sensory afferent neurons but is instead computed by the auditory system from representations of the physical cues.

Sounds Convey Multiple Types of Information to Hearing Animals

Hearing helps to alert animals to the presence of unseen dangers or opportunities and, in many species, also serves as a means for communication. Information about where sounds arise and what they mean must be extracted from the representations of the physical characteristics of sound at each of the ears. To understand how animals process sound, it is useful first to consider which cues are available.

Most vertebrates take advantage of having two ears for localizing sounds in the horizontal plane. Sound sources at different positions in that plane affect the two ears differentially: Sound arrives earlier and is more intense at the ear nearer the source (Figure 28–1A). Interaural time and intensity differences carry information about where sounds arise.

The size of the head determines how interaural time delays are related to the location of sound sources; the neuronal circuitry determines the precision with which time delays are resolved. Because air pressure waves travel at roughly 340 m/s in air, the maximal interaural delay in humans is approximately 600 μs; in small birds, the greatest delay is only 35 μs. Humans can resolve the location of a sound source directly ahead to within approximately 1 degree, corresponding to an interaural time difference of 10 μs. Interaural time differences are particularly well conveyed by neurons that encode relatively low frequencies. These neurons can fire at the same position in every cycle of the sound and in this way encode the interaural time difference as an interaural phase difference. Sounds of high frequencies produce *sound shadows* or intensity differences between the two ears. For many mammals with small heads, high-frequency sounds provide the primary cue for localizing sound in the horizontal plane.

Mammals can localize sounds in the vertical plane and with a single ear using spectral filtering. High-frequency sounds, with wavelengths that are close to or smaller than the dimensions of the head, shoulders, and external ears, interact with those parts of the body to produce constructive and destructive interference, introducing broad spectral peaks and deep, narrow spectral notches whose frequency changes with the location of the sound (Figure 28–1B). High-frequency sounds from different origins are filtered differently because in mammals the shape of the external ear differs back-to-front as well as top-to-bottom. Animals learn to use these spectral cues to locate sound sources. If the shape of the ear is experimentally altered, even adult humans can learn to make use of a new pattern of spectral cues. If animals lose hearing in one ear, they lose interaural timing and intensity cues and must depend completely on spectral cues for localizing sounds.

How do we make sense of the complex and changing sounds that we hear? Most natural sounds contain energy over a wide range of frequencies and change rapidly with time. The information used to recognize sounds varies among animal species, and depends on listening conditions and experience. Human speech, for example, can be understood in the midst of noise, over electronic devices that distort sounds, and even through cochlear implants. One reason for its robustness is that speech contains redundant cues: The vocal apparatus produces sounds in which multiple parameters covary. At the same time, this makes the task of understanding how animals recognize patterns a complicated one. It is not clear which cues are used by animals under various conditions.

Music is a source of pleasure to human beings. Musical instruments and human voices produce sounds that have energy at the fundamental frequency that corresponds to its perceived pitch, as well as at multiples of that frequency, giving sounds a quality that allows us, for example, to distinguish a flute from a violin when their pitch is the same. Musical pitches are largely in the low-frequency range in which auditory nerve fibers fire in phase with sounds. In music, sounds are combined simultaneously to produce chords and successively to produce melodies. Euphonious, pleasant chords elicit regular, periodic firing in cochlear nerve fibers. In dissonant sounds, there is less regularity both in the sound itself and in the firing of auditory nerve fibers; the component frequencies are so close that they interfere with one another instead of periodically reinforcing one another.

The Neural Representation of Sound in Central Pathways Begins in the Cochlear Nuclei

The neural pathways that process acoustic information extend from the ear to the brain stem, through the midbrain and thalamus, to the cerebral cortex (Figure 28–2). Acoustic information is conveyed from cells in the cochlear ganglion (see Figure 26–17) to the cochlear nuclei in the brain stem. There information is received by several different types of neurons, most of which are arranged tonotopically.

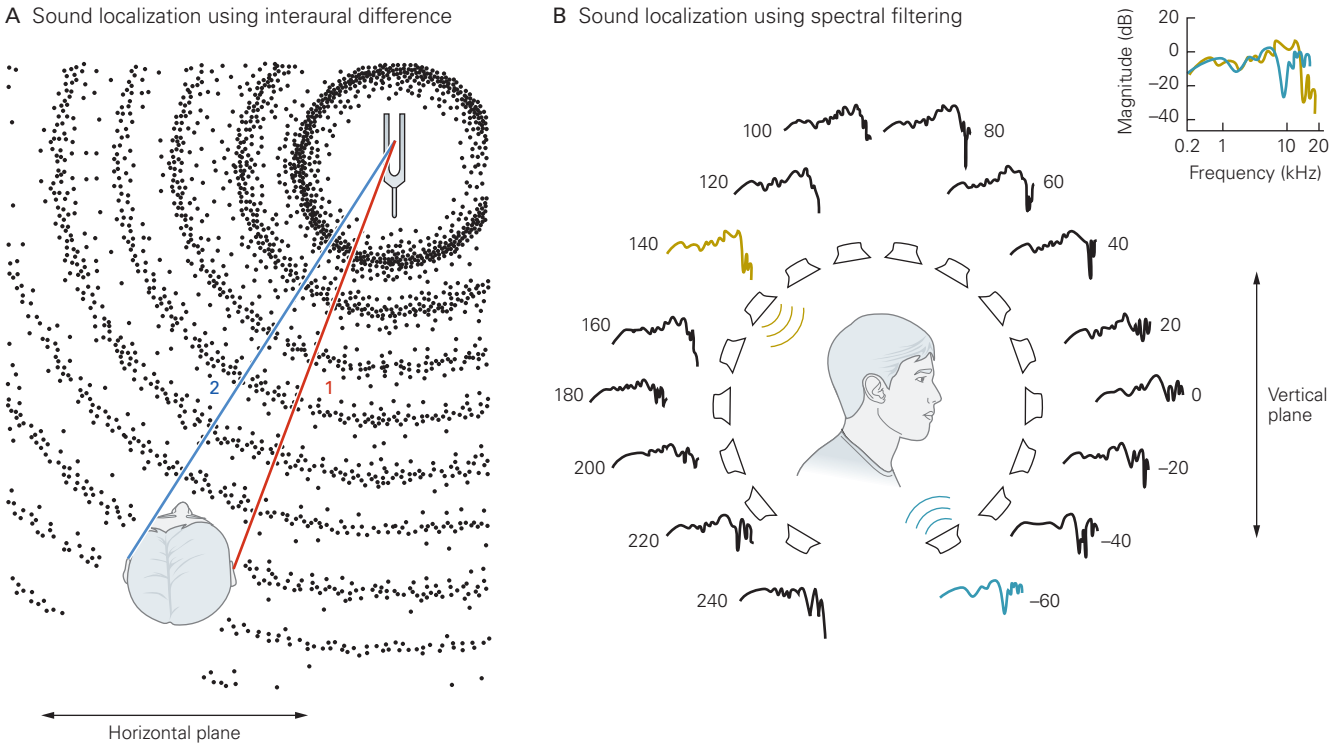


Figure 28–1 Cues for localizing sound sources in the horizontal plane.

A. Interaural time and intensity differences are cues for localizing sound sources in the horizontal plane, or azimuth. A sound arising in the horizontal plane arrives differently at the two ears: Sounds arrive earlier and are louder at the ear nearer the source. A sound that arises directly in the front or back travels the same distance to the right and left ears and thus arrives at both ears simultaneously. Interaural time and intensity do not vary with the movement of sound sources in the vertical plane, so it is impossible to localize a pure sinusoidal tone in the vertical plane. In humans, the maximal interaural time difference is approximately 600 μs. High-frequency sounds, with short wavelengths, are deflected by the head, producing a sound shadow on the far side. (Adapted, with permission, from Geisler 1998.)

B. Mammals can localize broadband sounds in both the vertical and horizontal planes on the basis of spectral filtering. When a noise that has equal energy at all frequencies over the human hearing range (*white noise*) is presented through a speaker, the ear, head, and shoulders cancel energy at some frequencies and enhance others. The white noise that is emitted from the speaker has a flat power spectrum, but by the time the noise has reached the bottom of the ear canal, its spectrum is no longer flat.

In the figure, the sound energy at each frequency at the eardrum relative to that of the white noise is shown by the traces beside each speaker; these traces plot the relative sound magnitude in decibels against spectral frequency (*head-related transfer function*). The small plot in the upper right compares two head-related transfer functions: one for a noise that arises low and in front of a listener (**blue**) and one for a noise from behind the listener's head (**brown**). Head-related transfer functions have deep notches at frequencies greater than 8 kHz, whose frequencies vary depending on where the sounds arose. Sounds that lack energy at high frequencies and narrowband sounds are difficult to localize in the vertical plane. Since spectral filtering also varies in the horizontal plane, it provides the only location cue to animals that have lost hearing in one ear.

You can test the salience of these spectral cues with a simple experiment. Close your eyes as a friend jingles keys directly in front of you at various elevations. Compare your ability to localize sounds under normal conditions and when you distort the shape of both ears by pushing them with your fingers from the back. (Data from D. Kistler and F. Wightman.)

The axons of the different types of neurons take different routes to the brain stem and midbrain, where they terminate on separate targets. Some of the pathways from the cochlear nuclei to the contralateral inferior colliculus are direct; others involve one or two synaptic stages in brain stem auditory nuclei. From the bilateral inferior colliculi, acoustic information flows two ways: to the ipsilateral superior colliculus, where it participates in orienting the head and eyes in response to sounds, and to the ipsilateral thalamus, the relay to auditory areas of the cerebral cortex. The afferent auditory pathways from the periphery to higher brain regions include efferent feedback at many levels.

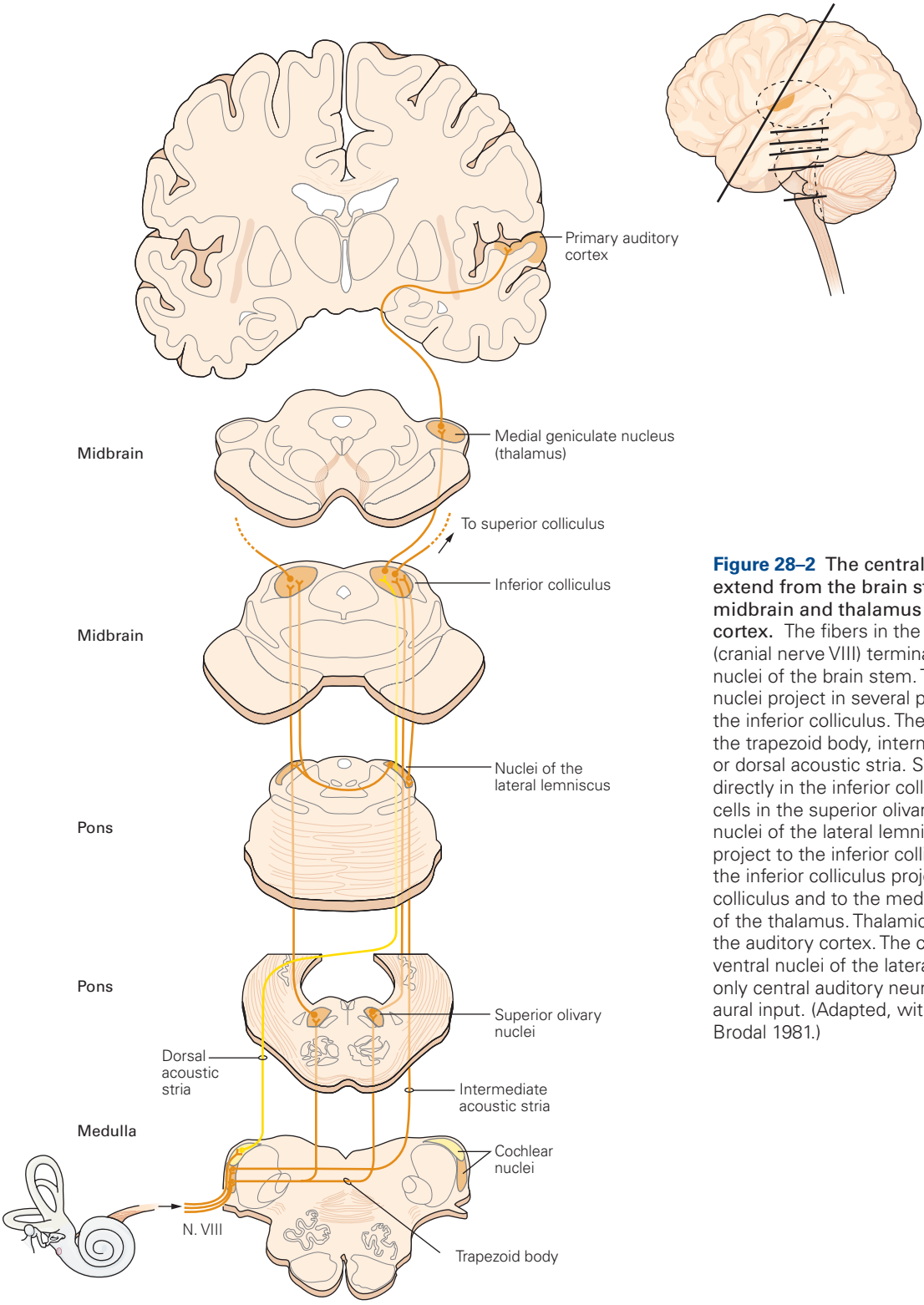


Figure 28–2 **The central auditory pathways extend from the brain stem through the midbrain and thalamus to the auditory cortex.** The fibers in the cochlear nerve (cranial nerve VIII) terminate in the cochlear nuclei of the brain stem. The neurons of these nuclei project in several parallel pathways to the inferior colliculus. Their axons exit through the trapezoid body, intermediate acoustic stria, or dorsal acoustic stria. Some cells terminate directly in the inferior colliculus. Others contact cells in the superior olivary complex and in the nuclei of the lateral lemniscus, which in turn project to the inferior colliculus. Neurons of the inferior colliculus project to the superior colliculus and to the medial geniculate nucleus of the thalamus. Thalamic neurons project to the auditory cortex. The cochlear nuclei and the ventral nuclei of the lateral lemniscus are the only central auditory neurons that receive monaural input. (Adapted, with permission, from Brodal 1981.)

The Cochlear Nerve Delivers Acoustic Information in Parallel Pathways to the Tonotopically Organized Cochlear Nuclei

The afferent nerve fibers from cochlear ganglion cells are bundled in the cochlear or auditory component of the vestibulocochlear nerve (cranial nerve VIII) and terminate exclusively in the cochlear nuclei. The cochlear nerve in mammals contains two groups of fibers: a large number (95%) of myelinated fibers that receives input from inner hair cells and a small number (5%) of unmyelinated fibers that receive input from outer hair cells.

The larger, more numerous, myelinated fibers are much better understood than the unmyelinated fibers. Each type detects energy over a narrow range of frequencies; the tonotopic array of cochlear nerve fibers thus carries detailed information about how the frequency content of sounds varies from moment to moment. The unmyelinated fibers terminate both on the large neurons in the ventral cochlear nuclei and also on the small granule cells that surround the ventral cochlear nuclei. Because it is difficult to record from these tiny fibers, the information they convey to the brain is not well understood. The unmyelinated fibers integrate information from a relatively wide region of the cochlea but are not responsive to sound. It has been suggested that these fibers respond to cochlear damage and contribute to hyperacusis—pain after exposure to loud sounds that damages the cochlea.

Two features of the cochlear nuclei are important. First, these nuclei are organized tonotopically. Fibers that carry information from the apical end of the cochlea, which detects low frequencies, terminate ventrally in the ventral and dorsal cochlear nuclei; those that carry information from the basal end of the cochlea, which detects high frequencies, terminate dorsally (Figure 28–3). Second, each cochlear nerve fiber innervates several different areas within the cochlear nuclei, contacting various types of neurons that have distinct projection patterns to higher auditory centers. As a result, the auditory pathway comprises at least four parallel ascending pathways that simultaneously extract different acoustic information from the signals carried by cochlear nerve fibers. Parallel circuits are a general feature of vertebrate sensory systems.

The Ventral Cochlear Nucleus Extracts Temporal and Spectral Information About Sounds

The principal cells of the unlayered ventral cochlear nucleus sharpen temporal and spectral information and convey it to higher centers of the auditory pathway. Three types of neurons are intermingled and form separate pathways through the brain stem (Figure 28–4).

Bushy cells project bilaterally to the superior olivary complex. This pathway has two parts. One courses through the medial superior olive and compares the time of arrival of sounds at the two ears; the other travels through the medial nucleus of the trapezoid body and the lateral superior olive and compares interaural intensity. Large spherical bushy cells sense low frequencies and project bilaterally to the medial superior olive, forming a circuit that detects interaural time delay and contributes to the localization of low-frequency sounds in the horizontal plane. The small spherical bushy cells and globular bushy cells sense higher frequencies. Small spherical bushy cells excite the lateral superior olive ipsilaterally. The globular bushy cells, through calyceal endings, excite neurons in the contralateral medial nucleus of the trapezoid body that in turn inhibit principal cells of the lateral superior olive. Neurons in the lateral superior olive integrate the ipsilateral excitation and contralateral inhibition to measure interaural intensity and to localize sources of high-frequency sounds in the horizontal plane (see Figure 28–6).

Stellate cells terminate widely. They excite neurons in the ipsilateral dorsal cochlear nucleus, the medial olivocochlear efferent neurons in the ventral nucleus of the trapezoid body, the periolivary nuclei in the vicinity of the ipsilateral lateral superior olive, and the contralateral ventral nucleus of the lateral lemniscus, inferior colliculus, and thalamus. The tonotopic array of stellate cells encodes the spectrum of sounds.

Octopus cells excite targets in the contralateral paraolivary nucleus and terminate in large excitatory calyceal endings on neurons of the ventral nucleus of the lateral lemniscus, which in turn provide sharply timed glycinergic inhibition to the inferior colliculus. Octopus cells detect onsets of sounds that allow animals to detect brief gaps. They mark the spectral components that come from one source that necessarily start together.

The differences in the integrative tasks performed by these pathways through the ventral cochlear nucleus are reflected in cell morphology. The shapes of their dendrites reflect the way they collect information from cochlear nerve fibers. The dendrites of the sharply tuned bushy and stellate cells receive input from relatively few cochlear nerve fibers, whereas those of the broadly tuned octopus cells, in contrast, lie perpendicular to the path of cochlear nerve fibers, poised to receive input from many cochlear nerve fibers. Many of the inputs to bushy cells are from unusually large

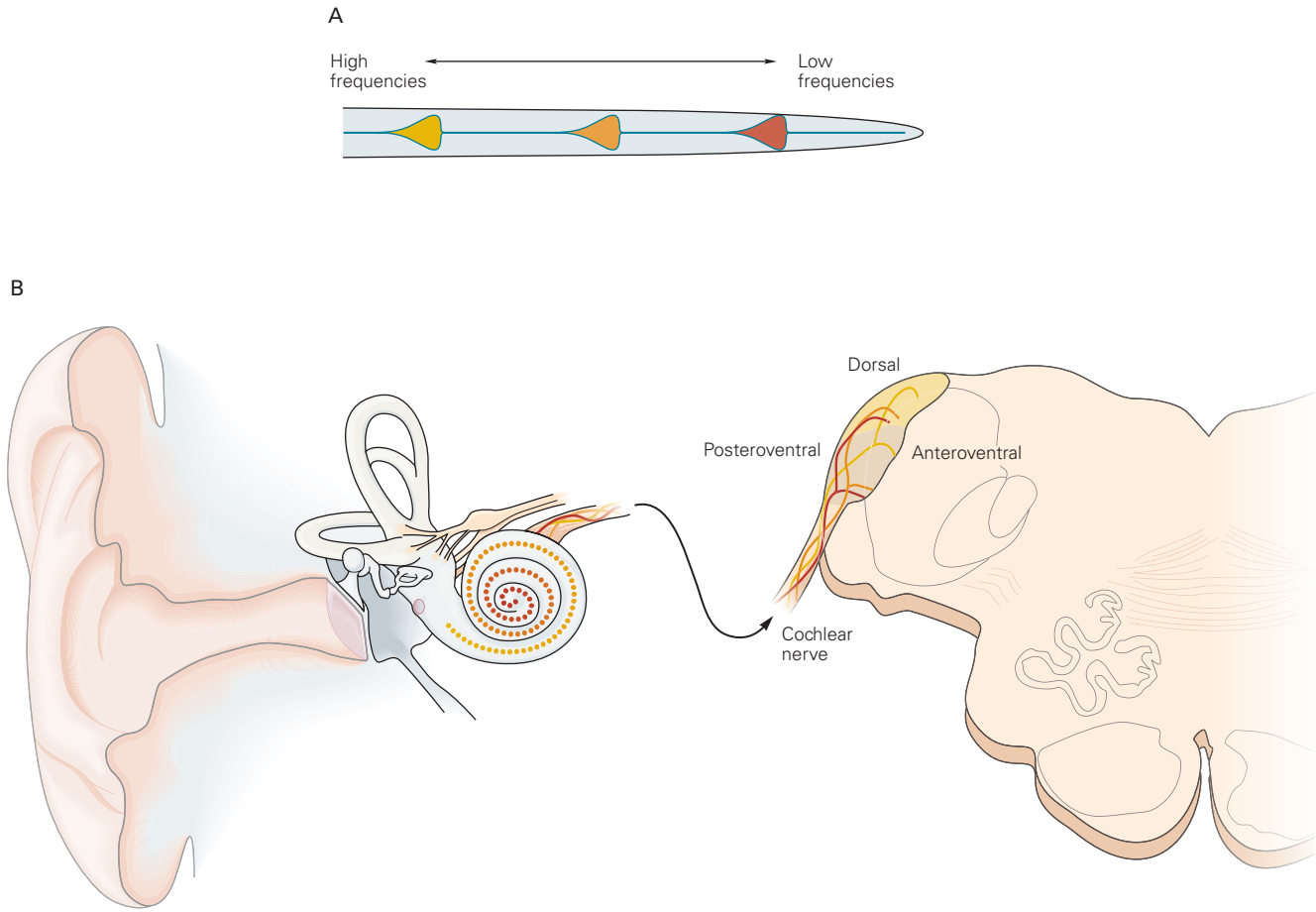


Figure 28–3 The dorsal and ventral cochlear nuclei.

A. Stimulation with three frequencies of sound vibrates the schematically uncoiled basilar membrane at three positions, exciting distinct populations of hair cells and their afferent nerve fibers.

B. Cochlear nerve fibers project in a tonotopic pattern to the cochlear nuclei. Those encoding the lowest frequencies (**red**) terminate most ventrally, whereas those encoding higher frequencies (**yellow**) terminate more dorsally. The cochlear nuclei include the ventral and dorsal nuclei. Each afferent fiber enters at the nerve root and splits into branches that run anteriorly (the ascending branch) and posteriorly (the descending branch). The ventral cochlear nucleus is thus divided functionally into anteroventral and posteroventral divisions.

terminals that envelop the bushy cell bodies, meeting their need for large synaptic currents. The need for large synaptic currents in octopus cells is met by summing inputs from large numbers of small terminals.

The biophysical properties of neurons determine how synaptic currents are converted to voltage changes and over how long a time synaptic inputs are integrated. Octopus and bushy cells in the ventral cochlear nucleus are able to respond with exceptionally rapid and precisely timed synaptic potentials. These neurons have a prominent, low-voltage-activated K^+ conductance that confers a low input resistance and rapid responsiveness and prevents repetitive firing (Figure 28–4C). The large synaptic currents that are required to trigger action potentials in these leaky cells are delivered through rapidly gated, high-conductance, AMPA-type (α-amino-3-hydroxy-5-methylisoxazole-4-propionate) glutamate receptors at many synaptic release sites. In contrast, stellate cells, in which even relatively small depolarizing currents produce large protracted voltage changes, generate slower excitatory postsynaptic potentials (EPSPs) in response to synaptic currents, and *N*-methyl-D-aspartate (NMDA)-type glutamate receptors enhance those responses.

The Dorsal Cochlear Nucleus Integrates Acoustic With Somatosensory Information in Making Use of Spectral Cues for Localizing Sounds

Among vertebrates, only mammals have dorsal cochlear nuclei. The dorsal cochlear nucleus receives input from two systems of neurons that project to different

layers (Figure 28–4A,B). Its principal cells, fusiform cells, integrate those two systems of inputs and convey the result directly to the contralateral inferior colliculus.

The outermost molecular layer is the terminus of a system of parallel fibers, the unmyelinated axons of granule cells that are scattered in and around the cochlear nuclei. This system transmits somatosensory, vestibular, and auditory information from widespread regions of the brain to the molecular layer.

The deep layer receives acoustic information. Not only cochlear nerve fibers but also stellate cells of the ventral cochlear nucleus terminate in the deep layer. Acoustic inputs are tonotopically organized in isofrequency laminae that run at right angles to parallel fibers.

Fusiform cells, the principal cells of the dorsal cochlear nucleus, integrate the two systems of inputs. Parallel fibers in the molecular layer excite fusiform cells through spines on apical dendrites in the molecular layer. Parallel fibers also terminate on spines of dendrites of cartwheel cells, interneurons that bear a strong resemblance to cerebellar Purkinje cells, which in turn inhibit fusiform cells. Cochlear nerve fibers and stellate cells in the ventral cochlear nucleus excite fusiform cells and inhibitory interneurons via synapses on the smooth basal dendrites in the deep layer.

Recent experiments suggest that the circuits of the dorsal cochlear nucleus distinguish between unpredictable and predictable sounds. An animal's own chewing or licking sounds, for example, are predictable and canceled through these circuits. The changes in spectral cues that arise when animals move their heads or ears or shoulders, changing the angle of incidence of sounds to the ears, are unpredictable, especially when an external sound source is moving. Somatosensory and vestibular information about the position of the head and ears, as well as descending information from higher levels of the nervous system about the animal's own movements, pass through the molecular layer to modulate acoustic information that arrives in the deep layer.

The Superior Olivary Complex in Mammals Contains Separate Circuits for Detecting Interaural Time and Intensity Differences

In many vertebrates, including mammals and birds, neurons in the superior olivary complex compare the activity of cells in the bilateral cochlear nuclei to locate sound sources. Separate circuits detect interaural time and intensity differences and project to the inferior colliculi.

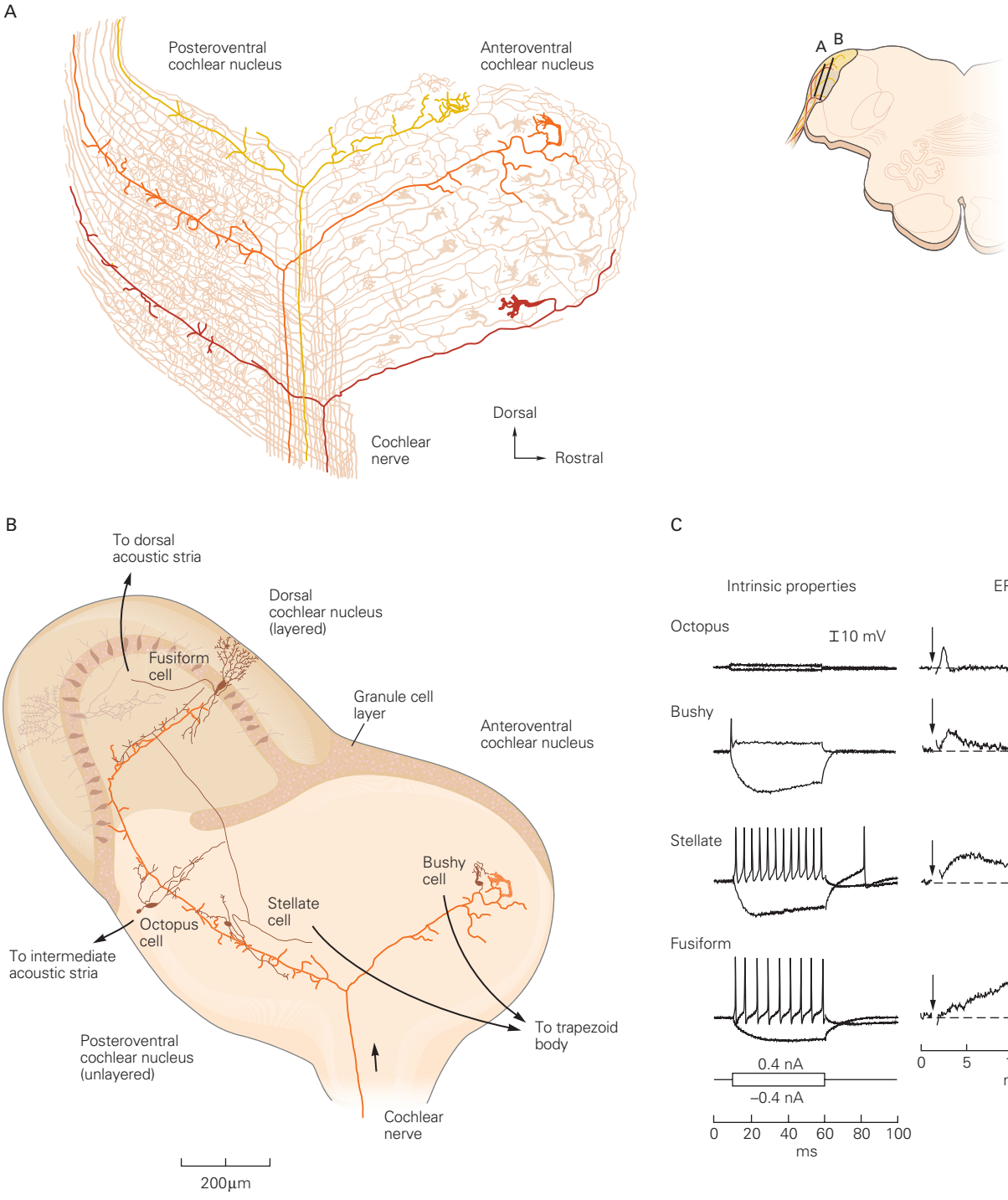
The Medial Superior Olive Generates a Map of Interaural Time Differences

Differences in arrival times at the ears are not represented at the cochlea. Instead, they are first represented in the medial superior olive where a map of interaural phase is created by a comparison of the timing of action potentials in the responses to sounds from the two ears. Sounds arrive at the near ear before they arrive at the far ear, with interaural time differences being directly related to the location of sound sources in the horizontal plane (Figure 28–5A).

Cochlear nerve fibers tuned to frequencies below 4 kHz and their bushy cell targets encode sounds by firing in phase with the pressure waves. This property is known as *phase-locking.* Although individual neurons may fail to fire at some cycles, some set of neurons fires with every cycle. In so doing, these neurons carry information about the timing of inputs with every cycle of the sound. Sounds arriving from one side evoke phase-locked firing that is consistently earlier at the near ear than at the far ear, resulting in consistent interaural phase differences (Figure 28–5A).

In 1948, Lloyd Jeffress suggested that an array of detectors of coincident inputs from the two ears, transmitted through *delay lines* comprised of axons with systematically differing lengths, could form a map of interaural time differences and thus a map of the location of sound sources (Figure 28–5B). In such a circuit, conduction delays compensate for the earlier arrival at the near ear. Interaural time delays increase systematically as sounds move from the midline to the side, resulting in coincident firing further toward the edge of the neuronal array.

Such neuronal maps have been found in the barn owl in the homolog of the medial superior olivary nucleus. Mammals and chickens use a variant of this input arrangement. The principal neurons of the medial superior olive form a sheet of one or a few cells' thickness on each side of the midline. Each neuron has two tufts of dendrites, one extending to the lateral face of the sheet, and the other projecting to the medial face of the sheet (Figure 28–5C). The dendrites at the lateral face are contacted by the axons of large spherical bushy cells from the ipsilateral cochlear nucleus, whereas the dendrites at the medial face are contacted by large spherical bushy cells of matching best frequency from the contralateral cochlear nucleus. The axons of bushy cells terminate in the contralateral


A
Posteroventral cochlear nucleus
Anteroventral cochlear nucleus
Cochlear nerve
Dorsal
Rostral
A B
B
To dorsal acoustic stria
Dorsal cochlear nucleus (layered)
Fusiform cell
Granule cell layer
Anteroventral cochlear nucleus
Bushy cell
Stellate cell
Octopus cell
To intermediate acoustic stria
To trapezoid body
Posteroventral cochlear nucleus (unlayered)
Cochlear nerve
200µm
C
Intrinsic properties
EPSPs
Octopus
10 mV
5 mV
Bushy
Stellate
Fusiform
0.4 nA
–0.4 nA
0 20 40 60 80 100
ms
0 5 10 15 20
ms

medial superior olive with delay lines just as Jeffress had suggested, but the branches that terminate in the ipsilateral medial superior olive are of equal length (see Figure 28–5C).

The conduction delays are such that each medial superior olive receives coincident excitatory inputs from the two ears only when sounds come from the contralateral half of space. As sound sources move from the midline to the most lateral point on the contralateral side of the head, the earlier arrival of sounds at the contralateral ear needs to be compensated by successively longer delay lines. This results in inputs from the two ears coinciding at successively more posterior and lateral regions of the medial superior olive. Inhibition superimposed on these excitatory inputs plays a significant role in sharpening the map of interaural phase.

In encoding interaural phase, individual neurons in the medial superior olive provide ambiguous information about interaural time differences. Phase ambiguities are resolved when sounds have energy at multiple frequencies, as natural sounds almost always do. The sheet of neurons of the medial superior olive forms a representation of interaural phase along the rostrocaudal and lateromedial dimensions. The array of bushy cell inputs also imposes a tonotopic organization in the dorsoventral dimension. Sounds that contain energy at multiple frequencies evoke maximal coincident firing in a single dorsoventral column of neurons that localizes sound sources unambiguously. The beauty of using interaural phase to encode interaural time disparities is that the brain receives information about interaural time differences not just at the beginning and end of the sound but with every cycle of an ongoing sound.

Principal cells of the medial superior olive also receive sharply timed inhibition driven by sounds from both the ipsilateral and contralateral sides through the lateral and medial nuclei of the trapezoid body, respectively. Remarkably, the inhibition through pathways from both sides precedes the arrival of excitation and sharpens the summation of excitation even though inhibition is mediated through a pathway that has an additional synapse. The great conduction speed through the disynaptic pathway through the medial nucleus of the trapezoid body is made possible by the large axons of globular bushy cells and the large calyceal terminals of Held that activate neurons in the medial nucleus of the trapezoid body with short and consistently timed delays. The pathway that brings ipsilateral inhibition through the lateral nucleus of the trapezoid body is less well understood.

Each medial superior olive thus forms a map of the location of sound sources in the contralateral hemifield. The striking difference between this spatial representation of stimuli and those in other sensory systems is that it is not the result of the spatial arrangement of inputs, like retinotopic or somatosensory maps, but is inferred by the brain from computations made in the afferent pathways.

The Lateral Superior Olive Detects Interaural Intensity Differences

Sounds with wavelengths that are similar to or smaller than the head are deflected by the head, causing the

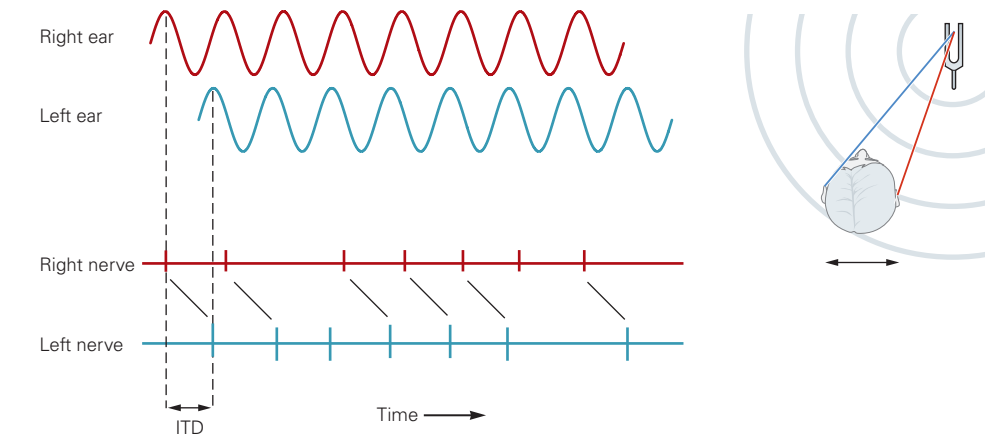
Figure 28–4 (Opposite) Different types of cells in the cochlear nuclei extract distinct types of acoustic information from cochlear nerve fibers.

A. The differing sizes and shapes of terminals along the length of each cochlear nerve fiber in the ventral cochlear nucleus of a newborn dog reflect differences in their postsynaptic targets. The large end bulbs form synapses on bushy cells; smaller boutons contact stellate and octopus cells. The nerve fibers shown here are color-coded as in Figure 28–3: the **yellow** fiber encodes the highest frequencies and the **red** fiber the lowest. (Adapted, with permission, from Cajal 1909.)

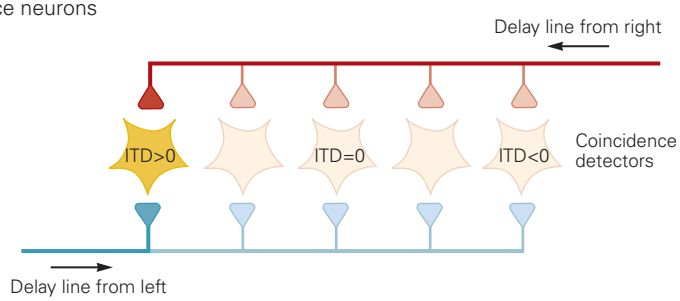
B. A layer of mouse granule cells (**light brown**) separates the unlayered ventral cochlear nucleus (**pink**) from the layered dorsal nucleus (**tan and light brown**). In the dorsal cochlear nucleus, the cell bodies of fusiform and granule cells are intermingled in a region between the outermost molecular layer and the deep layer. Cochlear nerve fibers, color-coded for frequency as in Figure 28–3, terminate in both nuclei but with different patterns of convergence on the principal cells. Each bushy, stellate, and fusiform cell receives input from a few auditory nerve fibers and is sharply tuned, whereas individual octopus cells are contacted by many auditory nerve fibers and are broadly tuned.

C. Differences in the intrinsic electrical properties of the principal cells of mouse cochlear nuclei are reflected in the patterns of voltage change in the cells. When steadily depolarized, stellate and fusiform cells fire repetitive action potentials, whereas repetitive firing in bushy and octopus cells is prevented by low-voltage-activated conductances. The low input resistance of bushy and octopus cells in the depolarized voltage range makes depolarizing voltage changes rapid but also small; the rise and fall of voltage changes in stellate and fusiform cells is slower. Synaptic potentials, too, are different. The brief synaptic potentials in bushy and octopus cells require larger synaptic currents but encode the timing of auditory nerve inputs more faithfully than do the longer-lasting synaptic potentials in stellate or fusiform cells. (Reproduced, with permission, from N. Golding.)

A Phase-locked firing in bushy cells



B Mapping of ITD onto array of neuronal coincidence neurons



C Bilateral medial superior olivary nuclei