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Epigenomics: The New Science of Functional and Evolutionary Morphology

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Abstract—Organisms are more than the genes that look after their assembly. Chemical and mechanical inputs from the environment, epigenomic (≈epigenetic) cues, also have an effect on the final phenotype. In fact, continued environmental influences on the adult phenotype continue to affect its characteristics. Despite its importance, it is a mistake to turn then to epigenomics as a causative agent of evolutionary modification. Within a biological hierarchy, higher levels result from lower-level processes (genes up to phenotype), and lower levels result from higher-level processes (natural selection of phenotypes down to gene pools), respectively, upward and downward causation. Predictable epigenomic cues are assimilated into the genome. The evolved genome therefore incorporates epigenomic cues or the expectation of their arrival, placing the current genome in the position of determining how much epigenomic information is included, what epigenomic information is incorporated, and when epigenomic information initiates gene expression during morphogenesis of the phenotype. Consequently scientific explanations of changes in phenotypes (*e.g.*, morphological design) are of two kinds, *causes* and *boundary conditions.* Causes are the events directly involved in producing changes in the state of a biological system; they act within limits or constraints, the boundary conditions. Confusion between these two types of explanation has misled some to equate epigenomic cues, which are boundary conditions, with natural selection, which is a causative explanation. Such confusion extends outside of biology *per se* where the consequences of non-equilibrium thermodynamics or chaos complexity unfortunately have been championed for their challenge to biological processes. However, because functional and evolutionary morphology employs analytical tools that describe the boundary conditions set by an integrated adaptation, the discipline is most favourably suited to providing explanations of biological diversity and evolution.

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> ". . .organisms, which we took to be primary examples of living nature, have faded away to the point where they no longer exist as fundamental and irreducible units of life. Organisms have been replaced by genes and their products as the basic elements of biological reality."
>
> — a lament by Brian Goodwin

INTRODUCTION

Certainly one of the current afflictions in biological sciences is the attitude that organisms can be reduced to just the properties of their genes. We see this in many forms. As the new century dawned, the separate human genome projects concluded with a description of the basic human genetic code. With the conclusion or near conclusion of genome descriptions of fruit fly, nematode, and a rapidly growing number of other organisms, the number of genome descriptions will soon reach the hundreds. Enthusiastic molecular biologists proclaim that now we have entered a 'post-genomic' age. The irony of this claim escapes them. With the DNA descriptions of only half a dozen species in hand out of perhaps 14 million animal species (Gibbs, 2001), such declarations seem premature. But such giddy claims by reductionist biologists have gone well beyond this. Now we are encouraged to find biological insights beyond the genes in proteomics, where we are awash in gene products.

The report of this collapse into reductionism offered by Brian Goodwin (Goodwin, 1994) at the top of this paper is a refreshing counterpoint to this reductionism. It reiterates what others have warned of before (Mayr, 1982; Russert-Kraemer and Bock, 1989), that organisms cannot be reduced to just the properties of their genes. Genes make sense only within the context of the whole organism and more goes into the making of the whole organism than just its genes. More goes into the finished phenotype of an organism than just the products of DNA-nutrition, morphogenetic events, immediate environment, to name a few. Unfortunately, Goodwin and others (*e.g.*, Kauffman, 1993) make the same mistake of extrapolation made early in the last century by D'Arcy Thompson (Thompson, 1917), namely that physical forces remain unknown to natural selection, and therefore physical forces are a separate engine of evolution.

As functional and evolutionary morphologists, we may find ourselves between these extremes. We do not expect to reduce the workings of an organism to its genes, nor do we expect the organism to be unprepared to meet and incorporate the physical/chemical influences in its environment. Certainly, events above the level of the genes influence the final outcome of embryonic development. But the way we think about these events, their influence on development, and their significance for evolution need to be more carefully incorporated into modern ideas about historical events. Functional and evolutionary morphologists are particularly well placed now to contribute to this task, as I will argue in this paper.

MORPHOGENESIS

Epigenomics

In contrast to 'genetics', Waddington (Waddington, 1942) coined the term 'epigenetics' in an attempt to focus attention on the processes above the level of the genes that bridge genes and phenotype. Within the hierarchy of biological systems, higher levels require for their implementation specific lower-level processes, 'upward causation' (*sensu* Campbell, 1974). Attempts to decipher these processes have focused primarily upon immediate gene influences and morphogenetic events, as Waddington himself illustrated in his later book on the subject, 'New Patterns in Genetics and Development' (Waddington, 1962). When pressed, most geneticists will likely concede the importance of events away from DNA in shaping the phenotype. However, such significant contributions to the phenotype often lie buried in working definitions. To some, epigenetics means nuclear inheritance not based on differences in DNA sequence; to others, epigenetics belongs in the province of expressed nucleic acid information (Lederberg, 1958).

Although serviceable, these views of epigenetic events tend to be very provincial. They neglect the current consequences of past history, and underestimate the non-genetic contributions to the phenotype. Perhaps, those working with animal behaviour have been most ready to include non-genetic influences in formulation of adult behaviours (phenotype). The development of bird songs (*e.g.*, Konishi, 1965; Marler, 1990) and of offspring imprinting (*e.g.*, Lorenz, 1965) would be a few examples. Similarly, morphologists are in a position to recognise the importance of non-genetic features that contribute to the phenotype of an organism and how it evolves. To do so, and place epigenetics in a modern idiom, I adopt and slightly expand on the term **epigenomics**, meaning the analysis of the normal non-genetic processes that influence the characteristics of the phenotype during the lifetime of the organism and the historical influences included. These events occur above (hence epi-) the level of the DNA (hence genomic). Note that, because the phenotype is also an historical product, evolutionary events important to epigenomics must similarly be incorporated into our analysis.

Taking Shape

Examples of non-genetic contributions to the phenotype have been known for some time, have been repeated frequently in scientific publications, and have received extensive reviews (Hall, 1970). The sex of many reptiles depends upon the temperature, or schedule of temperatures, the embryos experience while in the egg (Webb and Cooper-Preston, 1989). Nutritional deficiencies lead to phenotypic changes. Calcium deficiencies during infancy lead to rickets. In humans, bound feet, wrapped skulls and cradle boards all produce modified mechanical demands which result in modifications of the skeleton (Halstead and Middleton, 1973). Careful experimental manipulations illustrate the importance of mechanical events in the differentiation of the phenotype. Leg muscles of the developing chick contract

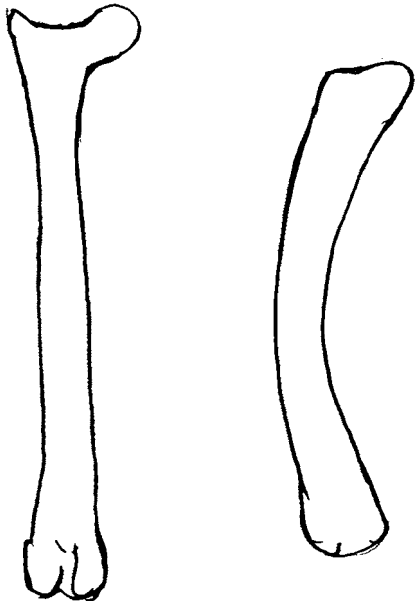

Figure 1. Chick femur. Normal (left) and experimental (right) wherein the musculature, and hence intermittent mechanical twitching, was detached from the developing leg while in the egg. Drawn from descriptions in Murray (1936).

irregularly while still in the egg, thereby producing an intermittent environment of mechanical stresses experienced by the femur (and other leg bones). If deprived of this mechanical environment, by removing embryonic muscles or growing the femur as an explant, then the developing femur is misshapen; its diaphysis is bowed, and its ends indistinct (Fig. 1) (Murray, 1936). Removing the temporalis jaw muscles and/or the cervical muscles in-day-old rats resulted (3-5 months) in morphological deficiencies later; the coronoid process was lost as were skull ridges at the site of what would be the muscle origin (Fig. 2) (Washburn, 1947). Less radical interventions in the mechanical environment produced by muscles have involved simply denervation of limb muscles, which similarly produce deficiencies in the bony phenotype (Fig. 3) (Lanyon, 1980).

In all these experiments, the genome remained unaltered; only the environment of mechanical influences was modified. These are influences outside the genes; part of the epigenomic environment that in turn controls selective gene expression. But these epigenomic contributions are more than just mechanical or nutritional in character. When grown in a bacteria-free environment, the usually leafy marine alga *Ulva* instead becomes filamentous (Provasoli and Pintner, 1980). A rotifer, when placed in an environment with its natural predators, grows protective spine-like projections (Fig. 4) (Beauchamp, 1952; Gilbert, 1966, 1980; Stemberger and Gilbert, 1984; Azgarese and Marinone, 1992). Biotic factors in the environment affect phenotypic outcomes. Ironically, the genes do not initiate these morphological

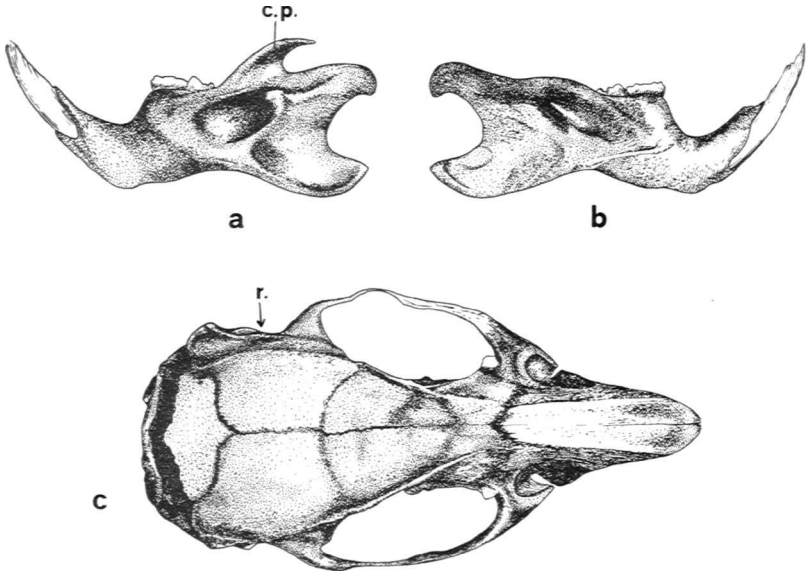

Figure 2. Rat skull. Muscles in tact (normal) or removed or detached from attachments. Mandible with (a) and without (b) attachment of temporalis. Note loss of coronoid process (c.p.). Skull, dorsal view (c), with (left side) and without (right side) temporalis muscle. Note loss of bony ridges (r.). From Dullemeijer (Dullemeijer, 1974), after Washburn (1947).

modifications to serve in a hostile environment, but instead the biotic information from the environment itself initiates gene action.

EPIGENOMICS AND EVOLUTION

Such epigenomic cues are well studied in embryonic development. Early in the 20th century, the mechanical and chemical influences of adjacent embryonic tissues were examined for their coordinated effects on morphogenetic outcomes (Lillie, 1930; Spemann, 1938). In fact, some have seen epigenomics (epigenetics) as centered on an 'analysis of development' and the elucidation of 'mechanisms by which genes express their phenotypic effects' (Hall, 1978). Certainly this is reflected in the current examination of epigenomics at the molecular level (*e.g.*, Riddihough and Pennisi, 2001, and related papers).

Although epigenomics has been recognised to hold significance for evolutionary events (Hall, 1983), the link between the two has largely been seen as a search for mechanisms by which morphogenetic cues activate gene expression producing adaptive features, or the ways in which epigenomic constraints limit or plasticity enhances phenotypic outcomes and thereby affect evolutionary possibilities (Langille and Hall, 1989). But epigenomic events do not cease when strictly embryonic processes are finished. For example, based upon a careful structural and functional analysis (Dullemeijer, 1956; Dullemeijer, 1959), the patterns of interaction

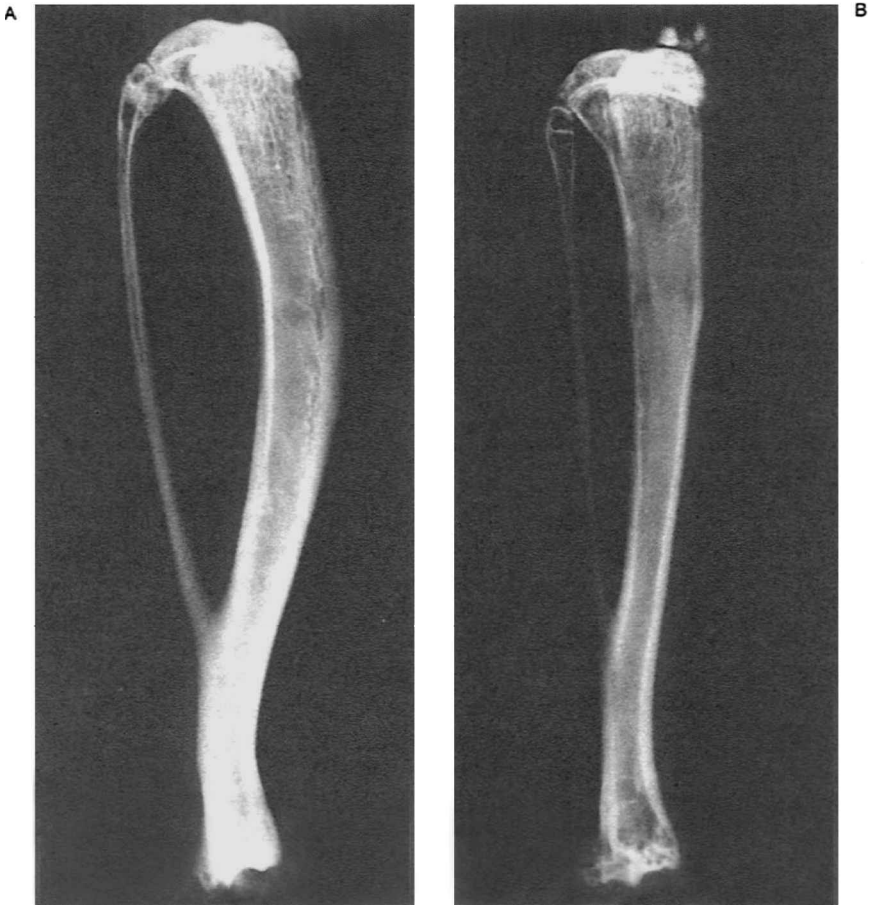

Figure 3. Radiographs of rat tibia and fibula, normal (left) and after denervation (right) of leg muscles during growth. Note loss of bone density and shape. From Lanyon (1980).

of phenotypic elements can be represented by a model of the adult skull of a venomous snake (Fig. 5), (Dullemeijer, 1968; Dullemeijer, 1970). To perform properly and deliver a successful envenomating bite, the structural and functional integrity of the skull elements must be maintained.

One way to evaluate the performance of a system is to compare it to an optimal engineering design (Zweers, 1979). Although limitations occur for use of this method in an evolutionary setting (Garland, 1998), optimisation methods help clarify the important elements. For example, using a basic comparative method, hypotheses about functional advantages in avian cranial design have been proposed (Bout, 2002).

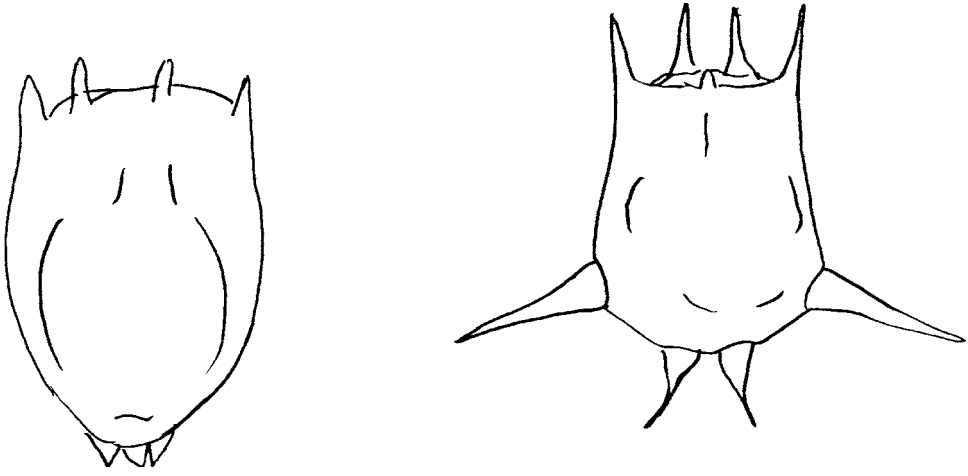

Figure 4. Rotifer (*Brachionus*) phenotype before (left) and after (right) exposure to its natural predator (*Asplanchna*), also a rotifer. After Gilbert (1966).

Downward Causation

Another way to evaluate the performance of a biological system is to compare its success within a biological context, namely within the context of its interaction with the environment (Bock, 1979). The consequence of this interaction is that those individuals possessing more suitable phenotypic characteristics, on average, fare better and survive (Darwin, 1859) carrying forward both the set of phenotypic characteristics and their lower level genotype. But the consequence of natural selection arising out of higher-level interactions (phenotype, populations) is to alter the design of lower levels within the hierarchy, namely a change in the subsequent gene pool. Consequently, natural selection, and the boundary conditions in which it operates, affect and alter the genome, or more particularly the pool of genomes that characterise a population. Stated another way, in terms of hierarchies, reductionist explanations represent an 'upward causation' (*sensu* Campbell, 1974), genes to organism, in that form-function features of higher levels are explained as the result of and restricted by lower level events (*e.g.*, DNA, epigenomic effects). However, evolutionary explanations represent 'downward causation' (*sensu* Campbell, 1974), organism to genes, in that the genome of lower levels is explained as the result of past survival and reproductive success at higher levels (natural selection of phenotypes) (Fig. 6).

Boundary Conditions

The interaction between phenotype (form-function complexes, Bock and Wahlert, 1965) and external environment places demands upon individual organisms with which they must cope to survive and reproduce. These demands that arise are selective agents (*sensu* Bock, 1993) if they participate directly in the culling of phenotypes from the population. Selective agents (=selective forces, =selective

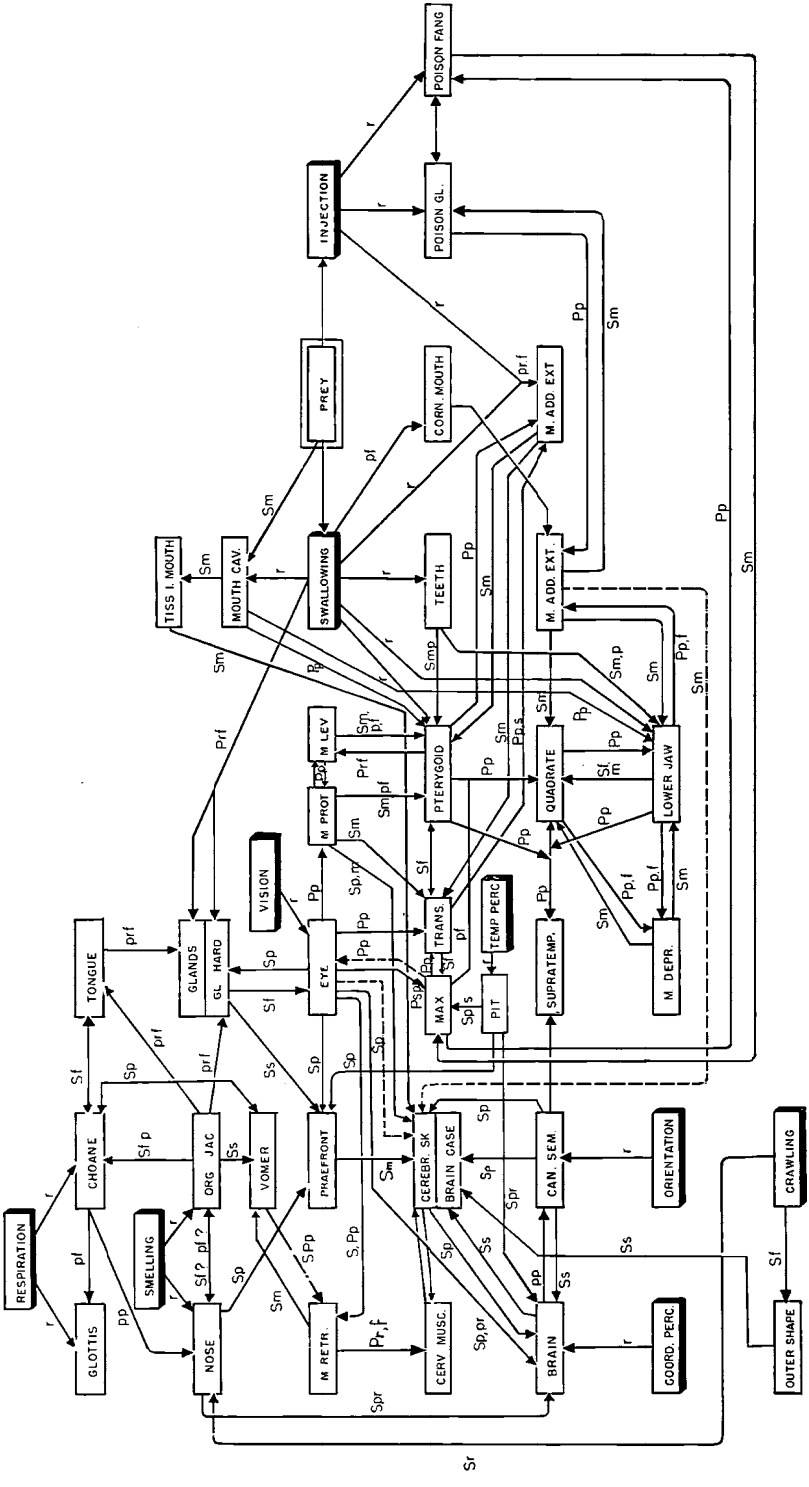

Figure 5. Structural and functional integration between features of a venomous snake skull. From Dullemeijer (1974).

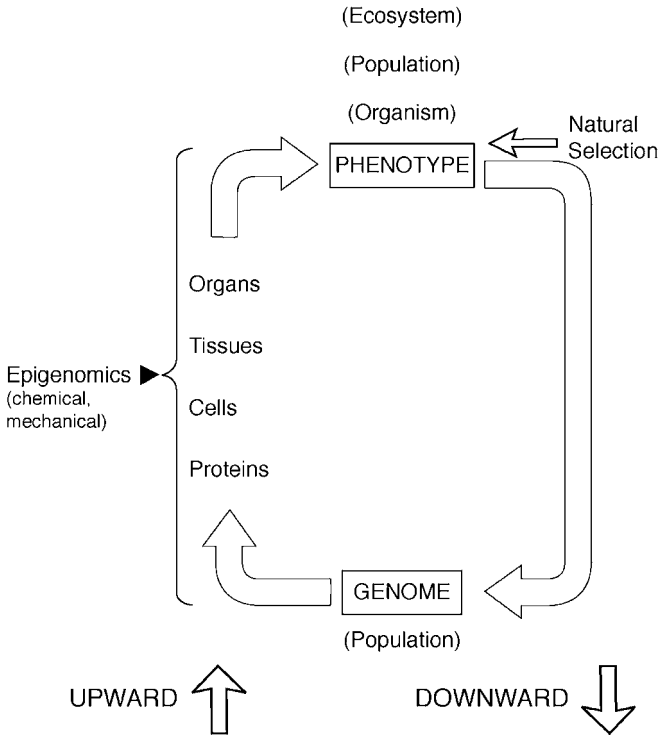

Figure 6. Upward and downward causation. Upward causation occurs from genome to phenotype with epigenomic cues participating. Downward causation results from the effects of natural selection on the population of phenotypes leaving some survivors that constitute the resulting gene pool.

demands), arising out of organismal interaction with the environment, are causative agents within an evolutionary context. They help explain (*sensu* Hempel, 1965) evolutionary outcomes.

Certainly, other interactions of organisms with their environment may result, eventually, in changes in the phenotype. One such interaction results in mutations, changes in the genome, as occurs for example in exposure to environmental radiation. Another is the epigenomic influence acting on an organism during its lifetime (Bock, 1993), examples supplied above.

Other influences may affect evolutionary outcomes, but it would be a conceptual mistake to speak of these as 'causes', and more productive to view these as **boundary conditions**. These are the constraints and influences within which natural selection, and other causes, operate as part of the evolutionary process. Selective agents are causes of evolutionary change, but they do not act independently of their surroundings nor independently of the impinging influences which direct their course. To paraphrase and borrow from Bock (Bock, 1993), boundary conditions describe the surroundings and the influence of these surroundings on the causative agents of evolutionary change. Both 'causes' and 'boundary conditions' help explain evolutionary change but only causes are the actual engines of evolutionary

change. By analogy, the network of railroad tracks from Paris to Amsterdam determines the path of a moving train and thereby sets the boundary conditions of its trajectory, but the tracks do not cause the train to move from Paris to Amsterdam. Conversely, the absence of train tracks from Amsterdam to the North Pole explains (*sensu* Hempel, 1965) the absence of a passenger-train service to the North Pole. In our explanations, we are carefully distinguishing between constraints/plasticity (boundary conditions) and initiators of change (causes). Selective agents cause evolutionary changes but they act within boundary conditions, constraints of all kinds including epigenomic and phylogenetic constraints.

Genetic Assimilation

Genetic assimilation (≈Baldwin effect) (Waddington, 1953, 1961; Hall, 2001) is a treacherous term, although most who use it seem to recognise its risks and pitfalls. The danger is that it will sound like a current effort to resurrect an old, discredited Lamarckian mechanism. Bluntly stated, phenotypic features produced by exposure to environmental or epigenomic influences are coded eventually into the genotype and assimilated. At first hearing, this sounds like the claim that favourable acquired characteristics are incorporated into the genome; Lamarckian indeed. Instead, what is intended is to identify how phenotypic features, once provoked by epigenomic events, get preprogrammed directly into the genome. A hypothetical example, paraphrased and borrowed from Frazzetta (1975), might illustrate. Terrestrial mammals scuff their feet as they frisk about on land. This mechanical abrasion stimulates development of calluses, adding protective features to the phenotype. We might easily imagine that individuals developing calluses first and early under genetic direction would be at an advantage compared to those acquiring calluses later under epigenomic stimulation. Individuals with calluses in place before they experience the abrasive environment might have the advantage over those with later onset of calluses in response to environmentally harsh stimuli. Those with early onset calluses would be favoured over those with late onset of calluses. The early onset phenotypic would spread within the population, consequently increasing its genotype within the gene pool. Despite its ring, genetic assimilation is a traditional Darwinian outcome (Hall, 2001).

Genomic Control

The current genome is the product of past history. The genome may incorporate, by genetic assimilation, preprogrammed information completing the phenotype independent of current epigenomic influences, which play no part in the expression of the phenotype. Or the genome may await the arrival of an epigenomic input before genes express the final phenotypic feature. From our example above, calluses may arise early, largely initiated independently by the genome, or calluses may arise later, when epigenomic events initiate gene expression. In rotifers, spines might be energetically expensive and cumbersome to wield, so preprogramming them in

genes and expressing them before a predator threatens may be disadvantageous. Ethology provides us with other examples.

Where distinctive behaviours (phenotypic feature) cannot be predicted ahead of birth (or hatching), the behaviour tends to be epigenomic, added to the effort of the genome itself. For example, the gosling chick will have parents that await it upon hatching, but the particular parents will be unknown before then, and specific recognition cannot be completely preprogrammed into the genome. Consequently, imprinting occurs after hatching, finishing the phenotypic behaviour. On the other hand, some behaviours cannot be learned ahead of time and must be ready to serve the first time they are deployed. A young hawk, perched on the edge of a nest several hundred metres above the canyon floor below ready to take its first flight, has no possibility of learning the basics of aerodynamic flight or growing flight feathers on the way down. Flight and feathers must now be ready to go and are likely coded largely into the genome. Some male birds, even if deprived of exposure to songs when growing up, nevertheless can produce, the following year when they first breed, territorial and courtship calls essentially indistinguishable from their parents.

The point to be made is that a phenotype may be preprogrammed in the genome, or the genome may await epigenomic inputs before completing the phenotype. The information needed to produce a completed phenotype may reside mostly in the genome, partially in the environment, or be a combination of both. As a consequence of upward causation, the genome determines how much epigenomic information is included, what epigenomic information is incorporated, and when (timing, context) epigenomic information initiates gene expression during morphogenesis of a phenotype. In turn, the phenotype meets the culling process of natural selection, and the survival outcome has the consequence, through downward causation, of reconstituting the pool of genomes in the population.

IMPLICATIONS

The consequences and implications of epigenomic inputs and evolutionary culling are several-fold.

Epigenomics and Evolution

It is possible and even productive to limit consideration of epigenomics to very narrow questions. This, for example, is commonly done in medicine where only the proximate influences of the immediate cellular or tissue environment on the phenotype might be considered. Within such a narrow scope, the immediate proximate affects of epigenomics can be evaluated and the medical implications determined. However, if our interest is in biological principles generally, then we cannot discuss epigenomics without discussing the history of the organisms (phenotypes) and for several reasons. First, the current genome includes the consequences of past history. How the current genome interacts with current epigenomic events is predetermined,

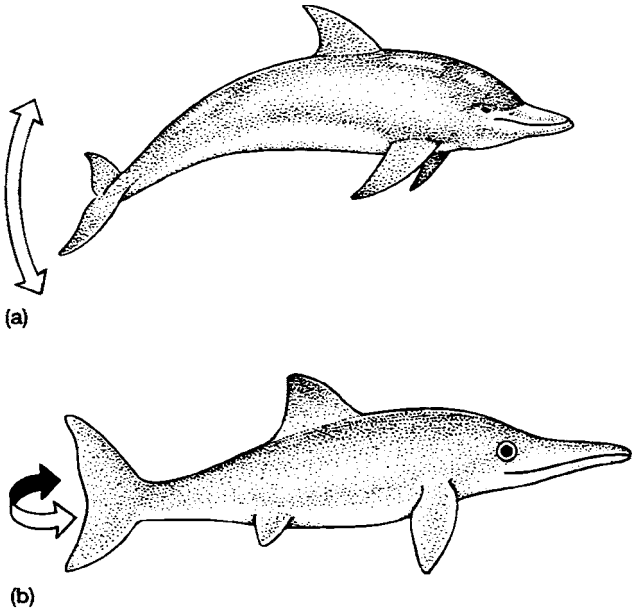

Figure 7. Convergent designs, different histories. Both the porpoise (a) and ichthyosaur (b) are designed for swimming by means of tail sweeps. However, tail flukes are oriented differently, horizontal *vs* vertical, probably explained by differences in their evolutionary histories, the porpoise out of a synapsid lineage, and the ichthyosaur out of a diapsid lineage. After Kardong (2002).

modulated and moulded by the outcomes of past selective events, assimilating these into the preprogrammed coding sequences of DNA. During development, the formative chick femur is exposed to the intermittent mechanical forces generated by twitching leg muscles. These epigenomic mechanical influences lead to the expression of genes that complete the morphogenesis of the well-defined femur. When predators threaten rotifers, associated epigenomic cues activate genes that in turn produce protective spines. If viewed as a proximate event, the mechanical influences on the chick and predator cues on the rotifer seem as if they contribute, independently of the genome, to the phenotype. However, if viewed as an ultimate event, these epigenomic influences (mechanical, predator) have already been assimilated into the genomes of each, a consequence of past evolutionary history. So assimilated and preprogrammed into the genome, these epigenomic influences become boundary conditions and help to explain the character of the phenotype, but are not themselves independent causes of the phenotype. It is therefore a mistake to equate, as some have done (Goodwin, 1994), natural selection (cause) with dynamical features of the environment (boundary conditions).

Second, a particular phenotypic solution cannot be explained completely without reference to the history out of which it came (*e.g.*, Garland *et al.*, 1991; Wolf *et al.*, 1998). The same selective demands acting on diverse organisms may produce different form-function outcomes (Bock, 1998). For example, both ichthyosaurs and dolphins exploit marine environments, using tail sweeps to propel themselves through

the water. If ichthyosaurs were available for careful study today, then along with dolphins, we could examine each species individually (Fig. 7). From a detailed functional analysis, each species might be shown to include phenotypic features that address the proximate hydrodynamic demands of locomotion in an aquatic environment. Both have streamlined bodies, fins, and fluted tails; in addition, both similarly exhibit features suited to diving (*e.g.*, dorsal nostrils, physiology). We could relate aquatic lifestyles and resulting hydrodynamic demands to phenotypic features of each. Such an analysis of form-function provides a proximate explanation of their respective phenotypes. However, propulsive tail sweeps are lateral or dorso-ventral; ichthyosaur and dolphin, respectively. No matter how rigorous and detailed our proximate analysis, we could not explain these particular phenotypic solutions to aquatic life with only proximate information. The full explanation must include attention to ultimate events, related to the different phylogenetic history out of which each evolved, diapsid and synapsid, respectively. Ichthyosaurs represent a secondary invasion of the water, evolving out of a reptilian history wherein terrestrial locomotion was built around lateral flexions of the vertebral column; dolphins represent a secondary invasion of the water, evolving out of a mammalian history wherein terrestrial locomotion was built around dorso-ventral flexion of the vertebral column. Historical events, particular to its own independent evolution, explain why different phenotypic solutions to aquatic life characterise the different species. If a full explanation of the variety of form-function features in living organisms is sought, then the history out of which each comes must be included in the analysis.

Boundary Conditions vs Causes of Evolution

Boundary conditions and selective agents contribute to an explanation of the form-function complex represented in the phenotype of an organism. But each contributes to that explanation in different ways. Epigenomic events are usually boundary conditions, already incorporated into the expectations of the genome. Epigenomic events of the past, with significant survival consequences, have been already assimilated into the programming of the current genome. Historically viewed, the arrival of predators is not a novel surprise for a rotifer. The genome already includes the consequences of past successful encounters with such threats to survival and the adaptive response (spines). Many (Kauffman, 1993; Goodwin, 1994) discuss evolutionary events within current organisms as if ancestors never met, survived, and adapted to chaos or complex events. Rather than correctly seeing these encounters of the past incorporated into the genome of the present, the temptation is to view these current epigenomic influences as causes, independent of the genome. However, complex systems are not necessarily complex causes, but usually boundary conditions. These contribute to the explanation of certain phenotypic outcomes, but they do not represent an equivalent explanation to that offered by the consequences of natural selection *via* selective agents.

Certainly stochastic events, chaotic events, and even thermodynamic events may lead to spontaneous order. But spontaneous order does not produce totally new

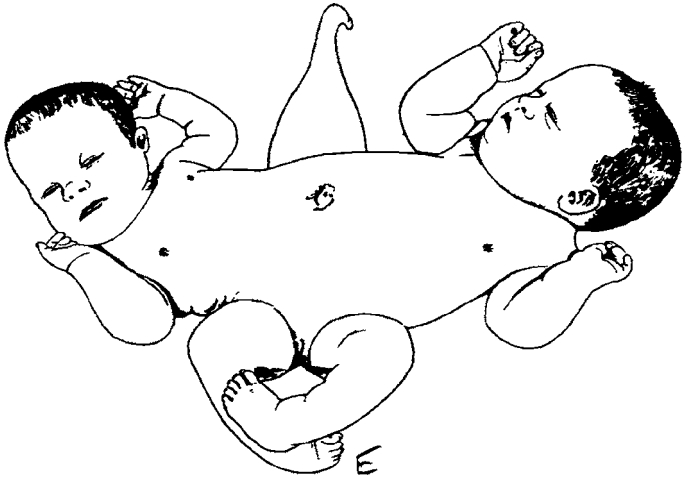

Figure 8. Conjoined twins. After Austin (1972) based on Potter (Pathology of the Fetus and the Infant, 2nd ed., 1961).

spontaneous organisms. For example, thermodynamics has been discussed for its possible relevance to biological systems (Prigogine and Stengers, 1984), with serious attempts to bring it intimately into a discussion of organismal evolution (Brooks and Wiley, 1988). Non-equilibrum thermodynamics, in particular, seems attractive to some physicists because it accounts for, or at least describes, the temporary appearance of organised matter contrary to the loss of order expected from the ways entropy should proceed. Others (Kauffman, 1993) have declared the importance of self-organising systems in producing order from chaotic beginnings, implying the relevance of such self-organisation in organismal systems.

Such heroic efforts are suspect until they produce convincing evidence that either thermodynamics or self-organising systems are in fact physical events of consequence to selective organismal survival and reproduction. Much has been claimed about their significance (Goodwin, 1994), but so far the proof is wanting. But there is a much more serious defect in these empty claims than their failure to deliver evidence of biological significance. Even if such events produced spontaneous organisms or non-equilibrium pockets of life resisting entropy, they would be little more than sources of biological variation or boundary conditions. Even if organisms were generated by self-organising events or thermodynamic outcomes, this newly minted biological life would still be exposed to the culling process of natural selection. Organisms must be internally organised and integrated to remain externally viable and adapted. Physical events cannot long sustain organised biological systems if these biological systems fail to meet the survival demands of the external environment.

An organism is not just a suite of internal, physical processes sustained under its own momentum. Organisms, however generated, must employ their phenotypes to meet the stringent demands of culling, resulting from the interaction of the organism with the external environmental in which it lives (Bock, 1979).

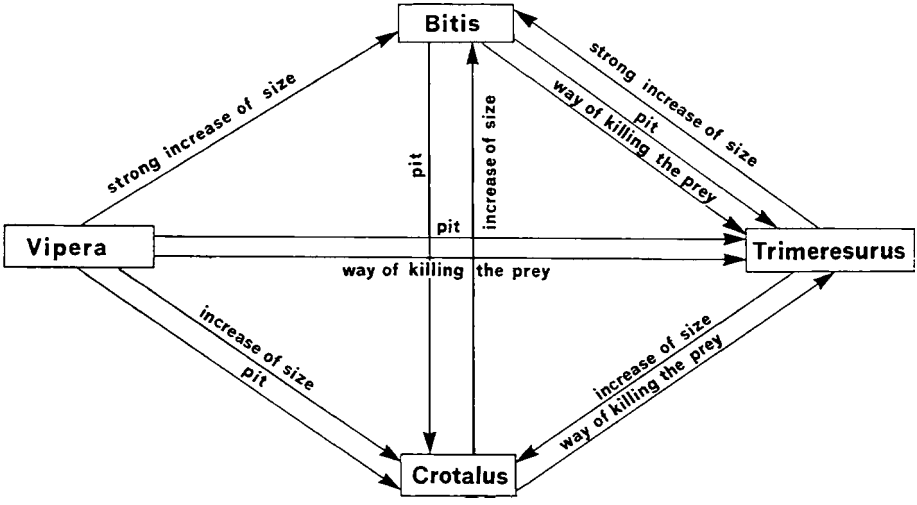

Figure 9. Structural and functional transformations between four genera (boxes) of viperid snakes. Arrows run in the direction of the transformation when the property is changed. From Dullemeijer (1974).

Boundary Conditions and Epigenomics

One attempt to discuss the factors contributing to the phenotype has been to describe epigenomic events as contributing through 'internal selection' and the environment through 'external selection' (Wagner and Schwenk, 2000). These are unfortunate terms because they do not describe equivalent processes with equivalent influences on the phenotype. Internal selection was meant here to characterise the constraints of morphogenesis, broadly understood, with subsequent evolutionary significance. But even if we allow it as a culling process, it is a very forgiving process. Rather anomalous phenotypes may 'survive' the morphogenetic processes that produced them (Fig. 8). But they will certainly meet the harsh fate of 'external selection' (=natural selection), which by far has an overriding affect on phenotypic survival. The intricacies and linked associations of morphological events may preserve stable configurations (constraints), but this is just a way of saying that these constraints limit phenotypic variety. Namely, these morphological constraints contribute to the boundary conditions within which natural selection occurs.

Examining morphological constraints as boundary conditions contributes an insight into phenotypic design, complementary to the causal events of natural selection. For example, predation in viperid snakes is based upon a common, underlying biomechanical mechanism. The linked, kinematic elements of the skull swing into position during the strike, advancing the fangs to a favourable location where they can penetrate the integument of the prey and inject the venom, which dispatches the prey. A theoretical analysis (Dullemeijer, 1959) suggests the transformations in the viperid head in response to addition or elimination of various characteristics to the constraints of the basic biomechanical mechanism (Fig. 9). This was proposed

initially not as an evolutionary hypothesis, but instead to illustrate structural accommodation of morphological additions or subtractions within an integrated system. However, this can be carried one step further, into predictions about evolutionary events. The use of a carefully defined biomechanical model of the viperid skull successfully predicted the boundaries of morphological change within viperids (Kardong, 2003).

CONCLUSIONS

Functional and Evolutionary Morphology

The analysis we do and implications we discover in the discipline of functional and evolutionary morphology are more than just antidotes to the reductionist paradigm. A reductionist paradigm is not intrinsically flawed if it aspires to only proximate goals. The interests of medicine and pharmaceuticals often reduce to genes or proteins (*e.g.*, Ezzell, 2002) where sufficient answers await discovery, and meet the purposes of these health science disciplines. To some extent, we also take a complex and bewildering biological organism, and, as a practical matter, reduce it to simpler functional units. These component features of an organism are more accessible to analysis. But we recognise we are doing so as a temporary convenience, and anticipate building back to the whole organism as our understanding of functional units builds. We do not philosophically expect that our analysis is complete when only a reduced unit of the organism is evaluated and modeled (Homberger, 1988).

Focusing on the integrated phenotype

Because interaction with the external environment shapes the genotype (downward causation), no evaluation of evolution of anatomical features can be centered exclusively on the genotype, a product itself of evolution. If we aspire to ultimate explanations for change through time, to understand current solutions arising out of historical patterns, then the whole organism and its interaction with the environment are central (*e.g.*, Bock, 1990). Collectively, the integration of the survival features or adaptations of an individual determine that organism's ability to persist and reproduce within a given environment. The ability of individuals within a population to meet the challenges of their environment determines the overall culling effects of natural selection, and the subsequent consequences for the collective character of the gene pool (genomes). Necessarily then, our analysis is focused on the phenotype (form-function complex).

If we seek explanations for organismal change through time, or if we seek to explain form-function complexes in current organisms, then functional morphology provides an important conceptual and methodological basis for generating testable hypotheses. I do not propose that functional morphology holds exclusive rights to such scientific insights. Certainly accompanying use of other methodologies is

encouraged and welcome, if their limits are recognised (see above). Functional morphology can provide, through a careful description, an informative model (Dullemeijer, 1974) of an adaptation (*sensu* Bock, 1980). This model, simplifying to essentials the defining elements, simulates function, and thereby also captures in its simulation the intrinsic restrictions (and opportunities) to its modification. As illustrated with this viperid model, if the function can be related to biological role (*sensu* Bock, 1980), then boundary conditions can be identified. In turn, boundary conditions lead to testable predictions about the limits of possible change and therefore provide an *explanation* of evolutionary outcomes.

With a functional analysis, the interdependence of characters is not ignored (*e.g.*, as in much of phylogenetics), but instead celebrated, a centerpiece of the methodology of functional analysis. In short, we enjoy the advantages of focusing upon the organism (form-function complex), where the phenotype is the center of evolutionary action. And we deploy the tools of analysis that give us direct access to the important survival features of the form-function complex, which in turn produce testable hypotheses of organismal design, diversity, and evolution.

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