Active sensation: insights from the rodent vibrissa sensorimotor system

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Rats sweep their vibrissae through space to locate objects in their immediate environment. In essence, their view of the proximal world is generated through pliable hairs that tap and palpate objects. The texture and shape of those objects must be discerned for the rat to assess the value of the object. Furthermore, the location of those objects must be specified with reference to the position of the rat's head for the rat to plan its movements. Recent *in vivo* and *in vitro* electrophysiological measurements provide insight into the algorithms and mechanisms that underlie these behavioral-based computations.

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Introduction

Active touch is a common behavior that animals use to discern the shape, size and texture of objects. The resulting haptic sensations are used to finely tune the position or the motion of tactile sensors. The transformation of sensory inputs into modulatory motor outputs during active touch is performed by sensorimotor feedback loops [1]. Here, we discuss active touch in the context of rhythmic, 5 to 25 Hz whisking by the rat [2] (Figure 1). These animals palpate objects with their vibrissae during a bout (see glossary) of whisking, which lasts for one second or more, to extract a stable picture of the world.

Can rats discriminate objects solely with their vibrissae?

Hutson and Masterton [3] devised sensory tests to isolate perceptual functions of the vibrissae. They found that blind rats with intact vibrissae would leap across wide gaps after contacting the opposite platform with their vibrissae. Rats with clipped vibrissae did not cross these wide gaps. Thus, sensory input from vibrissae enables animals to determine the existence and location of the far side of a gap, in a process that is well suited for electrophysiological studies [4,5]. A complementary role for the involvement of the vibrissae in detection tasks follows from studies on the discrimination of different textures, in which it is conjectured that rats discriminate with an acuity that rivals that of the human fingertip [6].

Texture is not the only fine sense transduced by the vibrissae. Recent experiments suggest that the vibrissae convey sufficient spatial information to enable rats to distinguish between differently shaped objects [7,8] and between alleys that differ in width by less than five percent [9,10].

Background
The rat vibrissa sensorimotor system consists of nested feedback loops

The vibrissae are embedded in feedback loops that form a closed topology at the level of brainstem up through loops that close at the level of the neocortex [11] (Figure 2). Our thesis is that these loops mediate active sensing, which involves a confluence of neuronal signals that represent touch with those that represent vibrissa position.

The brainstem sensorimotor loop is the lowest-order circuit in which sensorimotor integration occurs [12,13]. It contains secondary sensory nuclei as well as the motor nuclei that control motion of each vibrissa [14] through both intrinsic muscles in the mystacial pad (see glossary) and extrinsic muscles that move the pad as a whole [15]. These movements work in opposition to ensure active protraction and retraction in the whisk cycle (see glossary) [2,16]. The brainstem loop is believed to participate in rhythmic pattern generation [17•,18], based on evidence that whisking persists after lesions to vibrissae-related areas of neocortex [19,20] and the cerebellum [20], although the location of a central pattern generator in the brainstem in unknown.

The background firing-rate of motoneurons in the lateral aspect of the facial nucleus, which innervates the intrinsic muscles [21,22], depends on modulation by serotonergic neurons [18]. This modulation is analogous to the control of posture by spinal neurons [23] and, thus, probably controls the set-point (see glossary) of the vibrissae. We conjecture that the interplay between motoneurons in the medial aspect of the facial nucleus, which innervates the extrinsic muscles [14], and those in the lateral

aspect of the nucleus could be crucial for the control of whisking strategy, such as the change from large exploratory whisks to foveal whisks (see glossary) in the palpation of objects [2].

The midbrain, thalamic and cortical loops provide feedback pathways that parallel the monosynaptic pathway from the trigeminal nuclei to the facial nucleus (Figure 2) [24,25]. Three such pathways involve thalamic nuclei. The first is an extralemniscal pathway that ascends through the ventrolateral sector of ventral posterior medial (VPM-vl) thalamus to vibrissa primary sensory (S1) and secondary sensory (S2) cortex [26]. The second is a paralemniscal pathway that passes through posterior medial (POm) thalamus and projects down to the superior colliculus as well as up to S1, S2 and primary motor (M1) cortices [27–29]. The third is a lemniscal pathway that passes through the dorsomedial sector of ventral posterior medial (VPM-dm) thalamus to vibrissa S1 cortex. The extralemniscal pathway conveys primarily touch-based signals, the paralemniscal pathway conveys primarily vibrissa motion signals, which can be used to form positional reference signals, and

the lemniscal pathway conveys a combination of touch and motion signals [30•]. Despite this segregation of information, the thalamic nuclei interact through reciprocal connections to the reticular thalamic nucleus (Rt) [31,32], which can shape their dynamic response [33]. Furthermore, the pattern of corticothalamic descending connections [34,35] mirrors that of trigeminothalamic ascending inputs [28,36], a scheme that enables the thalamus to compare top-down predictions with sensory input [37].

Sensory and motor cortices interact through corticocortical projections and through thalamic-mediated connections among these cortical areas, principally involving POm thalamus [33–40] (Figure 2). This organization implies that the computations involved in sensory and motor functions are likely to be distributed throughout these cortical and thalamic areas [41]. Interestingly, the lemniscal pathway could suppress activity in the paralemniscal pathway through cortical activation of cells in the zona incerta [42,43], a process that is partially suppressed when animals are in the aroused state [44]. Activation of cells in the zona incerta subsequently inhibits neurons in POm thalamus [45,46,47•]. Thus, corticothalamic feedback from sensory cortex could gate the input of trigeminal sensory information to motor cortex. Nonetheless, the means by which neuronal activity in cortex can control information in ascending vibrissa pathways has only just begun to be addressed [48].

The neocortical loop is completed by projections from M1 cortex to the vibrissa areas of the facial nucleus [49•] as well as to other brainstem nuclei that connect to the facial nucleus [50,51]. Furthermore, projections from both S1 and M1 cortices to the superior colliculus are transformed into descending projections to the facial nucleus (Figure 2). A crucial question is how vibrissa motoneurons, which preferentially spike for transient inputs in the frequency range of natural whisking [52], merge inputs from brainstem, midbrain, thalamic and cortical feedback loops.

Object localization and vibrissa movement
Active vibrissa movements in free-ranging animals are always associated with active head and body movements. When rats are engaged in a horizontal localization task, in which they estimate the location of objects relative to their head in the azimuthal plane, they typically whisk [53]. However, whisking is not always necessary for vibrissa-based tactile sensation, as rats often rely solely on passive movement of the vibrissae secondary to body and head movements. In particular, rats use their vibrissae but do not whisk as they maintain contact with walls and surfaces [54] while running and while performing an aperture-size discrimination task [9].

The necessity and pattern of whisking could depend on the geometrical arrangement of the vibrissae. The altitude of an object can, in principle, be determined if the animal

Figure 1
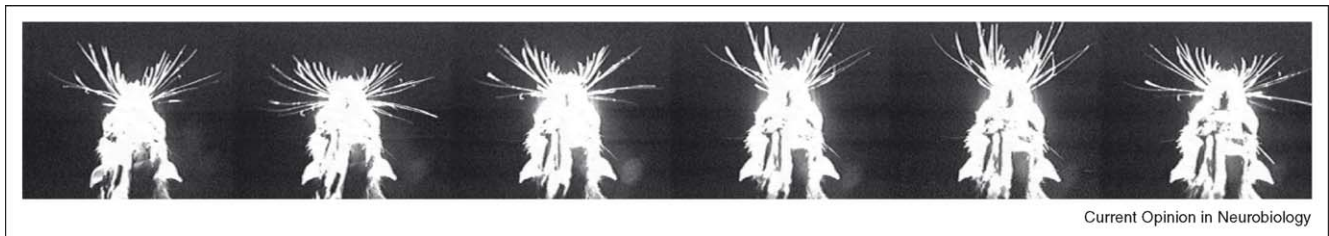
Successive strobed video images of a rat, using darkfield illumination from above, as she moves her vibrissae during a whisk cycle. The animal was trained, while blindfolded, to whisk in search of a food tube (not shown). Successive frames are at intervals of 33 ms. Data obtained as part of the study by Fee *et al.* [73].

senses which of the five possible rows of vibrissae the object is in contact with. The rows span $\sim 100^{\circ}$ range from contact with the ground to contact with objects above the head [55]. Thus, movement of the vibrissae is not necessary to assess altitude, but small movements can be used to locate objects on a scale finer than the $\sim 25^{\circ}$ spacing. In contrast to altitude determination, the $\sim 75^{\circ}$ span among the ~ 6 long vibrissae in a row covers less than a half of a hemifield in the azimuthal plane [21], so complete coverage of the sensory field requires that the vibrissa sweep along the anterior–posterior axis. The range of exploratory

whisking is consistent with this coverage and further includes limited movement in the dorsal–ventral direction to increase the resolution of altitude [56].

The distance of an object from the face is coded by a firing rate that appears to be independent of the azimuthal position of the vibrissa [57]. Thus, a reference of vibrissa position is not needed to specify this distance, which coincides with the radial coordinate of contact along the vibrissa with the follicle pore taken as the origin. A similar argument exists for the altitude of an object. By contrast, a

Figure 2
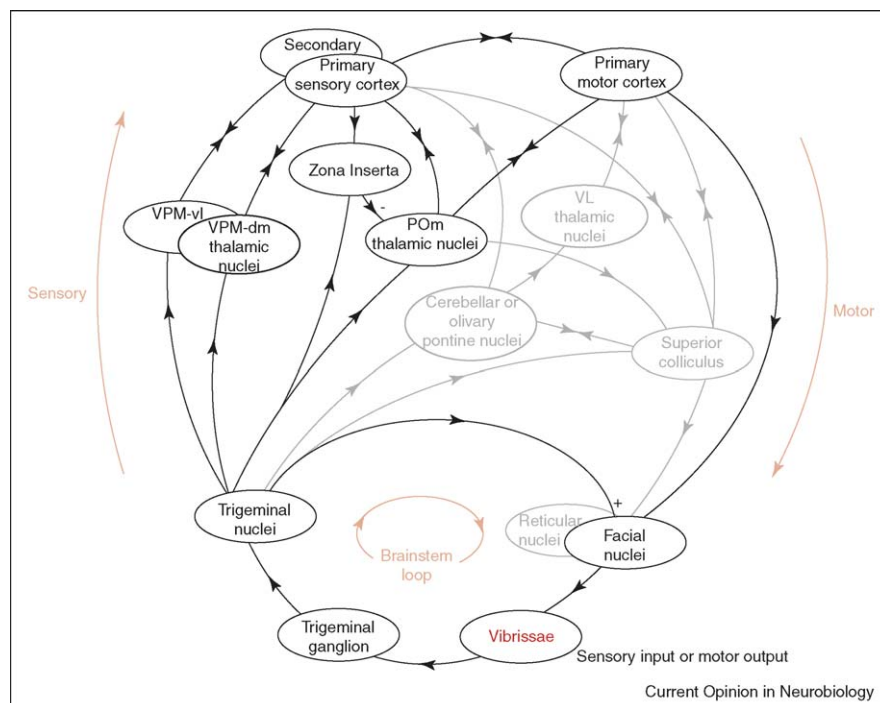
Simplified cartoon of the topologically nested vibrissa sensorimotor loops. The brainstem and thalamocortical pathways covered in this review are shown with black lines. Cerebellar pathways are shown in gray, whereas those that involve basal ganglia [114–116] are not shown. A complete description and a full set of references are found in Kleinfeld *et al.* [11]. Here, we have added a positive feedback connection (+) at the brainstem level [17•], a negative feedback connection (–) from zona incerta to POm thalamus [42,43], the division of VPM thalamus into dorsal medial (dm) and ventral lateral (vl) areas [26,30•], and a connection form POm thalamus to the superior colliculus [27].

reference of vibrissa position is essential to code the azimuth of contact as the vibrissae sweep along the anterior–posterior axis. Crucially, the pressure receptors in the follicle [58,59] respond to vibrissa contact in a manner consistent with compression of the follicle by motion that is predominantly along the azimuthal coordinate.

Coding rhythmic sensory signals
Common scaling for the cortical spike-rate
Here, we have grouped discrimination tasks into two classes. The first class concerns searching for and palpating edges and objects, for which animals exhibit large-angle exploratory whisking in the range of 5 to 15 Hz and foveal whisking up to 25 Hz [2]. Crucially, neurons throughout the entire sensory stream can follow with spike-by-spike precision at these frequencies [60,61], so that touch signals can be accurately timed relative to the position of the vibrissae. The second class concerns differentiation among textures, during which the vibrissae can vibrate at hundreds to thousands of Hertz as they sweep across a surface [62,63]. These high frequency signals are faithfully represented in the trigeminal nucleus [64,65]. However, cortical cells do not to follow inputs at such high frequency, although cortical oscillations at hundreds of Hertz, unrelated to texture, are documented [66,67]. It is thus of interest that high

frequency signals are represented in cortex as an irregular spiking process in which the spike rate is a monotonic function of the rate of stimulation [68[•],69].

Independent of the task and the phase-coherence between the sensory stimulation and the spike response in cortex, the stimulus is coded by logarithmic compression of the stimulation frequency (Figure 3). This universal representation is analogous to Weber's Law (see glossary) for the peripheral nervous system, with stimulus frequency replacing stimulus intensity. Phase-locking (see glossary) occurs for exploratory whisking, a strategy involved in object location, whereas an absence of locking is associated with texture discrimination. More refined analyses show that distinct temporal patterns of spikes emerge with textures of similar coarseness but differing details [68[•]], and that increases in firing rate with increasing stimulation frequency are primarily confined to neurons in the regions, denoted septa (see glossary), between cortical columns [70].

Active touch for object recognition and path finding
The essential issue in localization of an object in the azimuthal plane is to transform a touch signal into a measure of the angle relative to the face. In principle, this can be accomplished by contacting the object with an

Figure 3
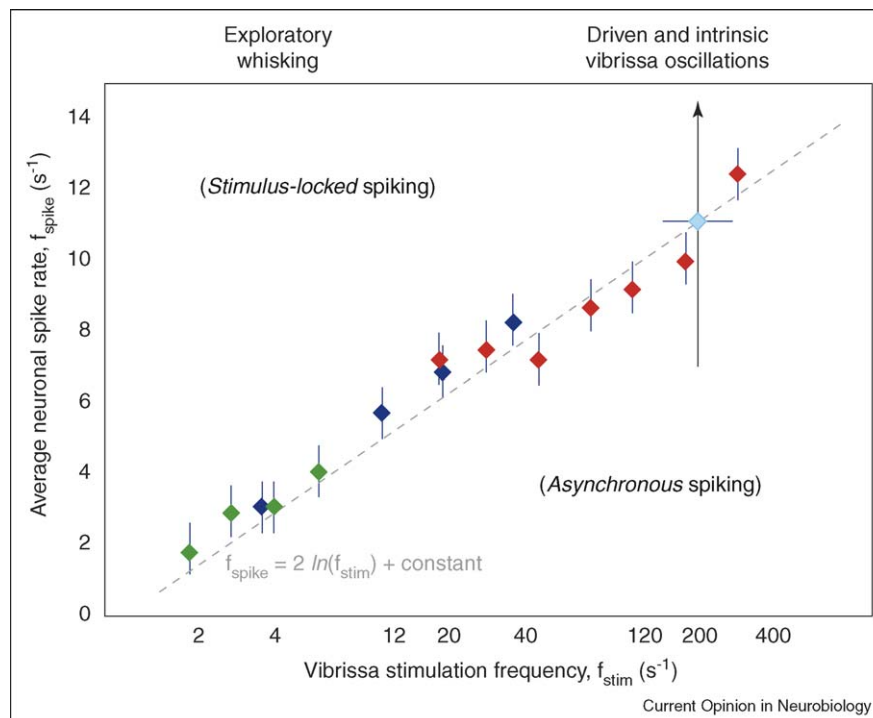
Coding of rhythmic vibrissa stimulation in S1 cortex of anesthetized animals. The data represent a composite extracted from the published results from multiple laboratories; green diamonds from Ahissar et al. [88], purple from Khatri et al. [117]; red from Arabzadeh et al. [68[•]], and blue from Andermann et al. [98]. Note that the results from Arabzadeh et al. [68[•]] are for a particular rhythmic amplitude; other angular speeds (speed = amplitude × frequency) with the same frequency are offset by a constant. The slope of the response across all data sets can be approximated by logarithmic scaling, as indicated by the dashed line and proposed on theoretical grounds [118].

array of vibrissae, together with triangulation (see glossary) [62], or by contacting the object with a single vibrissa and combining the touch signal with a reference signal of vibrissa position. New behavioral experiments are required to distinguish between these possibilities. Nonetheless, electrophysiological studies support the presence of a neuronal reference of vibrissa position. First, signals of vibrissa touch, as well as signals of vibrissa motion that are appropriate reference signals, exist at the

level of the trigeminal ganglion [71] (Figure 4a). Second, both active touch signals [72•] and reference signals [73,74•] (Figure 4b) are present in S1 cortex. Interestingly, the touch response is suppressed during whisking, at least as assayed in mice [72•] (Figure 5), consistent with both adaptation of the cortical response that occurs secondary to suppression of thalamocortical synaptic transmission in the aroused state [75,76] and possible gating by motor activity [77,78]. Furthermore, the reliability of the

Figure 4
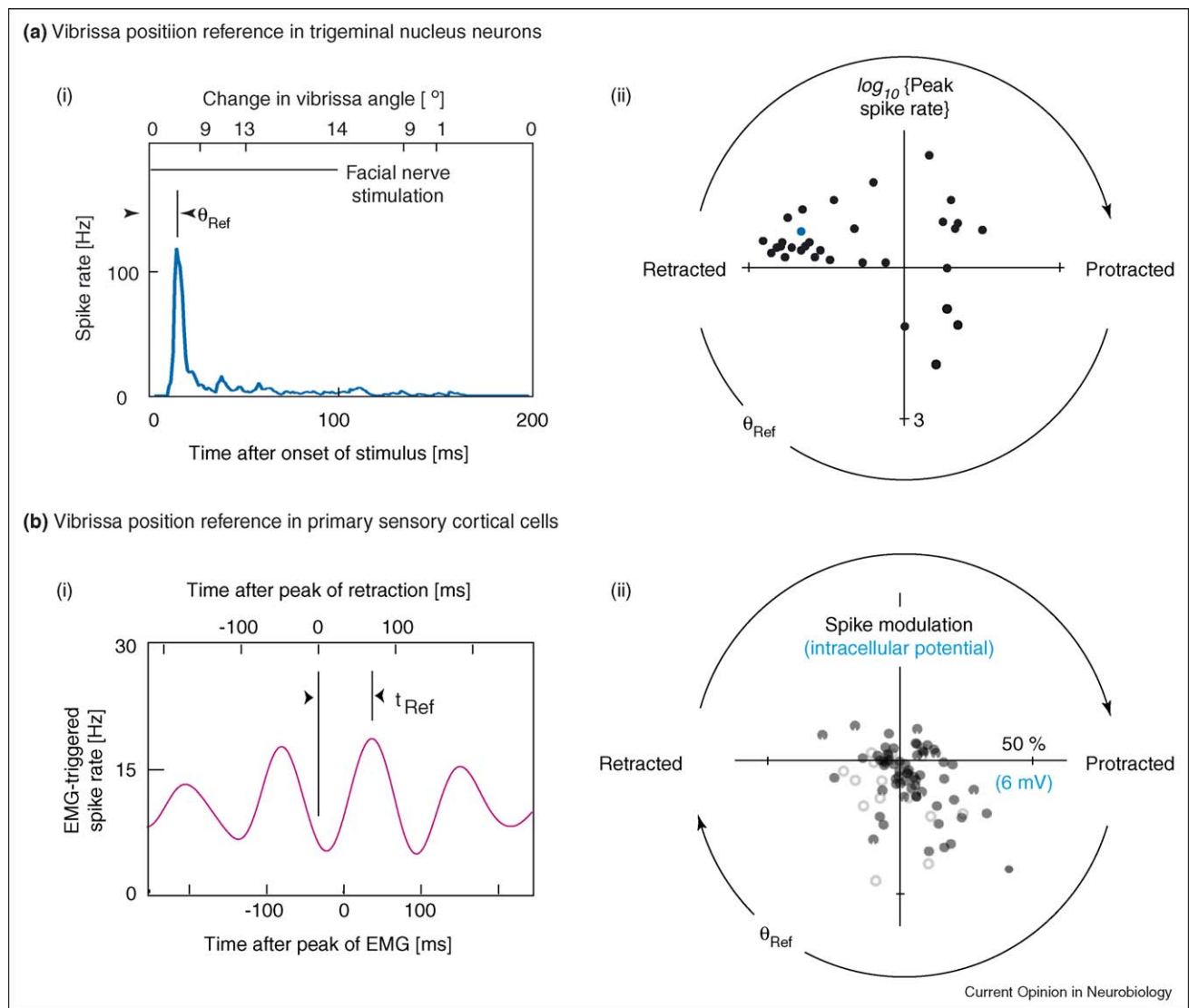
Encoding of vibrissa position. **(a)** Spiking output from primary sensory neurons of the trigeminal ganglion (TG) was recorded during vibrissa motion induced by 5 Hz elec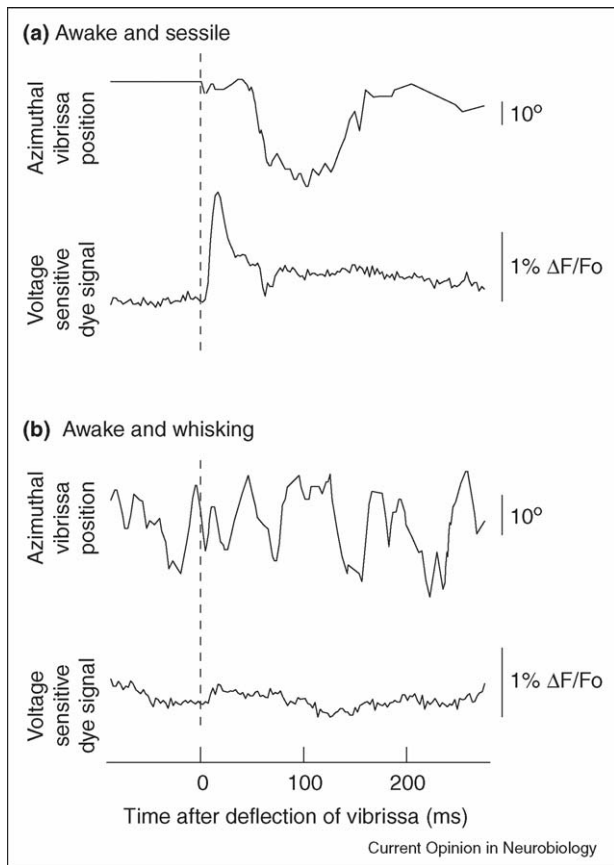trical stimulation of the facial motor nerve (FN). **(i)** The trial-averaged response of the reference signal for one neuron; the angle $\Delta\theta_{Ref}$ is the extent of protraction, relative to the initial retracted position, at the peak of the neuronal response. **(ii)** The summarized data for all cells [71]. The radial polar coordinate is the logarithm of the peak spike rate and the angular polar coordinate is the phase within the whisk cycle. **(b)** Responses in vibrissa S1 cortex measured while animals whisked without contact. **(i)** An example of the correlation between spiking and the peak of the electromyogram (EMG). The scale across the top accounts for the lag between vibrissa position and the EMG [2]; the time t_{Ref} is the peak of cortical spiking relative to the fully retracted position. **(ii)** Summarized data for all cells [62,73] from these extracellular measurements, for which the radial coordinate is the modulation of the spike–EMG correlation, as well as for cells from recent intracellular studies [74•], for which the radial coordinate is the maximum intracellular depolarization. The bias in spiking as a function of phase in the whisk cycle comes slightly earlier than that for the membrane depolarization, as expected for a threshold process.

Figure 5

(a) Awake and sessile

Azimuthal vibrissa position | 10°

Voltage sensitive dye signal | 1% ΔF/Fo

(b) Awake and whisking

Azimuthal vibrissa position | 10°

Voltage sensitive dye signal | 1% ΔF/Fo

Time after deflection of vibrissa (ms)

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The evoked sensory response in awake mice depends strongly on behavior [72•]. **(a)** The positional plot shows the measured change in azimuthal displacement. The voltage sensitive dye signal measures the average membrane potential within the focal volume and is reported as the fraction change in fluorescence ΔF/Fo. The dye signal shows a large amplitude response following transient magnetically induced displacement of the altitude of vibrissa C2, which served as the stimulus. Note that approximately 70 ms after this cortical response the mouse protracted its vibrissa. The scale ΔF/Fo refers to the fraction change in optical signal. **(b)** The dye signal of the mouse during active whisking when the magnetic deflection was applied. A much smaller sensory response was observed.

cortical reference signal is strongly enhanced when whisking is paired with reward [79]. Details aside, a nonlinear interaction between touch and reference signals, for example correlation, is sufficient to compute object location with single-vibrissa resolution in face centered coordinates. Evidence for an appropriate nonlinearity in S1 cortex exists [80,81]. Yet, a position-dependent touch signal remains to be demonstrated.

How are active touch signals processed in a cortical column? To answer this question, we consider experiments that used artificial whisking (see glossary) [82] to generate a sensory signal. The responses of neurons in the 'barrel' (see glossary) regions within layer 4 [83], which receive lemniscal (VPM-dm) input (Figure 2), in addition to those in layer 5a, which receive paralemniscal (POm) input, are facilitated with successive whisks [84]. The facilitation in layer 4 neurons is stronger when contact occurs during whisking, whereas responses in layer 5a neurons are usually unaffected by contact. By contrast, the responses in superficial layer 2/3 neurons, which mediate intercolumnar interactions [85], are depressed with repetitive contact [84]. These differences in cortical dynamics across laminae are suggestive of specialized processing within different layers [86] that relates to the associated afferent pathway [87–89]. Layer 4 neurons are posited to process spatial details of the palpated object, for which their columnar segregation [90] is consistent with single-vibrissa spatial resolution. By contrast, layer 5a neurons process vibrissa position and whisking kinematics. We thus hypothesize the existence of integration across neighboring columns within layer 5a [91•]. Finally, layer 2/3 neurons appear to integrate the outputs of layers 4 and 5a [88,92•]. The role of arousal [75,76] and adaptation [93,94] in this cortical computation remains to be evaluated.

From mechanics to spiking in texture discrimination

There are two current hypotheses on the mechanical origin of high frequency trigeminal signals that accompany texture discrimination tasks [63,95]. The first hypothesis involves mechanical resonance of the vibrissae [96,97] and is applicable when the drag on the vibrissa does not induce appreciable damping of the motion. This hypothesis originates from the observation that whiskers within a vertical arc, for example A2 through E2, are of similar length, whereas whiskers along a row, for example D1 through D6, decrease in length in the posterior–anterior dimension [7]. As a consequence, the longer, posterior vibrissa should exhibit a resonance with lower fundamental frequencies than the shorter, anterior vibrissae [95]. According to this hypothesis, as the vibrissae sweep along a textured surface, the vibrissa the resonance frequency of which most closely matches the texture-induced input frequency will transmit the greatest torque to the follicle [98]. Thus, an increase in firing rate at a specific position within the map of vibrissa position in S1 cortex would indicate the predominant frequency of whisker vibration and, consequently, the identity of the contacted texture [63]. Consistent with the predictions of the resonance hypothesis, vibrissae are observed to resonate when complex textures, such as sandpaper, are translated across the tip of the vibrissa [99]. The spike activity of neurons in the afferent pathway rises over a period of ∼500 ms, consistent with the Q-factor (see glossary) of the resonance [98], so that coding of textures by the rate of spiking is probably relevant when many arcs of vibrissae sweep the texture for an extended period of time [100].

The second hypothesis is that contact of the vibrissae with a surface is dominated by damping. In this hypothesis, resonant vibrations are suppressed while vibrations that reflect the topology of the surface dominate the stimulus-

induced motion of the vibrissa [68•]. Thus, the spatial modulation of the surface is reproduced by the pattern of spiking in trigeminal ganglion neurons. Experiments that used artificial whisking in the anesthetized animal provide proof-of-principle demonstration of this scheme [68•]. Distinguishing between these two coding strategies — one in which the underlying frequency components depend on intrinsic mechanical properties and the other in which the components depend upon extrinsic properties — will require quantification of vibrissa kinematics and associated neuronal activity while rats explore textured surfaces.

Sensory modulation of vibrissa motion
Although anecdotal evidence exists for changes in whisking strategy on the basis of the discrimination task [2,6,101,102], there is a paucity of quantitative data on both the psychophysics and the electrophysiology of sensory control of motor output. Nonetheless, recent work shows that the brainstem loop exerts transient positive feedback [17•] (Figure 2), such that the initiation of touch leads to a protracted period of contact [103]. This mechanism might increase the number of contact-mediated spikes and thus the reliability of a touch signal.

We conjecture that changes in whisking strategies are regulated at the corticothalamic level. Three classes of recent experiments support this view. A first class of experiments made use of awake, head-fixed animals that were trained not to whisk as a means to delineate the representation of rhythmic sensory input within M1 cortex [41]. Surprisingly, the observed response captured only the fundamental frequency of the input pattern for pulsatile stimuli with frequencies ranging from 5 to 20 Hz, the range of exploratory whisking. This nonlinear transformation resembles the synthesis of a sinusoidal feedback signal for servo-control (see glossary) of a motor.

A second class of experiments showed that M1 cortex supports oscillations in extracellular current-flow that are phase-locked to whisking as animals whisk in air [104]. These signals are preserved after lesions of the infraorbital branch of the trigeminal nerve block sensory input. Furthermore, ablation of M1 cortex leads to alteration of the whisking patterns [105]. Thus, motor cortex generates rhythmic signals that can drive normal exploratory whisking.

The third and final class of experiments built on early work by Welker and co-workers [106] and explored the motion of the vibrissa in response to activation of M1 cortex in both anesthetized and behaving animals. From a functional perspective, there are two contiguous motor areas [107•]. For the largest region, denoted 'retraction-face' (RF), activation of tissue with a brief train of extracellular current-pulses [107•,108], or even depolarization of a single cell [109,110], leads to retraction of the vibrissae. This

motion is transformed into a full whisk, with protraction and retraction, when animals are in the awake and aroused state [108], an effect that is mimicked by cholinergic activation of cortex [111•]. Furthermore, the induction of 5 to 15 Hz oscillations in motor cortex through pharmacologically induced disinhibition leads to cycles of retraction that are phase-locked to the cortical rhythm [112]. A similar effect occurs in response to prolonged electrical excitation to motor cortex [113]. For a smaller region near the midline, denoted 'rhythmic whisking' (RW), activation with a brief train of extracellular current-pulses leads to protraction [107•]. Rather remarkably, stimulation of the RW region in the awake animal, using a continuous train of high-frequency pulses, induces lower frequency rhythmic whisking [107•]. The set-point of whisking can be varied by simultaneous activation of the RF and RW regions. Collectively, these data show that M1 cortex, in principle, can subsume full control of vibrissa movement.

Conclusions
An analysis of the available data is consistent with the notion of motor control of the vibrissae by sensorimotor loops at the brainstem through cortical levels. Although neural correlates of vibrissa position and touch are already present in the brainstem loop, it appears that the convergence of these signals for object discrimination first occurs within sensory cortex, where we posit that representations of vibrissa position fuse with those of object contact. The available data further imply that rhythmic drive to the vibrissae can be under the control of motor cortex during active sensing. We thus hypothesize that the processed sensory stream is used to assess whisking strategy continuously and modify whisking on both cycle-by-cycle and bout-to-bout time-scales. To the extent that changes in motor drive can coincide with object identification, it might be useful to think of motor control as a 'read out' from sensory cortex.

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