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Human EvoDevo:
The Role of Development in Human Evolution

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organized by Philipp Gunz and Philipp Mitteroecker

Konrad Lorenz Institute
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The topic

Evolutionary developmental biology has played a significant role in extending evolutionary theory and has led to numerous novel insights into evolutionary processes and in the patterns of organismal variability.
While many EvoDevo studies have focused on macroevolutionary questions such as the evolution of animal body plans, recent studies addressing the «microevolution» of development, partly based on formal developmental models or selection experiments, have further aimed to bridge EvoDevo theory and quantitative genetics. The emergence of new journals, societies, conferences, and workshops, all devoted to EvoDevo, is testament to the importance of EvoDevo for contemporary biology
The idea that evolutionary modifications of primate development might have led to the appearance of modern humans has a long history in anthropology and can be traced back to early evolutionary biologists and anthropologists such as Geoffroy Saint-Hilaire, Ernst Haeckel, Lois Bolk, and Adolph Schulz.
The aim of this workshop is to contribute to the theoretical and empirical corpus of human EvoDevo, to discuss problems and limitations, and to identify the core themes underlying this scientific discipline. We are confident that the publication resulting from this workshop will be a strong signal to the anthropological community and also to evolutionary biologists, highlighting the importance of developmental approaches in the study of the evolution of mankind.

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Abstracts

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Skyhooks and spandrels: what can EvoDevo tell us about the evolution of syntax?

The capacity for human language is one of the central cognitive faculties with which humans are endowed, and the evolution of syntax in particular has been a topic of heated debate. From the adaptationist and modularist viewpoint (e.g. evolutionary psychology as represented by Pinker or Jackendoff), the language faculty is a complex mental organ, with many intricate parts, all related into a harmonious whole.
This combination of complexity and harmony is prima facie evidence that language, as a whole, and syntax, specifically, are adaptations in the fullest sense. In a long-running counterpoint to this viewpoint, various authors including Gould, Piatelli, Berwick and Chomsky have argued that many aspects of language are by-products of other adaptations (e.g. for vocal production, cognition, or audition), and that the intricacies of 19 syntax in particular mostly result from the interactions of such bona fide adaptations with the principles of neural development and self-wiring.
From this viewpoint, many phenomena that syntacticians study are better viewed as spandrels (a necessary byproduct caused by the constraints of cognitive architecture) than as adaptations. This debate has raged, mostly unproductively, for decades. I will argue that a resolution is to be found by detailed consideration of the mechanisms of neural computation and mammalian brain development. Many computational details of mature brain circuitry are likely to be byproducts of ancient systems of brain development, and have no direct adaptive value. Thus many details of syntax may be spandrels. It is only as part of a broader system — language in the broad sense — that they come to have adaptive value. From this viewpoint, it is not useful to ask whether «language» is an adaptation: we must rather inquire which of the component mechanisms of human neural computation, and neural development, have been specifically selected, and for what adaptive function(s). But we cannot use spandrels as «skyhooks» to explain all aspects of language evolution. We thus cannot avoid the question of what exactly the adaptive functions of various stages of protolanguage were during human evolution.

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An evolutionary and developmental perspective on congenital abnormalities in humans

Disturbances of early development in mammals are frequent and cause common congenital abnormalities, e.g. cervical ribs, extra digits and asymmetry in mammals. During early development all parts of an embryo are interconnected and form part of a large regulatory network. Due to this interconnectivity, mutations that cause these common abnormalities are associated with many negative side-effects (additional malformations and childhood cancers).
The negative side-effects of these mutations dramatically lower fitness, and consequently, are selected against. Selection against most changes leads to conservation of body plan traits that are determined during early development, e.g. the number of eyes, kidneys, limbs, digits, cervical vertebrae. Hence, the interactivity of early development is highly relevant for both the developmental origins of diseases, and for the evolutionary conservation of body plans.
However, despite the severe medical risks associated with these common congenital abnormalities, the underlying developmental and genetic mechanisms remain largely unknown. Furthermore, it is surprising that despite the substantial frequency of cervical ribs and extra digits not more is known

about their medical significance. Such knowledge of the underlying mechanisms is also essential for understanding the importance of developmental constraints in the evolution of body plans.
We will discuss progress that we are making in the understanding of the developmental and genetic processes involved in the high interactivity during early organogenesis. We will discuss the results in the light of evolutionary novelties and the conservation of body plans. Finally, we argue that changes of evolutionary conserved traits, such as the number of digits and cervical vertebrae, are reliable indicators of medical risks.

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An EvoDevo perspective on hominin cranial evolution

Differences in morphology between adults of different species ultimately owe to differences in patterns of growth and development. We will demonstrate how understanding the ontogenetic changes in extant groups can help unravel the evolutionary relationships among fossil species.
Phylo genetic relationships cannot be inferred directly from phenetic data. However, applying the methods of geometric morphometrics in a comparative developmental framework one can formulate predictions that would lend support to an ancestor-descendent relationship. Whether an EvoDevo approach can be applied successfully to the few available fossil specimens depends largely on the complexity of the growth pattern. Many cranial differences among hominins can be attributed to alterations of common growth factors, mainly by extension or truncation of otherwise conserved developmental pathways. The growth trajectories of the brain and its encasing bony capsule are relatively complex and comprise several distinct phases of shape change, whereas the postnatal trajectories of the face are almost linear. We will build this presentation around two examples:
(1) Approaching phylogenetic questions concerning robust and gracile australopithecines studying the more complete australopithecine crania in a comparative framework of hominin growth. We examine support for two alternative evolutionary scenarios based on predictions derived from theoretical models of quantitative genetics.
(2) Illustrating the ontogenetic changes that underlie the evolution of the large brain and globular braincase in modern humans that set Homo sapiens apart from other large-brained species of archaic Homo. To this end, we contrast the ontogenetic patterns found in recent humans and chimpanzees and consider the evolutionary mechanisms that contributed to the unique adult morphology of modern humans.

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Taking the middle road: a model organism-based approach to human evolutionary developmental biology

Development structures the phenotypic variation on which natural selection acts. For this reason, understanding the developmental basis for morphological variation is crucial to evolutionary explanation.
Humans and other model-less organisms pose a significant problem because human development is not amenable to direct study using the techniques of experimental developmental biology. Human evolutionary developmental biology must thus be based on inference from work on model organisms combined with human genetics and comparative anatomy. The middle-out approach, which emphasizes the relationship between developmental processes and their phenotypic outcomes is ideally suited to this form of inference.

We present examples from our work and the work of our collaborators with both mouse and chick to demonstrate how model organisms can be used to better understand the evolutionary developmental biology of humans. We illustrate through these examples, how understanding the developmental for phenotypic variation in model organisms can inform the explanation of hominid evolutionary change.

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Molecular and developmental mechanisms of evolutionary change in the primate limb skeleton

A key feature characterizing mammalian adaptive radiations is diversification in the relative lengths of the digits on the hands and feet. Associated hands and feet of early (40-50 mya) primates show that primate origins was accompanied by several novel features observed today among modern euprimates including the absence of claws, a divergent grasping hallux, and relatively long fingers and toes. Outgroup comparisons with sister taxa such as plesiadapiforms suggest that these features may have been acquired incrementally, with certain plesiadapiforms also exhibiting relatively elongate digits. Experimental evidence from model organisms has demonstrated the importance of developmental patterning genes in regulating the size, shape, and relative growth of specific bony elements within the limb.
Comparative studies reveal that evolutionary change in the expression of these patterning genes is likely to have played a major role in morphological diversification and evolution of the vertebrate skeleton.
A phylogenetic bracketing approach, employing evidence from mouse mutants and human congenital anomalies, can be employed to identify those genes that are likely to have played a key role in the evolution of primate hand and foot proportions. This approach implicates growth and differentiation factors, fibroblast growth factors, and posterior hox genes in the developmental control of primate metapodial and phalangeal proportions.
Together, these data suggest that the origin and adaptive radiation of primates in an arboreal milieu likely involved changes in the expression of specific developmental patterning genes affecting relative digit length and the size and shape of the nail-bearing phalanges.

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Did ancient hominins grow up like modern humans?

Among primates, modern humans display a unique developmental pattern. This peculiar life history is characterized by an extended growth period and a long dependency on the mother and adults in general.
After a well-marked adolescence period, individuals reach the age of first reproduction quite late. Many scholars have related these traits to our large adult brain. Indeed, the development of this «costly» organ results in a series of biological challenges. To start with, obstetrical as well as physiological constraints impose limits on brain size at birth, while brain size in adults has constantly increased over the course of human evolution.
Part of our social complexity and cognitive skills must be seen in light of the costs and benefits of our peculiar life history and from our unique pattern of brain development.
Until recently, it has been difficult to assess birthing as well as life history patterns in extinct species of hominins. However, today, new approaches that are primarily based on the study of microstructures in accretional hard tissues, such as tooth enamel, help us to tackle these issues. Although models based on the life history theory suggest the emergence of a primarily modern pattern as early as the emergence

of the first Homo representatives, empirical data yielded by the paleontological evidence may indicate a more varied spectrum of adaptations in ancient hominins .

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Simple rules and the evolution of hominin molars

Mammalian dentition is a functionally highly integrated system where details of occluding cusp patterns are critical for function. Furthermore, the overall complexity of molar tooth features closely reflects species specific diets. In addition to functional integration, teeth are also developmentally integrated. For example, molar teeth develop sequentially along the distally elongating dental lamina. Recent experimental evidence on mouse molar development shows that the initiation and size of distal molars depend on previous molars through a dynamic balance between intermolar inhibition and mesenchymal activation. Small species specific differences in the intermolar inhibition can have ratcheting effects on size and number of distal molars. This inhibitory cascade model predicts that mammalian molar proportions should evolve in a specific manner where the second molar makes up one- third of total molar area.
We first test this using living taxa by examining how well the model predicts variation within and among primate species. Next we show how closely the evolution of hominin molars has followed the inhibitory cascade predictions. The results point to an exceedingly simple rule in predicting hominin molar size and proportions, illustrating how developmental perspectives can provide insights into even well studied systems.

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Brain ontogeny and human life history evolution

Brain ontogeny appears to be fundamentally important in the evolution of primate life histories, especially through ties to maternal metabolic costs. This study examines patterns of brain growth in nonhuman primates, hominin fossils, and modern humans to assess both life history correlates and the phenotypic history of human brain growth evolution.
Adult brain size differences in nonhuman primates are not the product of simple extensions of brain growth periods: nonhuman primate brain growth patterns vary in many different ways. Modern human absolute brain size grows very rapidly relative to chimpanzees, although time differences in growth periods between the species are difficult to detect.
The rapid early brain growth pattern characteristic of modern humans is not evident in australopiths, but may be present during infancy in Homo erectus . Neandertals appear to grow brains even more rapidly than modern humans, suggesting very high metabolic costs of brain growth. These results indicate taxonomic differences in terms of maternal metabolic costs, suggesting clear life history differences among human ancestors (with important archaeological implications). Comparatively slow later brain growth in modern humans may reduce tradeoffs between current and future reproduction that impacted Neandertals.
Phenotypic differences among hominin species provide a basis for hypotheses about the molecular control of brain size ontogeny, suggesting complexity in molecular factors affecting brain size in modern humans.
Moreover, evolutionary changes in rate and timing of brain growth suggest the potential for positive selection on alleles affecting certain aspects of growth. New results for comparative primate samples

reveal dynamic patterns contemporary nonhuman primate brain ontogeny, both in terms of size and organization. These findings serve as a comparative baseline for assessing the evolutionary developmental history of human brain ontogeny beyond general size.

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Connecting the dots: insights from and limitations of studying ontogenetic processes in the human fossil record

Since discovery of the first Neanderthal specimens in the caves of Europe, the fossil record of human evolution has become surprisingly well populated. Compared to our African ape relatives, the large sample of geographically, temporally, and morphologically diverse human fossils has enabled paleoanthropologists to generate surprisingly robust scenarios about the course of hominin evolution. An important part of this record is the sample of juveniles that stretches across both taxonomic and age-class categories. These snapshots of ancestral ontogenetic processes provide insight into the role that developmental differences have played in the diversification of hominin species. Nevertheless, those seeking to apply the principles of evolutionary development to the fossil record face a fundamental obstacle: fossils neither evolve nor develop.
Just as phylogenetic lines drawn between fossil species are hypotheses of how taxa are related, so ontogenetic lines between juvenile and adult fossils are, at best, hypotheses about developmental change. This obvious statement is not merely rhetorical, but defines the parameters within which our assumptions, analyses, and conclusions must operate. The extent to which evolutionary development is applicable to and verifiable in the fossil record is limited by the static nature of paleontological data. Here I review the human fossil record focusing on insights gained from analyses of juvenile hominins. I also include examples in order to illustrate what we can and cannot (yet?) learn about the ontogeny of fossil species. If a fossil is a snapshot in evolutionary and developmental time, then inferring a temporal component represents overexposure of the image, blurring the boundaries of the individual to estimate the broader dynamics of biological change. Yet, within this framework, evolutionary development can greatly inform our understanding of the processes underlying human evolutionary diversity.

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Evolution of hominoid cranial development: classical theories and modern approaches

Already in the 1830s Geoffroy Saint-Hilaire observed the striking resemblance of juvenile apes to modern humans, particularly in their cranial morphology. In the early 19th century this led Lois Bolk to propose his fetalization theory of human evolution, very much in the spirit of Haeckel's theory of recapitulation. At the same time, other anatomists such as Adolph Schulz documented apparent similarities among infant primates and a subsequent divergence in the pattern of growth and development, reflecting von Baer's view of divergent rather than recapitulatory development. To some degree these two schools of thought are still present in the recent anthropological literature, usually under the headings of allometric scaling and heterochrony.
While, ultimately, a combination of both temporal and structural changes of development seems to account for modern human morphology, other researchers focused on the «dissociability» or «modularity» of these modifications. Did only a few developmental changes with many orchestrated effects account for all human-specific features? Or, instead, was a larger range of different and independent modifications responsible for modern human anatomy? King and Wilson, for example,

speculated in the 1970s that a single or a few mutations of regulatory genes with wide pleiotropic effects could have led to the appearance of modern humans. In contrast, many studies in evolutionary anthropology treat morphological differences between humans and other primates as largely independent.
I address these classical questions of human EvoDevo by a geometric morphometric approach focusing on hominoid cranial morphology. In Procrustes form space, the species-specific ontogenetic trajectories diverge postnatally but also differ by birth.
In particular, humans are already distinctive prenatally, indicating evolutionary modifications of early development, whereas other primates differentiate to a large extent postnatally. Pure heterochrony, operationalized as overlapping but differently truncated ontogenetic trajectories, does not sufficiently explain human craniofacial morphology nor the differences among the African apes. Modifications of developmental factors with wide pleiotropic effects account for a large part of primate shape variability, but modern human morphology could not have arisen without the evolutionary change of local or modular factors. While the pleiotropic factors evolved mainly by extension or truncation of otherwise conserved developmental pathways, local factors (modular shape characteristics) seem to have more degrees of freedom for evolutionary change. The data even indicate that constructional selection, the increase of local developmental factors, for example by gene duplication, may have been essential for human evolution.

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EvoDevo's theoretical consequences

The emergence EvoDevo in the 1980s was both a response to the incompleteness of the Modern Synthesis framework of evolutionary theory and a result of methodological advances in developmental biology, foremost in developmental genetics.
Today EvoDevo is a highly productive discipline that has diversified into several branches of empirical research. It has generated new results that have revolutionized our understanding of how development evolves and how this influences the evolutionary process. Less attention has been given to the important ways in which EvoDevo has informed evolutionary theory. One characteristic consequence is a shift away from the population dynamic emphasis of the Modern Synthesis towards a causal-mechanistic explanation of organismal evolution. Moreover, EvoDevo's inclusion of the dynamic relations between genes, cells, and tissues, and of the interactions of developmental processes with the environment, enables the understanding not only of what is adaptively varied but also of what is possible to arise in phenotypic evolution.
This takes evolutionary theory beyond the explanatory capacities of the Modern Synthesis. Together with theoretical advances in other biological disciplines, EvoDevo becomes a key component of an Extended Evolutionary Synthesis.

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Virtual quantitative functional morphology: a 21st century toolkit for the study of form and function

During both evolution and development, form is often said to relate to function; is there a coherent approach that we can develop to exploration of such hypothesized relationships? Recent mathematical, statistical and computational advances for the study of form and function are beginning to synergise, making a 21st century toolkit for the analysis of form-function relationships. Thus geometric

morphometric methods enable the analysis of covariances with form and connect with modern graphical tools to provide realistic visualizations. These can also be thought of as virtual representations of predicted form. Where the covariates are biomechanically interesting variables then these virtual predictions are usefully subjected to mechanical modelling and simulation both as a test of the predictions and to understand their mechanical function.
This is virtual, quantitative functional morphology in its infancy; there are many other interesting ways in which these computational toolkits can synergise and an exploration of these links will form the core of this presentation.

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Evolution of gene expression: human- and primate-specific enhancers

It has long been surmised that primate-specific or uniquely human phenotypes arise in large part from novel cis- regulatory sequences that effect lineage-specific gene expression. It is now feasible to identify these cis-regulatory determinants of uniqueness on a large scale, thanks to the sequencing of multiple nonhuman primate genomes. Using a statistical technique termed the surprisal test, we previously identified a whole-genome set of human-accelerated conserved noncoding sequences (HACNSs) that potentially evolved adaptively since the human-chimpanzee divergence. These included HACNS 1, an enhancer that drives human-specific gene expression in the region of the developing thumb.
We have now characterized additional high-scoring HACNSs using transient transgenesis in zebrafish, and identified additional examples of human-specific enhancer function, including one element with human- specific function in the developing brain. Although accelerated evolution is the commonly accepted signature of positive selection, clade-specific decelerated evolution could also be an indicator. This is because new transcription factor binding sites fixed by positive selection in the stem lineage of a clade are likely to be subsequently constrained within the clade. One such example is the enhancer downstream of the LDL receptor gene, which gained at least one new function-altering binding site in the stem lineage of anthropoid primates, and subsequently evolved under significantly higher sequence constraint in the descendant primate lineages. Efforts are under way to expand our locus-specific analysis of primate-specific constraint to the whole genome, in order to identify on a large scale the cis-regulatory elements that potentially set humans and other anthropoid primates apart from distant mammals.

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Postnatal developmental patterns and papionin cranial diversity: a model for hominin evolution?

The comparative study of cranial morphology is a central focus of paleoanthropology. To the extent that living taxa reflect developmental, biomechanical, and phylogenetic constraints on primate craniofacial form generally, extant primates offer a comparative basis for interpreting craniofacial diversity in the hominin fossil record.
The Old World monkey tribe Papionini has been put forward as an apt analog for hominin morphological variation and is a popular model for investigating homoplasy, particularly parallelism and convergence, within recent primate radiations. Ontogenetic scaling has long been recognized as a major contributor to primate craniofacial diversity, and studies of papionin cranial ontogeny, framed predominately within the rubric of bivariate allometry, have yielded essential insights into the primate cranial ontogeny. But studies grounded in geometric morphometrics, multivariate analysis,

developmental simulation, and 3D visualization offer complementary angles on the ontogeny of primate cranial form.
In this discussion, I draw on multivariate studies of papionin ontogeny to explore fundamental topics including: early establishment of interspecific differences in cranial shape; conservation of developmental patterns within morphologically diverse primate lineages; the impact of developmental trajectory differences on adult cranial shape; and the interplay between developmental programs and epigenetic factors in the ontogeny of diagnostic adult morphologies. Parallels with early hominins will be discussed and the relevance of the papionin model considered.

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The possible shapes of the human brain

The anatomy of the human brain is remarkably more variable than that of any other primate species. This variability seems to be, however, tightly constrained by the underlying neurodevelopmental mechanisms.
I will present an analysis based on magnetic resonance imaging, whole genome genotyping and mathematical modelling suggesting that brain size is a major determinant of human brain anatomy.