Good Vibrations: The Silent Symphony of Life

KENNETH WEISS

A century ago a leading biologist suggested that repetitively structured biological traits resembled interference patterns used in tuning violin plates. Are such ideas in tune with modern biology?

Look at the life around you. Everywhere, you are confronted with modularity and repetition, from the leaves and branches on plants, to your hair and the skeletal and other structures within you. Modularity, segmentation, and repetition are, like measures and tones in music, the way in which the living opus has been assembled by the composing processes of evolution. In his elegant book *Evolution Emerging,* W.K. Gregory (1951) likened modular ("polyisomeric") organization to "the notes in an octave . . . evolution emerging has involved an infinite number and variety of natural polyisomeres in both space and time." This has long been known, but little analyzed, in modern evolutionary terms until very recently. To continue the musical analogy, we can view patterned structures as a harmony of organization, with many parts integrated to form an organism, the way the violins, horns, flutes, and so on, form an orchestra. In fact, old ideas and new facts suggest that musical similes are relevant to the symphony of life.

Soon after Darwin published his *Origin of Species,* opponents of his views began marshaling their evidence. One of the first prominent biologists to assemble objections was St George Jackson Mivart (1870), previously respected by and on good terms with Darwin, Huxley, and the rest of the biological "in" crowd. The main issue was whether adaptive natural selection could explain species variation and evolution. Mivart so irritated Darwin that he responded at great length in the 6th edition of *Origin.* Some of Mivart's objections involved the nature of inheritance and homology in regard to discontinuous variation, such as repetitive, serially homologous structures. Mivart became a *bête noir* who was ostracized by the Darwinian community then becoming the mainline of biology. Mivart also tried to reconcile evolution and Catholicism, and was excommunicated from that church, too, poor fellow. But his theme was picked up by W.K. Brooks in the US who credited Mivart and then by William Bateson (1892, 1894, 1913, see Webster, in Bateson, 1894; Webster and Goodwin, 1996).

Bateson coined the term "genetics" and was a strong promoter of Mendelian genetics, but he did not think that the darwinian evolution by gradual natural selection could generate species or their diversity (e.g., Bateson, 1913). He pointed out problems in interpreting modular (repetitive, serially homologous, or meristic) structures: "Segmentation . . . is almost universally present . . . greater or less repetition of various structures is one of the chief factors in the composition of animal forms." (Quoted in Webster's preface to Bateson, 1894). But discrete segment numbers cannot evolve incrementally. What is actually inherited? A different gene for each hair or vertebra? That made no sense to him, and it may have been a reason for the non-specific suggestion a century later that evolution was a "punctuated" process.

One of his ideas about this[1] is strikingly modern in concept. The suggestion drew biological parallels with concepts of fields and vibrations or oscillations borrowed from physics. As we'll see, Bateson used a musical analogy that makes some evolutionary genetic points easy to understand. There were then no actual genes known and his views were ignored or even ostracized during the decades of ascendance of the neodarwinian synthesis. But the basic ideas are enjoying a justified revival in a profound advance in our understanding of the role of genes in the evolution and generation of complex morphologies. We can trace these ideas, at least fancifully, back to the famous Geoffroy-Cuvier debates in 1830 on the nature of animal form itself, and perhaps even push the musical analogy back to that time as well.

A FEW BASIC QUESTIONS

How Fundamental Is Modular Patterning?

It's worth stressing how very modular structure is in the construction of life. If the canonical essence of evolution is *descent with modification* among individuals across generations, to me an equally important principle is *duplication with variation* within the individual. From DNA to proteins to morphology, among plants and animals (even bacterial colony

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[1]Bateson's reference to Chladni figures was made most clearly in a letter to his sister (see B. Bateson, 1928).

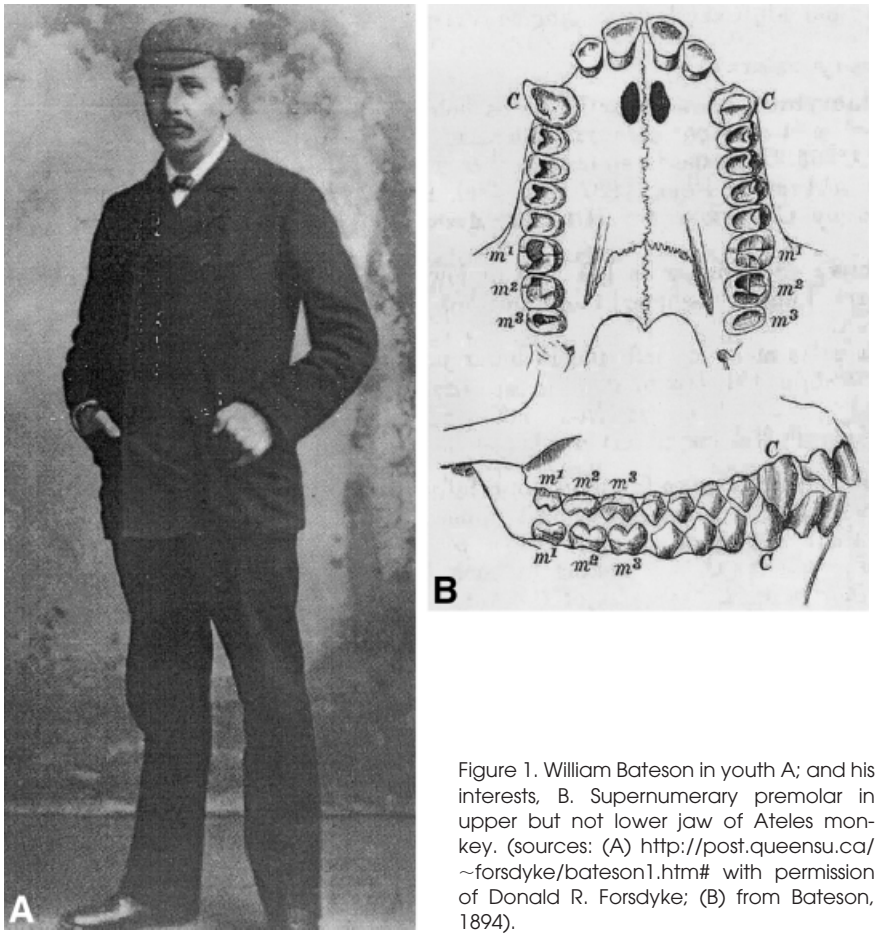

Figure 1. William Bateson in youth A; and his interests, B. Supernumerary premolar in upper but not lower jaw of Ateles monkey. (sources: (A) http://post.queensu.ca/~forsdyke/bateson1.htm# with permission of Donald R. Forsdyke; (B) from Bateson, 1894).

formation), from cells to ants in a colony, there is modular organization everywhere. This is built by gene duplication to form the genome, protein polymerization or multimerization to form functional biochemical units, and at the morphological level, beginning with cells themselves.

Across the plant and animal world, if you look at structures, organs, or organ systems you will see how commonly they are built of repeated subunits (themselves sometimes hierarchically modified). To make this happen, sets of differently programmed cells are produced in periodic or episodic fashion, and become the precursors of each unit within the structure. In this way, duplication with variation has allowed life to become complex, and organisms to achieve larger size and functional specialization.

Recognition of modularity is thoroughly built into modern biology. We routinely search for gene family members to explain comparable structures within an organism and for repeated regulatory sequences around genes expressed in similar cellular contexts. Wavelike patterning mechanisms have been a widely observed phenomenon in development.

How Does Modular Structure Relate to Genes?

Bateson's "vibratory" theory of patterning was that repeated structures were manifestations of sympathetic vibration or similar interference phenomena. His imagery was that of Chladni figures. These are the wavelike interference patterns that form when a source of oscillating energy diffuses through a material of some sort (Waller, 1961). The pattern is a function of the location, frequency, and energy level of the source of vibration. Ernst Chladni was a Leipzig lawyer, musician, and amateur scientist. As early as 1787, he had reported a way to make the vibrations caused by sound waves visible. He covered glass, metal, and wooden plates with sand and ran a violin bow against them. The vibrations moved the sand into patterns that are known today as "Chladni's figures." The vibration jostles the powder to areas or nodes of the plate in which vibration waves cancel each other out and there's no net motion.

The idea of using a tuning fork as a source of oscillating energy suggested an interesting way to illustrate the phenomenon. A physician named Félix Savart was interested in applying Chladni's notions to this problem, by dusting the plate with black powder, applying a tone to the plate and observing the interference waves or nodes, as shown in Figure 3. Plates of great violins have consistent patterns within, and consistent differences between them. Makers of great violins "tune" the top and back plates by shaving small amounts of wood here and there until appropriate frequencies generate the standard "modes." An important point to note is that the *same* plate has different patterns if the energy, location, or frequency of the source is changed.

In 1952, Alan Turing (known for deciphering the Nazi cryptographic system during World War II and ideas on designing programmable computers) suggested that two interacting substances diffusing through a uniform fluid could generate wavelike interference patterns. One substance is known as an activator, and diffuses from some source, inducing its own activity as well as that of the second substance, known as an inhibitor. In such a "reaction-diffusion" process, the inhibitor reduces the level of the activator. Depending on the production and diffusion levels of the two substances, and their interaction dynamics, an initially uniform area or "field" will generate wavelike patterns of high and low levels of the activator.

Look in the Mirror

(Virtual) Figure 2. Modular structure in life: left-right symmetry, hair, pores, teeth, cusps, papillae on the tongue, . . .

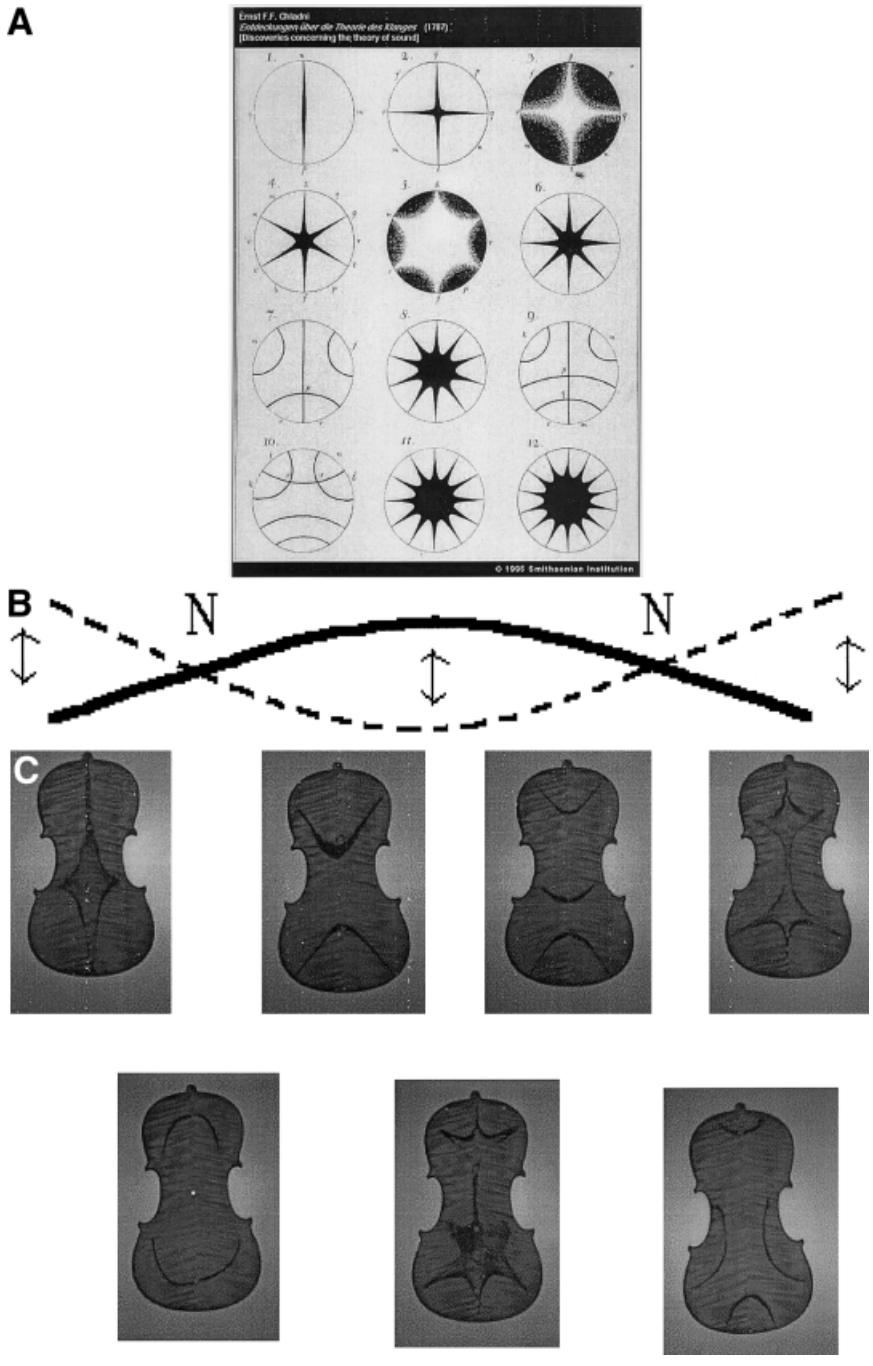

Figure 3. A: Chladni's figures shown here are 12 engravings of these acoustically produced patterns (Source: Chladni, 1787, copied from http://www.sil.si.edu/Exhibitions/Science-and-the-Artists-Book/phys.htm). B: Cross section of vibrating plate to show nodes (N) of no motion. C: Chladni figures of the 7 classical "modes" of a handmade violin (tonal frequencies 91, 138, 196, 231, 306, 312, 392 Hz, respectively). (Source: J. Wolfe, http://www.phys.unsw.edu.au/~jw/chladni.html)

Turing did not acknowledge that Bateson had thought of this in regard to biology, but several biologists noticed the relevance of Turing's ideas to diverse repetitive or wavelike biological traits. Bateson (1913) referred to the nodes and internodes as "the seat of appropriate and distinct chemical processes leading to the differentiation of the parts" of organisms. Structures can develop at the peaks, for example, if expression of developmental cascades occurs when activator levels cross some threshold, with the valleys the structure-free inhibition zones.

In recent years, the ability to detect cell-specific levels of expression of specific gene products (proteins or mRNA) has put these ideas to direct tests. Embryonic tissue is tested for spatiotemproal distribution of signaling factor molecules diffusing from cells of origin across the tissue. Initially broad patterns narrow to stripes and then periodic spots surrounded by expression of diffusible inhibitors. For example, hair and feathers develop in zones expressing the Fgf and Wnt signaling factors, but are inhibited in areas where Bmp factors are found. These gene products have patchy distribution that presages the location and spacing of future feathers, sometimes appearing first as an initial line of expressing cells (e.g., the dental lamina), that resolves into spots, and then spreads laterally to form other spots. Short distance spacing among adjacent cells may be patterned by additional activator-inhibitor interactions (e.g., the Notch-Delta system). These are highly conserved processes; for example, the same Notch-Delta signaling helps pattern the ommatidia in insect eyes, teeth, and feathers. These patterning systems then activate "selector" genes that initiate cascades of gene expression that lead to organ formation (see Gilbert and Gerhart references).

In addition to direct molecular examples, activation-inhibition processes have been shown by computer simulation to apply in varying ways to coloration in mammals, fish, seashells, butterfly wings, the location of mammary glands, feathers, scales, and digits in animals and flower parts. This is probably just the first peek at the wide distribution of such patterning mechanisms in nature.

The concepts are highly relevant to anthropology. My own interest is in dental patterning, in which it seems likely that the number, location, and differential morphology of teeth along the jaws are due to such mechanisms. Indeed, the same genes demonstrably expressed in this way in feather and other vertebrate patterning processes are expressed in teeth in ways consistent with activation-inhibition

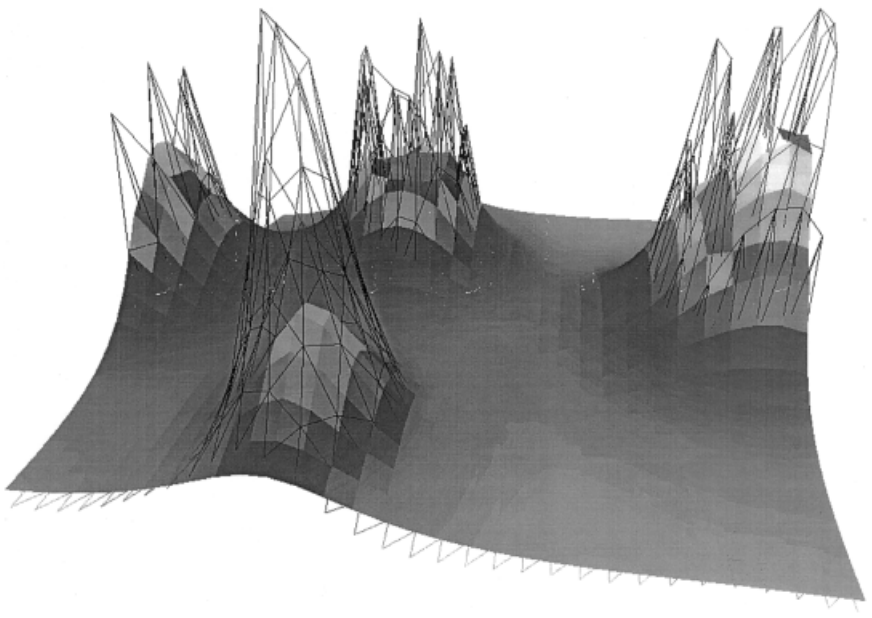

Figure 4. Peaks erupting from a simple reaction-diffusion process. Wire-screen is concentration of activator (this could be proportional to growth, for example), grey-scale of inhibitor (courtesy Brian Lambert).

patterning. (Jervall and Jung, 2000; Weiss et al., 1998). In elegant experiments that I wish I had done rather than they, Jukka Jernvall, Soile Keranen, and others in Irma Thesleff's lab in Helsinki have shown that gene expression and expression-manipulation are consistent with this general type of patterning process. Zones known as enamel knots expressing Fgf and other growth factors appear along the dental lamina; cusps form when this induces down-growth in surrounding tissue, while the knots themselves are self-inhibiting (Fig. 5B). Indeed, an earlier round of patterned expression of similar genes appears to be involved in the serially patterned location of tooth germs.

Salazar-Ciudad and Jernvall have subsequently shown by computer simulation that activation-inhibition processes modeling the behavior of enamel knots can generate strikingly realistic molariform cusplike crown patterns (Salazar-Ciudad and Jernvall, 2002; Fig. 5). In an important test, the authors tried the darwinian gradualism experiment of simply computer "morphing" a tooth from its initial to its final states (both of which matched between program and actual tooth embryos), and compared the resulting *intermediate* states with the intermediate states of real tooth germs that are closely imitated by the dynamic process simulation (J. Jernvall, personal communication). As far as the morphed intermediates go, art does not imitate life. Only the dynamic patterning process resembled the real thing.

Bateson could only speculate about such matters, but a century later we have at least some examples vindicating the idea at the molecular level. Dynamic patterning mechanisms like this seem to a ubiquitous means by which complex animals and plants are produced from single fertilized egg cells. Of course, to credit Bateson for his prescience does not mean that we would expect to see his—or Turing's, or anyone's—ideas fulfilled exactly, and repetitive patterning is brought about in many ways.

How Does Modular Structure Evolve?

A long-standing question of the "tempo and mode" of evolution has been the way complex traits evolve. Arguments about this pitted darwinian gradualism versus saltational evolution. As noted earlier, this problem bothered Bateson and others and kept them from adopting Darwin's solution to the species question. In the 20th century, Richard Goldschmidt (1940) suggested that mutational hopeful monsters may from time to time be produced that have new structures or traits. On rare occasions, these might pass the selective screen as adaptations to a new form of life. Saltational evolution was and is generally held to be a serious kind of heresy (or madness). Nobody thinks wings can evolve suddenly from legs, but patterned organ systems do normally vary in their number and morphology of elements (teeth, cusps, feathers, limbbones, regions of the gut, etc., Figure 1B). This could address Bateson's objection that neither darwinian gradualism nor simple mendelian segregation were consistent with the evolution of meristic traits. As Bateson (1928) said, an eight-petal form is to a four-petal form as one octave is to another. A mutationally derived shift in the dynamics of an interaction process can bring about such differences, and there are many examples.

Recognition of dynamic patterning processes has a second important implication for evolutionary thinking. As Bateson (1894) said, "Of course, heredity becomes quite a simple phenomenon in light of this." There is no single gene "for" a specific feather or tooth or intestinal villus or nephron. All the elements in each system express essentially the same genes. In principle, all that need differ along the jaw would be the position of the peaks of expression of say odontogenic genes. Not only need there not be separate genes for each iteration of a structure, but what may differ between the dentitions of carnivores and herbivores may mainly, or only, involve the interaction dynamics—things like diffusion rates, activation or inhibition efficiencies—of the same patterning genes.

What About Homology?

All of this affects notions of homology (see Abouheif, 1997; Hall, 1999). It may be evolutionary non-questions to ask whether the diastema in a mouse jaw represents "missing" teeth, or what the homologous digits are in a bird and mammal. Homology may really lie in the patterning process itself—a common generative mecha-

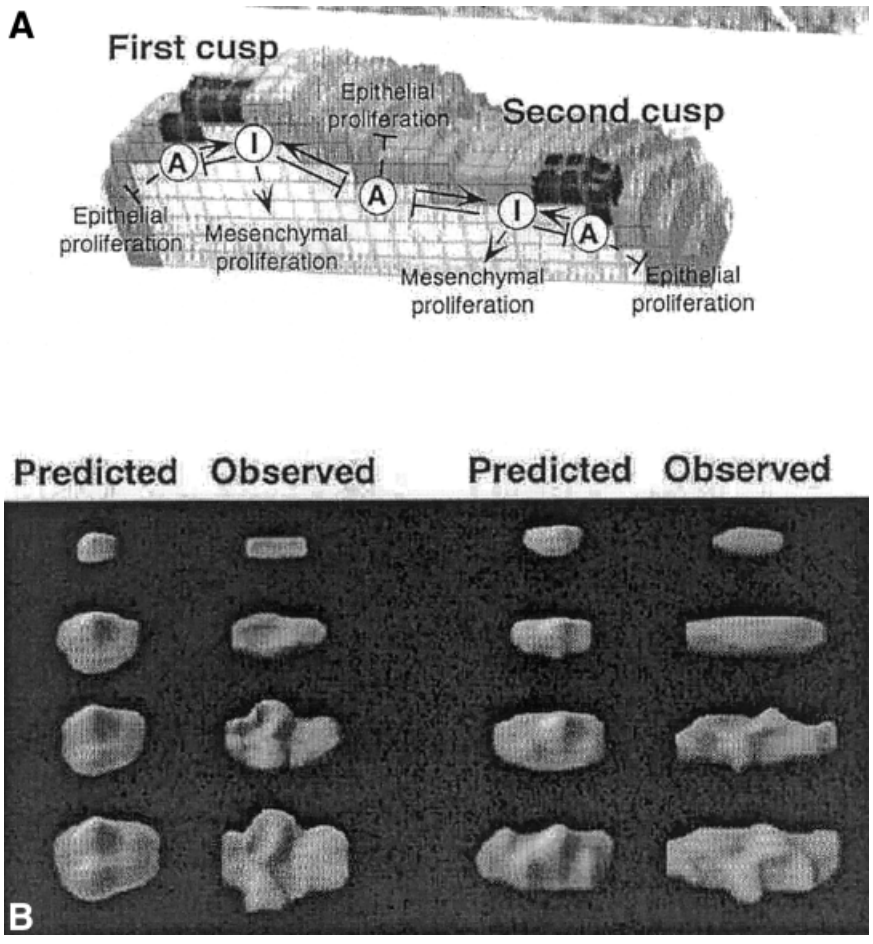

Figure 5. Simulation of tooth crown shape by a class of reaction-diffusion-like mechanism. A: Basic model of simulated spatial units showing activator (A) and inhibitor (I) relative to enamel knot (dark) and differential cell growth. B: Predicted (simulated) and observed mouse (left) and vole (right) first molar crown surfaces (with permission from Salazar-Ciudad and Jernvall, 2002).

nism, in Bateson's terms. The patterning process and genes may be shared, and the patterning genes may be the same, but there may be no specific gene or gene combination that is a particular member and can form the basis of taxonomic homologies. An example may be the transitory dental rudiments that appear in the (upper but not lower) diastema region of an embryonic mouse jaw (Keranen et al., 1999), but are not obviously identical to the teeth absent in the mouse.

It seems likely that one problem that taxonomy has is its tacit reliance on a *gene-for* notion of the relationship between genes and traits. Such assignments may not explain dynamically patterned serially homologous traits, of which there are so many. We have the same problem assigning homology to members of gene families that have undergone repeated duplication, such as globin or photoreceptor genes between birds and mammals. Should we call teeth and feathers or insect eyes homologous because at some point in their development the same patterning circuitry is used?

The Hairs on Your Head May Be Numbered, But What About the Wave?

Dynamic patterning processes are typically nested. For example, hairs are individually periodic structures, but pelage is also striped in mammals—including humans (Figure 6).[2] Hair form is regionally differentiated and individual hairs can themselves be striped. Thus, hair is patterned by several simultaneously occurring wave-generating processes. Murray (1993) provides a Chladni-like simulation of haircolor patterning in just that way.

Similarly nested patterning is seen along the mammalian dentition, in feathers, intestinal epithelial structure, tongue, limb, and vertebral patterning, bristles in various parts of a fly, and many others. As in tooth development, the same activation-inhibition process may be involved in multiple traits at different times or places in the same organism.

THE MUSIC OF EVOLUTION

Chemical "vibration" is harmonious to the organism and has properties similar to those of music. Ideas about this relate to age-old debates in biology. These ideas were applied to paleontological, comparative, and embryological data, and they may even have been relevant to early 19th century discussions of animal form. In 1830, Georges Cuvier and Etienne Geoffroy St. Hilaire held famous debates in Paris (Appel, 1987). Cuvier believed that complex animal form was due to independent adaptation (at that time, in the functional, not darwinian, sense of the term) of different body structures, such as limbs, claws, teeth, and so on. Geoffroy held that variations among animals reflected underlying body plans that could be distorted and modified but represented functional wholes.

These were bitter and celebrated debates. A new edition of Chladni appeared in 1830, and I have speculated (Weiss et al., 1998) that Félix Savart, as a member of the Paris intellectual set, may have attended the debates. Might he have seen the similarities between biological patterning and the way Chladni figures demonstrate variation on an underlying plan (the basic structure of a violin plate), and sided with Geoffroy?

Ideas about serial homology were around for most of the 20th century,

[2] I can personally attest that in their younger years, these stripes were clearer.

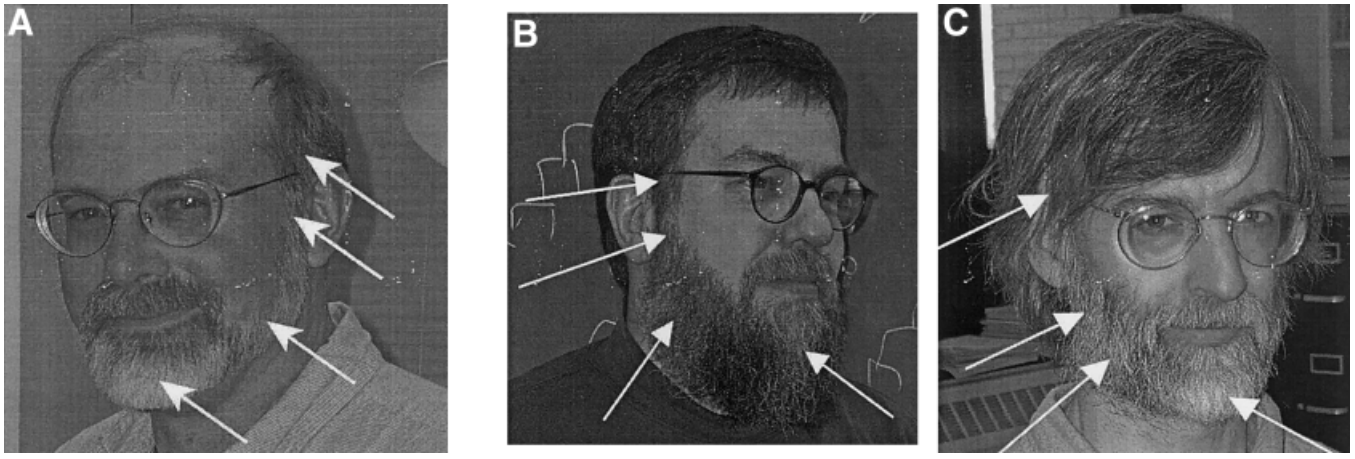

Figure 6. Variably striped humans.[2] A: George Milner, archeologist. B: James Wood, demographer. C: Andrew Clark, geneticist.

though suggestions as to cause did not get very far, and were often denigrated as untestable, or unscientific. But that was then and this is now. Dynamic patterning processes are a fundamental part of the developmental toolkit, that are used and re-used, and deeply conserved phylogenetically. But it is tempting to over-extend the implication of these generalities. Similar genes are used in diverse traits, but this does not mean that the same genes will be used in any particular trait, or even in the same trait among different species. Two *logically* similar patterning mechanisms can involve different, perhaps entirely unrelated sets of genes. For example, similar periodic patterning processes are involved in plants, but not with animal signaling factors.

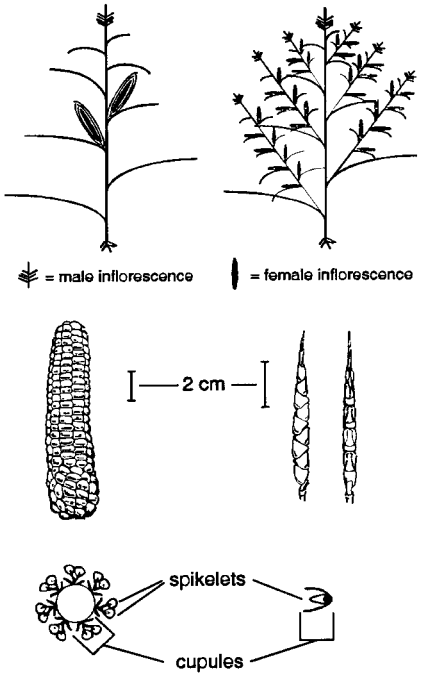

Figure 7. Pattern variants in teosinte and maize that are phenotypically invariant within strain but with underlying variation revealed by gene mapping in crosses. Are these differences due to genes for dynamic-patterning mechanisms rather than for specific traits? (from Lauter and Doebley, 2002, courtesy John Doebley).

Interestingly, a recent paper has examined various patterning differences between teosinte and maize (Lauter and Doebley, 2002). A long-standing question is how these traits, that are invariant within each species, could have evolved. Did it involve a Goldschmidt leap? We can't say, but Lauter and Doebley have shown by clever cross-breeding experiments that there is variation within teosinte that does not lead to trait variation, but that could be the latent source of rapid evolution of the trait. A small amount of mutational change might have sufficed to reconfigure this silent background variation to jump teosinte to maize form, creating this most important cultivar—just as a Chladni figure can jump when the sound frequency changes. The developmental timing of a single gene can change the shape of a leaf from simple to complex (Bharatham et al., 2002).

The musical analogy is probably not a bad one. Throughout an embryo as it develops, a highly orchestrated program of "vibrational" patterning mechanisms enables a single cell to become a harmonious complex organism, with tones and overtones. This is a developmental orchestra that all organisms can play, but none can hear.[3] We are probably just beginning to discover the degree to which we owe our nature to the good vibrations of this silent symphony of life.

NOTES

I welcome any comments on this column: kmw4@psu.edu. I maintain a *CrotcheyComments* page at www.anthro.psu.edu/rsrch/weiss_lab.

I thank Anne Buchanan and Jukka Jernvall for helpful comments.

TO READ

Most things discussed here can be profitably explored by web searching.

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[3]DNA sequences can be made into much more than a 4-tone exercise in minimalism, but translations to date are more aesthetic than biological. CDs and software are available; for example http://algoart.com/dnamusic/ or http://education.llnl.gov/msds/music/midi-dna.html or http://www.dnamusiccentral.com/.

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