Smell & Taste
Smell and taste are generally classified as visceral senses because of their close association with GIT function. Physiologically, they are related to each other.

The flavors of various foods are in large part a combination of their taste and smell. Consequently, food may taste different if one has a cold that depresses the sense of smell.

Both taste and smell receptors are chemo-receptors that are stimulated by molecules in solution in mucus in the nose and saliva in the mouth.

These two senses are anatomically quite different:

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<td>1. The taste receptors are NOT distance receptors</td>
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<td>2. The smell pathways have no relay in the thalamus</td>
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Smell

Olfactory epithelium
Olfactory epithelium covers an area of 5 cm² in the roof of the nasal cavity near the septum.
Olfactory epithelium contains odorant receptor (Olfactory sensory neurons).

Olfactory epithelium contains:
1. 10 to 20 million bipolar olfactory sensory neurons interspersed
2. glia-like supporting (sustentacular) cells and
3. basal stem cells.

Olfactory sensory neurons has
1. a short, thick dendrite that projects into the nasal cavity
2. it terminates in a knob containing 10 to 20 cilia.
3. The cilia are unmyelinated processes contain specific receptors for odorants (odorant receptors).
4. Olfactory sensory neurons axons pass through the cribriform plate of the ethmoid bone and enter the olfactory bulbs.

New olfactory sensory neurons are generated by basal stem cells as needed to replace those damaged by exposure to the environment; where this process is inhibited by bone morphogenic protein (BMP).
Olfactory bulbs

In the olfactory bulbs, the axons of the olfactory sensory neurons (first cranial nerve) contact the primary dendrites of the mitral cells and tufted cells to form anatomically discrete synaptic units called olfactory glomeruli.
Olfactory cortex

The axons of the mitral and tufted cells pass posteriorly through the lateral olfactory stria to terminate on apical dendrites of pyramidal cells in Layer V regions of the olfactory cortex (primary olfactory cortex):

1. anterior olfactory nucleus,
2. olfactory tubercle,
3. piriform cortex,
4. amygdala, and
5. entorhinal cortex.

1. piriform cortex ►
   a. directly to the frontal cortex
   b. via the thalamus to the orbitofrontal cortex.

Conscious discrimination of odors is dependent on the pathway to the orbitofrontal cortex. The orbitofrontal activation is generally greater on the right side than the left; thus, cortical representation of olfaction is asymmetric.

2. the amygdala is probably involved with the emotional responses to olfactory stimuli

3. the entorhinal cortex is concerned with olfactory memories.
Signal transduction in an odorant receptor

The olfactory epithelium is covered by a thin layer of mucus secreted by the supporting cells and Bowman glands, which lie beneath the epithelium.

1. The mucus bathes the odorant receptors on the cilia and provides the appropriate molecular and ionic environment for odor detection.

2. The olfactory mucus might contain one or more odorant-binding proteins (OBP) that concentrate the odorants and transfer them to the receptors.

The concentration of an odor-producing substance must be changed by about 30% before a difference can be detected. The comparable visual discrimination threshold is a 1% change in light intensity.

The direction from which a smell comes may be indicated by the slight difference in the time of arrival of odoriferous molecules in the two nostrils.

Odor-producing molecules are generally small, containing from 3 to 20 carbon atoms, and molecules with the same number of carbon atoms but different structural configurations have different odors.

Relatively high water and lipid solubility are characteristic of substances with strong odors.
The binding of an odorant molecule to an odorant receptor (OR) leads to the interaction of the receptor with a GTP-binding protein Golf. This interaction in turn leads to the release of a GTP-coupled Gaolf subunit, which then stimulates adenylyl cyclase III (ACIII) to produce elevated levels of cyclic AMP (cAMP). The increase in cyclic AMP opens cyclic nucleotide-gated (CNG) cation channels, allowing both Ca$^{2+}$ and Na$^+$ to enter the cell through the cilia. This causes a membrane depolarization, leading to an action potential transducing the signal to the olfactory bulb.

About 1000 different types of odorant receptors make up the largest gene family so far described in mammals; larger than the immunoglobulin and T-cell receptor gene families combined.

Increase cytoplasmic calcium:
1. Ca$^{2+}$ opens a Ca$^{2+}$-activated Cl$^-$ channel leading to Cl$^-$ efflux which further depolarizes the cell.
2. Ca$^{2+}$ binds to calmodulin
   a. lowering the cAMP sensitivity of the cyclic nucleotide-gated (CNG) cation channels is the explanation phenomenon of fairly rapid adaptation, or desensitization, that occurs in the olfactory system.
   b. stimulates the activity of a phosphodiesterase (PDE).
3. Ca$^{2+}$ is extruded by a Na$^+$/Ca$^{2+}$ exchanger.
Sniffing

The portion of the nasal cavity containing the olfactory receptors is poorly ventilated in humans.

Most of the air normally moves smoothly over the turbinates with each respiratory cycle, Eddy currents pass some air over the olfactory epithelium. These eddy currents are probably set up by convection as cool air strikes the warm mucosal surfaces. The amount of air reaching this region is greatly increased by sniffing.

Sniffing is a semi-reflex response that usually occurs when a new odor attracts attention.
Role of pain fibers in the nose:
Naked endings of many trigeminal pain fibers are found in the olfactory epithelium. They are stimulated by irritating substances and leads to the characteristic “odor” of such substances as peppermint, menthol, and chlorine. Activation of these endings by nasal irritants also initiates sneezing, lacrimation, respiratory inhibition, and other reflexes.

Abnormalities in Odor Detection
Anosmia (inability to smell) and hyposmia or hypesthesia (diminished olfactory sensitivity) can result from
①simple nasal congestion or be a sign of a more serious problem including
②damage to the olfactory nerves due to fractures of the cribriform plate,
③tumors such as neuroblastomas or meningiomas,
④infections (such as abscesses).
⑤Alzheimer disease can also damage the olfactory nerves.
⑥Aging is also associated with abnormalities in smell sensation; more than 75% of humans over the age of 80 have an impaired ability to identify smells.
Studies have shown that people who are unable to smell one or more class of odors frequently have small genetic differences from the general population.
"Hyperosmia," a heightened sense of smell, can be a genetic trait.
**Taste**

**Taste buds**
The specialized sense organ for taste (gustation) consists of approximately 10,000 taste buds, which are ovoid bodies measuring 50–70 μm.

There are four morphologically distinct types of cells within each taste bud:

1. Basal cells ~3% of cells
   - The basal cells arise from the epithelial cells surrounding the taste bud. The basal cells differentiate into new taste cells, and the old cells are continuously replaced with a half-time of about 10 days.

2. Dark cells (Type I taste cells) 60% of cells
3. Light cells (Type II taste cells) 30% of cells
4. Intermediate cells (Type III taste cells) 7% of cells

   The three cell types may represent various stages of differentiation of developing taste cells, with the light cells being the most mature.
The apical ends of taste cells have microvilli that project into the taste pore, a small opening on the dorsal surface of the tongue where tastes cells are exposed to the oral contents.

Each taste bud is innervated by about 50 nerve fibers, and conversely, each nerve fiber receives input from an average of 5 taste buds.

In humans, the taste buds are located in the mucosa of:

1. the epiglottis,
2. palate, and
3. pharynx and
4. in the walls of papillae of the tongue.
Types of taste buds:

1. The fungiform (النفرت) papillae:
   ① rounded structures
   ② most numerous near the tip of the tongue;
   ③ fewer in number,
   ④ lightly keratinized and scattered taste buds
   ⑤ Each fungiform papilla has up to five taste buds, mostly located at the top of the papilla

2. The circum-vallate (المحاطة أو المكسوة) papillae:
   are prominent structures arranged in a V on the back of the tongue

3. The foliate (ورقي) papillae:
   are on the posterior edge of the tongue.

4. The filiform (خيطي) papillae –
   ① cover the majority of the anterior surface,
   ② highly keratinized and
   ③ lack taste buds.
   ④ most abundant type of papillae
   ⑤ found on the surface on the tongue.

Each vallate and foliate papilla contain up to 100 taste buds, mostly located along the sides of the papillae.
Taste pathway

First order neurons: the sensory nerve fibers from the taste buds
1. on the anterior two-thirds of the tongue travel in the chorda tympani branch of the facial nerve
2. on the posterior third of the tongue travel in the glossopharyngeal nerve
3. on the areas other than the tongue (pharynx, throat, palate) travel in the vagus nerve

On each side, the myelinated but relatively slowly conducting taste fibers in these three nerves unite reach the brain stem in the gustatory portion of the nucleus of the solitary tract (NTS) in the medulla oblongata.

From there, axons of second-order neurons ascend in the ipsilateral medial lemniscus and, in primates, pass directly to the ventral posteromedial nucleus of the thalamus.

From the thalamus, the axons of the third-order neurons pass to neurons in the anterior insula and the frontal operculum in the ipsilateral cerebral cortex. This region is rostral to the face area of the Post-central gyrus, which is probably the area that mediates conscious perception of taste and taste discrimination.
Basic taste modalities
Humans have five established basic tastes: sweet, sour, bitter, salt, and umami.

It used to be thought that the surface of the tongue had special areas for each of the first four of these sensations, but it is now clear that all tastants are sensed from all parts of the tongue and adjacent structures. Afferent nerves to the NTS contain fibers from all types of taste receptors, without any clear localization of types.
Taste receptors and transduction

1. The salty taste is triggered by NaCl.
Salt-sensitive taste is mediated by a Na\(^+\)-selective channel known as amiloride-sensitive epithelial sodium channel (ENaC). The entry of Na\(^+\) into the salt receptors depolarizes the membrane, generating the receptor potential.

2. The sour taste is triggered by protons (H\(^+\) ions).
   a. ENaCs permit the entry of protons and may contribute to the sensation of sour taste.
   b. The H\(^+\) ions can also bind to and block a K\(^+\)-sensitive channel► The fall in K\(^+\) permeability ► depolarize the membrane.
   c. hyperpolarization-activated cyclic nucleotide-gated cation channel (HCN)

3. Umami taste is due to
   a. activation of a truncated metabotropic glutamate receptor-4 (mGluR4), in the taste buds.
   b. Glutamate in food may also activate ionotropic glutamate receptors to depolarize umami receptors.
4. Bitter taste is produced by a variety of unrelated compounds. Many of these are poisons, and bitter taste serves as a warning to avoid them.

a. Some bitter compounds bind to and block $K^+$-selective channels.

b. Many G protein-linked receptors in the human genome are taste receptors (T2R family) and are stimulated by bitter substances such as strychnine.

c. In some cases, these receptors couple to the heterotrimeric G protein, gustducin.

Gustducin $\rightarrow$ lowers cAMP $\rightarrow$ increases IP3 $\rightarrow$ depolarization.

d. Some bitter compounds are membrane permeable and may not involve G proteins; quinine is an example.

5. Substances that taste sweet act via the G protein gustducin (a primarily taste-specific G protein alpha-subunit involved in both bitter and sweet taste transduction).

A proposed mechanism for alpha-gustducin involves coupling specific cell-surface receptors with a cyclic nucleotide phosphodiesterase which would open a cyclic nucleotide-suppressible cation channel leading to influx of calcium, and ultimately leading to release of neurotransmitter.

The T1R3 family of G protein-coupled receptors is expressed by about 20% of taste cells, some of which also express gustducin.
6. Sugars taste sweet, but so do compounds such as **saccharin** that have an entirely different structure. It appears at present that natural sugars such as sucrose and synthetic sweeteners act via **different receptors on gustducin**.

Like the bitter-responsive receptors, **sweet-responsive receptors** act via **cAMP+IP3**

Taste exhibits **after reactions and contrast phenomena** that are similar in some ways to visual after images and contrasts.

Some of these are chemical “tricks,” but others may be true central phenomena.

A taste modifier protein, **miraculin**, has been discovered in a **plant**. When applied to the tongue, this **protein makes acids taste sweet**.
Signal transduction pathway of bitter (T2R), sweet (T1R2/3), and umami (T1R1/3) GPCRs in type II taste cells of the tongue. As described in the text and reviewed in [11, 32], ligand binding to taste GPCRs results in Ca\(^{2+}\) signaling through two G-protein-coupled pathways. Gbc activation of phospholipase C isoform b2 (PLCb2) results in production of inositol 1,4,5-trisphosphate (IP\(_3\)), which activates the IP\(_3\) receptor (IP\(_3\)R), an intracellular ion channel that allows calcium (Ca\(^{2+}\)) release from the intracellular endoplasmic reticulum (ER) calcium stores [254]. Simultaneously, Ga-gustducin activates phosphodiesterases (PDEs), which reduce the levels of cyclic-AMP (cAMP) and decrease protein kinase A (PKA) activity [28]. PKA can phosphorylate and inhibit the activity of the type III IP\(_3\)R [255, 256], the major IP\(_3\)R isoform found in type II taste cells [257–259], thus reduction of PKA activity can enhance IP\(_3\)R3-mediated calcium signaling. Calcium activates the plasma membrane-localized cation channel TRPM5 [137, 138], causing depolarization of cellular membrane potential, activation of voltage-gated sodium (Na\(^{+}\)) channels [260], and generation of an action potential that results in ATP release [11] through the CALHM1 ion channel [45, 46] and subsequent purinergic neurotransmission of taste sensations.
Transduction of Sweet Tastants

1. Sweet-tasting molecule (S) binds to sweet-taste receptor (SR), activating the G protein gustducin (G_{s}\text{gust}).
2. Gustducin or subunit activates adenylyl cyclase (AC) of the apical membrane, raising [cAMP].
3. PKA, activated by cAMP, phosphorylates a K+ channel in the basolateral membrane, causing it to close. The reduced efflux of K+ depolarizes the cell.
Diagrammatic representation of a rodent taste bud and important components of the bitter transduction pathway. A) A typical taste bud consists of 50-100 taste receptor cells (TRCs) that extend from the basal lamina to the taste pore. Taste stimuli interact with taste receptors on the apical membrane, while nerve fibers form chemical synapses with basal cells (labeled B) along the margin of the taste bud. Basal cells give rise to taste receptor cells. (B) Bitter stimuli interact with T2R/TRB receptors located on the apical membrane. These receptors couple to a heterotrimeric G protein consisting of α-gustducin, β3, and γ13. Alpha gustducin activates phosphodiesterase (PDE), causing decreases in intracellular cAMP, while β3γ13 activates phospholipase C β2 (PLCβ2) to produce the second messengers inositol 1,4,5 trisphosphate (IP3) and diacylglycerol (DAG). The IP3 binds to receptors located on smooth endoplasmic reticulum, causing a release of Ca2+ into the cytosol. The purpose of this study was to identify the IP3 receptor isotype that is expressed in taste cells.