Transformation in the Neural Code for Whisker Deflection Direction Along the Lemniscal Pathway

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Bale MR, Petersen RS. Transformation in the neural code for whisker deflection direction along the lemniscal pathway. J Neurophysiol 102: 2771–2780, 2009. First published September 9, 2009; doi:10.1152/jn.00636.2009. A prominent characteristic of neurons in the whisker system is their selectivity to the direction in which a whisker is deflected. The aim of this study was to determine how information about whisker direction is encoded at successive levels of the lemniscal pathway. We made extracellular recordings under identical conditions from the trigeminal ganglion, ventro-posterior medial thalamus (VPM), and barrel cortex while varying the direction of whisker deflection. We found a marked increase in the variability of single unit responses along the pathway. To study the consequences of this for information processing, we quantified the responses using mutual information. VPM units conveyed 48% of the mutual information conveyed by ganglion units, and cortical units conveyed 12%. The fraction of neuronal bandwidth used for transmitting direction information decreased from 40% in the ganglion to 24% in VPM and 5% in barrel cortex. To test whether, in cortex, population coding might compensate for this information loss, we made simultaneous recordings. We found that cortical neuron pairs conveyed 2.1 times the mutual information conveyed by single neurons. Overall, these findings indicate a marked transformation from a subcortical neural code based on small numbers of reliable neurons to a cortical code based on populations of unreliable neurons. However, the basic form of the neural code in ganglion, thalamus, and cortex was similar—at each stage, the first poststimulus spike carried the majority of the information.

INTRODUCTION

A common principle for the organization of sensory systems is a massive expansion in neuronal numbers from the periphery to the cerebral cortex. In the rat whisker system, for example, ~150 mechanoreceptors innervate each whisker follicle (Lee and Woolsey 1975), each thalamic barreloid contains ~250 neurons (Land et al. 1995), but each cortical barrel column contains ~10,000 neurons (Welker and Van der Loos 1986). Similarly, in the primate visual system, there are ~50 times as many neurons in layer 4 of V1 as there are retinal ganglion cells (Peters and Payne 1993). Neural codes at successive stages of the sensory pathway thus operate under markedly different anatomical constraints. Indeed, changes in neural circuitry from one stage to another can be associated with striking transformations of the neural code (Kara et al. 2000; Perez-Orive et al. 2002; reviewed by Quiñon Quiroga and Panzeri 2009).

The aim of this study was to compare, at successive stages of the whisker pathway, the neural code for an important sensory parameter—the direction in which a whisker is deflected. First-order whisker afferents are direction selective (Gibson and Welker 1983; Lichtenstein et al. 1990; Zucker and Welker 1969), as are many neurons at subsequent levels of the lemniscal pathway, from principal trigeminal nucleus (PrV), through ventro-posterior medial nucleus of thalamus (VPM), to primary somatosensory cortex (S1) (Minnery and Simons 2003; Simons 1978; Waite 1973). Direction tuning is more selective in the periphery than in thalamus or S1 (Minnery et al. 2003; Simons and Carvell 1989). Recent work has elucidated the mechanisms of directional tuning (Puccini et al. 2006; Wilent and Contreras 2005), its dependence on context (Khatri and Simons 2007; Kida et al. 2005; Lee and Simons 2004), its cortico-thalamic modulation (Li and Ebner 2007), and its fine-grained spatial organization (Andermann and Moore 2006; Bruno et al. 2003; Kerr et al. 2007; Timofeeva et al. 2003). However, the reliability of neuronal responses to directional stimuli has not been characterized. Unlike experimenters, behaving animals cannot average over many repetitions (trials) of a sensory event before reacting to it: they typically react to single events. Thus an effective neural code must be robust to trial-to-trial variability in neuronal responses. Such robustness might arise directly from high reliability of single neurons; alternatively, it might be generated from unreliable single neurons by population averaging (reviewed by Petersen et al. 2009). The aim of this study was to investigate how reliability influences the neural code for whisker direction.

Our first objective was to determine whether there is a transformation in how reliably neurons respond to whisker direction along the pathway. Our second objective was to test whether the form of the neural code is transformed. To this end, we recorded responses of neurons in trigeminal ganglion, VPM, and S1 to identical directional stimuli, under identical experimental conditions. To study reliability, we studied variability of neuronal responses. To quantify direction information, we used mutual information. This approach has the advantage that it provides an objective yardstick that can be used to compare different neurons in different brain regions and different neural codes in a manner that makes minimal assumptions about the precise relationship between stimulus and response (Poisson distribution, Gaussian distribution, etc.).

METHODS

Electrophysiology

For this study, it was essential to be able to deliver precisely controlled and repeatable whisker deflections. We therefore used an anesthetized preparation. All experiments were conducted in accordance with international and institutional standards for the care and use of animals in research. Adult Wistar rats (n = 28) were anesthetized with urethane (1.5 g/kg body weight) and placed in a stereotaxic...
instrument, and their body temperature was maintained at 37.5°C using a homeothermic heating system. In any one rat, recordings were made either in the trigeminal ganglion, the VPM, or barrel cortex. Craniotomies were made, relative to bregma, at 0–3.0 mm posterior, 0.5–3.5 mm lateral (ganglion); 2.0–4.5 mm posterior, 1.5–4.0 mm lateral (VPM); 0.5–3.5 mm posterior, 4.0–7.0 mm lateral (S1). The dura was reflected and either a tungsten microelectrode (8 MΩ at 1 kHz; FHC, Bowdoin, ME) or a silicon substrate, single shank 16-channel probe (2–4 MΩ at 1 kHz; NeuroNexus Technologies, Ann Arbor, MI) inserted into the brain using a customized piezoelectric motor (Lambda Photometrics, Harpenden, UK). The electrode penetration angle was vertical for ganglion and VPM recordings and normal to the pial surface for S1 recordings. Extracellular signals were preamplified, digitized (sampling frequency, 24.4 kHz), band-pass filtered (second-order Butterworth: for VPM and S1, 300–3,000 Hz; for ganglion, 500–6,000 Hz), and continuously stored to hard disk for off-line analysis (TDT, Alachua, FL).

**Whisker stimulation**

At each recording site, the principal whisker (PW) was identified by deflection of individual vibrissae using a handheld probe. Whiskers were cut at 10 mm from the skin, and the PW was inserted into a narrow tube attached to a custom-built, multidirectional mechanical stimulator, consisting of two orthogonally mounted piezoelectric multilayer benders (Physik Instrumente, Karlsruhe, Germany). Stimuli were generated as previously described (Montemurro et al. 2007a). At the start of each trial, the whisker was deflected by 400 μm in a given direction and held there for 250 ms, before being returned to the starting position. This square wave signal was smoothed to avoid mechanical resonances by convolution with a Gaussian function (SD, 1.6 ms). On each trial, the deflection direction was chosen at random from a uniform distribution. Each of 430 directions was presented once, at 0.5-s intervals, in the same random sequence for each recorded unit. We verified that the apparatus accurately reproduced the desired stimuli, using a custom-built LED-phototransistor device.

**Histological analysis**

Histological analysis was used to determine the location of recording sites in VPM and the depth of recording sites in S1. At the end of recordings, AC electrolytic lesions were made by applying 5–10 μA for 15 s. Animals were deeply anesthetized with urethane and perfused transcardially with 0.9% (wt/vol) formaldehyde in saline. Brains were removed and left in the buffered 30% (wt/vol) sucrose solution for a further 72 h. Coronal sections of 50 μm were cut using a freezing sliding microtome and stained with cresyl violet.

**Data analysis**

Spikes emitted by a given single unit were identified as previously described (Montemurro et al. 2007a). Ganglion units were classified as slowly adapting (SA) or rapidly adapting (RA) using a method similar to that of Lichtenstein et al. (1990). A unit was classified as SA if its spike rate in the interval 100–250 ms after deflection onset was significantly greater than its activity in the 150-ms interval immediately before deflection (Mann-Whitney U-test, P < 0.05). Units with no significant plateau response were classified as RA.

To compute the directional tuning curve for a given single unit, we first counted the number of spikes evoked by each of the 430 direction stimuli, within a time window of duration 100 ms, starting at deflection onset. The random stimulus design allowed us to flexibly classify the stimuli into a variable number of direction categories. We used 4 (0–90, 90–180°, etc.), 8 (0–45, 45–90°, etc.), and 16 categories (0–22.5, 22.5–45°, etc.); 0° corresponded to deflection in the ventral direction, 90° to caudal, and −90° to rostral.

We computed the mean firing rate for each category. Directional selectivity was quantified using a selectivity index, defined as the maximum firing rate across direction categories, divided by the firing rate averaged over categories. With n categories, a unit that fires exclusively in the preferred direction has selectivity index n; a unit that fires equally in all directions has index 1. However, as first noted by Kerr et al. (2007), the index can be inflated by sampling bias. For example, a unit completely unselective to direction fires, on average, equally in every direction. However, only in an imaginary experiment using an infinite number of stimulus repetitions would the n estimated firing rates be exactly equal, and the index be exactly 1. In a real experiment, the estimated firing rates will, because of chance, differ somewhat. One direction will evoke a greater estimated firing rate than the others, so the selectivity index will be >1. The magnitude of the bias depends strongly on firing rate. In the extreme case where a unit fires just one spike (at random) during presentation of the entire stimulus ensemble, one direction will, by chance, “evoke” the spike and the selectivity index will be n.

We corrected for this bias using the procedure of Kerr et al. 2007. First, to estimate the bias for a given unit, we randomly permuted its 430 responses with respect to the stimulus directions that evoked them and computed a “shuffled selectivity index.” This procedure randomizes the relationship between direction and response, so the amount by which the shuffled index exceeds 1 can be used as an estimate of the bias. We repeated the permutation procedure 10,000 times and averaged the 10,000 bias estimates. Finally, to produce a “bias-corrected selectivity index,” we subtracted the averaged bias from the selectivity index.

**Reliability analysis**

To quantify the reliability of a neuronal response to a given direction, we computed the mean response (number of emitted spikes) to a given stimulus and compared this to the variance of the response. The variance/mean ratio (Fano factor) is a useful measure of reliability. The response variance can be strongly constrained by the fact that a neuronal response consists of an integer number of spikes. For example, suppose that a single unit fires either one spike, with probability p, or zero spikes, with probability 1−p. The mean response is p; the variance is p−p². Thus the variance is a quadratic function of the mean. Additional spikes can only increase the variance, so p−p² is in fact the minimum possible variance. This gives rise to the “scalloped” structure in scatter plots of variance versus mean, apparent in Fig. 3, A and B.

**Information theoretic analysis**

Application of information theoretic methods to the whisker system is described in detail by Petersen et al. (2009). Briefly, we evaluated neural codes for direction based on two measures of neuronal response r—spike count and spike timing. For the spike count response of a single unit, r was the number of spikes fired within a time window of duration T ms, starting from deflection onset. For the spike count response of a pair of simultaneously recorded units, the response r was a vector consisting of the two single unit responses. To define the spike timing response, we subdivided the response window into L bins of width Δt ms (L = T/Δt) and registered whether each bin contained zero or at least one spike. In this way, for a single unit, r = [r₁, r₂, . . . , r₇] was a binary “word” of length L. R denotes the set of all possible responses, for a given type of code.

The set of stimuli S consisted of the 4, 8, or 16 different direction categories. We computed the unconditional probability P(s) of each category s as its relative frequency. The P(s) were approximately equal. We estimated the probability P(r|s) of response r being evoked by stimulus s for each possible stimulus-response combination and the unconditional probability P(r) as P(r) = ΣP(r|s)P(s).
If a neuron is direction selective, it emits different responses to different stimuli, and therefore the conditional probabilities $P(r|s)$ vary with $s$. Conversely, if a neuron is not direction-selective, the $P(r|s)$ are equal. Mutual information quantifies the stimulus coding of a neuron by measuring how much, on average, $P(r|s)$ differs from $P(r)$

$$I(S;R) = \sum_{r,s} P(r|s)P(s)\log_2 \frac{P(r|s)}{P(r)}$$

(1)

The value of $I(S;R)$ depends on the duration of the time window $T$ and (for spike timing), the bin size $\Delta t$.

Different spike patterns occur in response to different stimuli not only because different stimuli elicit different responses but also because of noise (variation in response to repetitions of the same stimulus). The total variability of the response caused by both sources (the response bandwidth) is quantified by the response entropy $H(R)$

$$H(R) = -\sum_r P(r)\log_2 P(r)$$

(2)

The component of the total variability caused specifically by noise is quantified by the noise entropy $H(R|S)$

$$H(R|S) = -\sum_s \sum_r P(s)P(r|s)\log_2 P(r|s)$$

(3)

Mutual information is the difference between these quantities: $I(S;R) = H(R) - H(R|S)$. Because $H(R|S) \geq 0$, $H(R)$ is an upper bound on $I(S;R)$. The tightness of this bound varies from one neuron to another. For an efficient encoder, most of the available bandwidth is used for transmitting information, and little is taken up by noise, so $I(S;R)$ accounts for a large fraction of $H(R)$. Conversely, for an inefficient encoder, most of the bandwidth is taken up by noise, so $I(S;R)$ is only a small fraction of $H(R)$. To quantify this, we computed the “coding efficiency” of a neuron $E(R)$ as (Rieke et al. 1995)

$$E(R) = \frac{I(S;R)}{H(R)}$$

(4)

Because they are computed from a finite number of trials, the probabilities $P(r)$ and $P(r|s)$ are estimates that fluctuate around their true values. Thus they are subject to sampling error. Sampling error typically leads to positive bias in estimates of mutual information and negative bias in estimates of entropies (reviewed by Panzeri et al. 2007). Because the magnitude of this bias varies for different types of codes and different neurons, it is important to eliminate it. We corrected for bias as previously described (Montemurro et al. 2007a). Briefly, to evaluate the spike count code, we corrected for sampling bias using quadratic extrapolation to infinite trials (Strong et al. 1998). To evaluate the spike timing code, we used two approaches: the shuffling procedure described by Montemurro et al. 2007b and the data-robust lower bound to Eq. 1, described by Pola et al. (2005). Both procedures were used together with quadratic extrapolation. We could reliably estimate mutual information for word lengths up to $L = 5$ bins. Because the two procedures gave very similar results (within 4.4% at $\Delta t = 5$ ms, $L = 5$), we report results only for the lower bound method.

Because some cells exhibited small values of mutual information (<0.1 bits), we tested statistically whether the information conveyed by each unit was significantly different to zero. We randomly permuted the responses of each neuron in turn with respect to the stimulus directions that evoked them and recomputed the mutual information as above. By repeating this procedure 10,000 times, we constructed a 95% confidence bound for the greatest mutual information value that could occur, given the null hypothesis that $I(S;R) = 0$.

RESULTS

We recorded the responses of 40 single units in the trigeminal ganglion, 25 in VPM, and 40 in S1 to deflection of their PWs in 430 different directions. To construct directional tuning curves, stimuli were divided into 4, 8, or 16 categories (0–90, 90–180°, etc.). For every unit, we calculated the evoked firing rate in each of the direction categories (time window, 100 ms; starting at deflection onset). To average tuning curves over units with different preferred directions (PDs), tuning curves were aligned by their PD. Figure 1A shows average tuning curves for ganglion, VPM, and S1 using eight direction categories. To compare the shapes of tuning curves independently of variations in maximum firing rate, we normalized the tuning curve of each unit by the firing rate in its PD (Fig. 1B). VPM and S1 directional tuning curves were broader than ganglion ones. To quantify direction selectivity, we computed a selectivity index for each unit (firing rate in the PD, divided by mean firing rate across directions). Consistent with previous observations (Bruno et al. 2003; Minnery et al. 2003), we found a decrease in direction selectivity along the pathway from trigeminal ganglion to S1. Mean selectivity indices were 2.64 ± 1.2 for ganglion; 2.34 ± 0.9 for VPM; and 1.77 ± 0.5 (SD) for S1. Because this index can be inflated by sampling bias (see METHODS), we also computed a bias-corrected selec-
tivity index (Kerr et al. 2007). The same decrease in selectivity across the pathway was evident with the corrected index: means for ganglion, VPM, and S1 were 2.38 ± 1.1, 1.97 ± 0.8, and 1.40 ± 0.5, respectively. To test whether this selectivity was limited by the number of categories used, the analysis was repeated using 16 direction categories. The resulting corrected index values were slightly higher, but not significantly so: means for ganglion, VPM, and S1 were 2.58 ± 1.9 (P = 0.94, Mann-Whitney U-test), 2.00 ± 0.9 (P = 0.92), and 1.41 ± 0.5 (P = 0.90), respectively. Hence most of the following analyses were conducted using eight direction categories.

Transformation of direction reliability across the pathway

Tuning curves, such as those of Fig. 1, show that the neuronal response is modulated by the direction of whisker deflection and therefore indicate that directional information is encoded. However, tuning curves do not show how much information is available in the neuronal response nor how reliable it is. Two neurons with similar tuning curves can differ greatly in the amount of information their responses convey, depending on their reliability.

To study reliability, we first examined the neuronal responses on a single trial basis. Figure 2, A1–A4, shows the spikes fired by typical single units, recorded from ganglion, VPM, and S1, in response to whisker deflection in each of the 430 different directions. For the ganglion, both an SA (n = 7) unit and an RA (n = 33) unit are shown. For the SA unit (Fig. 2A1), there was a qualitative difference in the response to different directions. The unit almost always responded to directions in the range 0–180° (response of ≥1 spike on 96% of trials) but rarely in the range −180 to 0° (response on 3% of trials). Similarly, the RA ganglion unit (Fig. 2A2) responded to directions in the range −180 to −45° (55% of trials) but almost never in other directions (0.4% of trials). For neurons such as these, the emission of a spike was a reliable event, which unambiguously signaled the occurrence of a whisker deflection within a preferred range of directions (0–180° for the SA unit, −180 to −45° for the RA unit).

![Figure 2](http://jn.physiology.org/)

**FIG. 2.** Response of single units to whisker direction at different stages of the whisker pathway. A1–A4: spikes fired in response to deflection of the principal whisker in 430 different directions for a slowly adapting (SA) ganglion unit, a rapidly adapting (RA) ganglion unit, a ventro-posterior medial thalamus (VPM) unit, and a primary somatosensory cortex (S1) unit, respectively. B1–B4: mean spikes per trial after a deflection in a given direction, for units corresponding to A1–A4. Bars denote SD. C1–C4: mutual information conveyed by the spike count about direction (8 categories) in time windows starting at stimulus onset, ending 1–100 ms later, for units corresponding to A1–A4.

J Neurophysiol • VOL 102 • NOVEMBER 2009 • www.jn.org
The example VPM unit also emitted spikes more frequently to some directions than others (response of ≥1 spike on 66% of trials for the preferred 135° compared with 26% for other directions). However, because all directions evoked responses, this unit’s spikes were an ambiguous signal. The example S1 unit was also directionally selective (response of ≥1 spike on 51% of trials for the preferred 135° compared with 27% for other directions) but, like the VPM unit, its spikes were ambiguous.

The hallmark of a reliable unit is that any trial-to-trial variations in its response are small compared with the mean response. The hallmark of an unreliable unit is that fluctuations are as large as (or larger than) the mean. To quantify the reliability of each neuron, we computed the ratio of the variance to the mean (Fano factor) of its response in each direction. For example, for the SA unit of Fig. 2A1, the mean response in the preferred direction (0–100 ms time window, 8 direction categories) was 3.7 spikes/trial and the variance was 0.26 spikes²/trial² (Fig. 2B1), resulting in a Fano factor of 0.069. For the S1 unit of Fig. 2A4, the mean was 0.89 spikes/trial, the variance was 0.94 spike²/trial² (Fig. 2B4), and the Fano factor was 1.1. The Fano factor data confirmed the intuitive impression from the raster plots that the SA unit’s response to direction was markedly more reliable than that of the cortical unit. Fano factors for the RA and VPM units of Fig. 2, A2 and A3, were 0.33 and 0.58, respectively.

To determine the general nature of the reliability at each stage of the pathway, we repeated the Fano factor analysis for every single unit in our database. For each unit, the Fano factor was computed for the response in each of eight direction categories (0–100 ms time window). We found that almost all ganglion responses exhibited Fano factors of <1 (Fig. 3A), with a mean of 0.31 ± 0.35 (Fig. 3D). The data for the RA units formed a clear scalloped structure (Fig. 3A, dots). This was a consequence of the fact that neurons fire integer numbers of spikes. For example, the RA unit shown in Fig. 2A2 had a mean response in the preferred direction of 0.67 spikes/trial. For a mean of 0.67, the minimum possible variance is 0.67 − 0.67² = 0.22 spikes²/trial² (see METHODS). The actual variance for this unit was indeed 0.22 spikes²/trial². The variability of the RA responses was typically the minimum possible, given their mean response. For VPM units, the Fano factor was also often <1, with an average of 0.53 ± 0.37 (Fig. 3D). Again, scalloping was evident in the scatter plot (Fig. 3B).

Although the mean response of cortical units to deflection in the preferred direction was similar to that of VPM units (0.9 vs. 0.8 spikes/trial), the response variance was markedly greater (1.3 vs. 0.4 spikes²/trial²). Thus the cortical Fano factor was typically >1 (Fig. 3C), with a mean of 1.3 ± 0.75 (Fig. 3D). Collectively, these results indicate a pronounced decrease in reliability along the pathway from receptors to barrel cortex.

This transformation in reliability has notable information processing implications. All else being equal, a reliable unit can potentially transmit much more information than an unreliable one. Our next aim was therefore to quantify the amount of information available in the responses of each unit. We did this by measuring the mutual information that the neuronal response (number of evoked spikes) conveyed about stimulus direction. Mutual information is expressed in binary logarithmic units (bits). With eight equally likely direction categories, the uncertainty about which direction might occur on any given trial was log₂8 = 3 bits. Mutual information measures how much, on average, this uncertainty might be reduced by observation of the neuronal response on a single trial. One bit of mutual information corresponds to a reduction of uncertainty by a factor of 2, two bits to a reduction of uncertainty by a factor of 2² = 4, and so on.

Figure 2, C1–C4, shows results for the example units from Fig. 2, A1–A4. We measured the response as the number of spikes emitted in a time window starting at deflection onset and systematically varied the window duration. The plots show mutual information as a function of window duration from 1 to 100 ms. For the SA ganglion unit, mutual information rose rapidly when the first spike occurred, reaching 0.71 bits at 15 ms of stimulus onset, and increased with subsequent spikes to 1.06 bits at 100 ms (Fig. 2C1). The RA unit information also increased rapidly, reaching its peak of 0.39 bits within 18 ms (Fig. 2C2). The VPM unit information peaked a little later, at 22 ms at 0.22 bits, before decreasing to 0.14 bits at 100 ms (Fig. 2C3). The S1 information peaked at the still lower value of 0.09 bits (Fig. 2C4). Thus the difference in reliability shown by Fano factor analysis was associated with a dramatic difference in direction information.

To determine the general nature of the transformation, we repeated the mutual information analysis for all units in our database (Fig. 4A). At 100 ms after stimulus onset, ganglion units conveyed an average of 0.49 ± 0.32 bits, VPM units conveyed 0.24 ± 0.24 bits, and S1 units conveyed 0.06 ± 0.07 bits. Thus there was an average reduction in mutual information of 52% from ganglion to VPM and a further reduction of 74% from VPM to S1. Remarkably, S1 units conveyed, on
average, only 12% of the mutual information conveyed by ganglion units. For shorter time windows, the reduction was even more marked. At 25 ms after stimulus onset, VPM units conveyed 50% of the mutual information conveyed by ganglion units, and S1 units conveyed 7%.

Within each stage of the pathway, neurons varied in their mutual information values (Fig. 4, B–D). Ganglion units (Fig. 4B) spanned a broad range from 0.08 to 0.95 bits (10th and 90th percentiles). VPM units (Fig. 4C) exhibited a skewed distribution with a number of weakly informative units (48% <0.1 bits) and a tail of informative units (90th percentile, 0.53 bits). S1 units (Fig. 4D) exhibited an even more skewed distribution (87.5% <0.1 bits; 90th percentile, 0.14 bits). In fact, whereas mutual information was significantly greater than zero ($P < 0.05$; see METHODS) for almost all ganglion and VPM units (100 and 92%, respectively), a significant minority of S1 units (32%) had mutual information statistically indistinguishable from 0. Within S1, layer 4 units conveyed slightly more mutual information than supragranular or infragranular layer units [median, 0.07 ($n = 5$), 0.04 ($n = 7$), and 0.04 bits ($n = 26$), respectively], but the differences did not reach statistical significance (Kruskal-Wallis test, $P = 0.39$). To check the robustness of the above results, we repeated the mutual information analysis using a measure of response that considers not just the number of evoked spikes but also their timing within the response window (see METHODS). We found a similar marked decrease in mutual information from the periphery to cortex. Using a response time window of 25 ms, subdivided into 5 ms bins, ganglion units conveyed, on average, 0.53 ± 0.30 bits, VPM units conveyed 0.30 ± 0.23 bits, and S1 units conveyed 0.04 ± 0.06 bits. This reduction—43% from ganglion to VPM, 92% from ganglion to S1—was similar to that reported above for spike counts in the same time window. In sum, these data indicate a dramatic transformation in the reliability with which direction information is represented along the whisker pathway.

In principle, the decrease in mutual information may not be entirely caused by differences in reliability. Another contributing factor might be that the decrease in firing rate from receptors to cortex lowers the bandwidth available for transmitting information. To test this possibility, we quantified bandwidth by measuring the “response entropy” (METHODS). We found (Fig. 5A) that, at 100 ms after stimulus onset, the average cortical response entropy was actually higher (1.27 ± 0.50 bits) than that of the ganglion (1.17 ± 0.62 bits) or the VPM (0.98 ± 0.42 bits). Thus limited bandwidth could not account for the low mutual information in cortex. The information theoretic measure of unreliability is the “noise entropy” (METHODS). Like the Fano factor, noise entropy is low for a reliable unit and high for an unreliable one. Consistent with the Fano factor results, we found (Fig. 5B) that noise entropy was 1.7 times larger, on average, in cortex compared with ganglion (1.21 ± 0.48 vs. 0.68 ± 0.41 bits) and 1.6 times larger compared with VPM (0.74 ± 0.43 bits). Thus a key factor underlying the reduced cortical mutual information was an increase in response variability. These data imply a markedly different form of direction code in the ganglion compared with cortex. In ganglion, a large fraction of a neuron’s bandwidth is accounted for by stimulus information: the “coding efficiency” (mutual information divided by response entropy) was 40 ± 20% (Fig. 5C). In contrast, in cortex, coding efficiency was only 5 ± 7%, with thalamus being intermediate (24 ± 22%).

![Figure 4](http://jn.physiology.org/)

**Fig. 4.** Transformation in direction information along the whisker pathway. A: mutual information conveyed by spike count in windows of progressively increasing duration, starting from deflection onset, averaged over all single units recorded from each brain area. Bars denote SE. B–D: distribution of mutual information values (100 ms time window) for ganglion, VPM, and S1, respectively.

![Figure 5](http://jn.physiology.org/)

**Fig. 5.** Transformation in coding efficiency along the pathway. A: response entropy of the spike count response (Eq. 2), plotted as in Fig. 4A. B and C: analogous data for noise entropy (Eq. 3) and coding efficiency (Eq. 4). Bars denote SE.
Cortical population coding

As noted in the Introduction, there is a profound expansion in neuron numbers from VPM to barrel cortex. This suggests that a decrease in reliability at the level of barrel cortex may be compensated by a change to larger-scale population coding. To test this possibility against the alternative possibility that directional information is simply lost, we recorded the responses of single cortical units simultaneously using a multi-microelectrode array (14 units, 32 pairs). If there is population coding, the mutual information conveyed by unit pairs should be substantially greater than that conveyed by the individual units. We estimated the mutual information conveyed by each pair of units (4 direction categories) and compared it with that conveyed by the constituent single units (Fig. 6). We found that, at 100 ms after stimulus onset, pairs of units conveyed a mean of 0.11 ± 0.06 bits, which was 2.1 times that conveyed by the constituent single units (0.05 ± 0.03 bits). This indicates that more information is available from the collective activity of groups of neurons than is available from that of single neurons and thus directly supports the population coding hypothesis.

Role of the first poststimulus spike

Might the form of the neural code also be different across the pathway? Previous work on location coding indicates that, in S1, the crucial element of the neuronal response is the first poststimulus spike, with later spikes being substantially redundant (Panzeri et al. 2001; Petersen et al. 2001). To test the role of the first spike in direction coding, we computed the mean number of spikes that each unit fired in response to deflection in its preferred direction and compared this to the unit’s mean number of first spikes (time window, 100 ms, starting from deflection onset). For RA ganglion, VPM, and S1, most spikes were first spikes: on average, RA units, 83.3 ± 19.8%; VPM units, 87.3 ± 15.9%; S1 units, 64.1 ± 20.4%. In contrast, for SA ganglion, on average, only 31.5% of spikes were first spikes (SD, 14.4%). This might reflect either a more complex, multispike SA code or, alternatively, a first spike code where subsequent spikes are redundant. To test the role of the first spike in the direction code, we computed the mutual information conveyed by the first spike only and compared it with the mutual information conveyed by the complete spike train (Fig. 7). We also computed the mutual information conveyed by the first and second spikes together and that conveyed by the first, second, and third spikes together. Despite the fact that SA ganglion units fired multiple spikes (mean 4.1 spikes in the PD), we found that the first spike of the SA cells accounted for the bulk (68.5%) of the mutual information conveyed by the complete response (Fig. 7A). Addition of the second spike added only an additional 10.0%; addition of the third spike added a further 9.1%.

For RA ganglion, VPM, and S1 units, the first spike was also dominant. For RA ganglion units, the first spike alone accounted for 85.5% of the mutual information carried by the complete response (Fig. 7B); for VPM units, 95.4% (Fig. 7C); for S1 units, 81.3% (Fig. 7D). Similar results were obtained when the possible role of spike timing on responses was also taken into account. First spike timing accounted the following mutual information conveyed by the complete response: ganglion SA units, 83.6%; RA ganglion, 91.2%; VPM, 96.6%; S1, 94.7% (25-ms time window, 5-ms bins).
DISCUSSION

This study presented an analysis of how neurons in the lemniscal pathway encode the direction of a whisker deflection and how the neural code is transformed at successive stages. Previous studies have reported a systematic broadening of directional tuning curves along the pathway from trigeminal ganglion to S1 (Minnery and Simons 2003; Minnery et al. 2003; Simons and Carvell 1989). The novel contribution of this study was to analyze the reliability of neuronal responses to directional stimuli. Our main results were that 1) there is a dramatic change in the nature of the direction code from highly reliable and efficient subcortically to unreliable and inefficient cortically and 2) the key information-bearing element of the response throughout the pathway is the first poststimulus spike.

Subcortical representation of whisker direction

As noted in the Introduction, there are strong anatomical constraints on neural coding in the subcortical whisker system. Each whisker is innervated by only ~150 mechanoreceptors. Because mechanoreceptors are heterogeneous—in morphology (Ebara et al. 2002), activation threshold (Gibson and Welker 1983), preferred direction (Zucker and Welker 1969), and response to object contact (Szwed et al. 2003)—the number responsive to any given stimulus may only be on the order of 10s of neurons per whisker. How can so few neurons convey reliable stimulus information? Our data indicate that a key factor is likely to be the remarkable reliability of stimulus coding in the mechanoreceptor population. We found that ganglion units exhibited sub-Poisson variability (Fano factor, 0.3) and conveyed a maximum of 1.3 bits (average, 0.5 bits) of information concerning the direction of deflection. To interpret such numbers, it is useful to consider the direction discrimination task of Narumi et al. (2007). This was a two-way task in which the two direction stimuli were equally likely. Thus there was log2 = 1 bit of stimulus uncertainty on every trial. Because rats performed with almost zero error, the underlying neural circuits must, at each level of the pathway, convey at least one bit of direction information. Our data indicate that just one to two mechanoreceptors, coding independent information, potentially provide sufficient afferent information to support this behavior.

These results are consistent with previous studies of how ganglion neurons encode other whisker parameters. Jones et al. (2004) showed that a white noise whisker stimulus elicits highly reproducible spikes and could be accurately decoded from the spike train. Arabzadeh et al. (2006) showed that texture-induced whisker vibrations could be accurately decoded from single neuron spike trains. In summary, in the trigeminal ganglion, single neurons, and even single spikes, are remarkably reliable and informative coding elements for a broad range of whisker stimuli.

Strong numerical constraints continue to operate in VPM, with each barreloid containing only ~250 relay cells. Our data show that a substantial fraction of the mechanoreceptor direction information is preserved across the two synapses between the mechanoreceptors and VPM relay cells. The average VPM unit exhibited a sub-Poisson Fano factor of 0.5 and conveyed 0.24 bits, the maximum being 0.88 bits. In the context of Narumi et al.’s two-way direction discrimination task, these results indicate that two to four VPM units, coding independent information, potentially suffice to supply the amount of information needed to support the observed behavioral performance. Previous studies have shown the likely mechanistic basis for this relatively reliable transmission. The trigeniculothalamic synaptic pathway—in marked contrast to intracortical circuitry—is mediated by potent synapses (Brecht and Sakmann 2002; Castro-Alamancos 2002; Deschenes et al. 2003; Montemurro et al. 2007a).

Overall, subcortical circuits in the lemniscal whisker system process directional information in a reliable manner. In this way, substantial information can be passed on to higher centers by means of remarkably small numbers of neurons.

Cortical representation of whisker direction

We found that S1 units exhibited substantial (approximately Poisson) variability (Fano factor, 1.3). In keeping with the substantial similarities in the anatomy of different cortical areas mentioned above, this result is entirely consistent with many previous studies of cat/primate visual cortex (Tolhurst et al. 1983). An analogous decrease in Fano factor along the sensory pathway has also been reported in the visual system (Kara et al. 2000).

We examined the functional implications of this transformation in reliability by estimating mutual information. We found that neurons in barrel cortex conveyed on average only 12.6% of the mutual information that ganglion units conveyed about whisker direction. In fact, consistent with Kerr et al. (2007), who reported that many supragranular layer neurons are directionally untuned, we found that, for a substantial minority of S1 neurons, mutual information was not statistically significant. Low mutual information was not caused by a limitation on the bandwidth of cortical units, because their response entropy was actually higher, on average, than that of ganglion units. Instead, a major factor contributing to low cortical mutual information seems to be a marked increase in response variability along the sensory pathway.

Collectively, these data suggest a marked change in the neural code for whisker direction at the cortical level. One possible interpretation is that direction is not encoded by all cortical neurons, but rather by a specific subpopulation. This hypothesis predicts that, even if the average mutual information is low, there should be a minority of units for which it is high. However, analysis of the distribution of mutual information values (Fig. 4, B–D) showed that the 10% most informative ganglion and VPM units were, respectively, 6.7 and 3.8 times more informative than the 10% most informative cortical units. We cannot completely exclude the possibility that a small subpopulation of cortical neurons exists that is highly informative about direction, but we were not able to detect it. An alternative interpretation of our data is that direction is coded in cortex by the collective activity of relatively many neurons, so that the low average information is offset by population size. Consistent with this hypothesis, we found that mutual information accumulated across units (pairs of simultaneously recorded S1 units conveyed 2.1 times as much information as single S1 units). Overall, our data may indicate a transition along the sensory pathway from local coding to population coding.

These changes may be a functional manifestation of the profound differences between subcortical and cortical cir-
Coding by the first poststimulus spike

In one respect, however, the neural code for direction seems to be remarkably similar at different stages of the whisker pathway. We found that the first poststimulus spike accounted for the bulk of the mutual information in the spike train, even for the highly responsive SA ganglion units. The early part of the response has previously been shown to be important for coding whisker location (Panzeri et al. 2001; Petersen and Diamond 2000; Petersen et al. 2001), sinusoidal whisker vibration (Arabzadeh et al. 2004), and texture (Arabzadeh et al. 2006). First spike coding has also been reported both elsewhere in the somatosensory system (Foffani et al. 2004; Johansson and Bizzi 2004) and the visual (Gollisch and Meister 2008; Reich et al. 2001) and auditory systems (Furukawa et al. 2000). This suggests that first spike coding is a general principle of coding.

In summary, our results indicate that there is a dramatic change in the reliability of the neural code for direction along the whisker pathway but that the essential nature of the code remains the same, with the first poststimulus spike being paramount.

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