Neural coding of passive lump detection in compliant artificial tissue

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Submitted 14 January 2013; accepted in final form 4 May 2014

Gwilliam JC, Yoshioka T, Okamura AM, Hsiao SS. Neural coding of passive lump detection in compliant artificial tissue. J Neurophysiol 112: 1131–1141, 2014. First published May 7, 2014; doi:10.1152/jn.00032.2013.—Here, we investigate the neural mechanisms of detecting lumps embedded in artificial compliant tissues. We performed a combined psychophysical study of humans performing a passive lump detection task with a neurophysiological study in nonhuman primates (Macaca mulatta) where we recorded the responses of peripheral mechanoreceptive afferents to lumps embedded at various depths in intermediates (rubbers) of varying compliance. The psychophysical results reveal that human lump detection is greatly degraded by both lump depth and decreased compliance of the intermediate. The neurophysiology results reveal that only the slowly adapting type 1 (SA1) afferents provide a clear spatial representation of lumps at all depths and that the representation is affected by lump size, depth, and compliance of the intermediate. The rapidly adapting afferents are considerably less sensitive to the lump. We defined eight neural response measures that we hypothesized could explain the psychophysical behavior, including peak firing rate, spatial spread of neural activity, and additional parameters derived from these measures. We find that peak firing rate encodes the depth of the lump, and the neural spatial spread of the SA1 response encodes for lump size but not lump shape. We also find that the perception of lump size may be affected by the compliance of the intermediate. The results show that lump detection is based on a spatial population code of the SA1 afferents, which is distorted by the depth of the lump and compliance of the tissue.

tactile; somatosensory; coding

The neural mechanisms underlying the perception of lumps embedded in tissue have not been studied directly. Although several studies have shown that there is a close relationship among a mechanical stimulus to the finger, the neural signals evoked in the peripheral afferents, and perception (see Hsiao and Gomez-Ramirez 2012 for a review), these studies have not investigated how combinations of stimulus features such as the combined effects of a soft intermediate between a rigid stimulus and the finger affect the neural representation of the stimulus and perception. Previous neurophysiological studies show that both the three-dimensional shape of spheres indented into the fingertip (Goodwin et al. 1995; Srinivasan and LaMotte 1987) and the roughness and softness of the tissue (Johnson et al. 2002; Srinivasan and LaMotte 1995) are represented by the population responses of the slowly adapting type 1 (SA1) afferents. Currently, it is not known how both the shape and texture of the lump and tissue are simultaneously represented in the SA1 neural response nor how the intermediate affects the neural representation and consequent perception of lumps.

In this study, we investigate the neural mechanisms underlying lump detection in artificial soft tissue in a combined psychophysical study of humans performing a passive lump detection task and a neurophysiological study of nonhuman primates (Macaca mulatta) where we recorded the responses of peripheral mechanoreceptive afferents using the same stimuli that were used in the psychophysical study. We show that the intermediates have a significant effect on both the neural representation and perception of the lump.

METHODS

Platen-Forcer Stimulator

Both psychophysical and neurophysiological experiments were performed using a platen-forcer stimulation system (see Lane et al. 2009 for details). On each trial, the stimulator is first positioned over the array of stimuli (Fig. 1A). A gripper is then lowered to grab the stem of the selected stimulus pattern. The stimulus is then raised and positioned over the finger, rotated to align with the major axis of the finger, and indented at the desired velocity into the skin to the desired depth (Fig. 1B).

Stimulus Set

The psychophysical and neurophysiological experiments used a set of stimuli (Fig. 1A) that simulate hard lumps embedded in soft tissue. The stimuli were molded as cubic shapes 35 mm on a side using Ecoflex 00-10 (28.2 kPa) or 00-30 (56.9 kPa) silicone rubber (Smooth-On, Easton, PA). Plastic Delrin spheres (diameters of 6.5, 9.5, and 12.5 mm) were used to represent hard lumps embedded 1.5, 2.5, and 3.5 mm beneath the surface of the rubbers. The three stimulus types are shown in Fig. 1A. The first (HLD-type) stimulus is defined

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Cancer often manifests as hard lumps (tumors) embedded in the soft tissues of the body such as the breast, prostate, and lung, which are significantly more compliant than the tumor (Hoyt et al. 2008; Krouskop et al. 1998; Phripps et al. 2005). Understanding how humans sense lumps is a complex process because the nervous system needs to encode the size and shape of the lump and the material properties of the surrounding tissue. Psychophysical studies by Adams et al. (1976) and Bloom et al. (1982) showed that humans can detect lumps in artificial tissue breast models as the lumps varied in size, depth, and mobility of the lump within the substrate. More recent studies showed that detection is affected by the compliance of the surrounding substrate and the velocity that the finger is moving. Platen-Forcer Stimulator

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subjects used a mouse to indicate at the desired velocity, held stationary for 500 ms, and then raised to (just touching the skin). The stimulus was indented to a target depth.

The HLD stimuli are a simplification of the complex characteristics exhibited between tumors and human tissue. The silicone rubber used in the stimuli had stiffness values comparable with those of normal tissue (25–50 kPa as described in Zhang et al. 2008), but the hardness of the Delrin lumps is stiffer than natural tumors. Thus there was a greater contrast between the simulated lumps and tissue than is normally observed in tactile tumor detection.

Psychophysics

During normal lump detection, doctors use both vertical motions orthogonal to the tissue surface and active scanning motions parallel to the surface of the tissue. However, studying active exploration of the tissues was beyond the scope of this work, and, as such, we restricted the study to investigate detection with passive vertical motions. The indentation depth for the stimulus to be picked up by the stimulator. There were 23 stimuli, consisting of 18 HLD stimuli (2 hardnesses, 3 sizes, and 3 depths), 3 L stimuli, and 2 H stimuli (Fig. 1C).

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Threshold was determined using a modified staircase paradigm with the indentation depth changed using a “two-up, one-down” paradigm. The indentation depth for the nth trial was defined by:

\[ X_n = X_0 (2^{-S/20}) \]

where \( X_0 \) is the initial indentation depth (in millimeters) and \( S \) is the stimulus intensity (in decibels). A reversal was defined as changing the direction of the indentation depth from increasing to decreasing and then back to increasing or vice versa. \( S \) was modified by \( \pm 2 \) dB before the first reversal, \( \pm 1 \) dB after the first and before the second reversal, and \( \pm 0.5 \) dB thereafter, such that the step-size magnitude decreased as the subjects approached the threshold (Cornsweet 1962). The two-up, one-down staircase algorithmic strategy converges at a detection threshold of 71% (Levitt 1971). The tracking algorithm terminated when the 10 most recent indentation depths were within a 2-dB range. The detection depth threshold was defined as the arithmetic mean of the last 5 indentation depths. The detection force threshold was defined as the arithmetic mean of the 5 corresponding force measurements. This procedure was repeated for each of the 18 HLD stimuli at 3 indentation velocities (20, 50, and 80 mm/s). On average, a subject achieved threshold criteria for a stimulus after 18.7 ± 6.6 trials. The entire protocol lasted ~1 h. The modified staircase paradigm was chosen to lower experiment duration (and thus subject fatigue) compared with the method of constant stimuli.

All of the psychophysical studies were performed in accordance with regulations governing human subject research and were approved by the Homewood Institutional Review Board of the Johns Hopkins University. A portion of the psychophysical study described above was originally presented in a brief conference manuscript (Gwilliam et al. 2010). The complete psychophysical data set with additional analysis is presented and further used in this study.

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Neurophysiology

Two macaque monkeys (*M. mulatta*: 5.9–11.5 kg) were used in this study. Single afferent recordings were made from the median and ulnar nerves using standard methods (Talbot et al. 1968). Animals were sedated intramuscularly with ketamine (20 mg/kg), and anesthesia was maintained by intravenous Nembutal (sodium pentobarbital; 25 mg/kg). Rectal temperature, heart rate, respiration rate, and oxygen saturation levels were monitored throughout the experiment. The animal’s hand was fixed to a rigid platform on the table with the palm facing upward. An incision was made into either the upper arm or forearm, and blunt dissection was performed to expose the median or ulnar nerve. Single afferent fibers innervating the distal fingerpads were then isolated using microdissection, and action potentials were discriminated using a custom-built time-amplitude window discriminator. Recordings were performed only on afferents with receptive fields (RFs) located near the center of the distal fingerpads of digits 2–5. Standard methods were used to classify each afferent as rapidly adapting (RA) or SA1 (Talbot et al. 1968). We did not record the responses from Pacinian afferents since it is known that they are insensitive to the two-dimensional form of the stimulus and as such it is unlikely that they are involved in lump detection (Phillips et al. 1988).

Each stimulus was vertically indented into a single fingerpad in a “+” pattern (Fig. 1D) centered over the RF of the neuron (Fig. 1E). The + pattern consists of a center point (a) and four symmetrical legs with spacing of 500 μm near the center and 1-mm spacing peripherally. The most central and distal points on each leg of the pattern are labeled alphabetically in order of stimulus presentation. Stimuli were indented along the distal-proximal and medial-lateral axes of the finger. The stimulus pattern was repeated five times.

Mean-Normalized Firing Rates

Average firing rates were calculated for each stimulus position in the pattern by averaging the number of spikes that occurred at that stimulus position (including all repeats) over the entire stimulus period. Since responses were spatially symmetrical, we averaged firing rates for horizontal and vertical positions to obtain a one-dimensional spatial event plot (SEP), which shows the average firing rate at each stimulus position on the pattern relative to the distance from the center of the RF. To account for interneuron differences in sensitivity, we computed the mean-normalized firing rate by dividing the firing rate of the responses recorded from each stimulus position by the mean firing rate of all stimulus points in the entire SEP.

Gaussian curves were fit to the mean-normalized firing rate SEPs for each stimulus using the following equation:

\[
y = \frac{1}{\sigma \sqrt{2\pi}} e^{-\frac{(x-\mu)^2}{2\sigma^2}}.
\]

These measures represent the peak firing rate (\(\alpha\)), spatial spread of the neural activity (\(\sigma\)), spatial offset on the finger (\(\mu\)), and the background spontaneous firing rate (\(\delta\)).

The animal experiments were performed in accordance with the guidelines and regulations of the National Institutes of Health *Guide for the Care and Use of Laboratory Animals* and the Johns Hopkins University Animal Care and Use Committee, which approved the protocol.

RESULTS

Psychophysical Results

We determined the detection thresholds for indentation depth and applied force for each of the HLD stimuli at three indentation velocities (20, 50, and 80 mm/s). We find that lump detection is greatly affected by lump depth (Fig. 2A; 1-way ANOVA, 0.0001 < \(P < 0.01\)) but not lump size (Fig. 2B; 1-way ANOVA, 0.02 < \(P < 0.58\)). For each indentation

![Fig. 2. Psychophysical lump detection thresholds. Data are organized by lump depth (**A**) and lump size (**B**). Rows show the average indentation depths (**top**) and associated forces (**bottom**) at which lumps were detected by human subjects. Columns denote different rubber hardnesses (H10 and H30). The smallest lump (L1) at the deepest depth (D3) requires the largest indentation depth for detection in every case. Increasing lump depth yields larger indentation depths and forces, indicating that lumps closer to the surface are easier to detect. Indentation velocity does not have a noticeable effect on detection thresholds. In general, \(P\) values (indicated) from 1-way ANOVAs suggest that lump depth affects lump detection more significantly than lump size.](http://jn.physiology.org/)

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velocity, the smallest lump (L1, 6.5 mm) at the deepest depth (D3, 3.5 mm) returned the largest indentation depth threshold. Smaller detection thresholds are observed as lump depth decreases. Tissue compliance has a considerable effect on detection thresholds with lumps embedded in the softer tissue (H10) being easier to detect (smaller detection thresholds; 1-way ANOVA,  是 smaller detection thresholds observed as lump depth decreases. Tissue compliance has a considerable effect on detection thresholds with lumps embedded in the softer tissue (H10) being easier to detect (smaller detection thresholds; 1-way ANOVA,  

The psychophysical detection thresholds for the 50 mm/s data were originally presented in Gwilliam et al. (2010). In this study, we find that lump detection is not affected over the full range of indentation velocities studied here (1-way ANOVA,  

Neurophysiological Results

SA1 afferents code for lumps. Typical responses of SA1 and RA afferents are shown in Fig. 3A. SA1 afferents had an initial onset response followed by a sustained firing rate that lasted throughout the indentation period. During the sustained period, firing rates were higher when the lump was centered over the RF of the neuron and declined as the lump was positioned away from the center along each of the four legs of the + stimulus pattern (Fig. 3B). In contrast, the RA afferents did not respond to the stimulus during the sustained period (Pei et al. 2009) and, as such, provide no information about the lump. During this period, whereas the SA1 afferents consistently provide spatial information about the lump, the RA afferents provide minimal information about the L stimuli and no significant information about the HLD stimuli. The results suggest that the RA afferents provide little, if any, information about lumps embedded in tissue. The neurophysiological results presented hereafter combine the response for both the sustained and transient periods.

Stimulus response symmetry. The responses were highly similar between the horizontal and vertical traces of the + pattern (Fig. 3B). We quantified the RF symmetry for the SA1 afferents by computing the sum of squared differences (SSD) values between the vertical and horizontal SEPs. The results for the H30-HLD stimuli (Fig. 4A), H10-HLD stimuli (Fig. 4B), and L stimuli (Fig. 4C) show that the SSD values are consistently larger for the shallowest depth (D1) and decrease with increasing depth. The largest lump size exhibits the largest SSD for both rubber intermediates. In contrast, no trend is observed in the L stimuli set (Fig. 4C). Since the embedded lumps used in this study were spherical, the asymmetry in the neural responses must be due to interactions between the asymmetries in the RFs of the peripheral afferents and the filtering effect of the intermediate. These inherent asymmetries in the RFs are small, as indicated by the low SSD observed in the responses to just the lump (Fig. 4C). These results suggest that lumps closer to the surface are more likely to show interactions between the lump and the tissue and that the difference becomes more pronounced for larger lumps. Similar to tumors in human tissue that move during palpation, the lumps in our stimuli could move due to the compliance of the rubber.

SA1 afferents also code for compliance. The peristimulus time histogram for all spikes obtained from the SA1 and RA neurons in response to the H stimuli (rubber only) are shown in Fig. 5. Even without the lump, the SA1 neurons show an initial onset peak followed by sustained activity during the sustained portion of the stimulus, and the RA neurons show activity only at the onset and offset of the stimulus. Only the SA1 afferents show differential responses to the two compliant surfaces during the sustained period. The observed firing rate for the H10 stimuli set during the static portion of the stimulus indentation is almost 10 spikes per second lower for the soft material than the harder rubber (H30). The differences in the SA1 response to the compliant surface is also observed during the onset response but is not observed in the RA afferents. These results support previous findings showing that both form and texture are carried by the SA1 population response (for a review, see Hsiao and Gomez-Ramirez 2012).
represented a 95% confidence interval of the mean, and error bars represent
stimulus set (A).

We fit Gaussians to the mean-normalized firing rates of H10-HLD stimuli, all Gaussian fits demonstrated
$r^2 > 0.95$, and for H30-HLD stimuli, all fits demonstrated $r^2 > 0.91$
with the exception of stimulus H30-L1-D3 ($r^2 = 0.80$) and
H30-L3-D3 ($r^2 = 0.85$). The large $r^2$ values indicate that the
Gaussian curves provide excellent fits to the neural responses.

RA afferents were insensitive to the lumps (shown in Fig. 6 for
only L2 stimuli). The results are similar during the initial
transient period while the stimulus is being indented into the
skin (Fig. 7). These results demonstrate that although the SA1
afferents respond differentially to lumps of varying size, the
spatial response profile is distorted. This is observed most
clearly for the HLD stimuli with the shape of the responses
being greatly affected by lump size, depth, and compliance of
the intermediate rubber. Evoked responses were greatest for
the L stimuli (no intermediate rubber) that showed an increase
in the spatial spread of the response as lump size increased,
suggesting that the neurons encode a representation of object
size. The full-width at half-maximum values for these curves
were 2.31, 2.58, and 3.02 mm, which provide a linear corre-
lation ($r^2 = 0.98$) with the actual lump sizes of 6.5, 9.5, and
12.5 mm, respectively. It is interesting to note that although
there is a linear correlation between the neural spread and the
actual lump size, the width of the neural responses do not
provide a vertical estimate of the actual size of the lump.

Furthermore, the spatial profiles for lumps embedded in the
softer rubber (H10) were more pronounced than spatial profiles
for lumps embedded in the harder rubber (H30), suggesting
that the perceived shape of the lump also changes as the
compliance of the intermediate changed. Profiles from the H30
stimulus set were relatively broad, demonstrating that the
change in response shape is due to the spatial filtering effect
of the rubber on the neural responses. The data show that whereas
the overall peak firing rates evoked by the lumps is only mildly
affected by lump size, the area under the Gaussian profile,
which approximates the overall population response of the SA1
afferents, is greatly affected by both rubber compliance and
depth.

The mean Gaussian profiles for the SA1 responses to the
H30 stimulus showing the effects of lump depth and size on the
intensity and spatial spread of the responses are shown in Fig. 8. As
the lump size increases, the spatial response broadens accord-
ingly. As the lump depth increases, the peak rate (amplitude)
decreases, whereas the spatial spread remains relatively une-
affected. Thus whereas the intermediate changes the firing rates
of the SA1 afferents, the overall information about the size of
the lump appears to be preserved.

**Neural coding of lumps.** We assessed potential neural codes
for lump detection by computing eight measures of the neural
responses based on the Gaussian fits (Fig. 9). The four primary
measures are the peak firing rate ($\alpha$), spatial spread of the
neural activity ($\sigma$), spatial offset on the finger ($\mu$), and the
background spontaneous firing rate ($\delta$). Four additional param-
ters were derived from these values that we hypothesized
could be used as potential neural codes underlying psycho-
physical behavior: 1) the contrast ratio ($\Phi$), a ratio of the peak
firing rate to the baseline offset; 2) contrast modulation ($\lambda$), a
ratio of the relative curve amplitude to the absolute amplitude
plus the baseline offset; 3) the volume under the curve ($\kappa$), a
measure of the population response that combines information
about spatial and intensive inputs; and 4) the signal-to-noise ratio ($\eta$), a ratio of the amplitude (signal, $\alpha$) to the spatial
spread (noise, $\sigma$).

![Fig. 4. Stimulus pattern and RF symmetry. Each plot marker shows sum of
squared error (SSD) between the mean-normalized firing rates of equivalent
stimulus points in the SPx and SPy stimulus pattern traces. Shaded bars
represent a 95% confidence interval of the mean, and error bars represent ±1
SD. SSD of stimulus symmetry is shown for H30 stimulus set (A), H10
stimulus set (B), and L stimuli (C). D: mean SSD values organized by lump
depth shows shallower lump depths are more sensitive to stimulus symmetry.

SA1 afferents do not give a vertical representation of lump shape. We fit Gaussians to the mean-normalized firing rates of
the SA1 afferent SEPs produced in response to the HLD and L
stimuli for the sustained (Fig. 6) and transient (Fig. 7) periods.

For H10-HLD stimuli, all Gaussian fits demonstrated $r^2 >
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spread (noise, $\sigma$).

![Fig. 5. Peristimulus time histogram (PSTH) for neuronal spike discharge
data for H stimuli for SA1 and RA neurons. The darker (H30) and lighter
(H10) traces represent the harder and softer H stimuli, respectively. The top
horizontal line depicts the 500-ms portion of stimulus, when object is
stationary. SA1 responses from the H30 stimulus exhibit higher firing rates
over the PSTH, particularly during the static portion of the stimulus. spks,
Spikes.](http://jn.physiology.org/Downloadedfrom)
In Fig. 10A, we show that the firing rate correlates with lump depth, with shallower depths evoking larger firing rates. Firing rates are higher for the softer H10 stimuli where there exists a greater contrast in stiffness between the lump and surrounding rubber. Figure 10B shows that whereas the rates evoked by the lump alone are greatly affected by size, adding the intermediate surface filters out this effect. Figure 10, C and D, shows the effect of depth and lump size on the spatial spread. Whereas lump depth has little effect on the spatial response (Fig. 10C), lump size has a large effect on the spatial response that is more pronounced for lumps embedded in the harder H30 rubber (Fig. 10D).

Next, we compared the psychophysical detection thresholds with the neural responses to determine which hypothetical neural code could explain the psychophysical data. Figure 11 shows the correlation between each hypothetical neural code (Fig. 9) to the psychophysical threshold for detection depth (Fig. 11A) and detection force (Fig. 11B). Markers on each plot correspond to the 18 HLD stimuli, with the y-axis of each representing the psychophysical detection threshold and the x-axis the hypothetical neural code computed for the same stimulus. Each subplot shows the correlation coefficient and statistical significance for the affine fit. Both psychophysical detection metrics (force and indentation depth) show statistical significance with spatial spread and volume under the Gaussian curve. Additionally, the correlation between psychophysical detection force and signal-to-noise ratio showed statistical significance ($P = 0.015$). These results suggest that detection of lumps is based on some measure related to the spatial population response of the SA1 afferents.

The question then remains as to whether the neural codes shown in Fig. 11 sufficiently explain the ability of humans to detect the lumps. To test this, we developed a detection model that assumes that the nervous system has access to all of the hypothetical neural codes. Figure 12, A and B, together shows a regression efficacy chart with each column corresponding to a specific number of model parameters with the complexity of the model (number of parameters) increasing from left to right. In both models, $r^2$ values plateau with approximately four parameter models used. The coefficients of the four-parameter model (Fig. 12C) and the final linear regressions obtained using these coefficients (Fig. 12D) are shown for the psychophysical detection forces and indentation detection depths. The results show that the correlation coefficients obtained between the model-estimated and detection thresholds for force ($r = 0.975$) and indentation depth ($r = 0.935$) are significantly higher for combinations of codes than for a single neural code, suggesting that detection may be based on combinations of neural codes.

**DISCUSSION**

**Effects of Substrate Compliance on Lump Detection**

In a previous psychophysical study investigating human lump detection abilities, Baumgart et al. (2010b) found that the compliance of the intermediate substrate (silicone rubber) was the primary factor affecting the ability of subjects to detect lumps even beyond lump depth and size. Our data also show that compliance of the intermediate greatly affects the ability of
subjects to detect lumps (Fig. 2). Furthermore, whereas the representation of the lump is affected by both the amplitude and spread of the neural response, lump detection is closely tied to a spatial representation of the neural response (Fig. 11).

The L stimuli used in this study are very similar to those used by Goodwin et al. (1995). SA1 profiles in this study support these authors’ original findings that the profile of SA1 responses correlate closely with actual curvature ($r^2 = 0.98$).

In contrast, the HLD stimuli contain a compliant medium separating the sphere (lump) from the finger. Figure 10D shows that the harder rubber results in an increased sensitivity of spatial spread ($\sigma$) to changes in the lump size. In contrast to the results observed for the softer intermediate (H10), where the spatial responses closely match the lump alone, the harder intermediate (H30) produces a spatial response that is significantly different from the lump-only stimuli. If indeed $\sigma$ is

![Figure 7](http://jn.physiology.org/)

Fig. 7. Mean-normalized firing rate profiles for SA1 and RA recorded for each stimulus during the transient indentation of the stimulus. Responses include the rising-phase (indentation of the stimulus) only and exclude the period of sustained hold and falling-phase of stimulus indentation. The number of neurons is shown for each stimulus. Rasters represent $SP_x$ and $SP_y$ profiles from mean normalized SEPs. Darker, small, circular markers denote the mean normalized firing rate at each individual stimulus pattern location. Curves represent a Gaussian fit to mean points. $r^2$ Values for each Gaussian fit to the mean points is shown at the bottom of each SA1 subplot.

![Figure 8](http://jn.physiology.org/)

Fig. 8. A: Gaussian curve fits overlaid for all H30-L1 stimuli across each lump depth. B: Gaussian curve fits for all H30-D1 stimuli across each lump size.

![Figure 9](http://jn.physiology.org/)

Fig. 9. Parameters used to describe Gaussian fits. The equation describes the offset ($\delta$) amplitude ($\alpha$) and standard deviation/spatial spread ($\sigma$) of the Gaussian curve. Other parameters used to describe attributes of the response are contrast ratio ($\phi = \frac{\alpha + \delta}{\alpha}$), contrast modulation ($\lambda = \frac{\alpha}{\alpha + 2\delta}$), signal-to-noise ratio (SNR) ($\eta = \frac{\alpha}{\sigma}$), and area under curve ($\kappa = \int (y - \delta)$).
involved in the estimation of lump size, this suggests that lumps are perceived to be larger for intermediate tissues that are relatively hard. The results also suggest that the process of detecting a lump is more than simply discriminating a hard surface below the tissue but is related to discriminating lump shape. If we assume that the perceived shape of the lump is based on an isomorphic representation of the lump in the neural response to the L stimulus, then the compliance of the intermediate must result in surgeons perceiving a distorted perception of the lump with lumps appearing to be larger in tissues that are less compliant.

**Encoding Compliance**

Srinivasan and LaMotte (1995) demonstrated that cutaneous information alone is sufficient to discriminate the compliance of objects with deformable surfaces even when the velocity and force of application are randomized. Although there are no combined psychophysical and neurophysiological experiments that address the neural mechanisms of softness perception, the SA1 system has been hypothesized to be responsible, in large part because these afferents, in contrast to RA afferents, show differential responses to surfaces of differing compliance. Our results support those findings and show that only the SA1 afferents gave significantly different responses to the two compliant surfaces during both the static and dynamic phases of the stimulus. An interesting question then arises: since lump detection, discrimination, and surface compliance are carried by the SA1 afferents, how can multiple codes be conveyed simultaneously in the population response? A clue comes from the results shown in Fig. 10 where the responses to the lumps are compared with the lumps embedded in the intermediate rubbers. Here, we can see that the relative spatial response is smaller in the soft rubber and greatly altered in the hard rubber. One possibility is that there may be dynamic differences in the changes in SA1 population response during indentation and that these dynamic changes may play a role in compliance discrimination. Future studies are needed to investigate these coding hypotheses.

![Fig. 10](http://jn.physiology.org/)

**Fig. 10.** A: firing rate (α) encodes for lump depth. Shallow lump depths evoke larger firing rates. Larger firing rates are observed for the softer rubber set (H10), which provides a greater contrast between lump and rubber hardness. B: the rubber separating the lump from the finger greatly filters the response to the lumps, reducing firing rate. C: the spatial response (σ) is affected more significantly for the harder rubber (H30) stimuli. No clear trend exists between σ and lump depth. D: lump size is more clearly encoded by the spatial response (σ) than firing rate (α). Sensitivity of spatial response to changes in lump size is more significant for the harder rubber stimuli (H30).

![Fig. 11](http://jn.physiology.org/)

**Fig. 11.** Correlation between each neurophysiology model parameter and psychophysical detection depths (A) or psychophysical detection forces (B). Each plot contains a marker for each of the 18 HLD stimuli. The vertical axis displays the indentation depth (or subsequent force value) measured at the psychophysical detection thresholds. The horizontal axis of each plot represents the value of the particular parameter obtained from the curves in Fig. 6. Each plot shows the correlation coefficient (r) and the statistical significance for the affine fit (P). Dashed lines indicate fits that are not statistically significant. Dark, solid lines indicate fits that are statistically significant at the level specified by P. Only the parameters that contain a spatial component (σ, κ, or η) show significance.
Neural Coding of Lump Size and Depth

Figure 10 illustrates that firing rate (α) encodes information about lump depth (Fig. 10A), whereas the spatial spread (σ) encodes information about lump size (Fig. 10D). This is also shown in Fig. 7 where the Gaussian curve fits for the SA1 responses to the H30 stimuli set are overlaid. The amplitude of the curves (α) decrease with increasing lump depth (Fig. 8A), and the spatial spread (σ) of the curves increases clearly with increasing lump size (Fig. 8B), suggesting that there is a potential neural code for both size and depth in the neural response.

Neural Coding of Lump Detection

Psychophysical studies investigating lump detectability are limited to providing detection thresholds and limits as stimulus variables (lump size, hardness, depth, etc.) are varied systematically (Adams et al. 1976; Baumgart et al. 2010a; Bloom et al. 1982; Peine and Howe 1998). In our study, a comparison of psychophysical thresholds with the parameters derived from the neural responses suggests that a combination of neural codes may play a role during lump detection.

The correlation and statistical significance between each neural parameter and the psychophysical detection depths (Fig. 11A) and detection forces (Fig. 11B) provide clues as to how information is coded. One observation is that the baseline offset (δ) shows no significant correlation with the lump detection thresholds (force nor depth), suggesting that background firing rate does not play a role in lump detection but instead depends on the change in the SA1 population response. These results are in agreement with work by Peine and Howe (1998), who suggested that humans detect lumps in soft tissue from deformation of the fingerpad induced by the lump and not changes in the pressure distribution. These results are also in agreement with Vega-Bermudez and Johnson (1999), who showed that firing rates of SA1 mechanoreceptors in response to indentation of a raised feature were independent of the baseline offset force applied as a flat surface to the fingerpad.

Results show that only spatial neural parameters are statistically significant when correlated with the psychophysical results. Of the six neural parameters that include a spatial component (σ, κ, and δ for both psychophysical force and depth), five show statistical significance (P < 0.05) when correlated with the psychophysical detection thresholds (Fig. 11). In contrast, no intensity-based neural parameters (δ, α, φ, or λ) show any statistical significance with either psychophysical depth or force thresholds. These results suggest that lump detection is based on a spatial population code of the SA1 afferents.

A brief discussion about the similarities and differences between human and nonhuman primate skin properties is warranted since stimuli were indented vertically into the skin of the human (psychophysical study) and monkey (neurophysiological study). Dandekar et al. (2003) did a systematic comparison of the fingers of monkeys and human using a three-dimensional finite-element modeling approach. They reported that the elastic moduli of the skin (0.18 human, 0.14 monkey) as well as the strain energy profiles under the skin for the two species are very similar. This is important since the SA1 afferents respond to strain. Although the ridge structure between the two species is not identical, receptor depths and innervation densities in the skin are similar between the two species. Additional studies have shown that there are close similarities in the neural responses and neural codes used.
between the two species for form and texture (see Hsiao and Gomez-Ramirez 2012 for a review).

Lump Detectability Model

The parameters we selected as potential neural codes (Fig. 3) are not exhaustive. However, they do encompass the most basic descriptive features of the neural response curves, including the peak firing rate ($\alpha$), spatial spread of the neural activity ($\sigma$), and the background spontaneous firing rate ($\beta$). All other neural codes are combinations of these parameters that may account for lump detection. The primary objectives in developing the lump detectability model are 1) to minimize model complexity (number of parameters) while simultaneously 2) maximizing correlation with the psychophysical responses. The regression efficacy chart (Fig. 12, A and B) accomplishes both objectives.

Figure 12 describes the construction of a lump detectability model of varying complexity (number of neural parameters) in which the neural parameter(s) that achieve(s) the best correlation with the psychophysical responses is/are shown in each column (Fig. 12B). In the 1st 2 levels of model complexity (1 or 2 parameters), $\sigma$ or $\kappa$ is present for both force and depth plots. Furthermore, as the number of model parameters increases, $\sigma$ and/or $\kappa$ continue to be present at every level of model complexity. This reinforces the significance and importance of the spatial component in the detectability of the stimulus. Furthermore, this result is in agreement with the results seen in Fig. 11, which show that $\sigma$ and $\kappa$ are the only two parameters that individually show statistical significance with both force and depth psychophysical detection thresholds.

Comparing the force and depth results of Fig. 12A shows that the force thresholds provide a better model fit than detection depths. One possible explanation for this observation is that the SA1 afferents are sensitive to the maximum compressive strain in the skin that is more closely tied to force than to depth. We selected a four-parameter lump detectability model because correlation values plateau after four parameters for both the force and depth scenarios. The superiority of the force-derived model is further observed in the final linear regressions (Fig. 12) between the four-parameter lump detectability models and psychophysical force and depth psychophysical indentation depths (left, $r = 0.975$) and psychophysical indentation depths (right, $r = 0.935$).

Active vs. Passive Scanning

The primary objective of the study was to gain a more thorough understanding of how lumps are detected in a compliant tissuelike substrate. As noted earlier, clinical methods used to detect lumps are twofold: scanning motions parallel to the tissue surface and direct probing orthogonal to the surface of the tissue. Indeed, scanning should provide additional information for lump detection because SA1 afferents are greatly sensitive to scan velocity (Katz and Krueger 1989).

In both the psychophysical and neurophysiological experiments, the stimuli were indented into the passively restrained finger. Early research by Gibson (1962) demonstrated noticeable differences in results during active and passive scanning for a tactual pattern recognition task. Phillips et al. (1983) compared the perception of tactile spatial form with static and scanned touch and found that whereas the perception of spatial form is mildly diminished with static touch (decline in performance of 25%), the perception of spatial form is unchanged. Whereas changing scanning velocity changes the responses of the SA1 afferents, it does not change their spatial RFs or their spatial responses (DiCarlo and Johnson 1999; Hsiao et al. 2002). Furthermore, two-dimensional tactile form perception is not affected by active or passive touch and is minimally affected by scan velocity (Vega-Bermudez et al. 1991). We believe that although the detection thresholds that we show in this paper may be lower for active scanning, because the firing rates evoked in the SA1 afferents would be higher, the overall findings would be the same.

Finally, the neural mechanisms of lump detection by the SA1 afferents may extend to the detection of multiple small lumps that form a rough textured surface (Johnson et al. 2002). However, in that case, the central mechanisms would depend on the spatial variation in firing rates and not on the spatial profile of the neural response.

GRANTS

This work was supported by National Institute of Neurological Disorders and Stroke Grants R01-NS-18787 and R01-NS-34086 and a National Science Foundation Graduate Research Fellowship.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

J.C.G. and S.S.H. conception and design of research; J.C.G. and T.Y. performed experiments; J.C.G. analyzed data; J.C.G., A.M.O., and S.S.H. interpreted results of experiments; J.C.G. prepared figures; J.C.G. drafted manuscript; J.C.G., A.M.O., and S.S.H. edited and revised manuscript; J.C.G., T.Y., A.M.O., and S.S.H. approved final version of manuscript.

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