Tactile innervation densities across the whole body

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Abstract

The skin is our largest sensory organ and innervated by afferent fibers carrying tactile information to the spinal cord and onto the brain. The density with which different classes of tactile afferents innervate the skin is not constant but varies considerably across different body regions. However, precise estimates of innervation density are only available for some body parts, such as the hands, and estimates of the total number of tactile afferent fibers are inconsistent and incomplete. Here we reconcile different estimates and provide plausible ranges and best estimates for the number of different tactile fiber types innervating different regions of the skin, using evidence from dorsal root fiber counts, microneurography, histology, and psychophysics. We estimate that the skin across the whole body of young adults is innervated by approximately 230,000 tactile afferent fibers (plausible range: 200,000-270,000), with a subsequent decrement of 5-8% every decade due to aging. 15% of fibers innervate the palmar skin of both hands and 19% the region surrounding the face and lips. Slowly and fast-adapting fibers are split roughly evenly, but this breakdown varies with skin region. Innervation density correlates well with psychophysical spatial acuity across different body regions, and additionally, on hairy skin, with hair follicle density. Innervation density is also weakly correlated with the size of the cortical somatotopic representation, but cannot fully account for the magnification of the hands and the face.

Keywords

afferent | mechanoreceptor | glabrous skin | hairy skin | homunculus

Introduction

Sensory processing cannot be studied without understanding the nature of sensory inputs. Careful study of the visual system has revealed that about 100 million photoreceptors in a single retina convert light into electrical impulses, which are relayed through roughly 1 million retinal ganglion cells in the optic nerve (Curcio et al., 1990). In audition, about 12,000 hair cells in each cochlea transmit auditory information to the brain (Ulehlová et al., 1987). The sense of touch puts to use our largest sensory organ, the skin, which is innervated throughout by cutaneous fibers signaling light touch, temperature, and pain. Despite the importance of touch for manipulation (Witney et al., 2004), movement (Panek et al., 2014), our sense of body ownership (Tsakiris, 2010), and affection (McGlone et al., 2014), we know little about the number and distribution of cutaneous fibers innervating different skin regions across the body. Estimates of tactile fiber innervation in the current literature are few, often incomplete and inconsistent, and range from a total innervation of around 45,000 fibers (Taube Navaraj et al., 2017) into the millions (Grunwald, 2017). Most textbooks do not even venture a guess (Bear et al., 2016; Goldstein, 2009; Kandel et al., 2000; Purves et al., 2018). Reliable estimates exist only for a few regions of glabrous skin. The gold standard is a study by Johansson and Vallbo (1979) that estimated that around 17,000 myelinated tactile fibers innervate the palmar surface of each hand.

Various techniques can be employed for counting fibers, but individually they all suffer from problems, which explains the discrepancy in estimates. Histological examination can provide estimates for the number of fibers in the peripheral nerves, but cannot distinguish between afferent and efferent fibers. Furthermore, peripheral nerves carry many types of sensory fibers other than tactile ones, for example, proprioceptive fibers or those innervating internal organs, such as the bladder. Immunohistochemistry of samples taken by skin biopsies allow receptor and fiber counts, but the regions covered are necessarily very small, and innervation of the skin is not uniform. Individual tactile fibers often branch and innervate tens of receptors, and estimates of branching and convergence factors differ widely. Another approach estimates innervation density from psychophysically determined two-point discrimination thresholds. Here, the idea is that higher innervation density enables improved spatial localization, so finer spatial discrimination should be associated with higher fiber count. However, such estimates are limited because discrimination thresholds likely rely predominantly on only one of the multiple different afferent classes that innervate the skin (Peters et al., 2009). A general problem is that none of the methods described above can be used to extrapolate between glabrous and hairy skin without taking into account the different composition in the types of tactile afferent fibers. Much valuable insight into the prevalence of different fiber types also comes from microneurography, a technique for obtaining electrophysiological recordings from individual fibers in human nerves. However, this technique has mostly been applied to fibers terminating in the hand, the foot, or the face. A handful of studies has investigated the hairy skin of the arms and legs, but data from the body trunk is sorely lacking, due to the technical challenges of applying the microneurography technique in these areas. Finally, data from animal models, specifically primates, can also provide valuable input, however stark differences in innervation density have been observed across different primate species (Verendeev et al., 2015), so such data can only be used with caution.

Here, we combine published evidence from multiple measures—fiber counts in the dorsal root ganglia, histology of the nerves and the skin, microneurography, and psychophysics—to estimate plausible ranges for innervation densities of Aβ myelinated tactile afferent fibers covering all skin regions of the body. We estimate that the skin of young adults in the third decade is innervated by approximately 230,000 tactile afferent fibers (plausible range: 200,000-270,000) in total, with a subsequent decrement due to aging of 5-8% every decade. The hands and the face are the most highly innervated skin regions, as might be expected from the exaggerated cortical representation of these body parts (Penfield and Boldrey, 1937). While we believe our estimates to be robust, more fundamental work remains to be done, especially concerning the innervation of hairy skin.

Tactile innervation of the skin

The tactile innervation of the skin has been extensively covered in reviews (Abraira and Ginty, 2013; Johansson and Flanagan, 2009; McGlone et al., 2014; Saal and Bensmaia, 2014) and textbooks (Goldstein, 2009; Mountcastle, 2005), so we will only provide a brief overview. Here, as well as in the rest of the paper, we will focus on data from humans. The main tactile fibers underlying discriminative touch are myelinated Aβ fibers. Some tactile information is also carried by slow, unmyelinated C fibers (e.g., C-tactile fibers), which are thought to be mainly responsible for affective touch (Löken et al., 2009). However, recent evidence has shown that C-tactile fibers are likely to contribute to tactile sensibility (Cole et al., 2006) and that the spinal pathways carrying signals from both types of fibers are more intertwined than had previously been thought (Marshall et al., 2019). For the purposes of this review, we will focus on myelinated Aβ fibers and discriminative touch exclusively. However, a similar approach to the one pursued here should allow estimation of innervation densities for C-tactile fibers in future work, completing the picture of tactile innervation.

Focusing on Aβ fibers, two major afferent classes exist, which are distinguished by their electrophysiological response properties: fast-adapting (FA) fibers (also called RA: rapidly-adapting or QA: quickly adapting in the literature) that respond exclusively to dynamic stimuli, that is when the skin is in motion; and slowly-adapting (SA) fibers, which, in addition to dynamic responsiveness, also respond to sustained static skin deformation or stretch. Both classes can be further subdivided into type I afferents, which are more numerous and terminate close to the surface of the skin, and type II afferents, which end in deeper skin layers. In the hairy skin, two further classes of fast-adapting afferents can be found, namely hair units and field units; both of these exhibit response properties similar to those of classical FAI units, but their receptive fields are much bigger, and they might be more sensitive to higher frequencies (see sections on the face and hairy skin below for further detail). The presence and prevalence of different afferent classes vary in glabrous (non-hairy) skin as found on the palm, sole, and the lips, as compared to hairy skin, which covers the rest of the body.

Tactile afferents are somatosensory neurons whose cell bodies reside within the dorsal root ganglia (DRG) and the cranial sensory ganglia, respectively. One branch of these sensory neurons penetrates the spinal cord (for DRG neurons) or targets the trigeminal nuclei of the brainstem (for trigeminal neurons). The other branch extends to the periphery and either terminates as a nerve ending or associates with cutaneous mechanosensory end organs. Some of these associations are still debated and might not apply to all skin types. In the following, we will note links between afferent classes and mechanoreceptive end organs that have been made in the literature, but our estimates will be based on electrophysiologically characterized afferent types, and we make no claim regarding their associated mechanoreceptors. We will report innervation densities as units/cm^2, where we take a unit as the structure composed of an afferent fiber and all the mechanoreceptors (if any) innervated by it. The following estimates apply to young adults; for a discussion of the decrease of innervation with age, please see *Tactile innervation over the lifespan*.

Glabrous skin of the hand

Unlike other body regions, the glabrous skin of the hand and its tactile afferent innervation have been extensively studied, owing to its importance in grasping and manipulation. The number of tactile afferent fibers in the glabrous skin of the hand of young adults is estimated to be around 17,000 (Johansson and Vallbo, 1979). There are slightly more fast-adapting fibers (56%) than slowly-adapting ones (44%), a common feature of glabrous skin (see section on the foot sole).

Four major afferent types have been identified in the palmar skin of the hand: fast-adapting type I (FAI) fibers that innervate Meissner corpuscles; slowly-adapting type I (SAI) fibers that innervate Merkel cells; slowly-adapting type II (SAII) fibers that innervate Ruffini corpuscles; and fast-adapting type II (FAII) fibers that innervate Pacinian corpuscles.

43% of tactile afferent fibers or around 7,310 fibers are fast adapting type I fibers (FAI). FAI afferents are densely packed in the human fingertip with 141 units/cm^2 at its distal end. The density decreases in the proximal direction and only 25 units/cm^2 are present in the palm (see Figure 1A). The end organs of FAI fibers are Meissner corpuscles (MCs). Each Meissner corpuscle is innervated by one or two FAI fibers (Matsuoka et al., 1983), and a single FAI fiber typically branches several times, with each branch innervating a small number of MCs (Cauna, 1956; Paré et al., 2002). In the human fingertip, 3-5,000 MCs/cm^2 can be found (Nolano et al., 2003; Verendeev et al., 2015). Meissner corpuscle density in the palm is considerably lower with 500 MCs/cm^2 at the thenar eminence (Bolton et al., 1966). These numbers suggest that there are at least twenty times more MCs than FAI fibers in the glabrous skin of the hand (> 155,000) and that each FAI fiber innervates around 40 MCs.

25% of tactile afferent fibers or around 4,250 fibers in the palmar region of a single hand are classed as slowly adapting type I fibers (SAI). SAI fibers are densely concentrated in the fingertips at around 70 units/cm^2 at its distal end, and less so in the more proximal area of the hand with 46 units/cm^2 in the middle phalanx and 10 units/cm^2 in the palm (see Figure 1A). SAI fibers repeatedly branch and innervate Merkel cell neurite complexes, which form clusters within the skin. In the fingerpad of normal adults, up to 10,000 Merkel cells/cm^2 can be found, but not all of them appear to serve mechanoreceptive functions or are connected to nerve fibers (Lacour et al., 1991).

19% of tactile afferent fibers or around 3,230 fibers are classed as slowly adapting type II fibers (SAII). These are uniformly distributed across the glabrous skin area of the hand at an innervation density of approximately 12 units/cm^2. However, there is some evidence for increased density at the skin/nail border on the fingertips (Birznieks et al., 2009; Johansson and Vallbo, 1979). SAII fibers innervate Ruffini corpuscles (Halata, 1988), but it is unclear whether all SAII-like responses originate from Ruffini corpuscles. Where they do, a one-to-one mapping between fibers and corpuscles is assumed (Johansson and Vallbo, 1980).

Finally, up to 13% of tactile afferent fibers or around 2,200 fibers are estimated to be fast-adapting type II (FAII). The innervation density of this fiber type is low and relatively uniform across the hand surface at around 10 units/cm^2, but appears more numerous in distal finger segments with around 25 units/cm^2. These numbers yield an estimated total of around 800 FAII fibers terminating in the palm and 350 in each finger. FAII fibers target Pacinian corpuscles, and each corpuscle is innervated by a single fiber. It is possible for a single fiber to innervate multiple corpuscles (Sathian and Devanandan, 1983), which often appear in clusters (Miller et al., 1958; Stark et al., 1998) close to the digital nerves and their branches, and thus a count of corpuscles can serve to establish an upper limit on the number of FAII fibers. Histological counts of Pacinian corpuscles show a steep decline between the fetal stage and old age. However, data from other age ranges is lacking, and the numbers presented here might be an over-estimation (see *Calculations and prior results* for further details).

Receptive fields of the type I fibers on the glabrous skin of the hand are small, circular, and well-defined with a mean area of 13 mm^2 for the FAI and 11 mm^2 for the SAI fibers. Receptive fields of type II fibers are larger with diffuse borders and a mean area of 101 mm^2 for FAII and 59 mm^2 for SAII fibers (Vallbo and Johansson, 1984).

Glabrous skin of the foot sole

Somatosensory feedback from the lower limb, and in particular from the foot sole, plays an important role in controlling balance, posture, and gait (Inglis et al., 2002; Pearcey and Zehr, 2019). The foot sole is covered with glabrous skin and innervated by the same four classes of tactile afferents as the hand (SAI, SAII, FAI, FAII).

We estimate the total number of plantar cutaneous tactile afferent fibers innervating a single foot sole to be around 4,000, divided as follows: 17% (~680) SAI fibers, 20% (~800) SAII fibers, 51% (~2,040) FAI fibers, and 12% (~480) FAII fibers. These numbers are higher than an earlier estimate provided by Strzalkowski et al. (2018) (see *Calculations and prior results* for details regarding our estimation methodology). Like the hand, the foot sole contains more fast-adapting (63%) than slowly-adapting fibers (37%). The distribution of cutaneous afferents is not uniform across the foot sole for type I afferents (Figure 1B). The overall highest innervation density is found in the toes (48 units/cm^2), followed by the lateral metatarsals (31 units/cm^2), the lateral arch (29.7 units/cm^2) and the heel (15.7 units/cm^2). Innervation density is lowest in the medial metatarsals (11.3 units/cm^2). FAI afferents are considerably more dense in the toes (24.5 units/cm^2) than in the metatarsal/arch (9.1 units/cm^2) and in the heel (8 units/cm^2). A similar distribution is observed for SAI afferents. Similar to the hand, SAII and FAII fibers are more uniformly distributed across the different areas of the foot sole (Figure 1B). In electrophysiological recordings, fewer tactile afferents have been found terminating in the great toe as would be expected given its size, and its innervation thus appears lower than that of the neighboring toes; whether this discrepancy reflects a statistical artefact or a genuine difference remains to be seen.

The size of the receptive fields varies considerably for the different tactile fibers and across different foot areas with a mean value of 76 mm^2 for the SAI fibers, 248 mm^2 for SAII fibers, 81 mm^2 for FAI fibers, and 873 mm^2 for FAII fibers. In general, larger receptive fields are reported in the middle metatarsal and heel, and smaller receptive fields are located in the toes (Strzalkowski et al., 2018). Receptive fields on the foot sole are thus several times larger than those measured in the hand, perhaps owing to the less dense innervation of this skin region and the different mechanical properties of the skin of the foot sole.

Face

The face is densely innervated by cutaneous fibers, especially the region around the mouth and lips, and also the inside of the oral cavity and the tongue, highlighting the essential sensory contribution to mastication and other eating-related behaviors. We estimate that around 43,000-46,000 tactile afferents innervate the hairy facial skin and the lips, excluding the oral cavity, which is likely to be innervated by around 16,000-19,000 fibers (see *Calculations and prior results* for details). For the purposes of this manuscript, we focus on the traditional notion of skin as the outer tissue of the body, which differs considerably in anatomy and physiology from the tissues within the oral cavity. Consequently we will not discuss the innervation of the oral mucosa further and instead refer the interested reader to reviews by Trulsson (2006) and Haggard and de Boer (2014).

Four different classes of tactile afferents have been found in the hairy skin of the face and the red zone of the lip: slowly-adapting type I and type II, fast adapting type I and fast adapting hair follicle afferents (Trulsson and Essick, 2010). Slowly adapting afferents are suggested to have two types of end-organs: Merkel cell-neurite complexes for SAI afferents and Ruffini endings for SAII afferents (Nordin and Hagbarth, 1989). The hair follicle afferents (FA hair units) encountered in the facial skin are likely similar to hair units described in other hairy skin, but appear in some cases associated with a single hair only (Trulsson and Essick, 2010). The nature of the end organs of FAI units in the facial skin is uncertain, as no Meissner corpuscles have been reported in this area (Nordin and Hagbarth, 1989); possibly they are related to field units in other hairy skin, though their receptive fields appear smaller. Notably, no FAII afferents have been reported in the literature, and vibrotactile thresholds on the face show no characteristic Pacinian sensitivity around 200 Hz (Barlow, 1987), so this afferent class might be absent on the face, while present in other body regions.

Slowly adapting afferents appear more abundant than fast adapting ones in the facial skin (Bukowska et al., 2010; Johansson et al., 1988), with around 65% SA, resulting in 29,000 fibers, and 35% FA, resulting in 15,500 fibers. However, this breakdown is extrapolated from relatively small samples, so should be treated with caution.

Innervation density is not uniform across the face: we estimate an innervation density of 48 units/cm^2 for the forehead, eyes, and nose (V1), 67 units/cm^2 for the central part of the face (V2) and 84 units/cm^2 for the lower lip, the chin, the jaw and an area around the ears (V3). Locally, some regions such as the area immediately surrounding the mouth and the lips are likely to exhibit much higher innervation densities.

The size of the receptive fields varies for the different tactile afferent fibers with a mean value of 4 mm^2 for the SAI fibers, 6 mm^2 for SAII fibers and 6 mm^2 for FA fibers (Bukowska et al., 2010). Most receptive fields have a circular or oval well-demarcated area of high and relatively uniform sensitivity (Johansson et al., 1988). The highest concentration and smallest size of the receptive fields are measured around the corner of the mouth and in the upper lip. The psychophysical and receptive field properties observed in these areas, including the tactile acuity, are similar to those found in the human fingertip (Nordin and Hagbarth, 1989), suggesting a similarly high innervation density.

Hairy skin

Studies investigating the sensory innervation of human hairy skin (other than facial) have often focused on C afferents or proprioceptive fibers, with relatively few targeting Aβ tactile afferents. Data exists for the hand dorsum (Edin and Abbs, 1991; Edin et al., 1995; Järvilehto et al., 1976, 1981; Kakuda, 1992; Konietzny and Hensel, 1977; Nagi et al., 2019), the arm (Ackerley et al., 2014; Löken et al., 2009; Vallbo et al., 1995), the leg (Aimonetti et al., 2007; Edin, 2001; Ribot-Ciscar et al., 1996), and the foot dorsum (Nagi et al., 2019; Ribot-Ciscar et al., 1989; Trulsson, 2001; Vedel and Roll, 1982), but not for the body core, back, or chest, where microneurography is technically challenging, due to the small size of the nerves involved and continuous movement of skin in this area during breathing.

Hairy skin is innervated by afferent classes with similar response characteristics as found in glabrous skin, though specific end organs might differ. As in all other types of skin, SAI afferents are present and innervate Merkel cells, which in hairy skin are organised into touch domes, as compared to the cell neurite complexes found in glabrous skin. Similarly, SAII afferents have been identified electrophysiologically, though it is unclear whether they always connect to Ruffini-like corpuscles, as is thought to be the case in the hand (Chambers et al., 1972). Afferents with response properties similar to FAI afferents are frequently observed, but unlike glabrous skin, hairy skin does not contain Meissner corpuscles. Instead, three different types of FA afferents have been identified in the hairy skin: hair units, field units, and FAII units (Vallbo et al., 1995). Hair units branch and terminate in close proximity to hair follicles. Each hair unit is estimated to innervate around 25 individual hair follicles in the forearm (Vallbo et al., 1995). Field units show remarkable similarities with hair units, having numerous high-sensitivity spots distributed over a fairly large area. The nature of the end-organs of field units is unclear. The presence of FAII afferents has been demonstrated both in electrophysiological recordings (Vallbo et al., 1995) and psychophysically (Verrillo, 1966), though Pacinian corpuscles appear to be extremely rare in hairy skin. Innervation patterns vary for different body regions, with a prevalence of SA afferents in the arms at 61% of all fibers, while they only make up 47% in the legs (see Calculations and prior results for further details).

Based on fiber counts and estimates of axon diameter distribution in the dorsal roots of the spinal cord (see Calculations and prior results), we estimate that around 140,000 Aβ fibers (range: 110,000-180,000) innervate the hairy skin of humans (excluding the face). Innervation is most dense in the back of the head and neck area with around 17 units/cm^2 and in the arms with 12 units/cm^2, while is almost uniform in the rest of the body, with 8.9 units/cm^2 covering the skin of the chest and abdomen, 9 units/cm^2 on the back, and 9.8 units/cm^2 for the legs.

Hair units terminate on hair follicles in hairy skin, suggesting a relationship between hair follicle density and FA afferent innervation. Hair follicle density is not uniform across the adult body but instead varies by more than an order of magnitude across different body regions (Szabo, 1967). If the number of hair follicles innervated by a single afferent was relatively constant across different areas, one would, therefore, expect a strong correlation between our estimates of FA innervation density and hair follicle density. Indeed, we found a strong correlation ($r = 0.94$, $p < 0.01$) between both quantities (Figure 2A). Our estimates imply that each FA hair fiber innervates, on average, 25 hair follicles (range: 15-52), in strong agreement with earlier estimates for the forearm (Vallbo et al., 1995). Hair follicles include both vellus and terminal hairs, both of which have been found to be innervated by nerve fibers (Hashimoto et al., 1990).

Whole body

Summarizing all information above, across the whole body the palmar skin of the hands and the perioral region of the face are the most densely innervated regions. Relatively high innervation can also be found in some sections of the foot, such as the toes, while the hairy skin of the arms and legs are the least densely innervated, closely followed by the trunk (see Figures 3, and Table 1).

Innervation density in context

Innervation density and tactile acuity

Innervation density limits the spatial resolution with which tactile features can be resolved on the skin: lower innervation results in a larger spacing between receptors and implies that two tactile stimuli need to be further apart to be discriminated. One might, therefore, expect a strong correlation between receptor spacing and perceptual tactile acuity as determined in psychophysical experiments. Previous work suggests that spatial acuity is largely driven by SAI afferents (Peters et al., 2009), which possess the smallest receptive fields and, therefore, the highest spatial resolution. Indeed, a close relationship between SAI receptor spacing and tactile acuity has been established across the different regions of the hand (Craig and Lyle, 2001, 2002). Following this line of research, we used psychophysical two-point discrimination thresholds obtained from different regions across the whole body (Mancini et al., 2014; Weinstein, 1968) and correlated these values with estimated SAI receptor spacing. We found a strong relationship between these two variables ($r = 0.93$, $p < 0.001$, see Fig. 2B). As prior research has shown, tactile acuity is not fixed but improves with training; while the eventual plateau performance is likely determined by innervation density, typical performance might not (Peters et al., 2009). Additionally, more reliable measures of spatial acuity than the classical two-point threshold do exist (Craig and Johnson, 2000), and these suggest that, for example, the lips in fact exhibit higher acuity than the fingertips (Sathian and Zangaladze, 1996; Van Boven and Johnson, 1994). Nevertheless, differences in innervation density across the whole body appear large enough to yield a reliable correlation with two-point psychophysical thresholds.

The reasoning above ignores the fact that receptive fields of type I afferents are not uniform, but contain several individual subfields or hot spots, as demonstrated in both glabrous (Johansson, 1978; Pruszynski and Johansson, 2014) and hairy skin (Vallbo et al., 1995). The number of such hot spots might ultimately determine perceptual limits on the spatial resolution of the skin. Indeed, one of the first studies aiming to relate the accuracy of tactile perception with afferent fiber counts (Ranson, 1933) based their analysis on perceptual threshold mapping of the skin on a spatial scale similar to individual subfields (Strughold, 1924). Based on the average estimated number of subfields per fiber (FAI: 15, SAI: 6 for glabrous skin; hair units: 25, field: 10, SAI: 3 for hairy skin) one might therefore expect around 1.5 million hot spots across the whole body, with around 150,000 on the palmar surface of each hand, mostly supported by FA fibers.

Innervation density and the cortical homunculus

As demonstrated by pioneering work in humans (Penfield and Boldrey, 1937; Penfield and Rasmussen, 1950) and non-human primates (Kaas et al., 1979; Marshall et al., 1937), body regions are mapped somatotopically onto the primary somatosensory cortex (S1), with nearby regions on the body generally represented by nearby patches in cortex. However, the size of individual body region representations in cortex is not proportional to that anatomical region's skin surface area. For example, the area devoted to the thumb in S1 is as large as the area devoted to the entire forearm (Goldstein, 2009). These findings have led to the famous homunculus, in which body parts are scaled by the size of their cortical representation, and which displays enlarged hands, face, and tongue. In how far cortical magnification is driven purely by innervation density, or whether usage effects such as increased contact with some body parts over others also play a part, has been debated. Many studies and textbooks argue for a close correlation between innervation density and cortical magnification (Catani, 2017; Kandel et al., 2000), though quantitative evidence is lacking. To test this idea directly, we took estimates of cortical magnification from the literature (Gandhoke et al., 2019; Penfield and Rasmussen, 1950), and compared these with the innervation density estimates described above. We found a positive, but non-significant, correlation between a region's peripheral tactile fiber count and the size of its representation in cortex ($r = 0.40$, $p = 0.42$, Figure 2C), when assessed as the length of the coronal section onto which that body part is mapped. Crucially, some regions exhibited much larger cortical magnification than would be expected from their peripheral innervation alone. This included the heavily enlarged cortical areas containing the hand and face representations. Thus, it appears that these body parts are further magnified cortically, perhaps reflecting the fact that they are more likely to receive tactile stimulation (Jenkins et al., 1990; Sur et al., 1980) or that they are especially behaviourally relevant. Interestingly, the apparent cortical magnification of regions with already high innervation mirrors the visual system, where the fovea is further magnified cortically beyond its already higher density of cone photoreceptors (Popovic and Sjöstrand, 2001).

Tactile innervation over the lifespan

Our estimates of innervation density are based on data from a range of ages, but we have tried, as much as possible, to focus on young adults. It has been widely demonstrated that tactile sensibility declines with age, as evidenced by increased sensory thresholds (Dyck et al., 1972; Gescheider et al., 1994; Thornbury and Mistretta, 1981; Verrillo, 1980) and decreased spatial acuity (Manning and Tremblay, 2006; Stevens and Choo, 1996; Stevens and Patterson, 1995; Tremblay et al., 2003; Woodward, 1993). This decline might be partially explained by age-related mechanical changes of the skin itself, such as in stiffness or moisture levels, but neural degeneration through changes in myelination, and receptor and fiber loss are likely to play a major part.

Focusing on the loss of tactile afferents specifically, a substantial decrease in the number of myelinated fibers in the spinal cord dorsal root from early middle age onwards has been well documented (see Spencer and Ochoa, 1981, for an overview of the literature). After a considerable increase in the number of myelinated fibers in the first life decade, a gradual loss of fibers occurs throughout the lifespan from the third decade onwards, with an approximate loss rate of 5-8% per decade (Corbin and Gardner, 1937; Gardner, 1940; Low and Dyck, 1977). Therefore, the proposed estimate of 230,000 tactile afferents in the whole body of a young adult might be reduced to about 160,000 tactile afferents for people over 80 years old. There is evidence that the decrease in the number of fibers due to aging is more pronounced in some body regions than others, and that the skin of the face, arms, legs, hands, and feet are most affected, while the number of fibers innervating the abdomen remains almost unchanged (Decorps et al., 2014).

The mechanoreceptive end organs themselves are also affected by aging and might change their morphology or disappear completely over time. This effect has been best documented for type I afferents. For example, the density of Meissner corpuscles at the fingertip decreases more than three-fold from young adulthood to old age, and that of Merkel cells declines more than five-fold (García-Piqueras et al., 2019).

Calculations and prior results

In the following, we provide an overview of measurements from the literature and detail the calculations that led to the estimates of innervation density described in the previous sections. Our approach relies on fiber counts from the dorsal root ganglia and the trigeminal nerve, estimates of the proportion of tactile Aβ fibers within each segment, and finally measurements for the surface area of skin innervated by each. The same basic idea has been pursued before (Ingbert, 1903b), but advances in histology and immunohistochemistry, along with a much advanced understanding of the different classes of fibers involved in tactile sensibility prompted us to provide a modern re-assessment.

Hand

For the palmar surface of the hand we follow the original estimates by Johansson and Vallbo (1979), which agree well with later histological analyses: a count of myelinated fibers at both the metacarpophalangeal (MCP) joint, covering all fibers innervating a given finger, and at the terminal trifurcation, covering innervation of the fingertips only, yielded 2,100-4,800 fibers per finger and roughly 1,900-2,600 per fingertip (Auplish and Hall, 1998). Assuming that around 45% of these fibers are tactile afferents in the Aβ range, similar to the proportion that has been estimated at the wrist (Vallbo and Johansson, 1978), yields 1,000-2,200 tactile afferents per finger and roughly 800-1,200 per fingertip. These numbers agree remarkably well with Johansson and Vallbo's original estimates of 2,500 for the whole finger and 1,000 for the fingertip of the index finger (Johansson and Vallbo, 1979). Psychophysical measurements also suggest that innervation density decreases dramatically between the fingertip and the palm, and SAI receptor spacing as calculated from Johansson and Vallbo's estimates correlates highly with spatial acuity across different regions of the hand (Craig and Lyle, 2001, 2002).

Pacinian corpuscles are relatively large and can, therefore, easily be identified in dissections, at least in principle. No dissection data has been reported from young adults and the few existing studies focus on either fetal tissue or cadavers of elderly individuals. These present a mixed picture. On the one hand, fetal studies are in good agreement with the estimates made by Johansson and Vallbo (1979). Cauna and Mannan (1958) counted Pacinian corpuscles in the radial half of a fetal index finger and found 178 in total, in almost perfect agreement with Johansson's estimates of afferent numbers (see also Brisben et al., 1999, for further analysis). In support of these findings, recent counts from the distal segment of several fetal fingers also yielded numbers in close agreement and confirmed that PC innervation is higher in the distal than in other finger segments (Kim et al., 2018). On the other hand, studies in elderly individuals report much lower numbers. Dissection of the whole hand of several old-age human cadavers has found around 300 corpuscles per hand (Stark et al., 1998). A more recent count in several distal finger segments yielded proportionally higher numbers (around 40 corpuscles per segment), but these counts were still much lower than those in fetal tissue (Kobayashi et al., 2018). Taken together, these results suggest a dramatic decrease in the number of Pacinian corpuscles with age, but it is unclear whether this decrease takes place early during development, later in life, or whether it is spread out across the lifetime. As the original estimates by Johansson and Vallbo (1979) are in good agreement with the fetal data, we used them in our report. However, it is possible that the true number of FAII fibers is lower than reported here, perhaps by half or more. More recently, it has been shown that Pacinian corpuscles can be resolved using high-field MRI (Laistler et al., 2018; Rhodes et al., 2019), opening the possibility to establish in-vivo counts across a range of age groups in the future.

Foot sole

A recent study estimated that around 1,700 tactile afferents innervate the plantar surface of a single foot (Strzalkowski et al., 2018). Our estimates suggest that the actual innervation is likely higher, by a factor of approximately two, based on several observations. First, the original estimate was based on a study demonstrating a ratio of roughly 10:1 in myelinated fibers between the hand and the foot (Auplish and Hall, 1998). However, fiber counts were only taken at the metacarpophalangeal and metatarsophalangeal joints, respectively, and because innervation density gradients are steeper on the hand than on the foot, this does not imply a ratio of 10:1 in the total fiber count. Instead, a ratio of 4-5:1 appears more realistic. Second, tactile acuity is higher on the foot sole compared to the foot dorsum or other regions on the leg (Mancini et al., 2014), suggesting a higher innervation density in this region, in line with our estimates for hairy skin (see below). Taken together, a total tactile innervation of 4,000 afferents per foot sole appears likely. To arrive at updated estimates for different regions of the foot sole, we took the total number of tactile afferents as estimated above and distributed them across the foot sole according to the relative densities established in Strzalkowski et al. (2018).

As has been done in the hand, Pacinian corpuscles can be identified and counted in human fetal samples. Comparing the results of a recent study that focused on the toes (Jin et al., 2020) with our estimates yielded 2-3 times more corpuscles in the experimental sample, a reasonably close match given the low numbers involved. The discrepancy might be explained by the fact that the number of corpuscles might decrease after the fetal stage, that several corpuscles might be innervated by a single fiber, or that we have underestimated the overall number of fibers innervating the foot sole. Finally, in the toes Pacinian corpuscles appear much more numerous at the proximal rather than the distal end, in contrast to the fingers, and given the difficulty of pinpointing FAII termination sites in microneurographic experiments, it is possible that some have been attributed to the forefoot region instead.

Face

The sensory innervation of the face is supplied by the sensory root of the trigeminal nerve or fifth cranial nerve. In this root, the total number of fibers is estimated at 170,000, and approximately 62,000 of these are myelinated and fall within the diameter range of Aβ fibers (Pennisi et al., 1991). The trigeminal nerve branches into three major divisions which supply different areas of the face; the ophthalmic branch, or V1, innervates the upper part of the face, covering approximately 38% of the facial skin; the maxillary branch, or V2, innervates the mid-third of the face, including part of the nose and down to the upper lip, corresponding to approximately 32% of the total facial area; finally, the mandibular branch, or V3, innervates the lower part of the face and the area around the ears, and covers around 30% of facial skin. The maxillary division V2 gives rise to six sensory branches, of which two are responsible for the sensory innervation of the hard palate inside the oral cavity (greater palatine and nasopalatine nerves). The mandibular division V3 includes five sensory branches, of which the lingual nerve and the buccal nerve innervate the floor of the oral cavity and the inside of the cheeks. Thus, four out of 11 branches of the V2 and V3 divisions innervate the inside of the mouth. Combining this fact with recent histological analyses, which found that skin within the V3 innervation area contains almost twice the number of fibers than skin innervated by V1 (Nolano et al., 2013), suggests by rough approximation that around 25-30% of the 62,000 myelinated fibers of the trigeminal nerve are responsible for the sensory innervation of the oral mucosa, leaving around 43,000 to innervate the facial skin and lips. The pattern of the sensory innervation changes across the three divisions and the density of myelinated fibers was estimated by Nolano et al. (2013) as 8.0, 15.9, and 16.4 per mm^2 in V1, V2, and V3, respectively. These estimates include multiple branches originating from the same afferent and also count any fibers merely traversing a given skin area rather than terminating there, and thus cannot be used directly to estimate the number of individual afferents. Nevertheless, in relative terms, these histological counts can be expected to scale proportionally to the actual afferent counts. To arrive at estimated innervation densities for V1, V2, and V3, we therefore divided the total number of fibers estimated above across V1, V2, and V3 in the proportions estimated by Nolano et al. (2013). A total facial skin area of 675 cm^2 was assumed (Siemionow and Sonmez, 2008). See Supplemental Table 1 for precise calculations (DOI: https://doi.org//10.15131/shef.data.12753650.

Hairy skin on arms, trunk, and legs

The dorsal roots of the spinal cord contain 1-1.2 million fibers in total, ranging from large, medium, and small myelinated to unmyelinated nerve fibers (Ingbert, 1903a; Liu et al., 2015). The region of skin innervated by all tactile afferents passing through a given dorsal root is known as a dermatome. While the specific territory innervated by each dermatome varies between people, and dermatomes also generally overlap within individuals, they nevertheless follow a systematic pattern. Fiber counts in individual dorsal roots can, therefore, be used to estimate the innervation of their associated dermatomes. The estimates presented here are based on recent fiber counts published by Liu et al. (2015). The territory of each dermatome is derived from an evidence-based map that assessed and combined multiple existing data sets (Lee et al., 2008); we traced the published dermatome outlines and then calculated the area of skin innervated by each dermatome as the sum of the areas covering the front and back of the body, respectively, assuming a total area of skin of 1.5 m2 (Yu et al., 2010). This analysis also takes into account that dermatomes generally overlap. We also compared the estimated peripheral fiber innervation densities derived from these maps with ones based on an older dermatome representation in a popular textbook (Grant and Anderson, 1983). We found only minor differences, suggesting that our results do not hinge on a particular dermatome map.

Only a subset of dorsal root fibers will be myelinated fibers in the Aβ range and underlie tactile innervation of the skin, rather than internal organs. The fraction of myelinated fibers varies across the spinal tract, being higher in the cervical and lumbar tract (Davenport and Bothe, 1934; O'Sullivan and Swallow, 1968) and, on average, around 40% of axons have been classified as unmyelinated (Sheehan, 1935). Assuming a 50:50 split between Aδ and Aβ myelinated fibers, and considering around 10% of Aβ fibers innervating deep structures (Vallbo and Johansson, 1978), an average fraction of 17% (range: 10%-25%) of the fibers in the dorsal roots are estimated to represent Aβ fibers involved in the transmission of tactile sensations. In the dermatomes C6-C8, for example, we estimate that about 53,500 of the 210,000 fibers are tactile afferents. Considering that approximately 36,000 of these are in the ulnar and median nerve and innervate the glabrous skin of the hand, the remaining tactile afferents in the C6-C8 dermatomes cover the hairy skin of the hand dorsum and forearm. This calculation leads to an estimated density of 12.7 units/cm^2 in these areas, which is consistent with the overall hairy skin estimations here proposed. Our estimates also agree well with a recent count in the L4 and L5 dorsal roots that found around 30% of axons had a diameter bigger than 5 µm, not all of which contribute to the tactile innervation of the skin (Sperry et al., 2019). Similarly, O'Sullivan and Swallow (1968) estimated around 6,000 fibers/mm2 in the sural nerve. 40% of these have a diameter in the range of 6-12 µm, which led to a total of 13,000 Aβ myelinated afferents in the sural nerve. Considering not all of these fibers are cutaneous afferents, and considering that the sural nerve contributes with other sacral nerves to the innervation of a skin area of around 4,500 cm^2 in the leg and foot, these measures result in good accordance with our estimates. Please see Supplemental Table 2 (DOI: https://doi.org//10.15131/shef.data.12753650) for full calculations split by dermatomes.

The main source of uncertainty in our estimates is the total number of fibers in the dorsal root and, most importantly, the proportion of myelinated Aβ fibers for each dermatome (Davenport and Bothe, 1934; Sperry et al., 2019). This question has only been investigated experimentally in a subset of dorsal roots, and different studies report conflicting results. For this reason, we repeated our calculations assuming a possible positive or negative variation of 20% on the number of tactile afferents for each dermatome. When doing so, we noticed that we fell short of or exceeded the physiologically plausible range in several instances, lending credibility to our original estimates. For example, in dermatomes C6, C7, and C8 considering that 18,000 of the total number of afferents can be expected to innervate the palmar surface of the hand, a reduction of more than 20% of the dorsal root fiber portion considered as tactile afferents, would result in a number close to zero (or even negative) for tactile afferents innervating the hairy skin of the back of the hand and part of the forearm. Similarly, an increase of more than 20% in the portion of dorsal root fibers considered to be tactile afferents would, in some dermatomes such as L1, result in areas of hairy skin having a density of afferents improbably close to that of the hairless skin of the foot and some areas of the palm of the hand. Taking these limits into account, the overall number of tactile afferents innervating the hairy skin is likely to fall in the range 110,000-180,000, leading to a total number of 200,000-270,000 afferents across the whole body.

To determine the proportion of SA and FA fibers, we tallied afferent numbers reported in different microneurography studies. For the hand dorsum and arm, we found a total of 267 reported afferents in the literature, 61% of which were slowly-adapting (Ackerley et al., 2014; Edin and Abbs, 1991; Edin et al., 1995; Kakuda, 1992; Löken et al., 2009; Nagi et al., 2019; Vallbo et al., 1995). For the foot dorsum and leg, our sample included 315 afferents, 47% of which were slowly adapting (Aimonetti et al., 2007; Edin, 2001; Nagi et al., 2019; Ribot-Ciscar et al., 1996, 1989; Trulsson, 2001). Thus, a higher proportion of slowly-adapting afferents innervates the arms than the legs. No data exists for the trunk. We assumed that the proportion of SA fibers for this region would fall in between those for the arms and the legs, as does overall innervation density, and settled on an estimate of 55% slowly-adapting fibers for the trunk. See Supplemental Table 3 (DOI: https://doi.org//10.15131/shef.data.12753650) for a detailed breakdown of afferent types reported in the literature on hairy skin.

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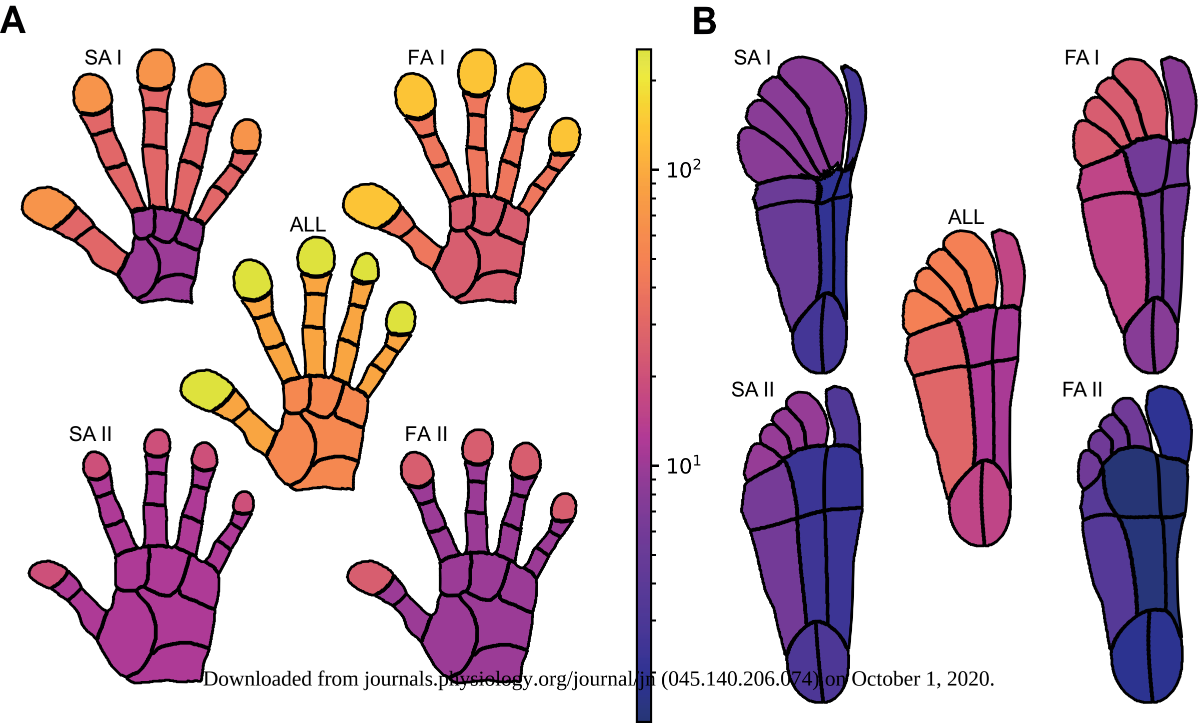
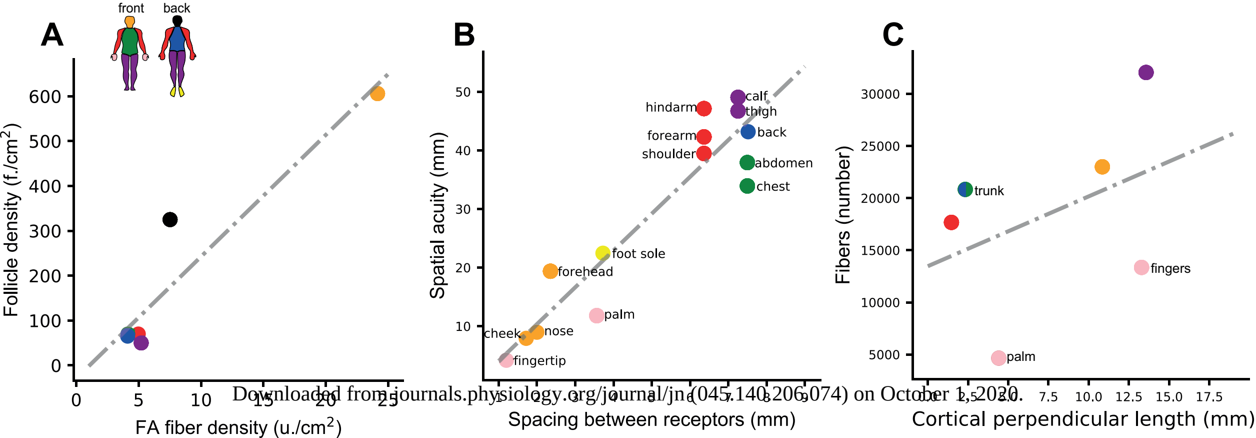
Figure captions

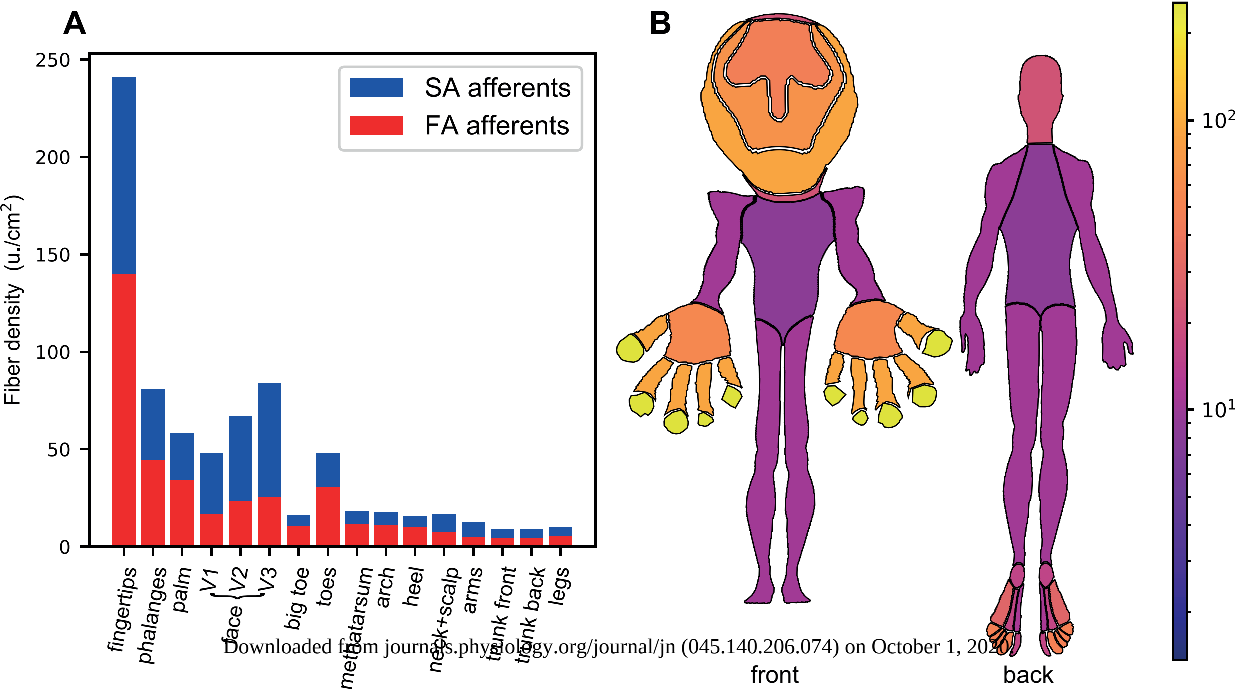
Figure 1. Innervation densities for (A) the palmar surface of the human hand, and (B) the plantar surface of the human foot. Each area is scaled and colored by its innervation density (units/cm^2) to reveal the hand and foot 'homunculi'. In the hand, both SAI and FAI fibers are densely packed in the distal ends of the fingertips and much less so in the palm, while the two other afferent classes are more evenly spread throughout the hand and exhibit much lower innervation density overall. Compared to the hand, the foot sole is less densely innervated but displays a similar proximal-distal gradient for type I afferents. Additionally, in the foot, a lateral gradient is evident with denser innervation of the lateral than the medial arch for all afferent classes. All illustrations were generated from 2D region outlines using a flow-based algorithm that scales each region according to a target value while preserving border relationships between regions (Gastner et al., 2018).

Figure 2. (A) Estimated fiber density for FA hair cells on different skin regions versus average hair follicle density for the same skin regions. Colours denote different body parts, as indicated in the inset. The grey line shows the line of best fit. (B) Estimated spacing between SAI termination sites versus perceptual tactile acuity as assessed by two-point discrimination tasks for different body regions (Weinstein, 1968). There is a strong relationship between a body region's tactile innervation and our ability to spatially discriminate tactile stimuli. (C) Size of cortical somatosensory representation for different body parts versus estimates for the total number of tactile fibers innervating that region. Innervation alone cannot explain cortical representation. Numbers refer to a single brain hemisphere.

Figure 3. Whole-body tactile innervation densities. The hand and face are the most densely innervated regions. (A) Total tactile innervation density for fast-adapting (red) and slowly-adapting (blue) afferents (including both type I and type II afferents), for different skin regions across the whole body. The ratio of fast and slowly adapting fibers is not constant but varies with skin region. (B) Illustration of the whole-body peripheral innervation homunculus using the same method as detailed in Figure 1. The color and scaling of each body area denotes its innervation density (units/cm^2), combining both SA and FA fibers.


A
SA I
FA I
ALL
SA II
FA II
10^2
10^1
B
SA I
FA I
ALL
SA II
FA II


A
front
back
Follicle density (f./cm^2)
FA fiber density (u./cm^2)
0
100
200
300
400
500
600
0
5
10
15
20
25
B
Spatial acuity (mm)
Spacing between receptors (mm)
10
20
30
40
50
hindarm
forearm
shoulder
calf
thigh
back
abdomen
chest
foot sole
forehead
palm
cheek
nose
fingertip
C
Fibers (number)
Cortical perpendicular length (mm)
5000
10000
15000
20000
25000
30000
0.0
2.5
5.0
7.5
10.0
12.5
15.0
17.5
trunk
fingers
palm



A
B
Fiber density (u./cm^2)
SA afferents
FA afferents
0
50
100
150
200
250
fingertips
phalanges
palm
V1
V2
V3
face
big toe
toes
metatarsum
arch
heel
neck+scalp
arms
trunk front
trunk back
legs
front
back
10^1
10^2

	# of afferents	Innerv. dens. $u./cm^2$	Skin area cm^2	SA afferents %
Hand	16,500	90	184	43
Fingertips	5,061	241	21	42
Fingers	6,156	81	76	45
Palm	5,046	58	87	41
Foot Sole	3,958	21	200	37
Big Toe	261	16	16	37
Toes	913	48	19	37
Metatarsal	912	18	51	37
Arch	1,362	18	76	37
Heel	597	16	38	37
Face	46,000	69	675	65
Face V1	12,307	48	255	65
Face V2	14,676	67	219	65
Face V3	16,820	84	200	70
Neck+Scalp	8,625	17	516	55
Front trunk	20,886	9	2,272	55
Back trunk	20,775	9	2,272	55
Arms	35,335	13	2,769	61
Legs	56,186	10	5,722	47
Total	~230,000	15	~15,000	53