6.11   Role of Primary Somatosensory Cortex in Perceptual Touch Detection and Discrimination

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Glossary

choice A choice is required when an organism is confronted with alternatives for which an action is necessary to acquire or avoid one or more of the alternatives because of a desire, goal, or preference.

choice probability A trial-to-trial correlation between neuronal signals and the monkey's choice behavior.

detection The simplest perceptual experiences that is a prerequisite for any further sensory processing. In detection tasks repeated presentations of a near-threshold stimulus might unpredictably fail or succeed in producing sensory percept.

discrimination The capacity to determine the difference between two stimuli.

difference limen In flutter discrimination, the difference limen is a measure of how a small increase in the frequency of a vibrotactile stimulus can be detected when compared to a standard stimulus frequency. A smaller difference limen implies a higher discrimination capacity.

flutter A type of somatosensory stimulation that is felt when touching an object that vibrates at frequencies between ~10 and ~50 Hz.

functional magnetic resonance imaging (fMRI) The use of MRI to measure the hemodynamic response related to neural activity in the brain or spinal cord of humans or other animals. It is one of the most recently developed forms of neuroimaging.

intracortical microstimulation A neurophysiological technique that is used to activate a population of neurons within a restricted cortical locus. Pulses of electric current delivered through a microelectrode drive the activation.

memory An organism's ability to store, retain, and subsequently recall information.

neurometric curve A plot of the percentage of correct behavioral responses that an ideal observer would make on the basis of observing the neuronal responses that are elicited by a given test stimulus.

perception The process of acquiring, interpreting, selecting, and organizing sensory information. The word perception comes from the Latin *capere*, meaning to take, the prefix per meaning completely.

primary somatosensory cortex (S1) It is located in the poscentral gyrus and in the depths of the central sulcus. It consists of four functional areas: Brodmann's areas 1, 2, 3a, and 3b, each of which has a somewhat different role in somatic sensation.

Projections from the thalamus to S1 arise chiefly from the ventral posterior nucleus, are somatotopically organized, and transmit information from the contralateral body.

psychometric curve A plot of the percentage of correct behavioral responses as function of changes in the properties of the test stimulus.

psychophysics A subdiscipline of psychology dealing with the relationship between physical stimuli and their subjective correlates, or percepts.

receptive field The area of the sensory space in which stimulus presentation leads to the response of a particular sensory neuron.

receiver operating characteristic (ROC) ROC analysis is often used to evaluate the results of a detection task with weak signals. A ROC curve is generated by plotting the probability of true positives (hits) against the probability of false positives (false alarms) for a binary classifier system and its criterion is varied. In neurophysiology, it is used to test whether an ideal observer could reliably identify a given stimulus or a behavior based on a neural response.

sensory threshold A theoretical concept used in psychophysics. A stimulus that is less intense than the sensory threshold will not elicit any sensation. The concept can be applied to detection and perception in all senses. Several different sensory thresholds have been defined:

- *Absolute threshold.* The lowest level at which a stimulus can be detected.
- *Recognition threshold.* The level at which a stimulus can not only be detected but also recognized.
- *Differential threshold.* The level at which an increase in a detected stimulus can be perceived.
- *Terminal threshold.* The level beyond which a stimulus is no longer detected.

stimulus A detectable change in the internal or external environment.

top-down and **bottom-up** Strategies of information processing. The first is applied to cerebral signals that transmit information derived from past experience and the second is applied to cerebral signals that transmit sensory information.

vibrotactile stimulus A mechanical oscillation in time delivered on the skin.

Weber fraction Weber made the observation that, within a fairly large range, the increase in a stimulus that is just noticeable (ΔI) is a constant proportion of the initial stimulus (I) from any one sense. The proportion $\Delta I/I$ is the Weber fraction.

6.11.1 Introduction

A fundamental goal of neuroscience is to understand how sensory experiences arise from activity in the brain (Adrian, E. D., 1928). A major component of this problem involves understanding how the brain represents sensory features. Pioneering investigations in several sensory systems have shown how neural activity represents the physical parameters of the sensory stimuli both in the periphery and in the central areas of the brain (Mountcastle, V. B. *et al.*, 1967; Talbot, W. H. *et al.*, 1968; Hubel, D. H. and Wisel, T. N., 1998). These investigations have paved the way for new questions that are more closely related to cognitive processing. For example, where and how in the brain do the neuronal responses that encode the sensory stimuli translate into responses that encode a perceptual decision (Romo, R. and Salinas, E., 2001; Schall, J. D., 2001)? What components of the neuronal activity evoked by a sensory stimulus are directly related to perception (Newsome, W. T. *et al.*, 1989; Romo, R. *et al.*, 1998)? Where and how in the brain sensory information is stored in memory (Romo, R. *et al.*, 1999)? These questions have been investigated in behavioral tasks where the sensory stimuli are under precise quantitative control and the subject's psychophysical performances are quantitatively measured (Hernández, A. *et al.*, 1997; de Lafuente, V. and Romo, R., 2005). One of the main challenges of this approach is that even the simplest cognitive tasks engage a large number of cortical areas, and each one might render the sensory information in a different way (Romo, R. and Salinas, E., 2003; Romo, R. *et al.*, 2004). Also, the sensory information might be combined in these cortical areas with other types of stored signals representing, for example, past experience and future actions (Hernández, A. *et al.*, 2002; Romo, R. *et al.*, 2002; 2004). Thus, an important issue in neuroscience is to decode from the neuronal activity all these processes that might be related to perception.

In this chapter, we review results obtained using the somatic modalities and that are relevant for understanding the link between neural representations of sensory events in areas 3b and 1 of the
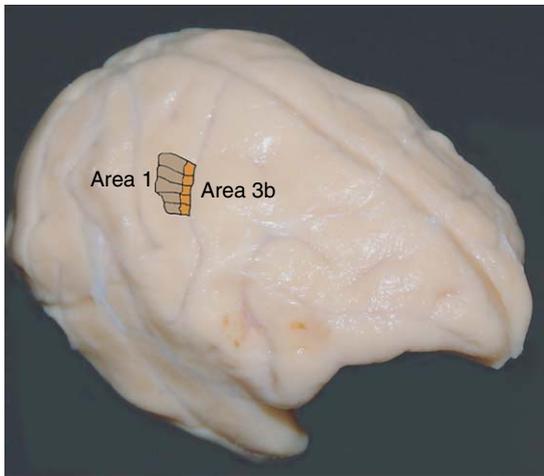
Figure 1 Picture of brain surface of one of the monkeys used to investigate the response properties of primary somatosensory cortex (S1) neurons during touch perception. Recordings were made in areas 3b and 1 of S1.

primary somatosensory cortex (S1; Figure 1) and psychophysically quantified behaviors during detection and discrimination tasks.

6.11.2   Sensory Detection

The detection of sensory stimuli is among the simplest perceptual experiences and is a prerequisite for any further sensory processing. A fundamental problem posed by the sensory detection tasks is that repeated presentation of a near-threshold stimulus might unpredictably fail or succeed in producing a sensory percept. Where in the brain are the neuronal correlates of these varying perceptual judgments? Pioneering studies on the neuronal correlates of sensory detection showed that in the case of vibrotactile stimuli the responses of S1 neurons account for the measured psychophysical accuracy (Mountcastle, V. B. *et al.*, 1969). However, direct comparisons between S1 responses and detection performance was not directly addressed and, therefore, it is not clear whether the activity of S1 accounts for the variability of the behavioral responses. Psychophysical performance was measured in human observers and S1 recordings were made in anesthetized monkeys.

6.11.3   Psychophysics of Sensory Detection

This problem has been recently addressed (de Lafuente, V. and Romo, R., 2005; 2006). These authors trained monkeys to perform a detection task. In each trial, the animal had to report whether the tip of a mechanical stimulator vibrated or not (Figure 2(a)). Stimuli were sinusoidal, had a fixed frequency of 20 Hz, and were delivered to the glabrous skin of one fingertip. Crucially, they varied in amplitude across trials. Stimulus-present trials were interleaved with an equal number of stimulus-absent trials in which no mechanical vibrations were delivered (Figure 2(a)). Depending of the monkeys' responses, trials could be classified into four types of responses: hits and misses in the stimulus-present condition, and correct rejections and false alarms in the stimulus-absent condition (Figure 2(b)). Stimulus detection thresholds were calculated from the behavioral responses (Figure 2(c)). Thus an important issue in this and similar tasks is to determine the neuronal correlates that account for these behavioral reports.

6.11.4   S1 Responses during Vibrotactile Detection

de Lafuente V. and Romo R. (2005) simultaneously characterized the activity of S1 neurons (areas 3b and 1) and the monkey's psychophysical performance by recording the extracellular spike potentials of single S1 neurons while the monkeys performed the detection task. Figures 2(c) and 3(a) show, respectively, the monkey's psychometric curve and the spike trains of an S1 neuron in the same trials. The firing rate of this example neuron varied smoothly as a function of stimulus amplitude, and no clear modulations in its firing rate could be appreciated during the stimulus-absent trials.

To test whether the responses of S1 neurons accounted for the monkey's psychophysical performance, de Lafuente V. and Romo R. (2005) calculated neurometric detection curves and compared them with the psychometric curves (Figures 3(b) and 3(c)). The proportion of yes responses for neurometric curves was defined, for a given amplitude, as the proportion of trials in which the neuron's firing rate reached or exceeded a criterion value (Green, D. M. and Swets, J. A., 1966;
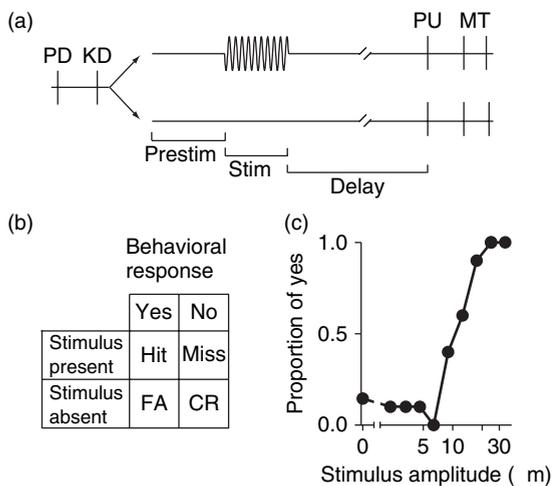
Figure 2 Detection task. (a) Trials began when the stimulator probe indented the skin of one fingertip of the right, restrained hand (probe down, PD). The monkey then placed its free left hand in an immovable key (key down, KD). On half of the randomly selected trials, after a variable prestimulus period (2.5–3.5 s), a vibratory stimulus (20 Hz, 0.5 s) was presented or not. Then, after a fixed delay period (3 s), the stimulator probe moved up (probe up, PU), indicating to the monkey that the response movement (MT) to one of the two push buttons could be made. The button pressed indicated whether the stimulus was felt or not (henceforth referred to as yes and no responses, respectively). (b) Depending on whether the stimulus was present or absent, and on the behavioral response, the trial outcome was classified as a hit, miss, false alarm, or correct rejection. Trials were pseudorandomly chosen; 90 trails were stimulus-absent (amplitude = 0) and 90 trials were stimulus-present with varying amplitudes (9 amplitudes with ten repetitions each). (c) Classical psychometric detection curve obtained by plotting the proportion of yes responses as a function of stimulus amplitude. Adapted from de Lafuente, V. and Romo, R. 2005. Neuronal correlates of subjective sensory experience. Nat. Neurosci. 12, 1698–1703.

de Lafuente, V. and Romo, R., 2005). For each neuron, this criterion was chosen to maximize the number of correct responses (Figure 3(b)). Pairwise comparisons of detection thresholds obtained from logistic fits to the simultaneously obtained neurometric and psychometric data showed that the detection thresholds of individual S1 neurons were not significantly different from the animals' psychophysical thresholds, and the two thresholds measures highly covaried. In addition, the shape of the mean neurometric curve resulting from the activity of the S1 neurons showed close correspondence with the shape of the mean psychometric curve (Figure 3(c)).

6.11.5 S1 Responses and Perceptual Reports

An important question addressed in this study is whether the activity of S1 neurons covaries with the perceptual yes–no judgments that the monkeys made on a trial-by-trial basis (de Lafuente, V. and Romo, R., 2005). To test this, these authors compared the activity during hit and miss trials for the near-threshold stimulus as well as for the corresponding activity in correct reject and false alarm trials in the stimulus-absent condition (Figure 4). They found no significant differences in the activity of S1 neurons between hits and misses (Figure 4, upper left panel) or between correct rejections and false alarms (Figure 4, upper right panel). This indicated that the activity of individual S1 neurons did not predict the monkey's behavior. To further quantify this, de Lafuente V. and Romo R. (2005) calculated a choice probability index, which estimates the probability with which the behavioral outcome can be predicted from the neuronal responses (Britten, K. H. *et al.*, 1996; Hernández, A. *et al.*, 2002). As shown in the lower panels of Figure 4, again they found no significant differences between hits and misses, or between correct rejections and false alarms trials.

6.11.6 Further Comments on the Functional Role of S1 in Sensory Detection

The low choice probability values are consistent with a detection model in which the activity of S1 serves as input to an additional processing stage(s) that determines whether a stimulus has occurred or not. Under this hypothesis, correlation between S1 activity and the final decision about the stimulus presence or absence is highly dependent on the amount of correlated noise among sensory neurons (Zohary, E. *et al.*, 1994). Indeed, de Lafuente V. and Romo R. (2005) found that the mean noise correlation coefficient across pairs of S1 neurons was 0.16 ± 0.02. This amount of correlated noise is similar to those reported in previous studies (Zohary, E. *et al.*, 1994; Bair, W. *et al.*, 2001; Romo, R. *et al.*, 2003), and is also consistent with the near chance choice probability values reported in the study of de Lafuente V. and Romo R. (2005). These results further support a detection model in which a central area(s) must be observing the activity of S1 neurons to judge about the stimulus
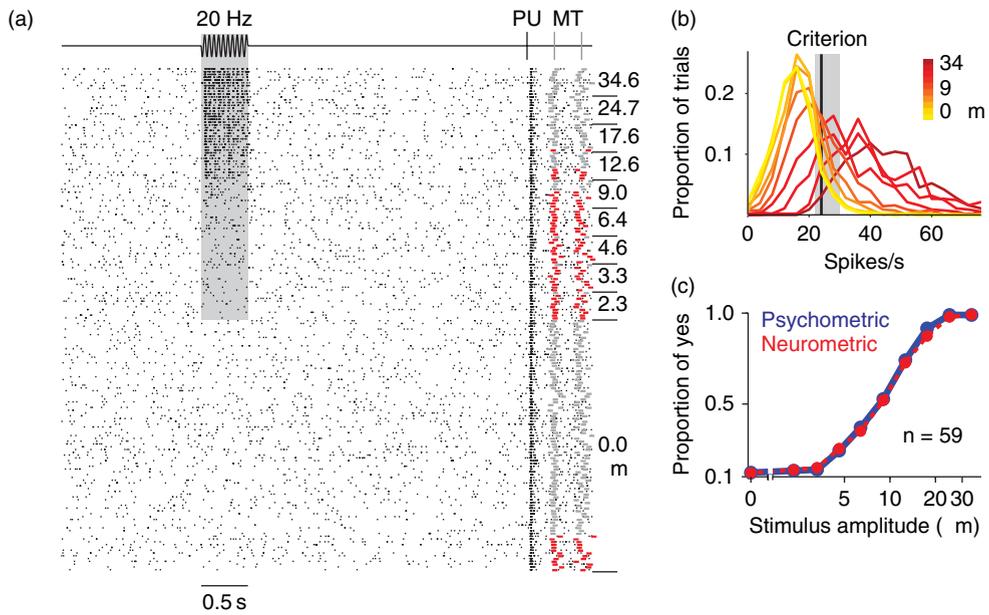
Figure 3 Activity of primary somatosensory cortex (S1) neurons during the detection task. (a) Raster plot of the spiking activity of an S1 neuron during the 180 trials of a typical detection experiment run. Each tick represents the time of spike occurrence and each row is a trial. Trials are arranged by stimulus amplitude, shown at right. Red markers at the end of the trial denote misses in stimulus-present trials, and false alarms in stimulus-absent trials. Gray box marks the time of stimulus presentation. (b) Activity distributions of the 59 neurons recorded in S1, grouped by stimulus amplitude (see calibration bar). Black vertical line marks the median criterion value (22 spikes per second) used to produce the neurometric proportion of yes for each neuron. Gray box indicates interquartile range. (c) Mean psychometric and neurometric detection curves (590 trials for each stimulus amplitude data point; 5310 trials for zero-amplitude data point). Adapted from de Lafuente, V. and Romo, R. 2005. Neuronal correlates of subjective sensory experience. Nat. Neurosci. 12, 1698–1703.
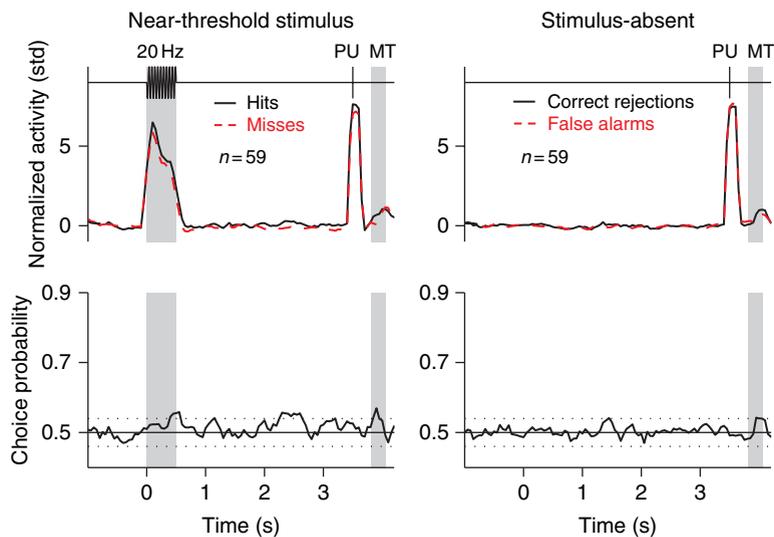
Figure 4 Correlation between psychophysical performance and neuronal responses during the detection task. Upper panels show the comparison of normalized neuronal population activity during hits and misses for near-threshold stimuli, and during correct rejections and false alarms in stimulus-absent trials. Lower panels show the choice probability index as a function of time. This index estimates the probability with which a trial's outcome can be predicted from the activity of neurons. Dotted lines mark significance levels (0.5 means chance levels) and n is the number of neurons. Adapted from de Lafuente, V. and Romo, R. 2005. Neuronal correlates of subjective sensory experience. Nat. Neurosci. 12, 1698–1703.

presence or absence. Therefore, the functional role of S1 in this and other perceptual tasks may be mainly to generate a neural representation of the sensory stimulus for further processing in areas central to it (Romo, R. *et al.*, 1999; Hernández, A. *et al.*, 2000; Salinas, E. *et al.*, 2000; Romo, R. *et al.*, 2002; 2003). However, a previous study found that functional magnetic resonance imaging (fMRI) signals in primary visual cortex (V1) reflected the percepts of human subjects rather than the encoded stimulus features (Ress, D. and Heeger, D. J., 2003). This result suggests that in V1 top-down signals (nonsensory inputs delivered to V1 via feedback projections) can be combined with bottom-up (sensory) information and this can contribute to sensory percepts (Ress, D. and Heeger, D. J., 2003). S1 data did not show evidence of this type of neural interaction; rather, they indicated that S1 represents the physical properties of stimuli and contributes little to near-threshold percepts (de Lafuente, V. and Romo, R., 2005). The discrepancy could be due to fundamentally different organizations across sensory cortices, or to differences between species. Another possibility to consider is that the modulation revealed through fMRI may have an effect that is invisible from the point of view of single neurons. This would happen if, for instance, such modulation acted only to synchronize the spikes of multiple target neurons (Fries, P. *et al.*, 2001a; 2001b).

6.11.7   Sensory Discrimination

The sensory detection task discussed above addressed the fundamental problem of whether the activity of S1 accounts for sensory detection. The results indicate that the S1 responses do not account for perceptual judgments in the detection task. However, there are reports suggesting a role for early sensory cortices in cognitive functions previously assigned to more central cortices. A more interesting cognitive task – sensory discrimination – was introduced by Mountcastle and colleagues several years ago (LaMotte, R. H. and Mountcastle, V. B., 1975; Mountcastle, V. B. *et al.*, 1990), and served to further explore the role of sensory cortices in perception. In the discrimination task they designed (LaMotte, R. H. and Mountcastle, V. B., 1975; Mountcastle, V. B. *et al.*, 1990), animals had to indicate whether the frequency of a comparison stimulus was lower or higher than the frequency of a base stimulus presented earlier (Figure 5). In principle, the task can be conceptualized as a chain of neural operations or cognitive steps: encoding the

first stimulus frequency, maintaining it in working memory, encoding the second frequency and comparing it to the memory trace left by the first stimulus, and communicating the result of the comparison to the motor apparatus. Thus the flutter task offers a number of advantages as a model for sensory processing in the brain (Romo, R. and Salinas, E., 2001; 2003): not only do humans and monkeys perform similarly, but the items to be compared are spread out across time and always activate the same well-defined population of primary receptors (Mountcastle, V. B. *et al.*, 1967; Talbot, W. H. *et al.*, 1968; Ochoa, J. and Torebjörk, E., 1983; Macefield, G. *et al.*, 1990; Vallbo, A. B., 1995). So spatial variations are basically taken out of the picture. However, for the flutter task to be a useful model it is essential that it generate a reliable sequence of cognitive events like the one just mentioned. How do we know that this is so?

A crucial step is to scrutinize the psychophysics. Importantly, in the original paradigm the base frequency did not vary from trial to trial during a run (LaMotte, R. H. and Mountcastle, V. B., 1975; Mountcastle, V. B. *et al.*, 1990). When Romo and colleagues reexamined the flutter discrimination task, they found the paradigm to be ambiguous: when the base stimulus frequency is kept constant, the task can be solved either by comparing the two stimuli or by categorizing the second stimulus as high or low, ignoring the base stimulus (Hernández, A. *et al.*, 1997). What were the monkeys actually doing? When the base frequency was held constant during long blocks of trials, as done originally, the measured discrimination limens (DLs) and Weber fractions were similar to those reported before. If the monkeys had been discriminating the differences in frequency between the two stimuli, they would also have been able to do so when the frequency of the base stimulus changed from trial to trial. However, this was not the case: their performance dropped to chance levels. It seemed that the monkeys were paying attention only to the second stimulus, categorizing it as low or high with respect to an internal reference, perhaps the base frequency used during training. To test this possibility, in separate runs the base stimulus was removed and single stimuli were delivered in each trial. In this new condition the monkeys were rewarded for correctly categorizing stimulus frequency as lower or higher than an arbitrary reference (20, 30, or 40 Hz) kept constant during a block of trials; monkeys had to determine this reference by trial and error. The monkeys learned this task very quickly, and the
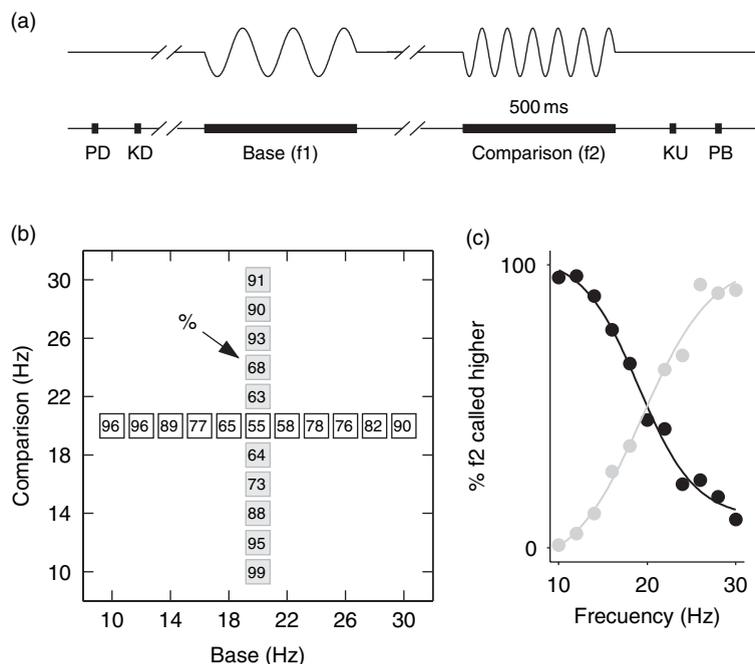
Figure 5 Discrimination task. (a) Sequence of events during discrimination trials. The mechanical probe is lowered, indenting the glabrous skin of one digit of the hand (PD); the monkey places his free hand on an immovable key (KD); the probe oscillates vertically, at the base frequency; after a delay, a second mechanical vibration is delivered at the comparison frequency; the monkey releases the key (KU) and presses one of two push buttons (PB) to indicate whether the comparison frequency was higher or lower than the base. (b) Stimulus set used to estimate psychometric thresholds. Each box indicates a base frequency/comparison frequency stimulus pair used; the number inside the box indicates overall percent correct trials for that base/comparison pair. (c) Psychometric curves computed from (b). Adapted from Romo, R., Hernández, A., Zainos, A., Brody, C. D., and Lemus, L. 2000. Sensing without touching: psychophysical performance based on cortical microstimulation. Neuron 26, 273–278 and Romo, R., Hernández, A., Zainos, A., and Salinas, E. 1998. Somatosensory discrimination based on cortical microstimulation. Nature 392, 387–390.

psychometric curves (Hernández, A. *et al.*, 1997) measured in this condition were practically identical to those measured during the classical discrimination task (Mountcastle, V. B. *et al.*, 1990).

For true discrimination, monkeys were retrained using multiple pairs of base and comparison frequencies. The key was to vary the base frequency in each trial but such that each frequency could be followed either by a higher or by a lower comparison; this forced the subjects to compare (Hernández, A. *et al.*, 1997). After retraining, which took a few months, performance in this situation was similar to that in the classical discrimination task. From these results it seems almost certain that the animals truly learned to discriminate between frequencies on a trial-by-trial basis.

The lesson is that although monkeys may indeed learn to discriminate they can also develop alternate strategies to solve a task, as suggested earlier based on theoretical arguments (Johnson, K. O., 1980). In particular, in the classical flutter discrimination paradigm,

monkeys tend not to compare the two stimuli at every trial; instead they classify the second stimulus, possibly setting the limits of each category during the first few trials in a run. Whenever animals are assumed to discriminate, this problem should not be underestimated, regardless of sensory modality (Johnson, K. O., 1980; Vogel, R. and Orban, G., 1990; Vázquez, P. *et al.*, 2000).

This appears as a simple observation, but it may reflect fundamentally different mechanisms at work. Consider a task that involves variations in a single feature across trials. To identify or classify a current sensory stimulus, it must be compared to a reference stored in long-term memory, but it is not clear how the comparison process can be studied in this situation. How is information stored in long-term memory read out and made comparable to current sensory events? Where is this information stored and how does it differ from the original sensory-evoked activity? In contrast, in discrimination tasks in which two stimuli are presented sequentially in each trial, the

comparison is made against the short-term memory trace left by the first stimulus. This means that if we can identify the neural correlate of the working-memory component, it might be possible to study the comparison or decision-making mechanisms that underlie task performance. Indeed, such neural correlate has been reported recently (Hernández, A. et al., 2002; Romo, R. et al., 2002; 2004).

6.11.8 Neural Coding of Vibrotactile Stimuli in S1

Mountcastle and colleagues recorded S1 responses in behaving monkeys trained to detect and discriminate the frequencies of flutter stimuli (Mountcastle, V. B. et al., 1990). The results support previous findings (Mountcastle, V. B. et al., 1969). First, it was found that quickly adapting (QA) neurons of S1 (areas 3b and 1), like their afferent fibers, fire periodically, in phase with mechanical oscillations. Second, their firing rates seem to change little in the flutter range (this conclusion was based, however, on data from 17 neurons). Third, psychophysical performance matched the inferred performance based on the discriminability of the periodic interspike intervals (Mountcastle, V. B. et al., 1990). It followed that, as proposed before, stimulus frequency could not be encoded by S1 firing rates; stimulus frequency had to be encoded temporally, in the serial order of evoked spikes (Talbot, W. H. et al., 1968; Mountcastle, V. B. et al., 1969; 1990).

In support of this proposal, using flutter stimuli, Merzenich and colleagues compared psychophysical data from monkeys to S1 recordings in separate experiments from the same animals (Recanzone, G. H. et al., 1992). The comparison was consistent with a temporal coding mechanism, and firing rates were not seen to vary with stimulus frequency (however, the range of frequencies tested was quite narrow, and animals were anaesthetized). Merzenich and colleagues made another important observation: that spike timing associated with the sine wave was much more precise in trained animals than in untrained monkeys (Recanzone, G. H. et al., 1992). Thus, based on these results, a psychophysical observer should exploit the periodic, spike timing evoked in the QA neurons of the S1 cortex for sensory discrimination.

Arguments in favor of the proposal reviewed above can be strengthened if a large number of neurons are studied and if neurons are studied in behaving animals during the flutter discrimination task. To this end, Romo and colleagues trained monkeys to discriminate

between flutter stimulus frequencies and recorded many neurons with QA properties in areas 3b and 1 of S1 (Hernández, A. et al., 2000; Salinas, E. et al., 2000; Luna, R. et al., 2005). Each recorded neuron with QA properties was studied during the discrimination task. There were three major results. First, the majority of neurons from S1 were phase-locked to the input stimulus frequency (Figures 6(a) and 6(b)); however, almost a third of QA neurons modulated their firing rates as a function of the stimulus frequency (Figures 7(a) and 7(b); Hernández, A. et al., 2000; Salinas, E. et al., 2000; Luna, R. et al., 2005). Second, the QA neurons that modulate their firing rates were affected by the task condition; that is, they increased their transmitted information about the stimulus frequency during task performance (Salinas, E. et al., 2000). Third, only those neurons that varied their firing rates as a function of the stimulus frequency were affected in error trials (Salinas, E. et al., 2000).

These findings question a unique role of periodic, spike timing in discrimination of flutter stimuli, and suggest that a firing rate code cannot be discarded (Salinas, E. et al., 2000). But, apart from this, what do these findings suggest? They suggest the presence of two subpopulations of QA neurons in S1 that behave differently in response to a periodic mechanical stimulus (Hernández, A. et al., 2000; Salinas, E. et al., 2000; Luna, R. et al., 2005). These two subpopulations might be arranged in a hierarchical fashion: QA neurons that respond periodically might be closer to the input stimulus, and those that modulate their firing rates might integrate the responses of the periodic neurons and transform them into a rate code (Hernández, A. et al., 2000). Such last-order neurons of the QA circuit could distribute the neural representation to those structures anatomically linked to S1, in order to solve the sensory discrimination task. However, further studies are needed to see whether this is so.

6.11.9 Neuronal Correlates of Flutter Discrimination in S1

A more direct test for the role of periodicity in flutter discrimination is measuring the discrimination capabilities of these subtypes of QA neurons associated with the psychophysical performance (Figures 6(c) and 6(d) and Figures 7(c) and 7(d)). A second test is to prove whether the evoked neural activity during discrimination in S1 cortex is sufficient for sensory performance. Finally, whether the temporal order of the spikes is important for sensory discrimination. These are
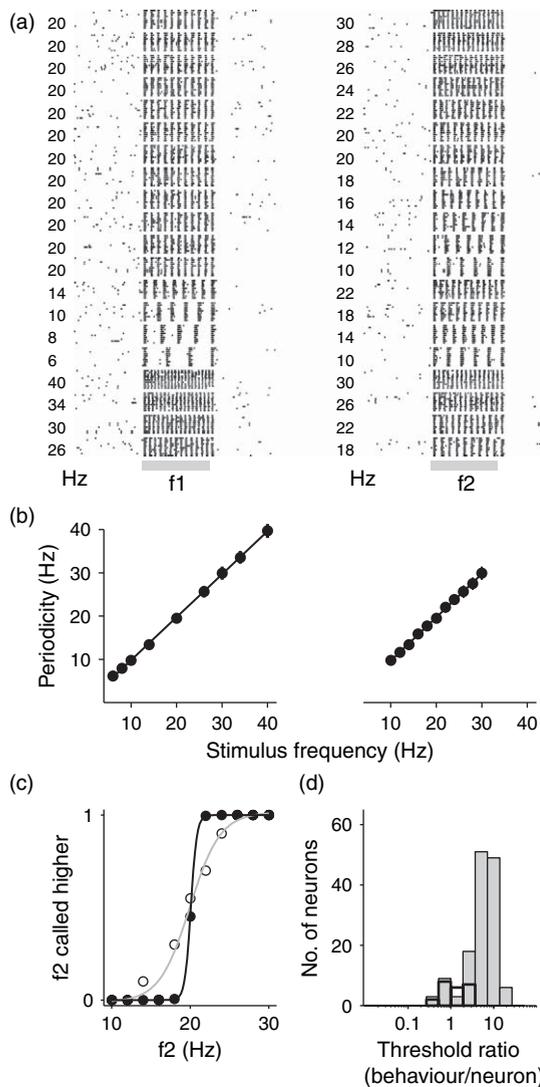
Figure 6 Periodic responses of a quickly adapting (QA) neuron of area 1 during the discrimination task. (a) Raster plots. Each row of ticks represents a trial, and each tick represents an action potential. Trials were randomly delivered. Gray horizontal lines indicate the first (f1) and the second (f2) stimulus. (b) Periodicity ($\pm$SD) as a function of the first (f1) and second stimulus (f2) frequencies. (c) Relationship between psychometric and neurometric discrimination functions. This is plotted as the probability that the second stimulus is judged higher than the first; data and sigmoidal fits (χ^2 test, $P < 0.001$) for 11 pairs of stimulus frequencies in which the base frequency was 20 Hz. Gray and black lines represent psychometric and neurometric functions, respectively. (d) Thresholds ratios (psychometric/neurometric thresholds) calculated from neurons with periodicity (gray bars). Open bars represent the threshold ratios between psychometric and neurometric thresholds calculated from a small number of neurons with modulations in their firing rate. Adapted from Hernández, A., Zainos, A., and Romo, R. 2000. Neuronal correlates of sensory discrimination in the somatosensory cortex. Proc. Natl. Acad. Sci. U. S. A. 97, 6091–6096.
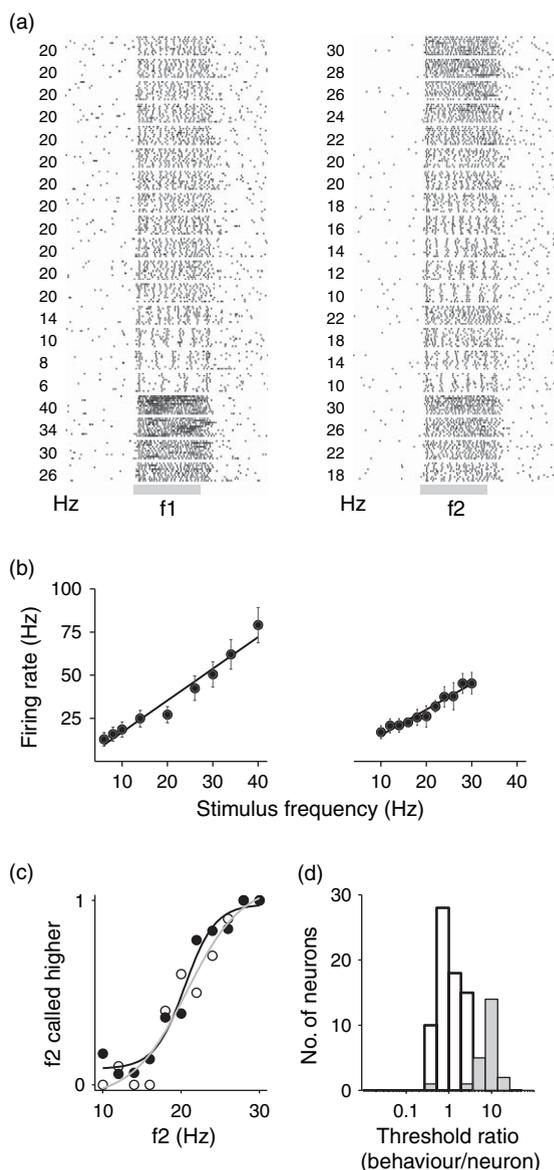
Figure 7 Firing rate modulation of a quickly adapting (QA) neuron of area 3b during the discrimination task. Same format as in Figure 6. (a) Raster plots. (b) Mean firing rate ($\pm$SD) as a function of the stimulus frequency. (c) Relationship between psychometric and neurometric discrimination functions. (d) Threshold ratios calculated between psychometric and neurometric thresholds for each neuron, which varied the firing rate as a function of the stimulus frequency (open bars). Gray bars represent the threshold ratios between psychometric and neurometric thresholds calculated from a small number of neurons that show periodicity. Adapted from Hernández, A., Zainos, A., and Romo, R. 2000. Neuronal correlates of sensory discrimination in the somatosensory cortex. Proc. Natl. Acad. Sci. U. S. A. 97, 6091–6096.

incisive tests to validate the meaning of the neural encoding of the flutter stimuli in the S1 cortex.

The vibrotactile discrimination task requires the comparison of the second stimulus frequency against the first (Hernández, A. et al., 1997). As indicated above, Romo and colleagues found two types of responses in QA neurons of the S1 cortex: one that is periodically entrained by the stimulus frequency, and a second that, although not periodically entrained, has average firing rates during the stimulus period that are modulated as a function of the stimulus frequency (Hernández, A. et al., 2000; Salinas, E. et al., 2000; Luna, R. et al., 2005). To investigate which of these two representations is associated with the psychophysical performance, these authors determined the probability that an observer (a cortical region central to S1 cortex) could distinguish the difference between the two stimuli (Hernández, A. et al., 2000; Salinas, E. et al., 2000; Luna, R. et al., 2005). This could be based on a comparison of the neuronal response distributions of the second stimulus frequency made against the neuronal response distributions of the first stimulus frequency. According to this, the observer could use a simple rule: if the number of spikes during the second stimulus is higher than during the first stimulus, then the second stimulus is higher than the first. The same rule can be used when considering the periodicity values: if the periodicity (estimated as the frequency with greatest power in a Fourier transform of the spiking responses) during the second stimulus period is higher than during the first stimulus period, then the second stimulus is higher than the first. The effect of this type of rule is equivalent to determining the area under the curve ROC (receiver operating characteristic; Green, D. M. and Swets, J. A., 1966) generated by the neuronal response distributions for each pair of stimulus frequencies, using both periodicity and firing rate values (Hernández, A. et al., 2000; Luna, R. et al., 2005). The areas under each of these two ROC curves are an estimate of the proportion of correct trials that an optimal observer would obtain by comparing the number of spikes or periodicity. In pairs of stimulus frequencies where the neuronal response distributions during the second stimulus are much higher than the neuronal distributions of the first stimulus, ROC values are close to 1; if the neuronal response distributions during the stimulus are much lower than the neuronal response distributions of the first stimulus, ROC values are close to 0; for overlapping distributions, intermediate ROC values are found. The ROC values were then used to compute neurometric functions. Psychophysical and neuronal discrimination thresholds are calculated as half the

difference between the stimulus frequency identified as higher than the standard in 75% of trials and that frequency identified as higher in 25% of the trials. These are read directly from the logistic functions expressed in terms of hertz. Using this analysis, Romo and colleagues are in the position to address the question of which of the two representations is meaningful for frequency discrimination.

Neurometric functions based on periodicity (Figures 6(c) and 6(d)) or firing rate (Figures 7(c) and (d)) of single S1 neurons were directly compared to the psychometric thresholds (Hernández, A. et al., 2000). The results of this analysis show that neurometric threshold values based on periodicity are far lower than the psychometric thresholds (Figure 6(d)). This is not the case when neurometric thresholds based on firing rate are compared to the psychometric thresholds (Figure 7(d)). They are very close to the psychometric thresholds. The goal of computing neurometric functions was not only to reveal the relationship between the neuronal responses of S1 to the mechanical stimulus, but also to discern whether these neural signals account for the psychometric behavior. However, what is then the functional meaning of the periodic neural signal in S1? One possible role is that they simply represent the temporal structure of the stimulus and that monkeys do not use this exquisite representation for frequency discrimination. This would be the case if, for example, discrimination were based on the mean number of spikes (or bursts) fired by the population of QA neurons as a function of the stimulus frequency. Consistent with this idea, Hernández A. et al. (2000) found that QA neurons in S1 whose firing rates are modulated by the stimulus frequencies and their neurometric thresholds based on firing rates are closely similar to the monkey's psychophysical thresholds. However, these correlations do not prove they are sufficient for discrimination (Romo, R. et al., 1998; 2000).

One experiment that could give an insight about the functional meaning of the periodic spike structure of the evoked activity in S1 is testing whether monkeys could discriminate the difference between the two stimuli when periodicity is broken. If monkeys fail to discriminate the difference in mean frequency between the two stimuli, this would strengthen the proposal that discrimination of flutter stimuli depends on the periodic structure of the spike trains evoked in S1 (Figure 8). However, monkeys were able to extract the mean frequency from the nonperiodic signals and the psychophysical measures were almost identical with the periodic stimuli (Romo, R. et al., 1998).
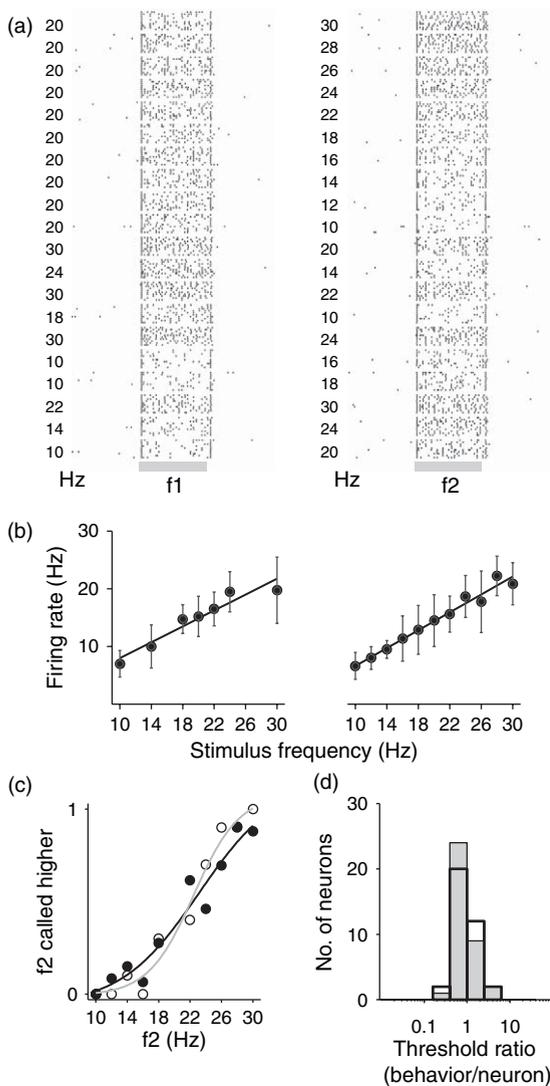
Figure 8 Firing rate modulation of a quickly adapting (QA) neuron of area 1 during the discrimination of aperiodic stimuli. Same format as in Figure 6, but both base (f1) and comparison (f2) frequencies (mean frequencies) lack periodicity. (a) Raster plots. (b) Mean firing rate ($\pm$SD) as a function of the stimulus frequency. (c) Relationship between psychometric and neurometric discrimination functions. (d) Threshold ratios calculated between psychometric and neurometric thresholds for each neuron during the discrimination of a periodic stimulus frequencies (open bars). Gray bars represent threshold ratios between psychometric and neurometric thresholds during the discrimination of aperiodic frequencies. Adapted from Hernández, A., Zainos, A., and Romo, R. 2000. Neuronal correlates of sensory discrimination in the somatosensory cortex. Proc. Natl. Acad. Sci. U. S. A. 97, 6091–6096.

Romo and colleagues then studied QA neurons in each of the two conditions: while monkeys discriminated between periodic stimuli and while monkeys discriminated between aperiodic stimuli (Hernández,

A. *et al.*, 2000). Due to the aperiodic stimulus design, even highly stimulus-entrained neurons do not carry information about stimulus frequency in their periodicity. Clearly, neurometric thresholds based on the firing rate were again closely associated with the psychometric thresholds (Figures 8(c) and 8(d)). As in the periodic condition, a psychophysical observer could exploit firing rate for frequency discrimination of aperiodic stimuli. These results suggest that an observer could solve this task with a precision similar to that of the monkey, based only on the firing rate produced during the stimulus periods.

There are, however, some further unexplored possibilities. For example, QA neurons of S1 typically respond to each stimulus pulse with a discrete burst of spikes. Encoding of vibrotactile stimuli could therefore be based on the number or rate of events, where each event is defined as a burst instead of being defined as a single spike. An observer counting bursts would obtain a good estimate of the count of stimulus pulses, and this estimate would be independent of variability in the number of spikes fired in response to each pulse. Indeed, there is experimental evidence suggesting that bursting activity could efficiently encode the stimulus features (Reinagel, P. *et al.*, 1999; Martínez-Conde, S. *et al.*, 2000; Kepecs, A. *et al.*, 2002; Krahe, R. and Gabbiani, F., 2004). But whether bursting actually contributes directly to the psychophysical behavior is not known. Finally, the temporal window on which vibrotactile discrimination is based has not been determined. In previous experiments carried out by Romo and colleagues, stimulus periods were always 500 ms long. Under these conditions, the use of a code based on counting events and the use of a code based on the rate of events could not be distinguished.

To distinguish between all these alternatives, Romo and colleagues conducted new combined psychophysical and neurophysiological experiments in the vibrotactile discrimination task (Luna, R. *et al.*, 2005). They reasoned that if an observer uses a firing rate, a bursting rate, or a measure of periodicity, then increases or decreases in the duration of either of the two stimuli used in each trial of the task should not lead to a systematic bias in discrimination, in either of the two possible directions. (On the other hand, under this hypothesis, stimulus duration could affect the sensory signal-to-noise ratio and therefore affect the psychometric threshold.) Alternatively, if the observer uses a strategy based on the total number of spikes or bursts fired in response to each stimulus, then manipulation of

the stimulus duration should systematically bias performance, with longer stimuli being perceived as having been of higher frequencies than they actually were. Romo and colleagues found that when the duration of one of the two stimuli was changed by 50% relative to the other stimulus, monkeys indeed biased their discrimination performance (Luna, R. et al., 2005). Monkeys treated shortened stimuli as if the applied stimulus frequency had been slightly but significantly lower than it actually was; conversely, monkeys treated lengthened stimuli as if the applied frequency had been slightly but significantly higher than it actually was. These effects were observed with both periodic and aperiodic stimuli. These investigators then sought an explanation for these psychophysical biases by recording QA neurons of S1 while the monkeys performed in variable-stimulus-length conditions (Luna, R. et al., 2005). They found that the effects can be qualitatively explained if one assumes that the neural signal used by the observer to solve the task is an integral of either spikes or bursts over a time window that concentrates most of its mass within the first 250 ms of the stimulus, but also has a small tail into later parts of the stimulus. Finally, examining trial-by-trial covariations of weighted counts of spikes and weighted counts of bursts, they found that only the weighted count of spikes covaried with performance on a trial-by-trial basis.

In summary, firing rates that vary as functions of stimulus frequency are seen in multiple areas activated during the task, in particular in S1, and there is evidence that these rate variations have a significant impact on behavior. Clearly, the brain must be able to extract at least some information from the precise timing of S1 spikes evoked during the task; for instance, humans can easily distinguish periodic stimuli from aperiodic. However, Romo and colleagues found no indication that the high periodicity found in S1 contributes to frequency discrimination, although this possibility is hard to rule out entirely.

6.11.10 Artificial Induction of Activity in S1 Underlying Flutter Discrimination

How can we be sure that the activity recorded in S1 is actually related to perception and behavior? Intracortical microstimulation is a powerful technique capable of establishing a causal link – not just a correlation – between the activity of localized neuronal populations and specific cognitive functions

(Salzman, D. et al., 1990; Britten, K. H. and van Wezel, R. J., 1998; Romo, R. et al., 1998; 2000). For flutter discrimination, this approach has provided the most compelling evidence that all the cognitive processes of the task may be triggered directly by the QA circuit in S1, and has also allowed us to explore questions about the neural code for flutter stimuli (Romo, R. et al., 1998; 2000). Importantly, S1 is organized in modules of neurons sharing the same receptive field and mechanoreceptor submodality (Mountcastle, V. B., 1957; Powell, T. P. S. and Mountcastle, V. B., 1959; Sur, M. et al., 1984). The experiments described below were aimed to drive a column(s) of S1 – mostly of the QA type – in a way that matched the dynamic responses recorded when mechanical stimuli were applied to a patch of skin of the fingertips.

Initially, the idea was to manipulate the comparison stimulus only (Romo, R. et al., 1998). The monkeys first learned to discriminate the frequencies of two sinusoidal vibrations delivered successively to the fingertips. Once they mastered the task, neurophysiological recordings were made in area 3b of S1, which allowed the identification of clusters of QA neurons. An applied microstimulation current spreads around a certain cortical area, activating many neighboring units. Thus, a key for the success of microstimulation experiments is that the microelectrode must be located in the midst of a functionally homogeneous cluster of neurons. Fortunately, area 3b is indeed organized into modules of units with similar properties, or into columns (Sur, M. et al., 1984). So, after the identificaton of a set of QA neurons, the comparison stimulus was substituted with microstimulation in one half of the trials. Artificial stimuli consisted of periodic current bursts delivered at the same comparison frequencies as mechanical stimuli. Microstimulation sites in S1 were selected to have QA neurons with receptive fields on the fingertip at the location of the mechanical stimulating probe. Remarkably, the monkeys discriminated the mechanical (base) and electrical (comparison) signals with performance profiles indistinguishable from those obtained with mechanical stimuli only (Figure 9(a)), so the artificially induced sensations probably resembled natural flutter quite closely (Romo, R. et al., 1998).

Going back to the question of whether periodicity is crucial for frequency discrimination, Romo and colleagues applied aperiodic microstimulation patterns that mimicked the random trains of mechanical pulses discussed earlier (Figure 9(b)). The same mean frequencies were used in this condition – 20 Hz still corresponded to 10 current bursts delivered
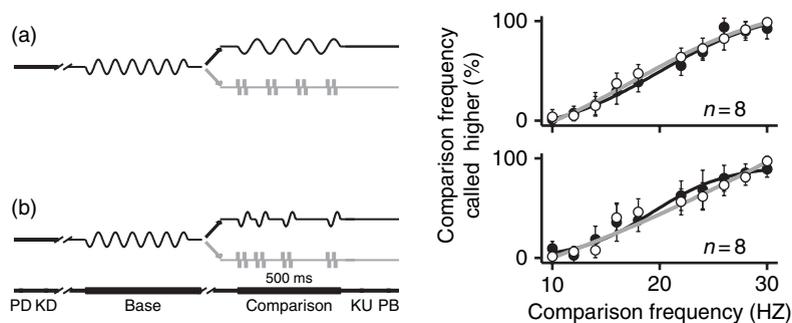
Figure 9 Psychophysical performance in frequency discrimination with natural mechanical stimuli and with artificial electrical stimuli injected into clusters of quickly adapting (QA) neurons of area 3b. The diagrams on the left show two types of trials that were interleaved during the experiments. In half of the trials, the monkeys compared two mechanical vibrations delivered on the skin. In the other half, one or both stimuli could be replaced by electrical frequencies microinjected into clusters of QA neurons of area 3b. The curves on the right show the animals' performance in the different situations, illustrated on the left. Filled and open circles indicate mechanical and electrical stimuli, respectively. In (a) and (b), the *y*-axis corresponds to the percentage of times the monkeys called the second stimulus frequency (*x*-axis) higher than the first (20 Hz). (a) Psychophysical performance using periodic stimuli; the comparison stimulus could be either mechanical or electrical frequencies. (b) Psychophysical performance when the comparison stimulus could be either aperiodic, mechanical or electrical stimulus frequencies. PD, indentation of the glabrous skin by the mechanical probe; KD, detection of indentation; KU, detection of the end of the comparison stimulus; PB, the monkeys presses one of two push buttons to indicate whether the second stimulus frequency was higher or lower than the first. Adapted from Romo, R., Hernández, A., Zainos, A., and Salinas, E. 1998. Somatosensory discrimination based on cortical microstimulation. Nature 392, 387–390.

in 500 ms – but the bursts were separated by random time intervals. Everything else proceeded as before, with mechanical and stimulation trials interleaved, as indicated in Figure 9(b). From the very first trials, the animals were able to discriminate both mechanical and electrical aperiodic signals (Figure 9(b)), with practically the same performance level reached with mechanical, periodic vibrations (Romo, R. *et al.*, 1998).

An interesting effect was observed as the intensity of the microstimulation current was varied. At very low intensities, artificial stimuli were not detected; the monkeys simply kept waiting. At intermediate intensities the monkeys detected the stimuli – they reacted and pushed a button – but their psychophysical behavior was at chance levels, as if they could determine the presence but not the frequency of the artificial stimuli. At higher intensities they discriminated normally (Romo, R. *et al.*, 1998). These transitions parallel those observed when the amplitude of mechanical vibrations is gradually increased; in particular, there is an atonal interval in which stimuli can be detected but their frequencies cannot be ascertained (LaMotte, R. H. and Mountcastle, V. B., 1975; Mountcastle, V. B. *et al.*, 1990). In an extra control experiment these authors investigated the effect of stimulus amplitude, which could potentially act as an alternate discrimination

signal (Romo, R. *et al.*, 1998). Four frequency pairs and all stimuli were mechanical, and the other half of the comparison stimulus was electrical. In both cases, the amplitude of the comparison could take one of three values, a standard amplitude A, 0.6A, or 1.4A. The changes in amplitude were, in terms of percentage, of the same magnitude (40%) as the differences between base and comparison frequencies. The results showed that performance was not affected by the large variations in amplitude; had the monkeys been guided by the amplitudes changes, one of the three combinations for each frequency pair would have fallen to <25% correct, because performance was normally >75% correct. Amplitude corrections, like those mechanical stimuli, were also applied to electrical currents in ∼60% of all runs; they had no marked impact on performance (Romo, R. *et al.*, 1998).

Because of the design of the paradigm, comparison of the second stimulus is made against a memory trace of the first one (Hernández, A. *et al.*, 1997). Having shown that the monkeys could use an artificial stimulus during the comparison, Romo and colleagues wondered whether they would be able to memorize and use an electrical stimulus delivered during the base period (Romo, R. *et al.*, 2000). In this case, in one half of the trials the base stimulus consisted of electrical microstimulation at a frequency equal to f1 (Figure 10), with the electric
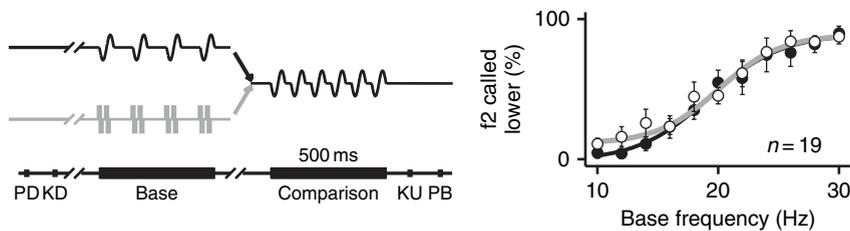
Figure 10 Psychophysical performance when the base stimulus could be either periodic, mechanical or electrical stimulus frequencies injected into clusters of quickly adapting (QA) neurons in area 3b. The same protocols and labels as in Figure 9, but here the base mechanical stimulus frequency was substituted by electrical stimulus frequencies. The y-axis corresponds to the percentage of times the monkeys called the comparison stimulus (20 Hz) lower than base stimuli at the frequency specified in the x-axis. Adapted from Romo, R., Hernández, A., Zainos, A., Brody, C.D., and Lemus, L. 2000. Sensing without touching: psychophysical performance based on cortical microstimulation. Neuron 26, 273–278.

current again being injected into QA neurons. The frequency pairs and event sequence during the task were the same as in previous experiments with natural stimuli; we stress this because careful design of the stimulus sets was particularly crucial here, in order to ensure that the monkeys paid attention to the base stimulus and stored it in working memory (Romo, R. *et al.*, 1999). The monkeys' psychophysical behavior was again indistinguishable from that observed with natural stimuli only (Figure 10), showing that the signals evoked by mechanical and artificial stimuli could be stored and recalled with approximately the same fidelity (Romo, R. *et al.*, 2000). Finally, they also investigated whether monkeys could perform the entire task on the basis of purely artificial stimuli. In most sessions in which the two mechanical stimuli were replaced by microstimulation patterns, monkeys were able to reach discrimination levels close to those measured with mechanical stimuli delivered to the fingertips. This demonstrates that activation of QA neurons is sufficient to drive all the cognitive processes involved in the task with little degradation in performance (Romo, R. *et al.*, 2000).

A couple of additional observations derived from these experiments are also noteworthy. First, early experiments with primary afferents had demonstrated that the flutter sensation is specifically mediated by QA fibers (Ochoa, J. and Torebjörk, E., 1983; Vallbo, A. B., 1995), but this was more difficult to test at the level of S1 (Romo, R. *et al.*, 1998). When microstimulation was applied to clusters of neurons identified as having slowly adapting (SA) properties (Figure 11(a)), the monkeys could barely discriminate, if at all (Romo, R. *et al.*, 2000). As the electrode was advanced to the border between SA and QA clusters, performance became somewhat better (Figure 11(b)), and it reached its usual degree of

accuracy when QA properties became most evident in the recordings (Figure 11(c); Romo, R. *et al.*, 2000). Hence, QA and SA units are still functionally segregated in S1, consistent with previous observations (Sur, M. *et al.*, 1984).

In some sessions, Romo and colleagues were able to introduce three microelectrodes into a cluster of QA neurons of area 3b that shared the same receptive field (Romo, R. *et al.*, 2000). They knew that the most anterior microelectrode was placed in the superficial layers, because another microelectrode was placed in front of it and recorded units in primary motor cortex that were driven by spontaneous or passive movements of the fingers and lacked cutaneous receptive fields. The most posterior microelectrode was placed, they believe, in the lower layers, and the microelectrode between these two in the middle layers. In separate runs, the frequency pairs and event sequence were the same in both mechanical and microestimulation trials, except that in the microstimulation trials the first mechanical stimuli were substituted with train of current pulses delivered at the frequency of the mechanical stimulus they were substituting. Figure 12 shows that discrimination is triggered by microstimulating each of the three different clusters. Thus, activation of any part of the cluster of neurons (probably a QA column) with similar functional properties is sufficient to initiate discrimination in this task (Romo, R. *et al.*, 2000).

6.11.11 Further Comments on the Functional Role of S1 to Flutter Discrimination

The results obtained in these sets of experiments suggest that QA neurons from S1 represent the stimulus frequencies both in the periodic spike intervals and
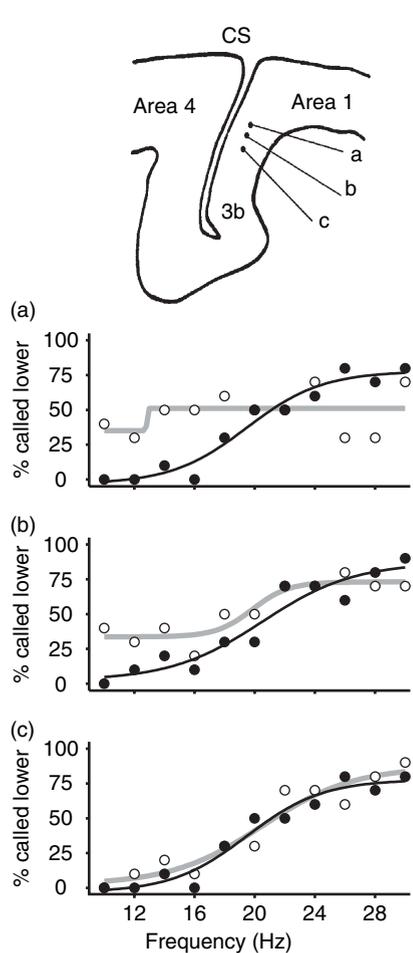
Figure 11 Psychophysical performance elicited by microstimulating at the base stimulus frequency in three different sites of area 3b. Same protocol and labels as in Figure 9. (a–c). Data collected in three separate runs during the same electrode penetration. (a) Psychophysical performance when microstimulation was applied in the center of cluster of slowly adapting (SA) neurons. (b) Psychophysical performance when microstimulation was applied in the border between quickly adapting (QA) and SA neurons. (c) Psychophysical performance when microstimulation was applied in a cluster of QA neurons. CS, central sulcus. Adapted from Romo, R., Hernández, A., Zainos, A., Brody, C.D., and Lemus, L. 2000. Sensing without touching: psychophysical performance based on cortical microstimulation. Neuron 26, 273–278.

Figure 12 Psychophysical performance elicited by microstimulating at the base stimulus frequency in three independent microelectrodes in three different sites of a cluster of quickly adapting (QA) neurons of area 3b. Protocols and labels as in Figure 9. CS, central sulcus. Adapted from Romo, R., Hernández, A., Zainos, A., Brody, C.D., and Lemus, L. 2000. Sensing without touching: psychophysical performance based on cortical microstimulation. Neuron 26, 273–278.

in the firing rate (Hernández, A. *et al.*, 2000; Salinas, E. *et al.*, 2000), and that activation of the QA circuit is sufficient to activate the entire chain of discrimination processes of this task (Romo, R. *et al.*, 1998; 2000).

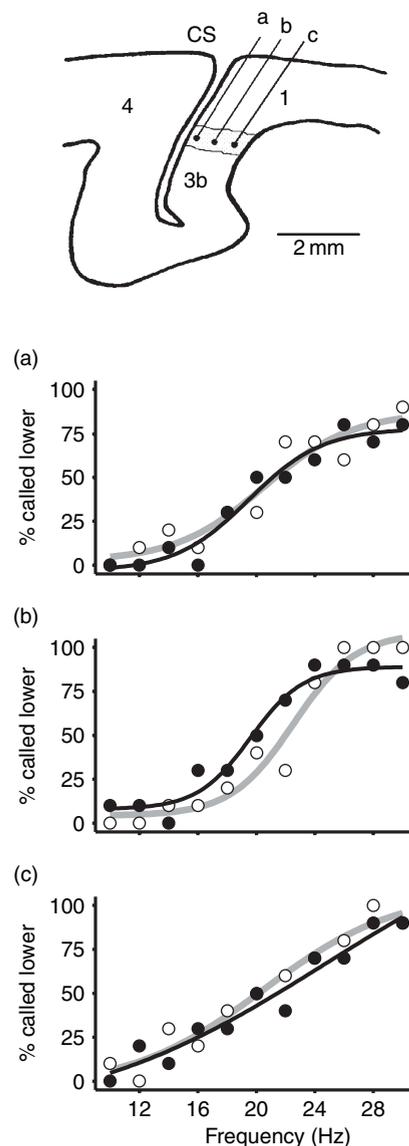The conclusion previously found in the literature – that frequency discrimination is based on periodicity – came from the observation that a small number of studied QA neurons from S1 reproduce in their activity the periodicity of the mechanical stimulus frequency, and also from the fact that these neurons did not have average firing rates that were modulated by the stimulus frequency (Mountcastle, V. B. *et al.*, 1990). However, the study that reached this conclusion only determined the relationship between the

neuronal responses to the mechanical stimulus frequencies; no attempt was made to quantify the neurometric thresholds based on periodicity and to compare these to the psychophysical thresholds. Romo and colleagues observed that neurometric thresholds using the periodicity values are far lower than the psychometric thresholds (Hernández, A. *et al.*, 2000). What is then the functional meaning of this neural signal? One possible role is that this simply represents the temporal structure of the stimulus and that monkeys do not use this exquisite representation for frequency discrimination. Consistent with this interpretation, these authors found QA neurons in S1 whose firing rates are modulated by the stimulus frequencies (Salinas, E. *et al.*, 2000), and their neurometric thresholds based on this measure are similar to the monkey's psychophysical thresholds (Hernández, A. *et al.*, 2000).

These results also suggest that QA neurons of S1, which are classified according to their capacity to react to a slight mechanical indentation applied to the center of their receptive fields, may in fact be composed of two subpopulations, each of which behaves differently in response to a periodic mechanical stimulus. These two subpopulations might be organized in a hierarchical fashion: QA neurons that respond periodically might be closer to the input stimulus, and those that modulate their firing rate might integrate the responses of the periodic neurons and transform them into a rate code. Such last-order neurons of the QA circuit could distribute the neural representation of the stimulus to those structures anatomically linked to S1 (Burton, H. and Fabri, M., 1995; Burton, H. *et al.*, 1995), to solve the sensory discrimination task. Relevant to this interpretation is the fact that neurons in secondary somatosensory cortex (S2) respond by encoding the stimulus frequencies in their firing rates and this encoding correlates closely with the subject's discrimination performance (Salinas, E. *et al.*, 2000; Romo, R. *et al.*, 2002; 2003). Ascending the cortical hierarchy, neurons in the prefrontal cortex and in the premotor cortices respond, encoding the entire sequence of the discrimination task, and correlate closely with the decision motor report (Romo, R. *et al.*, 1999; Hernández, A. *et al.*, 2002; Brody. C. D. *et al.*, 2003; Romo, R. *et al.*, 2004).

The results obtained in the microstimulation experiments show that the relationship between the neuronal responses and the animal's behavior in the flutter discrimination task are not simple coincidences (Romo, R. *et al.*, 1998; 2000). Monkeys were able to discriminate the stimulus frequencies either delivered to the fingertips or artificially injected into a cluster of QA neurons. The specificity of QA stimulation for frequency discrimination is suggested by the fact that SA stimulation cannot produce discrimination (Romo, R. *et al.*, 2000). Interestingly, it has been shown that activity in a single cutaneous afferent fiber could produce localized somatic sensations (Ochoa, J. and Torebjörk, E., 1983; Macefield, G. *et al.*, 1990; Vallbo, A. B., 1995), and frequency microstimulation of QA afferents linked to Meissner's corpuscles produced the sensation of flutter (Vallbo, A. B., 1995). These observations strongly support the notion that the activity initiated in specific mechanoreceptors is read out by S1; this reading is then widely distributed to those anatomical structures that are linked to S1 (Romo, R. and Salinas, E., 2001). The whole sequence of events associated with this sensory discrimination task must depend on this distributed neural signal (Romo, R. *et al.*, 1999; Hernández, A. *et al.*, 2002; Romo, R. *et al.*, 2002; Brody, C. D. *et al.*, 2003; Romo, R. and Salinas, E., 2003; Romo, R. *et al.*, 2004).

6.11.12   Conclusion

The highly simplified sensory tasks used here require perception of the stimuli and producing a decision that is communicated to the motor apparatus. The most salient result obtained in the detection task is that the S1 activity does not account for the variability in the detection responses at near-threshold stimuli. However, the S1 neural representation of the stimulus is necessary for further central processing. Indeed, the activity of areas central to S1 did covary with trial-by-trial judgments in the detection task (not reviewed here). This suggests that perceptual judgments in this task arise in the activity of those areas linked to S1. Experiments not reviewed here show that covariations between neuronal activities and perceptual judgments increase gradually, from lower covariations in the somatosensory cortices of the parietal lobe to higher covariations in some areas of the frontal lobe. Experiments in the vibrotactile discrimination task suggest that S1 transforms the phase-locked responses into a firing rate code that accounts for the variability of the discrimination performance. Activation of the QA circuit of S1 appears sufficient for vibrotactile discrimination; however, similar to the detection task, perceptual judgments arise in the activity of more central areas linked to S1.

Acknowledgments

References

Adrian, E. D. 1928. The Basis of Sensation. The Action of the Sense Organs. Christophers.

Bair, W., Zohary, E., and Newsome, W. T. 2001. Correlated firing in macaque visual MT: time scales and relationship to behavior. J. Neurosci. 21, 1676–1697.

Britten, K. H. and van Wezel, R. J. 1998. Electrical microstimulation of cortical MST biases heading perception in monkeys. Nat. Neurosci. 1, 59–63.

Britten, K. H., Newsome, W. T., Shadlen, M. N., Celebrini, S., and Movshon, J. A. 1996. A relationship between behavioral choice and the visual responses of neurons in macaque MT. Vis. Neurosci. 13, 87–100.

Brody, C. D., Hernández, A., Zainos, A., and Romo, R. 2003. Timing and neural encoding of somatosensory parametric working memory in macaque monkey. Cereb. Cortex 13, 1196–1207.

Burton, H. and Fabri, M. 1995. Ipsilateral intracortical connections of physiologically defined cutaneous representations in areas 3b and 1 of macaque monkeys. J. Comp. Neurol. 355, 508–538.

Burton, H., Fabri, M., and Alloway, K. 1995. Cortical areas within the lateral sulcus connected to cutaneous representations in areas 3b and 1: a revisited interpretation of the second somatosensory area in macaque monkeys. J. Comp. Neurol. 355, 539–562.

Fries, P., Neueschwander, S., Engel, A. K., Goebel, R., and Singer, W. 2001a. Rapid feature selective neuronal synchronization through correlated latency shifting. Nat. Neurosci. 4, 194–200.

Fries, P., Reynolds, J. H., Rorie, A. E., and Desimone, R. 2001b. Modulation of oscillatory neuronal synchronization by selective visual attention. Science 291, 1560–1563.

Green, D. M. and Swets, J. A. 1966. Signal Detection Theory and Psychophysics. Wiley.

Hernández, A., Salinas, E., Garcia, R., and Romo, R. 1997. Discrimination in the sense of flutter: new psychophysical measurements in monkeys. J. Neurosci. 17, 6391–6400.

Hernández, A., Zainos, A., and Romo, R. 2000. Neuronal correlates of sensory discrimination in the somatosensory cortex. Proc. Natl. Acad. Sci. U. S. A. 97, 6091–6096.

Hernández, A., Zainos, A., and Romo, R. 2002. Temporal evolution of a decision-making process in medial premotor cortex. Neuron 33, 959–972.

Hubel, D. H. and Wiesel, T. N. 1998. Early exploration of the visual cortex. Neuron 20, 401–412.

Johnson, K. O. 1980. Sensory discrimination: neural processes preceding discrimination decision. J. Neurophysiol. 43, 1793–1815.

Kepecs, A., Wang, X. J., and Lisman, J. 2002. Bursting neurons signal input slope. J. Neurosci. 22, 9053–9062.

Krahe, R. and Gabbiani, F. 2004. Burst firing in sensory systems. Nat. Rev. Neurosci. 5, 13–24.

de Lafuente, V. and Romo, R. 2005. Neuronal correlates of subjective sensory experience. Nat. Neurosci. 12, 1698–1703.

de Lafuente, V. and Romo, R. 2006. Neural correlate of subjective sensory experience gradually builds up across cortical areas. Proc. Natl. Acad. Sci. U. S. A. 10, 1266–1271.

LaMotte, R. H. and Mountcastle, V. B. 1975. Capacities of humans and monkeys to discriminate between vibratory stimuli of different frequency and amplitude: correlation between neural events and psychophysical measurements. J. Neurophysiol. 38, 539–559.

Luna, R., Hernández, A., Brody, C. D., and Romo, R. 2005. Neural codes for perceptual discrimination in primary somatosensory cortex. Nat. Neurosci. 8, 1210–1219.

Macefield, G., Gandevia, S. C., and Burke, D. 1990. Perceptual responses to microstimulation of single afferents innervating joints, muscles and skin of the human hand. J. Physiol. 429, 113–129.

Martínez-Conde, S., Mckinik, S. L., and Hubel, D. H. 2000. The function of bursts of spikes during visual fixation in the awake primate lateral geniculate nucleus and primary visual cortex. Proc. Natl. Acad. Sci. U. S. A. 99, 13920–13925.

Mountcastle, V. B. 1957. Modality and topographic properties of single neurons of cat's somatic sensory cortex. J. Neurophysiol. 20, 408–434.

Mountcastle, V. B., Talbot, W. H., Darian-Smith, I., and Kornhuber, H. H. 1967. Neural basis of the sense of flutter-vibration. Science 155, 597–600.

Mountcastle, V. B., Talbot, W. H., Sakata, H., and Hyvärinen, J. 1969. Cortical neuronal mechanisms in flutter-vibration studied in unanesthetized monkeys. Neuronal periodicity and frequency discrimination. J. Neurophysiol. 32, 452–484.

Mountcastle, V. B., Steinmetz, M. A., and Romo, R. 1990. Frequency discrimination in the sense of flutter: psychophysical measurements correlated with postcentral events in behaving monkeys. J. Neurosci. 10, 3032–3044.

Newsome, W. T., Britten, K. H., and Movshon, J. A. 1989. Neural correlates of a perceptual decision. Nature 341, 52–54.

Ochoa, J. and Torebjörk, E. 1983. Sensations evoked by intraneural microstimulation of single mechanoreceptor units innervating the human hand. J. Physiol. 342, 633–654.

Powell, T. P. S. and Mountcastle, V. B. 1959. Some aspects of the functional organization of the cortex of the postcentral gyrus of the monkey: a correlation of findings obtained in a single unit analysis with cytoarchitecture. Bull. Johns Hopkins Hosp. 105, 133–162.

Recanzone, G. H., Merzenich, M. M., and Schreiner, C. E. 1992. Changes in the distributed temporal response properties of SI cortical neurons reflect improvements in performance on a temporally based tactile discrimination task. J. Neurophysiol. 67, 1071–1091.

Reinagel, P., Godwin, D., Sherman, M., and Koch, C. 1999. Encoding of visual information by LGN bursts. J. Neurophysiol. 81, 2558–2569.

Ress, D. and Heeger, D. J. 2003. Neuronal correlates of perception in early visual cortex. Nat. Neurosci. 6, 414–420.

Romo, R. and Salinas, E. 2001. Touch and go: decision-making mechanisms in somatosensation. Annu. Rev. Neurosci. 24, 107–137.

Romo, R. and Salinas, E. 2003. Flutter discrimination: neural codes, perception, memory and decision making. Nat. Rev. Neurosci. 4, 203–218.

Romo, R., Brody, C. D., Hernández, A., and Lemus, L. 1999. Neuronal correlates of parametric working memory in the prefrontal cortex. Nature 399, 470–473.

Romo, R., Hernández, A., and Zainos, A. 2004. Neuronal correlates of a perceptual decision in ventral premotor cortex. Neuron 41, 165–173.

Romo, R., Hernández, A., Zainos, A., Brody, C. D., and Lemus, L. 2000. Sensing without touching: psychophysical performance based on cortical microstimulation. Neuron 26, 273–278.

Romo, R., Hernández, A., Zainos, A., Lemus, L., and Brody, C. D. 2002. Neuronal correlates of decision-making in secondary somatosensory cortex. Nat. Neurosci. 5, 1217–1225.

Romo, R., Hernández, A., Zainos, A., and Salinas, E. 1998. Somatosensory discrimination based on cortical microstimulation. Nature 392, 387–390.

Romo, R., Hernández, A., Zainos, A., and Salinas, E. 2003. Correlated neuronal discharges that increase coding efficiency during perceptual discrimination. Neuron 38, 649–657.

Salinas, E., Hernández, A., Zainos, A., and Romo, R. 2000. Periodicity and firing rate as candidate neural codes for the frequency of vibrotactile stimuli. J. Neurosci. 20, 5503–5515.

Salzman, D., Britten, K. H., and Newsome, W. T. 1990. Cortical microstimulation influences perceptual judgements of motion direction. Nature 346, 174–177.

Schall, J. D. 2001. Neural basis of deciding, choosing and acting. Nat. Rev. Neurosci. 2, 583–591.

Sur, M., Wall, J. T., and Kaas, J. H. 1984. Modular distribution of neurons with slowly adapting and rapidly adapting responses in area 3b of somatosensory cortex in monkeys. J. Neurophysiol. 51, 724–744.

Talbot, W. H., Darian-Smith, I., Kornhuber, H. H., and Mountcastle, V. B. 1968. The sense of flutter-vibration: comparison of the human capacity response patterns of mechanoreceptive afferents from the monkey hand. J. Neurophysiol. 31, 301–334.

Vallbo, A. B. 1995. Single-Afferent Neurons and Somatic Sensation in Humans. In: The Cognitive Neurosciences (*ed*. M. S. Gazzaniga), pp. 237–252. MIT Press.

Vázquez, P., Cano, M., and Acuña, C. 2000. Discrimination of line orientation in humans and monkeys. J. Neurophysiol. 83, 2639–2648.

Vogel, R. and Orban, G. 1990. How well do response changes of striate neurons signal differences in orientation: a study in the discriminating monkey. J. Neurosci. 10, 3543–3558.

Zohary, E., Shadlen, M. N., and Newsome, W. T. 1994. Correlated neuronal discharge rate and its implications for psychophysical performance. Nature 370, 140–143.

Further Reading

Mountcastle, V. B., LaMotte, R. H., and Carli, G. 1972. Detection thresholds for stimuli in humans and monkeys: comparison with thresholds events in mechanoreceptive afferent nerve fibers innervating the monkey hand. J. Neurophysiol. 25, 122–136.

Vallbo, A. B. and Johansson, R. S. 1984. Properties of cutaneous mechanoreceptors in the human hand related to touch sensations. Hum. Neurobiol. 3, 3–14.