PART II Neurophysiology

CHAPTER 4

Sensory Physiology

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CHAPTER OUTLINE

KEY CONCEPTS

1. Sensory transduction takes place in a series of steps, starting with stimuli from the external or internal environment and ending with neural processing in the central nervous system.
2. The structure of sensory organs optimizes their response to the preferred types of stimuli.
3. A stimulus gives rise to a generator potential, which, in turn, causes action potentials to be produced in the associated sensory nerve.
4. The speeds of adaptation of particular sensory receptors are related to their biological roles.
5. Specific sensory receptors for a variety of types of tactile stimulation are located in the skin.
6. Somatic pain is associated with the body surface and the musculature; visceral pain is associated with the internal organs.
7. The sensory function of the eyeball is determined by structures that form and adjust images and by structures that transform images into neural signals.
8. The retina contains several cell types, each with a specific role in the process of visual transduction.
9. The rod cells in the retina have a high sensitivity to light but produce indistinct images without color, while the cones provide sharp color vision with less sensitivity to light.
10. The visual transduction process requires many steps, beginning with the absorption of light and ending with an electrical response.
11. The outer ear receives sound waves and passes them to the middle ear; they are modified and passed to the inner ear, where the process of sound transduction takes place.
12. The transmission of sound through the middle ear greatly increases the efficiency of its detection, while its protective mechanisms guard the inner ear from damage caused by extremely loud sounds. Disturbances in this transmission process can lead to hearing impairments.
13. Sound vibrations enter the cochlea through the oval window and travel along the basilar membrane, where their energy is transformed into neural signals in the organ of Corti.
14. Displacements of the basilar membrane cause deformation of the hair cells, the ultimate transducers of sound. Different sites along the basilar membrane are sensitive to different frequencies.
15. The vestibular apparatus senses the position of the head and its movements by detecting small deflections of its sensory structures.
16. Taste is mediated by sensory epithelial cells in the taste buds. There are five fundamental taste sensations: sweet, sour, salty, bitter, and umami.
17. Smell is detected by nerve cells in the olfactory mucosa. Thousands of different odors can be detected and distinguished.

The survival of any organism, human included, depends on having adequate information about the external environment, where food is to be found and where hazards abound. Equally important for maintaining the function of a complex organism is information about the state of numerous internal bodily processes and functions. Events in our external and internal worlds must first be translated into signals that our nervous systems can process. Despite the wide range of types of information to be sensed and acted on, a small set of common principles underlie all sensory processes.

This chapter discusses the functions of the organs that permit us to gather this information, the sensory receptors. The discussion emphasizes somatic sensations, those dealing with the external aspect of the body, and does not specifically treat visceral sensations, those that come from internal organs.

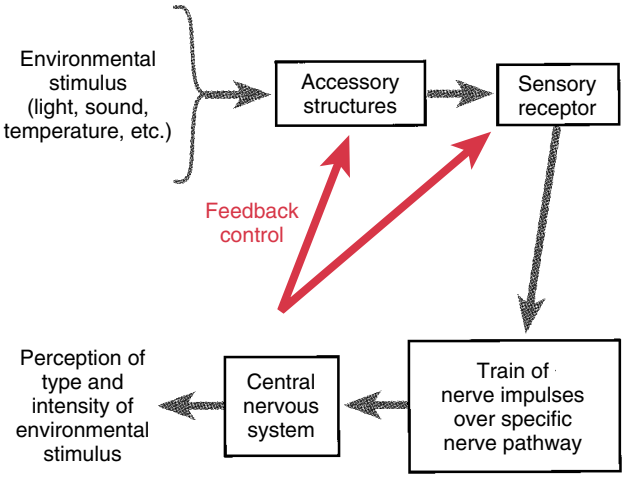


FIGURE 4.1 **A basic model for the translation of an environmental stimulus into a perception.** While the details vary with each type of sensory modality, the overall process is similar.

THE GENERAL PROBLEM OF SENSATION

While the human body contains a very large number of different sensory receptors, they have many functional features in common. Some basic themes are shared by almost all receptors, and the wide variety of specialized functions is a result of structural and physiological adaptations that adapt a particular receptor for its role in the overall economy of an organism.

Sensory Receptors Translate Energy From the Environment Into Biologically Useful Information

The process of sensation essentially involves sampling selected small amounts of energy from the environment and using it to control the generation of action potentials or nerve impulses (see Fig. 4.1). This process is the function of **sensory receptors,** biological structures that can be as simple as a free nerve ending or as complicated as the human eye or ear. The pattern of sensory action potentials, along with the specific nature of the sensory receptor and its nerve pathways in the brain, provide an internal representation of a specific component of the external world. The process of sensation is a portion of the more complex process of **perception,** in which sensory information is integrated with previously learned information and other sensory inputs, enabling us to make judgments about the quality, intensity, and relevance of what is being sensed.

The Nature of Environmental Stimuli. A factor in the environment that produces an effective response in a sensory receptor is called a **stimulus.** Stimuli involve exchanges of energy between the environment and the receptors. Typical stimuli include electromagnetic quantities, such as radiant heat or light; mechanical quantities, such as pressure, sound waves, and other vibrations; and chemical qualities, such as acidity and molecular shape and size. Common to all these types of stimuli is the property of **intensity**, a measure of the energy content (or concentration, in the case of chemical stimuli) available to interact with the sensory receptor. It is not surprising, therefore, that a fundamental property of receptors is their ability to respond to different intensities of stimulation with an appropriate output. Also related to receptor function is the concept of **sensory modality.** This term refers to the kind of sensation, which may range from the relatively general modalities of taste, smell, touch, sight, and hearing (the traditional five senses), to more complex sensations, such as slipperiness or wetness. Many sensory modalities are a combination of simpler sensations; the sensation of wetness is composed of sensations of pressure and temperature. (Try placing your hand in a plastic bag and immersing it in cold water. Although the skin will remain dry, the perception will be one of wetness.)

It is often difficult to communicate a precise definition of a sensory modality because of the subjective perception or **affect** that accompanies it. This property has to do with the psychological feeling attached to the stimulus. Some stimuli may give rise to an impression of discomfort or pleasure apart from the primary sensation of, for example, cold or touch. Previous experience and learning play a role in determining the affect of a sensory perception.

Some sensory receptors are classified by the nature of the signals they sense. For example, **photoreceptors** sense light and serve a visual function. **Chemoreceptors** detect chemical signals and serve the senses of taste and smell, as well as detecting the presence of specific substances in the body. **Mechanoreceptors** sense physical deformation, serve the senses of touch and hearing, and can detect the amount of stress in a tendon or muscle; and **thermal receptors** detect heat (or its relative lack). Other sensory receptors are classified by their "vantage point" in the body. Among these, **exteroceptors** detect stimuli from outside the body; **enteroceptors** detect internal stimuli; **proprioceptors** (receptors of "one's own") provide information about the positions of joints and about muscle activity and the orientation of the body in space. **Nociceptors** (pain receptors) detect noxious agents, both internally and externally.

The Specificity of Sensory Receptors. Most sensory receptors respond preferentially to a single kind of environmental stimulus. The usual stimulus for the eye is light; that for the ear is sound. This specificity is due to several features that match a receptor to its preferred stimulus. In many cases, **accessory structures,** such as the lens of the eye or the structures of the outer and middle ears, enhance the specific sensitivity of the receptor or exclude unwanted stimuli. Often these accessory structures are a control system that adjusts their sensitivity according to the information being received (Fig. 4.1). The usual and appropriate stimulus for a receptor is called its **adequate stimulus**. For the adequate stimulus, the receptor has the lowest **threshold**, the lowest stimulus intensity that can be reliably detected. A threshold is often difficult to measure because it can vary over time and with the presence of interfering stimuli or the action of accessory structures. Although most receptors will respond to stimuli other than the adequate stimulus, the threshold for inappropriate stimuli is much higher. For example, gently pressing the outer corner of the eye will produce a visual sensation caused by pressure, not light; extremes of temperature may be perceived as pain. Almost all receptors can be stimulated electrically to produce sensations that mimic the one usually associated with that receptor.

The central nervous pathway over which sensory information travels is also important in determining the nature of the perception; information arriving by way of the optic nerve, for example, is always perceived as light and never as sound. This is known as the concept of the **labeled line**.

The Process of Sensory Transduction Changes Stimuli Into Biological Information

This section focuses on the actual function of the sensory receptor in translating environmental energy into action potentials, the fundamental units of information in the nervous system. A device that performs such a translation is called a **transducer;** sensory receptors are biological transducers. The sequence of electrical events in the sensory transduction process is shown in Figure 4.2.

The Generator Potential. The sensory receptor in this example is a mechanoreceptor. Deformation or deflection of the tip of the receptor gives rise to a series of action potentials in the sensory nerve fiber leading to the central nervous system (CNS). The stimulus (1) is applied at the tip of the receptor, and the deflection (2) is held constant (dotted lines). This deformation of the receptor causes a

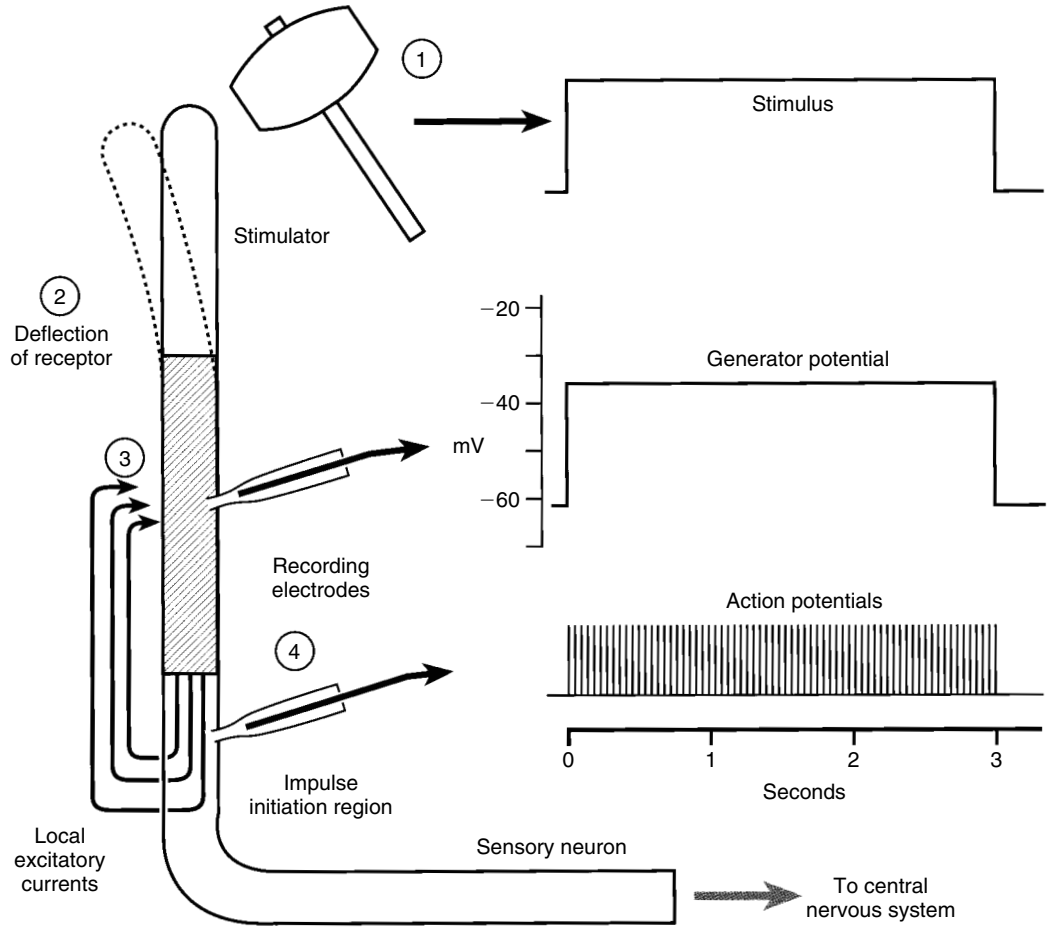


FIGURE 4.2 **The relation between an applied stimulus and the production of sensory nerve action potentials.** (See text for details.)

portion of its cell membrane (shaded region [3]) to become more permeable to positive ions (especially sodium). The increased permeability of the membrane leads to a localized depolarization, called the **generator potential.** At the depolarized region, sodium ions enter the cell down their electrochemical gradient, causing a current to flow in the extracellular fluid. Because current is flowing into the cell at one place, it must flow out of the cell in another place. It does this at a region of the receptor membrane (4) called the **impulse initiation region** (or coding region) because here the flowing current causes the cell membrane to produce action potentials at a frequency related to the strength of the current caused by the stimulus. These currents, called **local excitatory currents,** provide the link between the formation of the generator potential and the excitation of the nerve fiber membrane.

In complex sensory organs that contain a great many individual receptors, the generator potential may be called a **receptor potential,** and it may arise from several sources within the organ. Often the receptor potential is given a special name related to the function of the receptor; for example, in the ear it is called the cochlear microphonic, while an electroretinogram may be recorded from the eye. Note that in the eye the change in receptor membrane potential associated with the stimulus of light is a **hyperpolarization,** not a depolarization.

The production of the generator potential is of critical importance in the transduction process because it is the step in which information related to stimulus intensity and duration is transduced. The strength (intensity) of the stimulus applied (in Fig. 4.2, the amount of deflection) determines the size of the generator potential depolarization. Varying the intensity of the stimulation will correspondingly vary the generator potential, although the changes will not usually be directly proportional to the intensity. This is called a **graded response,** in contrast to the all-or-none response of an action potential, and it causes a similar gradation of the strength of the local excitatory currents. These, in turn, determine the amount of depolarization produced in the impulse initiation region (4) of the receptor, and events in this region constitute the next important link in the process.

The Initiation of Nerve Impulses

Figure 4.3 shows a variety of possible events in the impulse initiation region. The threshold (colored line) is a critical level of depolarization; membrane potential changes below this level are caused by the local excitatory currents and vary in proportion to them, while the membrane activity above the threshold level consists of locally produced **action potentials.** The lower trace shows a series of different stimuli applied to the receptor, and the upper trace shows the resulting electrical events in the impulse initiation region.

No stimulus is given at **A,** and the membrane voltage is at the resting potential. At **B,** a small stimulus is applied, producing a generator potential too small to bring the impulse initiation region membrane to threshold, and no action potential activity results. (Such a stimulus would not be sensed at all.) A brief stimulus of greater intensity is given at **C;** the resulting generator potential displacement is of sufficient amplitude to trigger a single action potential. As in all excitable and all-or-none nerve membranes, the action potential is immediately followed by repolarization, often to a level that transiently hyperpolarizes the membrane potential because of temporarily high potassium conductance. Since the brief stimulus has been removed by this time, no further action potentials are produced. A longer stimulus of the same intensity (**D**) produces repetitive action potentials because as the membrane repolarizes from the action potential, local excitatory currents are still flowing. They bring

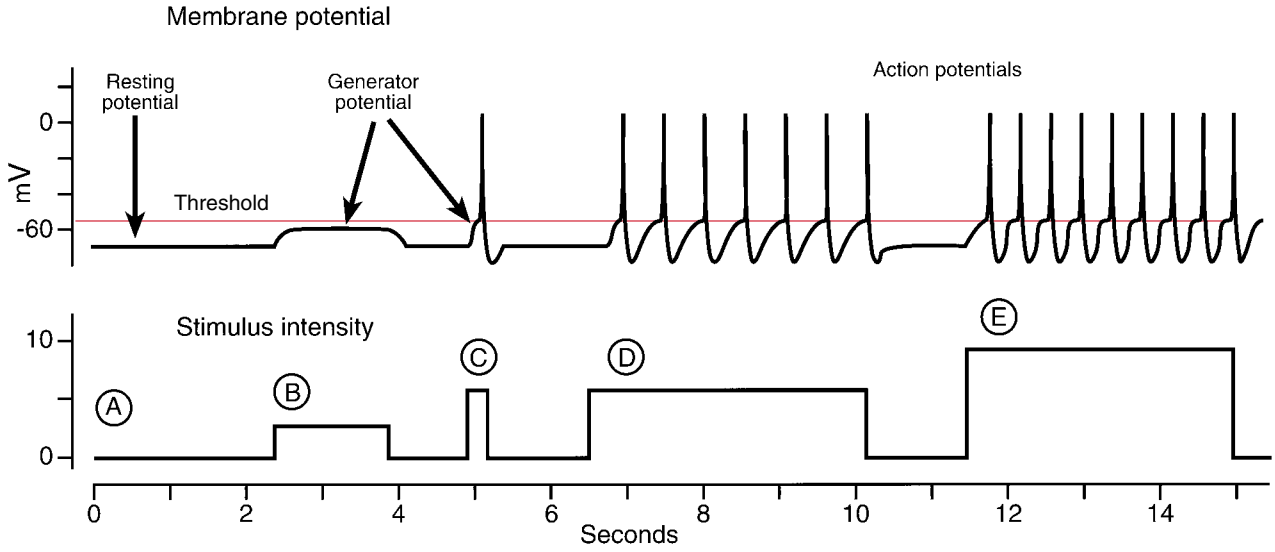


FIGURE 4.3 **Sensory nerve activity with different stimulus intensities and durations.** **A,** With no stimulus, the membrane is at rest. **B,** A subthreshold stimulus produces a generator potential too small to cause membrane excitation. **C,** A brief, but intense, stimulus can cause a single action potential. **D,** Maintaining this stimulus leads to a train of action potentials. **E,** Increasing the stimulus intensity leads to an increase in the action potential firing rate.

the repolarized membrane to threshold at a rate proportional to their strength. During this time interval, the fast sodium channels of the membrane are being reset, and another action potential is triggered as soon as the membrane potential reaches threshold. As long as the stimulus is maintained, this process will repeat itself at a rate determined by the stimulus intensity. If the intensity of the stimulus is increased (E), the local excitatory currents will be stronger and threshold will be reached more rapidly. This will result in a reduction of the time between each action potential and, as a consequence, a higher action potential frequency. This change in action potential frequency is critical in communicating the intensity of the stimulus to the CNS.

Adaptation. The discussion thus far has depicted the generator potential as though it does not change when a constant stimulus is applied. Although this is approximately correct for a few receptors, most will show some degree of **adaptation.** In an adapting receptor, the generator potential and, consequently, the action potential frequency will decline even though the stimulus is maintained. Part A of Figure 4.4 shows the output from a receptor in which there is no adaptation. As long as the stimulus is maintained, there is a steady rate of action potential firing. Part B shows **slow adaptation;** as the generator potential declines, the interval between the action potentials increases correspondingly. Part C demonstrates **rapid adaptation;** the action potential frequency falls rapidly and then maintains a constant slow rate that does not show further adaptation. Responses in which there is little or no adaptation are called **tonic,** whereas those in which significant adaptation occurs are called **phasic.** In some cases, tonic receptors may be called **intensity receptors,** and phasic receptors called **velocity receptors.** Many receptors—**muscle spindles**, for example—show a combination of responses; on application of a stimulus, a rapidly adapting phasic response is followed by a steady tonic response. Both of these responses may be graded by the intensity of the stimulus. As a receptor adapts, the sensory input to the CNS is reduced, and the sensation is perceived as less intense.

The phenomenon of adaptation is important in preventing "sensory overload," and it allows less important or unchanging environmental stimuli to be partially ignored. When a change occurs, however, the phasic response will occur again, and the sensory input will become temporarily more noticeable. Rapidly adapting receptors are also important in sensory systems that must sense the rate of change of a stimulus, especially when its intensity can vary over a range that would overload a tonic receptor.

Receptor adaptation can occur at several places in the transduction process. In some cases, the receptor's sensitivity is changed by the action of accessory structures, as in the constriction of the pupil of the eye in the presence of bright light. This is an example of feedback-controlled adaptation; in the sensory cells of the eye, light-controlled changes in the amounts of the visual pigments also can change the basic sensitivity of the receptors and produce adaptation. As mentioned above, adaptation of the generator potential can produce adaptation of the overall sensory response. Finally, the phenomenon of **accommodation** in the impulse initiation region of the sensory nerve fiber can slow the rate of action potential production even though the generator potential may show no change. Accommodation refers to a gradual increase in threshold caused by prolonged nerve depolarization, resulting from the inactivation of sodium channels.

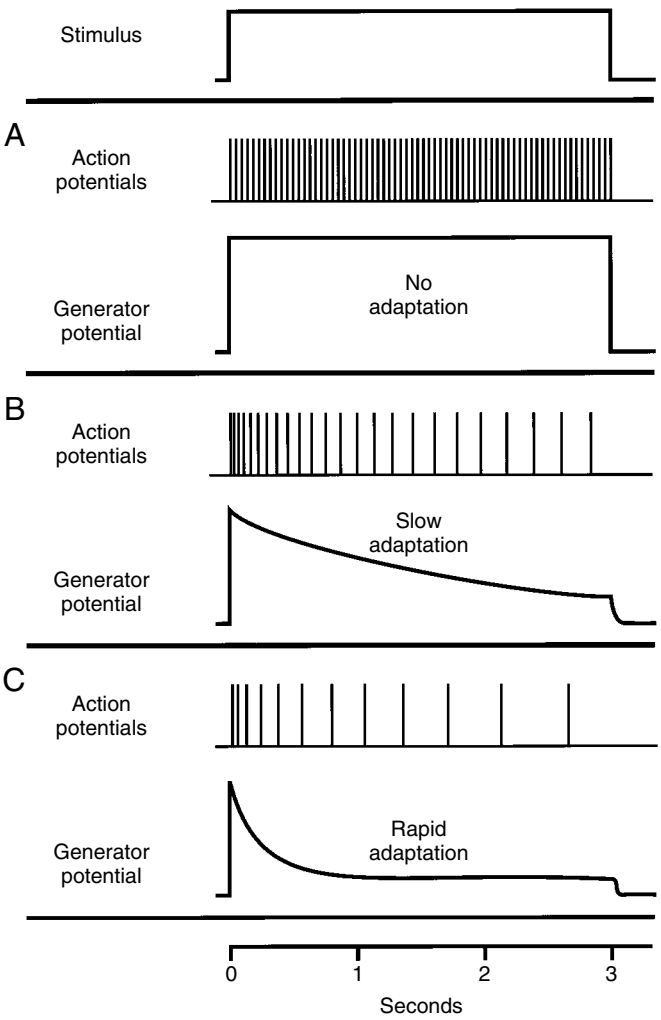


FIGURE 4.4 **Adaptation.** Adaptation in a sensory receptor is often related to a decline in the generator potential with time. **A,** The generator potential is maintained without decline, and the action potential frequency remains constant. **B,** A slow decline in the generator potential is associated with slow adaptation. **C,** In a rapidly adapting receptor, the generator potential declines rapidly.

The Perception of Sensory Information Involves Encoding and Decoding

After the acquisition of sensory stimuli, the process of perception involves the subsequent encoding and transmission of the sensory signal to the central nervous system. Further processing or decoding yields biologically useful information.

Encoding and Transmission of Sensory Information. Environmental stimuli that have been partially processed by a sensory receptor must be conveyed to the CNS in such

a way that the complete range of the intensity of the stimulus is preserved.

Compression. The first step in the encoding process is **compression.** Even when the receptor sensitivity is modified by accessory structures and adaptation, the range of input intensities is quite large, as shown in Figure 4.5. At the left is a 100-fold range in the intensity of a stimulus. At the right is an intensity scale that results from events in the sensory receptor. In most receptors, the magnitude of the generator potential is not exactly proportional to the stimulus intensity; it increases less and less as the stimulus intensity increases. The frequency of the action potentials produced in the impulse initiation region is also not proportional to the strength of the local excitatory currents; there is an upper limit to the number of action potentials per second because of the refractory period of the nerve membrane. These factors are responsible for the process of compression; changes in the intensity of a small stimulus cause a greater change in action potential frequency than the same change would cause if the stimulus intensity were high. As a result, the 100-fold variation in the stimulus is compressed into a threefold range after the receptor has processed the stimulus. Some information is necessarily lost in this process, but integrative processes in the CNS can restore the information or compensate for its absence. Physiological evidence for compression is based on the observed nonlinear (logarithmic or power function) relation between the actual intensity of a stimulus and its perceived intensity.

Information Transfer. The next step is to transfer the sensory information from the receptor to the CNS. The encoding processes in the receptors have already provided the basis for this transfer by producing a series of action potentials related to the stimulus intensity. A special process is necessary for the transfer because of the nature of the conduction of action potentials. As an action potential travels along a nerve fiber, it is sequentially recreated at a sequence of locations along the nerve. Its duration and amplitude do not change. The only information that can be conveyed by a single action potential is its presence or absence. However, relationships between and among action potentials can convey large amounts of information, and this is the system found in the sensory transmission process. This biological process can be explained by analogy to a physical system such as that used for transmission of signals in communications systems.

Figure 4.6 outlines a hypothetical **frequency-modulated** (**FM**) encoding, transmission, and reception system. An input signal provided by some physical quantity (1) is continuously measured and converted into an electrical signal (2), analogous to the generator potential, whose amplitude is proportional to the input signal. This signal then controls the frequency of a pulse generator (3), as in the impulse initiation region of a sensory nerve fiber. Like action potentials, these pulses are of a constant height and duration, and the amplitude information of the original input signal is now contained in the intervals between the pulses. The resulting signals may be sent along a transmission line (analogous to a nerve pathway) to some distant point, where they produce an electrical voltage (4) proportional to the frequency of the arriving pulses. This voltage is a replica of the input voltage (2) and is not affected by changes in the amplitude of the pulses as they travel along the transmission line. Further processing can produce a graphic record (5) of the input data. In a biological system, these latter functions are accompanied by processing and interpretation in the CNS.

The Interpretation of Sensory Information. The interpretation of encoded and transmitted information into a perception requires several other factors. For instance, the interpretation of sensory input by the CNS depends on the neural pathway it takes to the brain. All information arriving on the **optic nerves** is interpreted as light, even though the signal may have arisen as a result of pressure applied to the eyeball. The **localization** of a cutaneous sensation to a particular part of the body also depends on the particular pathway it takes to the CNS. Often a sensation (usually pain) arising in a visceral structure (e.g., heart, gallbladder) is perceived as coming from a portion of the body surface, because developmentally related nerve fibers come from these anatomically different regions and converge on the same spinal neurons. Such a sensation is called **referred pain.**

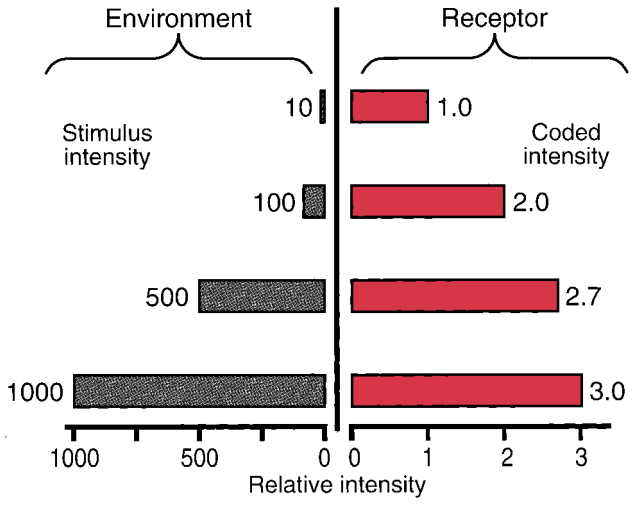


FIGURE 4.5 **Compression in sensory process.** By a variety of means, a wide range of input intensities is coded into a much narrower range of responses that can be represented by variations in action potential frequency.

SPECIFIC SENSORY RECEPTORS

The remainder of this chapter surveys specific sensory receptors, concentrating on the **special senses.** These traditionally include cutaneous sensation (touch, temperature, etc.), sight, hearing, taste, and smell.

Cutaneous Sensation Provides Information From the Body Surface

The skin is richly supplied with sensory receptors serving the modalities of touch (light and deep pressure), temperature (warm and cold), and pain, as well as the more compli-

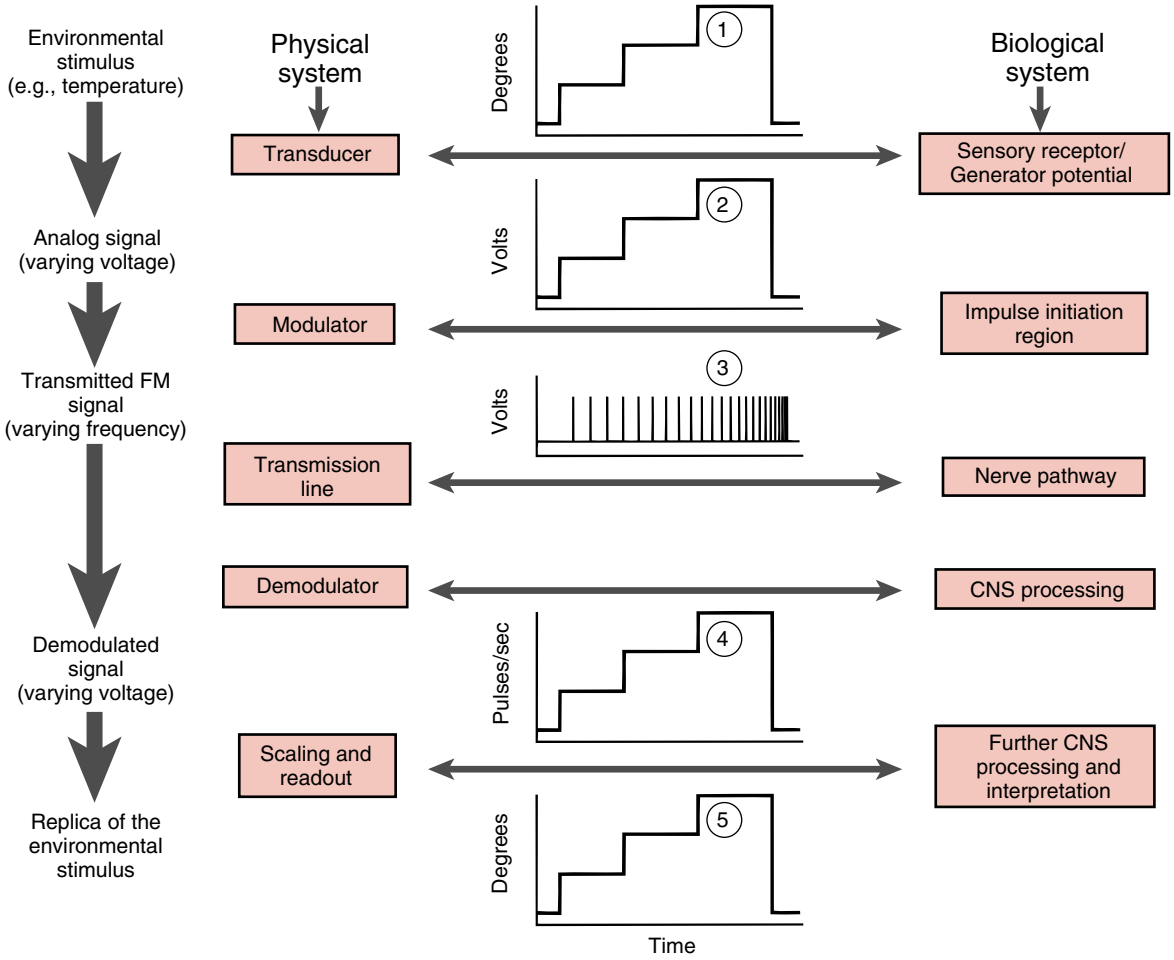


FIGURE 4.6 **The transmission of sensory information.** Because signals of varying amplitude cannot be transmitted along a nerve fiber, specific intensity information is transformed into a corresponding action potential frequency, and CNS processes decode the nerve activity into biologically useful information. The steps in the process are shown at the left, with the parts of a physical system that perform them (FM, frequency modulation). At the right are the analogous biological steps involved in the same process.

cated composite modalities of itch, tickle, wet, and so on. By using special probes that deliver highly localized stimuli of pressure, vibration, heat, or cold, the distribution of cutaneous receptors over the skin can be mapped. In general, areas of skin used in tasks requiring a high degree of spatial localization (e.g., fingertips, lips) have a high density of specific receptors, and these areas are correspondingly well represented in the somatosensory areas of the cerebral cortex (see Chapter 7).

Tactile Receptor. Several receptor types serve the sensations of touch in the skin (Fig. 4.7). In regions of hairless skin (e.g., the palm of the hand) are found Merkel's disks, Meissner's corpuscles, and pacinian corpuscles. **Merkel's disks** are intensity receptors (located in the lowest layers of the epidermis) that show slow adaptation and respond to steady pressure. **Meissner's corpuscles** adapt more rapidly to the same stimuli and serve as velocity receptors. The **Pacinian corpuscles** are very rapidly adapting (acceleration) receptors. They are most sensitive to fast-changing stimuli, such as vibration. In regions of hairy skin, small hairs serve as accessory structures for **hair-follicle receptors,** mechanoreceptors that adapt more slowly. **Ruffini endings** (located in the dermis) are also slowly adapting receptors. Merkel's disks in areas of hairy skin are grouped into **tactile disks.** Pacinian corpuscles also sense vibrations in hairy skin. Nonmyelinated nerve endings, also usually found in hairy skin, appear to have a limited tactile function and may sense pain.

Temperature Sensation. From a physical standpoint, warm and cold represent values along a temperature continuum and do not differ fundamentally except in the amount of molecular motion present. However, the familiar subjective differentiation of the temperature sense into "warm" and "cold" reflects the underlying physiology of the two populations of receptors responsible for thermal sensation.

Temperature receptors (**thermoreceptors**) appear to be naked nerve endings supplied by either thin myelinated fibers (cold receptors) or nonmyelinated fibers (warm receptors) with low conduction velocity. Cold receptors form a population with a broad response peak at about

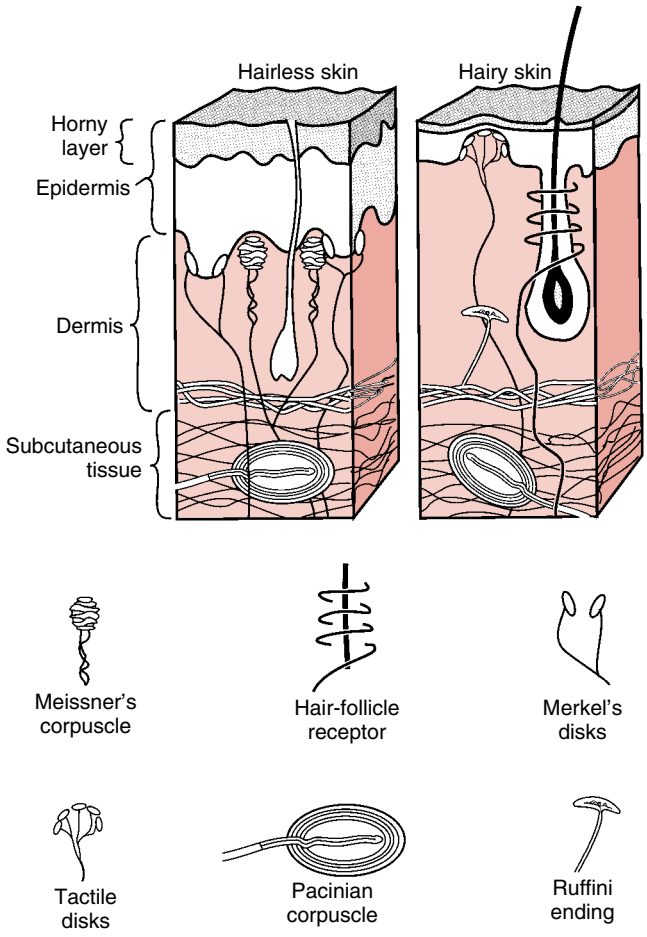


FIGURE 4.7 **Tactile receptors in the skin.** (See text for details.)

30°C; the warm receptor population has its peak at about 43°C (Fig. 4.8). Both sets of receptors share some common features:

- They are sensitive only to thermal stimulation.
- They have both a phasic response that is rapidly adapting and responds only to temperature changes (in a fashion roughly proportional to the rate of change) and a tonic (intensity) response that depends on the local temperature.

The density of temperature receptors differs at different places on the body surface. They are present in much lower numbers than cutaneous mechanoreceptors, and there are many more cold receptors than warm receptors.

The perception of temperature stimuli is closely related to the properties of the receptors. The phasic component of the response is apparent in our adaptation to sudden immersion in, for example, a warm bath. The sensation of warmth, apparent at first, soon fades away, and a less intense impression of the steady temperature may remain. Moving to somewhat cooler water produces an immediate sensation of cold that soon fades away. Over an intermediate temperature range (the "comfort zone"), there is no appreciable temperature sensation. This range is approximately 30 to 36°C for a small area of skin; the range is narrower when the whole body is exposed. Outside this range, steady temperature sensation depends on the ambient (skin) temperature. At skin temperatures lower than 17°C, **cold pain** is sensed, but this sensation arises from pain receptors, not cold receptors. At very high skin temperatures (above 45°C), there is a sensation of **paradoxical cold,** caused by activation of a part of the cold receptor population.

Temperature perception is subject to considerable processing by higher centers. While the perceived sensations reflect the activity of specific receptors, the phasic component of temperature perception may take many minutes to be completed, whereas the adaptation of the receptors is complete within seconds.

Pain. The familiar sensation of pain is not limited to cutaneous sensation; pain coming from stimulation of the body surface is called **superficial pain,** while that arising from within muscles, joints, bones, and connective tissue is called **deep pain.** These two categories comprise **somatic pain. Visceral pain** arises from internal organs and is often due to strong contractions of visceral muscle or its forcible deformation.

Pain is sensed by a population of specific receptors called nociceptors. In the skin, these are the free endings of thin myelinated and nonmyelinated fibers with characteristically low conduction velocities. They typically have a high threshold for mechanical, chemical, or thermal stimuli (or a combination) of intensity sufficient to cause tissue destruction. The skin has many more points at which pain can be elicited than it has mechanically or thermally sensitive sites. Because of the high threshold of pain receptors (compared with that of other cutaneous receptors), we are usually unaware of their existence.

Superficial pain may often have two components: an immediate, sharp, and highly localizable **initial pain**; and, after a latency of about 1 second, a longer-lasting and more diffuse **delayed pain.** These two submodalities appear to be mediated by different nerve fiber endings. In addition to

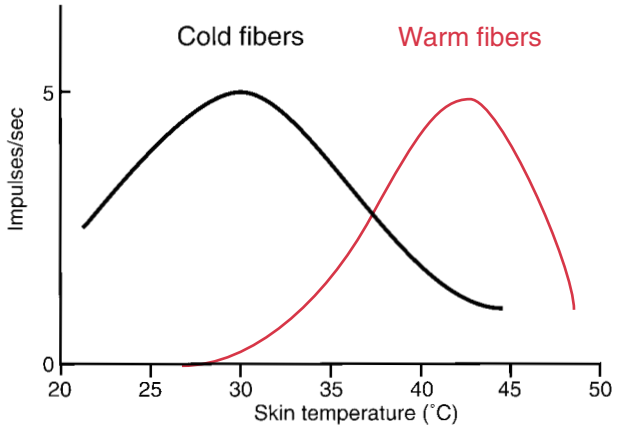


FIGURE 4.8 **Responses of cold and warm receptors in the skin.** The skin temperature was held at different values while nerve impulses were recorded from representative fibers leading from each receptor type. (Modified from Kenshalo. In: Zotterman Y. Sensory Functions of Skin in Primates. Oxford: Pergamon, 1976.)

their normally high thresholds, both cutaneous and deep pain receptors show little adaptation, a fact that is unpleasant but biologically necessary. Deep and visceral pain appear to be sensed by similar nerve endings, which may also be stimulated by local metabolic conditions, such as ischemia (lack of adequate blood flow, as may occur during the heart pain of angina pectoris).

The free nerve endings mediating pain sensation are anatomically distinct from other free nerve endings involved in the normal sensation of mechanical and thermal stimuli. The functional differences are not microscopically evident and are likely to relate to specific elements in the molecular structure of the receptor cell membrane.

The Eye Is a Sensor for Vision

The eye is an exceedingly complex sensory organ, involving both sensory elements and elaborate accessory structures that process information both before and after it is detected by the light-sensitive cells. A satisfactory understanding of vision involves a knowledge of some of the basic physics of light and its manipulation, in addition to the biological aspects of its detection.

The Properties of Light and Lenses. The adequate stimulus for human visual receptors is **light,** which may be defined as electromagnetic radiation between the wavelengths of 770 nm (red) and 380 nm (violet). The familiar colors of the spectrum all lie between these limits. A wide range of intensities, from a single photon to the direct light of the sun, exists in nature.

As with all such radiation, light rays travel in a straight line in a given medium. Light rays are **refracted** or bent as they pass between media (e.g., glass, air) that have different **refractive indices.** The amount of bending is determined by the angle at which the ray strikes the surface; if the angle is 90°, there is no bending, while successively more oblique rays are bent more sharply. A simple prism (Fig. 4.9A) can, therefore, cause a light ray to deviate from its path and travel in a new direction. An appropriately chosen pair of prisms can turn parallel rays to a common point (Fig. 4.9B). A **convex lens** may be thought of as a series of such prisms with increasingly more bending power (Fig. 4.9C, D), and such a lens, called a **converging lens** or **positive lens**, will bring an infinite number of parallel rays to a common point, called the focal point. A converging lens can form a **real image.** The distance from the lens to this point is its **focal length** (**FL**), which may be expressed in meters. A convex lens with less curvature has a longer focal length (Fig. 4.9E). Often the **diopter** (**D**), which is the inverse of the focal length (1/FL), is used to describe the power of a lens. For example, a lens with a focal length of 0.5 meter has a power of 2 D. An advantage of this system is that dioptric powers are additive; two convex lenses of 25 D each will function as a single lens with a power of 50 D when placed next to each other (Fig. 4.9F).

A **concave lens** causes parallel rays to diverge (Fig. 4.9G). Its focal length (and its power in diopters) is **negative,** and it cannot form a real image. A concave lens placed before a positive lens lengthens the focal length (Fig. 4.9H) of the lens system; the diopters of the two lenses are added algebraically. External lenses (eyeglasses or contact lenses) are used to compensate for optical defects in the eye.

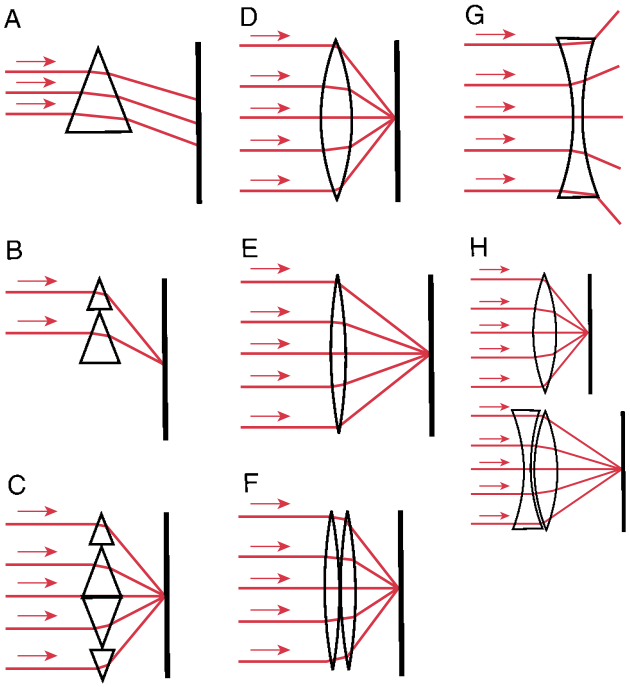


FIGURE 4.9 **How lenses control the refraction of light.** **A,** A prism bends the path of parallel rays of light. **B,** The amount of bending varies with the prism shape. **C,** A series of prisms can bring parallel rays to a point. **D,** The limiting case of this arrangement is a convex (converging) lens. **E,** Such a lens with less curvature has a longer focal length. **F,** Placing two such lenses together produces a shorter focal length. **G,** A concave (negative) lens causes rays to diverge. **H,** A negative lens can effectively increase the focal length of a positive lens.

The Structure of the Eye. The human eyeball is a roughly spherical organ, consisting of several layers and structures (Fig. 4.10). The outermost of these consists of a tough, white, connective tissue layer, the **sclera,** and a transparent layer, the **cornea.** Six **extraocular muscles** that control the direction of the eyeball insert on the sclera. The next layer is the **vascular coat;** its rear portion, the **choroid,** is pigmented and highly vascular, supplying blood to the outer portions of the retina. The front portion contains the **iris,** a circular smooth muscle structure that forms the **pupil,** the neurally controlled aperture through which light is admitted to the interior of the eye. The iris also gives the eye its characteristic color.

The transparent **lens** is located just behind the iris and is held in place by a radial arrangement of **zonule fibers,** suspensory ligaments that attach it to the **ciliary body,** which contains smooth muscle fibers that regulate the curvature of the lens and, hence, its focal length. The lens is composed of many thin, interlocking layers of fibrous protein and is highly elastic.

Between the cornea and the iris/lens is the **anterior chamber,** a space filled with a thin clear liquid called the **aqueous humor**, similar in composition to cerebrospinal

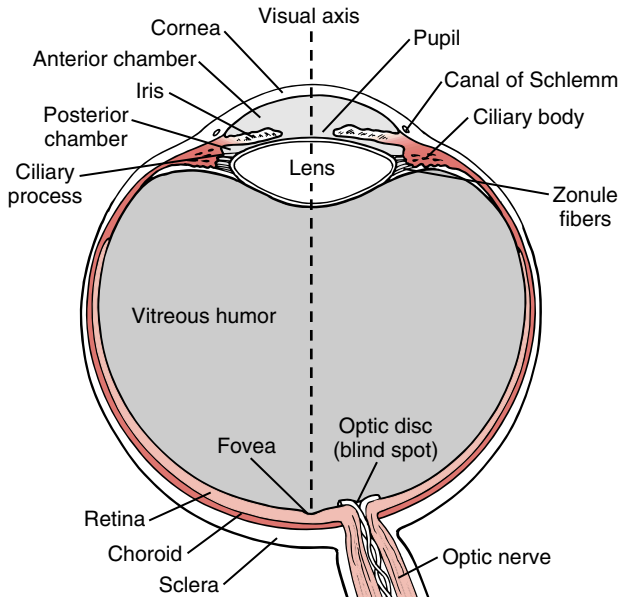


FIGURE 4.10 **The major parts of the human eye.** This is a view from above, showing the relative positions of its optical and structural parts.

fluid. This liquid is continuously secreted by the epithelium of the **ciliary processes,** located behind the iris. As the fluid accumulates, it is drained through the **canal of Schlemm** into the venous circulation. (Drainage of aqueous humor is critical. If too much pressure builds up in the anterior chamber, the internal structures are compressed and **glaucoma,** a condition that can cause blindness, results.) The **posterior chamber** lies behind the iris; along with the anterior chamber, it makes up the **anterior cavity**. The **vitreous humor** (or **vitreous body**), a clear gelatinous substance, fills the large cavity between the rear of the lens and the front surface of the retina. This substance is exchanged much more slowly than the aqueous humor.

The innermost layer of the eyeball is the **retina,** where the optical image is formed. This tissue contains the photoreceptor cells, called **rods** and **cones,** and a complex multilayered network of nerve fibers and cells that function in the early stages of image processing. The rear of the retina is supplied with blood from the choroid, while the front is supplied by the central artery and vein that enter the eyeball with the **optic nerve,** the fiber bundle that connects the retina with structures in the brain. The vascular supply to the front of the retina, which ramifies and spreads over the retinal surface, is visible through the lens and affords a direct view of the microcirculation; this window is useful for diagnostic purposes, even for conditions not directly related to ocular function.

At the optical center of the retina, where the image falls when one is looking straight ahead (i.e., along the **visual axis**), is the **macula lutea,** an area of about 1 mm^2 specialized for very sharp color vision. At the center of the macula is the **fovea centralis,** a depressed region about 0.4 mm in diameter, the **fixation point** of direct vision. Slightly off to the nasal side of the retina is the **optic disc,** where the optic nerve leaves the retina. There are no photoreceptor cells here, resulting in a **blind spot** in the field of vision. However, because the two eyes are mirror images of each other, information from the overlapping visual field of one eye "fills in" the missing part of the image from the other eye.

The Optics of the Eye. The image that falls on the retina is real and inverted, as in a camera. Neural processing restores the upright appearance of the field of view. The image itself can be modified by optical adjustments made by the lens and the iris. Most of the refractive power (about 43 D) is provided by the curvature of the cornea, with the lens providing an additional 13 to 26 D, depending on the focal distance. The muscle of the ciliary body has primarily a parasympathetic innervation, although some sympathetic innervation is present. When it is fully relaxed, the lens is at its flattest and the eye is focused at infinity (actually, at anything more than 6 meters away) (Fig. 4.11A). When the ciliary muscle is fully contracted, the lens is at its most curved and the eye is focused at its nearest point of distinct vision (Fig. 4.11B). This adjustment of the eye for close vision is called **accommodation.** The **near point** of vision for the eye of a young adult is about 10 cm. With age, the lens loses its elasticity and the near point of vision moves farther away, becoming approximately 80 cm at age 60. This condition is called **presbyopia;** supplemental refractive power,

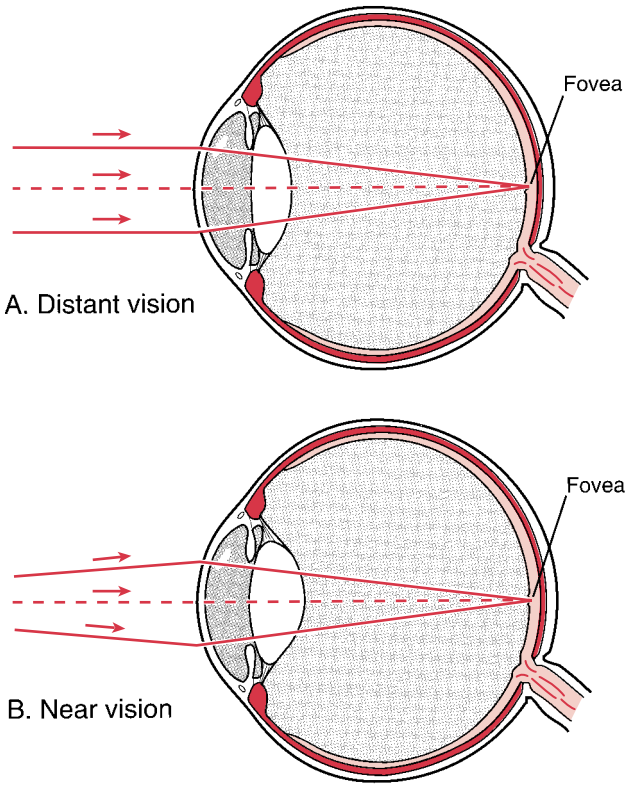


FIGURE 4.11 **The eye as an optical device.** During fixation the center of the image falls on the fovea. **A,** With the lens flattened, parallel rays from a distant object are brought to a sharp focus. **B,** Lens curvature increases with accommodation, and rays from a nearby object are focused.

in the form of external lenses (reading glasses), is required for distinct near vision.

Errors of refraction are common (Fig. 4.12). They can be corrected with external lenses (eyeglasses or contact lenses). Farsightedness or **hyperopia** is caused by an eyeball that is physically too short to focus on distant objects. The natural accommodation mechanism may compensate for distance vision, but the near point will still be too far away; the use of a positive (converging) lens corrects this error. If the eyeball is too long, nearsightedness or **myopia** results. In effect, the converging power of the eye is too great; close vision is clear, but the eye cannot focus on distant objects. A negative (diverging) lens corrects this defect. If the curvature of the cornea is not symmetric, **astigmatism** results. Objects with different orientations in the field of view will have different focal positions. Vertical lines may appear sharp, while horizontal structures are blurred. This condition is corrected with the use of a **cylindrical lens,** which has different radii of curvature at the proper orientations along its surfaces. Normal vision (i.e., the absence of any refractive errors) is termed **emmetropia** (literally, "eye in proper measure").

Normally the lens is completely transparent to visible light. Especially in older adults, there may be a progressive increase in its opacity, to the extent that vision is obscured. This condition, called a **cataract,** is treated by surgical removal of the defective lens. An artificial lens may be implanted in its place, or eyeglasses may be used to replace the refractive power of the lens.

The iris, which has both sympathetic and parasympathetic innervation, controls the diameter of the pupil. It is capable of a 30-fold change in area and in the amount of light admitted to the eye. This change is under complex reflex control, and bright light entering just one eye will cause the appropriate constriction response in both eyes. As with a camera, when the pupil is constricted, less light enters, but the image is focused more sharply because the more poorly focused peripheral rays are cut off.

Eye Movements. The extraocular muscles move the eyes. These six muscles, which originate on the bone of the **orbit** (the eye socket) and insert on the sclera, are arranged in three sets of antagonistic pairs. They are under visually compensated feedback control and produce several types of movement:

- Continuous activation of a small number of motor units produces a small tremor at a rate of 30 to 80 cycles per second. This movement and a slow drift cause the image to be in constant motion on the retina, a necessary condition for proper visual function.
- Larger movements include rapid flicks, called **saccades,** which suddenly change the orientation of the eyeball, and large, slow movements, used in following moving objects.

Organized movements of the eyes include:

- **Fixation,** the training of the eyes on a stationary object
- **Tracking movements,** used to follow the course of a moving target

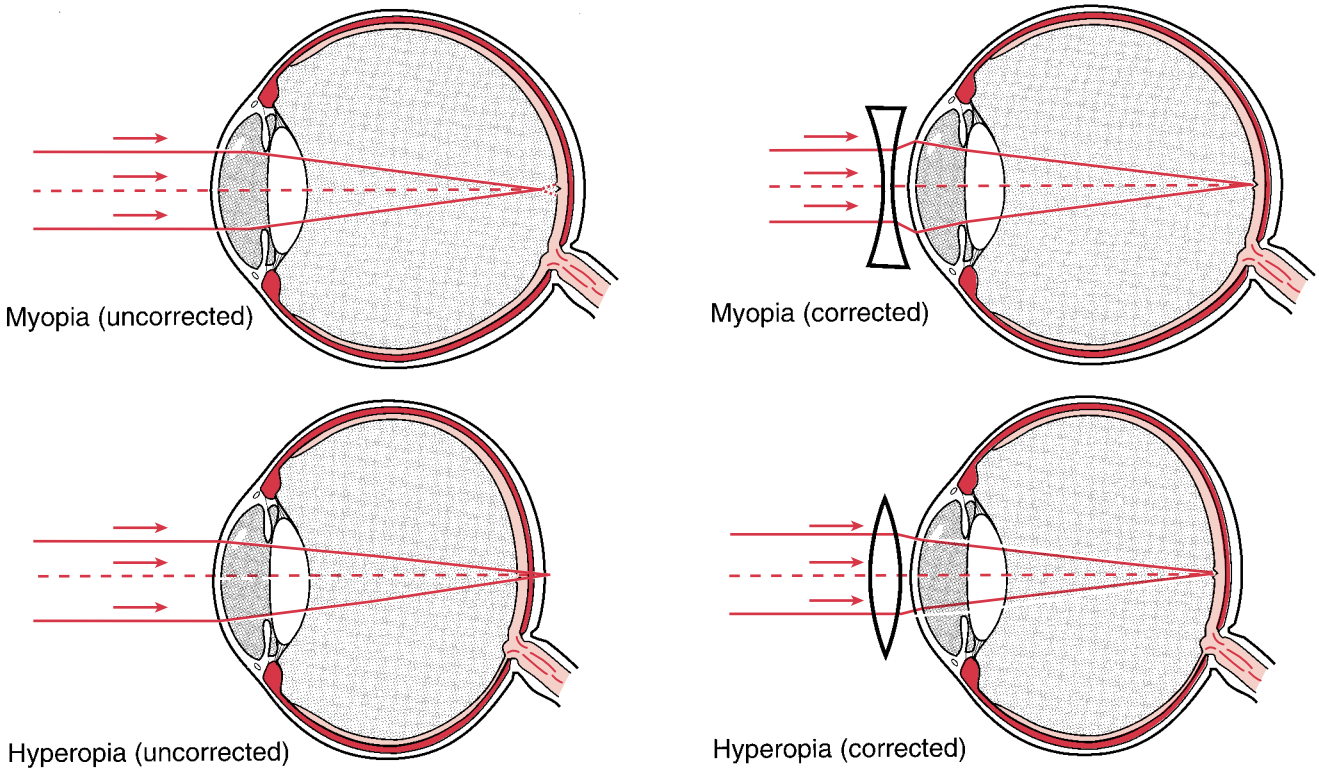


FIGURE 4.12 **The use of external lenses to correct refractive errors.** The external optical corrections change the effective focal length of the natural optical components.

- **Convergence** adjustments, in which both eyes turn inward to fix on near objects
- **Nystagmus,** a series of slow and saccadic movements (part of a vestibular reflex) that serves to keep the retinal image steady during rotation of the head.

Because the eyes are separated by some distance, each receives a slightly different image of the same object. This property, **binocular vision,** along with information about the different positions of the two eyes, allows **stereoscopic** vision and its associated **depth perception,** abilities that are largely lost in the case of blindness in one eye. Many abnormalities of eye movement are types of **strabismus** ("squinting"), in which the two eyes do not work together properly. Other defects include **diplopia** (double vision), when the convergence mechanisms are impaired, and **amblyopia,** when one eye assumes improper dominance over the other. Failure to correct this latter condition can lead to loss of visual function in the subordinate eye.

The Retina and Its Photoreceptors. The retina is a multilayered structure containing the photoreceptor cells and a complex web of several types of nerve cells (Fig. 4.13). There are 10 layers in the retina, but this discussion employs a simpler four-layer scheme: pigment epithelium, photoreceptor layer, neural network layer, and ganglion cell layer. These four layers are discussed in order, beginning with the deepest layer (pigment epithelium) and moving toward the layer nearest to the inner surface of the eye (ganglion cell layer). Note that this is the direction in which visual signal processing takes place, but it is opposite to the path taken by the light entering the retina.

Pigment Epithelium. The **pigment epithelium** (Fig. 4.13B) consists of cells with high **melanin** content. This opaque material, which also extends between portions of individual rods and cones, prevents the scattering of stray light, thereby greatly sharpening the resolving power of the retina. Its presence ensures that a tiny spot of light (or a tiny portion of an image) will excite only those receptors on which it falls directly. People with albinism lack this pigment and have blurred vision that cannot be corrected effectively with external lenses. The pigment epithelial cells also phagocytose bits of cell membrane that are constantly shed from the outer segments of the photoreceptors.

Photoreceptor Layer. In the photoreceptor layer (Fig. 4.13C), the rods and cones are packed tightly side-by-side, with a density of many thousands per square millimeter, depending on the region of the retina. Each eye contains about 125 million rods and 5.5 million cones. Because of the eye's mode of embryologic development, the photoreceptor cells occupy a deep layer of the retina, and light must pass through several overlying layers to reach them. The photoreceptors are divided into two classes. The cones are responsible for **photopic** (daytime) **vision,** which is in color (chromatic), and the rods are responsible for **scotopic** (nighttime) **vision,** which is not in color. Their functions are basically similar, although they have important structural and biochemical differences.

Cones have an **outer segment** that tapers to a point (Fig. 4.14). Three different photopigments are associated with cone cells. The pigments differ in the wavelength of light that optimally excites them. The peak spectral sensitivity for the **red-sensitive pigment** is 560 nm; for the **green-sensitive pigment,** it is about 530 nm; and for the **blue-sensitive pigment**, it is about 420 nm. The corresponding photoreceptors are called red, green, and blue cones, respectively. At wavelengths away from the optimum, the pigments still absorb light but with reduced sensitivity. Because of the interplay between light intensity and wavelength, a retina with only one class of cones would not be able to detect colors unambiguously. The presence of two of the three pigments in each cone removes this uncertainty. Colorblind individuals, who have a genetic lack of one or more of the pigments or lack an associated transduction mechanism, cannot distinguish between the af-

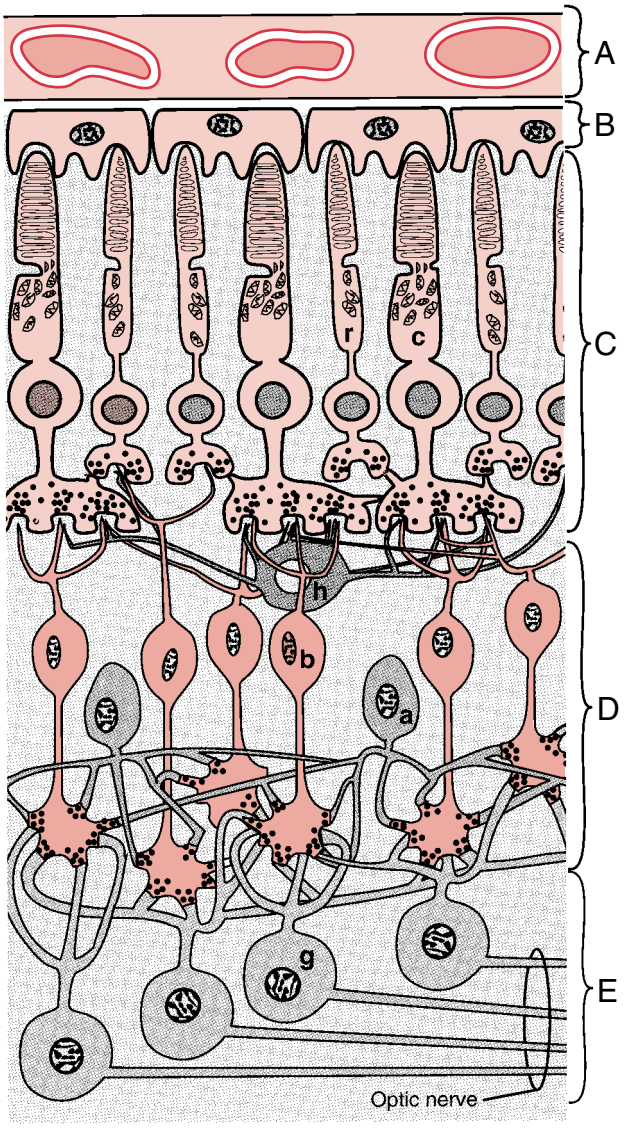


FIGURE 4.13 **Organization of the human retina.** A, Choroid. B, Pigment epithelium. C, Photoreceptor layer. D, Neural network layer. E, Ganglion cell layer. r, rod; c, cone; h, horizontal cell; b, bipolar cell; a, amacrine cell; g, ganglion cell. (See text for details.) (Modified from Dowling JE, Boycott BB. Organization of the primate retina: Electron microscopy. Proc Roy Soc Lond 1966:166:80–111.

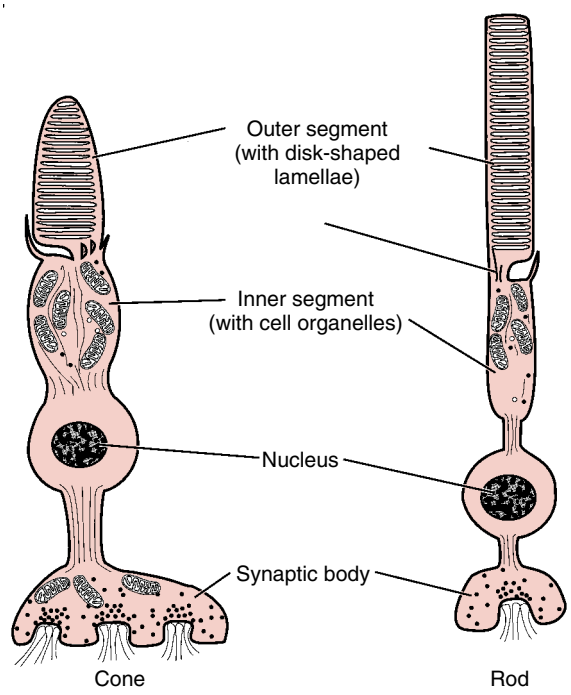


FIGURE 4.14 **Photoreceptors of the human retina.** Cone and rod receptors are compared. (Modified from Davson H, ed. The Eye: Visual Function in Man. 2nd Ed. New York: Academic, 1976.)

fected colors. Loss of a single color system produces **dichromatic vision** and lack of two of the systems causes **monochromatic vision**. If all three are lacking, vision is monochromatic and depends only on the rods.

A **rod cell** is long, slender, and cylindrical and is larger than a cone cell (Fig. 4.14). Its outer segment contains numerous photoreceptor disks composed of cellular membrane in which the molecules of the photopigment **rhodopsin** are embedded. The lamellae near the tip are regularly shed and replaced with new membrane synthesized at the opposite end of the outer segment. The **inner segment,** connected to the outer segment by a modified **cilium,** contains the cell nucleus, many mitochondria that provide energy for the phototransduction process, and other cell organelles. At the base of the cell is a **synaptic body** that makes contact with one or more bipolar nerve cells and liberates a transmitter substance in response to changing light levels.

The visual pigments of the photoreceptor cells convert light to a nerve signal. This process is best understood as it occurs in rod cells. In the dark, the pigment rhodopsin (or visual purple) consists of a light-trapping **chromophore** called **scotopsin** that is chemically conjugated with **11-cis-retinal**, the aldehyde form of vitamin A_1. When struck by light, rhodopsin undergoes a series of rapid chemical transitions, with the final intermediate form **metarhodopsin II** providing the critical link between this reaction series and the electrical response. The end-products of the light-induced transformation are the original scotopsin and an all-*trans* form of retinal, now dissociated from each other. Under conditions of both light and dark, the all-*trans* form of retinal is isomerized back to the 11-*cis* form, and the rhodopsin is reconstituted. All of these reactions take place in the highly folded membranes comprising the outer segment of the rod cell.

The biochemical process of visual signal transduction is shown in Figure 4.15. The coupling of the light-induced reactions and the electrical response involves the activation of **transducin,** a G protein; the associated exchange of GTP for GDP activates a **phosphodiesterase**. This, in turn, catalyzes the breakdown of cyclic GMP (cGMP) to 5′-GMP. When cellular cGMP levels are high (as in the dark), membrane sodium channels are kept open, and the cell is relatively depolarized. Under these conditions, there is a tonic release of neurotransmitter from the synaptic body of the rod cell. A decrease in the level of cGMP as a result of light-induced reactions causes the cell to close its sodium channels and hyperpolarize, thus, reducing the release of neurotransmitter; this change is the signal that is further processed by the nerve cells of the retina to form the final response in the optic nerve. An active sodium pump main-

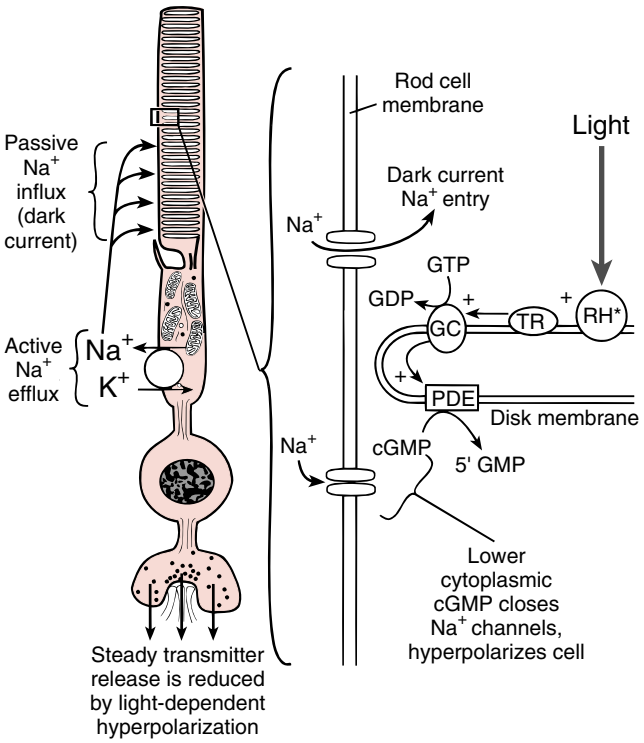


FIGURE 4.15 **The biochemical process of visual signal transduction.** Left: An active Na^+/K^+ pump maintains the ionic balance of a rod cell, while Na^+ enters passively through channels in the plasma membrane, causing a maintained depolarization and a dark current under conditions of no light. Right: The amplifying cascade of reactions (which take place in the disk membrane of a photoreceptor) allows a single activated rhodopsin molecule to control the hydrolysis of 500,000 cGMP molecules. (See text for details of the reaction sequence.) In the presence of light, the reactions lead to a depletion of cGMP, resulting in the closing of cell membrane Na^+ channels and the production of a hyperpolarizing generator potential. The release of neurotransmitter decreases during stimulation by light. RH*, activated rhodopsin; TR, transducin; GC, guanylyl cyclase; PDE, phosphodiesterase.

tains the cellular concentration at proper levels. A large amplification of the light response takes place during the coupling steps; one activated rhodopsin molecule will activate approximately 500 transducins, each of which activates the hydrolysis of several thousand cGMP molecules. Under proper conditions, a rod cell can respond to a single photon striking the outer segment. The processes in cone cells are similar, although there are three different opsins (with different spectral sensitivities) and the specific transduction mechanism is also different. The overall sensitivity of the transduction process is also lower.

In the light, much rhodopsin is in its unconjugated form, and the sensitivity of the rod cell is relatively low. During the process of **dark adaptation,** which takes about 40 minutes to complete, the stores of rhodopsin are gradually built up, with a consequent increase in sensitivity (by as much as 25,000 times). Cone cells adapt more quickly than rods, but their final sensitivity is much lower. The reverse process, **light adaptation,** takes about 5 minutes.

Neural Network Layer. **Bipolar cells, horizontal cells,** and **amacrine cells** comprise the **neural network layer**. These cells together are responsible for considerable initial processing of visual information. Because the distances between neurons here are so small, most cellular communication involves the **electrotonic spread** of cell potentials, rather than propagated action potentials. Light stimulation of the photoreceptors produces hyperpolarization that is transmitted to the bipolar cells. Some of these cells respond with a depolarization that is excitatory to the ganglion cells, whereas other cells respond with a hyperpolarization that is inhibitory. The horizontal cells also receive input from rod and cone cells but spread information laterally, causing inhibition of the bipolar cells on which they synapse. Another important aspect of retinal processing is **lateral inhibition.** A strongly stimulated receptor cell can, via lateral inhibitory pathways, inhibit the response of neighboring cells that are less well-illuminated. This has the effect of increasing the apparent contrast at the edge of an image. Amacrine cells also send information laterally but synapse on ganglion cells.

Ganglion Cell Layer. In the **ganglion cell layer** (Fig. 4.13E) the results of retinal processing are finally integrated by the **ganglion cells,** whose axons form the **optic nerve.** These cells are tonically active, sending action potentials into the optic nerve at an average rate of five per second, even when unstimulated. Input from other cells converging on the ganglion cells modifies this rate up or down.

Many kinds of information regarding color, brightness, contrast, and so on are passed along the optic nerve. The output of individual photoreceptor cells is **convergent** on the ganglion cells. In keeping with their role in visual acuity, relatively few cone cells converge on a ganglion cell, especially in the fovea, where the ratio is nearly 1:1. Rod cells, however, are highly convergent, with as many as 300 rods converging on a single ganglion cell. While this mechanism reduces the sharpness of an image, it allows for a great increase in light sensitivity.

Central Projections of the Retina. The optic nerves, each carrying about 1 million fibers from each retina, enter the rear of the orbit and pass to the underside of the brain to the **optic chiasma,** where about half the fibers from each eye "cross over" to the other side. Fibers from the temporal side of the retina do not cross the midline, but travel in the **optic tract** on the same side of the brain. Fibers originating from the nasal side of the retina cross the optic chiasma and travel in the optic tract to the opposite side of the brain. Hence, information from right and left visual fields is transmitted to opposite sides of the brain. The divided output goes through the optic tract to the paired **lateral geniculate bodies** (part of the thalamus) and then via the **geniculocalcarine tract** (or **optic radiation**) to the **visual cortex** in the **occipital lobe** of the brain (Fig. 4.16). Specific portions of each retina are mapped to specific areas of the cortex; the foveal and macular regions have the greatest representation, while the peripheral areas have the least. Mechanisms in the visual cortex detect and integrate visual information, such as shape, contrast, line, and intensity, into a coherent visual perception.

Information from the optic nerves is also sent to the **suprachiasmatic nucleus** of the hypothalamus, where it participates in the regulation of circadian rhythms; the **pretectal nuclei,** concerned with the control of visual fixation and pupillary reflexes; and the **superior colliculus,** which

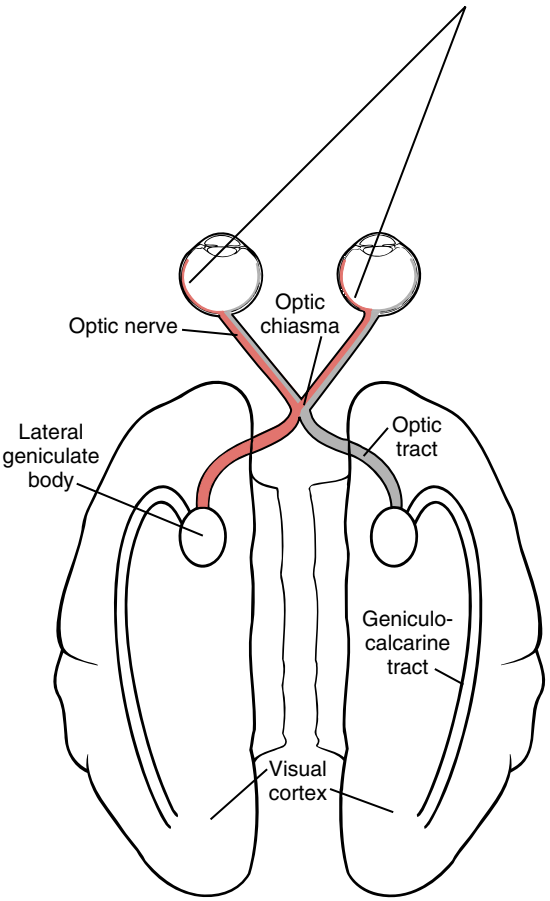


FIGURE 4.16 **The CNS pathway for visual information.** Fibers from the right visual field will stimulate the left half of each retina, and nerve impulses will be transmitted to the left hemisphere.

coordinates simultaneous bilateral eye movements, such as tracking and convergence.

The Ear Is Sensor for Hearing and Equilibrium

The human ear has a degree of complexity probably as great as that of the eye. Understanding our sense of hearing requires familiarity with the physics of sound and its interactions with the biological structures involved in hearing.

The Nature of Sound. **Sound waves** are mechanical disturbances that travel through an elastic medium (usually air or water). A sound wave is produced by a mechanically vibrating structure that alternately compresses and rarefies the air (or water) in contact with it. For example, as a loudspeaker cone moves forward, air molecules in its path are forced closer together; this is called **compression** or **condensation.** As the cone moves back, the space between the disturbed molecules is increased; this is known as **rarefaction**. The compression (or rarefaction) of air molecules in one region causes a similar compression in adjacent regions. Continuation of this process causes the disturbance (the sound wave) to spread away from the source.

The speed at which the sound wave travels is determined by the elasticity of the air (the tendency of the molecules to spring back to their original positions). Assuming the sound source is moving back and forth at a constant rate of alternation (i.e., at a constant **frequency**), a propagated compression wave will pass a given point once for every cycle of the source. Because the propagation speed is constant in a given medium, the compression waves are closer together at higher frequencies; that is, more of them pass the given point every second.

The distance between the compression peaks is called the **wavelength** of the sound, and it is inversely related to the frequency. A tone of 1,000 cycles per second, traveling through the air, has a wavelength of approximately 34 cm, while a tone of 2,000 cycles per second has a wavelength of 17 cm. Both waves, however, travel at the same speed through the air. Because the elastic forces in water are greater than those in air, the speed of sound in water is about 4 times as great, and the wavelength is correspondingly increased. Since the wavelength depends on the elasticity of the medium (which varies according to temperature and pressure), it is more convenient to identify sound waves by their frequency. Sound frequency is usually expressed in units of Hertz (Hz or cycles per second).

Another fundamental characteristic of a sound wave is its intensity or amplitude. This may be thought of as the relative amount of compression or rarefaction present as the wave is produced and propagated; it is related to the amount of energy contained in the wave. Usually the intensity is expressed in terms of **sound pressure,** the pressure the compressions and rarefactions exert on a surface of known area (expressed in dynes per square centimeter). Because the human ear is sensitive to sounds over a millionfold range of sound pressure levels, it is convenient to express the intensity of sound as the logarithm of a ratio referenced to the **absolute threshold of hearing** for a tone of 1,000 Hz. This reference level has a value of 0.0002 dyne/cm^2, and the scale for the measurements is the **decibel** (**dB**) scale. In the expression

$$dB = 20 \log (P/P_{ref}), \quad (1)$$

the sound pressure (P) is referred to the absolute reference pressure (P_{ref}). For a sound that is 10 times greater than the reference, the expression becomes

$$dB = 20 \log (0.002 / 0.0002) = 20. \quad (2)$$

Thus, any two sounds having a tenfold difference in intensity have a decibel difference of 20; a 100-fold difference would mean a 40 dB difference and a 1,000-fold difference would be 60 dB. Usually the reference value is assumed to be constant and standard, and it is not expressed when measurements are reported.

Table 4.1 lists the sound pressure levels and the decibel levels for some common sounds. The total range of 140 dB shown in the table expresses a relative range of 10 millionfold. Adaptation and compression processes in the human auditory system allow encoding of most of this wide range into biologically useful information.

Sinusoidal sound waves contain all of their energy at one frequency and are perceived as **pure tones**. Complex sound waves, such as those in speech or music, consist of the addition of several simpler waveforms of different frequencies and amplitudes. The human ear is capable of hearing sounds over the range of 20 to 16,000 Hz, although the upper limit decreases with age. Auditory sensitivity varies with the frequency of the sound; we hear sounds most readily in the range of 1,000 to 4,000 Hz and at a sound pressure level of around 60 dB. Not surprisingly, this is the frequency and intensity range of human vocalization. The ear's sensitivity is also affected by **masking:** In the presence of background sounds or noise, the auditory threshold for a given tone rises. This may be due to refractoriness induced by the masking sound, which would reduce the number of available receptor cells.

The Outer Ear. An overall view of the human ear is shown in Figure 4.17. The **pinna,** the visible portion of the outer ear, is not critical to hearing in humans, although it does

TABLE 4.1 The Relative Pressures of Some Common Sounds

Pressure (dynes/cm^2)	Sound Pressure Level (dB)	Sound Source	Relative Pressure
0.0002	0	Absolute threshold	1
0.002	+ 20	Faint whisper	10
0.02	+ 40	Quiet office	100
0.2	+ 60	Conversation	1,00
2	+ 80	City bus	10,000
20	+100	Subway train	100,000
200	+120	Loud thunder	1,000,000
2,000	+140	Pain and damage	10,000,000

Modified from Gulick WL, Gescheider GA, Frisina RD. Hearing: Physiological Acoustics, Neural Coding, and Psychoacoustics. New York: Oxford University Press, 1989, Table 2.2, p. 51.

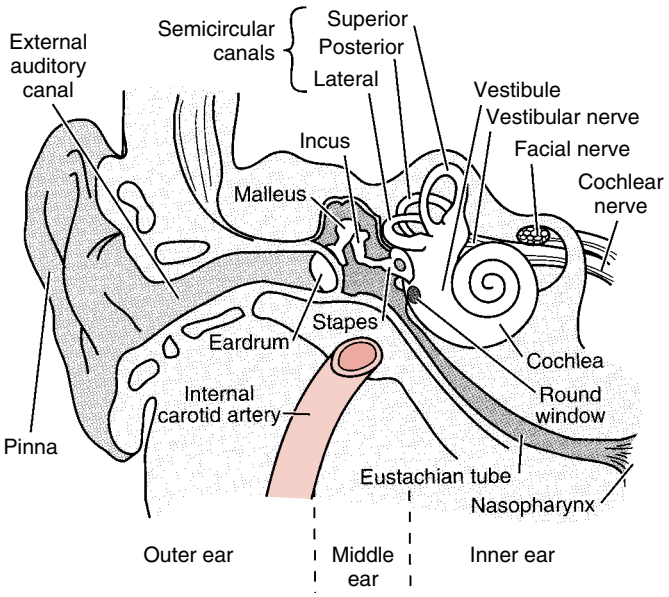


FIGURE 4.17 **The overall structure of the human ear.** The structures of the middle and inner ear are encased in the temporal bone of the skull.

slightly emphasize frequencies in the range of 1,500 to 7,000 Hz and aids in the localization of sources of sound. The **external auditory canal** extends inward through the **temporal bone.** Wax-secreting glands line the canal, and its inner end is sealed by the **tympanic membrane** or **eardrum,** a thin, oval, slightly conical, flexible membrane that is anchored around its edges to a ring of bone. An incoming pressure wave traveling down the external auditory canal causes the eardrum to vibrate back and forth in step with the compressions and rarefactions of the sound wave. This is the first mechanical step in the transduction of sound. The overall acoustic effect of the outer ear structures is to produce an amplification of 10 to 15 dB in the frequency range broadly centered around 3,000 Hz.

The Middle Ear. The next portion of the auditory system is an air-filled cavity (volume about 2 mL) in the mastoid region of the temporal bone. The middle ear is connected to the pharynx by the **eustachian tube.** The tube opens briefly during swallowing, allowing equalization of the pressures on either side of the eardrum. During rapid external pressure changes (such as in an elevator ride or during takeoff or descent in an airplane), the unequal forces displace the eardrum; such physical deformation may cause discomfort or pain and, by restricting the motion of the tympanic membrane, may impair hearing. Blockages of the eustachian tube or fluid accumulation in the middle ear (as a result of an infection) can also lead to difficulties with hearing.

Bridging the gap between the tympanic membrane and the inner ear is a chain of three very small bones, the **ossicles** (Fig. 4.18). The **malleus (hammer)** is attached to the eardrum in such a way that the back-and-forth movement of the eardrum causes a rocking movement of the malleus. The **incus (anvil)** connects the head of the malleus to the third bone, the **stapes (stirrup).** This last bone, through its oval **footplate,** connects to the **oval window** of the inner ear and is anchored there by an annular ligament.

Four separate **suspensory ligaments** hold the ossicles in position in the middle ear cavity. The superior and lateral ligaments lie roughly in the plane of the ossicular chain and anchor the head and shaft of the malleus. The anterior ligament attaches the head of the malleus to the anterior wall of the middle ear cavity, and the posterior ligament runs from the head of the incus to the posterior wall of the cavity. The suspensory ligaments allow the ossicles sufficient freedom to function as a lever system to transmit the vibrations of the tympanic membrane to the oval window. This mechanism is especially important because, although the eardrum is suspended in air, the oval window seals off a fluid-filled chamber. Transmission of sound from air to liquid is inefficient; if sound waves were to strike the oval window directly, 99.9% of the energy would be reflected away and lost.

Two mechanisms work to compensate for this loss. Although it varies with frequency, the ossicular chain has a lever ratio of about 1.3:1, producing a slight gain in force. In addition, the relatively large area of the tympanic membrane is coupled to the smaller area of the oval window (approximately a 17:1 ratio). These conditions result in a pressure gain of around 25 dB, largely compensating for the potential loss. Although the efficiency depends on the frequency, approximately 60% of the sound energy that strikes the eardrum is transmitted to the oval window.

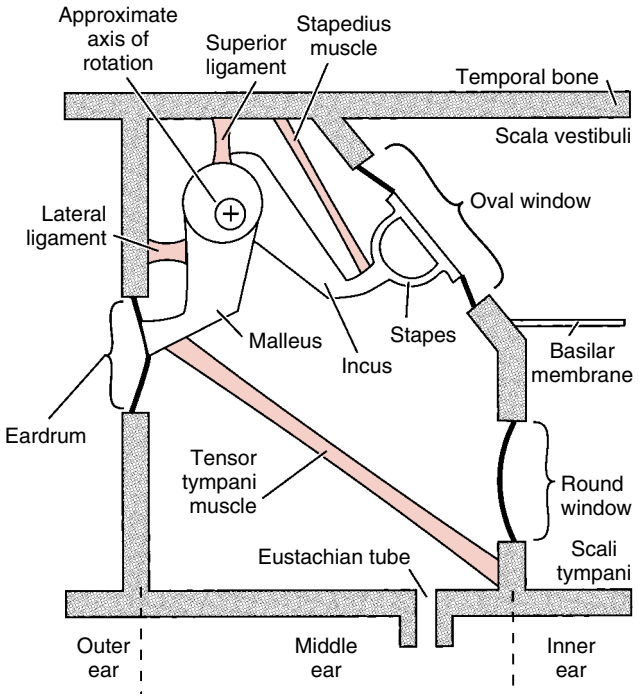


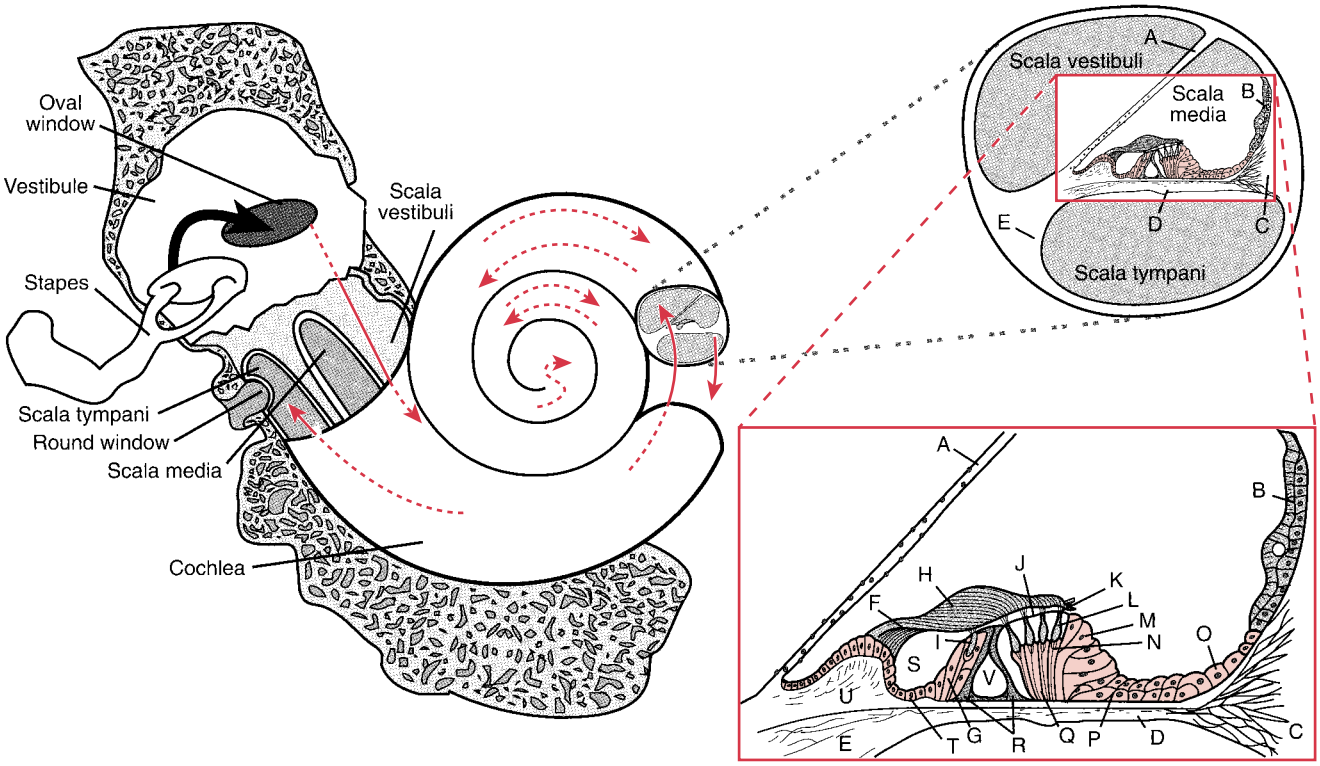
FIGURE 4.18 **A model of the middle ear.** Vibrations from the eardrum are transmitted by the lever system formed by the ossicular chain to the oval window of the scala vestibuli. The anterior and posterior ligaments, part of the suspensory system for the ossicles, are not shown. The combination of the four suspensory ligaments produces a virtual pivot point (marked by a cross); its position varies with the frequency and intensity of the sound. The stapedius and tensor tympani muscles modify the lever function of the ossicular chain.

Sound transmission through the middle ear is also affected by the action of two small muscles that attach to the ossicular chain and help hold the bones in position and modify their function (see Fig. 4.18). The **tensor tympani muscle** inserts on the malleus (near the center of the eardrum), passes diagonally through the middle ear cavity, and enters the **tensor canal,** in which it is anchored. Contraction of this muscle limits the vibration amplitude of the eardrum and makes sound transmission less efficient. The **stapedius muscle** attaches to the stapes near its connection to the incus and runs posteriorly to the mastoid bone. Its contraction changes the axis of oscillation of the ossicular chain and causes dissipation of excess movement before it reaches the oval window. These muscles are activated by a reflex (simultaneously in both ears) in response to moderate and loud sounds; they act to reduce the transmission of sound to the inner ear and, thus, to protect its delicate structures. Because this **acoustic reflex** requires up to 150 msec to operate (depending on the loudness of the stimulus), it cannot provide protection from sharp or sudden bursts of sound.

The process of sound transmission can bypass the ossicular chain entirely. If a vibrating object, such as a tuning fork, is placed against a bone of the skull (typically the mastoid), the vibrations are transmitted mechanically to the fluid of the inner ear, where the normal processes act to complete the hearing process. Bone conduction is used as a means of diagnosing hearing disorders that may arise because of lesions in the ossicular chain. Some hearing aids employ bone conduction to overcome such deficits.

The Inner Ear. The actual process of sound transduction takes place in the inner ear, where the sensory receptors and their neural connections are located. The relationship between its structure and function is a close and complex one. The following discussion includes the most significant aspects of this relationship.

Overall Structure. The auditory structures are located in the **cochlea** (Fig. 4.19), part of a cavity in the temporal bone called the bony labyrinth. The cochlea (meaning "snail shell") is a fluid-filled spiral tube that arises from a



A Reissner's membrane
B Stria vascularis
C Spiral ligament
D Basilar membrane
E Osseous spiral lamina
F Hensen's stripe
G Inner phalangeal cells
H Tectorial membrane
I Inner hair cell
J Reticular lamina
K Stereocilia
L Outer hair cells
M Cells of Hensen
N Arborized cuticular rods
O Cells of Claudius
P Cells of Böttcher
Q Deiters' cells
R Arch of Corti
S Internal sulcus
T Inner sulcus cells
U Spiral limbus
V Tunnel

FIGURE 4.19 **The cochlea and the organ of Corti.** Left: An overview of the membranous labyrinth of the cochlea. Upper right: A cross section through one turn of the cochlea, showing the canals and membranes that make up the structures involved in the final processes of auditory sensation. Lower right: An enlargement of a cross section of the organ of Corti, showing the relationships among the hair cells and the membranes. (Modified from Gulick WL, Gescheider GA, Frisina RD. Hearing: Physiological Acoustics, Neural Coding, and Psychoacoustics. New York: Oxford University Press, 1989.)

cavity called the **vestibule,** with which the organs of balance also communicate. In the human ear, the cochlea is about 35 mm long and makes about $2\frac{3}{4}$ turns. Together with the vestibule it contains a total fluid volume of 0.1 mL. It is partitioned longitudinally into three divisions (canals) called the **scala vestibuli** (into which the oval window opens), the **scala tympani** (sealed off from the middle ear by the **round window**), and the **scala media** (in which the sensory cells are located). Arising from the bony center axis of the spiral (the **modiolus**) is a winding shelf called the **osseous spiral lamina;** opposite it on the outer wall of the spiral is the **spiral ligament,** and connecting these two structures is a highly flexible connective tissue sheet, the **basilar membrane,** that runs for almost the entire length of the cochlea. The basilar membrane separates the scala tympani (below) from the scala media (above). The **hair cells,** which are the actual sensory receptors, are located on the upper surface of the basilar membrane. They are called hair cells because each has a bundle of hair-like **cilia** at the end that projects away from the basilar membrane.

Reissner's membrane, a delicate sheet only two cell layers thick, divides the scala media (below) from the scala vestibuli (above) (see Fig. 4.19). The scala vestibuli communicates with the scala tympani at the apical (distal) end of the cochlea via the **helicotrema,** a small opening where a portion of the basilar membrane is missing. The scala vestibuli and scala tympani are filled with **perilymph,** a fluid high in sodium and low in potassium. The scala media contains **endolymph,** a fluid high in potassium and low in sodium. The endolymph is secreted by the **stria vascularis,** a layer of fibrous vascular tissue along the outer wall of the scala media. Because the cochlea is filled with incompressible fluid and is encased in hard bone, pressure changes caused by the in-and-out motion at the oval window (driven by the stapes) are relieved by an out-and-in motion of the flexible round window membrane.

Sensory Structures. The **organ of Corti** is formed by structures located on the upper surface of the basilar membrane and runs the length of the scala media (see Fig. 4.19). It contains one row of some 3,000 **inner hair cells;** the **arch of Corti** and other specialized supporting cells separate the inner hair cells from the three or four rows of **outer hair cells** (about 12,000) located on the stria vascularis side. The rows of inner and outer hair cells are inclined slightly toward each other and covered by the **tectorial membrane,** which arises from the **spiral limbus,** a projection on the upper surface of the osseous spiral lamina.

Nerve fibers from cell bodies located in the **spiral ganglia** form **radial bundles** on their way to synapse with the inner hair cells. Each nerve fiber makes synaptic connection with only one hair cell, but each hair cell is served by 8 to 30 fibers. While the inner hair cells comprise only 20% of the hair cell population, they receive 95% of the afferent fibers. In contrast, many outer hair cells are each served by a single external spiral nerve fiber. The collected afferent fibers are bundled in the **cochlear nerve,** which exits the inner ear via the **internal auditory meatus.** Some efferent fibers also innervate the cochlea. They may serve to enhance pitch discrimination and the ability to distinguish sounds in the presence of noise. Recent evidence suggests that efferent fibers to the outer hair cells may cause them to shorten (contract), altering the mechanical properties of the cochlea.

The Hair Cells. The hair cells of the inner and the outer rows are similar anatomically. Both sets are supported and anchored to the basilar membrane by **Deiters' cells** and extend upward into the scala media toward the tectorial membrane. Extensions of the outer hair cells actually touch the tectorial membrane, while those of the inner hair cells appear to stop just short of contact. The hair cells make synaptic contact with afferent neurons that run through channels between Deiters' cells. A chemical transmitter of unknown identity is contained in synaptic vesicles near the base of the hair cells; as in other synaptic systems, the entry of calcium ions (associated with cell membrane depolarization) is necessary for the migration and fusion of the synaptic vesicles with the cell membrane prior to transmitter release.

At the apical end of each inner hair cell is a projecting bundle of about 50 **stereocilia,** rod-like structures packed in three, parallel, slightly curved rows. Minute strands link the free ends of the stereocilia together, so the bundle tends to move as a unit. The height of the individual stereocilia increases toward the outer edge of the cell (toward the stria vascularis), giving a sloping appearance to the bundle. Along the cochlea, the inner hair cells remain constant in size, while the stereocilia increase in height from about 4 μm at the basal end to 7 μm at the apical end. The outer hair cells are more elongated than the inner cells, and their size increases along the cochlea from base to apex. Their stereocilia (about 100 per hair cell) are also arranged in three rows that form an exaggerated *W* figure. The height of the stereocilia also increases along the length of the cochlea, and they are embedded in the tectorial membrane. The stereocilia of both types of hair cells extend from the **cuticular plate** at the apex of the cell. The diameter of an individual stereocilium is uniform (about 0.2 μm) except at the base, where it decreases significantly. Each stereocilium contains cross-linked and closely packed **actin filaments,** and, near the tip, is a cation-selective **transduction channel.**

Mechanical transduction in hair cells is shown in Figure 4.20. When a hair bundle is deflected slightly (the threshold is less than 0.5 nm) toward the stria vascularis, minute mechanical forces open the transduction channels, and cations (mostly potassium) enter the cells. The resulting **depolarization,** roughly proportional to the deflection, causes the release of transmitter molecules, generating afferent nerve action potentials. Approximately 15% of the transduction channels are open in the absence of any deflection, and bending in the direction of the modiolus of the cochlea results in hyperpolarization, increasing the range of motion that can be sensed. Hair cells are quite insensitive to movements of the stereocilia bundles at right angles to their preferred direction.

The response time of hair cells is remarkable; they can detect repetitive motions of up to 100,000 times per second. They can, therefore, provide information throughout the course of a single cycle of a sound wave. Such rapid response is also necessary for the accurate localization of sound sources. When a sound comes from directly in front of a listener, the waves arrive simultaneously at both ears. If the sound originates off to one side, it reaches one ear

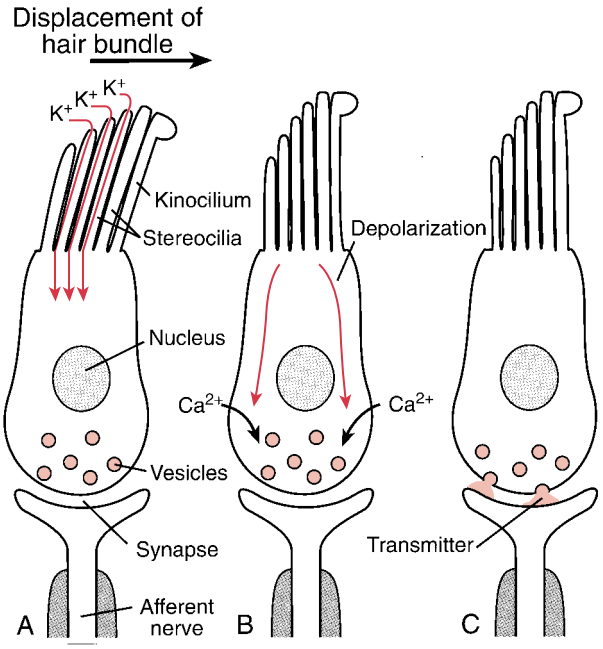


FIGURE 4.20 **Mechanical transduction in the hair cells of the ear.** **A,** Deflection of the stereocilia opens apical K^+ channels. **B,** The resulting depolarization allows the entry of Ca^{2+} at the basal end of the cell. This causes the release of the neurotransmitter, thereby exciting the afferent nerve. (Adapted from Hudspeth AJ. The hair cells of the inner ear. Sci Am 1983;248(1):54–64.)

sooner than the other and is slightly more intense at the nearer ear. The difference in arrival time is on the order of tenths of a millisecond, and the rapid response of the hair cells allows them to provide temporal input to the auditory cortex. The timing and intensity information are processed in the auditory cortex into an accurate perception of the location of the sound source.

Integrated Function of the Organ of Corti. The actual transduction of sound requires an interaction among the tectorial membrane, the arches of Corti, the hair cells, and the basilar membrane. When a sound wave is transmitted to the oval window by the ossicular chain, a pressure wave travels up the scala vestibuli and down the scala tympani (Fig. 4.21). The canals of the cochlea, being encased in bone, are not deformed, and movements of the round window allow the small volume change needed for the transmission of the pressure wave. Resulting eddy currents in the cochlear fluids produce an undulating distortion in the basilar membrane. Because the stiffness and width of the membrane vary with its length (it is wider and less stiff at the apex than at the base), the membrane deformation takes the form of a "**traveling wave**," which has its maximal amplitude at a position along the membrane corresponding to the particular frequency of the sound wave (Fig. 4.22). Low-frequency sounds cause a maximal displacement of the membrane near its apical end (near the helicotrema), whereas high-frequency sounds produce their maximal effect at the basal end (near the oval window). As the basilar membrane moves, the arches of Corti transmit the movement to the tectorial membrane, the stereocilia of the outer hair cells (embedded in the tectorial membrane) are subjected to lateral shearing forces that stimulate the cells, and action potentials arise in the afferent neurons.

Because of the tuning effect of the basilar membrane, only hair cells located at a particular place along the membrane are maximally stimulated by a given frequency (pitch). This localization is the essence of the **place theory** of pitch discrimination, and the mapping of specific tones (pitches) to specific areas is called **tonotopic organization**. As the signals from the cochlea ascend through the complex pathways of the auditory system in the brain, the tonotopic organization of the neural elements is at least partially preserved, and pitch can be spatially localized throughout the system. The sense of pitch is further sharpened by the resonant characteristics of the different-length stereocilia along the length of the cochlea and by the frequency-response selectivity of neurons in the auditory pathway. The cochlea acts as both a transducer for sound waves and a frequency analyzer that sorts out the different pitches so they

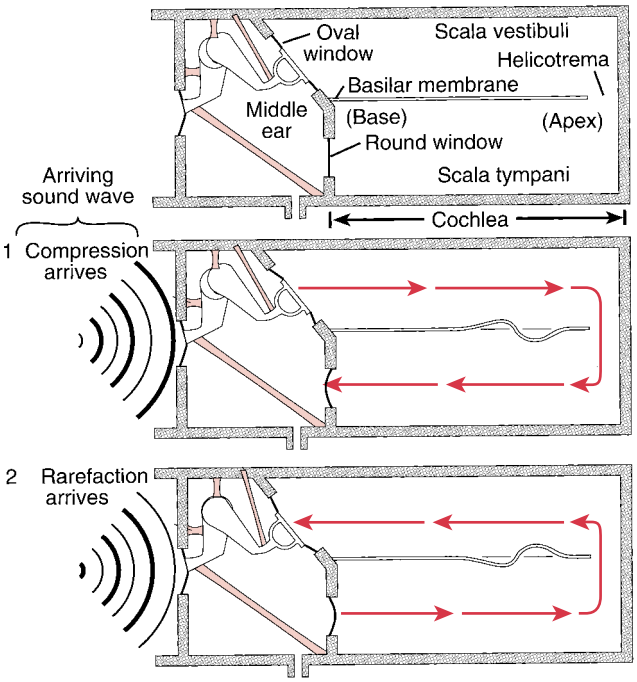


FIGURE 4.21 **The mechanics of the cochlea, showing the action of the structures responsible for pitch discrimination (with only the basilar membrane of the organ of Corti shown).** When the compression phase of a sound wave arrives at the eardrum, the ossicles transmit it to the oval window, which is pushed inward. A pressure wave travels up the scala vestibuli and (via the helicotrema) down the scala tympani. To relieve the pressure, the round window membrane bulges outward. Associated with the pressure waves are small eddy currents that cause a traveling wave of displacement to move along the basilar membrane from base to apex. The arrival of the next rarefaction phase reverses these processes. The frequency of the sound wave, interacting with the differences in the mass, width, and stiffness of the basilar membrane along its length, determines the characteristic position at which the membrane displacement is maximal. This localization is further detailed in Figure 4.22.

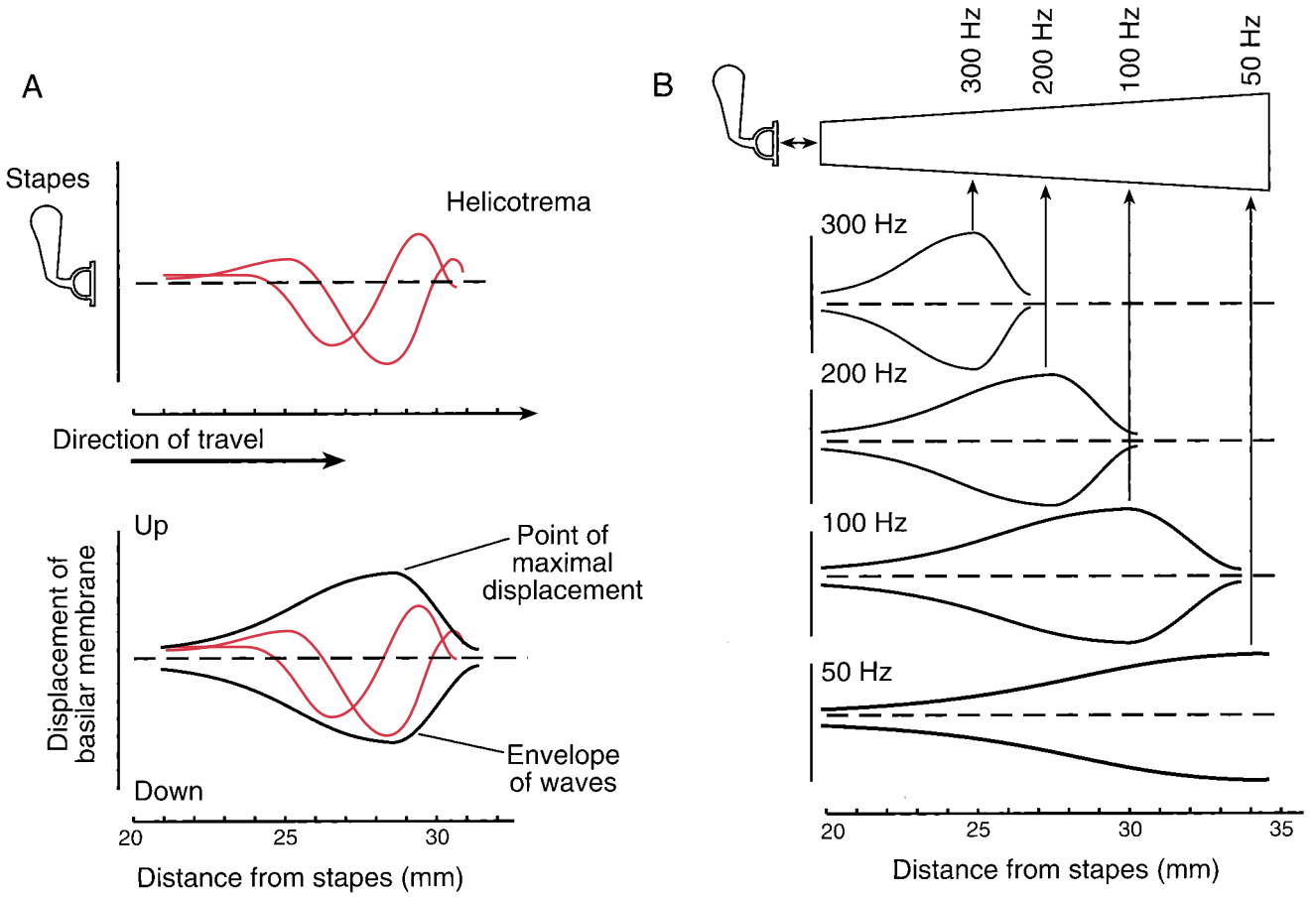


FIGURE 4.22 **Membrane localization of different frequencies. A,** The upper portion shows a traveling wave of displacement along the basilar membrane at two instants. Over time, the peak excursions of many such waves form an envelope of displacement with a maximal value at about 28 mm from the stapes (lower portion); at this position, its stimulating effect on the hair cells will be most intense. **B,** The effect of frequency. Lower frequencies produce a maximal effect at the apex of the basilar membrane, where it is the widest and least stiff. Pure tones affect a single location; complex tones affect multiple loci. (Modified from von Békésy G. Experiments in Hearing. New York: McGraw-Hill, 1960.)

can be separately distinguished. In the midrange of hearing (around 1,000 Hz), the human auditory system can sense a difference in frequency of as little as 3 Hz. The tonotopic organization of the basilar membrane has facilitated the invention of prosthetic devices whose aim is to provide some replacement of auditory function to people suffering from deafness that arises from severe malfunction of the middle or inner ear (see Clinical Focus Box 4.1).

Central Auditory Pathways. Nerve fibers from the cochlea enter the spiral ganglion of the organ of Corti; from there, fibers are sent to the **dorsal** and **ventral cochlear nuclei.** The complex pathway that finally ends at the **auditory cortex** in the superior portion of the **temporal lobe** of the brain involves several sets of synapses and considerable crossing over and intermediate processing. As with the eye, there is a spatial correlation between cells in the sensory organ and specific locations in the primary auditory cortex. In this case, the representation is called a **tonotopic map,** with different pitches being represented by different locations, even though the firing rates of the cells no longer correspond to the frequency of sound originally presented to the inner ear.

The Function of the Vestibular Apparatus. The ear also has important nonauditory sensory functions. The sensory receptors that allow us to maintain our equilibrium and balance are located in the **vestibular apparatus**, which consists (on each side of the head) of three **semicircular canals** and two **otolithic organs,** the **utricle** and the **saccule** (Fig. 4.23). These structures are located in the bony labyrinth of the temporal bone and are sometimes called the **membranous labyrinth**. As with hearing, the basic sensing elements are hair cells.

The semicircular canals, hoop-like tubular membranous structures, sense rotary acceleration and motion. Their interior is continuous with the scala media and is filled with endolymph; on the outside, they are bathed by perilymph. The three canals on each side lie in three mutually perpendicular planes. With the head tipped forward by about 30 degrees, the **horizontal** (**lateral**) **canal** lies in the horizontal plane. At right angles to this are the planes of the **anterior**

CLINICAL FOCUS BOX 4.1

Cochlear Implants

Disorders of hearing are broadly divided into the categories of **conductive hearing loss,** related to structures of the outer and middle ear; **sensorineural hearing loss** ("nerve deafness"), dealing with the mechanisms of the cochlea and peripheral nerves; and **central hearing loss,** concerning processes that lie in higher portions of the central nervous system.

Damage to the cochlea, especially to the hair cells of the organ of Corti, produces sensorineural hearing loss by several means. Prolonged exposure to loud occupational or recreational noises can lead to hair cell damage, including mechanical disruption of the stereocilia. Such damage is localized in the outer hair cells along the basilar membrane at a position related to the pitch of the sound that produced it. Antibiotics such as streptomycin and certain diuretics can cause rapid and irreversible damage to hair cells similar to that caused by noise, but it occurs over a broad range of frequencies. Diseases such as meningitis, especially in children, can also lead to sensorineural hearing loss.

In carefully selected patients, the use of a **cochlear implant** can restore some function to the profoundly deaf. The device consists of an external microphone, amplifier, and speech processor coupled by a plug-and-socket connection, magnetic induction, or a radio frequency link to a receiver implanted under the skin over the mastoid bone. Stimulating wires then lead to the cochlea. A single **extracochlear electrode,** applied to the round window, can restore perception of some environmental sounds and aid in lip-reading, but it will not restore pitch or speech discrimination. A **multielectrode intracochlear implant** (with up to 22 active elements spaced along it) can be inserted into the basal turn of the scala tympani. The linear spatial arrangement of the electrodes takes advantage of the tonotopic organization of the cochlea, and some pitch (frequency) discrimination is possible. The external processor separates the speech signal into several frequency bands that contain the most critical speech information, and the multielectrode assembly presents the separated signals to the appropriate locations along the cochlea. In some devices the signals are presented in rapid sequence, rather than simultaneously, to minimize interference between adjacent areas.

When implanted successfully, such a device can restore much of the ability to understand speech. Considerable training of the patient and fine-tuning of the speech processor are necessary. The degree of restoration of function ranges from recognition of critical environmental sounds to the ability to converse over a telephone. Cochlear implants are most successful in adults who became deaf after having learned to speak and hear naturally. Success in children depends critically on their age and linguistic ability; currently, implants are being used in children as young as age 2.

Infrequent problems with infection, device failure, and natural growth of the auditory structures may limit the usefulness of cochlear implants for some patients. In certain cases, psychological and social considerations may discourage the advisability of using of auditory prosthetic devices in general. From a technical standpoint, however, continual refinements in the design of implantable devices and the processing circuitry are extending the range of subjects who may benefit from cochlear implants. Research directed at external stimulation of higher auditory structures may eventually lead to even more effective treatments for profound hearing loss.

vertical (**superior**) **canal** and the **posterior vertical canal**, which are perpendicular to each other. The planes of the anterior vertical canals are each at approximately 45° to the midsagittal section of the head (and at 90° to each other). Thus, the anterior canal on one side lies in a plane parallel with the posterior canal on the other side, and the two function as a pair. The horizontal canals also lie in a common plane.

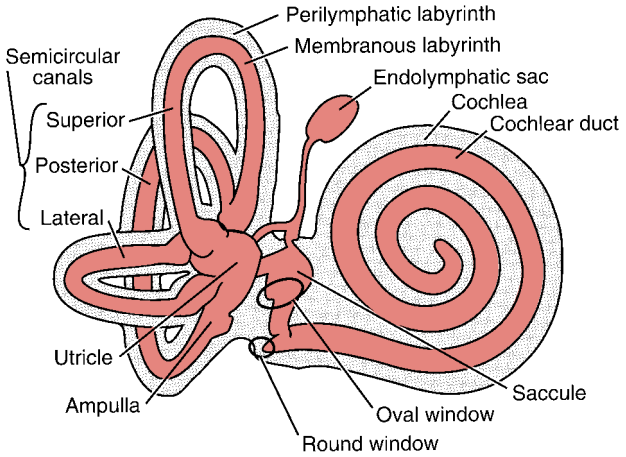


FIGURE 4.23 **The vestibular apparatus in the bony labyrinth of the inner ear.** The semicircular canals sense rotary acceleration and motion, while the utricle and saccule sense linear acceleration and static position.

Near its junction with the utricle, each canal has a swollen portion called the **ampulla**. Each ampulla contains a **crista ampullaris**, the sensory structure for that semicircular canal; it is composed of hair cells and supporting cells encapsulated by a **cupula**, a gelatinous mass (Fig. 4.24). The cupula extends to the top of the ampulla and is moved back and forth by movements of the endolymph in the canal. This movement is sensed by displacement of the stereocilia of the hair cells. These cells are much like those of the organ of Corti, except that at the "tall" end of the stereocilia array there is one larger cilium, the **kinocilium**. All the hair cells have the same orientation. When the stereocilia are bent toward the kinocilium, the frequency of action potentials in the afferent neurons leaving the ampulla increases; bending in the other direction decreases the action potential frequency.

The role of the semicircular canals in sensing rotary acceleration is shown on the left side of Figure 4.25. The mechanisms linking stereocilia deflection to receptor potentials and action potential generation are quite similar to those in the auditory hair cells. Because of the inertia of the endolymph in the canals, when the position of the head is changed, fluid currents in the canals cause the deflection of

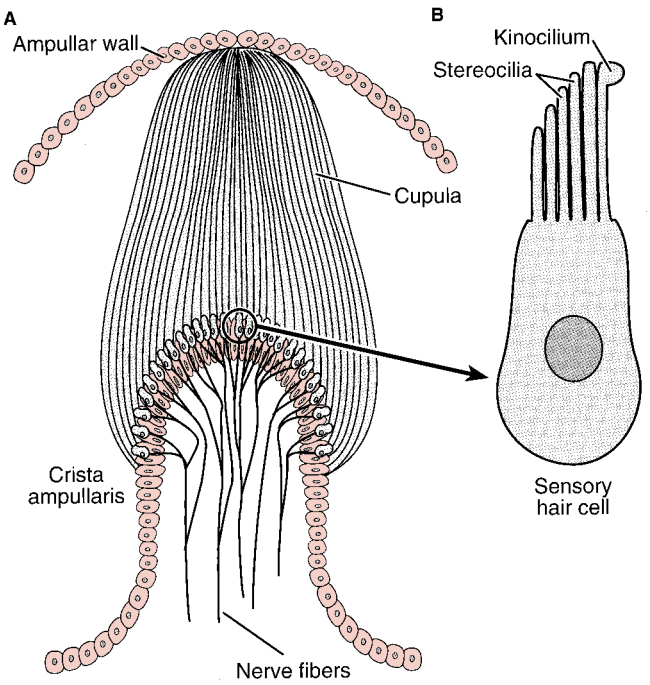


FIGURE 4.24 **The sensory structure of the semicircular canals.** **A,** The crista ampularis contains the hair (receptor) cells, and the whole structure is deflected by motion of the endolymph. **B,** An individual hair cell.

the cupula and the hair cells are stimulated. The fluid currents are roughly proportional to the rate of change of velocity (i.e., to the rotary acceleration), and they result in a proportional increase or decrease (depending on the direction of head rotation) in action potential frequency. As a result of the bilateral symmetry in the vestibular system, canals with opposite pairing produce opposite neural effects. The vestibular division of cranial nerve VIII passes the impulses first to the **vestibular ganglion,** where the cell bodies of the primary sensory neurons lie. The information is then passed to the **vestibular nuclei** of the brainstem and from there to various locations involved in sensing, correcting, and compensating for changes in the motions of the body.

The remaining vestibular organs, the saccule and the utricle, are also part of the membranous labyrinth. They communicate with the semicircular canals, the cochlear duct, and the endolymphatic duct. The sensory structures in these organs, called **maculae,** also employ hair cells, similar to those of the ampullar cristae (Fig. 4.26). The macular hair cells are covered with the **otolithic membrane,** a gelatinous substance in which are embedded numerous small crystals of calcium carbonate called **otoliths** (otoconia). Because the otoliths are heavier than the endolymph, tilting of the head results in gravitational movement of the otolithic membrane and a corresponding change in sensory neuron action potential frequency. As in the ampulla, the action potential frequency increases or decreases depending on the direction of displacement. The maculae are adapted to provide a steady signal in response to displacement; in addition, they are located away from the semicircular canals and are not subject to motion-induced currents in the endolymph. This allows them to monitor the position of the head with respect to a steady gravitational field. The maculae also respond proportionally to **linear acceleration.**

The vestibular apparatus is an important component in several reflexes that serve to orient the body in space and maintain that orientation. Integrated responses to

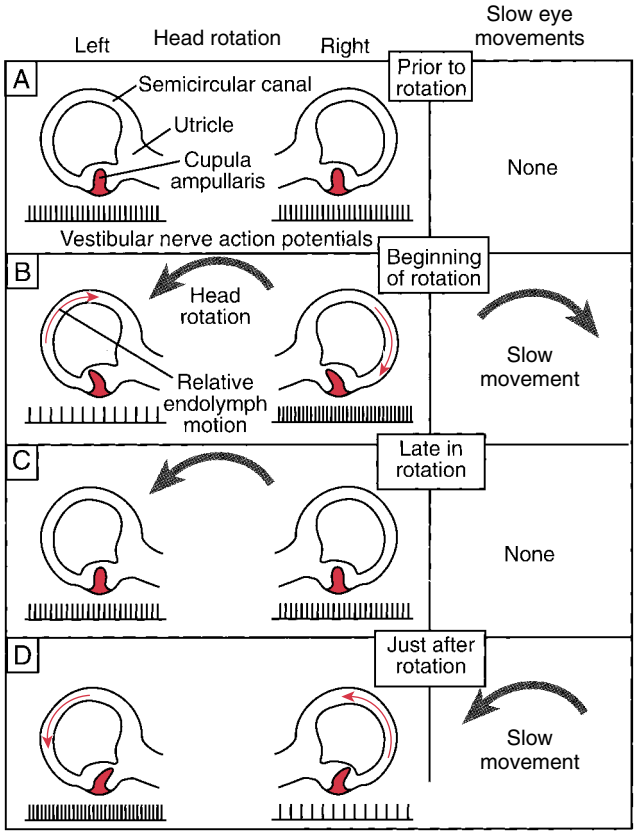


FIGURE 4.25 **The role of the semicircular canals in sensing rotary acceleration.** This sensation is linked to compensatory eye movements by the vestibuloocular reflex. Only the horizontal canals are considered here. This pair of canals is shown as if one were looking down through the top of a head looking toward the top of the page. Within the ampulla of each canal is the cupula, an extension of the crista ampullaris, the structure that senses motion in the endolymph fluid in the canal. Below each canal is the action potential train recorded from the vestibular nerve. **A,** The head is still, and equal nerve activity is seen on both sides. There are no associated eye movements (right column). **B,** The head has begun to rotate to the left. The inertia of the endolymph causes it to lag behind the movement, producing a fluid current that stimulates the cupulae (arrows show the direction of the relative movements). Because the two canals are mirror images, the neural effects are opposite on each side (the cupulae are bent in relatively opposite directions). The reflex action causes the eyes to move slowly to the right, opposite to the direction of rotation (right column); they then snap back and begin the slow movement again as rotation continues. The fast movement is called rotatory nystagmus. **C,** As rotation continues, the endolymph "catches up" with the canal because of fluid friction and viscosity, and there is no relative movement to deflect the cupulae. Equal neural output comes from both sides, and the eye movements cease. **D,** When the rotation stops, the inertia of the endolymph causes a current in the same direction as the preceding rotation, and the cupulae are again deflected, this time in a manner opposite to that shown in part B. The slow eye movements now occur in the same direction as the former rotation.

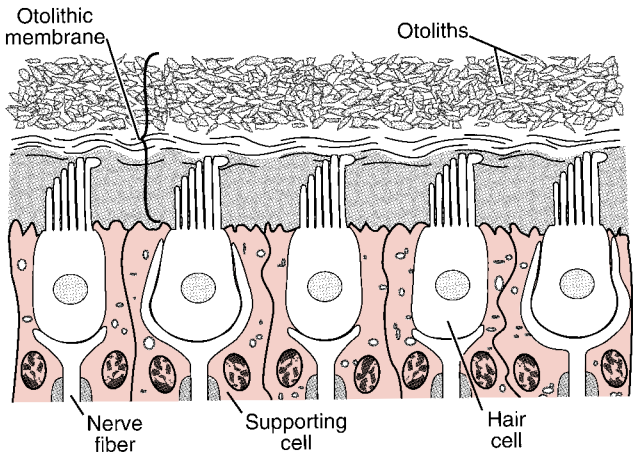


FIGURE 4.26 The relation of the otoliths to the sensory cells in the macula of the utricle and sacule. The gravity-driven movement of the otoliths stimulates the hair cells.

vestibular sensory input include balancing and steadying movements controlled by skeletal muscles, along with specific reflexes that automatically compensate for bodily motions. One such mechanism is the **vestibuloocular reflex.** If the body begins to rotate and, thereby, stimulate the horizontal semicircular canals, the eyes will move slowly in a direction opposite to that of the rotation and then suddenly snap back the other way (see Fig. 4.25, right). This movement pattern, called **rotatory nystagmus,** aids in visual fixation and orientation and takes place even with the eyes closed. It functions to keep the eyes fixed on a stationary point (real or imaginary) as the head rotates. By convention, the direction of the rapid eye movement is used to label the direction of the nystagmus, and this movement is in the same direction as the rotation. As rotation continues, the relative motion of the endolymph in the semicircular canals ceases, and the nystagmus disappears. When rotation stops, the inertia of the endolymph causes it to continue in motion and again the cupulae are displaced, this time from the opposite direction. The slow eye movements are now in the same direction as the prior rotation; the **postrotatory nystagmus** (fast phase) that develops is in a direction opposite to the previous rotation. As long as the endolymph continues its relative movement, the nystagmus (and the sensation of rotary motion) persists. Irrigation of the ear with water above or below body temperature causes convection currents in the endolymph. The resulting unilateral **caloric stimulation** of the semicircular canal produces symptoms of vertigo, nystagmus, and nausea. Disturbances of the labyrinthine function produce the symptoms of **vertigo**, a disorder that can significantly affect daily activities (see Clinical Focus Box 4.2).

Related mechanisms involving the otolithic organs produce automatic compensations (via the postural and extraocular musculature) when the otolithic organs are stimulated by transient or maintained changes in the position of the head. If the otolithic organs are stimulated rhythmically, as by the motion of a ship or automobile, the distressing symptoms of motion sickness (vertigo, nausea, sweating, etc.) may appear. Over time, these symptoms lessen and disappear.

The Special Chemical Senses Detect Molecules in the Environment

Chemical sensation includes not only the special chemical senses described below, but also internal sensory receptor functions that monitor the concentrations of gases and other chemical substances dissolved in the blood or other body fluids. Since we are seldom aware of these internal chemical sensations, they are treated throughout this book as needed; the discussion here covers only taste and smell.

Gustatory Sensation. The sense of taste is mediated by multicellular receptors called **taste buds,** several thousand of which are located on folds and projections on the dorsal tongue, called **papillae.** Taste buds are located mainly on the tops of the numerous **fungiform papillae** but are also located on the sides of the less numerous **foliate** and **vallate papillae**. The **filiform papillae**, which cover most of the tongue, usually do not bear taste buds. An individual taste bud is a spheroid collection of about 50 individual cells that is about 70 μm high and 40 μm in diameter (Fig. 4.27). The cells of a taste bud lie mostly buried in the surface of the tongue, and materials access the sensory cells by way of the **taste pore**.

Most of the cells of a taste bud are **sensory cells.** At their apical ends, they are connected laterally by tight junctions, and they bear **microvilli** that greatly increase the surface area they present to the environment. At their basal ends, they form synapses with the facial (VII) and glossopharyngeal (IX) cranial nerves. This arrangement indicates that the sensory cells are actually **secondary receptors** (like the hair cells of the ear), since they are anatomically separate from the afferent sensory nerves. About 50 afferent fibers enter each taste bud, where they branch so that each axon synapses with more than one sensory cell. Among the sensory cells are elongated **supporting cells** that do not have synaptic connections. The sensory cells typically have a lifespan of 10 days. They are continually replenished by new sensory cells formed from the **basal cells** of the lower part of the taste buds. When a sensory cell is replaced by a maturing basal cell, the old synaptic connections are broken, and new ones must be formed.

From the point of view of their receptors, the traditional four modalities of taste—**sweet**, **sour**, **salty**, and **bitter**—are well defined, and the areas of the tongue where they are located are also rather specific, although the degree of localization depends on the concentration of the stimulating substance. In general, the receptors for sweetness are located just behind the tip of the tongue, sour receptors are located along the sides, the salt sensation is localized at the tip, and the bitter sensation is found across the rear of the tongue. (The two "accessory qualities" of taste sensation are **alkaline** [soapy] and **metallic.**) The broad surface of the tongue is not as well supplied with taste buds. Most taste experiences involve several different sensory modalities, including taste, smell, mechanoreception (for texture), and temperature; artificially confining the taste sensation to only the four modalities found on the tongue (e.g., by

CLINICAL FOCUS BOX 4.2

Vertigo

A common medical complaint is dizziness. This symptom may be a result of several factors, such as cerebral ischemia ("feeling faint"), reactions to medication, disturbances in gait, or disturbances in the function of the vestibular apparatus and its central nervous system connections. Such disturbances can produce the phenomenon of **vertigo**, which may be defined as the illusion of motion (usually rotation) when no motion is actually occurring. Vertigo is often accompanied by autonomic nervous system symptoms of nausea, vomiting, sweating, and pallor.

The body uses three integrated systems to establish its place in space: the vestibular system, which senses position and rotation of the head; the visual system, which provides spatial information about the external environment; and the somatosensory system, which provides information from joint, skin, and muscle receptors about limb position. Several forms of vertigo can arise from disturbances in these systems. **Physiological vertigo** can result when there is discordant input from the three systems. Seasickness results from the unaccustomed repetitive motion of a ship (sensed via the vestibular system). Rapidly changing visual fields can cause visually-induced motion sickness, and space sickness is associated with multiple-input disturbances. **Central positional vertigo** can arise from lesions in cranial nerve VIII (as may be associated with multiple sclerosis or some tumors), vertebrovascular insufficiency (especially in older adults), or from impingement of vascular loops on neural structures. It is commonly present with other CNS symptoms. **Peripheral vertigo** arises from disturbances in the vestibular apparatus itself. The problem may be either unilateral or bilateral. Causes include trauma, physical defects in the labyrinthine system, and pathological syndromes such as Ménière's disease. As in the cochlea, aging produces considerable hair cell loss in the cristae and maculae of the vestibular system. Caloric stimulation can be used as an indicator of the degree of vestibular function.

The most common form of peripheral vertigo is **benign paroxysmal positional vertigo (BPPV)**. This is a severe vertigo, with incidence increasing with age. Episodes appear rapidly and are limited in duration (from minutes to days). They are usually brought on by assuming a particular position of the head, such as one might do when painting a ceiling. BPPV is thought to be due to the presence of **canaliths**, debris in the lumen of one of the semicircular canals. The offending particles are usually clumps of otoconia (otoliths) that have been shed from the maculae of the saccule and utricle, whose passages are connected to the semicircular canals. These clumps act as gravity-driven pistons in the canals, and their movement causes the endolymph to flow, producing the sensation of rotary motion. Because they are in the lowest position, the posterior canals are the most frequently affected. In addition to the rotating sensation, this input gives rise, via the vestibuloocular system, to a pattern of nystagmus (eye movements) appropriate to the spurious input.

The specific site of the problem can be determined by using the **Dix-Hallpike maneuver**, which is a series of physical maneuvers (changes in head and body position). By observing the resulting pattern of nystagmus and reported symptoms, the location of the defect can be deduced. Another set of maneuvers known as the **canalith repositioning procedure of Epley** can cause gravity to collect the loose canaliths and deposit them away from the lumen of the semicircular canal. This procedure is highly effective in cases of true BPPV, with a cure rate of up to 85% on the first attempt and nearly 100% on a subsequent attempt. Patients can be taught to perform the procedure on themselves if the problem returns.

Ménière's disease is a syndrome of uncertain (but peripheral) origin associated with vertigo. Its cause(s) and precipitating factors are not well understood. Typical associated findings include fluctuating hearing loss and tinnitus (ringing in the ears). Episodes involve increased fluid pressure in the labyrinthine system, and symptoms may decrease in response to salt restriction and diuretics. Other cases of peripheral vertigo may be caused by trauma (usually unilateral) or by toxins or drugs (such as some antibiotics); this type is often bilateral.

Central and peripheral vertigo may often be differentiated on the basis of their specific symptoms. Peripheral vertigo is more severe, and its nystagmus shows a delay (latency) in appearing after a position change. Its nystagmus fatigues and can be reduced by visual fixation. Position sensitive and of finite duration, the condition usually involves a horizontal orientation. Central vertigo, usually less severe, shows a vertically oriented nystagmus without latency and fatigability; it is not suppressed by visual fixation and may be of long duration.

Treatment for vertigo, beyond that mentioned above, can involve bed rest and vestibular inhibiting drugs (such as some antihistamines). However, these treatments are not always effective and may delay the natural compensation that can be aided by physical motion, such as walking (unpleasant as that may be). In severe cases that require surgical intervention (labyrinthectomy, etc.), patients can often achieve a workable position sense via the other sensory inputs involved in maintaining equilibrium. Some activities, such as underwater swimming, must be avoided by those with an impaired sense of orientation, since false cues may lead to moving in inappropriate directions and increase the risk of drowning.

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blocking the sense of smell) greatly diminishes the range of taste perceptions.

Recent studies have provided evidence for a fifth taste modality, one that is called **umami**, or savoriness. Its receptors are stimulated quite specifically by glutamate ions, which are contained in naturally occurring dietary protein and are responsible for a "meaty" taste. Glutamate ions can also be provided as a flavor-enhancer in the well-known food additive MSG, monosodium glutamate.

While the functional receptor categories are well defined, it is much more difficult to determine what kind of stimulating chemical will produce a given taste sensation. Chemicals that produce a sour sensation are usually acids, and the intensity of the perception depends on the degree

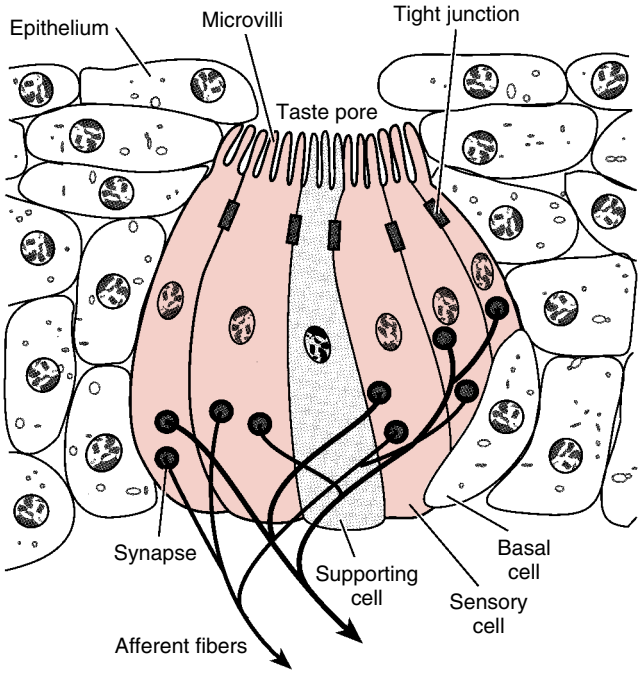

FIGURE 4.27 **The sensory and supporting cells in a taste bud.** The afferent nerve synapse with the basal areas of the sensory cells. (Modified from Schmidt RF, ed. Fundamentals of Sensory Physiology. 2nd Ed. New York: Springer-Verlag, 1981.)

of dissociation of the acid (i.e., the number of free hydrogen ions). Most sweet substances are organic; sugars, especially, tend to produce a sweet sensation, although thresholds vary widely. For example, sucrose is about 8 times as sweet as glucose. By comparison, the apparent sweetness of saccharin, an artificial sweetener, is 600 times as great as that of sucrose, although it is not a sugar. Unfortunately, the salts of lead are also sweet, which can lead to ingestion of toxic levels of this poisonous metal. Substances producing a bitter taste form a heterogeneous group. The classic bitter substance is quinine; nicotine and caffeine are also bitter, as are many of the salts of calcium, magnesium, and ammonium, the bitter taste being due to the cation portion of the salt. Sodium ions produce a salty sensation; some organic compounds, such as lysyltaurine, are even more potent in this regard than sodium chloride.

The intensity of a taste sensation depends on the concentration of the stimulating substance, but application of the same concentration to larger areas of the tongue produces a more intense sensation; this is probably due to facilitation involving a greater number of afferent fibers. Some taste sensations also increase with time, although taste receptors show a slow but definite adaptation. Elevated temperature, over some ranges, tends to increase the perceived taste intensity, while dilution by saliva and serous secretions from the tongue decreases the intensity. The specificity of the taste sensation arising from a particular stimulating substance results from the effects of specific receptor molecules on the microvilli of the sensory cells. Salty substances probably depolarize sensory cells directly, while sour substances may produce depolarization by blocking potassium channels with hydrogen ions. Bitter substances bind to specific G protein-coupled receptors and activate phospholipase C to increase the cell concentration of inositol trisphosphate, which promotes calcium release from the endoplasmic reticulum. Sweet substances also act through G protein-coupled receptors and cause increases in adenylyl cyclase activity, increasing cAMP, which, in turn, promotes the phosphorylation of membrane potassium channels. The resulting decrease in potassium conductance leads to depolarization. In the case of the umami taste, there is evidence of specific G protein-coupled receptors in the cell membranes of sensory taste cells.

Olfactory Sensation. Compared with that of many other animals, the human sense of smell is not particularly acute. Nevertheless, we can distinguish 2,000 to 4,000 different odors that cover a wide range of chemical species. The receptor organ for olfaction is the **olfactory mucosa,** an area of approximately 5 cm^2 located in the roof of the nasal cavity. Normally there is little air flow in this region of the nasal tract, but sniffing serves to direct air upward, increasing the likelihood of an odor being detected.

The olfactory mucosa contains about 10 to 20 million receptor cells. In contrast to the taste sensory cells, the olfactory cells are neurons and, as such, are **primary receptors.** These cells are interspersed among **supporting** (**sustentacular**) **cells**, and **tight junctions** bind the cells together at their sensory ends (Fig. 4.28). The receptor

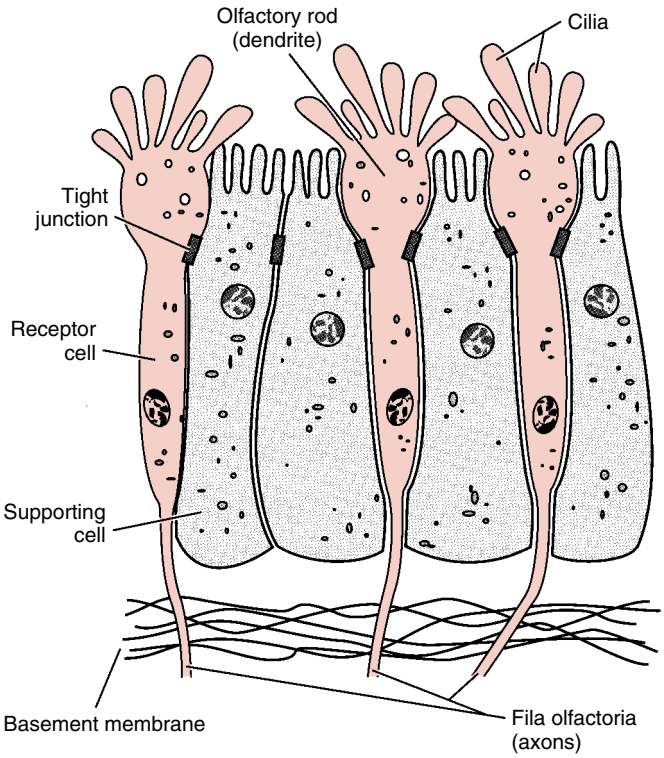

FIGURE 4.28 **The sensory cells in the olfactory mucosa.** The fila olfactoria, the axons leading from the receptor cells, are part of the sensory cells, in contrast to the situation in taste receptors. (Modified from Ganong WF. Review of Medical Physiology. 20th Ed. Stamford, CT: McGraw-Hill, 2001.)

cells terminate at their apical ends with short, thick dendrites called **olfactory rods,** and each cell bears 10 to 20 cilia that extend into a thin covering of mucus secreted by **Bowman's glands** located throughout the olfactory mucosa. Molecules to be sensed must be dissolved in this mucous layer. The basal ends of the receptor cells form axonal processes called **fila olfactoria** that pass through the **cribriform plate** of the **ethmoid bone.** These short axons synapse with the **mitral cells** in complex spherical structures called **olfactory glomeruli** located in the **olfactory bulb,** part of the brain located just above the olfactory mucosa. Here the complex afferent and efferent neural connections for the olfactory tract are made. Approximately 1,000 fila olfactoria synapse on each mitral cell, resulting in a highly convergent relationship. Lateral connections are also plentiful in the olfactory bulb, which also contains efferent fibers thought to have an inhibitory function.

The olfactory mucosa also contains sensory fibers from the trigeminal (V) cranial nerve. They are sensitive to certain odorous substances, such as peppermint and chlorine, and play a role in the initiation of reflex responses (e.g., sneezing) that result from irritation of the nasal tract.

The modalities of smell are numerous and do not fall into convenient classes, though some general categories, such as flowery, sweaty, or rotten, may be distinguished. Olfactory thresholds vary widely from substance to substance; the threshold concentration for the detection of ethyl ether is around 5.8 mg/L air, while that for methyl mercaptan (the odor of garlic) is approximately 0.5 ng/L. This represents a 10 million-fold difference in sensitivity. The basis for odor discrimination is not well understood. It is not likely that there is a receptor molecule for every possible odor substance located in the membranes of the olfactory cilia, and it appears that complex odor sensations arise from unique spatial patterns of activation throughout the olfactory mucosa.

Signal transduction appears to involve the binding of a molecule of an odorous substance to a G protein-coupled receptor on a cilium of a sensory cell. This binding causes the production of cAMP that binds to, and opens, sodium channels in the ciliary membrane. The resulting inward sodium current depolarizes the cell to produce a generator potential, which causes action potentials to arise in the initial segments of the fila olfactoria. The sense of smell shows a high degree of adaptation, some of which takes place at the level of the generator potential and some of which may be due to the action of efferent neurons in the olfactory bulb. Discrimination between odor intensities is not well defined; detectable differences may be about 30%.

REVIEW QUESTIONS

DIRECTIONS: Each of the numbered items or incomplete statements in this section is followed by answers or completions of the statement. Select the ONE lettered answer or completion that is BEST in each case.

1. An increase in the action potential frequency in a sensory nerve usually signifies
   (A) Increased intensity of the stimulus
   (B) Cessation of the stimulus
   (C) Adaptation of the receptor
   (D) A constant and maintained stimulus
   (E) An increase in the action potential conduction velocity
2. Why is the blind spot on the retina not usually perceived?
   (A) It is very small, below the ability of the sensory cells to detect
   (B) It is present only in very young children
   (C) Its location in the visual field is different in each eye
   (D) Constant eye motion prevents the spot from remaining still
   (E) Lateral input from adjacent cells fills in the missing information
3. The condition known as presbyopia is due to
   (A) Change in the shape of the eyeball as a result of age
   (B) An age-related loss of cells in the retina
   (C) Change in the elasticity of the lens as a result of age
   (D) A loss of transparency in the lens
   (E) Increased opacity of the vitreous humor
4. What external aids can be used to help a myopic eye compensate for distance vision?
   (A) A positive (converging) lens placed in front of the eye
   (B) A negative (diverging) lens placed in front of the eye
   (C) A cylindrical lens placed in front of the eye
   (D) Eyeglasses that are partially opaque, to reduce the light intensity
   (E) No help is needed because the eye itself can accommodate
5. At which location along the basilar membrane are the highest-frequency sounds detected?
   (A) Nearest the oval window
   (B) Farthest from the oval window, near the helicotrema
   (C) Uniformly along the basilar membrane
   (D) At the midpoint of the membrane
   (E) At a series of widely-spaced locations along the membrane
6. Motion of the endolymph in the semicircular canals when the head is held still will result in the perception of
   (A) Being upside-down
   (B) Moving in a straight line
   (C) Continued rotation
   (D) Being upright and stationary
   (E) Lying on one's back
7. A decrease in sensory response while a stimulus is maintained constant is due to the phenomenon of
   (A) Adaptation
   (B) Fatigue
   (C) The graded response
   (D) Compression
8. Sensory receptors that adapt rapidly are well suited to sensing
   (A) The weight of an object held in the hand
   (B) The rate at which an extremity is being moved
   (C) Resting body orientation in space
   (D) Potentially hazardous chemicals in the environment
   (E) The position of an extended limb
9. Adaptation in a sensory receptor is associated with a
   (A) Decline in the amplitude of action potentials in the sensory nerve
   (B) Reduction in the intensity of the applied stimulus
   (C) Decline in the conduction velocity of sensory nerve action potentials

(continued)

(D) Decline in the amplitude of the generator potential
(E) Reduction in the duration of the sensory action potentials

10. Which of the following is the principal function of the bones (ossicles) of the middle ear?
(A) They provide mechanical support for the flexible membranes to which they are attached (i.e., the eardrum and the oval window)
(B) They reduce the amplitude of the vibrations reaching the oval window, protecting it from mechanical damage
(C) They increase the efficiency of vibration transfer through the middle ear
(D) They control the opening of the eustachian tubes and allow pressures to be equalized
(E) They have little effect on the process of hearing in humans, since they are essentially passive structures

11. On a moonlit night, human vision is monochromatic and less acute than vision during the daytime. This is because
(A) Objects are being illuminated by monochromatic light, and there is no opportunity for color to be produced
(B) The cone cells of the retina, while more closely packed than the rod cells, have a lower sensitivity to light of all colors
(C) Light rays of low intensity do not carry information as to color
(D) Retinal photoreceptor cells that have become dark-adapted can no longer respond to varying wavelengths of light
(E) At low light levels, the lens cannot accommodate to sharpen vision

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