

## Smell and Taste: The Chemical Senses

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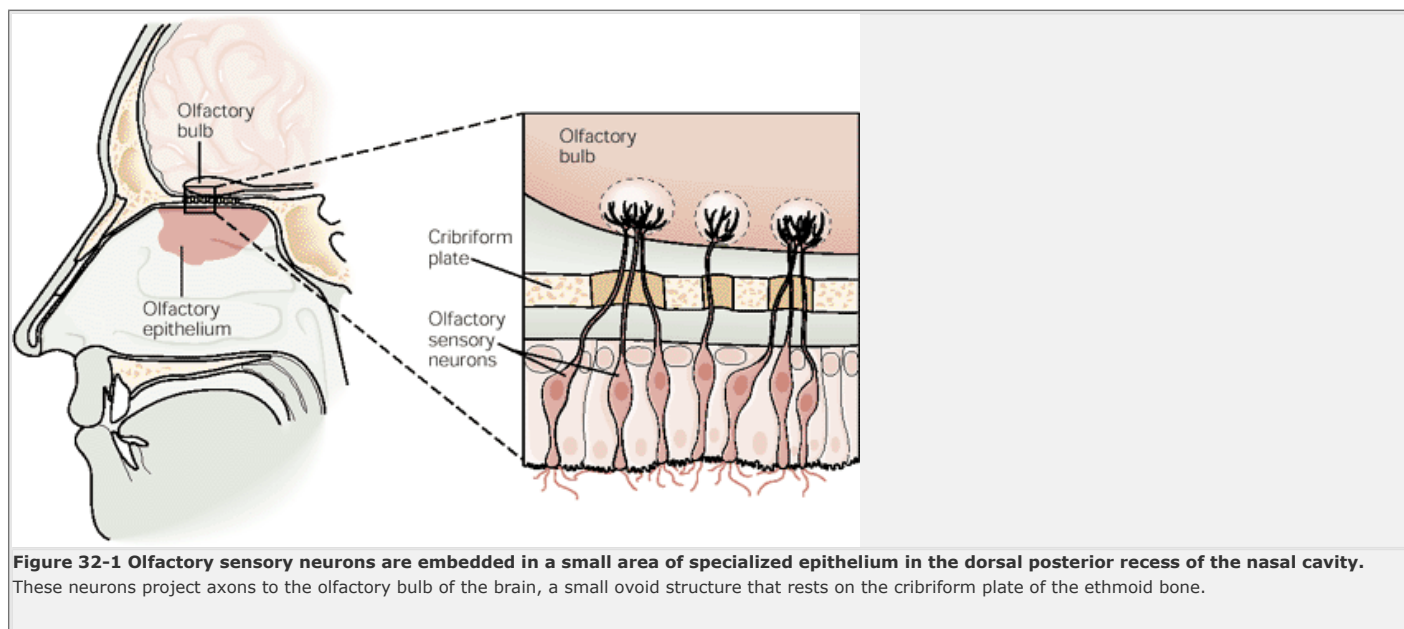
WE ARE CONTINUOUSLY bombarded by molecules released into our environment. Through the senses of smell and taste these molecules provide us with important information that we use constantly in our daily lives. They inform us about the availability of foods and the potential pleasure or danger to be derived from them. They also initiate physiological changes required for the digestion and utilization of ingested foodstuffs. In many mammals the sense of smell plays an additional role, eliciting physiological and behavioral responses to members of the same species.

Humans and other mammals are capable of discriminating a great variety of odors and flavors. Although the olfactory capability of humans is somewhat limited compared with that of some other mammals, we are nevertheless able to perceive thousands of different odorous molecules (*odorants*). Perfumers, who are highly trained to discriminate odorants, say that they can distinguish as many as 5000 different types of odorants, and wine tasters report that they can distinguish more than 100 different components of taste based on combinations of flavor and aroma.

Molecules that are smelled or tasted are sensed by specialized sensory cells in the nose or mouth that relay information to the brain. In the olfactory system the sensory cells are olfactory sensory neurons that lie within a specialized neuroepithelium in the back of the nasal cavity. The sensory cells of the mouth that sense taste

P. 626

stimuli (*tastants*) are specialized epithelial cells, called taste cells, that are clustered together in the taste buds. Taste cells are capable of sensing four basic types of taste stimuli: bitter, sweet, salty, and sour. The large variety of flavors that we associate with taste are generated by complex mixtures of molecules that fall into these four categories, together with volatile molecules that reach the olfactory system from the back of the nasal cavity during chewing and swallowing. The somatosensory system also plays a role in taste. It senses the textures of foods and localizes to the mouth sensations of flavors contributed by the olfactory system.



**Figure 32-1** Olfactory sensory neurons are embedded in a small area of specialized epithelium in the dorsal posterior recess of the nasal cavity. These neurons project axons to the olfactory bulb of the brain, a small ovoid structure that rests on the cribriform plate of the ethmoid bone.

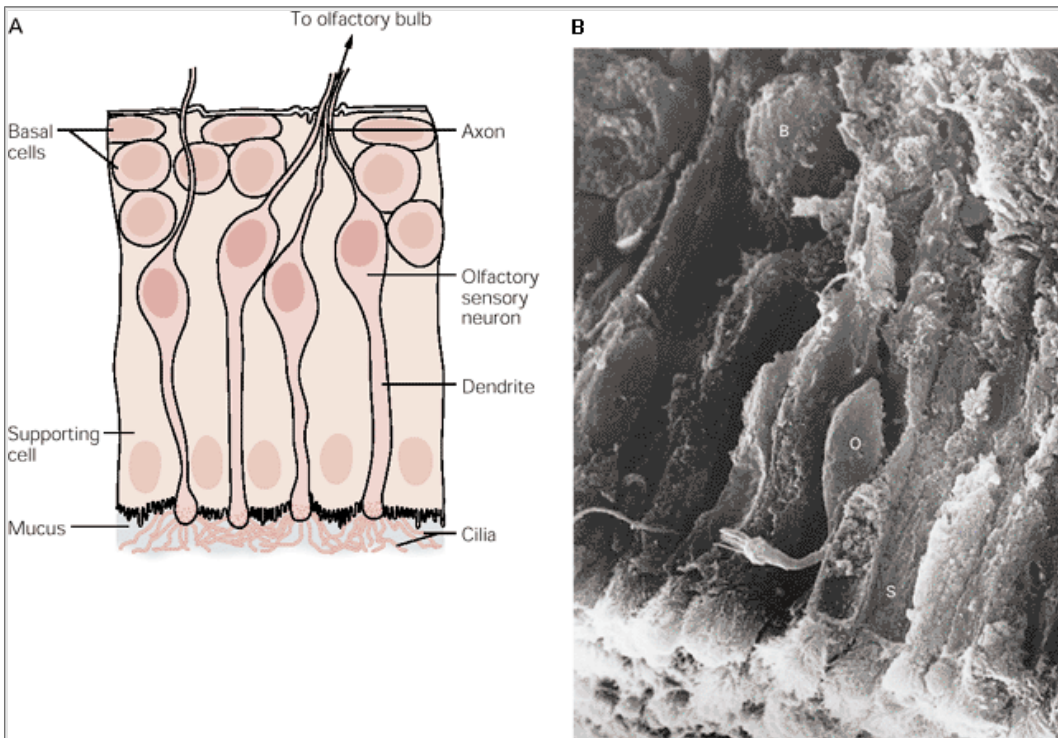
In this chapter we consider how odor and taste stimuli are detected and how they are encoded in patterns of neural signals transmitted to the brain. In recent years much has been learned about the mechanisms of signal detection and transduction in olfactory sensory neurons and taste cells. We shall see that the strategies employed by these cells to sense and transmit information involve specific receptors, signal transduction molecules, and ion channels similar to those of other neural and nonneural systems. We also consider the neural pathways through which olfactory and gustatory information is transmitted, and the organizational strategies used by the olfactory and gustatory systems to discriminate a large variety of chemical stimuli in the environment.

### Odors Are Detected by Nasal Olfactory Sensory Neurons

The initial events in olfactory perception occur in olfactory sensory neurons in the nose. These neurons are embedded in the olfactory epithelium, a small patch of specialized epithelium that in humans covers a region in the back of the nasal cavity about 5 cm<sup>2</sup> in size (Figure 32-1). The human olfactory epithelium contains several million olfactory sensory neurons interspersed with glia-like supporting cells, both of which lie above a basal layer of stem cells (Figure 32-2). Olfactory neurons are distinctive among neurons in that they are short-lived, with an average life span of only 30-60 days, and are continuously replaced from the basal stem cell population.

The olfactory sensory neuron is a bipolar nerve cell (Figure 32-2). From its apical pole each neuron extends a single dendrite to the epithelial surface, where the dendrite expands into a large knob. From this knob 5-20 thin cilia protrude into the layer of mucus that coats the epithelium. From its basal pole each neuron projects a single axon through the bony cribriform plate above the nasal cavity to the olfactory bulb, where the axon forms synapses with olfactory bulb neurons that relay signals to the olfactory cortex.

The cilia of the olfactory neuron are specialized for odor detection. They have specific receptors for odorants as well as the transduction machinery needed to amplify sensory signals and generate action potentials in the neuron's axon. The mucus that bathes the cilia is secreted by the supporting cells of the olfactory epithelium and by Bowman's glands, which lie under the epithelium and have ducts that open onto the epithelial surface. The mucus is thought to provide the appropriate molecular and ionic environment for odor detection. It also contains soluble odorant-binding proteins, produced by a gland that empties into the nasal cavity. While they are not themselves the olfactory receptors, these soluble odorant-binding proteins could contribute to odorant concentration or removal.



**Figure 32-2 Structure of the olfactory epithelium.**

**A.** The olfactory epithelium contains three major cell types: olfactory sensory neurons, supporting cells, and basal stem cells at the base of the epithelium. Each olfactory sensory neuron extends a single dendrite to the epithelial surface. From the dendritic terminus numerous cilia protrude into the layer of mucus lining the nasal lumen. From its basal pole each neuron projects a single axon to the olfactory bulb. Odorants bind to specific odorant receptors on olfactory cilia and initiate a cascade of signal transduction events that lead to the production of action potentials in the sensory axon.

**B.** This scanning electron micrograph illustrates the structure of the olfactory epithelium and the dense mat of receptive olfactory cilia at the epithelial surface (bottom of image). Supporting cells (**S**) are columnar cells that have apical microvilli and thin extensions attached to the base of the epithelium. An olfactory sensory neuron (**O**) with its dendrite and cilia and a basal stem cell (**B**) can be seen among the supporting cells (**S**). (From [Morrison and Constanzo 1990](#).)

P.627

## Different Odorants Stimulate Different Olfactory Sensory Neurons

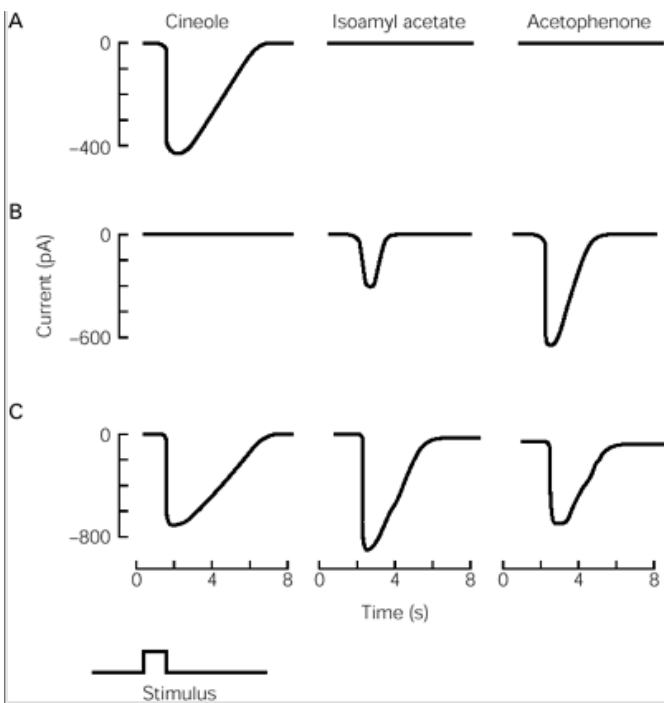
To be discriminated, an odorant must cause a distinct signal to be transmitted from the nose to the brain. This is accomplished primarily by the differing sensitivities of individual olfactory sensory neurons to different odorants ([Figure 32-3](#)). The usual response of the neuron to an odorant consists of depolarization and the production of action potentials. The number of neurons that respond to an odorant varies with odorant concentration; higher concentrations of an odorant stimulate a larger number of neurons. This may explain why odorants presented to human subjects at different concentrations can be perceived as being different.

## A Large Family of Odorant Receptors Permits Discrimination of a Wide Variety of Odorants

Volatile odorants that enter the nasal cavity and dissolve in the nasal mucus are detected by odorant receptors on the cilia of olfactory sensory neurons. A large multigene family, first identified in the rat, appears to

P.628

code for as many as 1000 different types of odorant receptors. This gene family, which is also present in humans, is extremely diverse. Although odorant receptors all have the same general structure and have some amino acid sequence motifs in common, each is unique ([Figure 32-4](#)). The unprecedented size and diversity of this receptor family are likely to allow for the discrimination of a wide variety of odorants having different sizes, shapes, and functional groups.

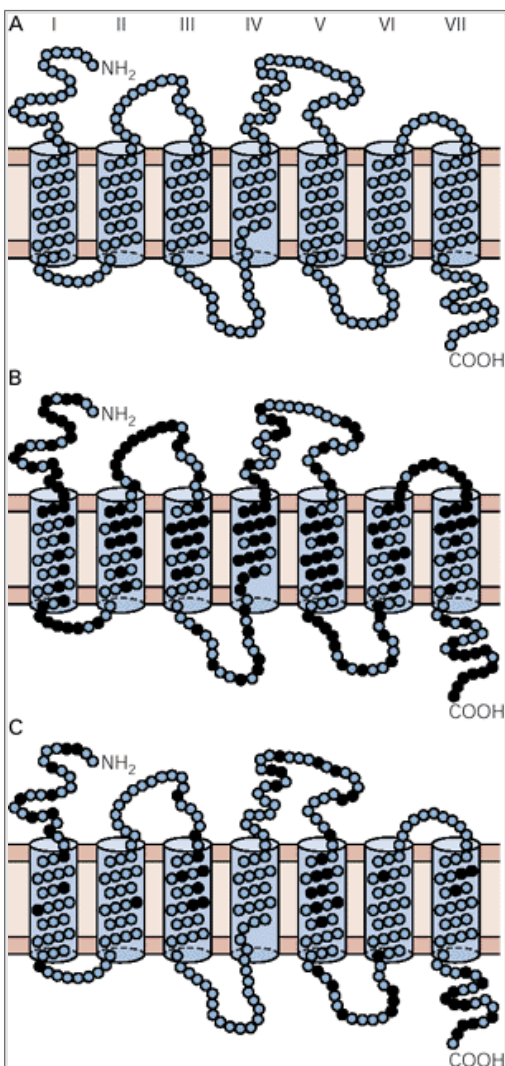


**Figure 32-3 Individual olfactory sensory neurons respond to different odorants.** The records are from patch clamp recordings of the responses of three neurons (A, B, C) to three odorants, each at a concentration of  $5 \times 10^{-4}$  M. One cell responded only to one of the odorants while another responded to two odorants; the third cell was stimulated by all three odorants. (Adapted from Firestein et al. 1993.)

The odorant receptors belong to a large superfamily of structurally related receptor proteins that transduce signals by interactions with heterotrimeric GTP-binding proteins (G proteins). Like other G protein-coupled receptors (see Chapters 5 and 13), the odorant receptors have seven hydrophobic regions that are likely to serve as transmembrane domains (Figure 32-4). Detailed studies of some other G protein-coupled receptors (eg, the  $\beta$ -adrenergic receptor) suggest that in many of these receptors the interaction with the ligand occurs

P.629

in a ligand-binding pocket that is formed by a combination of the transmembrane regions. Interestingly, the amino acid sequences of odorant receptors are especially variable in several transmembrane domains, providing a possible mechanism for the recognition of a variety of structurally diverse ligands.



**Figure 32-4 The amino acid sequences of odorant receptors are extremely diverse.**

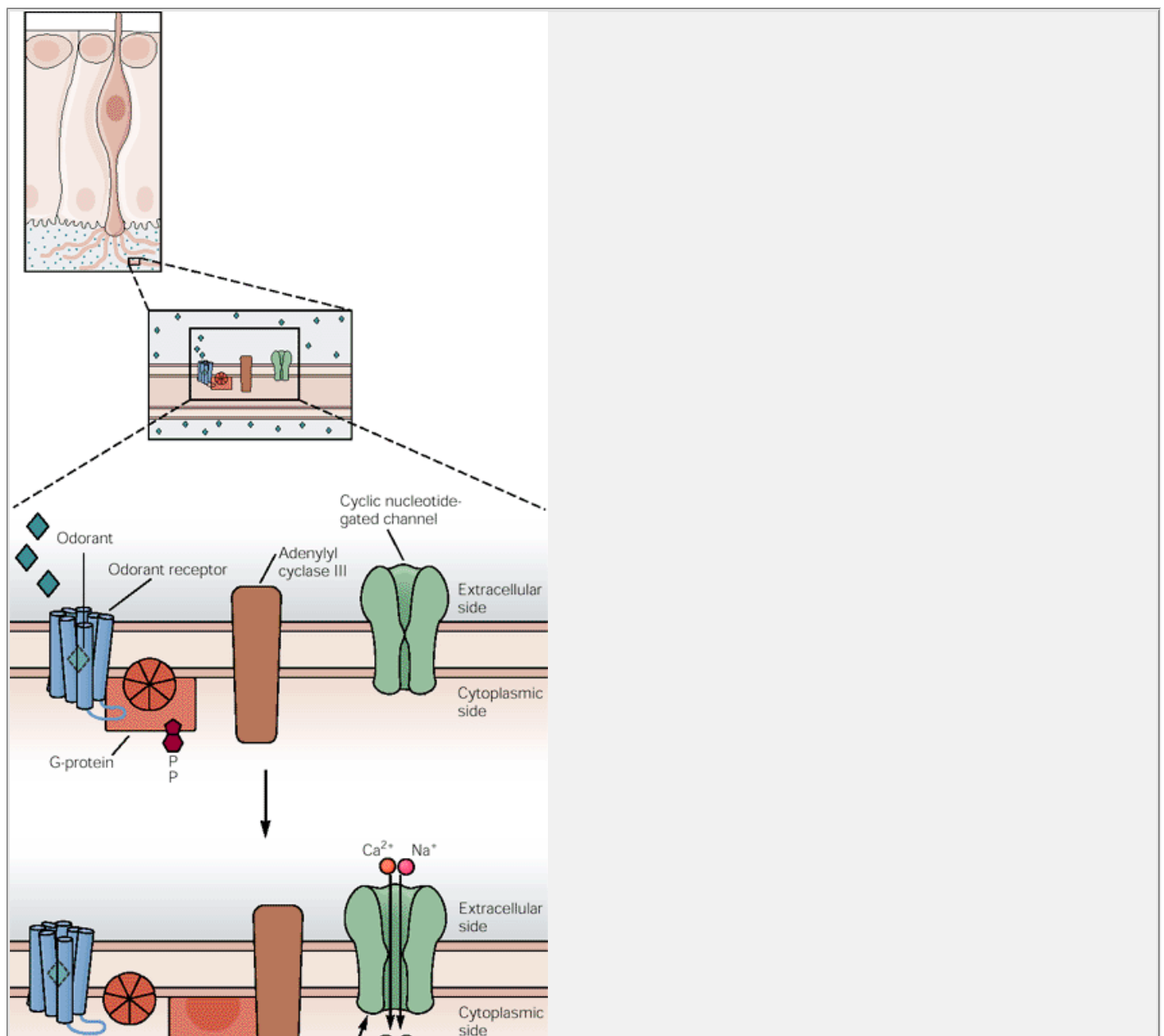
- A.** A typical odorant receptor (I15) is shown in its presumed configuration in the membrane, with seven hydrophobic membrane-spanning domains. Each amino acid is represented by a ball.
- B.** Odorant receptors are extremely diverse in amino acid sequence. The **black balls** indicate amino acids that are different in two odorant receptors (I15 and F6). The extreme diversity in the amino acid sequences of several of the transmembrane domains is consistent with the possibility that a ligand binding pocket is formed in the plane of the membrane by a combination of the transmembrane domains.
- C.** Although odorant receptors, and the genes that encode them, are extremely variable in sequence, some are closely related. Groups of receptor genes that are more than 80% identical in nucleotide sequence are considered to belong to the same subfamily. The receptors they encode are similar in amino acid sequence and therefore might interact with similar odorants. The **black balls** indicate amino acids that are different in two receptors (I15 and I9) that belong to the same subfamily.

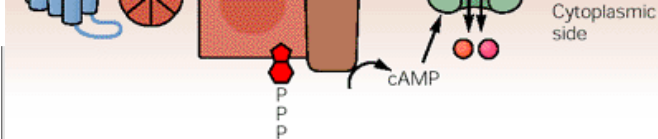
## The Interaction Between Odorant and Receptor Activates a Second-Messenger System That Leads to Depolarization of the Sensory Neuron

Odorants induce increases in adenylyl cyclase activity and cAMP in preparations of olfactory cilia. This effect is GTP dependent, suggesting that olfactory transduction, like visual transduction, proceeds via a G protein-coupled mechanism. The existence of an ionic conductance in olfactory cilia that is gated by cyclic nucleotides further suggests a mechanism by which odorant-induced elevations in cAMP could be translated into changes in membrane potential.

Our current understanding of the molecular events underlying olfactory signal transduction is illustrated in [Figure 32-5](#). In this model the interaction of an odorant with its receptor induces an interaction between the receptor and a heterotrimeric G protein. This interaction causes release of the G protein's GTP-coupled  $\alpha$ -subunit,  $G\alpha_{olf}$ , which then stimulates adenylyl cyclase to produce cAMP. The increased cAMP leads to the opening of cyclic nucleotide-gated cation channels in the cilia membrane, causing a depolarization that leads to the generation of action potentials in the sensory axon and the transmission of signals to the olfactory bulb. Additional signal transduction cascades involving inositol 1,4,5-trisphosphate ( $IP_3$ ), cyclic GMP, and carbon monoxide are also activated after odorant binding, but their roles in transduction are not currently understood.

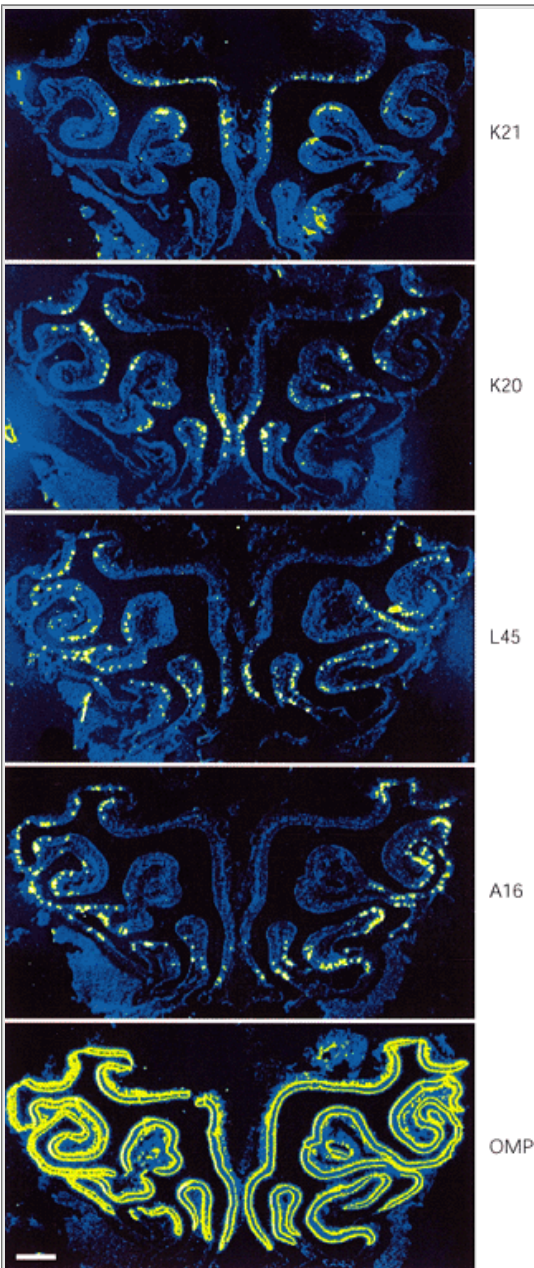
When we are continuously exposed to a disagreeable odor we cease to notice it after a short time. However, a brief exposure to fresh air allows us to smell the unpleasant odor again. This *adaptation* to odorants is thought to derive from at least two different physiological mechanisms. First, the interaction of an odorant receptor with its ligand may be followed by inactivation, or *desensitization*, of the receptor due to phosphorylation of the receptor by a protein kinase. Second, the olfactory neuron may adapt to different concentrations of an odorant by adjusting the sensitivity of its cyclic nucleotide-gated ion channels to cAMP, an effect conceptually analogous to light adaptation in the visual system, where light sensitivity is adjusted to match the intensity of light in the environment (see [Box 26-2](#)).





**Figure 32-5 Olfactory signal transduction.**

In this model binding of an odorant to an odorant receptor causes the receptor to interact with a G protein whose GTP-coupled  $\alpha$ -subunit ( $G\alpha_{olf}$ ) then stimulates adenylyl cyclase type III. The resultant increase in cAMP opens cyclic nucleotide-gated cation channels, leading to cation influx and a change in membrane potential in the cilium membrane.



**Figure 32-6 Each odorant receptor type is localized in one of four zones in the olfactory epithelium of the mouse.** Sections of mouse olfactory epithelium were hybridized to  $^{35}\text{S}$ -labeled probes prepared from genes encoding four different odorant receptors (K21, K20, L45, and A16) or olfactory marker protein (OMP), which is expressed in all olfactory sensory neurons. The nasal septum is in the center of each section, with the two nasal cavities on either side. The pattern of OMP mRNA expression indicates that most of the nasal cavity in this part of the nose is lined by olfactory epithelium. Each receptor probe labeled a small percentage of olfactory sensory neurons. These neurons are confined to one of four zones but are randomly scattered throughout that zone. Each of the receptor probes used here hybridized to neurons in a different zone. Note that the zones are bilaterally symmetrical in the two nasal cavities. Scale bar = 400  $\mu\text{m}$ . (From [Sullivan et al. 1996.](#))

## Different Olfactory Neurons Express Different Odorant Receptors

How is the information provided by 1000 different types of odorant receptors organized in the olfactory system? In situ hybridization studies indicate that each odorant receptor gene is expressed in only about 0.1% of olfactory sensory neurons, suggesting that each neuron expresses only one type of odorant receptor. Analysis of receptor expression in single neurons using the polymerase chain reaction also supports this conclusion. Thus each neuron is likely to transmit to the brain information that is derived from only one receptor type.

In rodents different sets of odorant receptor genes are expressed in four zones of the olfactory epithelium ([Figure 32-6](#)). Neurons with the same receptors are all located in one zone but are scattered throughout that zone along with neurons expressing other receptors. This arrangement suggests that sensory information is broadly organized into four large sets prior to transmission to the brain. The purpose served by this segregation is unknown. However, the different epithelial zones project axons to different domains in the olfactory bulb, indicating that the organization of epithelial inputs is preserved at the next level in the olfactory pathway.

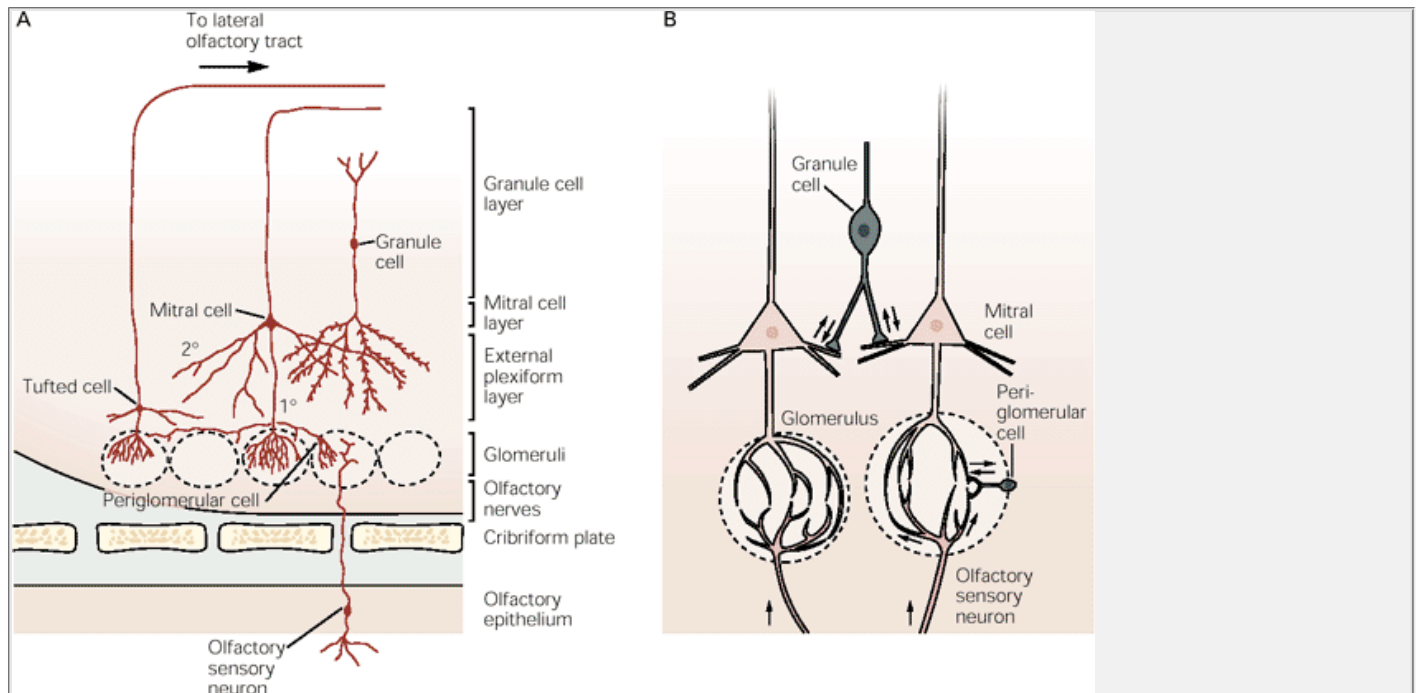
The highly distributed nature of information coding implied by this arrangement is likely to maximize the information-collecting function of the olfactory epithelium. Since any odorant can be recognized by receptors in many regions of the nasal cavity, responsiveness to an odorant is assured, even if part of the epithelium is damaged, as can occur during respiratory infection or with aging.

## Odorant Information Is Encoded Spatially in the Olfactory Bulb

Sensory information from the nose, is transmitted to the olfactory bulbs of the brain, paired structures that lie just above and behind the nasal cavities. In the olfactory bulb, incoming sensory axons synapse on the dendrites of olfactory bulb neurons within anatomically discrete synaptic units called glomeruli, of which there are about 2000 per bulb in the mouse (Figure 32-7). In the glomerulus the sensory axon makes synaptic connections with three types of neurons: mitral and tufted relay neurons, which project axons to the olfactory cortex, and periglomerular interneurons, which encircle the glomerulus. The axon of each olfactory sensory neuron synapses in only one glomerulus. Similarly, the primary dendrite of each mitral and tufted relay neuron is confined to a single glomerulus. In each glomerulus the axons of several thousand sensory neurons converge on

P.631

the dendrites of about 20-50 relay neurons, resulting in an approximately 100-fold decrease in the number of neurons transmitting olfactory sensory signals.



**Figure 32-7 The olfactory bulb receives signals from olfactory sensory neurons.** (Adapted from Shepherd and Greer 1990.)

**A.** Each sensory axon terminates in a single glomerulus, forming synapses with the dendrites of periglomerular interneurons and mitral and tufted relay neurons. The primary dendrite of each mitral and tufted cell enters a single glomerulus, where it arborizes extensively. Mitral and tufted cells also extend secondary dendrites into the external plexiform layer, where granule cell interneurons make reciprocal synapses with these secondary dendrites. The output of the bulb is carried by the mitral cells and the tufted cells, whose axons project in the lateral olfactory tract.

**B.** Within each glomerulus periglomerular cells form inhibitory dendrodendritic synapses with mitral cell dendrites. The periglomerular cells also sometimes make inhibitory contacts with mitral cells that receive input in nearby glomeruli. The secondary dendrites of mitral and tufted cells form excitatory synapses on the dendrites of granule cell interneurons, which form inhibitory synapses on numerous secondary dendrites. These inhibitory connections may provide a curtain of inhibition that must be penetrated by the peaks of excitation generated by odorant stimuli. They may also serve to sharpen or refine sensory information prior to transmission to the olfactory cortex.

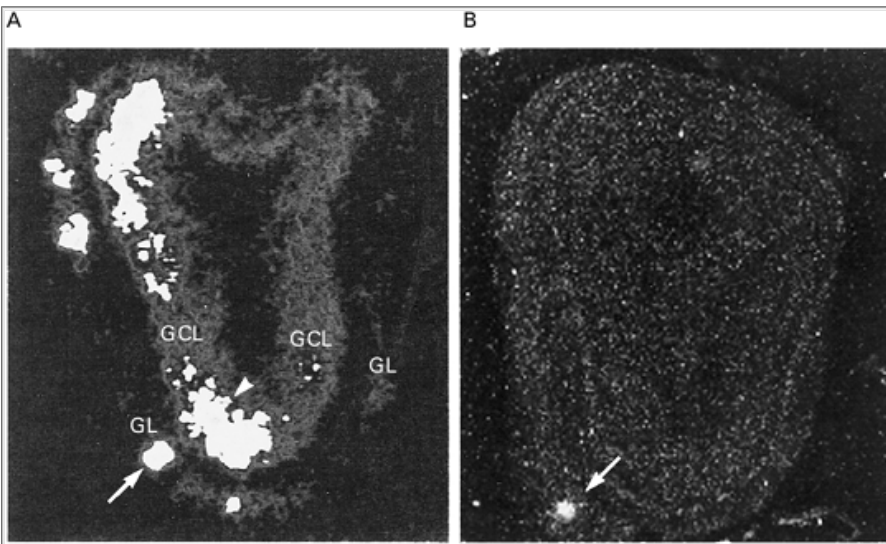
How is olfactory sensory information organized in the olfactory bulb? Insight into this question has come from experiments that took advantage of the fact that the survival of the olfactory sensory neurons in the nose depends on the integrity of the olfactory bulb. Relatively small lesions in the olfactory bulb lead to the degeneration of individual neurons that are widely dispersed in the olfactory epithelium, suggesting that the axons of sensory neurons in many areas of the epithelium converge on glomeruli in one region of the bulb. Further evidence for this convergence is provided by the observation that a single mitral relay neuron can be stimulated by odorants applied to many different areas of the olfactory epithelium.

The presence of anatomically discrete synaptic units (glomeruli) in the olfactory bulb led early researchers to suggest that the glomeruli might serve as functional units and that information about different odorants might be mapped onto different glomeruli. Evidence for this hypothesis is provided by exposing an animal to different odorants while recording the activity of a single mitral cell. Each mitral cell responds to multiple odorants, but mitral cells connected to different glomeruli generally respond to different sets of odorants. Labeling techniques that monitor neural activity over the entire olfactory bulb also show that each odorant typically stimulates many different glomeruli (Figure 32-8).

What characteristics of the afferent connections explain these observations? Analysis of the patterns of synapses formed in the bulb by sensory neurons expressing

P.632

different odorant receptors shows that the axons of neurons that express the same receptor all converge on a few glomeruli (Figure 32-8). It appears that each glomerulus may receive input from only one type of receptor. Remarkably, glomeruli that receive input from a specific type of receptor have the same locations in the olfactory bulbs of different animals. Thus, at the level of input to the olfactory bulb, sensory neuron's expressing a stereo-typed spatial map of sensory information is formed by different odorant receptors projecting to different glomeruli.



**Figure 32-8 Spatial mapping of sensory information in the olfactory bulb of rodents.**

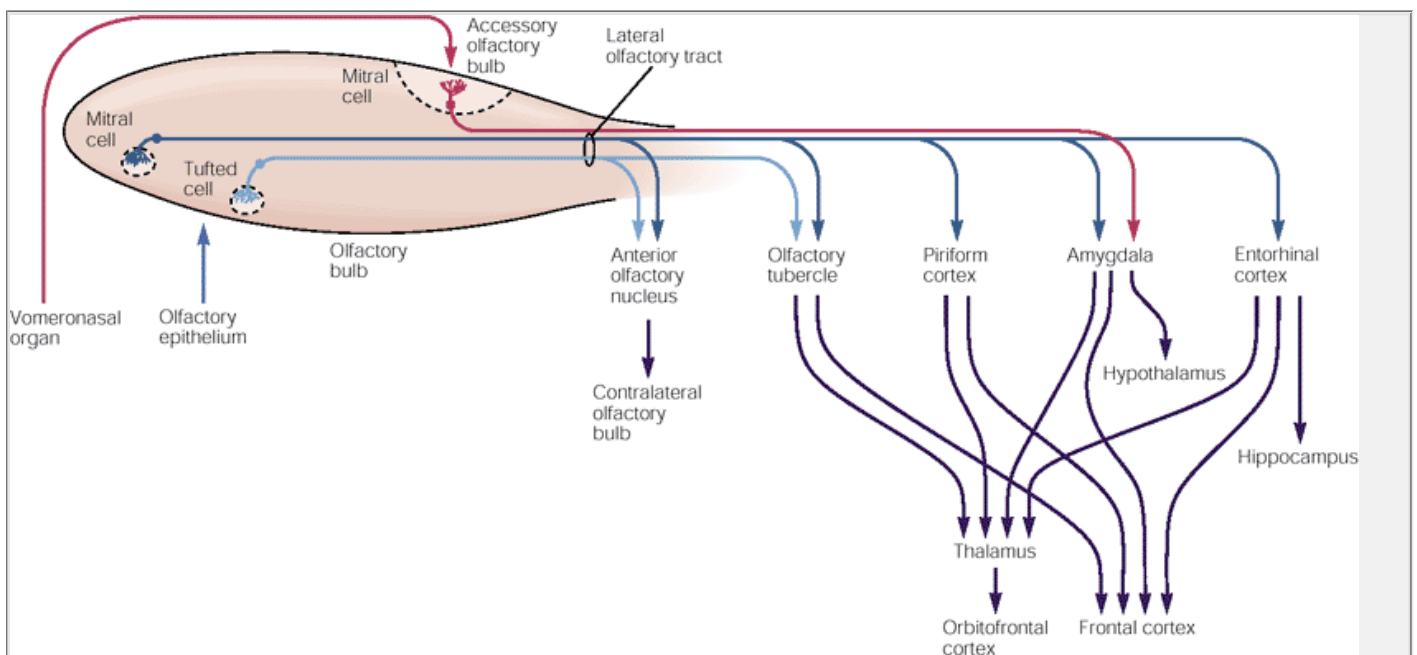
**A.** The pattern of labeling of a  $^{35}\text{S}$ -labeled *c-fos* probe in a section through the olfactory bulb of a rat exposed to peppermint odor. Intense hybridization to the probe is observed at several foci in the glomerular layer (**GL**; **arrow**) as well as in regions of the granule cell layer (**GCL**; **arrowhead**) deep to those foci. The intense signal in one or more glomeruli at several locations in this section illustrates the finding of numerous studies that a single odorant typically stimulates multiple glomeruli. Elevated neural activity is reflected here by increases in *c-fos* RNA. (From Guthrie et al. 1993.)

**B.** A section through the olfactory bulb of a mouse shows intense hybridization of a  $^{35}\text{S}$ -labeled odorant receptor gene (*M50*) probe to sensory axons in a single glomerulus (**arrow**). The axons of olfactory sensory neurons that express the *M50* odorant receptor gene are concentrated in only a few glomeruli. (From Ressler et al. 1994.)

This arrangement suggests that an odorant that stimulates many glomeruli is recognized by many different receptors. It also implies that different odorants that activate the same glomerulus are all recognized by the same receptor. Thus, the identity of an odorant may be encoded by a combination of receptors that recognize different structural features of that odorant. That is, each receptor may serve as one component of the code for many odorants, thus allowing for the discrimination of a large number of different odorants. In this model the information map in the olfactory bulb might not be based on different odors but rather on different molecular features, each of which might be shared by a variety of odorants, including those with very different perceived qualities.

Sensory information is likely to be extensively processed, and perhaps refined, in the olfactory bulb before it is sent to the olfactory cortex. Periglomerular interneurons encircling a glomerulus appear to make inhibitory dendrodendritic synapses with mitral cell dendrites in that glomerulus, and sometimes in adjacent glomeruli (see Figure 32-7). In addition, granule cell interneurons deep in the bulb provide negative feedback circuits. These interneurons are excited by the basal dendrites (secondary dendrites) of mitral cells and also inhibit those mitral cells and others with which they are connected (see Figure 32-7).

Another potential source of signal refinement, or adjustment, is the multiple inputs to the olfactory bulb from olfactory areas of the cortex as well as the basal forebrain (horizontal limb of the diagonal band) and midbrain (locus ceruleus and raphe). These connections may provide a way of modulating olfactory bulb function, so that odors might have different behavioral significance depending on the physiological state of the animal. For example, some centrifugal projections might heighten the perception of the aroma of foods when the animal is hungry.



**Figure 32-9 Olfactory information is processed in several regions of the cerebral cortex.**

Information is transmitted from the olfactory bulb by the axons of mitral and tufted relay neurons, which travel in the lateral olfactory tract. Mitral cells project to the five different regions of olfactory cortex: the anterior olfactory nucleus, which innervates the contralateral olfactory bulb; the olfactory tubercle; the piriform cortex; and parts of the amygdala and entorhinal cortex. Tufted cells appear to project primarily to the anterior olfactory nucleus and the olfactory tubercle, while mitral cells in the accessory olfactory bulb project only to the amygdala. The conscious discrimination of odors is thought to depend on the neocortex (orbitofrontal cortex and frontal cortex), which may receive olfactory information via two separate projections: one through the thalamus and one directly to the neocortex. The emotive aspects of olfactory sensation are thought to derive from limbic projections involving the amygdala and hypothalamus. The effects of pheromones are also thought to be mediated by signals from the main and accessory olfactory bulbs to the amygdala and hypothalamus.

## Odorant Information Is Transmitted From the Olfactory Bulb to the Neocortex Directly and via the Thalamus

The axons of the mitral and tufted relay neurons of the olfactory bulb project through the lateral olfactory tract to the olfactory cortex ([Figure 32-9](#)). The olfactory cortex, defined roughly as that portion of the cortex that receives a direct projection from the olfactory bulb, is divided into five main areas: (1) the anterior olfactory nucleus, which connects the two olfactory bulbs through a portion of the anterior commissure; (2) the piriform cortex; (3) parts of the amygdala; (4) the olfactory tubercle; and (5) part of the entorhinal cortex. From the latter four areas, information is relayed to the orbitofrontal cortex via the thalamus; however, the olfactory cortex also makes direct contacts with the frontal cortex ([Figure 32-9](#)). In addition, olfactory information is transmitted from the amygdala to the hypothalamus and from the entorhinal area to the hippocampus.

The afferent pathways through the thalamus to the orbitofrontal cortex are thought to be responsible for the perception and discrimination of odors, because people with lesions of the orbitofrontal cortex are unable to discriminate odors. In contrast, the olfactory pathways leading to the amygdala and hypothalamus are thought to mediate the emotional and motivational aspects of smell as well as many of the behavioral and physiological effects of odors.

## Pheromones Are Species-Specific Chemical Messengers

Some species release chemical substances into their surroundings to influence the behavior or physiology of members of the same species. Pheromones play an important role in sexual and social behaviors and reproductive physiology in many animals. Pheromones can influence estrus cycles, regulate the age of onset of puberty,

P.634

prevent implantation of fertilized embryos, and signal receptivity of females for mating in many species, including mice, rats, cattle, and pigs. The source of pheromones is typically urine or glandular secretions. However, very few pheromones have been chemically defined.

## The Vomeronasal Organ Transmits Information About Pheromones

Two separate olfactory systems appear to be involved in sensing pheromones: the main olfactory system, which we have already discussed, and the *accessory olfactory system* or *vomeronasal system*. The accessory system includes the paired vomeronasal organs, which are located at the base of the nasal septum; the vomeronasal nerves; and the accessory olfactory bulbs.

The vomeronasal organ is a fluid-filled, tubular structure that opens into the nasal cavity via a duct at its anterior end. It is lined, in part, with a sensory epithelium that resembles the olfactory epithelium of the nasal cavity. Molecules that dissolve in the mucus of the nasal cavity are pumped into the vomeronasal organ by changes in local blood volume, which change the size of its lumen. The axons of neurons in the vomeronasal organ are bundled in the vomeronasal nerve and project to the accessory olfactory bulb, an anatomically distinct region of the olfactory bulb.

The accessory olfactory bulb differs from the main olfactory bulb in its pattern of projections ([Figure 32-9](#)). Mitral cells in the accessory olfactory bulb project almost exclusively to regions of the amygdala that project to the hypothalamus. The anatomical layout of this pathway suggests that molecules sensed by the accessory olfactory system stimulate regions of the hypothalamus that are involved in reproductive physiology and behavior but are not consciously perceived. Consistent with this idea, male hamsters whose vomeronasal nerves have been cut exhibit a severe dysfunction in mating. Similar studies have implicated the vomeronasal system in a variety of behavioral and physiological responses to pheromones.

There has been considerable speculation as to whether humans communicate via body odors. There has also been debate as to whether humans have an accessory olfactory system, although evidence is accumulating that we do not.

## Sensory Transduction in the Vomeronasal Organ Differs From That in the Nose

Although sensory neurons in the vomeronasal organ resemble those in the nasal olfactory epithelium, they use different molecules to transduce sensory stimuli. Vomeronasal neurons completely lack several major components of the olfactory sensory transduction cascade ( $G_{\text{olf}}$ , adenylyl cyclase type III, and one subunit of the olfactory cyclic nucleotide-gated cation channel). In addition, only a rare vomeronasal neuron expresses "classical" odorant receptors. The vomeronasal neurons appear to use two entirely different families, of approximately 100 different receptor types each, to detect sensory ligands.

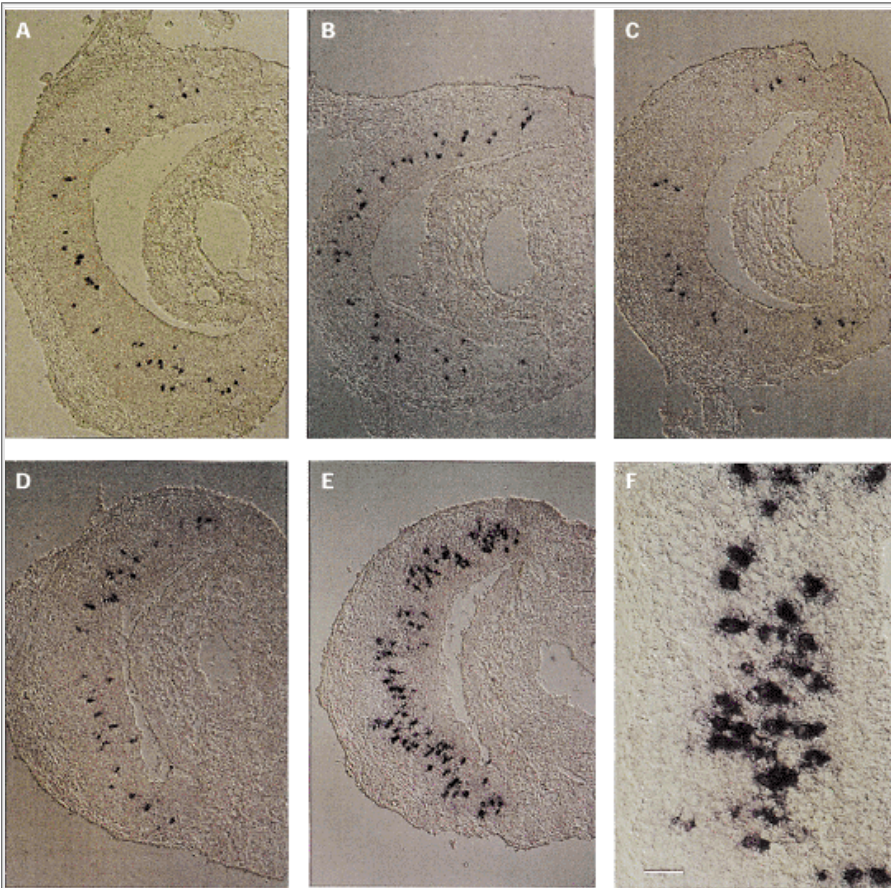
Although the members of both candidate pheromone receptor families are unrelated in sequence to odorant receptors, they resemble odorant receptors in that they have seven potential transmembrane domains, a feature characteristic of G protein-coupled receptors. The vomeronasal receptor families resemble the odorant receptor family in other ways as well. First, members of these families are diverse, suggesting that they recognize different ligands. Second, it appears that each vomeronasal neuron may express only one type of vomeronasal receptor. And third, neurons that express different receptor types are interspersed in the vomeronasal neuroepithelium ([Figure 32-10](#)).

The two families of vomeronasal receptors are expressed in two different spatial zones. In contrast to the spatial zones of odorant receptor expression, the vomeronasal zones consist of two parallel layers of neurons that extend throughout the neuroepithelium. Interestingly, neurons in the upper layer express high levels of the G protein  $G_{\alpha_2}$ , while those in the lower layer express high levels of  $G_{\alpha_3}$ , suggesting that the two receptor families might couple to different G proteins. An important question still to be answered is what ligands are recognized by the vomeronasal receptors. Another is whether information provided by the two receptor families is transmitted to different areas of the amygdala or hypothalamus that mediate different behavioral or physiological effects of pheromones.

## Olfactory Acuity Varies in Humans

Olfactory acuity varies considerably among humans. Sensitivity may vary as much as a thousandfold, even among people with no obvious abnormality. The most common olfactory aberration is *specific anosmia*. An individual with a specific anosmia has lowered sensitivity to a specific odorant even though sensitivity to other odorants appears normal. Specific anosmias to some odorants are common, a few occurring in 1-20% of people. For example, 12% of individuals tested in one study exhibited a specific anosmia for musk. Lack of a specific odorant receptor may explain specific anosmias.





**Figure 32-10 The pattern of expression of candidate pheromone receptors in the vomeronasal organ.** The expression of one family of vomeronasal receptor genes in the rat was examined by hybridizing digoxigenin-labeled probes to sections through the vomeronasal organ. Probes were prepared from different receptor genes (**A-D**) or a mix of six such probes (**E** and **F**). Each receptor probe hybridized to a small percentage of vomeronasal neurons scattered throughout the upper region of the vomeronasal neuroepithelium. With the mixed probe a much larger percentage of hybridized neurons is seen, indicating that the different receptor genes are expressed in different cells. Although the vomeronasal receptors are likely to recognize pheromones, no differences in hybridization were observed in male versus female rats (**A** vs **B**). Scale bar = 120  $\mu\text{m}$ . (From [Dulac and Axel 1995](#).)

P.635

Far rarer abnormalities of olfaction, such as *general anosmia* (complete lack of olfactory sensation) or *hyposmia* (diminished sense of smell), can derive from respiratory infections and are often transient. Chronic anosmia or hyposmia can result from damage to the olfactory epithelium caused by infections; from head trauma that severs the olfactory nerves passing through holes in the cribriform plate, which then become blocked by scar tissue; or from particular diseases, such as Parkinson disease. Olfactory hallucinations of repugnant smells (*cacosmia*) can occur as a consequence of epileptic seizures.

## Invertebrates and Vertebrates Use Different Strategies to Process Chemosensory Information

Chemosensory mechanisms have been studied in both vertebrates and invertebrates. Certain features are highly conserved in evolution, including the use of chemosensory cells with specialized cilia or microvilli exposed to the external environment. Explorations into the molecular mechanisms underlying chemoreception in several invertebrate species suggest that, like vertebrates, they use G protein-coupled receptors to detect chemosensory stimuli. However, recent studies indicate that the strategies used by the nematode worm *Caenorhabditis elegans* to sort out the complexity of chemical information in its environment are different from those of vertebrates.

The nervous system of *C. elegans* is composed of only 302 neurons, each of which has a characteristic location in the animal. Thirty-two of these cells are chemosensory neurons, which have cilia in contact with the external milieu. *C. elegans* can discriminate between a variety of volatile and nonvolatile chemicals. By killing individual cells with a laser beam, investigators can determine which cells respond to a given chemical. Such studies indicate that responses to volatile and nonvolatile chemicals are generally mediated by different chemosensory neurons. Different neurons respond to different chemicals, but each neuron can recognize a variety of chemicals. The worm moves toward some

P.636

chemicals but moves away from others, and different chemosensory neurons mediate these attraction and repulsion responses.

Molecular genetic studies have begun to provide insight into the mechanism by which *C. elegans* discriminates among different chemicals. A receptor for a volatile chemical, diacetyl, was identified by cloning genes that are mutated in worms that cannot sense diacetyl ([Figure 32-11](#)). Although the diacetyl receptor is unrelated to vertebrate odorant receptors, its structure suggests that it may also transduce signals by interacting with G proteins. The diacetyl receptor belongs to a family of receptors, members of which are expressed by different chemosensory neurons. These receptors are expressed in chemosensory neurons that detect both volatile and nonvolatile chemicals. In striking contrast to vertebrate olfactory systems, a single chemosensory neuron in *C. elegans* expresses several different receptors that belong to the diacetyl receptor family. Each neuron also appears to express several receptors that belong to other families of G protein-coupled receptors, suggesting that each neuron employs a variety of receptor types to detect chemicals in the external environment.

Functional studies indicate that a worm with only one functional chemosensory neuron can distinguish some chemicals. The expression of different classes of receptors in a single cell suggests the intriguing possibility that this discrimination derives from the existence of multiple signaling cascades, each of which is activated by a different receptor type.

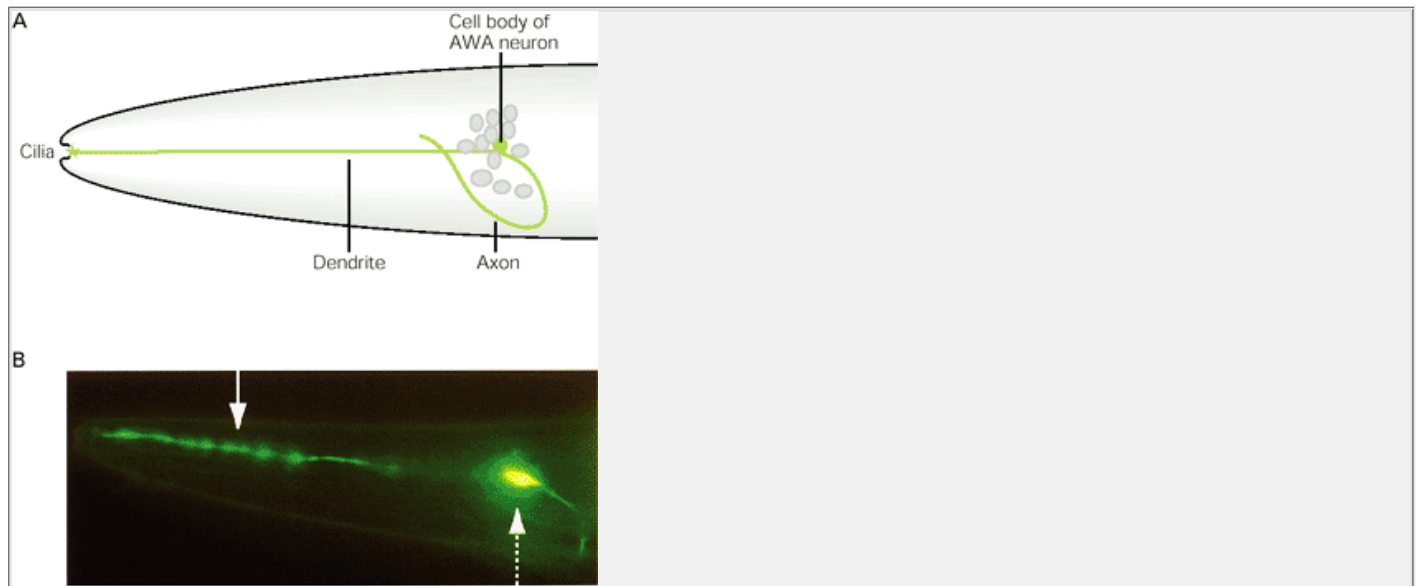
## Taste Stimuli Are Detected by Taste Cells in the Mouth

### Taste Cells Are Clustered in Taste Buds

Molecules that can be tasted are detected by taste cells clustered in taste buds on the tongue, palate, pharynx, epiglottis, and upper third of the esophagus. On the

tongue, taste buds are located primarily in the papillae, which are embedded in the epithelium.

In humans three morphological types of papillae are found in different regions of the tongue (Figure 32-12). Several hundred fungiform papillae, which have a peg-like structure, are located on the anterior two-thirds of the tongue. On the posterior third are the large circumvallate papillae, each of which is surrounded by a groove. The foliate papillae, situated on the posterior edge of the tongue, are leaf-like structures, each of which is also surrounded by a groove. Each fungiform papilla contains one to five taste buds, while each circumvallate or foliate papilla contains hundreds of taste buds.

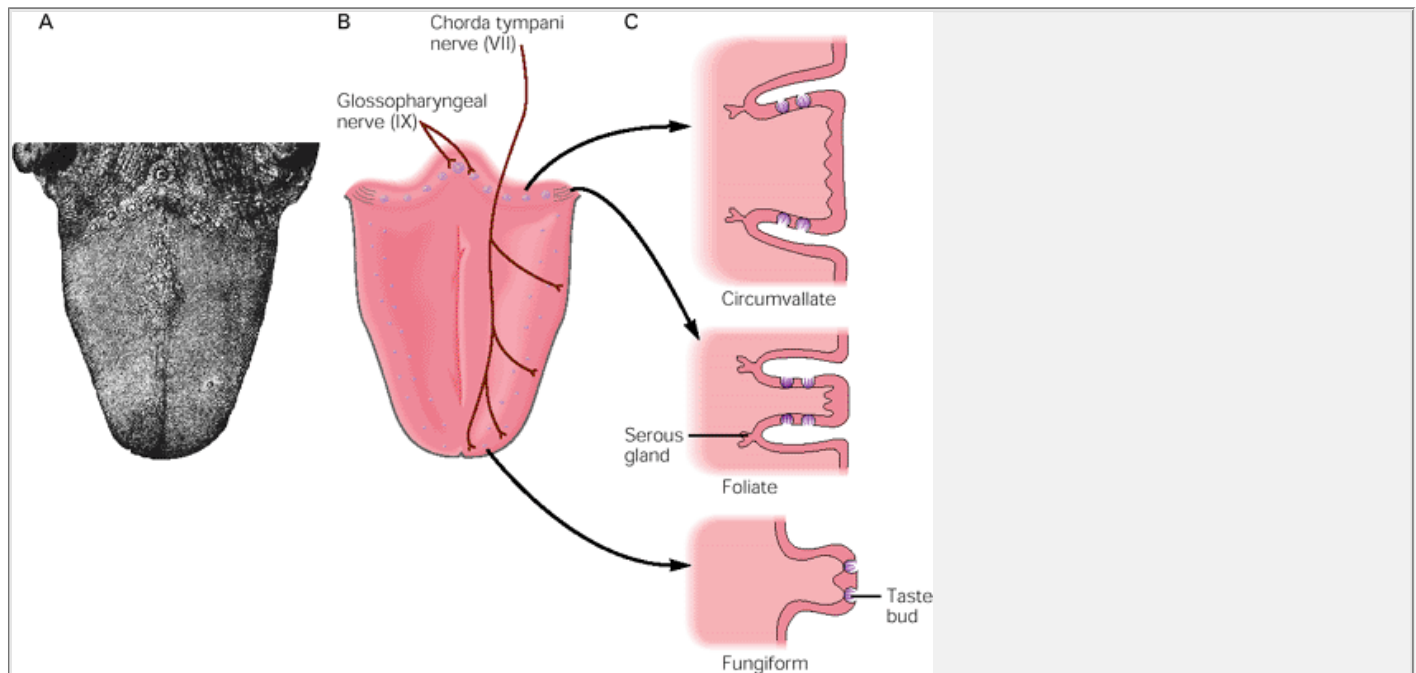


**Figure 32-11 The receptor for diacetyl is expressed in a specific chemosensory neuron in the nematode worm *Caenorhabditis elegans*.**

**A.** Diagram of a lateral view of the anterior end of the nematode *C. elegans* showing the cell body and processes of the AWA chemosensory neuron. The dendritic process of the AWA neuron terminates in cilia that are exposed to environmental chemicals. The AWA neuron detects the volatile chemical diacetyl; animals with a mutation in the *odr-10* gene are unable to sense diacetyl.

**B.** The pattern of expression of the *odr-10* gene was examined by preparing transgenic animals carrying a fusion gene consisting of part of the *odr-10* gene fused to a gene encoding a fluorescent protein (green fluorescent protein). In this lateral view of a transgenic animal, fluorescence is seen only in the AWA neuron, indicating that the *odr-10* gene is normally expressed in this neuron. This is consistent with the conclusion that the *odr-10* gene encodes the diacetyl receptor. **Arrows** indicate the AWA dendrite and cell body. (From [Sengupta et al. 1996.](#))

Four morphologically distinguishable types of cells are found in each taste bud: basal cells, dark cells, light cells, and intermediate cells (Figure 32-13). Basal cells, small round cells at the base of the taste bud, are thought to be the stem cells from which the other cells are derived. Taste cells are very short-lived and are continuously regenerated. The three nonbasal cell types may represent various stages of differentiation of the developing taste cell, with the light cells being the most mature. Alternatively, the light, intermediate, and dark cells could represent different cell lineages. All three types are referred to as taste cells; all have an elongate, bipolar shape and extend from the epithelial opening of the taste bud to its base.



**Figure 32-12 Taste buds are located in three types of papillae found in different regions of the human tongue.**

**A.** Surface of the dorsum and root of the human tongue. (From [Bloom and Fawcett 1975.](#))

**B.** The taste buds of the anterior two-thirds of the tongue are innervated by the gustatory fibers that travel in a branch of the facial nerve (VII) called the chorda tympani. The taste buds of the posterior third of the tongue are innervated by gustatory fibers that travel in the lingual branch of the glossopharyngeal nerve (IX). (Adapted from Shepherd 1983.)

**C.** The main types of taste papillae are shown in schematic cross sections. Each type predominates in specific areas of the tongue, as indicated by the arrows from **B**

Each taste bud has a small opening at the surface of the epithelium called a taste pore. The hundred or so taste cells in each bud extend microvilli into the taste pore (Figure 32-13). The microvilli, where sensory transduction takes place, are the only parts of the taste cell that are exposed to the oral cavity. The taste cell is innervated by sensory neurons (primary gustatory afferent fibers) at its basal pole. Although taste cells are nonneuronal epithelial cells, the contacts between taste cells and sensory fibers have the morphological characteristics of chemical synapses. In addition, taste cells, like neurons, are electrically excitable cells with voltage-gated  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{Ca}^{2+}$  channels capable of generating action potentials.

## The Four Different Taste Qualities Are Mediated by a Variety of Mechanisms

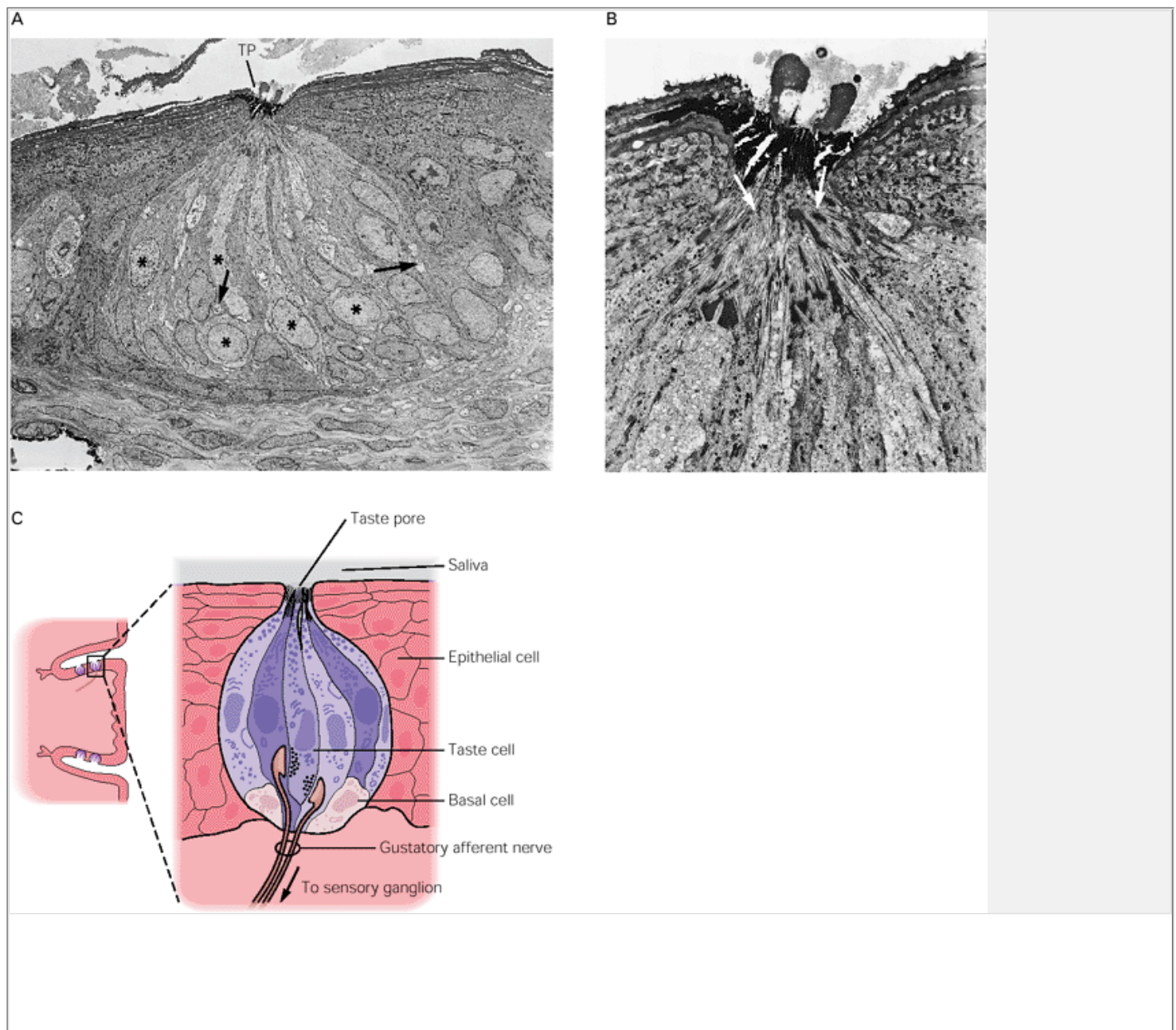
The gustatory system distinguishes four basic stimulus qualities: bitter, salty, sour, and sweet. Monosodium glutamate may represent a fifth stimulus category, called *umami*. The molecular mechanisms by which taste stimuli are transduced have been explored in studies using a variety of experimental techniques, including electrophysiology, biochemistry, and molecular biology. These studies have shown that each type of taste stimulus is transduced by a different mechanism (Figure 32-14). In addition, two stimuli may elicit the same taste sensation by different mechanisms. Furthermore, the molecular mechanisms used by different vertebrate species to sense the same tastant may differ.

In general, tastants interact with either ion channels or specific receptors in the apical membrane of the taste cell. These interactions typically depolarize the cell, either directly or via the action of second messengers. The resulting receptor potential generates action potentials in the taste cell, which, in turn, lead to  $\text{Ca}^{2+}$  influx through voltage-dependent  $\text{Ca}^{2+}$  channels and the release of neurotransmitter at synapses formed with sensory fibers. Another alternative mechanism may involve the release of  $\text{Ca}^{2+}$  from intracellular stores. As discussed below, salty and sour tastes involve permeation, or blockade, of ion channels by  $\text{Na}^+$  ions (salty taste) or  $\text{H}^+$  ions (sour taste), while sweet and bitter tastes appear to be mediated in some cases by specific G protein-coupled receptors, but in other cases they may result from direct effects on ion channels.

## Sweet

Sweet taste is thought to be mediated by the binding of sweet tastants to specific receptors on the apical membrane of the taste cell (Figure 32-14). There may be two different mechanisms for the transduction of sweet tastants. In rodents, one appears to involve a cAMP-dependent closure of basolateral  $\text{K}^+$  channels. Since these channels are normally open at the resting membrane potential, their closure leads to depolarization of the cell. The binding of sweet tastants to G protein-

coupled sweet receptors induces an increase in intracellular cAMP, activating a cAMP-dependent kinase that phosphorylates  $\text{K}^+$  channels, thereby inactivating them. Evidence for this pathway is provided by studies showing that mouse taste cells depolarize in response to sucrose and that this response can be mimicked by the intracellular injection of cyclic nucleotides or a chemical that specifically blocks  $\text{K}^+$  channels. In addition, sucrose causes a dose-dependent rise in cAMP in intact circumvallate taste buds. The observation that increases in cAMP that are induced by sweet tastants require the presence of GTP further suggests the existence of G protein-coupled receptors for sweet molecules.



**Figure 32-13 Each taste bud contains many taste cells.**

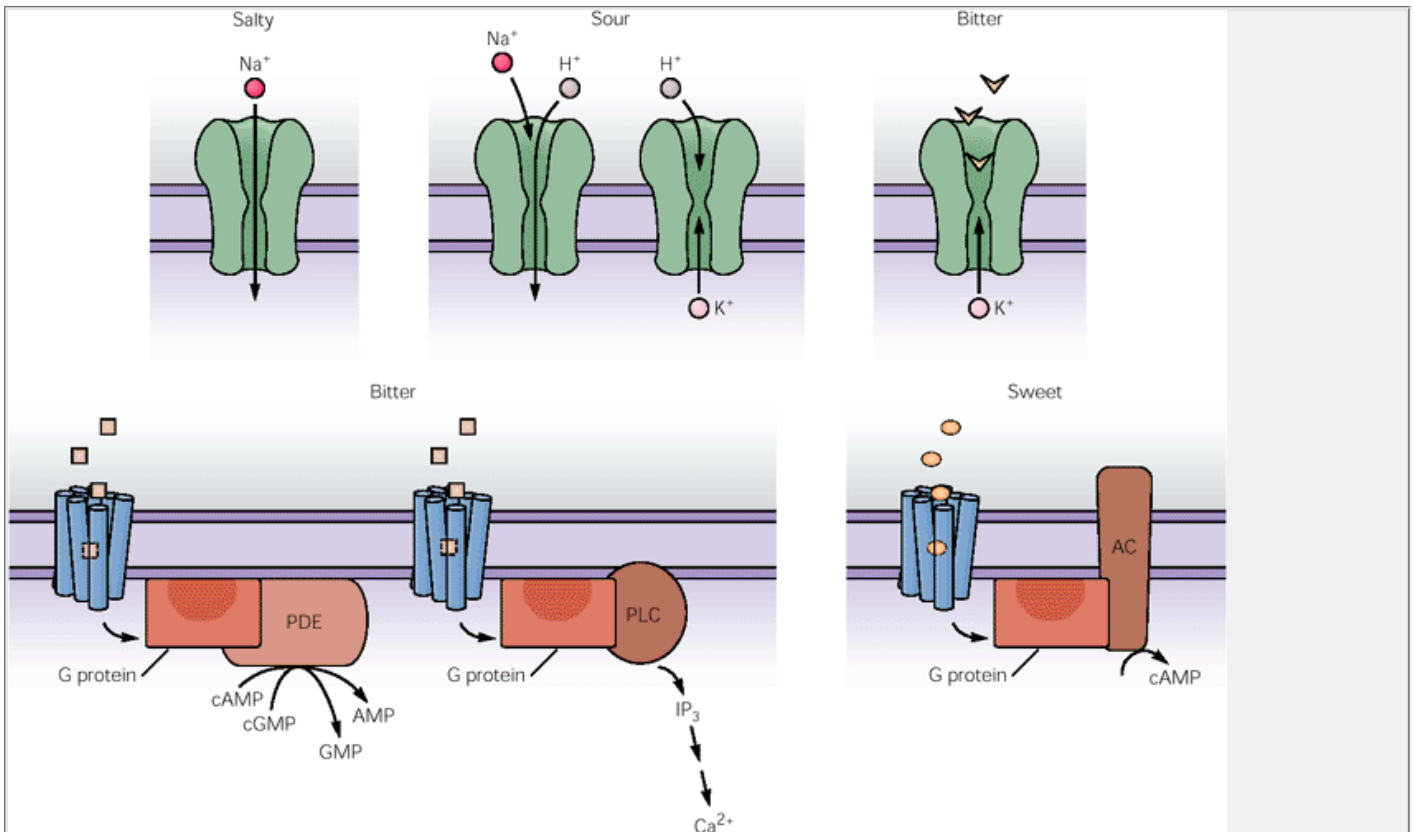
**A, B.** Transmission electron micrographs of longitudinal sections through a rabbit foliate taste bud show microvilli (**arrows in B**) projecting into the taste pore (**TP**). Also seen are the nuclei and apical processes of the taste cells (**asterisks in A**). Afferent nerve fibers are indicated by **arrows in A**. Magnification approximately  $\times 860$ . (**A**, from [Royer and Kinnamon 1991](#); **B**, courtesy of Royer and Kinnamon.)

**C.** Each taste bud contains 50-150 taste cells that extend from the base of the taste bud to the taste pore, where the apical microvilli of taste cells have contact with tastants dissolved in saliva and taste pore mucus. Access of tastants to the basolateral regions of these cells is generally prevented by tight junctions between taste cells. Taste cells are short-lived cells that are replaced from stem cells at the base of the taste bud. Three types of taste cells in each taste bud (light cells, dark cells, and intermediate cells) may represent different stages of differentiation or different cell lineages. Taste stimuli, detected at the apical end of the taste cell, induce action potentials that cause the release of neurotransmitter at synapses formed at the base of the taste cell with gustatory fibers that transmit signals to the brain.

A second mechanism of sweet taste transduction in rodents is suggested by the finding that some artificial sweeteners stimulate increases in  $IP_3$ . By analogy with signal transduction cascades involving  $IP_3$  induction in some other cell types, some sweet taste receptors may transduce signals via interactions with one or more G proteins that change intracellular concentrations

P.639

of  $IP_3$  rather than cAMP. Such increases in  $IP_3$  are likely to cause the release of  $Ca^{2+}$  from intracellular stores.



**Figure 32-14 Four basic taste stimuli are transduced into electrical signals by different mechanisms.**

**Salty** taste is mediated by  $Na^+$  influx through amiloride-sensitive  $Na^+$  channels. **Sour**. Sour taste can result from either the passage of  $H^+$  ions through amiloride-sensitive  $Na^+$  channels or from the blockade of  $K^+$  channels, which are normally open at resting potential. **Bitter**. Although at least one bitter stimulus, quinine, may depolarize taste cells by blocking apical  $K^+$  channels, most bitter stimuli are thought to bind to G protein-coupled receptors. There is evidence for two different pathways of bitter taste transduction that involve G proteins. In one the G protein stimulates phospholipase C (**PLC**) to increase production of inositol 1,4,5-trisphosphate ( **$IP_3$** ), which then causes the release of  $Ca^{2+}$  from intracellular stores. In the other pathway the G protein gustducin activates a phosphodiesterase (**PDE**) that may reduce intracellular levels of both cAMP and cGMP. **Sweet**. Some sweet tastants are also thought to bind to receptors that couple to gustducin or a G protein that stimulates  $IP_3$  production. However, other sweet receptors may couple to a G protein that interacts with adenylyl cyclase, causing an increase in cAMP that leads to the phosphorylation of  $K^+$  channels by protein kinase A.

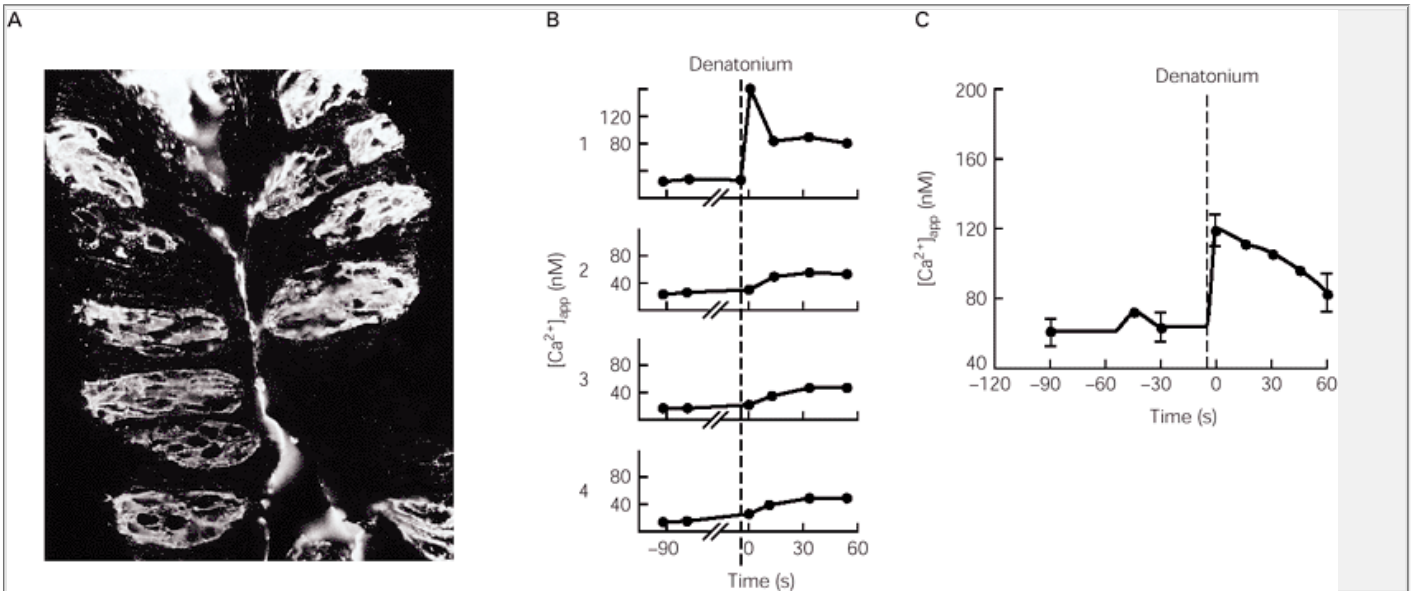
Yet another possibility has been raised by the observation that mice mutant for the G protein gustducin have defective responses to some sweet substances. Gustducin is similar to transducin, which causes cyclic nucleotide degradation in the visual system. The relative contributions of cAMP production and degradation, and  $IP_3$  turnover in sweet taste transduction, are currently unclear.

## Bitter

Bitter taste is often associated with toxic compounds and is thought to have evolved as a means of preventing ingestion of these molecules. Bitter taste sensations are elicited by a variety of compounds, including divalent cations, some amino acids, alkaloids, and denatonium, the most bitter compound known. The molecular heterogeneity of these bitter-tasting substances and the fact that some are membrane-permeable (eg, quinine) while others are not (eg, denatonium) suggest that bitter taste

P.640

might be transduced by more than one mechanism. Current evidence supports this idea.



**Figure 32-15 Responses of single taste cells to a bitter tastant.** (From Akabas et al. 1988.)

**A.** Taste buds in a circumvallate papilla of the rat tongue labeled with a monoclonal antibody. Many taste cells are clustered in buds lining the wall of the papilla.

**B.** Intracellular  $Ca^{2+}$  concentration increases in a taste cell responsive to a bitter stimulus, denatonium chloride (**1**). Three adjacent nonreceptive cells (**2, 3, 4**) showed no change in intracellular  $Ca^{2+}$  concentration. The  $Ca^{2+}$  concentration was calculated using a  $Ca^{2+}$ -sensitive dye, Fura-2.

**C.** Increases in intracellular  $Ca^{2+}$  concentration in the taste cell are caused by a release of  $Ca^{2+}$  from intracellular stores. When taste cells isolated in culture were bathed in a  $Ca^{2+}$ -free medium, denatonium remained an effective stimulus.

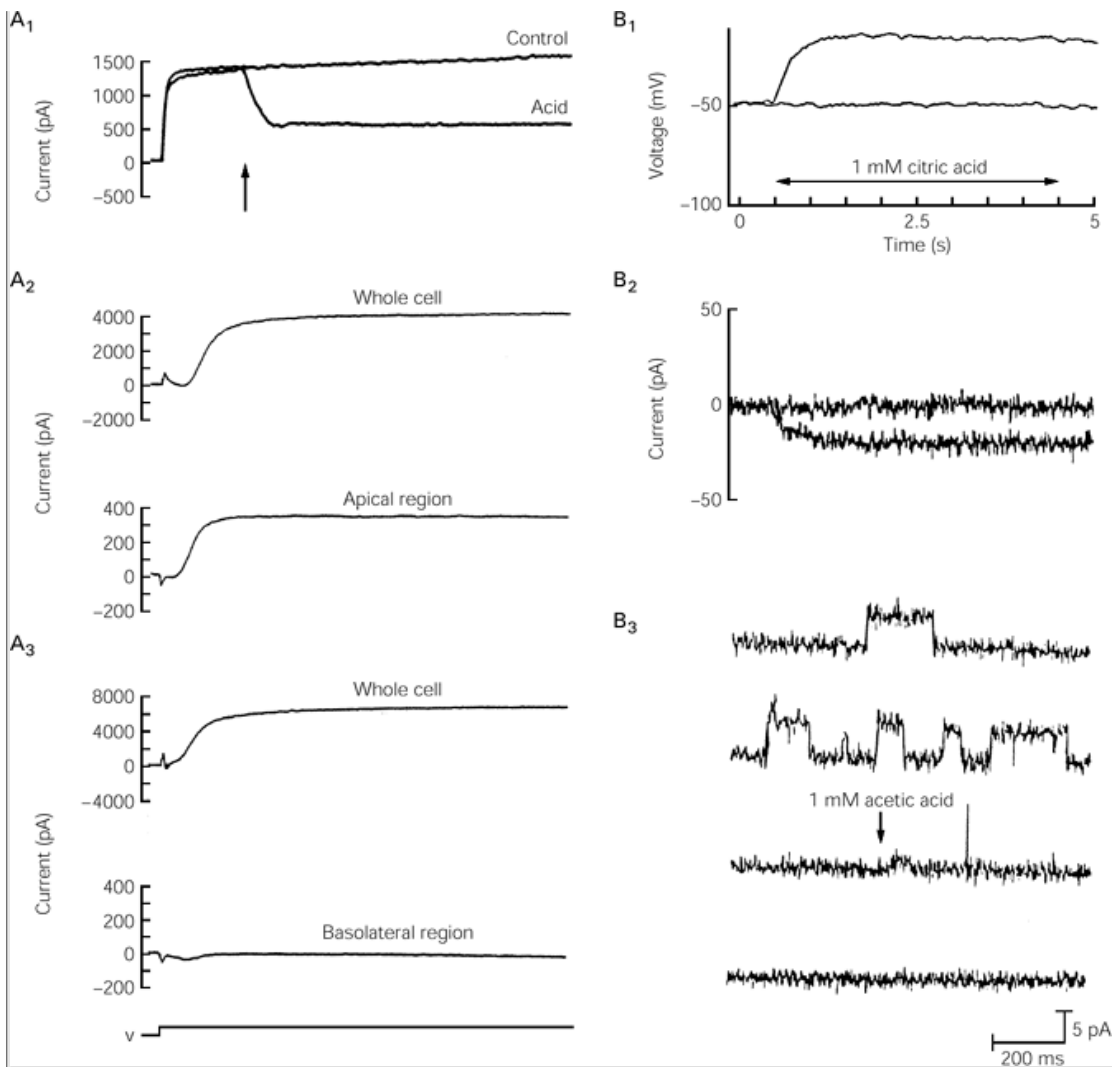
The transduction of many bitter tastes may involve specific G protein-coupled membrane receptors that bind to bitter-tasting compounds (Figure 32-14). This mechanism was suggested by the observation, in optically imaged taste cells impregnated with a calcium-sensitive dye, that intracellular  $Ca^{2+}$  changes after exposure to denatonium. Denatonium, as well as some other bitter stimuli, has been found to cause increases in intracellular  $IP_3$  and the release of  $Ca^{2+}$  from intracellular stores (Figure 32-15), which are changes elicited by G protein-coupled receptors in many other cell types.

Receptors for some bitter substances, like those for some sweet tastants, may be coupled to the taste cell-specific G protein gustducin. As already mentioned, gustducin is related to transducin, the G protein  $\alpha$ -subunit that stimulates cGMP phosphodiesterase in response to visual stimuli in photoreceptor cells. Recent studies suggest that gustducin similarly stimulates a taste cell phosphodiesterase, which then lowers intracellular levels of both cAMP and cGMP. Mice in which the gustducin gene has been deleted are defective in their ability to perceive some bitter compounds as well as some sweet ones.

Some bitter compounds that are membrane-permeable may be sensed by mechanisms that do not involve G proteins (see Figure 32-14). For example, quinine is able to block apically located  $K^+$  channels. This mechanism of bitter taste transduction may explain why a number of different chemicals that block  $K^+$  channels have a bitter taste.

## Salty

Salty stimuli, such as NaCl, are transduced at least in part by a diffusion of  $Na^+$  ions down an electrochemical gradient through apical amiloride-sensitive  $Na^+$  channels. This  $Na^+$  influx directly alters the membrane potential of the taste cell (see Figure 32-14). Evidence for this mechanism is provided by studies showing that amiloride interferes with the ability of human subjects to taste  $Na^+$  salts and that it blocks the response of the chorda tympani nerve to NaCl placed on the tongue. The transduction of  $K^+$  salts may similarly involve influx of  $K^+$  ions through apical  $K^+$  channels. Differences in the perceived qualities of various  $Na^+$  salts may be the consequence of differences in the ability of different  $Na^+$  salt anions to penetrate the tight junctions between taste cells and affect ion channels on the basolateral membranes of taste cells.



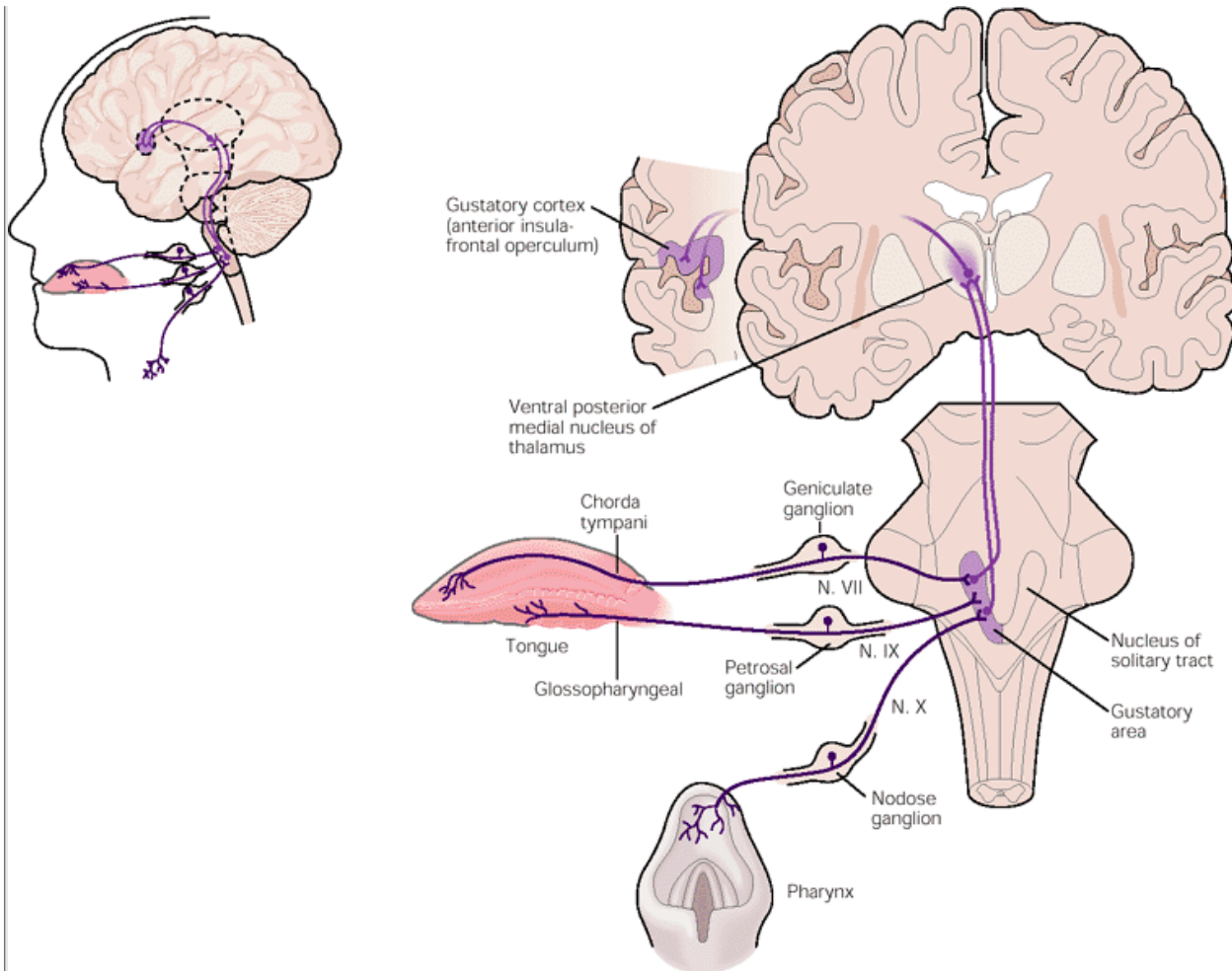
**Figure 32-16 Signal transduction of sour tastants can result from a blockade of apical K<sup>+</sup> channels.**

**A.** Recordings from isolated mudpuppy taste cells. **1.** Focal application of citric acid to the taste cell reduces the whole-cell K<sup>+</sup> current. **2-3.** Approximately 10% of the whole-cell K<sup>+</sup> current was recorded near the apical region (**2**), but less than 0.5% near the basolateral region (**3**). Potassium current was recorded in response to a 20 mV depolarization from -100 mV. (From [Kinnamon et al. 1988.](#))

**B.** Responses of isolated salamander taste cells and cell-free patches to acids. **1.** Citric acid elicited a slow depolarization of the taste cell, which was associated with an increase in membrane resistance (not shown). **2.** Under voltage clamp the acid-induced response was observed as a sustained inward current. **3.** Continuous recording of single K<sup>+</sup> channels in outside-out patches of taste cell membrane showed that the channels were rapidly (and reversibly) blocked by acetic acid. (From [Teeter et al. 1989.](#))

## Sour

Transduction of sour tastants appears to involve the permeation or blockade of apical ion channels by protons. In the mudpuppy sour taste is mediated by a blockade of apical K<sup>+</sup> channels by H<sup>+</sup> ions ([Figures 32-14](#) and [32-16](#)). Since the K<sup>+</sup> channels are generally open at resting potential, their blockade produces membrane depolarization. In the hamster a different mechanism seems to operate. In this species sour taste results from an influx of H<sup>+</sup> ions through amiloride-sensitive Na<sup>+</sup> channels (see [Figure 32-14](#)). These channels are thought to be permeable to protons when salivary Na<sup>+</sup> concentration is low; when Na<sup>+</sup> concentrations are high, protons block Na<sup>+</sup> flux through the channels and inhibit the response to NaCl. Consistent with this idea, acids reduce the perceived intensity of salts in humans.



**Figure 32-17 Taste information is transmitted from the taste buds to the cerebral cortex via synapses in the brain stem and thalamus.** Signals carried by fibers that innervate the taste buds travel through several different nerves to the gustatory area of the nucleus of the solitary tract, which relays information to the thalamus. The thalamus transmits taste information to the gustatory cortex.

P.642

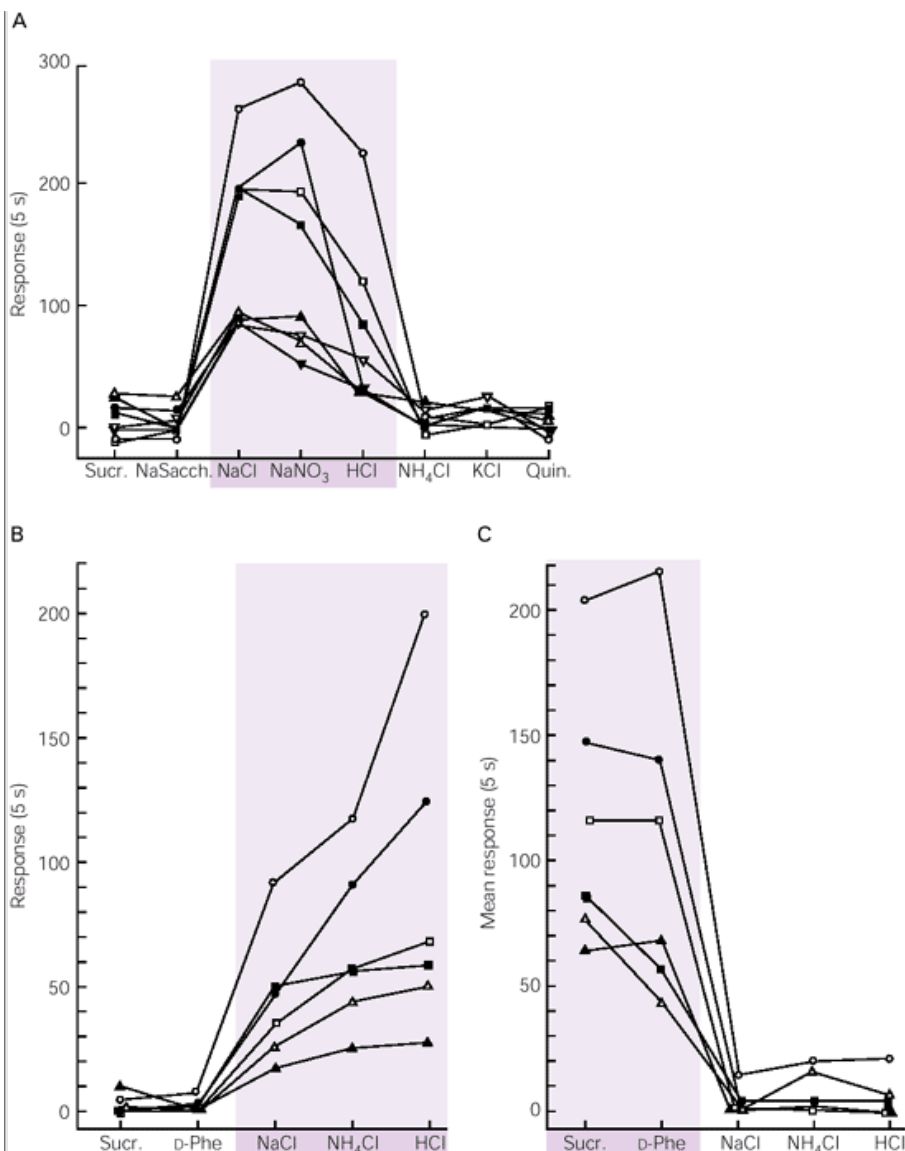
## Umami

Some consider the taste of monosodium glutamate to represent a fifth category of taste stimuli, umami. Umami taste may be transduced by a specific type of metabotropic glutamate receptor, which is also expressed in certain regions of the brain.

It is clear that a variety of mechanisms serve to transduce sensory stimuli in taste cells and that these mechanisms fall into two general categories: those involving specific membrane receptors and second messengers and those based on the direct permeation or blockade of ion channels. Proteins in the saliva may further contribute to taste sensation by binding taste stimuli and delivering them to the taste cell or, alternatively, by removing taste stimuli.

## Information About Taste Is Relayed to the Cortex via the Thalamus

There is some evidence that different taste cells respond to different taste stimuli. However, it is not known whether each cell responds to one tastant or a combination of tastants. Each taste cell is innervated at its base by the peripheral branches of primary gustatory fibers (see [Figure 32-13C](#)). Each sensory fiber branches many times, innervating numerous taste buds and, within each taste bud, several taste cells. Thus, the electrical activity recorded from a single sensory fiber represents the input of many taste cells. As already discussed, the release of neurotransmitter from taste cells onto the sensory fibers induces action potentials in the fibers and the transmission of signals to the brain.



**Figure 32-18 Response profiles of chorda tympani fibers of the hamster.** (From Frank 1985.)

**A.** Response profiles for eight fibers that responded more to two sodium salts than to HCl. (**Sucr.** = sucrose; **NaSacch** = sodium saccharide; **NaCl** = sodium chloride; **NaNO<sub>3</sub>** = sodium nitrate; **HCl** = hydrogen chloride; **NH<sub>4</sub>Cl** ammonium chloride; **KCl** = potassium chloride; **Quin.** = quinine.)

**B.** Profiles for six fibers that responded to HCl, NaCl, and NH<sub>4</sub>Cl. (**D-Phe** = D-phenylalanine.)

**C.** Profiles for six fibers that responded rather specifically to sucrose and D-phenylalanine, which are both sweet.

P.643

The taste buds in the anterior two-thirds of the tongue (those in the fungiform papillae) are innervated by sensory neurons of the geniculate ganglion whose peripheral branches travel in the chorda tympani, a branch of the facial nerve (cranial nerve VII) (Figures 32-12 and 32-17). Taste buds in the posterior third of the tongue are innervated by sensory neurons of the petrosal ganglion, whose peripheral branches travel in the lingual branch of the glossopharyngeal nerve (cranial nerve IX). The taste buds on the palate are innervated by the greater superficial petrosal branch of cranial nerve VII, and the buds on the epiglottis and esophagus by the superior laryngeal branch of cranial nerve X. Some of these nerves also carry somatosensory afferents that innervate regions of the tongue surrounding the taste buds

The sensory fibers that receive input from the taste cells and run in cranial nerves VII, IX, and X enter the solitary tract in the medulla (Figure 32-17) and then form synapses on a thin column of cells in the gustatory area of the rostral and lateral part of the nucleus of the solitary tract.

Neurons in the gustatory area project to the thalamus, where they terminate in the small-cell (parvocellular) region of the ventral posterior medial nucleus. There the cells serving taste are grouped separately from neurons concerned with other sensory modalities of the tongue.

Neurons in the parvocellular region of the thalamus that receive taste input project to neurons along the border between the anterior insula and the frontal operculum

P.644

in the ipsilateral cerebral cortex (Figure 32-17). This region is rostral to the somatosensory (ie, touch, pain, and temperature) representation of the tongue. This projection is believed to provide for the conscious perception and discrimination of taste stimuli.

It was once believed that taste cells responsive to each of the four basic categories of taste stimuli were concentrated exclusively in different areas of the tongue. This is not the case; taste buds responsive to sweet, salty, bitter, and sour tastes are found in all regions of the tongue. However, information derived from different areas of the tongue is spatially segregated in the nucleus of the solitary tract, thalamus, and cortex.

## Different Taste Sensations Derive From Variations in Patterns of Activity in the Afferent Fiber Population

How does the gustatory system discriminate among a variety of taste stimuli? One clue has come from studying activity in single afferent gustatory fibers caused by exposure of an animal to different taste stimuli. It has been found that a single gustatory fiber may respond best to one stimulus but may also respond to other



types of taste stimuli to varying degrees. For example, a fiber that responds vigorously to salt might also respond to acid (sour taste) and a fiber that responds primarily to acid might also respond to bitter stimuli (Figure 32-18).

This implies that each fiber receives signals from a population of taste cells with a distinctive set of response specificities. It also suggests that different tastes are encoded by different patterns of activity in the entire fiber population or by activation of different, but overlapping, sets of fibers. In this respect, taste coding may resemble sensory information coding in other systems, including the visual and auditory systems, where late steps in the processing of information involve a comparison of the activity of different cells that respond preferentially, but not exclusively, to certain features of sensory stimuli.

## The Sensation of Flavors Results From a Combination of Gustatory, Olfactory, and Somatosensory Inputs

Much of what we think of as the flavor of foods derives from information provided by the olfactory system. Volatile molecules released from foods or beverages in the mouth are pumped into the back of the nasal cavity (retronasally) by the tongue, cheek, and throat movements that accompany chewing and swallowing. Although the olfactory epithelium of the nose clearly makes a major contribution to sensations of taste, we experience taste as being in the mouth, not in the nose. It is thought that the somatosensory system is involved in this localization and that the coincidence between somatosensory stimulation of the tongue and retronasal passage of odorants into the nose causes the odorants to be perceived as flavors in the mouth.

Sensations of taste also frequently have a somato-sensory component. This component includes the texture of food as well as sensations evoked by spicy and minty foods and by carbonation.

## An Overall View

The senses of smell and taste provide us with a means to evaluate volatile molecules in our environment and both volatile and nonvolatile components of foodstuffs. The basic design and functional capacities of these systems are highly conserved across vertebrate species. In addition to providing a means of distinguishing between appropriate and potentially harmful substances prior to ingesting them, in many species these senses, particularly the sense of smell, play an important role in predator-prey relationships as well as in the regulation of social relationships critical to the production and rearing of offspring.

In the olfactory system, chemical stimuli are detected by olfactory sensory neurons that transmit signals to the olfactory bulb of the brain. From the olfactory bulb, olfactory information is relayed through the olfactory cortex to a variety of brain regions that allow for both the conscious discrimination of odors and their various effects on our emotions and behavior. The detection of odorants is accomplished by specific odorant receptors, of which there are as many as 1000 different types. There are millions of olfactory sensory neurons in the nose. Each receptor type is expressed by several thousand neurons, each of which expresses only one type of receptor.

Neurons that express the same type of odorant receptor are restricted to one zone in the nose, but in that zone they are interspersed with neurons expressing other receptor types. In the olfactory bulb the axons of those neurons converge on only a few glomeruli at fixed locations. The olfactory bulb appears to contain a highly organized sensory map in which information provided by different odorant receptors is focused onto different glomeruli. Each odorant may be recognized by several odorant receptors, and each receptor may recognize many odorants. The identity of an odorant is therefore

P.645

likely to be encoded in the olfactory bulb not by unique odor-specific glomeruli but by unique sets of glomeruli, each of which serves as one component of the multicomponent codes for a variety of odorants. Olfactory information may be processed, or refined, by local circuits within the olfactory bulb prior to transmission to the olfactory cortex. The means by which olfactory information is encoded in the cortex is not yet known.

Taste stimuli are detected in the mouth by taste cells, specialized epithelial cells that are clustered in structures called taste buds. The taste cells are innervated by sensory fibers that transmit signals to the gustatory area of the nucleus of the solitary tract. From there, gustatory information is transmitted to the cortex (through a relay in the thalamus). Four basic categories of taste stimuli—bitter, sweet, salty, and sour—are detected by taste cells. Sweet and some bitter tastants may be detected by specific G protein-coupled receptors on taste cells, while other bitter tastants may stimulate taste cells via direct interactions with ion channels. The detection of salty taste stimuli is mediated by Na<sup>+</sup> ion influx through Na<sup>+</sup> channels, whereas sour tastes can result either from the permeation of Na<sup>+</sup> channels by protons or by proton blockade of apical K<sup>+</sup> channels.

The detection of tastants is transduced into a receptor potential that induces action potentials in the taste cell and the release of neurotransmitter at synapses formed between the taste cell and sensory fibers. Each sensory fiber contacts a number of taste cells and each taste cell synapses with numerous sensory fibers. Each sensory fiber carries information derived from a variety of taste stimuli but is generally dominated by one of these stimuli. Thus, the identity of a taste stimulus appears to be encoded by a unique pattern of inputs from many separate fibers that provide components of the patterns for different stimuli. The multitude of different flavors that one can experience derives from a combination of gustatory, olfactory, and somatosensory components.

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P.646

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P.647

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