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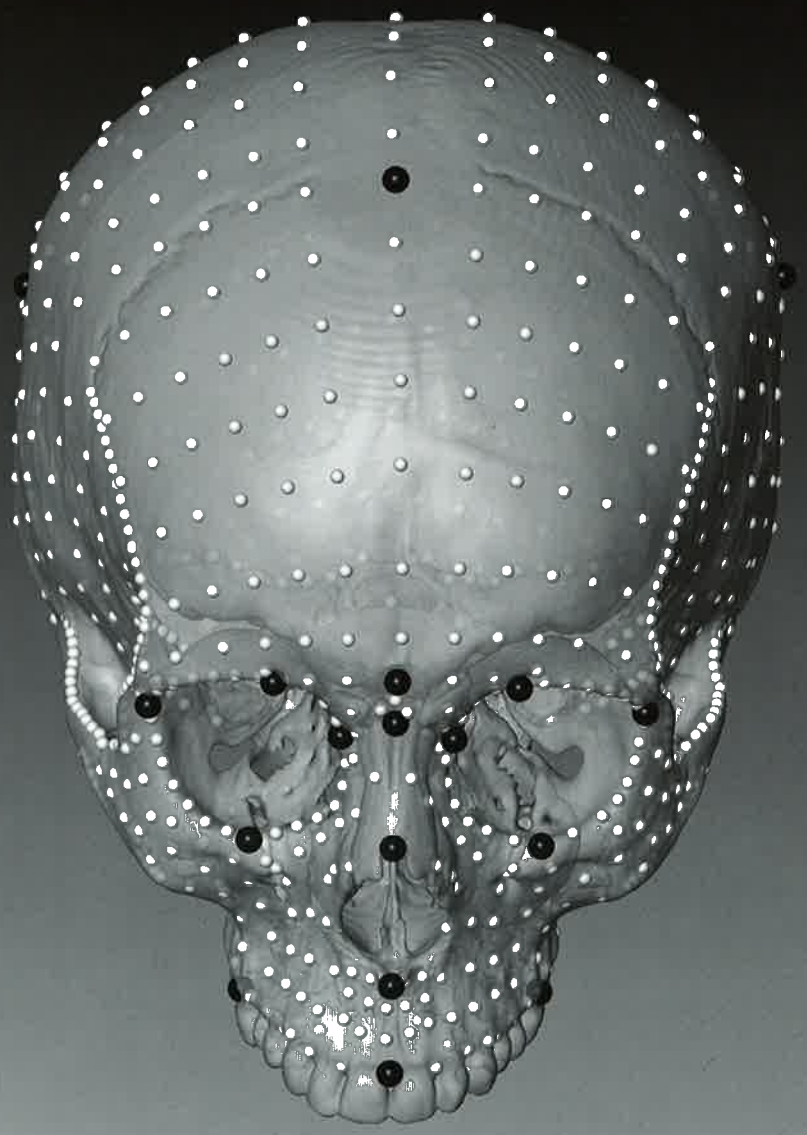

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Virtual Anthropology

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KEY WORDS virtual anthropology; comparative morphology; functional morphology; geometric morphometrics; human evolution; shape and form analysis; virtual morphology; biomechanics

ABSTRACT Comparative morphology, dealing with the diversity of form and shape, and functional morphology, the study of the relationship between the structure and the function of an organism's parts, are both important subdisciplines in biological research. Virtual anthropology (VA) contributes to comparative morphology by taking advantage of technological innovations, and it also offers new opportunities for functional analyses. It exploits digital technologies and pools experts from different domains such as anthropology, primatology, medicine, paleontology, mathematics, statistics, computer science, and engineering. VA as a technical term was coined in the late 1990s from the perspective of anthropologists with the intent of being mostly applied to biological questions concerning recent and fossil hominoids. More generally, however, there are advanced methods to study shape and size or to manipulate data digitally suitable for application to all kinds of primates, mammals, other vertebrates, and invertebrates or to issues regarding plants, tools, or other objects. In this sense, we could also call the field "virtual morphology." The approach yields permanently available virtual copies of specimens and data that comprehensively quantify geometry, including previously neglected anatomical regions. It applies advanced statistical methods, supports the reconstruction of specimens based on reproducible manipulations, and promotes the acquisition of larger samples by data sharing via electronic archives. Finally, it can help identify new, hidden traits, which is particularly important in paleoanthropology, where the scarcity of material demands extracting information from fragmentary remains. This contribution presents a current view of the six main work steps of VA: digitize, expose, compare, reconstruct, materialize, and share. The VA machinery has also been successfully used in biomechanical studies which simulate the stress and strains appearing in structures. Although methodological issues remain to be solved before results from the two domains can be fully integrated, the various overlaps and cross-fertilizations suggest the widespread appearance of a "virtual functional morphology" in the near future. Yrbk Phys Anthropol 156:22–42, 2015. © 2014 American Association of Physical Anthropologists

INTRODUCTION

Morphology deals with the study of shape and form of organisms and the relationships among their parts. The field qualitatively and quantitatively investigates normal and pathological variation of organisms, their growth and development during ontogeny, and it is a keystone for studies of the fossil record. There are two major subdisciplines in morphological research: comparative morphology, dealing with the diversity of form and shape, and functional morphology, the study of the relationship between the structure and the function of an organism's parts.

The technological opportunities that arose with computer power and software in the last two decades offered entirely new approaches in comparative morphology to investigate and compare carefully the external and internal structures of organisms, including humans. Major goals are to capture the size and shape of any structure quantitatively and comprehensively apply advanced statistical methods, combine results from different approaches, and generate data sets that can be easily evaluated for reproducibility. Virtual anthropology (VA) exploits digital technologies and pools experts from different domains such as anthropology, paleontology, primatology, medicine, mathematics, statistics, computer science, and engineering. The term "virtual anthropology" was coined in the mid-1990s and first published in the late 1990s (Weber et al., 1998) from the perspective of anthropologists. A more developed definition is presented in one of the discipline's textbooks by Weber and Bookstein (2011b). VA is characterized as "a multidisciplinary approach to studying morphology, particularly that of humans, their ancestors, and their closest relatives, in three or four dimensions (space or space-time)." Nonetheless, advanced methods to study shape and size or to manipulate and reconstruct data digitally were already applied early on to all kinds of organisms such as primates, mammals, other vertebrates and invertebrates, as well as plants, and of course to all other kinds of objects such as artifacts or buildings. Nevertheless, paleoanthropology was one of the important triggers to promote the development of methods based on computer power and software (cf. also "computer-assisted paleoanthropology"; Zollikofer et al., 1998). The suite of approaches that are part of VA can clearly be applied elsewhere; we could therefore also speak of a "virtual zoology," "virtual biology," or, as one of the reviewers of this contribution has cleverly suggested, the most inclusive term would be "virtual morphology."

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More important than the label is that the new approaches offer new opportunities, for instance, fairly easy access to spatial information. Clearly, 3D approaches allow gathering more relevant spatial information from three-dimensional objects than projections and 2D images do. As we will see, data acquisition in VA is often based on 3D technologies, which entails the need for algorithms to analyze them suitably. A key to all the "virtual" disciplines mentioned above is to perform morphological analysis using digital data. Many persons have contributed in this field. For reasons of brevity, only selected pioneers in the area of evolution are mentioned here (for a more comprehensive history of the field, see Spoor et al., 2000, or Weber and Bookstein, 2011b). These pioneers include Fleagle and Simons (1982), who used computed tomography (CT) to study long bones of an Oligocene primate; Wind (1984) used 2D tomographic slices to work on the Pithecanthropus IV fossil from Java; Conroy and Vannier used 3D data from CT to electronically remove matrix from a fossil to investigate the cranial cavity (Conroy and Vannier, 1984) and somewhat later (Conroy and Vannier, 1987) determined the dental development of the Taung child; Seidler et al. (1992) virtually exposed the cranium of the Tyrolean Iceman based on CT data and applied rapid prototyping (RP) models; Spoor et al. (1994) revealed the inner details of the bony labyrinth based on CT technology; and Zollikofer et al. (1995) virtually reconstructed Neanderthals and other fossils using the same approach. The first paleontologist to use radiological methods for the study of hominin fossils, although not digitally and not 3D, was Gorjanović-Kramberger (1902), who published on the inner details of the Krapina material only 7 years after the discovery of X-rays by Röntgen (1895).

What is the gain of the virtual disciplines for studying morphology? The most obvious and self-explanatory difference to traditional approaches is that work is done using "virtual" objects (which derive from digitization processes such as CT or surface scanning; see below) instead of "real" objects. They are analyzed in 3D (or 4D if time is included) within a computer environment, which entails some crucial advantages:

1. the accessibility throughout the "entire" object, including usually "hidden features" such as the braincase, the sinuses, the dentine below the enamel, the medullary cavities of long bones, trabecular bone, or, if we take living subjects, the brain or the heart including its chambers,
2. the "permanent" availability of virtual copies of the specimen (24/7) on hard drives or servers, where the actual location of the researcher and the specimen no longer play any role,
3. the possibility of obtaining a dense mesh of measurements across the whole geometry for "powerful" quantitative analyses of form and shape,
4. the "great range of options" for data handling, statistics, visualization, and data sharing for increasing sample size, and
5. the "reproducibility" of procedures and measurements, where each step can be electronically logged.

MORE DATA FROM SMALL SAMPLES

In the author's own work, the virtual objects were mostly fossils as well as bones and teeth of extant hominoids. Many algorithms and methods were developed to cope with specific problems in the field of hominoid evolution, but even stone tools and other artifacts can be analyzed in the same manner (Weber, 2014). Particularly paleoanthropology struggles with a serious limitation: the very few sources of evidence. Even if the number of discovered fossils has increased impressively in the last few decades, we have no hope of closing all gaps in the record or ever collecting sample sizes that will allow us to accurately characterize the morphological variation of hominin taxa.

The scarcity of fossil material raises an important demand: to extract as much information as possible from the few and often tiny remains. We need to think hard about experimental designs, methods, and collaborations with other sciences to meet this obligation. There have been huge advances in all fields of science based on the machines that now offer nearly endless computing power and storage. Who would have thought 50 years ago that we would know the complete sequence of the Neanderthal genome (Prüfer et al., 2014) or that the shape of the semicircular canals in the inner ear would suggest a species assignment (Hublin et al., 1996)? However, if we desire to consider paleoanthropology as a part of the natural sciences (Tattersall and Schwartz, 2002), we need to think about reproducibility. "The ability of an entire experiment or study to be reproduced, either by the researcher or by someone else working independently" is so common a statement that it is taught in every science introductory course for undergraduates and can be found in Wikipedia (http://en.wikipedia.org/wiki/Reproducibility). The latter adds in the next sentence "It is one of the main principles of the scientific method. . .." If we ignore it, paleoanthropology remains at the level of a narrative science—story telling in the sense of Landau (1984). The line to walk is thin between exploiting every possible bit of information stored in a fossil, but not exaggerating the interpretation and keeping in mind the uncertainties inherent in our data. Darwin (1871, p 385) himself recognized the poisonous influence of erroneous data: "False facts are highly injurious to the progress of science, for they often long endure; but false views, if supported by some evidence, do little harm, as everyone takes a salutary pleasure in proving their falseness; . . .."

Virtual anthropology offers the potential to make every manipulation or measurement public, and, of course, virtual objects and electronic data are easy to share electronically. This does not in itself guarantee proper investigations. White (2000, p 288) took it to an extreme when he stated in his Millennium essay: "The careerist leaps on each passing technological bandwagon. [. . .] Results can be instant, irreproducible, and irrelevant. When applied without appropriate biological background, they simply muddle fundamental issues in human evolution." We must indeed exercise caution and ensure that methods and machines are used advisedly and that researchers understand the prerequisites and limits of their use. Importantly, there are meanwhile enough documents in support of useful applications out there, including White and colleagues (e.g., Suwa et al., 2009), who later used the VA toolkit for describing and analyzing their fossils.

The limitations occurring during work with fossils warrant some extra words. Although a fossil appears to be a simple static object for the layperson—actually nothing more than a piece of stone of some specific shape—it may convey a rich variety of data for the expert. The examples include macroanatomy (e.g., the

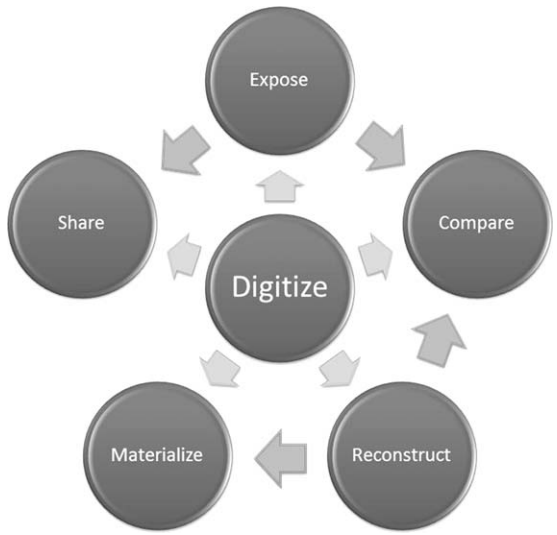

Fig. 1. The six operational areas of Virtual Anthropology: Digitize is in the center and naturally connected to all other actions. The most common pathways between the other modules Expose, Compare, Reconstruct, Materialize, and Share are indicated.

shape of the cranial vault, jaws, or teeth), microanatomy (e.g., the orientation of trabecular structures or the prisms of dental enamel), taphonomy (e.g., the degree of mineralization and the presence of cut marks), individual life history (e.g., traumata, pathologies and incorporated trace elements), or even genetics (ancient DNA from cell mitochondria or the nucleus). A virtual fossil can only offer a small fraction of this information. In most cases, it does so for the macroanatomy. In some cases, depending on the resolution, it can also supply information on microanatomy, and probably on taphonomy and life history. In the case of volume data (e.g., from CT), no color or texture information is transferred from the real to the virtual object. In the case of surface data, such information might be available on texture and color (together with the digitized surface); however, no internal structures are accessible beneath the surface. Some other data channels are missing entirely; for instance, a virtual fossil cannot be used to detect DNA or trace elements. Virtual fossils are thus not intended as a substitute for real fossils. They are useful for specific purposes only, particularly to work on all kinds of aspects of comparative and functional morphology (which of course does not exclude working on the real specimen as well). As our senses are not well adapted to rely solely on screen simulations, it is also advisable to look at the original or a premium cast during work.

VIRTUAL ANTHROPOLOGY IN PRACTICE

In the early days, VA was a rather exclusive endeavor, demanding machines that were otherwise available only to advanced film studios, such as those generating animations for the 1993 movie "Jurassic Park" (http://www.sgistuff.net/funstuff/hollywood/jpark.html). Today, it is much more feasible for any commonly equipped laboratory to start working in VA. The most typical infrastructural requirements are fast PCs with multiple-core processors, high-end graphic cards, and large storage systems (depending on the applications in the range from 10 to 100 TB, whose costs are often dramatically underestimated), along with software for image processing, 3D manipulation, visualization, programming, and statistics. More challenging are the personal requirements because a highly trained staff is necessary to handle all these components. The team would ideally include people with training in biology, anatomy, mathematics, statistics, programming, physics, and radiology. The data acquisition itself can be simple or demanding, depending on the technology used (see below); however, it does not have to occur in the same laboratory or university, as long as collaborations offer access to the respective facilities.

The following division of VA into six operational areas (Fig. 1) has proven to be convenient for didactic reason and thus is maintained throughout this article:

1. Digitize—mapping the physical world
2. Expose—looking inside
3. Compare—quantitative evaluation
4. Reconstruct—dealing with missing data
5. Materialize—coming back to the real world
6. Share—collaboration using electronic data transfer

All six are described extensively in a textbook on this discipline (Weber and Bookstein, 2011b).

THE SIX OPERATIONAL AREAS OF VIRTUAL ANTHROPOLOGY

Digitize

The first step, which also provides the framework for all further ones, is the transfer of the real object into the world of digital data. The latter is a projection of continuous data into the space of integers. The range of numbers used for quantification is therefore limited to a discrete set of values, and the number of elements recorded is limited by the resolution of the sensor. A variety of technologies is available, some still sophisticated and costly, and others simple in use and inexpensive. The VA researcher has to answer two questions right at the beginning:

1. Will it be sufficient for the research question at hand (e.g., classification, hypothesis testing, or modeling) to capture the surface of the object or are data needed throughout the volume of the object?
2. Independent of the first question, what resolution is reasonable (how small is the smallest structure to be detected; see below)?

Many interesting features of an investigated object are substructures, often reaching far into the interior of the object or completely hidden beneath the surface, for example, the cranial sinuses or the enamel–dentin junction (EDJ) of teeth. Others are difficult to measure on an intact specimen from an osteological collection such as bone and enamel thicknesses. All of them, however, can carry important information with regard to morphology, including taxonomic assessment. Volume data, that is, 3D data throughout the structure such as CT, are therefore often necessary. In archaeology or face recognition of living subjects, in contrast, surface data would satisfy most applications because the inner composition might be known, as in the case of stone tools, or not be part of the investigation. To save time and money, surface scans are often ideal. Even if it would be desirable to render internal structures or even if volume scans

would be faster (e.g., for numerous small objects like teeth or carpals in one run), surface scans could nevertheless be the choice of digitalization. One reason might be because volume data acquisition is simply not possible, for instance, for fossils that were just discovered in the field or because no permission for transporting them to a volume scanner is available.

For volume scans, "tomographic" procedures (imaging by sections) are used. CT is a standard medical imaging procedure applied to scan living patients. For more detail in the micron (μm) range, micro-CT (μ-CT), an industrial imaging routine to examine materials in very high resolution (Illerhaus et al., 2001), is available. Magnetic resonance tomography (MRT), in turn, is limited in resolution but has the advantage of avoiding ionizing radiation and thus some ethical problems when scanning living subjects. It is designed to capture soft tissues but hardly delivers usable signals for hard tissues such as bones and teeth (see below). Because the brain, the heart, the cartilage in joints, and similar structures can be visualized, biological anthropologists use it to scan, for instance, extant primates for comparative purposes [e.g., early work such as the relative size of frontal lobes (Semendeferi et al., 1997) or cranial base flexion during ontogeny (Jeffery and Spoor, 2002)]. In contrast, CT and μ-CT cope easily with dense and very dense objects such as bones, teeth, ivory, antlers, shells, and even stones.

All of the tomographic methods can deliver a stack of two-dimensional (2D) images (which are termed "slices") that are combined into a 3D volume. In the case of CT and μ-CT, images are acquired on the basis of X-ray technology. Radiation is emitted by the X-ray tube, the rays penetrate the object, are partly absorbed, and the remaining X-rays impact on a detector behind the object, where they are recorded (Brant and Helms, 2012; Bushberg et al., 2012). In medical scanners (CT), the object or patient rests on a moving table and the tube-detector system rotates around the body. In cone beam CT (CBCT) for dental practice, the patient sits upright while the tube-detector system rotates around the head. In contrast, in most μ-CTs, the object rotates but the tube-detector system is fixed. This implies the necessity of rigidly fixing the object to the rotation table and of objects that are stiff to avoid motion artifacts (blurred images as a result of shaking). Although scans in medical CTs or CBCTs usually take seconds or several minutes, μ-CT scans vary between half an hour and many hours, depending on the machine and object properties. Thus, it is also important to ensure that the object does not change its shape and size. For instance, collection specimens taken out of alcohol or formaldehyde can shrink during the scans due to evaporation, producing disturbances similar to motion artifacts. In addition, the fresh cadavers of laboratory mice and rats are not rigid enough to reliably avoid motion artifacts due to the rotation of the platform during a scan. Care has to be taken to fix the bodies appropriately. For fresh cadavers and particularly living animals, however, special facilities are available, that is "mini medical computed tomographs," where the mouse or rat can even be kept alive and anesthetized during the scan (in vivo μ-CT; e.g., Recheis et al., 2005). Another kind of μ-CT scanners is designed for extremities (distal tibia and radius, hand, and foot) of patients (e.g., Scanco XtremeCT, http://www.scanco.ch/en/systems-solutions/clinical-microct/xtremect.html).

Paleoanthropologists deal by definition with dead material, making the issue of radiation dose of low interest in all modalities (there might, however, be effects on color and preserved DNA; Parades et al., 2012; Richards et al., 2012). When it comes to living subjects, ethical questions become a vital part of each project. In most countries, using X-ray technology without medical reasons is treated as a physical assault against a person. Therefore, radiologists will refuse to undertake such scans for pure research purposes. Moreover, for animal experiments, applications are very restricted. Although great progress has been made in recent decades in minimizing the exposure per scan, the radiation doses of CT and dental CBCT scans are still high in comparison with 2D radiography, and the net dose for the population increases due to frequent applications (Brenner and Hall, 2007; Horner et al., 2013). A wide range of potential studies can thus not be undertaken. A back door here could be MRT, which can be applied to volunteers, but only for those questions that do not involve representations of bones and teeth (at least in high resolution; however, for attempts using bones, see, e.g., Salas and Maddock, 2008, or Kermi and Laskri, 2012).

Each slice of a volume data set is composed of arrays of raster elements, which may take different tonal values, like those of any digital photo. Although these elements in 2D are called "pixels," we call elements of 3D volume data "voxels" because they offer a third dimension, a thickness. Voxels carry information about their individual position in the *x*-, *y*-, and *z*-grid of the volume, plus a specific value for their color or gray value. The different densities of materials lead to different gray values of the voxels (a function of the attenuation of the X-rays; for technical details, see Bushberg et al., 2012), which is why we can detect the inner composition of a scanned object. If that inner composition is expected to be homogeneous, then there is no argument for using a tomographic technology. If, in contrast, different materials or change of material throughout the volume can be expected, then it is the appropriate procedure. Medical CTs usually deliver a resolution of roughly between one to half a millimeter (Brant and Helms, 2012), sometimes even down to ~200 μm; dental CBCT is in approximately the same range of several hundred microns. μ-CT starts somewhere around 100 μm and can go down as low as 1 μm (Ritman, 2004; Burghardt et al., 2011); however, this depends on the capabilities of the system (e.g., on the diameter of the microfocused X-ray beam and the size of the detector elements) and the applied magnification (zoom), the latter in turn depending on the size of the object and the scanner geometry. Although most recording chambers of μ-CTs are limited to relatively small objects (usually 1–15 cm in diameter; see below), only a few machines can handle large objects of the size of a human skull or a femur (e.g., see www.micro-ct.at, VISCOM X8060 II). A further increase in contrast quality and resolution is possible with synchrotron microtomography, with resolutions as low as 0.7 μm (Sanchez et al., 2012). This particular type of particle accelerator was occasionally used for fossils (e.g., Tafforeau et al., 2006; Le Cabec et al., 2014). However, research times at those facilities are in high demand and therefore very difficult to obtain.

Discussing CT and μ-CT naturally evokes the question of the appropriate resolution? This relates to the second issue raised at the beginning of this section. There is a general and very obvious answer: "good enough for the purpose" (Weber and Bookstein, 2011b). However, what does this mean in practice? In our experience, for

example, it rarely makes sense for the investigation of the gross geometry of skulls to go down to resolutions lower than 200 μm (corresponding roughly to 1/1,000 of the length of a skull). For the analysis of tooth wear facets, another scan at 50 μm would still be too coarse. In the first case, where the geometry of the whole object is the objective, a proportional resolution of 1/500 to 1/2,000 of the greatest length is sufficient. If, however, small details of a larger object need to be studied (e.g., trabeculi of a femur or the tooth wear facets in the above-mentioned example), then the scan, and the reconstructed data from it, have to be zoomed accordingly. A good question to raise at the start here is "How small is the smallest structure that needs to be detected?" For instance, perikymata (incremental growth lines on the enamel surface) have a depth of 2–5 μm and a spatial periodicity of 50–100 μm (Elhechmi et al., 2013). It would thus be useless to try measuring their depth on a scan with 40 μm resolution. Depending on the machine's capability to accommodate the object in its recording chamber and the possible zoom factor, a decision has to be made whether the resulting scan resolution would allow for the intended study.

"Why not digitize everything in the highest resolution possible?" First, the accessibility to machines offering the highest resolution technically possible is very restricted. They are immobile or, at best, can be transported only with great difficulty. Second, the emerging data volumes are gigantic. For example, a human cranium with 50 μm voxels (which is possible with specialized scanners; e.g., http://www.micro-ct.at/) yields a data set of 4,000 × 3,000 × 3,000 voxels; each voxel needs two bytes for color coding, hence we have roughly 72 GB of data—for one specimen. Fifty micrometers is still insufficient for each possible question we might have; however, the data set is certainly too big for the memory of a typical desktop computer, and a moderate sample of 100 specimens together would require significant storage capacity. Currently, the technical and financial development of computers and storage media still lags behind the possibilities of the scan. Third, in many available scanners, only small objects can be examined (e.g., Skyscan 1272 <75 mm diameter; GE v|tome|x s <135 mm diameter; and Scanco μCT 100 <160 mm diameter), whereas crania, jaws, or long bone fragments do not fit into the recording chambers.

For rarely accessible objects such as important hominin fossils or artifacts such as the Venus from Willendorf (Fig. 2), maximum resolution is definitely justifiable, mainly because those objects can undergo an examination perhaps only infrequently. The resulting data are good enough for virtually all purposes, and at least for the middle-term future (even if we have to await technical development to fully use them).

Resolution is less an issue in surface scanning because the amount of data is generally much less. Surface scanning does not allow looking even a micrometer below the exterior interface, but, depending on the system used, might also deliver very high resolutions (also in the micrometer range). Common scanners are based on laser beams or structured light (dark and bright stripes) that are projected over the object. A sensor measures the reflected light or the pattern of stripe distortion, respectively. Because the geometry of the light/pattern emitting and receiving system is known, the object geometry can be computed by means of triangulation. The acquisition of one such "shot" can be very quick (within seconds); however, it does not represent more than merely a single view (like a photo). To digitize the whole object, the latter has to be rotated and captured again and again, with overlapping areas. Most scanners come with software that can stitch together the different views until the whole object surface is recorded in all dimensions. In some cases, texture/color information can also be recorded to a certain extent. Usually, a photo is overlain with the surface data, leading to a more or less realistic appearance, but some systems can actually scan the color, which can be an important addition. This is not possible with any of the tomographic procedures. Surface scanners are usually smaller and lighter (easier to transport) than CT or μ-CT scanners, and one or several orders of magnitude cheaper. As long as there is a power source available, they can be applied even in the field. Another alternative to obtain 3D data from multiple images taken from different views is stereoscopic photography. Recent software packages (e.g., PhotoModeler®; http://www.photomodeler.com) can assist in calibrating the camera system and identifying overlapping points on images to create a 3D model of the object (Paul et al., 2013).

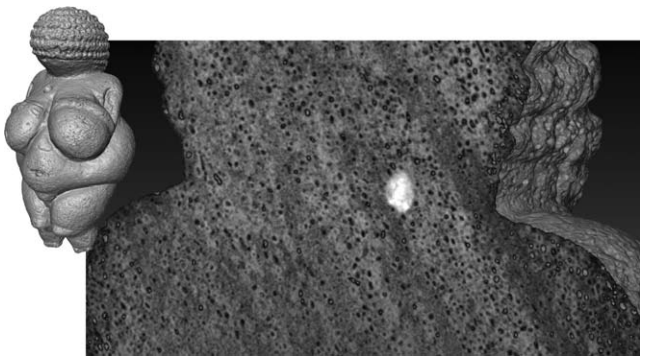

Fig. 2. The Venus from Willendorf (curated at the Natural History Museum Vienna) and a zoom into the head–neck region of the μCT scan (resolution: 53 μm). The volume was clipped to show the internal structures. Clearly, the figurine shows a quite heterogeneous inner life with stratification (bright and dark stripes), inclusions (the white spot), and high porosity in general which helps to identify the source of its raw material.

Finally, there is the possibility of combining "slicing" with "digital photography." This combination is an invasive approach that destroys the sample but delivers 3D volume data. When abundant material is available and noninvasive approaches such as CT do not deliver usable signals (e.g., because the object and the surrounding matrix are of equal density or the resolution is too low), this might be the method of choice. Thin sections of the object are removed, for example, by grinding or cutting, and each slice is photographed. At the end of the process, the object has disappeared but the stack of spatially registered photos can be treated like any other tomographic data set. The examples are the colored cryosections of the Visible Human Project (Ackerman et al., 1995) or a study on paleocurrents based on the orientation of ammonites in a limestone block (Lukeneder et al., 2014).

Each digitizing method has its own rules and pitfalls. Some effort is necessary to obtain usable results, and in some cases, tailored protocols have to be developed. For scanning living patients or animals, collaborations with radiologists are advisable (the daily procedures in the

clinic do not necessarily deliver good results for specific research purposes, but the radiologist might know how to adjust the machine). For bones and fossils, there are a number of best practices. For instance,

- remove all metal parts (e.g., fixing pins and clips) from the object to avoid image artifacts,
- keep the gantry tilt in medical devices at zero (otherwise the image stack is shifted and needs cumbersome recalculations),
- choose an appropriate field of view (to maximize resolution) and the smallest possible slice thickness (to minimize the partial volume effect),
- maximize the contrast and avoid CT-scale overflow artifacts,
- select a kernel (the convolution filter used for back projection) that is neutral or slightly hard,
- store the raw data because different or optimized reconstructions can be computed afterward from this source, and
- as a matter of courtesy, offer to share the data and leave a copy with the institution that hosts the collection or fossils.

The brevity of this article does not allow for a lengthy technical discussion; however, for more advice, see, e.g., Spoor et al. (2000), Zollikofer and Ponce de León (2005), or Weber and Bookstein (2011b).

Expose

VA allows observing internal structures. In contrast to dissection and other invasive techniques such as histological thin sections or grinding (see above), the natural assemblage of parts is not disturbed and the object itself is not destroyed. A major drawback of surface data is that no internal data are recorded; only tomographic data can be used to look inside.

The machinery cannot know about the internal features that might be present on tomographic images. For the software, every voxel has solely a position and a gray value, but no other characteristics or relations to its neighbors. One can browse through the stack of images on the screen and build a map of meaningful structures in one's mind. This is what most radiologists still do with their light box, examining hundreds of CT or MRT images of patients, searching, for instance, for a tumor or a thrombus. To use the full range of possibilities in VA, however, the researcher has to "tell" the machine which image area is representing what. We call this labeling of structures as segmenting. Segmentation means to separate particular areas of the image from their neighbors and to address them as different logical entities. The result is a scalar field of labels for each voxel where the label indicates different types of material. For instance, the brain in an MRT scan is often segmented from the surrounding cerebrospinal fluid (CSF), meninges, bones, and muscles to work on its morphology. In osteology and paleoanthropology, braincases are used instead of brains. They are the only source in fossils (except natural endocasts) to infer about our ancestors' cognitive capacities. In many fossils and in all dried skulls from collections, the braincase is empty and filled with air. Air has quite different gray values (blackish based on its low density) than bone (medium to light gray based on its much higher density). This makes it relatively easy to label the borders between air and bone using semiautomated algorithms (mostly "thresholded region growing" is applied). Those algorithms are available in many 3D programs (e.g., Amira™ and Analyze™) and work without much manual intervention. The latter is important to approximate the goal of reproducibility, consequently avoiding subjective influences. Clearly, the empty skull is the easiest example. Segmenting the brain from the CSF, for example, or the dentine from the enamel can be much more difficult, sometimes even impossible.

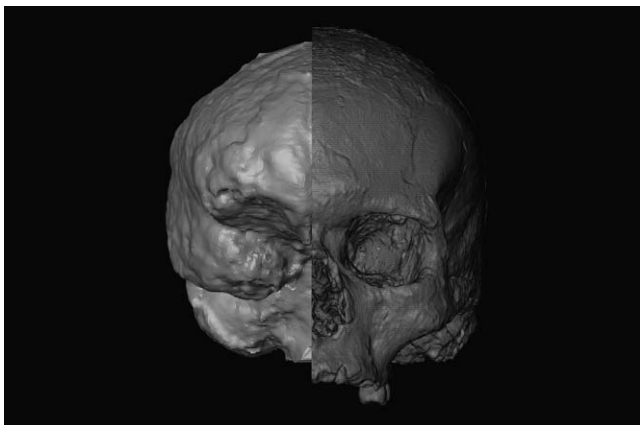

Fig. 3. The virtual endocast and half of the cranium of the Upper Paleolithic specimen Mladeč 1 (curated at the Natural History Museum Vienna).

After successfully labeling each single slice of the volume (which can number in the hundreds or thousands), the new object can be addressed. The voxels in the image stack are now no longer a homogeneous mass of equal entities; rather, some of them have been given a new quality, marking them as belonging together. They form a virtual object that can be rendered on the computer screen (Fig. 3). In the case of a "positive" of a formerly hollow cavity, we refer to the resulting object as a "virtual endocast" (Weber et al., 1998). If it derives from the braincase, surface details such as imprints of brain convolutions or vessels can be described, and the cranial capacity (volume) can be measured. Likewise, other hollow structures can be created as virtual endocasts, for instance, the frontal and the maxillary sinuses, the semicircular canals, or the pulp of a tooth.

As brain enlargement is one of the critical issues in human evolution, endocranial endocasts are important sources to compute indices such as the encephalization quotient, which is based on the estimated brain to body size ratio (Martin, 1983). Cranial capacity, that is, the volume of the endocranial cavity, is, however, not equal to the size of the brain but about 10% larger (Holloway et al., 2004, p 8). Virtual endocasts have been used in many fossil studies to infer an approximate brain volume or provide other descriptions of endocranial morphology (e.g., Conroy et al., 1998, 2000; Weber et al., 1998; Recheis et al., 1999; Falk et al., 2000; Tobias, 2001; Prossinger et al., 2003; Bräuer et al., 2004; Ryan et al., 2008; Wu et al., 2008; Falk et al., 2009; Carlson et al., 2011; Kranioti et al., 2011; Curnoe et al., 2012; Neubauer et al., 2012; Liu et al., 2014). Such endocasts have, of course, also been used for extant hominins, primates, and vertebrates in general (e.g., Colbert et al., 2005; Rowe et al., 2005; Macrini et al., 2007; Dong, 2008; Balzeau et al., 2009; Sakai et al., 2011; Bienvenu

et al., 2011; Arsznov and Sakai, 2012; Ni et al., 2012; Holloway et al., 2013).

As accurate as a virtual endocast can be, it will never provide direct information about the internal organization of the brain such as the number of neurons, their density, and structure or the connectivity between areas of the brain. Nonetheless, beyond a mere volume estimation, the full range of the morphometric tool kit (including landmarks [LMs], curves, and surfaces; see below) can be used to quantitatively compare the internal morphology of skulls, just as for their outer surface. Not only size changes are informative with regard to hominin evolution, changes in the overall proportions of skull components or supply structures are also being investigated. This includes the relative size of the frontal cortex and cerebellum (Seidler et al., 1997), the parietal lobes (Bruner et al., 2003), or the pattern of vascular supply (Neubauer et al., 2004). The ontogenetic patterns of brain development were modified over the course of evolution as well, which can be studied in fossils and in comparison with extant apes (Neubauer and Hublin, 2012).

Segmentation of structures is very common in medical research. Fetal alcohol syndrome, for instance, leaves its traces in the connecting structure between the brain hemispheres, the corpus callosum. Bookstein et al. (2006) clearly showed that a specific geometric signal appears indicating brain damage in this class of birth defect, which is triggered by alcohol abuse during pregnancy. The corpus callosum is well visible in standard MRT scans and easy to segment; however, its shape is quite difficult to compare quantitatively because it offers few LMs. By segmenting and putting semilandmarks (sLMs; explained below in "Compare" section) along its midline, the shape can be captured in great detail. The method is even used in the American courtrooms to detect damage in the brains of certain convicted murderers at risk of a death sentence (Weber and Bookstein, 2011b). Virtual endocasts of recent persons have also been used to explore the background of an innovative surgical intervention to relieve intracranial pressure in cases of severe brain edema. Such a "posterior-hinged circular craniotomy" (Traxler et al., 2002) can be applied when conventional therapy and trepanation fail. Instead of drilling holes, the whole calotte is cut open, with a single exception: a small region at the occiput is left intact to protect the vital blood drainage via the sagittal sinus. The relationships between frontal elevation of the calotte and volume gain are impossible to measure on a real patient or cadaver. Yet this is quite simple using virtual endocasts (Traxler et al., 2002), where frontal elevation can be simulated on the computer and volume increase can be measured in relation to skull shape (e.g., brachycephaly vs. dolichocephaly) and other factors such as sex and ethnic group.

Besides the brain and the braincase, there are endless other opportunities to successfully render structures accessible for research questions. The full list of "expose (looking inside)" applications cannot be elaborated here; however, two examples that were and are of great significance for biological anthropology should be mentioned.

The size and shape of the semicircular canals in the inner ear became famous in the 1990s when Spoor et al. started to measure them based on CT scans of extant and fossil primates (Spoor et al., 1994; Hublin et al., 1996). This research is a good example for adding traits to the list of diagnostic features that were simply unavailable for study before we could "look inside." The inner ear features are used to discriminate between taxa and in attempting to understand evolutionary adaptations (Spoor et al., 2003; Gunz et al., 2012). [The first case adding a trait using radiological methods was Gorjanović-Kramberger (1906), who published his observations of enlarged pulp cavities and shortened tooth roots seen on X-rays of the Krapina Neanderthals. A new and important, previously hidden trait (introduced later as "taurodonty"; Keith, 1913) was discovered.]

Another example is the segmentation of the dentine body of teeth (EDJ). It offers abundant information about the morphology of teeth and enamel thickness (e.g., Olejniczak et al., 2008; Skinner et al., 2008, 2009; Bailey et al., 2011) that is less often or less severely affected by wear. Tooth cusps are also present on the dentine; even if the enamel tip might be worn away, however, the dentine tips might still be present. Crests and fossae can also be detected on the EDJ. Dentine and enamel have different biomechanical properties. Accordingly, segmenting them accurately and attributing the proper characteristics greatly benefits biomechanical studies, for instance demonstrating actual tooth-loading scenarios derived from the individual wear pattern (Benazzi et al., 2011b, 2014).

All of the examples above dealt with internal structures of objects or patients; however, the specimen itself might not yet be ready for analysis. Paleoanthropologists and archaeologists know this situation: many fossils or artifacts are not (or only partly) accessible because they are covered by some foreign material, often called "matrix" or "encrustation." The foreign material must be removed without jeopardizing the surface of the object any more than necessary (see "Reconstruct" section). Physical preparation is a manual procedure that requires highly trained and experienced staff. Miniature chisels, air hammers, sandblasters, and the like are used to remove the matrix bit by bit. Nevertheless, a considerable element of risk remains because the matrix could be excised too deeply, destroying the actual fossil. Good preparators avoid such errors by working very slowly. Still, internal features such as sinuses or cranial cavities are nearly impossible to uncover.

"Electronic preparation," in contrast, is based on volume data (typically CT or μ-CT scans), which allows access at any point of the object. Segmentation can be used again to separate the object from the matrix (Prossinger et al., 2003; Zollikofer and Ponce de León, 2005; Benazzi et al., 2011a; Bolliger et al., 2012). This is a fairly straightforward job in cases where the fossilized bone displays a distinctly different range of gray values (densities) than the matrix does. The material properties of the matrix vary widely, as do the difficulties associated with their virtual removal. There is, however, one striking advantage of computer-based removal of matrix: the original specimen is not impaired and we have the "undo" button available.

The task becomes difficult when the gray values between fossilized bone and matrix overlap or when the matrix is heterogeneous, as is often the case when gravels and grains of rock are embedded in calcareous sand. Because of the digital image filtering methods, the boundaries between bone and matrix can be enhanced. Such filters may involve a single application of a Sobel, Laplace, Low Pass, or other filter (Weber and Bookstein, 2011b) or it may even be necessary to apply a fine-tuned sequence of many filters (e.g., Prossinger et al., 2003).

Morphological filtering is another routine to support the separation of logically different units by breaking up bridges between them (often just a voxel or two in thickness, potentially remaining after an automated region-growing procedure) or to smooth the results. An enormous body of literature is available on digital image processing, not necessarily related to VA-specific tasks but still very helpful to consult (e.g., Gonzalez and Woods, 2008; O'Gorman et al., 2008; Yoo, 2004).

Scanning the specimens and evaluating their interior is even advisable when the intention is to remove the matrix physically. The preview obtained provides a very useful aid for the preparator to plan the task in advance and to highlight potentially problematic areas (Maiolino et al., 2012). Likewise, mummies are scanned and inspected virtually to avoid, or at least to plan, physical unwrapping (Marx and D'Auria, 1988; Magid et al., 1989; Hoffman and Hudgins, 2002; Jansen et al., 2002; Lynnerup, 2003; Gardner et al., 2004).

Compare

One of the major strengths of VA is the readily available data in digital form. From there, it is only a small step to convert the outer or inner form of an object into a comprehensive set of descriptive numbers. Typical questions that arise in comparative biology and evolutionary sciences are as follows:

- What does the average shape and form of a population look like?
- How does shape and form vary in that population around its average?
- What is the impact of size on shape; is there allometry in the sample?
- How exactly do shapes and forms of two populations differ from each other?
- What might be the functional meaning of those differences?
- Are some substructures (modules) of the shape under examination more tightly integrated with others?

Traditional anthropological approaches often tend to "atomize" a biological form by describing or rating numerous separate traits (e.g., occipital bun, high parietal boss, low cranium, or projecting midface) or they merely use a fairly restricted set of (partly unrelated) measurements (e.g., maximum cranial length, width and height, bregma–lambda chord, or occipital subtense). The aim in VA is to provide an additional or alternative approach to cladistics and traditional morphometrics. Using it means considering the shape or form of specimens or groups of specimens as a whole and representing them by numbers. The advantages of this approach are many. Subjective assessments and ratings can be reduced. The object is not treated as a set of features that are independent of each other. Moreover, using computing power and memory allows us to handle hundreds of "traits" (actually then, it is the whole form at once) that come from hundreds or even thousands of individuals simultaneously. The human mind can extract peculiarities of objects quite well or group them according to eye-catching features. However, it also tends to overlook facts or to be overattracted by others, and we are constantly struggling to avoid introducing opinions rather than observing facts. Importantly, it might be the coincidence of features in individuals rather than the appearance of sole traits here and there that characterizes a population. The measurement template in Figure 4 is an example based on 25 traditional LMs and 824 sLMs (see below). It comes fairly close to the actual goal of capturing the geometry of a whole cranium. It enables appreciating even subtle shape changes in smooth regions such as the parietals or the zygomatic arch. It also considers all the 849 points at once and can be applied to hundreds of individuals in only one run. A similar approach was used by Gunz et al. (2009a; see Fig. 1 ibid.) to demonstrate the shape differences and similarities of anatomically modern humans, Neanderthals, and archaic humans. The data at the same time inform about the magnitude of variation within groups and allow computing most similar or mean shapes.

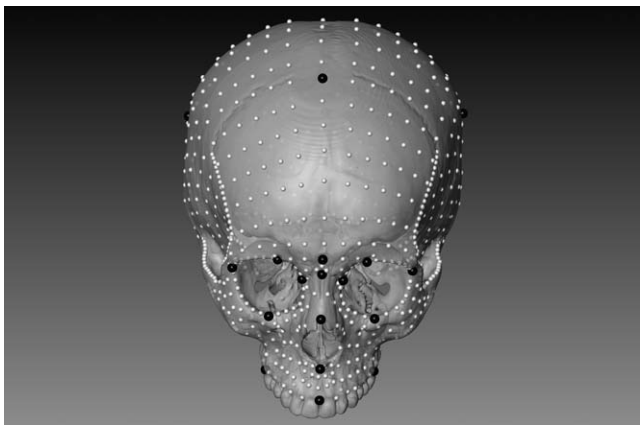

Fig. 4. Rendered 3D model of a modern human cranium with 25 classical landmarks (biologically homologous measuring points) as dark spheres and 824 semilandmarks (geometrically homologous measuring points) as bright spheres. Almost the complete geometry of the cranium can be captured with this approach.

The credo here is not to source out science to machines. On the contrary, only the researcher's brain can design a proper study and meaningfully interpret the powerful statistics computed by the machine. Nevertheless, between the stages of mere observations on the one hand and concluding interpretations on the other, machines can condense vast amounts of information and render peculiarities easily visible via simulations. Accordingly, they are a step toward reaching the goal of reproducible results.

With regard to the individual techniques for quantifying shape and form, the many choices clearly depend on the research question and material available. For instance, outline approaches such as elliptic Fourier analysis (Kuhl and Giardina, 1982) can capture closed contours quite well and are not dependent on evenly spaced points or equal numbers of points across specimens. Euclidean distance matrix analysis (Lele and Richtsmeier, 1991) is based on distances between LMs and thus suitable for sufficiently large sets of caliper measurements. Another approach is "geometric morphometrics" (GM) which uses multivariate statistics based on 3D coordinate data. GM retains all geometric information contained within the data and avoids distances completely; such distances have certain disadvantageous statistical properties, for example, introducing artifactual covariance structures (Rohlf, 1999) and biased mean estimates for realistic sample sizes (Rohlf, 2003; Slice, 2005). GM also does not require any specific

orientation of the object for the measurements: only whole sets of coordinates are taken (e.g., as in Fig. 4). A combination of outline- and LM-based approaches would be desirable in some cases (Baylac and Friess, 2005). As in many fast-developing fields, there are of course discussions on the individual pros and cons of the approaches. This review article cannot comprehensively encompass them all, but selected articles are suggested to form an opinion (e.g., Bookstein, 1991; Rohlf and Marcus, 1993; Bookstein, 1996; Dryden and Mardia, 1998; Lele and Richtsmeier, 2001; Slice, 2005; Weber and Bookstein, 2011b; Bookstein, 2014).

Quantitative comparisons of biological forms have to be kept within the framework of a central biological theory, that of homology (Bookstein, 1991). The concept of homology was long debated and continues to be. The correspondence of parts, as seen by Owen (1847), came into new light after Darwin (1859). A common concept is to speak of homology when traits of two or more organisms to be compared are derived from a common ancestor (cf. Remane, 1971), the classical example being the forearm of a dog, the wing of a bat, and the front flipper of a seal—all of which are derived from the forearm of tetrapods, even if they look very different and serve different functions. Another view of homology is "continuity of information," that is, information inherited with modifications from an ancestor that produces homologous features during the individual's development (Van Valen, 1982). Opposite to homologies are homoplasies, which look very similar but are not inherited from a last common ancestor (and thus are not based on the continuity of inherited information). If the same features are used, there is, however, an inherent circularity in the identification of homology, as it depends on information about evolutionary history, and knowledge about evolutionary history depends on the study of homologous structures (Sneath and Sokal, 1973). Other issues also affect the discussion, for instance, "correspondence" needs different definitions (and different measurements) for different purposes such as for phylogenetic, developmental, or functional studies (Schmitt, 1989; O'Higgins, 1997; Oxnard and O'Higgins, 2009). For morphometrics, there is another applicable concept than that of "topographic homology" (Jardine, 1969) or "geometric homology" (Gunz et al., 2005). Working with images or pictorial densities derived from biological entities (which is precisely what we do in VA), the view was recently expressed that curves and surfaces might be more adequate means to extract geometric information than LMs (Bookstein, 2014, p 406–407; see also Oxnard and O'Higgins, 2009).

Although the discussion of homology and the choice of correspondence criteria are far from being definitively settled (e.g., see Rieppel, 2007), LMs were traditionally, and still are, used in many biological/medical studies that compare developing structures and populations (cf. also cephalometry in orthodontics). LMs are specific points on a form (or an image of that form). The rules to locate them vary, yielding several types of LMs. For instance, they may be located at the crossing of bony structures (actually, the intersection of curves) or at extreme points (actually, the extreme property of a curve) or along sharp ridges (a curve as well). For a current classification, see the LM Types I–VI in Weber and Bookstein (2011b). Once LMs have been located, there is a set of accepted procedures to bring them into GM analysis. Aside from homology criteria, another central demand (and simultaneously a serious disadvantage of GM) is that the number of measurement points has to be equal on all specimens in the analysis. If parts of one form are missing, they either have to be excluded from the rest of the sample as well or they have to be estimated (reconstructed) on the defective specimen (see below; Gunz et al., 2009b).

The first step then is to convert the Cartesian coordinates into shape variables, which means to eliminate variation in orientation, location, and size. This kind of "registration step" is done by means of a generalized Procrustes analysis (GPA; Gower, 1975; Marcus et al., 1996), which also separates shape from size. The latter can be retained or otherwise be excluded from the analysis (form is shape and size). Shape variables (or form variables if size is reintroduced) are then treated with multivariate statistics. To generate an overview of the variation in the sample, a common next step is to subject shape or form variables to principal component analysis (PCA) to reduce dimensions and then to visualize shape/form changes by thin-plate spline (TPS) warping (Bookstein, 1978, 1991). Importantly, the way in which such data are represented allows scientists to compute the means and variances of groups at the same time that differences between two specimens or mean configurations are visualized as deformation grids. Multivariate regressions are used to determine dependencies, for instance, between shape and external variables such as sex, age, or geographical population. Partial least squares analysis inform about patterns of covariance, e.g, looking at different parts or modules of structures. Reflected relabeling is applied to symmetrize specimens and to analyze different components of asymmetry (Mardia et al., 2000; Schäfer et al., 2006). Permutation tests can be applied in cases where significance tests are useful. For a more comprehensive representation of references and examples demonstrating these workflows, see Weber and Bookstein (2011b).

Landmarks have been used for more than 100 years (see for instance, Rudolf Martin's first textbook of anthropology in 1914); however, the number of identifiable LMs can be very small in some structures and anatomical regions. The cranium in Figure 4 illustrates this quite well: only a handful of LMs are available on the braincase, leaving out whole regions on the frontal, parietal, occipital, and temporal bone. The viscerocranium shows similar problems, and likewise other structures such as the postcranium, the teeth, and of course the living face, body, and organs.

Note, however, that there is another class of "LMs" featuring a remarkable difference to the traditional ones in the textbooks of Martin (1914) or Howells (1973): their identification cannot be realized in the physical world. Nonetheless, the GM machinery allows identifying these so-called sLMs both on curves or surfaces. These points are geometrically homologous, which means that they relate to the homology of entire curves or surfaces (Bookstein, 1989; Gunz et al., 2005) and can be placed in all previously unattended regions. The 3D model of the human cranium (Fig. 4) uses 25 traditional LMs including many of those that are usually applied, plus 824 sLMs on curves (temporal lines, zygomatic arches, orbitae, and alveolar rim of the maxilla) and surfaces (frontal, parietal, occipital, temporal, sphenoid, zygomatic, nasal bone, and maxilla) that capture the unattended regions of the cranial bones. The sLM approach clearly considers more information than the

traditional one (for discussion on limitations, see Gunz and Mitteröcker, 2013). Importantly, these sLMs cannot be identified using a caliper or pen. Rather, they must be constructed following certain principals that can only be followed in the virtual world. All geometries of the complete sample are necessary. In an initial step, sLMs are identified on one template specimen (which can be any from the sample, preferably not the most atypical one) and then projected to all other specimens in the sample. After this step, they need to be "slid" (curve sLM have one degree of freedom, surface sLM have two degrees of freedom, and free points have three degrees of freedom). This step is impossible in the real world because sLMs are matched between specimens under the control of a global energy term, such as the bending energy of the TPS, which can only be computed, not intuitively "drawn" (see Thompson, 1917). After the first round, the template specimen is replaced by the new Procrustes average configuration, and the process is repeated until the changes are below a certain threshold. The number of sLMs needs to be sufficient to capture the spatial nature of variation or covariation that will emerge from multivariate analysis of these shape coordinates (Weber and Bookstein, 2011b).

Alternative approaches are available that use automated geometric morphometric methods and LM-free methods. Recently, Boyer et al. (2011) presented an idea to create correspondence maps between specimens, avoiding manual LM identification on anatomical surfaces. In contrast to earlier trials to register forms (e.g., Besl and McKay, 1992), no initial guess is needed. The approach promises shape analyses for nonmorphologists and other persons with no training in LM identification. The future will show how well it works in applications undertaken by nonspecialists. Attempts with regard to automating measurement procedures were made early on, for instance, Thirion and Gourdon (1996) detected curves on 3D surfaces or Subsol et al. (1998) detected crest lines on skulls.

The LM–sLM-based GM approach in any case works well with skulls and bones, and also with soft tissues, stones and artifacts, or other objects. Recent years have seen applications in the context of quantitative analysis, for instance of lithic assemblages using LM–sLM approaches (Archer and Braun, 2010; Buchanan and Collard, 2010; Lycett et al., 2010) or surface areas (Lin et al., 2010). GM is widely used to characterize facial shape and its asymmetries and relations to other tissues (e.g., Fink et al., 2005; Bugaighis et al., 2010; Meindl et al., 2012; Pflüger et al., 2012; Kustár et al., 2013). Even the shape of "car faces" was associated with trait attribution (Windhager et al., 2012).

One big issue in the context of using advanced approaches such as GM and others mentioned above is that they need a fairly rich theoretical background before they can be used properly. Often, programming knowledge is necessary to translate theory into results. A decade ago, sophisticated mathematical packages such as Mathematica™ (Wolfram Research) or Matlab™ (MathWorks) had to be used to develop routines that execute GPA or TPS warping. Not every good biologist, however, is a good programmer, and vice versa. Such applications therefore often left users stranded. The development of new algorithms is still mainly a task for interdisciplinary expert teams (a core domain of VA) involving biologists, mathematicians/statisticians, and

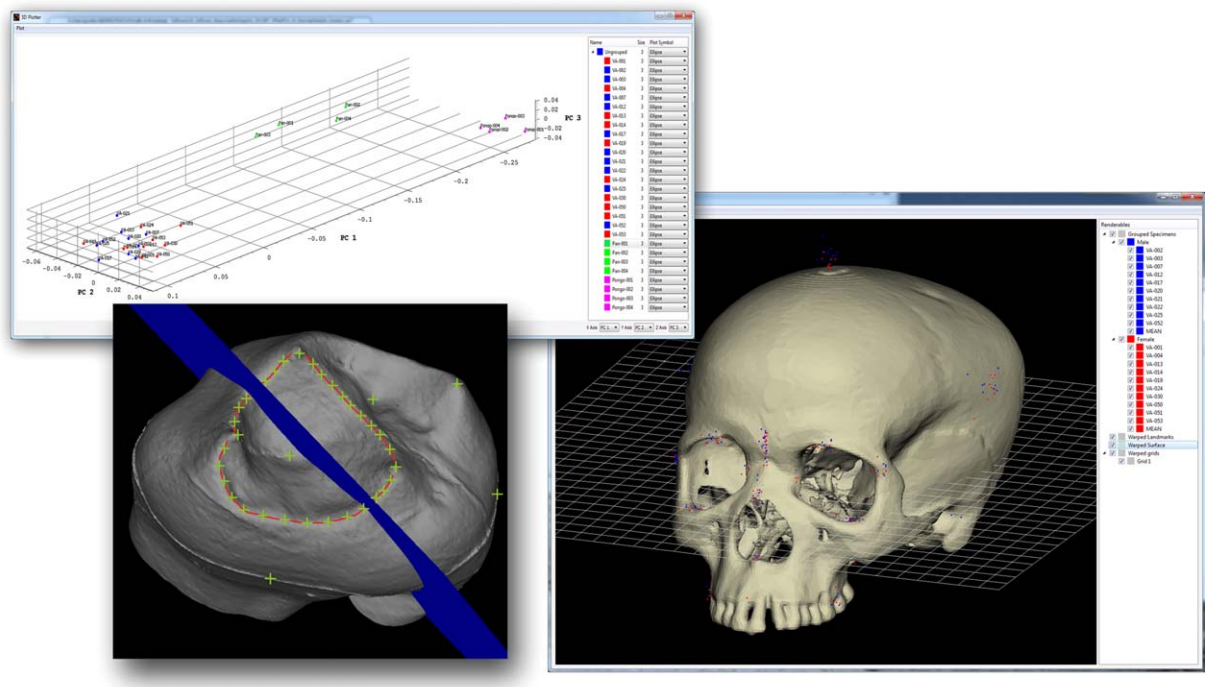

Fig. 5. GM results produced without programming knowledge (examples from the EVAN Toolbox). Top left: Principal component analysis of shape (first three relative warps) for modern humans (blue males, red females), chimps (green), and orangutans (purple); bottom right: the acquisition of landmarks and semilandmarks (green crosses along the red ridge curve) on the enamel–dentine junction of a molar; and bottom right: warped surface and deformation grid indicating shape changes (actually better viewed as a movie) between the two sexes.

software engineers. Nevertheless, the application of established procedures has become much easier because some software packages emerged.

"Morphologika" (https://sites.google.com/site/hymsfme/downloadmorphologica), developed under Paul O'Higgins, was one of the first solutions that could process 2D and 3D data and handle GPA, PCA, regression, and warping. "Morpheus" (http://www.morphometrics.org/) by Dennis Slice, "Viewbox" (http://www.dhal.com/viewboxindex.htm) by Demetrios Halazonetis, the suite of "tps" programs (http://life.bio.sunysb.edu/ee/rohlf/software.html) by James Rohlf, "geomorph" in R (http://www.r-project.org/), "MorphoJ" by Klingenberg Laboratory (http://www.flywings.org.uk/morphoj_page.htm), or "edgewarp" (http://brainmap.stat.washington.edu/edgewarp/) by Bill Green offer access to some or most GM routines. A major EU-funded consortium (European VA Network [EVAN]) attempted to spread knowledge among young European scientists and concurrently developed and released a software solution available for members (EVAN-Toolbox, http://www.evan-society.org/node/23). It is still being further developed (Fig. 5) and, beyond research purposes, has also turned out to be a fairly good teaching tool. This has helped issues of GPA, PCA, TPS, group mean comparisons, regression, reflected relabeling, and the analysis of asymmetry to lose some of their "frightening flavor" during practical application with real data. All operations can be put together in visual programming networks, just as modules that are connected by lines. Programming is not necessarily involved, although possible for the expert user, and definitely required for leaving the stereotype pathways of analysis.

Regardless of the approach or software used, most importantly, young people have to be trained on a broad scale to use such 21st century techniques. In this sense, some universities and research institutions are called on to consider upgrading their curricula.

Reconstruct

As the given examples show, many of the applications in VA concern fossil specimens or medical cases. Reconstruction is quite often necessary in this context, but as well in others such as archaeology. Reconstruction in VA refers to the form and shape of biological objects (however, in archaeology, it refers to the form and shape of artifacts or buildings). A reconstruction is needed when the form or shape of an object must be analyzed or compared with others; however, its present status does not clearly correspond with its original form. In fossils, various taphonomic processes can lead to disturbances of a form, as can damage potentially occurring during excavation or manipulation. When it comes to patients, for instance, trauma or cancer may cause the loss or alteration of structural parts. We distinguish four principal kinds of disturbances of a form. All of these apply similarly to archaeological or other objects (Fig. 6; Weber and Bookstein, 2011b).

- Type 1 disturbance: An object can be broken, but (almost) all pieces are preserved, for example, a broken cranium, even if it consists of many pieces, which can be fully restored using glue.
- Type 2 disturbance: Whenever parts of an object are missing, for example, a humerus that is basically intact but missing its head.
- Type 3 disturbance: An object can be deformed, for example, a fossilized pelvis that shows plastic deformation due to million-year-long pressure of the overlying rocks.
- Type 4 disturbance: An object can be intact but not be directly accessible because it is covered by a foreign material (cf. electronic preparation above), for example, a finger bone that is embedded in calcareous sands.

In fact, one frequently finds all kinds of combinations of these principal types of disturbances—it is rather the exception if only one appears alone in a fossil. In practice, we may observe "broken" and "missing" (Types 1 and 2), "broken" and "covered" (Types 1 and 4), "missing" and "deformed" and "covered" (Types 2, 3, and 4), and so forth. When a disturbance has been recognized and corrected, we refer to reconstruction. The types of disturbances introduced above are aids to consider different reconstruction problems that one will face during the process (Weber and Bookstein, 2011b). Unique solutions, at least in principle, are only possible with Type 1 or Type 4 problems. There are only very limited degrees of freedom to put together a complete 3D puzzle (Type 1), and e-preparation can entirely eliminate matrix in many cases (Type 4). Nonetheless, for most Type 2 problems, there is no unique solution. In addition, for most Type 3 problems, only approximations can be expected; exceptions are when the deformation forces are known exactly (which is very unrealistic for taphonomic processes that took place over thousands or millions of years) or when one half of a bilaterally symmetric structure is unaffected and can be mirrored. Any missing or deformed parts have to be estimated. This involves assumptions and data from comparable—but undisturbed—forms of the same or a similar group of objects.

We must therefore accept that a reconstruction can rarely, if ever, duplicate the original. It can, however, approximate it in most cases. Nevertheless, this can be a big step forward, for instance, when an important but slightly defective specimen can be included in an analysis that requires complete data sets (such as in GM; see above). The real advantage of VA in reconstruction is that manipulations are reproducible because such manipulations can be logged and quantitative reference data are used [for an exemplary documentation of a virtual fossil reconstruction (OH 5), see Benazzi et al., 2011b].

Biological forms follow constraints, for instance, laws of physics such as gravity and mechanical stress; they respond to the mechanisms of evolution such as the selection of environmentally favorable traits, and anatomical modules develop in concert (integration). Hence, we know a lot already about a form even if it is disturbed. The manifold genetic, developmental, and functional factors applying to the form of biological objects reduce the "degrees of freedom," the uncertainties, in a reconstruction process. Importantly, growth and evolution do not follow only a handful of constraints, as in the case of mass-produced goods. If a portion of a ceramic vase is missing, it could be relatively easy to re-create its initial form because it would follow a rather strict rule of a smooth surface (especially if done with a potter's wheel). In biology, we have to deal with an almost incalculable number of interacting factors, from genes and their expression to individual life histories. A

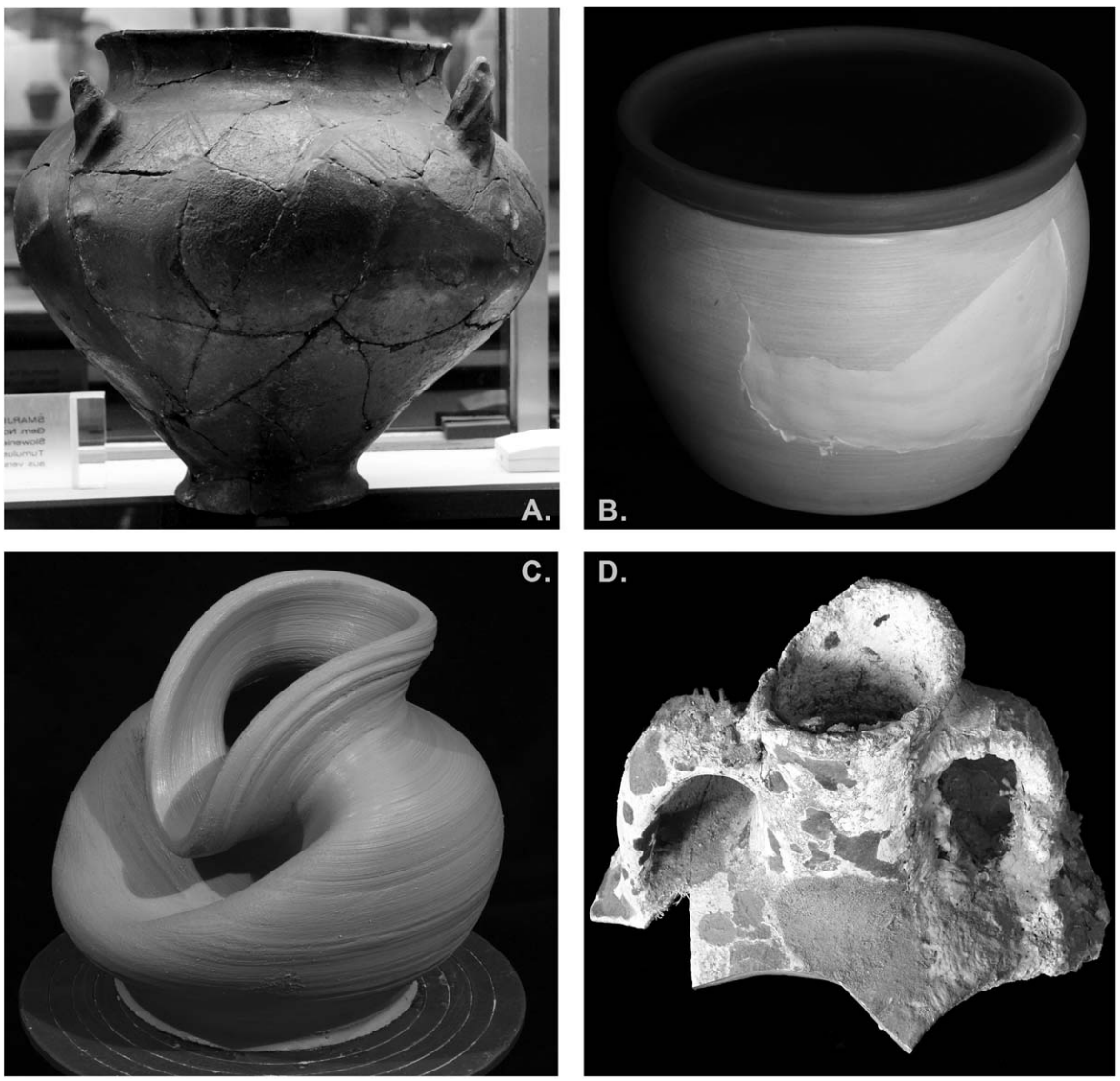

Fig. 6. The four types of disturbance illustrated with examples from pottery: (**A**) Type 1: broken, but (almost) all pieces preserved; (**B**) Type 2: missing part (here reconstructed in white); (**C**) Type 3: deformed; and (**D**) Type 4: covered by a foreign material (in this case, actually a combination with Type 2).

prerequisite of natural selection is the presence of inter-individual variation in populations. Although there is a basic form of, for example, a modern human maxilla, each of us has a slightly different maxilla form. It depends on the inherited skull form, the individual loadings that influence bone remodeling throughout life (related to muscles and diet), the preservation and position of teeth (e.g., some might be lost and some inclined forward or backward), or other behavioral aspects (e.g., teeth might be used as a tool or clenched during the night). We can thus reconstruct parts only with a particular likelihood when we use reference data (e.g., a sample of similar organisms). In the case of fossils, the task is clearly even more difficult because a reference sample might be very small or even absent. In those cases, reconstruction resorts to the closest sample available—a compromise.

Although reconstruction remains a challenging endeavor, some striking advantages of VA versus physical reconstructions are worth mentioning. First, reference data and applied assumptions that accompany the difficult cases of Type 2 and Type 3 disturbances are explicit factors of the reconstruction process, for instance, which particular reference specimen (or group average) was chosen or which LMs were preserved and measured, or which a priori knowledge about the form was applied when estimating missing parts (e.g., geometric constraints such as smoothness of curvature, radial or bilateral symmetry). Although such explicit information can be included in traditional approaches, this information *must* be present prior to a virtual reconstruction, where there is much less room left for intuitive manipulations. It is thus only a tiny step further to make it public in the latter case. Moreover, the whole process, including different trials and alternatives, can be saved stepwise. In some lucky cases, such as a Type 1 disturbance, the task may boil down to limiting the six degrees of freedom (three to translate and three to

rotate) to possibly zero when putting pieces together which makes the documentation even easier. Second, and in opposition to a physical reconstruction, a virtual one does not depend on sources of irritation such as gravity, glue, or having only one trial. For this reason, and despite some inherent difficulties of the virtual approach (e.g., necessary training for handling software and manipulating objects by a mouse or trackball), virtual reconstructions appeared already very early in the history of VA (Kalvin et al., 1995; Zollikofer et al., 1995; Thompson and Illerhaus, 1998). Computer manipulations offer absolute control over fragment translations and rotations, particularly when advanced computer-aided design (CAD) environments are used. The latter also support the process with construction aids such as B-splines (basis splines, mathematical functions for curve fitting) or NURBS (nonuniform rational B-splines, mathematical models for generating and representing curves and surfaces). The highly controlled merging of pieces on the screen and the possibility of mirroring pieces (seen frequently in "anatomical" reconstructions; e.g., Zollikofer and Ponce de León, 2005; Zollikofer et al., 2005; Ryan et al., 2008) are already important improvements. Moreover, some other technologies introduced above under "Compare" section can also be applied in VA reconstructions to help estimate missing or deformed parts (i.e., problems of Types 2 and 3).

The TPS warping used to visualize shape and form changes is also deployable for another kind of reconstruction: "geometric" reconstruction (Weber et al., 2003; Neubauer et al., 2004; Gunz et al., 2009b; Grine et al., 2010; Weber and Bookstein, 2011b; Senck et al., 2013, 2014). A "reference" or "template" specimen is necessary. This can be a particular individual or a computed mean configuration. A map of measured LMs and sLMs from the complete specimen is used, along with whatever is left of the specimen to be reconstructed (the "target"). A deformation of the reference is then computed to match the location of those corresponding points which are preserved on the target. A particular feature of the TPS warping, namely, that all locations between the measured ones are automatically interpolated, ensures that missing parts of the target are filled in. This is not a simple "copy and paste" action. Rather, the algorithm takes the still preserved morphology of the target into account and adapts those missing parts, which are filled in from the template, to this form. It is not only applied to fossil reconstructions (Gunz et al., 2009b; Benazzi et al., 2011a, 2013b) but also to preoperative implant planning, for example, for large skull defects (Heuzé et al., 2008). TPS is an almost perfect tool to reconstruct smooth surfaces, such as the neurocranium, and works particularly well when coordinate-based LMs and sLMs are sampled densely. Note, however, a serious caveat of TPS-based reconstruction. As mentioned above, it is an interpolation function and should not be used when an extrapolation is necessary, that is, when the region being reconstructed extends substantially beyond the limits of the region present in the target. In the extreme case, do not reconstruct the face if you have only the braincase at hand.

Alternatively, a whole sample (reference database) can drive reconstructions via multivariate regressions, which rely on the covariation among the observed coordinates from LMs and sLMs (Gunz et al., 2009b; cf. Neeser et al., 2009). As always in statistics, the certainty of an estimate depends on the sample size—the larger, the better, a demand that is rarely met in paleoanthropology but more easily achieved in biological and medical studies of recent humans or other animals. As mentioned above, TPS is fine with just one reference specimen; however, the consequence is that its results are entirely dependent on that particular specimen. If, however, there is more than one reference specimen available, then multiple reconstructions can be computed. This is a clever way to assess the range of possible shape or form variation of resulting reconstructions (Gunz et al., 2009b; Benazzi et al., 2011a; Weber and Bookstein, 2011b). Another solution is to compute the sample average configuration and use it for the TPS warping (Senck et al., 2013, 2014).

The gain of VA reconstructions versus physical reconstructions is quite clear; however, we have to keep in mind that compromises are often inevitable, particularly in paleoanthropology, where only a few intact templates exist. This discipline is highly dependent on reconstructed forms. In the sense of a heuristic process, even a composite fossil (introduced by Kalvin et al., 1995) might be a solution. For instance, Strait et al. (2009, 2010) have used a fairly complete but otherwise edentulous cranium of *Australopithecus africanus* (Sts 5) and another fairly complete dentition of a member of this taxon (Sts 52) to simulate cranial loadings during premolar and molar bites. Although both specimens show a similar dental stage, and the preserved tooth roots of Sts 5 were matched with the teeth of Sts 52, such a composite reconstruction would certainly contain deviations from the original appearance of Sts 5. However, those possible deviations (e.g., tooth position, inclination, and elevation) are within such a very limited range that they otherwise only minimally impact the global biomechanical simulation. The situation is admittedly not ideal until a more persuasive solution is possible, that is, until a complete and undeformed cranium with dentition is unearthed and accessible.

Materialize

Anthropologists are used to working with two sources for appraising morphology in the classic approach: original specimens and their casts. VA adds two other sources: digital copies and RP models derived from these copies.

Although the meaning of virtual specimens has been pointed out above, one might ask why a real copy of a virtual model has any value. They are very good aids when it comes to teaching and training purposes and for permanent museum display. They are indispensable when no computer is available. For the researcher as well, a real object provides a substantial aid to understanding three-dimensional relationships of spatially complex structures. Consider architects who undergo a rigorous selection in their career with regard to their abilities in spatial imagination. Nonetheless, we see them still building real models of constructions to appraise complex interactions of structures. There is a German word that neatly illustrates the connection: the word is "begreifen" and, likely not by accident, has two meanings: "to touch" and "to understand."

The first stereolithographic model in anthropology was produced for the Tyrolean Iceman "Ötzi" to provide noninvasive access to the skull of the precious mummy (Seidler et al., 1992; zur Nedden et al., 1994). Since then, the usefulness of RP models has been amply argued and demonstrated over the years (e.g., Hjalgrim

et al., 1995; Zollikofer et al., 1995; Seidler et al., 1997; Recheis et al., 1999; Ponce De León and Zollikofer, 1999; Weber et al., 2001; Kimbel et al., 2004). In the medical sciences, RP models have been used since the early 1990s, particularly with regard to implant planning (Klein et al., 1992; Anderl et al., 1994; Yau et al., 1995). There is thus a considerable overlap in the techniques used in (paleo)anthropology and surgery planning, which opens opportunities for collaborations and jobs.

Rapid prototyping technology, the approach used to materialize virtual models, has its roots in the industrial sector of the 1980s (for a historical review, see Beaman et al., 1997). It was invented to facilitate quick and relatively inexpensive manufacturing of industrial prototypes. They are necessary whenever something was created in a computer environment and now needs evaluation in the real world: a newly designed smartphone before mass production, a custom implant to train with before surgery, a downscaled model of an oil-tanker to test its fluid mechanics, and thousands of other applications. There are several different methods to realize RP models; however, there is one common principle behind them: the object is built layer by layer using tiny elements. This idea is very old: we can go back roughly 4,500 years and look at the Great Pyramids of Giza, which are constructed in the same manner, namely, layers of stones over layers of stones. The approach is slow but has one striking advantage: even hollow spaces and undercuts can be built, which is not possible with other techniques, for example, with computer numerical control (CNC) machinery.

One of the first and still one of the most advanced procedures is stereolithography (STL), which produces accurate models down to a resolution of ~0.1 mm or lower. All kinds of 3D data such as volume or surface data (e.g., CT, MRT, or surface scans), constructed surfaces from CAD, or a virtually reconstructed fossil can be used as data input. They are converted into a specific format, STL data, which was developed for driving RP machines. In the case of STL, data serve to control a mobile mirror that directs an ultraviolet (UV) laser beam in accordance with the layer geometry. Where the UV laser beam comes into contact with a photosensitive liquid acrylate or epoxide resin, it hardens that material. Then the part is lowered deeper—by the thickness of one layer—into the liquid polymer bath. A recoating system levels the surface before the next layer can be hardened. The process continues without manual intervention until the production of the 3D part has been completed. Supporting constructions permit the fabrication of "overhanging" parts that would otherwise float away before they are connected to the structures above.

Besides STL, there are many other methods using powders rather than liquids (e.g., Z-printing and laser sintering) or meltable plastics (e.g., fused deposition modeling), applied through heating nozzles, comparable with an inkjet printer. The resulting models have different properties, and there are huge differences in price, speed, as well in the quality of models (for an overview, see Weber and Bookstein, 2011b). Some of the options to be considered with regard to the desired application are price, accuracy, endurance, speed of production, transparency, and color.

Independent of the choice of RP method, all those modes offer some advantages over conventional casts in the following respects:

1. No physical mold (which will age) is needed. Of course the model itself will age, but it can be reproduced at any time to 100%. The only time-related aspect is to safely store the digital data.
2. Contact with the original object can be completely avoided during the process because only a contactless scan is required. This is a serious issue in many cases of fragile and brittle specimens or for those with porous surfaces.
3. Biological objects usually feature hollow structures and undercuts, which are handled perfectly by RP approaches. To build hollow structures makes sense if the model is transparent or those structures are accessible, for example, when models are built in separate parts like a skull with removable calotte to allow inspection of the cranial cavity and sinuses or a proximal femur with two separable halves to inspect trabecular structures.
4. RP models can be manufactured in any scale. Thus, they can be upscaled or downscaled.

Of course, RP procedures have certain inherent disadvantages: models can be rather expensive (depending on the quality and the method applied). This is usually negligible in industry but a real factor for limited science budgets. Interestingly, there is now a growing market for desktop 3D printers for home use, which enable producing models in a very low price range (whole machines can even be cheaper than one stereolithographic model, e.g., 3DSystems Cube3 and Makerbot Replicator Mini). Another drawback is the partly limited resolution of RP models, often somewhere in the 100 μm range for common applications (e.g., ZPrinter 650, Stratasys FDM, and 3DSystems SLA700 Fastmode). Nonetheless, technology improves rapidly, and there are some machines that can go down to a layer thickness of 16 μm (e.g., 3D Systems ProJet 3510 HDPlus or Stratasys Objet Eden500V). Limiting factors are the incoming digital data, which in the case of medical CT are even lower in resolution (typically 200–500 μm), and some inherent characteristics of the RP procedure itself. All digital images show an aliasing effect (jagged surface), and the same applies to all RP models due to the digital nature of the data and the layered manufacturing mode. A smooth surface can often only be achieved by intensive reworking. Conventional casts can offer a much finer resolution. Recent developments, however, do have the potential to improve resolution considerably using a combination of μ-CT and μ-STL. The size of objects is still limited; however, a layer thickness of less than 25 μm, both in data acquisition and model production, is possible. To see the first application with regard to a fossil object (lower molar of an *Australopithecus afarensis*), consult Weber and Bookstein (2011b, p 321).

Share

Scientific progress can be substantially supported by sharing methods and data resources. In most biological and evolutionary questions, intragroup and intergroup variation are common targets of attention. As the access to the Internet is widespread, some sciences have seen an increase in information sharing. Open-access journals are proliferating, and data archives have been created in different fields of research. A good example is in genetics, where the human sequences and meta-information are published as a matter of course (e.g., http://www.ncbi.nlm.nih.gov/gene and http://www.genecards.org/). Physical anthropology, and particularly paleoanthropology, are fields where the idea of sharing data for the

sake of creating knowledge is less pervasively accepted. The first electronic archive for hominin fossils was created in 1999 (http://www.virtual-anthropology.com/3d_data/3d-archive) and the idea of an opening—a "Glasnost in Paleoanthropology"—was expressed soon after the Millennium (Weber, 2001). The community saw reviews and conferences on the topic (Gibbons, 2002; Soares, 2003; Delson et al., 2007; Kullmer, 2008; Mafart, 2008), and some further archives were established (e.g., NESPOS, EVAN-Society, ORSA, Digimorph, Paleoanthportal, RHOI, AHOB, Visible Human Server, or Morphosource). However, more than a few researchers and curators remain reluctant to share data (Weber and Bookstein, 2011a). The digital@rchive of Fossil Hominoids (http://www.virtual-anthropology.com/3d_data/3d-archive) is still the largest database providing access to a significant number of very important hominin fossils without restrictions.

Certainly, difficult questions remain, for instance, how to protect the legitimate interests of the discoverers, who often invested considerable amounts of time and money, in some cases even risking their lives. There are rules somewhere in the fine print of agreements with funding agencies and journals; however, this has not changed the situation much. Most colleagues would agree that it is reasonable to allocate sufficient time for the discoverers to work on their specimens. Yet, even decades after their discovery, many fossils are not generally accessible for the scientific community, neither digitally nor physically (including casts). Scientific results must be verifiable, particularly if a new taxon is described and established. It is therefore, in my opinion, a reasonable demand that at least electronic data from specimens should be accessible after publication, or, if nothing is published, after a certain number of years. Such data also protect the original specimen because it has to be taken out physically only once for scanning (if no data embargo is established).

Besides being an important resource for various scientific and financially driven actions, gene sequences of humans represent our common evolutionary heritage and are openly accessible. Unearthed fossils are usually owned by the country in which they were discovered. The remains are then stored in one of the national institutions such as a natural history museum and administered by the local curator. A hominin fossil contains data about our common evolutionary heritage, as do genes. Each country has exclusive control over its property, and it can decide about its own strategies to support the increase of knowledge. Permission for access and international collaboration are an optional choice, which can in return lead to exchange of know-how and technology, and the stimulation of further joint projects.

When we discuss about data, access, and archives, there are some technical issues to consider as well. Data have diverse characteristics which depend on the mode of recording and also on the context of the user. These qualities of data are relevant for access policies and the structuring of data archives. There are other issues beyond the ethical approval for data collections on living subjects. A typical data archive for paleoanthropologists will no doubt contain data from hominids such as a CT scan of an Australopithecus skull or a gorilla pelvis. This type of data can be termed "source data" because they were mainly acquired by a machine (e.g., CT, μ-CT, MRT, and surface scanner). They are therefore much less biased by any intellectual treatment by colleagues than another kind of data that can be termed "derived data" (Weber and Bookstein, 2011b). The latter would include, for instance, 3D coordinate measurements of LMs or a virtual reconstruction of missing parts. Both require a lot of interaction and involve an observer's perception and individual interpretation (observer A's notion of where the LM "porion" on a particular specimen can be different from observer B's notion of the same LM on the same specimen). "Source" and "derived" entail fundamentally different issues for access rights on one hand and for further application of data on the other. Beyond these two types of core data, the paleoanthropologist will likely also need access to data of the geochronologists, the paleontologists, or the pathologists to incorporate yet another sort of data in the study, namely, "contextual data," which pertains to the specimen under examination. Electronic archives have to be structured and organized according to these needs.

When compared with other fields (e.g., genetics), we are still in the infancy of anthropological databases. A first essential step would be that all organizations curating collections formulate clear access policies, even if they include denial of access. At a minimum, the author argues that museums and other organizations holding valuable material in their collections should publish a list of specimens that are curated and the statements about their access policies. The increasing availability, cost reduction, and, nota bene, dependency on digital data will sooner or later lead to an intensified data sharing. We should also not forget that the number of young colleagues (the generation of "digital natives") in our field is inexorably growing as time goes by, and their attitude is generally more oriented toward opening than restricting data access.

HOW VA COULD CONTRIBUTE TO A "VIRTUAL FUNCTIONAL MORPHOLOGY"?

The achievements and applications introduced so far have related to comparative morphology. There are reasons, however, to think that VA, and similar approaches, have the potential to contribute to another major subdiscipline, functional morphology (O'Higgins et al., 2011; Weber et al., 2011). The idea of "form follows function" in biology is an old one, as expressed by Georges Cuvier (1769–1832) in his "conditions d'existence" (roughly speaking, Cuvier argued that all organismal parts that we see are already optimized toward their functional demands, otherwise the animal would not survive). Although we have learned in the meantime that shape and form may deviate from this strong statement, the importance of the relationship between form and function is generally recognized. Functional morphology is thus a fundamental approach to study biology on a macrolevel and microlevel with the goal of understanding how structure, shape, and size might relate to function or what the function of a structure might be at all. It is amazing how little we still know. For example, we speculate about ecology, diet, and their relationship with the masticatory apparatus. At the same time, we have only very weak ideas how, for instance, tooth shape is related to the shape and mechanics of the skull. For example, what impact do large teeth with flat reliefs have on jaw shape, what are the effects during the resulting jaw movements that might lead to specific anatomical proportions, or to the formation of strengthening structures to prevent bone failure? We do not even have a full

understanding of the shape variation of internal tooth structures (enamel thickness, EDJ, root shape and length, and pulp chamber)—we are only now on our way to discover them in the early 21st century (Smith et al., 2005; Olejniczak et al., 2008; Skinner et al., 2008; Bailey et al., 2011; Le Cabec et al., 2013).

If we wish to integrate morphology with functional data, other digital technologies are available that enable simulating biomechanics. The last decade saw many applications with regard to vertebrate biomechanics using either multibody dynamics analysis (Curtis et al., 2008; O'Higgins et al., 2012) or finite element analysis (FEA; Rayfield et al., 2001; Koolstra and Van Eijden, 2005; Rayfield, 2005; Ross, 2005; Dumont et al., 2009; Strait et al., 2009, 2010; Kupczik et al., 2009; Wroe et al., 2010; Benazzi et al., 2011b; Gröning et al., 2011). The former is used to study how mechanical systems such as the musculoskeletal apparatus move under the influence of forces. FEA, in turn, is an engineering technique that allows an assessment of how objects with complex geometry and material properties respond to complex loads. Digital representations (models) rely on the same source of data as VA, that is, captured geometries. However, it is not the shape analysis that is central to FEA but the deformations that a solid body experiences under loadings. For this reason, various other input parameters have to be assigned to the model, such as different material properties (for cortical bone, trabecular bone, dentin, enamel, etc.), forces (depending, among other things, on the muscle cross sections), and constraints such as the location of bite points or joints. Models can be validated by comparing results with in vivo or in vitro experimental data. Although in vitro experiments can use isolated anatomical elements or cadavers (Bhatia et al., 2014), in vivo experimentation is difficult (Dumont et al., 2009). For obvious ethical reasons, some experiments with human beings are impossible, for instance, implanted strain gages. Values have to come from analogous animal experiments (Richmond et al., 2005; Ross et al., 2011), which are also very difficult to conduct. The typical outputs of FEA mostly relate to stress, which is a measure of the amount of force per unit area, to strain, which is a measure of deformation representing the relative displacement between units in the material body, and to strain energy, which is the net potential energy stored in a solid that has been deformed by forces.

Because FEA is a deterministic process, two simulations using different parameters—varying geometry, material properties, forces, or constraints—will always lead to different results. FEA delivers a multitude of useful data but is not designed as a comparative tool. Although the morphometric approaches introduced in this contribution can deliver computed group mean configurations of shapes/forms or data on intragroup and intergroup variation or even compute a warped intermediate geometry between two stages, FEA regularly establishes a relation between shape and loadings via comparisons of colored images or of some isolated parameters such as strain measured at a few homologous LMs. As outlined in a recent publication (Bookstein, 2012), there is a discrepancy between the mathematical physics of elastic theory (the quantity minimized there derives from the sum of squared deviations of the first derivatives from unity, and the integral is taken only over the region occupied by actual material), which is essential for mechanics, and the quite different mathematics used in shape analysis (in the TPS approach, instead, the quantity being minimized is the integral of the squared second derivatives, and the integral is taken over all of space). A missing mathematical bridge between the two domains is a major problem in the biomechanical analysis of biological forms (Weber et al., 2011). A theoretical solution was introduced recently (Bookstein, 2012) but has not yet been tested with real data. Many researchers are currently experimenting with other attempts to bridge the two domains. Strain frequency plots, however, such as used in a recent publication (Parr et al., 2012), cannot relate strains to the actual location. They merely provide a summed picture of appearing strains. Moreover, the LM point strains cannot be based on sLMs for the mentioned mathematically incompatible differential equations. Others (Strait et al., 2009; Wroe et al., 2010; Cox et al., 2011; Gröning et al., 2011; O'Higgins et al., 2011) relied on visual comparisons between strain plots, have tried to compare the mean of stresses and strains, and invoked profiles along a structure to demonstrate strains. These measures, however, provide only quite scant pictures of the whole structure under investigation. Displacement plots (Gröning et al., 2011; O'Higgins et al., 2011) again carry information only on the direction of displacements but cannot inform about the quantity of work to impose particular simulated strains.

Despite the current problems, even today some VA methods are an essential component of biomechanical studies, for instance, in paleoanthropology to virtually reconstruct or electronically prepare a fossil form prior to FE model creation (Strait et al., 2009; Wroe et al., 2010; O'Higgins et al., 2011). In the case of extant species, the approach is used to determine a limited set of extreme forms within a group to be modeled later in the FE process (Smith et al., 2014). These examples and the ongoing efforts to combine results from the two domains give the author justified hope that something like a "virtual functional morphology" is not too far away.

CONCLUSIONS

Virtual anthropology, or "virtual morphology" if we put it into a wider context, offers the 21st century machinery that enables working with virtual copies of specimens and analyzes of shape and size based on a comprehensive quantitative basis that can capture the complete geometry. This approach visualizes shape and form changes that support understanding by their intuitive nature, supports reproducible and database-driven reconstructions of form, and helps to increase sample size considerably by sharing data.

Although these developments have revolutionized the methods applied in comparative morphology, there are also overlaps with other emerging digital approaches. For example, the simulation of biomechanics, which uses similar input data (virtual specimens), would profit substantially from statistically connecting loadings with geometry. Algorithms to fully bridge the two domains are still imperfect and in development. Combining the domains will, however, lead to a new dimension of computer-based analysis that we can conceive as a "virtual functional morphology." A case in point is the masticatory apparatus, which is certainly a key to studies of anthropoid variation and hominin evolution. The type of unresolved questions is quite fundamental:

- We have no good statistical data about the relationship between variation of skull shape and variation of mechanical loadings.
- The hominin skull underwent significant evolutionary form changes, for example, jaws became smaller, the braincase grew bigger, and cranial base flexion increased. What were the biomechanical consequences of these changes and how do changes in one part (module) mechanically relate to changes in another?
- The reproducing members of a taxon were all successful in an evolutionary sense. Nevertheless, individual shape varies significantly within groups. Within a given frame of functional demands (depending of the environment, e.g., diet), how far can geometry deviate from the mean shape to still meet these demands? This also introduces taxon assessment from a mechanical perspective.
- What feeding strategies could have favored the changes we recognize in the fossil record, and are they in agreement with paleoecological data?

Similar lists of pending questions with regard to functional morphology exist for many other anatomical regions, particularly in connection with locomotion. It is true that virtual techniques can only build models which are simulating the real world. Nevertheless, they can be validated using in vitro or in vivo experiments to avoid drifting away from the actual facts. We are at the very beginning with the list of issues mentioned above, for example, regarding knowledge on mechanical integration of modules or taxonomic assessment based on mechanical properties. Even for the most basic facts, such as variation of mechanical performance of structures in a given group of forms, we know only very little. In such a phase, modeling is particularly essential to develop ideas about possible interrelations and to generate new hypotheses.

A holistic approach to study complex interactions within biological systems is systems biology. In contrast to reductionist approaches, it focuses on the emergence of system properties at different levels of organisms. This integrative approach and the advent of phenomics—the large-scale study of high-dimensional phenotypes—mark a new era in biological and biomedical research. In a recent review, Houle (2010, p 1793) pointed out that "the causation of key phenomena such as natural selection and disease takes place in a continuous phenotype space whose relationship to the genotype space is only dimly grasped." We are going at full speed in the molecular sciences, and there is no reason to pause on the side of comparative and functional morphology, which are a vital part of phenomics. The further development of the above-sketched "virtual functional morphology" is eminently suitable as a cornerstone in this process.

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