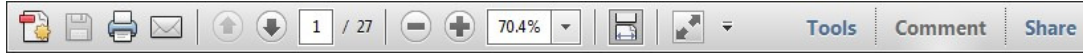
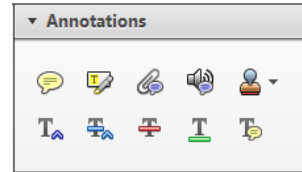


Once you have Acrobat Reader open on your computer, click on the [Comment](#) tab at the right of the toolbar:



This will open up a panel down the right side of the document. The majority of tools you will use for annotating your proof will be in the [Annotations](#) section, pictured opposite. We've picked out some of these tools below:



1. [Replace \(Ins\)](#) Tool – for replacing text.

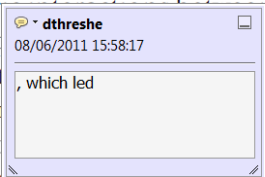


Strikes a line through text and opens up a text box where replacement text can be entered.

How to use it

- Highlight a word or sentence.
- Click on the [Replace \(Ins\)](#) icon in the Annotations section.
- Type the replacement text into the blue box that appears.

standard framework for the analysis of microeconomic activity. Nevertheless, it also led to the development of a new paradigm of strategic behavior. The number of competitors in the industry is that the structure of the industry is a key component of the main components of the industry. At the microeconomic level, are exogenous variables important? (M henceforth) we open the 'black b



2. [Strikethrough \(Del\)](#) Tool – for deleting text.



Strikes a red line through text that is to be deleted.

How to use it

- Highlight a word or sentence.
- Click on the [Strikethrough \(Del\)](#) icon in the Annotations section.

there is no room for extra profits as mark-ups are zero and the number of firms (net) values are not determined by market structure. Blanchard ~~and Kiyotaki~~ (1987), perfect competition in general equilibrium. The effects of aggregate demand and supply shocks in the classical framework assuming monopolistic competition. An exogenous number of firms

3. [Add note to text](#) Tool – for highlighting a section to be changed to bold or italic.



Highlights text in yellow and opens up a text box where comments can be entered.

How to use it

- Highlight the relevant section of text.
- Click on the [Add note to text](#) icon in the Annotations section.
- Type instruction on what should be changed regarding the text into the yellow box that appears.

dynamic responses of mark-ups consistent with the VAR evidence

sation of the industry. The number of competitors in the industry is a key component of the main components of the industry. At the microeconomic level, are exogenous variables important? (M henceforth) we open the 'black b



4. [Add sticky note](#) Tool – for making notes at specific points in the text.

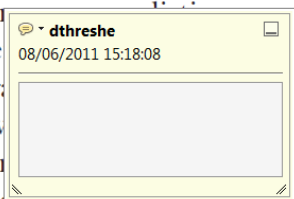


Marks a point in the proof where a comment needs to be highlighted.

How to use it

- Click on the [Add sticky note](#) icon in the Annotations section.
- Click at the point in the proof where the comment should be inserted.
- Type the comment into the yellow box that appears.

and supply shocks. Most of the evidence is consistent with the VAR evidence. The number of competitors in the industry is a key component of the main components of the industry. At the microeconomic level, are exogenous variables important? (M henceforth) we open the 'black b



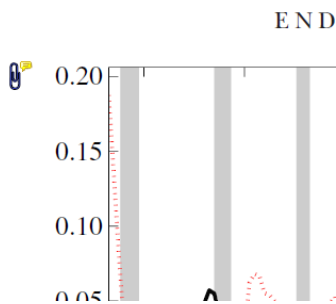
5. **Attach File** Tool – for inserting large amounts of text or replacement figures.



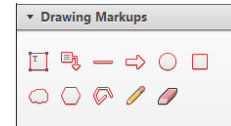
Inserts an icon linking to the attached file in the appropriate place in the text.

How to use it

- Click on the **Attach File** icon in the Annotations section.
- Click on the proof to where you'd like the attached file to be linked.
- Select the file to be attached from your computer or network.
- Select the colour and type of icon that will appear in the proof. Click OK.

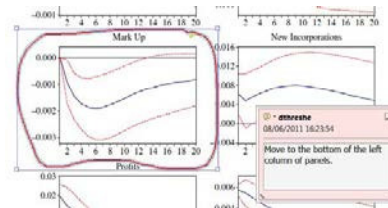


6. **Drawing Markups** Tools – for drawing shapes, lines and freeform annotations on proofs and commenting on these marks. Allows shapes, lines and freeform annotations to be drawn on proofs and for comment to be made on these marks.



How to use it

- Click on one of the shapes in the Drawing Markups section.
- Click on the proof at the relevant point and draw the selected shape with the cursor.
- To add a comment to the drawn shape, move the cursor over the shape until an arrowhead appears.
- Double click on the shape and type any text in the red box that appears.



REVIEW ARTICLE

A review of trabecular bone functional adaptation: what have we learned from trabecular analyses in extant hominoids and what can we apply to fossils?

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Abstract

Many of the unresolved debates in palaeoanthropology regarding evolution of particular locomotor or manipulative behaviours are founded in differing opinions about the functional significance of the preserved external fossil morphology. However, the plasticity of internal bone morphology, and particularly trabecular bone, allowing it to respond to mechanical loading during life means that it can reveal greater insight into how a bone or joint was used during an individual's lifetime. Analyses of trabecular bone have been commonplace for several decades in a human clinical context. In contrast, the study of trabecular bone as a method for reconstructing joint position, joint loading and ultimately behaviour in extant and fossil non-human primates is comparatively new. Since the initial 2D studies in the late 1970s and 3D analyses in the 1990s, the utility of trabecular bone to reconstruct behaviour in primates has grown to incorporate experimental studies, expanded taxonomic samples and skeletal elements, and improved methodologies. However, this work, in conjunction with research on humans and non-primate mammals, has also revealed the substantial complexity inherent in making functional inferences from variation in trabecular architecture. This review addresses the current understanding of trabecular bone functional adaptation, how it has been applied to hominoids, as well as other primates and, ultimately, how this can be used to better interpret fossil hominoid and hominin morphology. Because the fossil record constrains us to interpreting function largely from bony morphology alone, and typically from isolated bones, analyses of trabecular structure, ideally in conjunction with that of cortical structure and external morphology, can offer the best resource for reconstructing behaviour in the past.

Key words: cancellous bone; cortical bone; functional morphology; hominin; locomotion; Wolff's law.

Introduction

The goal of palaeoanthropologists, and palaeontologists in general, is to reconstruct behaviour in the past. The accuracy with which behaviour can be reconstructed has obvious implications for understanding the evolutionary history, environment, diet or phylogenetic relationships of past and present species. However, a primary problem when investigating fossil morphology is that one is limited by the functional inferences one can make from the preserved external

morphology alone. The external shape of a bone largely reflects a genetic blueprint in the sense that, for example, a gorilla femur or metacarpal is distinct from those of a chimpanzee or a human. Furthermore, the similarities in external morphology shared among gorillas, chimpanzees and humans compared with other primates also reflect their shared phylogenetic history.

The external shape of a bone is also obviously functional. For example, the length and degree of curvature of long bones correlate well with habitual locomotor behaviours (e.g. quadrupedalism vs. suspension vs. bipedalism; Jungers et al. 1997; Fleagle, 2013). Furthermore, the shape and size of articular facets are strongly correlated with joint mobility (Ruff, 1988; Ruff & Runestad, 1992; Ruff et al. 1994; Currey, 2002). However, articular facets are also functionally and physiologically constrained by the need for congruence

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with articulating bones and the interdependence of all the components of a particular joint that allow it to function effectively (Ruff & Runestad, 1992; Lieberman et al. 2001; Currey, 2002). As such, the external size and shape of articular facets remain relatively constant throughout life (apart from pathological conditions; Ruff & Runestad, 1992; Lieberman et al. 2001). Other aspects of external bone shape are more malleable and can reflect differences in function during one's lifetime, such as variation in the position or robusticity of muscle attachments (Churchill & Morris, 1998; Hawkey, 1998; Eshed et al. 2004; Zumwalt, 2006), but the utility of such skeletal markers for inferring behaviour has been questioned (Eliot & Jungers, 2000; Djukic et al. 2015; Miszkiewicz et al. 2015; Rabey et al. 2015). In short, although external morphology provides a wealth of functional information, it encompasses both primitive and derived features influenced by both genetic and non-genetic factors that can make it challenging to determine which aspects of external shape and size are functionally important for reconstructing the finer details of behaviour, particularly in fossils (Lieberman, 1997).

This confounding nature of external bony morphology has caused much debate among palaeoanthropologists regarding the behavioural reconstructions of many fossil hominoid (Madar et al. 2002; Susman, 2004; Moyà-Solà et al. 2005; Begun & Kivell, 2011) and hominin taxa (Stern, 1975; Rose, 1991; Richmond & Strait, 2000; Dainton, 2001; Lovejoy, 2009; Wood & Harrison, 2011; Almécija et al. 2013). The clearest example of this debate is the over 40-year-long discussion about the degree of arboreality in *Australopithecus afarensis* (for review, see Ward, 2002, 2013; Niemitz, 2010). Some view the primitive features of external morphology as retentions from a more arboreal ancestor that were either in the process of being lost or were selectively neutral and, as such, were considered largely non-functional and adaptively insignificant (Lovejoy et al. 1973; Latimer & Lovejoy, 1989). Other researchers aim to reconstruct behaviour as a whole and thus consider the primitive features as functionally useful with adaptive value retained under stabilizing selection (Stern, 1975; Rose, 1991; Stern & Susman, 1991). Palaeoanthropologists run into similar problems when interpreting the unusual morphology of Miocene apes like *Oreopithecus* (Moyà-Solà et al. 2005; Susman, 2005) and *Sivapithecus* (Madar et al. 2002; Begun & Kivell, 2011), or the mosaic morphology of *Australopithecus sediba* (Berger et al. 2010; Kivell et al. 2011a,b; DeSilva et al. 2013) and *Homo naledi* (Berger et al. 2015; Kivell et al. 2015). Thus, fossilized morphology often leaves us questioning which features are functionally important for reconstructing behaviour and exactly how extinct taxa interacted with their environments.

Resolution of this debate requires a better understanding of aspects of bony morphology that are more sensitive to loading (i.e. force or stress) during life than external bone shape and size and, as such, can better reflect how a bone

was used during an individual's lifetime (Ruff & Runestad, 1992; Lieberman, 1997). Analyses of internal bone structure – both the compact cortical shell and the spongy trabecular (also called cancellous) bone found underneath joints – can offer this functional insight. There is a general consensus that all bone is initially formed via a genetic blueprint but, because bone remodels throughout life, it can adapt to the magnitude and direction of mechanical loading during one's lifetime (Martin et al. 1998; Carter & Beaupré, 2001; Currey, 2002). This is true for both external and internal bony morphology. However, variation in the internal cortical and trabecular structure reflects more directly how a joint or bone was used during life because it is more responsive to the predominant directions of mechanical stress (which cause strain in the bone; Lieberman, 1997; Ruff et al. 2006). Furthermore, it is argued here that trabecular structure in particular is especially informative for inferring function and behaviour in the past for several reasons.

Trabecular bone is more porous than cortical bone. As such, trabecular bone has greater surface area and an increased number of bone cells that make it more metabolically active than densely-packed cortical bone (Huiskes et al. 2000; Jacobs, 2000; Currey, 2002). Trabecular bone typically remodels at a faster rate than cortical bone; the annual turnover rate of trabecular bone is approximately 25% compared with only about 2–3% of cortical bone in adult humans (Eriksen, 1986, 2010). Therefore, it is generally accepted that trabecular bone is more responsive and malleable to variations in magnitude and direction of load throughout life than cortical bone and, as such, may more clearly reflect function (Jacobs, 2000; Carter & Beaupré, 2001; Rubin et al. 2001, 2002; but see Lovejoy et al. 2003 and below). *In vivo* experimental studies of trabecular remodelling show that the basic genetic blueprint of trabecular structure can be subsequently changed by variation in load and/or habitual activities of an individual (Biewener et al. 1996; Guldberg et al. 1997; Mittra et al. 2005; Pontzer et al. 2006; Chang et al. 2008; Polk et al. 2008; Barak et al. 2011; Harrison et al. 2011). These experimental studies are further supported by computational analyses modelling trabecular bone response to variation in load (Huiskes et al. 2000; Jacobs, 2000; Fox & Keaveny, 2001). Thus, quantifying how trabecular structure varies (e.g. trabecular bone volume or BV/TV, mean thickness or spacing of trabecular struts, degree of anisotropy) across individuals or species could reveal differences in how a particular joint or bone was used during an individual's lifetime. As such, variation in trabecular structure can hold more detailed functional information than can be gleaned from external morphology alone and, when trabeculae are preserved, can be particularly informative for reconstructing behaviour in extinct taxa.

The dynamic adaptability of trabecular bone can help shed new light on several challenges that inherently come with analyses of (often unusual and fragmentary) fossilized

morphology and, in particular, the longstanding palaeoanthropological debates founded on differing functional interpretations of external morphology. For example, recent studies, reviewed in more detail below, using comparative and/or experimental analyses, have demonstrated the functional insight that can be gained from analyses of trabecular structure when applied to fossil hominin morphology (Barak et al. 2013a,b; Su et al. 2013; Skinner et al. 2015). A more precise insight into how bones and joints were loaded in extinct taxa can, in turn, provide a greater understanding of the functional significance (or lack thereof) of variation in their external morphology (Ryan & Ketcham, 2002b). The behavioural and mechanical flexibility (Wainwright et al. 2008) that characterizes extant primates means that external morphology does not always predict or reflect behaviour. This is particularly important for the numerous extinct Miocene and Pliocene taxa that are characterized by combinations of morphologies for which we have no good modern analogues (e.g. *Sivapithecus*, *Ardipithecus ramidus*, *Australopithecus sediba*). Furthermore, in fragmentary fossil specimens in which an epiphysis (and its underlying trabeculae) are preserved (e.g. a femoral head or distal ulna), more functional information can be gleaned about joint loading and potential behaviour than might be possible from just the external morphology alone. Trabecular analyses are non-invasive and can provide additional functional insight that, in combination with cortical and external morphology, can allow one to make the most out of such rare finds (Fig. 1).

This paper will review what is known about trabecular bone's functional response to load, how this has been applied to primate taxa, with a focus on extant hominoids and, finally, how this information can be (and has been) used to infer behaviour in fossil hominoids and hominins. Ideally, reconstructions of behaviour from bone should incorporate both trabecular and cortical bone structure, in combination with functional analyses of external morphology. Although the underlying physiological processes responsible for modelling and remodelling of trabecular and cortical bone are generally the same (Eriksen, 2010), there are several insightful reviews on the complexity of cortical bone functional adaptation (Lieberman, 1997; Pearson & Lieberman, 2004; Ruff et al. 2006; Judex & Carlson, 2009; Robling, 2009) and thus this will only be discussed briefly here.

The history of trabecular bone functional adaptation

The concept that the structure of bone (be that cortical or trabecular bone) can adapt over time to mechanical loading throughout life is commonly referred to as 'Wolff's law' (Wolff, 1892; Cowin, 2001; Pearson & Lieberman, 2004). However, Julius Wolff was not the first to recognize the correlation between bone structure and mechanical use.

Nearly 50 years before Wolff, Julius Ward (1838) compared the distinct trabecular pattern of the human femoral neck to the support bracket of a street lamp, which is the origin of 'Ward's triangle' for the sparse triangular area of trabeculae within the 'bracket' (Fig. 2; Koch, 1917; Martin et al. 1998). In 1867, Georg Hermann von Meyer, a Swiss anatomist, was the first to recognize variation in trabecular orientation within different bones. When German engineer Karl Culmann saw von Meyer's trabecular illustrations, he noticed that the orientation of the trabecular struts within the human femoral neck was remarkably similar to the internal compressive and tensile stress lines of a crane (similar to a cantilevered beam) he was designing at the time (Fig. 2; Martin et al. 1998; Hammers, 2015). The collaboration between von Meyer and Culmann has been called the 'first cooperation in the field of bone biomechanics' (Roesler, 1987: 1029). However, it was Wolff that made the concept popular (Wolff, 1870, 1892), and his 'trajectorial theory' of how forces are distributed throughout bone was well accepted by many in the scientific community at the time (Jacobs, 2000; but see Roux, 1881).

Wolff, however, considered there to be a static mathematical relationship between trabecular structure and stress trajectories, i.e. that they must be perpendicular to each other (Wolff, 1986; Jacobs, 2000; Hammers, 2015). Wolff also focused solely on adult structure, and made no reference to growth and development or processes that may have formed the 'final' adult structure, as he had no understanding of bone modelling and remodelling as we know them today (Townsend, 1948; Wolff, 1986; Martin et al. 1998; Pearson & Lieberman, 2004). Thus, Wolff's idea of how trabecular bone reflected mechanical loading was actually quite different from our current understanding that we still regularly subsume under the title 'Wolff's law'. In fact, it was Roux (1881) that recognized that bone cells were capable of responding to local mechanical stresses and that organisms had the ability to adapt their bony structure to new environments. These two important principles are much more similar to the general understanding and use of Wolff's law today, so much so that many researchers have suggested that the more general version of Wolff's law be called 'Roux's law' instead (Cowin, 2001; for further historical review, see Roesler, 1987; Martin et al. 1998).

Although many have found fault in Wolff's specific mathematical explanation for how bone adapts to mechanical loads (Pauwels, 1980; Carter et al. 1989; Frost, 1990; Bertram & Swartz, 1991; Cowin, 2001; Lovejoy et al. 2003), the current, more general version of 'Wolff's law' is well accepted (Cowin, 2001; Currey, 2002; Ruff et al. 2006). Thus, given that Wolff himself did not fully recognize the potential dynamic adaptability of bone, more appropriate terms are the 'mechanical adaptability hypothesis' (Martin et al. 1998) or 'bone functional adaptation' (Roux, 1881; Cowin et al. 1985; Lanyon & Rubin, 1985; Ruff et al. 2006), the latter of which will be used from here on in.

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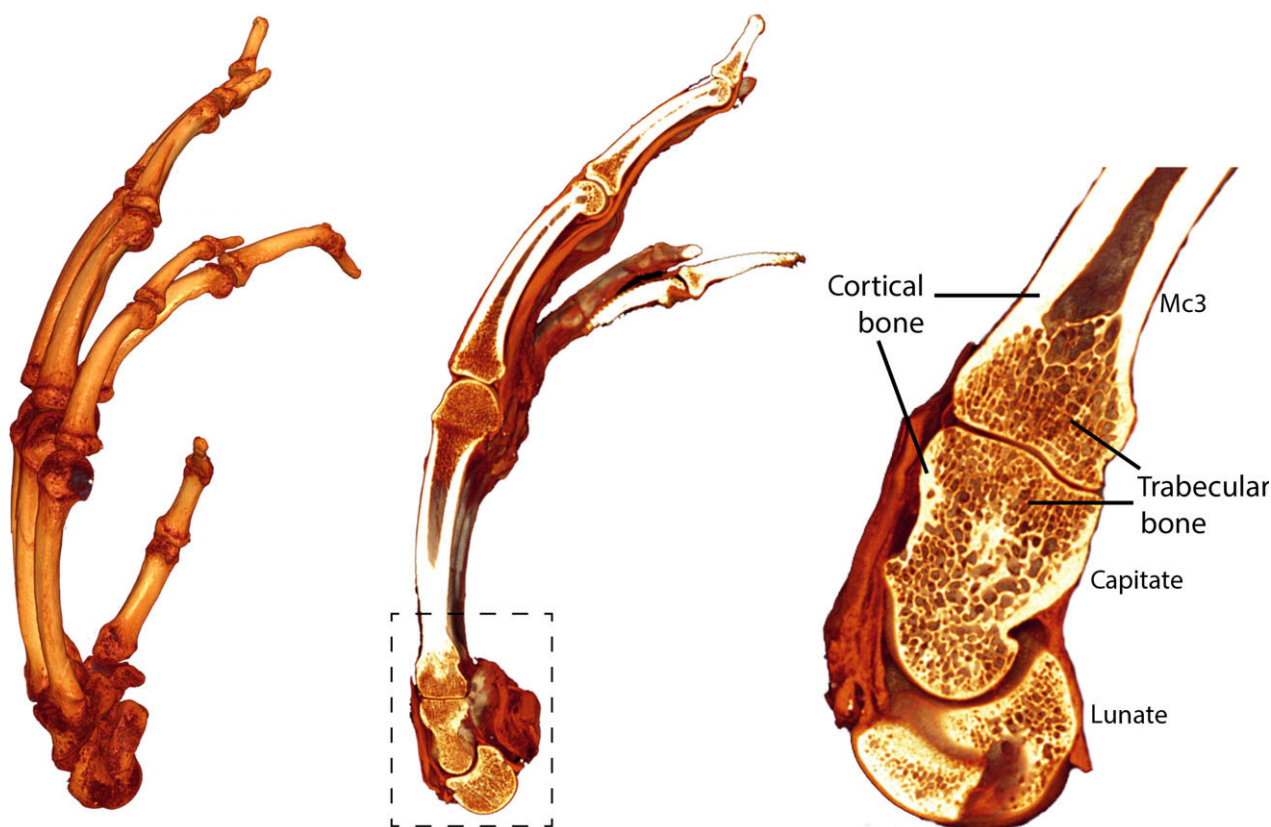


Fig. 1 Trabecular and cortical bone structure in a chimpanzee hand. A 3D rendering from a micro-CT scan of an extant chimpanzee hand (*Pan troglodytes*; left), a sagittal cross-section through the third ray, revealing the internal bone structure (middle) with the area outlined in the dashed box blown up (right) to show the dense cortical shell and the trabecular meshy network inside. Note that trabeculae fill just the epiphyses of long bones, like the third metacarpal (Mc3), while short bones, like the capitate and lunate, are filled completely with trabeculae.

Evidence of trabecular bone functional adaptation

The general functional role of trabecular bone is to provide strength and transfer external load away from the joint and toward the cortical bone (Currey, 2002; Barak et al. 2008). The relative amount of trabecular bone (BV/TV, sometimes also referred to as 'density') and its degree of alignment (i.e. anisotropy) are the most biomechanically informative aspects of trabecular architecture (Goldstein et al. 1993;

14 Odgaard et al. 1997; van Rietbergen et al. 1998); 88% of trabecular stiffness (Young's modulus of elasticity) can be explained by BV/TV (Stauber et al. 2006), while an additional 10% can be explained by degree of anisotropy

15 (Maquer et al. 2015). Indeed, Odgaard et al. (1997) demonstrated that the fabric (i.e. a characterization of the anisotropy) and mechanical (or elastic) principal directions are closely aligned. Thus, BV/TV and degree of anisotropy are among the most commonly quantified parameters in trabecular studies, often in concert with other variables that can provide more detailed information about variation in shape and size of the trabecular struts (Table 1; Odgaard, 1997, 2009). These descriptive variables, such as trabecular

thickness or number, are quantified in an effort to better understand heterogeneity in trabecular strength and/or the optimization of its structure. However, little is known about the effect these descriptive parameters have on the mechanical properties of the trabecular structure as a whole. For example, the number of trabeculae is thought to have no importance (Gibson, 1985; Gibson & Ashby, 1997), while the interconnectedness (i.e. connectivity; Hodgkinson & Currey, 1990) or shape of the individual struts (plate- vs. rod-shape; Liu et al. 2008) seem to play a more substantial mechanical role. In short, some descriptive parameters may be unimportant (Maquer et al. 2015), while others may be highly correlated with BV/TV and anisotropy, making their specific mechanical role challenging to identify (Hodgkinson & Currey, 1990; Goldstein et al. 1993).

Regardless of the potential limitations of describing and quantifying trabecular structure, the concept that trabecular bone structure can adapt to its mechanical environment has been demonstrated by numerous empirical studies. Firstly, several comparative studies of primate trabecular bone across individuals or species have revealed variation in trabecular structure that fits well with predictions of differences in habitual mechanical loading during locomotion

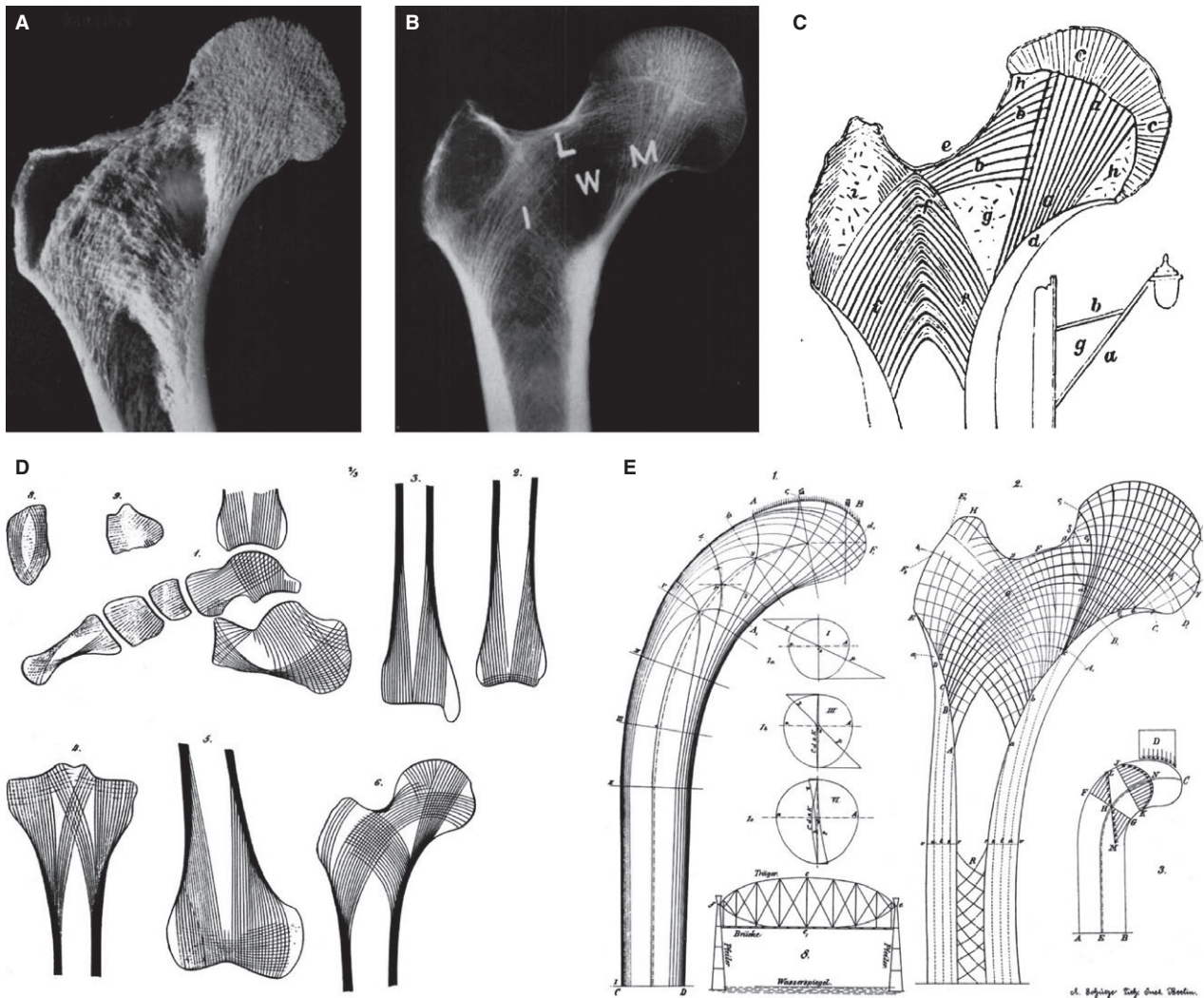


Fig. 2 Historical description of trabecular bone functional adaptation. (A) Coronal cross-section and (B) radiograph of a human proximal femur showing the distinct trabecular pattern related to bipedal loading. (C) Ward's (1838) drawing of the trabecular structure that he related structurally to the bracket street lamp post. The sparse area of trabeculae in the femoral neck is equivalent to the empty space within the bracket ('g'), which is known as 'Ward's triangle' (W). (D) von Meyer's (1867) stylized illustrations of trabecular patterns in human bones. (E) Wolff's (1970) composite diagram including the compressive and tensile strain patterns in Culmann's cantilevered beam and 'crane' (left), and the similarity to the trabecular pattern in the human proximal femur (right). Images (A–C) adapted from Garden (1961), and images (D and E) adapted from Skedros & Baucom (2007).

(Fajardo & Müller, 2001; Ryan & Ketcham, 2002a, 2005; Ryan & Shaw, 2012, 2015; Scherf et al. 2013; Tsegai et al. 2013; Matarazzo, 2015; but see below). Within humans, for example, more mobile, foraging populations show significantly greater BV/TV and thicker trabeculae in their proximal femur than that of less mobile, agricultural populations (Ryan & Shaw, 2015). The distinctive trabecular pattern of the adult proximal femur (Fig. 2) appears between the ages of 1 and 2 years, when human infants develop independent bipedal walking and the femur becomes weight-bearing in a human-like way (Townsend, 1948; Ryan & Krovitz, 2006; but see Cunningham & Black, 2009a,b). Raichlen et al. (2015) have recently followed on this study, suggesting that

subtle changes in trabecular structure of the human distal tibia reflect the increased biomechanical stability during bipedalism that is gained between the ages of 1 and 8 years.

Secondly, several computational studies can explain the maintenance of a particular trabecular structure as optimal for the mechanical load it experiences (Levenstone et al. 1994; Huiskes et al. 2000; Fox & Keaveny, 2001; Keaveny et al. 2001; Gupta et al. 2007). For example, in one of the first computer simulations of trabecular bone remodelling, Huiskes et al. (2000) showed that there is a balance in the metabolic process of bone resorption (osteoclasts) and bone formation (osteoblasts) that is governed by mechanical

Table 1 Commonly used trabecular parameters.

Parameter	Symbol (unit)	Description
Bone volume fraction	BV/TV	The proportion of trabecular bone voxels relative to the total number of voxels in a given region or VOI
Degree of anisotropy	DA	DA describes the trabecular orientation in 3D space. Anisotropic structure has a preferred orientation to the trabecular struts, while isotropic structures show symmetry of the orientation in all directions. DA is usually calculated using the mean intercept length (MIL) algorithm (see Harrigan & Mann, 1984), where the eigenvectors give the main directions. DA is reported as a dimensionless value, with fully isotropic structure represented by 0 or 1, and higher values representing relatively more anisotropic structures
Trabecular thickness	Tb.Th (mm)	The mean thickness of the trabecular struts in a given region or VOI. This is typically measured via 'sphere-fitting', i.e. by the diameter of spheres that can be fully contained within the structure
Trabecular separation	Tb. Sp (mm)	The mean width of the spaces between adjacent trabeculae in a given region or VOI
Trabecular number	Tb.N (mm ⁻¹)	The number of trabecular struts per mm. It is calculated as the inverse of the mean distance between the mid-axes of the trabecular struts
Structure model index	SMI	SMI is a dimensionless measure of the relative proportion of plate-like vs. rod-like structures in a given region or VOI. Values typically range from 0 (idealised plates) to 3 (idealised rods), and can be positive or negative values. Negative values indicate a more concave or closed structure, like a honeycomb; positive values indicate a more convex and open structure
Connectivity density	Conn.D	The number of interconnected trabeculae per unit volume (Odgaard & Gundersen, 1993)
Trabecular bone pattern factor	Tb.Pf (mm ⁻¹)	A proxy measure of trabecular connectivity within a given region or VOI. Lower values indicate greater connectivity and structural integrity within the trabecular structure; higher values indicate greater fragmentation and the presence of isolated trabecular struts. It can also have positive (connected structures are more convex) or negative (connected structures are more concave) values and the basis of its calculation is similar to SMI (Hahn et al. 1992). Thus, changes in SMI and Tb.PF values are closely correlated. Importantly, Odgaard (1997) demonstrates that quantification of Tb.Pf in 2D is not representative of connectivity in 3D
Bone surface density	BS/BV	The ratio of trabecular bone surface area relative to total trabecular bone volume in a given region or VOI

load. When mechanical load remained stable (i.e. homeostasis), remodelling continued without affecting the overall bone mass or structure. However, when the external load was rotated by 30°, the main orientation of the trabeculae gradually reoriented as well to align with the external load and optimize mechanical strength. A 20% decrease or increase in the external loading reduced or increased trabecular bone mass by a comparable degree (15.8% and 17.5%, respectively). When the original homeostatic loading conditions were applied again, the trabecular structure and bone mass gradually returned to its original form (Huiskes et al. 2000).

Since the 1990s, finite element (FE) modelling has been used successfully in various ways to quantify and validate the mechanical properties and functional significance of trabecular bone (Hollister et al. 1994; van Rietbergen et al. 1995, 1999; Kabel et al. 1999; Ulrich et al. 1999; Homminga et al. 2004; Ryan & van Rietbergen, 2005; Nguyen et al. 2013, 2014). For example, Homminga et al. (2004) used micro-FE modelling to show that osteoporotic human vertebrae were just as resistant to normal daily loading as healthy vertebrae. The osteoporotic trabeculae were more longitudinally oriented, compensating for the effects of bone loss and ensuring adequate stiffness for normal daily

loading (although they were less resistant to non-normal loads; Homminga et al. 2004).

Thirdly, and most convincingly, are *in vivo* experimental analyses that test directly trabecular bone functional adaptation (Lanyon, 1974; Skerry & Lanyon, 1995; Biewener et al. 1996; Mittra et al. 2005; Pontzer et al. 2006; Chang et al. 2008; Polk et al. 2008; Barak et al. 2011; Harrison et al. 2011). Many of the initial experimental studies focused on the mammalian calcaneus due to its predictable loading environment (Lanyon, 1973, 1974; Skerry & Lanyon, 1995; Biewener et al. 1996; Skedros et al. 2004, 2012; Sinclair et al. 2013). In mammals in which the calcaneus does not touch the ground during locomotion, it experiences a regular cantilever-like loading (i.e. bending) from the Achilles tendon during ankle extension. These studies found that the trabeculae underlying the Achilles tendon attachment were aligned with the compressive (and tensile) principal direction of stress (Lanyon, 1974; Biewener et al. 1996). Furthermore, after 8 weeks of disuse (in individuals in which the Achilles tendon was detached from the calcaneus), there was a reduction in BV/TV, trabecular thickness and number (although the orientation did not change) that reflected the absence of an external load (Biewener et al. 1996).

1 More recent *in vivo* studies have expanded on this work
 2 to test how variation in the direction and magnitude of the
 3 external load affect trabecular structure (Pontzer et al.
 4 2006; Chang et al. 2008; Barak et al. 2011; Harrison et al.
 5 **22** 2011). For example, Barak et al. (2011) showed that trabec-
 6 ular orientation varied predictably in the hindlimb joints of
 7 sheep that were loaded differently through daily exercise
 8 on level and inclined treadmills. The inclined sheep had a
 9 more extended ankle joint by 3.6 ° at midstance (i.e. at peak
 10 ground reaction force). After roughly 1 month, these sheep
 11 showed a change in trabecular orientation 2.7–4.3 ° in the
 12 distal tibia, corresponding closely with the change in the
 13 orientation of the external load at the ankle. In contrast,
 14 the carpal joint remained at a stable orientation in both
 15 groups and there were no significant differences in the tra-
 16 17 becular orientation in the distal radius. Thus, even small
 18 changes in joint angle can be reflected in the trabecular
 19 structure. Pontzer et al. (2006) also found a strong corre-
 20 spondence between changes in the orientation of external
 21 joint loading of the knee and trabecular orientation of the
 22 distal femur in guinea fowl.

23 Similar results have also been found in *in vivo* studies
 24 of humans. Elite athletes whom engage in sports that
 25 cause irregular-impact loading of the femur (i.e. forces
 26 from high acceleration/deceleration and from varied direc-
 27 tions, such as during soccer or squash), showed approxi-
 28 mately 10% higher trabecular bone density (i.e. bone
 29 mineral density quantified *in vivo* via magnetic resonance
 30 imaging), compared with elite athletes who engaged in
 31 sports of high-magnitude but primarily vertical loading
 32 (e.g. power-lifting), and 20% higher than non-athletes
 33 (Harrison et al. 2011). Trabecular bone mass (i.e. increased
 34 BV/TV and trabecular number, decreased trabecular spac-
 35 ing) was also higher in the knee in both gymnasts (Mod-
 36 lesky et al. 2008a) and Olympic fencers (Chang et al.
 37 2008) compared with the respective control groups. Con-
 38 versely, trabecular bone structure has been shown to be
 39 severely underdeveloped in children with cerebral palsy
 40 (Modlesky et al. 2008b), and to decrease in non-gravita-
 41 tional environments (Jee et al. 1983; Bikle & Halloran,
 42 1999).

43 Altogether, there is a large body of empirical evidence
 44 across a variety of different animals from the last several
 45 decades supporting trabecular bone functional adaptation.
 46 Trabecular bone structure is clearly capable of responding
 47 during life, often within a relatively short period of time,
 48 to the magnitude and direction of load (or unloading). How-
 49 ever, there is still much that we do not understand about
 50 trabecular bone, including the genetic and developmental
 51 role in shaping trabecular architecture, if and how trabecu-
 52 lar bone might respond differently to variation in the dura-
 53 tion, frequency or magnitude of the external load, or how
 54 all of these factors might vary depending on the species,
 55 age, anatomical region or differences in body mass. All of
 these factors can confound our interpretations of joint

loading and bone function from trabecular structure in
 extant and, particularly, fossil taxa.

The complexity of trabecular bone functional adaptation

Despite the evidence described above, there are also several
 empirical studies that have found that trabecular bone does
 not respond to mechanical stimuli in ways that one might
 predict. For example, Carlson et al. (2008) conducted an **23**
 experimental analysis on mice to see how trabecular struc-
 ture varied in the distal femur with differences in locomo-
 tion during growth. They had three groups of mice: (i) a
 free-ranging control group; (ii) a 'linear' group, which were
 encouraged to travel through a straight tube; and (iii) a
 'turning' group, in which the mice moved through a twist-
 ing tube. Despite their predictions that there should be vari-
 ation in external load on the femur in the 'linear' vs.
 'turning' mice, the trabecular structure did not significantly
 differ between the two groups. Furthermore, the 'free-ran-
 ging' control mice had significantly higher BV/TV than the
 exercised linear/turning mouse groups, which was also
 counterintuitive (Carlson et al. 2008). These results highlight
 some of the complexity of trabecular bone functional adap-
 tation and the challenges of testing hypotheses in living
 animals. For example, the Carlson et al. (2008) results may
 suggest that the free-ranging mice were actually more
 active than the 'linear/turning' mice, or that the trabecular
 structure of such small animals scales differently (Barak
 et al. 2013a,b; Christen et al. 2015) or experiences less strain
 (and thus there is less response) than that of larger animals
 (Biewener, 1990), especially when the cortical bone has
 responded to the changes in midshaft loading (Carlson &
 Judex, 2007), or reflect differences in bone modelling and
 remodelling based on anatomical location (Bass et al. 1999;
 Morgan & Keaveny, 2001; Morgan et al. 2003; Yeni et al.
 2011; R ath et al. 2013) or species (Chow et al. 1993; Erben,
 1996; Turner, 2001; Barak et al. 2013a). Below, some of the
 complicating factors that suggest trabecular bone func-
 tional adaptation is not as straightforward as functional
 morphologists might wish it to be are discussed.

When, how and to what kind of load does trabecular bone respond?

There is ongoing debate regarding what kind of external
 load trabecular bone is most responsive to. Is it primarily
 loading from muscles (i.e. contractile forces) or gravitational
 loading (i.e. substrate reaction forces; for review, see
 Robling, 2009; Judex & Carlson, 2009, respectively)? Is there
 a minimum magnitude of loading that is required to stimu-
 late bone growth and remodelling (Frost, 1987)? Is trabecu-
 lar structure reflecting more frequent but low-magnitude
 loading, or rare but high-magnitude loading? How much
 does adult trabecular structure reflect loading that occurred

during earlier development when bone was still growing? There are several studies that have tried to address these issues and have yielded conflicting results (for review, see Bertram & Swartz, 1991).

Many of the *in vivo* experiments described above (Pontzer et al. 2006; Carlson et al. 2008; Barak et al. 2011) are conducted on juvenile animals because bone is both actively modelling and remodelling during this time, and is considered to be more responsive to mechanical stimuli than adult bone (Pearson & Lieberman, 2004). Indeed, Pettersson et al.

(2010) found that variation in physical activity during growth (i.e. childhood and adolescence) was the strongest predictor for differences in adult trabecular bone density (i.e. bone mineral density) in the calcaneus of a large sample of men. Thus, this work highlights how activity during growth can have a lasting effect on trabecular structure later in life, even in inactive adults (Pettersson et al. 2010; but see Karlsson et al. 2000).

However, trabecular bone modelling and remodelling throughout ontogeny are influenced by a number of factors, such as the underlying genetic patterning (Cunningham & Black, 2009a,b), vascular patterning and the positioning of growth plates (Cunningham & Black, 2010), changes in hormone levels (Simkin et al. 1987; Karlsson et al. 2001; Yeni et al. 2011), and variation in cellular processes and constraints on bone design, that go beyond the scope of this paper (for review, see Lieberman, 1997). In early ontogeny, several studies have demonstrated that trabecular bone (and bone in general) follows particular patterns of growth during the modelling and remodelling process. For example, in a sample of healthy human children and adults, Parfitt et al. (2000) found that trabecular bone in the ilium (analysed via biopsy) formed with a roughly uniform trabecular number that was retained throughout life in healthy individuals (e.g. without osteopenia). In other words, between the ages of 1.5 and 23 years, there was an increase in BV/TV and trabecular thickness, but trabecular number did not change (Parfitt et al. 2000). In addition, during early ontogeny BV/TV and trabecular thickness tend to increase first, during periods of more dramatic increases in body mass, while trabecular orientation (i.e. anisotropy) is adapted later in development (Parfitt et al. 2000; Tanck et al. 2001). For example, in humans, trabecular structure of the femur and tibia reaches an adult-like pattern (BV/TV, anisotropy) at approximately 8 years old (Ryan & Krovitz, 2006; Gosman & Ketcham, 2009; Raichlen et al. 2015). The same ontogenetic pattern is found in the trabecular structure of human vertebrae (Roschger et al. 2001). Thus, overall trabecular architecture appears to be optimized later in life (Huiskes et al. 2000; Nafei et al. 2000; Tanck et al. 2001; Ryan & Krovitz, 2006; Cunningham & Black, 2009a).

However, this does not imply that adult trabecular bone is not also capable of responding and adapting to changes in external load. To the contrary, several *in vivo* experimen-

tal studies have been conducted on adult animals demonstrating changes in trabecular structure in response to variation in mechanical stress (Smith et al. 1989; Biewener et al. 1996; Rubin et al. 2001, 2002). Trabecular structure can respond to increased load even late in life, such as in postmenopausal women (Simkin et al. 1987; Smith et al. 1989) or, conversely, resorbing with removal of load, such as in quadriplegics (Frey-Rindova et al. 2000). However, adult trabecular structure seems to respond to external mechanical stimuli in different ways than during earlier ontogeny. Saporin et al. (2011) noted that in areas of higher loading in the adult primate femoral neck, BV/TV was higher due to increased trabecular thickness, while trabecular number did not change. In contrast, in areas of lower loading, BV/TV was lower due to a reduction in trabecular number, but trabecular thickness remained constant (Saporin et al. 2011; see also Rubin et al. 2001, 2002; Shaw & Ryan, 2012). The latter result is contrary to the finding that trabecular number remains uniform throughout life (Parfitt et al. 2000). However, Saporin et al. (2011) suggest that in areas of lower loading, reducing trabecular number is 'safer' than reducing trabecular thickness because of risk that resorption during remodelling will weaken or sever a trabecula, thus making it non-functional (Skedros et al. 2012). Instead, the reduction in trabecular number is not random, but is associated with increased anisotropy, thus preferentially removing specific and mechanically unnecessary trabeculae (Saporin et al. 2011; Skedros et al. 2012). This hypothesis is also consistent with the *in vivo* experimental results of Biewener et al. (1996).

There also appears to be a minimum load (either in magnitude, frequency and/or duration) that is required to stimulate trabecular bone remodelling. Frost's (1987) 'mechanostat' hypothesis puts forth strain thresholds for bony response: strains below 100–300 microstrain ($\mu\epsilon$) elicit remodelling of trabecular (and cortical) bone, while much higher strains (1500–3000 $\mu\epsilon$) stimulate bone modelling to increase cortical bone mass (Burr, 1985; Rubin & Lanyon, 1985). However, the duration of the strain (or external stress) is also important. For example, Skerry & Lanyon (1995) immobilized the calcaneus in several sheep, reducing the external load significantly. In a subset of these sheep, the immobilization device was removed and they were allowed to walk on the treadmill for 20 min/day. Even though the strain experienced by the calcaneus during this short time was 'normal' (Lanyon, 1973, 1974) and supposedly enough to stimulate trabecular remodelling (147 $\mu\epsilon$), after 12 weeks both groups of sheep showed the same degree of trabecular bone loss in the calcaneus. This result suggests that the magnitude and/or duration of load experienced during the short periods of walking were not sufficient to reduce the degree of trabecular bone loss due to immobilization. Barak et al. (2011) found a similar result; loading during 'normal' activity in non-exercised sheep wearing shoes that altered their ankle joint angle was not

enough to stimulate the reorientation of the trabecular alignment that was found in exercised sheep. In an experimental study on mice, Lambers et al. (2013) found that it required 10 weeks for trabecular bone (quantified as BV/TV and bone stiffness) within the vertebrae to 'fully adapt' to a new increased external load (applied at a high frequency for 5 min, three times/week). The BV/TV and stiffness values remained the same after 10 weeks, and the remodelling rates returned to those of the control group by this time as well (Lambers et al. 2013). Such studies suggest that bone functional adaptation requires both a minimum magnitude and duration of loading to affect trabecular growth and remodelling (Rubin & Lanyon, 1985; Skerry & Lanyon, 1995; Biewener et al. 1996; Barak et al. 2011), but determining what these minimum thresholds are, in particular skeletal elements or particular species, especially in primates, is challenging.

That being said, many experimental studies (Simkin et al. 1989; Smith et al. 1989; Basse & Ramsdale, 1994), including several discussed above (Pontzer et al. 2006; Barak et al. 2011; Lambers et al. 2013), have shown that relatively short periods of external loading can, sometimes dramatically, affect changes in trabecular structure if the orientation or magnitude is 'unusual' compared with that of normal daily activity. Thus, bone adaptation may be driven by an animal's most infrequent but dynamic behaviours, rather than habitual loading (Burr, 1990). If so, this has important implications for interpreting function and behaviour from trabecular structure in fossils. If only 10 or 15 min/day [as was the case in Pontzer et al. (2006) and Barak et al. (2011), respectively] of loading from a particular 'unusual' behaviour is enough to significantly alter trabecular structure, what can we infer about the overall locomotor behaviour of a fossil hominoid or hominin? Might the trabecular structure primarily retain a functional signal for those behaviours that loaded the skeleton in relatively rare and unusual ways, overriding the functional signal of the most common daily behaviours?

Rubin et al. (2001, 2002) tested this hypothesis specifically; is bone functional adaptation dependent on peak skeletal stress or can very low-level stress during less vigorous but much more frequent activities (e.g. standing) influence trabecular bone structure? In an experiment with adult sheep, they constrained some individuals and exposed their hindlimbs to extremely low-level (0.3 g) external loads at a high frequency (30 Hz) using an oscillation plate for 20 min/day for 1 year. These sheep showed a 34.2% increase in the trabecular bone density (decreasing trabecular spacing by 36.1% and increasing trabecular number by 45.6%) compared with the control group. Furthermore, there was no significant difference in cortical structure in any of the hind- or forelimb bones, demonstrating that trabecular bone is more responsive to low-magnitude but high-frequency loading than the cortex [Rubin et al. 2001, 2002; but see Carlson & Judex, 2007; Carlson et al. 2008 for the opposite

results]. These results suggest that very low-level external loading during habitual activities can be a determining factor of the overall trabecular pattern.

Trabecular bone and body mass

The relationship between variation in trabecular structure and body mass has been recently well studied in primates (Scherf, 2008; Cotter et al. 2009; Hernandez et al. 2009; Fajardo et al. 2013; Ryan & Shaw, 2013), and across a wider variety of mammals and birds (Swartz et al. 1998; Doube et al. 2011; Barak et al. 2013a; Christen et al. 2015). Generally, larger primates (and mammals) have absolutely thicker and more widely-spaced trabeculae but, relative to body mass, their trabecular struts are thinner and more tightly packed (Swartz et al. 1998; Doube et al. 2011; Barak et al. 2013a; Ryan & Shaw, 2013; Fig. 3). In other words, these aspects of trabecular structure scale with negative allometry across primates and mammals (but not within a particular taxon). In fact, the trabeculae of a whale are not much wider or more widely spaced than that of a human (Odgaard et al. 1997). In contrast, BV/TV scales with weak positive allometry while the degree of trabecular anisotropy shows no significant relationship with body mass (Doube et al. 2011; Barak et al. 2013a; Ryan & Shaw, 2013; but see Fajardo et al. 2013). However, scaling of specific trabecular parameters with body mass does seem to vary depending on bone (e.g. femur vs. vertebra) and taxonomic group (e.g. hominoids vs. strepsirrhines; Cotter et al. 2009; Fajardo et al. 2013; Ryan & Shaw, 2013).

The relationship between trabecular structure and body mass suggests that there are a number of constraining metabolic and biomechanical factors that govern trabecular architecture in general. Swartz et al. (1998) proposed that relative differences in trabecular structure between small and large animals may be driven by requirements to maintain an adequate surface area for the release and deposition of calcium (Kerschnitzki et al. 2013). Furthermore, trabecular thickness is constrained by the size of the regions that can be effectively regulated by osteocytes (Mullender & Huiskes, 1995; Mullender et al. 1996; Cowin, 2001; Christen et al. 2015). For example, there appears to be a minimum trabecular thickness, regardless of how small the animal, because the lacunae created by osteoclasts are about 30–60 μm in depth (Eriksen et al. 1985; Cowin, 2001; McNamara et al. 2006; Mulvihill et al. 2008; Eriksen, 2010). Trabeculae any thinner than this would simply be cut in two with remodelling, and thus would not be functional (Barak et al. 2013a). Conversely, there also appears to be a maximum trabecular thickness (i.e. approximately 460 μm ; Lozupone, 1985; Lozupone & Favia, 1990) that allows for optimal positioning of the osteocytes relative to bone surface while also maintaining the necessary biomechanical strength (i.e. stiffness; Ryan & Shaw, 2013). Indeed, Christen et al. (2015) recently demonstrated via computer modelling

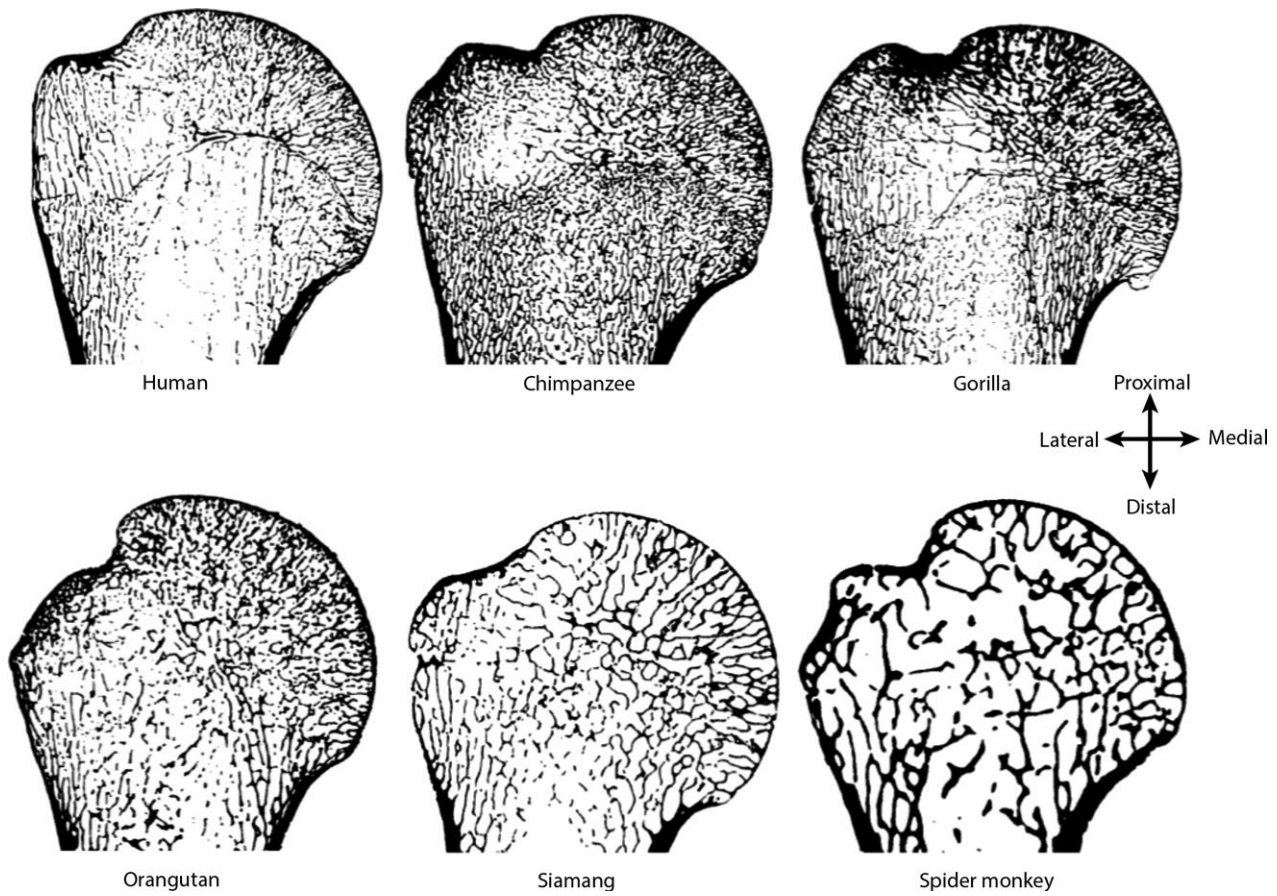


Fig. 3 Trabecular bone in the primate humerus. Coronal cross-section of the proximal humerus showing variation in trabecular structure, particularly in relation to body size. All humeri are scaled to approximately the same size. Note that the trabeculae in larger-bodied primates (e.g. chimpanzee, gorilla and orangutan) tends to be thinner and more densely-packed compared with smaller-bodied primates (siamang and spider monkey), which have relatively thicker trabeculae that are more spaced out. Humans are unique in having thin and somewhat densely-packed trabeculae, but have a comparatively low trabecular bone volume (BV/TV) compared with other great apes.

that the underlying mechanism for negative allometric trabecular bone scaling in terrestrial mammals may be variation in osteocyte density and the distance an osteocyte signal can travel towards osteoblasts at the bone surface (i.e. influence distance).

Larger animals experience relatively higher skeletal loading than smaller animals (Biewener, 1989, 1990). Given the metabolic constraints on trabecular size outlined above, the trabecular structure of larger animals must mitigate these increased loads in other ways. For example, they can alter other aspects of trabecular structure, such as increasing the BV/TV or trabecular anisotropy, or changing the shape of trabecular struts (i.e. plates vs. rods; Ryan & Shaw, 2013). It is also important to remember that trabeculae do not exist independently but within bones, such that larger animals may adapt the cortical distribution instead, highlighting the importance of studying both trabecular and cortical structure together (see below). Finally, it is also well documented that larger animals alter their locomotor kinematics [e.g. more extended limb postures (Biewener, 1983, 1989)

or complaint gaits (Schmitt, 1999; Polk, 2002)], which would reduce joint loading and, ultimately, strain on the trabecular structure. Such metabolic and biomechanical constraints should be considered when interpreting function from trabecular bone, especially in comparative analyses of extant and fossil primates that vary greatly in body size.

Systemic skeletal patterns of trabecular bone

A well-known experimental study by Lieberman (1996) investigated the potential reasons for variation in cranial vault thickness across hominins. Although this study investigated cortical bone only, the results raise an important and potentially confounding issue with regards to making functional inferences from internal bony morphology: a systemic response of bone throughout the skeleton. Lieberman (1996) had young pigs run on a treadmill for 60 min/day for 3 months and compared their cortical structure with that of controls (confined to walking in a small pen all day). Predictably, the exercised pigs had significantly higher

cortical thickness in their limb bones compared with that of the controls. However, they also had significantly thicker (28%) cranial vault bones, as well as thicker cortex in the caudal vertebrae and the last and penultimate ribs, neither of which are weight-bearing during locomotion or would indirectly incur higher external loading from running (Lieberman, 1996). Similar systemic patterns have been found in non-weight-bearing skeletal elements (e.g. mandible) in rats when external loads are reduced (e.g. absence of gravity; Simmons et al. 1983). Thus, these results make a strong argument for systemic adaptations of bone that are unrelated to load.

However, trabecular bone functional adaptation appears to be more localized than that of cortical bone (Rubin et al. 2001, 2002; Judex et al. 2004; Barak et al. 2011). For example, in the sheep experiment by Rubin et al. (2001, 2002) described above, the externally loaded hindlimb bones showed increased trabecular bone mass, but the radius (which did not experience the low-magnitude, high-frequency oscillations) did not. Judex et al. (2004) have shown in different genetic strains of inbred mice that changes in trabecular bone due to disuse varied not only across the mouse groups, but also varied depending on anatomical location (more so than changes in cortical bone).

That being said, this does not mean that there are not underlying systemic and genetic factors that must be considered in functional analyses of trabecular structure. All bone growth is mediated by hormones at both localized and systemic levels (Lieberman, 1996). Several studies have found that certain aspects of trabecular structure, primarily BV/TV and its mechanical properties (i.e. Young's modulus), are strongly influenced by genetics in baboons (Havill et al. 2010) and rodents (Alam et al. 2005). Furthermore, there appear to be systemic patterns in trabecular bone density or BV/TV that are consistent throughout several skeletal elements within a particular taxon and that are distinctive across different primate taxa (Chirchir et al. 2015). For example, compared with other extant primates and fossil hominins, modern humans may have recently evolved a remarkably low trabecular bone density throughout the epiphyses of both the upper limbs and, counterintuitively, the weight-bearing lower limbs as well (Chirchir et al. 2015; but see Ryan & Shaw, 2015). Independent analyses of trabecular structure across extant hominoids have revealed that there are consistent differences in BV/TV in several elements of the skeleton, with *Pan*, and particularly bonobos, having especially high BV/TV in the metacarpals (Tsegai et al. 2013), humerus (Davenport, 2013), manual phalanges and talus (unpublished data) compared with *Gorilla* and *Pongo*, and much higher than humans (Maga et al. 2006; Cotter et al. 2009; Hernandez et al. 2009; Griffin et al. 2011; Ryan & Shaw, 2012; Scherf et al. 2013). Thus, there appears to be an underlying blueprint of trabecular structure that is systemic throughout the skeleton, at least in some taxa, which is not fully understood. Such systemic

patterns could bias functional inferences when only one anatomical element is being investigated, which is often the case in trabecular studies (Maga et al. 2006; DeSilva & Devlin, 2012; Su et al. 2013; Ryan & Shaw, 2015).

Lovejoy et al. (2003) take a more extreme view. They critique the concept of 'Wolff's law' [referring to the strict version of this concept (i.e. that the bones' response is based on mathematical laws), rather than the more generalized version accepted by most researchers today] from a genetic and developmental perspective, suggesting that the structure and distribution of bone (both trabecular and cortical) reflects primarily the expression of positional information from mesenchymal cells during early growth. While the material properties and maintenance of bone structure can also be influenced by localized strain, this process is relatively minor compared with the genetic and development underpinnings of bone morphology, particularly in adults (Lovejoy et al. 2003). In other words, 'bones of the ... skeleton are almost entirely determined by the PI (positional information) of their original cartilage anlagen' (Lovejoy et al. 2003: 96). Their view has some empirical support; Skedros et al. (2004) found that the characteristic arched trabecular pattern of the adult deer calcaneus, which is ideal for resisting bending stress, is already present in the calcanei of foetal deer. Cunningham & Black (2009a,b) also found correspondence between the trabecular pattern of the human newborn ilium (i.e. prior to weight-bearing bipedalism) and the distinctive pattern found in adults. However, the position of Lovejoy et al. (2003) generally runs counter to the vast experimental literature showing bone's response to variation in load, even in adults. The value of their critique is the recognition of the significant genetic role in establishing and constraining (at least to some degree) bony morphology and that we still have much to learn about the mechanosensory mechanisms of bone in general.

Bone functional adaptation is not sufficient (but is all we have)

The numerous influences on how bone may (or may not) respond and adapt to mechanical stimuli discussed above demonstrate the complexity of drawing functional inferences from bone structure. In addition, Hall (1985) cautioned: 'Theoretical approaches which treat bones as idealized, isolated units ... simply fall short of reality. A particular bone's response to altered mechanical stress might be compromised by the simultaneous response of the attached muscles or connective tissue ... by altered blood flow, by associated mineral requirements, etc.' (Hall, 1985: xxvi-xxvii). Thus, in analyses of trabecular bone structure, one should ideally consider the broader context of cortical bone (both its external and internal morphology), the muscles and connective tissues acting on the bone, and the articulating bones and joints that together provide the

environment in which bone may respond to mechanical stimuli.

The human femoral neck is a particularly good example of the increased biomechanical understanding one can gain when trabecular bone is not investigated in isolation. Trabecular bone density in the femoral neck has an upper threshold due to weight constraints and limitations on energy absorption and haematopoietic function (Gibson & Ashby, 1997; Currey, 2002). However, there is also a lower threshold of trabecular bone density, clearly demonstrated by increased risk of fracture when trabecular stiffness is reduced (Lotz et al. 1995; Fox & Keaveny, 2001). There are kinematic limitations on the cortical thickness and maximum neck diameter that ensure the necessary range of motion at the hip joint (Fox & Keaveny, 2001). Therefore, trabecular bone in the human femoral neck is among the stiffest in the human skeleton, capable of coping with the significantly higher compressive strain compared with the proximal tibia, vertebrae and femoral trochanter (Morgan & Keaveny, 2001; Morgan et al. 2003; also see Amling et al. 1996) and carry approximately 50% of the compressive load at midneck (Lotz et al. 1995).

However, in the world of palaeontology, we are limited to the information that is preserved in the fossil record. Associated or articulated skeletal remains are rare within palaeoanthropology (Napier & Davis, 1959; Moyà-Solà & Köhler, 1996; White et al. 2009; Berger et al. 2010, 2015), and information regarding soft tissues, metabolism or genetics is at best ambiguous and usually absent. Thus, contrary to Hall's valid caveat, palaeontologists are generally forced to treat bones as isolated units. To move forward with any inferences about behaviour in the past, we must assume that there is at least some correlation between bone form and function, that bone responds to external load by minimizing bone mass and risk of fracture, while simultaneously optimizing stiffness, even if we are not exactly sure if this is true or how it works (Martin et al. 1998). Because trabecular bone appears to be particularly sensitive to mechanical stimuli during life, it can provide greater insight into bone and joint function, and ultimately behaviour, than analyses of external morphology alone.

What we already know about primate trabecular bone

The overwhelming majority of studies on trabecular bone morphology are on humans, usually within the context of better understanding osteopenia and osteoporosis (Eriksen, 1986; Simkin et al. 1987; Smith et al. 1989; Dempster, 2000). Living or cadaveric/osteological human samples are abundant, come with ethical consent and can be studied via radiography, such as dual-energy X-ray absorptiometry (DEXA) or peripheral quantitative computed tomography (pQCT) that can measure bone mineral density with relatively minimal effort. However, non-human primate osteo-

logical samples are much more rare, and the use of radiography on living individuals is usually ethically and logistically unfeasible. Thus, much less is known about trabecular bone in non-human primates. Pauwels (1948), Kummer (1966, 1972) and Oxnard (1972, 1982, 1993) pioneered new 2D methods for assessing stress trajectories in relation to trabecular structure, focusing primarily on human vertebrae or ilia but often within a broader, comparative and/or evolutionary context. Some of the first 2D studies of trabecular morphology in non-human primates were on the femur and vertebrae of a rhesus macaque (Beddoe, 1978), and talus and calcaneus of two sympatric species of lemur (Ward & Sussman, 1979). It was not until much later that Rafferty (1996; Rafferty & Ruff, 1994) conducted the first extensive comparative 2D trabecular analysis, looking at the humerus and femur in a large sample of prosimian and anthropoid primates.

However, 2D analyses provide only a single image of trabecular structure within an entire epiphysis or bone, and thus are limited in what can be inferred with regards to trabecular architecture and ultimately function. If one wishes to investigate trabecular structure in 3D in any extant or fossil primate, access to high-resolution (e.g. voxel size of ~30 µm) micro-CT is required. The resolution limits of medical CT (e.g. ~200 µm) are usually greater than the thickness of individual trabeculae and thus cannot reliably reproduce trabecular architecture (for a review of technological limitations, see Scherf, 2008). Limited access to micro-CT and the time-consuming and costly nature of dealing with large 3D data sets were the main limitations on 3D analyses of trabecular bone in non-human primates. Furthermore, when it comes to fossils, one can only study trabecular structure if the trabeculae themselves are sufficiently preserved.

Fajardo & Müller (2001) conducted one of the first 3D analyses of non-human hominoid trabecular bone using micro-CT. They investigated how differences in trabecular morphology of the proximal humerus and femur varied with arboreal and terrestrial locomotor behaviour in one gibbon, spider monkey, rhesus macaque and baboon. Fajardo & Müller (2001) found that variation in the degree of anisotropy correlated with locomotor differences in a predictable way: the more arboreal gibbon and spider monkey, which presumably have more variable loading of their humerus and femur, had more isotropic (i.e. less aligned) trabecular structure than the macaque and baboon with more stereotypical loading at the shoulder and hip. This research also laid important groundwork for investigating trabecular bone across different species that can vary greatly in morphology and body size; in particular, the challenges associated with making sure one is comparing homologous trabecular morphology with regards to anatomical location and amount of trabeculae being quantified [i.e. size and location of a volume of interest (VOI); Fajardo & Müller, 2001; Kivell et al. 2011a,b; Lazenby et al. 2011].

40 However, Fajardo et al. (2007) conducted a more extensive analysis of trabecular structure in the proximal femur (superior and inferior femoral neck) on a larger primate sample that contradicted the results of their previous study (Fajardo & Müller, 2001). They did not find a clear correlation between variation in trabecular structure and differences in locomotor behaviour. Instead, they found a high degree of overlap in trabecular parameters (including, among others, BV/TV and degree of anisotropy) across quadrupedal (*Colobus*, *Macaca*, *Papio*) and climbing/suspensory (*Ateles*, *Symphalangus*, *Alouatta*) taxa. Despite the addition of potential inherent differences in body size and phylogeny across the sample, 'taxa in this study share more similarities in femoral neck trabecular structure than differences and these similarities belie any correlation of structure with locomotor mode' (Fajardo et al. 2007: 431). They suggested that there may be greater similarity in hip joint loading across quadrupedal and climbing/suspensory primates than previously considered and/or that current models of anthropoid hip joint mechanics are overly simplistic.

The absence of a clear correlation between trabecular structure and predicted loading differences based on locomotor behaviour found by Fajardo et al. (2007) is just one of many studies on extant primates, or hominoids specifically, that have yielded equivocal results (Viola, 2002; Maga et al. 2006; Scherf, 2007, 2008; Cotter et al. 2009; Ryan et al. 2010; Ryan & Walker, 2010; DeSilva & Devlin, 2012; Shaw & Ryan, 2012; Schilling et al. 2014). For example, Ryan & Walker (2010) investigated variation in proximal humeral and femoral trabecular structure in relation to relative differences in forelimb and hindlimb use across five anthropoid primates. Despite predictions of higher loading of the humerus in brachiators (*Symphalangus*), higher loading of the femur in climbing arboreal quadrupeds (*Pan* and *Alouatta*) and equal loading of both limbs in terrestrial quadrupeds (*Papio* and *Presbytis*), all taxa had significantly higher BV/TV in the femur and greater isotropy in the humerus (see also Shaw & Ryan, 2012). Thus, similar to the findings of Fajardo et al. (2007), these results also suggest broad similarities in trabecular bone structure of the humerus and femur across anthropoid primates.

Although most trabecular studies to date have focused on the proximal humerus and femur (Rafferty & Ruff, 1994; Rafferty, 1996; MacLatchy & Müller, 2002; Ryan & Ketcham,

41 2002a,b, 2005; Viola, 2002; Ryan & van Rietbergen, 2005; Ryan & Krovitz, 2006; Fajardo et al. 2007; Scherf, 2007, 2008; Saporin et al. 2011; Ryan & Shaw, 2013; Scherf et al. 2013), equivocal results are not limited to just these bones.

42 For example, Ryan et al. (2010) also found no significant differences in the trabecular structure of the mandible in platyrrhines that habitually engage in gouging feeding behaviour (*Callithrix*) vs. non-gouging species (*Sanguinus*

43 and *Saimiri*). Schilling et al. (2014) found that variation in wrist bone (scaphoid, lunate and capitate) trabecular structure did not correlate with predicted loading differences

from locomotor behaviour. Similar equivocal results have been found in the hominoid calcaneus (Maga et al. 2006), talus (DeSilva & Devlin, 2012) and thoracic vertebrae (Cotter et al. 2007; but see Oxnard & Yang, 1981; Oxnard, 1997). 44

In contrast to hominoids and studies of anthropoid primates more generally, more clear functional signals have been found in the trabecular structure of extant strepsirrhines (MacLatchy & Müller, 2002; Ryan & Ketcham, 2002a, 2005). Leaping galagines (*Galago*), indriids (*Avahi*) and tarsiers (*Tarsius*), predicted to have more stereotypical hip joint loading than quadrupedal or slow climbing taxa, have more anisotropic trabeculae than non-leaping taxa (*Cheirogaleus*, *Loris*, *Perodicticus* and *Otolemur*; Ryan & Ketcham, 2002a, 2005). An earlier study by MacLatchy & Müller (2002) on a smaller sample (*Perodicticus* and *Galago*) found similar results. Furthermore, a comparative analysis of two fossil omomyid (*Omomys* and *Shoshonius*) femora showed variation in the trabecular structure suggesting important differences in joint loading and locomotor behaviour not revealed by the external morphology (Ryan & Ketcham, 2002b). Although Ryan & Ketcham (2002a) also noted a large degree of intraspecific variation in all taxa, suggesting that the trabecular structure was potentially also responding to subtle differences in individual behaviour, these results suggest that the locomotor behaviours of strepsirrhines may engender more divergent and/or stereotypical loading of the joints than is typical of a comparable sample of anthropoid primates (Demes et al. 1994; Hirasaki et al. 2000; Schmitt & Hanna, 2004).

Why so many equivocal results in analyses of hominoid trabecular bone?

Within primates, most trabecular studies have focused on hominoids, in part because of their close relationship to humans and their potential to help infer behaviour in fossil hominoids and hominins (Macchiarelli et al. 1999; Rook et al. 1999; Griffin, 2008; DeSilva & Devlin, 2012; Shaw & Ryan, 2012; Barak et al. 2013b; Scherf et al. 2013; Su et al. 2013; Tsegai et al. 2013; Schilling et al. 2014; Raichlen et al. 2015). Despite substantial variation in locomotion across extant hominoids, including highly specialized brachiation and suspension in Asian apes, and distinct knuckle-walking locomotion in African apes, many of these studies have yielded results that neither fit specific predictions of differences in external joint loading, nor broader 'suspensory' or 'quadrupedal' signals when compared with other non-hominoid primates that engage in similar behaviours (e.g. *Ateles* or *Alouatta*; DeSilva & Devlin, 2012; Shaw & Ryan, 2012; Schilling et al. 2014). There may be several reasons for these ambiguous results.

First, locomotion and body size are highly variable within hominoids. This includes variation in frequency of certain behaviours, even between species (e.g. *Gorilla* vs. *Pan* or *P. troglodytes* vs. *P. paniscus*), that are generally catego-

1 rized in the same broad locomotor categories (e.g.
 2 'knuckle-walkers'; Hunt, 1991; Doran, 1993; Remis, 1995).
 3 Reasons for variation in certain locomotor behaviours can
 4 relate to ecology (Doran & Hunt, 1994), body size (Cant,
 5 1992; Hunt, 1994) or even social rank (Hunt, 1992; Remis,
 6 1995), which is often information not associated with osteo-
 7 logical specimens. If, for example, trabecular bone is
 8 responding to more infrequent but dynamic loads (Burr,
 9 1990) rather than habitual daily activity, then slight differ-
 10 ences in the frequency of certain behaviours (e.g. suspen-
 11 sion, climbing) may have significant effects on the overall
 12 trabecular structure, creating greater intraspecific variation
 13 and greater overlap among different locomotor groups.
 14 Indeed, several recent trabecular studies demonstrate a
 15 high degree of intraspecific variation in trabecular structure
 16 in many taxa, such as *Pongo* (Tsegai et al. 2013) and
 17 humans (Ryan & Shaw, 2012, 2015). Furthermore, there can
 18 be substantial intraspecific variation in body mass between
 19 sexes (Plavcan & van Schaik, 1997), which can be challeng-
 20 ing to accommodate and investigate in the typically small
 21 samples available for micro-CT scanning. Although most tra-
 22 becular parameters have recently been shown to be nega-
 23 tively allometric across different primate or mammalian
 24 taxa (Doube et al. 2011; Ryan & Shaw, 2013), potential vari-
 25 ation in scaling within a taxon [i.e. between sexes and in
 26 the absence of broad-scale differences in body mass, such as
 27 when comparing dwarf shrews and elephants (Doube et al.
 28 2011) or galagos and gorillas (Ryan & Shaw, 2013)] is not
 29 well understood.

30 Second, the majority of trabecular studies to date have
 31 focused on the proximal humerus and/or femur. Although
 32 their globular epiphyses makes them relatively easy
 33 anatomical structures in which to analyse trabeculae, the
 34 shoulder and hip are complex joints, loaded in multiple
 35 directions from both soft tissues and substrate reaction
 36 forces. The kinematics of these joints during different types
 37 of locomotion, particularly arboreal behaviours, is not well
 38 understood (Bergmann et al. 1984; Larson, 1995; Chan,
 39 2007, 2008). Our predictions of joint loading across differ-
 40 ent species may be either too simplistic (Fajardo et al. 2007)
 41 or, alternatively, loading at these joints may actually be
 42 **45** more similar than we would instinctively expect. For exam-
 43 ple, there are broad similarities in hip joint loading
 44 between bipeds and quadrupeds (Bergmann et al. 1984,
 45 1993, 1999). Finally, the proximal humerus and femur are
 46 relatively removed from the external loading of substrate
 47 reaction forces compared with more distal skeletal elements
 48 (e.g. metacarpals or distal tibia), which may obscure the
 49 adaptive response of trabecular bone. In short, it may be
 50 that the trabecular structure of the hip and shoulder are
 51 limited in their value for containing a strong locomotor-spe-
 52 cific functional signal (Rafferty, 1996; Fajardo et al. 2007;
 53 Shaw & Ryan, 2012).

54 Third, such problems understanding joint loading at the
 55 shoulder and hip highlight a more general problem in

trabecular studies: that most trabecular analyses are based
 on relatively simplistic and coarse biomechanical models
 (Fajardo et al. 2007; Ryan & Walker, 2010; Ryan & Shaw,
 2012; Tsegai et al. 2013). Collection of the necessary biome-
 mechanical data, such as the kinematics of joint movement,
 ground reaction forces or electromyography of muscles, are
 all inherently challenging in extant primates for a number
 of logistical and ethical reasons (Vereecke et al. 2011). Thus,
 in the absence of specific biomechanical data, researchers
 are often forced to make predictions about how trabecular
 structure might vary based on relatively crude assumptions
 about habitual joint postures. The coarseness of the biome-
 mechanical models is in direct contrast to the incredibly precise
 information on trabecular structure that one can gain from
 micro-CT.

Fourth, phylogeny may also confound potential func-
 tional signals in trabecular bone, particularly in studies that
 have focused mainly on closely related taxa like hominoids.
 Only recently have trabecular studies addressed the influ-
 ence of phylogeny on individual parameters (that also
 account for variation in body size) using, for example, inde-
 pendent contrasts (Doube et al. 2011), the *K* statistic (Ryan
 & Shaw, 2012), phylogenetic generalized least squares (Ryan
 & Shaw, 2013) or independent evolution and phylogenetic
 general least squares (Smaers & Vinicius, 2009; Tsegai et al.
 2013). Some studies found only a minor phylogenetic influ-
 ence (Doube et al. 2011), while others found a more com-
 plex pattern of influence that varied across elements and
 taxonomic groups (Ryan & Shaw, 2013). Thus, the potential
 influence of phylogeny and how this might confound func-
 tional interpretations should not be ignored in comparative
 primate studies. **46**

Finally, some of the equivocal results from trabecular
 studies may be, in part, a consequence of methodology.
 Over the last decade, the traditional method of analysing
 trabecular structure in 3D is to quantify trabecular bone in
 a VOI, such as a sphere or cube within an epiphysis
 (Fig. 4A). The main advantage of the VOI method is that it
 is computationally feasible; it allows one to extract and
 quantify a portion of a complex structure from a much lar-
 ger and cumbersome micro-CT data set. There have been
 varied methods of determining VOI size and position (Ryan
 & Ketcham, 2002a; Griffin et al. 2011; Schilling et al. 2014),
 and further discussion about the potential bias resulting
 from variation in VOI size and position (Fajardo & Müller,
 2001; Maga et al. 2006; Kivell et al. 2011a,b; Lazenby et al.
 2011). Studies using VOIs aim to quantify a functionally
 informative trabecular subsection that is considered repre-
 sentative of the region or epiphysis being analysed.

However, there are several inherent limitations to the
 VOI method that are difficult to avoid. VOI size and posi-
 tion are constrained by the trabecular morphology itself,
 such that a VOI must be large enough to quantify a mean-
 ingful amount of trabecular structure (e.g. at least four tra-
 becular struts; Gross et al. 2014), but small enough that it

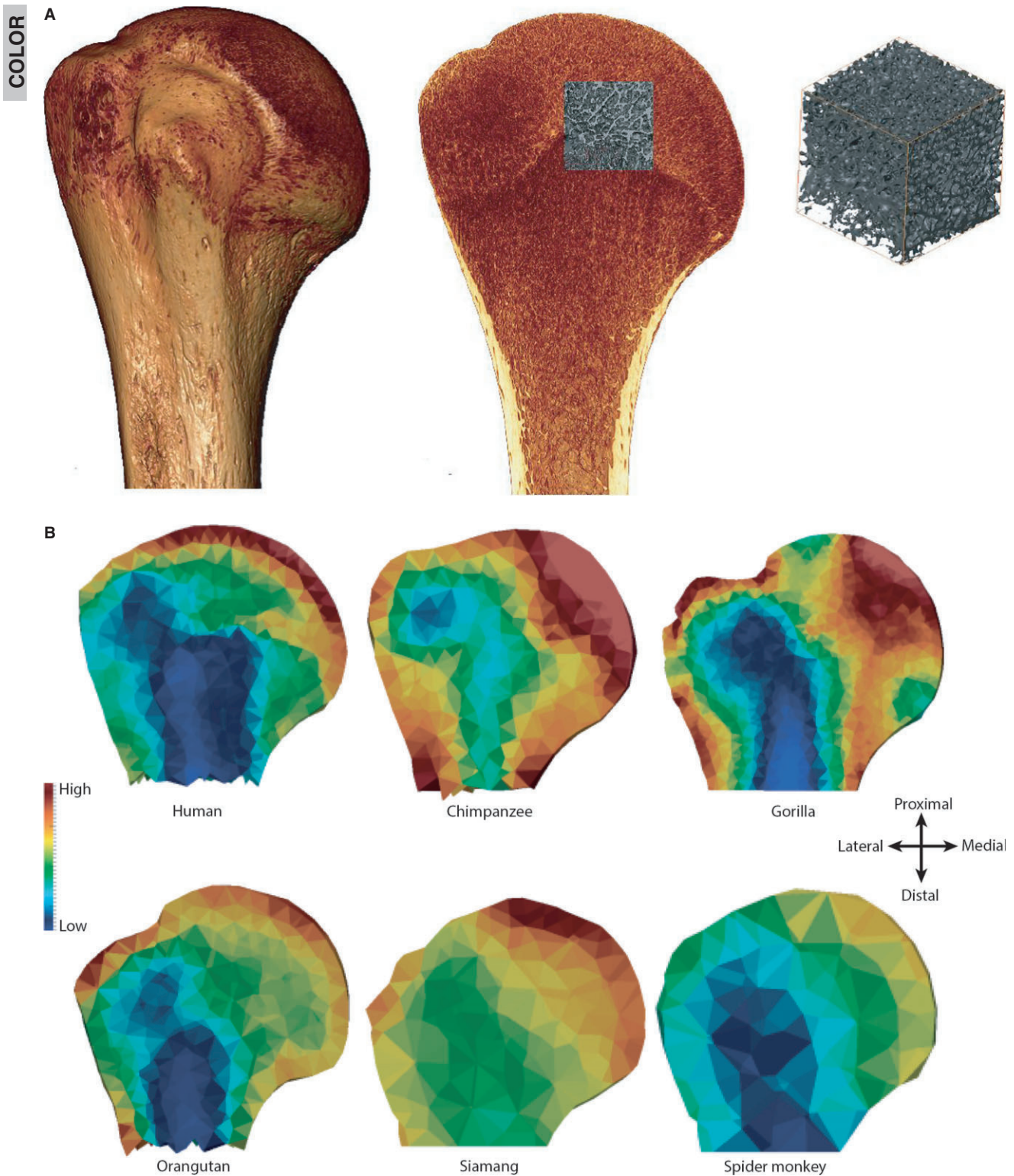


Fig. 4 Different methodological approaches to investigating trabecular bone. (A) The traditional volume of interest (VOI) method that analyses trabecular structure in a subsection of the epiphysis or bone. Here, an example is shown in the human proximal humerus in which the VOI is 30% of the geometric mean of the articular dimensions. (B) A new, holistic method [Medtool (Pahr & Zysset, 2009a; Gross et al. 2014)] that quantifies and visualizes variation in trabecular bone distribution (BV/TV) and stiffness throughout the entire epiphysis or bone. Here, variation in BV/TV is shown in a coronal cross-section throughout the proximal humerus in the same taxa and specimens shown in Fig. 3. Red indicates high BV/TV; blue indicates low BV/TV.

quantifies only trabeculae (i.e. avoiding cortical bone or anatomical features such as foramina). Therefore, it is often challenging to position VOIs near the subarticular surface where external joint loading is initially incurred, and the trabecular structure can be different from that deeper within the epiphysis (Singh, 1978; Currey, 2002). Positioning of VOIs is particularly difficult in small, irregular-shaped bones, such as tarsals and carpals (Schilling et al. 2014). Furthermore, there are several challenges associated with determining anatomically and/or biomechanically 'homologous' VOIs across a sample, especially when morphology is complex or there is a large degree of morphological and size variation (Maga et al. 2006; Kivell et al. 2011a,b; Lazenby et al. 2011). Although such methodological issues have been recognized by many researchers (Fajardo & Müller, 2001; Ryan & Ketcham, 2002a,b; Maga et al. 2006), these traditional methods have remained the standard in non-human primate studies due to computational limitations and the lack of alternative methods (see below).

A way forward

Recently, methods of analysing trabecular structure have evolved and improved. Several studies have taken an approach of placing multiple VOIs within an anatomical region with the aim of quantifying more detailed information about joint loading, albeit with varied success (DeSilva & Devlin, 2012; Su et al. 2013). Analysis of multiple trabecular parameters (derived from a single VOI) together using, for example, principal components analysis, has revealed combined patterns of trabecular structure that more clearly differentiate primate locomotor behaviour than specific parameters in isolation (Kivell et al. 2012; Ryan & Shaw, 2012; Scherf et al. 2013; Matarazzo, 2015). For example, Scherf et al. (2013) found a clear separation in the humeral trabecular structure across humans, orangutans and chimpanzees when BV/TV, rod- vs. plate-like trabeculae, trabecular number and spacing were considered together. Ryan & Shaw (2012), in a much larger anthropoid sample, also found that distinct combinations of variation in similar trabecular parameters could reasonably differentiate (via discriminant functional analysis) between different primate locomotor groups in the femur and, to a lesser degree, in the humerus. However, Ryan & Shaw (2012) also found that there was still a large degree of overlap in trabecular morphology, even across locomotor groups that would presumably have quite distinct loading of their shoulder and hip joints [e.g. bipeds (humans), quadrumanus climbers (orangutans) and arboreal quadrupeds (crab-eating macaques)].

The recent use of both comparative and experimental data in trabecular analyses by Barak et al. (2013b) is an ideal approach for better understanding the potential functional significance of variation (both inter- and intraspecific) in trabecular structure in extant and fossil taxa. They used kinematic and ground reaction force data collected on

chimpanzees during terrestrial knuckle-walking and humans during bipedalism (with both extended- and bent-hip-bent-knee gaits) to interpret variation in the trabecular structure of the distal tibia. They found that the principal trabecular orientation in chimpanzees was more obliquely angled than in humans, reflecting a more dorsiflexed tibio-talar joint at midstance than the more extended ankle joint in normal (i.e. extended hip and knee) human bipedal walking. Furthermore, they used these results to interpret the trabecular structure of fossil hominin distal tibiae; the principal trabecular orientation of the fossil hominin specimens was most similar to that of normal human bipedalism than the more dorsiflexed ankle joint loading of the bent-hip-bent-knee gait, suggesting that *Australopithecus africanus* (and a tibia putatively assigned to early *Homo*) likely used an extended-hip-extended-knee bipedal gait (Barak et al. 2013a,b).

More recently, a method originally developed for *in vivo* clinical studies of osteoporosis (Pahr & Zysset, 2009a,b) has been adapted for analyses of high-resolution trabecular bone across primates (Gross et al. 2014). This method uses an in-house script written for medtool (http://www.dr-pahr.at/index_en.php) that allows one to visualize and quantify trabecular (and cortical) morphology throughout the entire epiphysis or bone, rather than just a small VOI subsection of trabeculae (Fig. 4B). In particular, one can visualize via colour maps the distribution of trabecular bone and how BV/TV or stiffness vary throughout the epiphysis/bone, including just below the cortical bone where external load is first incurred. Thus, this method provides the ability to better reconstruct joint position of peak loading during habitual behaviours than is possible from, for example, a VOI positioned within the centre of an epiphysis (Shaw & Ryan, 2012; Scherf et al. 2013) or bone (Schilling et al. 2014). The downside of medtool, however, is that it does not yet provide the ability to statistically compare differences in trabecular structure across individuals or taxa, which is possible with traditional VOI methods.

The holistic medtool approach has been applied successfully to hominoid metacarpals (Stephens, 2012; Tsegai et al. 2013; Skinner et al. 2015), humeri (Davenport, 2013) and carpal bones (Bird, 2014; Fig. 4B). For example, the region of greatest BV/TV and trabecular stiffness throughout the third metacarpal head (Mc3) fits predictions of peak loading during habitual locomotor and manipulative behaviours across hominoids; a more dorsal concentration of trabecular bone on the Mc3 head in *Pan* and *Gorilla* is consistent with the extended metacarpophalangeal joint position during knuckle-walking (Jenkins & Fleagle, 1975), while a more palmar concentration is found in *Pongo*, hylobatids and humans, consistent with a flexed metacarpophalangeal joint during arboreal grasping (Asian apes) and manipulation (humans; Tsegai et al. 2013). A similar correlation between trabecular bone distribution and inferred joint position was also found in the Mc1 and Mc5 epiphyses; in

particular, highlighting a distinct pattern in humans consistent with forceful opposition between the thumb and the fingers (Stephens, 2012; Foote, 2013; Skinner et al. 2015). A human-like distribution of trabecular bone in some fossil hominins was used to suggest the ability for forceful precision or power squeeze gripping in *Australopithecus africanus* (Skinner et al. 2015). Although the average BV/TV or trabecular thickness values derived from the entire epiphyses revealed some overlap across extant (and fossil) hominoids (Tsegai et al. 2013; Skinner et al. 2015), similar to the results of previous VOI studies (Shaw & Ryan, 2012), the ability to visualize how trabecular structure varies throughout the bone can be more informative for reconstructing joint position, and ultimately behaviour, in fossil taxa. Currently, medtool is limited to quantifying BV/TV and trabecular stiffness (Gross et al. 2014), but can be used in conjunction with traditional VOI methods to quantify additional trabecular parameters (e.g. trabecular thickness or number) in regions of interest (Davenport, 2013) and calculate mean values for the entire trabecular structure using freeware, such as BoneJ (Doubé et al. 2010; Tsegai et al. 2013).

Trabecular bone functional adaptation in fossils

The decades-long debates regarding fossil hominoid or fossil hominin behaviour can only be resolved, at least to some degree, with analyses of bony morphology that is more responsive to load during life than the external bone shape and size. Trabecular bone can provide this insight. However, to move forward, palaeoanthropologists must make some assumptions about trabecular bone functional adaptation, despite the caveats and ambiguity from analyses of extant taxa discussed above. For example, we generally assume that the patterns and variation we see in trabecular bone structure in fossil taxa reflect loading from habitual behaviours, rather than more rare, but dynamic loading. Several comparative and experimental studies support this assumption (Rubin et al. 2001, 2002; Barak et al. 2013b; Tsegai et al. 2013), but others do not (Barak et al. 2011). We must also assume that the general genetic, developmental or metabolic factors that influence trabecular bone structure, growth and remodelling in extant taxa are the same in fossil taxa as well. The general similarity in some of these processes across different mammals provides support for this assumption (Turner, 2001), but important exceptions have been noted (Chow et al. 1993; Erben, 1996; Aerssens et al. 1998; Barak et al. 2013a). Furthermore, for ethical reasons, those interested in primates are forced to rely on other animal models (e.g. rodents, sheep) for *in vivo* testing of trabecular bone functional adaptation, or computer simulation methods. Thus, there will always be some degree of the 'unknown' in analyses of extant and fossil primates that cannot be avoided.

However, the disconnect between trabecular bone functional adaptation and variation in hominoid trabecular bone that has been prevalent in the last decade of research can be improved upon. Access to micro-CT is now easier and more affordable. Thus, larger extant samples that accommodate intraspecific variation in sex, body size or locomotor behaviour may help tease out functional signals in trabecular bone that have been previously obscured (Kivell et al. 2012). We continue to increase our understanding of variation in ecology and behaviour across different extant hominoid (and primate) taxa, particularly subspecies (Thorpe & Crompton, 2006; Pruetz & Bertolani, 2009; Wich et al. 2009) that were once lumped together into a sample of, for example, '*Pan*' or '*Pongo*'. Although rare, the use of behavioural and ecological data that has been collected on specific individuals (e.g. Tai chimpanzees; Carlson et al. 2006) may further help to elucidate how particular frequencies of behaviours might be reflected in trabecular structure.

Methodological advancements in the analyses of bone structure are now more accessible and can provide more informed functional interpretations of fossil morphology. Holistic approaches such as medtool (Pahr & Zysset, 2009a; Gross et al. 2014) provide clear and specific information about individual and species differences in joint loading, and when used in combination with traditional VOI methods that allow for statistical comparisons we are much better equipped to quantify and interpret variation in trabecular structure. *In vivo* validation testing of trabecular strength (i.e. Young's modulus) is not possible in fossil specimens, but micro-FE modelling of fossil morphology within the context of a comparative, validated extant sample can be used to test the effectiveness of fossilized morphology (both internal and external) in different loading regimes (Richmond et al. 2005; Nguyen et al. 2014) that can ultimately shed light on behaviour (Fig. 5).

Kinematic data on joint posture and loading (e.g. force and pressure) during primate locomotor and manipulative behaviours are essential for accurately interpreting the functional significance of variation of trabecular structure across extant and fossil primates. There have been numerous studies over the last few decades, particularly on quadrupedal or bipedal gaits on horizontal substrates (Schmitt, 1999, 2003; Vereecke et al. 2003; D'Août et al. 2004; Hannah et al. 2006; Wunderlich & Jungers, 2009). However, there have been far fewer studies on arboreal primate behaviours, such as climbing and suspension (Isler, 2002a,b, 2004; Schoonaert et al. 2006; Channon et al. 2010). To better reconstruct behaviour in fossil hominoids and hominins, more detailed analyses on joint kinematics and loading in primates engaged in more naturalistic locomotor behaviours, particularly arboreal locomotion (Vereecke et al. 2011), and manipulative behaviours (Shaw et al. 2012; Williams et al. 2012) are needed. Such data will improve on the simplistic biomechanical models that are used, by necessity,

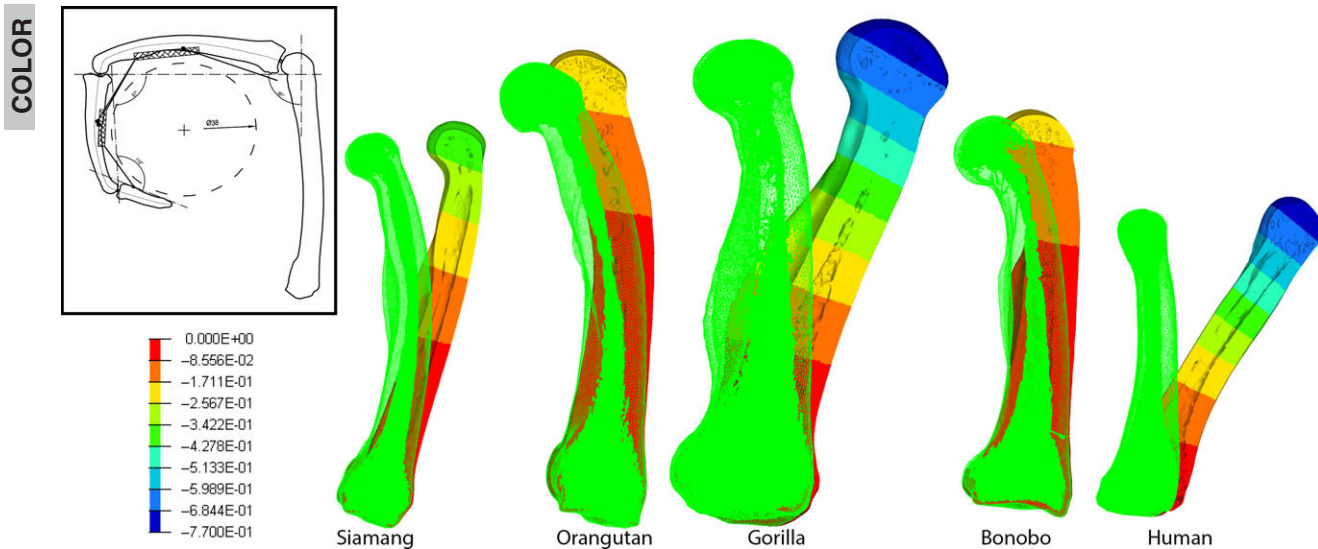


Fig. 5 Micro-finite element (μ FE) modelling of the primate phalanx. Using micro-CT, the true trabecular and cortical structure of the third proximal phalanx is modelled using μ FE in a static, suspensory posture (left inset image). The biomechanical model was validated by Richmond (2009) and tested via μ FE (Nguyen et al. 2014) on siamang phalanges. Here, this model is used to look at the displacement (how much the bone deforms under loading) across different extant hominoid taxa. Here, the displacement is $30 \times$ greater than actual so the deformation can be visualized. Due to variation in trabecular structure, cortical thickness and phalangeal curvature, one can see substantial variation in how well each phalanx copes with the external loading during a suspensory posture. Orangutans and bonobos show the least displacement, while gorilla and humans show the most. Adding fossil phalanges to this comparative context will provide greater insight into how well their external and internal morphology could cope with the compression and bending stress of suspensory grasping.

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in most trabecular studies to date. Together, incorporating biomechanical data and new trabecular methods into analyses of extant taxa, as well as knowing the potential limitations of trabecular bone structure and remodelling discussed above, will provide a better comparative context in which to make more informed functional interpretations of fossil specimens.

Although this review argues that trabecular bone is particularly informative for reconstructing behaviour in the past, it is, of course, not an isolated structure. Trabecular bone exists within a bone and its cortical shell that together, with soft tissues, serve to optimize biomechanical function within the skeleton as a whole. Thus, there are trade-offs between trabecular and cortical bone that, if analysed together, will provide a more informed reconstruction of behaviour in the past. Several studies of extant taxa have shown that cortical cross-sectional shape largely reflects biophysical loads rather than genetic factors (Jones et al. 1977; van der Meulen et al. 1993; Ruff et al. 1994, 2006; van der Meulen & Carter, 1995; van der Meulen et al. 1996). The cortical cross-sectional shape of long bones has been shown to differentiate locomotor behaviours across primates (Marchi, 2005; Ruff, 2009), or variation in behaviour and mobility across different human populations (Stock & Pfeifer, 2001; Shaw & Stock, 2013). However, because of the denser structure and slower remodelling rate of cortical bone (Eriksen, 1986), functional signals can be more ambiguous than that of trabecular bone. For example,

in vivo studies in a variety of animals have shown that limb bone shaft cross-sections are not always reinforced in the planes in which they are habitually loaded (Lanyon & Rubin, 1985; Judex et al. 1997; Demes et al. 1998; Lieberman et al. 2004; Wallace et al. 2014; but see Brassey et al. 2013). Thus, many have suggested caution when inferring functional loading patterns from cross-sectional shape, especially when one does not know the habitual loading behaviour or how bone may respond, such as in fossil taxa (Demes et al. 1998; Pearson & Lieberman, 2004; Wallace et al. 2014; but see Ruff et al. 2006; Brassey et al. 2013).

Regardless of the inherent complexity of cortical bone functional adaptation, the few primate studies that have analysed trabecular and cortical bone together have revealed interesting compensatory effects between the two structures (Skedros et al. 2004, 2012; Carlson & Judex, 2007; Carlson et al. 2008; Lazenby et al. 2008; Shaw & Ryan, 2012). For example, Shaw & Ryan (2012) showed in a sample of anthropoid primates that as trabecular bone increases in the humeral head, cortical diaphyseal strength also increases. Thus, even though loading at the shoulder joint and humeral midshaft is biomechanically distinct, when the humerus as a whole is loaded there is a morphological response in both trabecular and cortical bone. However, in other anatomical regions, the relationship between cortical and trabecular bone is more complex. In contrast to their humeral results, Shaw & Ryan (2012) found no correlation between trabecular structure in the femoral head and mid-

shaft cross-sectional geometry of the femur across their sample. In the femoral neck, variation in cortical bone may reflect more clearly differences in external load than trabecular bone across anthropoid primates (Fajardo et al. 2007), while in the specialized bipedal loading of human femoral neck, trabecular bone seems to play a more specific biomechanical role. The external loads elicit a pattern of 'trabecular eccentricity'; the asymmetrical (i.e. non-central) distribution of trabecular bone within the human femoral neck helps to reduce stress on the inferior aspect of the neck where strain and fracture risk is typically highest (Fox & Keaveny, 2001). Thus, analyses of both trabecular and cortical structure in extant taxa will provide a more holistic biomechanical interpretation and allow for more informed behavioural reconstructions in fossil taxa.

Concluding remarks

Like external bone morphology, trabecular bone architecture is the product of both genetic and non-genetic influences (Judex et al. 2004; Havill et al. 2010; Barak et al. 2011; Raichlen et al. 2015). However, it can be argued that the ability for trabecular bone to respond and adapt to mechanical stimuli throughout life, more so than external bone shape and size, makes it a particularly important source of functional information for reconstructing behaviour in the past. Teasing out the relevant functional signals (from the genetic, developmental or metabolic influences) in trabecular structure is not straightforward, as many of the comparative, experimental and computational modelling studies have demonstrated. However, variation in trabecular structure is our best source of morphological information that is preserved in the fossil record, particularly when analysed in conjunction with cortical bone, for reconstructing actual, rather than potential, behaviours in fossil hominoids and hominins.

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References

Aerssens J, Boonen S, Lowet G, et al. (1998) Interspecies difference in bone composition, density and quality; potential implications for *in vivo* bone research. *Endocrinology* **139**, 663–670.

- Alam I, Sun Q, Liu L, et al. (2005) Whole-genome scan for linkage to bone strength and structure in inbred Fischer 344 and Lewis rats. *J Bone Miner Res* **20**, 1589–1596.
- Almécija S, Tallman M, Alba DM, et al. (2013) The femur of *Orrorin tugenensis* exhibits morphometric affinities with both Miocene apes and later hominins. *Nat Comm* **4**, 2888.
- Amling M, Herden S, Posl M, et al. (1996) Heterogeneity of the skeleton: comparison of the trabecular microarchitecture of the spine, the iliac crest, the femur, and the calcaneus. *J Bone Miner Res* **11**, 36–45.
- Barak MM, Weiner S, Shahar R (2008) Importance of the integrity of trabecular bone to the relationship between load and deformation in rat femora: an optical metrology study. *J Mater Chem* **18**, 3855–3864.
- Barak MM, Lieberman DE, Hublin J-J (2011) A Wolff in sheep's clothing: trabecular bone adaptation in response to changes in joint loading orientation. *Bone* **49**, 1141–1151.
- Barak MM, Lieberman DE, Hublin J-J (2013a) Of mice, rats and men: trabecular bone architecture in mammals scales to body mass with negative allometry. *J Struct Biol* **183**, 123–131.
- Barak MM, Lieberman DE, Raichlen D, et al. (2013b) Trabecular evidence for a human-like gait in *Australopithecus africanus*. *PLoS ONE* **8**, e77687.
- Bass S, Delmas PD, Pearce G, et al. (1999) The differing tempo of growth in bone size, mass, and density in girls is region-specific. *J Clin Invest* **104**, 795–804.
- Bassey EJ, Ramsdale SJ (1994) Increase in femoral bone density in young women following high-impact exercise. *Osteoporosis Int* **4**, 72–75.
- Beddoe AH (1978) A quantitative study of the structure of trabecular bone in man, rhesus monkey, beagle and miniature pig. *Calcif Tissue Res* **25**, 273–281.
- Begun DR, Kivell TL (2011) Knuckle-walking in *Sivapithecus*? The combined effects of homology and homoplasy with possible implications for pongine dispersals. *J Hum Evol* **60**, 158–170.
- Berger LR, de Ruiter DJ, Churchill SE, et al. (2010) *Australopithecus sediba*: a new species of *Homo*-like australopithecine from South Africa. *Science* **328**, 195–204.
- Berger LR, Hawks J, de Ruiter DJ, et al. (2015) *Homo naledi*, a new species of the genus *Homo* from the Dinaledi Chamber, South Africa. *elife* **4**, e09560.
- Bergmann G, Siraky J, Rohlmann A (1984) A comparison of hip joint forces in sheep, dog, and man. *J Biomech* **17**, 907–921.
- Bergmann G, Graichen F, Rohlmann A (1993) Hip joint loading during walking and running measured in two patients. *J Biomech* **26**, 969–990.
- Bergmann G, Graichen F, Rohlmann A (1999) Hip joint forces in sheep. *J Biomech* **32**, 769–777.
- Bertram JEA, Swartz SM (1991) The 'law of bone transformation': a case of crying Wolff? *Biol Rev* **66**, 245–273.
- Biewener AA (1983) Allometry of quadrupedal locomotion: the scaling of duty factor, bone curvature, and limb orientation to body size. *J Exp Biol* **105**, 147–171.
- Biewener AA (1989) Scaling body support in mammals: limb posture and muscle mechanics. *Science* **245**, 45–48.
- Biewener AA (1990) Biomechanics of mammalian terrestrial locomotion. *Science* **250**, 1097–103.
- Biewener AA, Fazzalari NL, Konieczynski DD, et al. (1996) Adaptive changes in trabecular architecture in relation to functional strain patterns and disuse. *Bone* **19**, 1–8.
- Bikle DD, Halloran BP (1999) The response of bone to unloading. *J Bone Miner Metab* **17**, 233–244.

- Bird EE** (2014) Getting in touch with the hominoid wrist: locomotion, mobility and trabecular bone structure in the capitate. MSc dissertation, University College London.
- Brassey CA, Margetts L, Kitchener AC, et al.** (2013) Finite element modelling versus classic beam theory: comparing methods for stress estimation in morphologically diverse sample of vertebrate long bones. *J R Soc Interface* **10**, 20120823.
- Burr DB** (1985) Bone remodeling in response to *in vivo* fatigue microdamage. *J Biomech* **18**, 189–200.
- Burr DB** (1990) Experimental overload and bone adaptation. In: *Bone Morphometry* (ed. Takahashi HE), pp. 140–148. Japan, Nishimura: ??????????
- 55 Cant JGH** (1992) Positional behaviour and body size of arboreal primates: a theoretical framework for field studies and an illustration of its application. *Am J Phys Anthropol* **88**, 273–283.
- Carlson KJ, Judex S** (2007) Increased non-linear locomotion alters diaphyseal bone shape. *J Exp Biol* **210**, 3117–3125.
- Carlson KJ, Doran-Sheehy DM, Hunt KD, et al.** (2006) Locomotor behaviour and long bone morphology in individual free-ranging chimpanzees. *J Hum Evol* **50**, 394–404.
- Carlson K, Lublinsky S, Judex S** (2008) Do different locomotor modes during growth modulate trabecular architecture in the murine hind limb? *Integr Comp Biol* **48**, 385–393.
- Carter DR, Beaupré GS** (2001) *Skeletal Function and Form: Mechanobiology of Skeletal Development, Aging, and Regeneration*. Cambridge: Cambridge University Press.
- Carter DR, Orr TE, Fyhrie DP** (1989) Relationships between loading history and femoral cancellous bone architecture. *J Biomech* **22**, 231–244.
- Carter DR, Wong M, Orr TE** (1991) Musculoskeletal ontogeny, phylogeny, and functional adaptation. *J Biomech* **24**, 3–16.
- 56 Chan LK** (2007) Scapular position in primates. *Folia Primatol* **78**, 19–35.
- Chan LK** (2008) The range of passive arm circumduction in primates: do hominoids really have more mobile shoulders. *Am J Phys Anthropol* **136**, 265–277.
- Chang G, Pakin SK, Schweitzer ME, et al.** (2008) Adaptations in trabecular bone microarchitecture in Olympic athletes determined by 7T MRI. *J Magn Reson Imaging* **27**, 1089–1095.
- Channon AJ, Crompton RH, Günther MM, et al.** (2010) Biomechanics of leaping in gibbons. *Am J Phys Anthropol* **143**, 403–416.
- Chirchir H, Kivell TL, Ruff CB, et al.** (2015) Recent origin of low trabecular bone density in modern humans. *Proc Natl Acad Sci USA* **112**, 366–371.
- Chow JW, Badve S, Chambers TJ** (1993) Bone formation is not coupled to bone resorption in a site-specific manner in adult rats. *Anat Rec* **236**, 366–372.
- Christen P, Ito K, van Reitbergen B** (2015) A potential mechanism for allometric trabecular bone scaling in terrestrial mammals. *J Anat* **226**, 239–243.
- Churchill SE, Morris AG** (1998) Muscle marking morphology and labour intensity in prehistoric Khoisan foragers. *Int J Osteoarchaeol* **8**, 390–411.
- Cotter MM, Simpson SW, Latimer BM, et al.** (2009) Trabecular microarchitecture of hominoid thoracic vertebrae. *Anat Rec* **292**, 1098–1106.
- Cowin SC (ed.)** (2001) *Bone Biomechanics Handbook*. 2nd edn. Boca Raton: CRC Press.
- Cowin SC, Hart RT, Baleser JR, et al.** (1985) Functional adaptation in long bones: establishing *in vivo* values for surface remodeling rate coefficients. *J Biomech* **18**, 665–684.
- Cunningham CA, Black SM** (2009a) Anticipating bipedalism: trabecular organization in the newborn ilium. *J Anat* **214**, 817–829.
- Cunningham CA, Black SM** (2009b) Development of the fetal ilium – challenging concepts of bipedality. *J Anat* **214**, 91–99.
- Cunningham CA, Black SM** (2010) The neonatal ilium – metaphyseal drivers and vascular passengers. *Anat Rec* **293**, 1297–1309.
- Currey JD** (2002) *Bones: Structure and Mechanics*. Princeton: Princeton University Press.
- Dainton M** (2001) Did our ancestors knuckle-walk? *Nature* **410**, 324–325.
- D’Aout K, Vereecke E, Schoonaert K, et al.** (2004) Locomotion in bonobos (*Pan pansicus*): differences and similarities between bipedal and quadrupedal terrestrial walking, and a comparison with other locomotor modes. *J Anat* **204**, 353–361.
- Davenport R** (2013) Does internal bone structure of the humerus reflect locomotor behaviour in extant apes and fossil hominins? MSc dissertation, University College :London.
- Demes B, Larson J, Stern J, et al.** (1994) The kinetics of primate quadrupedalism: ‘hindlimb drive’ reconsidered. *J Hum Evol* **26**, 353–374.
- Demes B, Stern JT Jr, Hausman MR, et al.** (1998) Patterns of strain in the macaque ulna during functional activity. *Am J Phys Anthropol* **106**, 87–100.
- Dempster DW** (2000) The contribution of trabecular architecture to cancellous bone quality. *J Bone Min Res* **15**, 20–23.
- DeSilva JM, Devlin MJ** (2012) A comparative study of the trabecular bony architecture of the talus in humans, non-human primates, and *Australopithecus*. *J Hum Evol* **63**, 536–551.
- DeSilva JM, Holt KG, Churchill SE, et al.** (2013) The lower limb and mechanics of walking in *Australopithecus sediba*. *Science* **340**, 123299.
- Djukic K, Milovanovic P, Hahn M, et al.** (2015) Bone microarchitecture at muscle attachment sites: the relationship between macroscopic scores of entheses and their cortical and trabecular microstructure design. *Am J Phys Anthropol* **157**, 81–93.
- Doran DM** (1993) Comparative locomotor behaviour of chimpanzees and bonobos: the influence of morphology on locomotion. *Am J Phys Anthropol* **91**, 83–98.
- Doran DM, Hunt KD** (1994) Comparative locomotor behavior of chimpanzees and bonobos: species and habitat differences. In: *Chimpanzee Cultures*. (eds Wrangham RW, McGrew WC, deWaal FB, Heltne PG), pp. 93–106. Cambridge, Massachusetts: Harvard University Press.
- Doube M, Klosowski MM, Aganda-Carreras I, et al.** (2010) BoneJ: free and extensible bone image analysis in ImageJ. *Bone* **47**, 1076–1079.
- Doube M, Klosowski MM, Wiktorowicz-Conroy AM, et al.** (2011) Trabecular bone scales allometrically in mammals and birds. *Proc R Soc B* ?????, ???–?????. doi:10.1098/rspb.2011.0069.
- 57 Eliot DJ, Jungers WL** (2000) Fifth metatarsal morphology does not predict presence or absence of fibularis tertius muscle in hominids. *J Hum Evol* **38**, 333–342.
- Erben RG** (1996) Trabecular and endocortical bone surfaces in the rat: modeling or remodeling? *Anat Rec* **246**, 39–46.
- Eriksen EF** (1986) Normal and pathological remodeling of human trabecular bone: three dimensional reconstruction of the remodeling sequence in normals and in metabolic bone disease. *Endocr Rev* **7**, 379–408.

- Eriksen EF** (2010) Cellular mechanisms of bone remodelling. *Rev Endocr Metab Disord* **11**, 219–227.
- Eriksen EF, Mosekilde L, Melsen F** (1985) Trabecular bone resorption depth decreases with age: differences between normal males and females. *Bone* **6**, 141–146.
- Eshed V, Gopher A, Galili E, et al.** (2004) Musculoskeletal stress markers in Natufian hunter gatherers and Neolithic farmers in the Levant: the upper limb. *Am J Phys Anthropol* **123**, 303–315.
- Fajardo RJ, Müller R** (2001) Three-dimensional analysis of non-human primate trabecular architecture using micro-computed tomography. *Am J Phys Anthropol* **115**, 327–336.
- Fajardo RJ, Müller R, Ketcham R, et al.** (2007) Nonhuman anthropoid primate femoral neck trabecular architecture and its relationship to locomotor mode. *Anat Rec* **290**, 422–436.
- Fajardo RJ, DeSilva JM, Manoharan RK, et al.** (2013) Lumbar vertebral body bone microstructural scaling in small to medium-sized strepsirrhines. *Anat Rec* **296**, 210–226.
- Fleagle JG** (2013) *Primate Adaptation and Evolution*, 3rd edn. New York: Academic Press.
- Footo AC** (2013) Getting a grip on the past: trabecular structure in the fifth metacarpal head of extant and fossil hominoids. MSc dissertation, University College :London.
- Fox JC, Keaveny TM** (2001) Trabecular eccentricity and bone adaptation. *J Theor Biol* **212**, 211–221.
- Frey-Rindova P, de Bruin ED, Stüssi E, et al.** (2000) Bone mineral density in upper and lower extremities during 12 months after spinal cord injury measured by peripheral quantitative computed tomography. *Spinal Cord* **38**, 26–32.
- Frost HM** (1987) Bone ‘mass’ and the ‘mechanostat’: a proposal. *Anat Rec* **219**, 1–9.
- Frost HM** (1990) Skeletal structural adaptations to mechanical usage (SATMU): 1. Redefining Wolff’s law: the bone modelling problem. *Anat Rec* **226**, 403–413.
- Garden RS** (1961) The structure and function of the proximal end of the femur. *J Bone Joint Surg* **43B**, 576–589.
- Gibson LJ** (1985) The mechanical behaviour of cancellous bone. *J Biomech* **18**, 317–328.
- Gibson LJ, Ashby MF** (1997) *Cellular Solids: Structure and Properties*. New York: Cambridge University Press.
- Goldstein SA, Goulet R, McCubbrey D** (1993) Measurement and significance of three-dimensional architecture to the mechanical integrity of trabecular bone. *Calcif Tissue Int* **53**(S1), S127–S133.
- Gosman JH, Ketcham RA** (2009) Patterns in ontogeny of human trabecular bone from SunWatch Village in the prehistoric Ohio Valley: general features of microarchitectural change. *Am J Phys Anthropol* **138**, 318–332.
- Griffin NL** (2008) Bone architecture of the hominin second proximal pedal phalanx: a preliminary investigation. *J Hum Evol* **54**, 162–168.
- Griffin NL, D’Aouit K, Ryan TM, et al.** (2011) Comparative fore-foot trabecular bone architecture in extant hominids. *J Hum Evol* **59**, 202–213.
- Gross T, Kivell TL, Skinner MM, et al.** (2014) A CT-image-based framework for the holistic analysis of cortical and trabecular bone morphology. *Paleontol Electron* **17**, A17333.
- Guldberg RE, Caldwell NJ, Guo XE, et al.** (1997) Mechanical stimulation of tissue repair in the hydraulic bone chamber. *J Bone Miner Res* **12**, 1295–1302.
- Gupta A, Bayraktar HH, Fox JC, et al.** (2007) Constitutive modeling and algorithmic implementation of a plasticity-like model for trabecular bone structures. *Comput Mech* **40**, 61–72.
- Hahn M, Vogel M, Pompesius-Kempa M, et al.** (1992) Trabecular bone pattern factor: a new parameter for simple quantification of bone microarchitecture. *Bone* **13**, 327–330.
- Hall BK** (1985) *Research and the development and structure of the skeleton since the publication of Bones. And introduction to Bones: a study of the development and structure of the vertebrate skeleton by Murray PDF (originally published in 1936, reissued 1985)*, pp. xi–xlix. Cambridge University Press, Cambridge.
- Hammers A** (2015) The paradox of Wolff’s theories. *Ir J Med Sci* **184**, 13–22.
- Hannah JB, Polk JD, Schmitt D** (2006) Forelimb and hindlimb forces in walking and galloping primates. *Am J Phys Anthropol* **130**, 529–535.
- Harrigan TP, Mann RW** (1984) Characterization of microstructural anisotropy in orthotropic materials using a second rank tensor. *J Mater Sci* **19**, 761–767.
- Harrison LCV, Nikander R, Sikiö M, et al.** (2011) MRI texture analysis of femoral neck: detection of exercise load-associated differences in trabecular bone. *J Magn Reson Imaging* **34**, 1359–1366.
- Havill LM, Allen MR, Bredbenner TL, et al.** (2010) Heritability of lumbar trabecular bone mechanical properties in baboons. *Bone* **46**, 835–840.
- Hawkey DE** (1998) Disability, compassion and the skeletal record: using musculoskeletal stress markers (MSM) to construct an osteobiography from early New Mexico. *Int J Osteoarchaeol* **8**, 326–340.
- Hernandez CJ, Loomis DA, Cotter MM, et al.** (2009) Biomechanical allometry in hominoid thoracic vertebrae. *J Hum Evol* **56**, 462–470.
- Hirasaki E, Kumakura H, Matano S** (2000) Biomechanical analysis of vertical climbing in the spider monkey and the Japanese macaque. *Am J Phys Anthropol* **113**, 455–472.
- Hodgskinson R, Currey JD** (1990) Effects of structural variation on Young’s modulus of non-human cancellous bone. *J Eng Med* **204**, 43–52.
- Hollister SJ, Brennan JM, Kikuchi N** (1994) A homogenization sampling procedure for calculating trabecular bone effective stiffness and tissue level stress. *J Biomech* **27**, 433–444.
- Homminga J, van Reitbergen B, Lochmüller EM, et al.** (2004) The osteoporotic vertebral structure is well adapted to the loads of daily life, but not to infrequent ‘error’ loads. *Bone* **34**, 510–516.
- Huiskes R, Ruimerman R, van Lenthe GH, et al.** (2000) Effects of mechanical forces on maintenance and adaptation of form in trabecular bone. *Nature* **405**, 704–706.
- Hunt KD** (1991) Mechanical implications of chimpanzee positional behaviour. *Am J Phys Anthropol* **86**, 521–536.
- Hunt KD** (1992) Social rank and body size as determinants of positional behaviour in *Pan troglodytes*. *Primates* **33**, 347–357.
- Hunt KD** (1994) Body size effects on vertical climbing among chimpanzees. *Int J Primatol* **15**, 855–865.
- Isler K** (2002a) Characteristics of vertical climbing in gibbons. *Evol Anthropol* **11**, 49–52.
- Isler K** (2002b) Characteristics of vertical climbing in African apes. *Senckenb Lethaea* **82**, 115–124.
- Isler K** (2004) Footfall patterns, stride length and speed of vertical climbing in spider monkeys (*Ateles fusciceps robustus*) and woolly monkeys (*Lagothrix lagotricha*). *Folia Primatol* **75**, 133–149.
- Jacobs CR** (2000) The mechanobiology of cancellous bone structural adaptation. *J Rehab Research Devel* **37**, 209–216.

- 1 Jee WS, Wronski TJ, Morey ER, et al. (1983) Effects of space-
2 flight on trabecular bone in rats. *Am J Physiology* **244**, 310–
3 314.
- 4 Jenkins FA Jr, Fleagle JG (1975) Knuckle-walking and the func-
5 tional anatomy of the wrists in living apes. In: *Primate Func-*
6 *tional Morphology and Evolution*. (ed. Tuttle RH), pp. 213–
7 231. The Hague: Mouton.
- 8 Jones HH, Priest JD, Hayes WC, et al. (1977) Humeral hypertro-
9 phy in response to exercise. *J Bone Joint Surg A* **59**, 204–208.
- 10 Judex S, Carlson KJ (2009) Is bone's response to mechanical sig-
11 nals dominated by gravitational loading? *Med Sci Sports Exerc*
12 **41**, 2037–2043.
- 13 Judex S, Gross TS, Zernicke RF (1997) Strain gradients correlate
14 with sites of exercise-induced bone-forming surfaces in the
15 adult skeleton. *J Bone Miner Res* **12**, 1737–1745.
- 16 Judex S, Garman R, Squire M, et al. (2004) Genetically based
17 influences on the site-specific regulation of trabecular and
18 cortical bone morphology. *J Bone Miner Res* **19**, 600–606.
- 19 Jungers WL, Godfrey LR, Simons EL, et al. (1997) Phalangeal cur-
20 vature and positional behavior in extinct sloth lemurs (Pri-
21 mates, Palaeopropithecidae). *Proc Natl Acad Sci USA* **94**, 11
22 998–12 001.
- 23 Kabel J, van Rietbergen B, Odgaard A, et al. (1999) Constitutive
24 relationships of fabric, density, and elastic properties in can-
25 cellous bone architecture. *Bone* **25**, 481–486.
- 26 Karlsson MK, Linden C, Karlsson C, et al. (2000) Exercise during
27 growth and bone mineral density and fractures in old age.
28 *Lancet* **355**, 469–470.
- 29 Karlsson C, Obrant KJ, Karlsson M (2001) Pregnancy and lacta-
30 tion confer reversible bone loss in humans. *Osteoporos Int* **12**,
31 828–834.
- 32 Keaveny TM, Morgan EF, Niebur GL, et al. (2001) Biomechanics
33 of trabecular bone. *Annu Rev Biomed Eng* **3**, 307–333.
- 34 Kerschnitzki M, Kollmannsberger P, Burghammer M, et al.
35 (2013) Architecture of the osteocyte network correlates with
36 bone mineral quality. *J Bone Min Res* **28**, 1837–1845.
- 37 Kivell TL, Kibii JM, Churchill SE, et al. (2011a) *Australopithecus*
38 *sediba* hand demonstrates mosaic evolution of locomotor and
39 manipulative abilities. *Science* **333**, 1411–1417.
- 40 Kivell TL, Skinner MM, Lazenby R, et al. (2011b) Methodological
41 considerations for analyzing trabecular architecture: an exam-
42 ple from the primate hand. *J Anat* **218**, 209–225.
- 43 Kivell TL, Skinner MM, Lazenby RL, et al. (2012) Trabecular
44 architecture of fossil hominin first metacarpals. *Am J Phys*
45 *Anthropol* **147**(S54), 182.
- 46 Kivell TL, Deane AS, Tocheri MW, et al. (2015) The hand of
47 *Homo naledi*. *Nat Comm* **6**, 8431.
- 48 Koch JC (1917) The laws of bone architecture. *Am J Anat* **21**,
49 177–298.
- 50 Kummer B (1966) Photoelastic studies on the functional struc-
51 ture of bone. *Folia Biotheoretica* **6**, 31–40.
- 52 Kummer B (1972) Functional adaptation to posture in the pelvis
53 of man and other primates. In: *The Functional and Evolutionary*
54 *Biology of Primates*. (ed. Tuttle R), pp. 281–290. Chicago:
55 Aldine-Atherton.
- Lambers FM, Koch K, Kuhn G, et al. (2013) Trabecular bone
adapts to long-term cyclic loading by increasing stiffness and
normalization of dynamic morphometric rates. *Bone* **55**, 325–
334.
- Lanyon LE (1973) Analysis of surface bone strain in the sheep
during normal locomotion. *J Biomech* **6**, 41–49.
- Lanyon LE (1974) Experimental support for the trajectorial the-
ory of bone structure. *J Bone Jt Surg* **56B**, 160–166.
- Lanyon LE, Rubin CT (1985) Functional adaptation in skeletal
structures. In: *Functional Vertebrate Morphology*. (eds Hilde-
brand M, Bramble DM, Liem KF, Wake BD), pp. 1–25. Cam-
bridge, Massachusetts: Belknap Press.
- Larson SG (1995) New characters for the functional interpreta-
tion of primate scapulae and proximal humeri. *Am J Phys*
Anthropol **98**, 13–35.
- Latimer B, Lovejoy CO (1989) The calcaneus of *Australopithecus*
afarensis and its implications for the evolution of bipedality.
Am J Phys Anthropol **78**, 369–386.
- Lazenby RA, Cooper DML, Angus S, et al. (2008) Articular con-
straint, handedness, and directional asymmetry in the human
second metacarpal. *J Hum Evol* **54**, 875–885.
- Lazenby RA, Skinner MM, Kivell TL, et al. (2011) Scaling VOI size
in 3D μ CT studies of trabecular bone: a test of the over-sam-
pling hypothesis. *Am J Phys Anthropol* **144**, 196–203.
- Levenstone ME, Beaupr e GS, Jacobs CR, et al. (1994) The role of
loading memory in bone adaptation simulations. *Bone* **15**,
177–186.
- Lieberman DE (1996) How and why humans grow thin skulls:
experimental evidence for systemic cortical robusticity. *Am J*
Phys Anthropol **101**, 217–236.
- Lieberman DE (1997) Making behavioral and phylogenetic infer-
ences from hominid fossils: considering the developmental
influence of mechanical forces. *Annu Rev Anthropol* **26**, 185–
210.
- Lieberman DE, Devlin MJ, Pearson OM (2001) Articular area
responses to mechanical loading: effects of exercise, age, and
skeletal location. *Am J Phys Anthropol* **116**, 266–277.
- Lieberman DE, Polk JD, Demes B (2004) Predicting long bone
loading from cross-sectional geometry. *Am J Phys Anthropol*
123, 156–171.
- Liu XS, Sajda P, Saha PK, et al. (2008) Complete volumetric
decomposition of individual trabecular plates and rods and its
morphological correlations with anisotropic elastic moduli in
human trabecular bone. *J Bone Miner Res* **23**, 223–235.
- Lotz JC, Cheal EJ, Hayes WC (1995) Stress distributions within
the proximal femur during gait and falls: implications for
osteoporotic fracture. *Osteoporos Int* **5**, 252–261.
- Lovejoy CO (2009) Reexamining human origins in light of *Ardip-*
ithecus ramidus. *Science* **326**, 74–74e8.
- Lovejoy CO, Heiple KG, Burstein AH (1973) The gait of *Australo-*
pithecus. *Am J Phys Anthropol* **38**, 757–780.
- Lovejoy CO, McCollum MA, Reno PL, et al. (2003) Developmen-
tal biology and human evolution. *Ann Rev Anthropol* **32**, 85–
109.
- Lozupone E (1985) The structure of the trabeculae of cancellous
bone. I: the calcaneus. *Anat Anz* **159**, 211–229.
- Lozupone E, Favia A (1990) The structure of the trabeculae of
cancellous bone. 2: long bones and mastoid. *Calcif Tissue Int*
46, 367–372.
- Macchiarelli R, Bondioli L, Galichon V, et al. (1999) Hip bone tra-
becular architecture shows uniquely distinctive locomotor
behaviour in South African australopithecines. *J Hum Evol* **36**,
211–232.
- MacLatchy L, M uller R (2002) A comparison of the femoral head
and neck trabecular architecture of *Galago* and *Perodicticus*
using micro-computed tomography (μ CT). *J Hum Evol* **43**, 89–
105.

- 1 **Maga M, Kappelman J, Ryan TM, et al.** (2006) Preliminary obser-
 2 vations on the calcaneal trabecular microarchitecture of
 3 extant large-bodied hominoids. *Am J Phys Anthropol* **129**,
 4 410–417.
- 5 **Maquer G, Musy SN, Wandel J, et al.** (2015) Bone volume frac-
 6 tion and fabric anisotropy are better determinants of trabecu-
 7 lar bone stiffness than other morphological variables. *J Bone*
 8 *Min Res* **30**, 1000–1008.
- 9 **Marchi D** (2005) The cross-sectional geometry of the hand and
 10 foot bones of the Hominoidea and its relationship to locomotor
 11 behaviour. *J Hum Evol* **49**, 743–761.
- 12 **Martin RB, Burr DB, Sharkey NA** (1998) *Skeletal Tissue Mechan-*
 13 *ics*. New York: Springer.
- 14 **Matarazzo SA** (2015) Trabecular architecture of the manual ele-
 15 ments reflects locomotor patterns in primates. *PLoS ONE* **10**,
 16 e0120436.
- 17 **McNamara LM, van der Linden JC, Weinans H, et al.** (2006)
 18 Stress concentrating effect of resorption lacunae in trabecular
 19 bone. *J Biomech* **39**, 734–741.
- 20 **van der Meulen MCH, Carter DH** (1995) Developmental mechan-
 21 ics determine long bone allometry. *J Theor Biol* **172**, 323–327.
- 22 **van der Meulen MCH, Beauprè GS, Carter DR** (1993) Mechanobi-
 23 ologic influences in long bone cross-sectional growth. *Bone*
 24 **14**, 63–642.
- 25 **van der Meulen MCH, Ashford MW Jr, Kiralti BJ, et al.** (1996)
 26 Determinant of femoral geometry and structure during adoles-
 27 cent growth. *J Orthop Res* **14**, 22–29.
- 28 **von Meyer GH** (1867) Die architektur der spongiosa. *Arch Anat*
 29 *Physiol Wiss Med* **34**, 615–628.
- 30 **Miszkievicz JJ, Kivell TL, Schlecht SH, et al.** (2015) Investigating
 31 the extent to which enthesal changes reflect bone remodel-
 32 ing at the modern human femoral midshaft. *Am J Phys*
 33 *Anthropol* **156**(S60), 227 (abstract).
- 34 **Mitra E, Rubin C, Qin Y** (2005) Interrelationship of trabecular
 35 mechanical and microstructural properties in sheep trabecular
 36 bone. *J Biomech* **38**, 1229–1237.
- 37 **Modlesky CM, Majumdar S, Dudley GA** (2008a) Trabecular bone
 38 microarchitecture in female collegiate gymnasts. *Osteoporosis*
 39 *Int* **19**, 1011–1018.
- 40 **Modlesky CM, Subramanian P, Miller F** (2008b) Underdeveloped
 41 trabecular bone microarchitecture is detected in children with
 42 cerebral palsy using high-resolution magnetic resonance imag-
 43 ing. *Osteoporosis Int* **19**, 169–176.
- 44 **Morgan EF, Keaveny TM** (2001) Dependence of yield strain of
 45 human trabecular bone on anatomic site. *J Biomech* **34**, 569–
 46 577.
- 47 **Morgan EF, Bayraktar HH, Keaveny TM** (2003) Trabecular bone
 48 modulus-density relationships depend on anatomic site. *J Bio-*
 49 *mech* **36**, 897–904.
- 50 **Moyà-Solà S, Köhler M** (1996) A *Dryopithecus* skeleton and ori-
 51 gins of great-ape locomotion. *Nature* **379**, 156–159.
- 52 **Moyà-Solà S, Köhler M, Rook L** (2005) The *Oreopithecus* thumb:
 53 a strange case in hominoid evolution. *J Hum Evol* **49**, 395–404.
- 54 **Mullender MG, Huiskes R** (1995) Proposal for the regulatory
 55 mechanism of Wolff's law. *J Orthop Res* **13**, 503–512.
- Mullender MG, Huiskes R, Versleyen H, et al.** (1996) Osteocyte
 density and histomorphometric parameters in cancellous bone
 of the proximal femur in five mammalian species. *J Orthop*
Res **14**, 972–979.
- Mulvihill BM, McNamara LM, Prendergast PJ** (2008) Loss of tra-
 beculae by mechano-biological means may explain rapid bone
 loss in osteoporosis. *J R Soc Interf* **5**, 1243–1253.
- Nafei A, Danielsen CC, Linde F, et al.** (2000) Properties of grow-
 ing trabecular ovine bone. *J Bone Joint Surg (Br)*, **82-B**, 910–
 920.
- Napier JR, Davis PR** (1959) The forelimb skeleton and associated
 remains of *Proconsul africanus*. *Fossil Mammals of Africa* **16**,
 1–70.
- Nguyen NH, Pahr DH, Gross T, et al.** (2013) The biomechanical
 role of trabecular bone in the siamang (*Symphalangus syn-*
dactylus) manual proximal phalanx. *Eur Soc Study Hum Evol*
3, 162.
- Nguyen NH, Pahr DH, Gross T, et al.** (2014) Micro-finite element
 (μ FE) modeling of the siamang (*Symphalangus syndactylus*)
 third proximal phalanx: the functional role of curvature and
 the flexor sheath ridge. *J Hum Evol* **67**, 60–75.
- Niemitz C** (2010) The evolution of the upright posture and gait:
 a review and a new synthesis. *Naturwissenschaften* **97**, 241–
 263.
- Nowlan NC, Prendergast PJ, Murphy P** (2008) Identification of
 mechanosensitive genes during embryonic bone formation. *PLoS*
Comp Biol **4**, 1–10.
- Odgaard A** (1997) Three-dimensional methods for quantification
 of cancellous bone architecture. *Bone* **20**, 315–328.
- Odgaard A** (2009) Quantification of cancellous bone architec-
 ture. In: *Bone Mechanics Handbook*, 2nd edn. (ed. Cowin SC),
 pp. 14–19. New York: Informa Healthcare USA.
- Odgaard A, Gundersen HJG** (1993) Quantificaton of connectivity
 in cancellous bone, with special emphasis on 3-D reconstruc-
 tions. *Bone* **14**, 173–182.
- Odgaard A, Kabel J, van Reitbergen B, et al.** (1997) Fabric and
 elastic principal directions of cancellous bone are closely
 related. *J Biomech* **30**, 487–495.
- Oxnard CE** (1972) The use of optical data analysis in functional
 morphology: investigation of vertebral trabecular patterns. In:
The Functional and Evolutionary Biology of Primates. (ed. Tut-
 tle R), pp. 337–347. Chicago: Aldine-Atherton.
- Oxnard CE** (1982) The association between cancellous architec-
 ture and loading in bone: an optical data analytic view. *Physi-*
ologist **25**, 37–40.
- Oxnard CE** (1993) Bone and bones, architectures and stress, fos-
 sils and osteoporosis. *J Biomech* **26**, 63–79.
- Oxnard CE** (1997) From optical to computational fourier trans-
 forms: the natural history of an investigation of the cancellous
 bone structure of bone. In: *Fourier Descriptors and their*
Applications in Biology. (ed. Lestrel P), pp. 379–408. Cam-
 bridge: Cambridge University Press.
- Oxnard CE, Yang HCL** (1981) Beyond biometrics: studies of com-
 plex biological patterns. *Symp Zool Soc Lond* **46**, 127–167.
- Pahr DH, Zysset PK** (2009a) From high-resolution CT data to
 finite element models: development of an integrated modular
 framework. *Comp Meth Biomech Biomed Eng* **12**, 45–57.
- Pahr DH, Zysset PK** (2009b) A comparison of enhanced contin-
 uum FE with micro FE models of human vertebral bodies. *J*
Biomech **42**, 455–462.
- Parfitt AM, Travers R, Rauch F, et al.** (2000) Structural and cellu-
 lar changes during bone growth in healthy children. *Bone* **27**,
 487–494.
- Pauwels F** (1948) Die bedeutung der Bauprinzipien des Stutz
 und Bewegungsapparates für die Beanspruchung der Rohren-
 knochen. *Z Anat EntwGesch* **114**, 129–166.
- Pauwels F (ed.)** ((1980) *Biomechanics of the Locomotor Appara-*
tus: Contributions on the Functional Anatomy of the Locomo-
tor Apparatus. Berlin: Springer.

- 1 **Pearson OM, Lieberman DE** (2004) The aging of Wolff's 'law':
2 ontogeny and responses to mechanical loading in cortical
3 bone. *Yrbk Phys Anthropol* **47**, 63–99.
- 4 **Pettersson U, Nilsson M, Sundh V, et al.** (2010) Physical activity
5 is the strongest predictor of calcaneal peak bone mass in
6 young Swedish men. *Osteoporos Int* **21**, 447–455.
- 7 **Plavcan JM, van Schaik CP** (1997) Intrasexual competition and
8 body weight dimorphism in anthropoid primates. *Am J Phys
9 Anthropol* **103**, 37–68.
- 10 **Polk JD** (2002) Adaptive and phylogenetic influences on muscu-
11 loskeletal design in cercopithecine primates. *J Exp Biol* **205**,
12 3399–3412.
- 13 **Polk JD, Blumenfeld J, Ahlumwalia D** (2008) Knee posture pre-
14 dicted subchondral apparent density in the distal femur: an
15 experimental validation. *Anat Rec* **291**, 293–302.
- 16 **Pontzer H, Lieberman DE, Momin E, et al.** (2006) Trabecular
17 bone in the bird knee responds with high sensitivity to
18 changes in load orientation. *J Exp Biol* **209**, 57–65.
- 19 **Pruetz JD, Bertolani P** (2009) Chimpanzee (*Pan troglodytes*
20 *verus*) behavioural responses to stress associated with living in
21 a savanna-mosaic environment: implications for hominin
22 adaptations to open habitats. *PaleoAnthropolgy* ???, 252–262.
- 23 **Rabey KN, Green DJ, Tayler AB, et al.** (2015) Locomotor activity
24 influences muscle architecture and bone growth but not mus-
25 cle attachment site morphology. *J Hum Evol* **78**, 91–102.
- 26 **Rafferty KL** (1996) Joint design in primates: external and subar-
27 ticular properties in relation to body size and locomotor behav-
28 iour. PhD Dissertation, Johns Hopkins University.
- 29 **Rafferty KL, Ruff CB** (1994) Articular structure and function in
30 *Hylobates*, *Colobus*, and *Papio*. *Am J Phys Anthropol* **94**, 395–
31 408.
- 32 **Raichlen DA, Gordon AD, Foster AD, et al.** (2015) An ontoge-
33 netic framework linking locomotion and trabecular bone
34 architecture with applications for reconstructing hominin life
35 history. *J Hum Evol* ????, ???-???? (in press) [http://dx.doi.org/](http://dx.doi.org/10.1016/j.jhevol.2015.01.003)
36 [10.1016/j.jhevol.2015.01.003](http://dx.doi.org/10.1016/j.jhevol.2015.01.003).
- 37 **Räth C, Baum T, Monetti R, et al.** (2013) Scaling relations
38 between trabecular bone volume fraction and microstructure
39 at different skeletal sites. *Bone* **57**, 377–383.
- 40 **Remis M** (1995) Effects of body size and social context on arbo-
41 real activities of lowland gorillas in the Central African Repub-
42 lic. *Am J Phys Anthropol* **97**, 413–433.
- 43 **Richmond BG, Strait DS** (2000) Evidence that humans evolved
44 from a knuckle-walking ancestor. *Nature* **404**, 382–385.
- 45 **Richmond BG, Wright BW, Grosse I, et al.** (2005) Finite element
46 analysis in functional morphology. *Anat Rec* **283A**, 259–274.
- 47 **van Rietbergen B, Weinans H, Huiskes R, et al.** (1995) A new
48 method to determine trabecular bone elastic properties and
49 loading using micromechanical finite element models. *J Bio-
50 mech* **28**, 69–81.
- 51 **van Rietbergen B, Odgaard A, Kabel J, et al.** (1998) Relation-
52 ships between bone morphology and bone elastic properties
53 can be accurately quantified using high-resolution computer
54 reconstructions. *J Orthop Res* **16**, 23–28.
- 55 **van Rietbergen B, Müller R, Ulrich D, et al.** (1999) Tissue stresses
and strain in trabeculae of the canine proximal femur can be
quantified from computer reconstructions. *J Biomech* **32**, 165–
173.
- Robling AG** (2009) Is bone's response to mechanical signals dom-
inated by muscle forces? *Med Sci Sports Exercise* **41**, 2044–
2049.
- Robling AG, Castillo AB, Turner CH** (2006) Biomechanical and
molecular regulation of bone remodeling. *Ann Rev Biomed Eng* **8**, 455–498.
- Roesler H** (1987) The history of some fundamental concepts in
bone biomechanics. *J Biomech* **20**, 1025–1034.
- Rook L, Bondioli L, Köhler M, et al.** (1999) *Oreopithecus* was a
bipedal ape after all: evidence from the iliac cancellous archi-
tecture. *Proc Natl Acad Sci USA* **96**, 8795–8799.
- Roschger P, Grabner BM, Rinnerthaler S, et al.** (2001) Structural
development of the mineralized tissue in the human L4 verte-
bral body. *J Struct Biol* **136**, 126–136.
- Rose MD** (1991) The process of bipedalization in hominids. In:
Origine(s) de la bipédie chez les Hominidés. (eds Senut B, Cop-
pens Y), pp. 37–48. Paris: CNRS.
- Roux W** (1881) *Der zu"chtende Kampf der Teile, oder die 'Tei-
lauslee'im Organismus (Theorie der 'funktionellen Anpas-
sung')*. Leipzig: Wilhelm Engelmann.
- Rubin CT, Lanyon LE** (1985) Regulation of bone mass by
mechanical strain magnitude. *Calcif Tissue Int* **37**, 411–417.
- Rubin C, Turner AS, Bain S, et al.** (2001) Anabolism: low
mechanical signals strengthen long bones. *Nature* **412**, 603–
604.
- Rubin C, Turner AS, Mallinckrodt C, et al.** (2002) Mechanical
strain, induced noninvasively in the high-frequency domain is
anabolic to cancellous bone, but not cortical bone. *Bone* **30**,
445–452.
- Ruff C** (1988) Hindlimb articular surface allometry in Homi-
noidea and *Macaca*, with comparisons to diaphyseal scaling. *J
Hum Evol* **17**, 687–714.
- Ruff C** (2009) Relative limb strength and locomotion in Homo
hablis. *Am J Phys Anthropol* **138**, 90–100.
- Ruff C, Runestad JA** (1992) Primate limb bone structure adapta-
tions. *Annu Rev Anthropol* **21**, 407–433.
- Ruff C, Walker A, Trinkaus E** (1994) Postcranial robusticity in
Homo. III: Ontogeny. *Am J Phys Anthropol* **65**, 191–197.
- Ruff C, Holt B, Trinkaus E** (2006) Who's afraid of the big bad
Wolff?: 'Wolff's law' and bone functional adaptation. *Am J
Phys Anthropol* **129**, 484–498.
- Ryan TM, Ketcham RA** (2002a) The three-dimensional structure
of trabecular bone in the femoral head of strepsirrhine pri-
mates. *J Hum Evol* **43**, 1–26.
- Ryan TM, Ketcham RA** (2002b) Femoral head trabecular bone
structure in two omomyid primates. *J Hum Evol* **43**, 241–263.
- Ryan TM, Ketcham RA** (2005) The angular orientation of trabecu-
lar bone in the femoral head and its relationship to hip joint
loads in leaping primates. *J Morphol* **265**, 249–263.
- Ryan TM, Krovitz GE** (2006) Trabecular bone ontogeny in the
human proximal femur. *J Hum Evol* **51**, 591–602.
- Ryan TM, Shaw CN** (2012) Unique suites of trabecular bone fea-
tures characterize locomotor behaviour in human and non-
human anthropoid primates. *PLoS ONE* **7**, e41037.
- Ryan TM, Shaw CN** (2013) Trabecular bone microstructure scales
allometrically in the primate humerus and femur. *Proc R Soc B*
280, 20130172.
- Ryan TM, Shaw CN** (2015) Gracility of the modern *Homo sapiens*
skeleton is the result of decreased biomechanical loading.
Proc Natl Acad Sci USA **112**, 372–377.
- Ryan TM, van Rietbergen B** (2005) Mechanical significance of
femoral head trabecular bone structure in *Loris* and *Galago*
evaluated using micromechanical finite element models. *Am J
Phys Anthropol* **126**, 82–96.

- Ryan TM, Walker A (2010) Trabecular bone structure in the humeral and femoral heads of anthropoid primates. *Anat Rec* **293**, 719–729.
- Ryan TM, Colbert M, Ketcham RA, et al. (2010) Trabecular bone structure in the mandibular condyles of gouging and non-gouging platyrrhine primates. *Am J Phys Anthropol* **141**, 583–593.
- Saparin P, Scherf H, Hublin J-J, et al. (2011) Structural adaptation of trabecular bone revealed by position resolved analysis of proximal femoral of different primates. *Anat Rec* **294**, 55–67.
- Scherf H (2007) Locomotion-related femoral trabecular architectures in primates. Ph.D. Dissertation, Darmstadt University of Technology, Darmstadt, Germany.
- Scherf H (2008) Locomotion-related femoral trabecular architectures in primate: high-resolution computed tomographies and their implications for estimates of locomotor preferences of fossil primates. In: *Imaging Anatomical*. (eds Endo, Frey RH, FreyR), pp. 39–59. Japan: Springer.
- Scherf H, Harvati K, Hublin J-J (2013) A comparison of proximal humeral cancellous bone of great apes and humans. *J Hum Evol* **65**, 29–38.
- Schilling A-M, Tofaneli S, Hublin J-J, et al. (2014) Trabecular bone structure in the primate wrist. *J Morph* **275**, 572–585.
- Schmitt D (1999) Compliant walking in primates. *J Zool* **248**, 149–160.
- Schmitt D (2003) Substrate size and primate forelimb mechanics: implications for understanding the evolution of primate locomotion. *Int J Primatol* **24**, 1023–1036.
- Schmitt D, Hanna J (2004) Substrate alters forelimb to hindlimb peak force ratios in primates. *J Hum Evol* **46**, 149–159.
- Schoonaert K, D'Août K, Aerts P (2006) A dynamic force analysis system for climbing of large primates. *Folia Primatol* **77**, 246–254.
- Shaw CN, Ryan TM (2012) Does skeletal anatomy reflect adaptation to locomotor patterns? Cortical and trabecular architecture in humans and nonhuman anthropoids. *Am J Phys Anthropol* **147**, 187–200.
- Shaw CN, Stock JT (2013) Extreme mobility in the Late Pleistocene? Comparing limb biomechanics among fossil *Homo*, varsity athletes and Holocene foragers. *J Hum Evol* **64**, 242–249.
- Shaw CN, Hofmann CL, Petraglia MD, et al. (2012) Neandertal humeri may reflect adaptation to scraping tasks, but not spear thrusting. *PLoS ONE* **7**, e40349.
- Simkin A, Ayalon J, Leichter I (1987) Increased trabecular bone density due to bone-loading exercises in postmenopausal osteoporotic women. *Calcif Tissue Int* **40**, 59–63.
- Simkin A, Leichter I, Swissa A, et al. (1989) The effect of swimming activity on bone architecture in growing rats. *J Biomech* **22**, 845–851.
- Simmons DJ, Russeel JE, Winter F, et al. (1983) Effect of space-flight on the non-weight-bearing bones of rat skeleton. *Am J Physiol* **244R**, 319–326.
- Sinclair KD, Farnsworth RW, Pham TX, et al. (2013) The artiodactyl calcaneus as a potential 'control bone' cautions against simple interpretations of trabecular bone adaptation in the anthropoid femoral neck. *J Hum Evol* **64**, 366–379.
- Singh I (1978) The architecture of cancellous bone. *J Anat* **127**, 305–310.
- Skedros JG, Baucom SL (2007) Mathematical analysis of trabecular 'trajectories' in apparent trajectorial structures: the unfortunate historical emphasis on the human proximal femur. *J Theor Biol* **244**, 15–45.
- Skedros JG, Hunt KJ, Bloebaum RD (2004) Relationships of loading history and structural and material characteristics of bone: development of the mule deer calcaneus. *J Morph* **259**, 281–307.
- Skedros JG, Knight AN, Farnsworth RW, et al. (2012) Do regional modifications in tissue mineral content and microscopic mineralization heterogeneity adapt trabecular bone tracts for habitual bending? Analysis in the context of trabecular architecture of deer calcanei. *J Anat* **220**, 242–255.
- Skerry TM, Lanyon LE (1995) Interruption of disuse by short duration walking exercise does not prevent bone loss in the sheep calcaneus. *Bone* **16**, 269–274.
- Skinner MM, Stephens NB, Tsegai ZJ, et al. (2015) Human-like hand use in *Australopithecus africanus*. *Science* **347**, 395–399.
- Smaers JB, Vinicius L (2009) Inferring macro-evolutionary patterns using an adaptive peak model of evolution. *Evol Ecol Res* **11**, 991–1015.
- Smith EL, Gilligan C, McAdam M, et al. (1989) Detering bone loss by exercise intervention in premenopausal and postmenopausal women. *Calcif Tissue Int* **44**, 312–321.
- Stauber M, Rapillard L, van Lenthe GH, et al. (2006) Importance of individual rods and plates in the assessment of bone quality and their contribution to bone stiffness. *J Bone Min Res* **21**, 586–595.
- Stephens NB (2012) Trabecular bone architecture in the thumb of recent *Homo sapiens*, *Pan* and Late Pleistocene *Homo*. MSc dissertation, University College London.
- Stern JT Jr (1975) Before bipedality. *Yr Phys Anthropol* **19**, 59–68.
- Stern JT Jr, Susman RL (1991) 'Total morphological pattern' versus the 'magic trait': conflicting approaches to the study of early hominid bipedalism. In: *Origine(s) de la bipédie chez les Hominidés*. (eds Senut B, Coppens Y), pp. 99–112. Paris: CNRS.
- Stock J, Pfeiffer S (2001) Linking structural variability in long bone diaphyses to habitual behaviors: foragers from the southern African Later Stone Age and the Andaman Islands. *Am J Phys Anthropol* **115**, 337–348.
- Su A, Wallace IJ, Nakatsukasa M (2013) Trabecular bone anisotropy and orientation in an Early Pleistocene hominin talus from East Turkana, Kenya. *J Hum Evol* **64**, 667–677.
- Susman RL (2004) *Oreopithecus bambolii*: an unlikely case of hominidlike grip capability in a Miocene ape. *J Hum Evol* **46**, 103–115.
- Swartz SM, Parker A, Hou C (1998) Theoretical and empirical scaling patterns and topological homology in bone trabeculae. *J Exp Biol* **201**, 573–590.
- Tanck E, Homminga J, van Lenthe GH, et al. (2001) Increase in bone volume fraction precedes architectural adaptation in growing bone. *Bone* **28**, 650–654.
- Thorpe SKS, Crompton RH (2006) Orangutan positional behaviour and the nature of arboreal locomotion in hominoidea. *Am J Phys Anthropol* **131**, 384–401.
- Townsley W (1948) The influence of mechanical factors on the development and structure of bone. *Am J Phys Anthropol* **6**, 25–45.
- Tsegai ZJ, Kivell TL, Gross T, et al. (2013) Trabecular bone structure correlates with hand posture and use in hominoids. *PLoS ONE* **8**, e78781.
- Turner AS (2001) Animal models of osteoporosis – necessity and limitations. *Eur Cell Mater* **1**, 66–81.

- 1 Ulrich D, van Reitbergen B, Laib A, et al. (1999) The ability of
2 three-dimensional structural indices to reflect material aspects
3 of trabecular bone. *Bone* 25, 55–60.
- 4 Vereecke EE, D'Août K, De Clercq D, et al. (2003) Dynamic plan-
5 tar pressure distribution during terrestrial locomotion in
6 bonobos (*Pan paniscus*). *Am J Phys Anthropol* 120, 373–383.
- 7 Vereecke EE, D'Août K, Aerts P (2011) Studying captive ape
8 locomotion: past, present, and future. In: *Primate Locomotion:
9 Linking Field and Laboratory Research*. (eds D'Août K, Ver-
10 eecke EE), pp. 29–46. New York: Springer.
- 11 Viola TB (2002) Locomotion dependent variation in the proximal
12 femoral trabecular pattern in primates. MSc Thesis, University
13 of Vienna, Vienna, Austria.
- 14 Wainwright PC, Mehta RS, Higham TE (2008) Stereotypy, flexi-
15 bility and coordination: key concepts in behavioral functional
16 morphology. *J Exp Biol* 211, 3523–3528.
- 17 Wallace IJ, Demes B, Mongle C, et al. (2014) Exercise-induced
18 bone formation is poorly linked to local strain magnitude in
19 the sheep tibia. *PLoS ONE* 9, 99108.
- 20 Ward FO (1838) *Outlines of Human Osteology*. London: Henry
21 Renshaw.
- 22 Ward CB (2002) Interpreting the posture and locomotion of
23 *Australopithecus afarensis*: where do we stand? *Yrbk Phys
24 Anthropol* 45, 185–215.
- 25 Ward CB (2013) Postural and locomotor adaptations of *Australo-
26 pithecus* species. In: *The Palaeobiology of Australopithecus*.
27 (eds Reed KE, Fleagle JG, Leakey RE), pp. 235–245. Dordrecht:
28 Springer.
- 29 Ward SC, Sussman RW (1979) Correlates between locomotor
30 anatomy and behavior in two sympatric species of *Lemur*. *Am
31 J Phys Anthropol* 50, 575–590.
- 32 White TD, Asfaw B, Beyene Y, et al. (2009) *Ardipithecus ramidus*
33 and the paleobiology of early hominids. *Science* 326, 75–86.
- 34 Wich SA, Utami Atmoko SS, Setia TM, et al. eds ((2009) *Oran-
35 gutans: geographic variation in behavioral ecology and con-
36 servation*. Oxford: Oxford University Press.
- 37 Williams EM, Gordon AD, Richmond BG (2012) Hand pressure
38 distribution during Oldowan stone tool production. *J Hum
39 Evol* 62, 520–532.
- 40 Wolff J (1870) Über die innere Architektur der Knochen und ihre
41 bedeutung für die Frage vom Knochenwachstum. *Virchows
42 Archiv für Pathologische Anatomie und Physiologie* 50, 389–453.
- 43 Wolff J (1892) *Das Gesetz der Transformation der Knochen*. Ber-
44 lin: A. Hirchwild.
- 45 Wolff J (1986) *The law of bone remodelling*. Berlin: Springer.
- 46 Wood B, Harrison T (2011) The evolutionary context of the first
47 hominins. *Nature* 470, 347–352.
- 48 Wunderlich RE, Jungers WL (2009) Manual digital pressures dur-
49 ing knuckle-walking in chimpanzees (*Pan troglodytes*). *Am J
50 Phys Anthropol* 139, 394–403.
- 51 Yeni YN, Zinno MJ, Yerramshetty JS, et al. (2011) Variability of tra-
52 becular microstructure is age-, gender-, race- and anatomic site-
53 dependent and affects stiffness and stress distribution properties
54 of human vertebral cancellous bone. *Bone* 49, 886–894.
- 55 Zumwalt A (2006) The effect of endurance exercise on the mor-
56 phology of muscle attachment sites. *J Exp Biol* 209, 444–454.

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