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Neural codes for perceptual discrimination in primary somatosensory cortex

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We sought to determine the neural code(s) for frequency discrimination of vibrotactile stimuli. We tested five possible candidate codes by analyzing the responses of single neurons recorded in primary somatosensory cortex of trained monkeys while they discriminated between two consecutive vibrotactile stimuli. Differences in the frequency of two stimuli could be discriminated using information from (i) time intervals between spikes, (ii) average spiking rate during each stimulus, (iii) absolute number of spikes elicited by each stimulus, (iv) average rate of bursts of spikes or (v) absolute number of spike bursts elicited by each stimulus. However, only a spike count code, in which spikes are integrated over a time window that has most of its mass in the first 250 ms of each stimulus period, covaried with behavior on a trial-by-trial basis, was consistent with psychophysical biases induced by manipulation of stimulus duration, and produced neurometric discrimination thresholds similar to behavioral psychophysical thresholds.

Investigations in several sensory systems have shown how neural activity represents the physical parameters of sensory stimuli in both the periphery and central areas of the brain. This knowledge has paved the way for new questions that are more closely related to cognitive processing. For example, are the neural representations of sensory stimuli related to perception? In this respect, it has been shown that quickly adapting neurons of the primary somatosensory cortex (S1) are directly involved in frequency discrimination of vibrotactile stimuli[1,2]. But exactly which components of these neurons' stimulus-evoked activity are associated with the discrimination process is not known. Most of the quickly adapting neurons of S1 show phase-locked responses to the periodic mechanical sinusoids, in the form of single spikes or bursts of spikes[3–6]. This suggests that discrimination could be based on observing the temporal intervals between responses to each stimulus period[3]. However, about one-third of the quickly adapting neurons in S1 also have a firing rate, averaged over the duration of a stimulus, that is a function of the periodic stimulus frequency, with higher firing rates in response to higher stimulus frequencies[5,6]. Thus, an observer of the stimulus-evoked activity in the quickly adapting neuronal population of S1 could discriminate between two periodic vibrotactile stimuli either by comparing the precise temporal intervals between spikes or by comparing the overall spike rates elicited by the two stimuli[7,8].

Previously, we have computed neurometric thresholds[6] for both spike periodicity–based codes and overall firing rate–based codes; we found that periodicity-based neurometric thresholds were far smaller than psychometric thresholds. In contrast, firing rate–based neurometric thresholds were similar to psychometric thresholds. This result favored firing rate over spike timing as the neural code for perception of vibrotactile stimuli[5,6]. Notably, monkeys are also able to discriminate the mean frequency of aperiodic stimuli, which lack any temporal regularity[1,5,6]. It is assumed that under aperiodic stimulation, discrimination would be based on a comparison of overall spike rates[5,6]. Monkeys could use different coding strategies for periodic versus aperiodic stimuli, but a parsimonious account covering both the periodic and aperiodic cases once again favored firing rate as the neural code.

There are, however, some further unexplored possibilities. For example, quickly adapting 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[9–12]. But whether bursting actually contributes directly to psychophysical behavior is not known. Finally, the temporal window on which vibrotactile discrimination is based has not been determined. In our previous experiments, stimulus periods were always 500 ms long. Under those 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, we conducted new combined psychophysical and neurophysiological experiments in the vibrotactile discrimination task. We reasoned that if an observer uses firing rate, bursting rate or a measure of periodicity, then increases or decreases in the duration of either of the two stimuli used in each trial

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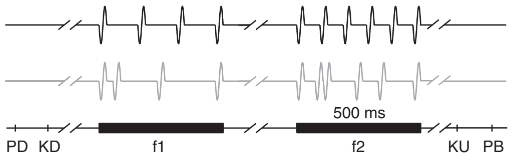

Figure 1 Discrimination task. Sequence of events during each trial. The mechanical probe is lowered (PD), indenting the glabrous skin of one digit of the hand, and the monkey places its free hand (KD) on an immovable key. The probe oscillates vertically at base frequency f1, and after a delay (3 s), a second mechanical vibration is delivered at the comparison frequency (f2). The monkey releases the key (KU) after a delay (3 s) between f2 and KU and presses one of two push buttons (PB) to indicate whether the second stimulus was higher or lower. In separate stimulus sets, monkeys discriminated between periodic (black line) and aperiodic (gray line) stimulus frequencies.

of the task should not lead to a systematic bias in discrimination in either of the two possible directions. (However, under this hypothesis, stimulus duration could affect the sensory signal-to-noise ratio and therefore 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 frequency than they actually were. We 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. 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. We sought an explanation for these psychophysical biases by recording quickly adapting neurons of S1 while the monkeys performed in variable–stimulus length conditions. We found that the effects can be qualitatively explained if one assumes that the neural signal used by the observer to solve the task is a weighted sum of either spikes or bursts over a time window that concentrates most of its weight within the first 250 ms of the stimulus but also has a small tail in later parts of the stimulus. Finally, examining trial-by-trial covariations of weighted counts of spikes and weighted counts of bursts, we found that only the weighted count of spikes covaried with performance on a trial-by-trial basis.

RESULTS

Stimulus duration biases performance

Two monkeys (*Macaca mulatta*) were trained in the vibrotactile discrimination task (**Fig. 1**). Initially, the monkeys were trained to discriminate between pairs of periodic stimulus frequencies of equal duration (500 ms) up to their psychophysical thresholds[3,13]. We then asked whether they could discriminate between pairs of aperiodic stimuli[1,6]. In each of these two task conditions, and in separate trial blocks, monkeys compared a second stimulus frequency that varied from trial to trial (range, 14–30 Hz) against a fixed first stimulus frequency (22 Hz), or they compared a fixed second stimulus frequency (22 Hz) against a varying first stimulus frequency (range, 14–30 Hz). The differences between the psychometric thresholds for the four cases (data not shown) were not significant (permutation test, $n = 1{,}000$, $P = 0.32$)[14].

Experiments using fixed-duration stimuli cannot distinguish between a code based on the total number of events produced in response to each stimulus and a code based on the rate at which the events are produced. However, if discrimination is based on a total number of events over the stimulus periods, changing this number by changing the stimulus period durations should affect discrimination performance. In contrast, if we assume that the periodicity measure and the spike and burst rate measures are time invariant during a stimulus, and one of these is the code used, then changing stimulus duration should not affect discrimination performance. We used blocks of trials in which, on a pseudorandom trial-by-trial basis, monkeys were required to discriminate either between two vibrotactile stimuli of equal duration (500 ms, control condition) or between two stimuli where one of the two stimuli was modified in length. In separate blocks, the modified stimulus either shortened by 50% to 250 ms, or lengthened by 50% to 750 ms. The other stimulus was kept at 500 ms. As before, in some blocks of trials we kept f1 fixed at 22 Hz and varied f2 (**Fig. 2a,b**); in other blocks of trials, we varied f1 and kept f2 fixed (**Fig. 2c,d**). We compiled psychometric curves for the different stimulus conditions and fit a logistic function to each psychometric curve.

Quantitative changes in the psychometric curves can be assessed through two parameters of the logistic fits (**Fig. 2**): (i) the psychometric

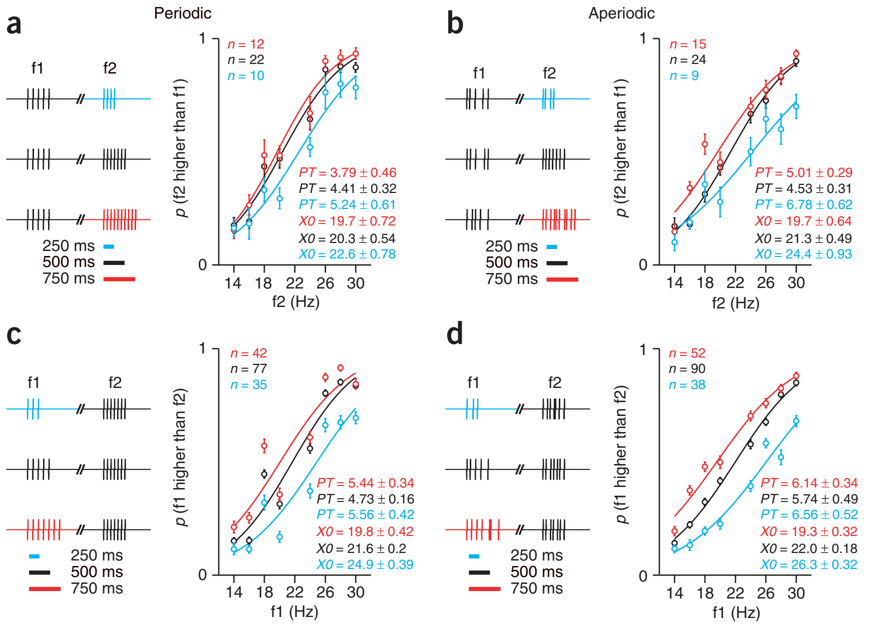

Figure 2 Psychophysical performance during the manipulation of the duration of one of the two stimuli. (**a**) Psychophysical performance when the duration of the second (f2) periodic stimulus increased (red) or decreased (cyan) with respect to the first (f1) periodic stimulus. (**b**) The same as in **a**, but with aperiodic stimuli. (**c**) Psychophysical performance when the duration of the periodic f1 stimulus increased (red) or decreased (cyan) with respect to f2. (**d**) The same protocol as in **c**, but with aperiodic stimuli. *n*, number of sessions for each stimulus condition; *PT*, psychometric thresholds for each stimulus condition (mean ± s.d.); *X0*, the frequency (mean ± s.d.) that corresponds to a *y*-axis value of 0.5 value in the logistic fit for each stimulus condition.

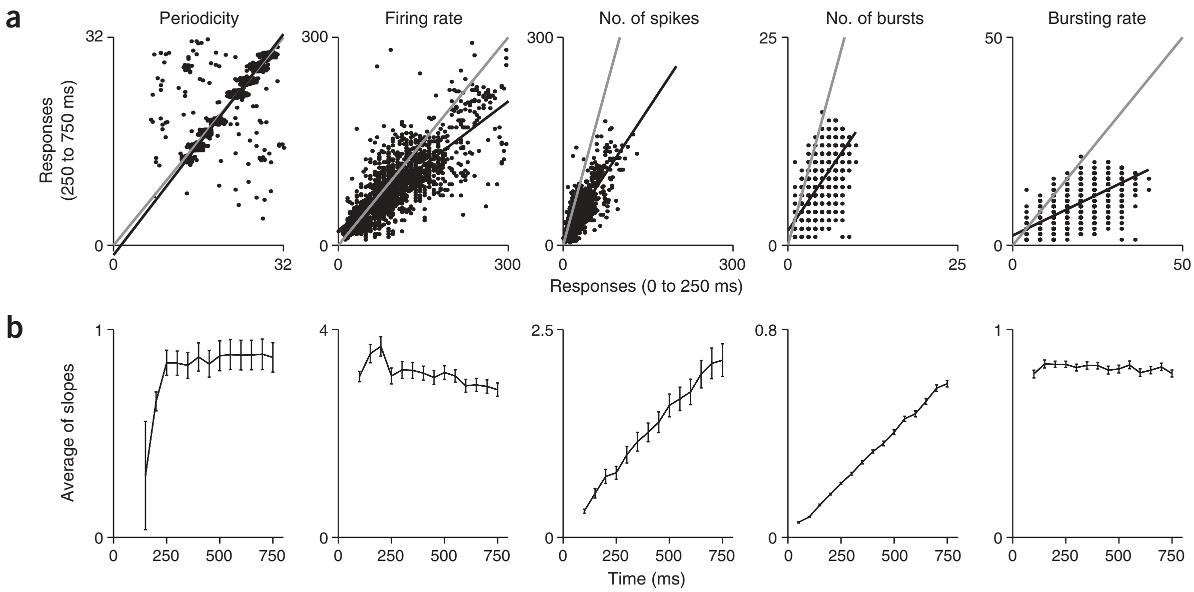

Figure 3 Responses of S1 neurons as a function of time during the stimulus period. (**a**) Comparison of responses, using 750-ms-long stimuli, from the first 250 ms versus the last 500 ms for each of the five measures. Each point represents data for one stimulus condition from one neuron. In the first panel, only the periodic stimulus trials are used, as no information can be calculated from the periodicity for aperiodic stimuli. Measures calculated during both periodic and aperiodic stimuli are plotted in all other panels. Diagonal gray line is the expected value when the response is time invariant; black line is the value obtained using the regression analysis in the data. (**b**) Response measure sensitivity, expressed as the linear regression slope (in units of response measure change per 1 Hz change in stimulus frequency), averaged over all neurons, as a function of time for each of the five measures in panel **a**. Aperiodic stimulus trials are not used in the first panel; both periodic and aperiodic trials are used in all other panels.

threshold, which measures the steepness of the logistic curve and represents the minimal change in stimulus frequency that produces a reliable change in behavior, and (ii) the *X0* value, which is a measure of the displacement of the curve along the horizontal axis and which represents the frequency at which the stimulus being varied (f1 or f2) is indistinguishable from the stimulus kept fixed at 22 Hz. Values of *X0* greater than 22 Hz (rightward displacement of the psychometric curve) indicate that the subject judges the varying stimulus to have a lower frequency than its actual value. Values of *X0* lower than 22 Hz (leftward displacement of the psychometric curve) indicate that the subject judges the varying stimulus to have a higher frequency than its actual value. In extreme cases, large displacements of the logistic curve preclude an accurate estimation of *X0*.

In general, we found that psychometric thresholds were only minimally affected by changes in stimulus duration (**Fig. 2**). The single exception was the condition in which f2 was decreased in length by 50% with respect to f1 for aperiodic stimuli (**Fig. 2b**, cyan; permutation test, $n = 1{,}000$, $P < 0.001$)[14]. In contrast, *X0* values were systematically and significantly affected by stimulus duration. Monkeys treated shortened stimuli as if they had a frequency that was 2.3–4.3 Hz lower than the actual applied value (compare *X0* values and psychometric curve shifts in **Fig. 2a–d** for shortened stimuli (cyan) versus control-length stimuli (black); permutation test, $n = 1{,}000$, $P < 0.04$)[14]. This bias effect was observed for both periodic (**Fig. 2a,c**) and aperiodic (**Fig. 2b,d**) stimuli. The opposite effect was observed when lengthened stimuli were used: monkeys treated lengthened stimuli as if they had a frequency that was 0.6–2.7 Hz higher than the actual applied value (compare *X0* values and psychometric curve shifts in **Fig. 2a–d** for lengthened stimuli (red) versus control-length stimuli (black); permutation test, $n = 1{,}000$, $P < 0.04$)[14]. Although the sign of the lengthening effect was the same in all conditions, the effect was strongest and statistically significant only when the first stimulus, f1, was lengthened (red in **Fig. 2c,d**; Permutation test, $n = 1{,}000$, $P < 0.001$)[14]. Again, the effect was observed for both periodic (**Fig. 2c**) and aperiodic (**Fig. 2d**) stimuli. The bias effects persisted over many trials despite the fact that monkeys were rewarded only for correct discrimination of the actual applied frequencies.

These results show that manipulations of the stimulus duration biased psychophysical performance in a direction consistent with an accumulative–event number code, such as integrating the number of spikes or bursts over each stimulus. However, the magnitude of the effect suggests that the accumulation of spikes or bursts does not occur equally over the entire stimulus period. For example, if firing rates were constant over the stimulus periods, and spikes were accumulated with equal weight over the entire period, then halving the stimulus length would have halved *X0* values with respect to the control (that is, shortened stimuli would have had $X0 = 11$ Hz), and increasing stimulus lengths by 50% should have led to an increase of 50% in *X0* values (lengthened stimuli would have had $X0 = 33$ Hz). Although the sign of the observed effect was in all cases consistent with the sign of this prediction, the observed magnitude was much lower. In addition, the effect was consistently stronger for shortening of stimuli than for lengthening of stimuli, which suggests that the initial part of the stimulus may have greater weight than the later part of the stimulus in determining discrimination performance. However, as there was a discernible effect when stimuli were lengthened from 500 to 750 ms, the later part of the stimulus must also have some influence on the perceptual process, though perhaps less influence than the earlier part of the stimulus.

There are two distinct alternatives that could contribute towards a greater weighting for the initial part of this stimulus than for the later part. First, the response of S1 neurons, which are known to be causally

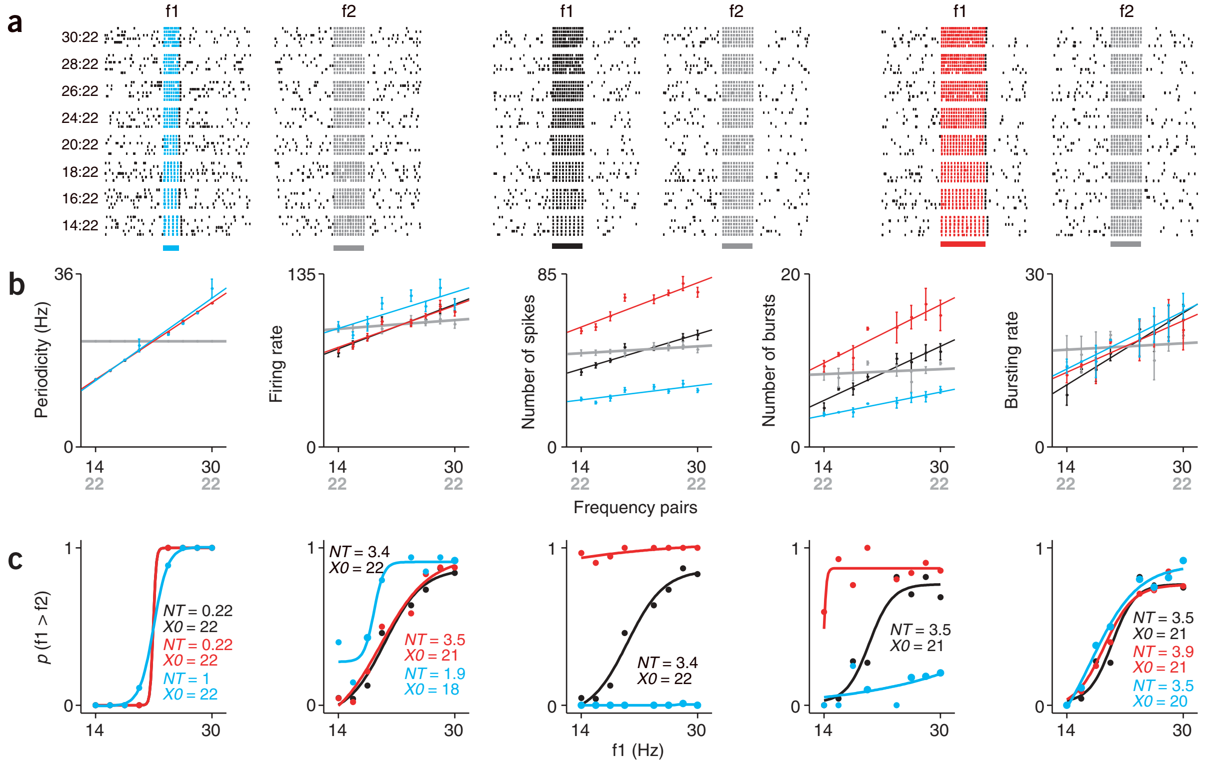

Figure 4 Responses of an area 1 neuron during the discrimination of the periodic stimulus set in **Figure 2c**. (**a**) Raster plots. Here, the duration of the first stimulus (f1) decreased (50%, cyan) or increased (50%, red) with respect to the comparison frequency (500 ms, gray). Middle panel: responses during discrimination of frequencies of equal duration. (**b**) Five different response measures, plotted as a function of stimulus frequency, during the manipulation of the stimulus duration. (**c**) Neurometric curves using the different measures during each stimulus condition. *NT*, neurometric threshold; *X0*, the frequency that gives a *y*-axis value of 0.5 value from the logistic fit.

related to perception of vibrotactile stimuli[1,2], could adapt during the stimulus, being more sensitive to stimulus parameters during the earlier versus the later parts of the stimulus[15–18]. Alternatively, a process subsequent to S1 involved in perception could preferentially weight the S1 responses from the earlier, versus the later, parts of the stimulus. We first explore S1 neuron adaptation and then turn to the second alternative.

Response adaptation in S1 does not explain performance

To investigate whether S1 neuron responses were differentially stimulus-sensitive during different portions of the stimulus, we recorded single, quickly adapting neurons in S1 (**Table 1**) while the monkeys discriminated between the periodic or aperiodic stimulus pairs shown in **Figure 2**. We examined the sensitivity over time of five candidate neural codes: spike timing periodicity, overall spike rate, overall spike count, overall burst rate and overall burst count. We took responses to 750-ms-long stimuli and compared, for each measure, the first 250 ms of the stimulus to the last 500 ms of the stimulus (**Fig. 3a**). We found that spike periodicity was time invariant (**Fig. 3a**) but that for all other measures, responses were significantly attenuated from the initial 250 ms to the final 500 ms of the stimulus (black slope below gray line; permutation test on distribution of responses for initial versus later part of the stimulus period, $n = 1{,}000$; $P < 0.01$)[14]. We also compiled trials in which both the first (f1) and the second (f2) stimulus were 500 ms long, and compared the response attenuation in the first stimulus with the response attenuation in the second stimulus (data not shown). No significant differences were found (permutation test, $n = 1{,}000$; $P = 0.41$)[14]. The initially stronger response to the stimulus could carry information about the stimulus value itself, or it could be a response common to all stimulus values and therefore uninformative. For each measure, we calculated a linear regression of the measure as a function of stimulus frequency (as in **Fig. 4** below) and used the slope of this linear regression to quantify the sensitivity of each measure to changes in stimulus frequency. We did this for a range of time windows all beginning at the start of the stimulus and extending into the stimulus in steps of 50 ms. We averaged these sensitivity slopes over neurons (**Fig. 3b**, lower panels) and found that the sensitivity of the periodicity and burst rate measures remained roughly constant over time during the stimulus. However, the sensitivity of the spike rate measure peaked approximately 200 ms after stimulus onset, suggesting that spikes from this time period would be particularly informative when used for stimulus discrimination.

These results suggest that for some codes, differential stimulus sensitivity in S1 neurons to different times during the stimulus could contribute to psychophysical biases induced by using varying stimulus lengths. But for each of the five candidate codes (periodicity, spike number, spike rate, burst number and burst rate), we must address the issue in a manner that allows quantitative comparison between the neuronal response measure and psychophysical results. We therefore used our five candidate measures to compute neurometric thresholds from S1 neuron responses[6]. These can be directly compared with the monkeys' psychometric threshold[6,19]. In our initial neurometric calculations, we weighted all parts of each stimulus equally, corresponding to an observer central to S1 that weights all parts of the stimulus equally.

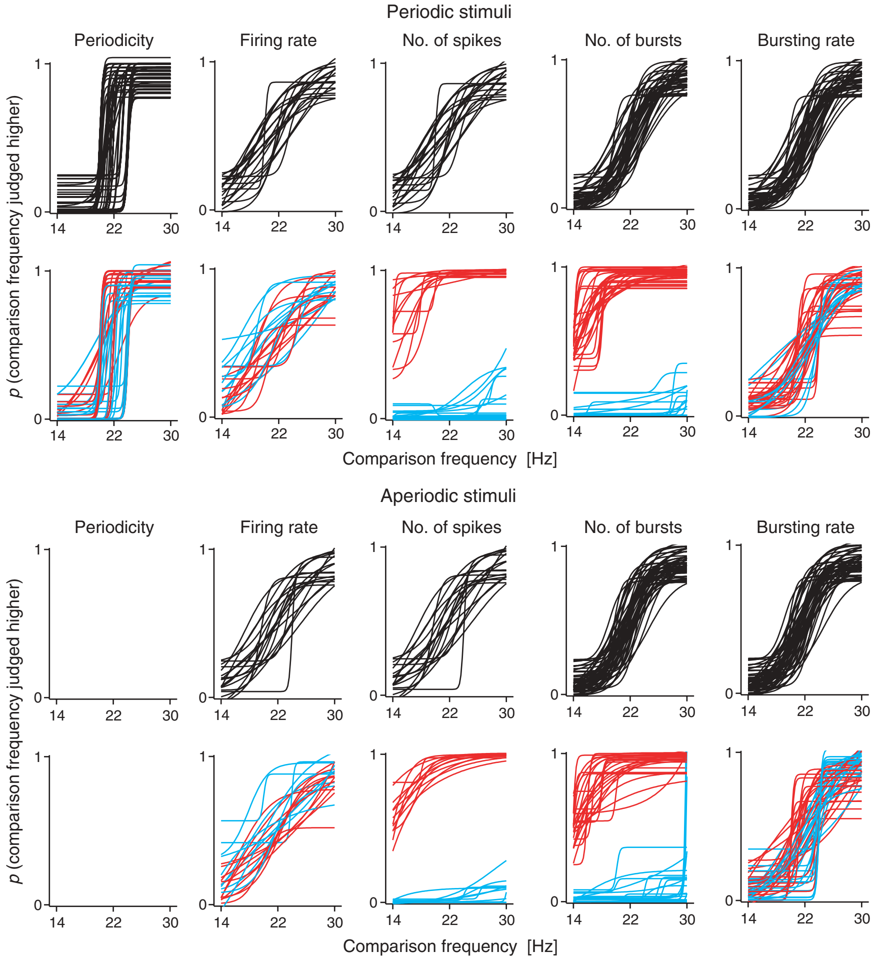

Figure 5 Individual neurons' neurometric functions, using different measures, while monkeys performed the discrimination task using the stimulus sets in **Figure 2**. Color codes and display format as in **Figure 4c**. Note the large changes produced by manipulation of the stimulus duration compared to the control neurometric functions (black). These changes occurred for both periodic and aperiodic stimulus discriminations. Black, equal duration of the two stimuli: 500 ms. Cyan, the duration of one of the two stimuli decreased (50%) as compared with the other. Red, the duration of one of the two stimuli increased (50%) as compared with the other.

The results for one sample neuron are shown in **Figure 4**. As can be seen in the spike rasters of **Figure 4a**, this neuron was strongly entrained by the periodic stimuli. Consistent with **Figure 3a**, the periodicity measure for this neuron was similar for all stimulus durations (leftmost panel, **Fig. 4b**). Similarly, the burst rate measure was similar for all stimulus durations (rightmost panel, **Fig. 4b**). However, other measures were significantly affected by stimulus duration. Spike rates, calculated over each stimulus period length, were slightly but significantly higher for the short, 250-ms stimulus durations (**Fig. 4b**, cyan), compared with spike rates for 500 and 750 ms durations (**Fig. 4b**, black and red lines, respectively). Compared with control-stimulus period lengths, total spike or burst numbers were markedly higher for long, 750-ms stimulus durations (**Fig. 4b**, red versus black) and markedly lower for 250-ms stimulus durations, (**Fig. 4b**, cyan versus black). Similar trends were observed during discrimination of aperiodic stimuli (with the exception of periodicity, which cannot be calculated when aperiodic stimuli are used). Thus, except for periodicity and burst rate, different measures were considerably affected by the manipulation of the stimulus duration.

The neuronal response distributions elicited by the stimuli are the basis for constructing neurometric functions, which can then be compared directly to the psychometric functions. **Figure 4c** shows neurometric curves, based on response distributions using different measures, for the neuron of **Figure 4a**. As expected from **Figure 4b**, *X0* values based on the periodicity measure were not affected by the stimulus duration. In contrast, neurometric *X0* values calculated from a spike-rate code were affected by stimulus duration but in a direction opposite to the effect found with psychometric *X0* values (compare **Fig. 4c** with **Fig. 2c**). Neurometric *X0* values for either spike number or burst number calculated from a total-event-number code were affected in the same direction as the psychometric *X0* values, but the magnitude of the neurometric effect was far stronger than the psychometric effect. Finally, neurometric *X0* values calculated from a burst-rate code were not significantly affected by stimulus duration. The trends shown for the example neuron of **Figure 4** were similar across the population of recorded neurons (**Fig. 5**).

This result shows that when all parts of the stimulus response of S1 neurons are weighted equally, none of the five codes considered so far produces stimulus duration effects on neurometric curves that mimic those seen in the psychometric curves. Thus, none of the five codes can explain the psychophysical biases produced by the manipulation of the stimulus duration.

Weighted integration of S1 responses explains performance

We therefore considered the alternative option: namely, that a process involved in perception but subsequent to S1 could differentially weight different portions of the stimulus. This corresponds to carrying out neurometric calculations that assign different weights to different portions of the stimulus response. Because the periodicity code did not depend on the portion of time used to measure it, we did not include periodicity in this analysis, restricting ourselves to spike- and burst-based codes.

Having measured psychometric curves at three different stimulus lengths, we used a weighting window composed of three fixed-duration intervals corresponding to the three stimulus lengths (**Fig. 6a**). We now assume that an observer central to S1 would use the same weighting window for all stimulus lengths. This makes event-rate and event-count codes equivalent to each other: the relationship between event-rate and event-count codes is defined by the weighting window in that rate can be defined as the weighted event count divided by the area of the weighting window. In this sense, **Figures 4** and **5** assume a rectangular weighting window whose width varies with the stimulus length and is always as long as the stimulus. But here we turn to the assumption that the weighting window is constant over all stimulus lengths. The rate

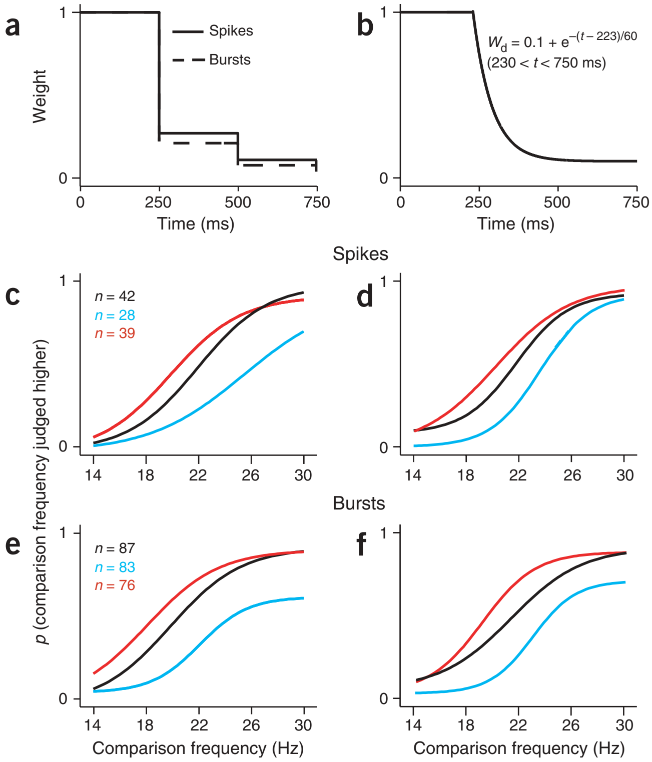

Figure 6 An integration time window, for event-number codes, that produces neurometric biases consistent with the psychophysical biases induced by stimulus lengthening and shortening. (**a**) Weighting windows, $W(t)$, composed of three rectangular portions, each 250 ms wide. The response measure for events at time t_i using this kernel is defined as the sum over i of $W(t_i)$. Time $t = 0$ corresponds to the start of the stimulus. The windows for spike events and for burst events shown here are those that produced the neurometric curves in **c** and **e** below most similar to the psychometric curves. (**b**) A smoother weighting window with properties similar to those shown in **a**. (**c**) Neurometric curves, averaged over neurons, that follow from using the spike weighting window in **a** when each event is an individual spike. (**d**) Neurometric curve as in **c** but using the weighting window of **b**. (**e**) The neurometric curves that follow from using the burst weighting window in **a** when each event is a burst of spikes. (**f**) Neurometric curve as in **e** but using the weighting window of **b**.

codes and weighted-event-count codes therefore differ only in a fixed normalization constant (the area of weighting window) and thus become equivalent to each other.

What should be the shape of this weighting window? Only the relative weights for the different stimulus portions are of importance in determining shape. We therefore kept the weight of the initial 250-ms portion fixed at an arbitrary value of 1 and systematically varied the weights for each of the other two intervals in the range [0, 1.9] in steps of 0.1 (20 different values for each interval, leading to 400 different total window shapes). Each of the possible window shapes was used to integrate spikes or bursts, and the resulting values were considered as spike- or burst-response measures. Distributions of these response measures were then used to compute neurometric functions as before, and the result was averaged over neurons. We computed the sum of squared differences between the averaged neurometric curves and the monkeys' psychometric curves. The window shapes that gave the minimal squared difference are shown in **Figure 6a**. **Figures 6c** and **e** show the corresponding neurometric curves, averaged over neurons, for spike integration and for burst integration, respectively. Results based on these integration measures show that such windows can indeed lead to psychophysical biases of a sign and magnitude comparable to those found experimentally, with shortening (cyan) having a greater effect than lengthening (red). These results are also consistent with the idea that the earlier components of the neuronal responses have a greater impact than later components on the perceptual signal used to perform the task.

The weighting window in **Figure 6a** was based on three rectangular portions, but this was determined by data from three specific stimulus lengths. In general, our data are roughly consistent with window shapes that have a gradual fall-off as a function of time, and any actual window used by the subjects is unlikely to have a strictly stepwise shape. We therefore constructed a time window with a square shape for 230 ms followed by an exponential fall-off, with a time constant of 60 ms (**Fig. 6b**). We used this window, placed beginning at stimulus onset, as a weighting window to integrate spikes or bursts. The results of using this window (**Fig. 6d** and **f**, for spike integration and for burst integration, respectively, with the same window used for both) are essentially similar to those obtained using the stepwise window of **Figure 6a**, with shortening (cyan) having a greater effect than lengthening (red). The window is placed at the peak of spike sensitivity to stimulus frequency.

Figure 7 Weighted counts of spikes covary with behavior on a trial-by-trial basis, but weighted counts of bursts do not. Each panel shows the cumulative distribution of normalized responses for correct (solid lines) versus incorrect (dotted lines) trials for trials with the stimulus lengths shown. Events in each stimulus are integrated using the weighting window of **Figure 6a**. In the top row, events are defined as single spikes, whereas in the bottom row, events are defined as bursts of spikes. Only neurons for which the weighted measure (spikes or bursts) was significantly stimulus-dependent were used in each panel, leading to different numbers of neurons in upper versus lower panels. ROC, receiver operating characteristic measure comparing the two distributions. The probability of observing this ROC value or greater by chance is 0.5, estimated using a permutation test. n, number of permutations.

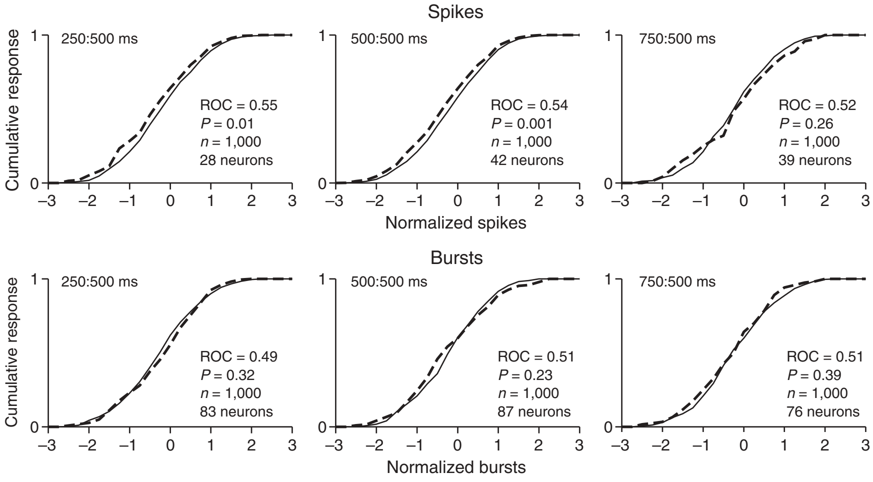

Table 1 **Neurons recorded in primary somatosensory cortex (S1) during vibrotactile discrimination with variable stimulus length**

f1:f2 duration (ms)	Periodic (f1: 14–30 Hz, f2: 22 Hz)	Aperiodic (f1: 14–30 Hz, f2: 22 Hz)	Periodic (f1: 22 Hz, f2: 14–30 Hz)	Aperiodic (f1: 22 Hz, f2: 14–30 Hz)
250:500	83 ($p = 61$, $fr = 22$, $b = 63$)	86 ($p = 5$, $fr = 27$, $b = 64$)	–	–
750:500	101 ($p = 75$, $fr = 31$, $b = 78$)	131 ($p = 6$, $fr = 38$, $b = 95$)	–	–
500:250	–	–	23 ($p = 16$, $fr = 8$, $b = 17$)	15 ($p = 0$, $fr = 6$, $b = 11$)
500:750	–	–	29 ($p = 20$, $fr = 9$, $b = 21$)	40 ($p = 2$, $fr = 7$, $b = 28$)

f1, first stimulus. f2, second stimulus. First number in each column under 'periodic' or 'aperiodic' represents number of those neurons tested with a modification in the stimulus duration of a total of 146 neurons. Each stimulus set of variable stimulus length had an equal number of trials in which the two stimulus periods were always 500 ms long. Numbers in parentheses after '=' correspond to the numbers of neurons that had significant slopes for the measures of periodicity (*p*), firing rate (*fr*) and bursts (*b*). The slopes were calculated using the stimulus periods of 500:500 ms.

Weighted sum of spikes covaries with performance

Our results using the weighting windows suggest that either spikes or bursts, when integrated using the windows of the top panels of **Figure 6**, could form the basis for an S1 neuronal code that is consistent with the psychophysical results of **Figure 2**. To further test the relationship between these two neuronal response measures and behavioral performance, we carried out an analysis that distinguished between correct and error trials. We assumed that on each trial, the animal's performance was based on comparing the activity of S1 neurons during the first stimulus with the activity of S1 neurons during the second stimulus. Trial-to-trial variations in the activity of these neurons is then expected to affect the animal's performance[5,19]. For each neuron, for each trial and for each of the two response measures (weighted spikes and weighted bursts, using the window of **Fig. 6a**), we calculated the difference between the measure applied to the spikes fired in response to the second stimulus in the trial, and the measure applied to the response to the first stimulus in the trial. We then grouped trials into classes defined by the f1, f2 stimulus frequency pair used in each trial. When f2 > f1, we expected correct trials to be associated with more positive measure differences than error trials; conversely, when f2 < f1, we expected correct trials to be associated with more negative measure differences. We multiplied each trial's measure difference by the sign of (f2 – f1) so that all trial classes would have the same expected tendencies. We then normalized each trial's measure difference into a *Z*-score by (i) subtracting the mean measure difference over those trials that shared the same (f1,f2) stimulus values and were recorded from the same neuron and then (ii) dividing by the standard deviation of that group of trials. We could now collapse together all trials from all classes, allowing us to search for what could be very weak correlations between single S1 neurons and behavior. We asked whether the distribution of normalized measure differences for correct trials had a significantly more positive mean than the distribution of normalized measure differences for error trials. We found that the two distributions were very slightly but quite significantly different only for the weighted spiking rate measure (**Fig. 7**; permutation test, $n = 1{,}000$, $P < 0.01$)[14], but not for the weighted bursting rate measures (**Fig. 7**; permutation test, $n = 1{,}000$, $P > 0.2$)[14]. The effect was of a magnitude comparable to similar correct-versus-error trial tendencies found in the middle temporal area during a perceptual discrimination task[20]. The effect was found for weighted spike measures during comparison of 250-ms-long stimuli with 500-ms-long stimuli, as well as during comparison of 500-ms-long stimuli with 500-ms-long stimuli. However, no significant effect was found when one stimulus was 750 ms long and the other was 500 ms long (upper panels of **Fig. 7**); we have no explanation for the lack of effect in this case.

DISCUSSION

The frequency of the vibrotactile stimulus can be defined as (i) the number of pulses per unit of time, or as (ii) the inverse of the period of time between two consecutive mechanical sinusoid periods. To identify the stimulus frequency, a subject could count the number of mechanical sinusoid periods per unit of time or measure the interval between two consecutive sinusoid periods. Here, we have addressed the following questions: first, whether we can identify in the neuronal activity of S1 which strategy an observer might use to discriminate between two vibrotactile stimuli, and second, which of the potential strategies are actually used by the subjects. Quickly adapting neurons of S1 typically produce a brief burst of spikes in response to each mechanical sinusoid period. We found that depending on the stimulus sets and conditions, an observer of the evoked-neuronal responses in S1 could extract information from either (i) the overall spiking rates during the stimuli, (ii) the rates of bursting, (iii) a count of the number of spikes or (iv) a count of the number of bursts elicited by the vibrotactile stimuli. Count and rate codes are different only when the stimulus can vary in duration. We note that by 'count codes' we do not necessarily mean that the observer consciously counts the exact number of pulses during the stimulus—an observer could simply judge whether there are more pulses in one stimulus period that there are in the other. However, as we explain further below, when we further consider which of these potential codes might be actually used by subjects performing the task, we find reasons to reject burst-based codes, suggesting that the most likely neural code for vibrotactile discrimination is one based on spike rate or count.

To distinguish whether a code based on spike rate or a code based on spike count was more to be used by subjects when discriminating between two stimuli, we manipulated stimulus duration. We assumed that if the observer used a rate-based code, or even a periodicity-based code, manipulation of stimulus duration should have no effect on psychometric curves. But if the observer used a simple accumulative counting strategy, stimulus duration manipulation should result in consistent and predictable biases in behavior. Monkeys biased their psychophysical performance in a manner consistent with an accumulative counting strategy. In other words, when the duration of one of the two stimuli increased, monkeys behaved as if the frequency of that stimulus were higher than it actually was, and when the duration of a stimulus was shortened, monkeys behaved as if the frequency of that stimulus were lower than it actually was. However, although the sign of the bias was consistent with an accumulative-counting code, the magnitude of the bias was much smaller than that predicted by accumulation over the entirety of the stimulus periods. Consequently, we considered a weighting window, defining a kernel over which spikes might be accumulated (that is, integrated), with most of the window concentrated over a time period significantly shorter than the standard 500-ms-long stimulus. We found that a spike integration time window with a 230-ms width, followed by an exponential fall-off with a time constant of 60 ms, can qualitatively account for both sign and magnitude of the psychophysical biases observed experimentally, can be used for both periodic and aperiodic stimuli, covaries on a trial-by-trial basis with behavior and produces neurometric discrimination thresholds that are similar to psychometric thresholds. We do not propose this time window as the precisely shaped unique window with these properties; other windows of approximately the same shape and size, but differing in the details of their shape (for instance, a gamma function instead of flat followed by exponential fall-off) would share the same properties. In sum, spike integration over a window of this form is the single candidate neural code for vibrotactile discrimination that is consistent with all the data examined to date. The output of such spike integration from quickly adapting neurons of S1 could form the input to more central areas, in which a spike-rate code encodes the stimulus frequency during the stimulus presentation, working memory, comparison and decision-making processes of this task[6,21–26]. The specific mechanisms by which integration over such a time window might be carried out remain to be determined.

Our findings are closely reminiscent of psychophysical evidence found for integration time windows during detection of vibrotactile stimuli in the vibration frequency range (250 Hz; ref. 27). Some of these authors found no evidence for integration in sensations transduced by non-Pacinian receptors, which are thought to underlie perception of stimuli in the flutter frequency range (6–40 Hz; ref. 27). But their use of a detection task at high frequencies, as opposed to the discrimination task in the flutter frequency range we used here, precludes a direct contrast between the two studies.

We have previously found that modifying the amplitude of the mechanical stimuli has no detectable effect on discrimination bias or performance, as long as the stimuli remain well above threshold for detection[1], as they are here. This is consistent with our present results: well above detection threshold, modest changes in stimulus amplitude do not change the firing rate of mechanosensory afferents with receptive fields centered at the stimulation site. Instead, amplitude changes affect the number of afferents with receptive field centers away from the stimulation site that are recruited into responding to the stimulus[28]. Thus, we might expect S1 neurons with receptive fields centered at the stimulation site to be similarly insensitive to modest changes in stimulus amplitudes[29]. If discrimination is based on the weighted integration of spikes from these neurons, then discrimination would not be affected by amplitude changes that keep the stimulus above detection threshold.

An important criterion for accepting any of the neural measures we have considered as candidates for encoding the stimuli is that the code should covary, on a trial-by-trial basis, with behavior[19]. In S1, we found that weighted spike counts, but not weighted burst counts or our periodicity measure, covaried with discrimination performance (in ref. 6 and the current study), supporting weighted spike count (that is, spike rate when computed with a kernel window with a shape similar to those of **Fig. 6**) as the most likely neural code for frequency discrimination (**Fig. 7**). In all areas central to S1 studied during the vibrotactile task, spike rate not only carries information about stimulus frequency during the different phases of the vibrotactile discrimination task, but also covaries, on a trial-by-trial basis, with the behavioral performance[6,21–26].

In conclusion, over the past several years there has been a debate over how information of sensory stimuli is encoded by cortical neurons. Depending on the stimulus characteristics, tasks and brain areas chosen, some investigators have proposed the firing rate[30,31], detailed precision of the neuronal responses[3,29,32–35], bursting rate[9–12,36] and sparse temporal codes[37] as codes for the sensory stimuli. In our case, we have shown that the frequency of the vibrotactile stimulus is encoded in several different measures of the stimulus-evoked responses of S1 neurons. However, the acid test is whether any of these neural codes accounts for behavior during task performance. Our results show that firing rate of S1 neurons, computed as a weighted spike count with a weighted window that has most of its mass in the first 250 ms and yet has a small tail extending beyond 500 ms, best covaries with the animal's psychophysical performance and therefore is the most likely neural code for vibrotactile discrimination. Although we have rejected all but one of the corresponding codes as the basis of vibrotactile discrimination, there is nevertheless the possibility that each of the rejected codes might be useful for different purposes during the vibrotactile task. Given that our analysis is based on single units, it is possible that a temporal code based on interactions between multiple neurons (for example, one based on spike synchrony), for either or both periodic or aperiodic stimuli, has escaped our scrutiny.

METHODS

General. Two monkeys (*Macaca mulatta*) were trained to discriminate the difference in frequency between two mechanical vibrations delivered sequentially to their fingertips (**Fig. 1**). Neurophysiological recordings were made in S1 (areas 3b and 1) contralateral to the mechanical stimulation while the monkeys performed the discrimination task[1,3,5,6,13]. The neurons selected for study had small, cutaneous receptive fields confined to the smooth, glabrous skin of one fingertip of digits 2, 3 or 4. All neurons had quickly adapting properties. The neuronal responses from S1 were collected while the monkeys discriminated frequencies at psychophysical thresholds (**Figs. 1** and **2**). Animals were handled according to institutional standards of the US National Institutes of Health and the Society for Neuroscience.

Discrimination task. The discrimination task used here has been described before[3,13]. Briefly, stimuli were delivered to the skin of the distal segments of one digit of the right, restrained hand by means of a computer-controlled motor 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 single-cycle sinusoid lasting 20 ms. Stimulus amplitudes were adjusted to equal subjective intensities[3,13]: for example, 71 μm at 12 Hz and 51 μm at 34 Hz (1.4% per Hz). During trials, two vibrotactile stimuli were delivered consecutively to the glabrous (hairless) skin, separated by an inter-stimulus delay period of 3 s, and the animal was rewarded with a drop of liquid. Discrimination was indicated by pressing one of two push-buttons. Performance was measured through psychometric techniques[1,3,6,13]. Initially, the two monkeys were trained to discriminate between pairs of periodic stimulus frequencies up to their psychophysical thresholds[3,13]. We then tested whether the two animals could discriminate between pairs of aperiodic stimuli. Aperiodic stimuli were also composed of pulses that were each 20 ms wide. To generate an aperiodic stimulus with N pulses, the 500-ms-long stimulus period was first divided into 20-ms bins, the first and last of the bins were then assigned to contain a pulse, and $(N - 2)$ of the remaining bins were randomly chosen to also contain a pulse. Fixing the initial and final pulse ensured that aperiodic stimuli could not be discriminated based on total stimulus length. Periodic and aperiodic stimuli were used in different blocks of trials. For both periodic and aperiodic conditions, and again in separate blocks of trials, monkeys either compared a variable second stimulus frequency (range 14–30 Hz) against a fixed first stimulus frequency (22 Hz; **Fig. 2a,b**), or they compared a fixed second stimulus frequency (22 Hz) against a variable first stimulus frequency (range 14–30 Hz; **Fig. 2c,d**). In these stimulus sets, monkeys discriminated between stimulus frequencies of equal duration (500 ms) or unequal duration (**Fig. 2**), with one stimulus 50% longer (750 ms) or shorter (250 ms) than the other.

Recording sessions and sites. Neuronal recordings were obtained with an array of seven independent, moveable microelectrodes (2–3 MΩ, inserted into S1; areas 3b and 1; two monkeys)[1,3]. Recording sites changed from session to session, and standard histological procedures were used to construct surface maps of all of the penetrations in S1. This was done first by marking the edges of the small chamber (7 mm in diameter) placed above S1. Additionally, in the last recording sessions, we made small lesions at different depths in the recording area. Neurons recorded from the top of the cortex to

2,500 μm below the surface fell into area 1; neurons recorded 2,500 μm from the insertion site and below fell into area 3b. All of these neurons had small cutaneous receptive fields confined to the distal segments of fingertips 2, 3 or 4 and had quickly adapting properties.

Data analysis. For each neuron studied during the discrimination task, offline analysis and statistical tests were done with custom and Matlab software (Mathworks). The analysis was restricted to the stimulus periods according to three criteria. First, we devised a measure that quantified the capacity of the neurons to represent the periodicity of the stimulus. For each trial, the power spectrum of the spike train evoked during the stimulus period was computed (fast Fourier transform, $n = 216$; sampling frequency, 10 kHz; resolution, 0.15; range, 6–100 Hz)[38,39]. As an estimate of the periodicity, we calculated the median frequency around the peak power spectrum frequency. The frequencies used for this measure were limited to those within a factor of 1.8 of the peak (to avoid contamination by harmonics) and to frequencies with a power greater than 0.15 of the power at the peak (to avoid noise). The median frequency calculated in this way was considered a quantitative measure of periodicity evoked in S1 neurons by the periodic or aperiodic mechanical stimuli. Second, neurons were classified as responding with bursts to the mechanical stimuli according to two criteria. First, an elevated firing rate criterion: we required the number of spikes recorded during the interval that separates two consecutive mechanical sinusoids to be higher than the activity of 950 of 1,000 intervals of the same duration, randomly selected within the period of 1.5 s that preceded the stimulus presentation (permutation test, $n = 1{,}000$, $P < 0.05$)[14]. Second, a mechanical event detection criterion: we required that in 95% of the intervals between two mechanical stimuli, the number of spikes in the first half of the interval was higher than the number of spikes in the second half of the same interval (**Supplementary Fig. 1**). Individual cycles for which the mechanical event detection criterion was satisfied were considered as containing a burst. This definition of bursts was intended to capture how an observer of an S1 neuron might try to detect the application of individual mechanical pulse events. The definition was not intended to capture detection of spike bursts caused by intrinsic biophysical properties of the neuron. Third, for each trial, we calculated the mean firing rate over the stimulus periods. For each stimulus frequency, we computed the mean ± s.d. of periodicity, bursting rate and firing rate over all trials with that stimulus frequency. For further analysis, we selected those neurons that had the best linear fit (χ^2, $Q > 0.05$) of the periodicity, bursting rate, number of bursts, number of spike or firing rate values as a function of the stimulus frequency[38,39]. We also required the slope of this linear fit to be significantly different from zero (permutation test, $n = 1{,}000$, $P < 0.05$)[14]. Under this combined test, not all neurons carried information in all of the codes tested. For each of the codes tested, we selected for further analysis only the subset of neurons that carried statistically significant stimulus information using that code. The discrimination task requires the comparison of the second stimulus frequency against the first. The quickly adapting neurons of S1 provide a reliable representation of the two stimulus frequencies[3,5,6]. We determined the probability that an observer (for example, a cortical region central to S1) could distinguish the difference between the two stimuli. This could be based on a comparison of the neuronal response distributions of the second stimulus frequency (f2) made against the neuronal response distributions of the first stimulus frequency (f1). According to this, the observer could use a simple rule: if the number of spikes or bursts during f2 is higher than during f1, then f2 is higher than f1. The same rule can be used when considering the periodicity values: if the periodicity values during f2 are higher than during f1, then f2 is higher than f1 (refs. 6,40). This rule can be tested by determining the area under the curve receiver operating characteristic (ROC) generated by the neuronal response distributions for each pair of stimulus frequencies, using periodicity, bursting rate and firing rate values[6,40]. In pairs of stimulus frequencies in which the neuronal response distributions of f2 are much higher than the neuronal distributions of f1, ROC values are close to 1. If the neuronal response distributions of f2 are much lower than the neuronal response distributions of f1, ROC values are close to 0. For overlapping distributions, intermediate ROC values are found (0.5). The ROC values were then used to compute neurometric functions. Psychometric and neurometric discrimination thresholds were calculated as half of the difference between the stimulus frequency identified as higher than the base in 75% of the trials and that frequency identified as higher in 25% of the trials[3,6,13]. These were directly read from the logistic functions (Boltzmann's equation) expressed in Hz. Because the manipulation of the stimulus duration altered both psychometric and neurometric curves, these changes can be quantified by calculating two parameters in the logistic function: (i) the psychometric and neurometric threshold is the minimal difference (in Hz) between f1 and f2 that the subject and the neuron can discriminate, and (ii) the $X0$ value is the frequency with a 0.5 probability in the logistic function. The $X0$ value measures the displacement of the logistic function along the x-axis. Rightward displacement of the psychometric function (compared with the control psychometric function calculated in the same run) indicates that the observer judges the comparison stimulus frequency lower than the first, whereas leftward displacement indicates the opposite.

Note: Supplementary information is available on the Nature Neuroscience website.

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COMPETING INTERESTS STATEMENT

The authors declare that they have no competing financial interests.

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