reproduction have a short evolutionary future (Maynard Smith, 1978).

A major difficulty stands in the way of this approach to the plasticity and directive power of the genome. It stems from the fact that selection between populations or species is likely to be a weak force compared to selection between individuals or genes. If genetic structures are to evolve because they promote evolution, this "weakness" of selection between populations and species must be compensated by the cumulative advantageous effect of the operation of those structures over long spans of evolutionary time (for a discussion, see Campbell, in press). We disagree among ourselves about the likelihood that attaches to such a scenario, but we agree that to test it properly one must analyze the evolution of genetic mechanisms

by means of models that explicitly appraise the strength and effect of selection at all of the relevant levels.

The issues raised in this section cannot yet be resolved. To advance the investigation into such issues, the present review has presented a clear definition of developmental constraints, clarified the problems encountered in identifying them and distinguishing them from selective constraints, and presented a series of cases and methods useful in attacking such problems. The examples illustrating the interplay between developmental processes and selection operating simultaneously at various levels are of particular interest in that they enforce the need for further clarification of the issues. If we are to understand the role of developmental constraints in evolution, it will be necessary to see more clearly than at present in what ways development and selection interact to yield constraints. Only then will it be possible to determine the best method for factoring out the respective contributions of development and selection in the generation of evolutionary pattern. The present review is intended as a step in this direction.

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REFERENCES

ALBERCH, P. 1982. Developmental constraints in evolutionary processes. In J. T. Bonner (ed.), *Evolution and Development*, p. 313-332. Springer-Verlag, Berlin.

——. 1983. Morphological variation in the neotropical salamander genus *Bolitoglossa*. *Evolution*, 37: 906-919.

ALBERCH, P., and E. A. GALE. 1983. Size dependence during development of the amphibian foot. Colchicine-induced digital loss and reduction. *J. Embryol. Exp. Morphol.*. 76: 177-197.

——, and ——. 1985. A developmental analysis of an evolutionary trend: Digital reduction in amphibians. *Evolution*, 39: 8-23.

ATCHLEY, W. R., J. J. RUTLEDGE, and D. E. COWLEY. 1981. Genetic components of size and shape. II. Multivariant covariance patterns in the rat and mouse skull. *Evolution*, 35:1037-1055.

BAILEY, D. 1956. A comparison of genetic and environmental principal components of morphogenesis in mice. *Growth*, 20: 63-74.

BATESON, W. 1894. *Materials for the Study of Variation Treated with Especial Regard to Discontinuity in the Origin of Species*. Macmillan, London.

BURIAN, R. M. 1983. "Adaptation." In M. Grene (ed.), *Dimensions of Darwinism*, p. 287-314. Cambridge University Press, Cambridge.

CAMPBELL, J. H. 1982. Autonomy in evolution. In R. Milkman (ed.), *Perspectives on Evolution*, p. 190-201. Sinauer, Sunderland.

——. 1983. Evolving concepts of multigene families. *Curr. Top. Biol. Med. Res.*, 10: 401-417.

——. 1985. A biological interpretation of evolution. In B. H. Weber and D. J. Depew (eds.), *Biology and New Philosophy of Science*, p. 133-167. MIT Press, Cambridge.

CARSON, H. L., and R. LANDE. 1984. Inheritance of a secondary sexual character in *Drosophila silvestris*. *Proc. Natl. Acad. Sci. USA*, 81:6904-6907.

CARSON, H. L., F. C. VAL, C. M. SIMON, and J. W. ARCHIE. 1982. Morphometric evidence for incipient speciation in *Drosophila silvestris* from the Island of Hawaii. *Evolution*, 36: 132-140.

CHARLESWORTH, B., R. LANDE, and M. SLATKIN. 1982. A neo-Darwinian commentary on macroevolution. *Evolution*, 36: 474-498.

CHARNOV, E. L. 1982. *The Theory of Sex Allocation*. Princeton University Press, Princeton.

CHEVERUD, J. M. 1982. Phenotypic, genetic, and environmental morphological integration in the cranium. *Evolution*, 36: 499-516.

CHEVERUD, J. M., J. J. RUTLEDGE, and W. R. ATCHLEY. 1983. Quantitative genetics of development: genetic correlations among age-specific trait values and the evolution of ontogeny. *Evolution*, 37: 895-905.

CLARK, A. H. 1973. The freshwater molluscs of the Canadian Interior Basin. *Malacologia*, 13: 1-509.

CLARKE, C. A., and P. M. SHEPPARD. 1963. Interactions between major genes and polygenes in the determination of the mimetic patterns of *Papilio dardanus*. *Evolution*, 17: 404-413.

COX, E. C., and C. YANOFKSY. 1967. Altered base ratios in DNA of an *Escherichia coli* mutator strain. *Proc. Natl. Acad. Sci. USA*, 58: 1895-1902.

ECHOLS, H. 1981. SOS functions, cancer and inducible evolution. *Cell*, 25: 1-2.

FALCONER, D. S. 1981. *Introduction to Quantitative Genetics*. 2nd ed. Longmans, London.

FISHER, R. A. 1930. *The Genetical Theory of Natural Selection*. Clarendon Press, Oxford.

FRANKEL, J. E., L. M. JENKINS, J. BAKOWSKA, and E. M. NELSON. 1984. Mutational analysis of patterning of oral structures in *Tetrahymena*. I. Effects of increased size on organization. *J. Embryol. Exp. Morphol.* 82: 41-66.

FRANKEL, J., E. M. NELSON, J. BAKOWSKA, and L. M. JENKINS. 1984. Mutational analysis of patterning of oral structures in *Tetrahymena*. II. A graded basis for the individuality of intracellular structural arrays. *J. Embryol. Exp. Morphol.*, 82: 67-95.

GARCIA-BELLIDO, A. 1975. Genetic control of wing disc development in *Drosophila*. In *Cell Patterning (Ciba Foundation Symposium No. 29)* p. 161-182. Elsevier, Amsterdam.

——. 1983. Comparative anatomy of patterns in the genus *Drosophila*. In B. C. Goodwin, N. Holder and C. C. Wylie (eds.), *Development and Evolution*, p. 227-255. Cambridge University Press, Cambridge.

GLASS, L., and A. T. WINFREE. 1984. Discontinuities in phase resetting experiments. *Am. J. Physiol.*, 246: R251-R258.

GOODWIN, B. C. 1984. A relational or field theory of reproduction and its evolutionary implications. In M.-W. Ho and P. T. Saunders (eds.), *Beyond Neo-Darwinism*, p. 219-241. Academic Press, New York.

GOULD, S. J., and N. ELDREDGE. 1977. Punctuated equilibria: the tempo and mode of evolution reconsidered. *Paleobiology*, 3: 115-151.

HALDANE, J. B. S. 1932. *The Causes of Evolution*. Longmans, Green, London.

——. 1954. The statics of evolution. In J. Huxley, A. C. Hardy, and E. B. Ford (eds.), *Evolution as a Process*, p. 109-121. Allen & Unwin, London.

HALL, B. G. 1982. Evolution of a regulated operon in the laboratory. *Genetics*, 101:335-344.

HAMILTON, W. D. 1967. Extraordinary sex ratios. *Science*, 156: 477-488.

HARVEY, P. H., M. KAVANAGH, and T. H. CLUTTON-BROCK. 1978. Sexual dimorphism in primate teeth. *J. Zool.*, 186: 475-485.

HILU, K. 1983. The role of single-gene mutations in the evolution of flowering plants. *Evol. Biol.*, 16: 97-128.

HOOD, L., J. H. CAMPBELL, and S. C. R. ELGIN. 1975. The organization, expression, and evolution of antibody genes and other multigene families. *Annu. Rev. Genet.*, 9: 305-353.

HUXLEY, J. S. 1932. *Problems of Relative Growth*. MacVeagh, London.

KAUFFMAN, S. 1983a. Developmental constraints: Internal factors in evolution. In B. Goodwin, N. Holder, and C. C. Wylie (eds.), *Development and Evolution*, p. 195-225. Cambridge University Press, Cambridge.

——. 1983b. Filling some epistemological gaps: New patterns of inference in evolutionary theory. In P. D. Asquith and T. Nickles (eds.), *PSA 1982*, Vol. 2, p. 292-313. Philosophy of Science Association, East Lansing.

KAUFFMAN, S., R. SHYMKO, and K. TRABERT. 1978. Control of sequential compartment formation in *Drosophila*. *Science*, 199: 259-270.

KAY, R. F. 1975. Functional adaptations of primate molar teeth. *Am. J. Phys. Anthropol.*, 43: 195-216.

KURTÉN, B. 1953. On the variation and population dynamics of fossil and recent mammal populations. *Acta Zool. Fenn.*, 76: 1-122.

LANDE, R. 1978. Evolutionary mechanisms of limb loss in tetrapods. *Evolution*, 32: 73-92.

——. 1979. Quantitative genetic analysis of multivariate evolution, applied to brain:body size allometry. *Evolution*, 37: 402-416.

——. 1981. Models of speciation by sexual selection on polygenic traits. *Proc. Natl. Acad. Sci. USA*, 78: 3271-3275.

LANDE, R., and S. J. ARNOLD. 1983. The measurement of selection on correlated characters. *Evolution*, 37: 1210-1226.

LEAMY, L. 1977. Genetic and environmental correlations of morphometric traits in randombred house mice. *Evolution*, 31: 357-369.

LEVINTON, J. In press. Developmental constraints and evolutionary saltations: a discussion and critique. In J. P. Gustafson, G. L. Stebbins, and F. Ayala (eds.), *Seventeenth Stadler Genetics Symposium: Genetics, Development, and Evolution*. Plenum Press, New York.

LEWIS, E. B. 1978. A gene complex controlling segmentation in *Drosophila*. *Nature*, 276: 565-

570.

LEWONTIN, R. C. 1980. Adaptation. *The Encyclopedia Einaudi*, Milan. [Reprinted in E. Sober (ed.), *Conceptual Issues in Evolutionary Biology*, p. 235-251. MIT Press, Cambridge, 1984.]

MADEN, M. 1981. Experiments on anuran limb buds and their significance for principles of vertebrate limb development. *J. Embryol. Exp. Morphol.*, 63: 243-265.

MAYNARD SMITH, J. 1978. *The Evolution of Sex.* Cambridge University Press, Cambridge.

MAYNARD SMITH, J., and R. J. G. SAVAGE. 1956. Some adaptations in mammals. *J. Linn. Soc.*, 42: 603-622.

MAYNARD SMITH, J., and K. C. SONDHI. 1960. The genetics of a pattern. *Genetics*, 45: 1039-1050.

MCGREGOR, H. C. 1982. Big chromosomes and speciation amongst amphibia. In G. A. Dover and R. B. Flavell (eds.), *Genome Evolution*, p. 324-341. Academic Press, London.

MEINHARDT, H. 1977. A model of pattern formation in insect enbryogenesis. *J. Cell Sci.*, 23: 117-139.

MITCHESON, G. 1977. Phyllotaxis and the Fibonacci series. *Science*, 196: 270-275.

MORTLOCK, R. P. 1984. The utilization of pentitols in studies of the evolution of enzyme pathways. In R. P. Mortlock (ed.) *Microorganisms as Model Systems for Studying Evolution*, p. 1-21. Plenum Press, New York.

NIJHOUT, H. F. 1978. Wing pattern formation in Lepidoptera: a model. *J. Exp. Zool.*, 206: 119-136.

NÜSSLEIN-VOLHARD, C. 1979. Maternal effect mutations that alter the spatial coordinates of the embryo of *Drosophila melanogaster.* In S. Subtelny and I. Konigsberg (eds.), *Determinants of Spatial Organization*, p. 185-211. Academic Press, New York.

NÜSSLEIN-VOLHARD, C., and E. WIESCHAUS. 1980. Mutations affecting segment number and polarity in *Drosophila. Nature*, 287: 795-801.

ODELL, G., F. G. OSTER, B. BURNSIDE, and P. ALBERCH. 1981. The mechanical basis of morphogenesis. *Dev. Biol.*, 85: 446-462.

OSTER, G., and P. ALBERCH. 1982. Evolution and bifurcation of developmental programs. *Evolution*, 38: 444-459.

OUWENEEL, W. I. 1976. Developmental genetics of homoeosis. *Adv. Genet.*, 18: 179-248.

PEDLEY, T. J. 1977. *Scale Effects in Animal Locomotion.* Academic Press, London.

RAUP, D. M. 1966. Geometric analysis of shell coiling: General problems. *J. Paleontol.*, 40: 1178-1190.

———. 1967. Geometric analysis of shell coiling: Coiling in ammonoids. *J. Paleontol.*, 41: 43-65.

RAUP, D. M., and S. J. GOULD. 1974. Stochastic simulation and evolution of morphology—towards a nomothetic paleontology. *System. Zool.*, 23: 305-332.

RAUP, D. M., and A. MICHELSON. 1965. Theoretical morphology of the coiled shell. *Science*, 147: 1294-1295.

RENDEL, J. M. 1959. Canalization of the scute phenotype of Drosophila. *Evolution*, 13: 425-439.

REX, M. A., and K. J. Boss. 1976. Open coiling in recent gastropods. *Malacologia*, 15: 289-297.

RICHARDS, C. S. 1970. Genetics of a molluscan vector of schistosomiasis. *Nature*, 227: 806-810.

RISKA, B., W. R. ATCHLEY, and J. J. RUTLEDGE. 1984. A genetic analysis of target growth in mice. *Genetics*, 107: 79-101.

SANDER, K. 1975. Pattern specification in the insect embryo. In *Cell Patterning (Ciba Foundation Symposium No. 29)*, p. 241-263. Elsevier, Amsterdam.

SAUNDERS, P. T., and M-W. Ho. 1984. The complexity of organisms. In J. W. Pollard (ed.), *Evolutionary Theory: Paths into the Future*, p. 121-139. Wiley, New York.

SHEPPARD, P. M. 1959. *Natural Selection and Heredity.* Hutchinson, London.

SINNOTT, E. W. 1935. Evidence for genes controlling shape. *Genetics*, 20: 12-21.

SLACK, J. 1980. A serial threshold theory of regeneration. *J. Theoret. Biol.*, 82: 105-140.

SPURWAY, H. 1949. Remarks on Vavilov's law of homologous variation. *La Ricerca Scientifica*, Suppl.: 3-9.

TARTOF, K. D. 1975. Redundant genes. *Annu. Rev. Genet.*, 9: 355-385.

THOMPSON, D'A. W. 1942. *On Growth and Form.* 2nd ed. Cambridge University Press, Cambridge.

TURING, A. M. 1952. The chemical basis of morphogenesis. *Phil. Trans. Roy. Soc., B*, 237: 37-72.

TURNER, R. J. G. 1977. Butterfly mimicry: the genetical evolution of an adaptation. *Evol. Biol.*, 10: 163-206.

VAN VALEN L. 1962. A study of fluctuating asymmetry. *Evolution*, 15: 125-142.

VAVILOV, N. I. 1922. The law of homologous series in variation. *J. Genet.*, 12: 67-87.

WADDINGTON, C. H. 1957. *The Strategy of the Genes.* Allen & Unwin, London.

———. 1960. Experiments on canalizing selection. *Genet. Res.*, 1: 140-150.

WAGNER, G. P. 1984. On the eigenvalue distribution of genetic and phenotypic dispersion matrices: Evidence for a nonrandom organization of quantitative character variation. *J. Math.*

Biol., 21: 77-95.

WAKIMOTO, B., and T. C. KAUFMAN. 1981. Analysis of larval segmentation in lethal genotypes associated with the *Antennapedia* gene complex in *Drosophila melanogaster*. *Dev. Biol.*, 81: 51-64.

WHITE, M. J. D. 1965. Principles of karyotype evolution in animals. In S. J. Geerts (ed.), *Proc. XI. Int. Cong. Genet.*, Vol. 2, p. 391-397. Pergamon Press, Oxford.

WINFREE, A. T. 1980. *The Geometry of Biological Time*. Springer-Verlag, New York.

WINFREE, A. T., and S. H. STROGATZ. In press. Organizing centers for waves in excitable media. *Science*.

WOLPERT, L. 1981. Positional information and pattern formation. *Phil. Trans. Roy. Soc.*, *B*, 295: 441-450.

WRIGHT, S. 1968. *Evolution and the Genetics of Populations, Vol. I: Genetic and Biometric Foundations*. University of Chicago Press, Chicago.