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First spikes in ensembles of human tactile afferents code complex spatial fingertip events

Roland S Johansson & Ingvars Birznieks

It is generally assumed that primary sensory neurons transmit information by their firing rates. However, during natural object manipulations, tactile information from the fingertips is used faster than can be readily explained by rate codes. Here we show that the relative timing of the first impulses elicited in individual units of ensembles of afferents reliably conveys information about the direction of fingertip force and the shape of the surface contacting the fingertip. The sequence in which different afferents initially discharge in response to mechanical fingertip events provides information about these events faster than the fastest possible rate code and fast enough to account for the use of tactile signals in natural manipulation.

Since Adrian's discoveries in the 1920s[1], it has been broadly assumed that primary sensory neurons transmit information by their firing rates. To estimate firing rates, at least two impulses in a given neuron are required, and for reliable estimates, neural responses are generally averaged over a substantial time window and over several trials. While carrying out tasks in the natural world, however, people must quickly extract information about single stimuli. For example, in dexterous manipulations, tactile afferent information about mechanical fingertip events is rapidly expressed in the control of fingertip actions. Both friction between the object and the fingertips and the shape of grasped surfaces, recognized by tactile mechanisms, are reflected in the applied fingertip forces within ~100 ms of initial contact[2–4]. Accidental slips and unexpected perturbations of a grasped object elicit responses in tactile afferents that trigger specific behavioral consequences even faster (~65 ms)[3,5–7]. Peripheral nerve conduction times and muscular force generation delays account for ~45 ms of the delay[5,8], and at least 15 ms is required for central processing[8–10]. Given these neuromuscular time constraints and the limited firing rates of tactile afferents in natural manipulation tasks[3,7,11], it can be assumed that information about object features and fingertip events is transmitted when the majority of afferents recruited have only had time to fire a single impulse. Therefore, we hypothesized that information about important parameters of discrete mechanical fingertip events can be efficiently transmitted by the relative timing of the first impulses ('spikes') evoked in individual units in ensembles of afferents. A code based on relative timing of first spikes has been discussed and analyzed theoretically in relation to fast object categorization in central vision[12].

Firing rates of individual human tactile afferents are tuned broadly to a preferred direction of fingertip force, and this preferred direction varies among afferents such that ensembles of afferents can encode force direction[13]. Likewise, changes in object shape influence firing rates differentially among afferents such that curvature contrast signals are present within populations of tactile afferents[14]. In the present study, we tested whether these fingertip parameters can be encoded by the timing of the first spikes evoked in populations of tactile afferents. We also asked how quickly this code might convey tactile information compared to the earliest possible rate code defined by the interval between the first and the second spike in neurons engaged, termed the 'first interspike rate'. We show that the relative timing of the first-spikes contains reliable information about direction of fingertip force and object shape and provides this information appreciably faster than rate codes. The first-spikes elicited in the population of fast-adapting type-I afferents ('Meissner afferents') were most efficient in this capacity.

RESULTS

Using one flat and two spherically curved objects with radii of 10 and 5 mm (curvatures 100 and 200 m^{-1}, respectively), we applied forces at magnitudes and time courses representative of manipulation to a standard site at the fingertip (**Fig. 1**a). Each object applied force in each of five directions: normal to the fingertip and at an angle of 20° relative to normal with the tangential force component in the radial, distal, ulnar and proximal directions (**Fig. 1a**). The primary site of contact was the center of the nearly flat portion of the volar surface of the fingertip, which is a primary target for object contact in fine manipulation[13]. To obtain a picture of the population response, we recorded signals in representative samples of afferents terminating all over the distal phalanx (**Fig. 1b**)[13]. In total, unitary action potentials of 196 afferents were recorded from the median nerve in the upper arm[15]. Based on adaptation to sustained skin indentation and properties of the cutaneous receptive field[16], 72 of those afferents were classified as fast-adapting type I (FA-I), 10 as fast-adapting type II (FA-II), 73 as slowly-adapting type I (SA-I), and 41 as slowly-adapting type II (SA-II). The end organs of the FA-I, FA-II and SA-I afferents are very likely Meissner corpuscles,

Department of Integrative Medical Biology, Physiology Section, Umeå University, SE-901 87 Umeå, Sweden. Correspondence should be addressed to R.S.J. (roland.s.johansson@physiol.umu.se).

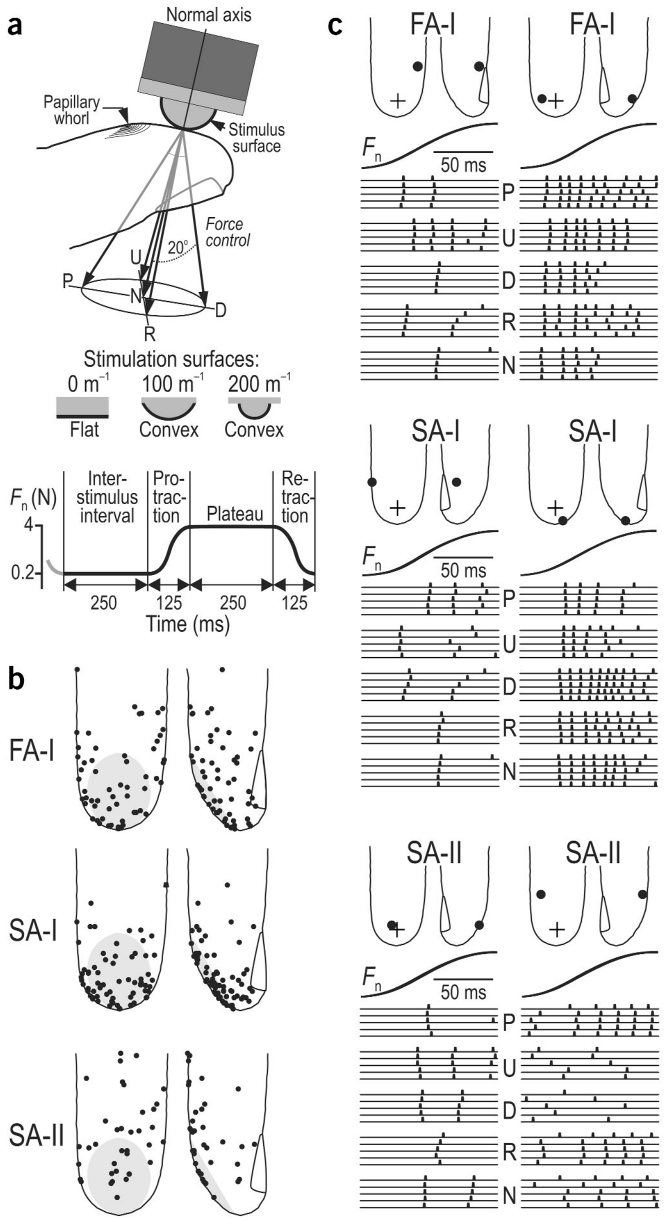

Figure 1 Force stimulation, afferent sample and responses to fingertip forces applied in different directions with the flat surface. (**a**) Superimposed on a 0.2 N normal force (F_n), force was applied to the fingertip in the normal direction only (N), and together with tangential components in the radial (R), distal (D), ulnar (U) and proximal (P) directions. Each stimulus consisted of a force protraction phase, a plateau phase and a retraction phase. (**b**) Locations of receptive field centers of sampled afferents on contours of the generic fingertip; side view includes afferents terminating on either side of the finger. Shaded zone represents an estimate of the area of contact between the stimulus surface and the fingertip at 4 N normal force[13]. (**c**) Impulse ensembles exemplify responses in two afferents of each type to the repeated force stimuli ($n = 5$) applied in each force direction; responses sorted in the same order as recorded. Traces above show the normal force component (F_n) superimposed for all trials. Force direction influenced consistently the first-spike latencies of all of these afferents except for the rightmost SA-II afferent that responded also during inter-stimulus intervals. Circles on the finger indicate the centers of the afferents' receptive fields and (+) indicates the primary site of stimulation.

Pacinian corpuscles and Merkel cells, respectively, and the SA-IIs are thought to terminate in Ruffini corpuscles[16]. The type-I afferents (FA-I and SA-I) possessed small and well-delineated receptive fields (~10 mm^2) as defined by weak point-indentations of the skin, whereas the fields of the type-II afferents (FA-II and SA-II) were an order of magnitude larger and less well defined[17,18]; the FA-II afferents responded to remote percussive stimuli and the SA-II afferents often to planar skin stretch. However, due to the widespread distributions of complex tensions all over the phalanx with fingertip forces representative of manipulation, in functional terms the receptive fields of nearly all FA-I, SA-I and SA-II afferents of the fingertip encompass the primary site of contact[13,14].

We focused on neural data obtained with the flat surface when examining effects of force direction. When examining effects of object shape, we focused on data obtained with forces normal to the skin at the contact site. For each afferent we analyzed data obtained from five stimuli from each stimulation condition (force direction and curvature). Our force stimuli did not consistently excite the FA-II afferents because of their preferential sensitivity to high-frequency mechanical transients, so their responses were not analyzed.

Direction of fingertip force

Although they terminated at various locations in the fingertip with reference to the primary stimulation site, nearly all of the recorded afferents responded reliably to at least one direction of force (61 FA-I, 73 SA-I and 40 SA-II afferents). Changes in force direction had substantial effects on the first-spike latency for afferents of the FA-I, SA-I and SA-II populations (**Fig. 1c**). Kruskal-Wallis ANOVAs applied to each individual afferent indicated that force direction reliably influenced ($P < 0.05$) the first-spike latency of nearly all responsive FA-I and SA-I afferents (92% and 90%, respectively) and for a majority of SA-II afferents (65%). As with the directional tuning of firing rates[13], for most directionally sensitive afferents the first-spike latency was tuned broadly to a direction in which it was shortest (**Fig. 2a**). Irrespective of direction of force, most afferents showed a remarkably small variability in the first-spike latency across the five repetitions of the stimulus (**Figs. 2a,b**). However, a two-way ANOVA applied to all afferents responsive in all five force directions indicated that the inter-trial jitter (expressed as the standard deviations of the latencies) differed among afferent types ($F_{2,122} = 4.81$; $P = 0.01$) but not with direction of force ($F_{4,488} = 1.42$; $P = 0.22$). The jitter was smaller for the FA-I afferents (median = 0.8 ms) than for the SA-I (1.0 ms) and SA-II afferents (1.0 ms).

For each directionally sensitive afferent that responded in all force directions, we estimated the direction of force in the tangential plane that would fire the afferent at the shortest latency (*i.e.*, the afferent's 'preferred direction'). In analogy with computations of preferred direction based on firing rates[13], we computed the vector sum of the mean latency leads observed in each direction over the mean latency observed for the direction with the longest latency. The direction of the resultant vector gave the afferent's preferred direction, and the length of the vector, termed 'directional sensitivity,' indicated the range of the latency changes resulting from changes in force direction. As with firing rates[13], for afferents of each type the preferred directions were distributed in all angular directions (**Fig. 2c**). The directional sensitivity was 12.9 ± 8.0 ms (mean ± s.d.), 14.9 ± 12.6 ms and 12.9 ± 16.6 ms for the FA-I, SA-I and SA-II afferents, respectively. For neither the FA-I afferents nor the SA-I afferents was there a significant angular-angular correlation between preferred directions derived from the first-spike latencies and from the first-interspike rate assessed by vector addition of the rates obtained with the four forces

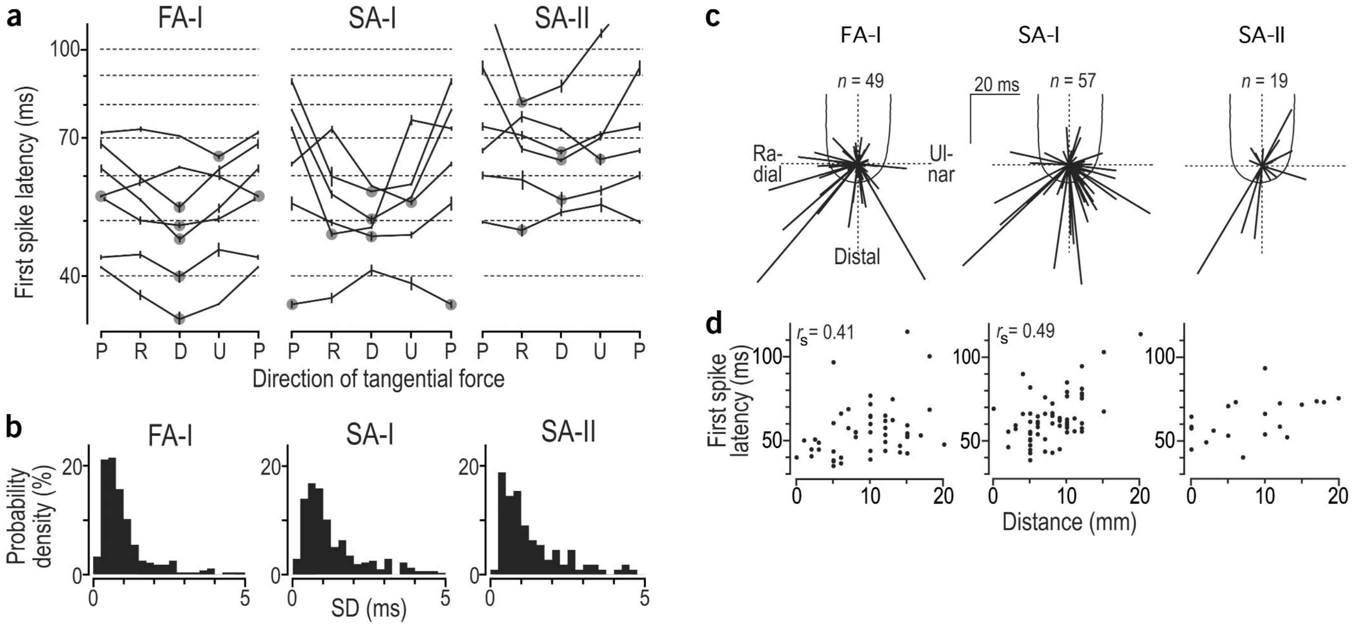

Figure 2 Afferents' directional sensitivity in the tangential plane. (**a**) Effect of direction of tangential force component on first-spike latencies exemplified by six afferents of each type that in most cases showed the shortest latency in the distal direction. Vertical bars give ± 1 s.d. of first-spike latencies computed across five stimuli. Gray circles indicate for each afferent the stimulus direction with the shortest latency. Note the logarithmic ordinate. (**b**) Frequency distribution of standard deviations of first-spike latencies; data pooled across stimulus directions and afferents. (**c**) Directional sensitivity vectors in the tangential plane with reference to the primary site of stimulation superimposed on the generic finger. (**d**) First-spike latencies with normal force stimulation plotted against distance from the primary stimulation site to the receptive field center. Correlation coefficients (r_s) are given in cases of significant correlation. Data from 6 SA-I and 17 SA-II afferents that could discharge during inter-stimulus intervals are not included in **b** and **d**.

with tangential components[13]. The maximum and the median angular difference between the preferred directions derived from the two response measures were 179° and 68°, respectively, for the FA-I afferents and 155° and 50° for the SA-I afferents. In contrast, for the SA-II afferents there was a reasonably high correlation between the preferred directions obtained by first-spike latencies and the rate code ($r_{aa} = 0.78$; see Methods).

The fact that first-spike latencies of individual afferents show directional tuning (**Fig. 2a**) with preferred directions distributed in all angular directions (**Fig. 2c**) suggests that information about force direction is contained in the sequence by which afferents are recruited. That is, with a single stimulus delivered to the fingertip in a given direction, the responsive afferents will be recruited in a particular order. With another force direction, the order will be different because some afferents would be recruited earlier, and others later. However, the efficacy of this code for conveying early directional information to the brain will depend on the variability in first-spike latencies and the number of afferents contributing impulses that quickly reach the brain. The latter will depend on the density of afferents in the fingertip, their mechanical sensitivities (which vary substantially for all afferents types and between types[19]) and the distance between an afferents' termination in the fingertip and the stimulation site (**Fig. 2d**; FA-I and SA- I (but not SA-II) afferents).

To evaluate how robustly and how early the recruitment sequence can code force direction, we computed, for our sample of afferents, the probability of correct discrimination of each force direction as a function of time (from force onset) using Monte Carlo simulations. The analysis used data from our entire sample of fingertip afferents, which we presume are unbiased except for the proportion of afferents of each type (see below). For each direction of force stimulation, we generated 1,000 possible recruitment sequences in which the individual afferents were ranked by recruitment order. For each sample sequence, the latency of an individual afferent was randomly selected from among the five latencies recorded from that afferent when stimulated (5 times) in the force direction in question. Thus, a sample sequence represents one of several possible recruitment sequences presented to the decoder during a single stimulus in a given direction, *i.e.*, the rank order of individual afferents could differ among sample sequences due to the variability in first-spike latencies. For each of these sample sequences, we then determined its predicted direction as follows. First, we obtained an estimate of the expected recruitment sequence for each force direction. Specifically, for each direction, we generated 20 sample sequences again by randomly selecting individual afferent latencies from among the five repeated force stimulations. We then computed the expected sequence from the mean ranks of the individual afferents in these 20 sample sequences. Note that these expected sequences may be conceived as representing learned recruitment sequences associated with stimuli in the different directions. Finally, we correlated the original sample sequence with each of these expected sequences. The expected sequence providing the highest correlation coefficient indicated the direction coded by the sample sequence. By determining the coded directions for all 1,000 sample sequences generated for a given force direction, we could compute the probability of correct discrimination of that direction. To estimate how the probabilities vary with time during the force stimulus, probability estimates were obtained for 124 progressively longer time windows (1-ms steps), starting at the onset of the force increase. For each window duration, the probability of correct discrimination was represented in time at the window's end (see Methods for further details).

The solid curves in the top panels of **Figure 3** show, for each afferent population and force direction, the time-varying probability of

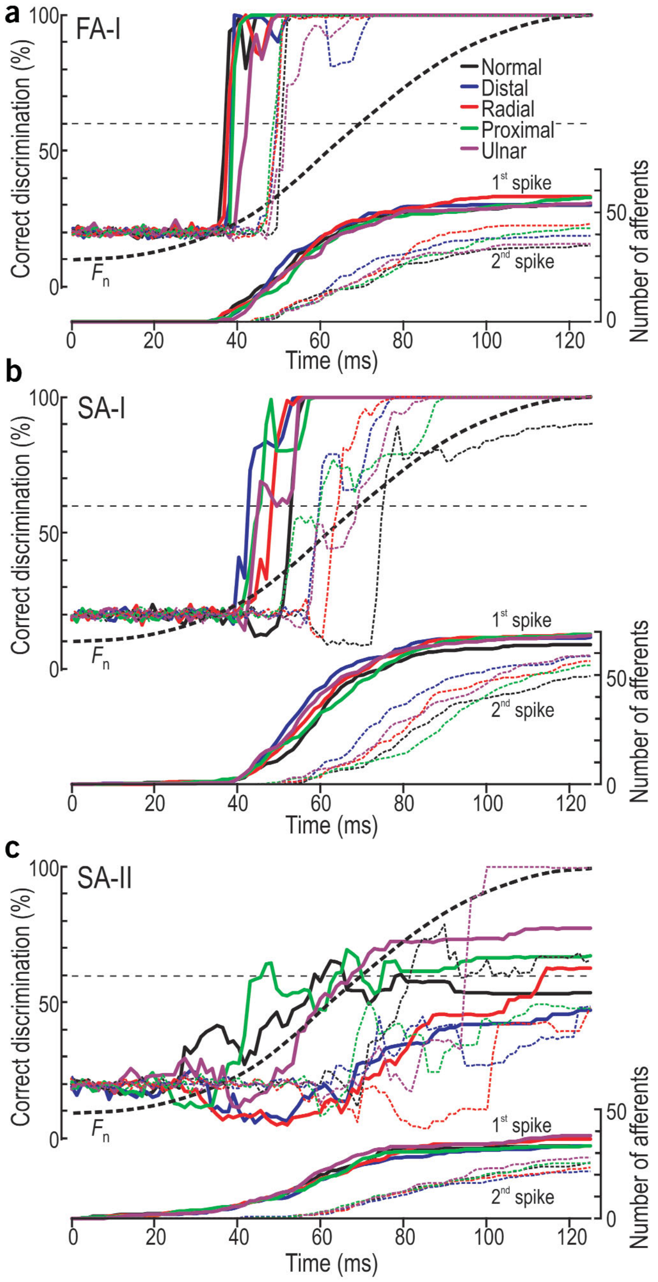

Figure 3 Discrimination of force direction by FA-I, SA-I and SA-II afferents based on the relative timing of first spikes and on first-interspike intervals. (**a**–**c**) Top, solid traces show the probability of correct discrimination of stimuli in each force direction (coded by different colors) by afferents' recruitment sequence as function of time during the force protraction phase. Black dashed curve shows the development of the normal force component (F_n). Horizontal line indicates the probability for one-half of the stimuli being discriminated correctly (*i.e.*, a probability of 60% given that chance performance is 20%). Thin dashed traces show the time-varying probability of correct discrimination based on first-interspike intervals. Bottom, solid curves give number of sampled afferents recruited as a function of time for stimuli in each force direction (*i.e.*, cumulative distributions of first-spike latencies). Thin dashed curves show the corresponding data for the second spike.

correct discrimination, and the solid curves in the lower panels represent the number of sampled afferents recruited with stimuli in each force direction, that is, cumulative distributions of first-spike latencies. Note that the distribution of first-spike latencies and thus the rates of afferent recruitment were hardly influenced by force direction. Separate repeated-measures ANOVAs applied to afferents of each type that responded in all directions revealed no systematic effects for the FA-I and SA-II populations, whereas with the SA-Is the latencies were on average marginally shorter with stimuli in the distal direction than in the proximal direction ($F_{4,224} = 2.48$; $P = 0.04$). Nevertheless, the SA-I and, in particular, the FA-I population discriminated force direction early and reliably based on the recruitment order. The FA-Is, which tended to be recruited earlier and had less variability in first-spike latencies, discriminated direction on average some 15 ms earlier than the SA-Is. About five FA-I afferents were recruited when half of the stimuli were effectively discriminated, corresponding to a probability of 60% (**Fig. 3**). This probability of discrimination was exceeded for all force directions ~42 ms after onset of the sinusoidal force increase, and ~6 ms after the appearance of the first spike at the electrode site in any FA-I afferent and any force direction. The time to exceed the same level of discrimination for all force directions with the SA-I afferents was ~53 ms and, depending on force direction, 8–16 afferents had to be recruited. The SA-II afferents discriminated force directions less well than did the FA-I and SA-I afferents (**Fig. 3c**). This may relate partially to ongoing background discharge in many of the SA-II afferents, which is reflected by the recruitment of afferents commencing already at the start of the force increase (**Fig. 3c**).

To identify the earliest possible information about force direction encoded in firing rates, we applied a similar rank correlation approach to the first-interspike intervals. As with first-spike latencies, early directional encoding based on first-interspike rate would need force direction to influence the first-interspike intervals of individual afferents differentially; correlated systematic influences with the first-interspike intervals of all afferents changing similarly would provide little directional information unless the decoder would know independently the exact time course of the stimulus. Thus, we ranked the durations of the first-interspike intervals for obtaining test and expected sequences to assess the best correlations. For each time window, the second spike had to occur within the current window for inclusion of an interspike interval in the correlation, and the probability obtained was represented in time at the end of the window. For the FA-I afferents, the first-interspike interval robustly discriminated each force direction, but 10–15 ms later than the discrimination provided by the first-spike latencies (compare thin and thick line curves in the top panel of **Fig. 3a**). With the SA-I afferents, the corresponding delay was on average ~20 ms, with a marked variation between force directions (**Fig. 3b**). As with the first-spike latencies, the SA-II afferents showed poor discrimination based on first-interspike rates (**Fig. 3c**). Notably, with both the FA-Is and SA-Is, at the time of the appearance of the first second spike in the afferent population (see bottom panels of **Fig. 3a**,**b**), force direction is nearly correctly predicted from the sequence of the first spikes.

Shape of stimulus surface

Fifty-four FA-I, 63 SA-I and 31 SA-II afferents were subjected to normal force stimuli with all three surfaces: the one flat and two curved surfaces (curvatures 100 and 200 m^{-1}). All afferents responded with at least one of the surfaces. As expected from the lack of systematic effects of surface shape on the average firing rates of these populations of afferents[14], separate repeated-measures ANOVAs applied to each of the three populations failed to indicate any systematic effect of shape on the first-spike latencies (see bot-

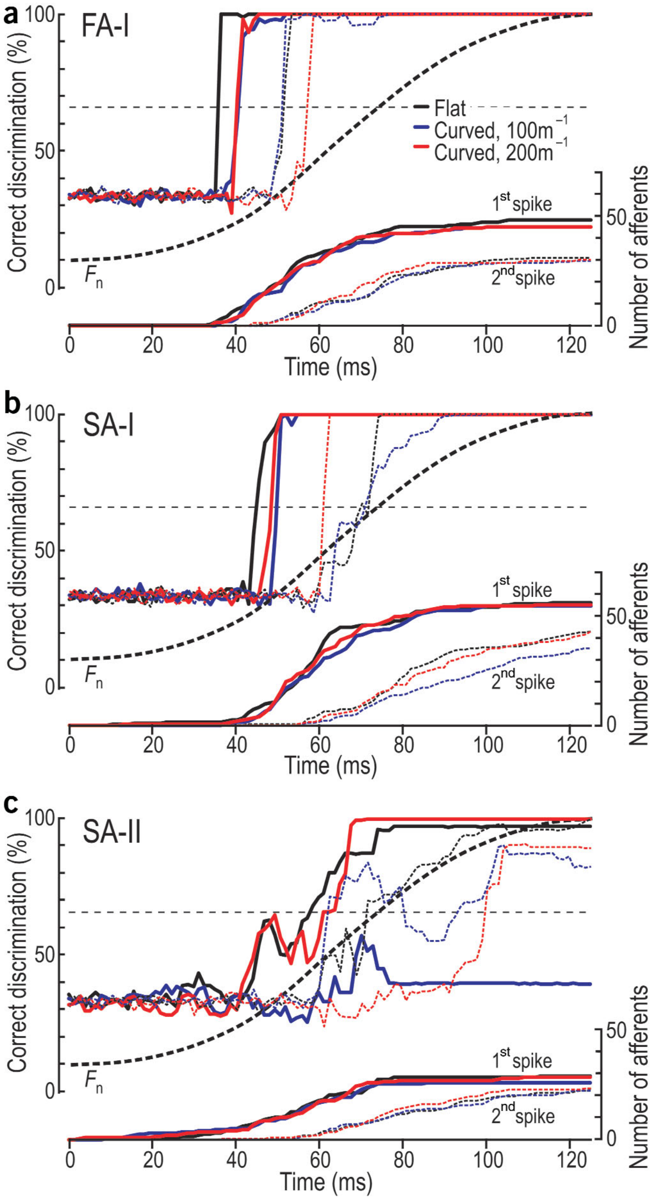

Figure 4 Discrimination of shape of stimulus surface by FA-I, SA-I and SA-II afferents based on the relative timing of the first spikes evoked in ensembles of tactile afferents and on the first-interspike intervals. (**a**–**c**) Top, solid traces show the probability of correct discrimination of each shape (coded by different colors) based on afferents' recruitment sequence as a function of time during the force protraction phase. Thin horizontal line indicates the probability for half of the stimuli being discriminated correctly (a probability of 66.5% given that chance performance is 33.3%). See **Figure 3** legend for further details.

tom traces in **Fig. 4a**–**c**). Yet, when individually tested the surface influenced reliably ($P < 0.05$) the first-spike latency for 79, 82 and 54% of the 42 FA-I, 56 SA-I and 24 SA-II afferents that responded with all surfaces, respectively. In agreement with the effect of surface shape on firing rates[14], for some afferents of each type the first-spike latency decreased with a change to a more curved surface and for others it increased (**Fig. 5a**). For the shape-sensitive FA-I, SA-I and SA-II afferents, the absolute value of the latency differences between responses to the flat and the most curved surfaces was 7.1 ± 8.2 ms, 12.9 ± 10.5 ms and 11.4 ± 12.3 ms, respectively.

The distance between the receptive field center and the primary stimulation site influenced the effect of shape on the first-spike latencies of the FA-Is and SA-Is: afferents that terminated farther from the primary stimulation site tended to show shorter latencies with curved surfaces than with the flat surface compared to those terminating at close locations (**Fig. 5b**). This stands in contrast to the effect of surface shape on the firing rates, which tend to increase with increasing curvature for afferents terminating close to the primary stimulation site[14,20]. The lack of a simple and consistent relationship between short latencies for response onsets and high firing rates is also apparent from the FA-I and SA-I afferents in **Figures 1c** and **5a**. This lack of correspondence indicates that the state of the mechanical link between the external stimulus and a nerve ending, somewhere inside the finger, can differ substantially when the ending elicits its first spike versus during subsequent firing, which occurs at higher fingertip forces. The complex nonlinear viscoelastic and anisotropic properties of the fingertip associated with its composite materials properties[13,14,21–23] most likely account for this phenomenon.

Using the same approach as with discrimination of force direction, we asked whether the relative timing of the first spikes could discriminate the three test surfaces. Both the FA-I and the SA-I populations quickly and unambiguously discriminated the three shapes (**Fig. 4a,b**). As with force direction, the FA-I afferents provided reliable information faster than the SA-Is, and for the FA-population in particular, surface can be discriminated when only a small fraction of the afferents has been recruited. For both populations the earliest possible rate code, represented by the first-interspike rate, provided shape discrimination, but substantially later than the first spikes (**Fig. 4a,b**; compare thin and thick traces in the top panels). Depending on surface, this delay ranged between 12 and 18 ms for the FA-Is and between 13 and 27 ms for the SA-Is. The SA-II afferents showed a poor capacity to discriminate object shape based on the relative timings of the first spikes as well as by the first-interspike rate (**Fig. 4c**).

DISCUSSION

Our central finding is that the relative timing of the first spikes in ensembles of primary sensory neurons contains rich information about the stimulus. Specifically, the relative timing of the first spikes elicited in populations of human tactile afferents in response to discrete mechanical fingertip events contain reliable information about the direction of force and the shape of the surface contacting the fingertip. Furthermore, the first spikes code this information faster than rate codes, which traditionally are thought to represent information in primary sensory neurons. The relative timing of the first spikes contains information about object shape and force direction because changes in either of these parameters differentially influenced the first-spike latency of individual afferents rather than having systematic effects on the latencies within an afferent population. Although our sampling of afferents from different digits undoubtedly introduced some variance in our data, it is unlikely that variation between fingers accounted for this differential effect. When we recorded from afferents of the same type terminating in the same fingertip, the effects of force direction and surface shape could differ substantially among the afferents. For example, the two FA-I afferents represented in **Figure 5a** terminated in the same digit, and the two SA-Is did as well.

Fast information transmission by the FA-I and SA-I afferents based on first spikes also depends on the capacity of fingertip stimuli to recruit quickly an adequate number of afferents. The tactile apparatus

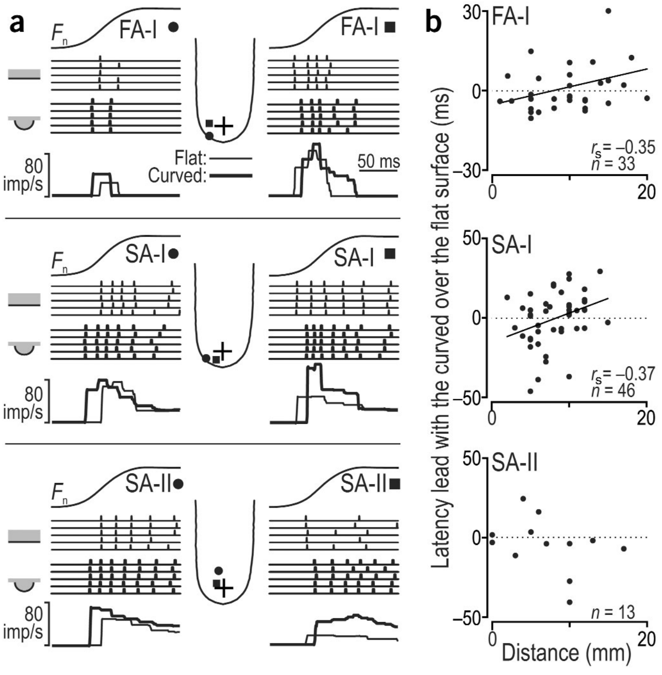

Figure 5 Effect of shape of stimulus surface on first-spike latencies of afferents responding to normal force stimulation with both the flat and the most curved surface (200 m^{-1}). (**a**) Impulse ensembles show responses of two single afferents of each type during all five of normal force stimuli with either surface. Traces above show normal force (F_n) superimposed for all trials and traces below instantaneous discharge frequency averaged over the five trials. (**b**) Difference in first-spike latencies recorded with the flat and the curved surface plotted against distance between receptive field center and primary site of stimulation for afferents with significant effect of surface shape on latency. Correlation coefficients (r_s) are given in cases of significant correlation.

of the human fingertip seems particularly suited in this respect: There is an exceptionally high density of FA-I and SA-I afferents in the fingertip (140 and 70 afferents/cm^2, respectively[24]) and their cutaneous termination, with multiple interdigitating nerve endings[17,25], ensures considerable recruitment of afferents even with weak localized stimuli[18]. Furthermore, with more natural stimuli, afferents located remote from the primary site of stimulation are recruited[13,14]. The key role of the FA-I afferents in fast discrimination of fingertip parameters, suggested by our results, agrees with the predominance of these afferents in body regions used for accurate object oriented actions, such as the glabrous skin of the hand[24], the tip of the tongue[26] and the sole of the foot[27]. The discrete event-driven sensory control in object-oriented actions[28,29] relies on the capacity of the tactile apparatus to quickly extract critical spatiotemporal events in a complex mechanical background, which typically involve low-frequency forces of appreciable amplitudes. The FA-I afferents are particularly suited to signal such dynamic events[3,7,11,30]. Under natural conditions, the discrimination of fingertip parameters based on relative timing of first spikes may be faster than suggested by our results because the size of that sample of afferents in our estimates was an order of magnitude lower than the actual number of afferents in the fingertip[24].

The variability in first-spike latencies with repetitions of the same stimulus was remarkably small (s.d. = ~1 ms) given inevitable noise in the stimulation apparatus and possibly non-stationary physiological conditions of the fingertip due to its viscoelastic properties[13,22,31]. The standardized stimulation history (see Methods) presumably contributed to the low intertrial jitter in our data. However, trends that suggest non-stationariness with repeated stimuli were observed occasionally (for example, **Fig. 1c**, left panels). Furthermore, we observed interactions between force direction and object shape on the first-spike latencies similar to those observed previously with firing rates[14]. How the brain in natural tasks deals with interactions between the current stimulus and the stimulation history[31] as well as those between different parameters of fingertip stimulation on the afferent responses are important problems for future research.

Precise timing of spikes seems to matter in the somatosensory system[32–35], and the timing of the first-spikes in ensembles of central neurons can contain more behaviorally significant information than the neurons' firing rates, both in the somatosensory[32,33] and visual system[12,36,37]. Our estimates of the information content of populations of peripheral afferents were based on a rank-order code similar to that proposed to explain fast object categorization in central vision[12]. These authors also offer a relatively simple neural decoding model for discrimination of first-spike sequences. In contrast to decoding approaches in which the precise timing of individual spikes is important (for overview, see ref. 38), decoding a rank order does not require information about the exact time a stimulus of interest commences if the background is reasonably noiseless. However, a rank order code should also function on the time-varying afferent input that occurs during active object manipulations: object manipulation is built on proactively controlled and well-demarcated sequential action phases[29] and proactive control of manipulation involves the prediction of distinct tactile and visual events that mark transitions between these phases and thus the attainment of their goals[11,39]. Hence, corollary discharges associated with the execution of action plans[40] could provide internal references that reset functionally the decoding in a phase-dependent manner. Indeed, descending corticothalamic and corticocuneate projections do control the signal processing in ascending somatosensory pathways[41–43]. As such, there is ample evidence that the processing of sensory stimuli is controlled by top-down influences that strongly shape the intrinsic dynamics of thalamocortical networks and constantly create predictions about forthcoming sensory events[44].

Possible decoding mechanisms that rely on determining precise relative timing of first spikes presumably requires more complex circuitry than those using a rank order code[12], including implementation of delay lines[38,45]. In this context, however, one may speculate whether the dispersion in peripheral conduction velocities are exploited as delay lines contributing to input synchrony at the cuneate and lemniscal levels, in a manner analogous to the axonal delay lines exploited in discrimination of interaural time differences in the mammalian auditory brainstem[46]. For example, different conduction velocities of afferents that project to a given higher-order neuron may for a certain direction of fingertip force result in highly synchronous inputs to this neuron early during the recruitment sequence, whereas with other force directions synchrony would occur at neurons receiving other patterns of afferent projections. The spread of cuneate afferents' firings due to the distributions of conduction velocities[16,47] is some 15 ms, which is within the range of most of the latency effects that we have observed in our experiments. Indeed, one influential idea in neuroscience is that synchrony is a means of representing features of sensory stimuli in task- and context-dependent manners[44].

We have shown a weak correspondence between first-spike latency and firing rate in the same afferents. This suggests that these two codes provide independent information about force direction and object shape to the brain. Given that multiple parallel pathways are used to process and transform somatosensory information, it is possible that these codes are used by the brain for different processes and perhaps different tasks. For example, the first spikes may be used for fast identification of a stimulus ('what') and for fast triggering of appropriate actions, whereas the firing rate may represent stimulus quantities ('how much'). Furthermore, the fact that the two codes appear to convey similar information but in apparently independent ways suggest that they represent rather independent monitoring systems. This may be useful for verification, learning and upholding the function of various control mechanisms.

METHODS

Subjects and procedure. Twenty-one females and twelve males (19–30 years of age) participated after providing written informed consent in accordance with the Declaration of Helsinki. Previous reports describe in detail the experimental procedure and the apparatus[13,14]. Briefly, impulses in single tactile afferents that terminated in the distal phalanx of the index, long or ring finger were recorded with tungsten needle electrodes[15] inserted into the median nerve ~10 cm proximal to the elbow and 0.5–0.6 m from the fingertips. For each afferent isolated, calibrated nylon filaments were used to delineate the field of skin from which a response could be elicited by a force four times the afferent's threshold force[18]. The receptive field center was defined as the intersection of the minor and major axes of the outlined field. For SA-II afferents that discharged in the absence of mechanical fingertip stimulation, the criterion of an afferent response was a clear modulation of the ongoing activity. To pool data from different digits in different subjects, we overlaid all data related to the location of the stimulation site and the locations of the afferents' receptive fields on a generic distal phalanx[13].

Force stimulation. The primary site of stimulation on the receptor-bearing finger was the midpoint of a line extending in the proximal-distal direction from the whorl of the papillary ridges to the distal end of the fingertip (**Fig. 1a**). All force stimuli were superimposed on 0.2 Newton (N) background force normal to the skin at this site and consisted of a force protraction phase (125 ms), a plateau phase at 4 N normal force (250 ms), and a force retraction phase (125 ms). The time course of the force change followed a half-sinusoid (**Fig. 1a**). The interval between successive stimuli was 250 ms. The first four stimuli of a stimulus sequence included a tangential force component orthogonal to the normal axis in the radial, distal, ulnar and proximal direction, respectively, which resulted in a force angle of 20° relative to the normal (**Fig. 1a**). Thus, the normal and tangential force components changed in parallel as in natural object manipulations[2]. The fifth stimulus of the sequence was in the normal direction only. With each stimulus surface, this stimulus sequence was run six times, but only the five repetitions were analyzed to reduce stimulation history effects.

Analysis. For each stimulus, the first-spike latency was measured as the time between the commencement of the force protraction and the appearance of the first nerve impulse. In the same way, we measured the latency of a second spike, if present, and we computed the first-interspike interval; the first-interspike rate was the inverse of this interval. For individual afferents, based on the responses to the five repetitions of each stimulus condition we used the non-parametric Kruskal-Wallis analysis of variance by ranks[48] to assess the effect of force direction and surface shape, respectively, on first-spike latency; stimuli in directions with no afferent response were assigned the highest rank. The Spearman rank correlation test[48] was used to assess correlation (r_s) and for analyses of vector data we used the angular-angular correlation test (r_{aa})[48]. ANOVAs were applied as detailed in the Results; when appropriate the dependent variable was logarithmically transformed to obtain approximately normal distributions. In these ANOVAs and in population analyses, unless otherwise indicated, each afferent was represented by its mean latency pertaining to the relevant experimental condition. In all tests, the probability selected as significant was $P < 0.05$.

In estimating the probability of correct discrimination of force direction, we used data from all sampled afferents, including those whose first-spike latency was not influenced by force direction and those SA-I ($n = 6$) and SA-II ($n = 17$) afferents that could show ongoing discharges during inter-trial periods. Each of the five expected recruitment sequences (representing the five force directions) used to determine the direction predicted by a sample sequence was based on afferents' mean ranks in 20 recruitment sequences created together with each sample sequence. The rank of an individual afferent in each of these 20 recruitment sequences was defined by its latency selected randomly from the five repetitions of the same stimulus in the relevant force direction using samples not included in the sample sequence but from the entire force protraction phase. To obtain integer expected ranks, the afferents were sorted based on their mean ranks in the 20 sequences. In cases when correlation of a sample sequence with the expected sequences resulted in identically high correlation coefficients with two or more expected sequences, the sample sequence was randomly assigned one of the directions represented by these expected sequences. For time windows without neural responses in the sample sequence, or responses in only one afferent, the sample sequence was assigned randomly to one of the five force directions. That is, the probability for correct discrimination (by chance) was 20%. We used the same protocol to estimate the capacity of tactile afferents to discriminate surface shape.

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COMPETING INTERESTS STATEMENT

The authors declare that they have no competing financial interests.

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