Circuit Dynamics and Coding Strategies in Rodent Somatosensory Cortex

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Pinto, David J., Joshua C. Brumberg, and Daniel J. Simons. Circuit dynamics and coding strategies in rodent somatosensory cortex. *J. Neurophysiol.* 83: 1158–1166, 2000. Previous experimental studies of both cortical barrel and thalamic barreloid neuron responses in rodent somatosensory cortex have indicated an active role for *barrel circuitry* in processing thalamic signals. Previous modeling studies of the same system have suggested that a major function of the barrel circuit is to render the *response magnitude* of barrel neurons particularly sensitive to the *temporal distribution* of thalamic input. Specifically, thalamic inputs that are initially synchronous strongly engage recurrent excitatory connections in the barrel and generate a response that briefly withstands the strong damping effects of inhibitory circuitry. To test this experimentally, we recorded responses from 40 cortical barrel neurons and 63 thalamic barreloid neurons evoked by whisker deflections varying in velocity and amplitude. This stimulus evoked thalamic response profiles that varied in terms of both their magnitude and timing. The magnitude of the thalamic population response, measured as the average number of evoked spikes per stimulus, increased with both deflection velocity and amplitude. On the other hand, the degree of initial synchrony, measured from population peristimulus time histograms, was highly correlated with the velocity of whisker deflection, deflection amplitude having little or no effect on thalamic synchrony. Consistent with the predictions of the model, the cortical population response was determined largely by whisker velocity and was highly correlated with the degree of initial synchrony among thalamic neurons ($R^2 = 0.91$), as compared with the average number of evoked thalamic spikes ($R^2 = 0.38$). Individually, the response of nearly all cortical cells displayed a positive correlation with deflection velocity; this homogeneity is consistent with the dependence of the cortical response on local circuit interactions as proposed by the model. By contrast, the response of individual thalamic neurons varied widely. These findings validate the predictions of the modeling studies and, more importantly, demonstrate that the mechanism by which the cortex processes an afferent signal is inextricably linked with, and in fact determines, the saliency of neural codes embedded in the thalamic response.

INTRODUCTION

Deciphering neural codes and discerning the structure of information in neural signals are key steps toward developing a more complete understanding of brain function. The predominant view has been that neurons encode information in terms of response magnitude, with a "preferred" input signal being defined as one that elicits the most spikes (Barlow 1953; Hubel and Weisel 1968). Another viewpoint maintains that information is better represented by the arrival times or temporal distribution of individual spikes (Alonso et al. 1996; Rieke et al. 1997). Regardless of the strategy, implicit in ascribing a particular code to a neural signal is the assumption that the neurons or networks receiving that code can decipher it. Surprisingly, there are few studies that deal directly with this issue (see, however, Burton and Sinclair 1993; McClurkin et al. 1991; Richmond et al. 1987).

Because of its anatomic and functional organization, the rodent somatosensory system is particularly well-suited for examining the encoding of stimuli by neural responses at multiple processing stages. In particular, layer IV of the primary somatosensory cortex contains anatomically distinct neuronal networks, called barrels, that correspond in one-to-one fashion to individual whiskers on the contralateral face (Welker 1976; Woolsey and van der Loos 1970). Neurons within a barrel are also related functionally, responding most robustly to deflection of the same principal whisker. In addition, evidence suggests that barrels receive input largely from their homologous barreloid, clusters of thalamic neurons also in one-to-one correspondence with facial whiskers, and that most neurons within a barreloid project to the corresponding barrel (Land et al. 1995; Swadlow 1995; Swadlow and Hicks 1996). Finally, receptive fields of neurons in thalamic barreloids and cortical barrels are such that both sets of neurons respond robustly to the same types of stimuli, allowing for a straightforward comparison of response properties.

In the present study, single-unit activity is recorded from either thalamic or cortical neurons in response to whisker deflections that differ in velocity and amplitude. Responses are measured in terms of both magnitude and temporal distribution to determine which measure provides the better representation of these deflection parameters at each processing stage.

A second question concerns the mechanism by which cortical barrels decipher the signal transmitted by the thalamus. Previous experimental studies of response properties of both barrel and barreloid neurons have indicated an active role for *barrel circuitry* in processing thalamic signals (Simons and Carvell 1989). Moreover, previous modeling studies of the same system have suggested that a major function of the barrel circuit is to render the *response magnitude* of barrel neurons particularly sensitive to the *temporal distribution* of thalamic input (Kyriazi and Simons 1993; Pinto et al. 1996). In the present study, we investigated whether real barrel neurons display the same sensitivity, suggesting that the dynamics and analysis of the model's mechanism apply equally well toward understanding real barrel circuits. Indeed, our results indicate that cortical neurons are more responsive to whisker velocity

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and that this is a reflection of their sensitivity to the temporal distribution of thalamic inputs.

METHODS

Preparation

Fifteen adult female rats weighing 250–350 g (Sprague-Dawley strain, Zivic Miller, Zelienople, PA) were used in the study. Details of the surgical procedure have been presented elsewhere (Simons and Carvell 1989). Briefly, animals were initially anesthetized using meto-fane (methoxyflurane, Pitman-Moore, Mundelein, IL) and maintained with 1.5–2.0% halothane anesthesia throughout the surgical procedure. A small area of skull and dura overlying either the barrel cortex or the ventral posterior medial nucleus of the thalamus (VPM) was removed to allow for single-unit recordings. Core body temperature was maintained at 37°C by a servo-controlled heating blanket (Harvard Apparatus, Cambridge, MA). For neuronal recordings, halothane was discontinued, and the rat was subsequently maintained in a lightly narcotized and sedated state by means of an intravenous infusion of fentanyl (Sublimaze, Janssen Pharmaceuticals; $5\text{–}10 \ \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$). Rats were immobilized with pancuronium bromide ($1.6 \ \text{mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$) and artificially respired ($\sim$90 breaths/min) using a positive pressure respirator. The condition of the rat was monitored throughout the experiment by assessing the electroencephalogram, mean arterial pressure, arterial pulse rate, pupillary reflex, perfusion of glabrous skin, and tracheal airway pressure. Experiments were terminated with an intravenously injected overdose of pentobarbital sodium if any of the above indicators could not be maintained within normal physiological ranges.

Electrophysiology

Extracellular single-unit recordings were obtained using double-barrel glass micropipettes (Simons and Land 1987). These were advanced in 4-μm steps through either the barrel field, perpendicular to the pial surface, or through VPM, in the dorsal/ventral plane of the Paxinos and Watson atlas (Paxinos and Watson 1982). One barrel was filled with 3 M NaCl ($\sim$1 μm tip diameter; 5–10 MΩ impedance at 135 Hz) and was used for unit recordings. The other barrel was filled with 10% wt/vol horseradish peroxidase (HRP) in 0.5 M Tris-HCl to mark recording sites and/or the end of recording tracks.

Whiskers on the contralateral mystacial pad were stimulated manually during electrode advancement to ascertain when the electrode entered into the whisker representation. Extracellularly recorded single units were determined by spike amplitude and waveform criteria using a digital oscilloscope. All of the thalamic data were obtained from spikes with waveforms that were initially negative, consistent with signals thought to emanate from cell bodies (see Simons and Carvell 1989). In the cortex, two types of neurons can be distinguished on the basis of the spike waveform, regular spiking units and fast spiking units (Kyriazi et al. 1996). In this study, only regular spiking units were encountered. Recordings were obtained from 63 thalamic barreloid neurons and 40 cortical barrel neurons.

Experiments were terminated using an overdose of pentobarbital, administered intravenously. Rats were perfused for HRP and cyto-chrome oxidase histochemistry. For cortical experiments, the right hemisphere was sectioned tangential to the pial surface overlying the barrel field. Alternate sections were processed for either HRP or cytochrome oxidase histochemistry (Simons and Land 1987). Thalami were sectioned in the coronal plane. Electrode tracks and HRP spots were used to verify that recordings originated from either a cortical barrel or from VPM; no attempt was made to identify individual thalamic barreloids histologically.

Stimulus control and data acquisition

The principal whisker (PW) was determined by manually deflecting whiskers while listening to an audio monitor; the whisker that elicited the strongest response was defined as the PW. The PW was then deflected using an electromechanical stimulator (Simons 1983), controlled by a laboratory computer (LSI 11/73, Digital Equipment). Sequential interspike intervals were measured with a resolution of 100 μs.

One whisker stimulator was modified and calibrated for different velocity and amplitude deflections before the start of the experiments. The actual motion of the stimulator, and hence of the whisker, was measured by deflecting it toward a light detecting circuit and examining the light level profile. Motion velocity was calculated using the highest amplitude ramp for each velocity and was computed as the average rate of rise over the entire range of deflection. Angular amplitude was calculated as the Arctan of the deflection distance divided by the distance of the stimulator from the base of the whisker (5 mm). To avoid mechanical resonance at high velocity, the modified stimulator was made shorter than standard stimulators used previously (Simons 1983); consequently, with this stimulator, whiskers could be deflected in only one direction. To maintain an angular deflection range consistent with previously used protocols, the stimulator was placed closer than normal to the base of the whisker (5 vs. 10 mm), and the whisker was deflected a shorter linear distance. The necessary modifications to both the stimulator and its controlling electronic circuitry produced a motion profile characterized by a sharper ramp onset as compared with the motion of the standard stimulator.

Stimulus protocol

Once the PW was determined for a given neuron, the whisker was deflected in eight directions, specified by 45° increments, to determine the deflection angle that evoked the most spikes; this was taken as the unit's preferred direction (Simons and Carvell 1989) (but see DISCUSSION). The PW was then deflected with a battery of 15 ramp-and-hold stimuli, systematically varied over five onset/offset velocities (210, 170, 145, 130, and 70 mm/s) and three amplitudes (7.4°/650 μm, 4.5°/390 μm, and 2.6°/225 μm). These values were centered around the standard deflection parameters used in our previous studies (e.g., Simons and Carvell 1989). They were chosen because we thought it likely that these stimuli would evoke suprathreshold responses that varied in both magnitude and temporal distribution. Each stimulus was repeated 10 times, with amplitude and velocity parameters randomized, and with an interstimulus interval of 2–3 s. The protocol was performed once with the whisker deflected in the cell's preferred direction, and once with the whisker deflected caudally, regardless of the cell's preferred direction, to provide a common stimulus for all neurons examined. To ensure accurate whisker motion, especially at low deflection amplitudes, the stimulator was positioned to immediately engage the whisker at stimulus onset. For this reason, only the responses produced by ramp onset are considered here.

Data analysis

Spike data from each of the 15 deflections were accumulated into peristimulus time histograms (PSTHs) summed over the sampled population. This was done separately for deflections in the caudal versus preferred direction for a total of 30 population response profiles in both thalamus and cortex. Histograms had binwidths of 100 μs. All response measures were computed from spikes occurring within a 25-ms response window beginning with the initial rise above baseline of the population response. This initial rise occurred within 2–4 ms of whisker deflection onset, depending on the stimulus. The 25-ms measurement window corresponds to the duration of evoked excitatory activity in either cortex or thalamus due to ramp-and-hold whisker deflections (Simons and Carvell 1989).

Two response measures were calculated. *Total response magni-*

$$TC40 = \frac{40\% \text{ of total spikes}}{\text{Time to produce } 40\%} = \frac{4 \text{ spks}}{4 \text{ ms}}$$

$$TC60 = \frac{6 \text{ spikes}}{8 \text{ ms}} = .75 \text{ spks/ms}$$

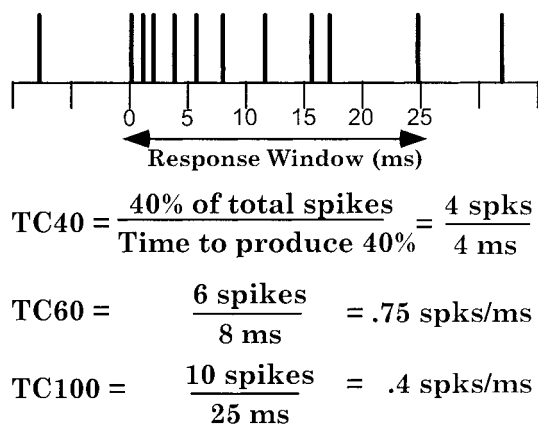$$TC100 = \frac{10 \text{ spikes}}{25 \text{ ms}} = .4 \text{ spks/ms}$$

FIG. 1. Example of measuring response magnitude and temporal contrast in a spike train. Response window is defined as the 25 ms beginning with the onset of activity due to whisker deflection (Simons and Carvell 1989). Response magnitude is the total number of spikes within the response window, which in this example is 10 spikes. Measures of temporal contrast are calculated as the average firing rate over time windows corresponding to the generation of fixed percentages of the response magnitude. The figure illustrates temporal contrast calculations over 40% (TC40), 60% (TC60), and 100% (TC100) of the total response.

tude is measured as the average number of spikes comprising the PSTH over the entire 25-ms response; hereafter it is equivalently referred to simply as response magnitude. *Temporal contrast* is a set of measures we devised to quantify the level of initial synchrony in the distribution of the population response; it is the average firing rate measured over specific initial segments of the 25-ms response. The duration of these initial segments are determined by the time required for the sampled population to generate a fixed proportion of the total response magnitude. Unlike measurement windows determined by a fixed interval of time or a set number of spikes, our measure of temporal contrast allows for comparison among responses that vary both in terms of their time course and in terms of their total activity.

As a specific example, temporal contrast measured over an interval corresponding to the first 40% of the total response magnitude (TC40) is defined as 40% of the total response magnitude divided by the amount of time (measured in 100-μs units) required to generate the *first* 40% of the total response magnitude. Temporal contrast over other response proportions are defined similarly (see Fig. 1 for an illustration of the measurement method). The term "temporal contrast" was chosen because responses having high values of the measure consist of many spikes occurring within a short period of time following response onset. This is reflected by a PSTH profile that initially changes very rapidly, i.e., it exhibits high *contrast* relative to the immediately preceding baseline (cf. Fig. 4). In the simulations on which the present experiments were based, such response profiles were represented by input triangles having a steep initial slope. Results are presented first using TC40 because our preliminary analyses indicated that this was a good measure of initial synchrony in the thalamic response. Interspike intervals from individual neurons were not considered because they generated, on average, <2 spikes per stimulus.

In this study, no attempt was made to distinguish between rapidly and slowly adapting categories of neurons. Although the majority of primary afferent neurons display slowly adapting responses (Lichtenstein et al. 1990), most neurons in the thalamus, and to an even greater extent in the cortex, have phasic responses, probably reflecting central inhibition. A subsequent report, describing responses of trigeminal ganglion neurons to the same stimuli used here, will address the issue of velocity and amplitude coding in rapidly and slowly adapting pathways in the whisker-to-barrel system.

RESULTS

Cortical representations of deflection amplitude and velocity

A central finding in the present study is that, for the ranges examined, the cortical response is significantly more dependent on whisker deflection velocity than amplitude. This is the case regardless of whether the response is measured in terms of total response magnitude or in terms of temporal contrast. Figure 2 presents 15 population PSTHs from the 40 cortical units studied. For a given amplitude, there is a clear increase in response magnitude as velocity increases. For a given velocity, deflection amplitude has little effect on the cortical response. Data in Fig. 2 are taken from caudal deflections. The same relationship holds for deflections in each unit's preferred direction. These data are quantified in Fig. 3.

A two-way ANOVA demonstrated that both velocity and amplitude have a significant effect on the response magnitude of the cortical population for both preferred and caudal deflections ($P < 0.05$; Fig. 3, *A* and *B*). However, amplitude has an effect only for the highest and lowest velocities. Linear regression analyses show that deflection velocity is a stronger determinant of response magnitude [$R^2 = 0.87$ (caud), 0.81 (pref)] than is deflection amplitude [$R^2 = 0.07$ (caud), 0.04 (pref)]. Moreover, a threefold change in deflection amplitude produces at *best* a change of ~0.30 spikes/stimulus in the cortical response. A threefold change in velocity, on the other hand, produces at *worst* a change of ~0.60 spikes/stimulus. From this it can be concluded that, over the ranges examined, the response magnitude of cortical neurons is more sensitive to whisker deflection velocity than amplitude. Figure 3, *C* and *D,* shows that, like response magnitude, temporal contrast at 40% (TC40, see METHODS) better represents stimulus velocity than amplitude. As expected, response magnitudes were larger for preferred direction deflections. Interestingly, however, correlations between deflection parameters (velocity, amplitude) and response measures (response magnitude, temporal contrast) were virtually identical regardless of whether the stimulus was applied in the unit's preferred angle or caudally.
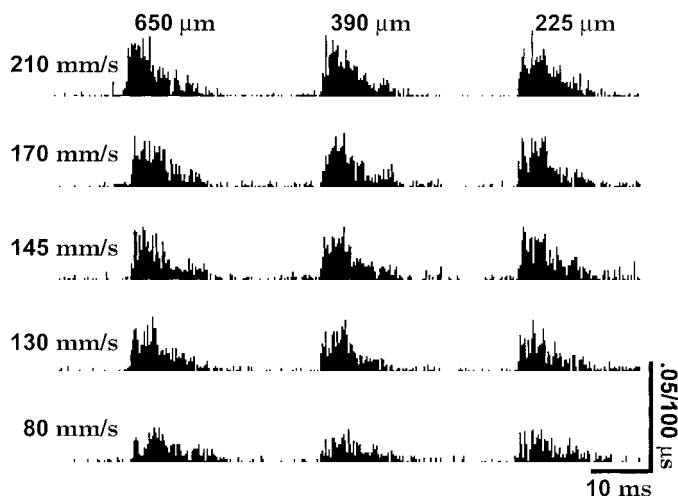

FIG. 2. Cortical population peristimulus time histograms (PSTHs). PSTHs represent the averaged response of 40 regular-spiking cortical neurons to caudal whisker deflections at 3 amplitudes and 5 velocities. Each stimulus was repeated 10 times in random sequence, for a total of 400 deflections per histogram. Vertical axis shows the probability that a spike will occur in each 100-μs bin.
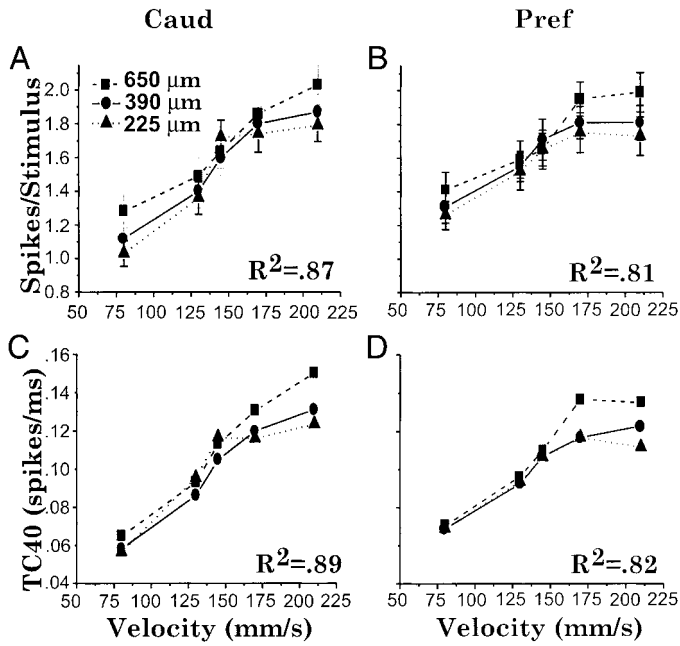
Caud

Pref

FIG. 3. Dependence of cortical response measures on deflection parameters. Quantitative data are shown for the same neurons as presented in Fig. 2. *A* and *B*: 15 data points represent average response magnitudes for whisker deflections at 5 velocities and 3 amplitudes (symbol shapes) in the caudal and preferred direction, respectively. The preferred direction was determined using a multidirectional stimulator deflected at ~125 mm/s and 5.6° (just above middle amplitude). Lines connect points corresponding to deflections of the same amplitude. *C* and *D*: same responses measured in terms of temporal contrast over 40% of the total response (TC40, see METHODS). R^2 values were calculated by collapsing the data across amplitudes.

Thalamic representations of deflection amplitude and velocity

With velocity such a strong determinant of the cortical response, the next question is how velocity is represented in the response of thalamic barreloid neurons. Figure 4 presents population PSTHs from the 63 thalamic neurons studied. Qualita-
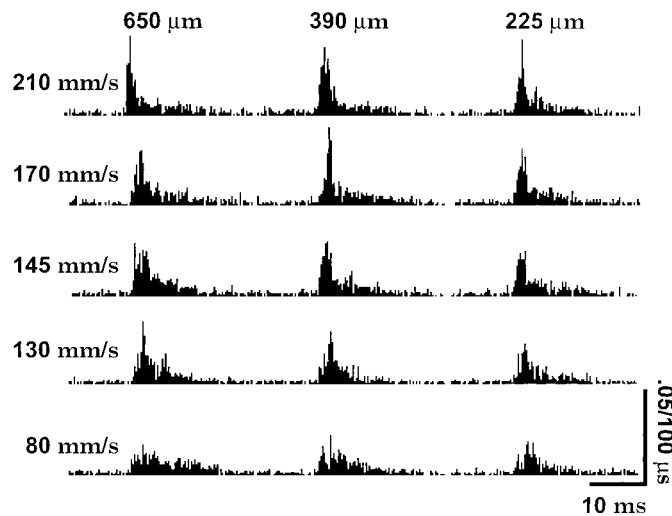

FIG. 4. Thalamic population PSTHs. PSTHs represent averaged response of 63 TCUs to caudal whisker deflections at 3 amplitudes and 5 velocities. Each stimulus was repeated 10 times in random sequence, for a total of 630 deflections per histogram. Vertical axis shows the probability that a spike will occur in each 100-μs bin.
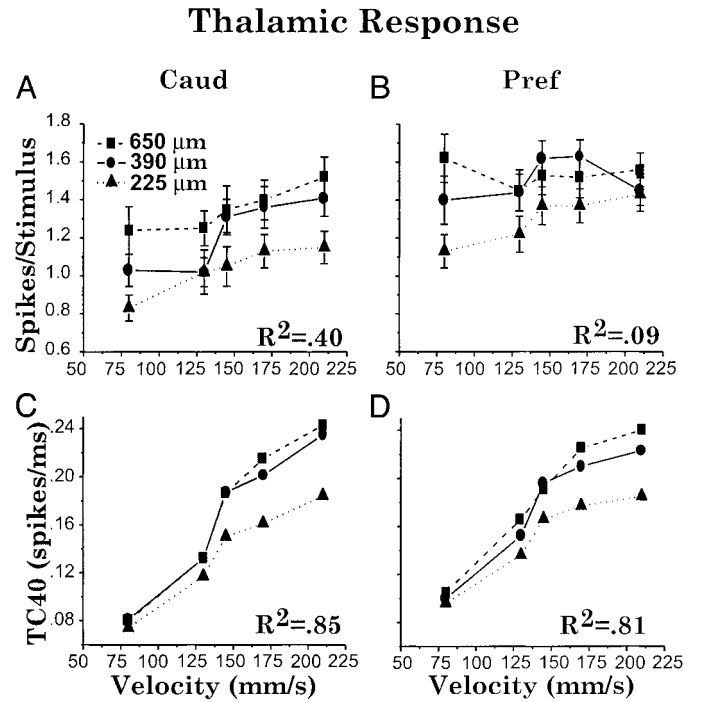
Thalamic Response

Caud

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FIG. 5. Dependence of thalamic response measures on deflection parameters. Quantitative data are shown for the same neurons as presented in Fig. 4. *A* and *B*: 15 data points represent average response magnitudes for whisker deflections at 5 velocities and 3 amplitudes (symbol shapes) in the caudal and preferred direction, respectively. The preferred direction was determined as in Fig. 3. Lines connect points corresponding to deflections of the same amplitude. *C* and *D*: same responses measured in terms of temporal contrast over 40% of the total response (TC40, see METHODS). R^2 values were calculated by collapsing the data across amplitudes.

tively, it can be seen that response magnitude remains fairly constant over the entire stimulus battery. However, the initial rate of change of the histograms clearly increases with increasing deflection velocity. Figure 5, *A* and *B,* quantifies the relationship between stimulus parameters and thalamic response magnitude for deflections in the caudal and preferred directions, respectively. Using a two-way ANOVA, both velocity and amplitude were found to have a significant effect on the magnitude of the thalamic response for both preferred and caudal deflections ($P < 0.05$). Examining the data more closely, it can be seen that deflection amplitude affects response magnitude at all velocities for caudal deflections. Preferred direction responses exhibit less sensitivity to velocity or amplitude due to the greater heterogeneity of single-cell responses at the preferred angle (see Fig. 8). Linear regression analyses show that deflection velocity has some effect on response magnitude [$R^2 = 0.40$ (caud), 0.09 (pref)], as does deflection amplitude [$R^2 = 0.47$ (caud), 0.41 (pref)]. Neither amplitude nor velocity, however, affect thalamic response magnitude to the same extent as velocity does in the cortex. In particular, in the thalamus, a threefold change in either velocity or amplitude produces at best a change of ~0.30 spikes/stimulus.

Figure 5, *C* and *D,* shows the relationship between stimulus parameters and thalamic TC40. Linear regression analysis shows that TC40 correlates more strongly with deflection velocity [$R^2 = 0.85$ (caud), 0.81 (pref)] than amplitude [$R^2 = 0.06$ (caud), 0.09 (pref)]. Deflection amplitude affects TC40

only within a limited range, at higher velocities and at the lowest deflection amplitude. Taken together with Fig. 5, *A* and *B,* it can be concluded that, over the range examined, the temporal contrast of the thalamic response provides a better reflection of whisker deflection velocity than does response magnitude.

Relationship between thalamic and cortical responses

The preceding analyses demonstrate that the cortical population response, measured in terms of either response magnitude or temporal contrast, is more dependent on deflection velocity than amplitude. Because thalamic barreloid neurons provide the major source of afferent input to cortical barrels, the neural code in the thalamus that best represents deflection velocity is likely to be the one to which the cortical circuit is most sensitive.

Figure 6 reexamines the data to illustrate directly the relationship between thalamic and cortical responses. As expected, the cortical response is better predicted by thalamic TC40 than by thalamic response magnitude. This is the case for both response magnitude and TC40 in the cortex (Fig. 6, *B* and *D*), at both preferred and caudal directions (open vs. filled symbols). Linear regression analyses show a weak correlation between either cortical response measure and thalamic response magnitude (Fig. 6, *A* and *C*). However, even the strongest correlation between thalamic response magnitude and the cortical response ($R^2 = 0.59$, Fig. 6*A,* filled symbols) is considerably less than the weakest correlation with thalamic TC40 ($R^2 = 0.89$, Fig. 6*D,* filled symbols). Thus as a measure of thalamic activity, temporal contrast not only provides a strong

reflection of whisker deflection velocity, but also a strong prediction of the cortical response.

As explained in METHODS, temporal contrast can be calculated for different proportions of the response magnitude. To examine more closely the relationships among deflection velocity, thalamic temporal contrast, and the subsequent cortical response, the same linear regression analysis was repeated for temporal contrast measures in cumulative 10% increments along the thalamic response (TC10–TC100, see METHODS). Because both cortical response magnitude and cortical temporal contrast yield similar results, only the former measure is considered here as the dependent variable. Regression lines and R^2 values were computed for data obtained from caudal deflections, from preferred direction deflections, and from the combined data. The results are presented in Fig. 7.

Figure 7*A* presents R^2 values obtained from linear regression analysis between each measure of thalamic temporal contrast and the velocity of whisker deflection, computed as in Fig. 5, *C* and *D.* The largest R^2 values are obtained using temporal contrast measured at 30 and 40% of the response magnitude. Figure 7*B* presents R^2 values obtained from regression analysis between each measure of thalamic temporal contrast and the cortical response magnitude, computed as in Fig. 6*B.* The thalamic response measures that exhibit the highest R^2 value in relation to the cortical response are again temporal contrast measured at 30 and 40%. Figure 7*C* illustrates the interesting result that, depending on velocity, 40% of the thalamic response is generated within 2–7 ms after the arrival of the first signal in the thalamus. Combined with the data from Fig. 7, *A* and *B,* this leads to the conclusion that the average firing rate of the thalamic population during the first 2–7 ms of the response provides the best reflection of whisker velocity in the thalamus and also the best prediction of the subsequent response in the cortex.

Relative importance of timing versus magnitude

The measures of response magnitude and temporal contrast are interdependent in that temporal contrast is computed as a proportion of the response magnitude divided by the amount of time required to generate that proportion. In Fig. 8, we consider the temporal and magnitude components separately to examine how each contributes to the correlation of temporal contrast with deflection velocity in both thalamus and cortex. Figure 8, *A* and *B,* presents the data in terms of the magnitude component of TC40; these data are equivalent to those of Fig. 5, *A* and *B,* and Fig. 3, *A* and *B,* respectively, with the ordinate scaled by 40%. Figure 8, *C* and *D,* presents the data in terms of the temporal component, expressed as the reciprocal of the time required to generate 40% of the response. This metric was used so that the ordinate values, derived as in Fig. 7*C,* increase linearly, allowing for straightforward comparison with the graphs in Fig. 8, *A* and *B.* In the thalamus, deflection velocity is well-represented by the temporal component (Fig. 8*C*) but poorly by the magnitude component (Fig. 8*A*); the converse is true in the cortex (Fig. 8, *B* and *D*). Hence, in the thalamus, temporal contrast is determined largely by the timing of the response, whereas in the cortex it is clearly dominated by the magnitude.
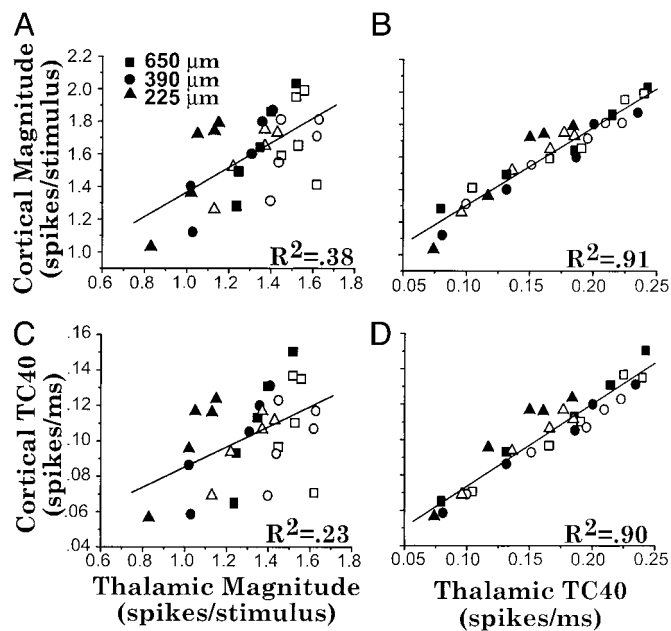

FIG. 6.   Relationship between thalamic and cortical responses. The 30 data points in each graph represent deflections at 5 velocities, 3 amplitudes, in both caudal (filled symbols) and preferred (open symbols) directions. Symbol shapes correspond to deflections using the same amplitude. *A* and *B*: relationship between cortical response magnitude and the thalamic response measured as response magnitude or temporal contrast at 40% (TC40, see METHODS), respectively. *C* and *D*: same relationship with the cortical response measured using TC40. R^2 values were calculated collapsing across both amplitude and direction.
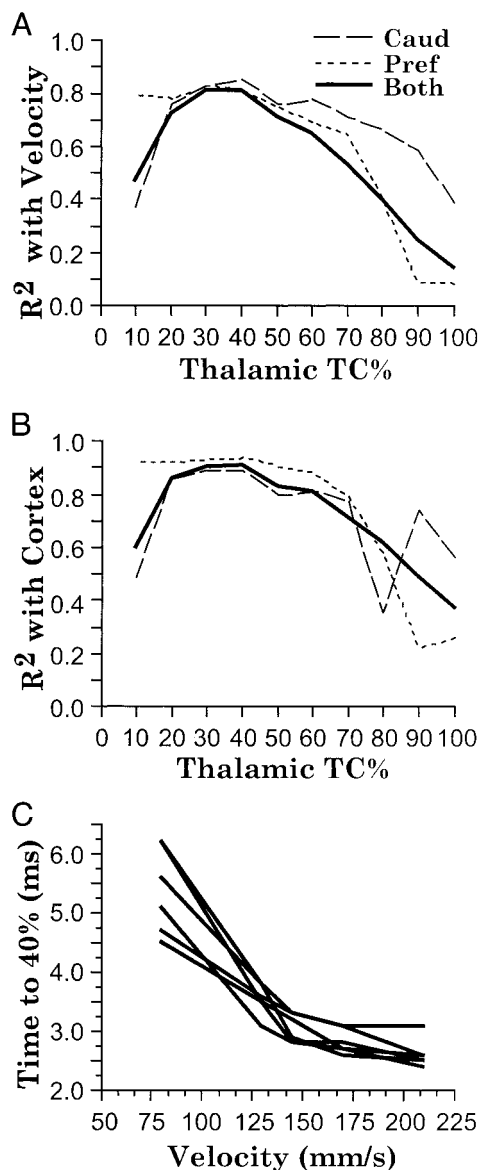
FIG. 7. Comparison between measures of temporal contrast in the thalamus. Thalamic responses were quantified using measures of temporal contrast in cumulative 10% increments along the total response magnitude (see METHODS). For each measure, R^2 values were calculated in relationship to either deflection velocity (*A*) or cortical response magnitude (*B*). Values were computed using responses to caudal deflections (– – –), preferred direction deflections (· · ·), and both sets combined (—). The time required to generate 40% of the total response for each stimulus condition is shown in *C;* the 6 lines represent data from deflections at 3 amplitudes in both caudal and preferred directions.

Neurons versus populations

The analyses presented thus far have focused on explaining the response of cortical neurons in terms of the entire population of the sampled thalamic neurons. Another possibility is that cortical sensitivity to deflection velocity can be explained in terms of thalamic responses measured at the level of individual neurons or subsets of neurons. For instance, it might be that deflection velocity is best represented in the interspike intervals of single thalamic neurons. The fact that thalamic neurons usually produce no more than a single spike per deflection, however, makes this particular coding strategy un-

likely. A more likely possibility is suggested by the fact that the response magnitude of the thalamic population response is affected, albeit slightly, by deflection velocity (Fig. 5, *A* and *B*). This might be explained by the existence of a subpopulation of thalamic neurons that robustly encode deflection velocity in terms of their individual response magnitudes. A disproportionate influence of these neurons on barrel circuitry would provide an alternative to temporal contrast for explaining the cortical response.

Figure 9 explores the possibility of such a thalamic code based on the response magnitude of single neurons. For each thalamic neuron we computed the average response to each stimulus condition for caudal and preferred deflections. These data were used to compute regression lines on a neuron-by-neuron basis between deflection velocity and response magnitude (Fig. 9*A*, as in Fig. 5, *A* and *B*). The slopes and R^2 values of the lines were also compiled (Fig. 9*B*). The same analyses were performed for the cortical neurons (Fig. 9, *C* and *D*). The most striking aspect of the thalamic data are the heterogeneity among individual units. Whereas response magnitudes of most neurons are positively correlated with velocity [45 of 63, 71% (caud); 34 of 63, 54% (pref)], a significant proportion exhibit a negative relationship [18 of 63, 29%(caud); 29 of 63, 46% (pref)]. At most, two units have R^2 values that reflect velocity as well as the measure of population temporal contrast (Fig. 9*B*, —, caud; · · ·, pref). Interestingly, whisker deflection in the preferred direction (□) is not associated with a reduction in heterogeneity nor an increase in the likelihood that individual units will show strong, positive correlations with velocity. This is consistent with the population data in Fig. 5*B*, wherein the stimulus/response function is actually flatter for preferred direction stimuli.
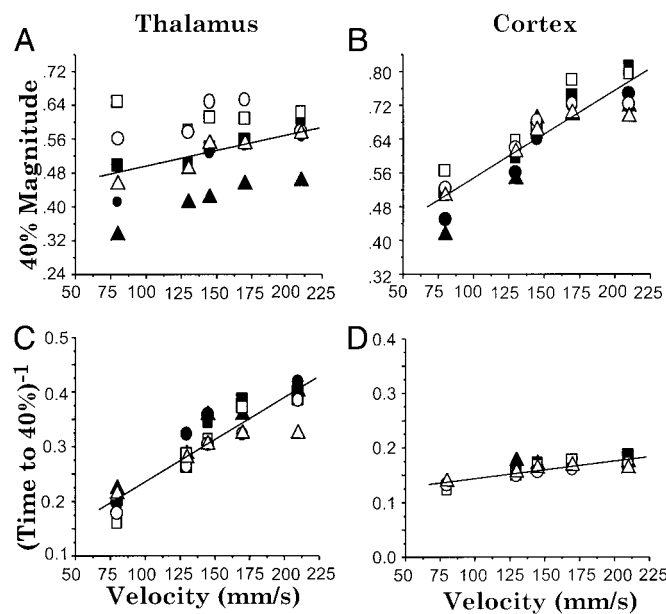

FIG. 8. Importance of magnitude vs. timing in thalamus and cortex. *A* and *B*: relationship between deflection velocity and the magnitude component of the TC40 measure (40% of response magnitude) in thalamus and cortex respectively. *C* and *D*: same relationship in terms of the temporal component of TC40 (time required to generate 40% of the response). The ordinates in *C* and *D* are expressed in reciprocal units of time to linearize the relationship. Symbol shapes correspond to deflection of the same amplitudes in both caudal (filled symbols) and preferred (open symbols) directions as in the previous figures.
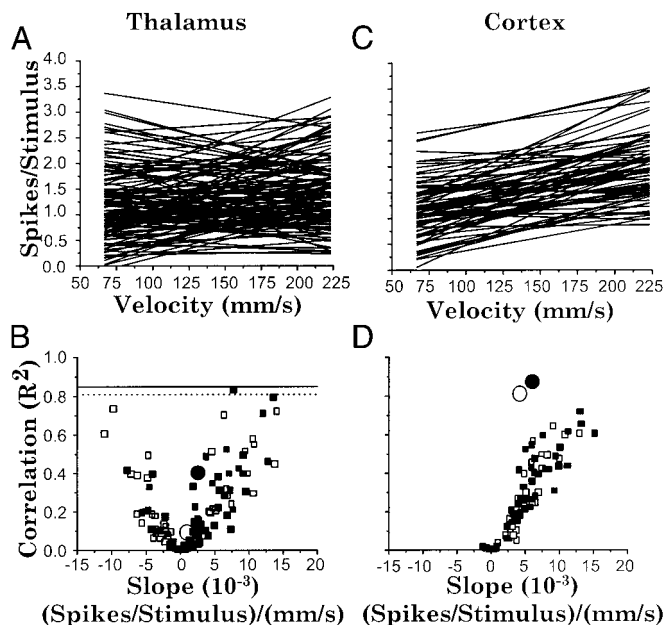
FIG. 9. Dependence of single-cell response magnitude on deflection parameters. *A* and *C*: individual regression lines, computed as in Fig. 3, *A* and *B*, for each of the 63 thalamic and 40 cortical neurons, respectively. Separate lines were computed for deflections in the caudal and preferred direction. *B* and *D*: slopes and R^2 values corresponding to each line in *A* and *C*. Each small square represents the statistics from a single neuron in response to deflections in the caudal (■) and preferred (□) direction. Large circles show the same values obtained from the population response magnitudes in both caudal (●) and preferred (○) directions. The horizontal lines in *B* show the R^2 value obtained from the thalamic response measured in terms of temporal contrast at 40% (—, caudal; ···, preferred).

Nearly one-half of the thalamic neurons displayed a negative relationship between response magnitude and velocity for at least one of the two directions tested. By contrast, virtually *all* of the cortical neurons displayed positive correlations in both directions (Fig. 9, *C* and *D*). If the cortical encoding of velocity indeed reflects the influence of a subpopulation of thalamic neurons that similarly encode deflection velocity in terms of their individual response magnitudes, one would have to conclude that ~50% of thalamic barreloid neurons have little or no influence on responses in the homologous cortical barrel.

DISCUSSION

This study has examined neuronal responses in thalamic barreloids and cortical barrels to whisker deflections varying in amplitude and velocity. Population responses were quantified using two measures of activity: total response magnitude and temporal contrast. Each was investigated for its ability both to encode whisker deflection parameters and, in the thalamus, to predict the subsequent cortical response. Using either measure, cortical neurons were found to encode deflection velocity more robustly than amplitude. In the thalamus, temporal contrast was found to encode velocity more robustly than response magnitude. Accordingly, temporal contrast, more specifically the average firing rate within 2–7 ms of the onset of thalamic activity, best predicted the cortical response. These results confirm the hypothesis, derived from modeling studies, that barrel circuitry is more sensitive to the level of initial synchrony in the thalamic input than to the total input spike count (Pinto et al. 1996).

Several studies have investigated the effects of deflection velocity and amplitude on neural responses in the whisker-to-barrel pathway. Comparisons among findings is somewhat complicated due to differences in the method of whisker stimulation and choice of response measures (for a complete discussion see Pinto 1997). However, findings in the trigeminal nerve (Gibson and Welker 1983; Gottschaldt et al. 1972; Lichtenstein et al. 1990), brain stem (Gottschaldt and Young 1977; Shipley 1974), and thalamus (Hellweg et al. 1977; Ito 1988; Waite 1973) generally indicate that, over ranges even broader than those used here, deflection amplitude and velocity are better represented by response magnitude and timing, respectively. The present results demonstrate that in the cortex, on the other hand, deflection velocity is better represented not by response timing but by response magnitude. Thus barrel circuitry transforms a temporally based thalamic code into a code based on response magnitude. Despite conflicting conclusions, an examination of published data reveals this to be consistent also with previous cortical studies (Hellweg et al. 1977; Ito 1985; Simons 1978).

The choice of deflection parameters used in the present study was based on two considerations. First, and foremost, we wished to evoke thalamic responses that were, on average, suprathreshold for most neurons and that varied in magnitude and initial synchrony, quantified using the temporal contrast measure. Second, the velocity and amplitude ranges were centered around those of our standard deflection protocol to allow for comparisons with previous findings from our laboratory; at least in terms of velocity (125 mm/s), the standard stimulus falls within the range of whisker motion observed during natural whisker deflection (Carvell and Simons 1990). The possibility remains that, outside of the ranges examined, the encoding and transformation of responses between thalamus and cortex may be different from revealed by the present study. For amplitudes greater than those used here, however, data from previous studies suggest that responses in both thalamus and cortex are relatively insensitive to deflection amplitudes up to 42° (Hellweg et al. 1977). On the other hand, stimuli evoking thalamic responses considerably less than 1 spike/stimulus might produce thalamic input that is too sparse to engage the timing-sensitive mechanisms of the barrel circuit. Recent findings, however, using low-frequency sinuisoidal whisker stimulation, indicate that temporal contrast robustly predicts cortical response magnitude even at thalamic response levels considerably lower than those examined here (J. A. Hardings and D. J. Simons, personal communication).

What is a "preferred" stimulus?

Because primary afferent neurons are sensitive to the direction of whisker displacement (Lichtenstein et al. 1990), the responses of central neurons in the whisker-to-barrel pathway are also determined in part by the angular direction in which the whisker is deflected (Simons 1978). In the present study, stimuli were delivered in two different directions for each neuron. Caudal deflections were used to assess directly how thalamic and cortical neurons respond to identical stimuli. Whiskers were also deflected in a "preferred" direction for each neuron, defined as the angle generating the largest number of spikes evoked by stimulus onset.

Previously (Simons and Carvell 1989), our working hypoth-

esis has been that cortical neurons having a particular "preferred" direction receive inputs from thalamic neurons having the same preference, in both cases measured in terms of response magnitude. The present results strongly indicate that this assumption is incorrect. Thalamic response magnitude is a poor predictor of the cortical response for caudal deflections, and the strength of this relationship is in fact even weaker for preferred angle deflections (Figs. 5 and 9B). A second previous assumption not supported by the present data are that responses to preferred direction stimuli should be more sensitive to changes in deflection parameters, and exhibit a greater dynamic range, than responses to nonpreferred deflections. Instead, in Fig. 9D, we unexpectedly found that the R^2 values obtained from deflections in an arbitrary direction (i.e., caudal) were significantly larger than those from preferred direction deflections.

These considerations bring into question the definition of a preferred stimulus. Our results suggest that, at least in the case of the cortical barrel, a preferred stimulus is one that evokes in thalamic neurons a response with high temporal contrast. Therefore it now appears likely that cortical neurons having a particular angular preference receive their strongest input from a group of thalamic neurons that respond to the same stimulus angle with uniformly short latencies. This thalamic subpopulation would generate a response having a high level of initial synchrony (i.e., temporal contrast) at the appropriate angle. Preliminary analysis of data from our laboratory indicate that, for a given thalamic neuron, the deflection angle that evokes the largest response is not necessarily the same as the one that evokes the response with shortest latency.

Coding strategies

Seminal studies of receptive field properties in the visual system (Barlow 1953; Hubel and Weisel 1968), and in fact most studies that followed, refer to a preferred stimulus as one that evokes the largest number of spikes from a neuron. Certainly, measured in this fashion, the individual *cortical* neurons examined here exhibit just such a preference to high-velocity stimuli. More recently, population magnitude codes have been postulated in which the pooled responses from an ensemble of neurons generate a more reliable and/or more accurate approximation of stimulus parameters (Georgopoulos et al. 1986; Wilson and McNaughton 1993). In the present study, the fact that the population response magnitude of cortical neurons relates better to deflection velocity than the response of any individual neuron suggests that barrel neurons may be participating in a similar strategy (Fig. 9D).

Temporal population codes often involve some form of synchrony (Gray et al. 1989; Singer 1993). In the present study, the encoding of stimulus parameters by population synchrony, here in the form of temporal contrast, is apparent in both thalamic and cortical responses. In terms of *individual* neurons in either thalamus or cortex, stimuli that lack a periodic temporal structure, such as those used here, typically evoke responses that are too brief, and produce too few spikes, to regard the interspike interval as a reasonable measure of the neuron's activity (Dear et al. 1993; Tovee et al. 1993).

Our results indicate that deflection velocity is encoded differently in the thalamus versus the cortex. In the thalamus, velocity is best represented by the measure of population temporal contrast. In the cortex, velocity is represented by at least three distinct codes: population response magnitude, population temporal contrast, and the response magnitude of individual neurons. Why might multiple codes be used in the cortex to represent what appears to be a *single* stimulus feature, i.e., velocity? One possibility is that the use of multiple codes reflects the fact that output from the barrel is received by a number of different circuits in the supra- and infragranular layers (Brumberg et al. 1999). As discussed below, the sensitivity of barrel circuits to the thalamic code is a consequence of the mechanism by which the circuit processes arriving signals. Processing mechanisms of cortical circuits outside the barrel are likely to vary considerably, rendering each type of circuit sensitive to a different type of barrel output.

Circuit dynamics

The barrel is a temporal contrast detector, responding best to rapid changes in thalamic input with an increase in neuronal firing. This is evidenced not only by the relationship between thalamic and cortical output in response to the deflection velocities examined here, but also from that same relationship using a variety of stimuli. That is, deflections of the principal versus an adjacent whisker, and also deflection onsets versus offsets, are characterized by responses having different temporal contrasts in the thalamus and different magnitudes in the cortex (Kyriazi et al. 1996). It was, in fact, the observation of different temporal contrasts between thalamic onset and offset responses that lead to the present set of experiments.

A primary goal in the present study has been to examine the prediction of previous modeling studies concerning temporal contrast sensitivity in real barrel neurons (Pinto et al. 1996). The experimental validation of this prediction provides evidence that the circuit dynamics governing barrel function have been effectively captured by the models. More importantly, it strongly suggests that the dynamics and analysis of the mechanisms in the model system provide an explanation for the behavior of the real system as well (Pinto 1997; Pinto et al. 1996). Briefly, a signal with high initial synchrony rapidly engages positive feedback among interconnected excitatory neurons, generating a strong excitatory response; inhibitory cells are driven in a more linear fashion by their thalamic inputs. The nonlinear buildup in the excitatory population is subsequently transferred to the inhibitory neurons that, because inhibitory synapses are strong and long-lasting, quickly dominate network activity, bringing the system back to its resting state. The time delay between the arrival of a thalamic signal in the cortex and the development of network inhibition represents a window of opportunity during which strong excitatory responses can be generated. Low temporal contrast signals, which generate smaller responses, are able to engage excitatory feedback mechanisms only weakly before the window is forced shut by a wave of inhibition. Thus it is the mechanism by which barrel circuits process arriving signals that render them more sensitive to the initial synchrony of a thalamic input and less sensitive to the input magnitude.

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