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## Intrinsic signal imaging of somatosensory function in non-human primates

Anna W. Roe<sup>1</sup>, Li Min Chen<sup>2</sup>, Robert Friedman<sup>1</sup>

<sup>1</sup>Department of Psychology, Vanderbilt University, Nashville, TN 37212

<sup>2</sup>Institute of Imaging Science, Vanderbilt University, Nashville, TN 37232

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Correspondence:

Anna W. Roe, Associate Professor

Department of Psychology

Vanderbilt University

301 Wilson Hall

111 21st Avenue South

Nashville, TN 37203

(615) 343-0901 phone

(615) 343-8449 fax

email: [anna.roe@vanderbilt.edu](mailto:anna.roe@vanderbilt.edu)

<http://www.psy.vanderbilt.edu/faculty/roeaw/index.html>

## **ABSTRACT**

Optical imaging studies of somatosensory cortex (SI) in primates has led to re-evaluation of our understanding of cortical functional organization. This chapter describes findings showing that somatosensory topography, long a foundation of cortical function, may not be as precise in the awake monkey, suggesting a re-evaluation of the relationship between topographic representation and sensory precision. Optical maps of the tactile funneling illusion, which demonstrate a map of how tactile stimuli are perceived rather than a map of skin topography, call for a re-evaluation of topographic representation in SI as a body map. With respect to representation of sensory submodalities, optical images of vibrotactile pressure, flutter, and vibration domains reveal striking similarities and differences between modality maps in visual and somatosensory cortices.

# OUTLINE

Intrinsic Signal Imaging of SI Organization

Topographic Representation in Primary Somatosensory Cortex (SI)

*Topography in somatosensory cortex.*

*Optical imaging of cortical topography in anesthetized monkeys.*

*Optical imaging of cortical topography in alert monkeys.*

Topographic Representation of the Tactile Perception in SI

*The funneling illusion*

*Two point stimulation produces cortical merging in Area 3b.*

*Intensity of funneling percept*

Modality Representation in SI

*Presence of interdigitated multiple maps*

*Relationship of vibrotactile domains to topography*

A New Model of SI organization

## Intrinsic Signal Imaging of SI Organization

This chapter reviews some exciting new studies on primate somatosensory cortex using intrinsic signal optical imaging methods. Previous electrophysiological approaches have provided a great deal of information regarding neural processes in SI. However, there is a limited understanding of the functional organization of such representation in SI. Optical imaging is a method well-suited for revealing such functional organizations. In the visual cortex, understanding functional organization has offered significant insight into the segregation and integration of different visual perceptual channels and has inspired a large number of studies. The hope is that greater understanding of functional organizations in somatosensory cortex will similarly illuminate the role of SI in tactile perceptual behaviors.

This chapter will be restricted to the imaging of intrinsic optical signals *in vivo* (i.e. without the use of dyes, cf. Bonhoeffer and Grinvald 1996 for review). The intrinsic signal arises from various sources including changes in blood volume due to local capillary recruitment, activity-dependent changes in the oxygen saturation level of hemoglobin (increase or decrease in deoxyhemoglobin), and light scattering changes that accompany cortical activation. In this method, stimulus-induced changes in neural activity produce local decreases in blood oxygenation detected as local decreases in tissue reflectance. These minute changes in optical absorption (typically in the 0.1% range), which are recorded by a CCD (charge-coupled device) camera, can be highly spatially localized because local capillary related bloodflow is highly localized. Thus, functional organizations in sensory cortices can be mapped at high resolution, permitting the visualization of 100  $\mu\text{m}$ -sized structures. The magnitude and timecourse of reflectance change is dependent on the illumination wavelength used (Vanzetta et al., 2005). In visual cortex, the typical intrinsic signal timecourse (under 600-630nm illuminant, wavelengths at which the oxymetry component is relatively large) peaks within 2-4 sec followed by a several second undershoot (Bonhoeffer and Grinvald 1996; Vnek et al., 1999). The optical signal in primate SI is similar in timecourse and magnitude (Chen et al 2001, 2003, 2005; for different wavelength see Tommerdahl et al. 1998, 1999). Although intrinsic imaging lacks the temporal resolution offered by dyes, it is a high spatial resolution imaging method that does not require application of any external agents to the brain. The intrinsic signal has been associated with so-called 'initial dip' in BOLD fMRI studies (e.g. Kim et al 2000, Cannestra et al 2001, Devor et al 2003, Sheth et al 2003, Thompson et al 2003, Fukuda et al 2006, Roe et al 2006) and has been shown to be correlated with both spiking and subthreshold components of neural response. For a recent review see Zepeda et al 2004.

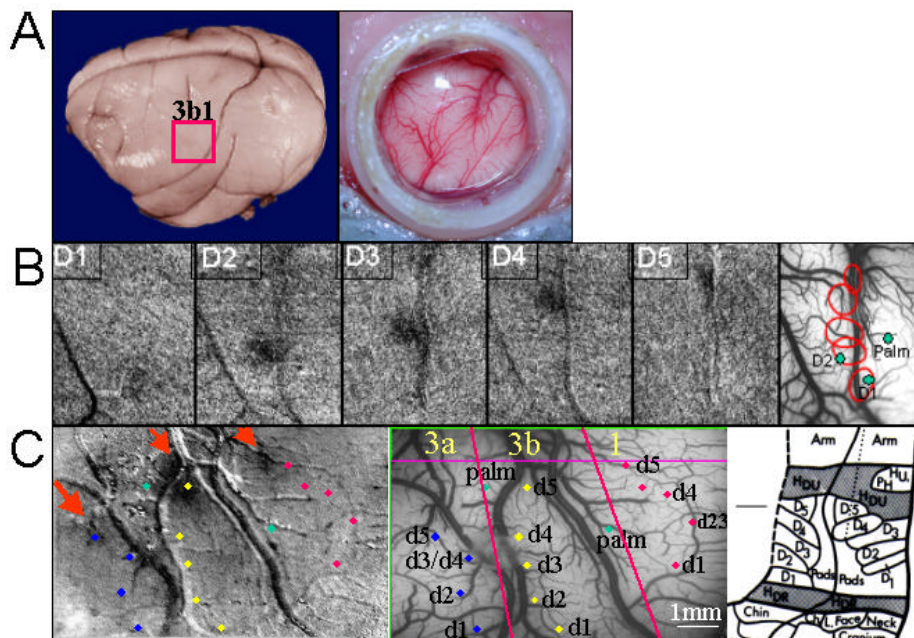
New world monkeys are an attractive species for optical imaging studies because their lissencephalic cortex allows unobstructed viewing of multiple visual cortical areas in both dorsal and ventral streams (see Fig 1A, cf. for visual cortex Malach et al 1994, Lyon et al 2002, Xu et al 2004; Roe et al 2005). Thus, it is possible, for example, to image Areas 3a, 3b, 1, and 2 simultaneously by optical methods. The functional organization of SI in new world monkeys largely parallels those in old world monkeys (cf. Sur et al., 1982) and has been studied extensively in physiological, anatomical, and behavioral studies, making them prime candidates for studies of functional organization of sensation and sensory behavior. For this reason, the studies summarized in this chapter are mostly derived from studies on New World monkeys.

To underscore the importance of this developing approach, one of the challenges of optical imaging is to understand the modular basis of cognition. How do networks of modules within and across cortical areas achieve vision or memory or emotion? Visualization of such modular activations during behavior is tantamount to watching the brain at work. Over the past decade, researchers have developed methods to visualize activations through implanted 'windows on the brain' (e.g. Chen et al 2002). By applying these methods to the awake, behaving animal, it is hoped that this method can open new vistas in our understanding of the neural basis of cognitive function. Furthermore, the ability of these studies to forge a critical link between a large body of work on animal models and functional imaging in humans will be

invaluable. There are now a handful of optical imaging studies on visual behaviors in the awake monkey (Grinvald et al 1991, Vnek et al 1999, Shtoyermann et al 2000, Seidemann et al 2002, Slovin et al 2002, Siegel et al 2003, Roe et al 2004). However, such studies in alert tactile behaviors are still few (Chen et al 2005).

## Topographic Representation in Primary Somatosensory Cortex (SI)

**Topography in somatosensory cortex.** Orderly topographic sensory maps in primary somatosensory cortex (SI) serve as an anchor for our understanding of somatosensory cortical organization (Woolsey et al. 1942; Nelson et al. 1980; Sur et al. 1982; Pons et al. 1985, 1987). Primate primary somatosensory cortex (SI) in the postcentral gyrus contains four complete topographic maps of the body surface that fall within the architecturally defined Brodmann's Areas 3a, 3b, 1, and 2 (e.g. Woolsey et al. 1942; Powell and Mountcastle 1959; Kaas et al 1979; Nelson et al. 1980; Sur et al. 1982; Pons et al. 1985, 1987). Areas 3b and 1 receive input primarily from cutaneous afferents where areas 3a and 2 receive input from deep afferents (muscle spindles and joints) (e.g. Tanji and Wise, 1981). Other parietal areas, such as areas 5 and 7, also process somatosensory information (Murray and Mishkin 1984; Dong et al. 1994; Burton et al. 1997; Duhamel et al. 1998; Debowy et al. 2001). Somatotopic maps are also found laterally in SII and adjacent area PV (Krubitzer et al. 1995; Burton et al. 1995) and there are other somatosensory areas in insular cortex that receive cutaneous and visceral information (Robinson and Burton 1980ab; Schneider et al. 1993; Craig 2003).



**Figure 1.** Optical imaging of digit topography in SI of anesthetized squirrel monkey. A) Locations of Areas 3b and 1 in squirrel monkey brain. Optical window over this area. Sur et al 1982. B) Five images obtained in response to indentation of digits D1 to D5, respectively. Dark pixels indicate cortical activation. D1-D5 activation locations overlaid on blood vessel map (from Chen et al 2001). C) Imaging of Areas 3a, 3b, and 1 in squirrel monkey in response to indentation of digit D5. D5 activation zones (orange arrows) correlate well with electrophysiological map (dots). Topography and size of focal activations (0.5-1 mm) area consistent with published maps (Sur et al 1982).

**Optical imaging of cortical topography in anesthetized monkeys.** A number of studies have employed the optical imaging approach to examine topographic representation in somatosensory cortex. Such studies have revealed organizations quite consistent with previous electrophysiological studies of SI topography (e.g. in rats: Masino and Frostig, 1993, 1996; Sheth et al., 1998; Goldreich et al., 1998; in non-human primates and humans: Narayan et al. 1994; Cannestra et al., 1998; Schwartz et al 2004). In the nonhuman primate, studies of somatotopy have produced images of the body map in the squirrel monkey (radial interdigital pad, D2 fingertip, and similar sites on the leg and foot) (Tommerdahl et al., 1999), distal fingerpads of the squirrel monkey (Chen et al. 2001, Tommerdahl et al 2002), and Area 1 of the Macaque monkey (Shoham and Grinvald 2001).

As shown in Figure 1B, focal activations roughly 0.5-1 mm in size are obtained following stimulation of individual digit tips with indenting probes. Comparison of D1 (thumb) to D5 digit tip activations reveals an orderly map within Area 3b of the squirrel monkey. These maps are quite consistent with published maps obtained with electrophysiological methods (e.g. Sur et al. 1982; Merzenich et al. 1987). Imaging a larger field of view reveals multiple representations, which include Areas 3a, 3b, and 1 (Figure 1C). For example, stimulation of a single digit tip (D5) elicits 3 activations in Area 3a, 3b, and 1 respectively (Fig 1C, orange arrows); the locations of these activations are consistent with electrophysiological recordings in this case (colored dots). Thus, intrinsic signal imaging is a useful tool for quickly and clearly revealing tactile topography in primates.

**Optical imaging of cortical topography in alert monkeys.** Our view of somatosensory topography is largely based on data collected in the anesthetized animal. However, little is known about these topographies in the awake primate (Iwamura et al. 1993; McKenna et al. 1982; Blankenburg et al. 2003). The question remains as to whether the fundamental structure of topographic maps is the same in the anesthetized and the awake, behaving animal. For example, does topography remain stable over time in the awake animal or is it dependent on behavioural context? Neither is much known regarding the relative activations of different cortical areas (within primary somatosensory cortex of the primate, SI, are cortical Areas 3a, 3b, 1 and 2). Since different cortical areas are characterized by distinct stimulus preferences (Mountcastle and Powell 1959; Hyvarinen and Poranen 1978; Costanzo and Gardner 1980; Carlson 1981; Sur et al. 1985; Iwamura et al. 1993), it is possible that different cortical areas become dominant under changing stimulus and behavioural contexts. A number of studies have investigated behavioral modulation of neuronal response within single cortical areas (Iwamura et al., 1983; Nelson et al 1987, 1991; Burton and Sinclair 2000; Meftah et al. 2002; Fitzgerald et al 2006); however, little is known about the modulation of inter-areal dominance or of patterned area-specific functional organizations during behavior (Hsiao et al 1993; Buchel and Friston 1997; Kastner et al 1998; Mesulam 1998; Friston 1998; Ungerleider et al. 1998). Indeed, what is the behavioural relevance of known functional organizations and topographies? Such studies would provide important constraints for studies on feedforward vs feedback influences in cortical processing (cf. Roe 2003).

One recent optical imaging study in somatosensory cortex revealed that activation patterns can differ significantly between anesthetized and awake preparations. Using intrinsic signal optical imaging of Areas 3b and 1, awake squirrel monkeys were imaged repeatedly for over a period of two years in awake and anesthetized states in response to vibrotactile and electrocutaneous stimuli presented to individual fingerpads. Imaged somatotopic maps were in general stable over this period in both the anesthetized and awake states, consistent with electrophysiologically recorded maps in Areas 3b and 1 in the anesthetized state.

However, in the awake animal, signal sizes were larger and more variable, leading to larger activations (both in area and amplitude), suggesting a less precise topography. Topographically, the map in the awake state appears less precise and also different from that in the anesthetized state. As shown in Figure 3, in the awake state the

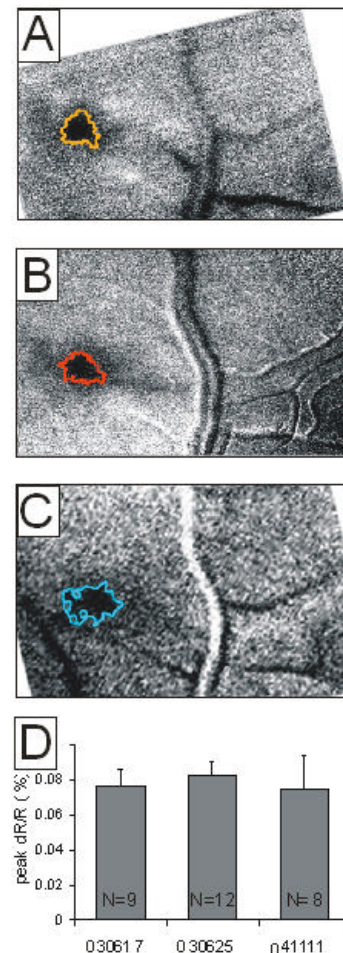


Figure 2. Cortical topography is stable over time in awake squirrel monkey SI (from Chen et al 2005). Images taken over 3 different imaging sessions.

activations to D3 and D4 stimulation are highly overlapped. The significance of this finding remains to be explored. Larger activations and larger receptive field sizes are traditionally associated with less refined topography and perhaps decreased discriminability. However, the possibility remains that larger imaged activations reflect a substrate for greater cortical dynamics. Indeed, these findings are consistent with some previous studies in the awake animal that have shown large receptive fields and dynamic changes in receptive fields (such as increases in receptive field size, shifting ‘hot spots’ or changes in spatial sensitivity profiles within receptive fields) or other modulation of cortical activity with behavioural context (Chapin and Lin 1984, Nelson 1987, Lee and Whitsel 1992, Nicolelis et al 1993, Schroeder et al 1995). Thus, topographic organizations present in the anesthetized animal may be used in different ways in the awake animal.

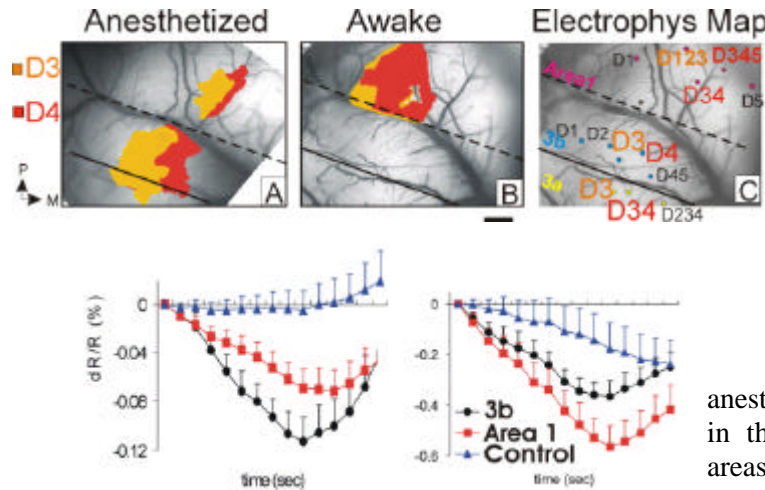


Figure 3. Comparison of topographic activations in the anesthetized and awake states. Cortical response to vibrotactile stimulation of D3 (orange) and D4 (red) in the squirrel monkey. A) Anesthetized activation is more prominent in Area 3b (see D). B) Awake activation is more prominent in Area 1 (see E). C) Electrophysiological mapping of Areas 3a, 3b, and 1. D) and E) Optical signal timecourse for D4 locations in anesthetized (d) and D3 locations in awake (e) in areas 3b and 1.

Another difference between anesthetized and awake activation patterns lies in the strength of activations across cortical areas. Whereas in the anesthetized animal strongest imaging signals are obtained from

Area 3b, in the awake animal Area 1 activation dominates over that in Area 3b, suggesting that inter-areal interactions in the alert animal differ substantially from that in the anesthetized animal. In the anesthetized state, we generally observe stronger activations in Area 3b than in Area 1 (Fig 3D). The opposite is observed in the awake state, where Area 1 activations are more prominent (Fig 3E). Whereas in the anesthetized animal strongest imaging signals are obtained from Area 3b, in the awake animal Area 1 activation dominates over that in Area 3b, suggesting that inter-areal interactions in the alert animal differ substantially from that in the anesthetized animal. These results suggest significant awake vs anesthetized differences in somatosensory activations, due to differences in neural response and/or vascular response.

## Topographic Representation of Tactile Perception in SI

The long-standing view that sensory topography in the somatosensory cortex reflects a 'body map' is well supported. However, a recent study has called into question traditional views of somatosensory cortical maps (Chen et al 2003). This study used the so-called ‘funneling illusion’ to demonstrate that topographic maps in SI can reflect the perceived location of tactile stimulation rather than the location of physical stimulation on the skin. This finding suggested that, in contrast to previous views, the topographic map in Area 3b is a perceptual map rather than a physical one.

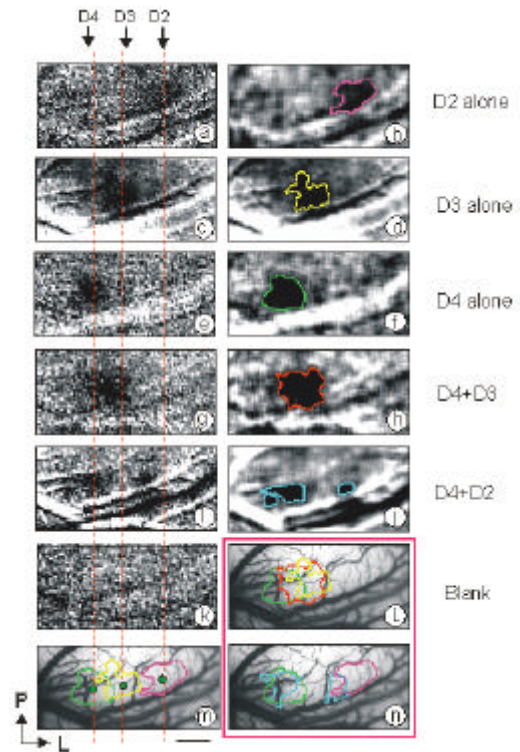
**The funneling illusion.** The funneling illusion is the illusory perception of skin stimulation at a single site central to a line of multiple stimulation sites (Sherrick 1964, von Békésy 1967, Gardner and Spencer 1972, Gardner and Tast 1981, Hashimoto et al 1999). Inputs at lateral sites are ‘funneled’ centrally so that perceived intensity at the central site is greater than that to stimulation at the middle site alone. With two point stimulation, a funneled sensation is produced at a central location which is without direct stimulation. This illusion has been reported on the forearm, palm, and fingers. When two digit tips

are simultaneously stimulated, subjects report sensations such as ‘a mound or trapezoid centered over a finger’, ‘a mound or trapezoid bridging fingers’, or ‘a mound bridging fingers with 2 lateral humps’ (Chen et al 2003 supplemental material). Thus, the funneling illusion is characterized by a perception of spatial mislocalisation and increased tactile intensity. The neural basis for this illusion is thought to involve a complex integration of inhibitory interactions. Previous studies have shown that the funneling illusion is encoded in primary somatosensory cortex (SI), and not peripherally at the skin (Gardner and Spencer 1972). Responses of SI neurons to three point skin stimulation have demonstrated that a broad distribution of cortical neurons are recruited (Gardner and Spencer 1972, Gardner and Costanzo 1980).

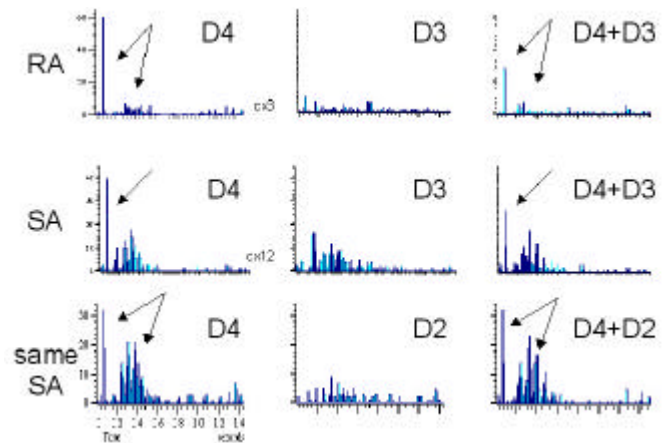
**Two point stimulation produces cortical merging in Area 3b.** The central representation of this phenomenon was not expected to be in primary somatosensory cortex. Since the illusion involves integration across multiple digits, it was unlikely to occur in Area 3b where receptive fields are confined to single digit tips. However, a recent study has demonstrated that this integration does indeed occur in early somatosensory areas. Figure 4 illustrates that stimulation of either D2 alone (a,b), D3 alone (c,d) or D4 alone (e,f) elicits single focal mm-sized activations. However, stimulation of adjacent digits D4+D3 (g,h) produces a single activation site whose center lies between the D3 and D4 sites (l). This merged activation is not observed for non-adjacent digits D4+D2 together (i,j) (n). Thus, stimulation of each location alone activates spatially distinct locations in the cortex, but together produces a single centrally located peak of activation (Gardner and Spencer, 1972; Gardner and Costanzo, 1980).

**Intensity of funneling percept.** The second notable characteristic of multi-point stimulation (two or more points) is the increased intensity of the funneled sensation in comparison to stimulation of a single point. Gardner and Costanzo (1980) demonstrated that responses of cortical neurons to multi-point stimulation were often similar in magnitude to single point stimulation and were always less than the sum of component single point responses. From this, they suggested that the increased intensity is not due to greater neuronal firing rates, but rather due to recruitment of a broader distribution of neurons. Such broader distribution can be reflected in either greater area of activation or greater amplitude of imaged signal.

Chen et al. (2003) found that both the area and amplitude of activation produced by paired



**Figure 4.** Cortical activations by 1- and 2-digit stimulation in Area 3b. Raw images of D2, D3, D4, D3+D4, D2+D4 stimulation (a,c,e,g,i); low-passed images with threshold outlines (b,d,f,h,j). Digit activation centers are indicated by red dashed lines. k, blank condition. l-n, overlay of outlines of adjacent digit (l), single digit (m), and non-adjacent digit (n) activations. m, penetrations show lateral to medial topographic locations of D2, D3 and D4 (green dots). Scale bar: 1 mm.



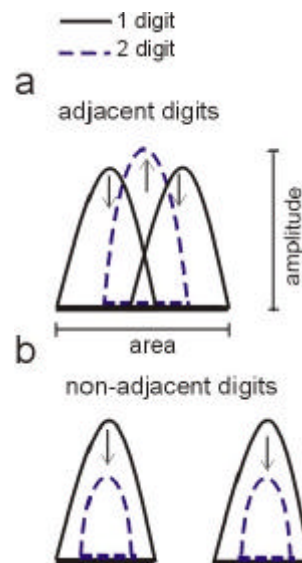
**Figure 5.** Two units recorded on D4 fingerpad. Top row: RA cell response to D4, D3, and D4+D3 stimulation. Middle row: SA cell response to D4, D3, and D4+D3 stimulation. Bottom row: same SA cell response to D4, D2, and D4+D2 stimulation. 20 trials, bin width 100msec. Arrows specify early and late components of response.

digit stimulation (both adjacent and non-adjacent) is *smaller* than the sum of the single digit activation areas. This reduction was observed in all digit pairs examined (both adjacent and non-adjacent). Thus, two finger stimulation leads to a *reduction* in activation area (for both adjacent and non-adjacent digit pairs).

Electrophysiological recording of single units also show similar reductions in activation. As shown in Figure 5, two units (one RA and one SA) were recorded with receptive fields on the D4 fingerpad. Stimulation of D4 alone (left column) revealed an early transient component and a weak late component (indicated by arrows) in both of the RA and SA cells' responses. Stimulation of either adjacent D3 or non-adjacent D2 alone produced no initial transient and relatively weak late response. Simultaneous stimulation of two adjacent fingerpads (right column, D4+D3) reduced the amplitude of the initial transient. This reduction of the initial transient was not observed with simultaneous stimulation of non-adjacent fingerpads (right, D4+D2). Thus, adjacent digit stimulation leads to weakening of digit activation as evidenced by decreased area and amplitude of optical signal, late component suppression in optical signal (not shown, Chen et al. 2003), and decline in size of single unit response.

We suggest that the decreased cortical activation observed during 2 digit stimulation may be due to inhibitory inter-digit interactions. Lateral inhibition is a well described phenomenon in the somatosensory pathways. Somatosensory afferents produce both inhibition as well as excitation in central neurons, including the dorsal horn, dorsal column nuclei, the ventrobasal complex, and the somatosensory cortex. These inhibitory processes are thought to be mediated by local feedforward or feedback circuits within the target nuclei. The spatial profiles of inhibition is often larger than that of excitation, producing a 'center-surround' receptive field organization (e.g. Janig et al., 1979); this sharpening has also been referred to as 'coning'. Stimulus induced inhibition has longer latencies than excitation and may last for 100 msec or more (e.g. Laskin and Spencer, 1979). These lateral inhibitory processes may serve to limit the spatial extent of discharge zones and enhance stimulus contrast, thereby improving spatial and form discrimination.

In sum, simultaneous digit stimulation produces a reduced activation at the sites of digit representation. This reduction is coupled with an increased response amplitude in the merged zone (where no actual stimulation occurs); this increased response at the merged zone is comparable in magnitude to that of single digit activations. In other words, even though no physical stimulus occurs at the merged site, the response is similar in size to that of an actual single digit stimulus. We speculate that a change in the balance of interaction between neurons at the merged site (increased amplitude) and those at nearby sites (decreased amplitudes) serves to heighten the perceived intensity and sharpen the focus (decreased area) during the funnelling illusion (Fig 6). The fact that activation of nearby cortical sites leads to single merged activations suggests that spatial percepts are strongly dictated by central representations. Indeed, physical perception can occur where no physical stimulus occurred. This study further suggests that, under certain contextual situations, receptive fields of neurons in Area 3b can span more than a single digit. The extent of these contextual influences are likely to be determined by mechanisms dependent on intra-cortical distance, center and surround interactions, and cortical feedback.



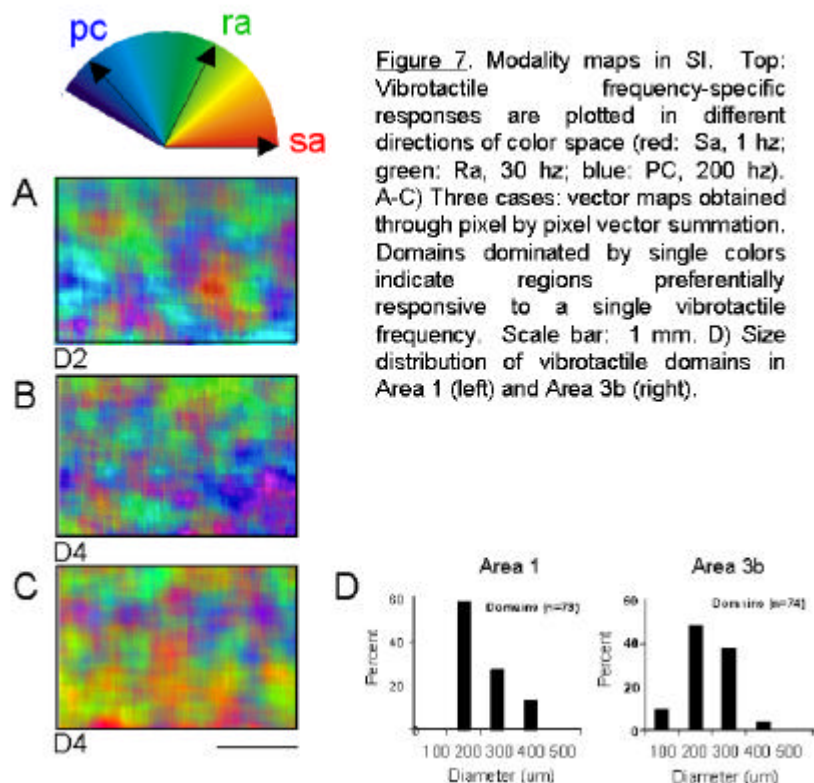
**Figure 6.** Summary of cortical merging. **a,** Adjacent digit stimulation results in merging to a single central site, and increased signal amplitude at the merged location concomitant with decreased amplitudes nearby. **b,** Non-adjacent digit stimulation results in decreased signal area and amplitude at each of the stimulation sites.

## Modality representation in SI

*Presence of interdigitated multiple maps.* Both anatomical and physiological evidence suggests ‘labelled lines’ of modality-specific cutaneous information (Verrillo 1966, Talbot et al. 1968, Verrillo and Bolanowski 1986). Psychophysically, vibrotactile stimuli produce three distinct sensations on the skin: 1) A pressure sensation is induced by stimuli below 2 Hz 2) A flutter sensation is evoked by stimulation in the 2-40 Hz range, and 3) a vibration sensation is evoked by higher frequencies (40-200 Hz) (Johansson et al. 1982). These pressure, flutter, and vibratory sensations are mediated by slowly adapting (SA), rapidly adapting (RA), and pacinian (PC) receptors, respectively (Mountcastle et al. 1972; LaMotte and Mountcastle 1975; Cohen and Vierck 1993). These modalities remain largely separate in their central projections. For example, direct electrical stimulation of single identified low threshold mechanoreceptive afferents (SA, RA, or PC) evoke only one type of perception (pressure, flutter, or vibration, respectively) (Torebjork and Ochoa 1980, Vallbo 1981). Psychophysical studies fail to find vibrotactile masking and adaptation between stimulus frequencies that produce pressure (0.5 Hz), flutter (20 Hz) and vibratory sensations (200 Hz) (Gescheider et al. 1979, 1985; Bolanowski et al. 1988). In addition, frequency-specific electrical stimulation of a cortical RA-dominated site in Area 3b mimics the effect of stimulating RA receptors of the skin (Romo et al. 1998). Remarkably, even the transfer of tactile learning from one digit to another is modality-specific (Harris et al 2001). These studies suggest a marked degree of separation in the experiences of pressure, flutter, and vibration, mediated by separate populations of receptors which remain separate in their central projections, and perhaps even to higher cortical areas involved in tactile learning and memory (also Romo et al. 2000). Thus, both psychophysical and neurophysiological studies suggest some degree of modality-specific functional segregation in somatosensory cortex.

Anatomical and physiological evidence also suggest parallel modality-specific pathways, from periphery through the dorsal column nuclei, to the thalamus, and into early somatosensory cortical areas. Dykes et al (1981) have described the segregation of RA, SA, and PC responses in the VPL and VPI. Jones and colleagues (1982) have suggested that ‘rods’ of topography and modality-specific cells project to similar modality specific bands in Area 3b, and perhaps also Area 1. Connections between Area 3b and 1 are topographically homotopic, with feedforward projections being more robust than feedback (e.g. Jones and Powell 1969, Jones et al. 1978, Cusick et al. 1985, Burton and Fabri 1995). Using 2-deoxyglucose labelling methods combined with anatomical tracer injections, Juliano et al. (1990) suggest that excitatory information is transmitted from area 3b to area 1 in a way that connects clusters of cells with similar response properties.

However, there is limited evidence as to whether different tactile features form multiple functional domains within each of Areas 3a, 3b, 1, 2. Electrophysiological mapping studies describe

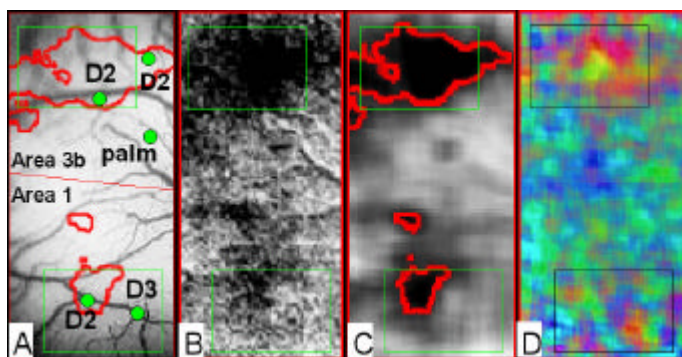


zones of neurons with SA, RA, and PC mechanoreceptor responses within Area 3b (Paul et al. 1972; Sur et al. 1981, 1984; Sretavan and Dykes 1983). Based on densely spaced electrode penetrations, Sur et al. (1981, 1984) found a segregation of SA and RA cells in the middle layers of Area 3b and suggested that these are organized in irregular antero-posterior ‘bands’. This ground-breaking work was the first to suggest the presence of multiple maps in single cortical areas in SI.

Recently, studies using optical imaging methods have revealed networks of vibrotactile domains in SI. Vibrotactile stimulation of the digit fingerpads at frequencies which produce the sensations of pressure (1 hz), flutter (30 hz), and vibration (200 hz) were used in the anesthetized squirrel monkey. These stimuli produced characteristic SA-dominated, RA-dominated, or PC-dominated responses, respectively. Intrinsic signal optical maps were obtained in response to each of these stimuli. A vector summation method was used to determine a pixel by pixel weighted response to the pressure, flutter and vibration stimuli (similar to that used for visual cortical orientation maps, methodology details are described in Friedman et al 2004). Clusters of pixels with saturated color indicate that one vector magnitude dominates the other two. Three examples of such pixel-wise SA/RA/PC vector summation are illustrated in Figure 8A-C. Pixel locations with a dominant SA response appear bright red, those with a dominant RA response appear bright green, and those with a dominant PC response appear bright blue. Patches of cortex that are coded white indicate areas with strong response to each of the pressure, flutter and vibratory stimuli. These vibrotactile domains are typically 200-300 um in size in both Area 3b and Area 1 (Fig 7).

Imaging using near-infrared signals has also shown a fine topography consistent with previous with electrophysiological methods (Tommerdahl et al. 2002). Further research using 25 Hz flutter and 200 Hz vibratory stimuli on the palm found that flutter stimulation led to focal topographic activation in area 3b, whereas vibration only led to delayed reduced activation or an inhibition in areas 3a and 3b that was supported by a reduced activation to paired stimulation (Tommerdahl et al. 1999). The apparent contradiction between a lack of activation to 200 Hz vibration in studies by Tommerdahl et al.(2005) and the focal activation observed by Chen et al (2001) and Friedman et al. (2004) in areas 3b and 1, has been reconciled by the finding that the responses to vibration are site dependent (i.e. digits vs palm). Further research has shown that the extent and magnitude of cortical response to flutter stimuli is duration-dependent (Simons et al. 2007, see also Simons et al. 2005, Chiu et al. 2005), with longer (2-5 sec) stimulation leading to suppression in surrounding regions. This finding parallels the improved ability to spatially localize following presentation of longer adapting stimulation (Tannan et al 2006). Surprising evidence demonstrates ipsilateral input can modify responses in SI, suggesting significant interhemispheric interactions (Tommerdahl et al. 2006). In sum, the research of Tommerdahl and associates in anterior parietal cortex has revealed complex spatial and temporal responses to relatively simple tactile stimuli that might reflect the sensations in humans to the same kinds of stimuli (Tommerdahl et al. 2005, Tannan et al, 2005, 2006).

**Relationship of vibrotactile domains to topography.** It is evident that the modality-specific response extends beyond the classically defined topographic map as revealed by simple indentation stimuli. As shown in Figure 8B, an indentation stimulus (which activates all three receptors types) to digit



D2 produces a fairly focal activation in both Area 3b and Area 1 (outline in red in Fig 8C). In response to pressure, flutter, and vibration stimulation, the vector summation map

**Figure 8.** Relationship of topography and vibrotactile response. D2 activation in Area 3b and 1. A) Vessel map. D2 activations in Area 3b (above) and Area 1 (below). B-C) Raw and filtered image of D2 indentation. Red outline delineates strongest activation zones. D) Modality vector map (red, green, blue: response for SA, RA, and PC, respectively) shows strongest activation in centers

reveals that the strongest responses (most saturated red, green, and blue regions) correspond with the topographic digit locations. However, clustered responses, though weaker, are also evident away from the location of D2 representation (outside the boxes). This additional non-topographic activation is reminiscent of the finding in visual cortex in which complete orientation maps are obtained even though only a single eye is stimulated (Blasdel 1992). Thus, modality maps and topographic maps exhibit some degree of independence. Whether this extended non-topographic region of activation is due to spiking and/or subthreshold activity remains to be determined.

## A New Model of SI organization

The finding that somatosensory cortical domains are roughly 200-300  $\mu\text{m}$  in size strengthen the view that modularity is a common organizational feature of cortical representation. Cortical domains of similar size have been described in multiple cortical areas [in V1 and V2 (see Roe 2003 for review), and V4 (Felleman et al 1997), IT (Tsunoda et al 2001), Area 7 (Siegel et al 2003), and in prefrontal areas (Kritzer and Goldman-Rakic 1995)]. These findings suggest a revision of previous views of SI organization which were based primarily on electrophysiological recordings. Previously, each cortical ‘hypercolumn’ was thought to contain segregated Sa and Ra columns innervated predominantly by thalamocortical fibers of a single vibrotactile modality (Sur et al 1980). Optical imaging evidence now suggests a modification of this view (Figure 9). As shown by reconstruction of single thalamocortical arbors (Garraghty et al 1989), inputs to SI have multiple arbors (200-300  $\mu\text{m}$  in size) that span several mm of cortex (see also Jones et al 1982). These and other cortico-cortical arbors are likely to give rise to clustered activations that have been observed in 2-deoxyglucose studies (Juliano et al 1981, 1987, 1990, cf. Burton and Fabri 1995). Such arbors could give rise either to an array of discrete clusters or, by varying arbor overlap, continuous modality maps. Thus, regions dominated by single SA, RA, or PC inputs would give rise to either SA (red), RA (blue), or PC (green) domains. Regions of some overlap would appear as magenta or yellow-green colors (not depicted). And regions of high SA, RA, and PC overlap could underly the so-called ‘hotspots’ commonly described in SI receptive fields (in optical images these locations would appear as black, gray, or white domains); these would be well activated by broadband stimuli such as skin indentation. Other arbors extend to non-topographic locations away from the hotspot and establish locally some degree of modality-specific dominance (cf. Figure 9). Thus, not unlike the way horizontal iso-orientation networks in V1 give rise to resulting orientation map structure, the observed maps result from overlapping horizontal networks of patchy, modality-specific dominance. In sum, in the revised view, each digit representation is served by collections of interdigitating Sa, Ra, and PC columns. The effect of topographic stimulation is therefore no longer so discrete and can, under certain stimulation conditions, have non-topographic consequences.

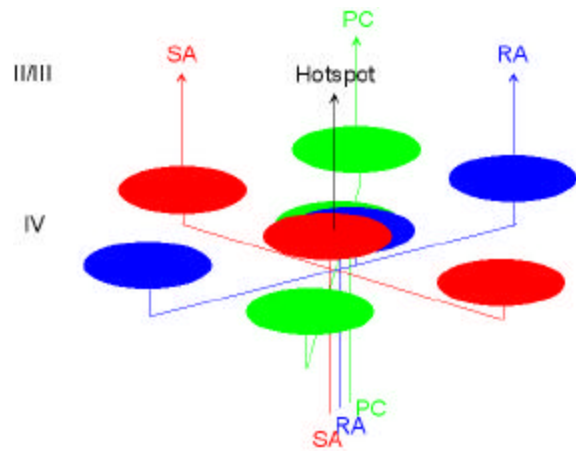


Figure 9. Proposed model of vibrotactile representation in SI. Single SA (red), RA (blue), or PC (green) fibers terminate in layer IV, each with several arbors (colored disks). These arbors project in turn to superficial layers II/III (vertical arrows). Thus, some cortical columns are dominated by a single SA, RA, or PC input, while others have mixed input (central overlapping disks).

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