Coding of Sensory Information (Abbreviated)

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SENSATION AND PERCEPTION provided the starting points for modern research into our mental processes. In the early nineteenth century the French philosopher Auguste Comte argued that the study of behavior should become a branch of the biological sciences and that the laws governing the mind should be derived from objective observation. Comte's new philosophy, which he called positivism, was influenced by the British empiricists John Locke, George Berkeley, and David Hume, who maintained that all knowledge is obtained through sensory experience—from what we see, hear, feel, taste, and smell. At birth, Locke proposed, the human mind is a tabula rasa, a blank slate upon which experience leaves its mark.

Let us then suppose the Mind to be, as we say, white Paper void of all Characters without any Ideas: How comes it to be furnished? Whence comes it by that vast store, which the busy and boundless Fancy of Man has painted on it with an almost endless variety? Whence has it all the materials of Reason and Knowledge? To this I answer, in one word, From Experience. In that all of our Knowledge is founded; and from that it ultimately derives itself.

It was this empiricist view that led to the emergence of psychology as a separate discipline apart from philosophy, which had long monopolized the study of the human mind. Thus, in its early days, psychology came to focus on the experimental study of mental processes by emphasizing sensation as the key to the mind. How does a stimulus lead to subjective experience? By what sequence of physiological events? For the fathers of experimental psychology—Ernst Weber, Gustav Fechner, Hermann Helmholtz, and Wilhelm Wundt—those were the central questions.

These researchers soon found that while the senses differed in their modes of reception, all the senses shared three common steps: (1) a physical stimulus, (2) a set of events transforming the stimulus into nerve impulses, and (3) a response to this signal in the form of a perception or conscious experience of sensation. Their findings gave rise to the fields of psychophysics and sensory physiology. Psychophysics focused on the relationship between the physical characteristics of a stimulus and the attributes of the sensory experience. Sensory physiology examined the neural consequences of a stimulus—how the stimulus is transduced by sensory receptors and processed in the brain. Some of the most exciting advances in our understanding of perception have come from merging these two approaches in, for example, recent human experiments that use positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) to scan brain function.

Early findings in psychophysics and sensory physiology, however, exposed one weakness in the empiricist argument: A newborn's mind is not blank, nor is our perceptual world formed simply from passive encounters with the physical properties of objects and stimuli. In fact, our perceptions differ qualitatively from the physical properties of stimuli because the nervous system extracts only certain pieces of information from each stimulus, while ignoring others, and then interprets this information in the context of the brain's intrinsic structure and previous experience. Thus we receive electromagnetic waves of different frequencies, but we perceive them as the colors red, blue, and green. We receive pressure waves from objects vibrating at

different frequencies, but we hear sounds, words, and music. We encounter chemical compounds floating in the air or water, but we experience them as smells and tastes.

Colors, tones, smells, and tastes are mental creations constructed by the brain out of sensory experience. They do not exist, as such, outside the brain. Thus we can now answer the old riddle: Does a falling tree make a sound if no one is near enough to hear it? Sound, as we know it, occurs only when pressure waves from the falling tree are perceived by the brain of a living being.

Although our perceptions of the size, shape, and color of objects are derived entirely from patterns of light that strike our retinas, our perceptions nevertheless appear to correspond to the physical properties of objects. In most instances we can use our perceptions to manipulate an object and to predict aspects of its behavior. Perception, we can show, organizes an object's essential properties well enough to let us handle the object appropriately.

In short, our perceptions are not direct records of the world around us. Rather, they are constructed internally according to constraints imposed by the architecture of the nervous system and its functional abilities. The philosopher Immanuel Kant referred to these inherent brain properties as a priori knowledge. In Kant's view the mind was not the passive receiver of sense impressions envisaged by empiricists. Rather the human mind was built to conform with certain preexisting conditions, such as space, time, and causality. The existence of these ideals was independent of any physical stimuli coming from beyond the body. So knowledge, according to Kant, was based not simply on sensory experience but on the brain's properties that organize sensory experience

As we shall see later, the dialectical tension between Kant's idealism and Comte's empirical positivism continues to reverberate in studies of perception. Kant's concept of a priori knowledge left its mark on Gestalt psychology, which holds that aspects of perception are the product of the brain's inborn capacity to order simple sensations in characteristic ways. Positivism, meanwhile, influenced behaviorist psychology, with its focus on the observable components of behavior—a person's motor response to the physical properties of a stimulus.

In this chapter we consider, in general, how a stimulus impinges on the body and how sensation leads to conscious awareness of events in our world. Specifically we shall consider how stimuli are transduced by sensory receptors and encoded into neural signals. While succeeding chapters will explore in detail the individual coding mechanisms for touch, pain, vision, hearing, balance, smell, and taste, here we shall emphasize the organizational principles that are universal to all sensory systems. Indeed, it is striking how sensory systems—not just in humans but in animals—rely on the same basic principles of information processing. The extent to which these features have been conserved in the course of evolution seems nothing short of astonishing.

Sensory Systems Mediate Four Attributes of a Stimulus That Can Be Correlated Quantitatively With a Sensation.

The modern study of sensation began in the nineteenth century with the pioneering work of Weber and Fechner in sensory psychophysics. They discovered that despite the diversity of

sensations we experience, all sensory systems convey four basic types of information when stimulated—modality, location, intensity, and timing. Together, these four elementary attributes of a stimulus yield sensation. The fact that all sensory systems convey the same type of information may be one reason why they have such similar organization.

Figure 21-1 The sensory systems encode four elementary attributes of stimuli—modality, location, intensity, and timing—which are manifested in sensation. The four attributes of sensation are illustrated in this figure for the somatosensory modality of touch.

1. In the human hand the submodalities of touch are sensed by four types of mechanoreceptors. Specific tactile sensations occur when distinct types of receptors are activated. Firing of all four receptors produces the sensation of contact with an object. Selective activation of Merkel cells and Ruffini endings produces sensations of steady pressure on the skin above the receptor. When the same patterns of firing occur only in Meissner's and Pacinian corpuscles, the tingling sensation of vibration is perceived.
2. Location and other spatial properties of a stimulus are encoded by the spatial distribution of the population of activated receptors. Each receptor fires action potentials only when the skin close to its sensory terminals is touched, ie, when a stimulus impinges on the receptor's receptive field (see Figure 21-5). The receptive fields of mechanoreceptors—shown as red areas on the finger tip—differ in size and response to touch. Merkel cells and Meissner's corpuscles provide the most precise localization of touch, as they have the smallest receptive fields and are also more sensitive to pressure applied by a small probe.
3. The intensity of stimulation is signaled by the firing rates of individual receptors, and the duration of stimulation is signaled by the time course of firing. The spike trains below each finger indicate the action potentials evoked by pressure from a small probe at the center of the receptive field. Two of these receptors (Meissner's and Pacinian corpuscles) adapt rapidly to constant stimulation, while the other two adapt slowly.

The four fundamental attributes of sensory experience are encoded within the nervous system by specialized subgroups of neurons. Modality defines a general class of stimulus, determined by the type of energy transmitted by the stimulus and the receptors specialized to sense that energy (Figure 21-1). Receptors, together with their central pathways and target areas in the brain, comprise a sensory system, and activity within a system gives rise to specific types of sensations such as touch, taste, vision, or hearing.

The location of the stimulus is represented by the set of sensory receptors within the sensory system that are active. Receptors are distributed topographically in a sense organ so that their activity signals not only the modality of the stimulus but also its position in space and its size. As a stimulus activates many receptors simultaneously,

The intensity of the stimulus is signaled by the response amplitude of each receptor, which reflects the total amount of stimulus energy delivered to the receptor. The timing of stimulation is defined by when the response in the receptor starts and stops and is determined by how

quickly the energy is received or lost by the receptor. Therefore, both the intensity and time course of stimulation are represented by the firing patterns of active sensory neurons.

Since ancient times five major sensory modalities have been recognized: **vision, hearing, touch, taste, and smell**. In addition to these classical senses we also consider the somatic senses of pain, temperature, itch, and proprioception (posture and the movement of parts of the body) and the vestibular sense of balance (the position of the body in the gravitational field).

An early insight into the neuronal basis of sensation came in 1826, when Johannes Müller advanced his "laws of specific sense energies." Müller proposed that modality is a property of the sensory nerve fiber. Each nerve fiber is activated primarily by a certain type of stimulus and each makes specific connections to structures in the central nervous system whose activity gives rise to specific sensations. Thus Müller's laws of specific sense energies identified the most important mechanism for neural coding of stimulus modality.

In each sensory system the initial contact with the external world occurs through specialized neural structures called sensory receptors. The sensory receptor is the first cell in each sensory pathway and transforms stimulus energy into electrical energy, thus establishing a common signaling mechanism in all sensory systems. The electrical signal produced by the receptor is termed the receptor potential. The amplitude and duration of the receptor potential are related to the intensity and time course of stimulation of the particular receptor. The process by which specific stimulus energy is converted into an electrical signal is called stimulus transduction.

Receptors are morphologically specialized to transduce specific forms of energy. Each receptor has a specialized anatomical region where stimulus transduction occurs. Most sensory receptors are optimally selective for a single stimulus energy, a property termed receptor specificity. The specificity of response in receptors underlies the labeled line code, the most important coding mechanism for stimulus modality. The fact that the receptor is selective for a particular type of stimulus energy means that the axon of the receptor functions as a modality- specific line of communication; activity in the axon necessarily conveys information about a particular type of stimulus. Excitation of a particular sensory neuron, whether naturally or artificially by direct electrical stimulation, elicits the same sensation. For example, electrical stimulation of the auditory nerve can be used to signal tones of different frequencies in patients with deafness caused by damage to receptors in the inner ear.

Figure 21-2 Mechanoreceptors are depolarized by stretch of the cell membrane and the depolarization is proportional to the stimulus amplitude.

> 1990.   The spindle organ in skeletal muscle mediates limb proprioception. These receptors signal muscle length and the speed at which the muscle is stretched. The receptor consists of a bundle of specialized (intrafusal) muscle fibers enclosed by a capsule. The sensory nerve endings respond to stretch of the muscle fibers. Stretch-sensitive ion channels in the nerve membrane are linked to the cytoskeleton by the protein spectrin. Mechanical deformation of the membrane opens these cation-selective channels. The influx of Na^+ and possibly Ca^{2+} depolarizes the nerve ending, producing the receptor potential. (Adapted from Sachs 1990.)

1991.	Response of an isolated muscle spindle to stretch. Upper records show the depolarizing receptor potentials recorded from the sensory axon when the muscle spindle is stretched to different lengths. Lower records show the amplitude and rate of stretch. Action potentials in this nerve have been blocked with tetrodotoxin to allow analysis of the receptor potentials. The initial depolarization of the muscle spindle in response to change in muscle length (dynamic response) is proportional to both the rate and amplitude of stretch. When stretch is maintained at a fixed length, the receptor potential decays to a lower value proportional only to the amount of stretch (static response). (Adapted from Ottoson and Shepherd 1971.)

1992.	Patch clamp records of a single stretch-sensitive channel recorded from skeletal myocytes. Pressure is applied to the receptor cell membrane by suction. At rest (top record) the stretch-sensitive channel opens sporadically for short time intervals, producing a transient depolarizing current. As the pressure on the membrane is increased (lower records), the channel opens more often and remains in the open state for longer time intervals (indicated by the bar above the channel openings). Each channel opening increases the membrane conductance to cations. The increase in the probability of opening and open time produces longer and larger depolarizations. (Adapted from Sachs 1990.)

Each class of sensory receptors makes connections with distinctive structures in the central nervous system, at least in the early stages of information processing. Thus, sight or touch is experienced because a particular central nervous structure is activated. Modality is therefore represented by the ensemble of neurons connected to a specific class of receptors. Such ensembles of neurons are referred to as sensory systems and comprise the somatosensory system, visual system, auditory system, vestibular system, olfactory system, and gustatory system.

Receptors Transduce Specific Types of Energy Into an Electrical Signal

Humans have four classes of receptors, each of which is sensitive primarily to one form of physical energy— **mechanical, chemical, thermal, or electromagnetic** (Table 21-1). The mechanoreceptors of the somatosensory system mediate the sense of touch, proprioceptive sensations (muscle stretch or contraction), and the sense of

joint position, whereas the mechanoreceptors of the inner ear mediate hearing and the sense of balance. Chemoreceptors are involved in the senses of pain, itch, taste, and smell. Thermoreceptors in the skin sense the body temperature and also the temperature of the ambient air and the objects that we touch. Humans possess only one type of receptor for electromagnetic energy: the photoreceptors in the retina.

The mechanisms for transducing stimulus energy into the receptor potential vary with the types of physical stimuli. Mechanoreceptors sense physical deformation of the tissue in which they reside. Mechanical pressure, such as pressure on the skin or stretch of muscles, is transduced into electrical energy by the physical impact of the stimulus on cation channels in the membrane that are linked to the cytoskeleton (Figure 21-2A). Mechanical stimulation deforms the receptor membrane, thus opening the stretch-sensitive channels and increasing ion conductances that depolarize the receptor (Figure 21-2B). The depolarizing receptor potential is therefore similar in

mechanism to the excitatory postsynaptic potential (see Chapter 10). The amplitude of the receptor potential is proportional to the stimulus intensity; by opening more ion channels for a longer time, strong pressure produces a greater depolarization than does weak pressure. Removal of the stimulus relieves mechanical stress on the receptor membrane and causes stretch-sensitive channels to close.

The mechanoreceptors of the inner ear demonstrate directional responses to mechanical stimulation. These receptors respond to bending of sensory cilia on their apical membrane. When the sensory hairs are deflected in one direction by a sound of the appropriate frequency, the receptor cell depolarizes, whereas deflection of the hairs in the opposite direction hyperpolarizes the receptor cell (Chapter 31).

Receptor potentials in chemoreceptors and photo-receptors are generated by intracellular second messengers activated when the stimulus agent binds to membrane receptors coupled to G proteins (Figure 21-3). The second messengers produce conductance changes locally or at remote sites. Chemoreceptors normally respond to the appropriate ligand with a depolarizing potential. Photoreceptors, by contrast, respond to light with hyperpolarization. As we have seen in Chapter 13, the great advantage of the second-messenger mechanism is that the sensory signal becomes amplified. A few quanta of light-activating photopigments, or a few odorant molecules binding to the receptor sites on olfactory neurons, can affect the conductance of many ionic channels in the receptor cell.

Each Receptor Responds to a Narrow Range of Stimulus Energy

Each of the major modalities has several constituent qualities or submodalities. For example, taste can be sweet, sour, salty, or bitter; objects that we see differ in color, shape, and movement; and touch has qualities of temperature, texture, and rigidity. Submodalities exist because each class of receptors—chemoreceptors, mechanoreceptors, thermoreceptors, and photoreceptors—is not homogenous. Instead, each class contains a variety of specialized receptors that respond to a limited range of stimulus energies.

The receptor behaves as a filter for a narrow range, or bandwidth, of energy. For example, individual photoreceptors are not sensitive to all wavelengths of light but to only a small part of the spectrum. We say that receptors are tuned to an adequate stimulus, the unique stimulus that activates a receptor at low energy. As a result, we can plot a tuning curve for each receptor based on physiological experiments. The tuning curve shows the receptor's range of sensitivity, including the preferred stimulus energy band at which it is activated by the smallest amplitude stimulus. At greater or lesser values, the stimulus intensity must be substantially increased to excite the receptor (Figure 21-4).

Figure 21-3 Transduction of stimulus energy into neural activity by chemoreceptors and photoreceptors requires intracellular second messengers.

(Adapted from Shepherd 1994.)

A.1. The olfactory hair cell is a chemoreceptor that mediates the sense of smell. The olfactory cilia on the mucosal surface bind specific odorant molecules and depolarize the sensory nerve via a second-messenger system. The firing rate signals the concentration of odorant in the inspired air. 2. Chemoelectric transduction is produced when the appropriate odorant binds to a receptor protein on the cell membrane, which activates G proteins linked to the receptor. Channel opening and depolarization in olfactory receptors and certain gustatory receptors are mediated by a second messenger (cAMP) stimulated by G protein activation. 3. Receptor currents evoked by the appropriate odorant. (Reproduced with permission from Maue and Dionne 1987).

B.1. Rod and cone photoreceptors are the sensory receptors of the retina. The outer segment of both receptors contains the photopigment rhodopsin, which changes configuration when it absorbs light. 2. Stimulation of the chromophore by light reduces the concentration of cGMP in the cytoplasm. This hyperpolarizes the photoreceptor by closing cation channels, decreasing the transmitter released by the photoreceptor terminals in the inner segment. 3. Receptor currents evoked by light flashes. (Reproduced with permission from Baylor et al. 1979.)

Figure 21-4 Tuning curves of sensory receptors measure the minimum amplitude of stimulation needed to activate a sensory receptor over a range of stimulus energies. Each sensory receptor responds optimally to a narrow range of intensities of a single type of energy. The tuning curve shown here is for an auditory receptor most sensitive to sound at 2.0 kHz. Higher and lower frequencies require stronger amplitude stimuli to evoke a response from the receptor. The tuning curve also illustrates the range of stimulus energies that can excite the receptor when presented at a given intensity. In this example, as the loudness of the tone rises, the receptor responds to a greater range of auditory frequencies. However, the receptor provides a stronger response at the preferred frequency than at other frequencies. Graded responses over the energy bandwidth provide a mechanism for sensory neurons to signal the particular type of stimulus energy that is presented. The auditory system tunes receptors in distinct parts of the sensory epithelium to different frequencies of sound. The relative response amplitude of these receptors to tones signals the sound frequency.

Under normal circumstances each sensory neuron is sensitive primarily to one type of stimulus. However, the sensitivity of a sensory nerve fiber to a particular type of stimulus is not absolute; if a stimulus is strong enough, it can activate several kinds of nerve fibers. For example, the retina is relatively insensitive to mechanical stimulation but very sensitive to light. Nevertheless, photoreceptors will respond to a blow to the eye, producing a perceptible flash of light (termed a phosphene). The mechanical stimulus produces a visual image because the receptor is connected to the visual centers of the central nervous system—an illustration of the principle that each sensory pathway conveys a specific modality.

The Spatial Distribution of Sensory Neurons Activated by a Stimulus Conveys Information About

the Stimulus Location

The spatial arrangement of activated receptors within a sense organ conveys important information concerning the stimulus. In the modalities of somatic sensation and vision the spatial

distribution of receptors conveys information about the location of the stimulus on the body or in the external world. In these modalities spatial awareness involves three distinct perceptual abilities: (1) locating the site of stimulation on the body or the stimulus source in space, (2) discriminating the size and shape of objects, and (3) resolving the fine detail of the stimulus or environment. These spacial abilities are linked to the structure of the receptive field of each sensory neuron—that area within the receptive sheet where stimulation excites the cell. The position of the receptive field is an important factor in the perception of the location of a stimulus on the body.

The Receptive Fields of Sensory Neurons in the Somatosensory and Visual Systems Define the

Spatial Resolution of a Stimulus

The receptive field of a sensory neuron in somatic sensation and vision assigns a specific topographic location to the sensory information. For example, the receptive field of a mechanoreceptor for touch is the region of skin directly innervated by the terminals of the receptor neuron and thus includes the entire area of skin through which a tactile stimulus can be conducted to reach the nerve terminals (Figure 21-5). The receptive field of a photoreceptor in the retina is the region of the visual field projected by the lens of the eye onto the portion of the retina in which the photoreceptor is located.

Each receptor responds only to stimulation within its receptive field. A stimulus that affects an area larger than the receptive field of one receptor will activate adjacent receptors. The size of a stimulus therefore influences the total number of receptors that are stimulated. A large object, such as a basketball, held between both hands will contact and activate more touch receptors than a pencil grasped between the thumb and index finger.

The density of receptors in a given part of the body determines how well the sensory system can resolve the detail of stimuli in that area. A dense population of receptors

leads to finer resolution of spatial detail because the receptors have smaller receptive fields (Figure 21-6). The spatial resolution of a sensory system is not uniform throughout the receptor sheet, however. For example, spatial discrimination is very acute in the finger tips and the central retina (or fovea), where sensory receptors

are plentiful and the receptive fields are small. In other regions, such as the trunk or the outer margins of the retina, the spatial information signaled by individual nerves is less precise because receptors in those areas are fewer and thus have larger receptive fields. These differences in receptor density are reflected in the central nervous system in the maps of the body created by the topographic arrangement of afferent inputs. In each map the most densely innervated regions of the body occupy the largest areas while sparsely innervated regions occupy smaller areas because of the smaller number of inputs.

Figure 21-5 Structural basis of the receptive field of receptors for the sense of touch. The receptive field of a touch-sensitive neuron in the skin includes the sensory transduction apparatus in the nerve terminals and the surrounding skin in which the terminals are located. A patch of skin contains many overlapping receptive fields innervated by individual sensory nerve fibers. When this region is touched, spikes are initiated at the node of Ranvier closest to the nerve terminals in the skin. They are conducted past the cell body, located in the dorsal root ganglion, to the synaptic terminals in the spinal cord or medulla.

The Sensory Neurons for Hearing, Taste, and Smell Are Spatially Organized According to Sensitivity

For hearing and the chemical senses (taste and smell), the receptors are spatially distributed following the energy spectrum for these modalities. For example, auditory receptors are arranged according to the sound frequencies to which they respond. Receptors at a specific location vibrate most strongly when stimulated by a particular range of sounds, with high frequencies located at the base of the cochlea and low frequencies at the apex. Thus the organization of the inner ear's receptor sheet represents the spectrum of sound, not the location of the sounds in space.

For taste and smell, receptors that have particular chemical sensitivities are located in different parts of the receptive surface of the tongue and inside the nose. For example, specific regions of the tongue contain receptors sensitive to salts, sugars, acids, bases, or proteins. Different foods will excite specific combinations of these receptors to evoke their characteristic tastes. The spatial distribution of activity in the chemoreceptor population allows the brain to differentiate salty from sweet or bitter tastes.

Intensity of Sensation Is Determined by the Stimulus Amplitude

Historically, the early scientific studies of the mind focused not on subjective perceptions of qualities such as color or taste but on phenomena that could be measured precisely: the size, shape, amplitude, velocity, and timing of stimuli. Psychophysics had its beginnings in the systematic study of the intensity of sensations produced by stimuli of defined magnitude.

Natural stimuli vary greatly in intensity. For example, we experience a range of sounds, from a whisper to a shout. The intensity or amount of a sensation depends on the strength of the stimulus. The capacity of sensory systems to extract information about the magnitude of the stimulus is important for two aspects of sensory discrimination: (1) distinguishing among stimuli that differ only in strength (as opposed to those that differ in modality or location) and (2) evaluating stimulus amplitude.

Figure 21-6 The density of sensory receptors in the retina and the size of the receptive field for each receptor determine the resolution of a visual image. Each square or pixel in these images represents a receptive field. The gray scale is proportional to the average light intensity in that region of the image. White pixels represent receptors with the highest firing rate, while black pixels represent receptors with the lowest firing rate. If there are a small number of receptors and each spans a large area of the scene, the result is a fuzzy, very schematic representation of the

scene (A). There is no cue from this representation what the picture actually shows. As the density of receptors increases, and the size of the receptive field of each receptor decreases, the spatial detail becomes clearer (B-D). Clouds, mountains, trees, grasslands, and water emerge, until the scenery is identifiable as Yosemite valley. However, the increased resolution comes at the cost of enlarging the total size of the receptor population.

The brain resolves the conflict between information overload from a huge number of receptors and the need for resolution of spatial detail by having a higher density of receptors in regions of the body where high resolution of detail is behaviorally important and using progressively lower numbers of receptors in surrounding regions. Spatial resolution for vision and touch parallels the density of receptors in the retina and skin. Spatial resolution on the fingertips approaches that of the image in D. Receptor density and tactile sensitivity on the palm is similar to the resolution in C. Resolution of spatial detail on the forearm approaches that in image B, while on the trunk it is similar to that in image A. (Photographs courtesy of Daniel Gardner.)

Psychophysical Laws Govern the Perception of Stimulus Intensity

The first psychophysicists—Weber, Fechner, Helmholz, and von Frey—developed simple experimental paradigms to compare how two stimuli of different amplitudes are distinguished. They quantitated the intensity of sensations in the form of mathematical laws that allowed them to predict the relationship between stimulus magnitude and sensory discrimination. For example, in 1834 Weber demonstrated that the sensitivity of the sensory system to differences depends on the absolute strength of the stimuli. We easily perceive that 1 kg is different from 2 kg, but it is difficult to distinguish 50 kg from 51 kg. Yet both sets differ by 1 kg! This relationship is expressed in the equation now known as Weber's law:

where δS is the minimal difference in strength between a reference stimulus S and a second stimulus that can be discriminated, and K is a constant. This is termed the just noticeable difference or difference limen. It follows that the difference in magnitude necessary to discriminate between a reference stimulus and a second stimulus increases with the strength of the reference stimulus.

Fechner extended Weber's law in 1860 to describe the relationship between the stimulus strength (S) and the intensity of the sensation (I) experienced by a subject: where S_0 is the threshold amplitude of the stimulus and K is a constant. In 1953 Stanley Stevens noted that, over an extended range of stimulation, the intensity of a

sensation is best described by a power function rather than by a logarithmic relationship. For some sensory experiences, such as the sense of pressure on the hand, there is a linear relationship between the stimulus magnitude and the perceived intensity.

This represents an example of a power function with a unity exponent (ie, $n = 1$).

The lowest stimulus strength a subject can detect is termed the sensory threshold. Thresholds are normally determined statistically by presenting a subject with a series of stimuli of random amplitude. The percentage of times the subject reports detecting the stimulus is plotted as a

function of stimulus amplitude, forming a relation called the psychometric function (Box 21-1). By convention, threshold is defined as the stimulus amplitude detected in half of the trials. Thresholds can also be determined by the method of limits, in which the subject reports the intensity at which a progressively decreasing stimulus is no longer detectible or an increasing stimulus is detectible.

The measurement of sensory thresholds is a useful diagnostic technique for determining sensory function in individual modalities. Elevation of threshold may signal an abnormality in sensory receptors (such as loss of hair cells in the inner ear caused by aging or exposure to very loud noise), deficits in nerve conduction properties (as in multiple sclerosis), or a lesion in sensory processing areas of the brain. Sensory thresholds may also be altered as a result of emotional or psychological factors related to the conditions in which stimulus detection is measured (Box 21-1).

The sensory threshold for a modality is limited by the sensitivity of receptors. The threshold energy is related to the minimum stimulus amplitude that generates action potentials in a sensory nerve. We define thresholds in terms of action potentials because receptor potentials are local signals; they are propagated passively, as are synaptic potentials, and therefore are not transmitted over distances greater than 1 mm. To convey a sensory message to the brain, the stimulus information must be represented as a series of action potentials.

Stimulus Intensity Is Encoded by the Frequency of Action Potentials in Sensory Nerves

The quantitative features of sensory stimuli measured in psychophysical studies are signaled by the firing patterns of the activated population of sensory neurons. The details of neuronal activity—how long a neuron fires, how fast, and how many neurons are firing— encode the intensity and time course of sensory experience. In the 1920s Edgar Adrian and Yngve Zotterman first noted that the discharge frequency of an afferent fiber increases with increasing stimulus intensity. This is because the activity of sensory receptors changes in relation to the stimulus amplitude. The change in membrane potential produced by the sensory stimulus is transformed into a digital pulse code, in which the frequency of action potentials reflects the amplitude of the receptor potential. Strong stimuli evoke larger receptor potentials, which generate a greater number and a higher frequency of action potentials .

Box 21-1 Sensory Thresholds Are Modified by Psychological and Pharmacological Factors

Sensory thresholds depend upon psychological factors and the context in which the stimulus occurs. The threshold for pain is often heightened during competitive sports or in childbirth, as reflected in a shift in the psychometric function to higher stimulus intensities (Figure 21-7B, curve c). Similarly, sensory thresholds can be lowered. Consider a runner at the starting line prepared to respond to the starter's shot. It is advantageous to respond as rapidly as possible, and the slightest noise resembling the start gun may trigger a leap to action. The runner's response to a lower stimulus intensity is represented as a shift in the psychometric function to lower stimulus intensities (Figure 21-7B, curve a).

The modifiability of sensory thresholds can be understood by considering two aspects of sensation: (1) the absolute detectability of the stimulus and (2) the criterion the subject uses to evaluate whether a stimulus is present. Detectability measures the capacity of a sensory system to process a stimulus, whereas the response criterion reflects an attitude or bias of the subject toward the sensory experience.

In the 1950s Wilson Tanner and John Swets developed the signal detection theory to explain the observation that subjects often report a sensory experience (ie, detection of a stimulus) when no stimulus is actually presented. A consequence of this decrease in response criterion (or bias) is that a subject is more likely to make mistakes. For example, the runner at the starting block is likely to make a false start in a crucial race. Similarly, elderly patients with sensory loss may falsely report feeling stimuli tested in a neurological examination as a denial of aging. The opposite condition—ignoring the occurrence of a stimulus such as pain—is also common.

The separate measures of stimulus detectability and response criterion can be combined with the concept of threshold to explain the mechanisms of drug action. For example, morphine, a potent analgesic, elevates the pain threshold both by reducing the detectability of a painful stimulus and by elevating the criterion the subject uses to determine whether a stimulus is painful or not. Marijuana also increases pain thresholds, but does so by increasing the response criterion rather than decreasing stimulus detectability—the stimulus is just as painful but the subject is more tolerant.

Figure 21-7 Sensory thresholds and the just noticeable difference (JND) between stimuli that differ in intensity, frequency, or other parametric features are quantifiable.

1. The psychometric function plots the percentage of stimuli detected by a human observer as a function of stimulus intensity. Threshold is defined as the stimulus intensity detected on 50% of the trials.
2. The absolute sensory threshold (curve b) is an idealized relationship between stimulus intensity and the probability of stimulus detection. If the sensory system's ability to detect the stimulus is increased or the subject's response criterion is decreased, curve a would be observed; curve c illustrates the converse.

Figure 21-8 The firing rates of sensory nerves encode the stimulus magnitude. (Adapted from Mountcastle et al. 1966.)
A. The number of action potentials per second in a slowly adapting mechanoreceptor action the amount of skin indentation. This receptor required a minimum indentation of 80 μm to respond. The relationship between increases in frequency of firing and pressure on the skin is linear.

1. Estimates made by a human subject of the magnitude of sensation produced by pressure on the hand increase linearly as a function of skin indentation. The relation between a subject's estimate of the intensity of the stimulus and its strength resembles the relation

between the discharge frequency of a sensory neuron and the stimulus strength. These data suggest that the neural coding of stimulus intensity is faithfully transmitted from the peripheral receptors to the cortical centers that mediate sensation.

The translation of the receptor potential amplitude into a frequency code is similar to the process governing repetitive firing of neurons in response to synaptic potentials. The timing of action potentials following depolarization of a neuron depends on the neuron's threshold for firing, which in turn varies depending on the neuron's previous firing. Immediately after the action potential there is an absolute refractory period, lasting 0.8-1.0 ms, during which action potentials cannot be generated because Na+ channels are inactivated. The upper limit on neuronal firing is about 1000-1200 spikes per second.

The nerve fires a second impulse when the amplitude of the receptor potential exceeds the neuronal threshold. Receptor potentials of small amplitude are only slightly larger than the resting threshold. Therefore, the second impulse is generated late in the refractory period or at its end, resulting in a long interval between the first and second spikes fired by the receptor's axon. However, a large-amplitude receptor potential produced by a strong stimulus allows the threshold to be reached earlier in the refractory period, reducing the time between impulses. Thus, a large depolarization produces a short interspike interval and high firing rates, whereas a small depolarization results in long interspike intervals and low firing rates.

In addition to increasing the frequency of firing of individual sensory neurons, stronger stimuli also activate a greater number of receptors. Therefore, the intensity of a stimulus is also encoded in the size of the responding receptor population. These population codes depend on the fact that individual receptors in a sensory system differ in their sensory thresholds. Most sensory systems have at least two kinds of receptors: low- and high-threshold receptors. When the stimulus intensity is increasing from weak to strong, low-threshold receptors are first recruited, followed by high-threshold receptors.

The Duration of a Sensation Is Determined in Part by the Adaptation Rates of Receptors

The temporal properties of a stimulus are encoded as changes in the frequency of sensory neuron activity. Stimuli appear, rise in intensity, fluctuate or remain steady, and eventually disappear. Many receptors signal the rate at which the stimulus increases or decreases in intensity by rapidly changing their firing rate. For example, when a probe touches the skin, the initial spike discharge is proportional to both the speed at which the skin is indented and the total amount of pressure (Figure 21-9A). During steady pressure the firing rate slows to a level proportional to skin indentation. Firing stops when the probe is retracted. Thus, neurons signal important properties of stimuli not only when they fire but also when they stop firing.

Figure 21-9 Measurements of firing rates quantify how sensory neurons represent the intensity of stimulation over time.

1966.   Slowly adapting mechanoreceptors respond throughout a continuous stimulus. Each successive trace illustrates the response to increases in the pressure applied to the skin; the trace below each spike record illustrates the amplitude and time course of the stimulus. As the pressure increases, the total number of action potentials discharged rises, leading to higher firing rates. The firing rate is higher at the beginning of skin contact than during steady pressure, as these receptors also sense how rapidly pressure is applied to the skin. When the probe is removed from the skin, the spike activity ceases. (Adapted from Mountcastle et al. 1966.)

1967.   Rapidly adapting mechanoreceptors respond only at the beginning and end of the stimulus, signaling the rate at which the stimulus is applied or removed. The slope of the pressure pulse indicates the speed of skin indentation in millimeters per second; all the stimuli have the same final amplitude. Slowly applied pressure evokes a long-lasting burst of low frequency firing; rapid indentation produces a very brief burst of high frequency firing. Motion of the probe against the skin is signaled by both the rate and duration of firing of this receptor. The receptor is silent when the indentation is maintained at a fixed amplitude and fires again when the probe is removed from the skin. (Adapted from Talbot et al. 1968.)

Although the continuous firing of a sensory neuron encodes the intensity of the stimulus, if the stimulus persists for several minutes without a change in position or amplitude, its intensity diminishes and sensation is lost. This decrease is called adaptation. All sensory receptors adapt to constant stimulation. Receptor adaptation is thought to be an important neural basis of perceptual adaptation in which a constant stimulus fades from consciousness.

Receptors can adapt slowly or rapidly. Receptors that respond to prolonged and constant stimulation are designated slowly adapting receptors. These receptors are able to signal stimulus magnitude for several minutes. The stimulus duration is signaled by persistent depolarization and generation of action potentials throughout the period of stimulation (Figure 21-9A). These receptors adapt gradually to a stimulus as a result of slow inactivation of Na+ or Ca2+ channels by the depolarizing receptor potential, or as a result of activation of calcium-dependent K+ channels.

Some receptors cease firing in response to constant-amplitude stimulation and are active only when the stimulus intensity increases or decreases. These rapidly adapting receptors respond only at the beginning and end of a stimulus, signaling the rate or velocity of stimulation (Figure 21-9B). Adaptation of rapidly adapting receptors depends on two factors. First, in many of these receptors the prolonged depolarization of the receptor potential inactivates the spike generation mechanism in the axon. Second, the receptor structure filters the steady components of the stimulus by changing shape, thus decreasing the electrical signal generated by the receptor (Figure 21-10)

The existence of two kinds of receptors—rapidly and slowly adapting sensors—shows another important principle of sensory coding. Sensory systems detect contrasts in discrete stimuli, ie, changes in the pattern of stimulation in time and space. Rapidly adapting receptors sense the time derivatives of stimuli (velocity and acceleration) that signal motion. The firing rates of these receptors are proportional to the speed of motion; they stop firing when the stimulus comes to

rest. Activation of rapidly adapting receptors at the beginning and end of stimulation conveys information about the changing sensory environment to the brain.

Many sensory receptors also sense spatial contrasts. In Chapters 22 and 25 we will learn that certain neurons mediating touch and vision are particularly sensitive to edges. These neurons fire much faster if the spatial properties of a stimulus in their receptive field change abruptly than if the stimulus has uniform spatial properties.

Sensory Systems Have a Common Plan

We have learned that the various sensory systems use similar neural codes for the properties of modality, location, intensity, and timing of physical stimuli. When a sensory neuron fires, it communicates to the brain that a certain form of energy has been received at a specific location in the sense organ. The details of the action potential code tell the brain how much energy was received at that place, when it began, when it stopped, and how quickly the energy changed in intensity. All sensory systems also have similar central processing mechanisms, which are briefly reviewed in this section and more fully described in later chapters.

Figure 21-10 Receptor morphology influences adaptation in rapidly adapting mechanoreceptors. The Pacinian corpuscle is a rapidly adapting mechanoreceptor located in the skin, in joint capsules, and in the mesentary of the abdominal wall. The receptor consists of concentrically arranged, fluid-filled lamellae of connective tissue that form a capsule surrounding the sensory nerve terminal. Because of this capsule, the sensory endings specialize in the detection of motion.

1. The capsule of the Pacinian corpuscle deflects steady pressure. The receptor responds with one or two action potentials at the beginning and end of a pressure stimulus but is silent when the stimulus is constant in intensity. When a stimulus first impinges on the skin, the capsule is deformed, compressing the nerve terminal. The pressure pulse activates stretch-sensitive channels in the nerve terminal, producing the response to stimulus onset. During steady pressure the capsule changes shape, reducing stretch of the nerve membrane. The outer lamellae of the capsule are compressed, absorbing the static load and preventing the deformation from being transmitted to the inner core of the capsule and the nerve terminal. When the pressure is removed, the capsule resumes its initial shape, and the resultant tissue movement stimulates the nerve terminal again, producing an "off" response.
2. Pacinian corpuscles are sensitive to vibration. Rapid movements are transmitted through the lamellae to the nerve terminal, generating a receptor potential and action potential for each vibratory cycle.

Figure 21-11 The functional and anatomical organization of sensory processing networks is hierarchical. Stimulation of a population of receptors initiates signals that are transmitted through a series of relay nuclei to higher centers in the brain (only one relay is shown). At each

processing stage the signals are integrated into more complex sensory information. (Adapted from Dudel 1983.)

1. In the somatosensory system excitatory synaptic connections from each receptor in the skin are widely distributed to a large group of postsynaptic neurons at each relay nucleus. 1. Each relay neuron receives sensory input from a large group of receptors and therefore has a bigger receptive field than any of the input neurons. 2. Receptors closest to the stimulus respond more vigorously than distant receptors.

B.1. The addition of inhibitory interneurons (gray) narrows the discharge zone. 2. On either side of the excitatory region the discharge rate is driven below the resting level by feedback inhibition.

Sensory Information Is Conveyed by Populations of Sensory Neurons Acting Together

The richness of sensory experience—the complexity of sounds in a Mahler symphony, the subtle layering of color and texture in views of the Grand Canyon, or the multiple flavors of a salsa—is obviously conveyed not by a single receptor or sensory axon but by populations of nerve fibers. The activity of whole populations of sensory neurons is orchestrated by the myriad of stimuli that typically impinge on receptors at once. The messages of individual sensors are integrated, not merely added up, as the signals converge on processing centers in the central nervous system. Understanding how sensory information conveyed by simultaneously activated receptors is processed in parallel pathways before it is combined in the highest centers of the cerebral cortex is key to understanding sensory perception.

Parallel processing is of particular importance in vision, where nearly all of the photoreceptors of the retina simultaneously receive light of varying hue and brightness. To make sense of a scene, the visual system needs to group the signals produced by individual objects, separate them, and distinguish objects of interest from the background. Thus in humans, of all sensory modalities, vision is the most highly developed; over half of the cortex processes visual information.

Specific submodalities, such as the color turquoise or the taste of a nectarine, depend upon the combined activity of populations of receptors sensitive to overlapping energy ranges rather than the unique firing of a single type of receptor. The subjective experience of a particular color or taste is constructed by the brain by integrating the inputs from these diverse receptors.

Sensory Systems Process Information in a Series of Relay Nuclei

The constituent pathways of sensory systems have a serial organization. Receptors project to first-order neurons in the central nervous system, which in turn project to second- and higher-order neurons. This sequence of connections gives rise to a distinct functional hierarchy. In the somatic sensory system, for example, primary afferent fibers converge onto second-order neurons, usually located in the central nervous system, and then onto third- and higher-order neurons (Figure 21-11).

The relay nuclei serve to preprocess sensory information and determine whether it is transmitted to the cortex. They filter out noise or sporadic activity in single fibers by transmitting only strong sequences of repetitive activity from individual sensory fibers or activity transmitted simultaneously by multiple receptors. The convergent connections from sensory receptors within the relay nucleus allow each of the higher-order neurons to interpret the sensory message in the context of activity in neighboring input channels.

Like receptor neurons, neurons in each sensory relay nucleus have a receptive field. The receptive field of each relay neuron is defined by the population of presynaptic cells that converge on it. The receptive fields of second-order and higher-order sensory neurons are larger and more complex than those of receptor neurons. They are larger because they receive convergent input from many hundreds of receptors, each with a slightly different but overlapping receptive field. They are more complex because they are sensitive to specific stimulus features, such as movement in a particular direction in the visual field.

Inhibitory Interneurons Within Each Relay Nucleus Help Sharpen Contrast Between Stimuli

Unlike the uniformly excitatory receptive field of the sensory receptor, the receptive field of higher-order sensory neurons in the visual and somatosensory systems usually has both excitatory and inhibitory regions. Inhibition is produced by inhibitory interneurons in the relay nuclei. The inhibitory region in a receptive field is an important way of enhancing the contrast between stimuli and thus gives the sensory systems additional power to resolve spatial detail.

Inhibitory interneurons are activated by three distinct pathways (Figure 21-12). The most important is the one in which the afferent fibers of receptors or lower-order relay neurons make connections with inhibitory interneurons which have connections with nearby projection neurons in the nucleus. This feed-forward inhibition by

afferent fibers allows the most active afferents to reduce the output of adjacent, less active projection neurons. It permits what Sherrington called a singleness of action, a winner-take-all strategy, which ensures that only one of two or more competing responses is expressed.

The inhibitory interneurons can also be activated by the projection neurons in the relay nucleus through recurrent axon collaterals from the projection neurons. This feedback inhibition allows the most active output neurons to limit the activity of less active neurons. Such inhibitory networks create zones of contrasting activity within the central nervous system: a central zone of active neurons surrounded by a ring of less active neurons (Figure 21-11B). As we shall see, in the visual system these cellular interactions contribute to selective attention, by which we attend to one stimulus and not to another

Figure 21-12 Inhibition of selected projection neurons in a sensory relay nucleus enhances the contrast between stimuli. The illustration shows three inhibitory pathways in the circuitry of the dorsal column nuclei, the first relay in the system for touch. The projection (or relay) cells (brown) send their axons to the thalamus. They receive excitatory input from touch receptor

axons traveling in the dorsal columns. These afferent fibers also excite inhibitory interneurons (gray) that make feed-forward inhibitory connections onto adjacent projection cells. In addition, activity in the projection cells can inhibit surrounding cells by means of feedback connections. Finally, neurons in the cerebral cortex can modulate the firing of projection cells by distal inhibition of either the terminals of primary sensory neurons or the cell bodies of projection neurons.

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In addition to the local feed-forward and feedback circuits for inhibition in a relay nucleus, the inhibitory interneurons can be activated by neurons in more distant sites, such as the cerebral cortex. In this way higher brain centers can control the flow of information through relay nuclei. Unlike the local feed-forward and feedback mechanisms, inhibition from distant regions of the brain is not necessarily related to the intensity of the sensory-evoked responses.

An Overall View

Our sensory systems are the way in which we perceive the external world, remain alert, form a body image, and regulate our movements. Sensations occur when external stimuli interact with receptors. Sensory information is conveyed to the brain as trains of action potentials traveling along individual sensory neurons and by populations of such neurons acting together. All sensory systems respond to four elementary features of stimuli—modality, location, intensity, and duration. The diverse sensations we experience, the sensory modalities, reflect different forms of energy that are transduced by receptors into depolarizing or hyperpolarizing electrical signals called receptor potentials. Receptors specialized for particular forms of energy, and sensitive to particular ranges of the energy bandwidth, allow humans to sense many kinds of mechanical, thermal, chemical, and electromagnetic events. To maintain the specificity of each modality within the nervous system, receptor axons are segregated into discrete anatomical pathways and processing areas.

The location and spatial dimensions of a stimulus are conveyed topographically, through each activated receptor's position in the sensory epithelium, called its receptive field. The identity of the active sensory neurons therefore signals not only the modality of a stimulus, but also the place where it occurs. The intensity and duration of stimulation, meanwhile, are reflected by the amplitude and time course of the receptor potential and by the total number of receptors activated. In the brain, intensity is conveyed by an action potential code in which the frequency of firing is proportional to the strength of the stimulus. The temporal features of a stimulus, such as duration and changes in magnitude, are signaled by the dynamics of the spike train.

The complex qualities of sounds, visual images, shapes, textures, tastes, and odors require the activation of large ensembles of receptors acting in parallel, each one signaling a particular stimulus attribute. For us to savor the richness and diversity of perception, the central nervous system must integrate the activity of an entire sensory population.

Sensory information in the central nervous system is processed in stages, in the sequential relay nuclei of the spinal cord, brain stem, thalamus, and cerebral cortex. Each of these processing

stations brings together sensory inputs from adjacent receptors and—using networks of inhibitory neurons—transforms the information to emphasize the strongest signals.

STUDY OF THE NEUROPHYSIOLOGICAL mechanisms of sensation began in 1925, when Edgar Adrian and Yngve Zotterman first recorded action potentials in a sensory nerve innervating the muscle spindle receptor. They discovered that the nerve transmits information from the receptor by modulation of the frequency of electrical impulses. Subsequently, Zotterman and other investigators clearly established the notion of specific nerve energies articulated by Johannes Müller in the early nineteenth century. This concept, as we have seen, states that morphologically distinct receptors transduce particular forms of energy and transmit this information to the brain through nerve fibers dedicated to that modality. Zotterman's studies demonstrated, for example, that pain is not the result of overstimulation of a generalized cutaneous receptor but results from electrical activity transmitted by specific sensory receptors called nociceptors.

We begin the study of the individual sensory systems with somatic sensation, the modality that was the subject of the first electrophysiological studies of sensation. Somatic sensibility arises from information provided by a variety of receptors distributed throughout the body. Somatic sensibility has four major modalities: discriminative touch (required to recognize the size, shape, and texture of objects and their movement across the skin), proprioception (the sense of static position and movement of the limbs and body), nociception (the signaling of tissue damage or chemical irritation, typically perceived as pain or itch), and temperature sense (warmth and cold).

Each of these modalities is mediated by a distinct system of receptors and pathways to the brain. However all share a common class of sensory neurons: the dorsal root ganglion neurons. Individual dorsal root ganglion neurons respond selectively to specific types of stimuli because of morphological and molecular specialization of their peripheral terminals.

In this chapter we describe in general the sensory response properties of dorsal root ganglion neurons that innervate the skin and mediate the senses of touch, temperature, pain, and itch. We consider how specialization of the nerve terminals allows these receptors to sense specific forms of energy. We will learn why some receptors sense light touch and others pressure, and why a painful stimulus, such as burning the skin, activates small-diameter sensory nerve fibers but not those neurons with thicker myelinated fibers that respond to light touch. In addition, we briefly consider nociceptors, proprioceptors, and visceral receptors, which are discussed in detail in later chapters when we consider, respectively, pain perception, voluntary movement, and the autonomic nervous system. Finally, we review the two major anatomical pathways that convey somatosensory information to the forebrain. Understanding the anatomy of these pathways is necessary to appreciate why certain lesions of the spinal cord may interrupt ipsilateral sensations of touch but not pain or temperature, while contralaterally producing the opposite deficits. In the next chapter, where we concentrate on touch, we will see how these afferent pathways convey somato-sensory information to the cerebral cortex and how the cortex processes and integrates this information.

The Dorsal Root Ganglion Neuron Is the Sensory Receptor in the Somatic Sensory System

Irrespective of modality, all somatosensory information from the limbs and trunk is conveyed by dorsal root ganglion neurons. Somatosensory information from cranial structures (the face, lips, oral cavity, conjunctiva, and dura mater) is transmitted by the trigeminal sensory neurons, which are functionally and morphologically homologous to dorsal root ganglion neurons. As we have seen in Chapter 5, the dorsal root ganglion neuron is well suited to its two principal functions: (1) stimulus transduction and (2) transmission of encoded stimulus information to the central nervous system. The cell body lies in a ganglion on the dorsal root of a spinal nerve. The axon has two branches, one projecting to the periphery and one projecting to the central nervous system (Figure 22-1). The terminal of the peripheral branch of the axon is the only portion of the dorsal root ganglion cell that is sensitive to natural stimuli. The properties of the nerve terminal determine the sensory function of each dorsal root ganglion neuron. The remainder of the peripheral branch, together with the central branch, is called the primary afferent fiber; it transmits the encoded stimulus information to the spinal cord or brain stem.

The peripheral terminals of dorsal root ganglion neurons are of two types. The terminal may be a bare nerve ending or the nerve ending may be encapsulated by a nonneural structure (Figure 22-2). Dorsal root ganglion neurons with encapsulated terminals mediate the somatic modalities of touch and proprioception (Table 22-1). They sense stimuli that indent or otherwise physically deform the receptive surface. In contrast, dorsal root ganglion neurons with bare nerve endings mediate painful or thermal sensations. Mechanoreceptors and proprioceptors are innervated by dorsal root ganglion neurons with large-diameter, myelinated axons that conduct action potentials rapidly. Thermal receptors and nociceptors have small-diameter axons that are either unmyelinated or thinly myelinated; these nerves conduct impulses more slowly.

Neurologists distinguish between two classes of somatic sensation: epicritic and protopathic. Epicritic sensations involve fine aspects of touch and are mediated by encapsulated receptors. These sensations include the ability to (1) detect gentle contact of the skin and localize the position that is touched (topognosis); (2) discern vibration and determine its frequency and amplitude; (3) resolve by touch spatial detail, such as the texture of surfaces, and the spacing of two points touched simultaneously (two-point discrimination); and (4) recognize

Figure 22-1 The morphology of a dorsal root ganglion cell. The cell body lies in a ganglion on the dorsal root of a spinal nerve. The axon has two branches, one projecting to the periphery, where its specialized terminal is sensitive to a particular form of stimulus energy, and one projecting to the central nervous system.

the shape of objects grasped in the hand (stereognosis). Protopathic sensations involve pain and temperature senses (as well as itch and tickle) and are mediated by receptors with bare nerve endings. Distinguishing between epicritic and protopathic sensation helps explain changes in sensation that take place following peripheral nerve damage. Protopathic sensations are considered to be cruder than epicritic sensations, in part because, more intense stimuli are needed to evoke pain. Nevertheless, the coding mechanisms for pain are very sensitive to the noxious or tissue-damaging aspects of the stimulus.

Touch Is Mediated by Mechanoreceptors in the Skin

Tactile sensitivity is greatest on the hairless (glabrous) skin on the fingers, the palmar surface of the hand, the sole of the foot, and the lips. Glabrous skin is characterized by a regular array of ridges formed by folds of the epidermis. The ridges are arranged in circular patterns called fingerprints and contain a dense matrix of mechanoreceptors. These receptors mediate the sense of touch; they are excited by indentation of the skin or by motion across its surface. When an object presses against the hand, the skin conforms to its contours. The depth of indentation depends on the force exerted by the object on the skin as well as its geometry. All mechanoreceptors sense these changes in skin contour but differ morphologically in important ways that affect their physiological function.

Mechanoreceptors Differ in Morphology and Skin Location

Virtually all mechanoreceptors have specialized end organs surrounding the nerve terminal. Although the sensitivity of these receptors to mechanical displacement is a property of the nerve terminal membrane, their dynamic response to stimulation is shaped by the specialized capsule. These nonneural structures must be deformed in particular ways in order to excite the sensory nerve. Histological and physiological studies have identified four major types of mechanoreceptors in glabrous skin. Two of these receptors are located in the superficial layers of the skin, and two are situated in the subcutaneous tissue (see Figure 22-2). The small superficial receptors sense deformation of the papillary ridges in which they reside. The larger subcutaneous receptors sense deformation of a wider area of skin that extends beyond the overlying ridges.

The two principal mechanoreceptors in the superficial layers of the skin are the Meissner's corpuscle and the Merkel disk receptor. The Meissner's corpuscle, a rapidly adapting receptor, is coupled mechanically to the edge of the papillary ridge, a relationship that confers fine mechanical sensitivity. The receptor is a globular, fluid- filled structure that encloses a stack of flattened epithelial cells; the sensory nerve terminal is entwined between the various layers of the corpuscle. The Merkel disk

Figure 22-2 The location and morphology of mechanoreceptors in hairy and hairless (glabrous) skin of the human hand. Receptors are located in the superficial skin, at the junction of the dermis and epidermis, and more deeply in the dermis and subcutaneous tissue. The receptors of the glabrous skin are Meissner's corpuscles, located in the dermal papillae; Merkel disk receptors, located between the dermal papillae; and bare nerve endings. The receptors of the hairy skin are hair receptors, Merkel's receptors (having a slightly different organization than their counterparts in the glabrous skin), and bare nerve endings. Subcutaneous receptors, beneath both glabrous and hairy skin, include Pacinian corpuscles and Ruffini endings. Nerve fibers that terminate in the superficial layers of the skin are branched at their distal terminals, innervating several nearby receptor organs; nerve fibers in the subcutaneous layer innervate only a single receptor organ. The structure of the receptor organ determines its physiological function.

receptor, a slowly adapting receptor, is a small epithelial cell that surrounds the nerve terminal. The Merkel cell encloses a semirigid structure that transmits compressing strain from the skin to the sensory nerve ending, evoking sustained, slowly adapting responses. Merkel disk receptors are normally found in clusters at the center of the papillary ridge.

The two mechanoreceptors found in the deep subcutaneous tissue are the Pacinian corpuscle and the Ruffini ending. These receptors are much larger than the Merkel cells and Meissner's corpuscles, and less numerous. The Pacinian corpuscle is physiologically similar to the Meissner's corpuscle. It responds to rapid indentation of the skin but not to steady pressure because of the connective tissue lamellae that surround the nerve ending (see Figure 21-10). The large capsule of this receptor is flexibly attached to the skin, allowing the receptor to sense vibration occurring several centimeters away. These receptors are activated selectively by the common neurological test of touching a tuning fork (oscillating at 200-300 Hz) to the skin or bony prominence. Ruffini endings are slowly adapting receptors that link the subcutaneous tissue to folds in the skin at the joints and in the palm or to the fingernails. These receptors sense stretch of the skin or bending of the fingernails as these stimuli compress the nerve endings. Mechanical information sensed by Ruffini endings contributes to our perception of the shape of grasped objects. The anatomical arrangement of mechanoreceptors in glabrous skin is shown in Figure 22-2.

Figure 22-3 Mechanoreceptors in glabrous skin vary in the size and structure of their receptive fields. Each colored area on the hands indicates the receptive field of a different sensory nerve fiber in the human median nerve. (Adapted from Johansson and Vallbo 1983.)

1. The Merkel disk receptor in the superficial skin and the subcutaneous Ruffini ending are slowly adapting receptors (see Figure 21-9A). The Merkel disk receptor has a small, highly localized receptive field, whereas the Ruffini ending has a large field (light purple) with a central zone of maximal sensitivity (dark purple). Depending on their location, individual Ruffini endings are excited by stretch of the skin in specific directions as indicated by arrows.
2. The Meissner's corpuscle in the superficial skin and the subcutaneous Pacinian corpuscle are rapidly adapting receptors (see Figure 21-9B). Meissner's corpuscles on the fingertips have receptive fields averaging 2-3 mm in diameter, while receptive fields on the palm average 10 mm in diameter. The receptive fields of Pacinian

corpuscles cover larger continuous surfaces on the fingers or palm (light pink) but have a central zone of maximal sensitivity located directly above the receptor (red).

1. Expanded view of the receptive fields of mechanoreceptors in the superficial and deep layers of glabrous skin. The relative sensitivity to pressure is shown as a contour map in which the most sensitive regions are indicated in red and the least sensitive areas in pale pink. Receptive fields in the superficial layers of the skin have many points of high sensitivity, marking the positions of the Meissner's corpuscles or Merkel disk receptors.

Receptive fields in the deep layers have a single point of maximal sensitivity overlying the Pacinian or Ruffini receptor.

Similar mechanoreceptors are found in the hairy skin that covers most of the body surface. The principal rapidly adapting mechanoreceptors of the hairy skin are the hair follicle receptor and the field receptor. Hair follicle receptors respond to hair displacement. The three separate classes of these receptors (down, guard, and tylotrich hairs) differ in sensitivity to hair movement and conduction velocity (see Table 22-1). Field receptors are located primarily over the joints of the fingers, wrist, and elbow. They sense skin stretch when the joint is flexed or when the skin is rubbed.

Figure 22-4 The distribution of receptor types in the human hand varies. The number of sensory nerve fibers innervating an area is indicated by the stippling density, with the highest density of receptors shown by the heaviest stippling. (RA = 5 rapidly adapting, SA = 5 slowly adapting.) Meissner's corpuscles (RA) and Merkel disk receptors (SA I) are the most numerous receptors; they are distributed preferentially on the distal half of the fingertip. Pacinian corpuscles (PC) and Ruffini endings (SA II) are much less common; they are distributed more uniformly on the hand, showing little differentiation of the distal and proximal regions. The fingertips are the most densely innervated region of skin in the human body, receiving approximately 300 mechanoreceptive nerve fibers per square centimeter. The number of mechanoreceptive fibers is reduced to 120/cm2 in the proximal phalanges, and to 50/cm2 in the palm. (Adapted from Vallbo and Johansson 1978.)

Mechanoreceptors in the Superficial and Deep Layers of Skin Have Different Receptive Fields

Each individual dorsal root ganglion neuron conveys sensory information from a limited area of skin determined by the location of its receptive endings. As we saw in Chapter 21, the region of skin from which a sensory neuron is excited is called its receptive field.

The size and structure of receptive fields differ for receptors in the superficial and deep layers of the skin. A single dorsal root ganglion cell innervating the superficial layers receives input from a cluster of 10-25 Meissner's corpuscles or Merkel disk receptors. The afferent fiber has a receptive field that spans a small circular area with a diameter ranging from 2 to 10 mm (Figure 22-3). These receptive fields are at least an order of magnitude greater in diameter than that of an individual receptor. Therefore, nerve fibers innervating the superficial layers of the skin sample the activity of many different sensory receptors of one particular sort. In contrast, each nerve fiber innervating the deep layers of skin innervates a single Pacinian corpuscle or Ruffini ending. Consequently, the receptive fields of these receptors cover large areas of skin, and their borders are indistinct (Figure 22-3). Usually, these receptive fields have a single "hot spot" where sensitivity to touch is greatest; this point is located directly above the receptor. The large receptive fields result from the ability of these receptors to sense mechanical displacement at some distance from the end organ.

The difference in size of the receptive fields of receptors in the superficial and deep layers of the skin plays an important role in the functions of the receptors. Meissner's corpuscle and Merkel disk receptors in the superficial layers resolve fine spatial differences because they transmit information from a restricted area of skin. As these receptors are smaller in diameter than the fingerprint ridges of glabrous skin, individual receptors can be stimulated by very small bumps on a surface. This very fine spatial resolution allows humans to perform fine tactile discrimination of surface texture and to read Braille. Pacinian corpuscles and Ruffini endings in the deep layers resolve only coarse spatial differences. They are poorly suited for accurate spatial localization or for resolution of fine spatial detail. Mechanoreceptors in the deep layers of the skin sense more global properties of objects and detect displacements from a wide area of skin.

Figure 22-5 Two-point discrimination varies throughout the body surface. The two-point threshold measures the minimum distance at which two stimuli are resolved as distinct. At smaller separations the stimuli are blurred into a single continuous sensation spanning the distance between the points. Two-point thresholds are measured clinically using a calibrated compass in which the separation of the tips is accurately scaled. Two-point thresholds can also be determined from measurements of the ability of subjects to discriminate the orientation of grating ridges as a function of their spacing. This method measures spatial acuity more accurately. The two-point threshold varies for different body regions; it is about 2 mm on the finger tip but increases to 10 mm on the palm and 40 mm on the arm. The two-point thresholds highlighted in pink match the diameter of the corresponding receptive fields shown in pink on the body. The greatest discriminative capacity is afforded in the finger tips, lips, and tongue, which have the smallest receptive fields. (Adapted from Weinstein 1968.)

The Spatial Resolution of Stimuli on the Skin Varies Throughout the Body Because the Density of

Mechanoreceptors Varies

In addition to the differences in spatial resolution between receptor classes due to differences in receptive field size, the skin area enclosed within receptive fields varies throughout the body. The smallest receptive fields are found on the tips of the fingers. Receptive fields are slightly larger on the proximal phalanges and even bigger on the palm. The receptive fields on hairy skin also increase in area as stimuli are moved proximally from the wrist to the trunk. These variations in receptive field size reflect the density of mechanoreceptors in the different regions of skin. Although individual dorsal root ganglion neurons innervate approximately the same number of sensory receptors in the skin, there are far more Meissner's corpuscles and Merkel disk receptors in the fingertip skin than on the palm. The spacing of mechanoreceptors is therefore smallest on the fingertips and widens proximally on the palm, where receptors are less densely packed (Figure 22-4).

Box 22-1 Vibration Sense Is Coded by Spike Trains in Mechanoreceptors in the Skin

Vibration is the sensation produced by sinusoidal oscillation of objects placed against the skin. Vibration may be produced by the hum of an electric motor, the strings of a musical instrument, or a tuning fork used in the neurological examination. Mechanoreceptors in the skin respond to these oscillations by a pulse code in which each action potential signals one cycle of the sinusoidal wave (Figure 22-6A). The vibratory frequency is signaled by the frequency of action potentials fired by the sensory nerves.

Individual mechanoreceptors differ in their threshold sensitivity to vibration (Figure 22-6B). Merkel disk receptors are most responsive to extremely low frequencies (5-15 Hz); Meissner's corpuscles are most sensitive to midrange stimuli (20-50 Hz). The Pacinian corpuscles have the lowest thresholds for high frequencies (60-400 Hz); at 250 Hz they detect vibrations as small as 1 = μm but at 30 Hz require stimuli with much larger amplitudes.

The receptor tuning thresholds determine the ability to sense vibration. Humans are most sensitive to vibration at frequencies of 200-250 Hz. To be felt, lower and higher frequencies must have proportionately larger amplitude vibrations.

The perception of vibration as a series of repeating events results from the fact that the receptors under the probe are activated synchronously and therefore fire action potentials simultaneously. The intensity of vibration is signaled by the total number of sensory nerve fibers that are active rather than the frequency of firing, which codes the vibratory frequency. If a patient is tested with a 250 Hz vibration near sensory threshold, only Pacinian corpuscles right under the contact point in the skin are activated. As the vibratory amplitude is increased, more distant Pacinian corpuscles as well as Meissner's corpuscles under the vibrator become activated. The total number of active sensory nerves is linearly related to the amplitude of vibration.

Figure 22-6A A rapidly adapting mechanoreceptor responds to sinusoidal mechanical stimuli with a single action potential for each cycle. The record here is for a receptor stimulated with a 25 Hz vibratory stimulus; the firing frequency of the receptor is 25 action potentials per second. The lowest stimulus intensity that evokes one action potential per cycle of the sinusoidal stimulus is called the receptor's "tuning threshold." (Adapted from Talbot et al. 1968.)

Figure 22-6B The threshold for detecting vibration corresponds to the tuning threshold of the mechanoreceptor. The sensitivity threshold for Meissner's corpuscles is lowest for frequencies of 20-50 Hz. Pacinian corpuscles sense higher frequencies. (Adapted from Mountcastle et al. 1972.)

The size of the receptive fields in a particular region of skin delimits the capacity to determine whether one or more points are stimulated. A sensory neuron innervating Meissner's corpuscles and Merkel disk receptors transmits information about the largest skin indentation within its receptive field. If two points within the same receptive field are stimulated, the neuron will signal only the larger indentation. But if the points are located in the receptive fields of two different nerve fibers, then information about both points of stimulation will be signaled. The

farther apart the points lie on the surface, the greater the likelihood that the two active nerves will be separated by silent nerve fibers. The contrast between active and inactive nerve fibers seems to be necessary for resolving spatial detail. Spatial resolution of stimuli on various regions of the skin can be quantified in humans by measuring their ability to perceive a pair of nearby stimuli as two distinct entities. The minimum distance between two detectable stimuli is called the two-point threshold. The two-point threshold varies for different body regions (Figure 22- 5). These variations are correlated with the size of sensory receptive fields and the innervation density of mechanoreceptors in the superficial layers of the skin. Thus, measurements of sensory function of the human hand reveal important information concerning the organization of peripheral sense organs.

Mechanoreceptors Differ in Adaptation Properties and Sensory Thresholds

Why is each layer of the skin endowed with two different sets of mechanoreceptors with similar receptive fields? The answer lies in their physiological function. Although all four types of mechanoreceptor are excited by indentation of the skin, they signal different information. As we learned in Chapter 21, mechanoreceptors respond to touch with sustained slowly adapting responses or with rapidly adapting bursts at the beginning and end of contact. The slowly adapting receptors signal the pressure and shape of objects by their average firing rate (see Figure 21-9A). The total number of action potentials evoked per second is proportional to the indentation force applied to the receptor. Rapidly adapting receptors sense motion of objects on the skin (see Figure 21-9B). These receptors respond during the period when the position of a stimulus changes, and they stop firing when it comes to rest. Their firing rates are proportional to the speed of motion, and the duration of activity signals the duration of the motion. They sense vertical impact such as the pressure wave produced when the hand contacts an object and vibration when the object oscillates (see Box 22-1). Rapidly adapting receptors are also stimulated by lateral motion such as stroking, rubbing, or palpation.

Mechanoreceptors also differ in sensory thresholds, the minimum intensity of stimulation required to generate an action potential in the nerve. Rapidly adapting receptors have lower touch thresholds than slowly adapting receptors. The Pacinian corpuscle is the most sensitive mechanoreceptor (Figure 22-6A,22-6B). These receptors are able to detect the minute vibrations produced by impacts on a surface on which the hand rests or caused by the hum of an electric motor. Pacinian corpuscles also sense the frictional displacement of the skin when the hand moves across an object, regardless of whether the surface is smooth or rough. The Meissner's corpuscle is particularly sensitive to abrupt changes in the shape of objects that occur at the edges or corners and to small irregularities on the surface sensed during palpation by the hand. Meissner's corpuscles are used to detect and localize small bumps or ridges on an otherwise smooth surface.

More salient bumps or edges are required to activate the slowly adapting Merkel disk receptors. However, once stimulated, the Merkel receptors provide a clearer image of contours by changes in the frequency of firing. If the surface is flat, these receptors fire continuously at relatively low rates. Convexities that indent the skin increase firing rates, whereas concavities silence these receptors. Responses are proportional to the surface curvature; large-diameter, gently curved objects evoke weaker responses than small-diameter objects (Figure 22-7). The strongest

responses occur when sharp edges or punctate probes, such as a pencil point, contact the receptive field. These changes in receptor activity are reflected in the corresponding perceptions of object shape experienced when we grasp spheres of different diameters between the thumb and index finger. A tiny sphere, such as a ball bearing, feels relatively sharp, whereas a ping-pong ball feels blunt.

The Spatial Characteristics of Objects Are Signaled by Populations of Mechanoreceptors

If the firing rate of slowly adapting receptors signals both pressure and shape, how does the brain decipher which parameter is signaled by an individual receptor? In fact, one receptor cannot signal both of these properties unambiguously. Information about size and shape is signaled by populations of receptors that are stimulated by different portions of the object. A small-diameter object, which indents the skin at a small localized spot, produces a sharply peaked response in which a small number of adjacent receptors fire at high rates. A gently rounded object, which contacts a large region of skin, evokes weak responses in a large population of receptors, forming a broad, low-amplitude profile (Figure 22-7A).

Information about texture is also mediated by populations of mechanoreceptors. Humans are able to sense the roughness of surfaces as well as the spacing and orientation of texture patterns, such as gratings or arrays of Braille dots. When the hand is rubbed over a set of Braille dots, the Merkel disk receptors and Meissner's corpuscles fire bursts of action potentials as each dot in the pattern crosses their receptive fields and are silent as the smooth regions between dots pass. The periodic firing of these receptors signals the spatial arrangement of the texture pattern (Figure 22-8).

However, each receptor axon is stimulated by only a small portion of the pattern. The overall picture is not contained in the firing patterns of any one individual nerve fiber but in the total ensemble of inputs provided by the active and inactive sensory nerves. The distribution of active and inactive nerve fibers represents the spacing and arrangement of the dots in the texture pattern. Therefore, a representation of the texture pattern is transmitted by a group of activated receptor axons in the peripheral nerve innervating the finger. We will learn in Chapter 23 how the central nervous system uses convergent connections to compare activity among members of the population to abstract the arrangement of dots comprising the textured surface.

Figure 22-7 The shape and size of objects touching the hand are encoded by populations of Merkel disk receptors.

1. The area of contact on the skin determines the total number of stimulated Merkel disk receptors in the population. The pink region on the fingertip shows the spread of excitation when probes of different diameters are pressed upon the skin with constant force. The intensity of color is proportional to the firing rates of the stimulated receptors. 1. A small-diameter, sharp probe activates a small population of Merkel receptors. However, the active receptors fire intensely because all of the force is concentrated at the small probe tip. 2. An intermediate-size probe excites more receptors but the peak firing

rate in the population is reduced. The probe does not feel as sharp as the small-diameter probe. 3. A gently rounded, large-diameter probe stimulates a large population of receptors spread across the width of the finger. These receptors fire at low rates because the force is spread over a larger area of skin. (Adapted from Goodwin et al. 1995.)

2. The firing rate of individual Merkel disk receptors signals the probe diameter. These recordings of action potentials fired by a Merkel disk receptor illustrate the responses evoked when probes of decreasing size are pressed on the center of the receptive field. All of the probes evoke a strong initial response as contact is made with the skin. The firing rate of the neuron during steady pressure is proportional to the curvature of each probe. The weakest responses are evoked by flat surfaces and gently rounded (large diameter) probes. The firing rate increases as the probe diameter becomes smaller. (Adapted from Srinivasan and LaMotte 1991.)

Figure 22-8 The firing patterns of mechanoreceptors in the superficial layers of the skin encode the texture of objects rubbed across the skin.

1. 1. The nerve responses to textures are measured with the hand immobilized. The receptive field of a single receptor on a monkey's finger is stimulated with an embossed array of raised dots on a rotating drum. The pattern moves horizontally over the receptive field as the drum rotates. The experimenter thus controls the speed of movement and the location of the dot pattern in the receptive field. The pattern is moved laterally on successive rotations to allow the dots to cross the medial, central, and lateral portions of the receptive field on successive rotations. The composite response of an individual nerve fiber to successive views of the raised dots simulates the distribution of active and inactive nerve fibers in the population. 2. Sequential action potentials discharged by individual receptors during each revolution of the drum are represented in spatial event plots in which each action potential is a small dot, and each horizontal row of dots represents a scan with the pattern shifted laterally on the finger.

2. Spatial event plots of three types of mechanoreceptors to dot patterns with different spacing. Slowly adapting Merkel disk receptors and rapidly adapting Meissner's corpuscles differentiate between dots and blank space when the spacing of the dots exceeds the receptive field diameter. A receptor fires bursts of action potentials for each dot, spaced by silent intervals. As the dots are brought closer together, the resolution of individual dots blurs. Pacinian corpuscles do not distinguish texture patterns because their receptive fields are larger than the dot spacing. (Reproduced from Connor et al. 1990.)

The spatial resolution of detail within a pattern depends on the total area of skin innervated by each sensory nerve (see Figure 21-6). The Merkel disk receptors provide the sharpest resolution of spatial pattern, as each receptor axon monitors a single dot. Meissner's corpuscles also resolve individual dots but the image of the pattern that they provide is not as sharp because they have slightly larger receptive fields. Pacinian corpuscles do not signal changes in surface contour because their large receptive fields encompass several dots in the textured surface. Instead they fire continuously, measuring the speed at which the hand moves across the surface. The activity of Pacinian corpuscles provides timing information that allows the brain to convert the number

of bursts per second fired by Meissner's corpuscles and Merkel disk receptors into spatial information about the number of dots per centimeter on the textured surface.

The pure sensory experiences evoked by the stimuli used in the neurological examination—a light tap, pressure from a pin, or a sinusoidal vibratory stimulus—are quite different from the tactile sensations evoked by the complex natural stimuli that we usually encounter. Natural stimuli rarely activate a single type of receptor; rather they activate different combinations of mechanoreceptors that act synergistically. For example, when we grasp, lift, and replace an object on a surface, the four classes of receptors signal important phases of the movement. Meissner's corpuscles are highly active during the initial period of contact as grasp force increases; these receptors also fire a second burst when the grip is released. Merkel disk receptors are also stimulated during the initial grip, but they continue to fire as the object is lifted, signaling grip force; they cease firing when the grip is released. Pacinian corpuscles are most sensitive to transient mechanical pressures at the start and stop of motion, when the object is lifted off and replaced on the surface. The vertical gravitational forces applied to the skin as the object is lifted are signaled by Ruffini endings. The coordinated sensory information from these receptors provides important signals to the motor system controlling the hand, which we shall study in Chapter 38.

Figure 22-11 Mechanical nociceptors are activated by strong stimuli and mediate sharp, pricking sensations. Pressure on the cell's receptive field with a blunt-tipped probe elicits no response even if the skin is indented by 2 mm (A), but the tip of a needle that punctures the skin produces a clear response (B). The bottom traces in parts A and B are the output of a force transducer coupled to the stimulator. Pinching the skin with serrated forceps (C), which is more traumatic than a pin prick, produces the strongest response. (Adapted from Perl 1968.)

Mechanical nociceptors require strong, often painful tactile stimuli, such as a pinch, in order to respond. They are also excited by sharp objects that penetrate, squeeze, or pinch the skin (Figure 22-11), and therefore mediate sensations of sharp or pricking pain. Their firing rates increase with the destructiveness of mechanical stimuli, from near-damaging to overtly destructive of the skin. The afferent fibers for mechanical nociceptors have bare nerve endings and, because they are myelinated, are the fastest-conducting nociceptive afferents.