Neuron, Vol. 26, 273–278, April, 2000, Copyright ©2000 by Cell Press

# Sensing without Touching: Psychophysical Performance Based on Cortical Microstimulation

**Ranulfo Romo,* Adrián Hernández, Antonio Zainos, Carlos D. Brody, and Luis Lemus**
Instituto de Fisiología Celular
Universidad Nacional Autónoma de México
04510 México, D. F.
México

## Summary

**Unequivocal proof that the activity of a localized cortical neuronal population provides sufficient basis for a specific cognitive function has rarely been obtained. We looked for such proof in monkeys trained to discriminate between two mechanical flutter stimuli applied sequentially to the fingertips. Microelectrodes were inserted into clusters of quickly adapting (QA) neurons of the primary somatosensory cortex (S1), and the first or both stimuli were then substituted with trains of current pulses during the discrimination task. Psychophysical performance with artificial stimulus frequencies was almost identical to that measured with the natural stimulus frequencies. Our results indicate that microstimulation can be used to elicit a memorizable and discriminable analog range of percepts, and shows that activation of the QA circuit of S1 is sufficient to initiate all subsequent neural processes associated with flutter discrimination.**

## Introduction

Intracortical microstimulation has provided the most compelling evidence to date of a causal link between the activity of localized populations of neurons and specific cognitive functions. Electrical microstimulation directly activates small clusters of neurons, and has been shown to determine or bias a monkey's choice during the decision stage of an ongoing perceptual task (Salzman et al., 1990, 1992; Britten and Wezel, 1998; Romo et al., 1998). However, it has not yet been shown that the neuronal activity induced by an electrical stimulus can be stored in memory, to be quantitatively compared to a subsequent perceptual stimulus, nor has it been shown that the activation of a specific group of neurons can, by itself, be sufficient basis for an entire cognitive process. A convenient model to approach these two questions is the flutter sensation, for which humans and monkeys have similar discrimination thresholds (Mountcastle et al., 1990; Hernández et al., 1997). Neurons in S1 with QA properties, which are arranged in a columnar fashion (Mountcastle, 1957; Powell and Mountcastle, 1959; Jones et al., 1975; Sur et al., 1981), are thought to mediate the sensation of flutter elicited by mechanical vibrations (5–50 Hz) delivered to the fingertips (Mountcastle et al., 1969, 1990). Extracellular recordings have shown that QA neurons fire with a probability that oscillates at the input frequency of flutter vibrations applied to their cutaneous receptive fields (Mountcastle et al., 1969, 1990; Recanzone et al., 1992). Microstimulation experiments have shown that when monkeys are trained to discriminate the difference in frequency between two sequentially applied flutter stimuli, the second mechanical stimulus can be replaced by an electrical stimulus applied to a cluster of QA neurons of area 3b at the frequency of the absent mechanical stimulus (Romo et al., 1998). Under these conditions, animals reliably indicate whether the second (artificial) signal is higher or lower frequency than the first (mechanical) stimulus, demonstrating that monkeys can make quantitative use of the artificial stimulus during the decision stage of the task (Romo et al., 1998). Because of the design of this task, comparison of the second stimulus frequency is made against the memory trace of the first stimulus (Mountcastle et al., 1990; Hernández et al., 1997; Romo et al., 1999). We wondered whether, in addition to using artificial stimuli during the decision stage of the task, monkeys could store the trace of an electrical stimulus delivered to QA neurons in S1 in place of the first mechanical stimulus. We also wondered whether monkeys could perform the entire task on the basis of purely artificial electrical stimuli. This would demonstrate that activation of QA neurons was sufficient to initiate the entire chain of cognitive processes involved in the task.

## Results

Two monkeys (*Macaca mulatta*) were trained to discriminate the difference in frequency between pairs of mechanical flutter stimuli delivered to the fingertips (Hernández et al., 1997; Romo et al., 1998). Each pair consisted of a base and a comparison stimulus (see Figure 1b). After training, neurophysiological experiments were made during performance of the task. In every session, single and multiunit activity was first recorded through microelectrodes inserted into area 3b of S1 (Mountcastle et al., 1990, 1991; Romo et al., 1998). We required small cutaneous receptive fields confined to the glabrous skin of one fingertip and possessing QA properties; once a neuron or cluster of neurons with such a receptive field was found, the mechanical stimulator tip was placed on the center of the receptive field. We then switched to the mixed mechanical/microstimulation protocol, in which microstimulation trials were randomly intermixed with standard, purely mechanical trials. The frequency pairs and event sequence were the same in both mechanical and microstimulation trials, except that in microstimulation trials the first or both mechanical stimuli were substituted with trains of current pulses injected into area 3b and delivered at the frequency of the mechanical stimulus they were replacing (Romo et al., 1998). Area 3b of S1 is organized in modules of neurons sharing the same receptive field and mechanoreceptor submodality (Mountcastle, 1957; Powell and Mountcastle, 1959; Jones et al., 1975; Sur

*To whom correspondence should be addressed (e-mail: rromo@ifisiol.unam.mx).

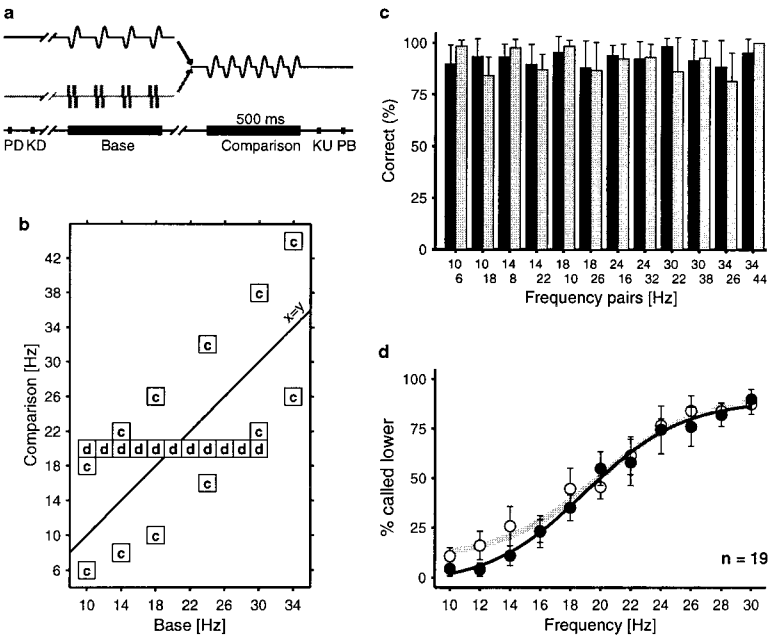


Figure 1. Psychophysical Performance Measured When the Base Stimulus Frequency Was Substituted in Half of the Trials by Trains of Current Pulses Injected into Clusters of QA Neurons of Area 3b

(a) Sequence of events during standard (down arrow, black) and microstimulation trials (up arrow, gray). The mechanical probe is lowered, indenting the glabrous skin of one digit of the restrained hand (PD). The monkey places his free hand on an immovable key (KD) within 1 s; after a delay period (1.5–3.5 s), the probe oscillates vertically, or a train of current pulses is delivered at the base frequency into area 3b. After an interstimulus interval (1.5–3.5 s), a second vibration is delivered at the comparison frequency; the monkey indicates detection of the end of the second stimulus by releasing the key (KU) within 600 ms and presses one of two push buttons (PB) to indicate whether the comparison frequency was higher or lower than the base.

(b) Stimulus sets used during both mechanical and microstimulation trials. The letter inside the box indicates the stimulus subset used to determine the working memory component ("c") and discrimination thresholds ("d") of the task.

(c and d) Psychophysical performance with pairs of trials used to reveal discrimination. Black bars and circles indicate standard discrimination trials; gray bars and white circles indicate microstimulation trials.

(c) Results from 12 frequency pairs (stimulus subset marked "c" in [b]); upper and lower rows of numbers on the x axis indicate, respectively, base and comparison frequencies for each pair of trials in hertz.

(d) Data and sigmoidal fits ($\chi^2$ test, $p < 0.01$) for 11 pairs in which the comparison stimulus was kept fixed at 20 Hz and the base stimulus frequency varied across trials (stimulus subset marked "d" in [b]). Each data point represents 190 trials collected in 19 uninterrupted runs. Stimulus pairs of "c" and "d" were randomly intermixed with each other within each of the 19 runs. Error bars are 1 SD with respect to the 19 runs.

et al., 1981). We aimed to drive a column(s) of area 3b—mostly of the QA type—in a way that matched the dynamic responses recorded when mechanical stimuli were applied (Mountcastle et al., 1990; Recanzone et al., 1992).

We first investigated whether monkeys could store a memory trace of an electrical stimulus delivered in place of the first mechanical stimulus. Figure 1a shows the sequence of events during standard (black, down arrow) and microstimulation (gray, up arrow) discrimination trials. Figure 1c shows the results obtained with the subset of frequency pairs marked "c" in Figure 1b, which test the working memory component of the task (see Experimental Procedures for a description of the stimulus set used). Performance with this subset of mechanical and microstimulation trials was, on average, 92% and 91% correct, respectively; the difference was not significant (permutation test [Siegel and Castellan, 1988], $n = 1000$, $p > 0.64$). Figure 1d shows the results obtained with the subset of frequency pairs marked "d" in Figure 1b. Within this subset, the base stimulus frequency varies above and below a fixed comparison frequency (20 Hz), in steps small enough to allow the determination of the monkeys' psychophysical discrimination threshold. This was defined here as the difference between base and comparison frequencies at which the animal performed at 75% correct (Mountcastle et al., 1990; Hernández et al., 1997; see Experimental Procedures). The psychophysical threshold during mechanical trials (3.97 Hz) was slightly lower than that found when the base stimulus was electrical (4.57 Hz), although the difference was not significant (permutation test, $n = 200$, $p > 0.35$). Overall performance with mechanical and microstimulation trials in subset "d" was also very similar, being 78% and 75% correct, respectively. The difference was not significant (permutation test, $n = 1000$, $p > 0.10$). These results show that monkeys were able to accurately memorize, over a range of several discriminable values, the percept induced by the base artificial stimulus frequency; they were then able to make a quantitative comparison of the memory trace left by the artificial stimulus against the second (mechanical) stimulus frequency.

The results above were specifically obtained when we microstimulated a cluster of neurons of area 3b that possessed QA properties. In ten sessions, we microstimulated clusters of neurons with slowly adapting (SA) properties. Figure 2 shows data for the subset of frequency pairs marked "d" in Figure 1b, for both electrical and mechanical stimuli, when the electrode tip was at the center of clusters of SA neurons. In all these cases, monkeys reacted normally to the end of the second stimulus but failed to discriminate between the two stimuli. That is, their reaction times (RT) during microstimulation trials were indistinguishable from those during mechanical trials (RT was defined as the difference between the end of the second stimulus and key release [KU]; see Figure 1a; in trials with electrical stimuli, RT = 339 ± 25 ms; in trials with mechanical stimuli, RT = 324 ± 31 ms; difference not significant [permutation test, $n = 1000$, $p > 0.26$]), but their performance fell to 54% correct

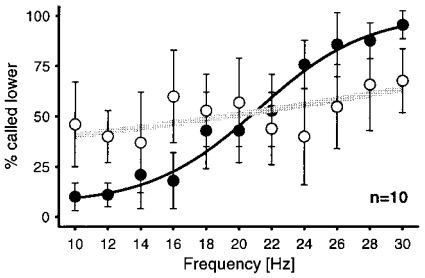


Figure 2. Psychophysical Performance When Clusters of SA Neurons of Area 3b Were Microstimulated at the Base Stimulus Frequency

We show data obtained with stimulus subset "d" of Figure 1b. Black circles indicate performance with mechanical trials. Open circles indicate psychophysical performance when the base stimulus frequency was substituted with artificial stimulus frequencies. The same protocol as in Figures 1a and 1b was used, and the results were plotted as shown in Figure 1d. Mechanical and microstimulation trials were randomly intermixed. Each data point represents 100 trials collected in ten uninterrupted runs. Error bars are 1 SD with respect to the ten runs.

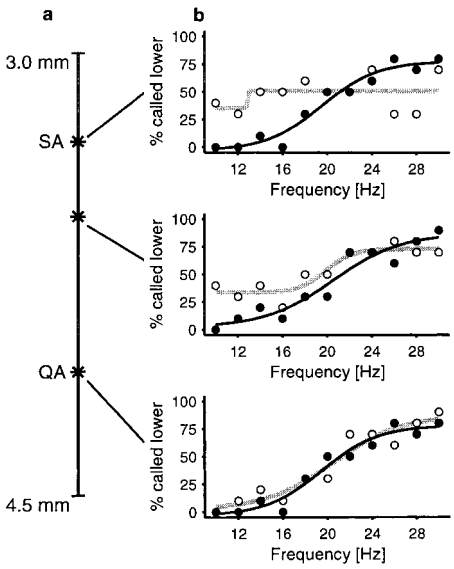


Figure 3. Psychophysical Performance Elicited by Microstimulating at the Base Stimulus Frequency in Three Different Sites of Area 3b

We show data obtained with stimulus subset "d" of Figure 1b.

(a) Electrode penetration in which microstimulation was made in clusters of SA or QA neurons, and in the border between clusters of SA and QA neurons.

(b) Psychometric performance elicited at the three sites of (a). Black circles indicate psychophysical performance with mechanical trials. Open circles indicate psychophysical performance when the base stimulus frequency was substituted with artificial stimulus frequencies. The same protocol as in Figures 1a and 1b was used, and the results were plotted as shown in Figure 1d. Mechanical and microstimulation trials were randomly intermixed. Each data point represents ten trials collected in three separate runs during the same electrode penetration.

with microstimulation trials while remaining above 80% correct with mechanical stimulation (results with both stimulus subsets marked "c" and "d" in Figure 1b). We also ran some "catch" trials, in which the first stimulus was not delivered at all (in neither mechanical nor electrical form). In these "catch" trials, the monkeys treated the second stimulus as if it were the first and sat still, waiting for many seconds for another stimulus. Normal RT during trials where the first stimulus was delivered in electrical form, therefore, indicates that monkeys detected the first stimulus and treated it as such, even when they were unable to use it for discrimination.

In five cases, we microstimulated at the border between a cluster of QA and SA neurons of area 3b; in these circumstances, monkeys performed less well (below 75% correct) than when the microstimulation was placed at the center of the cluster of QA neurons. Figure 3 shows an example of data taken from a single electrode penetration, for one data collection run when the electrode tip was at the center of a cluster of SA neurons, one data collection run when the electrode tip was near the border between an SA cluster and a QA cluster, and a final data collection run when the electrode tip was in the center of a QA cluster (we show only the discrimination threshold curves, from frequency pair subset "d" in Figure 1b). These results suggest that the activity of QA neurons, rather than that of SA neurons, is key to the performance of this sensory discrimination task.

In four sessions, we were able to introduce three microelectrodes into a cluster of QA neurons of area 3b that shared the same receptive field. We 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 (area 4) that were driven by spontaneous or passive movements of fingers and lacked cutaneous receptive fields. The most posterior microelectrode was placed, we believe, in the lower layers, and the microelectrode between these two in the middle layers. In separate runs, we applied the microstimulation protocol described above. Figure 4 shows that discrimination is triggered by microstimulating each of the three different clusters (we show only the discrimination threshold curves, from frequency pair subset "d" in Figure 1b). Thus, activation of any part of a column of neurons with similar functional properties is sufficient to initiate discrimination in this task.

If monkeys are consistently able to extract the base frequency from the artificially induced sensation, are they able to discriminate between two purely artificial stimulus frequencies injected into a cluster of QA neurons of area 3b? We investigated this possibility with the same protocol described above, but now both the base and comparison frequencies were substituted with trains of current pulses (Figure 5a). Once again, half of the randomly intermixed trials were standard (entirely mechanical, 23 frequency pairs) and half of the trials were artificial (now entirely microstimulation, 23 frequency pairs). Figure 5b shows the results obtained with the subset of pairs marked "c" in Figure 1b, which test the working memory component of the task. Monkeys were able to discriminate between the artificial stimulus frequencies with a performance almost identical to that obtained with mechanical stimuli (80% versus 89% correct, in artificial versus mechanical trials). The difference was small but statistically significant (permutation test, $n = 1000$, $p < 0.01$). Figure 5c shows the results with the subset of pairs marked "d" in Figure 1b, which are

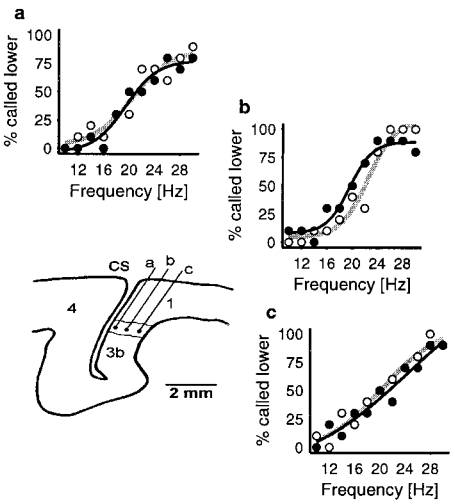


Figure 4. Psychophysical Performance Elicited by Microstimulating at the Base Stimulus Frequency with Three Independent Microelectrodes in Three Different Sites of a Cluster of QA Neurons of Area 3b

We show data obtained with stimulus subset "d" of Figure 1b. The key issue here is that all three microelectrodes "a," "b," and "c," recorded units that shared the same cutaneous receptive field and were of the QA submodality. Psychometric performance was quantified in three separate runs produced by microstimulation at each site. Black circles indicate performance with mechanical trials. White circles indicate psychophysical performance when the base stimulus frequency was substituted with artificial stimulus frequencies. The same protocol as in Figures 1a and 1b was used, and the results were plotted as shown in Figure 1d. Mechanical and microstimulation trials were randomly intermixed. Each data point represents ten trials collected in three separate runs. Abbreviations: CS, central sulcus; 4, area 4 of the primary motor cortex; 1 and 3b, somatosensory areas of S1.

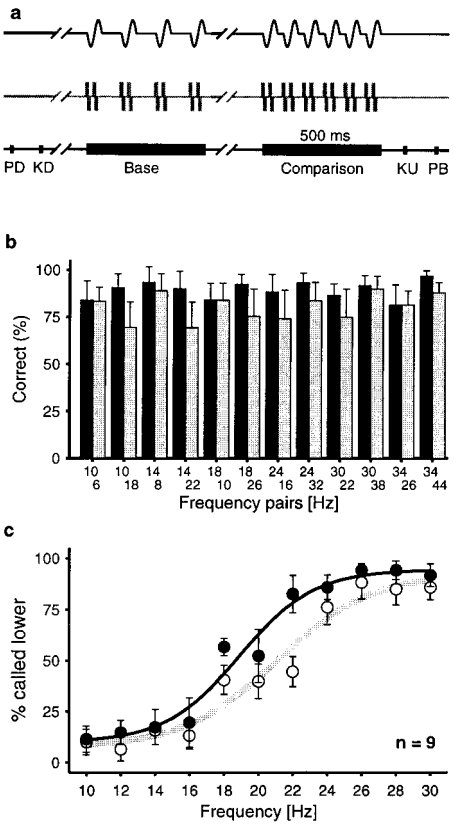


Figure 5. Psychophysical Performance When Both Base and Comparison Stimulus Frequencies Were Substituted in Half of the Trials by Trains of Current Pulses Injected into Area 3b

(a) Labels and trials as in Figure 1a, except that in half of the trials the two stimuli were substituted with trains of current pulses. Black bars and circles indicate trials in which the two stimuli were mechanical. Gray bars and white circles indicate intracortical microstimulation trials in which the two stimuli were electrical.

(b and c) Results with the frequency pairs designed to test discrimination.

(b) Results from 12 frequency pairs (stimulus subset marked "c" in Figure 1b).

(c) Data and sigmoidal fits for pairs in which the comparison frequency was kept fixed at 20 Hz and the base stimulus frequency varied across trials (stimulus subset marked "d" in Figure 1b). Each data point represents 90 trials collected in nine uninterrupted runs. Trials for (b) and (c) were randomly intermixed with each other within each of the nine runs. Error bars are 1 SD with respect to the nine runs.

designed to quantitate psychometric thresholds. The difference between psychophysical thresholds found with mechanical (2.88 Hz) and electrical (3.73 Hz) trials was once again small but significant (permutation test, $n = 200$, $p < 0.05$), and there was a consequent small but significant difference between overall performance in the mechanical and microstimulation trials of subset "d" (75% versus 80% correct, in artificial versus mechanical trials [permutation test, $n = 1000$, $p < 0.01$]). In two out of eleven sessions, monkeys were unable to discriminate between the two artificial frequencies (below 75% correct responses, averaged over all 23 frequency pairs). We could not find an explanation for these two negative results. One possibility is that the microstimulation was made at the border between QA and SA columns, but we could not determine this. According to these results, monkeys had more difficulties in discriminating frequencies when the two stimuli were artificial than when the base stimulus only was artificial. However, in nine out of eleven sessions, overall performance (with artificial stimuli) in each session was 75% correct or better, well above pure chance.

## Discussion

In our paradigm, the first stimulus has to be detected and memorized. Comparison of the second stimulus is made against the memory trace left by the first stimulus, and the decision is then projected to the motor apparatus to indicate discrimination. Accurate performance of the task can be consistent only with induction of a sensory percept during both stimulus periods. Our results indicate that the whole sequence of events that leads to discrimination could be initiated by artificial stimulus patterns injected into the QA circuit of area 3b. Thus, the neural activity produced by either the natural or the artificial stimulus can be used as the basis of sensory discrimination in a psychophysical observer.

The experiments described here followed on directly from our cortical microstimulation experiments of 1998 (Romo et al., 1998). However, the present results are more than a simple extension of our previous results.

First, previous microstimulation work, including our own, used microstimulation to affect a decision process which occurred simultaneously with the current injection (Salzman et al., 1990, 1992; Britten and Wezel, 1998; Romo et al., 1998). Thus, the lifetime of the percept directly induced by microstimulation could not be measured, even while it was shown that the results of the decision affected by this percept could be kept in memory (Seidemann et al., 1998). It therefore remained possible that the lifetime of a quantitative, microstimulation-induced percept was confined to the periods of stimulation. Our results conclusively demonstrate instead that a microstimulation-induced percept can be quantitatively memorized, with a lifetime and properties indistinguishable from those generated by mechanical stimuli: the working memory component of our behavioral task was reliably induced by the artificial activation of the QA circuit of S1. Second, correct behavioral performance after replacement of both base and comparison stimuli by cortical microstimulation demonstrates that activation of the QA circuit of S1 is, by itself, sufficient to initiate all neural processes that underlie this cognitive task. Most likely, our success with the artificial stimuli was facilitated by the modular organization of S1 (Mountcastle, 1957; Powell and Mountcastle, 1959; Jones et al., 1975; Sur et al., 1981), and by the fact that entire columns of QA neurons are driven to oscillate at the stimulus frequency by both mechanical and artificial stimuli.

The specificity of QA stimulation for frequency discrimination is suggested by the fact that SA stimulation cannot produce discrimination but can produce detection. Interestingly, it has been shown that activity in a single cutaneous afferent fiber could produce localized somatic sensations, and frequency microstimulation of QA afferents linked to Meissner's corpuscles produced the sensation of flutter (Ochoa and Torebjörk, 1983; Vallbo, 1995). These observations strongly support the notion that the activity initiated in specific peripheral mechanoreceptors is read out by S1; this reading is then widely distributed to those anatomical structures that are linked to S1. The whole sequence of events associated with this sensory discrimination task must depend on this distributed neural signal. We predict that recording of neuronal activity (Romo et al., 1999) and microstimulation of these structures linked to S1 will reveal the components of the discrimination task processed by each structure. This study, therefore, has directly established a strong link between neural activity and perception. However, we do not know yet whether microstimulation of the QA circuit in S1 elicits a subjective flutter sensation in the fingertips. This can only be explored by microstimulating S1 in an attending human observer.

## Experimental Procedures

### Mechanical Stimulation

Stimuli were delivered to the skin of the distal segment of one digit of the right, restrained hand, via a computer-controlled stimulator (BME Systems) (2 mm round tip). The initial indentation was 500 μm. Vibrotactile stimuli were trains of short mechanical pulses. Each of these pulses consisted of a single-cycle sinusoid lasting 20 ms. Stimulation amplitudes were adjusted to produce equal subjective intensities (Mountcastle et al., 1990; Hernández et al., 1997; Romo et al., 1998). During trials, two vibrotactile stimuli were delivered consecutively to the glabrous (hairless) skin, separated by an interstimulus delay period of 1.5–3.5 s, and the animal was rewarded for correct discriminations with a drop of liquid. Discrimination was indicated by pressing one of two push buttons. Performance was measured with psychophysical techniques (Mountcastle et al., 1990; Hernández et al., 1997; Romo et al., 1998). Animals were handled according to the institutional standards of the National Institutes of Health and the Society for Neuroscience.

### Recording and Electrical Microstimulation

Neuronal recordings were obtained with an array of seven independent microelectrodes (1–1.5 MΩ) inserted into area 3b of S1 of the left hemisphere of two monkeys (Mountcastle et al., 1990, 1991; Romo et al., 1998), one of which was used to microstimulate. Recording sites targeted the digit representation area and microstimulation sites changed from session to session. Microstimulation was applied in clusters of neurons with QA or SA properties. The borders of the cutaneous receptive field of each of these neurons were first defined with hand-held stimuli and then the submodality receptor property to which they belonged. QA neurons respond with a short burst of action potentials at the beginning and at the end of a slight, sustained mechanical indentation applied to the center of their receptive fields, while SA neurons respond during the whole period of the slight, mechanical indentation (Mountcastle et al., 1969, 1990; Sur et al., 1984). We could not test the effect of microstimulating Pacinian neurons because we did not record neurons in area 3b that had this submodality receptor property. These neurons are very rare in area 3b (Mountcastle et al., 1990). A computer-controlled pulse generator (Coulbourn), in series with an optical stimulus isolation unit, produced biphasic current pulses with the cathodal phase leading. Each phase lasted 0.2 ms, with 0.05 ms between phases. Two-pulse bursts, with 0.5 ms between pulses, were delivered at the base or at both base and comparison frequencies. Current amplitude varied between 65 μA and 100 μA; this range has been proven to be very effective to produce behavioral responses that are indistinguishable from those elicited by the mechanical stimuli delivered to the fingertips (Romo et al., 1998). Within each session, current amplitude was maintained fixed across all stimulus frequencies.

### Psychophysical Methods

We used a stimulus set that contained 23 different base/comparison frequency pairs (see Figure 1b). The stimulus pairs marked "c" in Figure 1b were chosen to ensure that the monkey could not perform the task correctly without using information from both base and comparison stimuli, and thus tested the working memory component of the task. These stimulus pairs correspond to stimulus set B in Romo et al. (1999). On the other hand, the stimulus pairs marked "d" in Figure 1b allowed compiling data with which to fit traditional one-dimensional psychometric curves (Mountcastle et al., 1990; Hernández et al., 1997; Romo et al., 1998). For each of the 23 frequency pairs, two stimulus classes were used: first, standard, purely mechanical stimuli trials (upper, black traces in Figures 1a and 5a); and second, artificial stimuli trials, i.e., trials in which one or both of the stimuli were artificial (lower, gray traces in Figures 1a and 5a). In each data collection run there were thus a total of 46 different frequency pair/stimulus class combinations. Trials using these combinations were presented in random order until ten trials for each combination had accumulated. Discrimination thresholds were determined by first fitting sigmoidal functions to the data obtained using subset "d" of Figure 1a (see Figure 1d); the threshold was then read off from the fit as half the difference between the base stimulus frequency that would be identified as lower than the comparison frequency (20 Hz) on 75% of the trials and the base stimulus frequency that would be identified as lower on 25% of the trials.

### Acknowledgments

The research of R. R. was supported by an International Research Scholars Award from the Howard Hughes Medical Institute and grants from DGAPA–UNAM and CONACyT. We thank E. Salinas

for invaluable comments and discussions and Sergio Méndez and Federico Jandete for technical assistance.

Received January 21, 2000; revised March 14, 2000.

**References**

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

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

Jones, E.G., Burton, H., and Porter, R. (1975). Commissural and cortico-cortical "columns" in the somatic sensory cortex of primates. Science *190*, 572–574.

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

Mountcastle, V.B., Talbot, W.T., Sakata, H., and Hyvärinen, J. (1969). Cortical neuronal mechanisms in flutter vibration studied in unanesthetized monkeys. J. Neurophysiol. *32*, 453–484.

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.

Mountcastle, V.B., Reitboeck, H.J., Poggio, G.F., and Steinmetz, M.A. (1991). Adaptation of Reitboeck method of multiple microelectrode recording to the neocortex of the waking monkey. J. Neurosci. Methods *36*, 77–84.

Ochoa, J.L., 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 S1 cortical neurons reflect improvements in performance on a temporally based tactile discrimination task. J. Neurophysiol. *67*, 1071–1091.

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

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.

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

Salzman, C.D., Murasugi, C.M., Britten, K.H., and Newsome, W.T. (1992). Microstimulation in visual area MT: effects on direction discrimination performance. J. Neurosci. *12*, 2331–2355.

Seidemann, E., Zohary, E., and Newsome, W.T. (1998). Temporal gating of neural signals during performance of a visual discrimination task. Nature *394*, 72–75.

Siegel, S., and Castellan, N.J. (1988). Nonparametric Statistics for the Behavioral Sciences (New York: McGraw-Hill).

Sur, M., Wall, J.T., and Kaas, J.H. (1981). Modular segregation of functional cell classes within the postcentral somato-sensory cortex of monkeys. Science *51*, 1059–1061.

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.

Vallbo, A.B. (1995). Single-afferent neurons and somatic sensation in humans. In The Cognitive Neurosciences, M.S. Gazzaniga, ed. (Cambridge, MA: MIT Press), pp. 237–252.