# Physiology of Smell (Olfaction)

**Lata Mullur**

Olfaction, also known as the sense of smell, is a chemosensory modality that is essential for taste, memory, emotion, and protective actions. It detects volatile chemicals in the environment. Olfactory epithelium is found in the roof of the nasal cavity and contains bipolar olfactory receptor neurons, supporting cells, and basal stem cells that can regenerate continuously. The olfactory epithelium is situated in such a location where the nervous system is directly connected with the external environment. Odorant molecules dissolves in the mucus layer and attach to certain receptors on olfactory neurons' cilia, start signal transduction through G-protein-mediated pathways that produce action potentials that are sent via the olfactory nerve. These inputs create synapses in the glomeruli of the olfactory bulb on mitral and tufted cells, whose axons travel to the piriform cortex, amygdala, and entorhinal cortex, among other key olfactory cortical areas, via the olfactory tract. Olfactory impulses, contrary to other sensory systems, do not require thalamic relay to reach the cortex, which facilitates quick emotional and memory-related reactions. Although sensitivity varies with stimulus parameters and exhibits rapid adaptation, humans are able to discriminate hundreds of odorants. Clinically, infections, age, trauma to the cribriform plate, neurodegeneration, or congenital abnormalities can cause olfactory dysfunctions such hyposmia and anosmia. To fully understand its functions in behavior, health, and illness, one must have an adequate knowledge of olfactory physiology.

***Keywords:*** *Olfactory epithelium, Odorant receptors, Olfactory bulb, Signal transduction, Olfactory pathways Olfactory dysfunction (anosmia/hyposmia)*

Lata Mullur
Professor& Head, Department of Physiology, BLDE (DU), Shri. B. M. Patil Medical College, Hospital and Research Center, Vijayapura, Karnataka, India.

Email: lata.mullur@bldedu.ac.in


Publisher: Cornous Publications LLP, Puducherry, India.
Introductory Human Physiology: New Approach and Recent Advances
Editor: Dr. Cornelius Nwozor
ISBN: 978-81-981855-7-0
DOI: https://doi.org/10.37446/edibook172024/45-51

## Introduction

Olfaction, also referred to as the sense of smell, is a specialized skill that allows organisms to detect and identify chemical molecules in their environment (Purves et al., 2018). Considering its close connection to gastrointestinal functions, olfaction is usually classified as a visceral sense. Taste, behavior, and memory are all significantly impacted (Doty, 2015). The olfactory epithelium, situated in the upper section of the nasal cavity, is the organ responsible for the sense of smell. Olfactory receptors are chemoreceptors activated by molecules dissolved in mucus within the nasal passage (Bear et al., 2015).

Since stimuli originate from an outside source, they are categorized as exteroceptors. In animals, the sense of smell is highly advanced. It is beneficial for them to find their partners and to recognize their territory (Pinel & Barnes, 2018). Olfaction serves a protective role by helping humans steer clear of spoiled food and avoid polluted surroundings. The olfactory system is the only sensory system that does not relay in the thalamus on its way to the cortex (Kandel et al., 2000). It is suggested that women have a stronger sense of smell than men do, and that it is at its sharpest during ovulation (Doty, 2015).

## 1. Functional Anatomy of the Olfactory System

The olfactory system consists of the olfactory epithelium, olfactory receptor neurons, and the olfactory bulb (Purves et al., 2018).

### a. Olfactory Epithelium

The olfactory receptor cells are located in a specialized area of the nasal mucosa lining the roof of the nasal cavity called the olfactory epithelium or the olfactory mucus membrane (Kandel et al., 2000). It is a patch of yellowish-pigmented mucus membrane Located on the roof of the nasal cavity, near the superior nasal concha and the nasal septum. In humans, it covers an area of 10 $cm^2$ in the roof of the nasal cavity and is covered by mucus produced by the Bowman's glands (Bear et al., 2015). The area is large in animals like dogs in which the sense of smell is pretty well developed (*microsmatic* animals). Human beings are *microsmatic*. A unique feature of olfactory mucosa is that it is one place in the body where the nervous system is exposed to the external environment (Purves et al., 2018).

The olfactory mucus membrane contains three main types of cells (Figure 1):

**1.** Olfactory receptor cells – bipolar neurons that detect odor molecules.

**2.** Supporting (sustentacular) cells – provide nourishment and support.

**3.** Basal cells – stem cells that regenerate receptor cells.

There are approximately 50 million bipolar olfactory sensory neurons in the human olfactory epithelium. (Purves et al., 2018)

The mucus layer dissolves the chemical particles and helps in their transport to reach the cilia of the receptor. Sniffing, or deep breathing channels the air to the olfactory mucus membrane.

In rodents and other mammals, another patch of olfactory mucus membrane is present along the nasal septum, called vomeronasal organ (Doty, 2015).

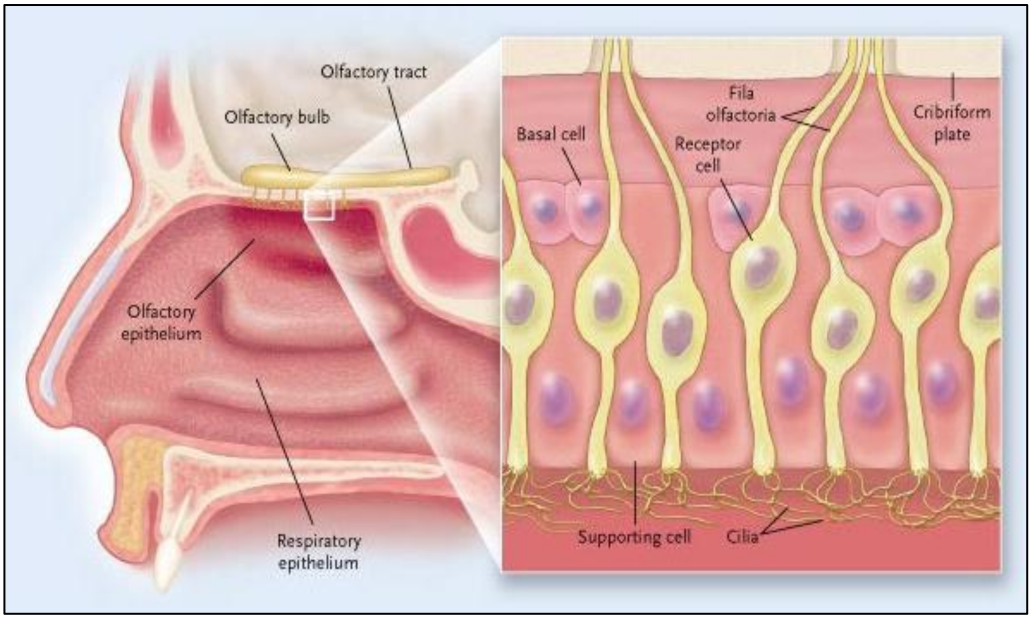


**Figure 1: Structure of the olfactory epithelium with three main types of cells.**
(Source: The New England Journal of Medicine. (n.d.). *Structure of the olfactory epithelium* [Figure]. Retrieved from https://www.nejm.org/doi/full/10.1056/NEJMoa022043)

**b. Olfactory Receptor Cell**

1. The olfactory receptor cell is a bipolar neuron. It has a short thick dendrite with an expanded end called an olfactory rod that gives off 10–20 cilia (Figure 1) (Bear et al., 2015).

2. Each cilium is about 2 μm long and 0.1 μm in diameter. The cilia are unmyelinated and project into the mucus where they interact with odorants dissolved in the mucus (Shipley & Ennis, 1996).

Odorant molecules dissolve in the mucus and bind to odorant receptors on the cilia of olfactory sensory neurons. Mucus offers an ideal ionic and molecular environment for smell sensing.

The axons of receptor cells form bundles known as the **olfactory nerves (cranial nerve I)** which pierce the cribriform plate of the ethmoid bone and enter the olfactory bulbs (Kandel et al., 2000).

**c. Olfactory Bulb**

The portion of the brain that projects forward above the cribriform plate of the ethmoid bone and below the orbital surface of the frontal lobe on each side is called the olfactory bulb.

In the olfactory bulbs, the axons of the olfactory sensory neurons contact the primary dendrites of the mitral cells and tufted cells (Figure 2) to form **olfactory glomeruli** that have anatomically unique synaptic units (Purves et al., 2018)**.**

Periglomerular cells, which are inhibitory neurons connected to glomeruli, and granule cells, which lack axons and form reciprocal synapses with the lateral dendrites of mitral and tufted cells, are also found in the olfactory bulbs (Shipley & Ennis, 1996). At these synapses, the granule cells inhibit the mitral or tufted cell by releasing GABA, while the mitral or tufted cells excite the granule cell by releasing glutamate.

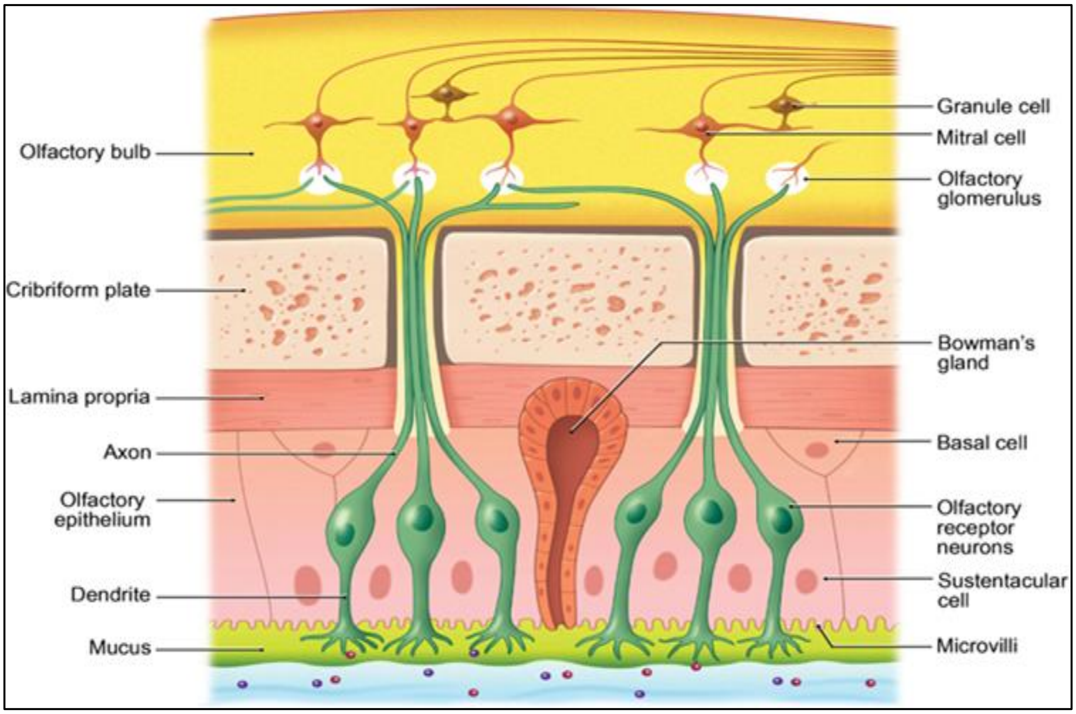


**Figure 2: Olfactory epithelium and the olfactory bulb.**
(Source: Enokey. (n.d.). *Anatomy of the olfactory system*. Retrieved from https://entokey.com/anatomy-of-the-olfactory-system/)

The olfactory epithelium has free terminals of many trigeminal pain fibers. They are triggered by irritating substances, which results in the distinctive "odor" of things like menthol, peppermint, and chlorine (Doty, 2015). Sneezing, lacrimation, respiratory inhibition, and other reflexes are also triggered when nasal irritants activate these endings.

The axons of mitral and tufted cells extend to the olfactory cortical areas as **olfactory tract.**

**d. Olfactory cortex**

While entering to the brain, the fibers of the olfactory tract divide into **lateral and medial olfactory stria**. The anterior olfactory nucleus, olfactory tubercle, piriform cortex, amygdala, and entorhinal cortex are the five areas of the olfactory cortex where the axons of the mitral and tufted cells terminate on apical dendrites of pyramidal cells after passing posteriorly through the **lateral olfactory stria** (Kandel et al., 2000). Information leaves these areas and either goes straight to the frontal cortex or via the thalamus to the orbitofrontal cortex. (Figure 3)

Olfaction is asymmetrically represented in the brain because orbitofrontal activation is typically higher on the right side than the left (Doty, 2015). The pathway to the entorhinal cortex is related to olfactory memories, while the pathway to the amygdala is likely involved in the emotional reactions to olfactory stimuli (Bear et al., 2015).

The medial olfactory stria projects to the septum and hypothalamus that mediates various autonomic responses associated with smell.

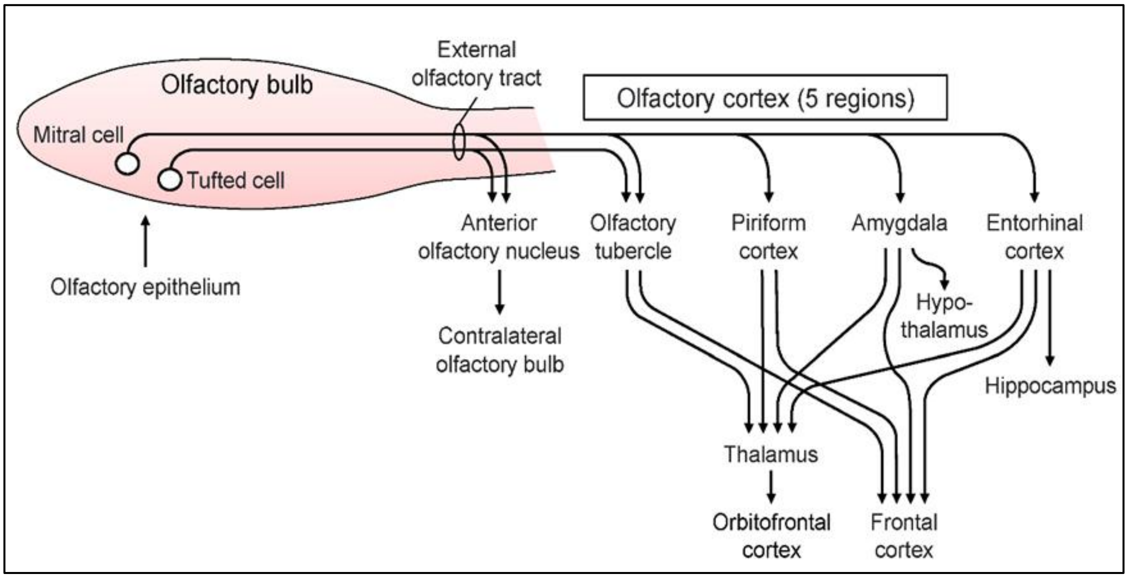


**Figure 3: Olfactory pathway**

(Source: Kandel ER, Schwartz JH, Jessell TM [editors]: *Principles of Neural Science,* 4th ed. McGraw-Hill, 2000)

**3. Mechanism of Olfaction**

When odoriferous chemicals dissolve in the thin layer of mucus covering the olfactory epithelium and come into contact with the cilia of the olfactory receptors, the receptors get activated (Purves et al., 2018).

To reach the cilia of the olfactory receptors, water-soluble odorants dissolve in the mucus covering the olfactory epithelium (Amoore, 1970). The lipid-soluble odorants bind to an Odorant-Binding protein to get transported in the hydrophilic mucus and reach the receptors.

The G protein is activated when the odorant attaches to the receptor, which opens cation channels and causes an influx of calcium (the main mechanism), activates the adenylyl cyclase-cAMP system and stimulates the phospholipase C-IP3, DAG system (Shipley & Ennis, 1996). Stimulation of one of these systems results in the depolarization of olfactory receptor cells, which in turn generates action potentials along the olfactory nerve fiber.

**Factors Affecting Olfaction**

a. **Type of odorant stimulus:** Volatile odorant chemicals are easily transported by air into the nose and quickly recognized.
b. **Threshold of olfactory receptors:** Some of the odoriferous compounds can be detected at extremely low concentrations by the olfactory receptors (Doty, 2015).
c. **Intensity of stimuli:** Humans can discriminate over 10,000 different odors (Leffingwell, 2002).
d. **Olfactory adaptation:** The olfactory receptors rapidly adapt when they are continuously stimulated.

## 4. Applied aspect

1. **Hyposmia:** Diminished sense of smell.
2. **Anosmia:** Sense of smell is absent.
3. **Parosmia**: Distorted smell perception
4. **Phantosmia**: Smell perception without stimulus (olfactory hallucination).

The most common causes of hyposmia or anosmia are the common cold, aging, and damage to the olfactory nerve or olfactory bulb, a fractured cribriform plate that damages the olfactory epithelium, atrophic rhinitis, and anomalies in receptors. When the olfactory nerve or other neural components in the olfactory neural pathway are injured, anosmia is usually irreversible (Purves et al., 2018).

A rare disorder known as congenital anosmia leads a person to be born without the ability to sense of smell (Doty, 2015).

## Conclusion

The physiology of smell plays a crucial role in detecting environmental chemicals, influencing taste, memory, and emotional responses. The olfactory system is unique in that it has specialized receptors, fast signal transduction, and direct cerebral projections that bypass the thalamus (Kandel et al. 2000). Its sensitivity and intricate nature are demonstrated by being able to differentiate among thousands of odorants. In addition to providing a deeper understanding of human perception, an understanding of this system helps identify and treat olfactory diseases such anosmia and hyposmia.

**Conflict of Interest Statement:**
The author declares that there is **no conflict of interest** regarding the preparation, content, or publication of this work.

## References

Amoore, J. E. (1970). *Molecular basis of odor*. Charles C. Thomas.

Bear, M. F., Connors, B. W., & Paradiso, M. A. (2015). *Neuroscience: Exploring the Brain* (4th ed.). Lippincott Williams & Wilkins.

Doty, R. L. (2015). *The Neurology of Olfaction*. Cambridge University Press.

Enokey. (n.d.). Anatomy of the olfactory system. Retrieved from https://entokey.com/anatomy-of-the-olfactory-system/

Ganong’s Review of Medical Physiology - Book 2 - Flip eBook Pages 1–50 | AnyFlip. https://anyflip.com/rvtsv/oumi/basic

Kandel, E. R., Schwartz, J. H., & Jessell, T. M. (2000). *Principles of Neural Science* (4th ed.). McGraw-Hill.

Kondo, K., Kikuta, S., Ueha, R., Suzukawa, K., & Yamasoba, T. (2020). Age-related olfactory dysfunction: Epidemiology, pathophysiology, and clinical management. *Frontiers in Aging Neuroscience*.

Leffingwell, J. C. (2002). Olfaction: A review. *Leffingwell Reports*, 1(1), 1–24.

NIH. (n.d.). Sense of smell and taste. National Institute on Deafness and Other Communication Disorders. https://www.nidcd.nih.gov/

Pinel, J. P. J., & Barnes, S. J. (2018). *Biopsychology* (10th ed.). Pearson.

Purves, D., Augustine, G. J., Fitzpatrick, D., et al. (2018). *Neuroscience* (6th ed.). Oxford University Press.

Shipley, M. T., & Ennis, M. (1996). Functional organization of olfactory pathways. *Journal of Neurobiology*, 30(1), 123–176.

The New England Journal of Medicine. (n.d.). Structure of the olfactory epithelium [Figure]. Retrieved from https://www.nejm.org/doi/full/10.1056/NEJMoa022043.