

# The Auditory System

## INTRODUCTION

## THE NATURE OF SOUND

Box 11.1 *Of Special Interest: Infrasound*

## STRUCTURE OF THE AUDITORY SYSTEM

## THE MIDDLE EAR

Components of the Middle Ear  
Sound Force Amplification by the Ossicles  
The Attenuation Reflex

## THE INNER EAR

Anatomy of the Cochlea  
Physiology of the Cochlea  
    Response of the Basilar Membrane to Sound  
    The Organ of Corti and Associated Structures  
    Transduction by Hair Cells  
        Box 11.2 *Path of Discovery: The Cellular Basis of Hearing*  
            by A. J. Hudspeth  
    The Innervation of Hair Cells  
    Amplification by Outer Hair Cells

## CENTRAL AUDITORY PROCESSES

## ENCODING SOUND INTENSITY AND FREQUENCY

Anatomy of Auditory Pathways  
Response Properties of Neurons in the Auditory Pathway

## MECHANISMS OF SOUND LOCALIZATION

Stimulus Intensity  
Stimulus Frequency and Tonotopy

## AUDITORY CORTEX

Localization of Sound in the Horizontal Plane  
    Sensitivity of Binaural Neurons to Sound Location  
Localization of Sound in the Vertical Plane  
    Box 11.3 *Path of Discovery: Bat Echolocation* by James Simmons

## CONCLUDING REMARKS

Neuronal Response Properties  
Effects of Auditory Cortical Lesions and Ablation  
    Box 11.4 *Of Special Interest: Auditory Disorders*

## KEY TERMS

## REVIEW QUESTIONS



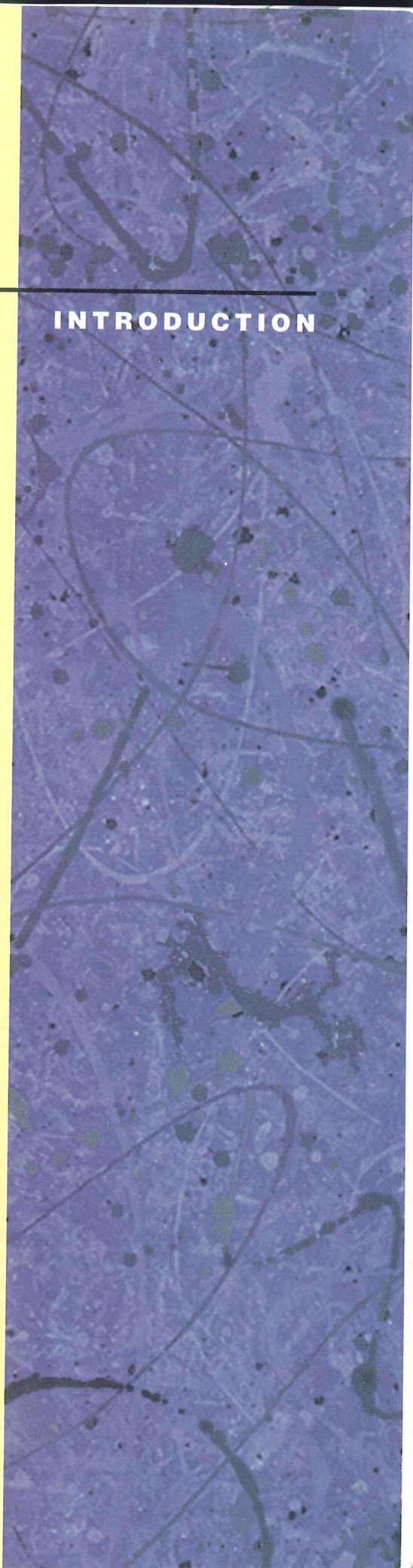




**T**he sense of hearing, also known as **audition**, plays many important roles in our daily lives. Even if we cannot see an object, we can detect its presence by hearing a sound that it makes. Anyone who has ever hiked through the forest in an area where there are bears or snakes knows that the sound of rustling leaves can be a powerful attention-grabber. From the sound, we can often identify the source and determine its location—an important piece of information if you have to make a run for it. Aside from the ability to detect and locate sound, we are able to perceive and interpret its nuances. We can immediately identify the bark of a dog, the voice of a friend, the crash of an ocean wave. Because humans are able to produce a wide variety of sounds as well as hear them, spoken language and its reception via the auditory system have become an extremely important means of communication. Audition in humans has even evolved beyond the strictly utilitarian functions of communication and survival: In a manner analogous to artists who use visual media, musicians explore the sensations and emotions evoked by sound.

In this chapter, we explore the mechanisms within the ear and brain that translate the sounds in our environment into meaningful neural signals. We will find that this transformation is carried out in stages rather than all at once. Within the ear, auditory receptors convert the mechanical energy in sound into a neural response. At subsequent stages in the brain stem and thalamus, signals from the receptors are integrated before they ultimately reach auditory cortex. By looking at the response properties of neurons at various points in the system, we begin to get some idea of the relationship between activity in the auditory system and our perception of sound.

## INTRODUCTION

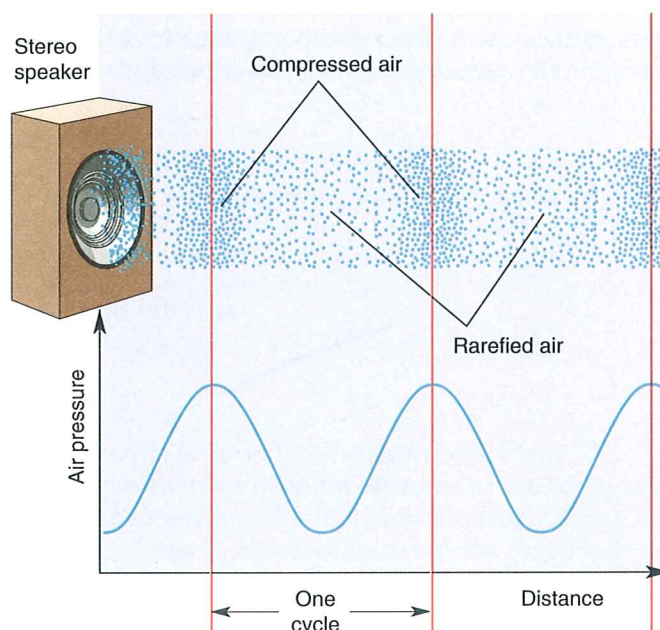




## THE NATURE OF SOUND

Sound consists of audible variations in air pressure resulting from a great variety of processes that move air molecules; these include the whisper of the human voice, the vibration of a string on a guitar, and the explosion of a firecracker. In general, when an object moves toward a patch of air, it compresses the air, increasing the density of the molecules. Conversely, the air is rarefied (made less dense) when an object moves away. This is particularly easy to visualize in the case of a stereo speaker, in which a paper cone attached to a magnet vibrates in and out, alternately rarefying and compressing the air (Figure 11.1). These changes in air pressure are transferred away from the speaker at the speed of sound, which is about 343 m/sec (767 mph) for air at room temperature.

Many sources of sound, such as vibrating strings or a stereo speaker reproducing the sound of a stringed instrument, produce variations in air pressure that are periodic. The **frequency** of the sound is the number of compressed or rarefied patches of molecules that pass by our ears each second. One cycle of the sound is the distance between successive compressed patches; the sound frequency, expressed in units called **hertz (Hz)**, is the number of cycles per second. Because sound waves all propagate at the same speed, high-frequency sound waves have more compressed and rarefied regions packed into the same space than low-frequency waves (Figure 11.2a). Our auditory system can respond to pressure waves over the remarkable range of 20–20,000 Hz (though this audible range decreases significantly with age and exposure to noise, especially at the high-frequency end). Whether a sound is perceived to have a high or low tone, or *pitch*, is determined by the frequency. In order to relate frequency to recognizable examples, remember that a room-shaking low note on an organ is about 20

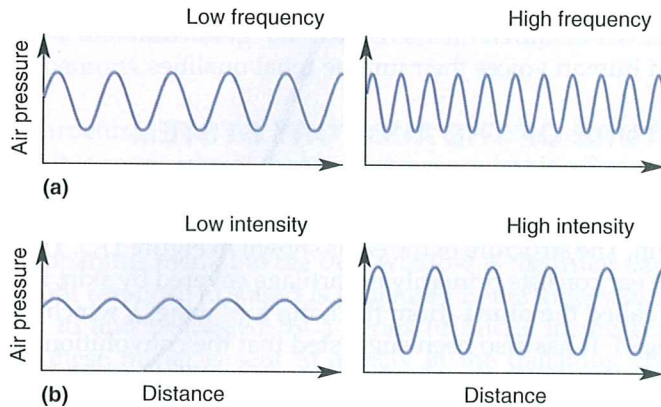


**Figure 11.1**

**The production of sound by variations in air pressure.** When the paper cone of a stereo speaker pushes out, it compresses the air; when the cone pulls in, it rarefies the air. If the push and pull are periodic, there will also be a periodic variation in the air pressure, as shown in the graph. The distance between successive compressed (high-pressure) patches of air is one cycle of the sound (indicated by the vertical lines). The sound wave propagates away from the speaker at the speed of sound.

Hz and an ear-piercing high note on a piccolo is about 10,000 Hz. Although humans can hear a great range of frequencies, there are high and low sound wave frequencies our ears cannot hear, just as there are electromagnetic waves of light our eyes cannot see (Box 11.1).

Another important property of a sound wave is its **intensity**, which is the difference in pressure between the compressed and rarefied patches of air



**Figure 11.2**

**The frequency and intensity of sound waves.** (a) We perceive high-frequency waves as having a higher pitch. (b) We perceive high-intensity waves as louder.

### Box 11.1

### OF SPECIAL INTEREST

## Infrasound

Most people are familiar with ultrasound (sound above the 20 kHz limit of our hearing) because it has everyday applications, from ultrasonic cleaners to medical imaging. Some animals can hear these high frequencies. For instance, dog whistles work because dogs can hear up to about 40 kHz. Less well known is infrasound, or sound at low frequencies, below about 20 Hz. Some animals can hear these frequencies; one is the elephant, which can detect 15 Hz tones at sound levels inaudible to humans. Whales produce low-frequency sounds, which are thought to be a means of communication over distances of kilometers. Low-frequency vibrations are also produced by the earth, and it is thought that some animals may sense an impending earthquake by hearing such sound.

Even though we usually cannot hear very low frequencies with our ears, they are present in our environment and can have unpleasant subconscious effects. Infrasound is produced by such devices as air conditioners, boilers, aircraft, and automobiles. Though even intense infrasound from these machines does not cause hearing loss, it can cause dizziness, nausea, and headache. Many cars produce low-frequency sound when they're moving at high-

way speeds, making sensitive people carsick. At very high levels, low-frequency sound may also produce resonances in body cavities such as the chest and stomach, which can damage internal organs. You might want to think twice before standing directly in front of a large speaker at a concert!

In addition to mechanical equipment, our own bodies generate inaudible low-frequency sound. When muscle changes length, individual fibers vibrate, producing low-intensity sound at about 25 Hz. While we cannot normally hear these sounds, you can demonstrate them to yourself by carefully putting your thumbs in your ears and making a fist with each hand. As you tighten your fist, you can hear a low rumbling sound produced by the contraction of your forearm muscles. Other muscles, including your heart, produce inaudible sound at frequencies near 20 Hz.

It's probably just as well that we aren't more aware of infrasound. It would be hard to get any work done listening to our bodies rumble and groan in a world filled with the drone of manmade machinery.

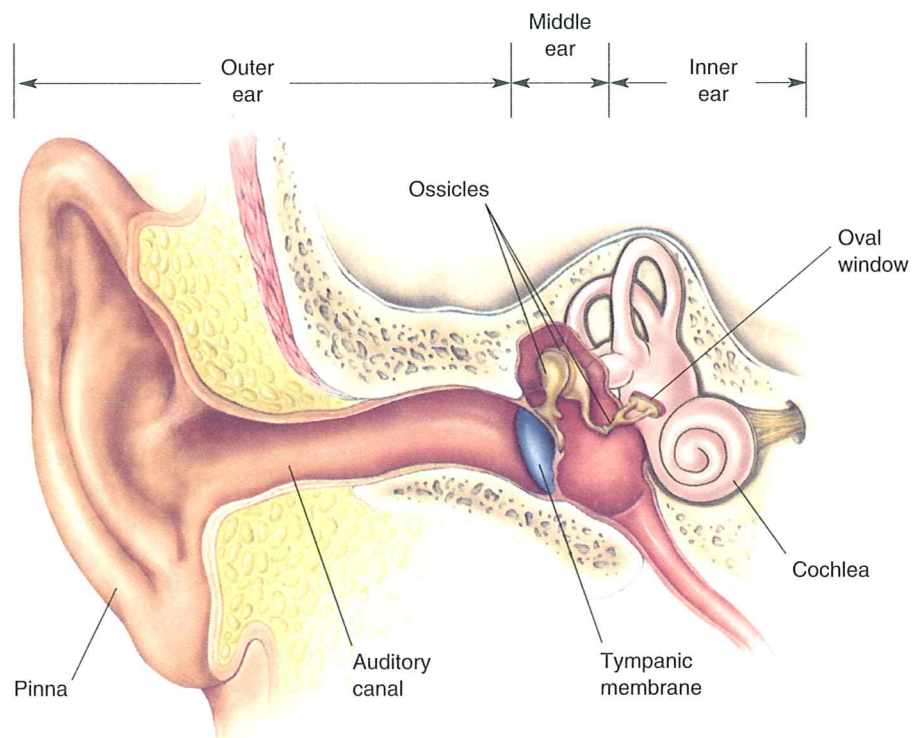


(Figure 11.2b). Sound intensity determines the *loudness* we perceive, loud sounds having higher intensity. The range of intensities to which the human ear is sensitive is astonishing: The intensity of the loudest sound that doesn't damage our ears is about a trillion times greater than the intensity of the faintest sound that can be heard. If we were any more sensitive, we would hear a constant roar from the random movement of air molecules.

Real world sounds rarely consist of simple periodic sound waves at one frequency and intensity. It is the simultaneous combination of different frequency waves at different intensities that gives different musical instruments and human voices their unique tonal qualities.

## STRUCTURE OF THE AUDITORY SYSTEM

Before exploring the details of translating variations in air pressure into neural activity, let's quickly survey the structural organization of the auditory system. The structure of the ear is shown in Figure 11.3. The visible portion of the ear consists primarily of cartilage covered by skin, forming a sort of funnel called the **pinna** (from the Latin for "wing"), which brings sound into the head. It has also been suggested that the convolutions in the pinna play a role in localizing sounds, something we will discuss later in the chapter. In humans, the pinna is more or less fixed in position, but animals such as cats and horses have considerable muscular control over the position of their pinna and can orient it toward a source of sound. The entrance to the internal ear is called the **auditory canal**, and it extends about 2.5 cm (1 inch) inside the skull before it ends at the **tympanic membrane**, also known as the *eardrum*. Connected to the medial surface of the tympanic membrane is a series of bones called **ossicles** (from the Latin for "little bones"). Located in a small air-filled chamber, the ossicles transfer movements of the tympanic membrane into movements of a second membrane covering a hole in the bone of the skull called the **oval window**. Behind the oval window is the



**Figure 11.3**  
The outer, middle, and inner ear.



fluid-filled **cochlea**, which contains the apparatus for transforming the physical motion of the oval window membrane into a neuronal response. Thus, the first stages of the basic auditory pathway look like this:

Sound wave moves the tympanic membrane→  
 Tympanic membrane moves the ossicles→  
 Ossicles move the membrane at the oval window→  
 Motion at the oval window moves fluid in the cochlea→  
 Movement of fluid in the cochlea causes a response in sensory neurons.

All of the structures from the pinna inward are considered components of the ear, and it is conventional to refer to the ear as having three main divisions. The structures from the pinna to the tympanic membrane make up the **outer ear**, the tympanic membrane and the ossicles compose the **middle ear**, and the apparatus medial to the oval window is the **inner ear**.

Once a neural response to sound is generated in the inner ear, the signal is transferred to and processed by a series of nuclei in the brain stem. Output from these nuclei is sent to a relay in the thalamus, the **medial geniculate nucleus**, or **MGN**. Finally, the MGN projects to **primary auditory cortex**, or **A1**, located in the temporal lobe. In one sense, the auditory pathway is more complex than the visual pathway because there are more intermediate stages between the sensory receptors and cortex. However, the systems have analogous components, including sensory receptors, early integration stages (which in the visual system are within the retina), a thalamic relay, and sensory cortex (Figure 11.4).

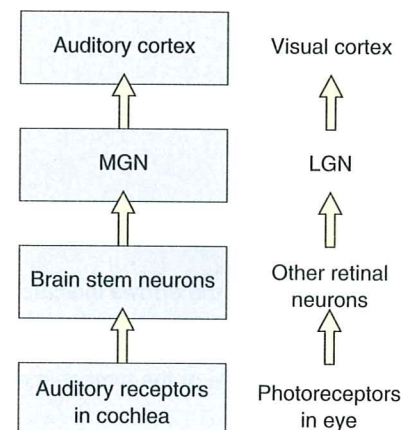
## THE MIDDLE EAR

The outer ear funnels sound to the middle ear, an air-filled cavity containing the first elements that move in response to sound. In the middle ear, variations in air pressure are converted into movements of the ossicles. In this section, we'll explore how this first transformation of sound energy occurs.

### Components of the Middle Ear

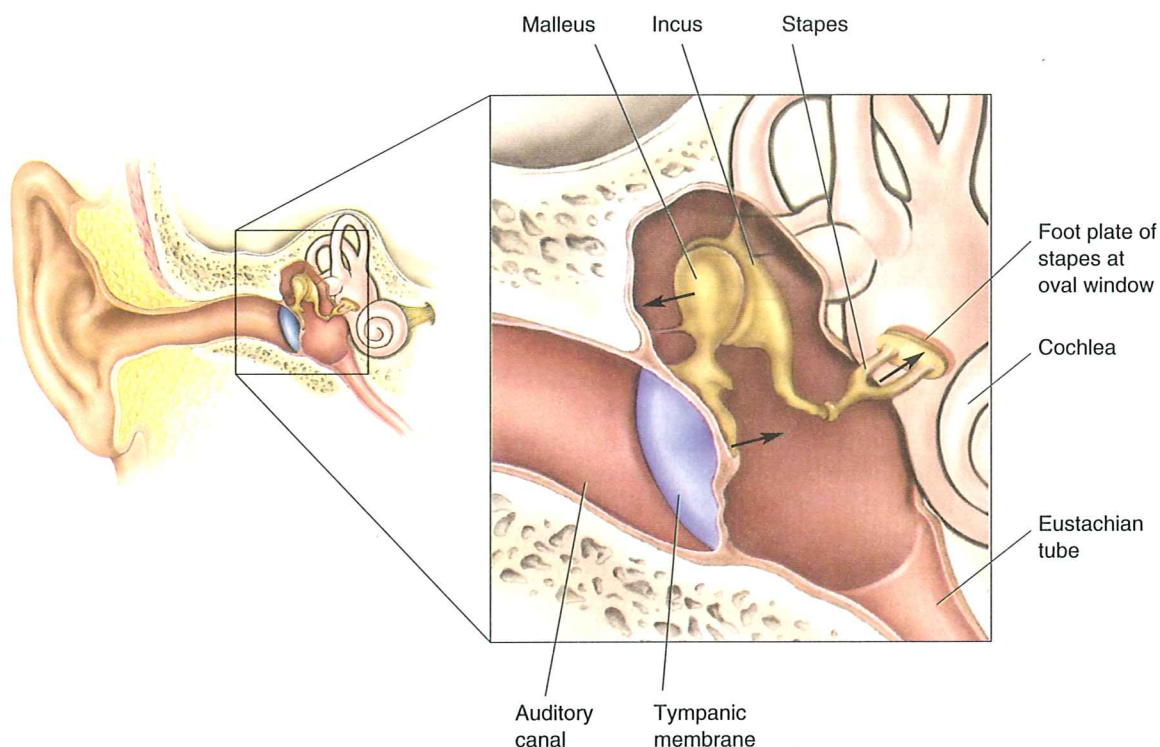
The structures within the middle ear are the tympanic membrane and the ossicles. The tympanic membrane is somewhat conical in shape, with the point of the cone extending into the cavity of the middle ear. There are three ossicles, each named (from the Latin) after an object it slightly resembles (Figure 11.5). The ossicle attached to the tympanic membrane is the **malleus** ("hammer"), which forms a rigid connection with the **incus** ("anvil"). The incus forms a flexible connection with the **stapes** ("stirrup"). The flat bottom portion of the stapes, the **footplate**, moves in and out like a piston at the oval window, thus transmitting sound vibrations to the fluids of the cochlea in the inner ear.

The air in the middle ear is continuous with that in the mouth via the **Eustachian tube**, although this tube is usually closed by a valve. When you're in an ascending airplane or a car heading up a mountain, the pressure of the surrounding air decreases. However, as long as the valve on the Eustachian tube is closed, the air in the middle ear is at the pressure of the air before you started to climb. As a result of the pressure inside the middle ear being higher than the air pressure outside, the tympanic membrane bulges out, and you experience unpleasant pressure or pain in the ear. The pain can be relieved by yawning or swallowing, either of which opens the Eustachian tube, thereby equalizing the air pressure in the middle ear with the ambient air pressure.



**Figure 11.4**  
**Auditory and visual pathways compared.** Following the sensory receptors, both systems have early integration stages, a thalamic relay, and a projection to neocortex.



**Figure 11.5**

**The middle ear.** As the arrows indicate, when the bottom of the malleus is pushed inward by the tympanic membrane, the lever action of the ossicles makes the footplate of the stapes push inward at the oval window. The pressure pushing at the oval window is greater than that at the tympanic membrane, in part because the surface area of the footplate of the stapes is smaller than the surface area of the tympanic membrane.

### Sound Force Amplification by the Ossicles

Sound waves move the tympanic membrane, and the ossicles move another membrane at the oval window. Why don't sound waves simply directly move the membrane at the oval window? The answer lies in the fact that the cochlea is filled with fluid, not air. If sound waves impinged directly on the oval window, the membrane would barely move, and most of the sound would be reflected because of the pressure the cochlear fluid exerts at the back of the oval window. If you've ever noticed how quiet it is under water, you know how well water reflects sound coming from above. Because the fluid in the inner ear resists being moved much more than air does (i.e., fluid has greater inertia), more pressure is needed to vibrate the fluid. The ossicles provide this necessary amplification in pressure.

To understand the process, consider the definition of pressure. The pressure on a membrane is defined as the force pushing it divided by its surface area. The pressure at the oval window can become greater than the pressure at the tympanic membrane if the force on the oval window membrane is greater than that on the tympanic membrane, or, conversely, if the surface area of the oval window is smaller than the area of the tympanic membrane. It turns out that the middle ear increases pressure at the oval window by altering both the force and the surface area. The force at the oval window is greater because the ossicles act like levers; a large movement of the tympanic membrane is transformed into a smaller but stronger movement of the oval window. And the surface area of the oval window is much smaller



than that of the tympanic membrane. These factors combine to make the pressure at the oval window about 20 times greater than that at the tympanic membrane, and this increase is sufficient to move the fluid in the inner ear.

## The Attenuation Reflex

Two muscles attached to the ossicles have a significant effect on sound transmission to the inner ear. The *tensor tympani muscle* is anchored to bone in the cavity of the middle ear at one end and attaches to the malleus at the other end. The *stapedius muscle* also extends from a fixed anchor of bone and attaches to the stapes. When these muscles contract, the chain of ossicles becomes much more rigid, and sound conductance to the inner ear is greatly diminished. The onset of a loud sound causes these muscles to contract, a response called the **attenuation reflex**. Sound attenuation is much greater at low frequencies than at high frequencies.

A number of functions have been proposed for this reflex. One function may be to adapt the ear to continuous sound at high intensities. Loud sounds that would otherwise saturate the response of the receptors in the inner ear could be reduced to a level below saturation by the attenuation reflex, thus increasing the dynamic range we can hear. The attenuation reflex also protects the inner ear from loud sounds that would otherwise damage it. Unfortunately, the reflex has a delay of 50–100 msec from the time that sound reaches the ear, so it doesn't offer much protection from very sudden loud sounds; damage might already be done by the time the muscles contract. This is why, despite the best efforts of your attenuation reflex, a loud explosion (or music on your Walkman) can still damage your cochlea. Because the attenuation reflex suppresses low frequencies more than high frequencies, it tends to make high-frequency sounds easier to discern in an environment with a lot of low-frequency noise. This capability enables us to understand speech more easily in a noisy environment than we could without the reflex. It is thought that the attenuation reflex is also activated when we speak, so we don't hear our own voices as loudly as we otherwise would.

## THE INNER EAR

Although considered part of the ear, not all of the inner ear is concerned with hearing. The inner ear consists of the cochlea, which is part of the auditory system, and the labyrinth, which is not. The labyrinth is an important part of the *vestibular apparatus*, which helps maintain the body's equilibrium (see Chapter 14). Here we are only concerned with the cochlea and the role it plays in transforming sound into a neural signal.

## Anatomy of the Cochlea

The cochlea (from the Latin for "snail") has a spiral shape resembling a snail's shell. One can approximate the structure of the cochlea by wrapping a drinking straw  $2\frac{1}{2}$  times around the sharpened tip of a pencil (Figure 11.6). In the cochlea, the hollow tube (represented by the straw) has walls made of bone. The central pillar of the cochlea (represented by the pencil) is a conical bony structure called the **modiolus**. The actual dimensions are smaller than the straw-and-pencil model, the cochlea's hollow tube being about 32 mm long and 2 mm in diameter. At the base of the cochlea there are two



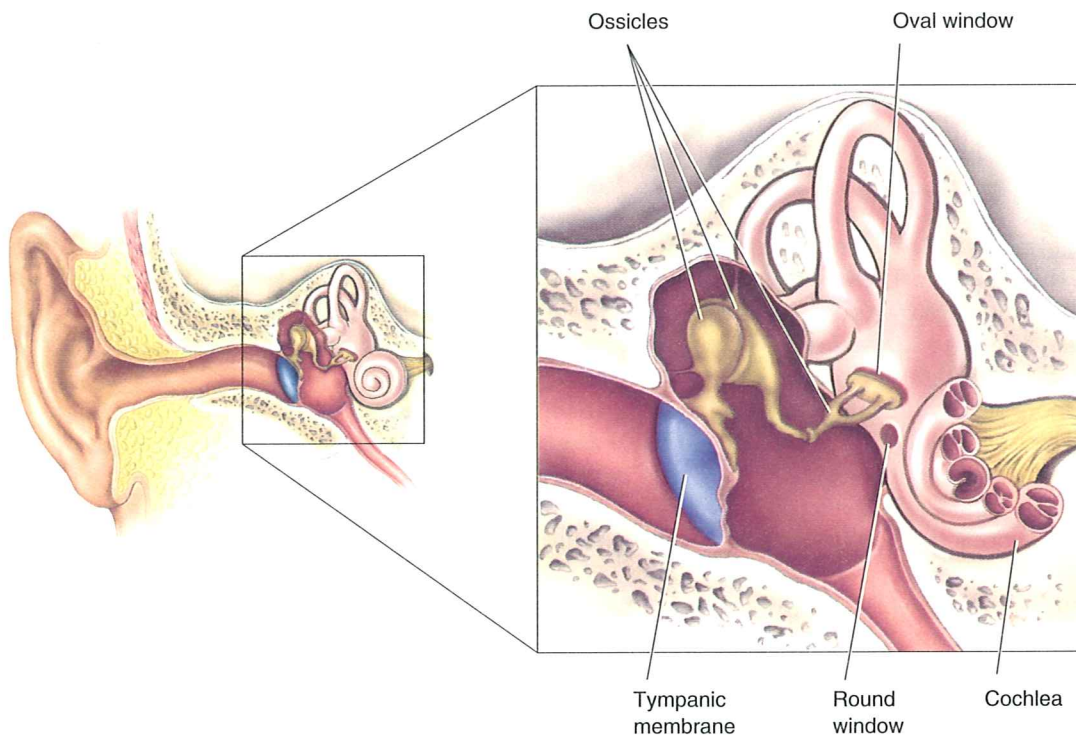


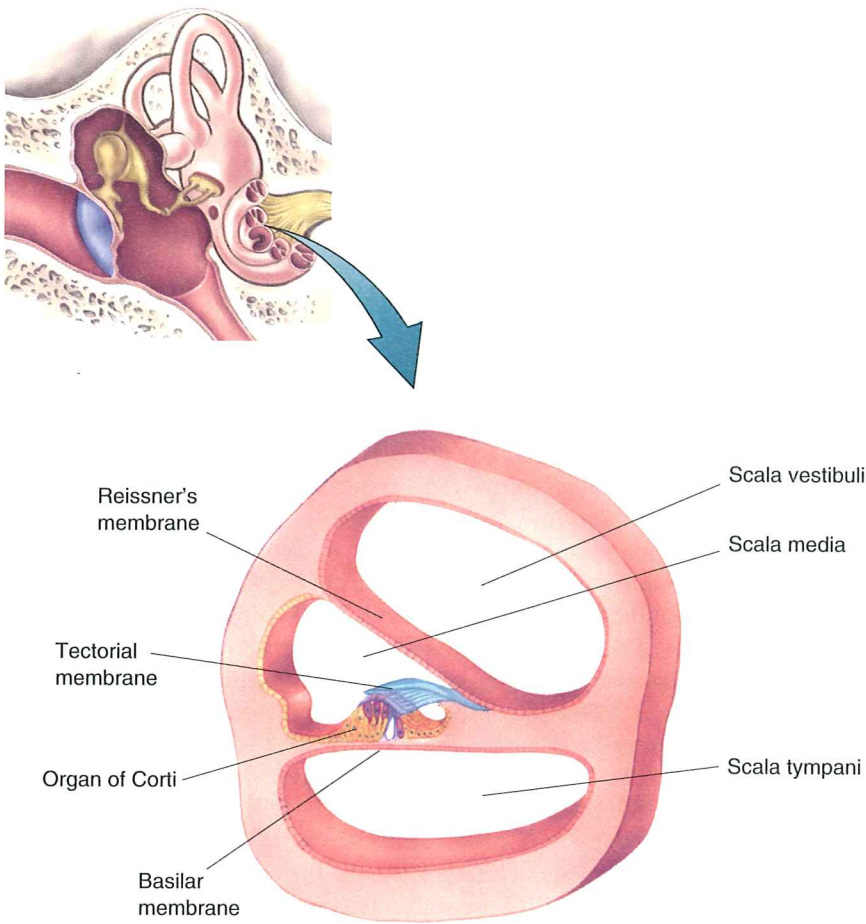
Figure 11.6  
The inner ear.

membrane-covered holes; the oval window, which as we have seen is below the footplate of the stapes, and the **round window**.

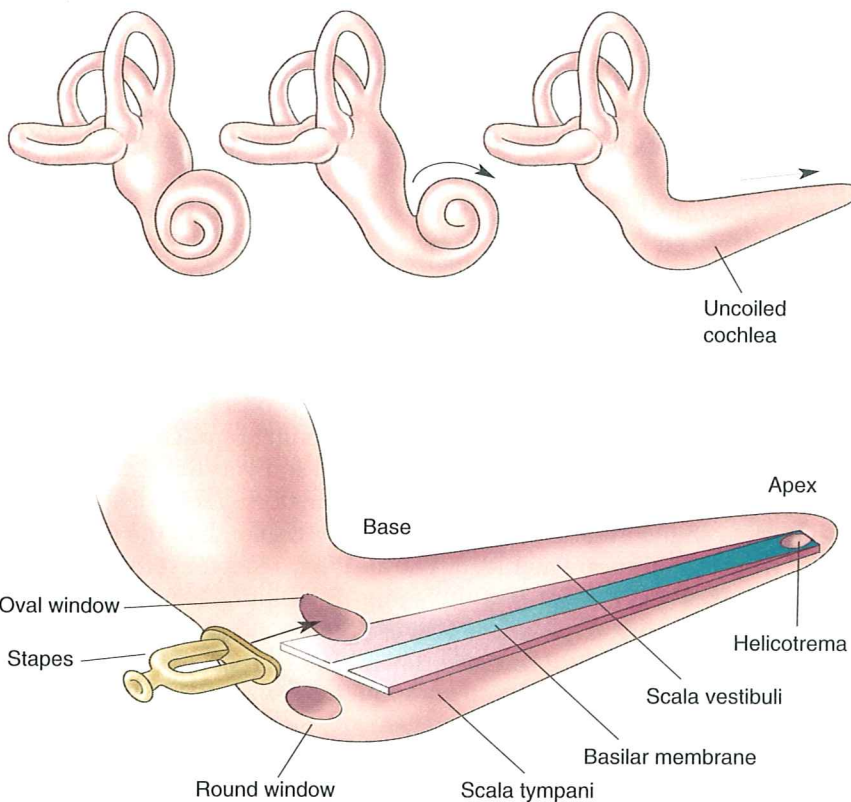
If the cochlea is cut in cross section, it can be seen that the tube is divided into three chambers: the **scala vestibuli**, the **scala media**, and the **scala tympani** (Figure 11.7). The three *scalae* wrap around inside the cochlea like a spiral stairway ("*scala*" is from the Latin for "stairway"). **Reissner's membrane** separates the scala vestibuli from the scala media, and the **basilar membrane** separates the scala tympani from the scala media. Sitting upon the basilar membrane is the **organ of Corti**, which contains auditory receptor neurons; hanging over this organ is the **tectorial membrane**. At the apex of the cochlea the scala media is closed off, and the scala tympani and scala vestibuli are connected by a hole in the membranes, the **helicotrema** (Figure 11.8). Consequently, the fluid in the scala vestibuli is continuous with that in the scala tympani. At the base of the cochlea, the scala vestibuli meets the oval window and the scala tympani meets the round window.

The fluid in the scala vestibuli and scala tympani, called **perilymph**, has an ionic content similar to that of cerebrospinal fluid: low  $K^+$  (7 mM) and high  $Na^+$  (140 mM) concentrations. The scala media is filled with **endolymph**, which is unusual in that it has ionic concentrations similar to intracellular fluid, high  $K^+$  (150 mM) and low  $Na^+$  (1 mM), even though it is extracellular. The explanation for this difference is that an active process taking place at the *stria vascularis* (the endothelium lining one wall of the scala media) reabsorbs sodium and secretes potassium against their concentration gradients. Because of the ionic concentration differences and the permeability of Reissner's membrane, the endolymph has an electrical potential that is about 80 mV more positive than that of the perilymph; this is called the **endocochlear potential**. We shall see that the endocochlear potential is important because it enhances auditory transduction.





**Figure 11.7**  
**Three parallel canals within the cochlea.** Viewed in cross section, the cochlea is seen to contain three smaller tubes running in parallel. These tubes, the *scala*e, are separated by Reissner's membrane and the basilar membrane. The organ of Corti contains the auditory receptors; it sits upon the basilar membrane and is covered by the tectorial membrane.



**Figure 11.8**  
**The basilar membrane in an uncoiled cochlea.** Although the cochlea narrows from base to apex, the basilar membrane widens toward the apex. The helicotrema is a hole at the apex of the basilar membrane, which connects the scala vestibuli and scala tympani.



## Physiology of the Cochlea

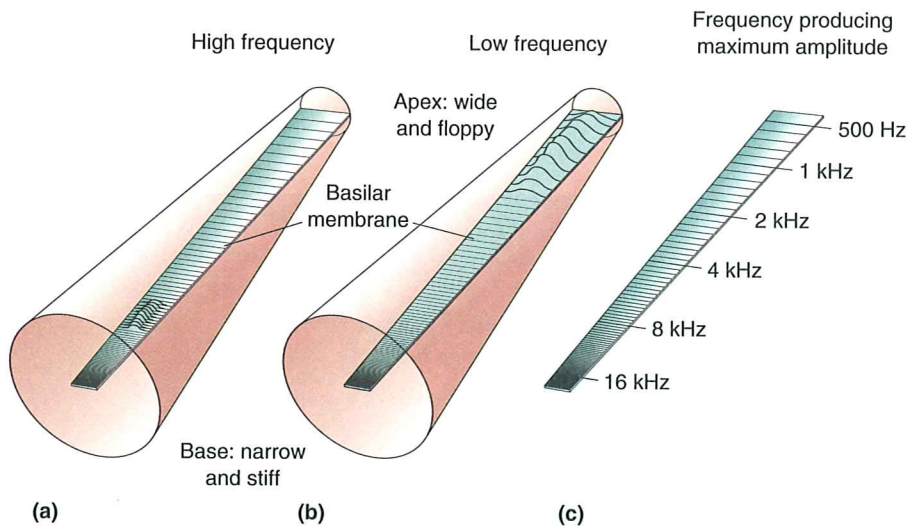
Despite its structural complexity, the basic operation of the inner ear is fairly simple. Look at Figure 11.8 and imagine what happens when the ossicles move the membrane that covers the oval window. Inward motion at the oval window pushes perilymph into the scala vestibuli. If the membranes inside the cochlea were completely rigid, then the increase in fluid pressure at the oval window would reach up the scala vestibuli, through the helicotrema, and back down the scala tympani to the round window. The membrane at the round window would bulge out in response to the inward movement of the membrane at the oval window. Although this isn't exactly what happens, the description conveys the very important point that any motion at the oval window must be accompanied by a complementary motion at the round window. Such movement must occur because the cochlea is filled with incompressible fluid held in a solid bony container. The consequence of pushing in at the oval window is a bit like pushing in one end of a tubular water balloon—the other end has to bulge out. The only reason the description of the events in the cochlea given above is not quite accurate is that the structures inside the cochlea are not rigid. Most importantly, the basilar membrane is flexible and bends in response to sound.

**Response of the Basilar Membrane to Sound.** The basilar membrane has two structural properties that determine the way it responds to sound. First, the membrane is wider at the apex than at the base by a factor of about 5. Second, the stiffness of the membrane decreases from base to apex, the base being about 100 times stiffer. Think of it as a flipper of the sort used for swimming, with a narrow, stiff base and a wide, floppy apex. When sound pushes the footplate of the stapes at the oval window, perilymph is displaced within the scala vestibuli, and endolymph is displaced within the scala media because Reissner's membrane is very flexible. We owe much of our understanding of the response of the basilar membrane to the research of Hungarian-American biophysicist Georg von Békésy. von Békésy determined that the movement of the endolymph makes the basilar membrane bend near its base, starting a wave that propagates toward the apex. The wave that travels up the basilar membrane is similar to the wave that runs along a rope if you hold one end in your hand and give it a snap. The distance the wave travels up the basilar membrane depends on the frequency of the sound. If the frequency is high, the stiffer base of the membrane will vibrate a good deal, dissipating most of the energy, and the wave will not propagate very far (Figure 11.9a). However, low-frequency sounds generate waves that travel all the way up to the floppy apex of the membrane before most of the energy is dissipated (Figure 11.9b). The response of the basilar membrane establishes a place code in which different locations of membrane are maximally deformed at different sound frequencies (Figure 11.9c). As we shall see, the differences in the traveling waves produced by different sound frequencies are responsible for the coding of pitch.

**The Organ of Corti and Associated Structures.** Everything we have discussed to this point involves the mechanical transformations of sound energy that occur in the middle and inner ear. Now we come to the point in the system where neurons are involved. The auditory receptor cells, which convert the mechanical energy into a change in membrane polarization, are located in the organ of Corti (named for the Italian anatomist who first identified it). The organ of Corti consists of hair cells, the rods of Corti, and various supporting cells.

The auditory receptors are called **hair cells** because each one has about 100 hairy-looking **stereocilia** extending from its top. The hair cells and stereocilia are shown in Figure 11.10 as they appear when viewed through



**Figure 11.9**

**Response of the basilar membrane to sound.** The cochlea is again shown uncoiled. (a) High-frequency sound produces a traveling wave, which dissipates near the narrow and stiff base of the basilar membrane. (b) Low-frequency sound produces a wave that propagates all the way to the apex of the basilar membrane before dissipating. The bending of the basilar membrane is greatly exaggerated for the purpose of illustration. (c) There is a place code on the basilar membrane for the frequency that produces the maximum amplitude deflection.

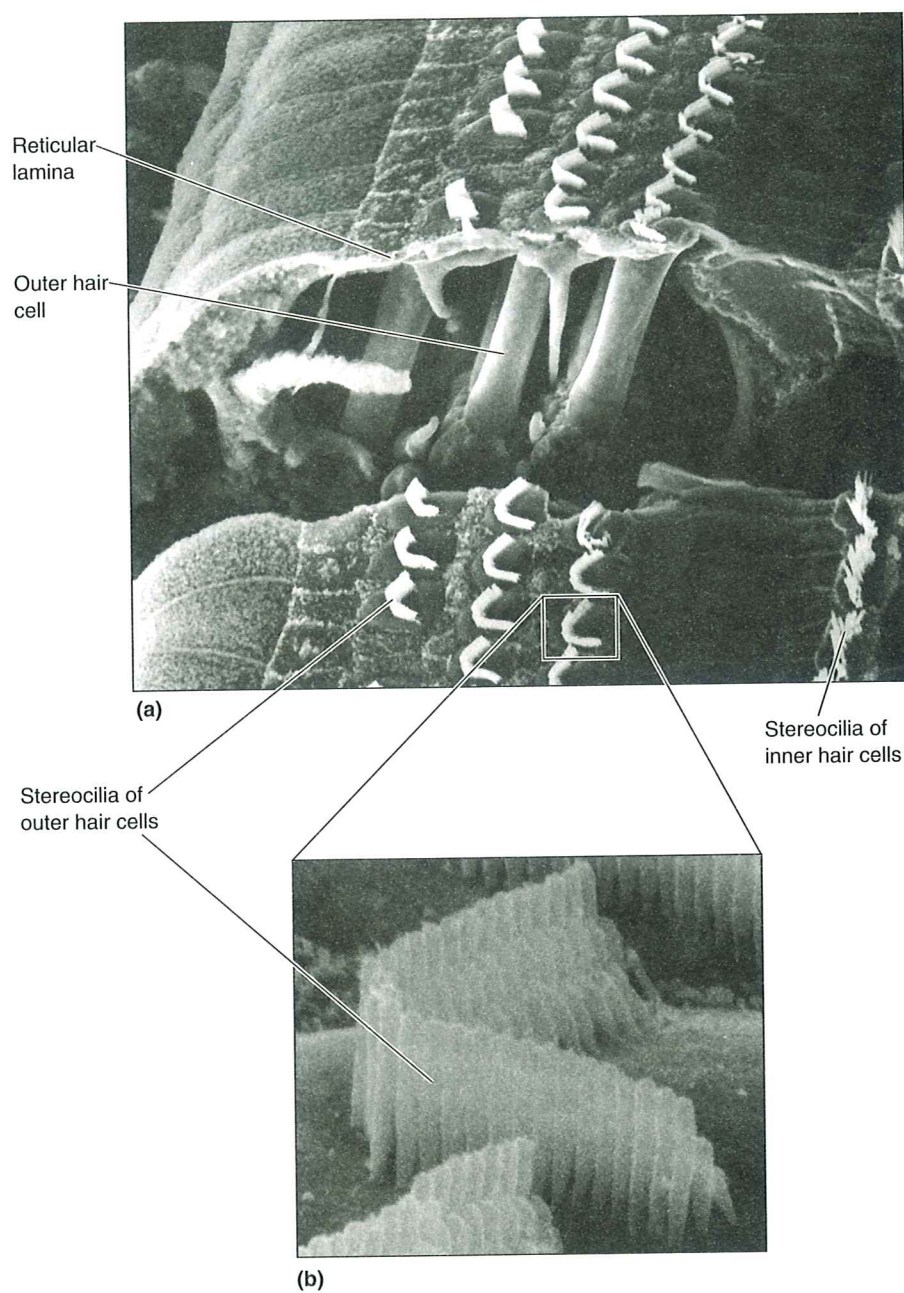
a scanning electron microscope. The critical event in the transduction of sound into a neural signal is the bending of these cilia. For this reason, we want to examine the organ of Corti in more detail to see how flexing of the basilar membrane leads to bending of the stereocilia.

The hair cells are sandwiched between the basilar membrane and a thin sheet of tissue called the **reticular lamina** (Figure 11.11). The *rods of Corti* span these two membranes and provide structural support. Hair cells between the modiolus and the rods of Corti are called **inner hair cells** (there are about 3500), and cells farther out than the rods of Corti are called **outer hair cells** (there are about 15,000–20,000 arranged in 3–5 rows). The stereocilia at the tops of the hair cells extend above the reticular lamina into the endolymph, and their tips end in the gelatinous substance of the tectorial membrane. To keep the membranes within the organ of Corti straight in your mind, remember that the *basilar* is at the *base* of the organ of Corti, the *tectorial* forms a *roof* over the structure, and the *reticular* is in the *middle*, holding onto the hair cells.

Hair cells form synapses on neurons whose cell bodies are located in the **spiral ganglion** within the modiolus. Spiral ganglion cells are bipolar, with neurites extending to the bases and sides of the hair cells, where they receive synaptic input. Axons from the spiral ganglion enter the **auditory nerve** (cranial nerve VIII), which projects to the cochlear nuclei in the medulla.

**Transduction by Hair Cells.** When the basilar membrane moves in response to a motion at the stapes, the entire foundation supporting the hair cells moves because the basilar membrane, rods of Corti, reticular lamina, and hair cells are all rigidly connected. These structures move as a unit, pivoting up toward the tectorial membrane or away from it. When the basilar membrane moves up, the reticular lamina moves up and in toward the modiolus. Conversely, downward motion of the basilar membrane causes the reticular lamina to move down and away from the modiolus. When the

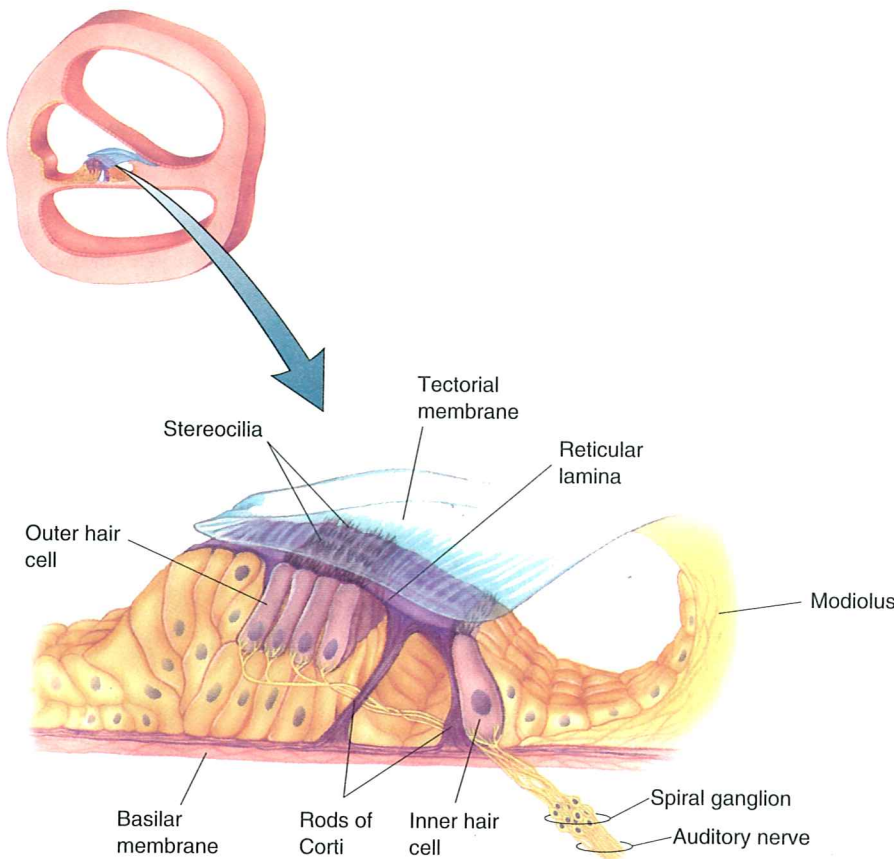




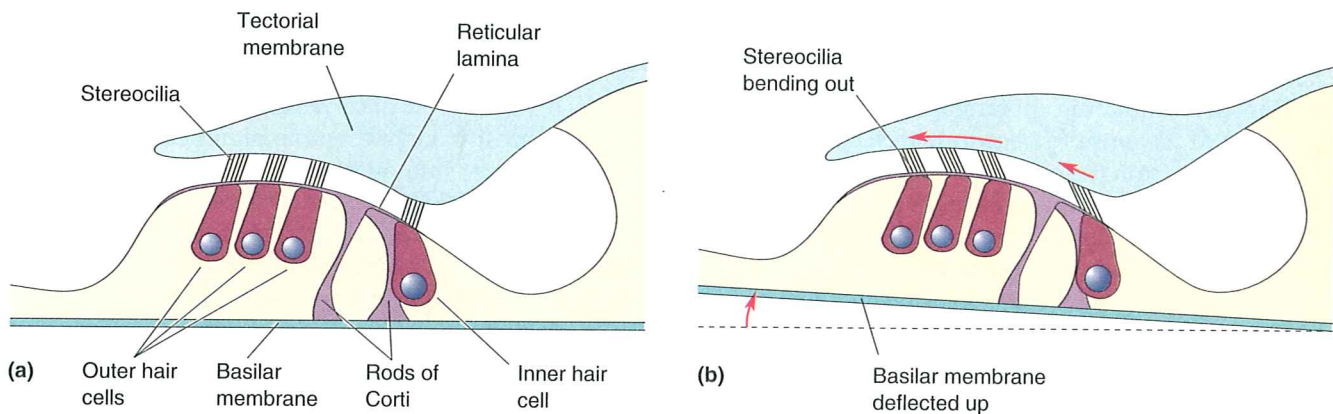
**Figure 11.10**

**Hair cells viewed through the scanning electron microscope. (a)** Hair cells and their stereocilia. **(b)** Higher resolution view of the stereocilia on an outer hair cell. The stereocilia are approximately 5  $\mu\text{m}$  in length. (Source: Courtesy of I. Hunter-Duvar and R. Harrison, The Hospital for Sick Children, Toronto, Ontario)





**Figure 11.11**  
The organ of Corti



**Figure 11.12**

**Bending of the stereocilia produced by upward motion of the basilar membrane.** (a) At rest, the hair cells are held between the reticular lamina and the basilar membrane, and the tips of the outer hair cell stereocilia are attached to the tectorial membrane. (b) When sound causes the basilar membrane to deflect upward, the reticular membrane moves up and inward toward the modiolus, causing the stereocilia to bend outward.

reticular lamina moves inward or outward relative to the modiolus, it also moves in or out with respect to the tectorial membrane. Because the tectorial membrane holds the tips of the hair cell stereocilia, the lateral motion of the reticular lamina relative to the tectorial membrane bends the stereocilia on the hair cells one way or the other (Figure 11.12). The stereocilia contain aligned actin filaments that make them stiff, so they bend as rigid rods. Cross-link filaments connect the stereocilia on each hair cell, making all the cilia on a hair cell move together as a unit.

Until recently, progress was slow in understanding how hair cells convert the mechanical deformation of stereocilia into neural signals. Because



the cochlea is encased in bone, it is quite difficult to record from the hair cells. In the 1980s, A. J. Hudspeth and his colleagues, now at the University of Texas, pioneered a new approach, in which hair cells are isolated from the inner ear and studied *in vitro* (Box 11.2). The *in vitro* technique has revealed much about the transduction mechanism. Recordings from hair cells indicate that when the stereocilia bend in one direction, the hair cell depolarizes, and when they bend in the other direction, the cell hyperpolarizes.

## Box 11.2 PATH OF DISCOVERY

### The Ear's Gears

by A. J. Hudspeth

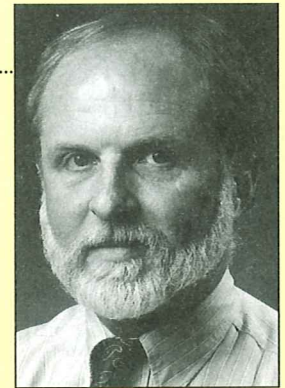
My research interest arose by accident. As graduate students, two colleagues and I were given the task of lecturing to the first-year medical class in neurobiology. This exercise was undoubtedly meant to build character, and incidentally freed the faculty from the necessity of lecturing on the three least palatable topics in neuroscience! We dutifully went about our preparation, then met to rehearse one another's talks. Although all the assigned subjects were challenging, the material on hearing and balance proved most opaque. We read that, in the darkness of the labyrinth, strangely named structures (basilar membranes, cupulae) performed arcane tasks, eliciting electrical signals of questionable significance (summing potentials, cochlear microphonics) in response to obscurely described stimuli. I came away from the experience with the conviction that the ear could not be as obscure as it seemed, that the unrivaled structural beauty of its cellular organization must reflect a comparable—if as yet unrevealed—precision of operation. I resolved to study how the internal ear's receptors, the hair cells, transduce mechanical stimuli into electrical responses.

The precedent of Theseus suggested that one should venture into a labyrinth only with due precautions. Indeed, the vestibular labyrinth's complexity, fragility, and position in the hardest bone of the body make experimentation on hair cells *in situ* very difficult. I therefore initiated a different approach, removing receptor organs from the internal ear and exploring the electrical responsiveness of their constituent hair cells *in vitro*. This strategy presented formidable problems. Isolating intact cells and maintaining them alive for hours was a challenge; stimulating and recording from such small cells was frustrating. It was especially difficult to achieve a mechanically stable experimental environment when working with cells sensitive to movements as small

as 0.3 nm, the diameter of a single atom. At the same time, though, experimentation with isolated hair cells offered important advantages. One could be certain from which cell a recording was made, and could employ a variety of extra- and intracellular recording techniques. Most importantly, the experimenter could confront a hair cell with stimuli of whatever amplitude, orientation, and timecourse he or she wished, without the necessity of dealing with the complex and incompletely understood mechanical and hydrodynamic properties of the intact ear.

Despite the differences between our various senses, all sensory receptors face similar challenges. Each such cell must transduce some significant form of stimulus energy into an electrical response that the nervous system can interpret. How can a receptor filter away irrelevant inputs and focus its attention on those of greatest behavioral importance? In order that the receptor organ be as sensitive as possible, the cell must detect the smallest possible amount of energy. How does the cell contrive to make such sensitive measurements without being overwhelmed by thermal, electrical, or other noise? The receptor must at the same time be able to adapt to maintained stimulation, so that its responsiveness is not impaired by large, maintained inputs. How can a receptor respond effectively to salient components of a stimulus, while ignoring background stimuli? These common demands are an important attraction of biophysical research on sensory transduction. Working in this field, one may attempt to understand how evolution has shaped a receptor to specific tasks that may be precisely defined in physical terms.

Some of the most important aspects of transduction by hair cells remain to be explored. The small



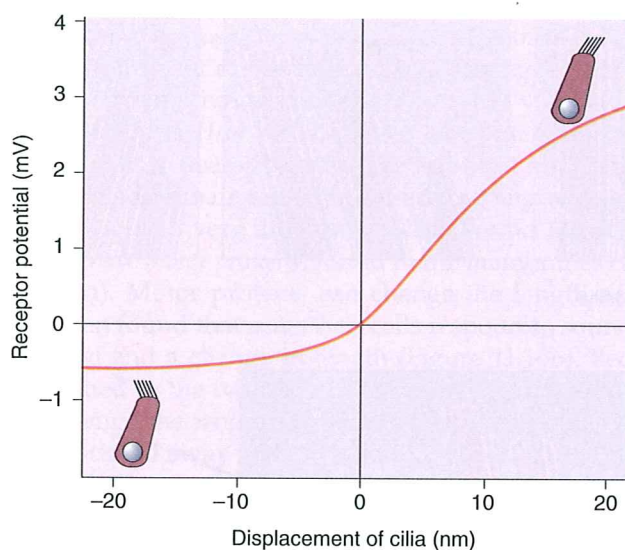
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Depolarization or hyperpolarization produced by bending of the stereocilia is the receptor potential, which is above or below the resting potential of  $-70$  mV (Figure 11.13).

These changes in cell potential result from the opening of potassium channels on the tips of the stereocilia. Figure 11.14 shows how these interesting channels are believed to function. Each channel is linked by an elastic filament to the wall of the adjacent cilium. When the cilia are straight, the tension on this filament holds the channel in a partially opened state, allowing a steady leak of  $K^+$  from the endolymph into the hair cell. Displacement of the cilia in one direction increases tension on the linking filament, increasing the inward  $K^+$  current. Displacement in the opposite direction relieves tension on the linking filament, thereby allowing the channel to



**Figure 11.13**

**Hair cell receptor potentials.** The hair cell depolarizes or hyperpolarizes depending on the direction in which the stereocilia bend. (Source: Adapted from Russel, Cody, and Richardson, 1986, Fig. 5.)

### Box 11.2

### PATH OF DISCOVERY

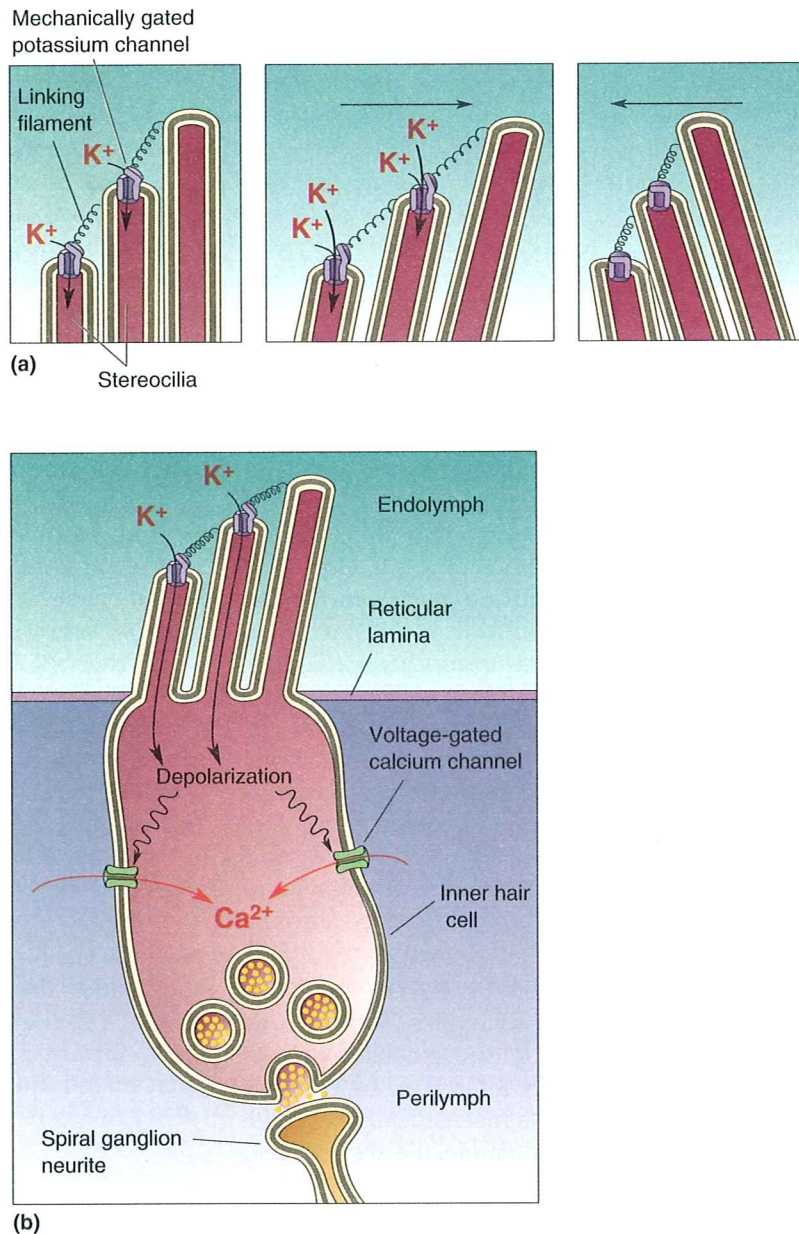
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number of cells in the internal ear has limited the application of biochemical techniques, so we know almost nothing about the molecular constituents of hair cells. It will be especially interesting to learn the structure of the hair bundle's mechanically sensitive ion channel, to see how that molecule responds to stimuli, and to ascertain whether it or a similar molecule subserves other forms of mechanoreceptivity—for example, touch. Perhaps the greatest challenge is understanding how the ear achieves its extraordinary sensitivity. Several lines of evidence suggest that hair cells are not just passive receptors of

mechanical stimuli, but that they are somehow capable of producing active motions that enhance the ear's inputs. The cochlear amplifier is so powerful that most human ears actually *produce* spontaneous tones that can be detected by a sensitive microphone placed in the ear canal! The contraction of electrically stimulated hair cells and the presence of myosin in hair bundles provide hints of mechanisms by which a hair cell could augment its mechanical inputs. It will be fascinating to learn not only how amplification occurs, but also how a hair cell regulates its amplifier so as to avoid instability.



close completely, preventing inward  $K^+$  movement. The entry of  $K^+$  into the hair cell causes a depolarization, which in turn activates voltage-gated calcium channels (Figure 11.14b). The entry of  $Ca^{2+}$  triggers the release of neurotransmitter, which activates the spiral ganglion fibers lying postsynaptic to the hair cell. It is interesting that the opening of  $K^+$  channels produces a depolarization in the hair cell, whereas the opening of  $K^+$  channels *hyperpolarizes* most neurons. The reason that hair cells respond differently from neurons is the unusually high  $K^+$  concentration in endolymph, which yields a  $K^+$  equilibrium potential of 0 mV compared to the equilibrium potential of -80 mV in typical neurons.



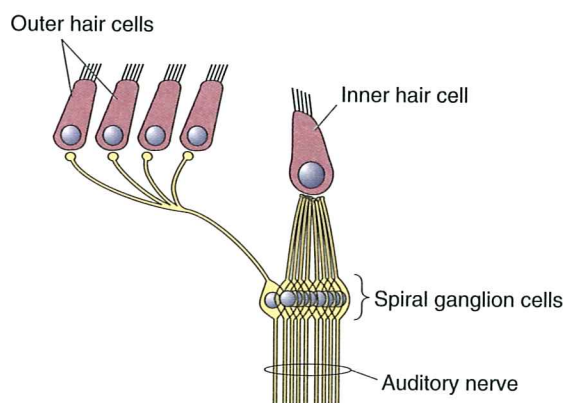
**Figure 11.14**

**Depolarization of a hair cell.** (a) Potassium channels are opened when the linking filaments joining the stereocilia are stretched. (b) Entry of potassium depolarizes the hair cell, which opens voltage-gated  $Ca^{2+}$  channels. Incoming calcium further depolarizes the cell, leading to the release of synaptic vesicles to the postsynaptic neurite from the spiral ganglion.

**The Innervation of Hair Cells.** The auditory nerve consists of the axons of neurons whose cell bodies are located in the spiral ganglion. Thus, the spiral ganglion neurons, which are the first in the auditory pathway to fire action potentials, provide all the auditory information sent to the brain. For this reason, it is important to note that there is a significant difference in the spiral ganglion innervation of the inner and outer hair cells. It is estimated that the number of neurons in the spiral ganglion is in the range of 35,000–50,000. Despite the fact that inner hair cells are outnumbered by outer hair cells by a factor of 5 to 1, more than 95% of the spiral ganglion neurons communicate with the relatively small number of inner hair cells, and less than 5% receive synaptic input from the more numerous outer hair cells (Figure 11.15). Consequently, one spiral ganglion fiber receives input from only one inner hair cell; each inner hair cell feeds about 10 spiral ganglion neurites. The situation is the opposite with outer hair cells. Because they outnumber their spiral ganglion cells, an individual spiral ganglion fiber synapses with numerous outer hair cells. Simply based on these numbers, we can infer that most of the information leaving the cochlea comes from the responses of inner hair cells.

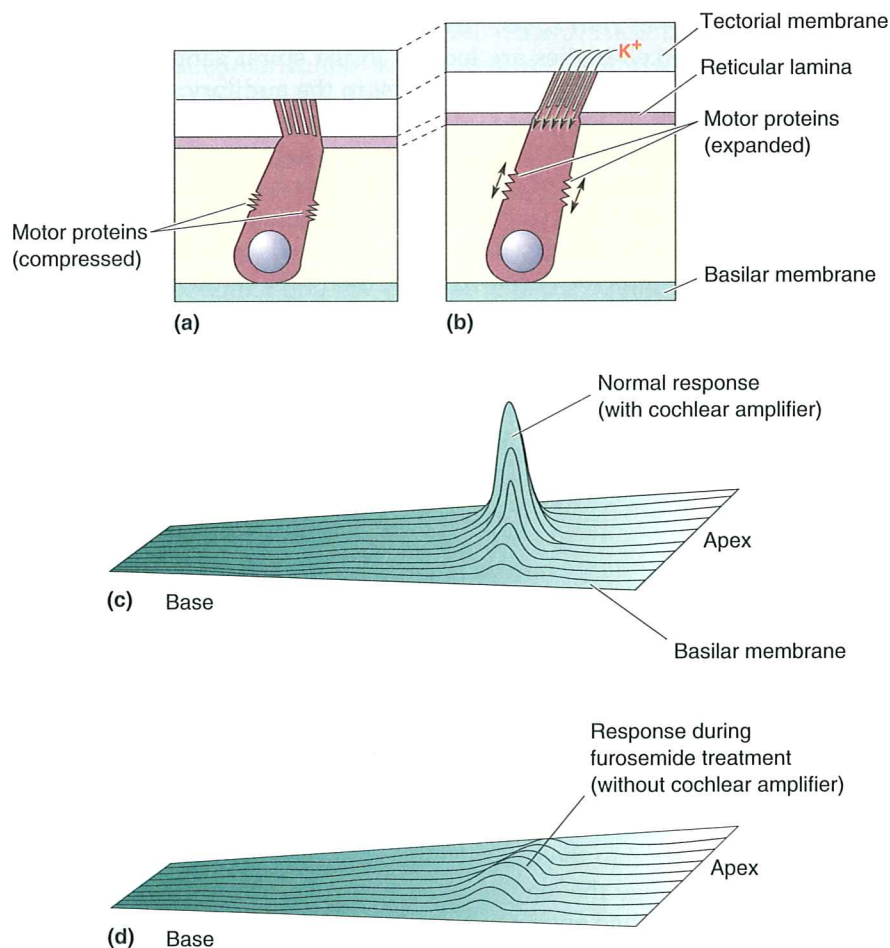
**Amplification by Outer Hair Cells.** Given that outer hair cells far outnumber inner hair cells, it seems paradoxical that most of the cochlear output is derived from inner hair cells. However, ongoing research suggests that outer hair cells play a very important role in sound transduction. The key to this function are *motor proteins*, found in the membranes of outer hair cells (Figure 11.16a). Motor proteins can change the length of outer hair cells, and it has been found that outer hair cells respond to sound with both a receptor potential and a change in length (Figure 11.16b). Because outer hair cells are attached to the basilar membrane and reticular lamina, when motor proteins change the length of the hair cell, the basilar membrane is pulled toward or pushed away from the reticular lamina and tectorial membrane. This is why the word *motor* is used—the outer hair cells actively change the physical relationship between the cochlear membranes.

The motor effect of outer hair cells makes a significant contribution to the traveling wave that propagates down the basilar membrane. This was demonstrated in 1991 by Mario Ruggero and Nola Rich at the University of Minnesota, who administered the chemical furosemide into experimental animals. Furosemide temporarily decreases the transduction that normally results from the bending of stereocilia on hair cells and it was found to significantly reduce the movement of the basilar membrane in response to sound (Figure 11.16 c, d). Reduction in the movement of the basilar membrane



**Figure 11.15**  
Innervation of hair cells by neurons from the spiral ganglion.



**Figure 11.16**

**Amplification by outer hair cells.** (a) Motor proteins in the membranes of outer hair cells. (b) When potassium enters the hair cell, motor proteins are activated and lengthen the hair cell. (c) The conformational change of the hair cell increases the bending of the basilar membrane and is therefore called cochlear amplification. (d) Furosemide decreases hair cell transduction, consequently reducing the bending of the basilar membrane. (Source: Adapted from Ashmore and Kolston, 1994, Fig. 2, 3.)

produced by furosemide is believed to result specifically from inactivation of the outer hair cell motor proteins. For this reason, it is sometimes said that the outer hair cells constitute a **cochlear amplifier**. When the outer hair cells amplify the response of the basilar membrane, the stereocilia on the inner hair cells will bend more, and the increased transduction process in the inner hair cells will produce a greater response in the auditory nerve. Through this feedback system, therefore, outer hair cells contribute significantly to the output of the cochlea. (In some situations, the cochlear amplifier can also produce sounds of its own; see Box 11.4.)

The effect of outer hair cells on the response of inner hair cells can also be influenced by neurons outside the cochlea. In addition to the spiral ganglion afferents that project from the cochlea to the brain stem, there also are about 1000 efferent fibers projecting *from* the brain stem *toward* the cochlea. These efferents diverge widely, synapsing onto outer hair cells. Stimulation of these efferents changes the shape of the outer hair cells, and, as we've already discussed, this affects the responses of inner hair cells. In this way, descending input from the brain to the cochlea can regulate auditory sensitivity.

The amplifying effect of outer hair cells explains how certain antibiotics (e.g., kanamycin) that damage hair cells can lead to deafness. After excessive exposure to antibiotics, the responses to sound of many inner hair cells

are reduced. However, the antibiotic almost exclusively damages outer hair cells, not inner hair cells! For this reason, deafness produced by antibiotics is thought to be a consequence of damage to the cochlear amplifier (i.e., outer hair cells), demonstrating just how essential this amplifier is.

## CENTRAL AUDITORY PROCESSES

Because there are more synapses at nuclei intermediate between the sensory organ and the cortex, the auditory pathway appears more complex than the visual pathway. Also, in contrast to the visual system, there are many more alternative pathways by which signals can get from one nucleus to the next. Nonetheless, the amount of information processing in the two systems is not that different when you consider that the cells and synapses of the auditory system in the brain stem are analogous to interactions in the layers of the retina. We will now look at auditory circuitry, focusing on the transformations of auditory information that occur along the way.

### Anatomy of Auditory Pathways

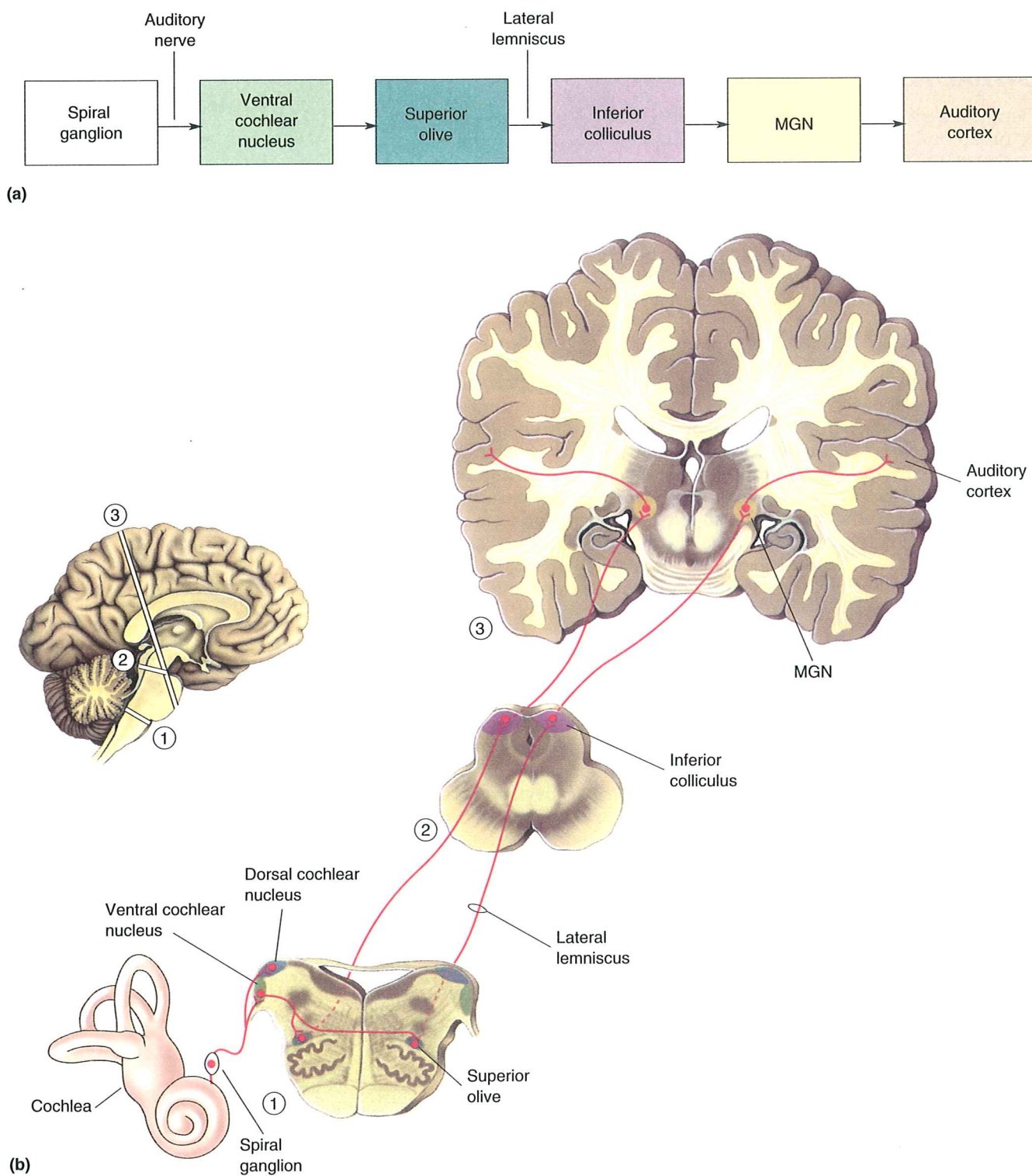
Afferents from the spiral ganglion enter the brain stem in the auditory nerve. At the level of the medulla, the axons innervate the **dorsal cochlear nucleus** and **ventral cochlear nucleus** ipsilateral to the cochlea where the axons originated. Each axon branches so that it synapses on neurons in both cochlear nuclei. From this point on, the system gets more complicated, and the connections are less well understood, because there are multiple pathways. Rather than trying to describe all of these connections, we will follow one pathway from the cochlear nuclei to auditory cortex (Figure 11.17). Cells in the ventral cochlear nucleus send out axons that project to the **superior olive** (also called the superior olivary nucleus) on both sides of the brain stem. Axons of the olivary neurons ascend in the *lateral lemniscus* (a lemniscus is a collection of axons) and innervate the **inferior colliculus** of the midbrain. Many efferents of the dorsal cochlear nucleus follow a similar route as the pathway from the ventral cochlear nucleus, but the dorsal path bypasses the superior olive. Although there are other routes from the cochlear nuclei to the inferior colliculus, with additional intermediate relays, *all ascending auditory pathways converge onto the inferior colliculus*. The neurons in the colliculus send out axons to the medial geniculate nucleus (MGN) of the thalamus, which in turn projects to auditory cortex.

Before moving on to the response properties of auditory neurons, we should make several points. (1) As we have said, there are projections and brain stem nuclei, other than the ones described, that contribute to the auditory pathways. For instance, the inferior colliculus sends axons not only to the MGN but also to the superior colliculus (where integration of auditory and visual information occurs) and to the cerebellum. (2) There is extensive feedback in the auditory pathways. For instance, the brain stem neurons send axons that contact outer hair cells, and auditory cortex sends axons to the MGN and inferior colliculus. (3) It is important to note that, other than the cochlear nuclei, auditory nuclei in the brain stem receive input from both ears. This explains the clinically important fact that the only way in which brain stem damage can produce deafness in one ear is if the cochlear nuclei (or auditory nerve) on one side are destroyed.

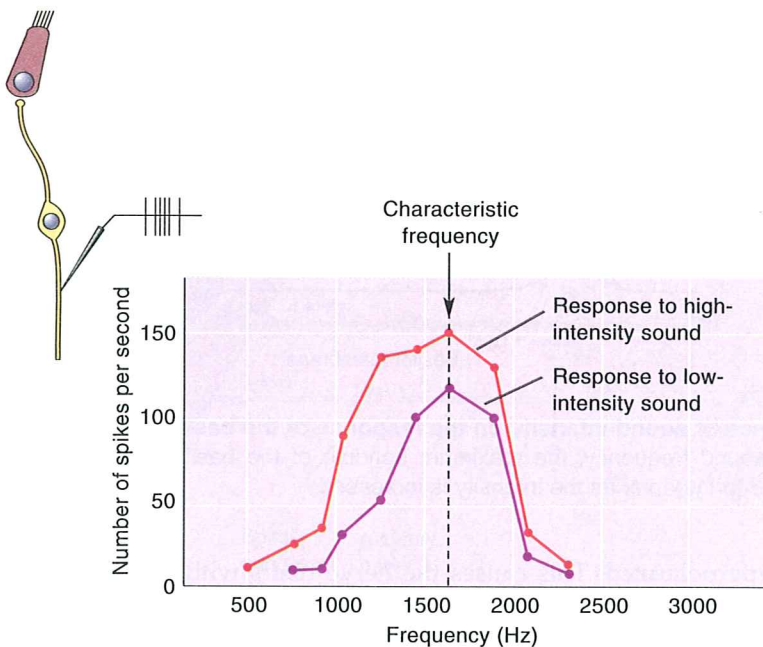
### Response Properties of Neurons in the Auditory Pathway

To understand the transformations of auditory signals that occur in the brain stem, we must first consider the nature of the input from the neurons in the spiral ganglion of the cochlea. Because most spiral ganglion cells receive input from a single inner hair cell at a particular location on the basilar membrane, they fire action potentials only in response to sound within a limited frequency range. After all, hair cells are excited by deformations of the basilar membrane, and each portion of the membrane is maximally sen-



**Figure 11.17**

**Auditory pathways.** There are numerous paths by which neural signals can travel from the spiral ganglion to auditory cortex. A primary pathway is shown (a) schematically and (b) through brain stem cross sections.

**Figure 11.18**

**Response of an auditory nerve fiber to different sound frequencies.** This neuron is frequency tuned and has greatest response at the characteristic frequency. (Source: Adapted from Rose, Hind, Anderson, and Brugge, 1971, Fig. 2.)

sitive to a particular range of frequencies. Figure 11.18 shows the results of an experiment in which action potentials were recorded from a single auditory nerve fiber (i.e., the axon of a spiral ganglion cell). The graph represents the firing rate in response to sounds at different frequencies. The neuron is most responsive to sound at one frequency, called the neuron's **characteristic frequency**, and it is less responsive at neighboring frequencies. This type of frequency tuning is typical of neurons at each of the relays from cochlea to cortex.

As one ascends the auditory pathway in the brain stem, the response properties of the cells become more diverse and complex, just as in the visual pathway. For instance, some cells in the cochlear nuclei are especially sensitive to sounds varying in frequency with time. In the MGN there are cells that respond to fairly complex sounds such as vocalizations, as well as other cells that show simple frequency selectivity as in the auditory nerve. An important development in the superior olive is that cells receive input from cochlear nuclei on both sides of the brain stem. As discussed below, such binaural neurons are probably important for sound localization.

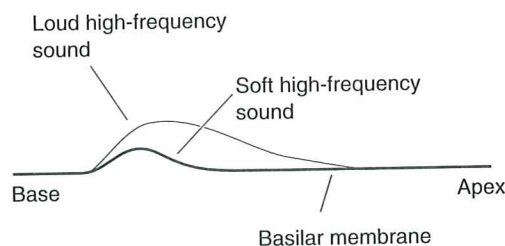
## ENCODING SOUND INTENSITY AND FREQUENCY

If you stop reading this book for a moment, you can focus on the many sounds around you. You can hear sounds you might have been ignoring, and you can selectively pay attention to different sounds occurring at the same time. There is truly an incredible diversity—from chattering people to cars to the radio to electrical noises. We cannot yet account for the perception of each of these sounds by pointing to particular neurons in the brain. However, most sounds have certain features in common, including intensity, frequency, and a location from which they emanate. Each of these features is represented in a different manner in the auditory pathway.

### Stimulus Intensity

Information about sound intensity is coded in two interrelated ways: the firing rates of neurons and the number of active neurons. As a stimulus gets more intense, the basilar membrane vibrates with greater amplitude, causing the membrane potential of the activated hair cells to be more depolar-



**Figure 11.19**

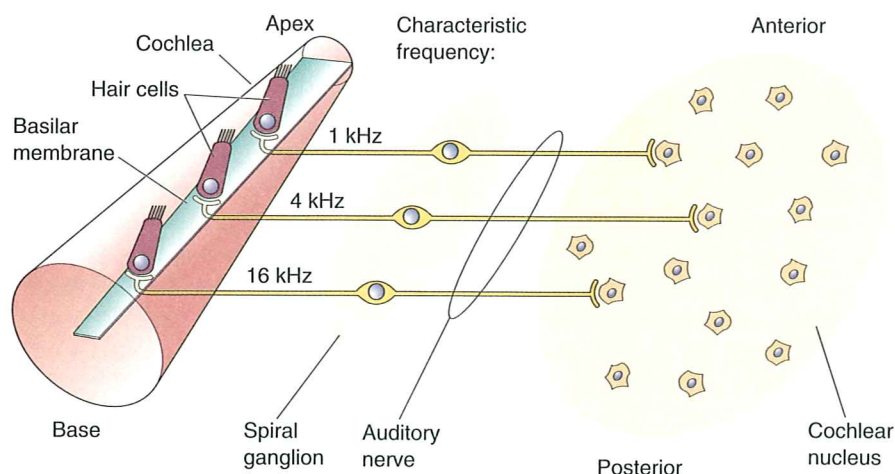
**The influence of sound intensity on the response of the basilar membrane.** At the same sound frequency, the maximum bending of the basilar membrane will occur closer to the apex as the intensity is increased.

ized or hyperpolarized. This causes the nerve fibers with which the hair cells synapse to fire action potentials at greater rates. In Figure 11.18, the auditory nerve fiber fires faster to the same sound frequencies when the intensity is increased. In addition, more intense stimuli produce movements of the basilar membrane over a greater distance (Figure 11.19), which leads to hair cell activation over a larger area. In a single auditory nerve fiber, this increase in the number of activated hair cells is seen as a broadening of the frequency range to which the fiber responds. The number of active neurons in the auditory nerve (and throughout the auditory pathway), and their firing rates, are thought to be the neural correlates of perceived loudness.

### Stimulus Frequency and Tonotopy

As already discussed, from the hair cells in the cochlea through the various nuclei leading to auditory cortex, most neurons are sensitive to stimulus frequency and are most sensitive at the characteristic frequency. This sensitivity is largely a consequence of the mechanics of the basilar membrane because different portions of the membrane are maximally deformed by sound of different frequencies. Moving from the base to the apex of the cochlea, there is a progressive decrease in the frequency that produces a maximal deformation of the basilar membrane. There is a corresponding representation of frequency in the auditory nerve; auditory nerve fibers connected to hair cells near the apical basilar membrane have low characteristic frequencies and those connected to hair cells near the basal basilar membrane have high characteristic frequencies (Figure 11.20). When neurons in the auditory nerve synapse in the cochlear nuclei, they do so based on characteristic frequency. Nearby neurons have similar characteristic frequencies, and there is a systematic relationship between position in the cochlear nucleus and characteristic frequency. In other words, there is a map of the basilar membrane within the cochlear nuclei. Systematic organization within an auditory structure based on characteristic frequency is called **tonotopy**, and it is analogous to retinotopy in the visual system. There are tonotopic maps within each of the auditory nerve relay nuclei, the MGN, and auditory cortex.

Because of the tonotopy present throughout the auditory system, the location of active neurons in auditory nuclei is one indication of the frequency of the sound. However, there are two reasons why frequency must be coded in some way other than the site of maximal activation in tonotopic maps. One reason is that these maps do not contain neurons with very low characteristic frequencies, below about 200 Hz. As a result, the site of maximal activation might be the same for a 50 Hz tone as for a 200 Hz tone, so there must be some other way to distinguish them. The second reason that

**Figure 11.20**

**Tonotopic maps on the basilar membrane and cochlear nucleus.** Going from the base to the apex of the cochlea, the basilar membrane resonates with increasingly lower frequencies. This tonotopy is preserved in the auditory nerve and cochlear nucleus. In the cochlear nucleus, there are bands of cells with similar characteristic frequencies; characteristic frequencies increase progressively from posterior to anterior.

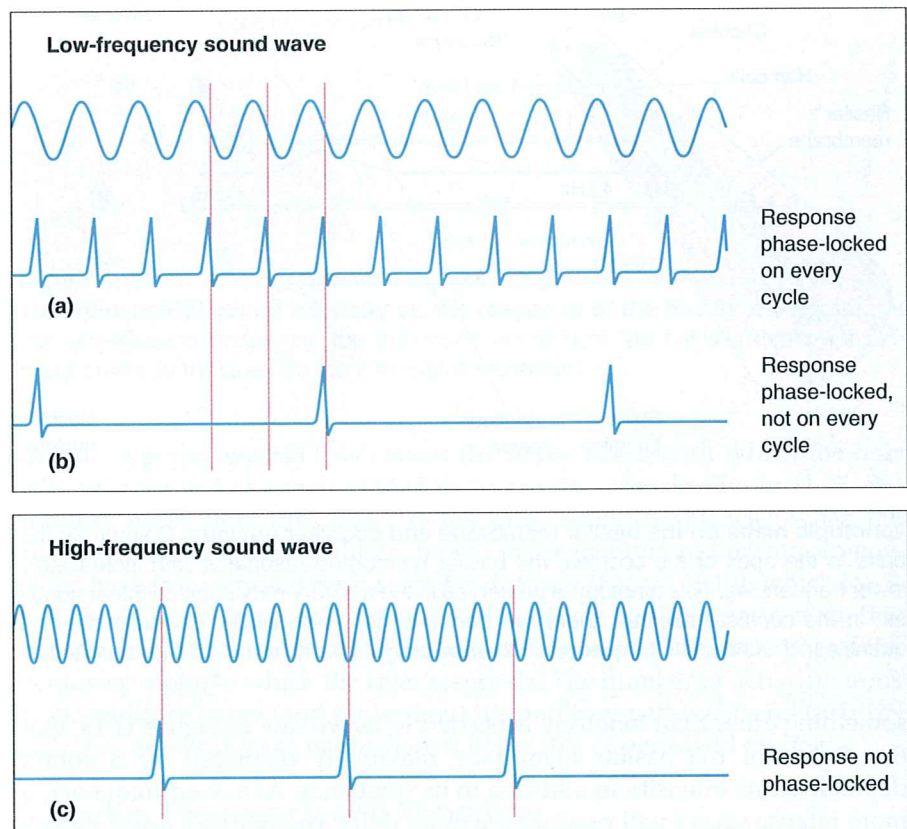
something other than tonotopy is needed is, as we saw in Figure 11.19, that the region of the basilar membrane maximally displaced by a sound depends on its intensity in addition to its frequency. At a fixed frequency, a more intense sound will produce a maximal deformation at a point further up the basilar membrane than a less intense sound.

The main source of information about sound frequency that complements information derived from tonotopic maps is the timing of neural firing. Recordings made from neurons in the auditory nerve show **phase locking**, the consistent firing of a cell at the same phase of a sound wave (Figure 11.21). If you think of a sound wave as a sinusoidal variation in air pressure, a phase-locked neuron would fire action potentials at either the peaks, the troughs, or some other constant location on the wave. At low frequencies, some neurons fire action potentials every time the sound has a particular phase (Figure 11.21a). This makes it easy to determine the frequency of the sound; it is the same as the frequency of the neuron's action potentials.

It is important to realize that there can be phase locking even if an action potential has not fired on every cycle (Figure 11.21b). For instance, a neuron may have a response phase-locked to a 1000 Hz sound in such a way that an action potential fires on perhaps 25% of the cycles of the input. If you have a group of such neurons, each responding to different cycles of the input signal, it is possible to have a response to every cycle (by some member of the group) and thus a measure of sound frequency. The idea that intermediate frequencies are represented in the pooled activity of a number of neurons, each of which fires in a phase-locked manner, is called the **volley principle**. Phase locking occurs with sound waves up to about 4 kHz. Above this point, the action potentials fired by a neuron are at random phases of the sound wave (Figure 11.21c) because the intrinsic variability in the timing of the action potential becomes comparable to the time interval between successive cycles of the sound.

To summarize, here is how different frequencies are represented. At very low frequencies, phase locking is used; at intermediate frequencies, both phase locking and tonotopy are useful; and at high frequencies, tonotopy must be relied on to indicate sound frequency.



**Figure 11.21**

**Phase locking in the response of auditory nerve fibers.** Sound at a low frequency can elicit a phase-locked response, either (a) on every cycle of the stimulus or (b) on some fraction of the cycles. At high frequencies, (c) the response does not have a fixed phase relationship to the stimulus.

## MECHANISMS OF SOUND LOCALIZATION

While the use of frequency information is essential for interpreting sounds in our environment, sound localization can be of critical importance for survival. If a predator is about to eat you, finding the source of a sudden sound and running away are much more important than analyzing the subtleties of the sound. Humans are not eaten by wild animals much anymore, but there are other situations in which sound localization can save your life. If you carelessly try to cross the street, your localization of a car's horn may be all that saves you. Our current understanding of the mechanisms underlying sound localization suggests that we use different techniques for locating sources in the horizontal plane (left–right) and vertical plane (up–down).

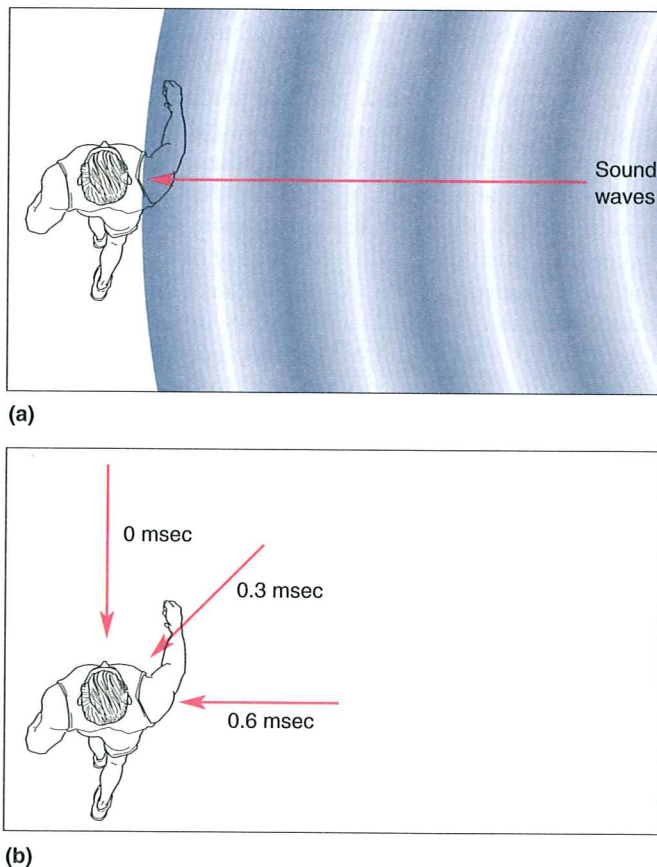
If you close your eyes and plug one ear, you can locate a bird singing as it flies overhead almost as well as with both ears open. But if you try to locate the horizontal position of a duck quacking as it swims across a pond, you'll find that you're much less able using only one ear. Thus, good horizontal localization requires a comparison of the sounds reaching the two ears, whereas good vertical localization does not.

### Localization of Sound in the Horizontal Plane

Perhaps the most obvious cue to the location of a sound source is the time at which the sound arrives at each ear. We have two ears, and if we aren't

facing a source directly, it will take the sound longer to reach one ear than the other. For instance, if a sudden noise comes at you from the right, it will reach your right ear first (Figure 11.22a); it will arrive at your left ear later, after what is known as an *interaural time delay*. If the distance between your ears is 20 cm, sound coming from the right, perpendicular to your head, will reach your left ear 0.6 msec after reaching your right ear. If the sound comes from straight ahead, there will be no interaural delay; and at angles between straight ahead and perpendicular, the delay will be between 0 and 0.6 msec (Figure 11.22b). Thus, there is a simple relationship between location and interaural delay. Detected by specialized neurons in the brain stem, the delay enables us to locate the source of the sound.

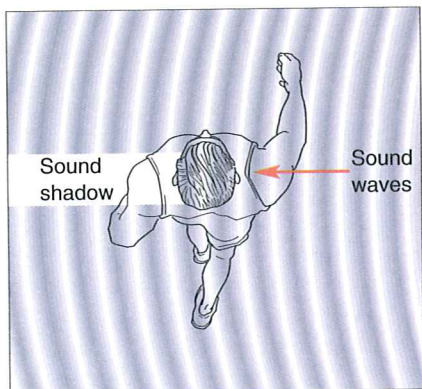
If we don't hear the onset of a sound because it is a continuous tone rather than a sudden noise, we cannot know the initial arrival times of the sound at the two ears. Thus, continuous tones pose more of a problem for sound localization because they are always present at both ears. We can still use arrival time to localize the sound but in a slightly different manner from localizing a sudden sound. The only thing that can be compared between continuous tones is the time at which the same *phase* of the sound wave reaches each ear. Imagine you are exposed to a 200 Hz sound coming from the right. At this frequency, one cycle of the sound covers 172 cm, which is much more than the 20 cm distance between your ears. After a peak in the sound wave passes the right ear, you must wait 0.6 msec, the time it takes



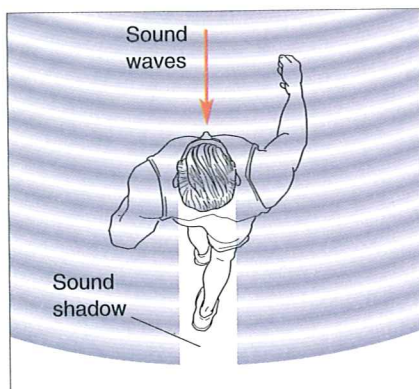
**Figure 11.22**

**Interaural time delay as a cue to the location of sound.** (a) Sound waves coming from the right side will reach the right ear first, and there will be a large interaural delay before the sound propagates to the left ear. (b) If the sound comes from straight ahead, there is no interaural delay. Delays for three different sound directions are shown.

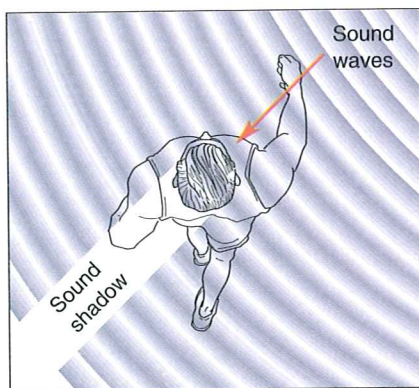




(a)



(b)



(c)

**Figure 11.23**

**Interaural intensity difference as a cue to sound location.** (a) With high-frequency sound, the head will cast a sound shadow to the left, when sound waves come from the right. Lower-intensity sound in the left ear is a cue that the sound came from the right. (b) If the sound comes from straight ahead, a sound shadow is cast behind the head but the sound reaches the two ears with the same intensity. (c) Sound coming from an oblique angle will partially shadow the left ear.

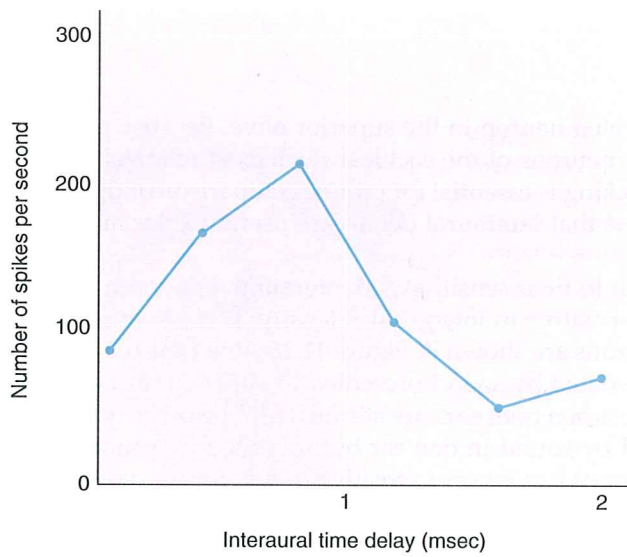
sound to travel 20 cm, before detecting a peak at the left ear. Of course, if the sound is straight ahead, peaks in the continuous tone will reach the ears simultaneously. Because the sound wave is much longer than the distance between the ears, we can reliably use the interaural delay of the peak in the wave to determine sound location.

However, things are more complicated with continuous tones at high frequencies. Suppose that the sound coming from the right now has a frequency of 20,000 Hz, which means that one cycle of the sound covers 1.7 cm. After a peak reaches the right ear, does it still take 0.6 msec before a peak arrives at the left ear? No! It takes a much shorter time because many peaks of such a high-frequency wave will fit between your ears. No longer is there a simple relationship between the direction the sound comes from and the arrival times of the peaks at the two ears. Interaural arrival time simply is not useful for locating sounds with frequencies so high that one cycle of the sound wave is smaller than the distance between your ears.

The brain has another process for sound localization at high frequencies: *interaural intensity difference*. An interaural intensity difference exists between the two ears because your head effectively casts a sound shadow (Figure 11.23). There is a direct relationship between the direction the sound comes from and the extent to which your head shadows the sound to one ear. If sound comes directly from the right, the left ear will hear a significantly lower intensity (Figure 11.23a). With sound coming from straight ahead, the same intensity reaches the two ears (Figure 11.23b), and with sound coming from intermediate directions, there are intermediate intensity differences (Figure 11.23c). Neurons sensitive to differences in intensity can use this information to locate the sound. The reason intensity information cannot be used to locate sounds at lower frequencies is that sound waves at these frequencies diffract around the head, and the intensities at the two ears are roughly equivalent. There is no sound shadow at low frequencies.

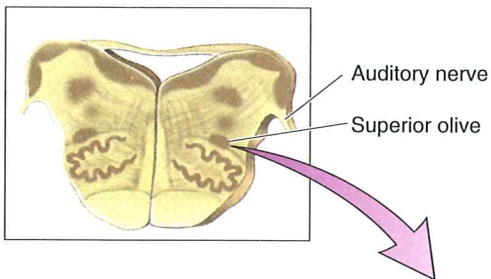
Let's summarize the two processes for localizing sound in the horizontal plane. With sounds in the range of 20–2000 Hz, the process involves *interaural time delay*. From 2000–20,000 Hz, *interaural intensity difference* is used. Together these two processes constitute the **duplex theory of sound localization**.

**Sensitivity of Binaural Neurons to Sound Location.** From our discussion of the auditory pathway, recall that neurons in the cochlear nuclei only receive afferents from the ipsilateral auditory nerve. Thus, all of these cells are *monaural*, meaning that they only respond to sound presented to one ear. At all later stages of processing in the auditory system, however, there are *binaural* neurons whose responses are influenced by sound at both ears. The response properties of binaural neurons imply that they play an important role in sound localization in the horizontal plane. The first structure where binaural neurons are present is the superior olive. While there is some controversy concerning the relationship between the activity of such neurons and the behavioral localization of sound, there are several compelling correlations. Neurons in the superior olive receive input from cochlear nuclei on both sides of the brain stem. Cells in the cochlear nuclei that project to the superior olive typically have responses phase-locked to lower-frequency sound input. Consequently, the olivary neuron receiving spikes from the left and right cochlear nuclei can compute interaural time delay. Recordings made in the superior olive show that the neurons typically give the greatest response to a particular interaural delay (Figure 11.24). One model for the circuitry that produces neurons sensitive to interaural delay involves *delay lines*. If the afferents reaching the superior olive are active with different delay times following sound in the left or right ear, the olivary neurons will have a preferred interaural delay (Figure 11.25). In other words, the left ear and right ear afferents are delay lines that determine the optimal interaural

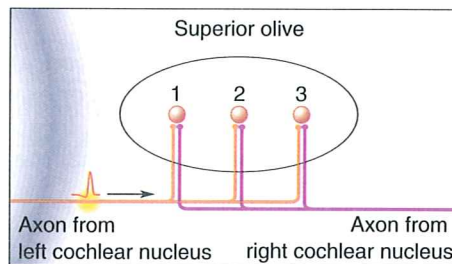


**Figure 11.24**

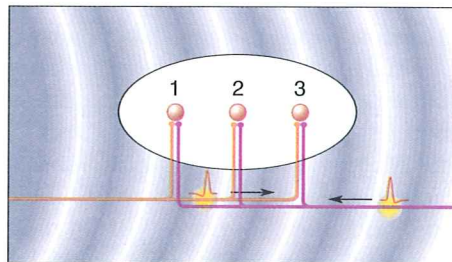
**A neuron in the superior olive sensitive to interaural time delay.** This neuron has an optimal delay of 1 second.



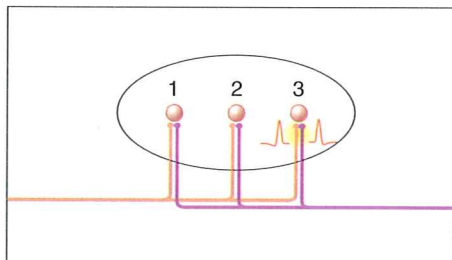
Sound from the left side initiates activity in the left cochlear nucleus, activity is then sent to the superior olive.



Very soon, the sound reaches the right ear, initiating activity in the right cochlear nucleus. Meanwhile, the first impulse has traveled farther along its axon.



Both impulses reach olivary neuron 3 at the same time, and summation generates an action potential.



**Figure 11.25**

**Delay lines and neuronal sensitivity to interaural delay.**



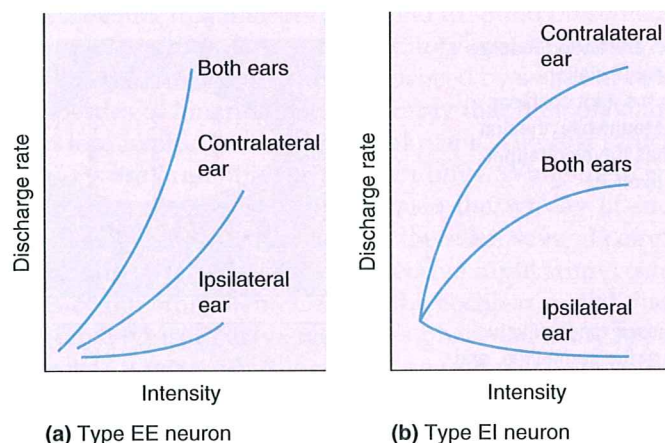
delay for a given neuron in the superior olive. Because phase locking only occurs in the neurons of the cochlear nucleus at relatively low frequencies, and phase locking is essential for precise comparison of the timing of inputs, it makes sense that interaural delays are useful for localization only at low frequencies.

In addition to their sensitivity to interaural delay, neurons in the superior olive are sensitive to interaural intensity. The responses of two types of binaural neurons are shown in Figure 11.26. One type of neuron (type EE) is moderately excited by sound presented to either ear but only gives a maximal response when both ears are stimulated. The other type of neuron (type EI) is excited by sound in one ear but inhibited by sound in the other ear. These EI neurons can be very sensitive to differences in intensity at the two ears because the effect of added excitation from one ear is compounded by the effect of decreased inhibition from the other ear. Presumably such a mechanism serves horizontal localization of high-frequency sound by means of differences in interaural intensity.

### Localization of Sound in the Vertical Plane

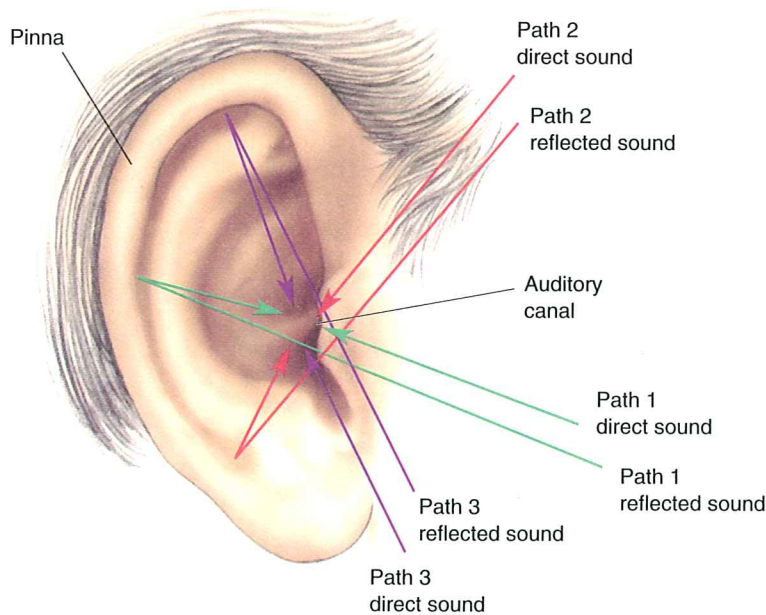
As mentioned above, localizing sounds in the vertical plane is much less affected by plugging one ear than localizing sounds in the horizontal plane. In order to seriously impair vertical sound localization, one must place a tube into the auditory canal to bypass the pinna. The necessity of this step indicates the importance of the shape of the outer ear for assessing the elevation of a source of sound. The bumps and ridges of the outer ear apparently produce reflections of the entering sound. The delays between the direct path and the reflected path make vertical localization possible (Figure 11.27). Consistent with the idea that reflections off the outer ear are important is the finding that vertical localization is seriously impaired if the convolutions of the pinna are covered.

Some animals are extremely good at vertical sound localization even though they do not have a pinna. For example, a barn owl can swoop down on a squeaking mouse in the dark, locating accurately by sound, not sight. Although owls do not have a pinna, they can use the same techniques we



**Figure 11.26**

**Binaural responses in the superior olive.** (a) At all sound intensities, this EE neuron gives a stronger response to *bilateral* stimulation than to *unilateral* stimulation. (b) The response of this EI neuron increases with increasing sound intensity in the contralateral ear but decreases as intensity rises in the ipsilateral ear. The response to bilateral stimulation is reduced from the contralateral response.



**Figure 11.27**  
Vertical sound localization based on reflections from the pinna.

use for horizontal localization (interaural differences) because their ears are at different heights on their head. Some animals have a more “active” system for sound localization than humans and owls. Certain bats emit sounds that are reflected off objects, and these echoes are used to locate objects without sight. Emission and reception of reflected sound, which is analogous to the sonar used by ships, is used by many bats to hunt insects. In 1989, James Simmons at Brown University made the startling discovery that bats can discriminate time delays that differ by as little as 0.00001 msec (Box 11.3). This finding challenges our current understanding of how the nervous system, using action potentials lasting almost a millisecond, can perform such fine temporal discriminations.

## AUDITORY CORTEX

Axons leaving the MGN project to auditory cortex via the internal capsule in an array called the *acoustic radiation*. Primary auditory cortex (A1) corresponds to Brodmann’s area 41 in the temporal lobe (Figure 11.28a). The structure of A1 and the secondary auditory areas is in many ways similar to corresponding areas of the visual cortex. Layer I contains few cell bodies, and layers II and III contain mostly small pyramidal cells. Layer IV, where the medial geniculate axons terminate, is composed of densely packed granule cells. Layers V and VI contain mostly pyramidal cells that tend to be larger than those in the superficial layers. Let’s look at how these cortical neurons respond to sound.

## Neuronal Response Properties

In general, neurons in monkey (and presumably human) A1 are relatively sharply tuned for sound frequency and possess characteristic frequencies covering the audible spectrum of frequencies. In electrode penetrations made perpendicular to the cortical surface in monkeys, the cells encountered tend to have similar characteristic frequencies, suggesting a columnar organization on the basis of frequency. In the tonotopic representation in A1, low frequencies are represented rostrally and laterally, whereas high



## Box 11.3

## PATH OF DISCOVERY

## Bat Echolocation

by James Simmons

One powerful approach to learning how the brain works is to study an animal whose behavior might embody, in an exaggerated form, some general principle of brain function. The same exaggeration that makes the chosen creature seem exotic might also make the workings of the system easier to observe than in a more conventionally studied species. My colleagues and I have been very fortunate in getting a glimpse of how the brain creates the images that constitute perception from an unlikely source: the sonar system that bats use to “see” in the dark. Bats are popularly regarded as truly strange animals; they have even been demonized in myths and in horror movies. The bat’s very body is unusual, with wings, tiny eyes, huge ears, and often a nose-leaf. But in reality these odd characteristics are fascinating adaptations of the animal to its nocturnal environment. Bats hunt flying insects in the dark with astonishing precision, using a form of biological sonar called *echolocation*. Bats actually *do* this—finding, tracking, and intercepting each flying insect—in only a second or so. In flight, the bat broadcasts ultrasonic chirps and perceives objects from their echoes, determining distance from the time it takes for the sound to travel out to the target and back to the ears. This mode of perception naturally places a premium on the brain’s capacity to register the timing of sounds with great precision. Echolocation in bats provides an opportunity to observe how the brain uses time as a dimension of perception when it must do its utmost to be accurate.

My interest in bats began in graduate school in 1965 in the laboratory of auditory physiologist E. G. Wever, at Princeton University. This laboratory was a virtual menagerie of strange and unusual creatures with interesting auditory systems: dolphins, fish, frogs, owls, lizards—and bats. Wever provided the best of atmospheres for scientific research: support, encouragement, and a true interest in knowledge. With one of the lab’s buildings to use as a sonar test range, I was told to try to find out just how accurate the bat’s sonar really was. My first experiments involved training bats to sit still on a platform and “tell” me how far away objects were; the bats got mealworms as a reward. This involved catching bats in abandoned buildings, then hand-feeding them until they ate from a dish, and then getting them to sit still long enough to begin learning what I wanted them to do. Many bat-hunting afternoons were spent tottering high up on a rickety ladder, getting strange stares from passers-by. Word got around that I was an exterminator, and calls kept coming in to “please take away the bats from my house.”

In the first experiments on perception of echo delay, the big brown bat could judge the distance to objects with an accuracy of about a centimeter. This is equivalent to telling a time difference of about 50 msec in echo delays from one object to another. It soon became apparent, however, that the

movements of the bat while it scanned the targets were introducing a blurring effect on the results. More refined experiments with echoes delivered electronically to the bat through a loudspeaker revealed that the bat’s echo-delay acuity actually was a fraction of a microsecond. Under quiet conditions the big brown bat can detect changes as small as 10 nanoseconds (0.01 microsecond) in the delay of echoes! Not surprisingly, there was a lot of skepticism about this result because it seemed biologically impossible. After all, individual neural action potentials are roughly 300,000 nsec (300 microseconds) wide, and the jitter in their timing is also hundreds of microseconds. How could bats possibly perceive changes of only 10 nsec using such inherently imprecise neural events to register echoes? Besides, aren’t these animals too strange to challenge assumptions drawn from studying more conventional laboratory species, in which perception appears to emerge from representing stimulus information on maps in the brain?

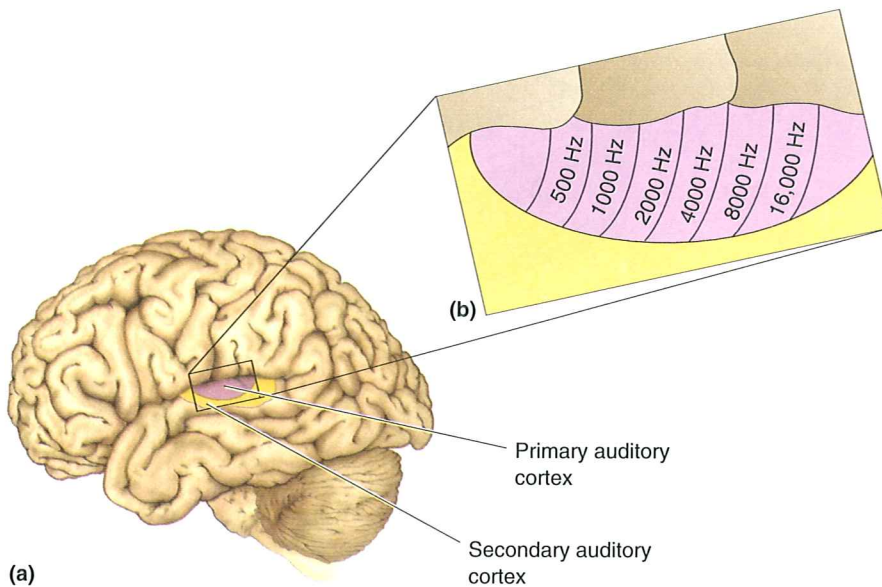
But behavior doesn’t lie; in fact, it is what the brain is for, so my colleagues and I searched long and hard to find the bat’s neural mechanism for registering echoes with submicrosecond precision. We eventually found that the bat stretches small differences of a few microseconds in the timing of sounds into differences of hundreds of microseconds in the timing of neural events. Furthermore, with Steven Dear in the Department of Neuroscience at Brown University, we have most recently seen how the bat might set up intricate timing patterns of neural responses to create the images the bat perceives.

D. R. Griffin, one of the discoverers of echolocation, has described progress in this field as a “state of dynamic habituation to successive surprises,” which seems to characterize scientific inquiry in general very accurately. The possible role of hearing in the bat’s orientation was greeted with much disbelief, and each subsequent discovery has revealed capabilities that at first seemed beyond reason. What is important to science? Being critical, even skeptical, about your own experiments while keeping an open mind for what is possible to find.



James Simmons



**Figure 11.28**

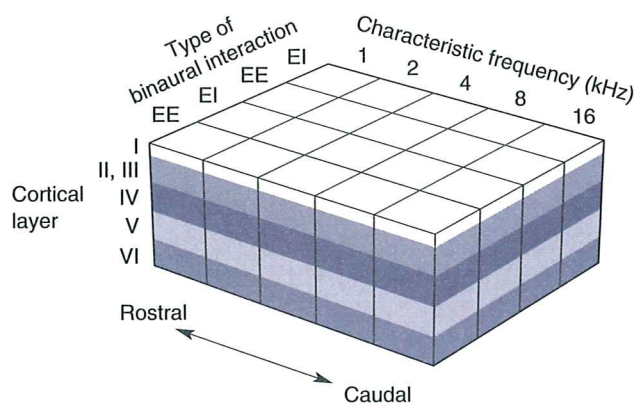
**Primary auditory cortex in humans.** (a) Primary auditory cortex (purple) and secondary auditory areas (yellow) on the superior temporal lobe. (b) Tonotopic organization within primary auditory cortex. The numbers are characteristic frequencies.

frequencies are represented caudally and medially (Figure 11.28b). Roughly speaking, there are *isofrequency bands* running mediolaterally across A1. In other words, there are strips of neurons running across A1 in which all the neurons have fairly similar characteristic frequencies.

In the visual system, it is possible to describe large numbers of cortical neurons as having some variation on a general receptive field that is either simple or complex. So far, it has not been possible to place the diverse auditory receptive fields into a similarly small number of categories. As at earlier stages in the auditory pathway, neurons have different temporal response patterns; some have a transient response to a brief sound, and others have a sustained response. In addition to the frequency tuning that occurs in most cells, some neurons are intensity tuned, giving a peak response to a particular sound intensity. Even within a vertical column perpendicular to the cortical surface, there can be considerable diversity in the degree of tuning to sound frequency. Some neurons are sharply tuned for frequency, and others are barely tuned at all; the degree of tuning does not seem to correlate well with cortical layers. Other sounds that produce responses in cortical neurons include clicks, bursts of noise, frequency-modulated sounds, and animal vocalizations. Attempting to understand the role of these neurons that respond to seemingly complex stimuli is one of the challenges researchers currently face.

Given the wide variety of response types that neurophysiologists encounter in studying auditory cortex, you can understand why it is reassuring to see some sort of organization or unifying principle. One organizational principle already discussed is the tonotopic representation in many auditory areas. A second organizational principle is the presence in auditory cortex of columns of cells with similar binaural interaction. As at lower levels in the auditory system, one can distinguish EE and EI neurons (see Figure 11.26). Recall that EE cells respond more to stimulation of both ears than to either ear separately, while EI cells are inhibited if both ears are stimulated. If one makes an electrode penetration perpendicular to the cortical



**Figure 11.29**

**Hypothetical ice cube model of auditory cortex.** In this model, characteristic frequencies increase moving rostral to caudal, and alternating bands of EE and EI cells run mediolateral.

surface, most of the cells encountered will be of one type, either EE or EI. In cat cortex, there are alternating patches of EE and EI cells within an isofrequency band, and evidence suggests that the binaural interaction columns (sometimes called *summation and suppression columns*) are roughly at right angles to the isofrequency bands (Figure 11.29). As we discussed for the superior olive, neurons sensitive to interaural time delays and interaural intensity differences probably play a role in sound localization.

In addition to A1, other cortical areas located on the superior surface of the temporal lobe respond to auditory stimuli. Some of these higher auditory areas are tonotopically organized, and others do not seem to be. As in visual cortex, there is a tendency for the stimuli that evoke a strong response to be more complex than at lower levels in the system. An example of specialization is Wernicke's area, which we will discuss in Chapter 21. Destruction of this area does not interfere with the sensation of sound, but it seriously impairs the ability to interpret spoken language.

### Effects of Auditory Cortical Lesions and Ablation

While deafness results from bilateral ablation of auditory cortex, it is more often the consequence of damage to the ear (Box 11.4). A surprising degree of normal auditory function is retained after lesions of auditory cortex that are unilateral. This is in marked contrast to the visual system, in which a unilateral cortical lesion of striate cortex leads to complete blindness in one hemifield. The reason for greater preservation of function after lesions of auditory cortex is that both ears send output to cortex in both hemispheres. In humans, the primary deficit that results from unilateral loss of A1 is an inability to localize the source of a sound. It may be possible to determine which side of the head a sound comes from, but there is little ability to locate the sound more precisely. Performance on such tasks as frequency or intensity discrimination is near normal.

Studies in experimental animals indicate that smaller lesions can produce rather specific localization deficits. Because of the tonotopic organization of A1, it is possible to make a restricted cortical lesion that destroys neurons with characteristic frequencies within a limited frequency range. Interestingly, there is a deficit in localization only for sounds roughly corresponding to the characteristic frequencies of the missing cells. This finding reinforces the idea that information in different frequency bands may be processed in parallel by tonotopically organized structures.



## Box 11.4 OF SPECIAL INTEREST

## Auditory Disorders

Although the effects of cortical lesions provide important information about the role of auditory cortex in perception, the perceptual deficit we all associate with the auditory system, deafness, usually results from problems in or near the cochlea. Deafness is conventionally subdivided into two categories: conduction deafness and nerve deafness. Loss of hearing resulting from a disturbance in sound conductance from the external ear to the cochlea is called *conduction deafness*. This sensory deficit can result from something as simple as excessive wax in the ear to more serious diseases of the ossicles. A number of diseases cause binding of the ossicles to the bone of the middle ear, impairing the transfer of sound. Fortunately, most of the mechanical problems in the middle ear that interfere with sound conductance can be treated surgically.

*Nerve deafness* is deafness associated with the loss of neurons in either the auditory nerve or the hair cells of the cochlea. Nerve deafness sometimes results from tumors affecting the inner ear. It also can be the result of drugs that are toxic to hair cells, such as quinine and certain antibiotics. Exposure to loud sounds, such as explosions and loud music, is another cause of injury to the cochlea. Depending on the degree of cell loss, different treatments are possible. If the cochlea or auditory nerve on one side is completely destroyed, deafness in that ear will be absolute. However, a partial loss of hair cells is more common. In these cases, a hearing aid can be used to amplify the sound for the remaining hair cells. In more severe cases in which there is considerable damage to the cochlea but an intact auditory nerve, it is sometimes possible to restore some hearing by implanting an artificial electronic cochlea. This device has an electrode that is placed over or within the cochlea in order to electrically stimulate the auditory nerve. The artificial cochlea is wired to a microphone, which receives the sound. The frequency coding usually provided by the mechanics of the basilar membrane and hair cells can be partially achieved by the use of multiple electrodes that stimulate different portions of the auditory nerve in response to sound of various frequencies. The success of these devices is quite variable, ranging from restoration of the ability to understand speech to only a crude perception of changes in sounds.

With deafness, a person hears less sound than normal. With a hearing disorder called *tinnitus*, a person

hears noises in the ears in the absence of any sound stimulus. The subjective sensation can take many forms, including buzzing, humming, and whistling. You may have experienced a mild and temporary form of tinnitus after being at a party with really loud music; the rest of your brain may have had fun, but your hair cells are in shock! Tinnitus is a relatively common disorder that can seriously interfere with concentration and work if it persists. You can imagine how distracting it would be if you constantly heard whispering or humming or the crinkling of paper. Tinnitus can be a symptom of any of a number of neurological problems. Although it frequently accompanies diseases involving the cochlea or auditory nerve, it may result from exposure to loud sounds or abnormal vasculature of the neck. Although clinical treatment of tinnitus is only partially successful, the annoyance of the noise can often be lessened by using a device to constantly produce a sound in the affected ear(s). For unknown reasons, the constant real sound is less annoying than the sound of the tinnitus that gets blocked out.

Perhaps the most interesting cause of tinnitus is sound produced by the ear itself. It is a curious fact that even normal ears not only respond to sound, they also can produce sound. Short sound clicks presented to the ear cause a faint "echo" that can be picked up with a microphone in the auditory canal. This echo is thought to be a by-product of the cochlear amplifier bending the cochlear membranes, which moves the ossicles and tympanic membrane, in the reverse order from normal sound transduction. This echo is not usually heard because it is faint and there are other sounds in the environment. However, in some cases, the ears emit sounds in the absence of any incoming sound at all. Called *spontaneous oto-acoustic emissions*, these sounds are thought to be a result of cochlear damage that makes the cochlear amplifier continuously active. As in the response of a normal ear to a click, the amplifier drives the cochlear membranes, ultimately moving the tympanic membrane and producing sound. If these spontaneous sounds are loud enough, they are heard as tinnitus.



## CONCLUDING REMARKS

We have followed the auditory pathway from the ear to cerebral cortex and seen the ways in which sound information is transformed. Variations in the density of air molecules are converted to movement of the mechanical components of the middle and inner ear that is transduced into a neural response. The structure of the ear and cochlea are highly specialized for the transduction of sound. However, this fact should not blind us to the considerable similarities between the organization of the auditory system and that of other sensory systems.

Many analogies can be made between the auditory and visual systems. In the sensory receptors of both systems, a spatial code is established. In the visual system, the code in the photoreceptors is retinotopic; the activity of a given photoreceptor indicates light at a particular location. The receptors in the auditory system establish a spatial code that is tonotopic because of the unique properties of the cochlea. In each system, the retinotopy or tonotopy is preserved as signals are processed in secondary neurons, the thalamus, and finally in sensory cortex.

The convergence of inputs from lower levels produces neurons at higher levels that have more complex response properties. Combinations of LGN inputs give rise to simple and complex receptive fields in visual cortex; similarly in the auditory system, the integration of inputs tuned to different sound frequencies yields higher-level neurons that respond to complex combinations of frequencies. Another example of the increase in complexity at higher levels is that in the visual system, the convergence of inputs from the two eyes yields binocular neurons, which are important for depth perception. Analogously, in the auditory system, input from the two ears is combined to create binaural neurons, which are used for horizontal sound localization. These are just a few of the many similarities in the two systems. Principles governing one system can often help us understand other systems. Keep this in mind while reading about the somatosensory system in the next chapter, and you'll be able to predict some features of cortical organization based on the types of sensory receptors.

## KEY TERMS

### Introduction

audition

### The Nature of Sound

frequency

hertz (Hz)

intensity

### Structure of the Auditory System

pinna

auditory canal

tympanic membrane

ossicle

oval window

cochlea

outer ear

middle ear

inner ear

medial geniculate nucleus (MGN)

primary auditory cortex (A1)

### The Middle Ear

malleus

incus

stapes

Eustachian tube

attenuation reflex

### The Inner Ear

modiolus

round window

scala vestibuli

scala media

scala tympani

Reissner's membrane

basilar membrane

organ of Corti

tectorial membrane

helicotrema

perilymph

endolymph

hair cell

stereocilium  
reticular lamina  
inner hair cell  
outer hair cell  
spiral ganglion  
auditory nerve  
cochlear amplifier

#### Central Auditory Processes

dorsal cochlear nucleus  
ventral cochlear nucleus  
superior olive

inferior colliculus  
characteristic frequency

#### Encoding Sound Intensity and Frequency

tonotopy  
phase locking  
volley principle

#### Mechanisms of Sound Localization

duplex theory of sound localization

1. How is the conduction of sound to the cochlea facilitated by the ossicles of the middle ear?
2. Why is the round window crucial for the function of the cochlea? What would happen if it were rigid instead of a flexible membrane?
3. Why is it impossible to predict the frequency of a sound simply by looking at which portion of the basilar membrane is the most deformed?
4. Why would the transduction process in hair cells fail if the stereocilia as well as the hair cell bodies were surrounded by perilymph?
5. If inner hair cells are primarily responsible for hearing, what is the function of outer hair cells?
6. Why doesn't unilateral damage to the inferior colliculus or MGN lead to deafness in one ear?
7. What mechanisms function to localize sounds in the horizontal and vertical planes?
8. What symptoms would you expect to see in a person who had recently had a stroke affecting A1 unilaterally? How does the severity of these symptoms compare with the effects of a unilateral stroke involving V1?
9. What is the difference between nerve deafness and conduction deafness?

## REVIEW QUESTIONS

