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Review

Biology and applications of olfactory sensing system: A review

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ABSTRACT

Various metal oxide and conducting polymer-based sensors have been used in electronic nose systems for the detection of volatile organic compounds (VOCs). Some of the major constrains of these sensor materials are their sensitivity and selectivity. Recently, much research has been towards the development of biosensors that mimic biological olfactory mechanism. The sensing materials based on biological olfactory system can be well adapted to detect low concentrations of VOCs as it exhibits high selectivity/specificity, fast response time, high sensitivity, simplicity in fabrication, and are not toxic resulting from their biocompatibility and rapid biodegradability. A better understanding of human olfactory system can aid in the development of an artificial olfactory sensing system. The application domain of such sensors/systems could be potentially expanded for rapid and accurate detection of VOCs in environment and other biological media. Therefore, this paper provides a brief overview of the biology, associated mechanisms, and the functional principles of the olfactory sensing system in humans. Moreover, it summarizes the recent research on the development of an olfactory sensor utilizing olfactory receptors, odorant binding proteins and olfactory epithelium for the detection of different VOCs, and research needs in this area.

Contents

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1. Introduction

Vertebrate olfactory systems can identify and distinguish volatile compounds (odorants) of diverse molecular structures with high accuracy. The mammalian nose can detect certain compounds in concentrations as low as few parts per trillion [1]. Such performances are due to numerous olfactory receptors (ORs) expressed by olfactory sensory neurons and their subsequent neuronal processing. Each of the ORs can bind to numerous odorants with specific affinities, although some receptors are relatively restricted to a set of few chemically related compounds [2]. In the process of sensing the smell, the binding of specific odorants to the OR proteins is the initiation step in odor recognition and triggering of signal transduction in a cell. Gomila et al. [2] stated that "Given the fantastic odor space detected by the olfactory receptors, it is tempting to harness them to some generic electronic devices that could be endowed with some of the most prominent properties of animal olfaction: discrimination, specificity and sensitivity."

Recent studies have led to a more refined understanding of olfactory neurons and the mechanisms involving odorant detection. Joint efforts of biologist and biochemists have revealed that olfactory receptor achieve odorant identification and signal transduction by employing molecular elements [3]. An olfactory system plays an important role in identifying food and recognizing environmental conditions. Olfactory sensing can be used for detecting human diseases [4–7], food contamination [8–11], or hazardous agents [12,13]. Currently, olfactory research is focused towards the discovery of potential commercial applications.

Biomimetic design of an electronic nose on the principle of the mammalian olfactory system can aid in increased sensitivity and selectivity [14] for various trace level odorant detection applications. Different components of the biological olfactory system are being used for fabricating sensors. Researchers are investigating the development of olfactory sensors based on olfactory receptors [15], odorant binding proteins (OBP) [10,12,16], olfactory neurons [14], and insect antennae [17–19] among others. For example, Lin et al. [4] simulated the three-dimensional structure of the OR protein and synthesized a peptide sequence for the breath analysis for uremia diagnosis. However, research on artificial olfactory sensor development has not reached to the point where one can mimic the sensitivity and selectivity of biological olfactory receptors [14]. Thus, it is imperative to understand the biological olfactory system for developing artificial olfactory sensors.

Some reviews on olfactory systems [20–23], biosensors [7,24–29] and electronic nose [30–33] are available in literature. There is a need to integrate the engineering and science for a better understanding for the development of olfactory sensors. Therefore, this study was aimed to develop an in-depth understanding of the biological olfactory sensing system, in order to develop suitable novel techniques of engineered olfactory sensors for odorant detection applications. Specifically, this review paper focuses on (i) conducting a state-of-the-art review of the biology and mechanisms of biological olfactory sensing systems and (ii) establishing a framework for developing intelligent sensors based on the biological olfactory system and their applications in volatile organic compound (VOC) sensing.

2. Biology and mechanism of olfaction

2.1. Structure of olfactory system

2.1.1. Olfactory region

The human olfactory system comprises of *an external nose* and *inner nasal cavity*. The nasal cavity consists of two chambers divided by a septum [34]. Inside the nostril is a slight dilation called the *vestibule*, lined with skin containing hairs and sebaceous glands. Entire nasal cavity, above and behind the vestibule is covered by mucous membrane. Human nose consists of three *turbinates/nasal concha* (superior, middle and inferior). Turbinates are long, narrow and curled bone shelf protruding into the nasal passage that direct the air towards the olfactory epithelium. The mucous membrane can be divided into two parts: *an olfactory region*, above the superior turbinate and corresponding to nasal septum, and *a respiratory region*, which comprises of rest of the nasal cavity. Ciliary action in the respiratory region aids in active drainage back and down into the nasopharynx. The highly vascular surface of nasal mucosa also helps in warming and humidifying the inspired air [34,35]. Olfactory regions are the sensory regions that sense the smell.

The mucous membrane lining the *olfactory region* is termed as the *olfactory epithelium* (Fig. 1). It is a specialized epithelium tissue inside the nasal cavity that plays an important role in olfaction. Olfactory epithelium consists of three major types of cells: (i) *the basal cells*, (ii) *the olfactory supporting cells*, and (iii) *the olfactory receptor cells/olfactory neuron cells*. The *basal cells* are the stem cells that give rise to the olfactory receptor cells. *Supporting cells* have numerous microvilli and secretory granules, which provide the epithelium with mucous. The *olfactory mucosa* bathes the olfactory epithelium protecting the sensory cells incorporated in them. The mucus layer contains molecules such as mucopolysaccharides, immunoglobulins, proteins (such as lysozymes, odorant binding proteins), pigmented cells and various enzymes (such as peptidases). Epithelium color depth is a factor that could be correlated with the sensitivity of the olfactory system, although their exact function in enhanced sensitivity is unknown. This color is light yellow in human, whereas dark yellow/brown in dogs.

2.1.2. Olfactory receptor cells and olfactory receptors

O*lfactory receptor cells* are principally the most important sensory cells with receptors that sense odor. The olfactory epithelium has more than 6–10 million olfactory receptor cells [20,21]. These cells are bipolar neurons, consisting of dendrites at one end (projecting into the mucus above the surface of the epithelium) and axons at the other end (projecting into the olfactory bulb). Receptor cells are distinct from other sensory cells, due to their ability to regenerate and replace themselves upon injury [20]. Another unique aspect of these cells is that as the age of the organism increases, cells tend to live longer [20]. The axons of olfactory receptor cells form bundles that are collectively known as *olfactory nerve* or the *first cranial nerve* that carries the sensory information from the olfactory epithelium to the olfactory bulb.

The dendritic end of the olfactory receptor cells ends in the form of *an apical dendritic olfactory knob* into the mucous of the olfactory epithelium. Each knob contains five to fifty long specialized cilia that extend into the olfactory epithelium [20,21,36,37]. The olfactory cilia are cylindrical with diameter ranging from 0.25 to 0.5 μm