Temporal Frequency of Whisker Movement. II. Laminar Organization of Cortical Representations

EHUD AHISSAR, RONEN SOSNIK, KNARIK BAGDASARIAN, AND SEBASTIAN HAIDARLIU
Department of Neurobiology, The Weizmann Institute of Science, Rehovot 76100, Israel

Received 13 October 2000; accepted in final form 9 February 2001

Ahissar, Ehud, Ronen Sosnik, Knarik Bagdasarian, and Sebastian Haidarliu. Temporal frequency of whisker movement. II. Laminar organization of cortical representations. *J Neurophysiol* 86: 354–367, 2001. Part of the information obtained by rodent whiskers is carried by the frequency of their movement. In the thalamus of anesthetized rats, the whisker frequency is represented by two different coding schemes: by amplitude and spike count (i.e., response amplitudes and spike counts decrease as a function of frequency) in the lemniscal thalamus and by latency and spike count (latencies increase and spike counts decrease as a function of frequency) in the paralemniscal thalamus (see accompanying paper). Here we investigated neuronal representations of the whisker frequency in the primary somatosensory ("barrel") cortex of the anesthetized rat, which receives its input from both the lemniscal and paralemniscal thalamic nuclei. Single and multi-units were recorded from layers 2/3, 4 (barrels only), 5a, and 5b during vibrissal stimulation. Typically, the input frequency was represented by amplitude and spike count in the barrels of layer 4 and in layer 5b (the "lemniscal layers") and by latency and spike count in layer 5a (the "paralemniscal layer"). Neurons of layer 2/3 displayed a mixture of the two coding schemes. When the pulse width of the stimulus was reduced from 50 to 20 ms, the latency coding in layers 5a and 2/3 was dramatically reduced, while the spike-count coding was not affected; in contrast, in layers 4 and 5b, the latencies remained constant, but the spike counts were reduced with 20-ms stimuli. The same effects were found in the paralemniscal and lemniscal thalamic nuclei, respectively (see accompanying paper). These results are consistent with the idea that thalamocortical loops of different pathways, although terminating within the same cortical columns, perform different computations in parallel. Furthermore, the mixture of coding schemes in layer 2/3 might reflect an integration of lemniscal and paralemniscal outputs.

INTRODUCTION

Primary cortical areas receive thalamic information via multiple channels (Bishop 1959; Diamond 1983). In the somatosensory system of rodents, vibrissal information reaches the barrel cortex via the lemniscal and paralemniscal pathways (Diamond and Armstrong-James 1992; Woolsey 1997). The lemniscal pathway, which ascends via the ventral posteromedial nucleus (VPM), projects to the barrels in layer 4 and to layers 5b and 6a (Chmielowska et al. 1989; Lu and Lin 1993). The paralemniscal pathway, which ascends via the medial division of the posterior nucleus (POm), projects to layers 1 and 5a and to the septa between the barrels in layer 4 (Koralek et al. 1988; Lu and Lin 1993). Recently we demonstrated that these two afferent pathways exhibit different coding schemes for the whisker temporal frequency (Ahissar et al. 2000). Both coding schemes result in a spike-count representation (we use the term "representation" here to refer to a neuronal variable that changes as a function of a stimulus quantity in such a manner that the quantity can be reconstructed from the variable). Whether these two coding schemes are shared by cortical layers other than 4 and 5a, and whether these neuronal representations are invariant to stimulus parameters, is not yet known.

Receptive field (RF) characteristics, and latency of responses to brief vibrissal stimulation, vary for the various cortical layers (Armstrong-James and Fox 1987; Armstrong-James et al. 1992; Simons 1978). RF characteristics—such as, sizes of RF center and surround, and the thresholds and magnitudes of responses—depend critically on several parameters, including arousal state and type of stimulation (Armstrong-James and Fox 1987; Diamond et al. 1992b; Nicolelis and Chapin 1994; Simons et al. 1992). However, for each given set of conditions, the RF characteristics of neurons in the lemniscal and paralemniscal layers consistently differ (Armstrong-James and Fox 1987; Brumberg et al. 1999; Simons 1978). Furthermore neurons of the lemniscal layers of the cortex respond with short and constant latencies, while paralemniscal neurons exhibit slower responses and more variable latencies (Armstrong-James et al. 1992; Sosnik et al. 2001). Most of these differences are similar to those found between responses of lemniscal and paralemniscal neurons in the thalamus (Diamond et al. 1992b; Sosnik et al. 2001) and can be attributed, in part, to the anatomical differences between the two pathways; the paralemniscal pathway contains axons with smaller diameters than those of the lemniscal pathway and form more diffuse connections (Bishop 1959; Chiaia et al. 1991; Williams et al. 1994).

Parallel pathways to cortex might result from a sequential evolutionary process in which a newer pathway performs (better) the same function performed by the old pathway (Bishop 1959). Alternatively, the two pathways could perform different types of processing. The data presented here are consistent with the latter possibility. By examining cortical responses to air-puff stimuli of constant and modulated frequencies and two pulse widths, we show that lemniscal (layer 4 barrels and layer 5b) and paralemniscal (layer 5a) neurons exhibit different coding schemes. These coding schemes are the same as those exhibited by thalamic lemniscal and paralemniscal neurons, respectively (see accompanying paper). Neurons in layer 2/3 seem to partially integrate these two coding schemes, which

Address reprint requests to E. Ahissar (E-mail: Ehud.Ahissar@weizmann.ac.il).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked "*advertisement*" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

suggests a convergence of two processing streams in the barrel cortex.

METHODS

Animal procedures, electrophysiology, whisker stimulation, histology, and data analysis were as described in the accompanying paper (Sosnik et al. 2001). Since mechanical stimuli induced frequency doubling in the brain stem (see accompanying paper), only results obtained using air-puff stimuli are presented here; data obtained with mechanical stimuli were used only for latency calibrations. The air puffs were directed to stimulate two to three rows of whiskers, rows that contained the entire RF (see accompanying paper) of most of the simultaneously recorded neurons; at least four whiskers were stimulated in each row. The neurons whose RFs were not stimulated were excluded from analysis. In addition to constant-frequency stimulations, trains of frequency modulated (FM) stimuli were applied in single blocks of 24 or 36 consecutive trains of 8 s with 2-s inter-trial interval. Each FM block was applied with the same pulse-width, 20 or 50 ms.

After staining the cortical coronal sections for cytochrome oxidase activity, layers 1, 2/3, 4, 5a, 5b/6a, and 6b were distinct. The border between layers 5b and 6a usually exhibited a staining density lighter than those in layers 5b and 6a. In sections where this border was not evident, it was defined midway across the dark staining region that corresponded to layers 5b and 6a.

The experimentation was conducted in conformity with the Guiding Principles for Research Involving Animals and Human Beings, and with the animal welfare guidelines of The Weizmann Institute of Science.

RESULTS

In this study, a total of 572 single units and 453 multi-units were recorded from 317 recording sites. Of these, 151 single units and 136 multi-units were recorded from sites that could be clearly assigned to the following layers: 26 single units and 22 multi-units from layer 2/3; 46 and 42, respectively, from layer 4 barrels; 51 and 47, respectively, from layer 5a; and 28 and 25, respectively, from layer 5b. The remaining units were recorded from layer 6, from the septa of layer 4, from the borders between the layers or between barrels and septa, or from sites that could not be reliably reconstructed. Consistent with previous studies (Moore and Nelson 1998), the percentage of responsive neurons was not high. About 40% of the multi-units (52/136), and 30% of the single units (50/151) exhibited responses to at least two stimulation frequencies (referred to as "responsive units" hereafter) and were analyzed.

Characteristics of neuronal responses to trains of air puffs

All responsive cortical neurons displayed responses that differed from the relay-like responses observed with the same stimuli in the brain stem (see accompanying paper). Whereas brain stem responses are constant along the stimulus train, cortical responses usually changed during the train with most changes usually occurring during the first stimulus cycles. Two types of dynamics for the cortical responses were usually observed: amplitude reduction and latency increments. Typically, neurons from all cortical layers displayed amplitude reduction along the train. However, latency increments were observed almost exclusively in layers 5a and 2/3. Examples of multi-unit recordings from all four layers during 8-Hz stimulations are depicted in Fig. 1. The lemniscal neurons (from layer 4 barrels and layer 5b) exhibited modulations of response magnitude during the first stimulus cycles, until the response stabilized, however, their response latencies were constant throughout the stimulus train. In contrast, paralemniscal (layer 5a) and layer 2/3 neurons exhibited stabilization of both amplitude and latency.

These stabilization processes occurred in the majority of the recorded neurons and thus were evident in the ensemble activity of each layer (Fig. 2*A*). The ensemble activities were composed from the activities of all neurons recorded from well-localized sites, i.e., sites that could be unambiguously affiliated with a specific layer, during 8-Hz stimulations. Response latencies of the lemniscal ensembles were constant, while latencies of the ensembles of layers 5a and 2/3 increased until stabilized at significantly higher values (Fig. 2*B*; latency to 0.3 peak value). Latencies to 0.2–0.5 peak value showed similar dynamics. Latencies to 0.1 peak value of layers 2/3 and 5a ensembles did not stabilize; these latencies oscillated between low and high values due to the small early response peaks and trended background activity appearing during some stimulus cycles in layers 2/3 and 5a, respectively. The latency of the small early response peaks in layer 2/3 was similar to the lemniscal latencies (Fig. 2*A*). In all the cortical layers, the response area (i.e., spikes per stimulus cycle, or "spike count") decreased and stabilized at lower values than those that followed the first stimulus cycle (Fig. 2*C*). The stabilized values are termed "steady-state values." Since stabilization processes were usually restricted to the first 0.5 s for all the frequencies tested, "steady-state periods" refer to the periods from 0.5 s after train onset until the end of the train.

Single units recorded from these layers, while displaying weaker responses and larger variabilities, usually followed the layer-specific patterns observed with multi-units and with layer ensembles: after a stabilization period (0.2–0.6 s), the responses were attenuated in all layers and delayed in layers 5a and 2/3 (Fig. 3). Of the responsive single units of layer 4 barrels and layer 5b, 73% (11/15) and 82% (9/11), respectively, exhibited constant latencies and spike-count reduction; and of the responsive single units of layer 5a and layer 2/3, 76% (13/17) and 86% (6/7), respectively, exhibited both spike-count reduction and latency increments [reductions and increments refer to the steady-state values, between 0.5 and 3 s from train onset, being consistently lower or higher, respectively, from the value that corresponded to the first stimulus cycle (see Fig. 2, *B* and *C*)]. Thus the response patterns of single units in layers 4 and 5b differed from those in layers 5a and 2/3 (χ^2, $P < 0.01$), whereas response patterns of single units in layers 4 and 5b, or layers 2/3 and 5a, were similar (χ^2, $P > 0.5$ for each).

Effect of the stimulus frequency

The main difference between the responses of the lemniscal and paralemniscal layers was in the temporal domain. Lemniscal neurons responded with a fixed latency, while the latencies of layer 5a neurons, as well as those of layer 2/3 neurons, were modulated during the dynamic period until they stabilized at longer latencies during the steady-state period. Whether these dynamic processes depend on the temporal frequency of the stimulus (for frequencies around the whisking frequency range) was tested by quantifying the response dynamics for

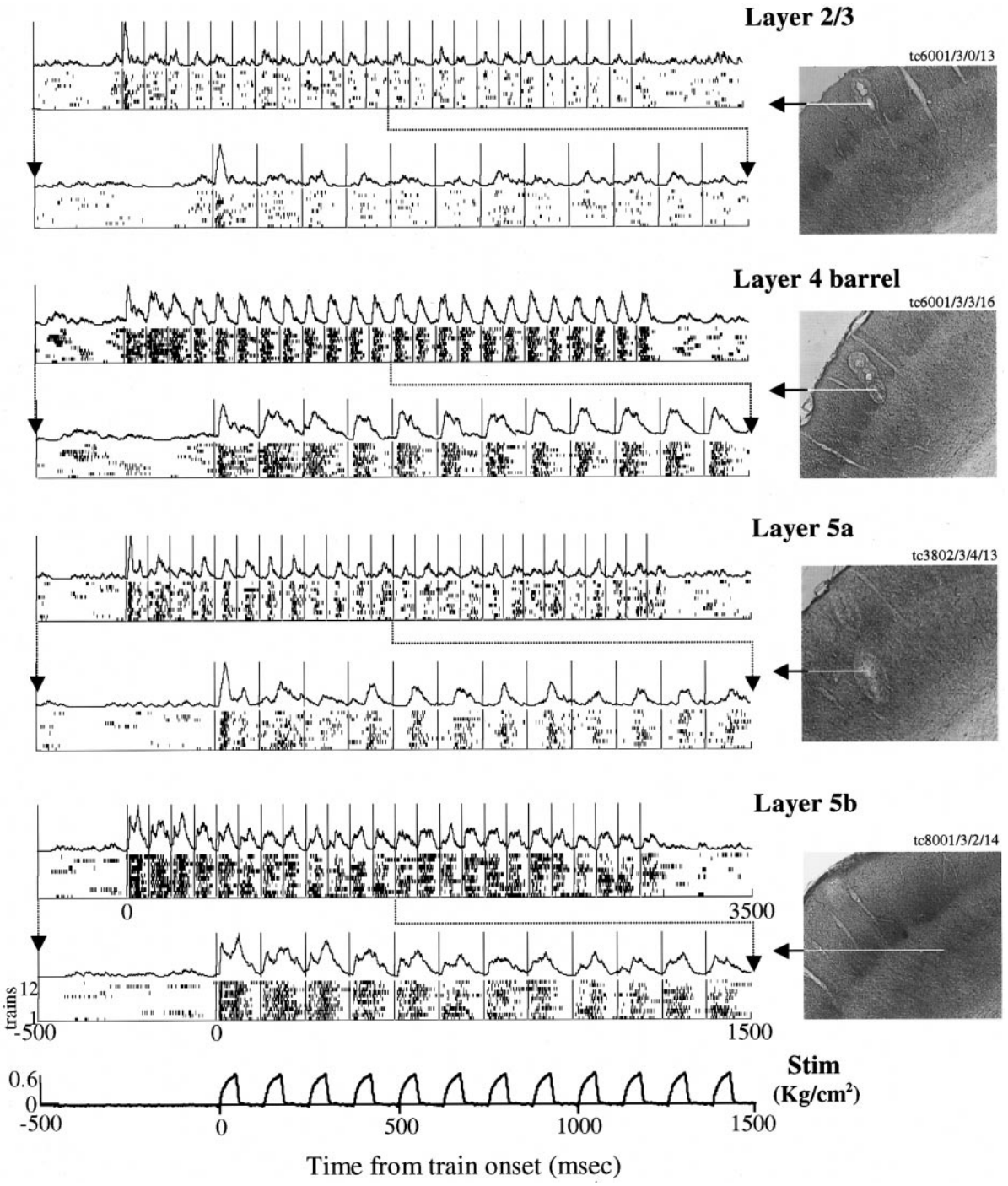

FIG. 1. Typical multi-unit responses for each of the 4 cortical layers studied. The peristimulus time histograms (PSTHs, *top curves*) describe the average responses along the entire stimulus train. In the corresponding rasters, each small vertical line represents a single spike, and each long vertical line represents the onset of a single air-puff pulse. The *bottom PSTHs* and rasters for each layer show the 1st 1,500 ms in expanded scale. The recording sites of these units (origins of arrows) are depicted on coronal cortical sections, which were stained for cytochrome oxidase activity (*right*). The *bottom trace* depicts the output pressure of the pneumatic pump in expanded scale. The multi-units from layers 2/3 and 4 were recorded simultaneously. Each recording depicts one block of 12 trains (3 s each) of 50 ms air-puff pulses at 8 Hz; in the layer 5a example, at $t = 2$ s, the stimulus frequency was changed to 8.7 Hz. Receptive fields (RFs): layer 2/3, D1, D2, D3, E1, E2; layer 4, D2; layer 5a, gamma, C1, C2, D1, D2, E1, E2; layer 5b, E4.

stimulus frequencies between 2 and 11 Hz. For all frequencies tested, the pulse width and train duration used were the same; the only differences between trains of different frequencies were the inter-pulse intervals and the number of pulses per train. The effect of the stimulus frequency on the steady-state response pattern was different for the lemniscal and paralemniscal layers (see simultaneous recording of local populations from layer 4 barrel and layer 5a in Fig. 4). The response of each local population to the first stimulus cycle was similar for all three frequencies tested. However, the steady-

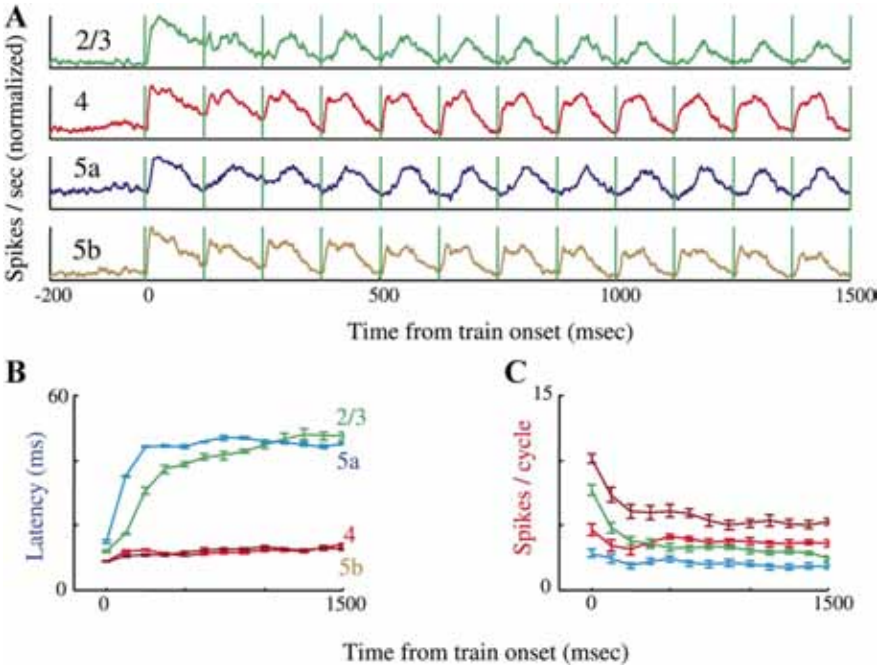

FIG. 2. Ensemble responses to 8-Hz stimulations. *A*: PSTHs of layer ensembles. For each layer, spike trains of layer ensembles were compiled from all spikes generated by all well-localized neurons recorded from that layer. Vertical green lines represent stimulus onsets (in the protraction direction). Spike rates were normalized to the highest level for each layer. *B*: dynamics of response latency. The latency to 0.5 peak value was computed and plotted for each stimulus cycle. Standard errors of the latency for each stimulus cycle were computed from the inter-train variability ($n = 24$ trains) of the ensemble latency to the 1st spike. *C*: dynamics of spike counts. The spike-count values are the means ± SE of the number of spikes within 125 ms after the onset of each stimulus pulse.

state responses differed. While the steady-state latencies of the lemniscal neurons were constant for all frequencies, those of layer 5a neurons increased with increasing stimulus frequencies (Fig. 4). In all layers, increased frequencies yielded reduced response magnitudes. However, the underlying causes for the magnitude reductions in the lemniscal and paralemniscal responses were different. Lemniscal neurons exhibited amplitude attenuation throughout the response burst, while maintaining a constant response duration (Fig. 4, layer 4). Paralemniscal neurons exhibited delayed and shorter responses with increasing frequencies, such that only the last part of the low-frequency response burst (observed during the 1st stimulus cycle or during 2-Hz stimulations) remained (Fig. 4, layer 5a). This is demonstrated both by the rasters and by the peristimulus time histograms (PSTHs). The PSTHs also revealed that for the remaining response bursts of the paralemniscal neurons, there was no amplitude reduction across the different frequencies up to 8 Hz (Fig. 4, layer 5a, the trailing edges of the PSTHs, from response peak and on, overlapped).

Population analysis of steady-state responses

The steady-state responses of all well-localized local populations were analyzed. The response patterns were consistent for the local populations of each layer (Fig. 5). Within the range of 2–11 Hz, almost all recordings from layer 4 barrels

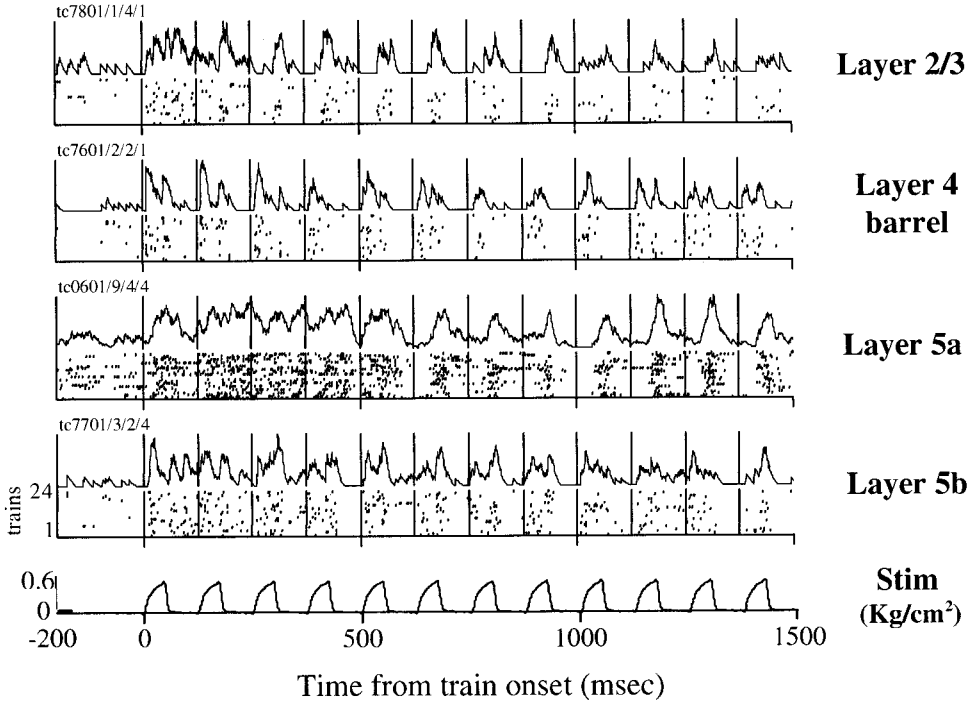

FIG. 3. Typical single-unit responses for each of the 4 cortical layers. Responses to 24 trains at 8 Hz (1st 1,500 ms) are shown. RFs: layer 2/3, D2, D3, E1, E2, E3, E4; layer 4, E2, E3; layer 5a, gamma, C1, C2, C3, C4, beta; layer 5b, E1. See legend of Fig. 1 for details.

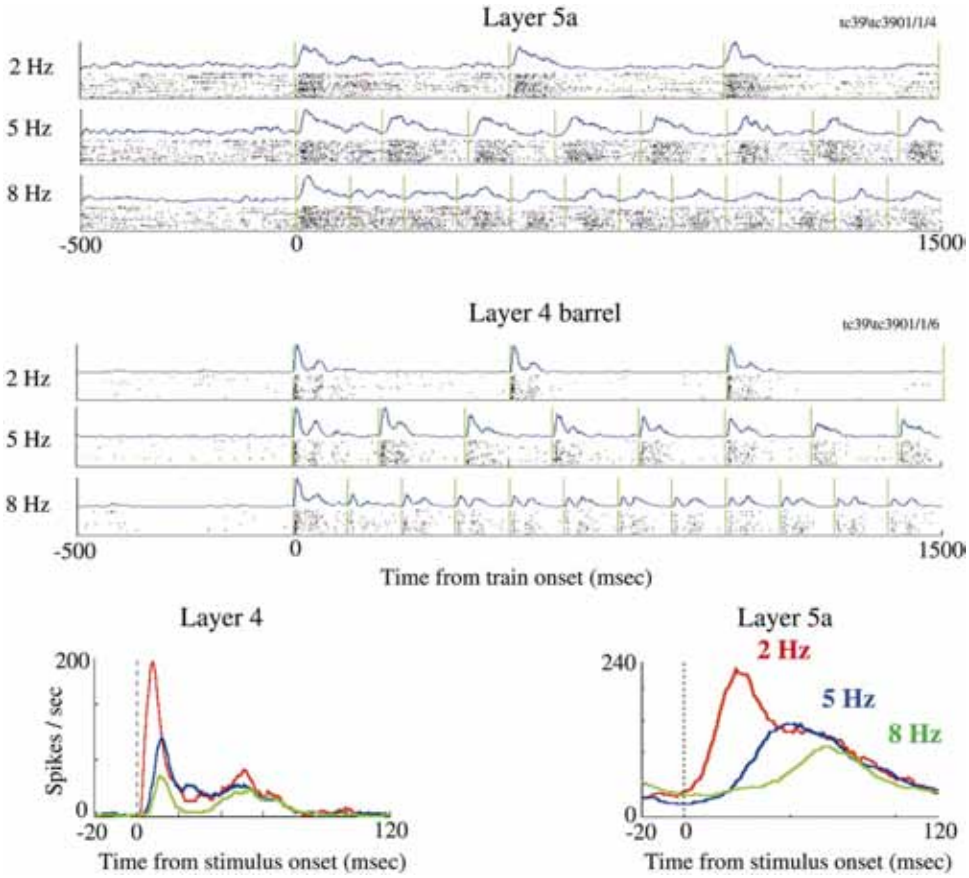

FIG. 4. Comparison of local populations recorded simultaneously from a barrel in layer 4 and from layer 5a. The PSTHs and raster displays for the 1st 1,500 ms of the stimulus trains at 3 frequencies are presented (*top*). The steady-state PSTHs for each stimulus frequency were averaged across all stimulus pulses between 0.5 and 3 s from train onset (*bottom*). RFs: layer 4, C1, C2, D1; layer 5a, D1, D2, D3, D4, E2.

and layer 5b revealed amplitude coding and almost all recordings from layer 5a revealed latency coding of the stimulus frequency; amplitudes decreased and latencies increased as a function of the frequency. Both amplitude and latency coding, in the lemniscal layers and layer 5a, respectively, resulted in spike-count coding; as the stimulus frequency increased the spike counts decreased, as indicated by the reduction in the areas of the PSTHs.

Local populations in layer 2/3 exhibited a response pattern in which the two distinct response patterns observed in the lemniscal (layer 4 barrels and layer 5b) and paralemniscal (layer 5a) layers were integrated. Responses of local populations from layer 2/3 displayed onset latencies similar to those displayed in layer 5a (Fig. 5). However, unlike local populations of layer 5a, those of layer 2/3 usually did not maintain the same offset latency across frequencies. This indicates that the response amplitudes of most layer 2/3 neurons were attenuated in addition to being delayed. Thus local populations of layer 2/3 exhibited both amplitude and latency coding of the stimulus frequency.

Figure 5 also depicts the variability in response patterns within each cortical layer. While all local populations of the lemniscal layers exhibited amplitude reduction as a function of frequency, some exhibited a uniform reduction along the entire response pulse while in others, the reduction was mainly restricted to the early response component. However, in all these recordings there was a response component of short (and constant) latency at all frequencies. In contrast, in almost all local populations of layers 5a (16/19) and 2/3 (6/8), response onset was significantly delayed with increasing frequencies. In the remaining two local populations of layer 2/3, a small early response component, with constant latency, was evident at all frequencies.

The difference among the steady-state response latencies in the various layers is demonstrated by the distributions of onset latencies (to 0.3 peak value) of all well-localized units (single and multi-units) recorded in these layers (Fig. 6). The distribution of onset latencies showed a constant mode ~10–15 ms in layers 4 and 5b (with the exception of layer 4 at 11 Hz) and increasing modes from 15 to 60 and 65 ms in layers 5a and 2/3, respectively. The distributions of latencies to 0.1 and 0.5 of peak value showed similar patterns; lemniscal latency modes were constant at ~10 and 15 ms, respectively (except for layer 4 barrels at 11 Hz and threshold of 0.5, which showed a uniform distribution between 5 and 50 ms), whereas the latency modes in layers 5a and 2/3 increased from 15 to 60–65 ms (except for layer 2/3 at 11 Hz and threshold of 0.1, which showed a uniform distribution between 10 and 65 ms). While the dispersion of layer 5a latencies remained more or less unchanged, that of the other layers increased at 11 Hz mainly due to strong attenuation of the early response component in layers 4 and 5b and of the entire response in layer 2/3 (Fig. 4). The latencies of layer 2/3 and 5a were significantly larger than those of layer 4 at all frequencies ($P < 0.002$, 2-tailed *t*-test) and those of layer 5b at 5, 8 and 11 Hz ($P < 0.05$; layer 5a latencies were longer than those of 5b also at 2 Hz, $P < 0.05$). The latencies of layers 4 and 5b did not differ ($P > 0.05$). The latencies of layers 2/3 and 5a were not significantly different except at 5 Hz ($P = 0.007$; medians: layer 2/3 33 ms and layer 5a 31 ms).

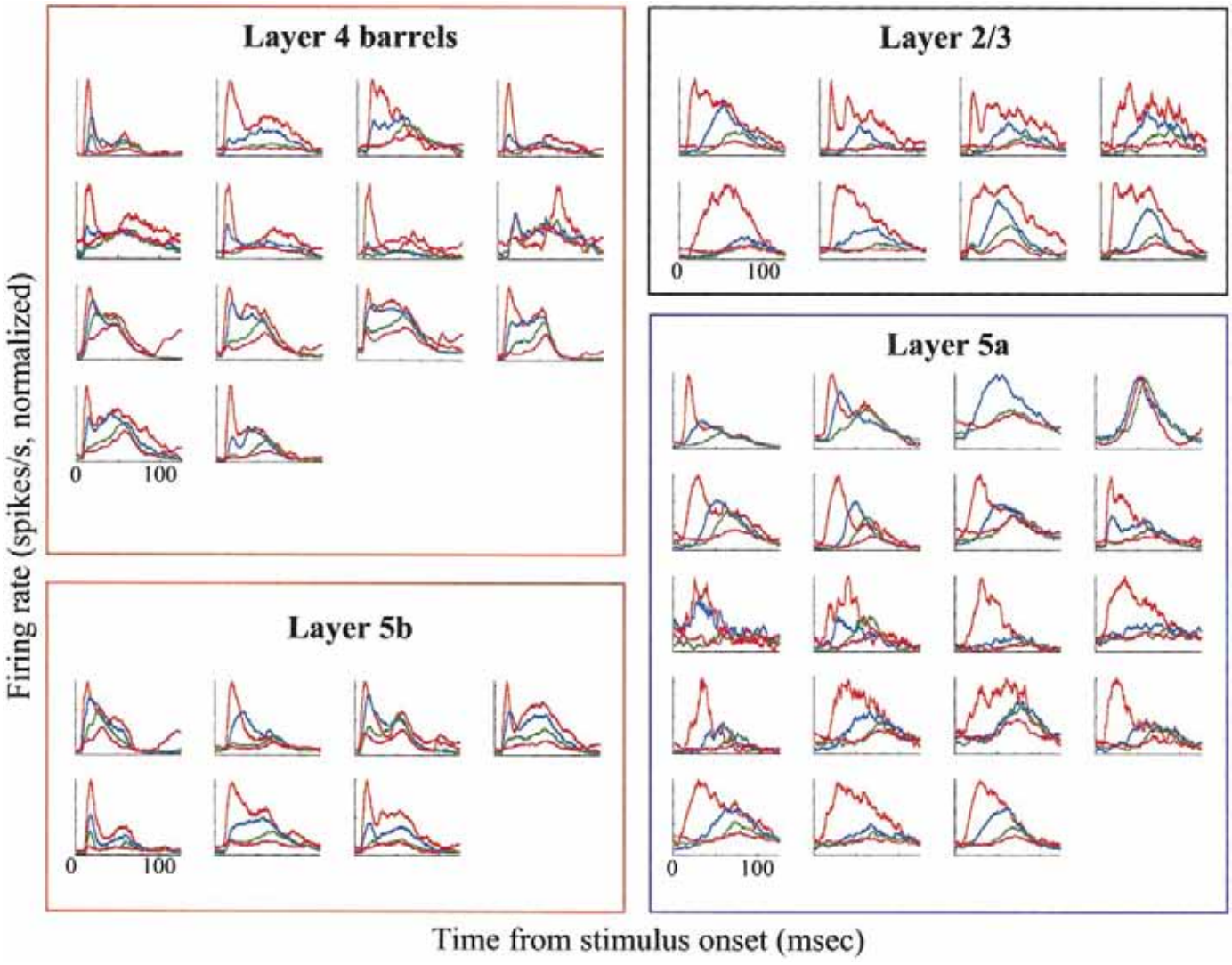

FIG. 5. Steady-state responses of local populations in different cortical layers to different stimulus frequencies. All responsive, well-localized local populations are included. The steady-state PSTHs for 2 (red), 5 (blue), 8 (green), and 11 Hz (magenta) are depicted. Firing rate scales were normalized independently for each local population. Arrangement of the graphs for each layer is random.

Latency distributions were computed also for the first stimulus cycle at all frequencies (data not shown). No significant difference was found between the latencies of the different layers in response to the first stimulus cycle. Means and medians of these latencies were slightly different in the various layers, probably reflecting the slight differences in the latencies of whisker-evoked intracellular potentials following low-frequency stimuli (Zhu and Connors 1999). For layers 2/3, 4, 5a, and 5b, the medians of the latencies to the first stimulus cycle were 15, 10, 16, and 14 ms, respectively, to 0.3 peak value, and 12.5, 9, 13, and 12 ms, respectively, to 0.1 peak value.

Figures 5 and 6 demonstrate that, with few exceptions in each layer, the common response modes differed significantly between layers 4–5b and layers 2/3–5a. This is also evident from the gross ensemble representations, generated by the summed activity of all well-localized neurons in each layer (Fig. 7). For each layer, the ensemble response is described by PSTHs (Fig. 7, *left*) and tuning curves (*right*). The tuning curves describe the dependencies of the onset latency (blue) and the spike count (red) on the stimulus frequency. The ensemble PSTHs and tuning curves demonstrate, once again, the basic differences between responses in the different layers. Whereas onset latencies were constant in the lemniscal layers, they increased with increasing frequencies in layers 5a and 2/3. In all layers, spike counts decreased with increasing frequencies (red tuning curves). However, as demonstrated by the preceding examples, this spike-count coding of the frequency was generated by different mechanisms in the lemniscal and paralemniscal layers. While the lemniscal ensembles displayed general amplitude attenuation, the reduction in layer 5a spike-counts was primarily due to increased onset latencies, at least for 5 and 8 Hz. For latencies in which spikes were generated, there was no difference in amplitude (of spike probability) among the responses to 2-, 5-, and 8-Hz stimulations; the time course of these responses was nearly identical after about 65 ms. In contrast, the response of layer 5a to 11 Hz appeared to be attenuated in addition to being delayed, since it was consistently weaker than the responses to other frequencies, during the entire response pulse.

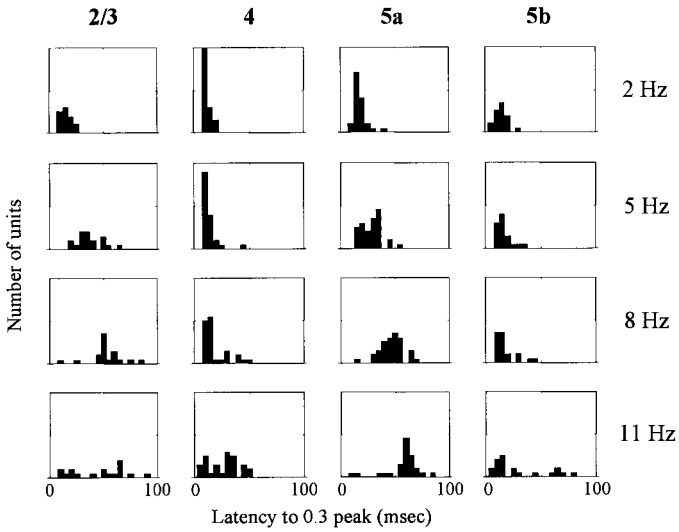

FIG. 6. Response latencies of all well-localized neurons. Distributions of latencies to 0.3 of peak value are depicted for each stimulation frequency. All well-localized and responding single and multi-units of layers 2/3 ($n = 18$), 4 ($n = 30$), 5a ($n = 34$), and 5b ($n = 20$) are included.

The ensemble response (like the individual ones) of layer 2/3 exhibited an integration of the amplitude and latency coding schemes in which, in addition to increased onset latencies, the entire response was attenuated, and thus offset latencies were shorter for higher frequencies.

Stimulus pulse-widths and internal representations

Both spike count and onset latency coded the stimulus frequency in layers 2/3 and 5a. Which of the two representations represents the input frequency for further cortical computations? According to our phase-locked loop (PLL) hypothesis, which is described in the accompanying paper and in Ahissar and Vaadia (1990), Ahissar et al. (1997, 2000), and Ahissar (1998), the spike count is the output variable representing the whisker frequency for further processing, whereas the latency is an internal variable of the thalamocortical loop and is dynamically adjusted to obtain the correct spike counts. Our thalamic recordings indeed show that paralemniscal spike-count coding is preserved with very short pulse widths of the stimulus (20 ms), while latency coding is much reduced (see accompanying paper). However, if paralemniscal thalamocortical loops indeed function as PLLs, paralemniscal cortical neurons should behave similarly.

To test this prediction, we applied the same 20-ms air puffs described in the accompanying paper. Although the peak pressure obtained with the 20-ms stimuli was lower than that obtained with the 50-ms stimuli, the peak neuronal input to the cortex was probably similar for the two pulse widths because the ensemble thalamic output displayed similar peak responses for both pulse widths (Fig. 7 in the accompanying paper). The effect of the pulse width on the responses of local populations at 5 Hz is depicted in Fig. 8. Whereas the responses in the lemniscal layers (layer 4 barrels and layer 5b) were significantly shorter with pulses of 20 ms, the duration of the responses in layers 5a and 2/3 were hardly affected by the pulse width at 5 Hz (Fig. 8). In contrast, the steady-state onset latencies were shorter during 20-ms pulses in layers 5a and 2/3 but constant in the lemniscal layers.

The effect of the pulse width on the steady-state responses at all frequencies is depicted in Fig. 9, which displays the ensemble responses of all the neurons stimulated with both 20- and 50-ms stimuli in each layer. In the lemniscal layers and with all tested frequencies, the durations of the responses were shorter for the 20-ms pulses. In layers 5a and 2/3, the response duration for the 20-ms pulses was also considerably shorter at 2 Hz, but at higher frequencies, the duration of responses to 20- and 50-ms stimuli were similar and only shifted to lower latencies with 20-ms stimuli (Fig. 9, PSTHs). As a result, latency coding in layers 5a and 2/3 decreased markedly (Fig. 9, tuning curves), whereas spike-count coding was almost unchanged (Fig. 9; areas under the PSTHs and tuning curves).

The effect of stimulus pulse width on cortical representations is summarized in Fig. 10. Reduction of the pulse width from 50 to 20 ms significantly affected the spike-count representation in layer 4 barrels and layer 5b and the latency representation in layers 5a and 2/3 (2-way ANOVA, $P < 0.0001$). However, latency representations in the lemniscal layers (layer 4 barrels and layer 5b) and spike-count representations in the paralemniscal layer (layer 5a) and layer 2/3 were not affected (2-way ANOVA, $P > 0.1$). Thus reduction of the stimulus pulse width resulted in opposite effects in different cortical layers: spike-count reduction with no latency change in the lemniscal layers and latency reduction with no spike-count change in layers 5a and 2/3. These opposite effects are similar to those observed in the lemniscal and paralemniscal thalamic

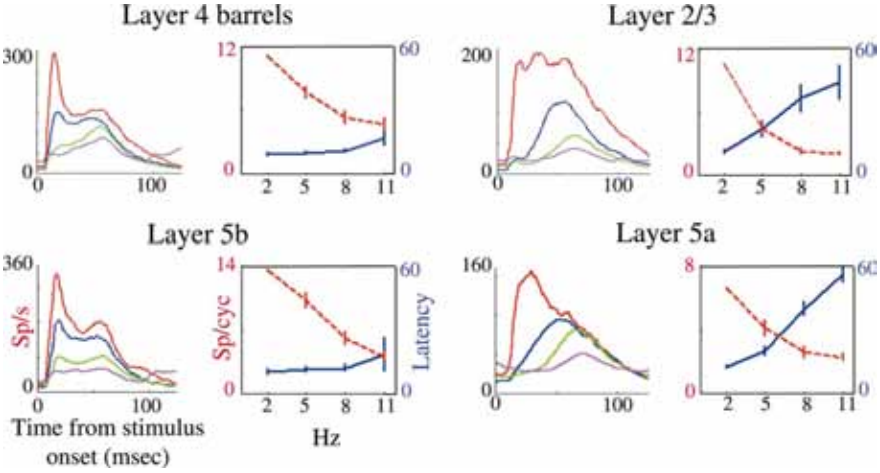

FIG. 7. Steady-state representations of the layer ensembles. PSTHs were averaged across all well-localized local populations of each layer (color coded as in Fig. 5). The latency (to 0.1 peak value) and spike-count tuning curves were computed for each local population and then averaged. Tuning curves of spike counts (dashed red curves) were normalized before averaging so that the response of each local population at 2 Hz was equal to the average response of all local populations of that layer at 2 Hz. Tuning curves of latency (solid blue curves) were not normalized. Mean ± SE values across all local populations are depicted, thus the SEs represent variability between local populations.

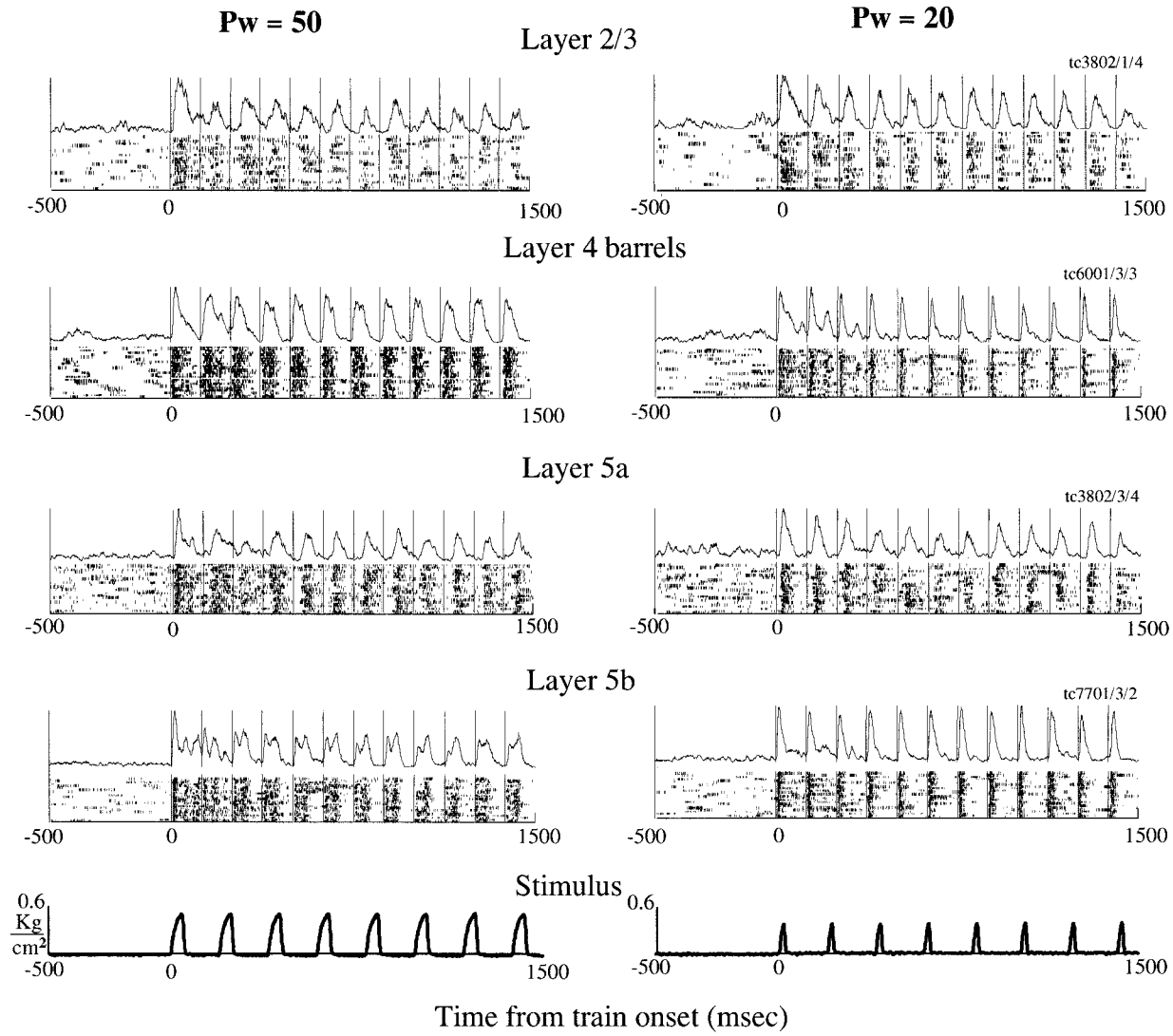

FIG. 8. Effect of stimulus pulse width on responses of local populations. Responses (rasters and PSTH) from all 4 cortical layers during stimulations (50 and 20 ms) at 5 Hz are depicted. See legend of Fig. 1 for details.

nuclei (see accompanying paper) and are consistent with the phase-locked loop model.

Representations of FMs

We examined the dynamic behavior of cortical representations by stimulating the whiskers with FM trains in which the stimulus pulse width remained constant but the inter-pulse interval changed continuously. In each train, FMs started after an initial constant-frequency period of 2 s (Fig. 11, black curves, *middle panels*). The initial constant frequency was 5 Hz, the modulation depth was 40% (i.e., frequency varied between 3 and 7 Hz), the modulation frequency was 0.5 Hz, and the initial modulation phase was 90°. In Fig. 11, the instantaneous latency modulation of the neuronal activities is depicted by blue curves in the *middle* and *bottom left panels*. As expected from the constant-frequency data, with pulse widths of 50 ms, neurons in layer 4 barrels and layer 5b essentially showed no latency modulations, whereas the response latencies of neurons in layers 5a and 2/3 increased with increasing instantaneous stimulus frequencies. In all layers, the instantaneous stimulus frequency was represented by spike counts (red curves in *middle* and *bottom left panels*), similar to the representations of constant stimulus frequencies.

However, as with the constant-frequency stimuli, the extent of cortical representations of FM stimuli depended on the pulse width of the stimulus. When the pulse width of the stimulus was reduced from 50 to 20 ms, the latency modulations in layers 5a and 2/3 were significantly reduced (Fig. 12). In contrast, spike-count modulations in these layers were only slightly affected. In the lemniscal layers, latencies were constant while spike-count modulations were reduced. This behavior was consistent across all well-localized local populations tested with both pulse widths (n = 6, 7, 12, and 7 local populations in layers 2/3, 4 barrels, 5a, and 5b, respectively) except for two local populations in layer 5b that exhibited larger spike-count modulations during 20-ms stimulations.

DISCUSSION

Our findings indicate that the cortical column in the rat barrel cortex cannot be considered as a single computational

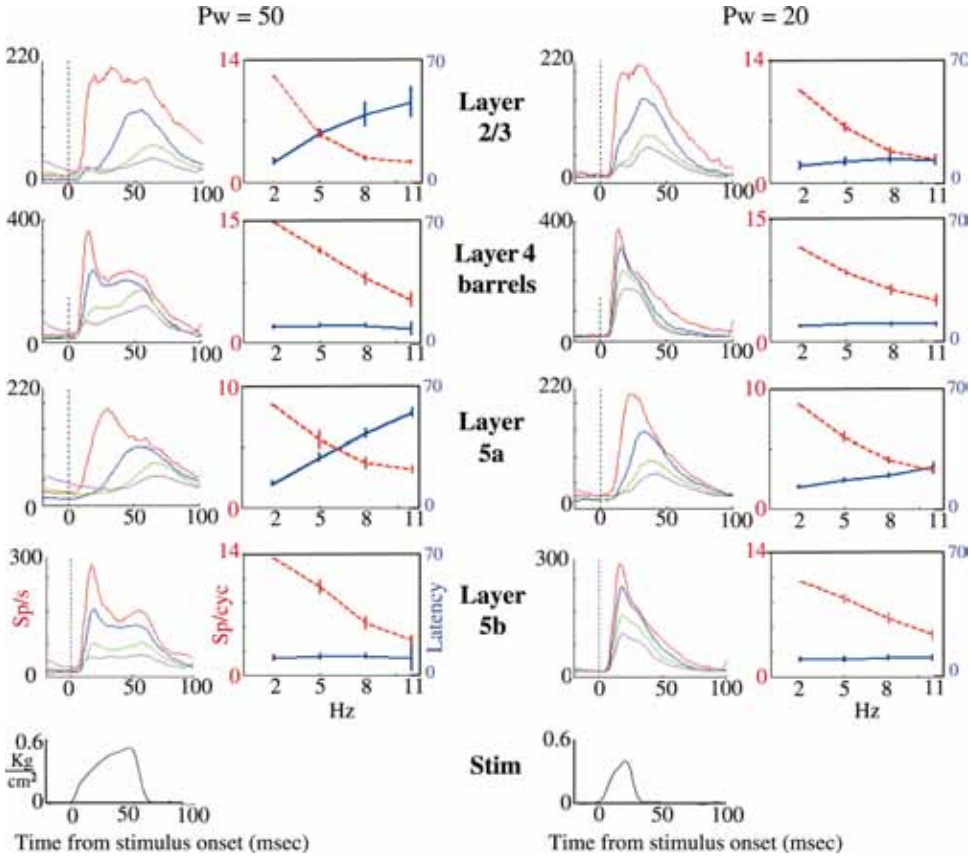

FIG. 9. Effect of stimulus pulse width on steady-state responses of neuronal ensembles. For each layer and pulse width, average PSTHs (*left*) and tuning curves (*right*) are presented. Only local populations that were stimulated with both 20- and 50-ms pulses were averaged in layer 2/3 ($n = 6$), layer 4 barrels ($n = 7$), layer 5a ($n = 12$), and layer 5b ($n = 7$). Tuning curves of spike counts (dashed red curves) were normalized before averaging (see legend of Fig. 7). Tuning curves of latency (to 0.3 peak value; solid blue curves) were not normalized. The *bottom traces* depict the output pressure of the pneumatic pump.

unit that processes a unitary thalamic input. Focusing on the laminar organization within barrel-columns, i.e., within the imaginary cortical columns defined by the borders of the barrels in layer 4 and extending across all layers, we showed that neurons in different layers represent the temporal frequency of a tactile stimulus using different coding schemes. These coding schemes depended strongly on the thalamic affiliation of the different layers: neurons in the barrels of layer 4 and in layer 5b, which receive lemniscal input from the VPM, displayed constant latencies and represented the input frequency by amplitude and spike count. In contrast, neurons in layer 5a, which receives paralemniscal input from the POm, represented the stimulus frequency by latency and spike count. These representations are similar to the neuronal representations observed in the corresponding thalamic nuclei in both the lemniscal and paralemniscal pathways (see accompanying paper). Overall, these findings are consistent with a parallel processing scheme, in which lemniscal and paralemniscal inputs are processed concurrently by parallel thalamocortical loops. Interestingly, neurons in the "output" layer 2/3 exhibited an integration of the two coding schemes, which indicates that the outputs of these two processing streams might be integrated, at least partially, already within the barrel cortex.

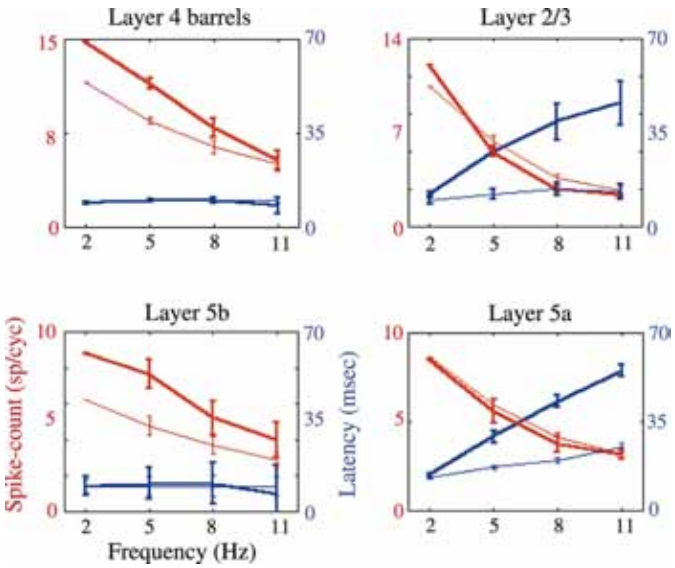

FIG. 10. Dependence of cortical representations on stimulus pulse width. Same data as those used for Fig. 9. Latency (blue curves), spike count (red curves), pulse widths of 50 and 20 ms (thick and thin curves, respectively).

Effects of anesthesia

Neurons in layer 4 barrels and layer 5b usually displayed two response components: an "early" component that peaked around 20 ms, and a "late" one that peaked around 50 ms after stimulus onset (see Fig. 5). The late component was probably significantly emphasized by the anesthesia (Simons et al. 1992). Also, part of the amplitude adaptation observed with 50-ms stimuli (e.g., Fig. 2) might be caused by anesthesia. In contrast, the latency shifts in the paralemniscal system cannot be attributed to the anesthesia because latency shifts due to anesthesia are an order of magnitude smaller (Fanselow and Nicolelis 1999; Friedberg et al. 1999; Simons et al. 1992). In our study, under the same conditions of anesthesia, the latency shifts were significantly reduced with pulse widths of 20 ms,

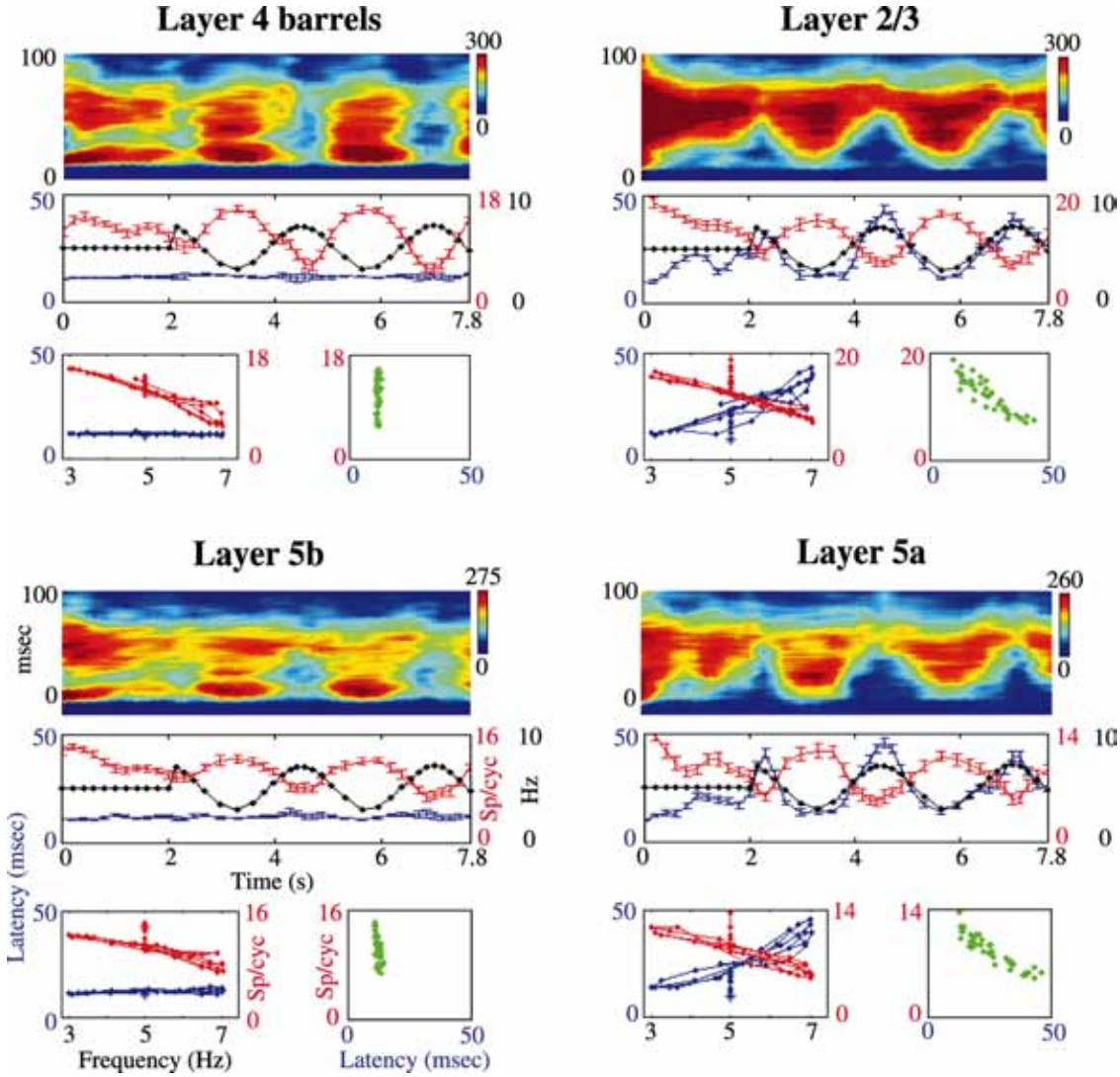

FIG. 11. Responses of local populations to FM stimuli (pulse-width = 50 ms). *Top* (for each layer): PSTHs as a function of train time (vertical axis depicts PSTH time, horizontal axis train time, and color axis firing-rate). *Middle*: instantaneous stimulus frequencies (black), response latencies (blue), and spike counts (red) as a function of train time. Means of 36 trials ± SE are presented. *Bottom left*: trajectories of the latencies and spike counts as functions of the instantaneous whisker frequency (data re-plotted from *middle*). Each dot represents a value during 1 stimulus cycle. Lines connect dots according to their temporal order (asterisk denotes the 1st stimulus cycle). *Bottom right*: spike counts as a function of latency (data re-plotted from *middle*). Each green dot represents the spike count and latency of a response to a single air-puff pulse. Responses to all air-puff pulses during the FM train are plotted. RFs: layer 2/3, delta, D1, D2, D3, E1, E2; layer 4, E4; layer 5a, gamma, E1, E2, E3, beta; layer 5b, E4;

which further indicates that anesthesia per se does not induce these latency shifts. Since latency shifts developed during each stimulus train, they probably reflect a dynamic process, specific to processing the sensory stimulus, rather than a general arousal effect.

Effect of stimulus type

We compared here cortical responses to air-puff stimuli at different frequencies and pulse widths. The movement induced by air-puff stimuli is usually less defined than that induced by mechanical stimuli in which the whisker is firmly attached to the stimulator. Unfortunately, due to this firm attachment, mechanical stimuli often produce afferent responses that are significantly different from those observed during self-initiated whisker movements in awake rats (see accompanying paper). Most disturbing for our study was the frequency doubling that occurred with mechanical stimuli due to the enforced backward movement at the end of the stimulus pulse. In contrast, video tracking of the whisker movement during our air-puff stimuli (Fig. 1 in the accompanying paper) revealed movements that resemble those observed during exploratory whisking (Carvell and Simons 1990). Furthermore, our air-puff stimuli evoked brain stem responses similar to those evoked by self-initiated whisker movements in awake rats (Nicolelis et al. 1995). Thus air-puff stimulations were selected here to investigate whisker-frequency coding in the cortex.

The use of air puffs helped us overcome another potential problem. While the central field of lemniscal RFs usually contains a single (the "principal") whisker, those of paralemniscal neurons usually contain a few, similarly effec-

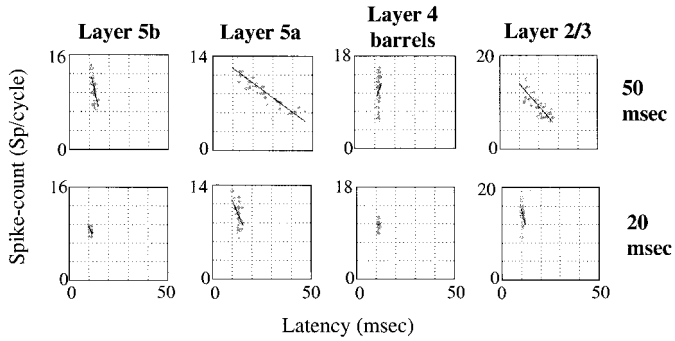

FIG. 12. Effect of stimulus pulse width on latency and spike-count modulations. Spike counts as a function of latency (during FM stimulations with 50 and 20 ms) are depicted for the same local populations presented in Fig. 11. Each dot represents the spike count and latency of a response to a single air-puff pulse. Responses to all air-puff pulses during the FM train are plotted. —, linear regressions.

tive, whiskers (Armstrong-James and Fox 1987; Diamond et al. 1992b; Ghazanfar and Nicolelis 1999; Simons 1978). Consequently, a comparison of lemniscal and paralemniscal responses based on single whisker stimulations would often be misleading (see DISCUSSION in the accompanying paper). Because during natural whisking all the whiskers are moving and thus the entire RFs of neurons are stimulated, we chose to base our laminar comparisons on stimulations of the entire RFs of both lemniscal and paralemniscal neurons. Our air-puff stimuli were thus directed to stimulate those two to three whisker rows containing the primary and surrounding whiskers included in the RF of the recorded neurons.

Due to the differences mentioned in the preceding text, we would not expect that fast mechanical stimulations of single whiskers would yield results similar to those obtained with our air puffs. We assume that the generation of cortical representations of the whisker frequency depends on the temporal dynamics of the stimulus and on the stimulation field. These dependencies have yet to be characterized, by using stimuli, either mechanical or air puffs, with controlled temporal dynamics and stimulation fields.

Comparison with previous findings

During the last 30 years, the spatial characteristics of cortical responses had been described in detail. Therefore we did not devote time to quantitatively analyze spatial parameters but rather focused on rigorously characterizing cortical responses to the temporal component of the stimuli. Previous studies that addressed the temporal domain of cortical responses mainly focused on responses to paired pulses with different inter-pulse intervals. When applied to an adjacent whisker, or to the same whisker as the first pulse, the second pulse usually evokes a weaker response if applied shortly after (less than ~200 ms) the first one (Brumberg et al. 1996; Fanselow and Nicolelis 1999; Moore et al. 1999; Shimegi et al. 1999; Simons 1985). Similarly, our stimulation paradigm also induced reductions in the response amplitude for frequencies above 5 Hz. However, our results indicate that the changes observed during the second stimulus pulse are usually the beginning of a longer stabilization process, during which the latency and spike-count coding develop.

When the thalamus or internal capsule are stimulated directly, cortical lemniscal neurons usually exhibit amplitude reduction while paralemniscal neurons exhibit response augmentation during the second pulse, if the instantaneous frequency is 7–14 Hz (Castro-Alamancos 1997; Dempsey and Morison 1943). Our results indicate that neurons in the barrel cortex usually do not display augmentation in response to *external* sensory stimuli. While some barrel cortex neurons did exhibit response augmentation during stimulus cycles that immediately followed the first cycle (see Figs. 1 and 3), the ensembles only exhibited reductions with frequencies above 5 Hz: for both lemniscal and paralemniscal neurons, the averaged responses to the second stimulus pulse were weaker than those to the first pulse with 8 (Fig. 2) and 11 Hz (not shown). Although differences in the stimulation parameters used, such as intensity and duration, could account for this, we believe that the difference is mainly due to the nature of the input to the cortex. Whereas during intracranial or in vitro stimulations, the strength of the second input pulse is equivalent to that of the first, with whisker stimulations, it is not. This is because thalamic neurons display significant transformations of brain stem signals (see accompanying paper), including magnitude reduction, in both lemniscal and paralemniscal pathways. These magnitude reductions would negate, at least partially, thalamocortical augmentation.

The mechanism underlying augmenting responses (Castro-Alamancos and Connors 1996) could be instrumental for the operation of thalamocortical loops during repetitive stimulations of the afferent pathways, such as during natural whisking. Immediately after the initiation of whisking (Fanselow and Nicolelis 1999), or a stimulus train (see accompanying paper), the response of thalamocortical neurons is attenuated, probably due to a shift into a gating mode (Sherman and Guillery 1996), a mode that enables sensory computation. In the paralemniscal system, augmentation mechanisms can increase cortical excitibility, at least during initial stages following whisking or stimulation onset, as a counterbalance to the thalamic attenuation, in order to maintain the activity along the thalamocortical loop during the initiation of thalamocortical computation.

Neurons in different cortical layers respond with different latencies to low-frequency (usually $\leq$1 Hz) stimuli (Armstrong-James et al. 1992; Ito 1985; Zhu and Connors 1999). In our paradigm, an equivalent low-frequency stimulus was the first stimulus pulse in each train, whose instantaneous frequency was $\leq$1 Hz (preceded by an interval of $\geq$1 s). In fact, in our experiments, with stimulation frequencies of $\leq$2 Hz, the response latencies in each layer remained constant. For the first stimulus cycles and 2-Hz stimuli, the latencies we observed were consistent with those previously observed (Armstrong-James et al. 1992; Ito 1985; Zhu and Connors 1999); layers 4 and 5b responded first, and layers 2/3 and 5a later. Armstrong-James et al. (1992) maintained that these latency differences support the notion of a "vertical column," excluding layer 5a. Our results clearly support the exclusion of layer 5a but further suggest that layer 5a is part of a different processing stream.

Pulse-width invariance and cortical representations

The frequency of the stimulus was coded primarily by the amplitude of the responses of neurons in layer 4 barrels and layer 5b and primarily by the latency of the responses of the neurons in layer 5a (Fig. 7). Both these types of coding yielded

a spike-count representation in which spike counts decreased as the stimulus frequency increased. Which of these cortical representations (spike-count, amplitude or latency) is used for further computations in the cortex is not yet known. However, one might assume that neuronal representations used for further processing are protected, at least to some extent, from variations in nonrelevant stimulus parameters. That is, neuronal representations of one parameter, the stimulus frequency in this case, should be invariant with respect to another parameter, for example the pulse width. The only invariant representation we observed was that of the spike-count in layers 5a and 2/3 (Fig. 10). Thus the spike count of local populations in these layers might be the output variable that encodes stimulus frequency. This finding is fully consistent with layer 5a neurons being components of thalamocortical phase-locked loops. If this is the case, latency coding in layer 5a, as in the POm, reflects internal loop computations (see accompanying paper).

The inconsistency of spike-count coding in the lemniscal layers (layer 4 barrels and layer 5b) suggests that, like in the VPM (see accompanying paper), this representation is not a "true" representation of the stimulus temporal frequency but rather a by-product of a different process, possibly one that performs a rate-code computation. The constant latency observed in the lemniscal layers under different stimulus conditions, i.e., with different frequencies and pulse widths, suggests that a constant latency is important for lemniscal processing. Interestingly, this would be expected if the lemniscal system performs spatial processing. If lemniscal processing focuses on extracting spatial details from whisker activation, e.g., the texture of an object scanned by the whiskers, the activity pattern across neurons that represent different whiskers should sustain the same response latency. If not, the spatial image extracted from the neural activities at a given time will be a distorted image of the external object (Ahissar and Zacksenhouse 2001).

Comparison of cortical and thalamic responses

The use of identical stimuli enables direct comparison between responses in the brain stem, thalamus (accompanying paper) and cortex (present paper). Comparison of response patterns reveals a clear segregation between the lemniscal (VPM, layer 4 barrels and layer 5b) and paralemniscal (POm and layer 5a) systems and general similarity of response patterns within each system. This implies that each system is involved in a separate processing, largely independent of the processing performed in the other system (see *Parallel processing?* below). However, use of average data and response distributions, even if obtained with identical stimuli, is not sufficient for deducing causal links required for detailed elucidation of the type of processing performed in each system. This is because similarity of average data can be induced without direct causal links, and differences can be explained by many variables that are hidden from the experimenter. For example, whether the temporal dynamics of POm and layer 5a neurons are causally linked cannot be determined from the average data presented here and in the accompanying paper. The general similarity in the dynamics can be explained by the existence of a common dominating input or by the operation of similar cellular processes. Differences between POm and layer 5a latencies can be attributed, for example, to differences in response sensitivities (which can dynamically change along the train and thus escape our fixed criteria for latency estimation), to cooperative mechanisms with peculiar time dependencies (such as those observed between the basal and apical dendritic inputs to layer 5 neurons) (Larkum et al. 1999), to effects of specific network dynamics, or simply to un-matched samples in thalamus and cortex. In order to reveal causal thalamocortical relationships, "on beam" (i.e., from neurons with similar RFs) simultaneous recordings, preferably including intracellular recordings, should be conducted from the thalamus and cortex during whisker stimulations, and the effects of perturbations induced in each site should be investigated.

Parallel processing?

The barrel cortex receives afferent input via the lemniscal and paralemniscal pathways. The major target of the lemniscal fibers are the barrels in layer 4 and that of the paralemniscal is layer 5a (Chmielowska et al. 1989; Lu and Lin 1993). Whereas the connections between layer 4 and 2/3 are mostly unidirectional (from layer 4 to layer 2/3), the connections between layers 5a and 2/3 are reciprocal (Bernardo et al. 1990; Gottlieb and Keller 1997; Keller 1995; Kim and Ebner 1999; Staiger et al. 2000). Thus while the processing order between layers 4 and 2/3 is clear, it is not clear whether layer 5a sends feedforward information to and receives feedback from layer 2/3 or vice versa. Analysis of onset latencies to low-frequency whisker stimulations could not provide additional information in this case. While layer 4 neurons (and in some studies also layer 5b neurons) consistently respond with the shortest latencies in the barrel cortex, the latencies of neurons in layers 2/3 and 5a are similar (Armstrong-James et al. 1992; Ito 1985; Swadlow 1995; Zhu and Connors 1999). Usually, the dispersions of these latencies are significantly larger than the laminar differences, making all these differences, including those between layer 4 and the other layers, statistically insignificant (Brumberg et al. 1999; Ito 1985). Similarly, this was the case with the low-frequency stimuli (2 Hz and 1st stimulus cycles of all frequencies) of the present study (see Fig. 6 and related text). However, during steady-state responses to higher frequencies, the laminar differences became clear: whereas lemniscal latencies remained constant, those in layers 5a and 2/3 increased significantly. Furthermore the latencies of layers 2/3 and 5a became significantly different at 5 Hz. With this frequency, layer 2/3 neurons usually lagged those of layer 5a (median latencies differed by 2 ms). In the other frequencies, the differences were not statistically significant. This result indicates that at least at some stimulation frequencies, afferent information usually arrives earlier to layer 5a and only later to layer 2/3. It should be interesting to see whether this processing order holds for the entire range of frequencies usually used by rats for exploratory whisking (4–10 Hz) (Carvell and Simons 1990; Fanselow and Nicolelis 1999; Kleinfeld et al. 1999; Welker 1964). In the present study, layer 2/3 neurons usually lagged those of layer 5a also at 8 Hz (Fig. 6, difference between medians was 4.5 ms); however, this difference was not statistically significant.

Although not conclusive, our latency measurements suggest that at least during steady-state operation ~5 Hz (and probably also 8 Hz), the activity of layer 5a neurons is not driven by layer 2/3 neurons. More direct evidence for the lack of a

feedforward drive from layer 2/3 to the deep layers comes from a recent study showing that lesioning of layer 2/3 has no detectable effect on the response latency, or other response properties, of neurons in layers 4, 5 and 6 when stimulating the principal whisker, although such effects were detected when stimulating nonprincipal whiskers (Huang et al. 1998). Thus layer 5a neurons should either be driven by neurons from layers 4 or 5b or by direct thalamic afferents. The clear difference between the frequency dependence and response dynamics of layer 5a neurons and those of the lemniscal neurons suggests that the former possibility is unlikely. On the other hand, the similarity between the frequency dependence and response dynamics of layer 5a neurons and those of the POm (see accompanying paper), which is the source of most of the thalamic projections to layer 5a, strongly suggests that the steady-state activity of layer 5a neurons is predominantly affected by their thalamic inputs rather than by intracortical inputs.

In general, the laminar distribution of neuronal representations observed here corresponds to the laminar pattern of thalamic inputs. The amplitude and latency codings we observed in the lemniscal and paralemniscal layers, respectively, were similar to those observed in the lemniscal (VPM) and paralemniscal (POm) thalamic nuclei, respectively. The similarity of these response patterns is remarkable, especially when they are compared with the essentially relay-like response pattern of the trigeminal brain stem neurons (see accompanying paper). This similarity suggests that, within each pathway (lemniscal and paralemniscal), thalamic and cortical neurons are strongly engaged in thalamocortical processing loops. The strong anatomical (Chmielowska et al. 1989; Deschenes et al. 1998; Hoogland et al. 1987) and functional (Diamond et al. 1992a; Swadlow 1989, 2000; Swadlow and Gusev 2000) coupling between thalamic and cortical neurons in these circuits, supports this notion. According to this scheme, layers 4 and/or 5b establish the cortical output of the lemniscal loop and layer 5a establishes the main output of the paralemniscal loop. According to our results, these outputs can be integrated in layer 2/3. This is suggested by late response components in layer 2/3 lagging responses in layer 5a (Fig. 6), the appearance in layer 2/3 of small early response components, with latencies similar to those observed in layers 4 and 5b (Fig. 2), and the combination of amplitude and latency coding in layer 2/3 (Fig. 7).

Whisking movements make whiskers move along the whisker rows and thus perpendicular to whisker arcs. This geometrical arrangement has important implications for the suitable encoding schemes in these two dimensions. Particularly in the context of object localization, this arrangement calls for temporal coding along the whisker rows and spatial coding along the whisker arcs (Ahissar and Zacksenhouse 2001). This observation leads to the question: are temporally and spatially coded information types processed by separate anatomical channels? First evidence in this direction is provided by a series of studies showing that the lemniscal system has better spatial sensitivity than the paralemniscal system (Armstrong-James and Fox 1987; Brumberg et al. 1999; Diamond et al. 1992b; Simons 1978). The results presented here and in the accompanying paper provide additional support for the suggested parallel processing scheme. Together all these results suggest that tactile information encoded by the whiskers along the rows and along the arcs are decoded in parallel by the paralemniscal and lemniscal systems, respectively (see Ahissar and Zacksenhouse 2001). Such parallel processing allows each system to maximize its efficiency in decoding the information encoded by one encoding scheme without compromising the processing of the information encoded differently. Most likely, before processing merges, the processed information should be re-coded according to a generic coding scheme, common to both systems and suitable for higher-level processing. Our results suggest that this generic code is the spike-count code and that the spike-count-coded information generated by both pathways is integrated in layer 2/3. These suggestions are, in our minds, worthy of further exploration. In particular, on-beam simultaneous recordings from the various computational levels (thalamus and related cortical layers) should facilitate the understanding of the actual thalamocortical computations performed in the two pathways, and intracellular recordings in layer 2/3 would elucidate the mechanisms of intracortical integration implemented in this system.

We thank A. Arieli for insightful comments and discussions and B. Schick for reviewing the manuscript.

This work was supported by grant No. 97-222 from the United States-Israel Binational Science Foundation (BSF), Jerusalem, Israel; the Abramson Family Foundation, USA; and The Dominic Institute for Brain Research, Israel. S. Haidarliu was supported by The Center for Absorption of Scientists, Ministry of Absorption, Israel.

REFERENCES

AHISSAR E. Temporal-code to rate-code conversion by neuronal phase-locked loops. *Neural Comput* 10: 597–650, 1998.

AHISSAR E, HAIDARLIU S, AND ZACKSENHOUSE M. Decoding temporally encoded sensory input by cortical oscillations and thalamic phase comparators. *Proc Natl Acad Sci USA* 94: 11633–11638, 1997.

AHISSAR E, SOSNIK R, AND HAIDARLIU S. Transformation from temporal to rate coding in a somatosensory thalamocortical pathway. *Nature* 406: 302–306, 2000.

AHISSAR E AND VAADIA E. Oscillatory activity of single units in a somatosensory cortex of an awake monkey and their possible role in texture analysis. *Proc Natl Acad Sci USA* 87: 8935–8939, 1990.

AHISSAR E AND ZACKSENHOUSE M. Temporal and spatial coding in the rat vibrissal system. *Prog Brain Res* 130: 75–88, 2001.

ARMSTRONG-JAMES M AND FOX K. Spatiotemporal convergence and divergence in the rat S1 "barrel" cortex. *J Comp Neurol* 263: 265–281, 1987.

ARMSTRONG-JAMES M, FOX K, AND DAS-GUPTA A. Flow of excitation within rat barrel cortex on striking a single vibrissa. *J Neurophysiol* 68: 1345–1358, 1992.

BERNARDO KL, MCCASLAND JS, WOOLSEY TA, AND STROMINGER RN. Local intra- and interlaminar connections in mouse barrel cortex. *J Comp Neurol* 291: 231–255, 1990.

BISHOP GH. The relation between nerve fiber size and sensory modality: phylogenetic implications of the afferent innervation of cortex. *J Nerv Ment Dis* 128: 89–114, 1959.

BRUMBERG JC, PINTO DJ, AND SIMONS DJ. Spatial gradients and inhibitory summation in the rat whisker barrel system. *J Neurophysiol* 76: 130–140, 1996.

BRUMBERG JC, PINTO DJ, AND SIMONS DJ. Cortical columnar processing in the rat whisker-to-barrel system. *J Neurophysiol* 82: 1808–1817, 1999.

CARVELL GE AND SIMONS DJ. Biometric analyses of vibrissal tactile discrimination in the rat. *J Neurosci* 10: 2638–2648, 1990.

CASTRO-ALAMANCOS MA. Short-term plasticity in thalamocortical pathways: cellular mechanisms and functional roles. *Rev Neurosci* 8: 95–116, 1997.

CASTRO-ALAMANCOS MA AND CONNORS BW. Cellular mechanisms of the augmenting response: short-term plasticity in a thalamocortical pathway. *J Neurosci* 16: 7742–7756, 1996.

CHIAIA NL, RHOADES RW, BENNETT-CLARKE CA, FISH SE, AND KILLACKEY HP. Thalamic processing of vibrissal information in the rat. I. Afferent input to the medial ventral posterior and posterior nuclei. *J Comp Neurol* 314: 201–216, 1991.

CHMIELOWSKA J, CARVELL GE, AND SIMONS DJ. Spatial organization of thalamocortical and corticothalamic projection systems in the rat SmI barrel cortex. *J Comp Neurol* 285: 325–338, 1989.

DEMPSEY EW AND MORISON RS. The electrical activity of a thalamocortical relay system. *Am J Physiol* 138: 283–296, 1943.

DESCHENES M, VEINANTE P, AND ZHANG ZW. The organization of corticothalamic projections: reciprocity versus parity. *Brain Res Brain Res Rev* 28: 286–308, 1998.

DIAMOND IT. Parellel pathways in the auditory, visual and somatic systems. In: *Somatosensory Integration in the Thalamus*, edited by Macchi G, Rustioni A, and Spreafico R. Amsterdam: Elsevier, 1983, p. 251–272.

DIAMOND ME AND ARMSTRONG-JAMES M. Role of parallel sensory pathways and cortical columns in learning. *Concepts Neurosci* 3: 55–78, 1992.

DIAMOND ME, ARMSTRONG-JAMES M, BUDWAY MJ, AND EBNER FF. Somatic sensory responses in the rostral sector of the posterior group (POm) and in the ventral posterior medial nucleus (VPM) of the rat thalamus: dependence on the barrel field cortex. *J Comp Neurol* 319: 66–84, 1992a.

DIAMOND ME, ARMSTRONG-JAMES M, AND EBNER FF. Somatic sensory responses in the rostral sector of the posterior group (POm) and in the ventral posterior medial nucleus (VPM) of the rat thalamus. *J Comp Neurol* 318: 462–476, 1992b.

FANSELOW EE AND NICOLELIS MAL. Behavioral modulation of tactile responses in the rat somatosensory system. *J Neurosci* 19: 7603–7616, 1999.

FRIEDBERG MH, LEE SM, AND EBNER FF. Modulation of receptive field properties of thalamic somatosensory neurons by the depth of anesthesia. *J Neurophysiol* 81: 2243–2252, 1999.

GHAZANFAR AA AND NICOLELIS MA. Spatiotemporal properties of layer V neurons of the rat primary somatosensory cortex. *Cereb Cortex* 9: 348–361, 1999.

GOTTLIEB JP AND KELLER A. Intrinsic circuitry and physiological properties of pyramidal neurons in rat barrel cortex. *Exp Brain Res* 115: 47–60, 1997.

HOOGLAND PV, WELKER E, AND VAN DER LOOS H. Organization of the projections from barrel cortex to thalamus in mice studied with Phaseolus vulgaris-leucoagglutinin and HRP. *Exp Brain Res* 68: 73–87, 1987.

HUANG W, ARMSTRONG-JAMES M, REMA V, DIAMOND ME, AND EBNER FF. Contribution of supragranular layers to sensory processing and plasticity in adult rat barrel cortex. *J Neurophysiol* 80: 3261–3271, 1998.

ITO M. Processing of vibrissa sensory information within the rat neocortex. *J Neurophysiol* 54: 479–490, 1985.

KELLER A. Synaptic organization of the Barrel cortex. *Cereb Cortex* 11: 221–262, 1995.

KIM U AND EBNER FF. Barrels and septa: separate circuits in rat barrel field cortex. *J Comp Neurol* 408: 489–505, 1999.

KLEINFELD D, BERG RW, AND O'CONNOR SM. Anatomical loops and their electrical dynamics in relation to whisking by rat. *Somatosens Mot Res* 16: 69–88, 1999.

KORALEK KA, JENSEN KF, AND KILLACKEY HP. Evidence for two complementary patterns of thalamic input to the rat somatosensory cortex. *Brain Res* 463: 346–351, 1988.

LARKUM ME, ZHU JJ, AND SAKMANN B. A new cellular mechanism for coupling inputs arriving at different cortical layers. *Nature* 398: 338–341, 1999.

LU SM AND LIN RC. Thalamic afferents of the rat barrel cortex: a light- and electron-microscopic study using Phaseolus vulgaris leucoagglutinin as an anterograde tracer. *Somatosens Mot Res* 10: 1–16, 1993.

MOORE CI AND NELSON SB. Spatio-temporal subthreshold receptive fields in the vibrissa representation of rat primary somatosensory cortex. *J Neurophysiol* 80: 2882–2892, 1998.

MOORE CI, NELSON SB, AND SUR M. Dynamics of neuronal processing in rat somatosensory cortex. *Trends Neurosci* 22: 513–520, 1999.

NICOLELIS MAL, BACCALA LA, LIN RCS, AND CHAPIN JK. Sensorimotor encoding by synchronous neural ensemble activity at multiple levels of the somatosensory system. *Science* 268: 1353–1358, 1995.

NICOLELIS MA AND CHAPIN JK. Spatiotemporal structure of somatosensory responses of many-neuron ensembles in the rat ventral posterior medial nucleus of the thalamus. *J Neurosci* 14: 3511–3532, 1994.

SHERMAN SM AND GUILLERY RW. Functional organization of thalamocortical relays. *J Neurophysiol* 76: 1367–1395, 1996.

SHIMEGI S, ICHIKAWA T, AKASAKI T, AND SATO H. Temporal characteristics of response integration evoked by multiple whisker stimulations in the barrel cortex of rats. *J Neurosci* 19: 10164–10175, 1999.

SIMONS DJ. Response properties of vibrissa units in rat SI somatosensory neocortex. *J Neurophysiol* 41: 798–820, 1978.

SIMONS DJ. Temporal and spatial integration in the rat SI vibrissa cortex. *J Neurophysiol* 54: 615–635, 1985.

SIMONS DJ, CARVELL GE, HERSHEY AE, AND BRYANT DP. Responses of barrel cortex neurons in awake rats and effects of urethane anesthesia. *Exp Brain Res* 91: 259–272, 1992.

SOSNIK R, HAIDARLIU S, AND AHISSAR E. Temporal frequency of whisker movement. I. Representations in brain stem and thalamus. *J Neurophysiol* 86: 339–353, 2001.

STAIGER JF, KOTTER R, ZILLES K, AND LUHMANN HJ. Laminar characteristics of functional connectivity in rat barrel cortex revealed by stimulation with caged-glutamate. *Neurosci Res* 37: 49–58, 2000.

SWADLOW HA. Efferent neurons and suspected interneurons in S-1 vibrissa cortex of the awake rabbit: receptive fields and axonal properties. *J Neurophysiol* 62: 288–308, 1989.

SWADLOW HA. Influence of VPM afferents on putative inhibitory interneurons in S1 of the awake rabbit: evidence from cross-correlation, microstimulaton, and latencies to peripheral sensory stimulation. *J Neurophysiol* 73: 1584–1599, 1995.

SWADLOW HA. Descending corticofugal neurons in layer 5 of rabbit S1: evidence for potent corticocortical, but not thalamocortical, input. *Exp Brain Res* 130: 188–194, 2000.

SWADLOW HA AND GUSEV AG. The influence of single VB thalamocortical impulses on barrel columns of rabbit somatosensory cortex. *J Neurophysiol* 83: 2802–2813, 2000.

WELKER WI. Analysis of sniffing of the albino rat. *Behaviour* 22: 223–244, 1964.

WILLIAMS MN, ZAHM DS, AND JACQUIN MF. Differential foci and synaptic organization of the principal and spinal trigeminal projections to the thalamus in the rat. *Eur J Neurosci* 6: 429–453, 1994.

WOOLSEY TA. Barrels, vibrissae and topographic representations. In: *Encyclopedia of Neuroscience*, edited by Adelman G and Smith B. Amsterdam: Elsevier, 1997, vol. I, p. 195–199.

ZHU JJ AND CONNORS BW. Intrinsic firing patterns and whisker-evoked synaptic responses of neurons in the rat barrel cortex. *J Neurophysiol* 81: 1171–1183, 1999.