

**Figure 28-14** The auditory system of the bat has specialized areas for locating sounds.

**A.** A sonogram of an animal's calls (solid lines) and the resultant echoes (dashed lines) illustrates the two components of the call: the protracted, harmonically related constant-frequency (CF) signal and the briefer frequency-modulated (FM) signal. The duration of the calls declines as the animal approaches its target. (Adapted, with permission, from Suga 1984.)

**B.** A view of the cerebral hemisphere of the mustached bat shows three of the functional areas within the auditory cortex. The FM area is where the distance from the target is computed; the CF area is where the velocity of the target is

computed; and the Doppler-shifted CF area is specialized for the identification of small fluttering objects. The expanded cortical representation of Doppler-shifted CF signals near the second harmonic of the call frequency (60–62 kHz) forms the acoustic "fovea." (Adapted, with permission, from Suga 1984.)

**C.** The FM-FM combination-sensitive neuron shown does not respond significantly to either pulses or echoes alone, but responds very strongly to a closely paired pulse-echo. However, the neuron is also sensitive to the time difference between the pulse and echo, as seen in the record on the right, where the neuron fails to respond to a pulse-echo combination that is not closely paired. (Adapted, with permission, from Suga et al. 1983.)

fields in cats, monkeys, and humans. Regardless, the choice of appropriate stimuli is likely to be as important in studying these other species as it has been in studies of bats.

### **The Auditory Cortex Is Involved in Processing Vocal Feedback During Speaking**

Vocal communication involves both speaking and hearing, often taking place concurrently. When we speak, the sound of our voice is delivered not only to the intended listener but also back to our own ears. Such feedback to our auditory system during vocal production is conducted not only through the air but also through bone and can be loud as a result of the proximity of the mouth and the ears.

The auditory system must distinguish an auditory percept as being self-generated or externally generated. To monitor external sounds from the acoustic environment during speaking, self-generated sounds have to be masked. At the same time, the auditory system must also monitor our own voice in order to detect errors in vocal production. An accurate representation of one's own voice through vocal feedback is crucial to maintaining desired vocal production and to the learning of a new language. In humans and animals, perturbations of the vocal feedback can lead to alterations in vocal production, and interruptions or blockages of the vocal feedback can result in degradation in vocal learning.

The evidence for the involvement of the auditory cortex in processing vocal feedback comes from both human and animal studies. Responses in the auditory cortex of human subjects to their own voice while speaking are smaller than the responses to the playback of the same sounds. This reduction can be observed in electrocorticographical (ECoG) recordings (Figure 28–15A) or with a variety of imaging methods (eg, fMRI, PET, magnetoencephalography [MEG]).

Single-neuron recordings from the auditory cortex of vocalizing monkeys have shown that self-initiated vocalizations result in suppression of cortical responses to monkeys' own vocalizations, of external sounds heard during vocalization, and also spontaneous activity (Figure 28–15B). Because in many instances firing rates are suppressed to below spontaneous activity, the suppression is likely caused by inhibition. Neurons suppressed by self-initiated vocalizations show frequency and intensity tuning, as is typical of auditory cortical neurons, and respond to the playback of vocalizations.

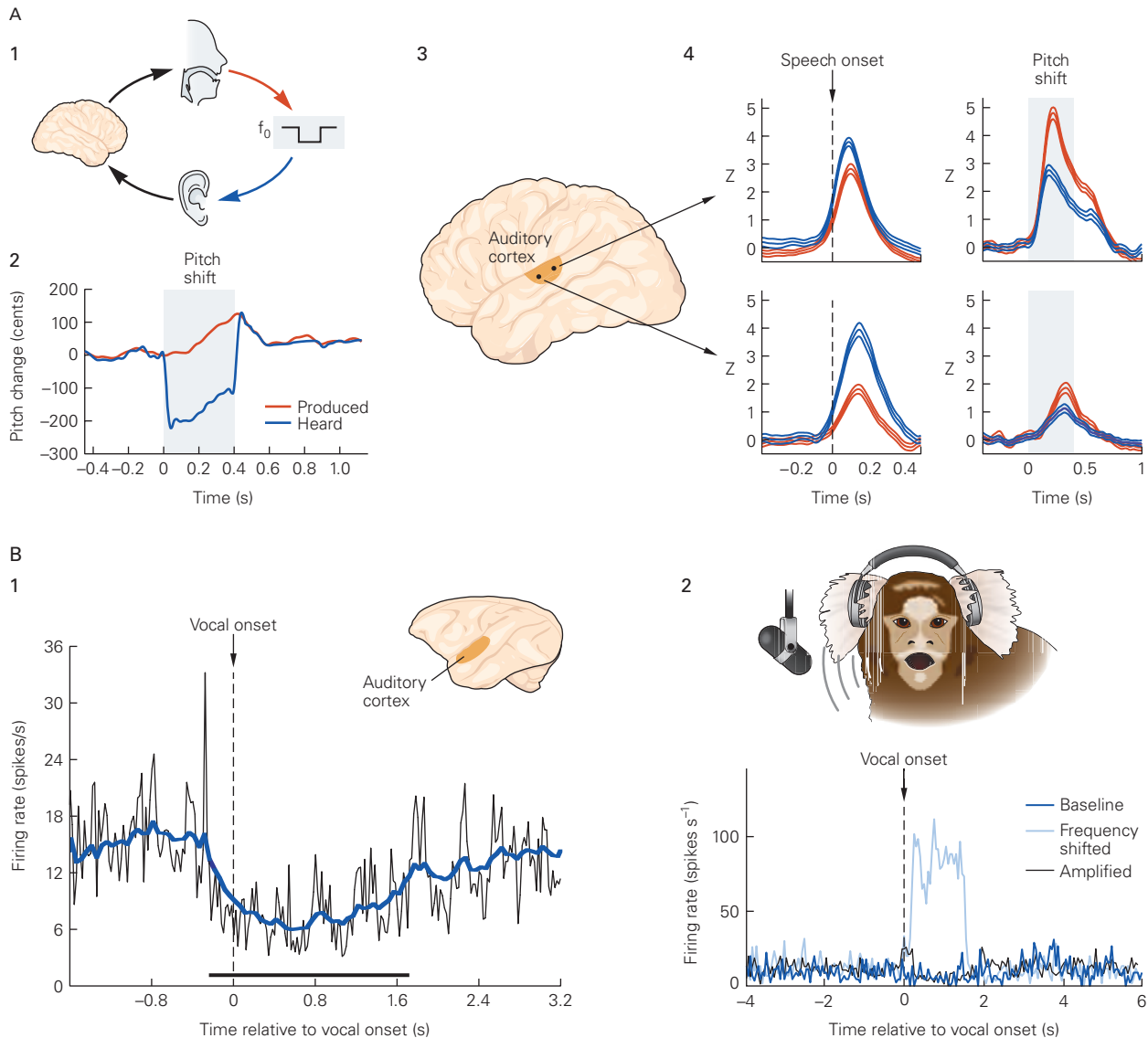
The vocalization-induced suppression begins several hundred milliseconds prior to the onset of vocalization (Figure 28–15B), suggesting that these neurons receive modulatory signals originating in vocal

production circuits. In humans, vocal production is carried out by cortical areas in the frontal lobe, from Broca's area to premotor and motor cortex. In humans and monkeys, axons from the premotor cortex to auditory regions of the superior temporal gyrus have been described, and presumably, they mediate the vocalization-induced suppression. This modulatory connection is not active when humans or monkeys simply listen to vocal sounds played to them.

Why do we suppress our auditory cortex when we speak? A simple answer is that this suppression helps reduce the masking effect of our own voice, which can be very loud. A more interesting answer is that this suppression results from a vocal feedback-monitoring network in auditory cortex. In humans, there is less or no suppression of auditory cortex if vocal feedback is experimentally altered through earphones, for example, when the pitch of the voice is shifted (Figure 28–15A). In marmoset monkeys, neurons suppressed by self-initiated vocalizations may become less suppressed or even excited when the animal hears its own frequency-shifted vocalizations (Figure 28–15C). This sensitivity to feedback perturbations suggests that neurons exhibiting vocalization-induced suppression are part of a network responsible for monitoring vocal feedback signals. The presence of vocal feedback-related neural activity in the auditory cortex of both humans and monkeys suggests that the auditory cortex combines both internal modulation and vocal feedback responses, rather than merely responding to sensory signals coming through the ears.

Not all neurons in the auditory cortex are suppressed by speaking or vocalizing. A smaller proportion (~30%) of neurons in marmoset A1 increase their responses during self-initiated vocalizations, consistent with their auditory response characteristics. In contrast to vocalization-induced suppression, vocalization-related excitation begins after the onset of vocalization and is likely the result of feedback through the ascending auditory pathway. The vocalization-related excitation may help maintain the sensitivity of the auditory cortex to the external acoustic environment during speaking or vocalizing.

Vocalization-induced suppression of auditory responses has been observed in several mammalian subcortical structures, including the brain stem and inferior colliculus. Such suppression begins a few milliseconds before or is synchronized with vocal production. In contrast, cortical suppression begins several hundred milliseconds before the vocal onset. It is possible that subcortical suppression of auditory responses during speaking or vocalizing is initiated by cortical commands.



**Figure 28-15** Vocal feedback processing in auditory cortex.

**A.** Examples of vocalization-induced suppression and sensitivity to pitch perturbation in human cerebral cortex. **1.** A subject's vocalizations (red arrow) went through a digital signal processor that shifted pitch and delivered the distorted auditory feedback (blue arrow) to the subject's earphones. **2.** Pitch track of an example trial shows the pitch recorded by the microphone (produced) and the pitch delivered to the earphones (heard). Shaded region indicates the time interval when the signal processor shifted the pitch by -200 cents (1 cent = 1/1200 octave). **3.** The locations of electrodes that recorded from two sites in the auditory cortex on the surface of the superior temporal gyrus. **4.** The Z variable represents the power in the 50 to 150 Hz (high- $\gamma$ ) range of cortical activity, which has been shown to correlate well with neuronal spiking activity. It was extracted from the signals recorded at each electrode in the speaking (red) and listening (blue) conditions. Vertical lines in the left column of plots indicate vocalization onset, and shaded regions in the right column of plots indicate the onset and offset of perturbation. The response of a subject's auditory cortex to his or her own self-produced vocalization is generally smaller than the response seen when the subject passively listens to playback of the same vocalization (left column). The response of auditory

cortex to the perturbation during active phonation (speaking) is enhanced (right column). (Adapted, with permission, from Houde and Chang, 2015.)

**B. 1.** Vocalization-induced suppression of neural activity in marmoset monkey auditory cortex. Population-averaged firing rate of all vocalization-suppressed responses are aligned by vocal onset (a "Phee" call). The blue line is a moving average (100 ms window) and shows that suppression begins prior to vocalization (indicated by arrow). The thick bar indicates the period over which suppression is continuously significant ( $P < 0.05$ ). (Adapted, with permission, from Eliades and Wang 2003.)

**2.** Neurons subject to vocalization-induced suppression are sensitive to vocal feedback perturbations. **Top:** Self-produced vocalizations with or without feedback alterations were delivered to the marmoset through a customized headphone. **Bottom:** This auditory cortical neuron was suppressed during normal vocalization (dark blue) but showed a large increase in firing rate when the auditory feedback of the vocalization was shifted in the frequency domain (light blue). Amplifying auditory feedback alone did not generate firing rate changes (black). (Adapted, with permission, from Eliades and Wang 2008; Crapse and Sommer 2008.)

## Highlights

1. Sound impinging on two ears carries information that the brain uses to compute where sounds arise and what they mean. Sounds are characterized by the amount of energy at one or more frequencies. To determine where sounds arise in the horizontal plane, many mammals compute differences in the time of arrival at the two ears for sounds less than approximately 3,000 Hz. To determine where sounds arise in the vertical dimension and whether they arise from the front or the back, mammals use spectral filtering of sounds greater than approximately 6,000 Hz by the head, shoulders, and external ears.
2. Acoustic information is brought to the brain from the cochlea by auditory nerve fibers, each sharply tuned to a narrow range of frequencies and together representing the entire hearing range of the animal. Auditory nerve fibers terminate in the ventral and dorsal cochlear nuclei, distributing acoustic information to four major groups of principal cells that form parallel ascending pathways through the brain stem. The topographic organization of the auditory nerve inputs imparts a tonotopic organization to the ipsilateral cochlear nuclei that is preserved all along the auditory pathway, including auditory cortex.
3. A marked feature of auditory neurons at processing stations along the ascending pathway is their progressively increasing stimulus selectivity.
4. The ventral cochlear nucleus extracts three features of sounds: (a) The monaural pathways through octopus cells of the ventral cochlear nucleus, the superior paraolivary nucleus, and ventral nucleus of the lateral lemniscus detect coincident firing of auditory nerve fibers that is useful for detecting onsets and gaps in sounds. (b) Stellate cells detect and sharpen the encoding of spectral peaks and valleys and convey that spectral information to the dorsal cochlear nucleus, olivocochlear neurons in the ventral nucleus of the lateral lemniscus, ventral nucleus of the lateral lemniscus, inferior colliculus, and thalamus. Spectral information is used for understanding the meaning of sounds and for localizing their sources. (c) Bushy cells sharpen and convey information about the fine structure of sounds, which is used in the binaural pathways through the medial and lateral superior olivary nuclei to make the interaural comparisons of timing and intensity of sounds at the two ears, which are used to localize sound sources along the azimuth.
5. The dorsal cochlear nucleus integrates acoustic signals with somatosensory information in its principal cells. Somatosensory information helps distinguish the spectral cues generated by an animal's own movements, which are biologically uninteresting, from those that arise from the environment.
6. Auditory brainstem pathways converge in the inferior colliculus. The inferior colliculus feeds acoustic information through the medial geniculate body of the thalamus to auditory cortex.
7. A projection from the inferior colliculus carries information about the location of sounds to the superior colliculus, a part of the brain that controls reflexive orienting movements of the head and eyes.
8. Within auditory cortex, auditory neurons continue to become more selective to the stimuli to which they respond. Subregions of the auditory cortex represent different biologically significant features such as pitch of tones that form harmonic complexes. Auditory cortex also transforms rapidly varying features of sounds into firing-rate-based representations, while representing slowly varying sounds using spike timing.
9. Auditory circuits in the cerebral cortex are segregated into separate processing streams, with dorsal and ventral streams concerned respectively with sound location in space and sound identification.
10. The cerebral cortex modulates processing in subcortical auditory areas. Projections from the auditory cortex innervate the thalamus, inferior colliculus, olivocochlear neurons, some basal ganglionic structures, and even the dorsal cochlear nucleus.
11. Auditory cortex is involved in processing vocal feedback signals during speaking. Speaking induces suppression of neural activity in auditory cortex that begins several hundred milliseconds prior to the vocal onset. This suppression results from a vocal feedback-monitoring network that functions to guide vocal production and learning.

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# Smell and Taste: The Chemical Senses

## A Large Family of Olfactory Receptors Initiate the Sense of Smell

Mammals Share a Large Family of Odorant Receptors  
Different Combinations of Receptors Encode Different Odorants

## Olfactory Information Is Transformed Along the Pathway to the Brain

Odorants Are Encoded in the Nose by Dispersed Neurons  
Sensory Inputs in the Olfactory Bulb Are Arranged by Receptor Type  
The Olfactory Bulb Transmits Information to the Olfactory Cortex  
Output From the Olfactory Cortex Reaches Higher Cortical and Limbic Areas  
Olfactory Acuity Varies in Humans

## Odors Elicit Characteristic Innate Behaviors

Pheromones Are Detected in Two Olfactory Structures  
Invertebrate Olfactory Systems Can Be Used to Study Odor Coding and Behavior  
Olfactory Cues Elicit Stereotyped Behaviors and Physiological Responses in the Nematode  
Strategies for Olfaction Have Evolved Rapidly

## The Gustatory System Controls the Sense of Taste

Taste Has Five Submodalities That Reflect Essential Dietary Requirements  
Tastant Detection Occurs in Taste Buds  
Each Taste Modality Is Detected by Distinct Sensory Receptors and Cells  
Gustatory Information Is Relayed From the Periphery to the Gustatory Cortex

Perception of Flavor Depends on Gustatory, Olfactory, and Somatosensory Inputs

Insects Have Modality-Specific Taste Cells That Drive Innate Behaviors

## Highlights

**T**HROUGH THE SENSES OF SMELL and taste, we are able to perceive a staggering number and variety of chemicals in the external world. These chemical senses inform us about the availability of foods and their potential pleasure or danger. Smell and taste also initiate physiological changes required for the digestion and utilization of food. In many animals, the olfactory system also serves an important social function by detecting pheromones that elicit innate behavioral or physiological responses.

Although the discriminatory ability of humans is somewhat limited compared with that of many other animals, odor chemists estimate that the human olfactory system may be capable of detecting more than 10,000 different volatile chemicals. Perfumers who are highly trained to discriminate odorants can distinguish as many as 5,000 different types of odorants, and wine tasters can discern more than 100 different components of taste based on combinations of flavor and aroma.

In this chapter, we consider how odor and taste stimuli are detected and how they are encoded in patterns of neural signals transmitted to the brain. In recent years, much has been learned about the mechanisms underlying chemosensation in a variety of animal species. Certain features of chemosensation have

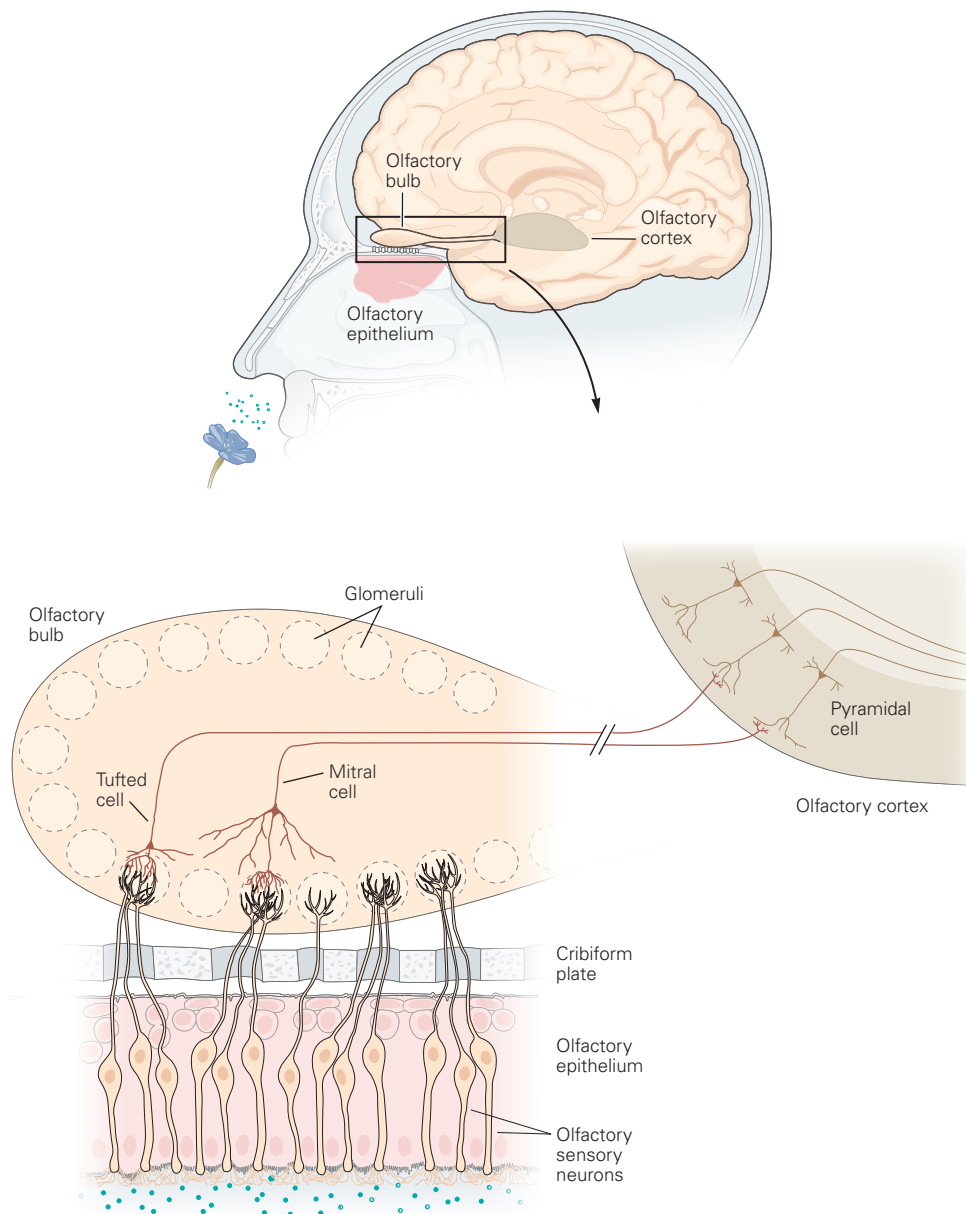
been conserved through evolution, whereas others are specialized adaptations of individual species.

### A Large Family of Olfactory Receptors Initiate the Sense of Smell

Odorants—volatile chemicals that are perceived as odors—are detected by olfactory sensory neurons in the nose. The sensory neurons are embedded in a

specialized olfactory epithelium that lines part of the nasal cavity, approximately 5 cm<sup>2</sup> in area in humans (Figure 29–1), and are interspersed with glia-like supporting cells (Figure 29–2). They are relatively short lived, with a life span of only 30 to 60 days, and are continuously replaced from a layer of basal stem cells in the epithelium.

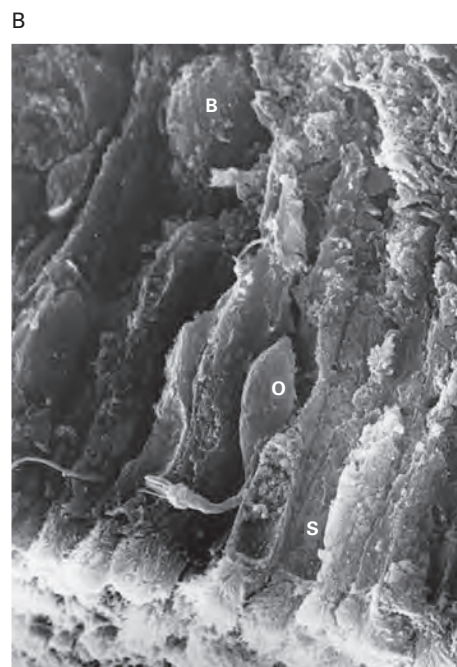
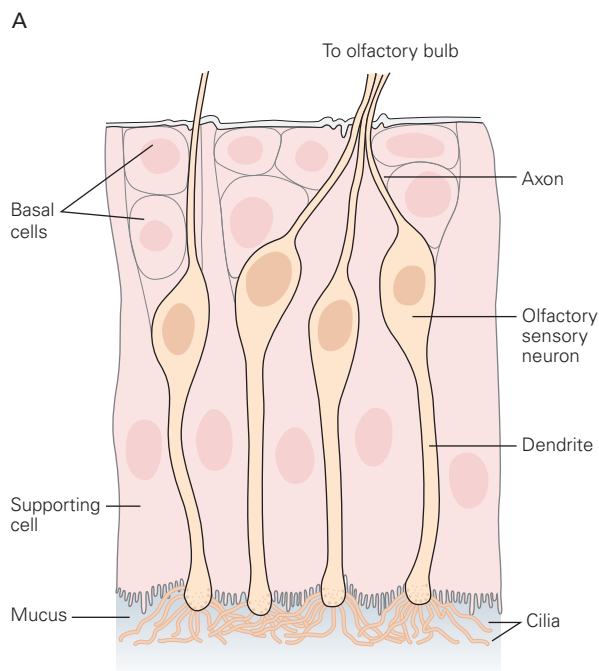
The olfactory sensory neuron is a bipolar nerve cell. A single dendrite extends from the apical end to the epithelial surface, where it gives rise to numerous



**Figure 29–1** The olfactory system. Odorants are detected by olfactory sensory neurons in the olfactory epithelium, which lines part of the nasal cavity. The axons of these neurons project to the olfactory bulb, where they terminate on the

dendrites of mitral and tufted cell relay neurons within glomeruli. In turn, the axons of the relay neurons project to the olfactory cortex, where they terminate on the dendrites of pyramidal neurons whose axons project to other brain areas.





**Figure 29–2** The olfactory epithelium.

**A.** The olfactory epithelium contains sensory neurons interspersed with supporting cells as well as a basal layer of stem cells. A single dendrite extends from the apical end of each neuron; sensory cilia sprout from the end of the dendrite into the mucus lining the nasal cavity. An axon extends from the basal end of each neuron to the olfactory bulb.

**B.** A scanning electron micrograph of the olfactory epithelium shows the dense mat of sensory cilia at the epithelial surface. Supporting cells (**S**) are columnar cells that extend the full depth of the epithelium and have apical microvilli. Interspersed among the supporting cells is an olfactory sensory neuron (**O**) with its dendrite and cilia, and a basal stem cell (**B**). (Reproduced, with permission, from Morrison and Costanzo 1990. Copyright © 1990 Wiley-Liss, Inc.)

thin cilia that protrude into the mucus that coats the nasal cavity (Figure 29–2). The cilia contain the odorant receptors as well as the transduction machinery needed to amplify sensory signals from the receptors and transform them into electrical signals in the neuron's axon, which projects from the basal pole of the neuron to the brain. The axons of olfactory sensory neurons pass through the cribriform plate, a perforated region in the skull above the nasal cavity, and then terminate in the olfactory bulb (see Figure 29–1).

### Mammals Share a Large Family of Odorant Receptors

Odorant receptors are proteins encoded by a multigene family that is evolutionarily conserved and found in all vertebrate species. Humans have approximately 350 different odorant receptors, whereas mice have approximately 1,000. Although odorant receptors belong to the G protein–coupled receptor superfamily, they share sequence motifs not seen in other superfamily members. Significantly, the odorant receptors vary considerably in amino acid sequence (Figure 29–3A).

Like other G protein–coupled receptors, odorant receptors have seven hydrophobic regions that are likely to serve as transmembrane domains (Figure 29–3A). Detailed studies of other G protein–coupled receptors, such as the  $\beta$ -adrenergic receptor, suggest that odorant binding occurs in a pocket in the transmembrane region formed by a combination of the transmembrane domains. The amino acid sequences of odorant receptors are especially variable in several transmembrane domains, providing a possible basis for variability in the odorant binding pocket that could account for the ability of different receptors to recognize structurally diverse ligands.

A second, smaller family of chemosensory receptors is also expressed in the olfactory epithelium. These receptors, called trace amine-associated receptors (TAARs), are G protein–coupled, but their protein sequence is unrelated to that of odorant receptors. They are encoded by a small family of genes present in humans and mice as well as fish. Studies in mice, which have 14 different olfactory TAARs, indicate that TAARs recognize volatile amines, one of which is present in high concentrations in the urine of male