Part 4, Sensory and Motor Systems

4.4. The Chemical Senses

Overview

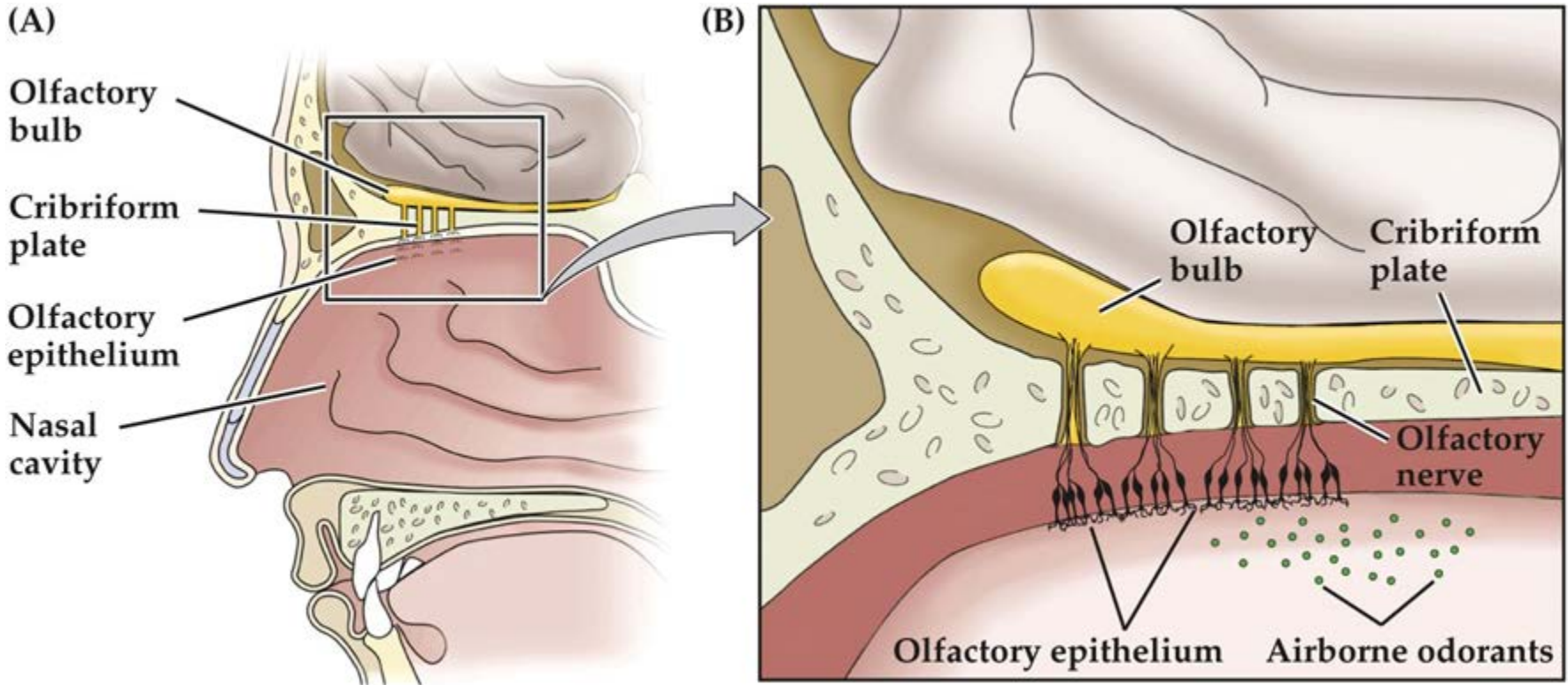
- Three sensory systems are associated with the nose and mouth: the olfactory (smell), gustatory (taste), and trigeminal (chemosensory irritant) systems.
- Each of these is dedicated to the detection of chemicals in the environment.
  - The olfactory system detects airborne molecules called odorants, which provide information about self and other people, animal and plants, as well as helping to identify food and noxious or hazardous substances in the environment in humans.
  - The gustatory system detects ingested tastants (primarily water- or fat-soluble molecules), which provide information about the quality, quantity, and safety of ingested food.
  - The trigeminal chemosensory system provides information about irritating or noxious molecules that come into contact with skin or the mucous membranes of the eyes, nose, and mouth.

4.4. The Chemical Senses

4.4.1 Olfactory system

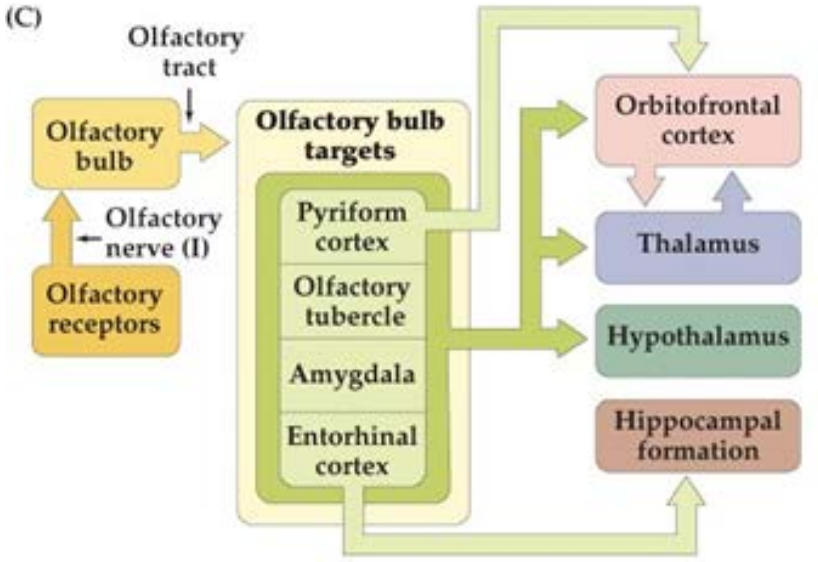
Organization of the olfactory system

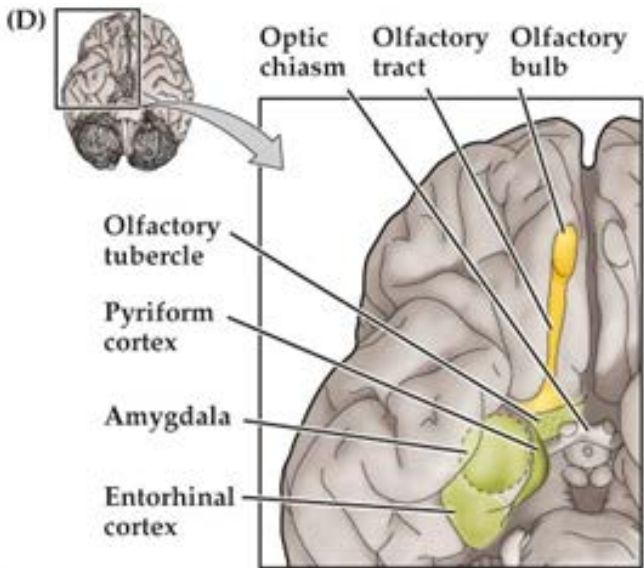
- The olfactory system processes information about the identity, concentration, and quality of a wide range of airborne, volatile chemical stimuli, called **odorants**.
- Odorants interact with olfactory receptor neurons found in an epithelial sheet, the **olfactory epithelium**, that lines the interior of the nose.
- Axons arising from receptor cells project directly to neurons in the **olfactory bulb**.



Organization of the olfactory system

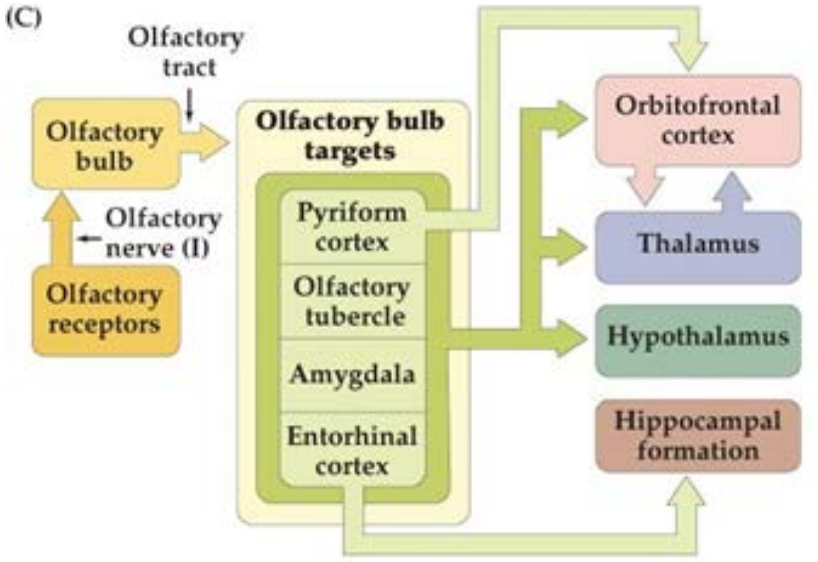
- Neurons in the olfactory bulb send projections to the pyriform cortex in the temporal lobe, as well as to other structures in the forebrain via an axon pathway known as the olfactory tract.
- The olfactory system is unique among the sensory systems in that it does not include a thalamic relay from primary receptors *en route* to a cortical region that processes the sensory information.
- Instead, after relaying through the olfactory bulb, olfactory sensory information is processed in the **pyriform cortex**, a three-layered archicortex dedicated to olfaction and considered to be phylogenetically older than the six-layered neocortex.

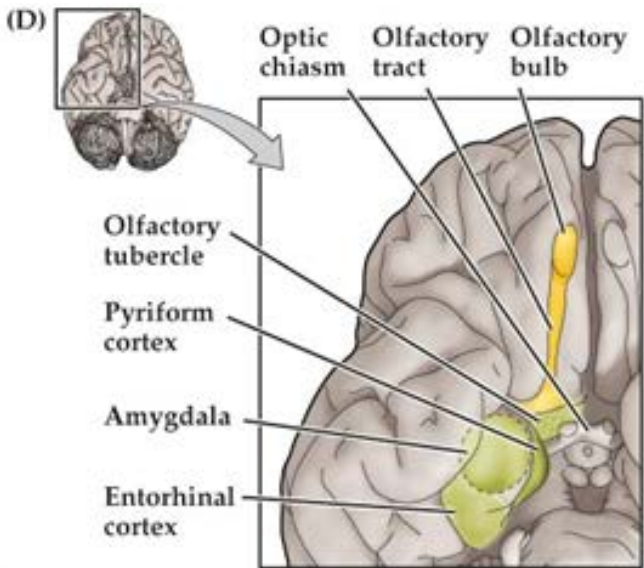




Organization of the olfactory system

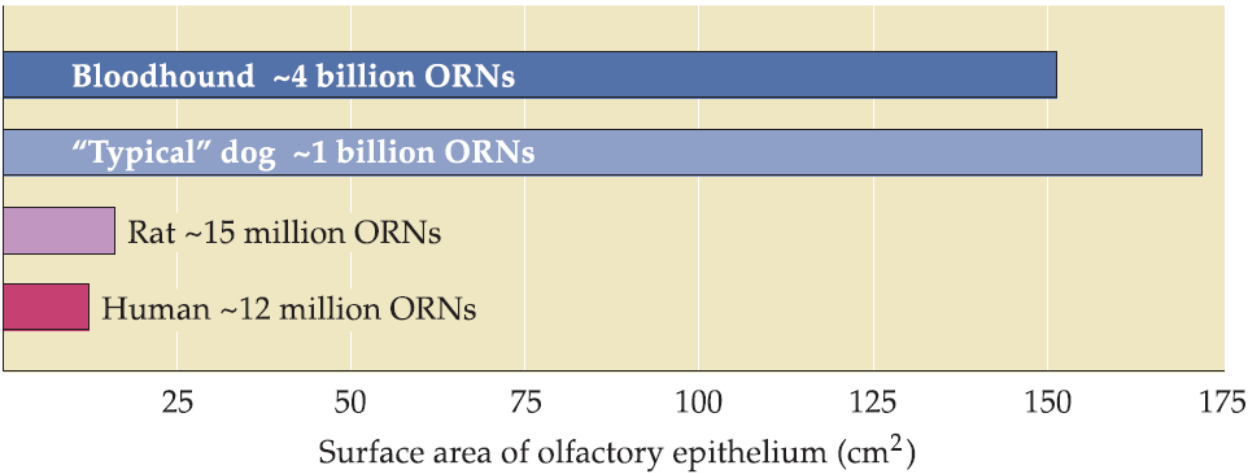
- Olfactory information from pyriform cortex is relayed to the thalamus *en route* to association areas in the neocortex, where further processing occurs
- The olfactory bulb relays information directly to a number of other targets in addition to the pyriform cortex, including the hypothalamus and amygdala.
- Despite its phylogenetic age and unusual trajectory to the cortex, the olfactory system abides by the same principle that governs other sensory modalities: Sensory stimuli--in this case, airborne chemicals--interact with receptors at the periphery and are transduced and encoded into electrical signals, which are transmitted to higher-order centers.

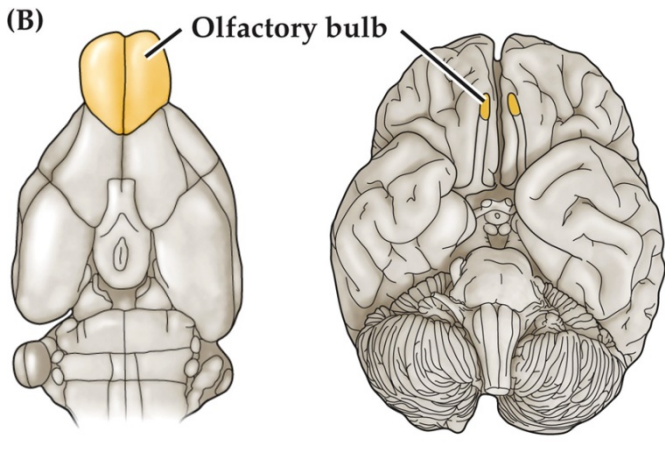




Olfactory perception in humans

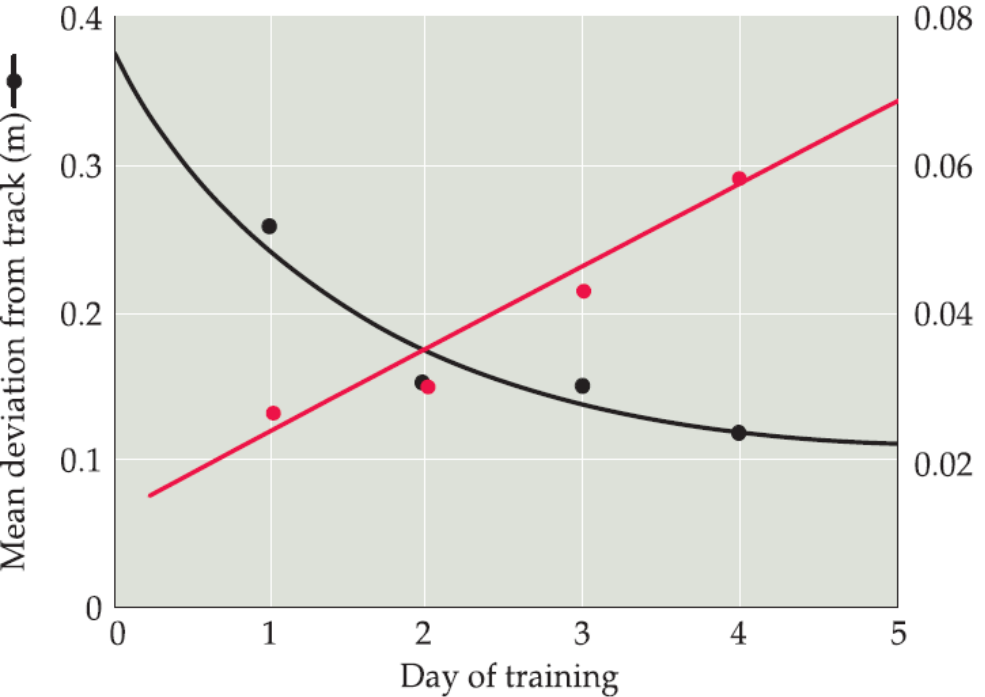
- In humans, olfaction is often considered the least acute of the senses, and many animals obviously possess far superior olfactory abilities.
- The greater chemosensory sophistication of such animals may be explained by increased numbers of olfactory receptor neurons and odorant receptor proteins in an expanded olfactory epithelium, as well as by a relatively larger portion of the forebrain devoted to olfaction.
- In a 70 kg human, the surface area of the olfactory epithelium is approximately 10 cm^2; in contrast, a rat has 15 cm^2, a 3 kg cat has about 20 cm^2, and dogs such as bloodhounds have 380 cm^2 of olfactory epithelium.





Olfactory perception in humans

- We seem to use scent-tracking strategies that are similar to our more olfactorally gifted counterparts:
  - we pursue a tracking path that constantly bisects the linear scent trail.
  - we sniff frequently and sniffing increases as scent tracking is learned.
  - our performance improves with practice.
- Humans are also quite good at detecting and identifying individual airborne odorants with a wide range of aesthetic (unpleasant/pleasant) and behavioral (irritant/attractant) significance.



Accessing olfactory function in the lab or clinic

- Some individuals consistently fail to identify one or more common odors.
- This chemosensory deficits, known as **anosmias**, are often restricted to a single odorant, suggesting that a specific element in the olfactory system—either an olfactory receptor gene or genes that control expression or function of specific odorant receptor genes—is inactivated.
- Anosmias can be congenital, or they may be acquired following chronic sinus infection or inflammation, traumatic head injury, or exposure to toxins.
- Olfactory loss is also a common consequence of aging.

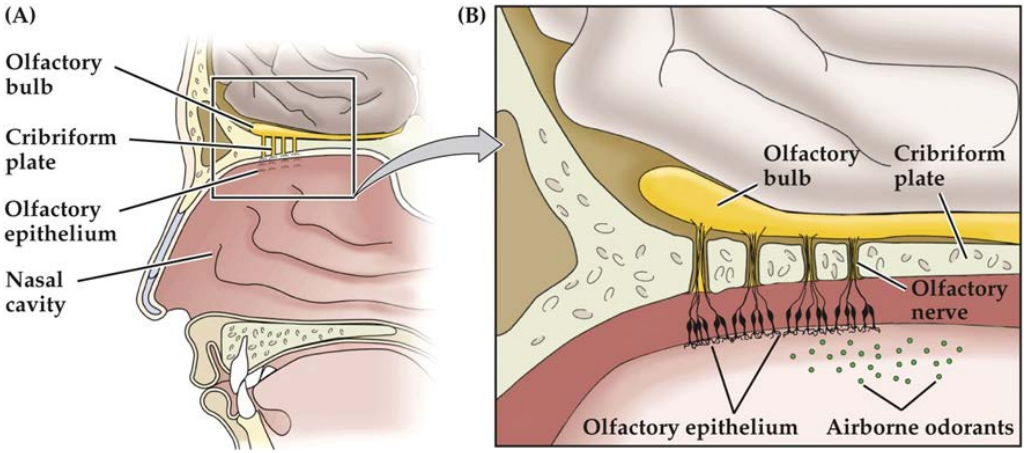
Physiological and behavioral responses to odorants

- Olfaction can influence reproductive and endocrine functions.
- For instance, women living in single-sex dormitories tend to have synchronized menstrual cycles, apparently mediated by olfaction.
- Experimental evidence reinforces the reality of this surprising phenomenon:
  - Volunteer women exposed to gauze pads from the underarms of other women at different stages of their menstrual cycles also experience synchronized menses, and this synchronization can be disrupted by exposure to analogous gauze pads from men.
- In other animals, including many mammals, species-specific odorants called **pheromones**--chemical signals, usually produced by conspecifics--play important roles in behavior, eliciting (or at least influencing) social, reproductive, and parenting behaviors.

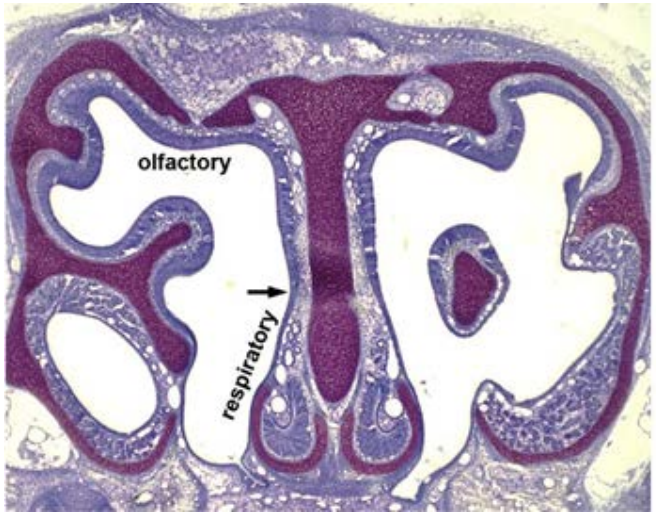
Olfactory epithelium and olfactory receptor neurons

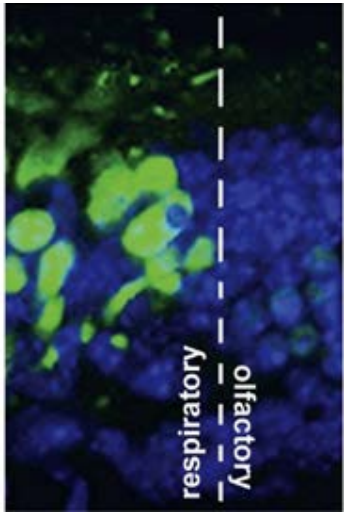
- The transduction of olfactory information--a series of neural events that ultimately results in the conscious sense of smell--begins in the olfactory epithelium, the sheet of neurons and supporting cells that lines approximately half of the surface of the nasal cavity.

- The remaining intranasal surface is lined by respiratory epithelium similar to that in the trachea and lungs.



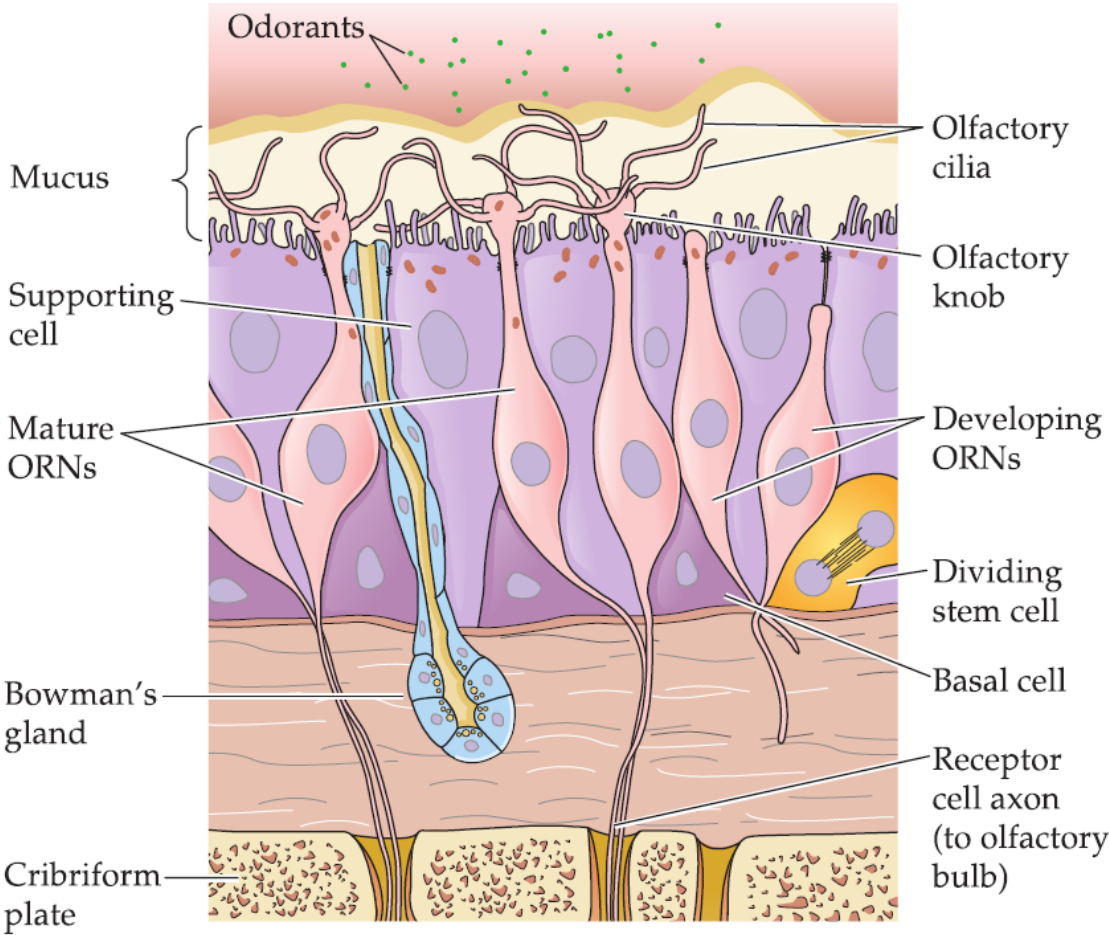
- There is a sharp boundary between respiratory epithelium (marked by expression of the transcription factor Forkhead1) and olfactory epithelium.





Olfactory epithelium and olfactory receptor neurons

- The neural portion of the olfactory epithelium includes several cell types:
  - The most important of these are the **olfactory receptor neurons** (**ORN**s).
    - These bipolar cells give rise to small-diameter, unmyelinated axons at their basal surface that transmit olfactory information centrally.
    - At the apical surface, an ORN gives rise to a single dendritic process that expands into a knoblike protrusion from which several microvilli, called **olfactory cilia**, extend into a thick layer of mucus.
    - The mucus that lines the nasal cavity protects the exposed receptor neurons and supporting cells of the olfactory epithelium and controls the ionic milieu of the olfactory cilia, the primary site of odorant transduction.
  - Mucus is produced by secretory specializations called **Bowman's glands** that are distributed throughout the olfactory epithelium.



Olfactory epithelium and olfactory receptor neurons

- When the mucus layer thickens, as during a cold, olfactory acuity decreases significantly.
  - Two other cell classes, **basal cells** and **sustentacular** (supporting) **cells**, are also present in the olfactory epithelium.

❖ This entire apparatus--mucus layer and epithelium with neural and supporting cells--is called the **nasal mucosa**.

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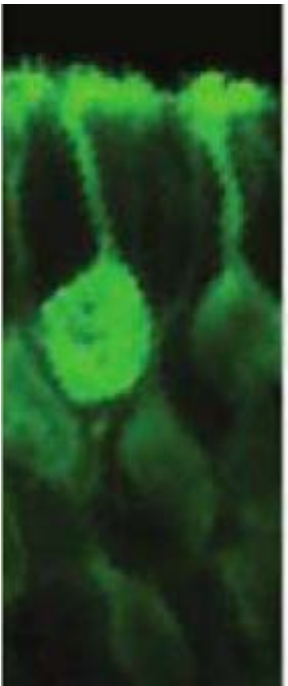
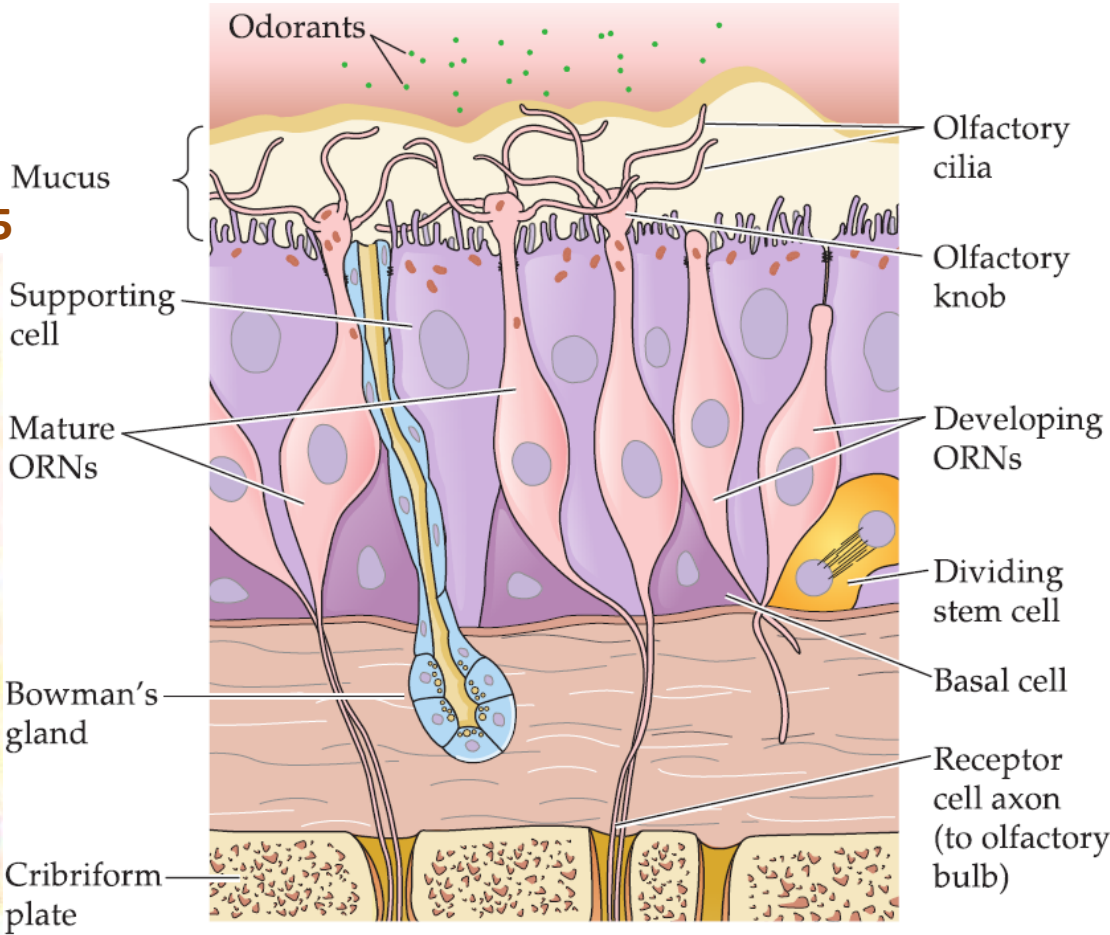
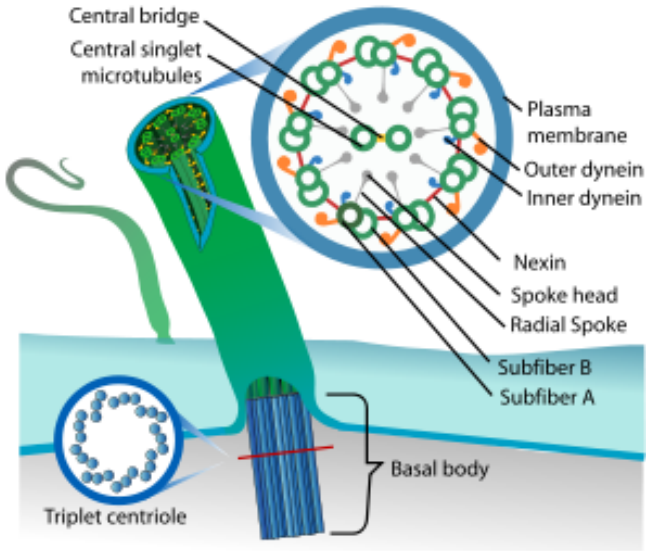


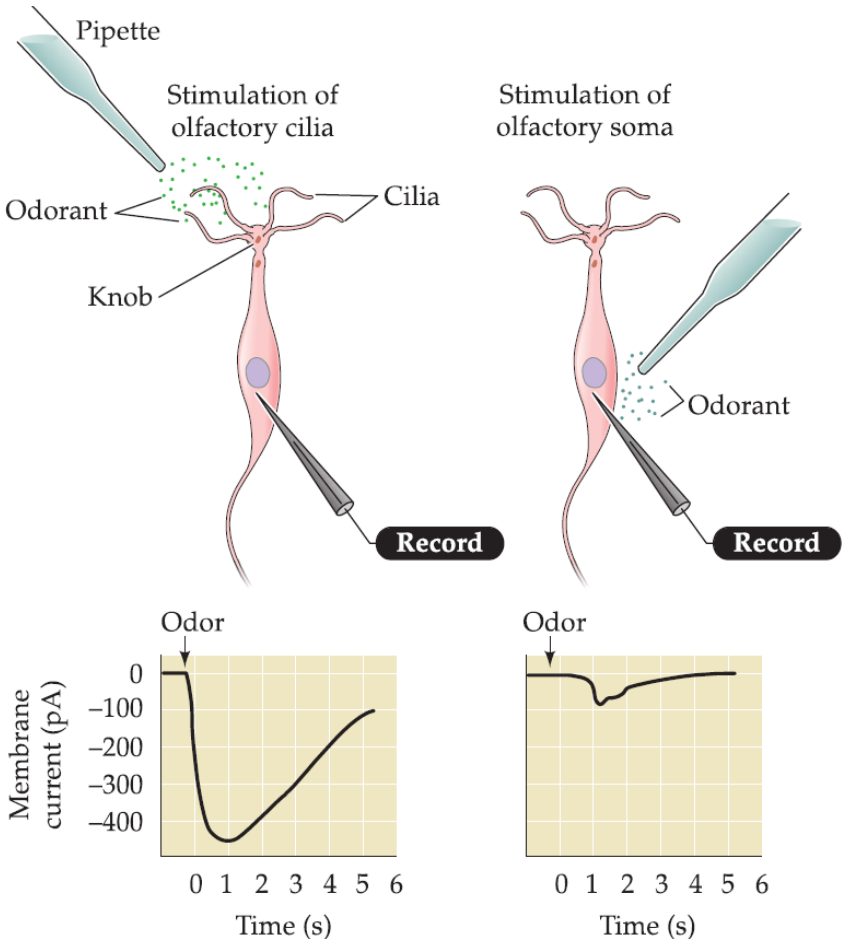
Cytokeratin5



Odor transduction

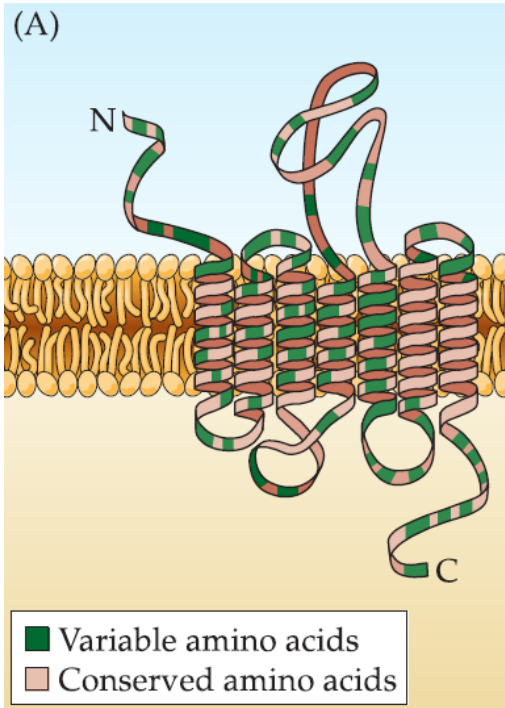
- Odorants presented to the cilia of an isolated olfactory receptor neuron elicit a robust electrical response.
- Those presented to the cell body do not.
- Despite their external appearance, olfactory cilia do not have the cytoskeletal features of motile cilia (i.e., the "9 + 2" arrangement of microtubules).
- The actin-rich olfactory cilia more closely resemble microvilli of other epithelia (such as the lung and gut) and thus have a greatly expanded cellular surface to which odorants can bind.





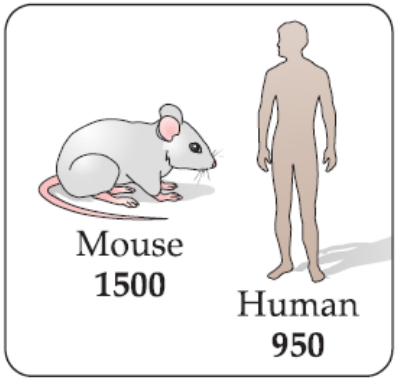
Odorant receptor proteins

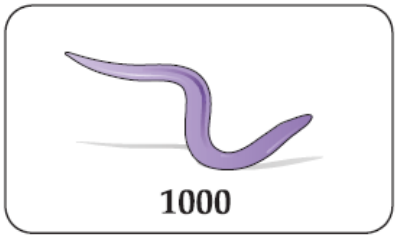
- The central role of odorant receptor proteins in the encoding of olfactory information was acknowledged in 2004 when a Nobel Prize was awarded to Richard Axel and Linda Buck for their discovery of the **odorant receptor gene family**.
  - Olfactory receptor molecules are homologous to G-protein-linked receptors.
  - In all invertebrates and vertebrates examined thus far, odorant receptor proteins have seven membrane-spanning hydrophobic domains, potential odorant binding sites in the extracellular domain of the protein, and the ability to interact with G-proteins at the carboxyl terminal region of their cytoplasmic domain.
  - The amino acid sequences for these molecules show substantial variability in several of the membrane-spanning regions, as well as in the extracellular and cytoplasmic domains.
  - As many as a thousand genes encode proteins of similar inferred structure in several mammalian species, including humans.
  - Each gene presumably encodes a receptor protein that detects a particular set of odorant molecules.
  - The molecular mechanism by which individual receptors bind specific odorants remains poorly understood.

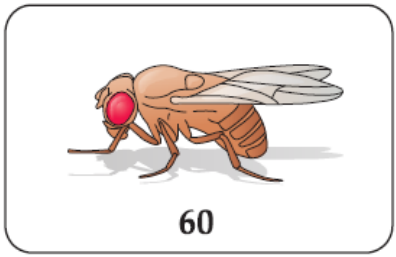


Odorant receptor genes

- The number of odorant receptor genes, though substantial in all species, varies widely.
  - In all mammals, odorant receptors are the largest known single gene family, representing 3-5% of the genome.
  - Analysis of the human genome has identified approximately 950 apparent odorant receptor genes.
  - Analysis of the mouse genome indicates about 1500 different odorant receptor genes, and in certain dogs, including those noted for their olfactory abilities, the number is around 1200.
  - Additional sequence analysis of apparent mammalian odorant receptor genes, however, suggests that many of these genes--around 60% in humans and chimps versus 15-20% in mice and dogs--are not transcribed due to changes that have rendered them pseudogenes.
  - The number of functional odorant receptor proteins encoded by stably transcribed and translated genes is estimated to be around 400 in humans and chimps versus about 1200 in mice and 1000 in dogs.
  - Similar analysis of complete genome sequences from the worm *C. elegans* and the fruit fly *D. melanogaster* indicate that the worm has approximately 1000 odorant receptor genes, but the fruit fly has only about 60.

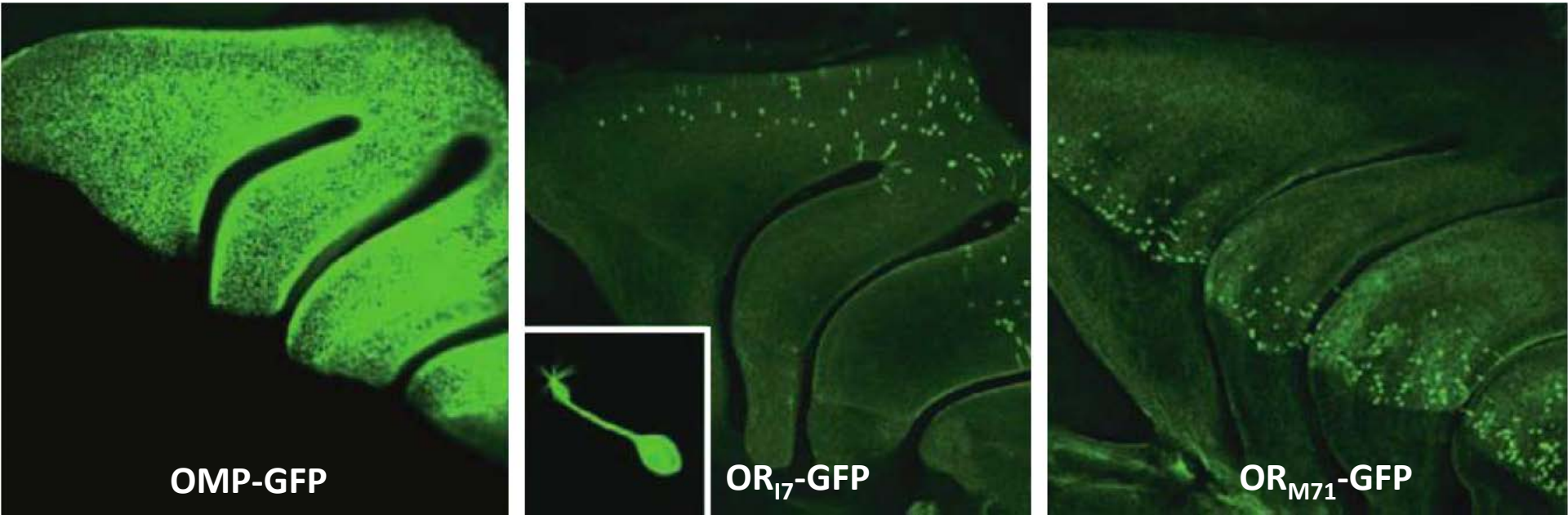






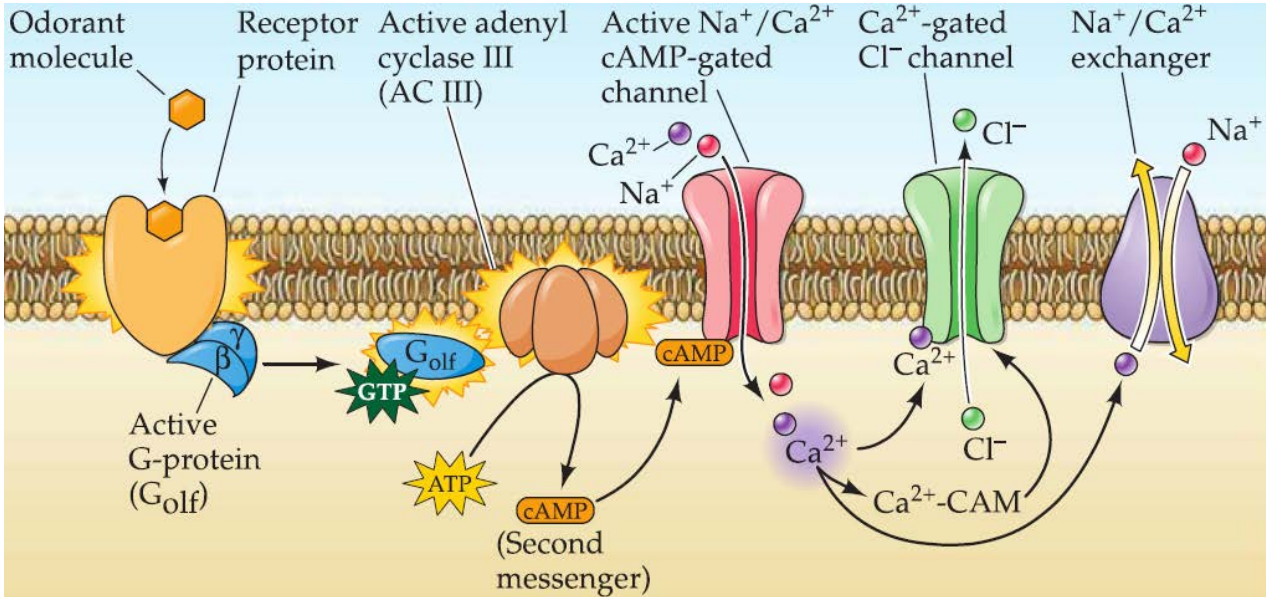
Odorant receptor gene expression

- Most mammalian ORNs express only one odorant receptor gene.
- Olfactory receptor neurons expressing a specific odorant receptor are restricted to a distinct domain or zone in the epithelium.



Physiological mechanisms of odor transduction

- Once an odorant is bound to an odor receptor protein, several additional steps are required to generate a receptor potential that converts chemical information into electrical signals that can be interpreted by the brain.
- In mammals, the principal pathway for generating electrical activity in olfactory receptors involves cyclic nucleotide-gated ion channels similar to those found in rod photoreceptors.
  - The olfactory receptor neurons express an olfactory-specific heterotrimeric G-protein, G_{olf}, whose alpha subunit dissociates upon odorant binding to receptor.
  - G_{olf} alpha activates adenyl cyclase Ill (ACIII), an olfactory-specific adenylate cyclase.
  - Stimulation of odorant receptor molecules leads to an increase in cyclic AMP (cAMP).

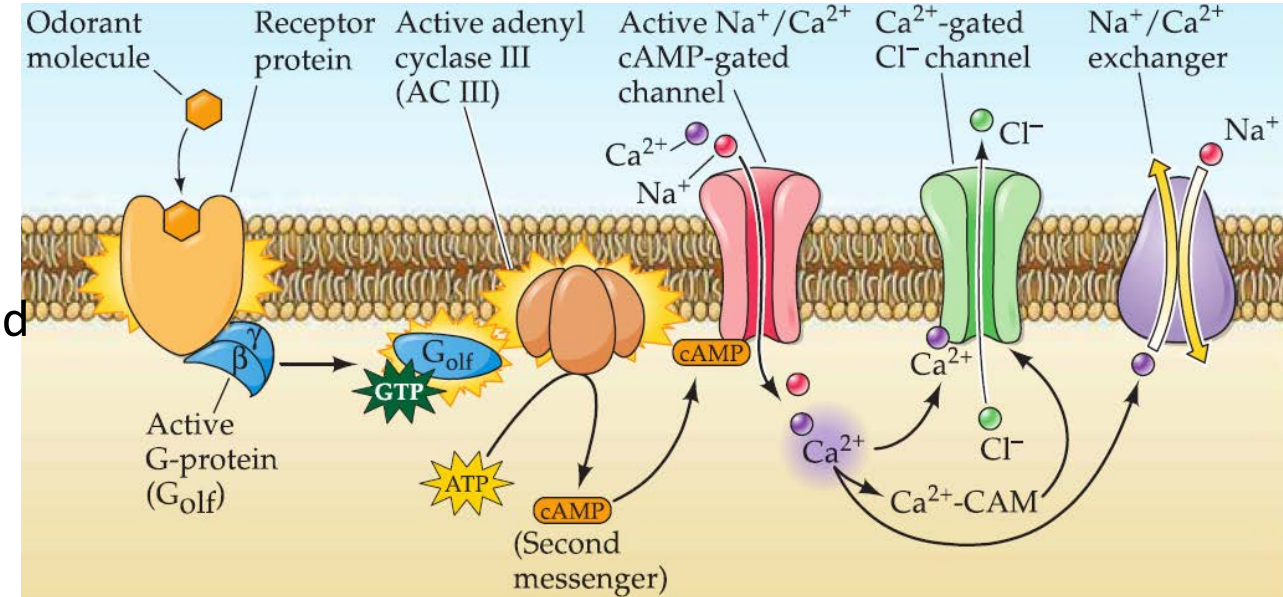


Physiological mechanisms of odor transduction

- cAMP opens cyclic nucleotide-gated channels that permit the entry of Na^+ and Ca^{2+} (mostly Ca^{2+}), thus depolarizing the neuron.
- This depolarization, amplified by a Ca^{2+}-activated Cl^- current, is conducted passively from the cilia to the axon hillock region of the olfactory receptor neuron, where action potentials are generated via voltage-regulated Na^+ channels and transmitted to the olfactory bulb.

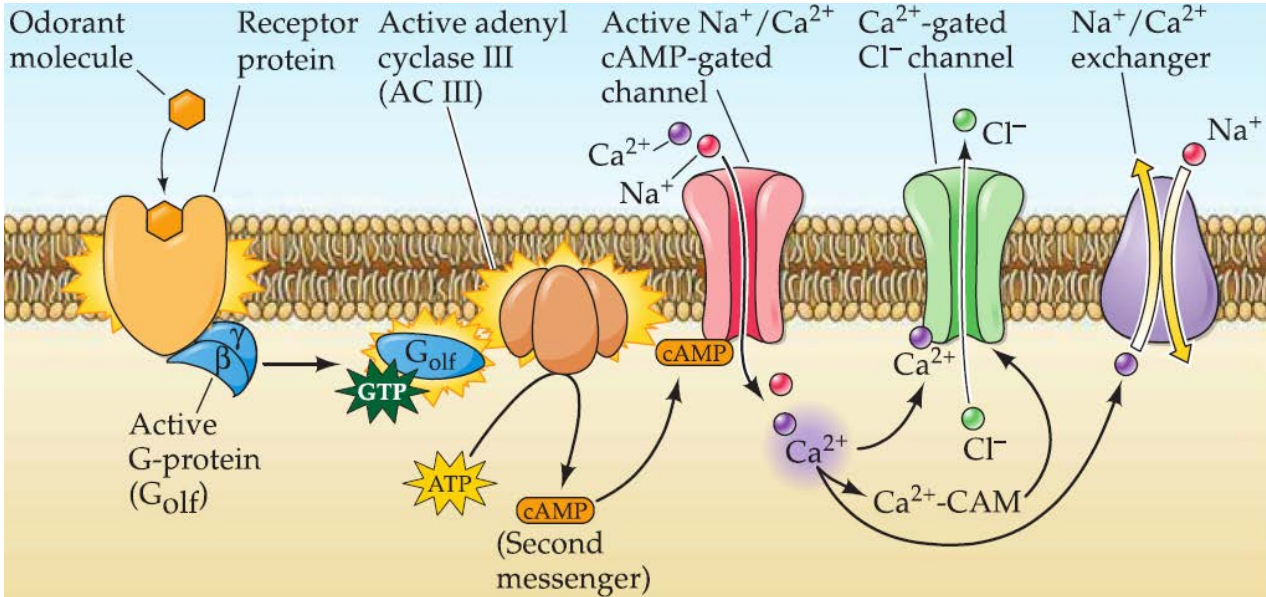
❖ There are also distinct signaling mechanisms for repolarization, recovery, and adaptation in response to odorants.

- In response to elevated Ca^{2+}, an Na^+/Ca^{2+} exchanger extrudes Ca^{2+} and transports Na^+ to re-polarize the membrane.
- Recovery relies on calcium/calmodulin kinase II-mediated mechanisms that restore the heterotrimeric G_{olf} and diminish cAMP levels via activation of phosphodiesterases.



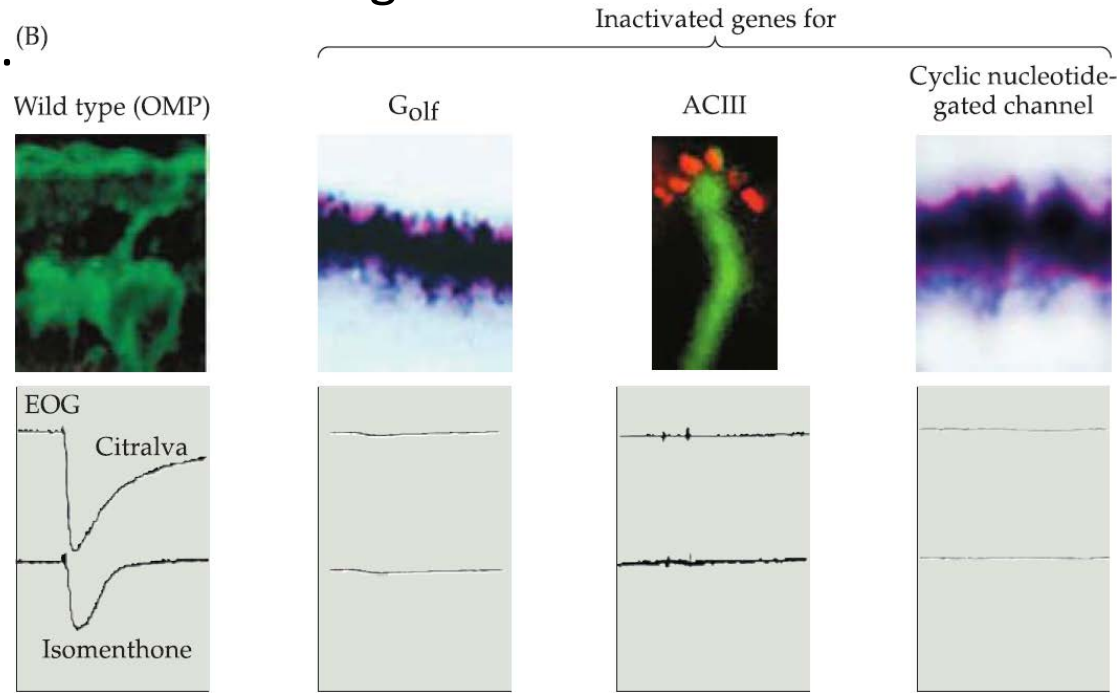
Physiological mechanisms of odor transduction

- Adaptation relies on cAMP-regulated phosphorylation of intracellular domains of the odorant receptor proteins, as well as engagement of β-arrestin (which serves a similar role in photoreceptor adaptation) to modify receptor sensitivity.
  - These mechanisms for adaptation likely play a large role in perceived changes in sensitivity to smells, such as initially noticing, but later not sensing, the smell of cigarette smoke in a "smoking" hotel room.



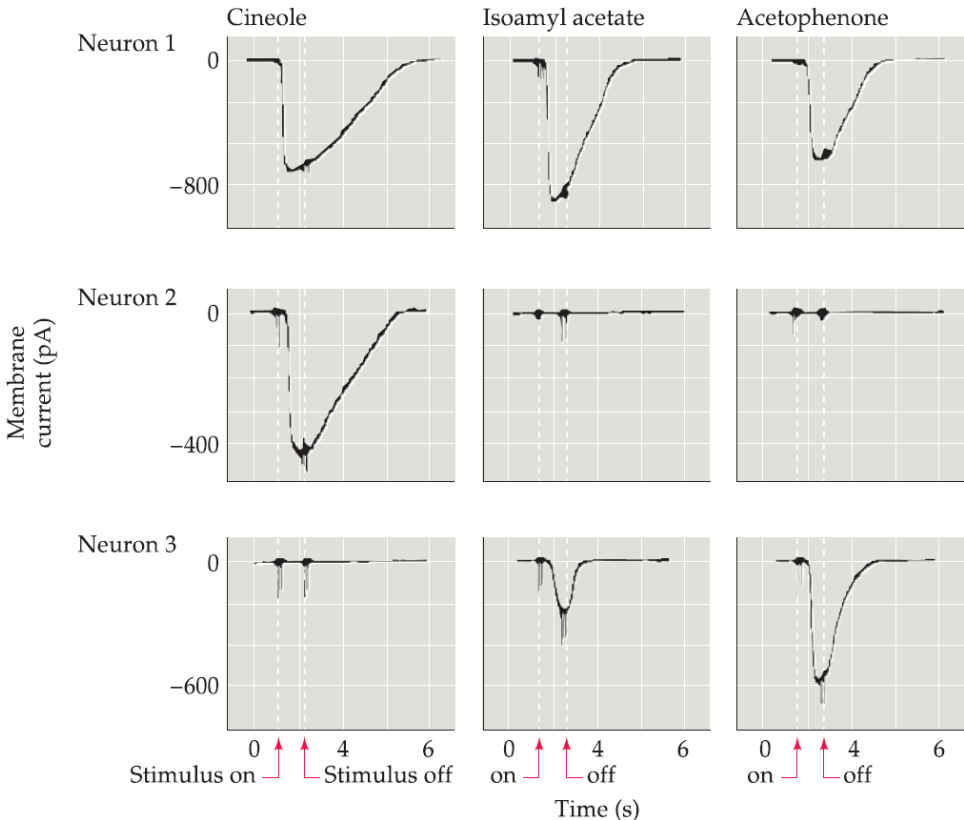
Physiological mechanisms of odor transduction

- In genetically engineered mice, inactivation of any one of the major signal transduction elements (G_{olf}, ACIII, or cyclic nucleotide-gated channel) results in a loss of receptor response to odorants in olfactory receptor neurons.
- There is also complete loss of behavioral response to most odorants; in other words, these mice are anosmic.
- This common endpoint following loss of function of each molecule demonstrates that each signaling step—receptor-mediated G-protein activation, adenyl cyclase-mediated elevation of cAMP levels, and Ca^{2+}-mediated activation of the cyclic nucleotide-gated channel--contributes to the transduction of odorants.



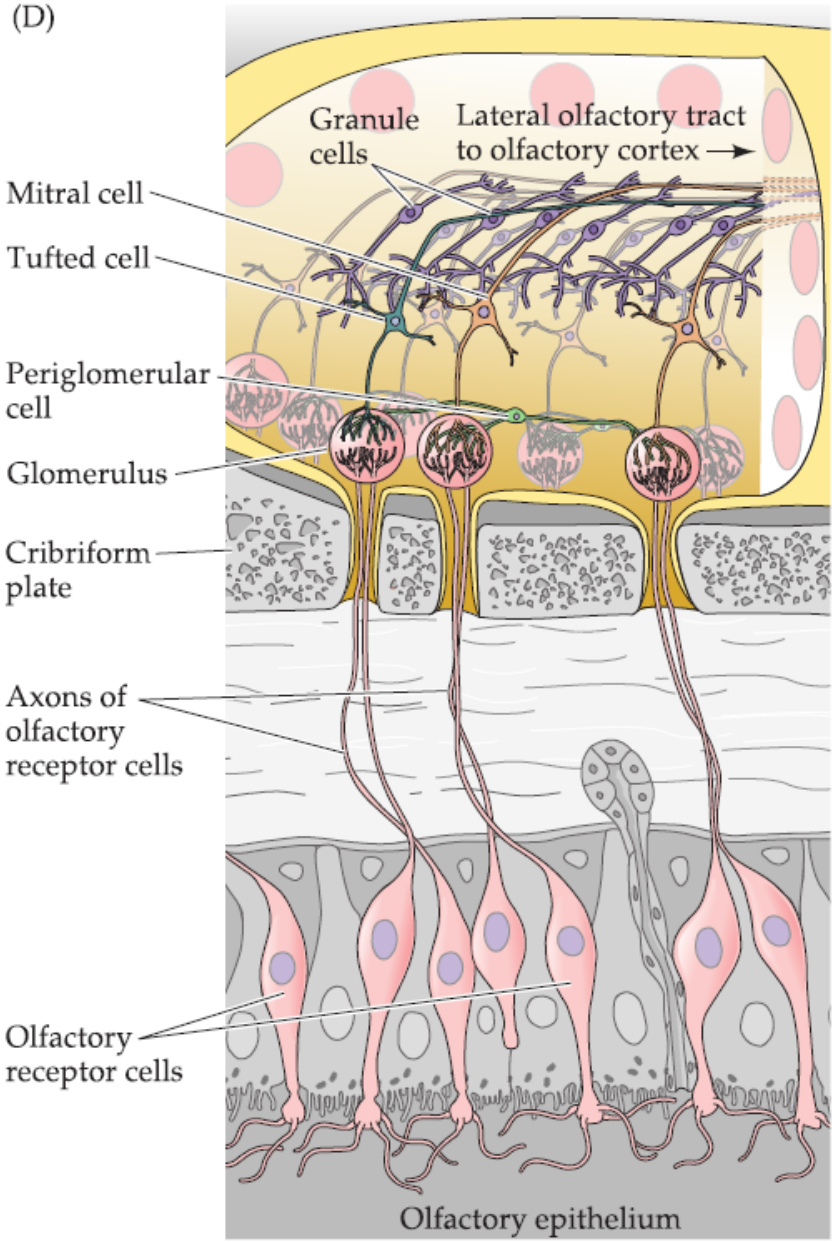
Physiological mechanisms of odor transduction

- Some olfactory receptor neurons exhibit marked selective to a single chemically defined odorant, whereas others are activated by a number of different odorant molecules.
- Presumably, these differences parallel the expression of a single odorant receptor gene in each olfactory receptor neuron.



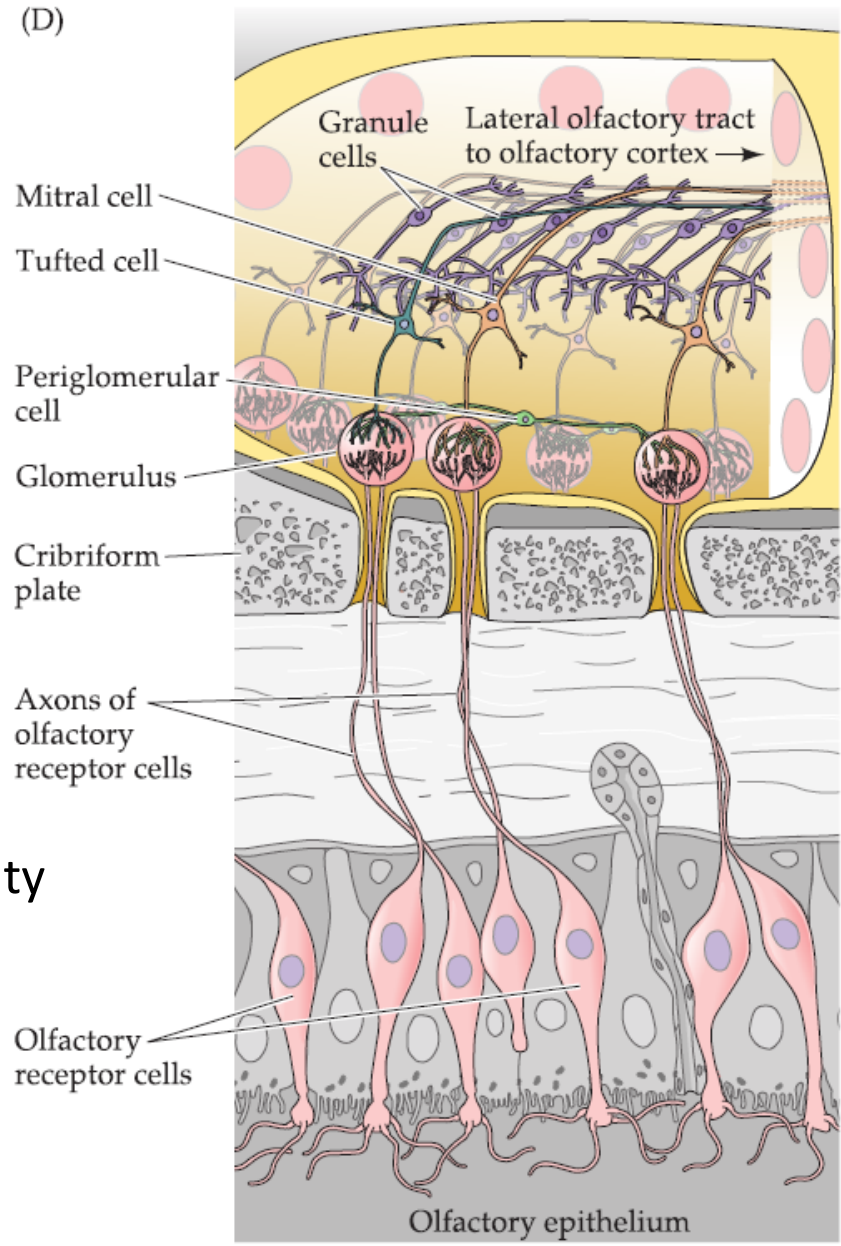
The olfactory bulb

- Olfactory receptor neurons have axons which relay odorant information directly to the brain via action potentials.
  - As the axons leave the olfactory epithelium, they coalesce to form a large number of bundles that together make up the olfactory nerve (cranial nerve I).
- Each olfactory nerve projects ipsilaterally to the olfactory bulb, which in humans lies on the ventral anterior aspect of the ipsilateral cerebral hemisphere.
- The most distinctive feature of the olfactory bulb is the array of **glomeruli**—more or less spherical accumulations of neuropil 100-200 μm in diameter.
  - Glomeruli lie just beneath the surface of the bulb and are the synaptic target of the primary olfactory axons.



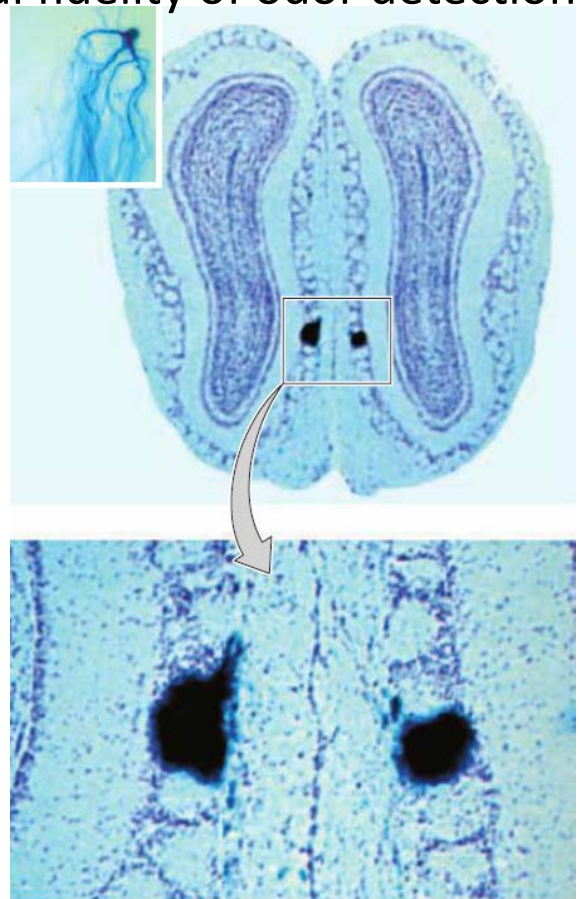
The olfactory bulb

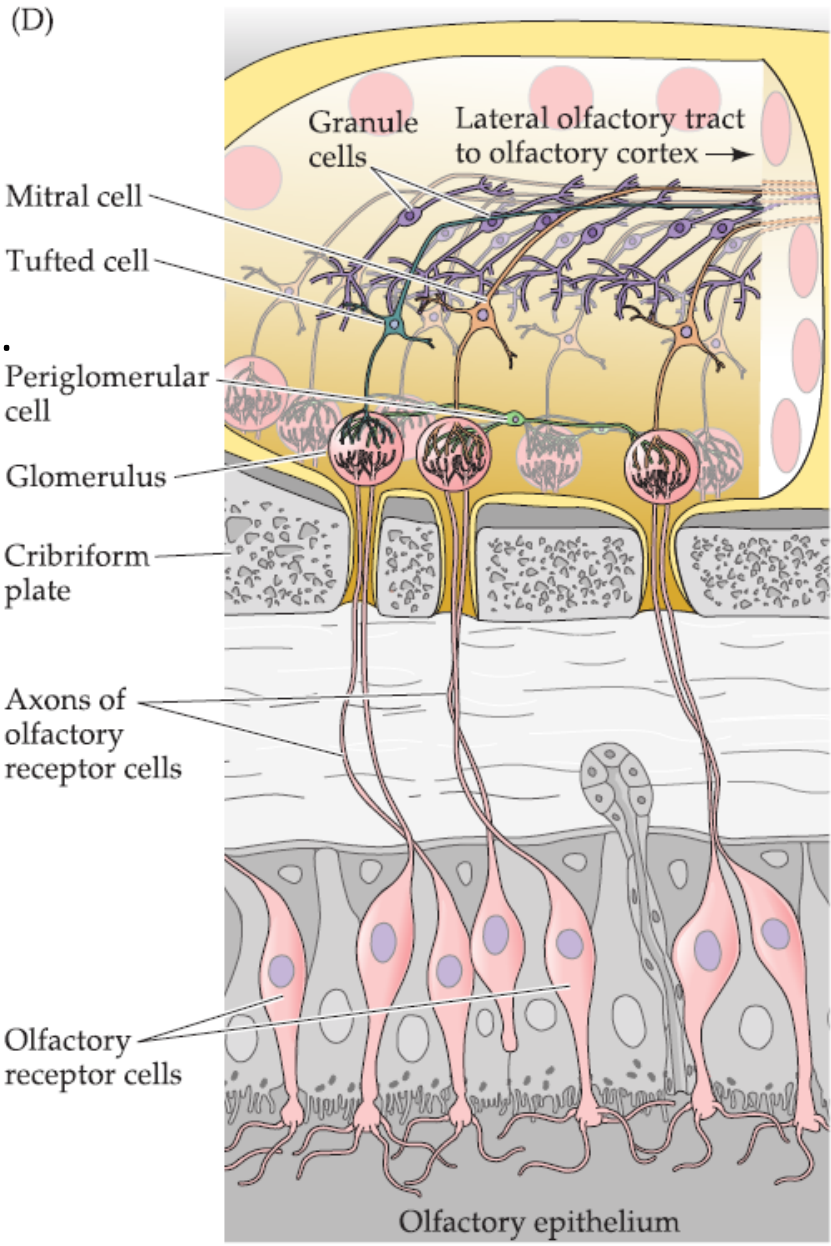
- In mammals, including humans, within each glomerulus the axons of the receptor neurons contact apical dendrites of **mitral cells**, which are the principal projection neurons of the olfactory bulb.
  - The cell bodies of the mitral cells are located in a distinct layer of the olfactory bulb deep within the glomeruli.
  - A mitral cell extends its primary dendrite into a single glomerulus, where the dendrite gives rise to an elaborate tuft of branches onto which the axons of olfactory receptor neurons synapse.
  - In the mouse, whose glomerular connectivity has been studied quantitatively, each glomerulus includes the apical dendrites of approximately 25 mitral cells, which in turn receive input from approximately 25,000 olfactory receptor axons.



The olfactory bulb

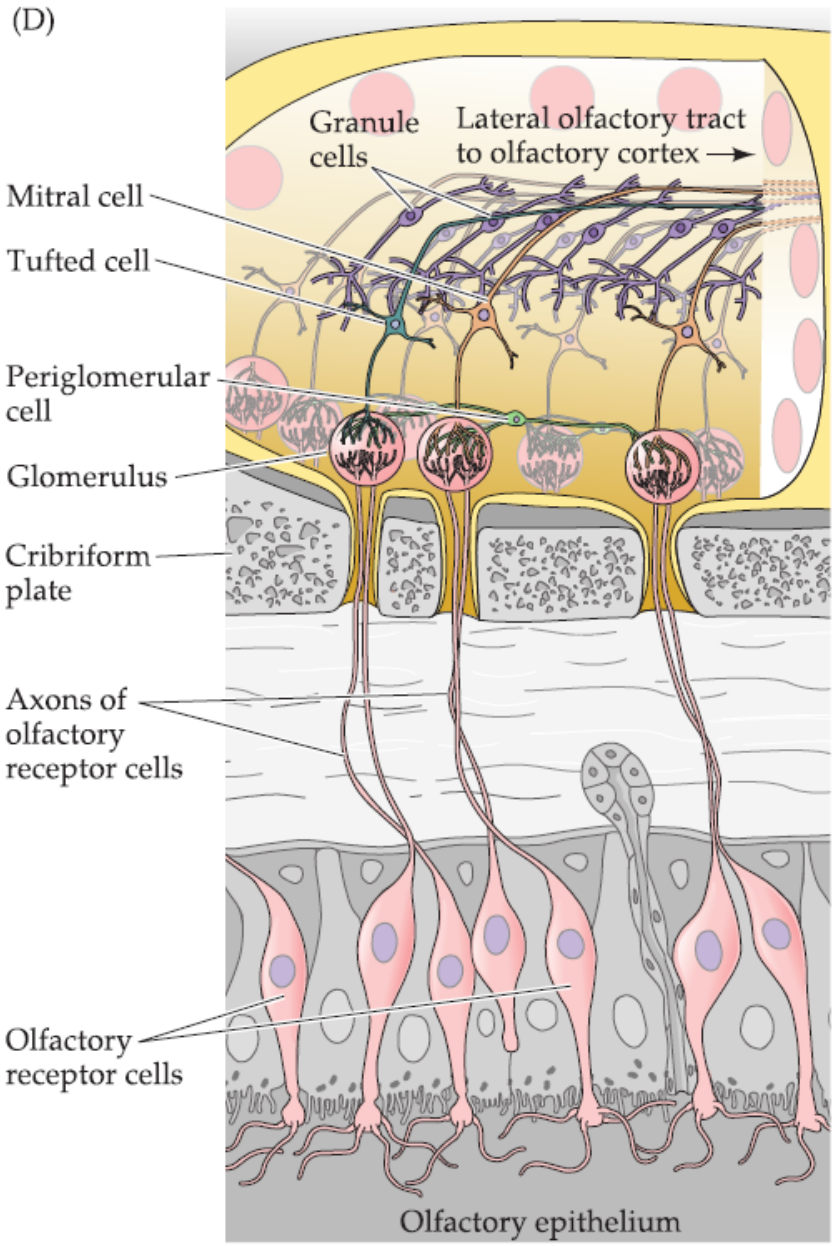
- Remarkably, most if not all 25,000 of these axons come from olfactory receptor neurons that express the same, single odorant receptor gene.
- This degree of convergence presumably increases the sensitivity of mitral cells to ensure maximal fidelity of odor detection.





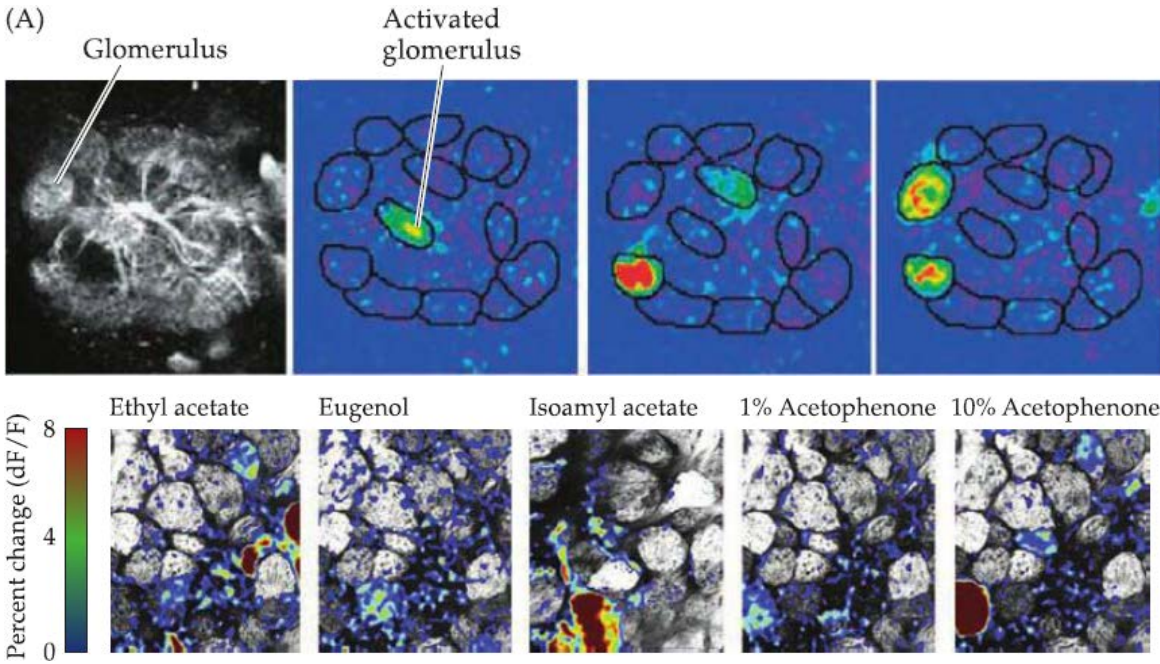
The olfactory bulb

- Each glomerulus also includes dendritic processes from two other classes of local circuit neurons: approximately 50 **tufted cells** and 25 **periglomerular cells** contribute to each glomerulus.
- **Granule cells**, which constitute the innermost layer of the vertebrate olfactory bulb, synapse primarily on the basal dendrites of mitral cells within the external plexiform layer.
  - Granule cells lack an identifiable axon, and instead make reciprocal dendrodendritic synapses with mitral cells.
  - Granule cells are thought to establish local lateral inhibitory circuits with mitral cells as well as participating in synaptic plasticity in the olfactory bulb.



The olfactory bulb

- The relationship between olfactory receptor neurons expressing one odorant receptor and small subsets of glomeruli suggests that individual glomeruli respond specifically (or at least selectively) to distinct odorants.
- The selective (but not singular) responses of subsets of glomeruli to particular odorants has been confirmed physiologically in invertebrates such as *Drosophila*, as well as in mice, using single and multiunit recordings, metabolic mapping, voltage-sensitive dyes, genetically encoded sensors of electrical activity, or intrinsic signals that depend on blood oxygenation.
  - Such studies show that increasing the odorant concentration increases the activity of individual glomeruli, as well as the number of glomeruli activated.
  - Different single odorants, or odorants with distinct chemical structures maximally activate one or a few glomeruli.

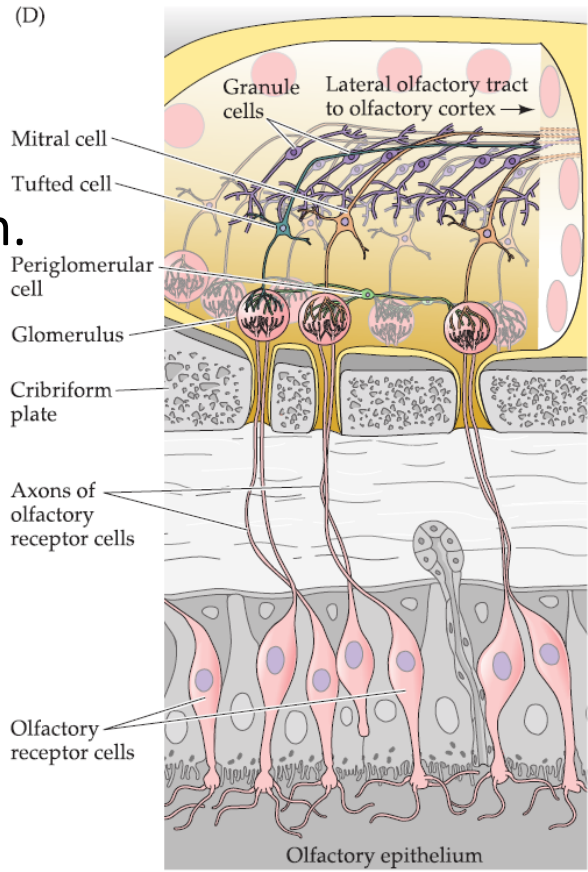


The olfactory bulb

- It is still not clear how (or whether) odor identity and concentration is mapped across the entire array, or reflects the activation of smaller subsets of glomeruli.
- Given the response of small numbers of glomeruli to single odorants, one might expect that complex natural odors such as those of coffee, fruits, cheeses, or spices--each of which is composed of more than a hundred compounds--would activate a very large number of olfactory glomeruli.
- In mice, natural odorants presented at their normal concentrations activate a relatively small number of glomeruli (up to 20), each of which responds selectively to one or two molecules that characterize the complex odor.
- One useful metaphor is to envision the sheet of glomeruli in the olfactory bulb as an array of lights on a movie marquee the spatial distribution of the active and inactive glomeruli ("lit and unlit lights") produces a message that is unique for a given odorant at a particular concentration.

Cortical processing of olfactory information

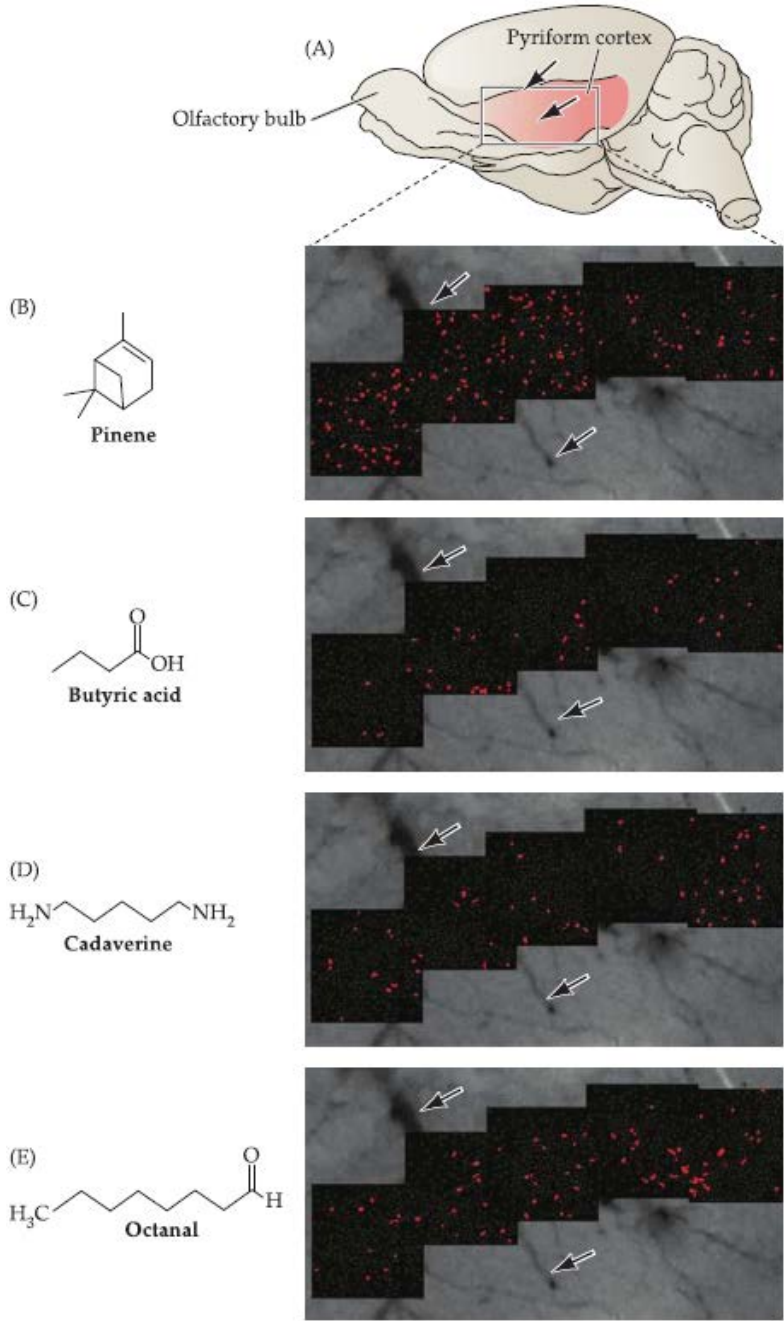
- Mitral cell axons provide the only relay for olfactory information to the rest of the brain.
- The mitral cell axons from each olfactory bulb form a bundle--the **lateral olfactory tract**--that projects to the accessory olfactory nuclei, the olfactory tubercle, the pyriform and entorhinal cortex, as well as to portions of the amygdala.
- Most projections of the lateral olfactory tract are ipsilateral; however, a subset of mitral cell axons cross the midline, presumably initiating bilateral processing of some aspects of olfactory information.
- The major target of the lateral olfactory tract is the three-layered pyriform cortex in the ventromedial aspect of the human temporal lobe, near the optic chiasm.
- Neurons in pyriform cortex respond to odors, and mitral cell inputs from glomeruli that receive odorant receptor-specific projections are distributed across the pyriform cortex.



Cortical processing of olfactory information

- Recent work suggests that the segregation of responses to single odors in the pyriform cortex is far less focal than that in the olfactory bulb.

- In fact, individual pyriform cortical cells seem to be more broadly tuned to different odors than is the case in the olfactory bulb, and the neurons that respond to single odors are distributed throughout extended regions of the pyriform cortex.



4.4. The Chemical Senses

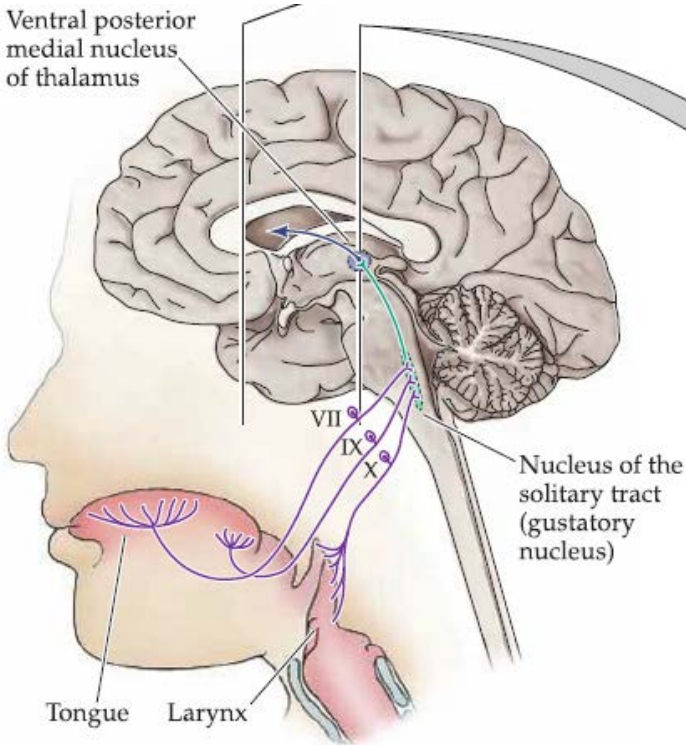
4.4.2 Taste system

Organization of the taste system

- The second chemosensory system, the taste system, represents the chemical as well as physical qualities of ingested substances, primarily food.
- Once in the mouth, the chemical constituents of food interact with receptor proteins on **taste cells**, which are located in epithelial specializations called **taste buds** in the tongue.
  - Taste cells transduce chemical stimuli to encode information about the identity, concentration, and qualities (pleasant, unpleasant, or potentially harmful) of the substance.
  - This information also prepares the gastrointestinal system to receive and digest food by causing salivation and swallowing--or, if the substance is noxious, gagging and regurgitation.
- Information about the temperature and texture of food (including viscosity and fat content) is transduced and relayed from the tongue and mouth via somatic sensory receptors from the trigeminal and other sensory cranial nerves to the thalamus and somatic sensory cortices.

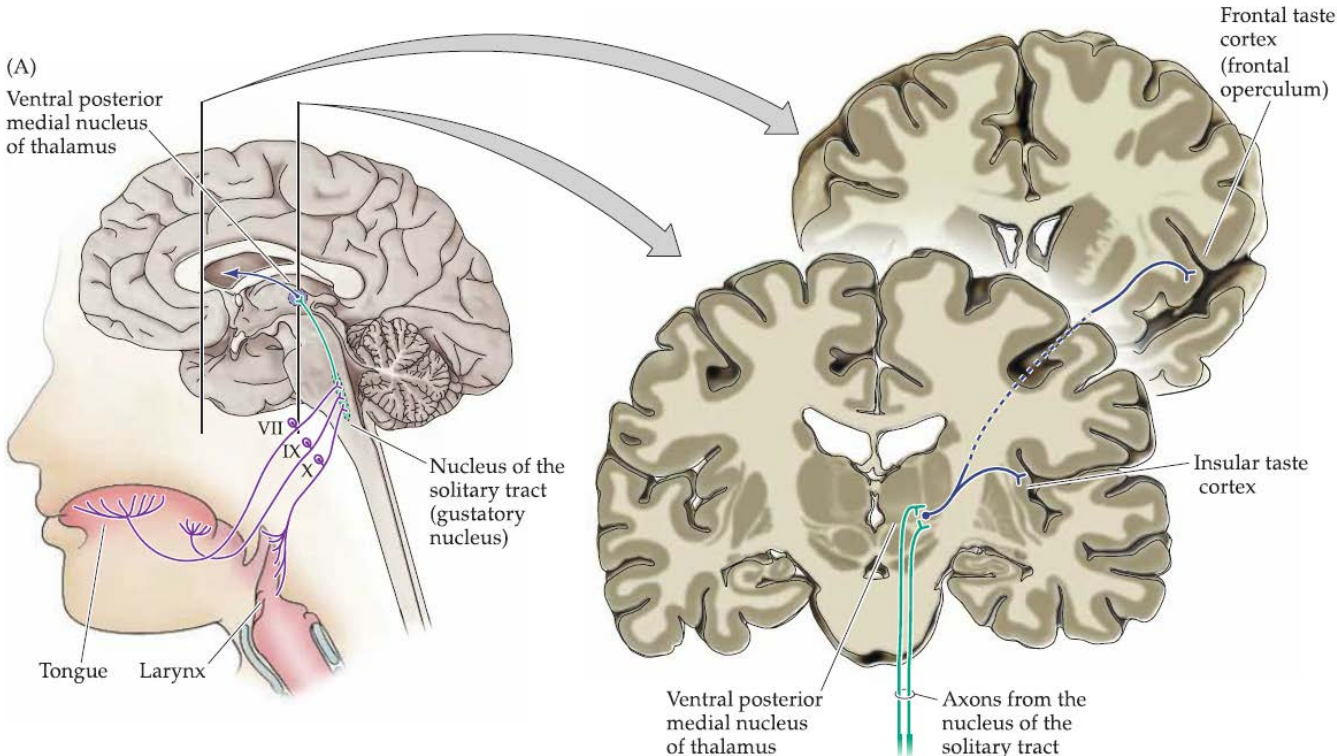
Organization of the taste system

- Taste cells (the peripheral receptors) are found in taste buds distributed on the dorsal surface of the tongue, soft palate, pharynx, and the upper part of the esophagus.
- Taste cells synapse with primary sensory axons that run in the chorda tympani and greater superior petrosal branches of the facial nerve (cranial nerve VII), the lingual branch of the glossopharyngeal nerve (cranial nerve IX), and the superior laryngeal branch of the vagus nerve (cranial nerve X) to innervate the taste buds in the tongue, palate, epiglottis, and esophagus, respectively.
- The central axons of these primary sensory neurons in the respective cranial nerve ganglia project to rostral and lateral regions of the **nucleus of the solitary tract** in the medulla, which is also known as the **gustatory nucleus** of the solitary tract complex.



Organization of the taste system

- The distribution of the cranial nerves that innervate taste buds in the oral cavity is topographically represented along the rostral-caudal axis of the rostral portion of the gustatory nucleus.
  - The terminations from the facial nerve are rostral, the glossopharyngeal are in the midregion, and those from the vagus nerve are more caudal in the nucleus.
- Axons from the rostral (gustatory) part of the solitary nucleus project to the ventral posterior complex of the thalamus, where they terminate in the medial half of the **ventral posterior medial nucleus**.
- This nucleus projects in turn to several regions of the neocortex, including the anterior insula in the temporal lobe (the **insular taste cortex**) and the operculum of the frontal lobe.

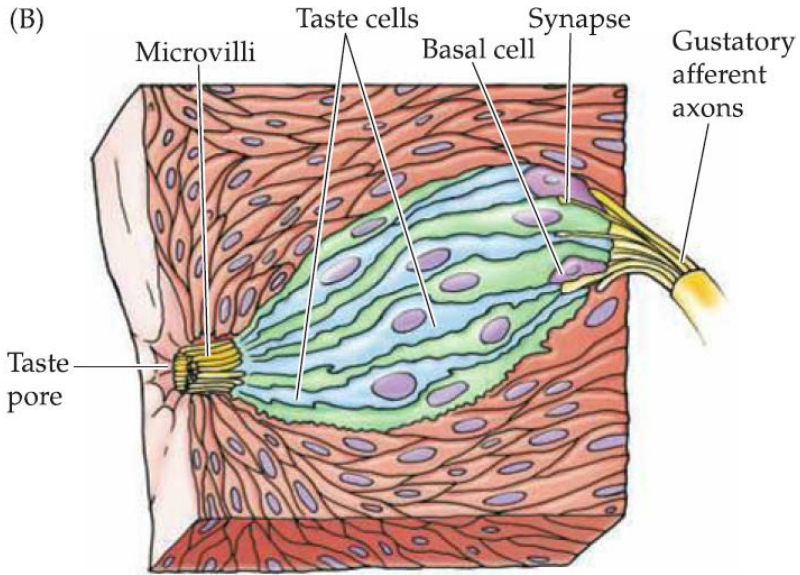


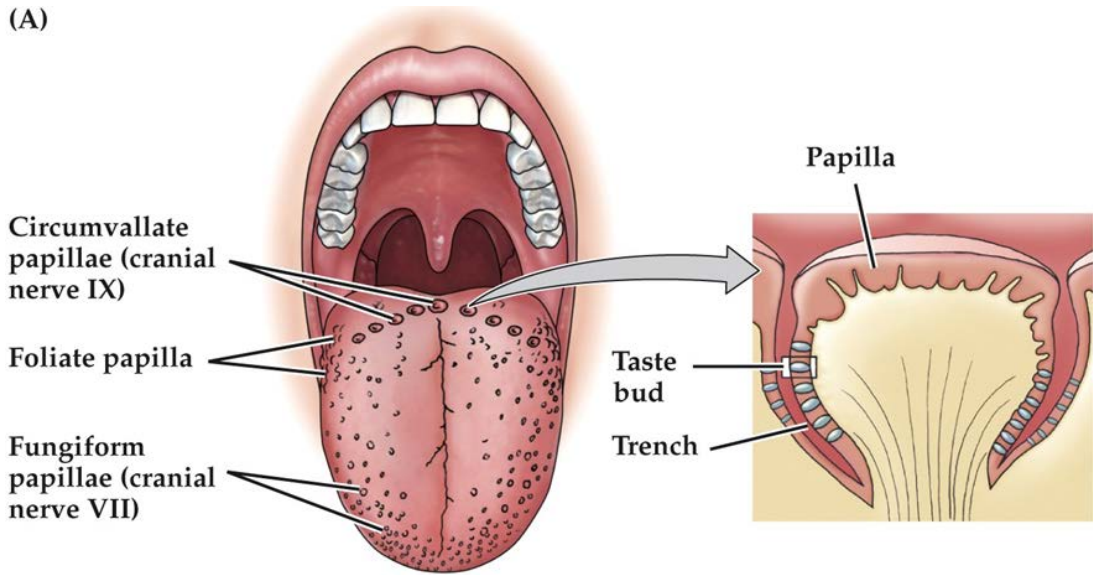
Taste perception in humans

- The taste system encodes information about the quantity as well as the identity of stimuli.
- In general, the perceived intensity of taste is directly proportional to the concentration of the taste stimulus.
- In humans, threshold concentrations for most ingested tastants are quite high:
  - The threshold concentration for citric acid is about 2 mM; for salt (NaCl) 10 mM; and for sucrose 20 mM.
  - In contrast, recall that the perceptual threshold for some odorants is as low as 0.01 nM.
  - Because the body requires substantial concentrations of salt and carbohydrates, taste cells may respond only to relatively high concentrations of these essential substances in order to promote an adequate intake.
- It is advantageous for the taste system to detect potentially dangerous substances (e.g., bitter-tasting plant compounds, which may be noxious or poisonous) at much lower concentrations.
- Thus the threshold concentration for such tastants is relatively low:
  - that for quinine is 0.008 mM, and for the deadly substance strychnine it is 0.0001 mM.

Taste papillae and taste buds

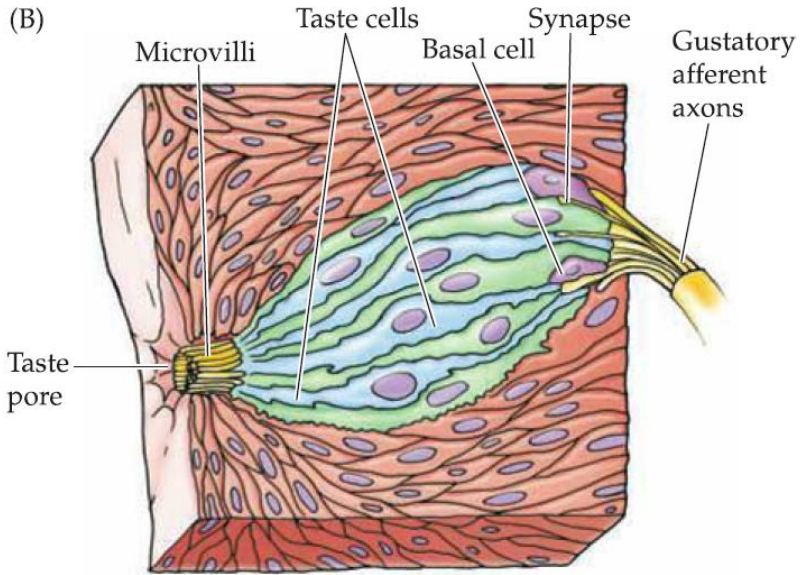
- Tastants are detected over the full surface the tongue in receptive specializations called **taste papillae**.
  - Papillae are defined by multicellular protuberances surrounded by local invaginations in the tongue epithelium.
  - These invaginations form a trench to concentrate solubilized tastants.
- **Taste buds** are distributed along the lateral surfaces of the papillar protuberance as well as in the trench walls.
  - They consist of specialized neuroepithelial receptor cells called **taste cells**, some supporting cells, and occasional basal cells.
  - In humans, approximately 4000 taste buds are distributed throughout the surface of the tongue as well as the palate, epiglottis, and esophagus.

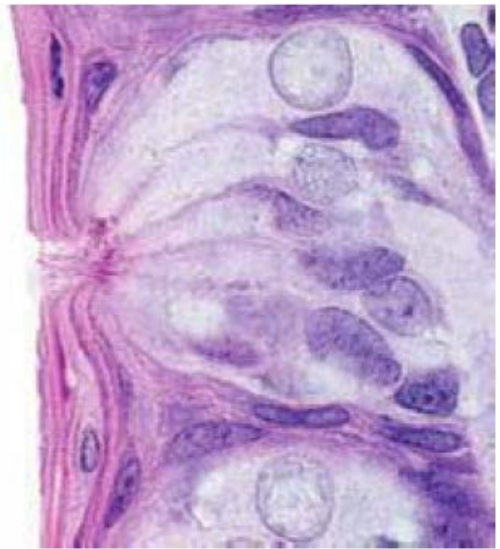




Taste papillae and taste buds

- Taste cells are clustered around a 1 mm opening called a **taste pore** in the taste bud near the surface of the tongue.
- Solubilized tastants are further concentrated and are presented directly to the exposed taste receptor cells in the relatively small region of the taste pore.
- Like olfactory receptor neurons (and presumably for the same reasons--exposure to infectious agents and environmental toxins), taste cells have a lifetime of about 2 weeks.
- Taste cells are apparently regenerated from **basal cells**, which constitute a local stem cell population that is retained in the mature tongue.





Taste papillae and taste buds

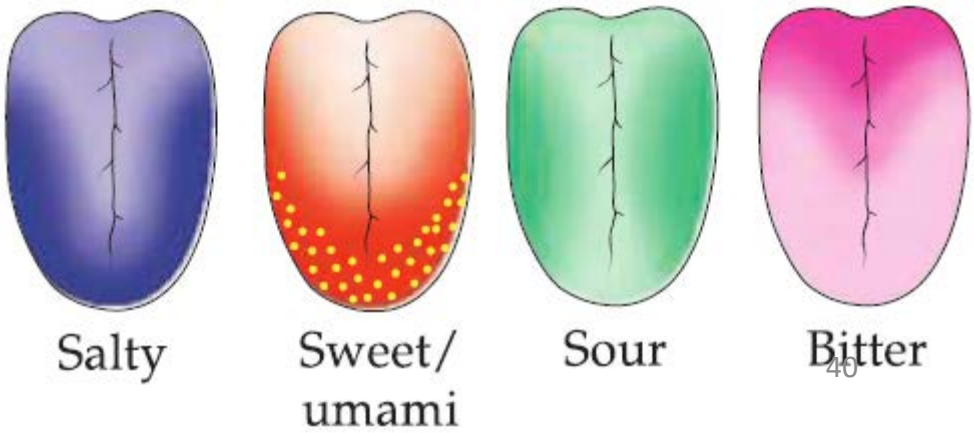
- There are three types of papillae:
  - **fungiform** (which contain about 25% of the total number of taste buds).
  - **circumvallate** (50%).
  - **foliate** (the remaining 25%).
- Fungiform papillae are found only on the anterior two-thirds of the tongue; the highest density (about 30 per cm^2) is at the tip.
  - Fungiform papillae have a mushroom-like structure (hence their name) and typically have about three taste buds at their apical surface.
- Nine circumvallate papillae form a chevron at the rear of the tongue.
  - Each consists of a circular trench containing about 250 taste buds along the trench walls.
- Two foliate papillae are present on the posterolateral tongue, each having about 20 parallel ridges with about 600 taste buds in their walls.
- Chemical stimuli on the tongue first stimulate receptors in the fungiform papillae and then in the foliate and circumvallate papillae.

Tastants

- Based on general agreement across cultures, the taste system detects five perceptually distinct categories of tastants: **salt**, **sour**, **sweet**, **bitter**, and **umami**.
- These five perceptual categories have dietary and metabolic significance:
  - salt tastes include NaCl, which is needed for electrolyte balance.
  - essential amino acids such as glutamate are needed for protein synthesis.
  - sugars such as glucose and other carbohydrates are needed for energy.
  - sour tastes, associated with acidity and thus protons (H^+), indicate the palatability of various foods (for example, the citric acid in oranges).
  - bitter-tasting molecules, including plant alkaloids such as atropine, quinine, and strychnine, indicate foods that may be poisonous.
- There are obvious limitations to this classification. People experience a variety of gustatory or ingestive sensations in addition to these five, including astringent (cranberries and tea), pungent (hot peppers and ginger), fat, starch, and various metallic tastes.

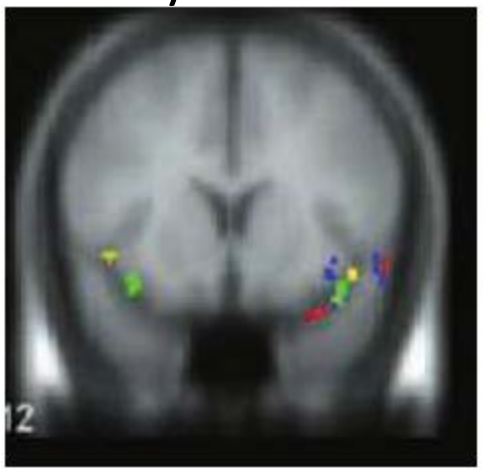
Peripheral innervation of the tongue

- Although all tastes can be detected over the entire surface of the tongue, different regions of the tongue have different thresholds for various tastes.
  - The tip of the tongue is most responsive to sweet, umami, and salty compounds, all of which produce pleasurable sensations at somewhat higher concentrations.
    - The acquisition of foods high in carbohydrates and amino acids is beneficial (in moderation), and thus it is not surprising that the most exposed region of the tongue is especially sensitive to these tastes.
  - Sour and bitter taste sensitivity is lowest toward the tip and greatest on the sides and back of the tongue.
    - It seems reasonable that, once it has analyzed for nutrient content, the receptor surface might next evaluate aesthetic characteristics like acidity and bitterness.



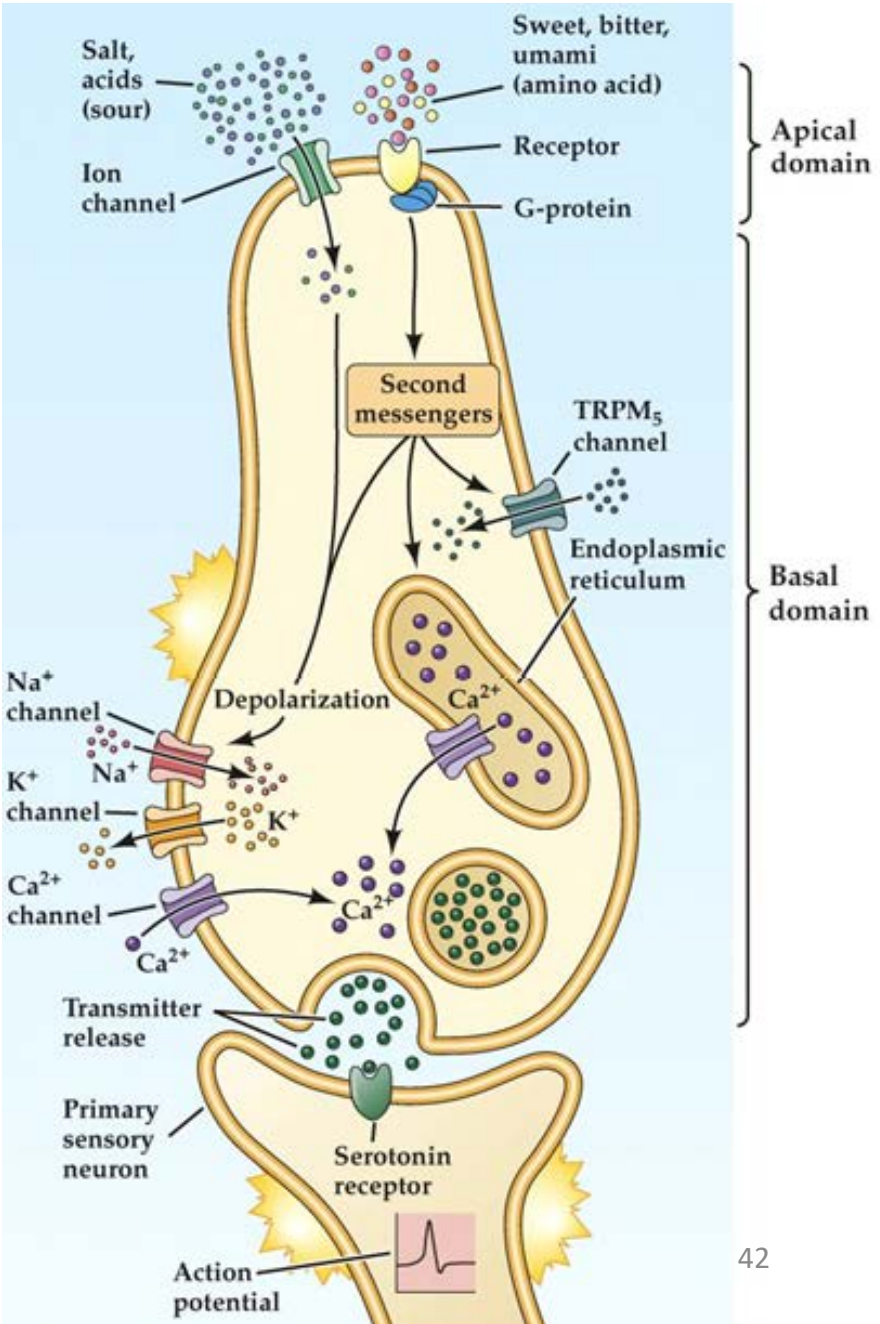
Taste categories

- Each of the primary tastes represented over the surface of the tongue corresponds to a distinct class of receptor molecules expressed in subsets of taste cells.
- Thus, representation in taste buds of the five primary categories of taste perception is closely linked to the molecular biology of taste transduction.
- These taste categories are also maintained in the representation of taste information in the central nervous system, including that in the insular taste cortex.
- Mapping of responses to sweet, bitter, salty, sour, and umami in normal human subjects shows that each of these tastes elicits focal activity in the taste cortex, suggesting that information about each taste category remains somewhat segregated throughout the taste system.



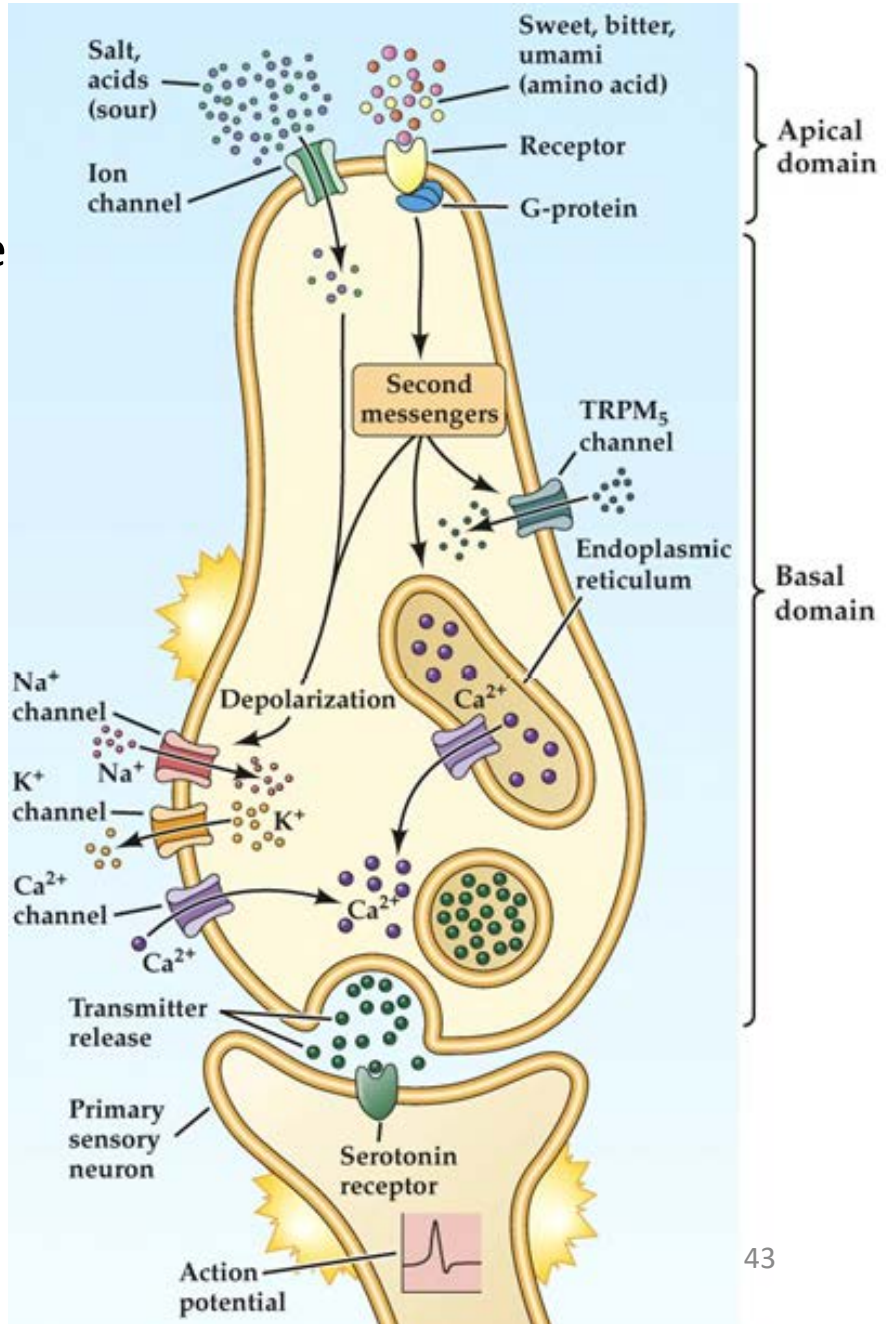
Taste receptor proteins and transduction

- Within the taste buds, only the taste cells are specialized for sensory transduction, their basic structure and function are uniform across all classes of papillae and their constituent taste buds.
  - Taste cells have distinct apical and basal domains, reflecting their epithelial character.
  - Chemosensory transduction is initiated in the apical domain of the taste cells, and electrical signals are generated at the basal domain via graded receptor potentials.
  - The specific neurotransmitters released by taste cells are thought to include serotonin, ATP, and GABA.



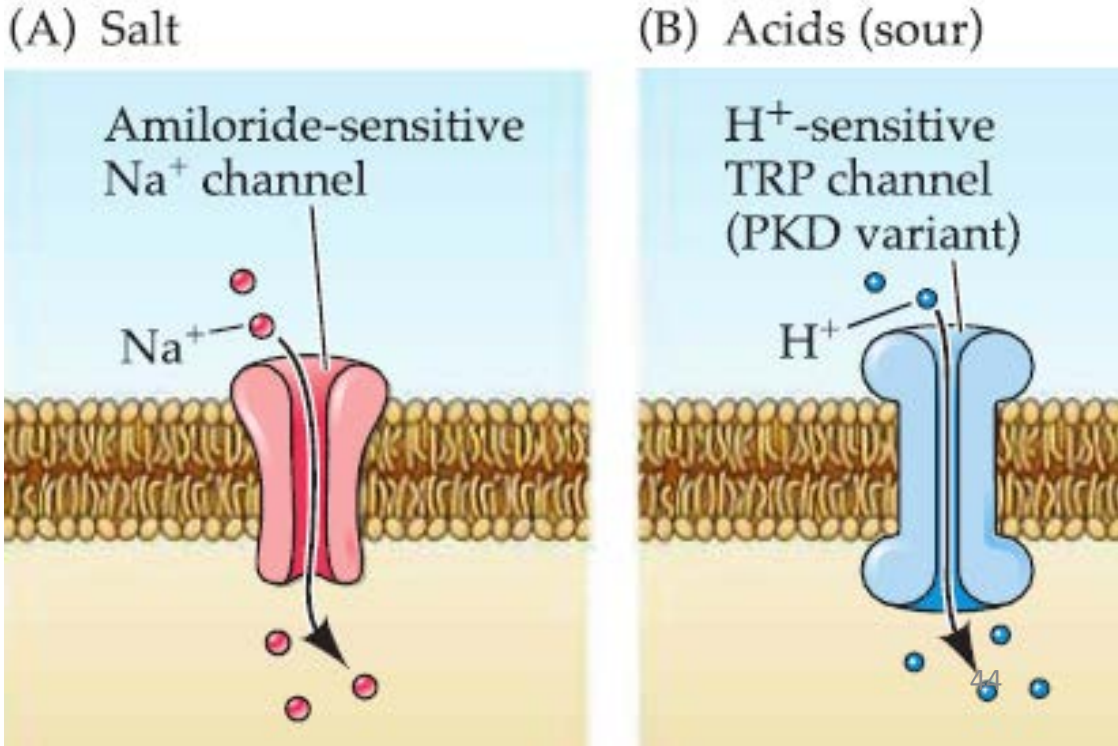
Taste receptor proteins and transduction

- Taste receptor proteins and related signaling molecules, like those in olfactory receptor neurons, are concentrated on microvilli that emerge from the taste cell apical surface.
- The basal domain is specialized for synaptic activation in response to tastant binding on apical receptor proteins.
- There are voltage-regulated ion channels as well as channels controlled by second messengers---especially members of the **transient receptor potential**, or **TRP** family.
- Local endoplasmic reticulum acts as a store that provides Ca^{2+} to facilitate synaptic vesicle fusion and neurotransmitter release at synapses made onto gustatory afferents at the basal surface.



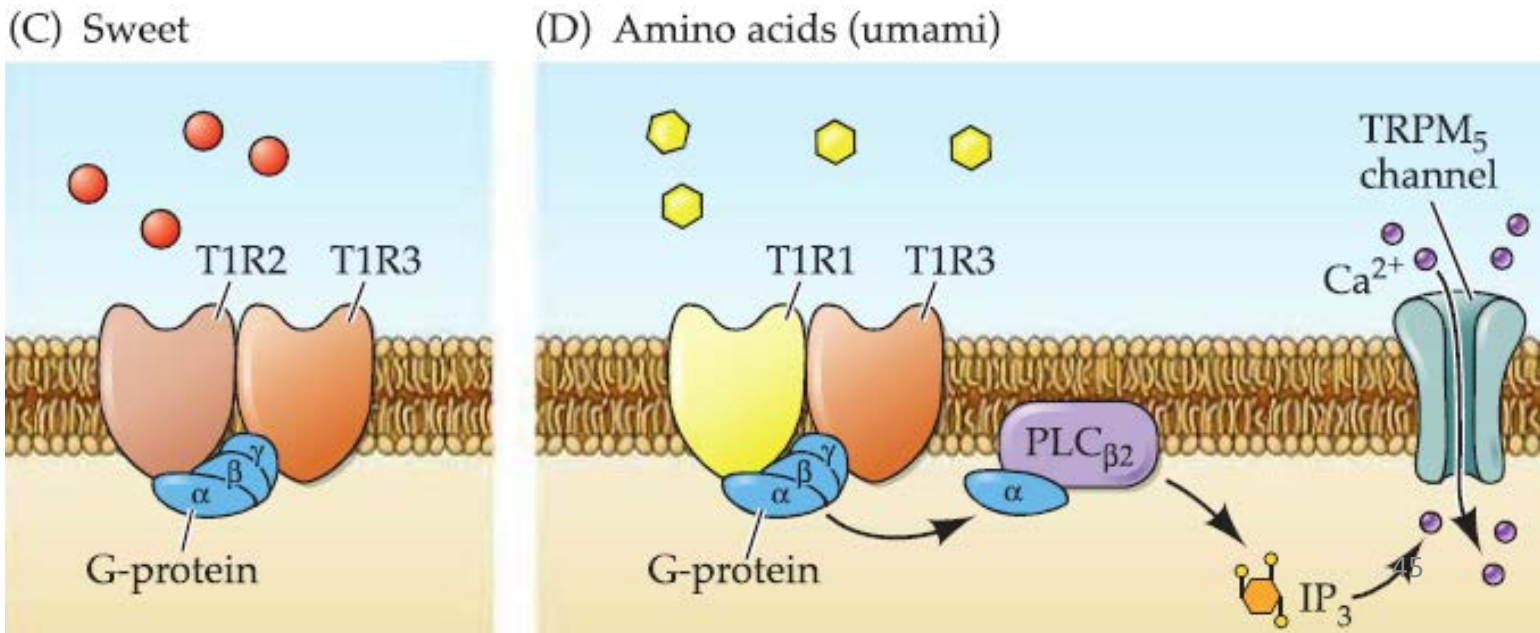
Taste receptor proteins and transduction

- Five distinct classes of taste receptor molecules represent tastants in the major perceptual categories-salty, sour, sweet, bitter, and umami.
  - Salty and sour tastes are elicited by ionic stimuli such as the positively charged ions in salts (e.g., Na^+ from NaCl), or the H^+ in acids (e.g., acetic acid, which gives vinegar its sour taste).
  - The ions in salty and sour tastants initiate sensory transduction via specific ion channels, most likely an amiloride-sensitive Na^+ channel for salty tastes and, for sour, an H^+-permeant, nonselective cation channel that is a member of the TRP family.



Taste receptor proteins and transduction

- In humans and other mammals, sweet and umami receptors are heterodimeric G-protein-coupled receptors that share a common 7-transmembrane receptor subunit called T1R3, paired with the T1R2 7-transmembrane receptor for perception of sweet, or with the T1R1 receptor for amino acids.
- Upon binding sugars or other sweet stimuli, the T1R2/T1R3 receptor heterodimer initiates a G-protein-mediated signal transduction cascade that leads to the activation of the phospholipase C isoform **$PLC_{\beta 2}$**, leading in turn to increased concentrations of inositol triphosphate (IP_3) and to the opening of TRP channels (specifically the $TRPM_5$ channel), which depolarizes the taste cell via increased intracellular Ca^{2+}.



Taste receptor proteins and transduction

- Another family of G-protein-coupled receptors known as T2R receptors transduces bitter tastes.
- Although the transduction of bitter stimuli relies on a mechanism similar to that for sweet and amino acid tastes, the taste cell-specific G-protein **gustducin**, found primarily in T2R-expressing taste cells, apparently contributes to the transduction of bitter tastes.
- The remaining steps in bitter transduction are similar to those for sweet and amino acids.