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Population Coding of Stimulus Location in Rat Somatosensory Cortex

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Summary

This study explores the nature of population coding in sensory cortex by applying information theoretic analyses to neuron pairs recorded simultaneously from rat barrel cortex. We quantified the roles of individual spikes and spike patterns in encoding whisker stimulus location. 82%–85% of the total information was contained in the timing of individual spikes: first spike time was particularly crucial. Spike patterns within neurons accounted for the remaining 15%–18%. Neuron pairs located in the same barrel column coded redundantly, whereas pairs in neighboring barrel columns coded independently. The barrel cortical population code for stimulus location appears to be the time of single neurons' first poststimulus spikes—a fast, robust coding mechanism that does not rely on "synergy" in crossneuronal spike patterns.

Introduction

It is widely accepted that sensory events are encoded in cortex by numerous spikes distributed across large numbers of neurons. This makes the neural population code highly complex, so that it has been difficult to determine systematically which components of neuronal activity constitute the basic units for carrying information. Two fundamental questions can help guide the inquiry. First, do neuronal populations convey messages by spike timing with millisecond precision or by spike counts accumulated over periods that are long compared to the typical interspike interval? Second, are the basic information units of the neural code independent spikes or spike patterns? Answering these questions will also reveal whether the functional unit is the single neuron, or the neuronal ensemble.

In the present report, we have tried to address these two questions using the rat somatosensory cortex as a model. Our inquiry builds upon the considerable progress that has been made in recent years in understanding neural coding. With regard to the first question, there is now evidence that single neuron spike timing on the millisecond scale can be a mechanism for information transmission about dynamic stimulus features both in nonmammalian neural structures (Bialek et al., 1991; Berry et al., 1997; Vickers et al., 2001) and in mammalian cortex (Buracas et al., 1998). Precise timing of spikes even increases the information transmitted about stimuli which contain no dynamic features (Panzeri et al., 2001; Reich et al., 2001): single neurons of the rat somatosensory cortex, for example, encode 44% more information about stimulus location when spikes are binned with 5 ms resolution than when they are simply counted over one long response window (Panzeri et al., 2001).

Regarding the second question, both single neuron and multi-neuron spike patterns have recently been studied. For single cells of the fly, closely spaced spike pairs carry more information than the spikes do individually (Brenner et al., 2000); for pairs of mouse retinal ganglion cells, the role of cross-cell patterns is under debate (Nirenberg et al., 2001; M.J. Berry II, personal communication). In cortex, although the information available in spike patterns compared to that available in independent spikes has not been quantified, there is evidence suggesting that patterns might play a role in neuronal coding. For example, some sensory stimuli (Gray et al., 1989; deCharms and Merzenich, 1996; Villa et al., 1999) and motor preparatory states (Abeles et al., 1993; Vaadia et al., 1995; Riehle et al., 1997) can elicit specific population crosscorrelation structures not predicted by the firing rates of individual neurons. Here, we wish to adopt a more comprehensive approach by quantifying and comparing the information transmitted by both within-cell and cross-cell spike patterns to that conveyed by the spikes individually.

By measuring the information conveyed by single spikes and spike patterns, one can characterize neuronal coding as *synergistic* or *redundant*. A synergistic code conveys its message only at the level of a spike ensemble, and the information transmitted by a set of spikes is *greater* than the summated information transmitted by the constituent spikes independently. Neural coding cannot be synergistic unless spike patterns are information bearing (either within cells or across cells). On the other hand, in a redundant code, different spikes convey similar messages: the information transmitted by the set of spikes is *less* than the summated information transmitted by the constituent spikes independently. Synergy has the advantage of high capacity, whereas redundancy affords simplicity and robustness.

The present evaluation of population coding mechanisms could also improve our understanding of the functional significance of cortical columns. Visual, auditory, and somatosensory areas consist of repeating modules, each of which contains several thousand neurons sensitive to similar stimuli. Because cortical columns are generally regarded as the information processing modules of the cerebral cortex (Mountcastle, 1997), we hope to elucidate whether they function as ensemble encoding units, or whether the constituent neurons convey information in an independent fashion.

Rat somatosensory cortex offers several advantages

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as an experimental model. Cortical columns are anatomically defined and have a one-to-one relationship with the whiskers on the rat's snout (Woolsey and Van der Loos, 1970; Welker, 1971), allowing the columnar location of each neuron to be identified. Another important feature is that neurons tend to fire few spikes per trial. This restricts the potential complexity of the code, allowing the experimenter to reliably estimate the information conveyed by the spike trains of simultaneously recorded neuron pairs (Panzeri and Schultz, 2001; Panzeri et al., 2001), and thereby permitting a comprehensive analysis of the role that individual spikes and spike patterns play in neural coding. Studying the coding of stimulus location, we have quantified the role of spike timing within and across neuron pairs, and assessed whether the mode of processing is redundant or synergistic. Under our conditions, precise spike timing of single neurons significantly increases the quantity of information available, but spike timing does not appear to be exploited to generate synergistic patterns across neurons. These findings suggest a robust population coding mechanism whose advantage—in comparison to complex synergistic coding—may be to ensure that each cortical column rapidly distributes the same message to multiple brain regions and to all neuronal targets within a brain region.

Results

We analyzed 212 pairs of simultaneously recorded cells from the barrel cortex of urethane-anesthetized rats. Only pairs where each cell was recorded at a different electrode were considered. In 52 cases, both neurons were located in barrel column D2. In other cases, the two neurons were located in different barrel columns: 80 D1-D2 pairs, 93 D2-D3 pairs, and 39 D1-D3 pairs. Vibrissae C1, C2, C3, D1, D2, D3, E1, E2, and E3 were stimulated one at a time in order to study how populations of cortical neurons encode stimulus location. The stimulus was an up-down step function of 80 μm amplitude and 100 ms duration, delivered once per second, 50 times for each vibrissa. Stimulus onset was defined as time = 0 ms.

To find out the time scale at which neurons transmit information, we measured the neuronal response in terms of both *spike count* and *spike timing*. The spike count of a neuron on a given trial was the number of spikes emitted in the time interval [*0-T*] ms. To evaluate spike timing, this interval was subdivided into a sequence of *dt* ms bins, each containing 0 or 1 spikes, and the response on a given trial was the one out of these $2^{T/dt}$ sequences that occurred. For each *pair* of simultaneously recorded cells, the two spike counts and the two spike sequences emitted on a given trial were considered. We measured the mutual information contained in each type of response about stimulus location, using the series expansion method (Panzeri et al., 1999; Panzeri and Schultz, 2001); see Experimental Procedures.

Role of Spike Timing within and across Barrel Columns

We showed previously that precise spike timing allows *single* neurons to transmit 44% more information about stimulus location than does the spike count alone (Panzeri et al., 2001). This analysis did not address the potentially important effect of spike timing across multiple neurons. Our first aim was therefore to uncover the role of spike timing at the level of multiple neurons. While our earlier work was able to examine timing within a 40 ms response window with a bin size as small as 5 ms, inclusion of two neurons allowed the current analysis to test for temporal resolution as fine as 10 ms. This limit was determined by the number of trials per stimulus available—see Experimental Procedures.

An example of a pair of cells recorded from barrel column D2 is shown in Figure 1a. At the left, the spike times relative to stimulus onset are shown for each of 50 deflections of whiskers D1 and D2. Both cells responded strongly and rapidly to the principal whisker D2, but weakly and with greater delay to nonprincipal whisker D1. This observation is consistent with the well-known functional properties of barrel cortex: in general, nonprincipal whiskers evoke spikes in a cortical barrel column at longer latencies than does the principal whisker (Armstrong-James and Fox, 1987). These properties are reflected in the poststimulus time histograms (PSTHs) to deflection of D2 and each of the eight surrounding whiskers (middle panel). The information about stimulus location transmitted in spike count by this pair of neurons (right panel, dashed line) increased with the length of the response window until 20 ms, reflecting the fact that different whiskers elicited different numbers of spikes. Initially, the information in spike timing (solid line) was similar to that in the spike count (dashed line). However, by 40 ms, there was 25% additional information in spike timing. Clearly, one factor contributing to the additional information in spike timing was that different whiskers elicited spikes at different latencies (left and middle panels), a code that is "washed out" in the spike count. Later, we consider whether a second factor could be precisely timed spike patterns.

Figure 1b illustrates a pair of cells recorded from *different* barrel columns: one neuron was located in barrel column D2, the other in barrel column D1. The spike times relative to stimulus onset for 50 deflections of whiskers D1 and D2 (left panel) and the PSTHs for the nine whiskers of interest (middle panel) again reveal that both neurons yielded the strongest and shortest latency response to their respective principal whiskers; nonprincipal whiskers elicited fewer spikes at longer latencies. Stimulus-dependent latency differences contributed to a large (50%) advantage for spike timing.

To show that this advantage of spike time coding compared to spike count coding was a general finding, Figure 2a gives results averaged over all pairs of cells. For cell pairs in barrel column D2 (left panel), the information in spike timing and spike count at 20 ms poststimulus was similar, 0.27 $\pm$ 0.09 bits (mean $\pm$ SD) and 0.25 $\pm$ 0.08 bits, respectively. However, by 40 ms poststimulus, D2 cell pairs conveyed 0.31 $\pm$ 0.10 bits by spike timing—25% more than by spike count. The advantage of spike timing compared to spike count for cell pairs located in different barrel columns tended to be greater: for D1-D2 pairs (middle panel), the advantage was 29%; for D2-D3 pairs, 33% (not shown). For D1-D3 pairs (right panel), the advantage was 52%.

In order to estimate better the precision of the tempo-

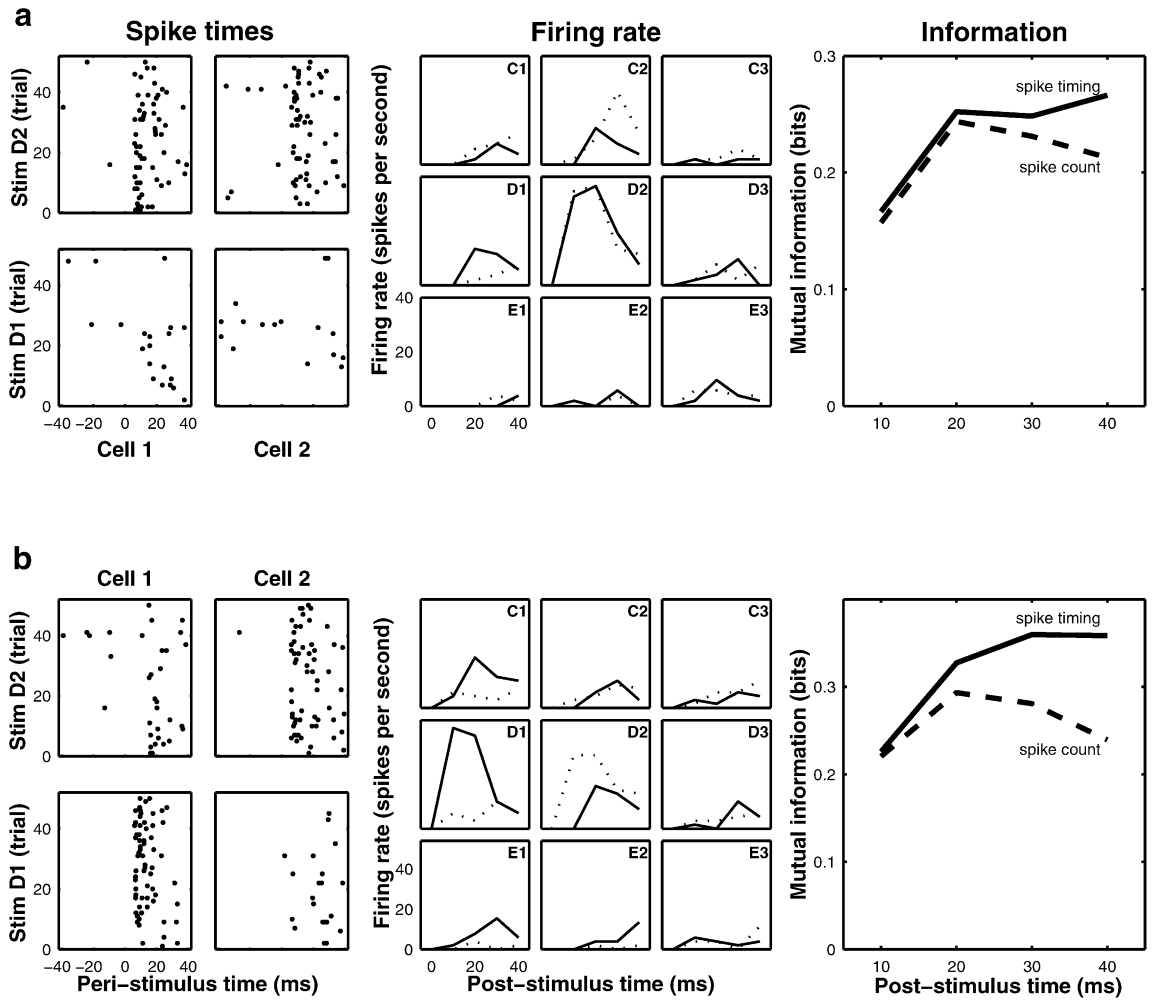

Figure 1. Coding by Cell Pairs, within Column and across Columns

(a) Cell pair located within barrel column D2. Left: Raster plots for each cell in response to whisker stimuli D1 and D2 at 0.1 ms resolution. Middle: PSTHs for each of the nine whisker stimuli: responses of one cell are shown as solid lines; the other as dotted lines. Bin size is 10 ms. Right: mutual information between the stimulus set and the spike timing response evaluated with 10 ms bins. The information that the two cells conveyed by spike timing (solid line) was substantially more than that conveyed by spike count (dashed line). (b) Cell pair distributed across two barrel columns, D1 and D2. PSTHs and mutual information plotted as for part (a).

ral code, we measured the spike timing information for the response interval 0–20 ms with a bin size as small as 5 ms. If information increases as bin size is decreased, timing must be precise on the scale of the smaller bin size. For neuron pairs in D2 barrel column, information increased from 0.25 ± 0.09 bits with 20 ms bins to 0.29 ± 0.09 bits with 5 ms bins. The increase in information obtained by considering a resolution of 5 ms was even greater for pairs located in different barrel columns: for D1-D2 pairs, information increased from 0.27 ± 0.11 bits for 20 ms bins to 0.36 ± 0.15 bits for 5 ms bins; for D2-D3 pairs, it increased from 0.22 ± 0.11 bits to 0.30 ± 0.12 bits; for D1-D3 pairs, it increased from 0.24 ± 0.12 bits to 0.36 ± 0.14 bits. Thus, the precision of the spike timing code was at least 5 ms, and the 25%–52% advantage for spike timing compared to spike count might be even larger at smaller time bins. These results show that spike timing is important for the population coding of stimulus location, extending the observations made earlier concerning single neurons (Panzeri and Schultz, 2001). Spike timing is particularly informative for populations that encompass separate barrel columns.

Information in Individual Spikes and Spike Patterns

The information in spike timing described in the previous section could be generated in two ways. The simplest is if all the information were coded by stimulus-dependent differences in the timing of individual spikes, within-trial correlations between spike times not being informative. In this case, information can only be coded by variations in the PSTH structure across stimuli. The second way is if particular spike patterns were to occur within the same trial, which could code information even in the absence of stimulus-dependent PSTH structure. The series expansion method permits us to quantify the relative contribution of these two mechanisms. As detailed in Experimental Procedures, the expansion expresses the

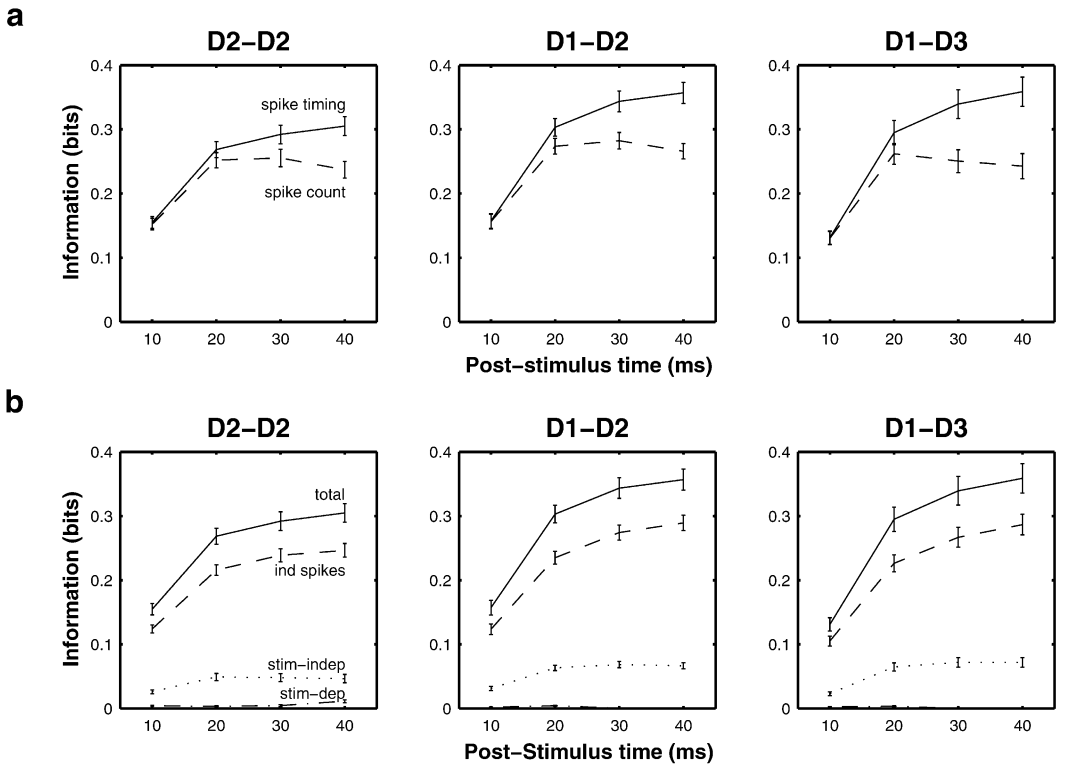

Figure 2. Role of Spike Timing and Spike Patterns in Population Coding

Labels above the graphs refer to neuronal locations. (a) Information in spike timing (solid line) is plotted as a function of poststimulus time, together with information in spike count (dashed line), averaged over cell pairs. (b) Total information in spike timing (solid line) is compared to the contribution of each component in the series expansion, averaged over cell pairs. The total contribution of individual spikes (dashed line) is the sum of the first order term, Equation 3, and the PSTH similarity second order term, Equation 4. Spike patterns contributed much less (stimulus-independent patterns, Equation 5, dotted line; stimulus-dependent patterns, Equation 6, dash-dotted line). Bars denote SEM.

total information in spike timing as an approximation consisting of the sum of two terms arising from individual spikes and two terms arising from spike patterns.

The amount of information that a neuronal population conveys by the timing of individual spikes is the sum of an *independent spike timing* term and a *PSTH similarity* term. The former term expresses the information that would be conveyed were the spikes to carry independent information; the latter term corrects this for any redundancy arising from similarity of PSTHs across stimuli. More precisely:

- *Independent spike timing*: if within-trial spike patterns do not convey information, then *all* information must be in the timing of individual spikes. Under these circumstances, the time-varying firing rate (PSTH) is a complete description of the neuronal response, and is the only statistic required in order to estimate the information. Equation 3 expresses the relationship between PSTH and mutual information: the greater the diversity in PSTH structure across stimuli, the greater is the information. If each spike provides *independent* information about the stimulus set, Equation 3 gives the total information available in the response (DeWeese, 1996; Brenner et al., 2000; Panzeri and Schultz, 2001).
- *PSTH similarity*: if there is any redundancy between spikes, Equation 3 can overestimate the information. Redundancy is present if the PSTH value at a given time bin correlates across the stimulus set with the PSTH value at a different time bin for the same cell, or correlates with the PSTH value at any time bin for a different cell. This type of correlation has been termed *signal correlation* (Gawne and Richmond, 1993), and Equation 4 quantifies the amount of redundancy that it introduces.

The remaining two terms in the series expansion approximation, given below, express any further effect that spike patterns might have beyond that of individual spikes.

- *Stimulus-dependent spike patterns*: a neuronal population can carry information by emitting patterns of spikes that "tag" each stimulus, without the differences in the patterns being expressed in the PSTHs. When the assumptions of the series expansion are satisfied, as in the present case, the only types of spike pattern it is necessary to consider are spike pairs—higher order interactions can be neglected (see Experimental Procedures). Patterns involving pairs of spikes are quantified, for each stimulus, as the probability of spikes occurring in each of two time bins. For *within-cell patterns*, the bins come from the same cell; for *cross-cell patterns*, they come from

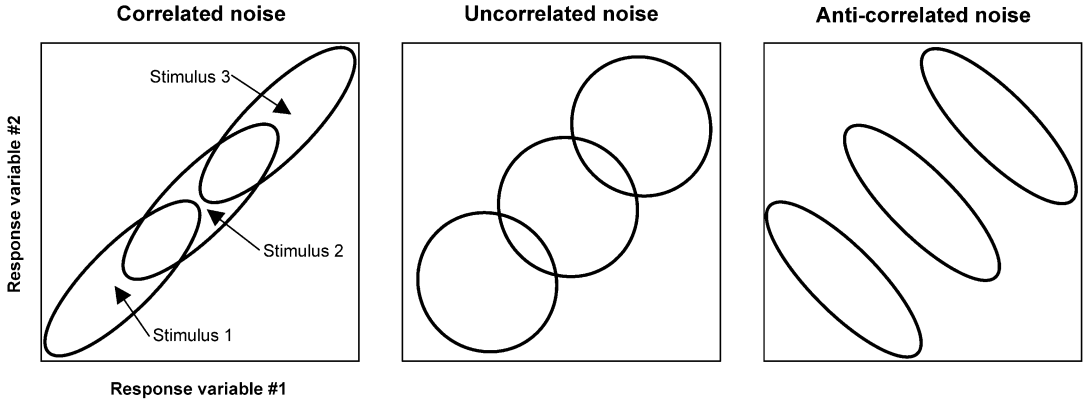

Figure 3. Effect of Stimulus-Independent Patterns on Population Coding

Each panel sketches hypothetical distributions of "responses" to three different stimuli. The response variables can be considered either to be different bins within the same cell or bins across different cells. Each ellipse indicates the set of responses elicited by a given stimulus. In each of these examples, signal correlations are positive whereas the sign of noise correlation differs. In the middle panel, noise correlation is zero, and stimulus-independent patterns exert no effect on the total information. When noise correlation is positive (left panel), responses to the stimuli are less discriminable and stimulus-independent spike patterns cause a redundant effect. When noise correlation is negative (right panel), responses are more discriminable and the contribution of stimulus-independent spike patterns is thus synergistic. In general, if signal and noise correlations have the same sign, the effect of stimulus-independent patterns is redundant, if they have opposite signs, it is synergistic.

different cells. In the terminology of Gawne and Richmond (1993), this joint probability is known as the *noise correlation*. In the case of cross-cell synchrony, for example, the noise correlation will be greater than expected from the PSTHs. In the case of within-cell refractoriness, where the presence of a spike in one bin predicts the absence of a spike in the next bin, the noise correlation will be *less* than that expected from the PSTH.

The amount of information conveyed by stimulus-dependent spike patterns depends, analogously to the PSTH information, on how much the noise correlations (normalized by firing rate) vary across the stimulus set: the greater the diversity, the greater the information available. This effect is quantified by Equation 6.

- *Stimulus-independent spike patterns*: even if not stimulus dependent, spike patterns can exert an effect on the neuronal code through a subtle interaction between signal correlation and noise correlation. In contrast to stimulus-dependent patterns, this less intuitive coding mechanism has received little attention in experimental work—it has been noted in theoretical papers by Snippe (1996), Oram et al. (1998), Abbott and Dayan (1999), and Panzeri et al. (1999). As shown schematically in Figure 3, this term—Equation 5—is positive if signal correlations and noise correlations have different signs, negative if the same signs. If signals are uncorrelated, the term is zero.

Figure 2b shows how these different, timing-dependent components contributed to the coding of stimulus location. The left panel shows results averaged over all pairs of neurons located in barrel column D2. At 40 ms poststimulus, the timing of *individual spikes* (dashed line) accounted for 83 $\pm$ 14% of the total information in spike timing (solid line). Stimulus-dependent spike patterns (dash-dotted line) accounted for 5 $\pm$ 7%, stimulus-independent patterns (dotted line) for 12 $\pm$ 14%. Similar results were obtained for pairs of neurons located in different barrel columns: D1-D2 pairs (middle panel) conveyed 17 $\pm$ 6% by spike patterns (stimulus-dependent and stimulus-independent patterns considered together), D2-D3 pairs (not shown) conveyed 15 $\pm$ 7%, D1-D3 pairs (right panel) conveyed 18 $\pm$ 6%. Thus spike patterns conveyed about 15%–18% of the total information in the population spike train, and we will analyze them below in more detail. Then, we will examine the component of the neuronal response which carried the most information about stimulus location—individual spike timing.

Nature of the Spike Pattern Information

As detailed in Experimental Procedures, we split the information components into separate *within-cell* and *cross-cell* parts, and these are plotted in Figure 4. The left panel shows results averaged over all pairs located within D2 barrel column, evaluated at 40 ms poststimulus. The major finding was that within-cell spike patterns gave a significant positive contribution to the information in the population code (0.07 $\pm$ 0.04 bits), and this contribution was a stimulus-*independent* one. In addition, there was a very small, positive contribution from stimulus-dependent patterns across cells (0.007 $\pm$ 0.02 bits) and a small negative effect of stimulus-independent patterns across cells ($-$0.02 $\pm$ 0.02 bits).

Corresponding data for neuron pairs located in different barrel columns are shown in the middle and right panels of Figure 4. Again, the major finding was that within-cell spike patterns exerted a positive effect. For D1-D2 and D1-D3 pairs, both stimulus-independent patterns across cells and stimulus-dependent patterns (within and across cells) were negligible.

Overall, neither within nor across barrel columns did cross-cell spike patterns seem to code information about

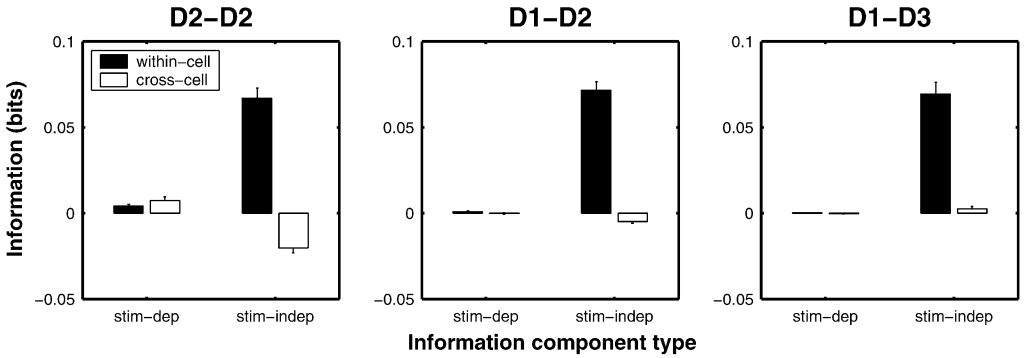

Figure 4. Contributions of Within-Cell Patterns and Cross-Cell Patterns to the Spike Timing Code

For each cell pair, the contribution to the second order terms of the series expansion was split into within-cell and cross-cell components. Labels above the graphs refer to neuronal locations. Results for stimulus-dependent patterns and signal-noise interaction are plotted averaged over cell pairs. Bars denote SEM.

stimulus location: the net contribution of spike patterns to the population code was almost entirely attributable to within-cell patterns. Since stimulus-independent spike patterns within individual neurons transmitted a significant quantity of information, we carried out additional analyses to determine the nature of these spike patterns. As noted above, the information conveyed by stimulus-independent spike patterns depends on the relationship between signal correlations and noise correlations. To find out which of the three modes of interaction illustrated in Figure 3 applied, for each cell pair, we plotted the (Pearson) signal correlation coefficient (averaged over time bin combinations) against the noise correlation coefficient (averaged over both time bin combinations and stimuli). Figure 5a shows results for within-cell patterns. For both same-column (left panel) and cross-column (middle and right panels) pairs, signal correlation coefficients were usually positive and noise correlation coefficients negative. A positive signal correlation coefficient means that pairs of PSTH bins tend to have similar values across different stimuli. A negative noise correlation coefficient means that spikes co-occur in pairs of bins less frequently than expected from the PSTHs. Since signal and noise correlations had different signs, their interaction resembled that shown schematically in Figure 3c, making the stimulus-independent spike pattern information term positive.

Figure 5b shows corresponding results for cross-cell patterns. For cell pairs located in barrel column D2 (left panel), both signal correlations and noise correlations tended to be positive (in contrast to the observation for within-cell patterns). Hence, their interaction resembled that shown in Figure 3a, making the stimulus-independent pattern term negative. For neuron pairs in different barrel columns (middle and right panels) noise correlations tended to be positive, but signal correlation values were scattered around zero (Figure 3b), consistent with the finding that the effect of cross-cell stimulus-independent spike patterns was negligible for neurons in different barrel columns (Figure 4).

Synergy or Redundancy?

A given pattern of spikes is synergistic if the transmitted information is greater than that conveyed by the constituent spikes independently; it is redundant if the information is less than that conveyed independently. The picture is complicated by the fact that some spike patterns produced by a neuron pair can be synergistic, while others are redundant. In the series expansion, the first order term, Equation 3, is precisely the information conveyed by spikes independently. Therefore, to evaluate whether the coding of stimulus location is synergistic or redundant, we evaluated the sum of the three higher order terms—Equations 4, 5, and 6. To examine the origin of the synergy/redundancy in more detail, we split these terms into separate within-cell and cross-cell components.

Figure 6 shows that neuron pairs in the same barrel column (D2-D2) were highly redundant (white bar). The value of 0.055 $\pm$ 0.067 bits of redundant information corresponds to 19% of the total information in spike timing. This was due exclusively to cross-cell contributions (gray bar). Within-cell contributions (black bar), by themselves, were slightly synergistic (0.005 bits); for cross-cell contributions, redundancy caused by spikes in different cells being correlated across stimuli was much stronger than any positive effect of information-bearing spike patterns.

For neuron pairs located in different barrel columns, the overall effect (white bars) was close to zero: 0.001 $\pm$ 0.023 bits for D1-D2 pairs (0.5% of the total information), -0.003 ± 0.026 bits for D2-D3 pairs (not shown, -0.4% of the total information), and 0.017 $\pm$ 0.042 bits for D1-D3 pairs (7% of the total information). Again, different types of spike pattern exerted opposing effects: within-cell patterns were synergistic; cross-cell patterns redundant.

Coding by the First Poststimulus Spike

The previous sections showed that the coding of stimulus location is achieved mainly by the timing of individual spikes—a simple mechanism that does not depend on cross-cell synergy. Beyond pointing out the remarkable amount of information carried by single spikes, we asked whether it is possible to further specify the nature of the code: is a similar quantity of information transmitted by any single spike or, alternatively, is a particular subset of individual spikes crucial? Indeed, a preceding study of barrel cortex showed that, in single cells, the

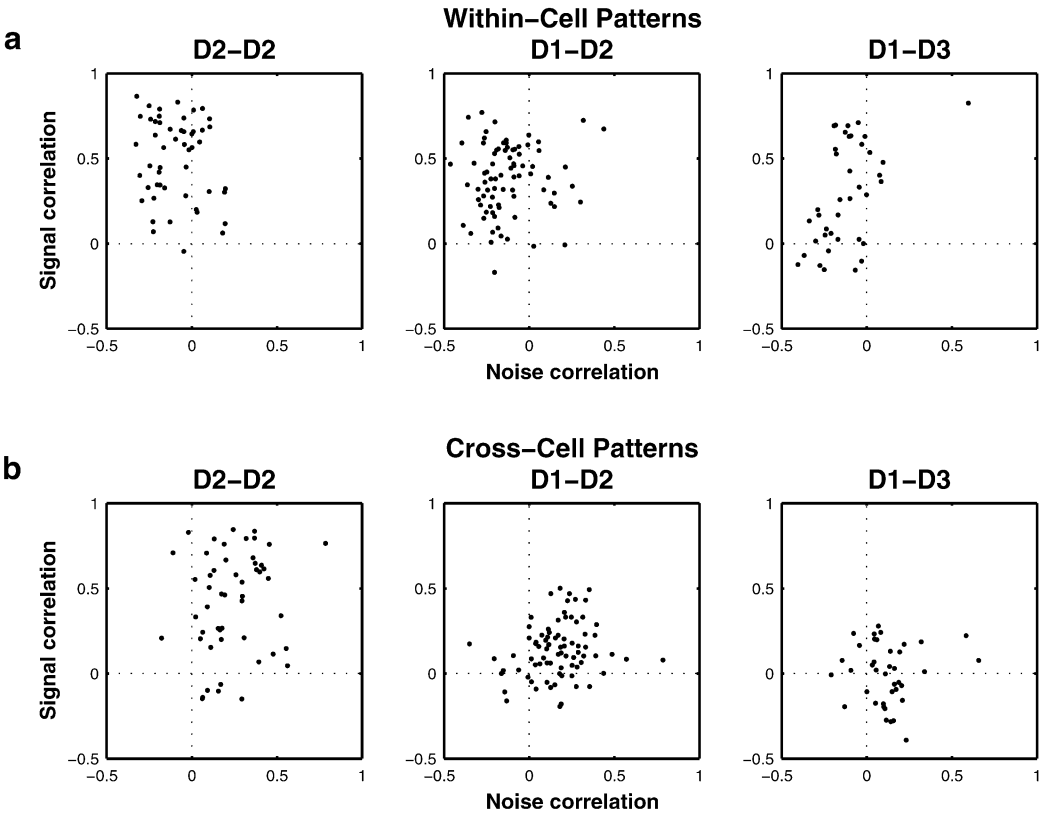

Figure 5. The Relationship between Signal Correlation and Noise Correlation, across and within Cells

Labels above the graphs refer to neuronal locations. (a) For each cell pair, average within-cell signal correlation coefficient is plotted against average within-cell noise correlation coefficient (see text for details). (b) Corresponding results for cross-cell correlations.

overwhelming part of the total information was accounted for by the timing of the *first* poststimulus spike (Panzeri et al., 2001). To examine the role of the first spike at the population level, we repeated the above analyses considering only the first, second, or third spikes per cell recorded on each stimulus trial. The information conveyed by the individual spike terms of the series expansion (Equations 3 and 4) was compared to the corresponding data for the whole spike train. For neuron pairs in barrel column D2, the first spikes conveyed almost as much information as the entire spike train (Figure 7). The mean first spike information was 91 ± 7% of that in the entire 40 ms spike trains. For neurons in different barrel columns (not illustrated), the corresponding values were 87 ± 7% (D1-D2 pairs), 91 ± 9% (D2-D3 pairs), and 89 ± 9% (D1-D3 pairs). The mean information conveyed by D2-D2 pairs in the second and third spikes was 43 ± 18% and 18 ± 14%, respectively, of that present in the individual spikes of the whole spike train. Similar results for second and third spikes were obtained for cell pairs distributed across different barrel columns. Since nearly all the information in the entire spike train was already present in the first poststimulus spike, the later spikes were almost completely redundant, both for neuron pairs within and across barrel columns.

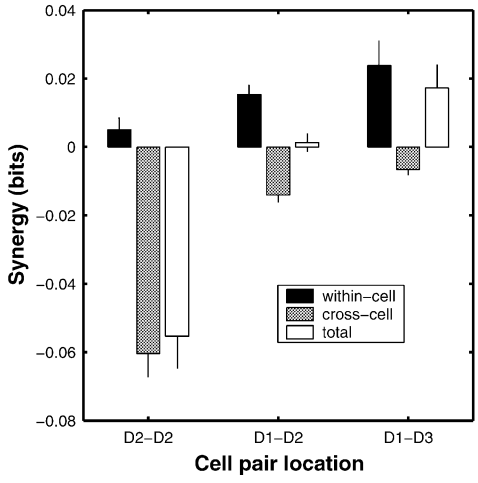

Figure 6. Synergy/Redundancy within and across Cells

Total synergy (white bars) was estimated as the sum of second order terms, as explained in Experimental Procedures. This was split into cross-cell (gray bars) and within-cell (black bars) constituents. Results were averaged over cell pairs according to location; bars denote SEM.

All the observations given in this report point toward the conclusion that, to a large extent, the barrel cortex population code for stimulus location consists of the time of individual cells' first spike after whisker deflection. We characterize this as a simple, spike-time popu-

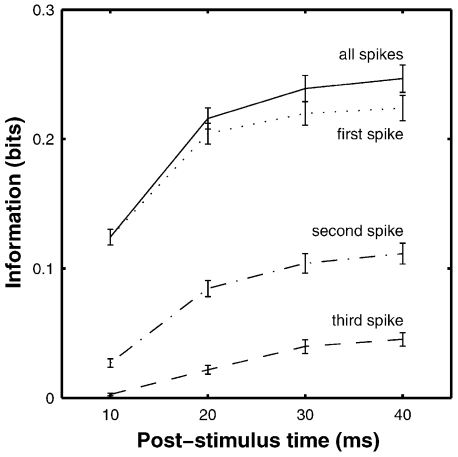

Figure 7. Information Conveyed by Single Spikes

Mean information conveyed by individual spikes in the whole spike train, averaged over all cell pairs within D2 barrel column (solid line), is plotted as a function of poststimulus time, together with that conveyed only by the first spike in each cell (dotted line), the second spike (dash-dotted line), and the third spike (dashed line). Bars denote SEM.

lation code. Under the conditions reported here, the basic functional unit of barrel cortex for stimulus localization seems to be the single neuron rather than the neuronal ensemble.

Discussion

Coding and Decoding Mechanisms

Neuronal populations can transmit information in three ways: (1) by individual spikes (Bialek et al., 1991); (2) by single neuron spike patterns (Berry et al., 1997; Brenner et al., 2000); and (3) by cross-neuron spike patterns (Gray et al., 1989; Abeles et al., 1993; Vaadia et al., 1995; Riehle et al., 1997; deCharms and Merzenich, 1996; Villa et al., 1999). Each of these processes can occur at short time scales ("spike timing information") or long time scales ("spike count information"). Previous studies have tended to focus on a single coding mechanism in isolation, but real biological systems are likely to employ some combination. For example, Fairhall et al. (2001) showed that the fly H1 neuron can signal image velocity by single spike timing while, simultaneously, signaling the "context" (variance of image velocity) by interspike interval (a spike pattern code).

Recent studies have considered mechanisms for the coding of whisker location in rat barrel cortex using the spike trains of many simultaneously recorded neurons, either by training an artificial neural network to reconstruct stimulus location (Ghazanfar et al., 2000), or by estimating stimulus discriminability using population d' (Petersen and Diamond, 2000). In both cases, the population code was found to be "distributed," in the sense that stimulus discriminability increased with the number of neurons included in the analysis. Having identified the distributed character of the code, the next question is: what are the specific information-bearing units within it? Under the present experimental conditions, the series expansion method permitted us to identify which aspects of neuronal activity carry sensory information—individual spikes, single cell spike patterns, or cross-cell spike patterns. The timing of individual spikes accounted for 82%–85% of the total information transmitted by neuron pairs, whereas the remaining 15%–18% was almost entirely due to within-cell, but not cross-cell, spike patterns.

The contribution of individual spikes could be accounted for primarily (87%–91%) by the times of the first spikes following whisker deflection, later spikes being redundant. Since these initial, information-rich spikes could also occur at long latencies (note the response of the D2 neurons to whisker D1 in Figure 1), the information grew progressively across poststimulus time (Figures 1 and 2): for D1-D2 neuron pairs, the available information was 127% greater at 40 ms than at 10 ms. Our analysis shows the amount of information that is available: whether the brain uses the earliest available signal, or the more reliable, later signal is a separate issue. One way the downstream targets of a brain region could exploit the benefits of both reliability and speed might be to integrate information from larger populations of neurons.

How might these results generalize when barrel cortex is studied under different conditions? Time scale is one issue to consider: most of the results presented here and previously (Panzeri et al., 2001) concern the contribution of spike timing with 5–10 ms time bins. We detected no trend toward spike patterns having a more important role at temporal resolutions as fine as 5 ms (Panzeri et al., 2001). Still, the present analysis cannot completely exclude the possibility that cross-cell spike patterns carry additional amounts of information at still finer temporal precision. A second issue is whether spike patterns might play a greater role for more naturalistic stimuli, e.g., whisker deflections varying in amplitude, velocity, or direction, and with a more complex temporal profile. In other sensory systems, the available data do not support the idea that spike patterns are the fundamental unit for encoding even dynamic stimuli. For example, complex visual stimuli can be accurately reconstructed from the timing of single spikes of both individual neurons (Bialek et al., 1991; Buracas et al., 1998) and neuronal populations (Warland et al., 1997). Thus, we expect that individual spikes are the major information bearing unit for dynamic whisker stimuli, just as they are for spatial whisker stimuli; this prediction must be tested in future investigations.

First spike time, which we found to be the crucial aspect of information transmission (Figure 7), also has an important role in other sensory systems. The first spike time of cortical responses encodes visual contrast (Gawne et al., 1996; Reich et al., 2001) and sound source location (Furukawa et al., 2000). Although information is thus *available* in first spike times, it is not always safe to assume that such information can be *used* by the rest of the animal's brain. Unlike the experimenter, an animal likely does not have independent knowledge of stimulus time. In the rat whisker system, two possible solutions to this decoding problem seem plausible. (1) Since the collection of vibrissal sensory data under natural conditions is an active process initiated by a motor command, the sensory system could use the output

from the motor system as an estimate of stimulus time. (2) Complementing information that might be available from *absolute* timing relative to the motor command, the sensory system could use the *relative* timing between spikes in the neuronal population (Buonomano and Merzenich, 1999; Jenison, 2001; Van Rullen and Thorpe, 2001). In the present case, for example, deflection of whisker D1 elicits spikes first in barrel column D1 and *subsequently* in barrel column D2; whereas deflection of whisker D2 elicits the opposite sequence of spikes.

The first of these decoding solutions (motor efference signal), acting alone, would probably not possess sufficient temporal precision (Kleinfeld et al., 1999) to permit the representation of information by first spike times, but it may constrain sensory analysis to a time window within which relative spike timing would convey the relevant information. In a broader context, use of a motor command for decoding first spike time information can apply only to modalities where sensory activity is elicited by motor output, but would not be relevant in cases where sensory activity is elicited purely by external changes.

Information Transmission in Columnar Systems

Given that nearly all the information in the entire spike train is already present in the first poststimulus spike, we argue that the efficiency of cortical processing of stimulus location is enhanced by mechanisms that suppress subsequent, redundant spikes. One such mechanism is represented by the powerful GABAergic intracortical inhibitory input that quickly curtails the excitatory discharge evoked by single whisker deflection (Simons and Woolsey, 1984; Kyriazi and Simons, 1993; Kyriazi et al., 1996; Swadlow and Gusev, 2000). The functional circuitry of barrel cortex ensures that there is a very short window after whisker stimulation during which cortical neurons are able to emit a few, information-rich spikes.

Because columns are thought to be the basic information processing modules of cerebral cortex, we set out to elucidate whether they function as ensemble encoding units, or whether the constituent neurons convey information in an independent fashion. The answer hinges on the nature of neuronal cross-correlations. We found the average cross-cell noise correlation coefficient within a cortical barrel column to be 0.25—a figure broadly consistent with studies of the primate visual (Gawne and Richmond, 1993; Zohary et al., 1994) and motor systems (Lee et al., 1998), as well as rat prefrontal cortex (Jung et al., 2000). The agreement among these reports suggests that a small, positive cross-cell noise correlation may be a general principle of cortical columnar operation. Zohary et al. (1994) argued that correlated noise between cells imposes a strict limit on the amount of information available from a neuronal population (it causes redundancy). The series expansion method makes explicit the connection between information and signal/noise correlations, showing that this limit holds *provided* both that cross-cell signal correlations are positive and that there is no strong stimulus-dependent structure in the cross-cell noise correlations. In the present case, both these conditions were true of cells within the same barrel column, so that cross-cell effects indeed caused redundancy. The same pattern of correlations has recently been reported in both rat prefrontal cortex and monkey extrastriate cortex (Jung et al., 2000; Bair et al., 2001).

Across barrel columns, however, signal correlations were weak. Stimulus-independent spike patterns have little effect under these circumstances, and the coding was consequently near independent. Thus, information can increase approximately linearly until the limit dictated by the information available in the stimulus set is approached (Gawne and Richmond, 1993; Rolls et al., 1997).

The redundancy that we found within barrel columns was mainly due to individual spikes conveying similar messages. Hence, sampling large populations of neurons within a given barrel column would confer little improvement in coding accuracy. This conclusion is consistent with previous studies of neighboring cells in primate neocortex (Gawne and Richmond, 1993; Zohary et al., 1994; Lee et al., 1998). Across different sensory systems and species, it appears that same column cortical cells have high (positive) signal correlation and positive noise correlation. Information theory tells us that redundancy is likely in this case. We suggest that redundant coding is a general characteristic of columnar processing. As compared to synergy, redundancy might seem to be an inefficient coding mechanism, causing thousands of neurons to produce a similar message, with little gain in accuracy. But its benefits could include (1) robustness and (2) transmission of the same message to multiple targets.

Experimental Procedures

Electrophysiology

Methodology is described in detail by Lebedev et al. (2000). All procedures conformed to N.I.H. and international standards concerning the use of experimental animals. Twenty-two adult male Wistar rats weighing ~350 g were used. Anesthesia was induced by urethane (1.5 g/kg body weight, i.p.). The subject was placed in a stereotactic apparatus (Narishige, Tokyo) and left somatosensory cortex exposed by a 4 mm diameter craniotomy. Body temperature was maintained near 37.5°C and, during the recording session, anesthetic depth was held at a consistent depth by monitoring hindpaw withdrawal, corneal reflex, and respiration rate.

At the end of the experiment, subjects were perfused with saline followed by 4% paraformaldehyde. After postfixation in 20% sucrose, a flattened slab of neocortex was frozen, cut into 40 μm tangential sections, and processed for nitric oxide synthase activity (Valtschanoff et al., 1993) in order to visualize barrel columns in layer IV. To determine the columnar location of sampled neurons, electrode penetration sites were identified relative to the histological sections.

An array of six tungsten electrodes, arranged either as a single row or as a 2 × 3 matrix, with 300 ± 50 μm horizontal separation between adjacent electrode tips, was advanced into the cortical barrel field, centered on barrel column D2. Typically, 1–2 electrodes penetrated any single barrel column under the array. The whole array was advanced in 100 μm steps. The great majority of neurons were likely to have been located between 300–950 μm, the depths at which thalamic axons from the ventral posterior medial nucleus terminate (Lu and Lin, 1993). Since the methodology did not permit us to register electrode depth with accuracy better than about 100 μm, we did not attempt to classify single neurons according to laminar position.

Neuronal activity was amplified and band-pass filtered in the range 300–7500 Hz. Action potentials were digitized at 25 KHz, 32 points per waveform, and time-stamped with 0.1 ms precision (Datawave, Boulder, CO). Offline, single unit action potentials were discriminated by differences in shape and amplitude.

Individual whiskers were stimulated 3 mm from their base by a piezoelectric wafer (Morgan Matroc, Bedford, OH), which was controlled by a signal generator (A.M.P.I., Jerusalem).

Information Analysis

To evaluate the mutual information using the direct (or "brute force") method, the key step is to estimate the conditional probability $P(n|s)$ of each possible response n, given each of the possible stimuli s. n can be a single cell response, or a cell pair response and either a spike count or a spike sequence. The stimulus-average response probability $P(n)$, and the stimulus probability $P(s)$ must also be estimated. The mutual information can be written (Shannon, 1948):

$$I(S,R) = \left\langle \sum_n P(n|s) \log \frac{P(n|s)}{P(n)} \right\rangle_s \quad (1)$$

Information quantifies *diversity* in the set of probabilities $P(n|s)$. If these are all equal, for a given response n, and hence equal to $P(n)$, the argument of the logarithm is one and the response contributes nothing to $I(S,R)$.

The problem with the direct method is that it is difficult to estimate the above conditional probabilities accurately, given the number of trials presented in a typical physiological experiment. Fluctuations in the estimated conditional probabilities lead to spurious diversity that mimics the effect of genuine stimulus-coding responses. Hence, the effect of limited sampling is an *upward* bias in the estimate of the mutual information; the size of the bias being inversely related to the number of trials. Provided that the number of trials is at least the number of different responses, there is a formula for the bias magnitude that can be used to improve the accuracy of information estimation (Panzeri and Treves, 1996; Golomb et al., 1997). Considering pairs of neurons, stimulated with 50 trials, response "words" of length not exceeding 2 can be considered using the direct method. The direct method is not, therefore, useful for studying coding by spike timing in neuronal populations.

The variety of possible spike sequences, and hence the potential complexity of the neural code, increases rapidly with the number of spikes emitted per trial; conversely, low firing rates limit the complexity. Since typical firing rates in the barrel cortex are just 0–3 spikes per whisker deflection, the mutual information can be well approximated by a second order power series expansion in the time window T, which depends only on PSTHs and pairwise correlations between spikes at different times (Panzeri et al., 1999, 2001; Panzeri and Schultz, 2001). These quantities are far easier to estimate from limited experimental data than are the full conditional probabilities required by the direct method. Hence the series expansion method is less susceptible to sampling bias and, for a given number of trials, permits information to be estimated at greater temporal resolution. In the present case, words of length 4 per cell in a pair could be analyzed. Most of the results reported here are for the time window 0–40 ms, divided into 10 ms bins. However, we checked that the basic pattern of results was similar at small bins, by considering smaller response intervals.

The series expansion approximation for the information conveyed by spike timing (Panzeri and Schultz, 2001) consists of one first order, and three second order terms:

$$I(S,R) = I_t + I_{tta} + I_{ttb} + I_{ttc} \quad (2)$$

(There is also a series expansion for spike counts—see Panzeri et al. [1999]). An important feature of the method is that the contribution of individual spikes (I_t and I_{tta}) is evaluated separately from that of spike patterns (I_{ttb} and I_{ttc}). The first order term is:

$$I_t = \sum_{a,i} \left\langle \bar{n}_{ais} \log_2 \frac{\bar{n}_{ais}}{\langle \bar{n}_{ais'} \rangle_{s'}} \right\rangle_s \quad (3)$$

n_{ais} is the response in time bin i of cell a to stimulus s on a particular trial. The bar $\bar{}$ means an average over trials, thus $\bar{n}_{ais}$ is simply the corresponding PSTH. The angle brackets $\langle \ldots \rangle_s$ denote an average over stimuli, weighted by the stimulus probabilities $P(s)$. Equation 3 conveys information contained in the timing of independent spikes.

The first of the second order terms (PSTH similarity) is:

$$I_{tta} = \frac{1}{2} \sum_{a,b,i,j} \left[CS_{aibj} \left(1 - \log_2 \frac{CS_{aibj}}{MS_{ai} MS_{bj}} \right) - ECS_{aibj} \right] \quad (4)$$

Here $MS_{ai} = \langle \bar{n}_{ais} \rangle_s$ is the average of the PSTH over stimuli for time bin i of cell a; $CS_{aibj} = \langle \bar{n}_{ais} \bar{n}_{bjs} \rangle_s$ is the signal correlation between time bin i of cell a and bin j of cell b; $ECS_{aibj} = MS_{ai} MS_{bj}$ is the expected value of CS_{aibj} for PSTHs that are uncorrelated across stimuli. I_{tta} is always negative or zero: it corrects I_t for any redundancy between spikes. I_{tta} and I_t together express any information that the population conveys purely by the timing of individual spikes (time-varying firing rate).

The influence of multi-spike patterns is expressed by the remaining two second order terms. The first of these (stimulus-independent patterns) is:

$$I_{ttb} = -\frac{1}{2 \log_2 e} \sum_{a,b,i,j} \left\langle CN_{aibjs} - ECN_{aibjs} \right\rangle_s \log_e \frac{CS_{aibj}}{ECS_{aibj}} \quad (5)$$

CN_{aibjs} (noise correlation) is the *joint* PSTH of bin i of cell a and bin j of cell b given stimulus s. It is equal to $\overline{n_{ais} n_{bjs}}$, unless $a = b$ and $i = j$, in which case it is zero. $ECN_{aibjs} = \bar{n}_{ais} \bar{n}_{bjs}$ is the expected value of CN_{aibjs} for statistically independent spikes. Note that "noise" is something of a misnomer since noise correlations can reflect the presence of information, as explained below. This expression is positive when the normalized signal and noise correlations have opposite sign; negative when they have the same sign—see Figure 3.

The final term (stimulus-dependent patterns) is:

$$I_{ttc} = \frac{1}{2} \sum_{a,b,i,j} \left\langle CN_{aibjs} \log_2 \left[\frac{CN_{aibjs}}{ECN_{aibjs}} \div \frac{\langle CN_{aibjs'} \rangle_{s'}}{\langle ECN_{aibjs'} \rangle_{s'}} \right] \right\rangle_{s'} \quad (6)$$

I_{ttc} is positive or zero and captures the effect of any stimulus-dependent structure in the normalized noise correlations CN/ECN.

Note that the relative contribution of within-neuron and cross-neuron spike patterns can be assessed simply by considering separately the $a = b$ and $a \neq b$ components in Equations 4, 5, and 6.

Estimating Synergy/Redundancy

The *total synergy* in the response of a neuronal population is the total information it conveys by spike timing less that conveyed by the constituent spikes independently; if the total synergy is negative, the code is redundant. In the series expansion, the information conveyed by spikes independently is precisely the first order term I_t. Thus the total synergy S is simply the sum of the second order terms:

$$S = I_{tta} + I_{ttb} + I_{ttc} \quad (7)$$

The series expansion also allows us to express the total synergy in terms of a within-cell part S_w and a cross-cell part S_c. S_w is the sum of the same cell ($a = b$) components of the second order terms and measures the net effect of within-cell spike patterns. S_c is the sum of the cross-cell ($a \neq b$) ones, and measures the net effect of cross-cell spike patterns.

Checking the Method

We performed several analyses to check that the series expansion approximation was accurate. In the following, results are given for D2-D2 cell pairs; those for cross-columnar pairs were similar. First, we verified that the formal mathematical assumptions of the method were satisfied: the stimulus-average firing rate in any time window must be less than one; correlations between spike times must have finite precision; the ratio CS_{abij}/ECS_{abij} must not diverge at any time resolution dt. Second, we estimated the response entropy in spike timing for each cell pair, both directly with the "brute force" method and using the series expansion (Schultz and Panzeri, 2001). For dt = 10 ms and T = 40 ms, these estimates differed by 1.3% averaged over pairs. Third, we compared information in the spike count, estimated using the series expansion, to that estimated using the direct method. For T = 40 ms, these values differed by 1.2% averaged over pairs. Fourth, as reported in Panzeri et al. (2001), we compared information in spike timing for single cells, with the direct ("brute

force") and series expansion methods at values of *dt* and *T* for which the former method was well sampled. For $dt = 10$ ms and $T = 40$ ms, the corresponding information estimates differed by 1.5%, averaged over cells. Fifth, we made the same comparison for pairs of cells. For $dt = 10$ ms and $T = 20$ ms, the estimates differed by 1.0%, averaged over pairs of cells. Lastly, we estimated a lower bound on the full spike timing information that is very robust to sampling problems (introduced to spike train analysis by Reich et al. [2000]) and compared this to the information in the spike train estimated using the series expansion. For $dt = 10$ ms and $T = 40$ ms, these values differed by 0.1%, averaged over pairs.

Collectively, these results indicate that the series expansion method was accurate in the present case.

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