Chapter 1
Introduction to Evo-Devo-Anthro

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Evolutionary developmental biology, or evo-devo, is a relatively young branch of biology concerned with how and why organismal development matters to evolution. Evo-devo encompasses a range of unified research questions and empirical approaches that can be grouped into two complementary research areas (Laublicher 2007). The first area concerns the process of organismal development. This research uses molecular tools such as studies of gene and protein expression patterns to understand how *processes* of organismal development have evolved and produced phenotypic diversification at macroevolutionary scales. The second approach focuses on the role that process plays in structuring the *pattern* of heritable phenotypic variation among individuals. This approach relies on quantitative genetic theory and morphometric tools to measure developmentally determined patterns of phenotypic variation, typically at the level of populations, and to understand how these patterns have biased or constrained the rate and direction of evolutionary change within and between species (Raff 2000).

In the past couple of decades, the types of research questions that evo-devo addresses have also become of great interest to biological anthropologists. The discipline is gaining traction among researchers interested in the role(s) played by organismal development in the evolution of uniquely human, and non-human primate, traits. This volume aims to provide an overview of past and ongoing research in evo-devo specifically as it applies to the study of human and primate evolution – Evolutionary Developmental Anthropology (EDA, or Evo-Devo-Anthro). In this

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introductory chapter, we begin with a brief survey of the origins and principal discoveries of evolutionary developmental biology. We then discuss the emergence of evo-devo in anthropology in the context of past research at the interface of human/primate development and evolution. Finally, we summarize the current state of affairs in the growing field of evo-devo anthropology, and highlight a number of knowledge gaps which are promising avenues for future research in this field.

A Brief History of Evo-Devo

As this volume attests, many different approaches to studying the reciprocal interactions of development and evolution fall under the broad umbrella of evolutionary developmental biology. As a result, finding consensus on a single definition of evo-devo that describes what the field is, and what it seeks to accomplish, can be challenging. The lack of consensus stems from two distinct goals: studying process at macro- and microevolutionary scales. These goals are driven by the desire to understand the broad developmental processes that drive the evolution and diversification of form among species and higher taxonomic levels, versus the lower level (but likely similar) processes that pattern the structure of phenotypic variation among individuals within populations, as the fuel for natural selection. This lack of consensus on what evo-devo is also stems from the fact that, although it is in some ways a "new" discipline (Carroll 2005), its roots run deep. The study of organismal development, evolutionary processes, and their complex interactions is at least 150 years old, dating back to 19th-century evolutionary embryologists such as Ernst Haeckel and Francis Balfour, and to Charles Darwin himself (Hall 1999). These pioneers focused on the comparative study of embryology as a window into organismal development, and were particularly interested in what these processes could reveal across taxa about phylogenetic relationships and the evolution of specific traits with a shared evolutionary origin but different morphologies and functions (i.e., homologies such as the hands of dolphins, bats, and humans) (Hall 1999; Maienschein 2007).

Many of these early studies in comparative embryology were concerned with comparing *patterns* of growth and development within and among species. These now-classic works inferred that differences in ontogenetic patterns must account for variation within populations, but especially morphological divergence among taxa in deep time. Evolutionary embryologists were less concerned with lower level biological *processes* (i.e., cellular dynamics) that would explain described developmental *patterns* across all vertebrates. This was largely a practical issue: describing macroscopic changes in vertebrate fetal development between taxa was considerably simpler than documenting changes in the spatial relationships of cells and tissues during morphogenesis. Productivity in this area of study has since increased dramatically with the advent and benefit of modern molecular tools.

In contrast to other fields in biology such as population genetics, progress in embryology for much of the 20th century was relatively slow, in part due to the technical challenges associated with studying embryonic development, to the extent that the discipline contributed relatively little to the modern evolutionary synthesis

of the 1940s (Carroll 2005; Maienschein 2007). The Modern Synthesis united several disciplines studying evolutionary biology from different angles, particularly population genetics and paleontology (Mayr and Provine 1998). It suggested that the evolution of quantitative traits is gradual, and occurs through mechanisms consistent with Mendelian genetics, namely through small genetic changes that produce continuous (i.e., bell-curved) variation within populations, which can then be acted upon by selective forces. Proponents further argued correctly that this process, occurring at the population level (microevolution), could be extrapolated to higher taxonomic levels and longer timescales to explain macroevolutionary patterns.

Despite the realization that development interposes itself between genes and phenotypes, and hence likely influences the transition from one to the other, the study of embryology was not revived after the synthesis. Rather, the synthesis served to affirm the primacy of genes and phenotypes in determining evolutionary change, relegating organismal development, not to mention the field of epigenetics (*sensu* Waddington, Jamniczky *et al.* 2010) to a secondary, less important, process linking genes to phenotypes. For several decades following the synthesis, organismal development continued to be viewed as a black box, something that was "hopelessly complex and would involve entirely different explanations for different types of animals" (Carroll 2005:6). However, the reasons for ignoring organismal development in the study of the evolution of animal form, in particular early embryological events such as morphogenesis, were not entirely philosophical. Considerable practical obstacles in developmental biology remained: although genes were now seen as primary drivers of evolutionary change, prior to the late 1970s no one had successfully identified and localized genes that *determine* animal form, let alone how changes in their structure or function could lead to the *evolution* of animal form and function.

Breakthroughs in developmental biology were finally achieved in the late 1970s and 1980s, first in fruit flies, and eventually in vertebrates. These breakthroughs were rooted in technological innovations in molecular genetics: especially the ability to identify, localize, and manipulate genes physically; in particular to visualize their expression patterns; and to relate these to temporal and spatial effects on the development of organismal form (for example through gene inactivation) (Anderson and Ingham 2003). Homeotic genes were among the first genes shown to control key aspects of development, and some consider their discovery to mark the birth of evo-devo (Hall 1999; Carroll 2005). Homeotic genes regulate segmental patterning in the metazoan embryo. Early analyses revealed that loss-of-function mutations in these genes in *Drosophila* caused segmental identity shifts (homeotic transformations), where one segment along the embryo's anterior-posterior axis would take on the likeness of an adjacent segment (Lewis 1978). Homeotic genes act as transcription factors, proteins that regulate the transcriptional activity of other genes (Mallo *et al.* 2010).

Soon after their discovery in *Drosophila,* similar genes with similar tasks in embryonic patterning were uncovered in vertebrates, including humans (Tournierlasserve *et al.* 1989; Krumlauf 1994). These discoveries led to a fundamental evo-devo concept: the developmental genetic toolkit (Carroll *et al.* 2005). Toolkits describe subsets of genes that specify animal form during embryological development. Toolkit genes are distinct from those involved in the routine functions of all cells (housekeeping genes,

Zhu *et al.* 2008), and those that are uniquely expressed in differentiated cell types. Toolkit genes belong to signalling pathways, many acting as transcription factors that regulate the activities of other genes that specify cell fates and/or establishing spatial and temporal expression patterns during morphogenesis. The same toolkits are recruited several times during an individual's development, and contribute to the development of vastly different structures. As a result, toolkit genes have pleiotropic effects on the phenotype, a fact amply demonstrated by disrupting the function of any of these genes (Goodman and Scambler 2001; Goodman 2002).

Developmental toolkits are also highly conserved – down to the level of the nucleotide sequence – across divergent animal phyla. This sequence conservation provided evidence that homology at the phenotypic level, which played such an important role in 19th-century evolutionary embryology, was reflected in homology at the genetic level. Put differently, morphological structures in related species look similar not only because they were inherited from a common ancestor with a similar character trait, but more specifically because these species inherited homologous developmental genetic toolkit(s) specifying these traits. Highly conserved toolkit genes were even found to specify anatomical structures that evolutionary embryologists would have identified as being analogous rather than homologous, such as the eyes of fruit flies and vertebrates (Mark *et al.* 1997). In other words, even though certain traits between vertebrates and invertebrates may not seem homologous in an anatomical sense, they are, with some cautions (Hall 2007), genetically and developmentally homologous via inheritance of the same toolkits from a last common ancestor deep in evolutionary time (Shubin *et al.* 1997).

The existence of seemingly universal developmental toolkits implies that morphology evolves not because of differences in the structure or complement of toolkit genes, but rather because of how and when they are expressed, in other words because of gene regulatory differences among taxa (Prud'homme *et al.* 2007). This idea had already been proposed by Mary-Claire King and A. C. Wilson in a seminal paper in 1975 (King and Wilson 1975). They compared the sequence homology at a macromolecular (i.e., amino acids among proteins) in *Pan* and *Homo*, highlighting a distinction between the well-known organismal differences of these sister taxa, and the high degree of conservation in the amino acid sequence of dozens of proteins primarily related to cell function. They concluded that the striking differences in biology between these taxa could not be explained by differences in the sequence and function of protein-coding genes, and were therefore due to mutations in the non-coding, regulatory regions that control the expression of these genes.

In the age of evo-devo, King and Wilson's observation was extended to anatomical structures. The discovery of homeotic genes and highly conserved developmental toolkits led to the realization that even the striking morphological differences between a human and a chimpanzee were due to differences in the regulation of the same/homologous toolkit genes. This idea is now commonly known as the "*cis*-regulatory hypothesis" (Carroll 2008; Wittkopp and Kalay 2012). C*is*-regulatory elements (CREs) are non-coding DNA regions located on the same DNA strand as the toolkit gene(s) they regulate. CREs typically bind transcription factors, modulating the expression of their targets in a context-specific manner (Wittkopp and Kalay 2012).

Thus CREs enable the same toolkits to be redeployed at different times and in different developmental contexts, for example in different types of tissues or body segments. This plasticity allows morphology to evolve via mutations in CREs rather than in their protein-coding targets. Mutations in CREs not only preserve the structural integrity of the toolkit genes, they also mitigate the potential pleiotropic effects of mutations in the coding sequence of the toolkit gene(s) they regulate. The importance of CREs at macroevolutionary scales is still a matter of debate (Hoekstra and Coyne 2007; Lynch and Wagner 2008; Wagner and Lynch 2008). Still, genetic change in CREs remains a strong candidate for enabling microevolutionary change; that is, producing continuous variation in quantitative traits at the level of the population.

Evolution, Development, and Anthropology

The study of primate development and ontogeny has a long history in biological anthropology. In the late 19th century, European anatomists contributed a number of studies on prenatal and juvenile specimens of apes, monkeys, and even humans (reviewed in Schultz 1926). Many were based on the description of anatomy in primate fetuses, often obtained by chance from zoos or tropical expeditions. Although some were quite detailed (Deniker 1885), most tended to focus on a few readily measured, external characteristics such as body mass and head circumference (Figure 1.1), or more qualitative descriptions of the face, cranium, and soft anatomy. Detailed quantitative analyses were hampered by small sample sizes, which rarely exceeded half a dozen. Such small samples made it difficult to draw conclusions regarding variation among individuals, or even whether the few individuals described were representative of their species. Moreover, samples rarely included longitudinal ontogenetic

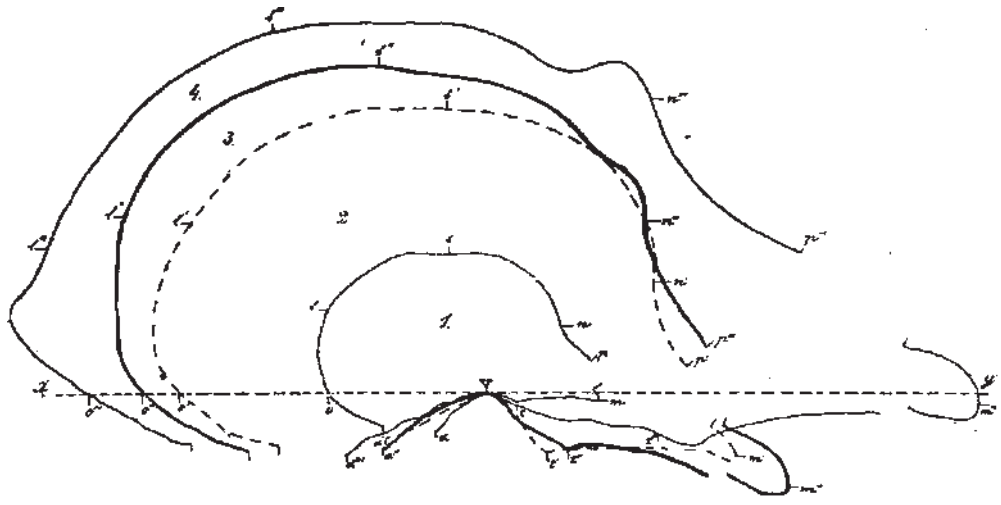

Figure 1.1. Figure from Deniker's 1885 study on cranial growth in hominoids. The figure depicts cranial shape changes over ontogeny in gorillas, starting with a fetus (1, center) to near-adult crania (4, outermost).

series, precluding a temporal dimension to the study of primate development. Most importantly, however, despite the prior publication of both Charles Darwin's *On the Origin of Species* and *The Descent of Man*, few of these studies were conducted in an explicitly evolutionary framework.

Still, these early studies made important contributions to the increasingly intertwined fields of human/primate development and evolution. These comparative studies were some of the earliest to illustrate key evolutionary developmental concepts, such as homology and heterochrony, as they apply to primates and humans. Taken together, they revealed that many interspecific differences in morphology observed in adults first appear prenatally, during fetal growth or even earlier in embryonic patterning. Beyond simply affirming a link between embryology, ontogeny, and evolution, this relatively simple observation led to the recognition that phenotypic divergence among primates, even among closely related taxa such as hominoids, is driven by organismal development, including not only observable differences in postnatal growth rates, but also earlier stages of embryonic and fetal development.

These studies laid the foundation for the more systematic and quantitative comparative ontogenetic studies of European anatomists in the first half of the 20th century, culminating in the work of Adolph Schultz. Between about 1920 and 1960, Schultz published close to 50 articles dealing with growth, development, and variability in different regions of the body, including the head, teeth, vertebral column, limbs, and internal organs in dozens of primate taxa (Howells 1977; Wood 1996). The importance of his contributions is not only in their quantitative nature, but also because, by the same token, they provided a detailed account of variation and variability in morphology within and among primates. Schultz published the bulk of this work before the Modern Synthesis, and long before the advent of molecular embryology. He thus lacked a framework for explaining how, mechanistically, the various parts of the vertebrate body are patterned, grow, and interact, and more importantly, how heritable variation in these complex traits arises. Nonetheless, his contributions highlight the fact that much can be learned about primate evolutionary diversification by studying patterns of growth and development among closely related taxa, and presage the importance of studying phenotypic variation and variability (i.e., the propensity of a trait to vary) for understanding the relationship between organismal development and evolution.

Following in the tradition of evolutionary embryologists and Adolph Schultz, much of the evo-devo research in anthropology in the second half of the 20th century continued to focus on comparative patterns of embryonic, fetal, and postnatal ontogeny within and among taxa. Specifically, many studies addressed heterochrony, or how differences in the timing and rate of development between different parts of the body, and/or between the same parts in different taxa, could explain the evolution of size and shape differences across species (i.e., allometry, Gould 1975, 1977; Alberch *et al.* 1979; Shea 1981, 1983; Shea and Bailey 1996; Minugh-Purvis and McNamara 2002; Mitteroecker *et al.* 2004). Heterochronic shifts are readily tractable with cross-sectional ontogenetic samples, even when the non-adult sample is limited to a few individuals or a few developmental stages. This is especially useful for studying primate evo-devo, because of the relative paucity of prenatal collections of primates.

Moreover, comparative studies of heterochrony, ontogenetic allometry, and evolutionary shifts in life history events using extant primates are useful for understanding the evolution of development as documented in the hominin fossil record, even when single juvenile samples are recovered (e.g., Alemseged *et al.* 2006). This presents an inherent advantage over a developmental genetics approach, which is challenging in a primate framework (see below).

Integration, Modularity, and Evolvability in Biological Anthropology

In parallel with comparative studies of allometry, heterochrony, and other ontogenetic processes in primates, the second half of the 20th century also saw the application of concepts such as morphological integration and modularity to the study of primate evolutionary developmental biology. Morphological integration and modularity describe the interconnectedness of different structures in the vertebrate body (Wagner 1995; Cheverud 1996a; Wagner and Altenberg 1996). These concepts are based on two simple observations: (1) the body of a complex organism is organized into discrete, internally consistent structures that share a common developmental origin or function (i.e., modules), (2) these modules do not develop independently, but rather must interact and grow in such a way that they preserve the proper function of the whole organism throughout its ontogeny (i.e., integration). From a quantitative perspective, modularity and integration are typically assessed in a hierarchical fashion through the magnitude of phenotypic covariation among traits. Specifically, sets of traits that covary more strongly in size and shape with each other than they do with other traits form a module. At the level of the whole organism, some of these modules interact with each other, for example due to their physical proximity, and grow in a coordinated fashion in response to changes in the overall size of the organism (i.e., growth, Hallgrímsson *et al.* 2002). In this sense, the whole organism is also integrated. A good example can be found in the mammalian skull: the cranial base, face, and neurocranium are neighboring structures that form independent modules with different developmental origins and functions, yet the growth of all three is coordinated even while the function of each part (e.g., mastication, sensory input) is preserved (e.g., Hallgrímsson *et al.* 2004, 2007; Bastir and Rosas 2005, 2009; Mitteroecker and Bookstein 2008).

The idea of modularity and integration traces its origins as far back as Georges Cuvier and Charles Darwin, both of whom recognized that body parts are functionally and developmentally correlated, to the extent that "when slight variations in one part occur, and are accumulated through natural selection, other parts become modified" (Darwin 1859:147). The idea that organisms are integrated entities made of correlated parts remained largely qualitative, until 1948, when Everett Olson and Robert Miller published their seminal volume *Morphological Integration* (Olson and Miller 1958). Olson and Miller proposed that both developmental and functional interactions were important sources of correlation among body parts, contributing towards building "integrated" organisms in which these parts function in concert with all

others. Olson and Miller also developed the first quantitative methods, mostly based on statistical correlation, for empirically identifying groups of phenotypic traits that are more strongly integrated on the basis of shared developmental and/or functional factors. One of the examples they used were the teeth of owl monkeys (*Aotus*), revealing stronger patterns of integration (correlation) within teeth than, for example, between the lower and upper molars.

Since then, there have been many publications dealing with morphological integration in primates, beginning with the pioneering work of James Cheverud on the monkey cranium (Cheverud 1982, 1996b). To date, integration and modularity has been studied most extensively in the primate cranium (reviewed in Mitteroecker and Bookstein 2008) and dentition (reviewed in Grieco *et al.* 2013), but also increasingly in the postcranial skeleton (e.g., Young 2004; Young and Hallgrímsson 2005; Rolian 2009; Young *et al.* 2010; Lewton 2012). Many of these studies assess shape (co)variation using geometric morphometric tools, and determine the extent to which these patterns constrain or facilitate evolutionary change in skeletal form (evolvability, Rolian *et al.* 2010; Young *et al.* 2010; Grabowski 2011). These types of studies formulate and test models of integration/modularity based on genetic and developmental processes that, at least in theory, affect the strength of correlations among parts (e.g., pleiotropy); and in this sense, they are studies in evolutionary developmental anthropology. It is important to emphasize, however, that they are not empirical analyses of these genetic and developmental processes *per se*. Instead, most rely on existing developmental evidence from model organisms to test hypotheses regarding the outcome of development on patterns of integration, and what these mean for the evolvability of the primate and hominin skeleton (Rolian 2014).

Developmental Genetics: Next Steps and New Frontiers in Evo-Devo-Anthro

The field of evo-devo is just over 30 years old, and that of vertebrate evo-devo as applied to primates about half that age (e.g., Weiss and Buchanan, this volume). Within this timeframe, and due in no small part to technological breakthroughs in rapid and high-throughput genomics and developmental biology research tools, substantial progress has been made in understanding how processes of organismal development relate to the patterns of macroevolutionary diversity across vertebrate species. In terms of understanding mammalian evo-devo, the primary animal model system remains the very well characterized, now-universal laboratory rodent (e.g., Boughner, Lacruz, Martínez-Abadías *et al.*, Reno, this volume). The success of mouse (and other rodent models such as rats and voles), is due to the relative ease with which these small mammals can be housed and manipulated experimentally, including the benefit of relatively short gestational periods of less than a month and larger litters of about 8–12 pups.

Experimental developmental biology work of the sort routinely done using rodent models is largely impractical in primates, not least because of longer gestational periods, single-births, greater costs of housing, and ethical challenges in handling these larger animals. In this respect, EDA invariably has limitations in terms of

collecting data directly from the developmental genetic processes that regulate primate ontogeny and on which selection can act. The news is not all bad, however, and there is one very good reason to continue to use rodent models for work in EDA: developmental processes in rodents are to a high degree homologous with those of other mammals, including primates (Rolian 2014; Reno, this volume). This homology encompasses morphological modularity in the skull and postcranial skeleton (e.g., Hallgrímsson *et al.* 2002, 2004; Willmore *et al.* 2009) and in the dentition (Chai *et al.* 2000; Jernvall and Thesleff 2012), to the extent that it is tenable to generate and use, for example, mouse mutants that replicate macroevolutionary change evidenced in the hominin fossil record to model the developmental-genetic processes that underlie phenotypic variation in primates living and extinct (Martínez-Abadías *et al.*, this volume). Thus it is possible to meaningfully address fundamental questions in paleoanthropology even if the data are collected from experimental model systems other than primates.

Yet even distantly related model organisms, such as yeast, share with vertebrates, including humans, fundamental cellular processes (e.g., chromatin assembly, Harkness 2005) that help build our understanding of these most basic units – cells – of body tissues and parts including organism maintenance, ageing, and life history. Also, non-mammalian models offer various unique advantages in terms of experimental techniques and options. For example, in mouse it is virtually impossible to perturb development *in utero* without sacrificing both the pregnant mother and her prenatal offspring, or time consuming and costly to create new mouse mutants via genetic engineering approaches. In contrast, the chick/avian model is ideally suited to prenatal *in ovo* surgeries and grafts; and not only does the zebrafish model offer transparent embryos as literal windows into development, but also fish morphogenesis can be perturbed quickly and effectively by adding varying amounts of mutagens to the tank water. Thus, using a variety of model organisms (i.e., yeast, worm, chick, frog, and zebrafish) to describe and experimentally manipulate highly conserved low-level developmental-genetic processes is a feasible and valid solution to gain new mechanistic insights into primate ontogeny and evolution. As other model organisms are adopted and characterized alongside new molecular genetic and developmental biology techniques, the options available to evo-devo anthropologists will no doubt increase as well.

Cross-discipline work is also important to get traction in research areas that to date have proven more intangible. As the degree of cognition and culture appears to distinguish anatomically modern *Homo sapiens* among other primates living and fossil, new frontiers in EDA could tackle the evolutionary-developmental mechanisms underlying behavioral traits such as complex language and abstract thought (Charvet and Finlay, Crespi and Leach, Lalueza-Fox, this volume). Also, the developmental-genetic basis of primate life history demands further attention as an absolutely longer life history period, due in no small part to a protracted childhood, appears to be another trait that is specific, if not unique, to *Homo sapiens* (Gunz, this volume). While the evolutionary patterns of life history variation among primates are now well established, how evolutionary changes in life history are genetically and developmentally regulated remain fascinating and underexplored topics in EDA. In this and all EDA contexts, knowledge of the fossil record and the major transitions it documents is paramount to frame, and then properly test, the right hypotheses.

A related challenge is how to accurately model ontogeny in fossil primates using what is known, or might yet be gleaned from, a relatively few existing fossil specimens. At first glance, the fossil record seems ill-suited to studies of evolution and development, as McNulty writes, "for the simple reason that fossils neither evolve nor develop" (McNulty 2012, p.488). In other words, we can't do developmental genetics or embryology with vertebrate fossils; and except perhaps for our most recent Neanderthal relatives (Green *et al.* 2010), evolutionary genomics in fossil hominins are also impossible. To this, we may add a further complication: with few exceptions (e.g., the Pleistocene site of Sima de los Huesos, De Castro *et al.* 2004; Rosas and Bastir 2004; Gomez-Robles and Polly 2012), hominin fossil samples are generally too small or too distant in time and space to derive reliable "population" estimates of phenotypic (co)variation patterns required for the types of integration and modularity analyses described above. Despite these limitations, there is still an important role for fossils in human evo-devo studies. Although fossil samples are small, more often than not consisting of single data points, they can serve as "yardsticks" by which to test or validate evolutionary hypotheses derived from developmental analyses in neontological taxa (Thewissen *et al.* 2012). For example, fossils can be used to: confirm if different patterns of integration observed among *living* primate taxa have influenced the evolutionary sequence of skeletal changes in our past (Young *et al.* 2010); or test development-based hypotheses about adaptive versus non-adaptive origins of derived skeletal features in hominins (Ackermann and Cheverud 2004; Rolian *et al.* 2010); and, more generally, validate models of life history and ontogenetic evolution within hominoids and hominids (e.g., Bromage 1989; Ackermann and Krovitz 2000; Dean *et al.* 2001; McNulty 2012).

Given the practical difficulties of working with primates in an evo-devo context, biological anthropologists can also explore the utility of *in silico* experiments to test predictions about developmental-evolutionary change during the morphogenesis of a body part (e.g., teeth, limbs), including over longer periods of time in a population (see, e.g., Salazar-Ciudad and Marin-Riera 2013; Rolian, this volume). These increasingly sophisticated computation-driven insights should help build useful theories about phenotypic and ontogenetic plasticity, and subsequently phenotypic evolution, in extant and extinct primates. Also, compared to many developmental genetic methods, classic approaches of studying phenotypic evolvability, integration, and variation using skeletal specimens (e.g., evolutionary quantitative genetics; geometric morphometrics; and other measures of morphological modules and their change) is straightforward and inexpensive with access to large collections, and thus sample populations that more likely capture normal ranges of variation. In this sense, these types of studies will likely continue to be fruitful avenues for research in EDA. These skeleton-based studies can also reasonably be applied to the fossil record, and – no less importantly – fossils used appropriately as yardsticks by which to gauge theories of integration.

As the power of *in vivo*, *in vitro*, and *in silico* techniques increases, another important step to advance EDA is not only for anthropologists to build expertise in developmental biology but also to talk and work directly beside developmental biologists, who continue to cultivate new experimental animal models and *in vivo* and *in vitro* techniques as well as transgenic and other genetic engineering approaches. Further,

the unique ethos and methodologies of each field are driven by fundamental questions that reflect a collective curiosity about why species, as well as individuals, look different from each other; as well as why pathologies (i.e., extremes of phenotypic variation) occur and how they can be diminished or prevented.

Lastly, the field of Evolutionary Developmental Biology itself continues to change, witnessed, for example, by a recent push to incorporate ecological principles, as well as epigenetic influences and mechanical stimuli, into contemporary models of organismal development (Gilbert and Epel 2009; Jamniczky *et al.* 2010; Mammoto and Ingber 2010; Abouheif *et al.* 2014). These new directions and their unique breakthroughs will surely feed into EDA research; and potentially vice versa. For instance, persistent "black boxes" in our understanding include how natural selection (i.e., survival in a particular ecological context) shapes developmental process to effect evolutionary change; and how developmental processes beyond the genetic code constrain evolutionary potential. Beyond these broad questions, there also remain proximate questions regarding primate evolution and development for which we have few answers. This is undoubtedly a long list, and we mention but a few topics here. For example, considering the amount of data already available for other regions of the vertebrate skeleton (e.g., limbs and skulls), it is remarkable that we know relatively little regarding developmental evolution in the axial skeleton (Burke *et al.* 1995). In light of differences in vertebral patterning among hominoids and within the hominin lineage, using mouse models to understand, for example, the underlying mechanisms of homeotic changes in the axial skeleton could give useful insight into important events in human evolution such as the transition to bipedalism (Pilbeam 2004; Williams 2012; Young and Capellini, this volume). Another research area that remains underexplored in EDA, as in developmental biology more broadly, concerns soft tissues (Diogo and Wood, this volume). Little is known regarding the developmental evolution of soft tissues such as muscles, sensory tissues, and the integument, despite the tremendous amount of phenotypic diversity across primates in these traits (Hamrick 2003; Diogo *et al.* 2014). Thus we make the case that now, more than ever, those working or training to work in evolutionary developmental anthropology cast their intellectual nets widely to capture and then make use of as great a wealth of new methods, insights, and inspirations as possible. The end goal of this book is to stimulate interest and build momentum in the burgeoning field of Evolutionary Developmental Anthropology by sharing current EDA work to highlight scientific ground covered thus far as well as suggest new and needed forays into uncharted research territories.

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