Patterns in the brain: Neuronal population coding in the somatosensory system

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Abstract

The aim of this article is to review some basic principles of neural coding, with an emphasis on mechanisms of stimulus representation in ensembles of neurons. The theory of “across-neuron response patterns” (ANRPs), first suggested by Thomas Young (1802) and fully developed by Robert Erickson (1963–2000), is summarized and applied to the problem of coding in primary afferent fibers and cortical neurons of the somatosensory system. The basic premise of the theory is that precise information about stimulus features cannot be encoded by single neurons, but is encoded by patterns of activity across populations of neurons. Different stimuli produce uniquely different patterns of ensemble activity (ANRPs)—discrimination between two stimuli is based on the absolute difference in total amount of activity (neural mass difference) of the ANRPs for those stimuli. Review of the literature shows that ANRPs and related population codes can accurately represent and differentiate among various stimulus parameters that cannot be distinguished by single neurons alone. Finally, the behavior of neuronal ensembles can be used to account for the sensory-perceptual changes associated with plasticity of thalamocortical circuits following selective sensorimotor deprivation or experience. © 2000 Elsevier Science Inc. All rights reserved.

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1. Introduction

1.1. Purpose of the review

The sense of touch constitutes the interface between the external world of objects and our internal world of self. It is both an active sense for exploring and manipulating the environment, and a passive sense for receiving touch that can stir the emotions as well as inform. Unlike other senses, touch is simultaneously given and received by simple mutual contact of the skin. It is a young girl caressing her silken, gray cat, a carpenter feeling the grain of his newly carved table, a physician palpating a sensitive abdomen, a lover’s touch that leads to a kiss, a blind man fingering a pattern of raised dots in order to “see.”

How does this sense of touch come about? What are the neural mechanisms responsible for the rich variety of somatosensory experiences? As G. E. Smith [107] observed “... all the kaleidoscopic manifestations of mental activity are dependent upon, and determined by, physiological processes taking place in the nervous system.” But what is the nature of those processes, especially as they apply to somesthesia? The aim of this review is to address those questions, based primarily on the author’s own research in sensory processing and on related neural coding studies by others. The review concentrates on stimulus coding by populations (ensembles) of neurons and is limited mainly to discussion of the somatosensory system.

1.2. Brief history of neural coding

The history of neural coding is marked by a pervasive tension between two seemingly contradictory ideas—that different sensory functions are mediated by activation of distinctly different neurons with highly specific stimulus sensitivities, or that different functions are represented by unique patterns of activity in populations of neurons with relatively broad stimulus sensitivities. The “specificity” theory had its origins in Johannes Müller’s doctrine of “specific nerve energies” [79], which emphasized the unique functional characteristics of the nerves mediating different sense modalities. That doctrine was subsequently extended by von Helmholtz [48] and von Frey [39] to become the principle of “specific fiber energies,” which held that each stimulus submodality or quality within a sense modality is encoded by excitation of different specific nerve fibers or...
neurons. The modern version of this theory is often referred to as the “labeled-line” code. Support for this view was driven largely by new electrophysiological techniques that made it possible to determine the physiological properties, response characteristics, and receptive fields of individual neurons. The predominance of the specificity idea is exemplified by the ubiquitous phrase, “place- and modality-specific neurons,” in the neuroscience literature. This notion is also reflected in various proposals for different classes of cells signaling “touch, vibration, pain, cold, position, movement, etc.” in somesthesis, “red, green, edge, orientation, direction of movement, etc.” in vision, and “salty, sweet, sour, etc.” in gustation. With its emphasis on individual cells, the labeled-line notion has been explicitly or implicitly advocated by many investigators [4,19,38,52,64,66,76,78,90,93–95].

In contrast, the “pattern” theory had its origins in the theory of color vision proposed by Thomas Young [124] and elaborated by von Helmholtz [49]. The theory stated that the retina contains three different receptors that are broadly, but differentially, sensitive to all portions of the spectrum—any wavelength of light (color) can thus be uniquely represented by the ratios of responses across the different types of receptors. This basic idea was adopted in varying form or developed independently by others including Adrian et al. [3], Pfaffmann [91,92], Weddell [118], Erickson [25,26], Towe [111], Mountcastle [76,78], Doetsch and Erickson [14], John [56], Doetsch and Towe [15], Whitfield [120], Ray and Doetsch [99], and Nicolelis et al. [82,83]. In the modern period, Pfaffmann [92] was the first to make a formal statement of the pattern theory in his description of gustatory coding; surprisingly, he later adopted a position more consistent with the labeled-line theory [93]. However, it was Robert Erickson [25] who put the matter most succinctly: “... the neural message for gustatory quality is a pattern made up of the amount of neural activity across many neural elements.” Erickson [23,24,26,27] then proceeded to develop this notion into a comprehensive theory, and extended its application to all sensory, motor, and cognitive systems of the brain, suggesting that “across-neuron response patterns” constitute the fundamental language of the nervous system. The basic difference between the two theories is illustrated schematically in Fig. 1.

Some versions of the pattern theory tended to neglect the role of specialized receptors and neurons, suggesting that different patterns of excitation in space and time were the sole determinants of different sensory experiences [80,118]. This view was later modified to include the role of differentially sensitive receptors and central neurons [70,106]. In contrast, the original Young–Helmholtz theory did not have this problem, because it explicitly required different types of retinal receptors. Likewise, the pattern theory developed by Erickson [23–27] demands the existence of differentially tuned neural elements at all levels of the nervous system, from receptors to cerebral cortex. Furthermore, the theory incorporates the idea of specificity in terms of anatomically and functionally distinct systems mediating different sensory, motor, and cognitive processes. Hence, neural specificity, within certain broad limits, and population coding are not mutually exclusive. A peripheral nerve, nucleus, or brain area is developmentally specified to perform or contribute to certain functions (such as somatosensory or visual perception)—but precise coding of information within that anatomical/functional entity is accomplished by patterns of activity across neuronal populations that are unique for each sensory-perceptual experience (see [89] for a catalogue of candidate neural codes).

2. Theory of coding by across-neuron response patterns

The central principle of the across-neuron response pattern (ANRP) theory, sometimes referred to as the “across-
The “fiber pattern” theory [23–27], is that information is encoded by neuronal populations and not by individual neurons. More specifically, precise information is represented in the nervous system by spatiotemporal patterns of activity and amounts of activity in ensembles of nerve fibers and central neurons. The basis for this proposition is that the sensitivity functions or neural response functions (NRFs) of single cells are typically broad compared with the ability to discriminate between stimuli [26,31]. Young [124] recognized this when he first proposed his trichromatic theory of color vision. Furthermore, most cells are sensitive to more than one stimulus dimension. For example, somatosensory neurons may respond to variations in stimulus quality (submodality), location, intensity, orientation, direction of movement across the skin, etc. Consequently, there are certain values of each stimulus dimension that elicit identical firing rates in a given cell. It follows that an individual neuron cannot differentiate among those multidimensional stimulus variables, and cannot precisely encode information as a strictly labeled line.

The general solution to this problem is that neurons with broad, overlapping NRFs can accurately encode a specific stimulus by the ratios or patterns of activity across those neurons—hence, across-neuron response patterns (ANRPs). Each distinguishable stimulus is encoded by a uniquely different ANRP. The qualitative form or profile of the ANRP determines the quality of the sensation elicited. The quantity or total amount of activity in the ANRP is referred to as neural mass (NM) and determines the quantitative or intensive aspects of the sensation [21]. More specifically, NM is defined as: number of excited neurons × number of impulses × time (duration of response).

The concept of neural mass is the basis for understanding the mechanism of sensory discrimination. The ability to discriminate between any two stimuli is directly related to the NM difference (NMD) between the ANRPs for those stimuli [21]. The NMD is equal to the sum of the absolute differences in number of impulses produced by the stimuli across all neurons. A just noticeable difference (jnd) is presumed to be represented by a constant NMD—a jnd in sensory quality is given by a constant NMD with a change in pattern, whereas a jnd in intensity is given by a constant NMD with little or no change in pattern. The basic principles of the ANRP theory are illustrated in Fig. 2.

Fig. 2. Theoretical changes in across-neuron response patterns (ANRPs) for two different stimuli (A and B) produced by changes in intensity and quality. The profiles (slopes) of the curves indicate stimulus quality; the absolute heights reflect total neural mass (NM) and indicate stimulus intensity. The shaded areas give the NM differences between each set of ANRPs and are directly related to discriminability of the stimuli. (A) ANRPs for stimuli A and B differing in quality but not intensity. (B) ANRPs after an increase in the intensity of stimulus B. (C) ANRPs after a change in the quality of stimulus B, becoming more similar to the quality of stimulus A. (D) ANRPs after a change in the quality and a decrease in the intensity of stimulus B. Note that the quality and intensity of stimulus A remain the same in all graphs; all changes in stimulus B are described relative to the plot for B shown in graph A.
In short, the ANRP theory holds that sensory-perceptual distinctions are based on differences in neuronal population responses, differences in either the profile or amount of activity in the ANRP, or a combination thereof. All distinguishable features of a stimulus—quality, location, intensity, orientation, direction of movement, etc.—can be encoded simultaneously by an ensemble of neurons, without requiring a different coding mechanism for each stimulus feature. As demonstrated by Erickson [24], each discriminable stimulus property corresponds to a different ANRP in the same (or overlapping) neuronal ensembles.

Certain definable characteristics of individual neurons and neuronal populations can greatly influence the configuration of ANRPs. These variables include the height and width of NRFs (e.g., absolute sensitivity and size of receptive fields), innervation density or cortical magnification (number of neurons per unit area of receptor surface), and density or overlap of NRFs (e.g., overlap of receptive fields) [26,99]. Table 1 summarizes how different neuronal properties affect ANRPs and NM, and Table 2 shows how those properties are related to different somatosensory thresholds. Erickson and his students [14,18,25,29,31,40,68,104,105] first developed the ANRP theory to address the problem of coding for taste quality in the gustatory system. As a first approximation, they typically used the number of impulses per unit time as the measure of neuronal responses. Their success in predicting the behavioral discriminability of different taste stimuli led to the application of the model to other sense modalities, including color discrimination [24], sound localization [20], joint angle or limb position [24], skin temperature [22,28], and tactile stimulus location and intensity [24,99]. Erickson [23,27] argued that population coding is a mechanism common to all sensory domains but applies equally to other functions such as movement and more complex processes related to memory, motivation, emotion, and aspects of intelligence. The generality and predictive power of the theory is now readily apparent—transmission of information by population response patterns (ANRPs) may well be the most basic coding and processing mechanism of the mammalian brain.

### Table 1
<table>
<thead>
<tr>
<th>Neuronal variable</th>
<th>Effect on neural mass of single ANRP</th>
<th>Effect on neural mass difference between ANRPs</th>
</tr>
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<tbody>
<tr>
<td>Increase NRF height</td>
<td>Increase</td>
<td>Increase</td>
</tr>
<tr>
<td>Increase NRF width</td>
<td>Increase</td>
<td>Increase</td>
</tr>
<tr>
<td>Increase innervation density*</td>
<td>Increase</td>
<td>Increase</td>
</tr>
<tr>
<td>Increase NRF overlap or density*</td>
<td>Increase</td>
<td>Increase or decrease</td>
</tr>
</tbody>
</table>

*Number of neurons per unit area of skin; *NRF width × innervation density; † given minimum NRF overlap.

### Table 2
<table>
<thead>
<tr>
<th>Effect of neuronal variables on somatosensory thresholds</th>
<th>Neuronal variable</th>
</tr>
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<tbody>
<tr>
<td>Absolute threshold</td>
<td>(\propto (\text{ID})^{-1}, (\text{RF Overlap})^{-1})</td>
</tr>
<tr>
<td>Differential threshold</td>
<td>(\propto (\text{ID})^{-1}, (\text{RF Overlap})^{-1})</td>
</tr>
<tr>
<td>Point-localization threshold</td>
<td>(\propto (\text{ID})^{-1})</td>
</tr>
<tr>
<td>Two-point discrimination threshold</td>
<td>(\propto (\text{ID})^{-1}, (\text{RF Area}))</td>
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</tbody>
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ID = Innervation density; RF = receptive field.

## 2.1. Related coding models

Many approaches to neural coding have at least some basic features in common with those of the ANRP theory. Several models are especially noteworthy. In discussing the “coarse coding” principle of distributed representations, Hinton et al. [50] stated that “If you want to encode features accurately using as few units as possible, it pays to use units that are very coarsely tuned, so that each feature activates many different units and each unit is activated by many different features. A specific feature is then encoded by a pattern of activity in many units. . . .” Other recently developed approaches that are similar to the ANRP model include activation of “cortical fields and neuronal populations” (Roland [100]), “vector coding” or “distributed representing” (Churchland and Sejnowski [8]), coding by “cell assemblies” (Palm [87]), “neuronal population vectors” for encoding direction of limb movement (Georgopoulos et al. [44]), activity in “pools of neurons” for making perceptual decisions about visual motion (Newsome [81]), “distributed population coding” of faces (Abbott et al. [2]; Young and Yamane [122]), and others (see reviews [1,12,102]).

Surprisingly, most of these models make no reference to the seminal Young–Helmholz theory or Erickson’s detailed exposition of the ANRP theory. It seems that the idea of population coding has been reinvented several times, with relatively little acknowledgment of its origins and historical development.

## 3. Population coding in the somatosensory system

### 3.1. Developmental specification of function: Cerebral cortex and its inputs

How is cortical function initially specified in brain development, and how does this relate to the problem of neural coding? During the early cell migration phase of development, the neocortex is not segregated into unique sensory and motor areas, but appears to consist of a functionally homogeneous or equipotential “protocortex” [86]. A “protem-map” of prospective cortical areas may be present in the germinal epithelium, so that the final tangential location of a cortical neuron is determined mainly by the relative position of its precursor cell [96]. In any case, functionally unique areas emerge from protocortex after cell migration ceases, when thalamic neurons project their axons to target cells in specific cortical areas, and intracortical and callosal connec-
tions are made [53,69,73]. This presumably constitutes the major stage of functional specification. After the basic identity of each cortical area is established, the functional and anatomical microstructure of those areas can be fine-tuned by neuronal activity related to unique sensory experiences, motor activities, and learning. In the adult brain, major functional specification of a cortical area is very unlikely, although internal organizational changes may occur.

Thus, the parcelization of the cortex into somatosensory, visual, and auditory areas, etc., appears to be due primarily to the specific developmental wiring of subcortical and cortical circuits. These circuits are driven by spinal or cranial nerves that innervate specialized receptors in the end organs subserving a particular modality. Somatosensory cortex becomes “somatosensory” mainly because it receives input from the somatosensory thalamus, which in turn, receives afferent input from pathways that transmit sensory information from peripheral somatic structures. Whereas the modality specificity of different sensory cortical areas is defined by their selective interconnections, the submodality specificity of individual neurons within those areas may be quite “fuzzy,” given the broad NRFs and multidimensional sensitivity of those neurons. This leads directly to the idea that precise stimulus information within a particular modality is given, not by single neurons, but by neuronal ensembles located in the cortical areas devoted to that modality.

3.2. Neuronal typology and taxonomy: Basic issues

Can neuronal typology and classification help identify basic principles of neural coding? Historically, most studies of sensory coding focused on the specific response characteristics of individual neurons or nerve fibers. The physiological findings were often used to create a neuronal taxonomy based on a single criterion, such as maximal sensitivity to a specific stimulus feature (submodality), receptive field organization, rate of response adaptation, or conduction velocity. A common problem with such typologies is their essentialistic nature, using one or very few salient features to classify neurons and ignoring less prominent characteristics. Compounding this problem, the class to which a neuron is assigned has often been reified to indicate the specific function of that neuron. Hence, a category label such as “position, orientation, or edge detector” may implicitly be transformed into a labeled-line code for that discrete “function.”

When polythetic (multiple) taxonomic criteria are employed, the results more closely reflect the functional relationships among neurons, but the categories frequently become “fuzzy” or may even disappear [30,32,101,115]. In some cases, polythetic taxonomy yields relatively consistent subsets of neurons with differential characteristics that can be used to help determine synaptic interconnectivity, neuronal circuitry, and various functional properties of neural systems. These data are valuable as criteria for deciding whether a particular cell is a member of the coding population at a given synaptic level of the system. For example, it is important to differentiate between presynaptic and postsynaptic neurons at all levels, and to know the selective projections of those neurons to different targets that may be involved in sensory perception or some other function. To understand the flow of information in the cortex from one neuronal population to another requires knowledge of the laminar position and synaptic connectivity of those populations. Of course, the major criterion for determining whether a subset of neurons participates in stimulus coding is the degree to which inclusion of that subset enhances the ability of the neuronal population as a whole to represent (encode) specific stimulus features (for a list of criteria for candidate neural codes, see [88,89]).

3.3. Neuronal typology and taxonomy: Somatosensory nerve fibers

Can taxonomy of peripheral somatosensory fibers help solve the coding problem? Of all the sense modalities, the somatosensory system may appear most amenable to taxonomic analysis, with putative peripheral classes for touch, pressure, flutter-vibration, temperature, pain, joint position, etc., and their subcategories [9,76,78]. For instance, four main types of mechanosensitive nerve fibers innervating the glabrous skin of the human hand are now generally recognized—RA (QA), Pce, SAI, and SAI II fibers [9,55,58]. Each class is usually assigned a functionally different role, and the information it carries is thought to be analyzed separately at higher levels. Consistent with this notion, Dykes [19] developed a comprehensive model of somatosensory processing by anatomically segregated sets of parallel neural channels made up of different submodality-specific cell populations extending from peripheral receptors to cerebral cortex. The specific sets of neurons included, but were not limited to, the four types of glabrous skin mechanoreceptive afferents. Dykes [19] proposed that information in the different neuronal populations is processed independently, but noted that a “serious deficiency” of the model is its failure to provide a mechanism for the integration of information carried by different afferent channels.

At first glance, data obtained by microstimulation of single human peripheral nerve fibers seemed to provide strong support for the notion that different groups of fibers mediate discrete submodalities of sensation, especially near threshold [85,103,116,117]. However, as discussed by Ray and Doetsch [99], stimulation at different intensities and frequencies was found to produce considerable variations in the sensory qualities evoked—RA fibers were especially versatile, yielding sensations of touch, pressure, vibration, tickle, or combinations thereof. In contrast, no sensation could be elicited by stimulation of SAI II fibers alone. Schady et al. [103] made the interesting comment that changing stimulus frequency from 5 to 30 Hz evoked 24 “previously unrecognized sensations.” Similar variability was encountered in attempting to spatially match the projected sensory fields with the receptive fields of single fibers [85,103,116,117]. Finally, no simple relationship was found between the firing frequency of any one fiber and the
perceived intensity of the corresponding sensation. In short, individual nerve fibers seem to be limited in their ability to transmit precise information about stimulus submodality, location, intensity, etc. A population code is apparently required, even at the level of primary afferent fibers. The rare situation (near threshold) in which a single fiber or a small number of fibers signals precise information may represent a limiting case of the ANRP code—activation of the fiber(s) simply constitutes a small ensemble pattern that is distinguishable from other patterns.

It is now clear that many somatosensory neurons assigned to a given category (such as RA, SA, etc.) have complex profiles of sensitivity, and respond to more than one stimulus dimension. Gibson et al. [45] anticipated this situation when they used an extensive array of stimuli and different measures of neuronal responsiveness to study the “coding profiles” of single mechanosensitive nerve fibers of kittens. They concluded that the response properties of the fibers were highly variable and were “continuously and broadly distributed.” Given the diversity of coding profiles, the authors “were unable to find any justifiable basis for designation of discrete categories of S-R profiles.” The use of many different stimuli (and response measures) typically shows that single neurons have more complex, multidimensional sensitivity functions (NRFs) than is revealed by the use of only one or a few stimuli. Furthermore, the findings of such studies tend to break down taxonomic categories based on one or a few characteristics. Hence, strict “place and modality specificity” tends to become “fuzzy” indeed.

Consistent with that view, Ray and Doetsch [98] found that the size and organization of receptive fields, “on” and “off” responses, and even the rate of adaptation of mechanosensitive nerve fibers of the raccoon varied considerably with stimulus location and intensity. They concluded that fiber classification based on adaptation rate was unreliable, and that single fibers could not be assigned a specific coding function. Furthermore, the response properties of individual fibers had little psychophysical predictive power, and could not account for variations in tactile acuity across the skin. In this case at least, neuronal taxonomy was found to be of limited value in studying coding.

3.4. Receptive fields and brain maps

Can neuronal receptive fields (RFs) and somatotopic maps contribute directly to neural coding mechanisms? Specifically, do they convey useful information to the brain? These questions are especially appropriate because neurophysiologists have long been preoccupied with mapping the RFs of single neurons and mapping sensory/motor representations in the brain, with the hope of gaining insight into neural coding. It is clear that RFs and maps are both empirical constructs defined by the investigator in terms of an arbitrary level of neuronal firing in response to stimulation of specific skin locations. At any given moment, RFs and sensory maps are static and highly simplified representations of the skin by individual neurons (RFs) and populations of neurons (maps), respectively. In fact, the RFs of central neurons can vary greatly in size and organization, depending on various subcortical and cortical modulating influences; likewise, the topography of brain maps can change considerably with localized sensory deprivation and experience (see reviews [62,63,71,72]).

Thus, the momentary properties of a RF reflect not only the dominant input connectivity of a neuron, but also the current level of excitability of the cell. Similarly, the basic organization of a sensory map is established by developmental processes that provide for easy lateral cell interactions; short-term changes in the map reflect modifications in the balance of excitatory and inhibitory inputs reaching certain neurons. One might argue that the maximum size and location of neuronal RFs, and the maximum variability in map organization, provide markers that define the spatial limits on the skin to which sensation produced by neuronal excitation is projected. But, in fact, afferent input from the periphery finds its way to the appropriate set of central neurons without separate information about RFs or maps.

In short, neither RFs nor maps provide direct information about profiles or levels of neuronal activity produced by different stimuli. Fields and maps can be interpreted or “read” only by an external observer; they cannot be utilized internally by the brain, which “knows” only neuronal activity or the lack thereof. This leads to the conclusion that information about different stimuli and their functional significance is conveyed not by RFs or maps, but by afferent and central patterns of activity in ensembles of neural elements.

3.5. Population response patterns of primary somatosensory nerve fibers

Can activity in neuronal populations solve the coding problem? In 1931, Adrian et al. [3] commented on the overlapping distribution of the RFs of mechanosensitive nerve fibers: “. . . stimulation of any point on the skin will cause impulse discharges in several fibres, and the particular combination of fibres in action, together with the relative intensity of the discharge in each, would supply all the data needed for localization.” Hence, the notion of neuronal population coding in somesthesia is not new. However, most studies of ensemble activity have been based on extrapolations made from the responses of a “representative” single nerve fiber to stimulation of different points within the RF of that fiber. Moreover, population behavior was usually examined separately for each class of fibers [9,58].

In contrast, Ray and Doetsch [99] used a direct approach to determine the ANRPs of median (forepaw) and tibial (hindpaw) nerve fibers of the raccoon. They recorded the responses of single fibers to punctate stimulation at standard test locations (using a series of intensities) on the glabrous skin of the forepaw and hindpaw, regardless of the precise location of the stimulus within any one RF. Furthermore, they pooled the responses of the fibers from each nerve without making assumptions about the possible classification or function of the fibers. The ANRPs of the median and
tibial fiber samples were then reconstructed for each stimulus location and intensity, and the sample ANRPs were adjusted for differences in innervation density measured across each paw and between the two paws.

The results of this synthesis revealed that stimulus location and intensity on the skin were accurately encoded by ANRPs that were specific for each stimulus. Stimulation of different locations at the same intensity evoked uniquely different ANRPs that varied primarily in the form or profile of the response pattern, including differences in the sets of activated fibers (Fig. 3). Stimulation of any one test site at different intensities elicited different ANRPs that varied mainly in the magnitude (total amount of activity) of the response pattern (Fig. 4). NMDs (number of excited neurons × number of impulses × duration of response) between the ANRPs were measured and used to estimate variations in the discriminability of stimulus location and intensity across the skin of the two paws. The results showed that NMDs between the ANRPs, as a function of stimulus location and intensity, were greater for distal sites than for proximal sites on each paw. Moreover, NMDs between ANRPs were larger for locations on the forepaw than for comparable locations on the hindpaw. Because NMDs are directly related to stimulus discriminability, the NMD values reflect expected differences in tactile acuity across the skin surfaces. Ray and Doetsch [99] concluded that “... systematic differences in the population response profiles of median and tibial nerve fibers could account for regional variations in tactile acuity across each paw and differences between the two paws.” Similar conclusions could be drawn for intensity discrimination. The investigators stressed that such quantitative predictions could not be made on the basis of the characteristics of individual nerve fibers [98].

Other studies support the basic idea that somatosensory information is accurately encoded by patterns of activity in ensembles of fibers [9,58]. Those studies (using indirect methods to reconstruct the population behavior of different fiber classes in monkeys) include the neural representation of spatial features of localized tactile stimuli by populations of SA fibers [59], and the coding of amplitude [57] as well as spatial features [46] of vibrating tactile stimuli by populations of QA fibers. Darian-Smith and colleagues examined the response profiles produced by moving spatial gratings [10] and dot patterns [11] in ensembles of QA, SA, and PC fibers. They found that moving gratings were best represented by QA and PC fibers (depending on temporal frequency); dot patterns were best encoded by SA fibers and poorest by PC fibers. However, all three types of fibers clearly responded to both sets of stimuli in varying degrees. LaMotte et al. [67] reported that the size, shape, and orientation of objects moving across the fingertip were encoded by the spatial response profiles of both SAI and RA fibers. The third dimension of shape was best represented by the spatial distribution of SA activity, although RA fibers also responded well to that stimulus feature. How is such differential responsiveness among fiber types to be interpreted?

There is a tendency to believe that the activity of nerve fibers which respond at low rates (or with low fidelity) to a given stimulus pattern simply represents noise that degrades the neural representation of the stimulus. Hence, those types of fibers are often omitted from the population synthesis. However, given the high acuity of tactile perception and given that low-level responses are a normal component of the afferent input, there is no a priori reason to believe that those responses detract from or interfere with the neural code. Furthermore, the representation of a stimulus by neuronal populations need not be an isomorphic transformation of the physical properties of the stimulus. The issue of which fibers contribute to the code can only be resolved by experimental analysis and synthesis. In many cases, stimulus-related responses of low magnitude are part of the code, adding NM to the signal and enhancing the neural representation of the stimulus.

In this context, recent studies by Goodwin, Wheat, and colleagues [47,119] revealed that the population responses of SAI fibers in monkeys could unambiguously signal differences in the shape, location, and intensity (force) of curved surfaces placed in contact with the skin of the fingerpads. In contrast, a single fiber could not differentiate between changes in curvature and applied force. The investi-
gators showed that a change in position of the stimulus produced a corresponding shift in the SAI response profile, analogous to a change in NM of the ANRPs for different skin sites. Although 50% of the RA fibers responded to the stimuli used, those fibers were not included in the synthesis, despite the finding by Wheat et al. [119] that “. . . there was reliable information present about differences in the positions of . . . the stimuli.” Could inclusion of the RA fibers have yielded a more accurate stimulus representation?

3.5.1. Population studies based on simultaneous recordings

Almost all population studies have been based on sequential recordings from individual nerve fibers and subsequent extrapolations or pooling of the data from those fibers. An exception is the work of Johansson, Bergenheim, and colleagues [5,54], who examined population coding in samples of simultaneously recorded primary and secondary muscle spindle afferents and Golgi tendon organ afferents. These findings support the view that different “fiber types” can indeed contribute to the same neural code, and that populations of fibers with broad, overlapping NRFs can provide the basis for precise information coding. Bergenheim et al. [5] concluded that “. . . the greater discriminative ability of the mixed ensembles constitutes an even better argument against the labelled line theory than the earlier observation that ensembles comprising a single type of afferent have a better discriminative ability than single receptor afferents.”

3.6. Population response patterns of somatosensory cortical neurons

Although ideas about coding in primary afferents still tend to be dominated by notions of specific fiber classes and labeled lines, coding in the cerebral cortex by neuronal populations has become more generally accepted. This was not always the case. Towe and colleagues [15–17,74,111,113,114] were among the first to describe the response patterns of neuronal populations in sensorimotor cortex of cats. They found two major sets of neurons distributed unevenly throughout the cortex—small-field s neurons predominated in SI and were concentrated in the middle cortical layers; wide-field m neurons predominated in motor (MI) areas and were located in deeper layers. Earlier, Mountcastle [77] had proposed the idea that radially oriented cortical “columns” (later called “macrocolumns” [75]) are the fundamental units of somatosensory cortical operation—initially, all neurons in a column were thought to have very similar response properties, including submodality sensitivity, RF location, and response latencies. Doetsch and Towe [15] examined this notion, and reconstructed the spatiotemporal response profiles of sequentially recorded neurons located in a vertical cylinder of tissue (approximately equivalent to a macrocolumn) in the SI hindpaw cortex of the cat. They constructed spike density profiles as a joint function of depth in the cortex and time after electrical stimulation of each paw. The population response patterns of s and m neurons were studied separately to examine their differences and assess their contribution to overall ensemble activity (Fig. 5).

The authors found that s neurons responded only to stimulation of the contralateral hindpaw, and yielded an ensemble profile that was sharply demarcated in depth and time. The m neurons responded to stimulation of all four paws, but the ensemble profile for the contralateral hindpaw was much more circumscribed than those for the other three
paws; the latter were all similar to one another, but were shifted relative to each other in time. In short, the population response patterns of the two sets of neurons to stimulation of different skin locations varied greatly. The $s$ and $m$ neurons also differed in other respects, including number of spikes per response and submodality sensitivity. Thus, the “macrocolumn” cylinder in the SI hindpaw area contained diverse sets of neurons with different response properties and ensemble profiles. Identical studies in other sensorimotor areas yielded different “macrocolumns,” dominated to varying degrees by $s$ or $m$ neurons [17,74,111,113,114]. The evidence from this work suggests that a cortical macrocolumn—if it really exists as a functional entity [108,112]—does not operate as a homogeneous unit, but is capable of generating differential response patterns that encode various stimulus features, including location, submodality, intensity, and time. This conclusion is supported by the recent work of Favorov and Kelly [33–35], indicating that adjacent neurons located in the same macrocolumn (or “segregate”) have distinctly different RFs and time courses of activity following stimulation. The authors suggested that these differences provide for local spatiotemporal patterns of activity and spatial profiles of “temporal coherence” across the cortex. Indeed, local patterns of activity in such limited neuronal populations are thought to form the basis for cortical stimulus representation.

Other studies are consistent with the view that information is encoded by response patterns in ensembles of cortical neurons. Although cells in the dorsal column-medial lemniscus system and SI cortex are still often described as
being “place and modality specific,” there now seems to be agreement that a population code is required to accurately represent stimulus location and spatial stimulus features. Furthermore, the total amount of activity in a responding neuronal population is a generally accepted code for stimulus intensity [9,76,78]. For instance, Mountcastle and Darian-Smith [78] proposed that local stimuli applied to the skin produce spatially distributed patterns of activity that are limited in their extent by surround inhibition; such patterns represent “the transformation in neural space of the intensity, contour, and location of the peripheral stimulus.” Moreover, they suggested that spatial tactile discrimination is mediated by differences in spatial profiles of activity, and that intensity discrimination is based on the size of the active neuronal population and levels of neuronal firing. However, Mountcastle [76] has continued to adhere to the notion that submodality or sensory quality is encoded by distinct labeled lines, suggesting that submodality-specific neural channels can be incorporated into other types of codes.

Direct evidence for cortical ensemble coding was obtained by Gardner and colleagues, who reconstructed the response profiles of populations of SI neurons in cats [43] and monkeys [42] to shearing mechanical stimuli delivered to the skin. They demonstrated that each of three stimuli, delivered separately to different locations on the skin, elicited a spatially distributed pattern of activity with a sharp peak and rapidly decreasing activity on the sides; the patterns overlapped, but the peaks were shifted relative to each other across the cortex. In contrast, when the three stimuli were presented simultaneously to those locations, they evoked only one fused population profile, with a peak higher than that of the individual profiles. This “funneling” of activity into one cortical pattern can account for the perceptual illusion of one tactile sensation centered over the middle of three appropriately placed stimuli on the skin. More generally, the findings support the view that patterns of SI activity encode information about the location and spatial features of tactile stimuli, and account for the sensory phenomena associated with those stimuli. Interestingly, Gardner [41] later described the ability of single cortical neurons to extract specific features of cutaneous stimuli, such as contact area, edge orientation, and direction of movement (and even defined a set of “haptic neurons”), with little emphasis on population coding.

A different strategy for studying cortical population coding involves the use of metabolic mapping and various imaging techniques. Whitsel, Juliano, and colleagues [61,109,121] employed [14C]-2-deoxyglucose mapping to study the global profiles of SI activation evoked by repetitive stimulation of restricted skin regions on the limbs of monkeys. They found that vertical displacement or brushing of the skin produced complex spatial patterns of patchy metabolic labeling that were distributed across surprisingly large regions of SI. The patches extended from cortical layers II through V, and broad spatial patterns elicited in different animals by the same stimulus were very similar. The findings indicate that even very localized stimuli engage widespread ensembles of neurons, generating spatial patterns of activation that are unique for each stimulus. Whitsel et al. [121] concluded that the “S-I cortical network 2DG labeling pattern evoked by somatic stimulation reflects both the place and the mode of somatic stimulation—that is, it is stimulus-specific.” These kinds of studies paved the way for subsequent work on the cortical representation of various sensory-perceptual, motor, and other functions using modern imaging techniques [6,7,37,97,100,110].

3.6.1. Population studies based on simultaneous recordings

Perhaps the most direct approach to population coding is represented by the elegant work of Nicolelis et al. [82,83], based on simultaneous recordings from many neurons at several levels of the somatosensory system. These investigators showed that the RFs of neurons in the ventral posterior medial (VPM) nucleus in the thalamus of the rat were much larger and overlapped more extensively than generally thought, and often shifted considerably in location over time (within about 35 ms) following stimulation. Nicolelis et al. [83] suggested that “VPM contains a dynamic and distributed representation of the face, in which stimulus information is coded in both spatial and temporal domains.” Furthermore, simultaneous recordings made from up to five different relays of the trigeminal system (including VPM and SI cortex) in freely behaving rats revealed that neurons at those levels developed widespread 7–12-Hz synchronous oscillations related to rhythmic whisker twitching (WT). Moreover, tactile stimulation of individual whiskers elicited distributed spatiotemporal patterns of activity in neuronal ensembles located within the same areas displaying oscillatory behavior. Nicolelis et al. [82] concluded that “Dynamic patterns of neural ensemble activity in this sensory system were found not only to code tactile stimulus attributes but also to anticipate the occurrence of stereotyped WT behaviors associated with active tactile exploration of the surrounding environment.” This view is entirely consistent with the ANRP theory, and is a far cry from “labeled lines” or “place- and modality-specific neurons.”

3.7. Distributed neural networks

Information processing in the brain involves both serial (hierarchical) and parallel circuits that are all part of larger interconnected networks [36,50,123]. For example, local stimulus-induced patterns of activity (ANRPs) produced in SI areas 3a, 3b, 1, and 2 are transmitted to SII and to parietal areas 5 and 7b (Fig. 6). Furthermore, different cortical laminae project selectively to different targets—supragranular layers transmit information primarily to cortical areas in the ipsilateral and contralateral hemisphere; infragranular layers transfer information mainly to various subcortical targets, including the thalamus [60]. Hence, the patterns of output from different cortical layers to their respective targets may vary significantly in detail. For instance, Hsiao et al. [51] suggested that processing of information about tactile form...
within area 3b of monkeys involves a series of isomorphic-to-nonisomorphic transformations in progressing from layer 4 to supragranular and infragranular layers. The ANRPs transmitted from SI to other areas undergo further transformation as they produce “new” ANRPs or combine (interact) with existing ANRPs in those areas (Fig. 6). The result is a unique spatiotemporal response pattern distributed across the entire network affected by the stimulus. Functional imaging studies have shown that specific sensory and motor tasks produce differential changes in regional cerebral blood flow or metabolism that are widely and discontinuously distributed throughout the brain [6,7,97,110]; more complex tasks involving language, thinking, learning, and memory in humans are also associated with distributed areas of activation [37,100]. Although functional imaging gives few details about the specific patterns of excitation over time, the activation fields presumably reflect the spatial features of ANRPs—namely, the locations of responding neuronal ensembles. The ANRP of the network as a whole, not activation of a single circuit, conveys the full significance of a stimulus to the brain.

But how is the neural pattern in a distributed network decoded or “read out”? This question seems to imply that an active neuronal population converges onto a small set of “canonical” or “grandmother” neurons whose sole function is to decode the neural message and thereby to represent the stimulus. The problem is that few, if any, such neurons exist in complex brains (not even “specific face neurons”), and that such a process would annihilate the ANRP code, negating its considerable advantages over a labeled line code. Instead, population patterns of activity in presynaptic neurons are transmitted across synaptic relays only to generate other population patterns of activity in postsynaptic neurons. A pattern (ANRP) may be modified or transformed significantly during synaptic transmission (signal processing) for optimal utilization of neural information at different synaptic levels [24,27]. Nonetheless, each synaptic stage “reads” the pattern and then generates another pattern—there is no specialized “decoding or readout” point anywhere in the system. Or, as Erickson [27] expressed it “… an across-fiber pattern is not read out, but is utilized as is. . . .” Thus, ANRPs at different synaptic levels (brain areas) may lead directly to certain responses—such as a sensory percept or movement; ANRPs in other parts of the network may produce an emotion, memory, or other cognitive event. Of course, any modifications in the overall network response produced by changing stimulus inputs or perturbations of the system would have corresponding perceptual (and motor) consequences.

3.8. Somatosensory thalamocortical plasticity

A major source of change in the response characteristics of sensory (and motor) systems is sensorimotor deprivation

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Fig. 6. Diagram of some basic interactive components of the distributed thalamocortical somatosensory network. Three major cortical areas, their interconnections, and their thalamic inputs are illustrated. The shaded region within each area represents the across-neuron response pattern (ANRP) evoked by stimulation of the arm; the patterns for the arm have different spatial configurations in the three areas. The combined ANRPs of the network contain all the available information about the stimulus and mediate the sensory-perceptual phenomena produced by that stimulus.
and learning. Twenty years ago, the sensory systems of the adult mammalian brain were generally considered to be static, hard-wired entities. Since then, many studies have shown that selective loss of sensory input or specific sensorimotor training can modify the physiological properties of single neurons and cause reorganization of topographic sensory (and motor) maps (see reviews [62,63,65,71,72]). However, with several exceptions, most studies did not specifically examine the effects of sensorimotor perturbation on neuronal population behavior.

Nicolelis et al. [84] studied the changes produced in ensembles of simultaneously recorded neurons in the VPM nucleus of rats by blocking afferent input from localized whisker regions of the face. They found that injections of lidocaine caused single VPM neurons to show dramatic temporal and spatial shifts in the organization of their RFs, resulting in immediate (but reversible) reorganization of large portions of the face representation in VPM. Most importantly, the investigators reconstructed the neuronal population response patterns produced by stimulation, and compared those patterns before and after sensory block. The results showed that the block abolished responses to stimulation of whiskers in the anesthetized area and permitted new, short-latency responses to appear after stimulation of far-surround whiskers. Long-latency responses to stimulation of near-surround whiskers remained or increased in strength. These changes were qualitatively similar to deprivation-induced plasticity observed in SI cortex (see reviews [62,63,65,71,72]), but the findings revealed neuronal population dynamics that are not evident from static topographic maps. Nicolelis et al. [84] suggested that “... sensory deprivation disrupts the normal dynamic state of equilibrium between excitation and inhibition within the network that comprises the entire somatosensory system, producing reorganization at multiple levels of this pathway.”

Consistent with that approach, Doetsch [13] examined the perceptual significance of denervation-induced reorganization of somatotopic cortical maps, using the ANRP model as a guide. He discussed two competing hypotheses: (1) the idea of functional respecification suggests that excitation of partially deafferented neurons by inputs from new RFs is associated with a change in function (peripheral reference) to signal the new skin fields; (2) the notion of functional conservation suggests, instead, that the activity of those neurons continues to signal the original skin fields despite the responsiveness to stimulation of the new RFs. The weight of the behavioral evidence supports the idea of conservation—stimulation of skin regions adjoining an area of denervation or amputation in humans typically evokes sensation referred to the original (now phantom) skin regions.

This phenomenon can be explained by the ANRP model, with reference to the hand and arm. Stimulation of the intact hand and arm evokes two distinct ANRPs in slightly overlapping sets of SI neurons; the ANRPs constitute the neural basis for sensations projected to the hand and arm. If the hand is lost, stimulation of the arm still elicits the original “arm ANRP,” but simultaneously evokes responses in the neurons of the SI hand area that have developed new RFs on the arm. Because the new “hand ANRP” resembles the original pattern for the hand, sensation is referred to the (phantom) hand. Thus, stimulation of the arm typically yields two sensations—one projected to the arm, and the other to the phantom.

The idea that one population of neurons can generate similar ANRPs from stimulation of different skin fields (before and after reorganization) is supported by the findings of Nicolelis et al. [84] in VPM of the rat. Close inspection of the ensemble patterns shown in their Fig. 3B reveals that stimulation of whiskers 1–3 after reorganization evoked patterns (across neurons 1–11) that were similar to the patterns elicited before reorganization by stimulation of whiskers 4–6. Thus, stimulation of whiskers 1–3 may be interpreted by the rat as originating from the stimulated whiskers, but also from phantom whiskers 4–6. This line of argument is consistent with the idea that the functional significance of a given ANRP is not altered.

If the meaning (perceptual consequence) of activity in one brain area were to change due to plasticity, one would expect that the meaning of activity in the entire network must change to preserve perceptual and behavioral order. Indeed, Merzenich and deCharms [71] have argued that this probably occurs during cortical reorganization. They further suggested that the altered meaning of activity patterns must ultimately spread to involve the entire brain. Such radical changes in the functional significance of ANRPs—the neural code—are highly problematic. Continuously changing meanings attached to a given ANRP would appear to be incompatible with reliable transmission of information. How could the brain recognize when a particular pattern in a given circuit has acquired new meaning, i.e., when the code has changed? Such functional respecification would seem to require information other than, or in addition to, neural input—information that is not available to the brain. From this perspective, it is very unlikely that the functional meaning of ANRPs in neural networks can change significantly. In summary, population response patterns constitute the basic language of the brain, and the functional significance of those brain patterns appears to be highly conserved.

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