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Metameric variation of upper molars in hominoids and its implications for the diversification of molar morphogenesis

Abstract

Metameric variation of molar size is in part associated with the dietary adaptations of mammals and results from slight alterations of developmental processes. Humans and great apes exhibit conspicuous variation in tooth morphology both between taxa and across tooth types. However, the manner in which metameric variation in molars emerged among apes and humans via evolutionary alterations in developmental processes remains largely unknown. In this study, we compare the enamel-dentine junction of the upper molars of humans—which closely correlates with morphology of the outer enamel surface and is less affected by wear—with that of the other extant hominoids: chimpanzees, bonobos, gorillas, orangutans, and gibbons. We used the morphometric mapping method to quantify and visualize three dimensional morphological variation, and applied multivariate statistical analyses. Results revealed the following: 1) extant hominoids other than humans share a common pattern of metameric variation characterized by a largely linear change in morphospace. This indicates a relatively simple graded change in metameric molar shape; 2) intertaxon morphological differences become less distinct from the mesial to distal molars; and 3) humans diverge from the extant ape pattern in exhibiting a distinct metameric shape change trajectory in the morphospace. The graded shape change and lower intertaxon resolution from the mesial to distal molars are consistent with the concept of a ‘key’ tooth. The common metameric pattern observed among the extant nonhuman hominoids indicates that developmental patterns underlying metameric variation were largely conserved during ape evolution.

Furthermore, the human-specific metameric pattern suggests considerable developmental modifications in the human lineage.

KEYWORDS: Metameric variation; Morphometric mapping; Hominoid evolution; Enamel-dentine junction; Molar morphology

1. Introduction

Current fossil evidence indicates that hominoids (humans and apes) originated during the late Oligocene (Leakey et al., 1995; Perelman et al., 2011; Springer et al., 2012; Stevens et al., 2013). Diversity among extant apes and humans has resulted from subsequent species, subspecies and population level differentiation. Exploring phenotypic similarities and/or differences between extant apes and humans is essential to reconstruct the evolutionary history of apes and humans.

Dental morphology is among the most notable anatomical features that characterize each taxon and can be traced through evolutionary time. Numerous studies have intensively examined dental morphology, with a primary focus being on its relation with diet. Molars are of special relevance to feeding because of its major role in mastication. For example, Kay (1975) examined molar size and facet placement in living and fossil primates in relation to occlusal function and diets. He demonstrated that folivores possess larger and higher-crowned molars with higher and longer shearing crests than do frugivores. In great apes, the broad occlusal basin with thin enamel and marginal cusps (that support shearing crests) in chimpanzees, high cusps with elongated shearing crests in gorillas, and low cusps with thicker enamel in orangutans are thought to be associated with diets that emphasize ripe fruits,

fiber-rich foods, and hard-shelled fruits, respectively (Spears and Crompton, 1996; Kono, 2004; Kono and Suwa, 2008; Fleagle, 2013).

Teeth are also among the most abundant material in the vertebrate fossil record. Thus, in addition to dietary implications, dental morphology has also been used to infer phylogenetic relationships (Anapol and Lee, 1994; Suwa et al., 2007, 2009; Alba et al., 2013; Stevens et al., 2013; Moore et al., 2015; Déroit et al., 2019; Zanolli et al., 2019). However, adaptive modifications in tooth morphology can at times blur phylogenetic signals. For example, orangutans, some platyrrhines (*Cebus* and *Callicebus*) and some cercopithecids (*Cercocebus*) have flattened molar crowns/cusps, and orangutans and *Cebus* share wide and shallow occlusal basins. These morphologies have been interpreted as a result of convergent adaptation to diets rich in seeds and hard fruits (Rosenberger and Kinzey, 1976; Kay, 1981; Anapol and Lee, 1994). Abrasion and wear may be an additional complicating factor because of their situation dependency, although both wear and biomineralization reflect individual life history and are therefore informative (Bayle et al., 2009; Kelley and Schwartz, 2010; Smith et al., 2015; Zanolli et al., 2016). Teeth are actually designed to function in a worn state, extreme examples being hypsodont ungulates such as bovids and equids (Janis and Fortelius, 1988), or some rodents, elephants and so on. However, regarding bunodont molars, worn teeth are not always suitable for comparative morphological studies, especially in phylogenetic comparisons, because of obliteration of diagnostic morphologies with advanced wear and considerable individual variation in wear patterns.

One solution for such concerns is to focus on the enamel-dentine junction (EDJ). First, examining EDJ morphology enables larger samples with intact morphology. While tooth wear can also

reach the dentine and partially obliterate the EDJ, EDJ is affected later and less than the outer enamel surface. Importantly, the EDJ represents the three-dimensional shape of the epithelial basal membrane, which serves as a template for the outer enamel surface (Jernvall and Thesleff, 2000; Skinner et al., 2009b; Morita et al., 2014). Second, developmental processes and patterns can be inferred from the EDJ. This is important because morphological evolution occurs via modification of developmental processes. At the EDJ, activator–inhibitor signaling and mechanical interactions occur between the inner enamel epithelium and underlying mesenchymal tissues. Thus, in certain respects, the EDJ morphology serves as a proxy for the morphogenetic pathways that characterize crown formation (Jernvall and Jung, 2000; Jernvall and Thesleff, 2012; Renvoise et al., 2017). In apes, although it is difficult to investigate actual developmental processes, patterns of metameric variation help infer those processes (e.g., Evans et al., 2016; Morita et al., 2016). Metameric variation results from the repetition of molar morphogenesis, which Weiss (1990) described as ‘duplication with variation’ (Weiss, 1990; Hlusko, 2002). Therefore, taxon-specific patterns of metameric variation trace the manner in which molars are sequentially formed in each taxon.

Since Kavanagh et al. (2007) proposed the inhibitory cascade model as the underlying developmental mechanism that explains size proportions in sequential molars, numerous studies have used size as a variable to investigate metameric variation in molars (MVM), including in hominins (Schroer and Wood, 2015; Evans et al., 2016). Polly (2007) explained the relative sizes of M1, M2, and M3 (first, second, and third molars), that sequentially change in mammals, by the inhibitory cascade model in association with dietary adaptation. However, while mouse-based experimental data support the inhibitory cascade model, actual variation in molar size proportions may differ from expectations

(Renvoise et al., 2009; Labonne et al., 2012; Wilson et al., 2012; Asahara, 2013; Bernal et al., 2013; Asahara et al., 2016). Although primates share with rodents the general modular genetic architecture that regulates tooth patterning (Hlusko et al., 2011), a mouse-based model may not be readily applicable since the mouse dentition is highly specialized (e.g., lack of canines, premolars, and tooth replacement). From a quantitative morphological approach, Hlusko et al. (2016) demonstrated that size ratios of the last premolar and molars (i.e., M_3/M_1 and M_2/P_4) in nonhuman primates can be highly heritable and explain well the underlying genetic mechanisms that regulate molar size variation. However, molar size proportion is only one aspect of a highly complex pattern of metameric morphological variation. In particular, primates such as anthropoids with long life histories tend to deviate from the general mammalian pattern of metameric size variation, implying that multiple mechanisms determine primate dental variability (Carter and Worthington, 2016). Furthermore, in humans, it is well known that third molar size variation is greater than in the other molars (Garn et al., 1963; Sofaer et al., 1971; Townsend et al., 2003), which is the case also in nonhuman primates such as in chimpanzees (Swindler et al., 1998), thereby potentially impacting the patterns of between-molar size variation. Given the stochastic factors involved in sequential tooth development—perturbations that occur later in the cascade events are amplified by earlier ones—larger variation in later-forming teeth is expected (Polly, 1998; Jernvall, 2000; Townsend et al., 2003). In addition, variation in tooth shape can partly reflect size difference, so-called allometry, but shape variation in molars is not well-explained by size effects (Morita et al., 2016).

Although molar size proportions have been variously investigated as summarized above, the MVM inclusive of the details of EDJ morphology remains unexplored in hominoids. Accordingly, we investigate the MVM of EDJ shape in extant apes and humans. We aim to discuss molar shape variation

in hominoids in terms of development, phylogeny, and function. Comparative morphological analyses of postcranial, cranial, and dental features suggest that some of the key differences observed among living great apes and humans can be explained as specializations of each lineage/clade (White et al., 2009; Suwa et al., 2009; Almécija et al., 2015; White et al., 2015; Morita et al., 2017; Morimoto et al., 2018). Although the relationship between tooth morphology and diet in great apes has been considered to some extent, it has not been explicitly discussed whether MVM relates to such proposed adaptations or, more generally, reflects phylogenetic relationships. In this study, we examine whether living great ape and human MVM can be explained by phylogenetic ancestry, or if the ancestral patterns of MVM were modified by taxon-specific adaptations. Specifically, we address the following questions:

- (a) What does MVM indicate about dental developmental processes?
- (b) Are the specialized diets in apes associated with specific patterns of MVM, e.g., folivory/herbivory in gorillas and frugivory in chimpanzees?
- (c) Does MVM reflect phylogeny? Does a close phyletic relation result in similar MVM patterns?
- (d) Does the strength of the phyletic signal differ in M^1 , M^2 , and M^3 ?
- (e) Did humans acquire distinct MVM features subsequent to the split with chimpanzees?

In order to address the above issues, we use the morphometric mapping (MMap) method (Zollikofer and Ponce de León, 2001; Bondioli et al., 2010; Morimoto et al., 2011, 2012, 2014, 2018; Zanolli et al., 2014, 2017; Morita et al., 2016, 2017) to quantitatively evaluate MVM. Applying landmark-based conventional geometric morphometric methods to the analyses of MVM of entire EDJ surfaces is difficult due to the problem of non-correspondency of potentially homologous features of the complex and variable EDJ surfaces—but see Braga et al. (2010), Pan et al. (2017) and Skinner et al.

(2008, 2009a), for limited EDJ analyses of the occlusal fovea or the occlusal and basal crown outlines. This concerns comparisons across both taxa and molar elements. For example, the number of cusps differs among molars even in conspecific populations (e.g., the absence of hypocone or hypoconulid, and the presence of accessory cusps), and features such as secondary ridges and cingular structures are highly variable within and among taxa, and cannot be expected to correspond across specimens and samples. MMap is a homology-free geometric morphometric method that enables the quantification of surface topography. MMap is applicable to the quantitative analysis of metamerism variation in cases wherein not all specimens share a sufficient number of homologous structural entities (Morita et al., 2016).

2. Materials and methods

In quantifying metamerism variation in the upper molars of extant hominoids, we assembled a comparative sample comprising the maxillary permanent molars of the following taxa (Table 1): *Pan troglodytes* (chimpanzees; $n = 40$), *Pan paniscus* (bonobos; $n = 12$), *Gorilla gorilla* (gorillas; $n = 42$), *Pongo pygmaeus* (orangutans; $n = 45$), *Hylobates lar* (gibbons, $n = 23$), and *Homo sapiens* (humans; $n = 30$). The bonobo specimens were obtained from the collection of the Royal Museum for Central Africa, Tervuren, Belgium, and the orangutan specimens were mostly obtained from the Naturalis Biodiversity Centre, Leiden, Netherlands. The human sample comprises specimens from the Late to Final Jomon period (2000–300 BC; $n = 28$) and the Kamakura period (13–15th centuries AD; $n = 2$) of Japan housed at Kyoto University and St. Marianna University, Japan, respectively. The remaining hominoid teeth were obtained from the collections of the Anthropological Institute and Museum of the

University of Zurich, Switzerland; the Cleveland Museum of Natural History, USA; and the National Museum of Nature and Science, Tokyo, the Primate Research Institute, Kyoto University, and the University Museum, the University of Tokyo, Japan.

Volume reconstructions of the hominoid molars were constructed from various μ CT scans acquired with the following scanners: ScanXmateA080S, Comscantecno, Japan (housed at Kyoto University; scans made at voxel resolutions of 31–32 μ m); TX225-ACTIS, TESCO Corporation, Japan (housed at University Museum, the University of Tokyo; voxel resolutions of 28–42 μ m); μ CT80, Scanco Medical, Switzerland (housed at University of Zurich; voxel resolutions of 58–125 μ m); and XT H 225ST, Nikon Metrology, USA (housed at University of Zurich; voxel resolutions of 70–100 μ m). Images with voxel resolutions 58 μ m or greater were processed with resampling (up-sampling) by a factor of 2 using the software Amira 6.4 (Thermo Fisher Scientific, Waltham, Massachusetts, USA) to homogenize the image resolutions. The image stack for each tooth was filtered with a median filter to facilitate tissue segmentation, and triangular mesh models of the 3D EDJ surfaces were reconstructed. All specimens were considered as left by mirroring the teeth from the right side.

Prior to the morphometric analyses, each EDJ surface model was aligned as follows (Supplementary Online Material [SOM] Fig. S1). First, the occlusal basin outline was defined by the four main cusps (paracone, protocone, metacone, and hypocone) and their intercuspal ridges, manually digitized on the surface model, and the least-squares plane of the outline was computed. We traced the distolingual edge of the occlusal basin for specimens with an underdeveloped or absent hypocone (e.g., M³ in humans). Each molar was positioned so that the least squares plane of the occlusal basin outline was horizontal, and then the image was centered using the centroid of the occlusal basin outline.

Second, we digitized the cervical line to calculate its centroid. We then defined a plane parallel to the occlusal plane containing the cervical line centroid as the ‘basal plane’. Each specimen was then translated along the z-axis so that the xy-plane ($z = 0$) was located at a position 80% of total crown height (from the highest cusp tip to the basal plane), that is, ‘shifting-up’ each specimen along the z-axis without rotation. This was done so that the xy-plane lies at or above the cervical line in all parts of the specimens. To summarize, for each molar, the horizontal plane was defined by the occlusal basin outline, and the origin was placed directly below the centroid of the occlusal basin outline, at a vertical position below the highest cusp tip by a distance of 80% of crown height (from cusp tip to cervical line centroid; henceforth ‘crown base’).

Next, the EDJ surface was sectioned by 300 vertical planes radiating from the z-axis, perpendicular to the horizontal (x-y) plane, and cross-sectioning the molar in 300 equiangular sections ($L = 300$). In each vertical cross-section, 300 points were sampled along the intersection of the vertical section with the EDJ surface, running from the z-axis ($d = 0$ in SOM Fig. S1) to the outer intersection at $z = 0$ ($d = 1$ in SOM Fig. S1). This was done in 300 equidistant intervals ($K = 300$). For each of the 300 sampled points along the 300 equiangular sections, the following metrics were recorded:

local surface curvature (c), height from the basal plane (h), and horizontal distance (i.e., radius) from the z-axis (r). Notably, the surface curvature metric (c) was determined three-dimensionally by calculating the minimal local quadric surface at each sampled point. The morphometric data of each molar were thus represented as $K \times L$ matrices ($K = 300$, $L = 300$) for each of the three variables (c , h , and r).

Next, the morphometric variables were mapped onto a polar coordinate system (d , θ). Here, d denotes the normalized position along each cross-sectional outline ($d = 0 \rightarrow 1$: center $\rightarrow$ outer crown

base), and θ denotes the anatomical direction ($\theta = 0^\circ \rightarrow 360^\circ$: buccal $\rightarrow$ mesial $\rightarrow$ lingual $\rightarrow$ distal $\rightarrow$ buccal). The three-dimensional morphology of the EDJ was thus visualized in the form of two-dimensional morphometric maps $M(d, \theta)$. These morphometric maps are shown as false-color maps.

The effects of scaling were corrected by normalization of the variables c , h , and r using basal size (i.e., the square root of the summed squared distances of each value of r at the crown base [$d = 1$]). This approach is analogous to normalization by centroid size in standard geometric morphometrics (Bookstein, 1991). Finally, prior to the principal components analysis (PCA), each row of the $K \times L$ matrix for each specimen was weighted by two factors. First, each value was weighted by the length of each cross-sectional outline, which corrected point density that varies in inverse proportion to outline length. Next, each value was weighted by the r value for that point, which corrected lower point density in proportion to radial distance from the z axis.

We conducted our comparative analysis based on Fourier transforms, and by performing PCA of shape using the covariance matrix. First, 2D-Fourier transforms $F(M_i)$ of all M_i ($i = 1, 2, \dots, n$) were calculated (M had natural periodicity in θ). This resulted in $K \times L$ sets of Fourier coefficients representing a specimen's shape of the EDJ surface as a point in the multidimensional Fourier space. Each specimen was preoriented according to anatomical direction. Differences due to orientation were corrected prior to PCA, limiting the freedom of rotation to only around the z -axis. Optimal fitting was achieved by iteratively minimizing inter-specimen distance in Fourier space through rotation around θ (z -axis). After all specimens were aligned by best-fit, PCA was performed on the Fourier coefficients to identify the principal patterns of shape variation represented by the sample. We selected only the low-frequency domain of Fourier coefficients (i.e., low-pass filtering in Fourier space) to reduce the number

211 of variables relative to the number of specimens and to focus on the major pattern of variation. To
 212 facilitate visual inspection and morphological interpretation of the PCA results, morphometric maps
 213 were reconstructed by transforming an arbitrary point in PC space and/or along the PC axis into its
 214 corresponding sets of Fourier coefficients, and producing the morphometric maps by inverse Fourier
 215 transformation. Specimen density in PC space was visualized on the basis of the script ‘data density
 216 plot’ (McLean, 2014). Here, local density was calculated as the reciprocal of the sum of squared
 217 distance from all the specimens included in PC space. Red, green, and blue values were attributed to M^1 ,
 218 M^2 , and M^3 local densities, respectively, and integrated into a false-colored density plot. Finally, the
 219 overall trend seen in the metameric variation of each species was quantified by calculating the angle and
 220 the relative lengths of the M^1 – M^2 and M^2 – M^3 vectors in PC space. The angles range from 0° (two
 221 vectors with an identical direction) to 180° (two vectors with opposite directions). Relative vector
 222 lengths were calculated as the length of the M^2 – M^3 vector relative to that of the M^1 – M^2 (length was
 223 calculated as an Euclidean distance in PC space), so that a phenotypic change in M^2 – M^3 greater than in
 224 M^1 – M^2 would result in a ratio greater than 1. This index represents the relative degree of modification of
 225 the developmental program from M^1 to M^3 . As an indicator of molar size, EDJ centroid size was
 226 calculated from the h and r variables. All parametrization and calculations for MM were performed in
 227 MATLAB 9.3 (MathWorks, USA; see Morita et al., 2016 for details). Phenotypic distances among taxa
 228 (and between molar elements) were calculated as Euclidean distances between means using all PCs.
 229 The neighbor-net diagram was computed with SplitsTree4 (Huson and Bryant, 2006), based on all PCs.
 230 We used the multivariate K statistic for phylogenetic signals with a randomization test to assess the
 231 influence of phylogeny, using the R package geomorph (Blomberg et al., 2003; Adams, 2014; Goolsby,

2015; Adams et al., 2019). The phylogeny of extant hominoids was based on the consensus tree downloaded from the 10kTrees website ver. 3 (<http://10ktrees.fas.harvard.edu/>; Arnold et al., 2010) and modified with Mesquite v. 3.05 (Maddison and Maddison, 2015). Furthermore, we projected the phylogenetic tree onto PC space with reconstructed internal nodes (the position of ancestral states) using the maximum likelihood method for continuous data implemented with the R package ‘phytools’ (Revell, 2012).

3. Results

Figure 1 depicts metameric variation in a gorilla (Fig. 1A) and a chimpanzee (Fig. 1B) visualized by the 3D models of the EDJ and the corresponding morphometric maps of the three variables (c, h, and r). MMap of the surface curvature (c-Map) captures the well-defined anatomical features: the four major cusps (paracone, protocone, metacone, and hypocone), the ridges that connect the cusps and delimit the occlusal basin, the oblique crest that runs from protocone to metacone, and the lingual cingulum. The height map (h-Map) depicts the location, distribution, and height of the cusps. MMap of the radius (r-Map) comprehensively shows the horizontal distances at each EDJ positions, and shows a lingual or distolingual elongation at the basal crown relative to the center of the occlusal basin.

Figure 2 presents shape variation in the upper molar in PC space and corresponding patterns of shape variation along PC1 and PC2, which comprise 18.0% and 8.9% of the total variation, respectively. The PC axes are statistical constructs dependent on the input sample and do not necessarily convey biologically interpretable patterns of shape variation. We focused on the patterns of variation along PC1 and PC2, since they capture the intertaxon differences and metameric variation that

correspond to the questions addressed in this study.

All taxa analyzed in this study exhibited a shared pattern of metameric variation along PC1 ($M^1 \rightarrow M^2 \rightarrow M^3$: low to high PC1 scores), wherein the most prominent feature is variation in relative cusp height. The M^1 , with lower PC1 scores, tends to exhibit relatively high and massive crowns with sharp cusp tips, whereas the M^3 (higher PC1 scores) tends to have relatively indistinct cusps ultimately resulting in approximated buccal cusps (paracone and metacone) and reduced hypocone (Fig. 2D). Among taxa, PC1 distinguishes gorillas from the other hominoids.

PC2 captures other aspects of intertaxon differences, wherein gorillas/orangutans and humans represent the variation extremes. High PC2 scores (e.g., M^2 of humans) indicate decreased distal cusps, especially the hypocone, and gradual slope of buccal and lingual faces. Low PC2 scores (e.g., in M^2 of gorillas) correspond to retention of four distinct cusps and steep buccal and lingual faces (Fig. 2E).

Morphological transition from M^1 to M^3 is represented by the M^1-M^2 and M^2-M^3 vectors, denoted as ‘metameric change vectors’ (Fig. 2B). Furthermore, we traced intraindividual metameric variation (SOM Fig. S2), and the major patterns were consistent with the mean-based metameric change. However, some individuals exhibited peculiar differences from the mean-based results. General trends in metameric change across the entire sample are visualized by the false-colored density plot (SOM Fig. S3), indicating a gradual transition from M^1 (red) to M^2 (green) and M^3 (blue) along the PC1 axis. Morphological change proceeds fairly linearly in PC space, predominantly along PC1, except for humans, who exhibit an angled metameric change vector (Fig. 2B) involving both PC1 and PC2. The metameric shape change seen in the extant hominoids, from the mesial to distal molars, does not

correspond to that of relative size along the molar row (Fig. 2C). Whereas shape change in extant hominoids is fairly consistent from M^1 to M^3 (from lower to higher PC1 scores), relative molar sizes from M^1 to M^3 are variable: humans and *Pan* species show size reduction from M^1 to M^3 , while gorillas and gibbons have a relatively large M^2 , and orangutans comparable M^1 to M^3 sizes.

We used PC1–PC3 to further evaluate the metameric change vectors (summarized in Table 2). The results reveal that humans exhibit a peculiar pattern of metameric variation in contrast with the other hominoids in two respects. First, humans have a smaller interior vector angle than the other hominoids. Second, only humans exhibit a vector length ratio of less than 1. The latter means that morphological change between M^1 and M^2 is greater than that between M^2 and M^3 only in humans.

We separately analyzed molar shape variation among humans and apes to evaluate whether the taxon-specific MVM pattern is masked by between-group (human vs. ape) variation in PCA. The PCA of ape upper molars (apePCA) exhibits a pattern similar to that of the whole data (SOM Fig. S4). The pattern captured by apePC1 is highly correlated with PC1 of the combined ape and human sample ($r = 0.99, p < 0.001$). However, the human MVM pattern exhibited a more complex situation. Figure 3 illustrates the results of PCA performed among human molars (homoPCA). The homoPC1, which separates M^1 from M^2 and M^3 , reflects hypocone development or reduction. Positive values of homoPC1 in M^2 and M^3 are associated with the combination of a developed trigon with a diminished talon. Conversely, negative values in M^1 are associated with four well-developed main cusps. The homoPC1 correlates with PC2 of all the specimens ($r = 0.59, p < 0.001$). Thus, the major metameric shape differences observed in human molars only partially correspond to the PC2 of the combined ape and human analysis. Other MVM shape differences are represented in homoPC2 and homoPC3. Shape

differences in homoPC2 are associated with overall cusp development and distribution of lingual cusps. Positive homoPC2 indicates a higher trigon with relatively smaller hypocone. Negative values are associated with lower cusps and a distal shift of the lingual cusps. The homoPC2 largely separates M^2 from M^3 and correlates with PC1 of all the samples ($r = -0.52, p = 0.003$). The homoPC3 also captures the difference between M^2 and M^3 and reflects the difference in distribution between buccal and lingual cusps. Negative homoPC3 is characterized by high and distally positioned protocone, whereas positive values correspond to mesially positioned protocone and closely located buccal cusps.

Figure 4 visualizes taxon-specific patterns of metamer variation. Since the metamer change vectors of nonhuman taxa are largely linear, morphological transition proceeds gradually, particularly in chimpanzees, bonobos, and orangutans. The features represented in M^1 gradually diminish toward M^3 . The morphometric maps of each taxon reveal that taxon-specific features are mostly shared among the three molars in nonhuman hominoids. In humans, M^1 and M^2 exhibit contrasting shapes, mainly reflecting hypocone reduction in M^2 , and M^3 exhibits a contrasting pattern compared with M^2 , reflecting metacone reduction.

We calculated the multivariate generalization of Blomberg's K of each molar's morphology in extant ape taxa to detect phylogenetic signals and projected the resulting phylogenetic tree onto the morphospace (SOM Fig. S5). K of the three molars were less than 1 with no statistical significance for PC scores with 1000 permutations (M^1 : $K = 0.63, p = 0.09$; M^2 : $K = 0.57, p = 0.28$; M^3 : $K = 0.40, p = 0.76$). However, the statistical power (1 - Type II error rate) of the randomization test to detect phylogenetic signals in the data diminishes with the reduced number of terminal taxa analyzed (Blomberg et al., 2003). Furthermore, evolutionary changes in metamer variation were reconstructed

from the estimated ancestral morphology of each molar (SOM Fig. S5D). Metameric shape change is nearly linear in the common ancestors of both extant hominoids and great apes.

Distance-based similarity patterns were visualized as a neighbor-net diagram shown in Figure 5. Most of the conspecific specimens of extant apes are connected to each other and form taxon-specific clusters (SOM Fig. S6). Conversely, human molars do not cluster but are divided into an M^1 vs. M^2 – M^3 clusters. The neighbor-net diagram shows another type of classification, a tendency for M^1 – M^2 and M^3 to form separate clusters (SOM Fig. S7). However, in humans, only M^1 belongs to this common M^1 – M^2 cluster, whereas both human M^2 and M^3 belong to the common M^3 cluster.

4. Discussion

4.1. What does MVM indicate about dental developmental processes?

The results of the MMap-based PCA reveals that PC1 captures the overall morphological transition along the molar series (M^1 – M^2 – M^3) shared by humans and extant apes (Fig. 2). Except for humans, this morphological transition along tooth positions is fairly linear in PC morphospace. We checked whether this can be explained by size differences between molars in each taxon, i.e., allometry. Our data indicate that shape differences in molars are not associated with size differences across the taxa used in this study, since M^2 size is comparable to or larger than M^1 size in gorillas, orangutans, and gibbons (Fig. 2C; SOM Fig. S8). An analysis of the metameric change vector (Table 2) also supports a fairly linear pattern of shape change. This indicates that the morphological transitions between M^1 and M^2 and between M^2 and M^3 share comparable trajectories. MMap-based visualizations indicate that this morphological transition corresponds to a general reduction of the distal cusps in size, height and spatial

distinctness. More specifically, the metacone loses its distinctiveness from the adjacent cusps and ultimately approximates the paracone, and the hypocone becomes less distinct in the distal molar and ultimately indiscernible. Such morphological transitions reflect both between-molar and between-taxon variation; that is, the direction of the latter variation is similar to that of the former in the PC morphospace. This suggests that developmental modification pathways related to between-molar differences are, in part, paralleled by between-taxon differences, and supports the interpretation that the basic within-taxon pattern of metamerism along the molar row of extant apes and humans is shared and highly conserved.

What causes the reduction of the distal cusps? We hypothesize that this shape reduction (i.e., loss of distinctness) could be caused by a decline in cusp patterning potency. Multicusped teeth like hominoid molars is configured by iterative activation of the epithelial signaling centers, known as enamel knots (Jernvall and Thesleff, 2012). The primary enamel knot appears during the bud to cap stages, and the subsequent secondary enamel knots appear at the sites of the future cusps (Jernvall et al., 1994; Jernvall and Thesleff, 2000). This sequential activation of enamel knots is formulated as a quantitative morphodynamic model, the so-called patterning cascade model. In this model, cusp patterning is regulated by the balance between production and interaction of activator–inhibitor and their diffusion ratio (Salazar-Ciudad and Jernvall, 2002, 2010). The major trend of distal cusp reduction in hominoids captured by PC1 could thus be caused by a gradual decline in patterning ability associated with the attenuation of signaling molecules yielded from the later-forming secondary enamel knots.

We can interpret this inferred gradient of cusp patterning ability analogous to the field theory, wherein a gradation of diffusible substance, morphogens, generates the morphological gradient (Butler,

1939), and the clone theory, where tooth-type specific clones of cells sequentially grow and form primordia (Osborn, 1978). Under the inhibitory signaling of the earlier-formed tooth, the developmental program of M^2 would be a slightly modified version of the M^1 program (similarly from M^2 to M^3). Thus, the production of M^2 and M^3 can be considered as a ‘copy and paste with modification’ of the M^1 , with a graded attenuation of later signaling. Our data indicates that the pattern of modification varied among hominoids, such that the most ‘basic’ pattern appears to be seen in extant orangutans and *Pan* species. In these taxa, the trajectory and degree of developmental modification from M^2 to M^3 appears to be similar to that from M^1 to M^2 .

Our data show that the MVM of shape and size exhibit different patterns of transition from M^1 to M^3 . While the former exhibits a common pattern of graded change ($M^1 < M^2 < M^3$ along PC1), the latter varies in hominoids (e.g., $M^1 < M^2 > M^3$ in gorilla, and $M^1 > M^2 > M^3$ in humans and chimpanzees; Fig. 2C; SOM Fig. S8). Why do MVM of shape and that of size dissociate from each other? We hypothesize that the MVM of shape is more conservative than that of size, and that they are regulated by different developmental mechanisms that are only loosely interrelated. According to the inhibitory cascade model, each molar size depends on inhibition from the anterior tooth germ (Kavanagh et al., 2007). This indicates that the size of each molar is not determined at the time of M^1 development but is determined stepwise through the cascade. We speculate that the regulation of intermolar shape is more predetermined because cusp patterning potency is inherited by extending the dental lamina over the course of molar development from M^1 to M^3 . Though cusp patterning potency gradually declines from mesial to distal, the pattern itself may be largely determined at the morphogenetic phase of M^1 development. This stands in contrast to the regulation of molar size, which

can be altered by modulating the strength of inhibitory signaling at the time of development of each molar. Based on this hypothesis, we suggest that the dissociation of the regulatory mechanism of size and shape results in size MVM to be more flexible in response to dietary demands, while shape MVM can be evolutionarily more conservative.

Furthermore, there is another mechanism of dental reduction captured by PC2 and more accurately depicted by humanPC1. This shape change corresponds to hypocone reduction with trigon development and dominates human MVM (homoPC1). The spatially localized reduction of the last-forming cusp could be caused by a spatiotemporal factor, such as lack of space in the tooth germ, or late initiation of cusp formation at a later morphogenetic stage (Jernvall and Jung, 2000).

4.2. Are the specialized diets in apes associated with specific patterns of MVM?

A possibly diet-related signal was observed in gorillas. Although gorillas are more similar to the other apes than to humans in terms of MVM, they are located at a different position in morphospace, especially along the PC1 (Fig. 2), which could be explained by their dietary specialization. According to the inhibitory cascade model of molar size proportions, dietary habits correlate with intermolar size relations in a way that herbivorous species tends to have larger distal molars due to weaker inhibition from the M¹ (Kavanagh et al., 2007; Polly, 2007). Gorillas are known to be more dependent on a relatively folivorous or herbivorous diet than any other extant great ape (Yamagiwa and Basabose, 2006, 2009; Fleagle, 2013). Since cellulose-rich plant foods need more shearing force during mastication (Lucas and Luke, 1984; Janis and Fortelius, 1988), leaf-eating species have higher cusps and longer shearing crests than fruit-eating species (Kay, 1975, 1977, 1981). The EDJ shape of gorilla molars captured by the MMaps is

consistent with observed morphological features in gorilla molar, such as the relatively balanced arrangement of cusps, well-developed ridges, deep trigon and talon basins, and morphological similarity between the first two molars than in the other species (Figs. 2 and 4). Although these features have been captured by linear measurements, angles, and qualitative descriptions (Remane, 1922, 1960; Haug, 1977; Pilbrow, 2003; Olejniczak et al., 2004; Suwa et al., 2007), MMap enables the quantification of complex crown morphology and shows, for example, that in terms of cusp development and distinctness (as expressed in PC1) gorilla M^3 's are comparable to other species' M^1 in mean shape.

Looking into more detail, our data show that a distinct pattern of metameric variation occurs in the folivorous/herbivorous gorilla, in which the M^1 and M^2 are statistically indistinguishable from each other (in PC1–PC2 space, $p = 0.104$). Based on the inhibitory cascade model (Kavanagh et al., 2007), a larger M^2 results from weaker inhibition from M^1 to M^2 . The increased size of M^2 in gorillas (SOM Fig. S8) would partly offset the general reduction in pattern formation ability from mesial to distal in gorillas. Although M^1 and M^2 are relatively similar to each other, the MVM of gorillas is also fairly linear. Accordingly, the unique MVM pattern in gorillas can be considered as based on a shared developmental program with the other hominoids.

4.3. Does MVM reflect phylogeny and does a close phyletic relation result in similar MVM patterns?

Metameric variation observed in an organism results from a common developmental mechanism (Weiss, 1990). The nonhuman taxa studied here demonstrate moderate levels of homogeneity across conspecific molars (Fig. 5; SOM Fig. S6), indicating the existence of taxon-specific aspects of molar morphogenesis. However, extant hominoids share a linear pattern of shape change along the molar row,

with large intertaxon overlap in PC morphospace. Furthermore, a broad separation between the M^1 – M^2 and M^3 clusters suggest a common nesting pattern of similarity ($(M^1, M^2), M^3$) as a whole (SOM Fig. S7; Table 2). These results suggest that a common developmental mechanism of MVM can be largely maintained despite conspecific similarities across molar positions that reflect taxon-specific morphologies. Our data, however, do not necessarily indicate that a closer phylogenetic relationship between two groups result in similar patterns of MVM. For example, chimpanzees are distinct from humans and more similar to orangutans, and the gorilla MVM pattern does not resemble that of chimpanzees but equally differs from orangutans (Fig. 2; Table 2).

4.4. Does the strength of phyletic signal differ in M^1 , M^2 , and M^3 ?

Although there is no statistical significance probably due to the small number of terminal taxa (Blomberg et al., 2003), K in all molars is less than 1, indicating that EDJ morphology reflects morphological changes uncorrelated with a Brownian motion-like process. K becomes smaller from M^1 to M^3 along the molar row. This could also be explained analogous to Butler’s field theory which postulates that the mesial–distal gradient of diffusible signaling molecules, so-called morphogens, determines the morphology of each tooth type (Butler, 1939). The larger K value of M^1 is consistent with the concept of a ‘key’ tooth located at the mesial-most position, and indicates greater stability in size and morphology than in the other teeth of the same field. The distal molars exhibit a lower K , implying that variance is concentrated within each taxon rather than among taxa. Morphological variation is greater in the later-forming distal molars than that in the mesial molars, possibly due to increased developmental instability (Townsend et al., 2003; Harris and Dinh, 2006; Morita et al., 2016).

Our data thus indicate that the mode of tooth development in which distal molars emerge later during ontogeny would impinge on the strength of the phylogenetic signal. The interpretation of the phylogenetic signal, however, has to remain tentative due to the small sample sizes and number of taxa of this study. This could be tested more rigorously with an expanded dataset in the future.

4.5. Did humans acquire distinct features of MVM compared with other hominoids after the split with chimpanzees?

Humans are separated from the other hominoids along PC2 (perpendicular to the general hominoid MVM) in a positive direction. This corresponds to the reduction of the hypocone, and is more accurately captured by homoPC1 (Fig. 3). As discussed previously (Section 4.1), we hypothesized that this shape variation was related to spatiotemporal factors acting during tooth development (Jernvall and Jung, 2000).

The HomoPC2, which relates with general cusp distinctiveness, partially reflects common developmental mechanism of MVM among hominoids since it is significantly correlated with PC1 of the combined human and ape sample. Human MVM, however, cannot be explained by homoPC2 (which highlights the difference between M^2 and M^3) because morphological variation of human M^1 's extends along its full range of the axis. Along homoPC3, which also relates to the difference between M^2 and M^3 , protocone development is well maintained despite a change in cusp distribution (Fig. 3B). In humans, homoPC2 and homoPC3 combined separates M^2 and M^3 quite well, while this morphological transition is not graded from M^1 (i.e., M^2 and M^3 differ from M^1 in opposite directions). This shape variation probably underlies the non-linear human pattern observed in the combined human and ape analysis. It is

associated with the retainment of a well-developed protocone, and may be related with functional demands. The protocone is considered crucial to mastication since it occludes directly with the corresponding lower molar and is significant in all phases of the chewing cycle (Kay and Hiiemae, 1974; Spears and Macho, 1995). The protocone also forms before the distal molars, and could thus be developmentally more conserved than the other cusps.

Humans are characterized by a distinct pattern of upper molar morphology. The morphological change between M^1 and M^2 is notably greater than that between M^2 and M^3 (Table 2). The distance-based diagram (Fig. 5) indicates that humans exhibit a unique pattern of nesting (humans: M^1 vs. M^2 , M^3 ; nonhuman hominoids: M^1 , M^2 vs. M^3). Humans are separated from the other hominoids along PC2 (perpendicular to the general hominoid MVM) in a positive direction, and the MVM in humans diverges from the linear pattern of the other hominoids (M^1 to M^3 vectors are angled in higher PC space; Fig. 2; Table 2). Collectively, the human-specific MVM pattern appears to result from a combination of factors, which are captured by PC2, homoPC1 and homoPC3. In humans, a developed protocone occurs with extreme hypocone (and metacone) reduction. Developmental studies have revealed that no single factor is sufficient to explain dental diversity, and that cusp patterning is potentially affected by multiple signaling pathways in an additive manner (Jernvall and Thesleff, 2012; Harjunmaa et al., 2012). Our data suggest that the unique MVM dimension that we observed in human upper molars may have been induced by spatiotemporal factors that affect signaling patterns and/or intensities, associated with or accompanying extreme distal crown reduction.

When did this human-specific MVM emerge during the course of evolution? Reconstruction of the ancestral state of MVM by squared-change parsimony (SOM Fig. S5) suggests that the last

common ancestor (LCA) of humans and chimpanzees probably had a largely modern-ape like MVM with no clear PC2 component (which is mainly associated with hypocone reduction). This is likely because there is no tendency for a human-like distal cusp reduction in *Australopithecus* and *Ardipithecus* (Robinson, 1956; Johanson and White, 1979; White et al., 2006; Suwa et al., 2009; Gómez-Robles et al., 2012; Fornai et al., 2015). The ancestral MVM pattern would be worth verifying across known Middle and Late Miocene apes, including fossils suggested to be close to the LCA of African great apes and humans, such as *Nakalipithecus* (Kunimatsu et al., 2007), or by early hominins such as *Ardipithecus* (Suwa et al., 2009; White et al., 2015). Dental reduction in the postcanine tooth row, such as advanced hypocone reduction and simplification of the occlusal surface, becomes clear in *Homo* after the Middle Pleistocene (Martín-Torres et al., 2007, 2012; Gómez-Robles et al., 2012). This is relatively recent compared with the chimpanzee – human split (Langergraber et al., 2012; Moorjani et al., 2016; Besenbacher et al., 2019; but see Hobolth et al., 2007). A recent evolutionary simulation study suggested that aspects of hominin postcanine shape largely evolved at a rate consistent with neutral evolution, unlike, for example, brain evolution (Gómez-Robles et al., 2017). This suggests a relatively stable pattern of occlusal crown outline and major cusp positions before and after the emergence of the genus *Homo*. However, such an evolutionary scenario is based on various assumptions, and interpretations of rates and patterns of evolution in *Homo* need to be better documented both temporally and phenotypically. For the time being, we may infer that the human-specific MVM may reflect a combination of non-adaptive processes such as genetic drift, pleiotropic effects, and perhaps a shift in selective pressures (including relaxation) regarding the level of intermolar occlusal relationships to be maintained (Organ et al., 2011; Park et al., 2012; Gómez-Robles et al., 2017). A better understanding of the underlying developmental

mechanisms of dental reduction is necessary to further evaluate these possibilities.

Conclusions

We quantified metamer variation in the upper molars of extant hominoids using the MMap method. Results showed that extant apes shared a largely linear morphological transition along tooth positions in PC morphospace, associated with distal crown reduction with modification in cusp size, saliency and position. Such shape change in the molars of hominoids is independent of relative molar size. The high cusped molar morphology of gorillas is explained by a shift along this MVM axis. Among extant hominoids, humans exhibit the most distinct MVM characterized by remarkable hypocone reduction. In humans, in addition to developmental mechanism related to the linear pattern that they share with extant apes, other spatiotemporal and functional factors may have had an important role in attaining its molar morphogenetic pattern.

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795

Figure legends

Figure 1. Schema of metamereric variation (M^1 , M^2 , and M^3 , from left to right) in a gorilla (A) and a chimpanzee (B)—molars from individual specimens. Surface topography map (c-Map), 3D model, height map (h-Map), and radius map (r-Map), from top to bottom. Maps are Gaussian-filtered for visualization. Not to scale. Abbreviations: pa = paracone; pr = protocone; me = metacone; hy = hypocone; oc = oblique crest; lc = lingual cingulum.

Figure 2. Metamereric variation in hominoid upper molars. A) Molar shape variation in PC space (along PC1 and PC2). All three variables, c, h, and r were included to make the analysis comprehensive. Symbols used in the PC graph: open circles = M^1 ; asterisks = M^2 ; open stars = M^3 . Colors: green = humans, red = chimpanzees; black = bonobos; blue = gorillas; cyan = orangutans; magenta = gibbons. B) Taxon-specific metamereric change vectors from M^1 to M^3 . The markers indicate the location of mean molar shape. C) The relationship between molar shape change captured by PC1 and relative molar size. The markers indicate the location of mean molar shape. Molar shape changes from left to right. Size of each molar relative to M^1 increases upward and decreases downward. D) Major patterns of variation are represented by morphometric maps (c-Map, h-Map, and r-Map, from top to bottom) visualizing ± 1.5 SD along each PC axis: PC1: (–) c-Map: prominent crown relief with mesiolingual cingulum; h-Map: high and broad four main cusps; r-Map: larger dimension in each of the four cusp directions, particularly toward hypocone/ (+) c-Map: decreased relief and tendency to fuse buccal cusps; h-Map: generally lower cusp and hypocone reduction; r-Map: elongation at the middle of buccolingual axis. E) PC2: (–) c-Map: pointed four cusp tips; h-Map: high and relatively distant four cusps; r-Map: relatively vertical

817 buccal and lingual side and elongation toward distolingual direction/ (+) c-Map: clear buccal intercuspal
 818 groove and reduction in hypocone; h-Map: high and relative enlargement of protocone area; r-Map:
 819 larger buccolingual dimension in the mesial cusps. Abbreviations: b = buccal; m = mesial; l = lingual; d
 820 = distal.

821

822 **Figure 3.** Metameric variation in human upper molars. All three variables, c, h, and r were included. A)

823 Molar shape variation in PC space (PC1 and PC2) and associated morphometric maps (c-Map, h-Map,
 824 and r-Map, from left to right [PC1] and top to bottom [PC2]) visualizing ± 1 SD along each PC axis.

825 Symbols used in the PC graph: open circles = M^1 ; asterisks = M^2 ; open stars = M^3 . Major patterns of
 826 variation are as follows: PC1: (–) c-M: clear crown relief; h-M: high and relatively distant four cusps; r-
 827 M: elongation toward distolingual direction / (+) c-M: decreased crown relief with relatively clear
 828 buccal intercuspal groove; h-M: distinct trigon (paracone, protocone, and metacone) and hypocone
 829 reduction; r-M: larger buccolingual dimension at the middle. PC2: (–) c-M: decreased crown relief with
 830 hypocone reduction; h-M: generally lower cusps and distal displacement of protocone; r-M: relatively
 831 smaller dimension with elongation in a distolingual direction/ (+) c-M: relatively clear crown relief; h-
 832 M: higher trigon and smaller hypocone; r-M: lingual expansion with elongations toward buccal cusps.

833 B) Shape variation in PC3 and PC2 space and associated morphometric maps: PC3: (–) c-M: relatively
 834 pointed cusp tips; h-M: separated buccal cusps and higher protocone; r-M: lingual expansion / (+) c-M:
 835 relatively sharp mesial cusps and intercuspal ridge; h-M: mesial displacement of protocone and
 836 relatively centered metacone; r-M: larger dimension in each of the four cusp directions, particularly
 837 toward paracone. Abbreviations: b = buccal; m = mesial; l = lingual; d = distal.

838

839 **Figure 4.** Average morphometric maps of M^1 , M^2 and M^3 (from left to right) in humans, chimpanzees,
840 bonobos, gorillas, orangutans, and hylobates. Non-human taxa exhibit features (or trends) shared by all
841 three molars: chimpanzees, sharp cusps; bonobos, sharp cusp and marginal ridges; gorillas, high cusps;
842 orangutans, reduced relief; gibbons, generally low cusps but relatively high metacone. Humans show a
843 marked difference between mesial and distal cusps in M^2 and M^3 . Abbreviations: b = buccal; m =
844 mesial; l = lingual; d = distal.

845
846 **Figure 5.** Neighbor-net diagram of all specimens based on Euclidean distances in morphospace (based
847 on all PCs).

848

Figure 1

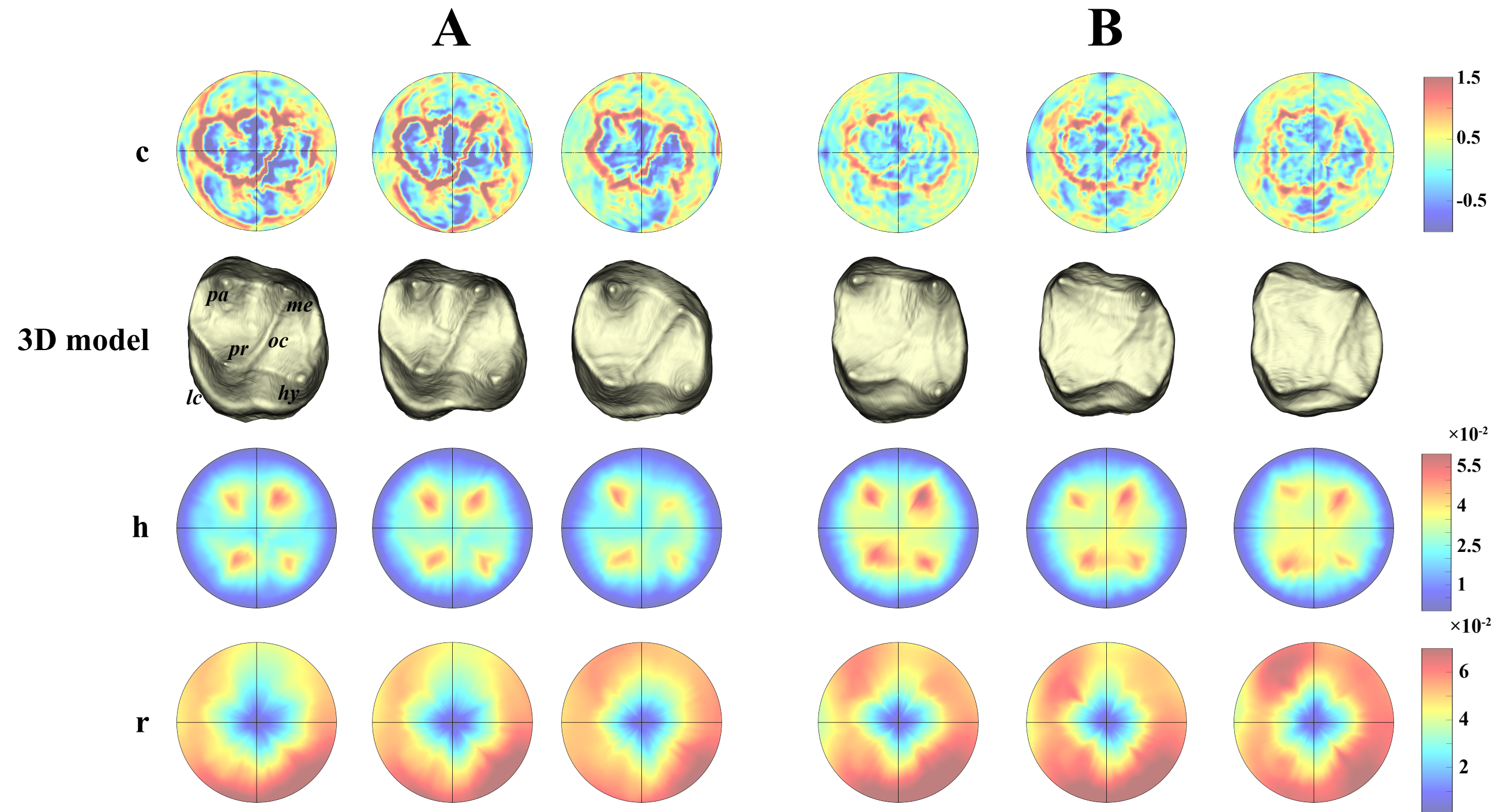


Figure 2

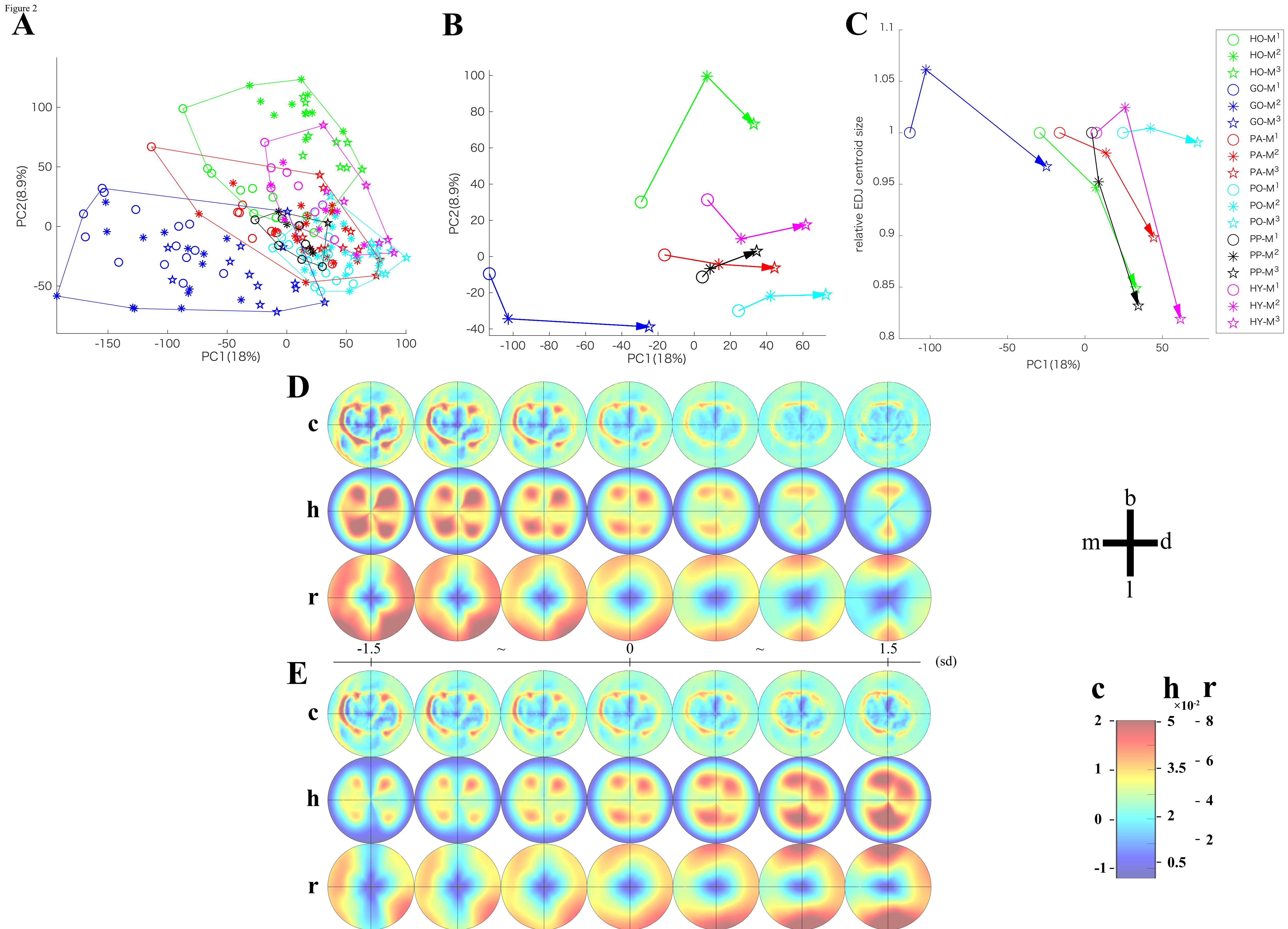


Figure 3

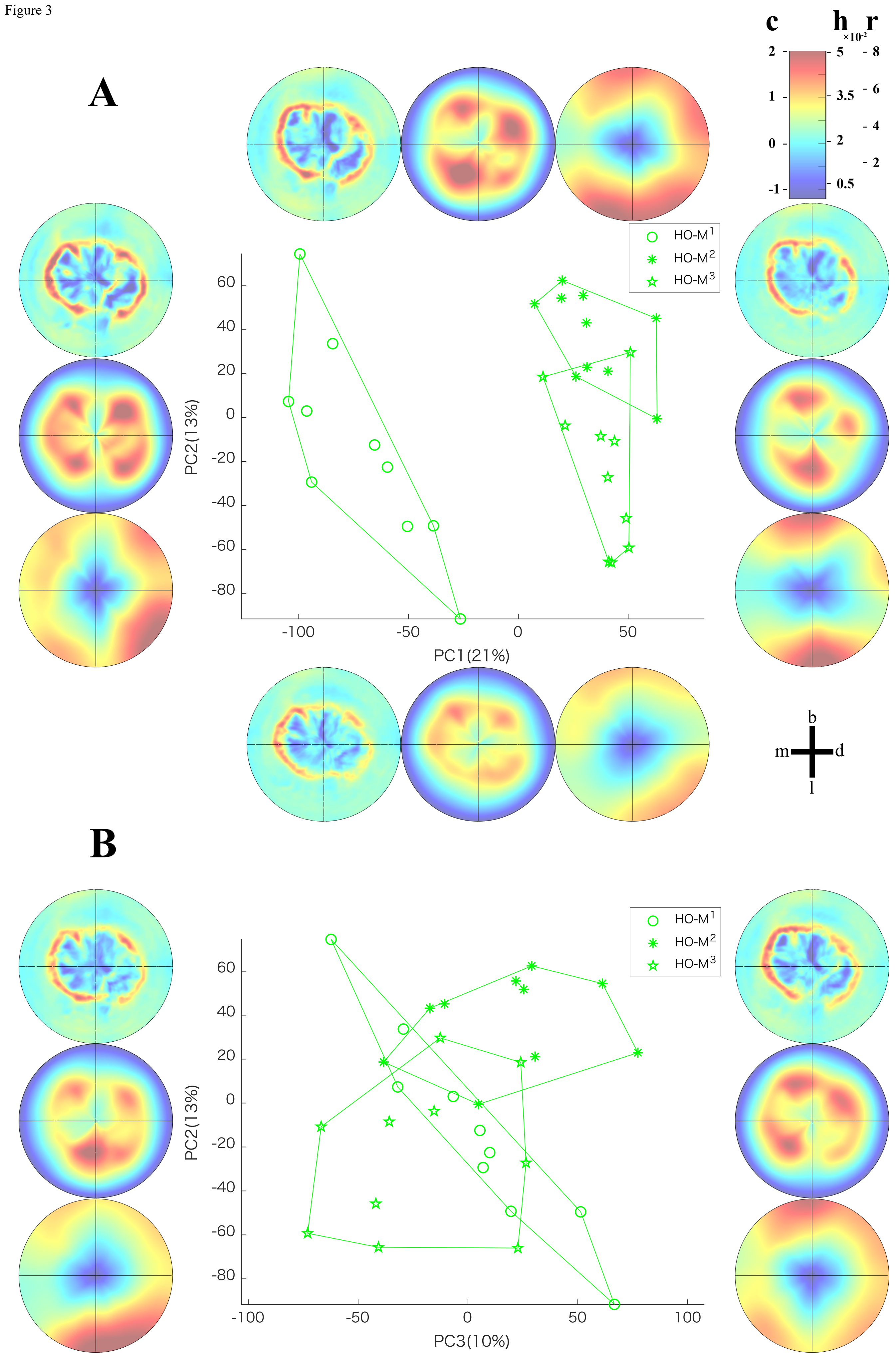
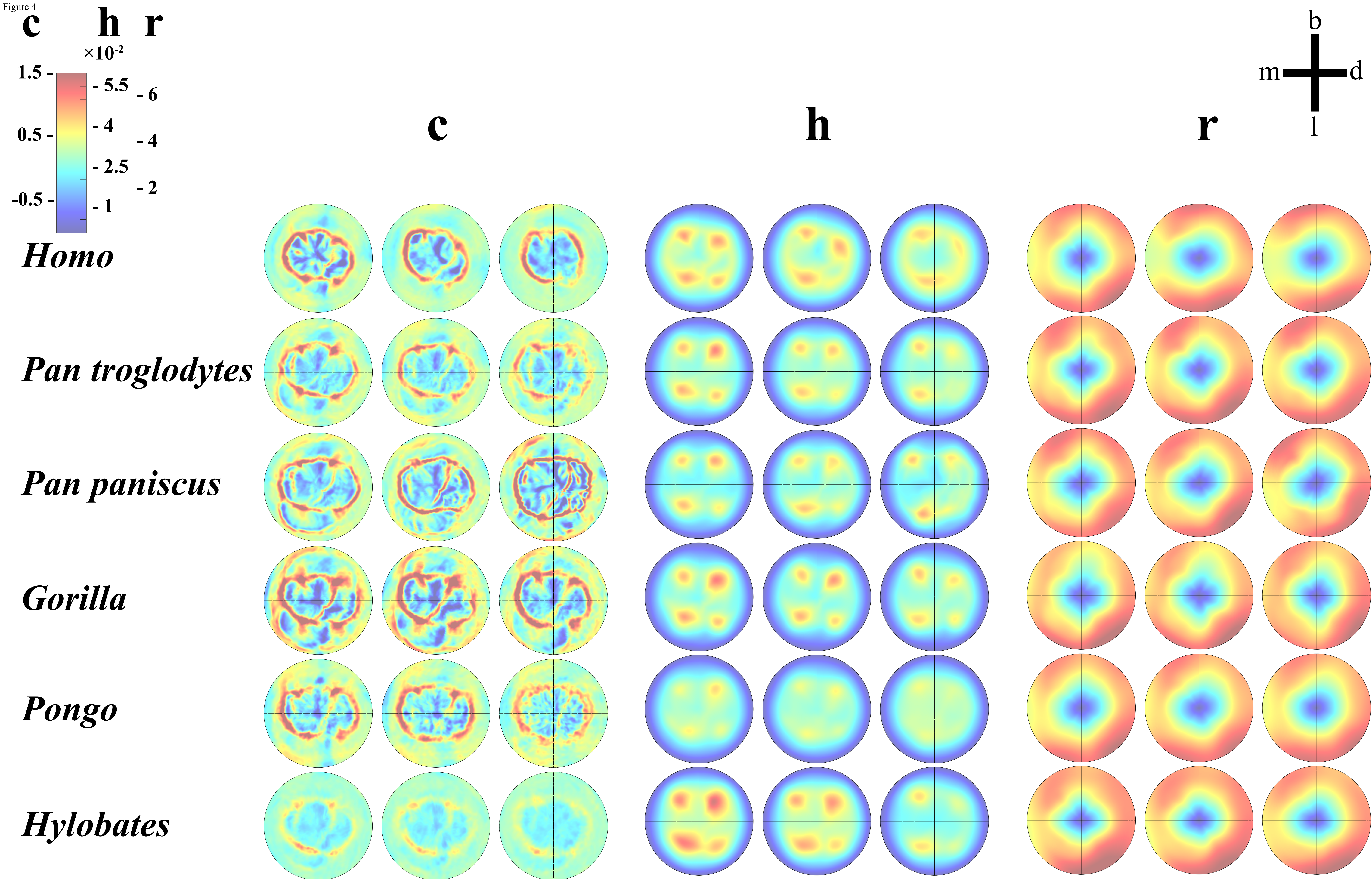


Figure 4



Supplementary Online Material (SOM):

Metameric variation of upper molars in hominoids and its implications for the diversification of molar morphogenesis

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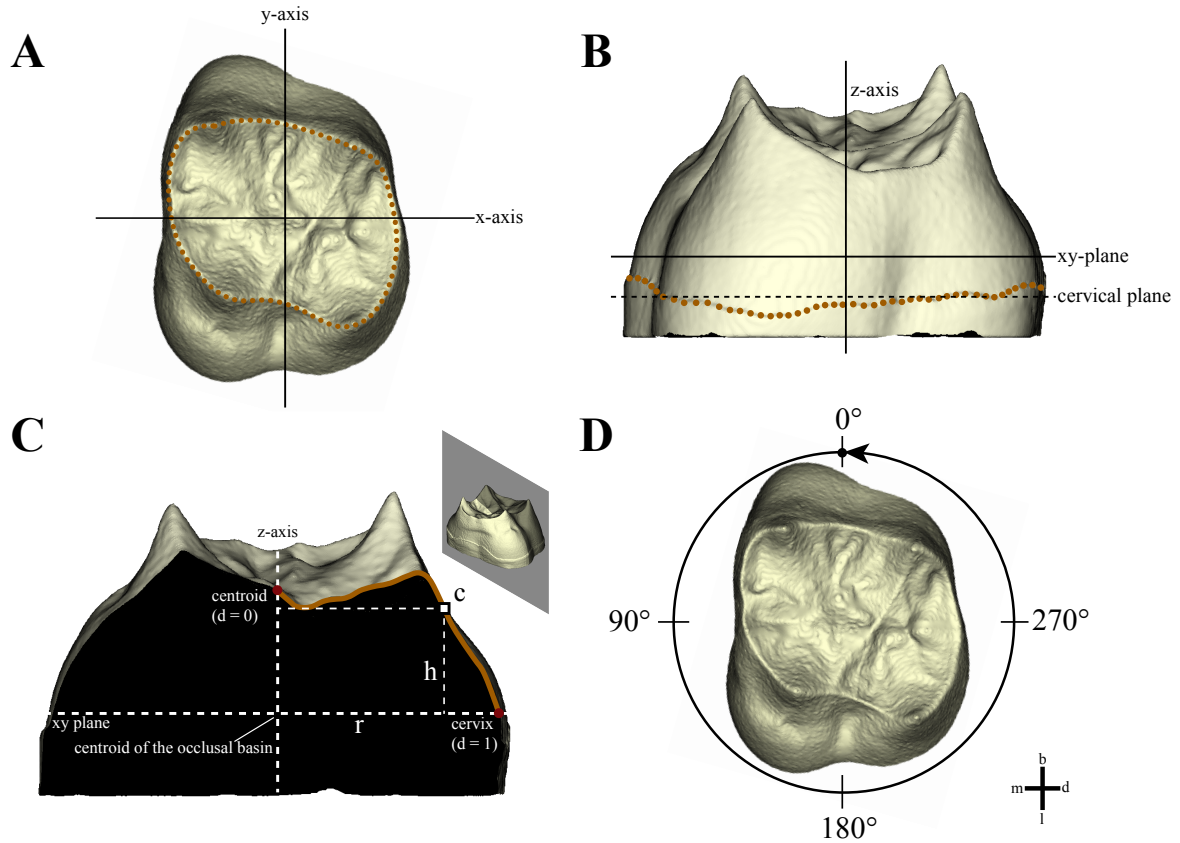
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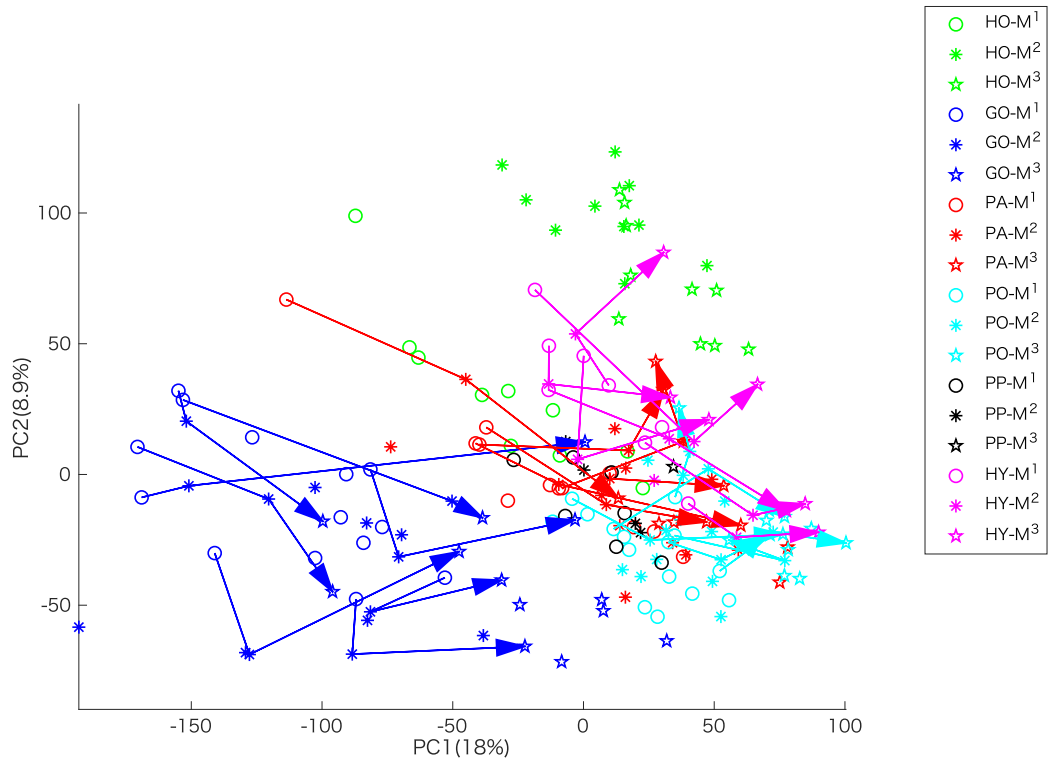
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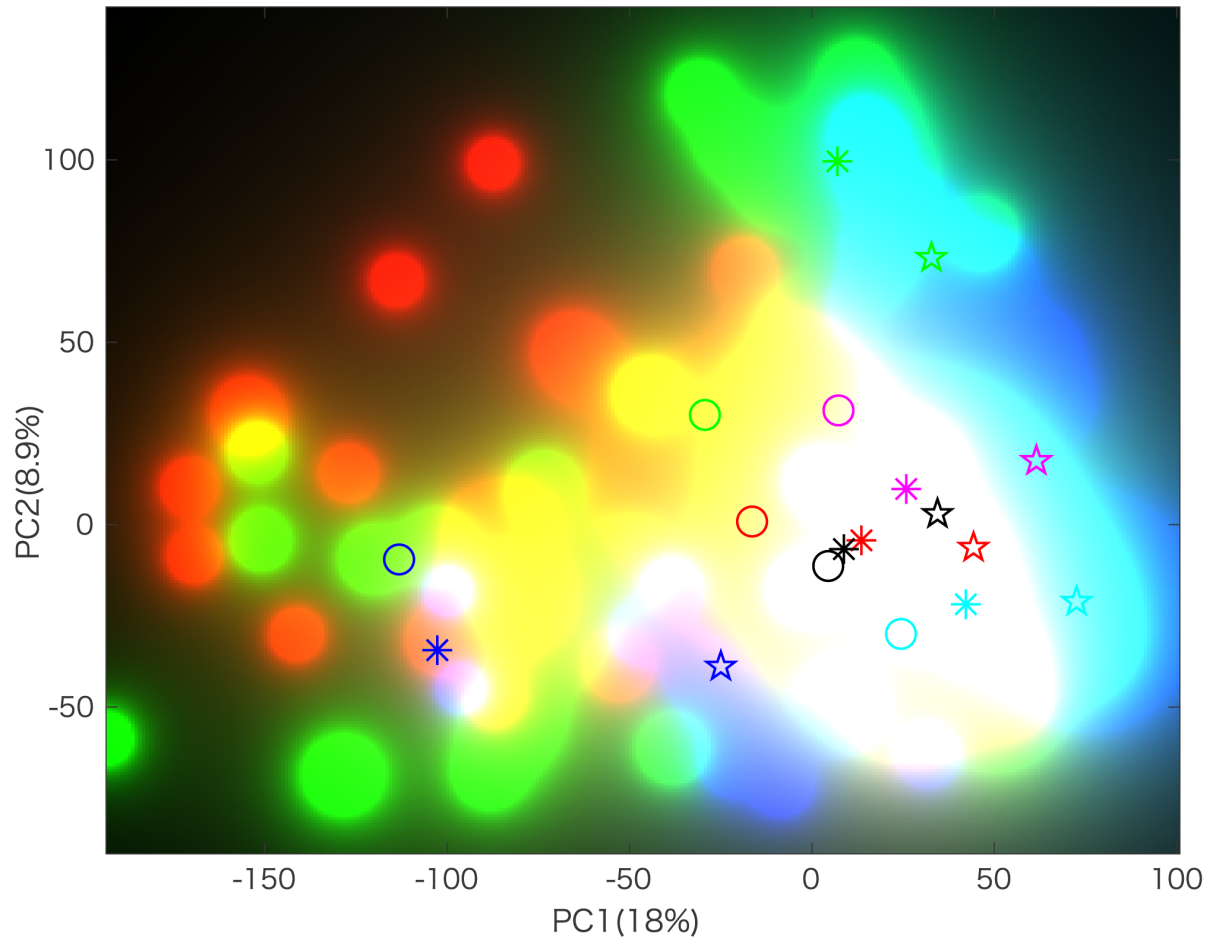
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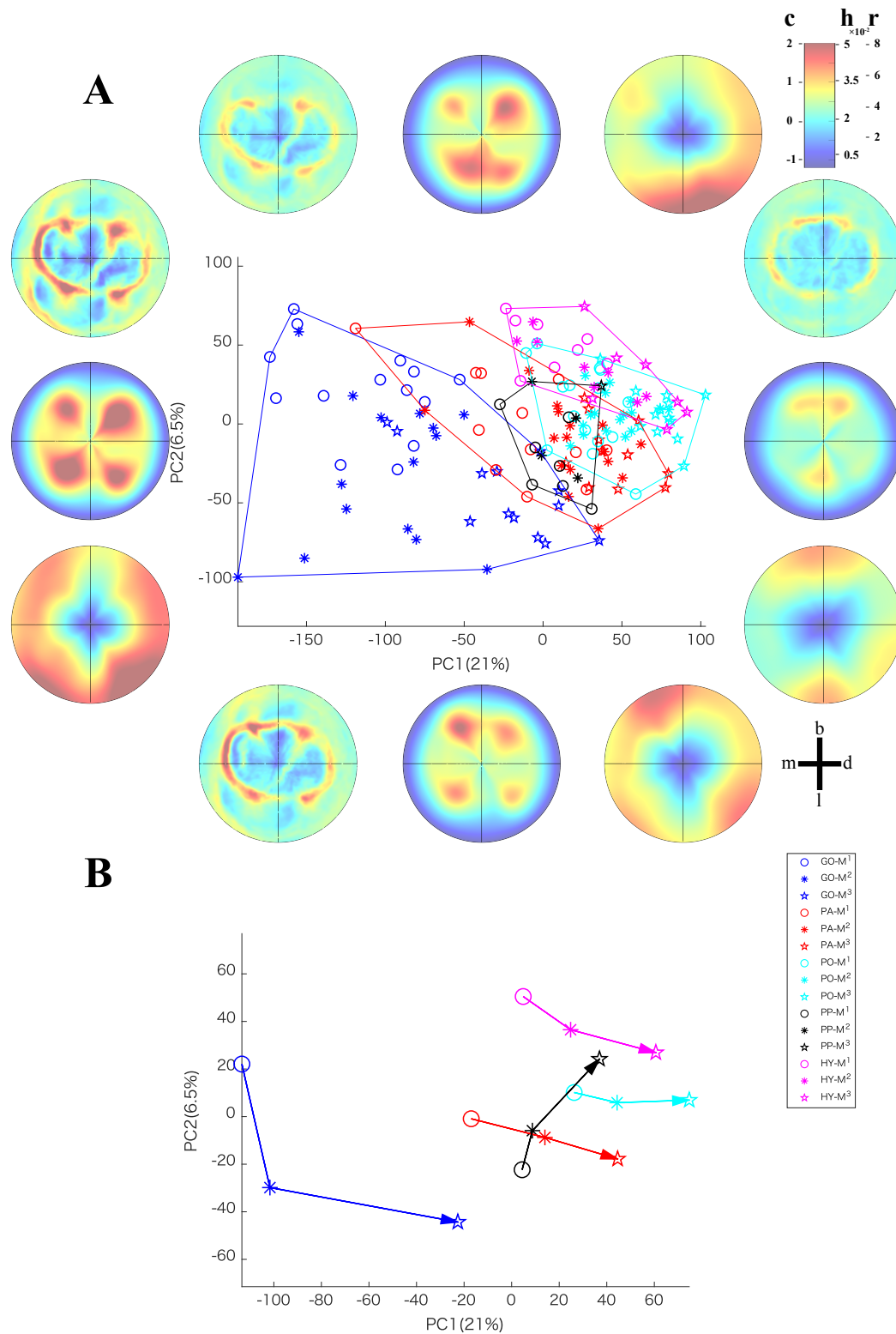
SOM Figure S1. Scheme of morphometric data acquisition. A) 3D representation of EDJ crown of left human M^1 (occlusal view). Dotted line indicates the digitized occlusal basin outline. The EDJ is aligned so that the least-squares plane of occlusal basin outline is parallel to the xy-plane of the Cartesian coordinate system, which origin is defined by the centroid of the occlusal basin. B) 3D model of the EDJ (distal view). Filled circles indicate the digitized cervical line. Finally, the EDJ is ‘shifted-up’ until 80% of total crown height lies above the least-squared centroid of the cervical line. C) Vertical section of the EDJ. The EDJ segment that runs from the z-axis to the cervix ($d: 0 \rightarrow 1$) is parameterized by elliptic Fourier analysis. Along the EDJ segment, we sampled three variables: c = curvature calculated in 3D; h = height from the basal plane; r = radius from the z-axis. This was done in 300 equidistant locations along each EDJ segment. D) 3D model of EDJ (occlusal view) that represents the anatomical direction: buccal (0°) $\rightarrow$ mesial (90°) $\rightarrow$ lingual (180°) $\rightarrow$ distal (270°) $\rightarrow$ buccal (360°). Parametrization was repeated in 300 equiangular sections. Abbreviations: b = buccal; m = mesial; l = lingual; d = distal.



SOM Figure S2. Individual-based metameric vectors from M1 to M3 along PC1 and PC2. The number of individuals for which all three molars examined were: chimpanzees, 6; gorillas, 8; orangutans, 6; gibbons, 7. The major trend of metameric change among molars is largely the same as that represented by mean shape in Figure 2B.

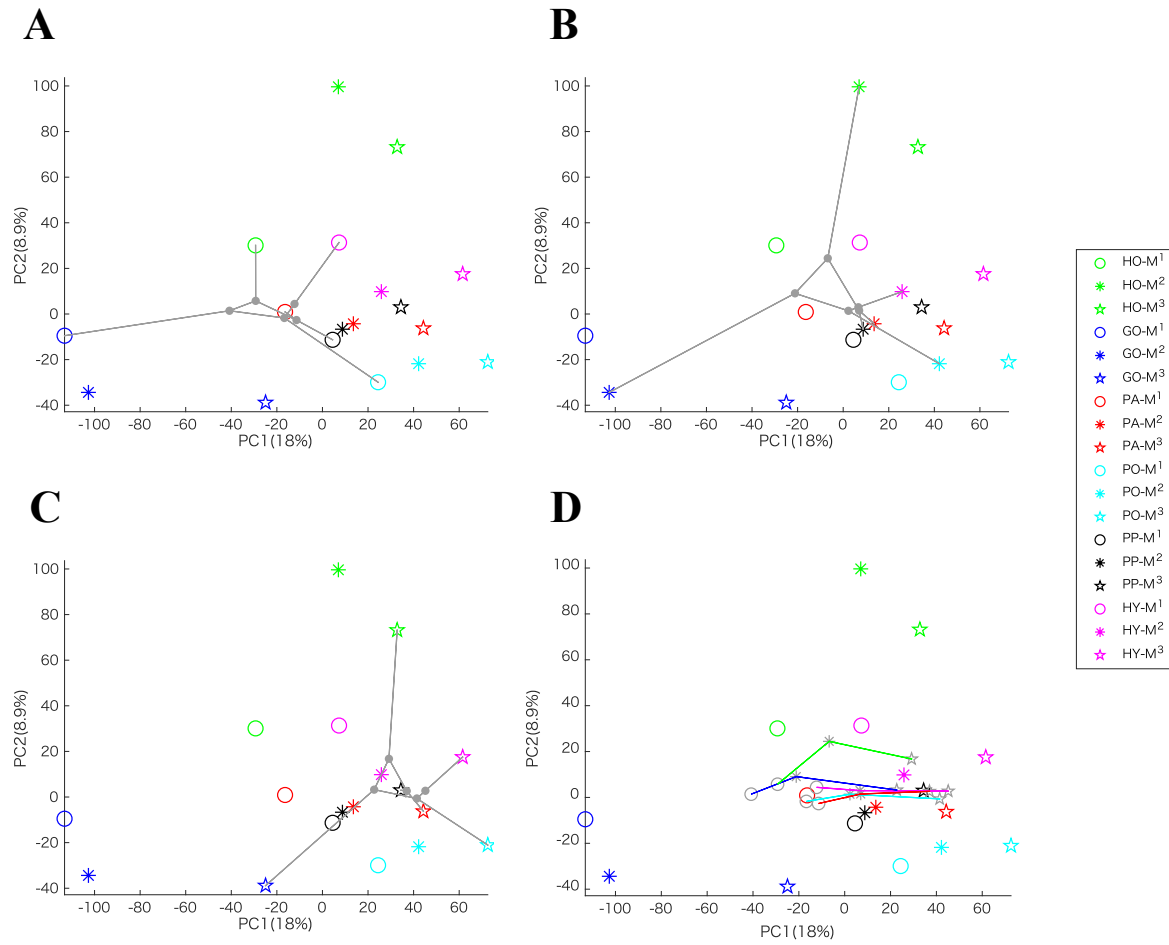


SOM Figure S3. The false color mapping of local density in PC1–PC2 space. The red, green, and blue RGB values correspond to M^1 , M^2 , and M^3 local density, respectively. Except for the high density (white) in the middle of the morphospace, the density map shows gradation from red to green and blue along PC1, which represents a shared pattern of metamerism variation among hominoids. The symbols are as in Figure 2. The markers indicate the locations of mean molar shape for each taxon.

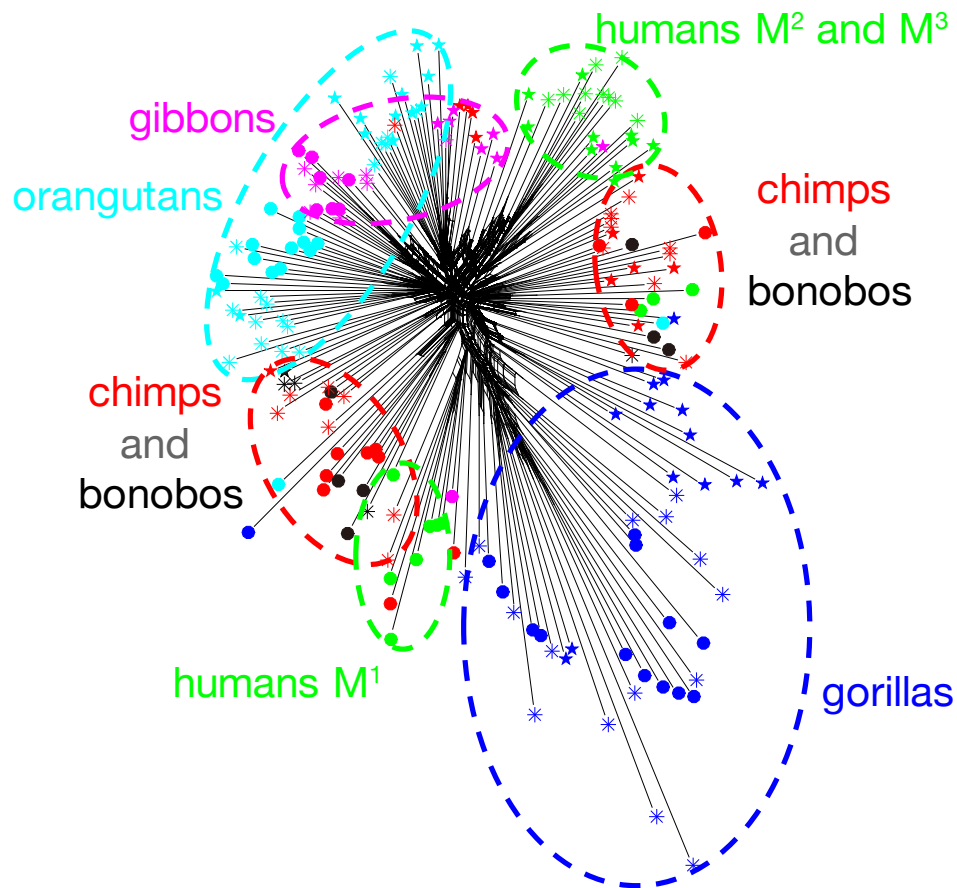


SOM Figure S4. Metameric variation in extant ape upper molars: results of the PCA of the nonhuman hominoid sample. A) Molar shape variation in PC space (along PC1 and PC2). Symbols used in the PC graph: open circles = M¹; asterisks = M²; open stars = M³. Colors: red = chimpanzees; black = bonobos; blue = gorillas; cyan = orangutans; magenta = gibbons. Major patterns of variation are as follows: PC1:

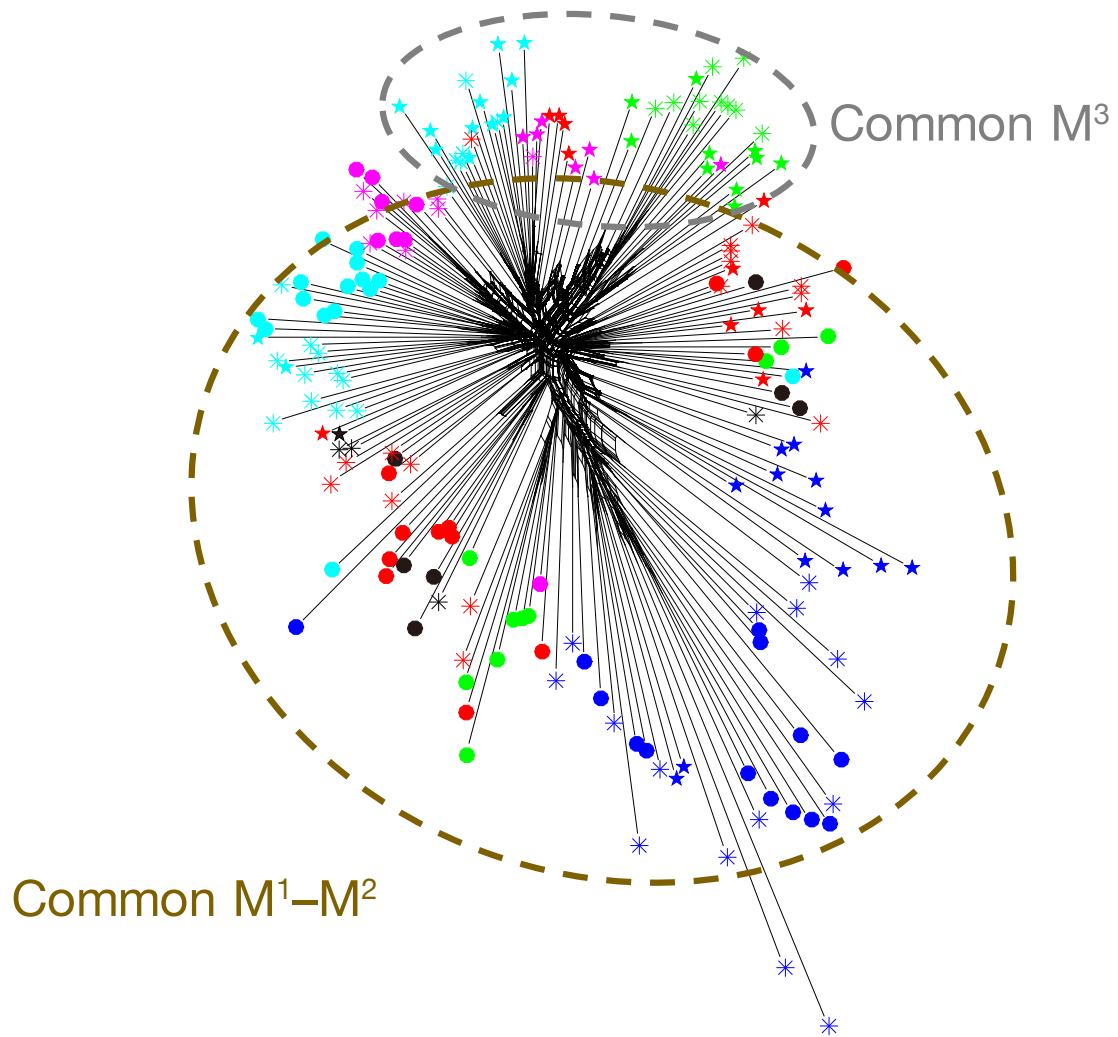
(-) c-Map: clear crown relief with mesiolingual cingulum; h-Map: high and broad four main cusps; r-Map: larger dimension in each of the four cusp directions, particularly toward hypocone / (+) c-Map: decreased relief and closely located buccal cusps; h-Map: generally lower cusp and hypocone reduction; r-Map: elongation at the middle of buccolingual axis. PC2: (-) c-Map: relatively clear crown relief with sharp mesial ridge; h-Map: high paracone and closely located buccal cusps; r-Map: larger mesiobuccal and distolingual direction / (+) c-Map: pointed four cusp tips; h-Map: distant buccal cusps and closely located lingual cusps; r-Map: expansion towards lingual direction. Abbreviations: b = buccal; m = mesial; l = lingual; d = distal. B) Taxon-specific metameric change vectors from M^1 to M^3 . The markers indicate the location of mean molar shape.



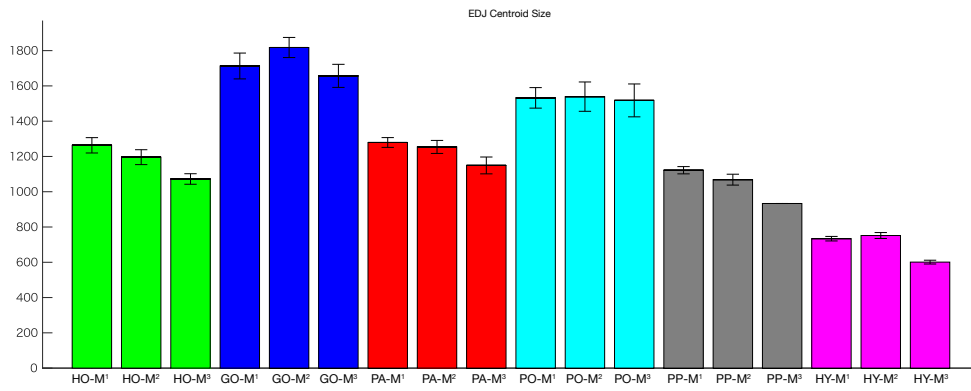
SOM Figure S5. A–C) Phylomorphospace of hominoid upper molars. The phylogeny of extant apes is projected into a plot defined by PC1 and PC2 of the covariance matrix among extant species means for M¹ (A), M² (B), and M³ (C), respectively. Internal node morphologies were reconstructed using squared-change parsimony. D) Estimated metamer variation of molars (MVM) for each ancestral node: magenta = all extant hominoids (crown hominoids); cyan = extant great apes and humans (crown hominids); blue = extant African great apes and humans (crown hominines); green = humans and chimpanzees; red = genus *Pan*.



SOM Figure S6. Taxon-based groupings of the neighbor-net diagram (main text Fig. 5). Gorillas form a clear cluster, whereas orangutans and gibbons partially overlap and chimpanzees and bonobos group together. Although there seems to be two distinct *Pan* clusters, they share a common root and are actually tightly connected. Humans are divided into two clusters: M¹ vs. M² and M³.



SOM Figure S7. Molar-based groupings of the neighbor-net diagram (main text Fig. 5). Most hominoid M¹s and M²s form a common cluster with the exception of gorilla M³s. Although the human M¹ groups with the common M¹–M² cluster, both M² and M³ of humans group with the common M³ cluster.



SOM Figure S8. Metameric variation of EDJ centroid size calculated from the square root of the summed squared distances of h and r value of each data point.