# Developmental biology and human evolution

**Jeffrey H. Schwartz**

*Departments of Anthropology and History and Philosophy of Science, University of Pittsburgh, USA*

## Abstract

The *Evolutionary* or *Modern Evolutionary Synthesis* (here identified as the Synthesis) has been portrayed as providing the foundation for uniting a supposed disarray of biological disciplines through the lens of Darwinism fused with population genetics. Rarely acknowledged is that the Synthesis's success was also largely due to its architects' effectiveness in submerging British and German attempts at a synthesis by uniting the biological sciences through shared evolutionary concerns. Dobzhansky and Mayr imposed their bias toward population genetics, population (as supposedly opposed to typological) thinking, and Morgan's conception of *specific genes for specific features* (here abbreviated as *genes for*) on human evolutionary studies. Dobzhansky declared that culture buffered humans from the whims of selection. Mayr argued that as variable as humans are now, their extinct relatives were even more variable; thus the human fossil record did not present taxic diversity and all known fossils could be assembled into a gradually changing lineage of time-successive species. When Washburn centralized these biases in the *new physical anthropology* the fate of paleoanthropology as a non-contributor to evolutionary theory was sealed. Molecular anthropology followed suit in embracing Zuckerkandl and Pauling's assumption that molecular change was gradual and perhaps more importantly continual. Lost in translation was and still is an appreciation of organismal development. Here I will summarize the history of these ideas and their alternatives in order to demonstrate assumptions that still need to be addressed before human evolutionary studies can more fully participate in what is a paradigm shift-in-the-making in evolutionary biology.

Correspondence: Jeffrey H. Schwartz, Departments of Anthropology and History and Philosophy of Science, University of Pittsburgh, 3302 WWPH, Pittsburgh, PA 15260, USA.
Tel. +1.412.6487509 – Fax: +1.412.6487535.
E-mail: jhs@pitt.edu

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## Introduction

The history of evolutionary thought is interesting especially because it is continually being rewritten. Consider Charles Darwin. It is commonplace to read in textbooks and popular works that had he slit the pages of the reprint of Mendel's publication of his sweet-pea experiments rumored to have been in his library he would have discovered the missing element in his theory of evolution by natural selection: namely, the role of population genetics in explicating evolution as the result of long-term adaptation. But he did not. The world thus had to wait for nearly a century for the population geneticist of the Synthesis, Theodosius Dobzhansky, to fill this lacuna. And he did with the assumption that the evolution of species and their clades (macroevolution, which no one can observe in a lifetime) could be understood by studying generational changes in gene/allelic frequencies as reflected in morphology (microevolution, which one can observe in a lifetime) (see historical review[1]). But Darwin could never have embraced Mendel's conception of particulate inheritance. Like many of his contemporaries, Darwin believed in blending inheritance, which he incorporated into his theory of heredity, pangenesis.[2] When Bateson and Saunders[3] at the request of Galton on behalf of the Royal Society applied Mendel's principles to animals, an intellectual rift emerged between *Darwinians* and their critics, *Mendelians*.[1,4-8]

Darwin's[9] emphasis on gradual evolutionary change and continuous variation led him to believe that had extinction or loss of geological deposits not eliminated morphologically intermediate forms, we would behold a continuum at any point in time between individuals, sexes, and species. Unfortunately, extinction and geological events created an artificial picture of discontinuity in a world that in reality is and was seamlessly continuous. Mendelism, however, with its emphasis on discrete, non-blending units of heredity, lent itself to believing that the morphological features they produced were also discrete and discontinuous. By insisting that gradual change through the accumulation of infinitesimally small variations over long periods of time constituted evolution, Darwin rejected a fact well-known to animal and plant breeders: namely, the plant or animal a breeder selected to serve as the progenitor of a new breed or variety often appeared in one generation not only without warning, but replete with its unique attributes.[2] Further, this *monstrosity* (to use 19th century language[2,10-12]) was capable of breeding with parental-type stock. Darwin's argument for rejecting *monsters* as evidence of evolution was that these individuals would not be able to survive in the wild. Yet for the saltationists Huxley[13] and especially Mivart[12], *monsters* did furnish material for the study of evolution.[1,14] Huxley criticized Darwin for dismissing *natura facit saltum* and invoked many of the examples Darwin rejected – such as the case of the emergence of the Ancon sheep – to argue that novel morphology, and thus also species, arose abruptly. Mivart argued further that changes important to the survival of an organism must emerge in or nearly in final form, most likely from major alterations of development.

In a monographic embrace of Mendelism and criticism of Darwin's insistence on gradual change, Morgan[6] also cited as evidence of the abruptness with which evolutionary novelty could arise the same examples of the *sudden origin* of *monsters* that Darwin dismissed as providing insight onto evolutionary change. It therefore is remarkable that it was Morgan who ultimately devised the argument for melding Darwinism and Mendelism.[15-17] And, also ironically, Morgan paralleled Darwin in accepting part of biological observation as necessary for evolution and rejecting the rest. Upon establishing the first fruit-fly population genetics laboratory Morgan and colleagues[18] carried out numerous experiments in an attempt to map the location on chromosomes of hereditary units. Although Johanssen[19] had earlier introduced the term *gene*, Morgan referred to units of heredity as hereditary *factors* perhaps because, like Bateson,[4,20] Johanssen believed that genes existed in the cytoplasm, not on chromosomes. Morgan's[15] initial argument was the following: i) mutations that occur in laboratory animals do not differ from those that occur in wild animals; ii) the same mechanisms/processes that produce small-scale mutations (and concomitantly small-scale phenotypic changes) also underlie large-scale mutations (and concomitantly large-scale phenotypic changes), both kinds of which he observed in his fruit-flies; iii) mutation is random relative to selection, which can only act on features once they have appeared; and iv) as with the odds in a sequence of coin tosses yielding heads versus tails, a mutation affecting one feature does not ensure that the next mutation would follow suit.

Curiously, though, after presenting this logical thought experiment Morgan[16,17] then rejected much of it. First, as Darwin had earlier denied to *monsters* the wherewithal to survive in nature, Morgan invoked the same fate for individuals bearing the phenotypic results of large-scale mutations. Consequently, he asserted, the only mutations and their phenotypic expressions that would be viable in nature were small-scale mutations, which would produce minor phenotypic change or variation. Second, Morgan declared, a mutation in one direction *would* bias subsequent mutations to follow suit. Over time, selection opting for these micromutations via their products would gradually change the population or species both phenotypically and genetically.

As for Mendelian *factors* and the features they produced being discrete and discontinuous, Morgan proclaimed that since the mutations and thus their phenotypic expressions must be so incredibly minuscule for an organism to survive, variation was essentially continuous. Thus in one fell swoop Morgan melded Darwinian notions of selection and gradualism with Mendelian inheritance, with the proviso that micromutation, not selection or blending inheritance,[2,9] produced the variation upon which selection then acted. Also with Morgan, the notion of their being *specific genes for specific morphological features* (abbreviated here as *genes for*) became an integral part of Darwinian evolutionary theory.

## The evolutionary synthesis[1] and the stultification of intellectual heterodoxy

The Synthesis that Dobzhansky[24], Mayr[25], and Simpson[26] contrived promoted population genetics over all other biological disciplines and its reliance on the notion of *specific genes for specific features*. Unfortunately, as the embryologist de Beer[27] bemoaned, this emphasis bypassed entirely the developmental processes that give rise to a functionally integrated adult organism because, in a *genes for* conception of biology, one need focus only on parental transmission of alleles to the zygote and the adult progeny.

Absent from the Synthesis' version of evolution was consideration of, or even a perceived need to consider development broadly, much less in its details: e.g. in the timing of induction, threshold effects, regulation of development, protein/enzyme-gene interactions, epigenetic interactions etc that are intricately intertwined in the development of an organism from its undifferentiated to fully adult state. But this is not to say that all evolutionary biologists were as narrow-minded.

For example, in his *Vibratory* or *Undulatory* theory of evolution, Bateson (e.g. Refs. *10,20*) sensed correctly[1] that the origination of organismal novelty – especially differences between taxa in repeated or meristic features – resulted from internal alterations of developmental oscillations. Beginning with his early work on amphibian metamorphosis (e.g.Refs. *28,29*), J. Huxley was keenly aware of the importance of incorporating development into a viable theory of evolution (e.g. Refs. *23,30*). In the preface to his 1942 monograph, *Evolution: The Modern Synthesis*, in addition to Dobzhansky, Huxley acknowledged the contributions of Goldschmidt [in developmental genetics[31] and evolution[32]] and Waddington [in developmental genetics and epigenetics[33]]. He then commented: *Equally obvious is my debt to the Morgan school and to Goldschmidt, but clearly this would apply to any modern book dealing with evolution* (p. 8). How mistaken Huxley was given the hostility with which Dobzhansky[24], Mayr[25], and even Simpson[26], who studied extinct mammals, attacked Goldschmidt.

By centralizing population genetics as the key to understanding evolutionary processes, Dobzhansky[24,34] shifted focus in evolutionary biology from systematic considerations of species to a more ambiguous notion of variation within populations and their change over time (see review in Ref. *35*), which consequently denied paleontology input into the formulation of theories of evolution, especially the origin of species. This is obvious in Simpson's[26] contribution to the synthesis, *Tempo and Mode in Evolution*, in contrast to Dobzhansky and Mayr's volumes, whose titles proclaimed relevance to the essential issue in evolutionary biology, the origin of species. Excluded from discussion of species' origins, a paleontologist was left to rail against neo- and paleosystematists whom he perceived as upholding outdated *typological thinking* or *essentialism* rather then adopting the tenets of the Synthesis (e.g. Refs. *36,37,38*). It was only in the late 1950s that Mayr took up this baton in earnest and through a biased reporting of history seduced most, especially English-speaking, evolutionists with a false dichotomy between *typological* with *population* thinking.[39] As Winsor has detailed, Mayr's assault was actually against saltationists, whom he painted with the brush of anti-Darwinism. From the perspective of an ill-defined notion of population thinking the Synthesis' embrace of Darwinian gradual evolution by natural selection blurred distinction between *races*, species, and higher taxa.[39] From a saltational perspective, the origin of species, including those that were ancestors of higher taxa, did not lie in natural selection but in other processes. And this was anathema to Mayr and fellow neo-Darwinians (see also Refs. *1,14*).

## Was the evolutionary synthesis a synthesis?

By excluding or minimizing all biological pursuits except for population genetics and population thinking it is difficult to embrace the Synthesis as having been synthetic in the sense of it integrating diverse biological fields. Indeed, as Jepsen[40] recounted, the goal of the Synthesis was to unite supposedly disparate biological disciplines under the same umbrella: Darwinism infused with population genetics. In contrast, efforts from the German school by Schindewolf[41] and Goldschmidt[32] to encompass development, genetics beyond the populational and its underlying *genes for* concept, and comparative morphology (including paleontology) in evolutionary models were more credible

[1] *The evolutionary dogma that Dobzhansky, Mayr, and Simpson promoted has been referred to even by Mayr differently at different times: e.g. "The Evolutionary Synthesis" 21. Mayr, E. and W. B. Provine 1981. The evolutionary synthesis. Bulletin of the American Academy of Arts and Sciences 34:17-32. and "The Modern Evolutionary Theory" 22. Mayr, E. 1996. The modern evolutiionary theory. Journal of Mammalogy 77:1-7. J. Huxley's work, which these three individuals ignored and whose emphases differed dramatically from theirs, was titled Evolution: The Modern Synthesis 23. Huxley, J. 1942. Evolution: The Modern Synthesis. New York, Harper & Brothers.. Here I will refer to the brainchild of Dobzhansky, Mayr, and Simpson as "the Synthesis."*

attempts at a synthesis. In further contrast to the Synthesis, intellectual openness characterized the British school, as witnessed in J. Huxley's convening scholars representing the breadth of biology not only to discuss problems specific to each discipline, but also to acknowledge their shared concerns about the relevance, meaning, and delineation of *species*.[42] Consequently, the title of Huxley[23] monograph *Evolution: The Modern Synthesis* was not meant to reflect the triumph of the Synthesis. Rather, as he expressed in the quote above regarding the relevance of Goldschmidt and others' work to evolutionary thought, Huxley's title reflects his appreciation of the topical breadth and degree of transdisciplinarity necessary to begin a true evolutionary synthesis.

The question then is not solely directed to understanding how or why the Synthesis survived, but that it so successfully submerged other, more pluralistic attempts to forge a biological synthesis. For indeed, the *ad hominem* assaults Dobzhansky *et al*. (e.g. Refs. *24-26,36,37*) levied against the proponents of the German school hardly constitute scientific refutation or falsification. But the underlying message was sufficient for the Synthesis to triumph over other endeavors. Namely, as Simpson[37] bluntly put it, after World War II those in the *East* (Germany), who had become isolated from those in the *West*, suffered intellectual stagnation while he and fellow *Western* evolutionists proceeded down the correct intellectual path.

As for the fate of the British school, World War II certainly had an impact on Britain's economy and thus on higher education and research. But this may not be the entire explanation. Rather, as a review of the evolutionary literature coming out of the United States for the next two decades or so reveals, there was little or no reference to Huxley or his colleagues' work.[43] In other words, the British school suffered the fate of being ignored.

When Simpson[38] eventually discussed the edited volume that emerged from Huxley's workshop, *The New Systematics*[42], he wrought an attack similar to his reviews of Schindewolf and others of the German school. He condemned Huxley's effort as insignificant and of no value to field. As Simpson (p. 64) wrote: *…from that book alone it is hardly possible to determine exactly what was new about its systematics or to draw up a formal statement of its principles, but it did make it clear that there was a ferment working in the field.* Simpson further demonstrated his disregard for Huxley's effort by summarizing his approach to systematics and taxonomy, which, he declared represented the *new, new systematics* (p. 64).

Unfortunately, by the time Simpson wrote these words, the evolutionary die had been cast. The only credible way in which one should think about evolution was through the lens of the Synthesis. This is historically interesting because, in the end, no one actually knew what the Synthesis was. Rather, because of the Synthesis's architects attacks or dismissal by other means of potentially viable syntheses, one really only knew what the Synthesis was not.

## Whither human evolutionary studies?

Given the intellectual battles waged on the evolutionary front during the first half of the 20th century, it is noteworthy that human paleontologists were silent. One can point to Henry Fairfield Osborn's[44] theory of *aristogenesis*, which was a version of orthogenesis or *purpose-driven* evolution.[45] But Osborn was a vertebrate paleontologist first and turned his attention to human evolution only later in his career (e.g. Ref. *46*).

This was, however, not unusual. Either one was a human anatomist who, as a student of human morphology, was deemed or thought himself qualified to issue declarations on the taxonomy and phylogenetic relationships of human-like fossils. Or one was a vertebrate paleontologist who gained authority from having tackled the systematics and phylogenetic relationships of other groups and then decided to wade into the arena of human fossils. Odd as it may seem, these activities did not also demand embracing the Synthesis or even contributing to evolutionary theory. To the contrary, by accepting evolution simply as descent with modification one could turn to what most paleontologists thought they should be doing: namely arguing that a particular fossil could plausibly be interposed chronologically and morphologically between others as a means to elaborating a picture of evolution through putative ancestor-descendent sequences.[43] But the individuals who defined the future of human evolutionary studies were neither human anatomists nor paleontologists: Theodosius Dobzhansky beginning with Ref.*47* and Ernst Mayr.[48]

Dobzhansky focused on human variability, both morphological and genetic, such as blood groups. His belief in the role of selection affecting gradual genetic and consequently morphological change after geographic isolation separated incipient daughter species from the parental lineage led him to this conclusion: *Since at some point in time humans developed culture, which removed them from the whims of selection, they "controlled" their own evolutionary destiny. Specifically, protected by the barrier of culture, humans would not speciate.*

Mayr's interpretation of the human fossil record, of which like Dobzhansky he lacked first-hand knowledge, reflected a different bias. Mayr proclaimed that while human variability is great now, it was even greater in the past. From this assumption Mayr asserted that since a comparative morphologist would err and not allocate Congo pygmies and Watusi to the same species, *Homo sapiens*, it was unreasonable to interpret the human fossil record as providing evidence of taxic diversity. Mayr (p. 109) then collapsed what he described as *a simply bewildering diversity of [taxonomic] names* into one genus, *Homo*, which he defined on the basis of bipedality. Within this genus, which he envisioned as a seamlessly transforming, non-diversifying lineage, Mayr lumped the known early hominids into the species *transvaalensis*, which was succeeded by a species *erectus* that morphed into the species *sapiens*.

One could suggest that Dobzhansky's and especially Mayr's constraining to one continually changing lineage a human fossil record that even then demonstrated taxic diversity was guided by their reaction to the ethnic cleansing enacted during World War II.[49] But it is odd not only that this scheme was accepted so readily, but also that so many who study human evolution still embrace it.

Why? Historically, it would seem, someone representing human evolution had to jump onto the Synthesis' wagon, and it was Sherwood Washburn.[50]

Echoing Simpson's denigration of the German school for engaging in *typological thinking* or *essentialism*, Washburn berated physical anthropologists for remaining in this outmoded mindset of thinking in terms of fixed types rather than adopting the *population thinking* of the Synthesis (e.g. Refs. *25,26,37,48,51*). Washburn thus became a convert of the central dogma of the Synthesis six years before Mayr's lecture to the Anthropological Society of Washington, which was the beginning of his unabashed campaign to demolish non- or anti-Darwinian alternatives to the Synthesis' version of Darwinism by pitting population against typological thinking (see review of Mayr in Ref. *39*).

The *new* physical anthropology that Washburn imposed on human evolutionary studies, with its emphasis on humans as descendants of an extremely, almost unnaturally variable and gradually transforming lineage species may have seemed reasonable at the time. Nevertheless, as with the tenets of the Synthesis, the intellectual stultification with which Mayr and then Washburn shackled human paleontology, and subsequently Mayr the anthropological community in general, has outlived its usefulness – if as hindsight suggests, they were ever useful. At the very least, alternatives to suggestions that have been so long-lived and even elevated to the level of truth should be considered.

## Species, speciation, and genes: the legacy of the synthesis

Although the title of Mayr's[25] monographic contribution to the Synthesis was *Systematics and the Origin of Species*, very little in it deals with the practice of systematics.[43] In contrast to J. Huxley and colleagues'[42] focus on how conceptualizing species depends on the type of organism under study, Mayr[25] provides no insight into the matter whatsoever. Rather, one of his primary objectives is to prove by assertion that the origin of species is a slow, continuous, and smoothly transformational process. For example:

> *That speciation is not an abrupt, but a gradual and continuous process is proven by the fact that we find in nature every imaginable level of speciation, ranging from an almost uniform species at one extreme to one in which isolated populations have diverged to such a degree that they can be considered equally well as separate, good species at the other extreme…A widespread species is more likely to represent the first stage of speciation than one with a narrowly restricted range.* (p. 159)

This quote is representative of Mayr's belief in his powers of observation being so finely honed that, as he proclaimed elsewhere,[5], he could actually identify species in the making. Mayr's dogmatism also led him to diminish or even reject the importance of all modes of speciation (e.g. sympatric, allopatric speciation via peripheral isolates, and especially polyploidy in plants) but one. Specifically, complete geographic isolation (= allopatry) of the sort that cleaves a parent species into two relatively large daughter populations. Subsequently, different selection pressures that geographic separation would presumably impose on daughter populations would guide them toward reproductive isolation. Mayr[25] combined these elements in his *biological species definition*:

> *A species consists of a group of population which replace each other geographically or ecologically and of which the neighboring ones intergrade or interbreed wherever they are in contact or which are potentially capable of doing so (with one or more of the populations) in those cases where contact is prevented by geographical or ecological barriers.*
>
> *Or shorter: Species are groups of actually or potentially interbreeding natural populations, which are reproductively isolated from other such groups* (p. 120).

It is not obvious how this definition clarifies anything. Indeed not only is it next to impossible to apply the *biological species definition* to extant organisms, it is inapplicable to extinct organisms. Yet Mayr was so convinced of the veracity of his definition and so dead-set on demolishing theoretical alternatives to the Synthesis' emphasis on gradualism that he could declare: *…the species concept has been clarified by the taxonomist, and we know now that species differ by so many genes that a simple mutation would, except for some cases in plants, never lead to the establishment of a new species* (p. 155).

How Mayr or his contemporaries knew *that species differ by so many genes* is a mystery except in the context of believing, in the Morganian sense, that there are specific *genes for* specific morphological features and then extrapolating from the speculation (*species differ by many features*) to the even more speculative claim that *species differ by many genes*. Of course, none of this has any connection to the conception of allopatry leading to reproductive isolation. Further, as Mayr knew from his own ornithological work, taxonomists often erect a new species, or even a new genus and species, on the basis of only one or a few features. This inconsistency notwithstanding, a legacy of the Synthesis that remains cemented in paleoanthropology is the unacknowledged inferring of *specific genes for specific morphologies* from the very morphological features these genes are supposed to underlie. This is obvious in the language of *multiregionalists* (e.g. Refs. *52-55*), as well as of those who embrace a gradual and smoothly continuous transition from *archaic* to *modern* humans (e.g. Refs. *56-59*). In particular it is commonplace to read in the literature of specimens deemed *intermediate* or providing evidence of *hybridization* described as presenting a mix of *Neanderthal* and *modern human* features. The implication and sometime overt claim is that there are *genes for* traits that are specifically Neanderthal and other *genes for* traits that are specifically modern human, and that the traits these genes supposedly underlie will be reflect in hybrids.

Interestingly, now that it is more feasible to sequence and compare both contemporary and ancient nDNA, a similar language and apparently more biological scenario of the *genes for* conception has emerged.[60-62] In this case, specific genes are identified as *Neanderthal* or *Homo sapiens* in comparison with *Pan* from which their transformation to generate features deemed Neanderthal or *Homo sapiens* are then extrapolated. Of further note is that genes identified as Neanderthal and present in the Eurasians but not in the sub-Saharan Africans in the sample are said to represent a period of interbreeding between Neanderthals and ancestors of modern Eurasians after the latter diverged from an African ancestor.[60] This scenario is reminiscent of an interpretation of human and chimpanzee nDNA sequences as reflecting a prolonged period of interbreeding between the forerunners of these two living hominoids.[63] Informing these investigations is the belief that one can identify genes that are specifically chimpanzee, *Homo sapiens*, and Neanderthal.

As to the interpretation of Neanderthal-*Homo sapiens* similarities and differences, Green *et al*.[60] assume a close human-chimpanzee relationship and then use chimpanzee DNA sequences to *determine* character polarity. In other words sequence data do not generate either a human-chimpanzee or a human-Neanderthal sister relationship. These relationships – to the exclusion of other primates – are first taken as real and then similarities between Neanderthal and chimpanzee sequences are interpreted as primitively retained in the extinct hominid. When Neanderthals and/or modern humans differ from the ape, the differences are interpreted as derived *character* states.

Yet while this approach to assessing molecular polarity – a single taxon is defined a priori as representing in its entirety the primitive state against which to judge the primitiveness or derivedness of two or a few taxa – is commonplace, it is also contradictory. Namely, as articulated by Zuckerkandl and Pauling[64] in their molecular assumption (see Ref. *65*), and subsequently embraced by other molecular systematists without question (e.g. Refs. *66,67-71*), if molecular change is supposed to be an ever-ongoing process (such that taxa acquire molecular difference as a function of time since divergence), how can a taxon also remain totally primitive (= unchanged)?[72] Furthermore, if the endeavor is to generate a theory of relatedness, how can one begin the analysis by assuming first which taxon will be the primitive sister of other taxa?[7]

With regard to hominid evolution, this contradiction is alive and well. For instance, Green *et al.*[60] analyze only three taxa: *Pan*, Neanderthal, and *Homo sapiens*. *Pan* is presumed primitive in the small portion of the DNA analyzed. When *H. sapiens* and *H. neanderthalensis* differ in DNA sequence or gene, the inference is that there are specific Neanderthal and specific human genes. The task is then to identify these genes in order to generate a scenario of how *H. neanderthalensis* morphology was converted into *H. sapiens* morphology. And Green et al. do just that. They propose (p. 717) *that an evolutionary change in RUNX2 was of importance in the origin of modern humans and that this change affected aspects of the morphology of the upper body [especially rib cage and clavicle shape] and cranium [especially frontal protrusion and bossing]* (notes from their text added). But while this makes a nice story, it does not actually reflect the developmental context of *RUNX2* (*CBGA1*) or the affects of altering it.

Mutations affecting the *RUNX2* (*CBGA1*) gene are autosomal dominant and reduce the amount of functional RUNX2 transcription factor in cells, thereby systemically impacting chondro- and osteo-genesis as well as tooth formation (e.g. Refs. *73,74*). The disorder caused by this dysregulation is cleidocranial dysplasia and its manifestations include short stature and arms, scoliosis, short tapering fingers, broad thumbs, hypo-/a-plastic clavicles (with concomitant medial approximation of shoulder joints), extreme medial approximation of distal femora, patent fontanelles and metopic/frontal suture, poorly pneumaticized mastoid processes, bulging frontals (as also seen in normal third-term fetuses and neonates with unfused frontal sutures), widespread orbits, flat nasal regions, small upper jaws, supernumerary or peg-shape teeth, and developmental inhibition of primary teeth. There are also significant soft-tissue anomalies.[75,76]

For Green *et al*.'s scenario to *work*, Neanderthals must be primitive relative to *H. sapiens*, with alteration of the *RUNX2* signaling pathway transforming features of the former hominid into those of the latter species. If we assume that mutations affecting *RUNX2* in modern humans convert to the primitive state, proper chondro-, osteo-, and odonto-genesis would be impaired. Yet morphologically normal Neanderthals do not present hypoplastic or aplastic bone or tooth formation. To the contrary, *H. neanderthalensis* had robust and *oversized* long bone epiphyses, medial outgrowths from the lateral walls of the nasal cavity, often thick diaphyseal bone, and relatively tall and in profile anteriorly curved supraorbital margins; some individuals also develop *taurodontism*, which is characterized by development of an extremely long, molar root with barely differentiated root tips (cf. Refs. *57,78-81*). Further, *H. neanderthalensis* developed noticeably protrusive nasal regions and large maxillae that taper anteriorly (producing a wedge-shape *snou*), an extremely long thumb, terminal manual phalanges that are distally compressed anteroposteriorly and broad laterally, and widely separated shoulder joints due in part to development of the relatively longest clavicle of any primate (ibid.).

From a broadly comparative, cladistic perspective, in the features cited above Neanderthals are clearly derived relative to other hominids, including *Homo sapiens*.[78,80-84] Only by assuming that evolutionary change is essentially orthogenetic can one interpret these and other Neanderthal features as primitive relative to their counterparts in *H. sapiens* (e.g. Refs. *57,60*).

From a developmental perspective, features such as thickened diaphyses, expanded articular regions, lengthening of the thumb, distal broadening of manual terminal phalanges, taurodontism, distinctly mounded supraorbital margin, and extraordinary clavicular elongation are characteristics of hyperostosis, not of hypostosis or hypoplasia, and certainly not of aplasia (cf. Ref. *85*). Indeed, since *RUNX2* is critical to normal chondro-, osteo-, and odonto-genesis (e.g.Refs. *73,74*) alterations of it as Green *et al*. suggest (or more properly, altering expression of the RUNX2 transcription factor with consequent downstream effects) would not convert skeletal and dental morphology distinctive of Neanderthal into that which is distinctive of *H. sapiens*. Rather, the result would be diagnosable as cleidocranial dysplasia.[75,76] Further, since the effects of RUNX2 are systemically critical for proper skeletogenesis, it is unlikely that only one or a few features – such as a clavicle, the frontal bone, some ribs – would be affected but the rest of the skeleton and the teeth, not to mention soft-tissue anatomy, would remain unaltered.

As for the uniquely bossed frontal bone of *H. sapiens*, this configuration is not also associated with delayed onset of fontanelle closure, metopism, widely spaced orbits, a flattened nasal region, and a reduced maxilla. But, then, specimens of *H. neanderthalensis* with bossed frontals do not express these features either, e.g. the adults La Ferrassie 1, Amud, Krapina C, or Monte Circeo 1, or the juveniles/adolescents Engis, Roc de Marsal, La Quina 5, or Le Moustier (see descriptions and illustrations in Ref. *79*).

On the other hand, in analogy to the correlation between overexpression of the transcription factor ectodysplasin and the development of more complex molar cusp and crest patterns in mice,[86] overexpression of the RUNX2 transcription factor, if part of a signaling pathway that induces hyperostosis and hyperodontogenesis, may have played a role in Neanderthals developing some of their unique cranial, postcranial, and dental morphologies. But we will not know if this is the case. As we do not know the signaling pathways that underlie *Homo sapiens*-specific morphology, it is doubtful we are close to understanding signaling pathways that underlie any of the derived features that distinguish extinct species of hominid.

## Biology versus wishful thinking

The notion that one might identify specific genes that *make* a modern human or a Neanderthal is appealing. Would it not be wonderful to point to a handful of genes as *the* underlying source of difference between our species and a potential fossil relative? Nevertheless, this is wishful thinking, even if specific genes or gene products implicated in the development of features or biological systems can be identified. For in Metazoa, unlike bacteria, ca. 97-98% of the genome is non-coding and a large proportion of that is comprised of developmentally regulated genes.[87]

But identifying similar genes or gene products in two or more taxa – even if one can experimentally determine their roles in the development of extant species – does not inform with regard to the recruitment of these molecules in developmental time and cellular space or to their interactions with other molecules.[88,89] The complexity and extent of such signaling pathways remain extremely difficult to determine in experimental organisms. It will be impossible in fossils.

This hurdle notwithstanding, what is interesting about the language of gene identification in analyses of ancient DNA is that it not only retains the conception of *specific genes for specific morphologies*. It also retains the element of population genetics thinking that so troubled de Beer.[27] Namely, that by focusing on mutation and hereditary transmission from parent to offspring, the developmental unfolding and differentiation of the individual is ignored. Simply identifying the *DLX* (distal-less) gene in butterflies and echinoderm larvae does not reveal that in butterflies this gene is recruited in the signaling pathway that produces wing eyespots,[90] while in sea urchins it is expressed simultaneously with the engrailed and orthodenticle homeobox genes to transform larvae from bilateral to radial symmetry.[91]

In short, simple comparisons of linear sequences of nucleotides do not reveal developmental and morphological differences between eukaryotes, and especially between metazoans. Rather, different and functionally different genes exist as a result of RNA- and transcription factor-mediated alternative intron splicing and exon frame reading, which together construct developmental genes from a stretch of DNA that is identified only by a start and stop codon.[92,93] Thus, in terms of organismal development – and not in terms of autosomal genes that may be correlated with, for example, eye color and with which population geneticists have been preoccupied – it is erroneous and certainly abiological to endeavor to identify *specific genes for specific structures* (e.g. Refs. *94,95*). But since such a gene-morphology relationship had been assumed, how surprising it must have been when, for example, the human genome consortium discovered that rather than >100,000 genes, the human genome comprises <23,000 genes, only ca. four times the number of genes in *Saccharomyces* (the budding yeast). How to make >100,000 genes from ca. 23,000? Multiple permutations of alternatively splicing introns and translating (both sense and antisense) exon-reading frames!

As Davidson and Erwin[96] argued, there is a developmentally integrated hierarchy of instructional information that spans basic gene regulatory networks (GRNs) fundamental to establishing basic body plans to differentiation gene batteries (DGBs) involved in the terminal specialization of tissues and structures. In other words, there is a *molecule-morphology* continuum that cannot be teased apart with *molecules* and *morphology* being treated as separate, independent entities.[97] Further, we are barely at the threshold of understanding the role in both plants and animals of non-Mendelian inheritance in developmental and epigenetic processes.[98,99]

I am not suggesting that *morphology* is not heritable. For after all, (multicellular) organismal form is ultimately tied to the DNA transmitted from one generation to the next. Also inherited is the hierarchy of integrated signaling pathways that orchestrate the transformation of, for instance, a morula into the adult of its species. But it is not because there are *specific genes for specific morphologies* that we might hypothesize derived features for subclades and ultimately species of any posited clade. To be redundant, it is the different ways in which introns are alternatively spliced and exon frames read, continuously in different ways from the least differentiated to the most differentiated state of development, with potential input from the developing organism's surroundings (e.g. cell-cell or organism-environment), that yields the *finished product*: *the* organism. Consequently, the quest should be not to identify single genes as smoking guns of species identity. Rather the endeavor should be focused on understanding how inherited DNA, especially developmentally regulated *genes*, are exploited to create one species rather than another.

## Final thoughts

It is a curious historical twist that the underlying presumption in paleoanthropology since Huxley[100] has been to diminish recognition of taxic diversity in the fossil record by referring to a vague notion of extreme variability among living humans and, by unjustified inference, also in their extinct relatives.[48]Although minimizing differences among fossil hominids may have been provoked by a post-World War II backlash to ethnic cleansing and racism,[49] the fact remains that two architects of the Synthesis imposed their non-synthetic view of evolution on human evolutionary studies, and the field succumbed to it. One may well wonder how different evolutionary biology, including paleoanthropology, would have been if the architects of the US-based evolutionist had not submerged the contemporaneous British or German attempts at a true evolutionary synthesis. At the very least, the spirit of alternative thinking that had characterized evolutionary biology for nearly 100 years would likely have made possible the co-existence of competing interpretations of the human fossil record and theories of hominid relationships.

Increasing technological sophistication, beginning with the re-emergence of molecular systematics in the 1960s and now the capacity for sequencing large portions of genomes, or the formulation of complex algorithms for managing huge databases, does not necessarily correlate with refinement of phylogenetic theory or methodology. Indeed, any such endeavor is no more sophisticated than the assumptions that underlie it. Hopefully, especially with the current pace of understanding the fundamentals of organismal development, attempts at a true synthesis in evolutionary biology will begin to surface. And as they do, perhaps they not only will spill over into human evolutionary studies, but will have the effect of broadening the scope of the discipline rather than provoking further intellectual retrenchment.

## References

1. J.H. Schwartz. Sudden Origins: Fossils, Genes, and the Emergence of Species. New York, John Wiley & Sons (1999).
2. C. Darwin. The Variation of Animals and Plants under Domestication. London, John Murray (1868).
3. W. Bateson, E.R. Saunders. Reports to the Evolution Committee of the Royal Society. Report 1. Experiments Undertaken by W. Bateson, F.R.S. and Miss E.R. Saunders. London, Harrison & Sons (1902).
4. W. Bateson. Mendel's Principles of Heredity. Cambridge, Cambridge University Press (1909).
5. B. Bateson. William Bateson, F.R.S., Naturalist: His Essays & Addresses Together with a Short Account of His Life. Cambridge, Cambridge University Press (1928).
6. T.H. Morgan. Evolution and Adaptation. New York, MacMillan (1903).
7. R. Olby. Origins of Mendelism. Chicago, University of Chicago Press (1985).
8. W.B. Provine. The Origins of Theoretical Population Genetics. Chicago, The University of Chicago Press (1971).
9. C. Darwin. On The Origin of Species by Means of Natural Selection, or the Preservation of Favored Races in the Struggle for Life. London, John Murray (1859).
10. W. Bateson. Materials for the Study of Variation, Treated with Especial Regard to Discontinuity in the Origin of Species. New York, Macmillan (1894).
11. H. de Vries. The Mutation Theory. Chicago, Open Court (1910).
12. S.G. Mivart. On the Genesis of Species. London, John Murray (1871).
13. T.H. Huxley. Review of "The Origin of Species". *The Westminster Review* ***17***, 22-79 (1860).
14. J.H. Schwartz. 2005. Darwinism versus Evo-Devo: a late 19th c. debate. In: S. Mueller-Wille, H.J. Reinberger (Eds.), A Cultural History of Heredity III: 19th and early 20th Centuries, pp. 67-84. Berlin, Max Planck Institute for the History of Science (2005).
15. T.H. Morgan. A Critique of the Theory of Evolution. Princeton, Princeton University Press (1916).
16. T.H. Morgan. On the mechanism of heredity. Proceedings of the Royal Society (Biology) ***94,*** 162-197 (1922).
17. T.H. Morgan. Evolution and Genetics. Princeton, Princeton University Press (1925).
18. T.H. Morgan et al. The Mechanism of Mendelian Heredity. New York, Henry Holt (1926).
19. W. Johanssen. The genotype conception of heredity. *Am. Nat.* ***45***, 129-159 (1911).
20. W. Bateson. Problems of Genetics. New Haven, Yale University Press (1913).
21. E. Mayr, W.B. Provine. The evolutionary synthesis. *B. Am. Acad. Arts Sci.* ***34***, 17-32 (1981).
22. E. Mayr. The modern evolutiionary theory. *J. Mammal.* ***77***, 1-7 (1996).
23. J. Huxley. Evolution: The Modern Synthesis. New York, Harper & Brothers (1942).
24. T.H. Dobzhansky. Genetics and the Origin of Species. New York, Columbia University Press (1941).
25. E. Mayr. Systematics and the Origin of Species. New York, Columbia University Press (1942).
26. G.G. Simpson. Tempo and Mode in Evolution. New York, Columbia University Press (1944).
27. G.R. de Beer. Embryology and Evolution. Oxford, Clarendon Press (1930).
28. E.B. Ford, J.S. Huxley. Mendelian genes and rates of development in *Gammarus chevreuxi*. *Br. J. Exp. Biol.* ***5***, 112-134 (1927).
29. J.A. Huxley. Time relations in amphibian metamorphosis, with some general considerations. *Sci. Prog.* ***17***, 606-618 (1923).
30. J. Huxley, J. Introductory: towards the new systematics. In: J. Huxley (Ed.) The New Systematics, pp. 1-46. Oxford, Clarendon

Press (1940).

31. R.B. Goldschmidt. Lymantria. *Bibliotheca Genetica* ***11***, 1-180 (1934).
32. R.B. Goldschmidt. The Material Basis of Evolution. New Haven, Yale University Press (1940).
33. C.H. Waddington. Organisers and genes. Cambridge, Cambridge University Press (1940).
34. T. Dobzhansky. Genetics and the Origin of Species. New York, Columbia University Press (1937).
35. J.H. Schwartz, I. Tattersall. Fossil evidence for the origin of *Homo sapiens*. *Yearb. Phys. Anthropol.* ***53***, 94-121 (2010).
36. G.G. Simpson. Review of O. Schindewolf, *Grundfragen der Paleontologie* and *Der Zeitfaktor in Geologie und Paleontologie*. *Q. Rev. Biol.* ***27***, 388-389 (1952).
37. G.G. Simpson. Essay-review of recent works on evolutionary theory by Rensch, Zimmermann, and Schindewolf. *Evolution* ***3***, 178-184 (1949).
38. G.G. Simpson. Principles of Animal Taxonomy. New York, Columbia University Press (1961).
39. M.P. Winsor. The creation of the essentialism story: an exercise in metahistory. *Hist. Phil. Life Sci.* ***28***, 149-174 (2006).
40. G.L. Jepsen. Forward. In: G.L. Jepsen, G.G. Simpson and E. Mayr (Eds.), Genetics, Paleontology, and Evolution, V-X. New York, Atheneum (1963).
41. O. Schindewolf. Basic Questions in Paleontology: Geologic Time, Organic Evolution, and Biological Systematics. Chicago, University of Chicago Press (1993).
42. J.H. Schwartz 2011. Systematics and Evolutionary Biology: uneasy bedfellows? *Rev. Mex. Biodivers.* ***82***, 1-18 (2011).
43. H.F. Osborn. Aristogenesis, the creative principle in the origin of species. *Am. Nat.* ***68***, 193-235 (1934).
44. G.L. Jepsen. Selection, 'orthogenesis,' and the fossil record. *P. Am. Philos. Soc.* ***93***, 479-500 (1949).
45. H.F. Osborn. Men of the Old Stone Age: Their Environment, Life, and Art. New York, C. Scribner (1915).
46. T. Dobzhansky. On species and races of living and fossil man. *Am. J. Phys. Anthropol.* ***2***, 251-265 (1944).
47. E. Mayr. Taxonomic categories in fossil hominids. *Cold Spring Harbor Symposium on Quantitative Biology* ***15***, 109-118 (1950).
48. J.H. Schwartz. "Race" and the odd history of paleoanthropology. *Anat. Rec. Part B* ***289***, 225-240 (2006).
49. S.L. Washburn. The new physical anthropology. *T. New York Acad. Sci.* ***13***, 298-304 (1951).
50. E. Mayr. Speciation and systematics. In: G.L. Jepsen, G.G. Simpson and E. Mayr (Eds.), Genetics, Paleontology, and Evolution, pp. 281-298. New York, Atheneum (1949).
51. M.H. Wolpoff et al. Modern human ancestry at the peripheries: a test of the replacement theory. Science ***291***, 293-297 (2001).
52. M.H. Wolpoff et al. 1994. Multiregional evolution: a worldwide source for modern human populations. In: M. Nitecki and D. Nitecki (Eds.), Origins of Anatomically Modern Humans, pp. 175-199. New York, Plenum (1994).
53. M.H. Wolpoff. Multiregional evolution: The fossil alternative to Eden. In: P. Mellars and C.B. Stringer (Eds.), The Human Revolution: Behavioral and Biological Perspectives on the Origins of Modern Humans, pp. 62-108. Edinburgh, Edinburgh University Press (1989).
54. A. Thorne, M.H. Wolpoff. Regional continuity in Australasian Pleistocene hominid evolution. *Am. J. Phys. Anthropol.* ***55***, 337-349 (1982).
55. H. Rougier et al. Pestera cu Oase 2 and the cranial morphology of early modern Europeans. *P. Natl. Acad. Sci. USA* ***105***, 1165-1170 (2007).
56. E. Trinkaus. Modern human versus Neandertal evolutionary distinctiveness (with CA comment). *Curr. Anthropol.* ***47***, 597-620 (2006).
57. C. Duarte et al. The early Upper Paleolithic human skeleton from the Abrigo do Lagar Velho (Portugal) and modern human emergence in Iberia. *P. Natl. Acad. Sci. USA* ***96***, 7604-7609 (1999).
58. E. Trinkaus. Western Asia. In: F. Smith and F. Spencer (Eds.), The Origins of Modern Humans, pp. 251-325. New York, Alan R. Liss (1984).
59. R.W. Green et al. A draft sequence of the Neandertal genome. *Science* ***238***, 710-722 (2010).
60. M. Krings et al. Neandertal DNA sequences and the origin of modern humans. *Cell* ***90***, 19-30 (1997).
61. J.P. Noonan et al. Sequencing and analysis of Neanderthal genomic DNA. *Science* ***314***, 1113-1118 (2006).
62. N. Patterson et al. Genetic evidence for complex speciation of humans and chimpanzees. *Nature* ***441***, 1103-1108 (2006).
63. E. Zuckerkandl, L. Pauling. Molecular disease, evolution, and genic heterogeneity. In: M. Kasha and B. Pullman (Eds.), Horizons in Biochemistry, pp. 189-225. New York, Academic Press (1962).
64. J.H. Schwartz, B. Maresca. Do molecular clocks run at all? a critique of molecular systematics. *Biol. Theory* ***1***, 1-15 (2006).
65. W.M. Brown et al. Mitochondrial DNA sequences of primates: tempo and mode of evolution. *J. Mol. Evol.* ***18***, 225-239 (1982).
66. M. Ruvolo et al. 1991. Resolution of the African hominoid trichotomy by use of a mitochondrial gene sequence. *P. Natl. Acad. Sci. USA* ***88***, 1570-1574 (1991).
67. A. Caccone, J.R. Powell 1989. DNA divergence among hominoids. *Evolution* ***43,*** 925-942 (1989).
68. A. Goldberg et al. Adaptive evolution of cytochrom *c* oxidase subunit VIII in anthropoid primates. *P. Natl. Acad. Sci. USA* ***100***, 5873-5878 (2003).
69. V. Sarich. A molecular approach to the question of human origins. In: P. Dolhinow and V. Sarich (Eds.), Background for Man, pp. 60-81. Boston, Little Brown (1971).
70. E. Zuckerkandl. On the molecular evolutionary clock. *J. Mol. Evol.* ***26***, 34-46 (1987).
71. J.H. Schwartz. Molecular systematics and evolution. In: R.A. Meyer (Ed.) Encyclopedia of Molecular Cell Biology and Molecular Medicine (EMCBMM), pp. 515-540. Weiheim, Wiley-VCH Verlag (2005).
72. L.F. Huang et al. Mouse clavicular development: analysis of wild-type and cleidocranial dysplasia mutant mice. *Dev. Dynam.* ***210***, 33-40 (1997).
73. S. Mundlos et al. Mutations involving the transcription factor CBFA1 cause cleidocranial dysplasia. *Cell* ***30***, 773-779 (1997).
74. G. D'Alessandro et al. Cleidocranial dysplase: etiology and stomotognathic and craniofacial abnormolaties. *Minerva Stomatol.* ***59***, 117-127 (2010).
75. R. Mendoza-Londono, B. Lee. Cleidocranial dysplasia. *Gene Reviews NBK* ***1513***, 1-15 (1993).
76. J. Radovcic et al. The Krapina Hominids: An Illustrated Catalog of Skeletal Collection. Zagreb, Mladost (1988).
77. J.H. Schwartz, I. Tattersall. Morphology, variability, and systematics: lessons from Krapina. *Periodicum Biologorum* ***108***, 389-401 (2006).
78. J.H. Schwartz, I. Tattersall 2002. The Human Fossil Record, Volume One, Terminology and Craniodental Morphology of Genus *Homo* (Europe). New York, Wiley-Liss (2002).
79. J.H. Schwartz et al. Architecture of the nasal complex in Neanderthals: comparison with other hominids and phylogenetic significance. *Anat. Rec.* ***291***, 1517-1534 (2008).
80. E. Trinkaus, W.W. Howells. The Neanderthals. *Sci. Am.* ***241***, 118-133 (1979).
81. I. Tattersall, J.H. Schwartz. Evolution of the genus *Homo*. *Annu.*

*Rev. Earth Planet. Sci.* ***37***, 67-92 (2009).

82. J.H. Schwartz, I. Tattersall. The Human Fossil Record, Volume Two, Craniodental Morphology of Genus *Homo* (Africa and Asia). New York, Wiley-Liss (2003).
83. J.H. Schwartz, I. Tattersall. Variability in Hominid Evolution: putting the cart before the horse? In: M. Antunes (Ed.) Últimos Neandertais em Portugal (Last Neandertals in Portugal) Odontologic and Other Evidence, pp. 367-401. Lisboa, Academia das Ciéncias de Lisboa (2000).
84. J.H. Schwartz. Skeleton Keys: an introduction to human skeletal morphology, development, and analysis. New York, Oxford University Press (2007).
85. A.T. Kangas et al. Nonindependence of mammalian dental characters. *Nature* ***432***, 211-214 (2004).
86. J.A. Eisen. Assessing evolutionary relationships among microbes from whole-genome analysis. *Curr. Opin. Microbiol*. ***3,*** 475-480 (2000).
87. J. Gerhart, M. Kirschner. Cells, embryos, and evolution: toward a cellular and developmental understanding of phenotypic variation and evolutionary adaptability. Malden, Blackwell (1997).
88. S. Gilbert. Developmental Biology. Sunderland, Sinauer (2006).
89. S.B. Carroll et al. Pattern formation and eyespot determination in butterfly wings. *Science* ***265***, 109-114 (1994).
90. C.J. Lowe, G.A. Wray. Radical alterations in the roles of homeobox genes during echinoderm evolution. *Nature* ***389***, 718-721 (1997).
91. G. Ast. The alternative genome. S*ci. Am.* ***292***, 59-65 (2005).
92. T.W. Nilsen, B.R. Graveley. Expansion of the eukaryotic proteome by alternative splicing. *Nature* ***463,*** 457-463 (2010).
93. H. Pearson. What is a gene? *Nature* ***441***, 399-401 (2006).
94. K. Stotz. With 'Genes' Like That, Who Needs an Environment?: Postgenomics's Argument for the 'Ontogeny of Information'. *Philos. Sci.* ***73***, 905-917 (2006).
95. E.H. Davidson, D.H. Erwin. Gene regulatory networks and the evolution of animal body plans. *Science* ***311***, 796-800 (2006).
96. J.H. Schwartz. Organismal innovation. In: M.J. O'Brien and S.J. Shennan (Eds.), Innovations in Cultural Systems: Contributions from Evolutionary Anthropology, pp. 53-67. Cambridge, MIT Press, (2009).
97. S.J. Lolle et al. Genome-wide non-mendelian inheritance of extragenomic information in *Arabidopsis*. *Nature* ***434***, 505-509 (2005).
98. M. Rassoulzadegan et al. RNA-mediated non-mendelian inheritance of an epigenetic change in the mouse. *Nature* ***441***, 469-474 (2006).
99. T.H. Huxley. On Some Fossil Remains of Man. In: Man's Place in Nature. New York, D. Appleton (1863).