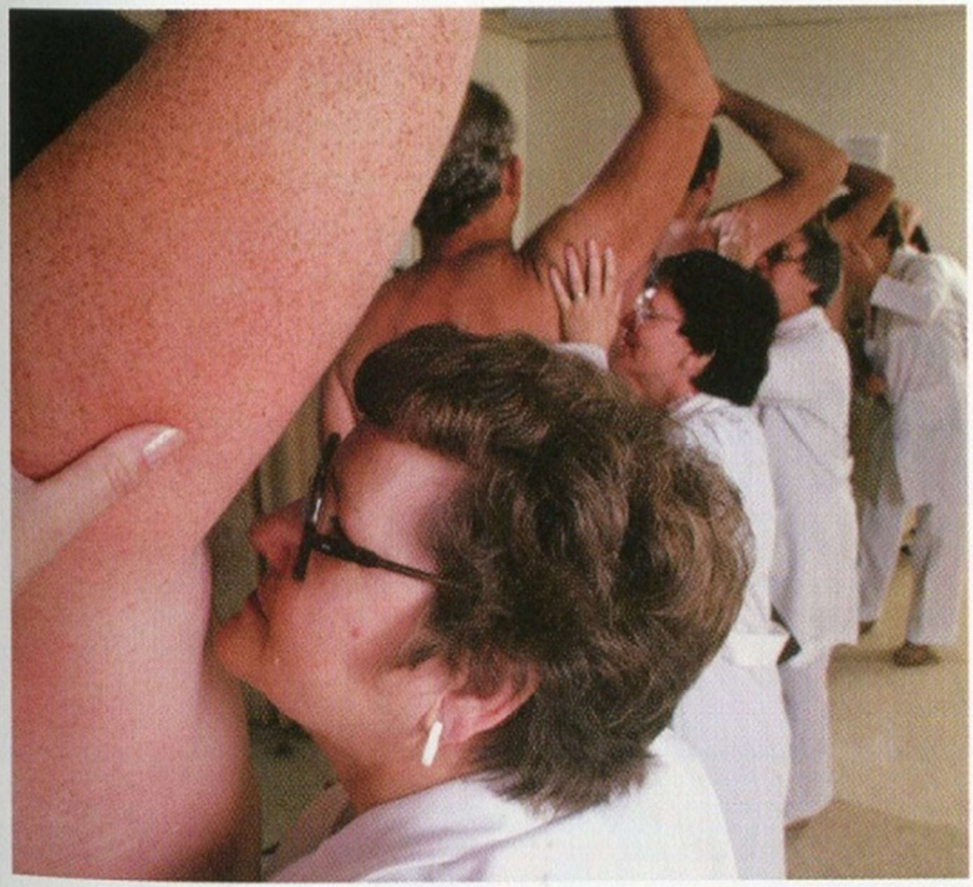
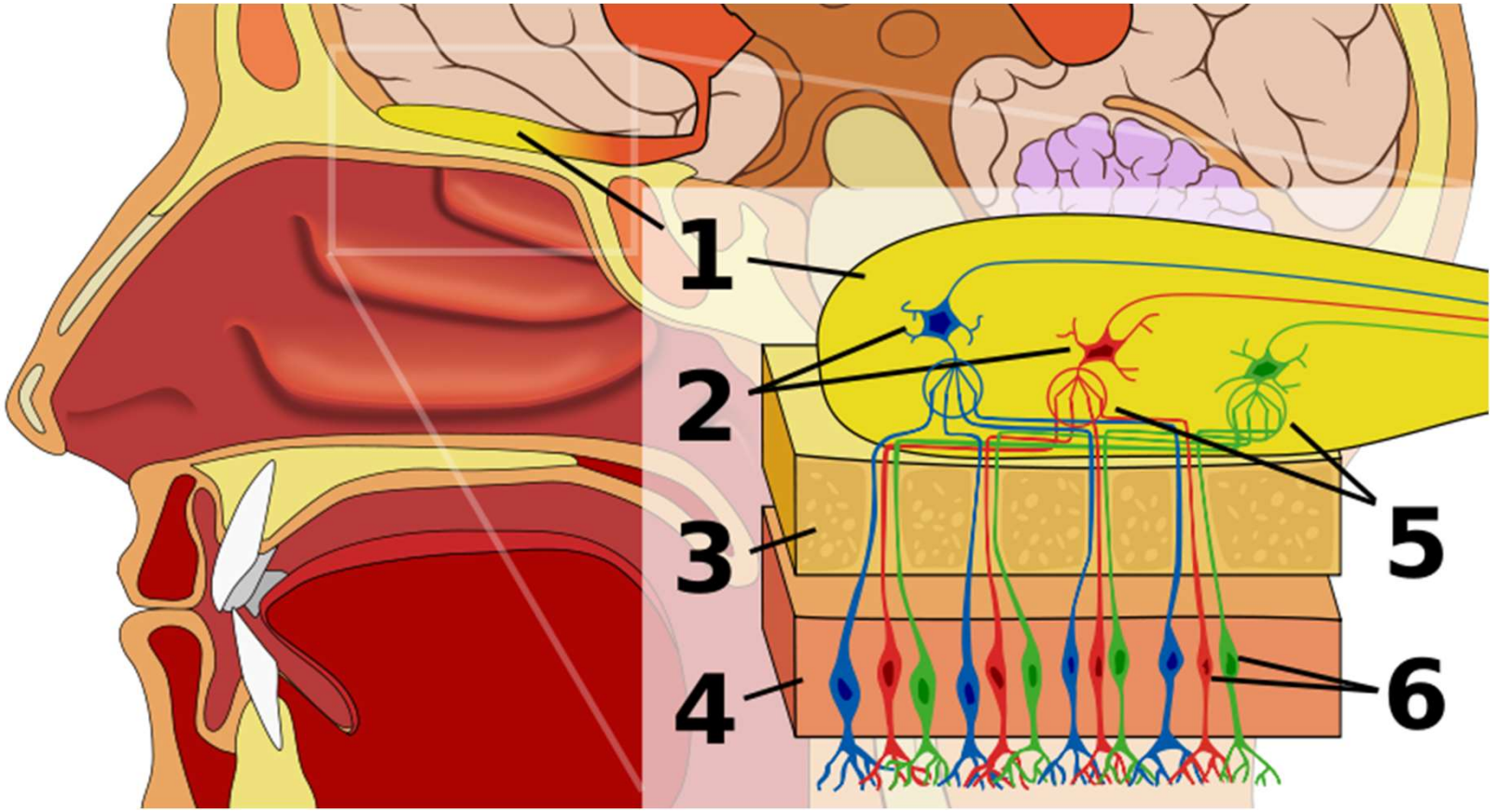
Smell this



MALE BODY SMELL

Male sweat contains androstenone, a musky compound. When sprayed onto a waiting-room chair, women are more likely to choose that chair. Women are more sensitive to it than men, even more so when they are ovulating, when they can pick up on a part per trillion.



1: Olfactory bulb 2: Mitral cells 3: Bone
4: Nasal Epithelium 5: Glomerulus 6: Olfactory receptor cells

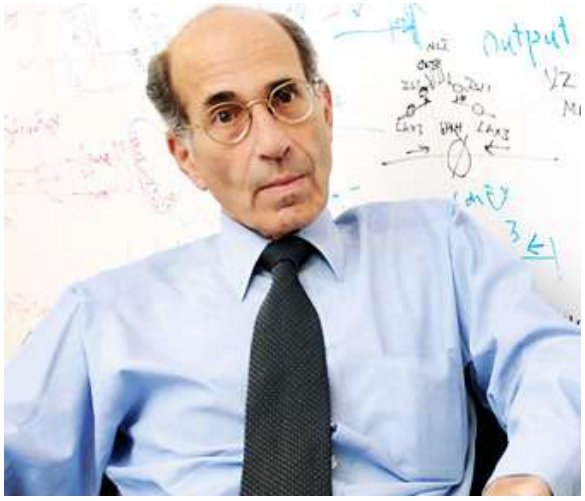
Sense of Smell

- Olfaction (also known as olfactics) refers to the sense of smell.
- Least understood of our senses
- Sense of smell is a subjective phenomenon that cannot be studied well in lower animals
- Sense of smell is poorly developed in the human being in comparison with the sense of smell in some lower animals

- **History**
  - the Roman philosopher Lucretius (1st Century BCE), different odors are attributed to different shapes and sizes of odor molecules that stimulate the olfactory organ.
  - The modern counterpart to that theory was the discovery of odorant receptor molecules by Linda B. Buck and Richard Axel (who were awarded the Nobel Prize in 2004).
  - Mammals have about a thousand genes expressing for odor reception. Of these genes, only a portion are functional odor receptors. Humans have far fewer active odor receptor genes than other mammals and primates.

The Scent of Surprise

- **The Hutchinson Center's Dr. Linda Buck 'surprised, overjoyed' to win 2004 Nobel Prize; honored for landmark discoveries of smell receptors**

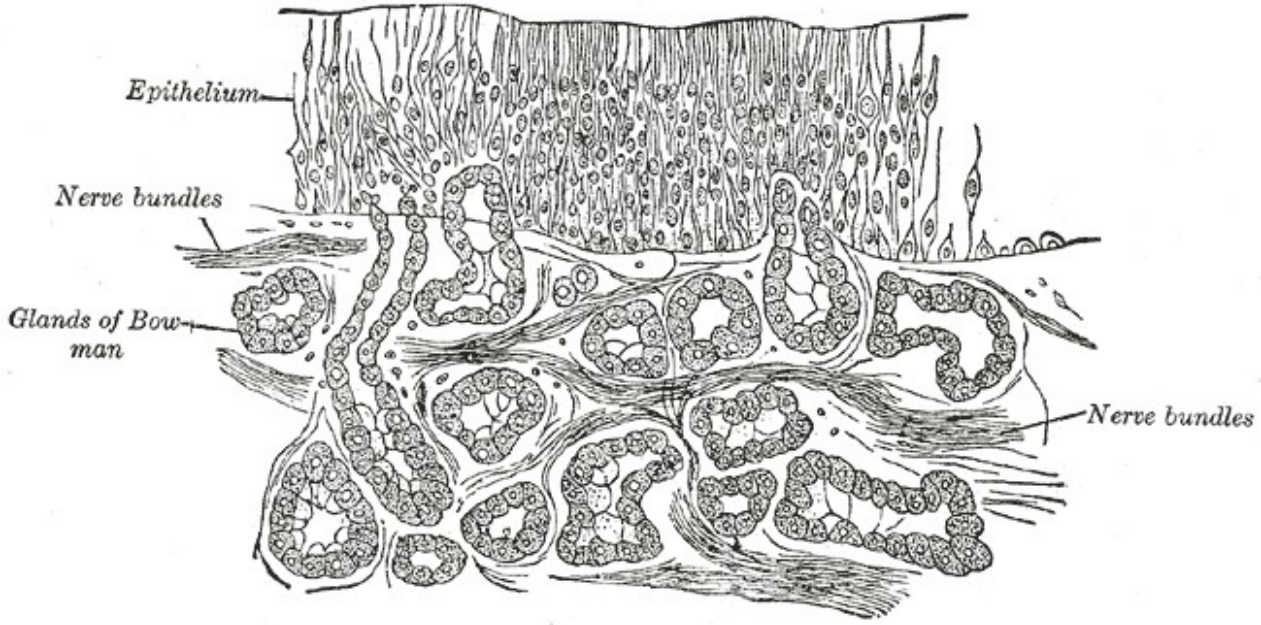


Richard Axel, Ph.D
Columbia Univ.

Linda Buck, Ph.D

- Humans have about 40 million olfactory receptor neurons.
- In vertebrates, olfactory receptor neurons reside on the olfactory epithelium in the nasal cavity. These cells are bipolar neurons with a dendrite facing the interior space of the nasal cavity and an axon that travels along the olfactory nerve to the olfactory bulb.

- **Olfactory membrane: Fig. 53-3**
  - The **olfactory epithelium** is a specialized epithelial tissue inside the nasal cavity that is involved in smell.
  - In humans, it measures about 1 inch wide by 2 inches long (about 2 cm by 5 cm) and lies on the roof of the nasal cavity about 3 inches (about 7 cm) above and behind the nostrils.
  - The olfactory epithelium is the part of the olfactory system directly responsible for detecting odors.
  - Olfactory epithelium consists of three distinct types of cells: Olfactory cells, supporting cells, and basal cells



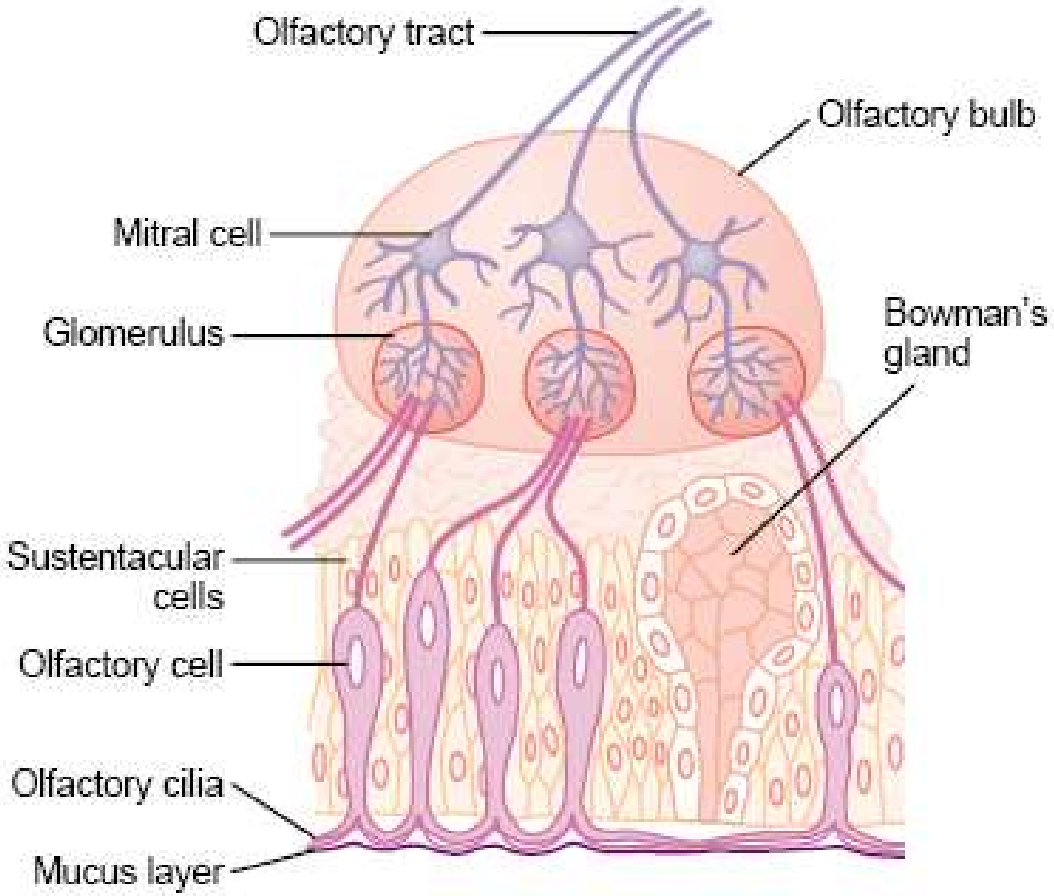
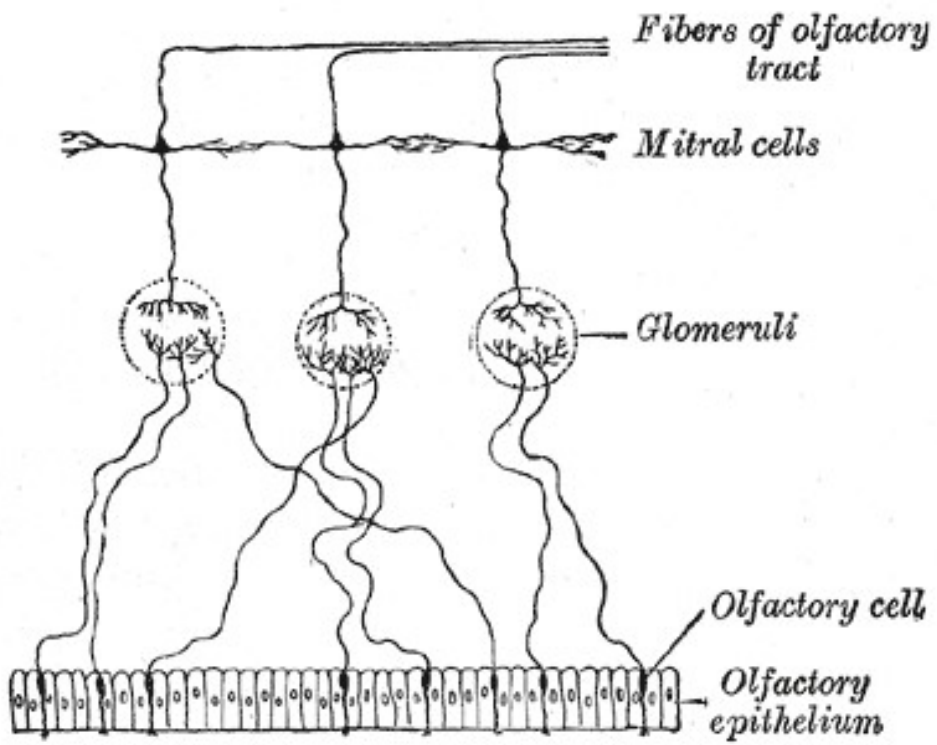


Figure 53–3

Organization of the olfactory membrane and olfactory bulb, and connections to the olfactory tract.

- Olfactory cells: bipolar nerve cells derived from the CNS itself. 100 million of these cells in the olfactory epithelium.
- Olfactory hairs or cilia: 0.3 um in diameter and up to 200 um in length. Hairs react to odors in the air and then stimulate the olfactory cells



- Membrane potentials and action potentials in olfactory cells
- Adaptation: adapt about 50% in the first sec or so after stimulation. Then they adapt very little and very slowly. We know smell sensations adapt almost extinction within a minute or so. The psychological adaptation is far greater than the degree of adaptation of the receptor themselves similar to taste sensations.
- Search for the primary sensations of smell: at least 100 primary sensations of smell and perhaps as many as 1000 – big contrast to primary color sensation which has 3

- Affection nature of smell: smell might be more important than taste in the selection of food
- Threshold for smell: minute quantity of the stimulating agent in the air can elicit smell sensation. Low threshold. Gas detection
- Gradations of smell intensities: only 10 to 50 times above the threshold values for many odorants evoke max intensity of smell. Smell is concerned more with detection of the presence of substance.

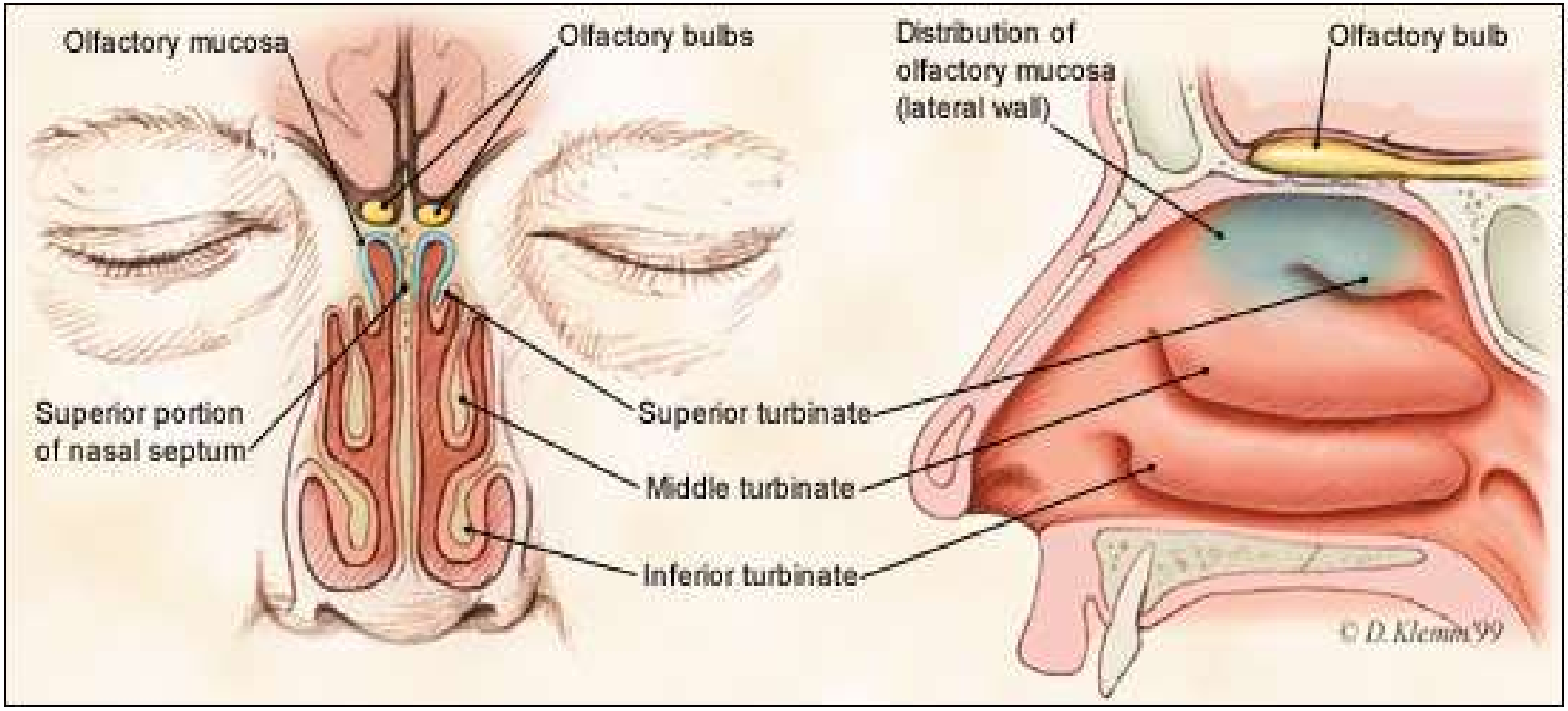
Olfactory System

- The **olfactory system** is the sensory system used for olfaction.
- Most mammals and reptiles have two distinct parts to their olfactory system: a **main olfactory system** and **an accessory olfactory system**.
- The main olfactory system detects volatile, airborn substances,
- while the accessory olfactory system senses fluid-phase stimuli.
- Behavioral evidence indicates that most often, the stimuli detected by the accessory olfactory system are pheromones.

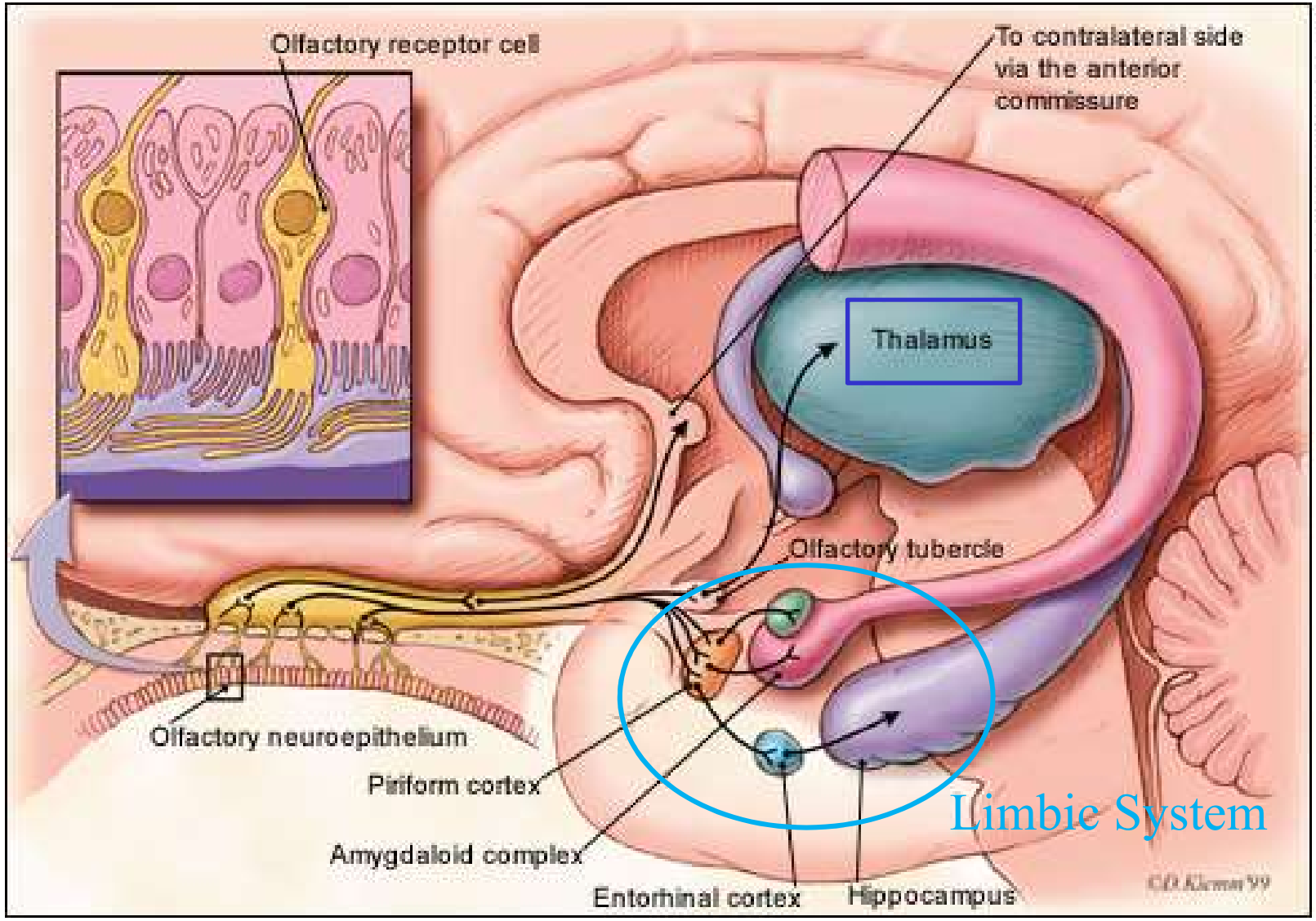
• Transmission of smell signals into the CNS: Fig. 53-4

- Very, Very Old olfactory system
- Less Old olfactory system
- Newer olfactory system

Anatomy of the olfactory neural pathways, showing the distribution of olfactory receptors in the roof of the nasal cavity.



Simplified diagram of cortical regions thought to be involved in the processing of olfactory information as it passes from the olfactory epithelium to the brain.



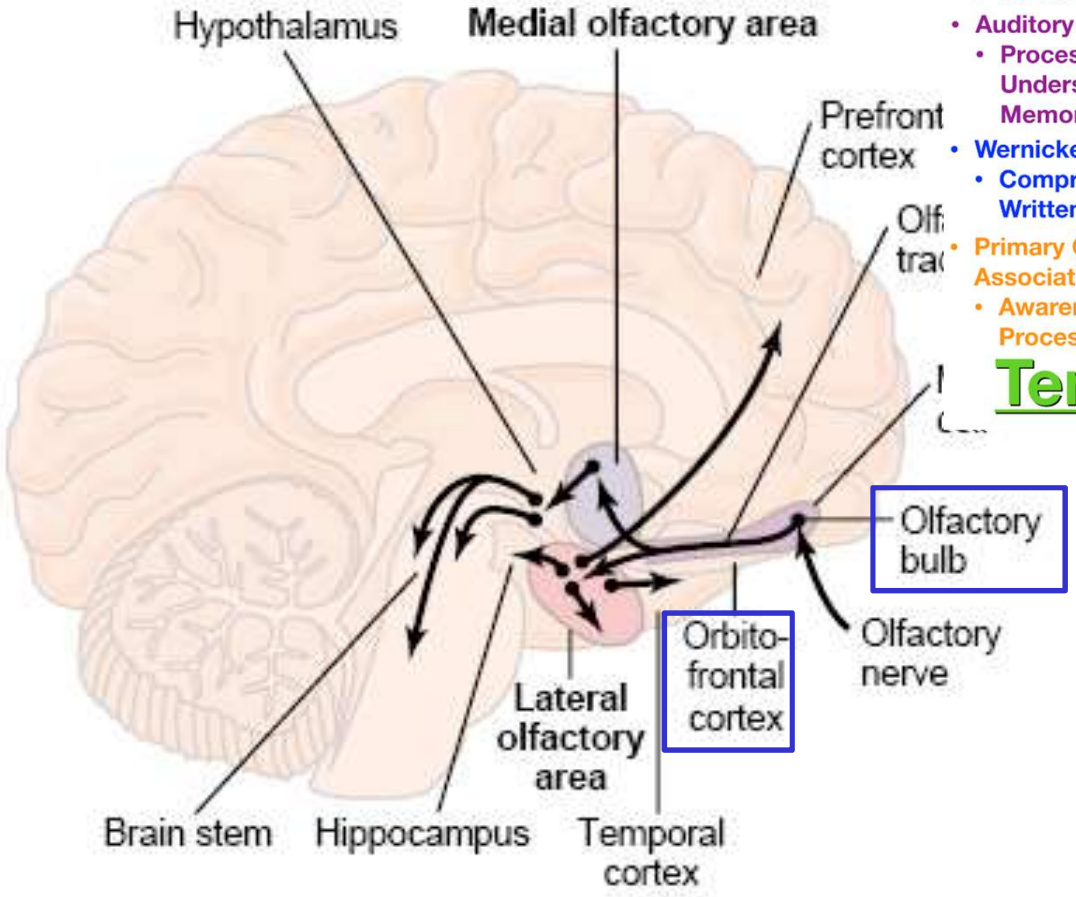


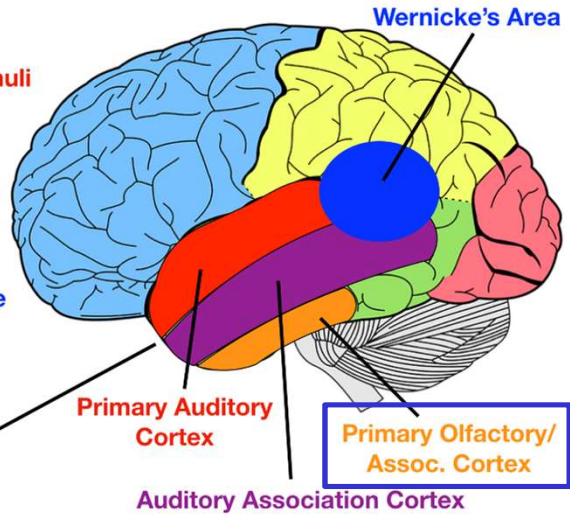
Figure 53–4

Neural connections of the olfactory system.

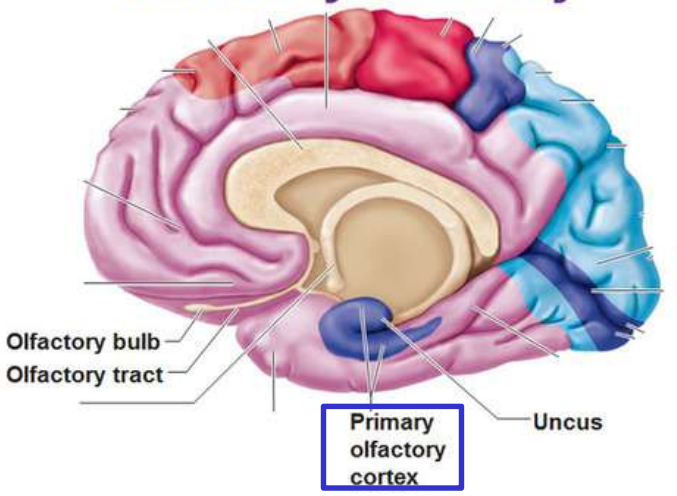
Functional Areas

- **Primary Auditory Cortex**
  - **Awareness of Auditory Stimuli**
- **Auditory Assoc. Cortex**
  - **Process, Analyze, Understand, Recognize, Memory of Sounds**
- **Wernicke's Area**
  - **Comprehend/Understand Written & Spoken Language**
- **Primary Olfactory Cortex/ Association Cortex**
  - **Awareness of Smell & Processing of Smell**

Temporal



Olfactory Pathway



Parasagittal view, right hemisphere

- Primary motor cortex
- Motor association cortex
- Primary sensory cortex
- Sensory association cortex
- Multimodal association cortex

Olfactory pathway

Olfactory receptor cell → Olfactory nerve

Olfactory bulb

Olfactory Tract

Medial Olfactory area

Septal Nuclei

Hypothalamus
Limbic system
(primitive parts)

(Very Old Olfactory System)

Lateral Olfactory area

Prepyriform cortex
Pyriform Cortex
Amygdala

Limbic system
(hippocampus)

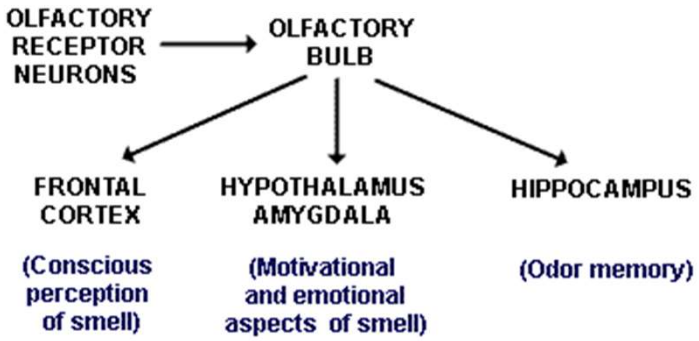
(Less Old Olfactory System)

Thalamus

Orbitofrontal Cortex

(Newer System)

Functional Olfactory



Which senses are ipsilateral?

For example, both taste and smell have ipsilateral ascending projections, whereas those of the other sensory systems are either contralateral or bilateral. 2018. 12. 31.

Answer and Explanation: Olfaction is neither ipsilateral nor contralateral. This is because there is no directional sense involved in the sense of smell. Further, the olfactory receptor cells are found in the nasal cavity and transmit information to a single olfactory bulb.

Shape Theory

- The **Shape theory** of smell states that the sensation of smell is due to a 'lock and key' mechanism by which a scent molecule fits into olfactory receptors in the nasal lamina of the nose.
- Dr. John E. Amoore came up with the shape theory in 1952 at Oxford University.
- Dr. Amoore postulated that seven primary odors combine in various ways to form all odors.
- The seven primary odors include sweaty, spermous, fishy, malty, urinous and musky.
- It is well proven that the olfactory receptors in all higher animals are special types of G-protein-coupled receptors.
- Since all types of G-protein receptors known to modern science are activated through binding of molecules with highly specific conformations, or shape, it is assumed that olfactory receptors operate in a similar fashion.

- Since only 347 olfactory receptors have been discovered in the human nose, it is assumed that humans distinguish between a multitude of experienced smells through a complex relationship between the receptors and the odorous molecules. This includes:
- Specific binding of certain molecular functional groups by one or many receptors
- Loose binding of molecular structures and functional groups with similar shapes by one or many receptors
- Specific binding of molecular elements in certain special conformations
- It is generally believed that signals from different olfactory bulb neurons are combined and processed by the brain, which results in the perception of different scents.

Vibration Theory

- The **Vibration theory,** proposed by Luca Turin, of smell is that the quality of a particular odor arises from olfactory receptors' responding to frequencies of vibrations of odor molecules in the infrared range.
- The theory is opposed to the more widely accepted shape theory of olfaction in which the *shape* of odorant molecules allow them to fit into membrane proteins in the olfactory receptors.
- Some evidence supports vibration theory; some evidence supports shape theory. Although vibration theory explains the quality of odors, it does not explain intensity of odors, why some odours are stronger than others at the same concentrations.
- And research goes on…

- Stimulation of the olfactory cells
  - Chemical mechanism of excitation of the olfactory cells: summary in the textbook
  - Physical factors (1) volatile substances (2) water-soluble (3) lipid soluble
- Clinical
  - Damage to the olfactory system can occur by traumatic brain injury, cancer, inhalation of toxic fumes, or neurodegenerative diseases such as Parkinson's disease and Alzheimer's disease.
  - These conditions can cause anosmia (lack of olfaction)
  - Doctors can detect damage to the olfactory system by presenting the patient with odors via a scratch and sniff card or by having the patient close their eyes and try to identify commonly available odors like coffee or peppermint candy.

[강석기의 과학카페] 마침내 밝혀진 냄새수용체 구조

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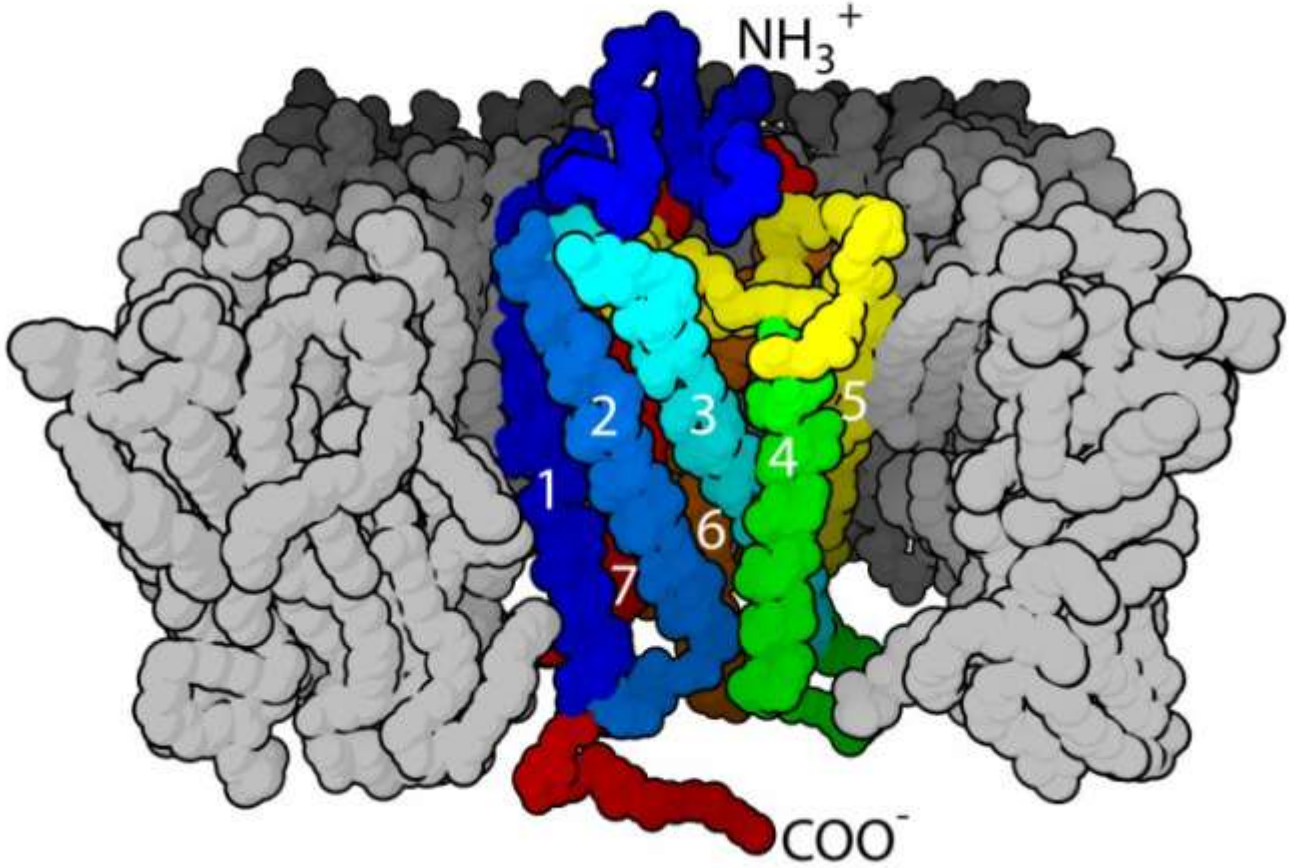


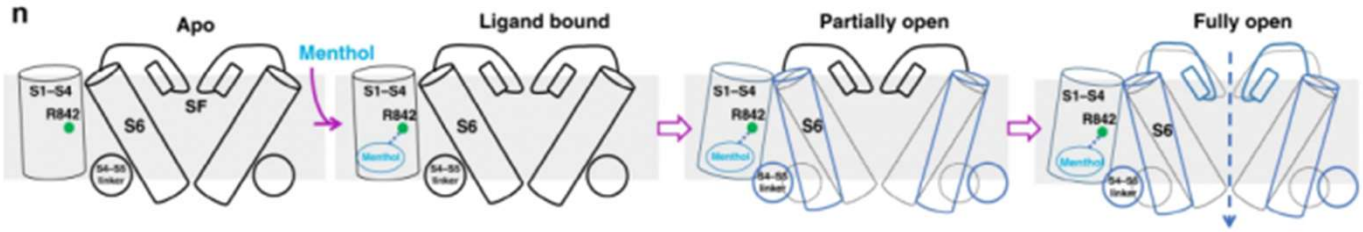
G 단백질 연결 수용체. 위키피디아 제공

https://www.dongascience.com/news.php?idx=59057

- 1990년 인간게놈프로젝트가 시작됐을 때만 해도 단백질 지정 유전자 개수가 10만 개는 될 것이라고 봤다. 그런데 작업이 진행되면서 예상값이 점점 줄어들었고 해독 결과 불과 2만 개라는 충격적인 사실이 밝혀졌다. 이에 대해 중요한 건 유전자 개수가 아니라 유전자 사이의 네트워크의 복잡성이라고 설명한다.

- 실제 다른 유전자의 발현을 조절하는 전사인자를 지정하는 유전자가 2000여 개로 전체의 10%를 넘는다. 세포 안팎의 신호를 전달하는 데 관여하는 유전자도 그 정도 되는데, 호르몬 같은 신호분자(리간드라고 부른다)의 유전자와 이를 인식하는 수용체 유전자로 이뤄져 있다.

- 한편 수용체의 대다수가 G단백질연결수용체(GPCR)로 거의 1000가지나 된다. GPCR은 세포막에 박혀있는 단백질로 바깥쪽에서 온 리간드가 달라붙으면 구조가 바뀌면서 세포 안쪽의 G단백질에 영향을 줘 신호를 전달한다. 시각, 후각, 미각 같은 감각 신호(각각 광자(빛)와 냄새분자, 맛분자)도 GPCR을 통해 전달된다. 특히 냄새수용체 유전자는 거의 400가지나 돼 전체 유전자의 2% 가까이 차지하고 있다.



냉각수용체 TRPM8은 세포막에 박힌 통로단백질로 상온에서는 통로가 막힌 비활성 상태다(맨 왼쪽). 온도가 떨어지거나 냄새분자인 멘톨(menthol)이 결합하면 구조가 바뀌며 통로가 열려 세포 밖 칼슘이온이 안으로 들어와 신호를 일으켜 우리는 춥거나 시원하다고 느낀다(오른쪽).

https://www.youtube.com/watch?v=wQJbsOWc344&ab_channel=AlilaMedicalMedia

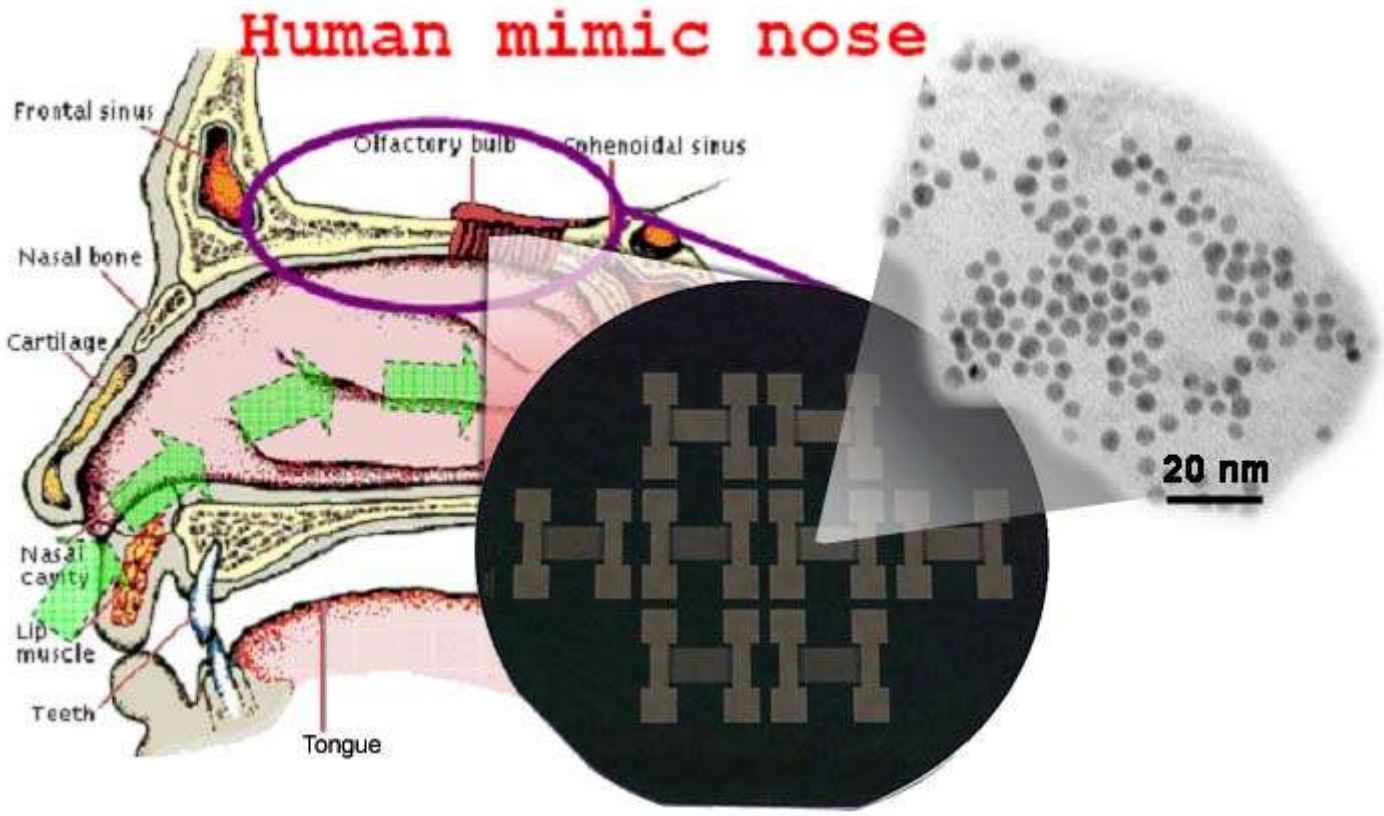
Artificial Nose

• The electronic nose was developed in order to mimic human olfaction that functions as a non-separative mechanism: i.e. an odor / flavor is perceived as a global fingerprint.
• Electronic Noses include three major parts: a sample delivery system, a detection system, a computing system.
• **Sample delivery system** enables the generation of the headspace (volatile compounds) of a sample, which is the fraction analyzed. The system then injects this headspace into the detection system of the electronic nose. The sample delivery system is essential to guarantee constant operating conditions.

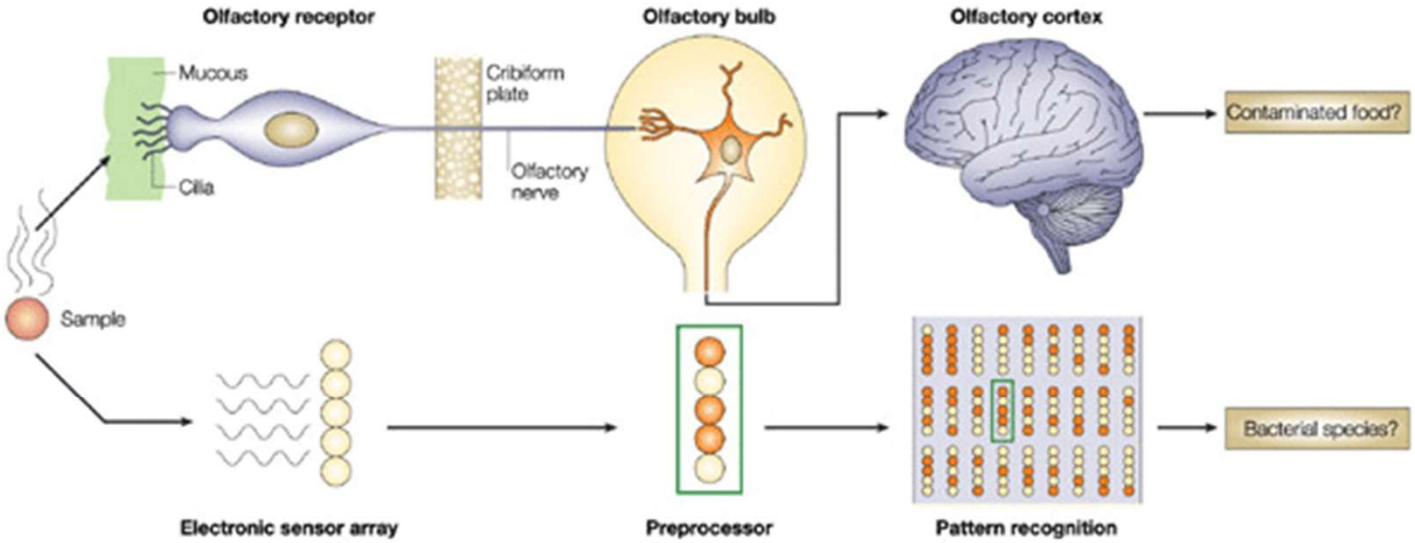
• **Detection system**, which consists of a sensor set, is the "reactive" part of the instrument.
• When in contact with volatile compounds, the sensors react, which means they experience a change of electrical properties.
• Each sensor is sensititive to all volatile molecules but each in their specific way.
• Most electronic noses use sensor-arrays that react to volatile compounds on contact: the adsorption of volatile compounds on the sensor surface causes a physical change of the sensor. A specific response is recorded by the electronic interface transforming the signal into a digital value.
•The more commonly used sensors include metal oxide semiconductors (MOS), conducting polymers (CP), quartz crystal microbalance, surface acoustic wave (SAW), and field effect transistors (MOSFET).

• **Computing system** works to combine the responses of all of the sensors, which represents the input for the data treatment.

• This part of the instrument performs global fingerprint analysis and provides results and representations that can be easily interpreted.



Electronic Nose



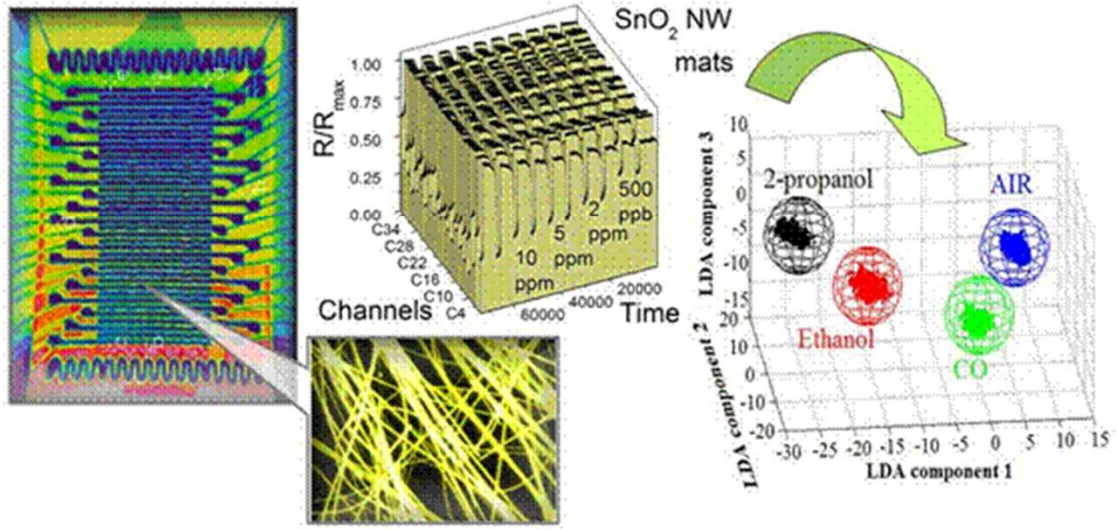


Figure 3. KAMINA electronic nose system equipped with sensing elements made of metal oxide percolating network. The resistance change data from the array of the nanowire based sensing elements is analyzed using LDA to recognize the analyte gas in air (Adapted from V. Sysoev et al. *Nano Letters* 2007)

The E-Nose Knows Infections

Electronic Nose

- How does an electronic nose work
  - https://www.youtube.com/watch?v=3-lHCkK5faM

Electronic Nose

- What is an electronic nose
  - https://www.youtube.com/watch?v=j-5ZTZx-2I4

Electronic Nose

- Electronic nose can detect 17 diseases

https://www.youtube.com/watch?v=bZgkSYKV4Rw&t=49s&ab_channel=MonellCenter