

Brain Intelligence and Artificial Intelligence

人脑智能与机器智能

Lecture 12 – Olfaction

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故事开始于去年，我在书房看书，突然灵光一闪。。

Friday 00:32

我刚刚读着读着书，突然有个想法。



我书房有瓶香氛，每次刚走进书房的时候，我觉得特别香。

不一会儿我的大脑就 habituate 了。我完全闻不到香味了，一点儿也感觉不到香气的存在。
所以我们花钱买香氛，其实只买了每次进门的那 30s 的愉悦感。

有没有一种 dynamic perfume，能把几种香水按照某种时间序列动态释放，让我们的嗅小球能避免 habituation，一直感受到不同的香味，保持香水的愉悦。

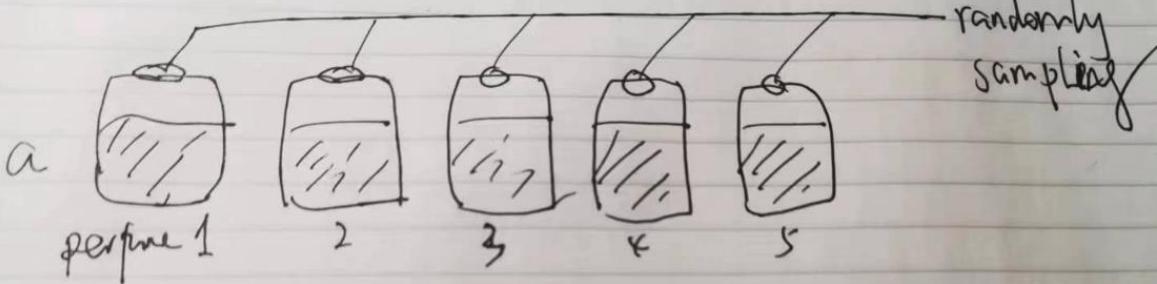
这个装置其实非常简单。而且嗅小球神经对香味 dynamics 的反应应该是比较慢的，可以比较缓慢地打开不同香水。比如，5 种香水组合，每 30s 随机打开一种香水。

Friday 00:34



像我们听音乐，肯定不是只听一个频率的声音，都是动态变化的声音才能称之为音乐，才能带来大脑的愉悦。

为啥香水就是单一的呢？也需要动态变化的香水，才能有长久的愉悦。



Neural
response
X

$a \xrightarrow{f(\cdot)} x \xrightarrow{g(\cdot)} s$

perfume neural pleasure

$$\max_a \sum_t S(t)$$

模型是这样的



我在京东搜了，还没有这种香水。
咱们赶紧写个专利？@魏晨



Friday 00:41

大家有啥想法？ comments?



Friday 00:46



魏晨 博士 21 级

感觉气味和弦一样有不同的色彩，不同气味的动态变化或许也有像音乐和弦转换一样的效果。可以加强某种气味的感受，也可以组合为一种全新的嗅觉体验



魏晨 博士 21 级

感觉挺有趣的 😄

当遥远的往昔已杳无印迹
当人民已经亡故
当器具已拆散、星散
但气息仍永久地弥漫，
幽灵般地唤起我们的记忆...
寂静、孤独、脆弱，
却又充满活力；
捉摸不定，
却更翔实而又挥之不去

——普鲁斯特《追忆似水年华》

药良气味苦，琴澹音声稀。

——白居易《寄唐生》

含桃最说出东吴，香色鲜秾气味殊。

——白居易《吴樱桃》

还有少年春气味，时时暂到梦中来。

——白居易《春眠》

萧条秋气味，未老已深谙。

——白居易《秋思其二》

可怜闲气味，唯欠与君同。

——白居易《闲卧寄刘同州》

语言对气味的描述如此贫瘠。

但是当你闻到一种味道时，你很明确你喜欢 or 不喜欢。

Diversity in preference to scents

皮蛋

century egg / hundred-year egg



2011年6月，美国CNN网站选出「全球十大最恶心食物」，皮蛋身居榜首。美国网友说皮蛋外型怪异，味道吓人，甚至给予它「恶魔煮的蛋」、「恶心至极」等等负面评价。

鲱鱼罐头

Surströmming



据报道瑞典政府也规定不许在住宅区内开启鲱鱼罐头。

国际航班也不允许携带这种罐头，因为气压的变化可能发生罐头破裂，后果很严重。



Lecture 12 – Olfaction

- **Olfactory system in animals and humans**

1. Olfactory receptor
2. Olfactory epithelium (OE)
3. Olfactory bulb (OB)

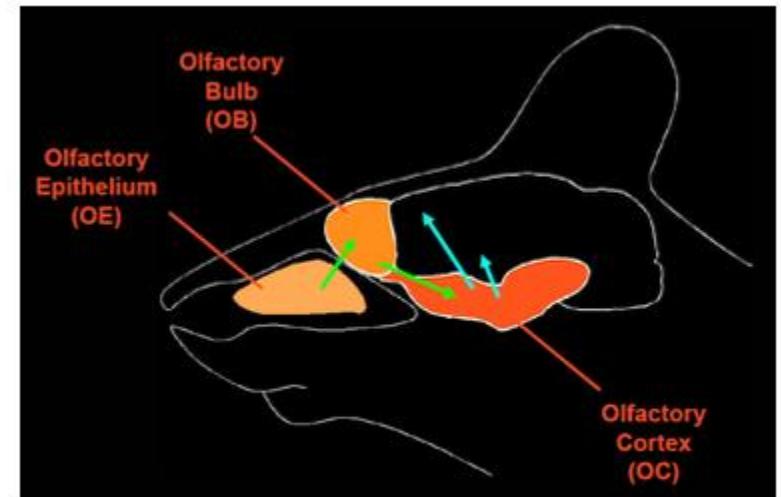
Glomerulus

Information representation

4. Olfactory cortex (OC)
5. Olfactory habituation vs olfactory adaption

- **Bio-inspired artificial olfactory system**

- Neuromorphic olfactory system
- AI for olfaction



当你闻花的时候，你会吸入花释放出来的分子，通过大脑中发生的电活动来建立花朵气味的内部表征

Olfactory receptors (ORs)

气味有数以百万计不同种类。

每种气味都由数十到数百个不同的分子组成。

这些分子在空气中飘荡，进入我们的鼻子，并与嗅觉受体 (olfactory receptors)结合。

人鼻子有超过 300 个ORs，相比于人眼只有3种颜色感受器（对应RGB波长的光）。

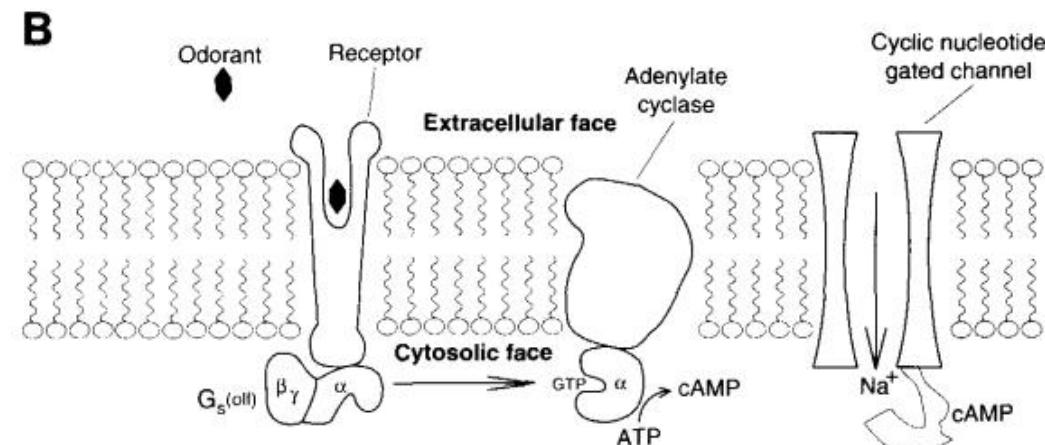
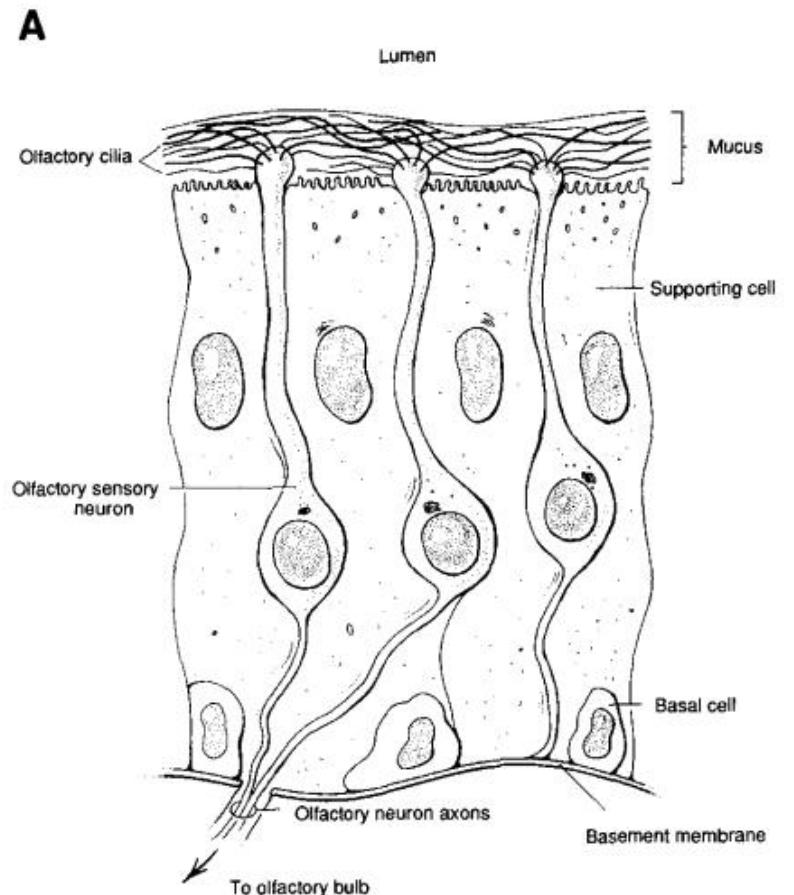
这300个ORs可以让人识别出100,000种气味。

A novel multigene family may encode odorant receptors: a molecular basis for odor recognition

L Buck, R Axel - Cell, 1991 - [cell.com](#)

The mammalian olfactory system can recognize and discriminate a large number of different odorant molecules. The detection of chemically distinct odorants presumably results from the association of odorous ligands with specific receptors on olfactory sensory neurons. To address the problem of olfactory perception at a molecular level, we have cloned and characterized 18 different members of an extremely large multigene family that encodes seven transmembrane domain proteins whose expression is restricted to the olfactory ...

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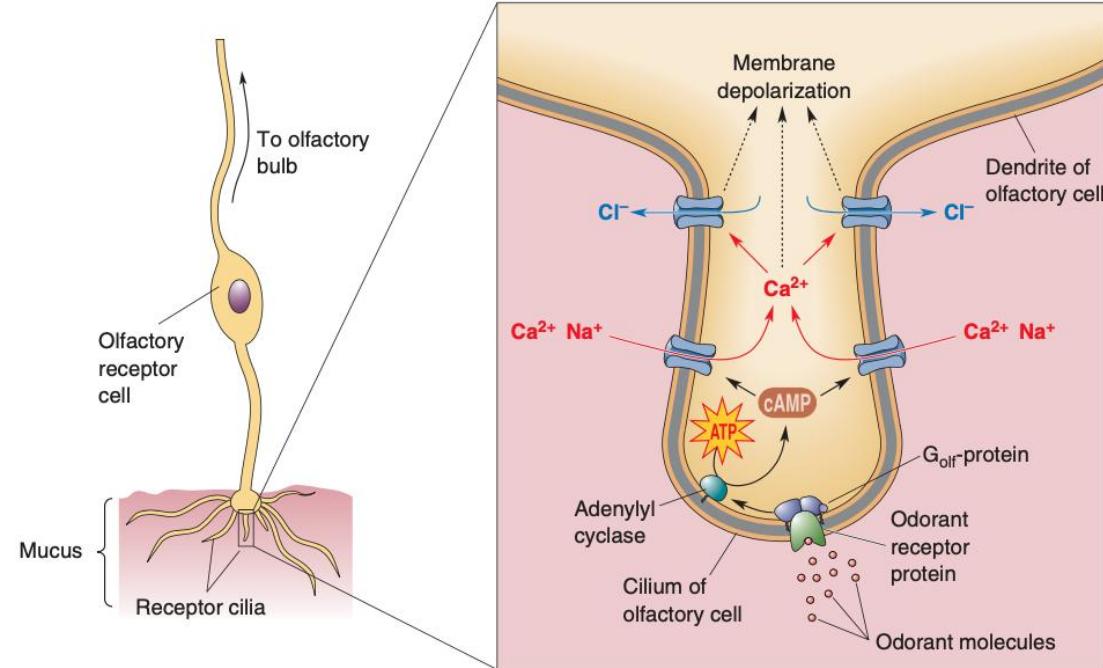
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▲ FIGURE 8.10

Transduction mechanisms of vertebrate olfactory receptor cells. The drawing at right shows a single cilium of an olfactory receptor cell and the signaling molecules of olfactory transduction that it contains. G_{olf} is a special form of G-protein found only in olfactory receptor cells.

Olfactory Transduction. Although taste receptor cells use several different molecular signaling systems for transduction, olfactory receptors probably use only one (Figure 8.10). All of the transduction molecules are located in the thin cilia. The olfactory pathway can be summarized as follows:

Odorants →
Bind to membrane odorant receptor proteins →
Stimulate G-protein (G_{olf}) →
Activate adenyl cyclase →
Form cAMP →
Bind cAMP to a cyclic nucleotide-gated cation channel →
Open cation channels and allow influx of Na^+ and Ca^{2+} →
Open Ca^{2+} -activated Cl^- channels →
Cause current flow and membrane depolarization (receptor potential).

Olfactory receptors (ORs)

Nobel Prize in Physiology or Medicine 2004

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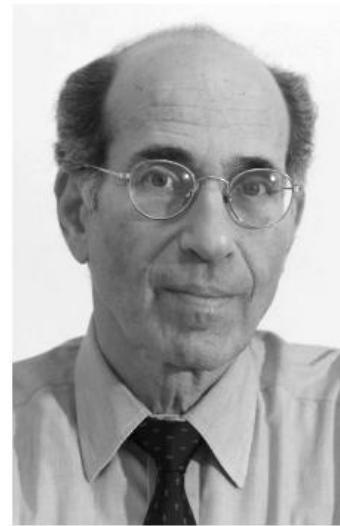


Photo from the Nobel Foundation archive.
Richard Axel

Prize share: 1/2



Photo from the Nobel Foundation archive.
Linda B. Buck

Prize share: 1/2

The Nobel Prize in Physiology or Medicine 2004 was awarded jointly to Richard Axel and Linda B. Buck "for their discoveries of odorant receptors and the organization of the olfactory system"

<https://www.bilibili.com/video/BV12e4y1z72g/>

2004年诺贝尔生理学或医学奖-气味受体和嗅觉系统组织方式

Olfactory receptors (ORs)

Nobel Prize in Physiology or Medicine 2004

请介绍2004年诺贝尔生理学奖



2004年诺贝尔生理学或医学奖授予了理查德·阿克塞尔（Richard Axel）和琳达·巴克（Linda B. Buck），以表彰他们在嗅觉系统的研究中所做出的重要贡献。他们的研究揭示了大脑如何识别、处理和区分大量不同的气味，这为我们理解嗅觉的神经基础带来了重要的突破。

主要发现和研究内容

1. 嗅觉受体的发现：阿克塞尔和巴克发现了一大类编码嗅觉受体的基因。这些基因编码的蛋白质就是嗅觉受体，每种受体对不同气味分子有特异性。哺乳动物的嗅觉系统中大约有1000种不同的嗅觉受体基因，每种受体仅表达于特定的嗅觉神经元中。
2. 嗅觉信号的编码方式：他们发现，每个嗅觉神经元只表达一种类型的嗅觉受体，并且该受体能够识别特定的气味分子。每种气味分子可以激活多种不同的受体，而大脑通过一组活跃的受体组合来识别气味。这种“组合编码”机制允许大脑区分成千上万种不同的气味，尽管受体种类有限。
3. 嗅觉信号传导路径：阿克塞尔和巴克还研究了嗅觉信号在嗅球中的传导路径。每一种受体类型的神经元将其信息传送到嗅球中相应的嗅小球（glomeruli），每个嗅小球只接收同一种受体类型的信号。嗅球的信息进一步传递到大脑的嗅觉皮层及其他高级区域，这些区域负责将气味信号与情绪、记忆等进行整合。

研究的影响与应用

阿克塞尔和巴克的研究极大地加深了人们对嗅觉系统的理解，揭示了嗅觉的分子和神经基础。这一发现对神经科学、基因学、行为科学以及人工嗅觉（例如电子鼻）等领域产生了深远影响，并为嗅觉系统如何与情绪和记忆系统相互作用的研究提供了基础。

通过揭示气味识别的分子机制和神经回路，这一成果帮助人们理解了嗅觉的生理和心理功能，并为探索其他感觉系统提供了模型。

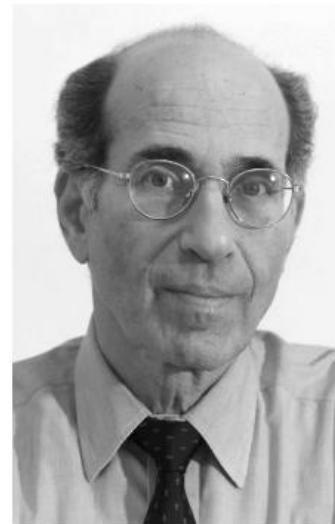


Photo from the Nobel Foundation archive.
Richard Axel

Prize share: 1/2



Photo from the Nobel Foundation archive.
Linda B. Buck

Prize share: 1/2

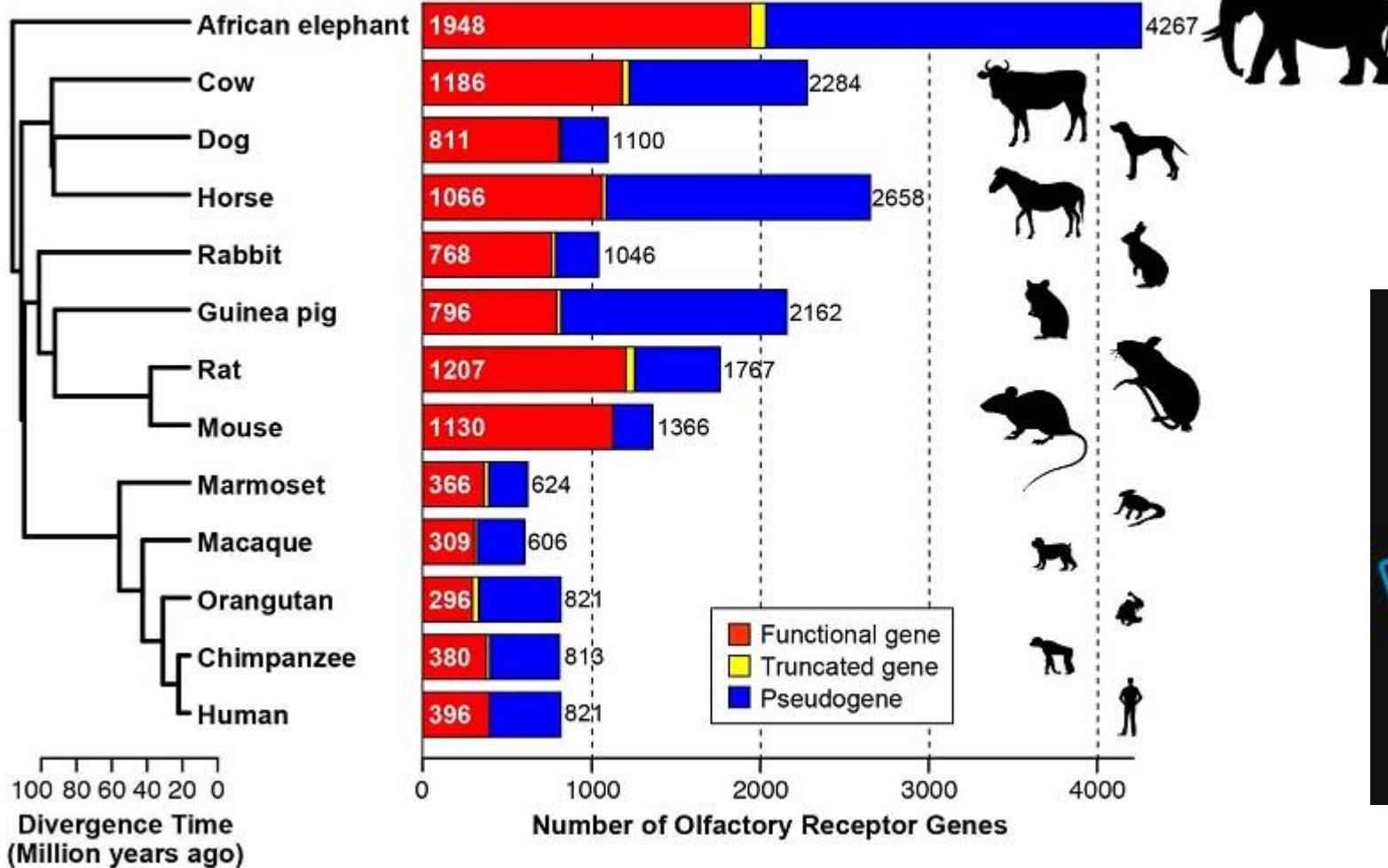
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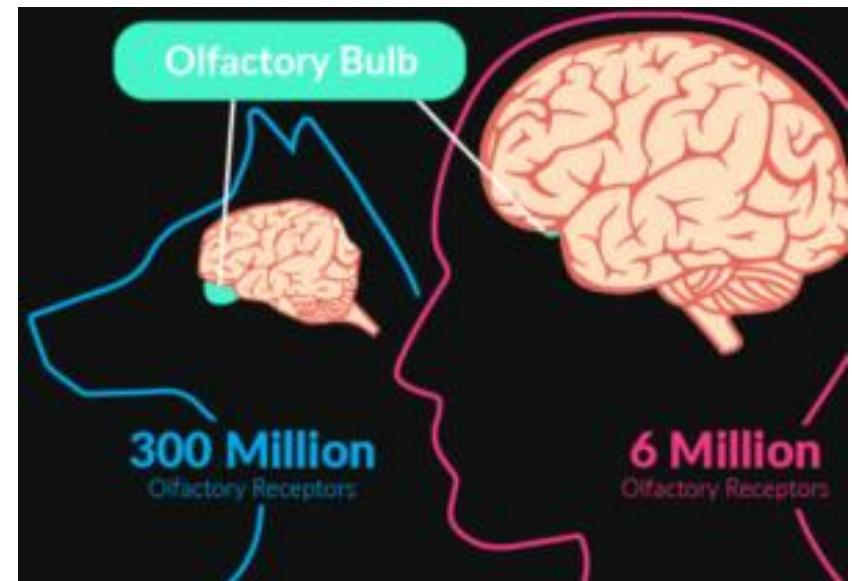
科学问题：

- 嗅觉受体ORs的工作机制是什么？人和动物的ORs的种类、数量有区别吗？
- 控制ORs表达的基因？这些基因是进化保守的吗？
- 气味编码：不同的ORs 如何对不同的气体分子反应？一对一映射？还是一对多映射？多对多映射？
- 气味解码：人如何根据不同ORs的反应和大脑的神经表征来识别气味？
- 气味感知：气味到大脑的神经环路是什么？
- 气味与记忆的关系？为什么气味能唤醒遥远的记忆？其神经机制是什么？
- 气味与情绪的关系？如何筛选\生成让人愉悦的气味分子？（闻香师？）
- . . .

Number of OR genes



Number of ORs



Yoshihito Niimura, Atsushi Matsui, and Kazushige Touhara, "Extreme expansion of the olfactory receptor gene repertoire in African elephants and evolutionary dynamics of orthologous gene groups in 13 placental mammals", Genome Research, 2014, doi: 10.1101/gr.169532.113.

Olfactory epithelium (嗅上皮)

嗅上皮 (olfactory epithelium) 是鼻腔内一层特殊的组织，位于鼻腔顶部，负责检测气味分子。它包含多种细胞类型，其中最主要的是嗅觉感受器细胞 (olfactory receptor neurons, ORNs)。

1. 气味分子进入鼻腔：当气味分子（挥发性化学物质）随空气进入鼻腔时，一部分气味分子到达嗅上皮。嗅上皮上覆盖有一层薄薄的黏液，气味分子首先溶解在黏液中。

2. 气味分子与嗅觉受体的结合：嗅觉感受器细胞的纤毛 (cilia) 伸入黏液中，表面携带着嗅觉受体 (olfactory receptors)。这些受体是位于细胞膜上的G蛋白偶联受体 (GPCRs)，每个受体对特定类型的气味分子具有高度的特异性。当气味分子与相应的嗅觉受体结合后，受体发生构象改变，激活胞内的G蛋白 (主要是Golf蛋白)。

3. 信号转导过程：受体与气味分子结合后，激活Golf蛋白，进一步激活腺苷酸环化酶 (adenylate cyclase)，从而将细胞内的ATP转化为环磷酸腺苷 (cAMP)。cAMP作为第二信使，与**环核苷酸门控离子通道 (CNG通道) **结合，导致这些通道打开。钠 (Na^+) 和钙 (Ca^{2+}) 离子流入嗅觉感受器细胞，使其去极化。此外，流入的钙离子还进一步激活氯 (Cl^-) 通道，导致氯离子外流，进一步增强了细胞的去极化。

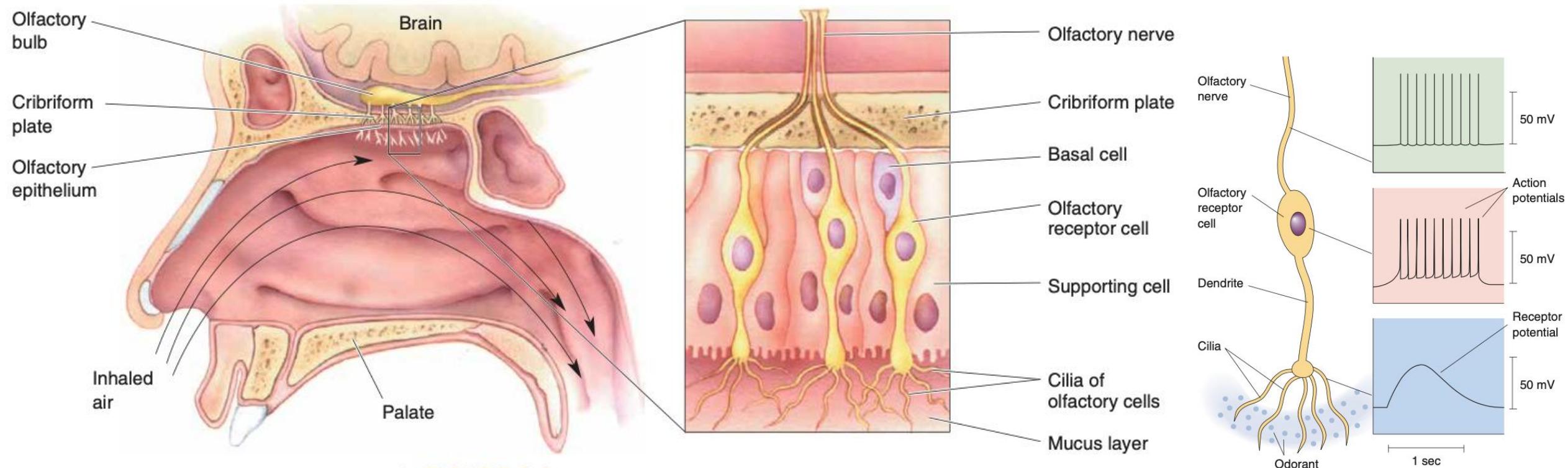
4. 动作电位的生成和传递：当膜电位去极化达到阈值时，嗅觉感受器细胞产生动作电位，沿着细胞轴突传递。这些轴突汇聚成嗅神经 (olfactory nerve)，将信号传递到嗅球 (olfactory bulb)。

5. 嗅觉信号的初步加工：在嗅球中，每一种嗅觉受体类型的嗅觉感受器细胞的轴突汇集到对应的嗅小球 (glomerulus)，在此处与二级神经元 (如束细胞和簇细胞) 建立突触连接。这种特定连接帮助将不同气味分子编码成特定的神经信号模式。

最终，这些信号通过嗅球中的神经通路传输到大脑的高级嗅觉处理区域，包括嗅皮层、杏仁核和前额叶皮层，与记忆和情绪等高级功能相整合。

6. 信号的编码和气味识别：嗅觉系统使用“组合编码”机制，即每种气味分子可以激活多个不同的嗅觉受体，产生特定的激活模式。这种激活模式形成了气味的“神经指纹”，帮助大脑识别和区分不同气味。

Olfactory epithelium (嗅上皮)



▲ FIGURE 8.9
The location and structure of the olfactory epithelium. The olfactory epithelium

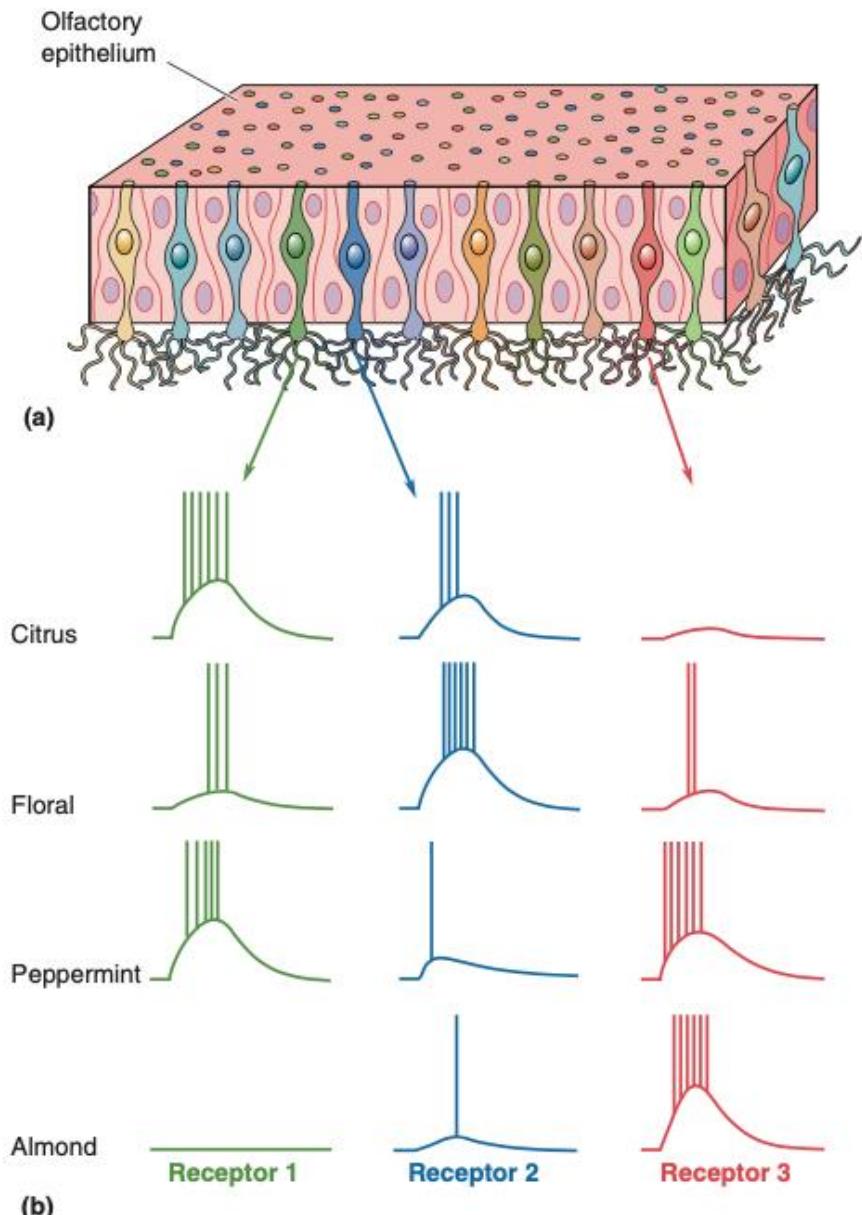
The surface area of the **human** olfactory epithelium(嗅上皮) is only about 10 cm^2 .

The olfactory epithelium of certain **dogs** may be over 170 cm^2 , and dogs have over 100 times more receptors in each square centimeter than humans.

Olfactory epithelium

气味的编码机制 many-to-many

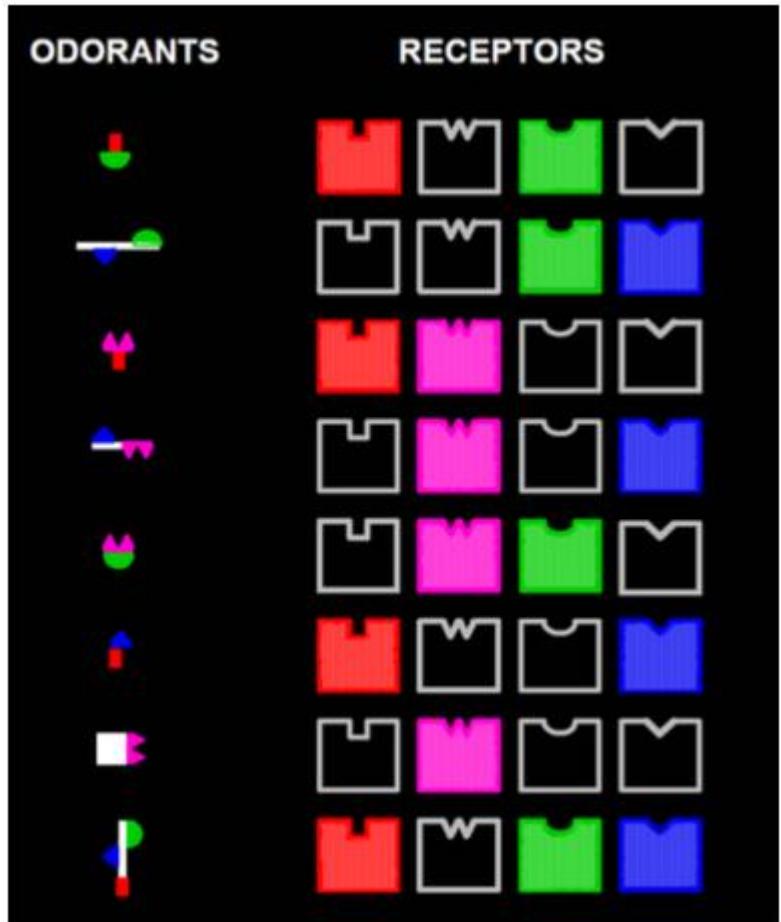
- (a) 每个OR cell表达一种嗅觉受体蛋白（此处由细胞颜色编码），不同的细胞随机分散在 Olfactory epithelium的某个区域内。
- (b) 三个不同OR cells的微电极记录表明，每个细胞对许多不同的气味做出反应，但具有不同的偏好。通过测量所有三个细胞的反应，可以清楚地区分四种气味中的每一种。



▲ FIGURE 8.13
Broad tuning of single olfactory receptor cells. (a) Each receptor cell ex-

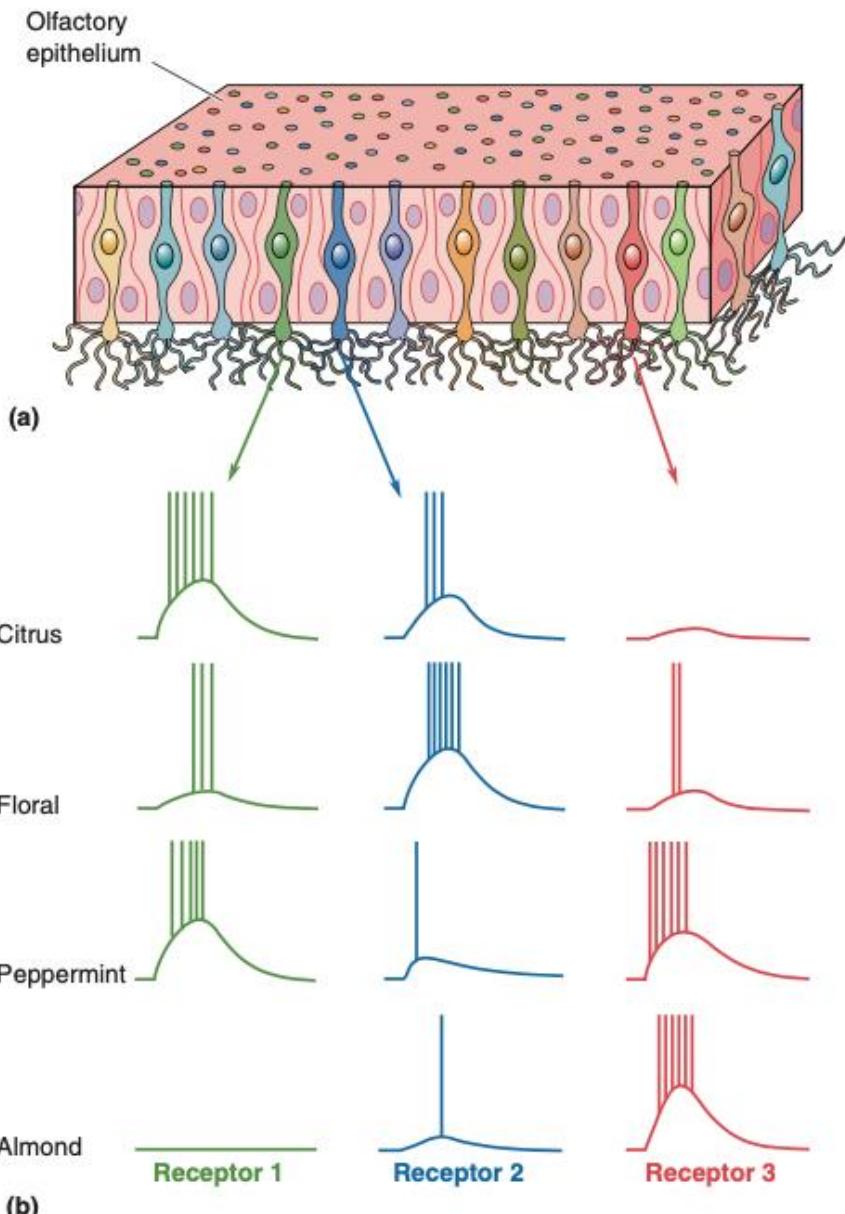
Figure is from *Neuroscience: Exploring the brain (Ed.4)*.

Olfactory epithelium



嗅觉系统使用“**组合编码**”机制，即每种气味分子可以激活多个不同的嗅觉受体，产生特定的激活模式。

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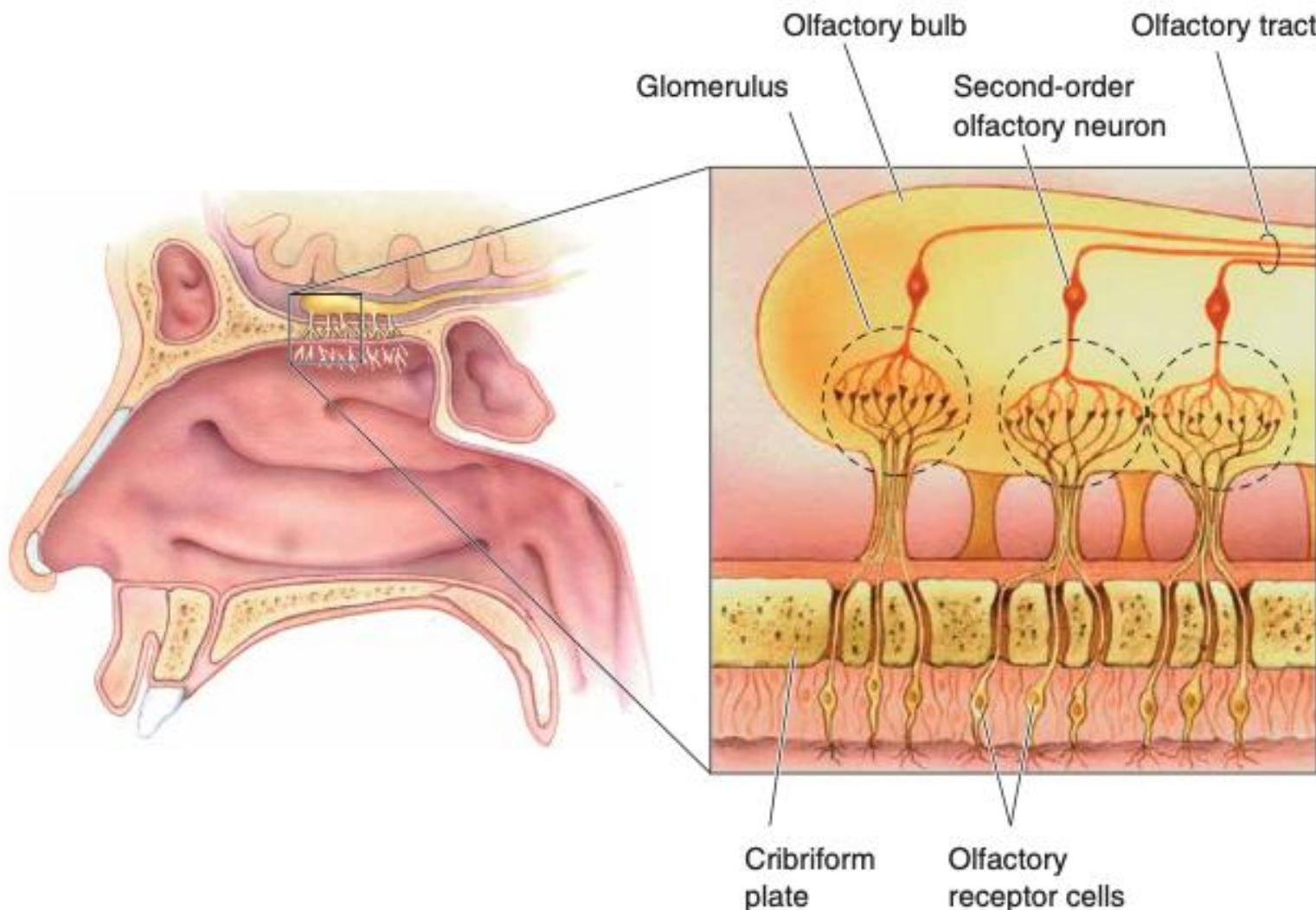


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L. B. Buck, “Unraveling the sense of smell (nobel lecture),” *Angewandte Chemie International Edition*, 2005.

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Olfactory bulb

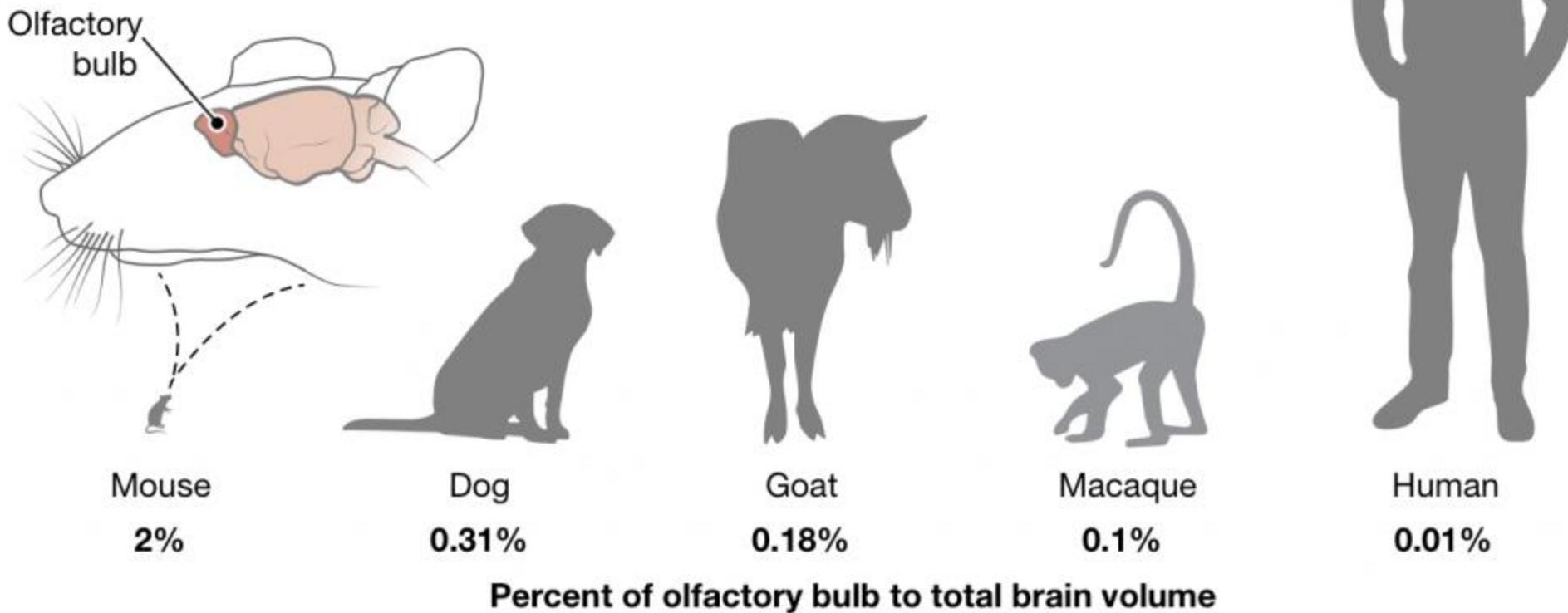


◀ **FIGURE 8.14**
The location and structure of an olfactory bulb. Axons of olfactory receptor cells penetrate the cribriform plate and enter the olfactory bulb. After multiple branching, each olfactory axon synapses upon second-order neurons within a spherical glomerulus. The second-order neurons send axons through the olfactory tract further into the brain.

Percent of olfactory bulb to total brain volume

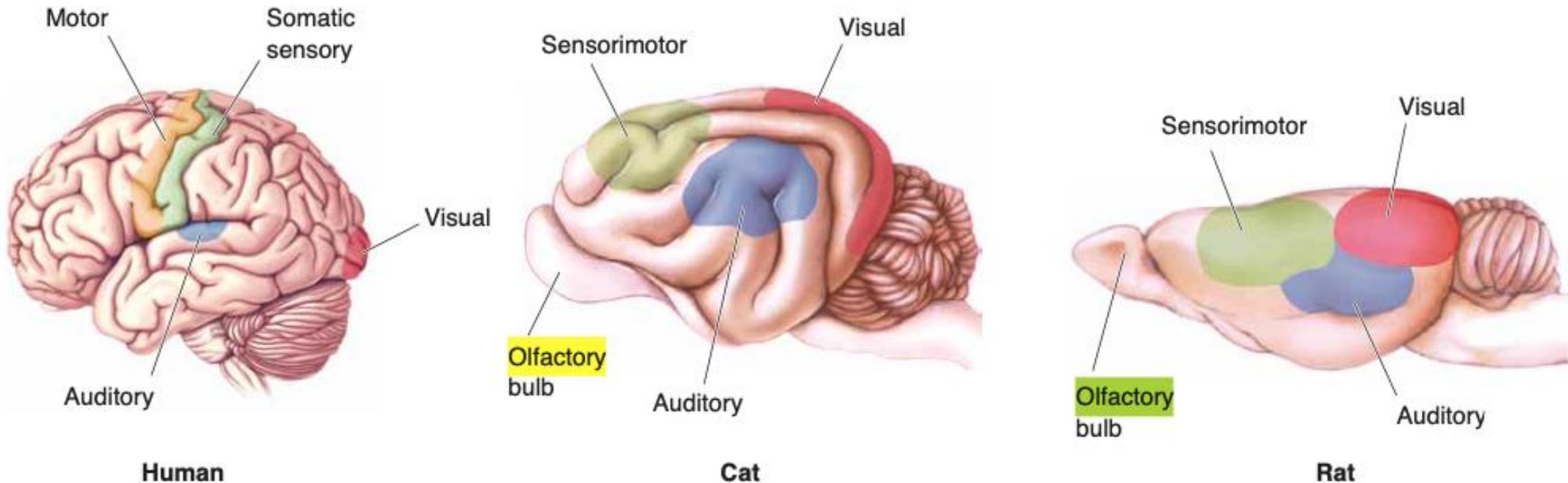
The smell test

The relatively small size of the human olfactory bulb—compared to other animals—has long been cited as a reason for human’s “inferior” scent of smell. New research is starting to overturn this notion.



Credits: (Graphic) C. Bickel/Science; (Data) McGann et al., *Science* **356** (12 May 2017)/Kavoi and Jameela, *Int. J. Morphol.* **29** (3): 939–946, 2011/Seidlitz et al., *NeuroImage* (28 April 2017)

Where is Olfactory bulb in human brain?



▲ FIGURE 7.29

A lateral view of the cerebral cortex in three species. Notice the expansion of the human cortex that is neither strictly primary sensory nor strictly motor.

Glomerulus

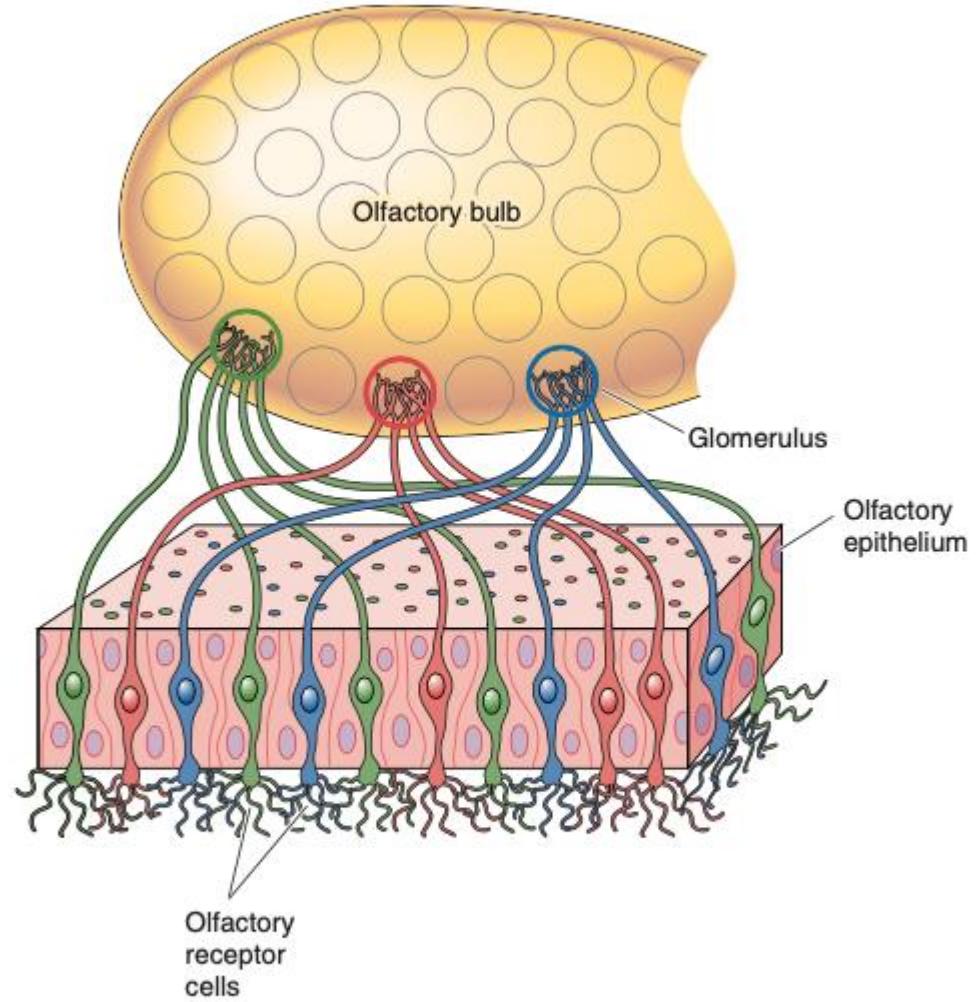
Each glomerulus receives input from only one particular type of receptor cells.

This means that the array of glomeruli within a bulb is a very orderly map of the receptor genes expressed in the olfactory epithelium (Figure 8.16), and, by implication, **a map of odor information**.

科学问题：

- Glomeruli的空间位置是怎么设计的？ORs的随机的，glomerulus的位置是最优化的？
- ORs如何找到其对应的glomerulus的？
- 这个设计原则能用来做嗅觉传感器电路设计吗？

Principal Odor Map (POM)



▲ FIGURE 8.16

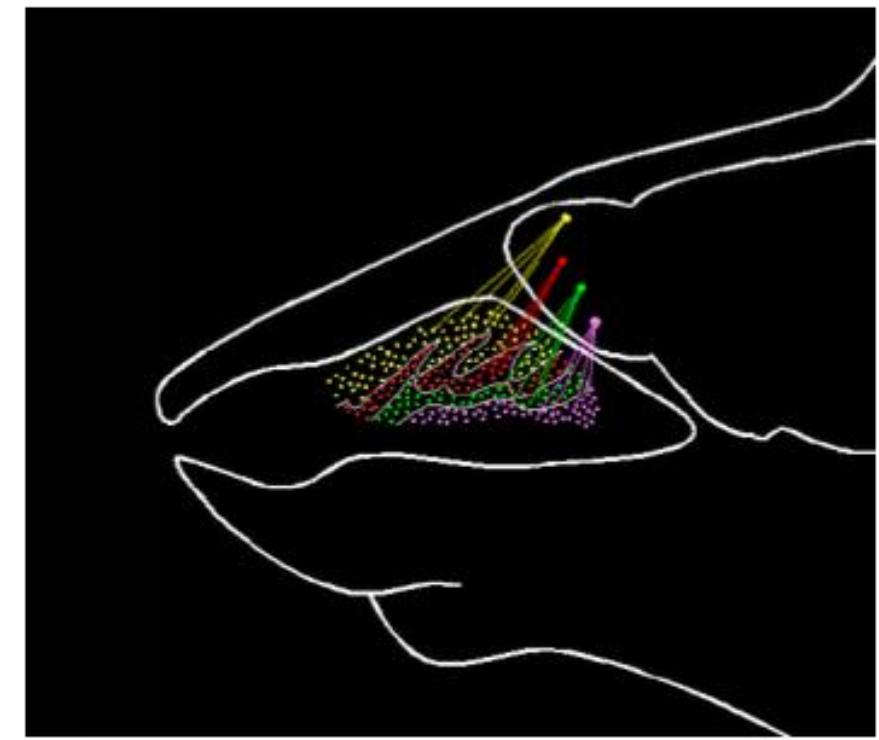
Specific mapping of olfactory receptor neurons onto glomeruli. Each glomerulus receives input only from receptor cells expressing a particular receptor protein gene. Receptor cells expressing a particular gene are color-coded.

Figure is from *Neuroscience: Exploring the brain (Ed.4)*.

Signal Integration in the Olfactory Bulb

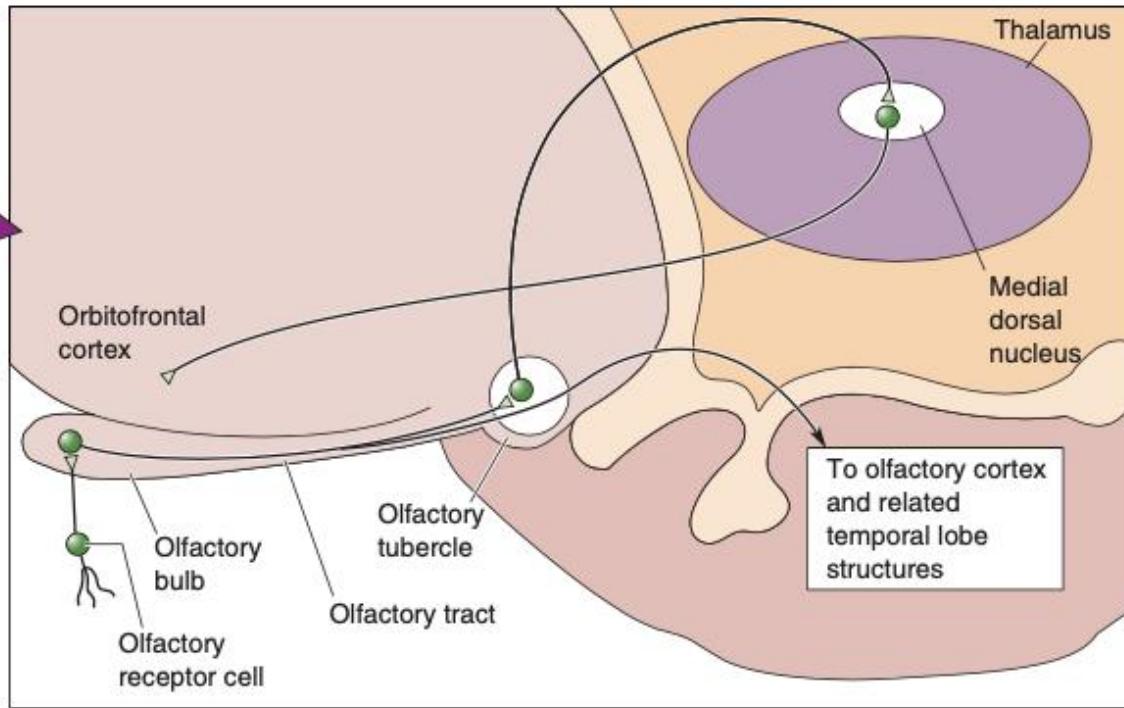
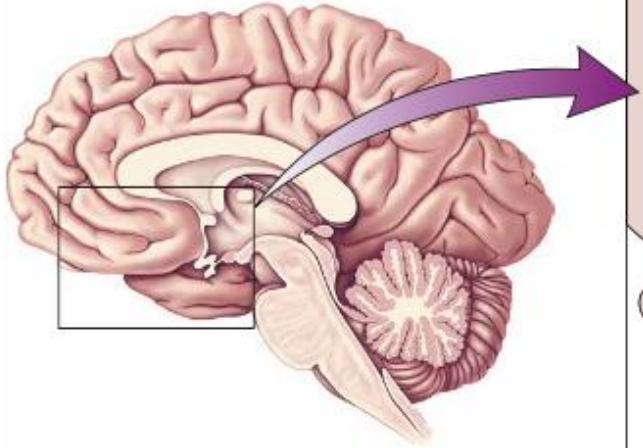
How does the brain translate an odorant's combinatorial receptor code into a perception? Each olfactory sensory neuron in the OE sends a single axon to a spherical structure called glomerulus in the OB. Since there are only **2000 glomeruli** while there are **10 million olfactory sensory neurons**, there is a massive convergence in the OB. Axons of thousands of olfactory sensory neurons expressing the same olfactory receptor converge in only 2-4 glomeruli dedicated to the same olfactory receptor. This allows a high degree of **signal integration**.

This further indicates that sensory information that is broadly organized and interspersed in different zones in the nose is transformed into **a stereotyped sensory map** in the bulb. Remarkably, this map is virtually **identical** in different individuals. This bulb map is likely to be important for stimulation of odor memories. Sensory neurons in the epithelium are **short lived** and are continuously replaced. However, the bulb map remains **constant** over time, assuring odorants can elicit **distant memories**.



Signal integration from the OE to the OB.

Olfactory cortex

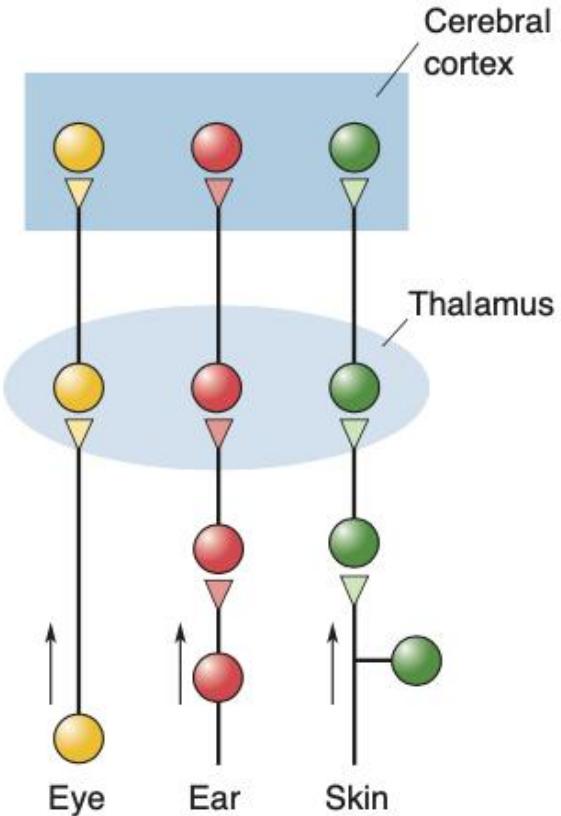


▲ FIGURE 8.17

Central olfactory pathways. Axons of the olfactory tract branch and enter many regions of the forebrain, including the olfactory cortex. The neocortex is reached only by a pathway that synapses in the medial dorsal nucleus of the thalamus.

The olfactory arrangement produces an unusually **direct** and **widespread** influence on the parts of the fore-brain that have roles in **odor discrimination, emotion, motivation, and certain kinds of memory**. Conscious perceptions of smell may be mediated by a path from the olfactory tubercle, to the medial dorsal nucleus of the thalamus, and to the orbitofrontal cortex (situated right behind the eyes).

Figure is from *Neuroscience: Exploring the brain (Ed.4)*.



▲ FIGURE 7.16

The thalamus: gateway to the cerebral cortex. The sensory pathways from the

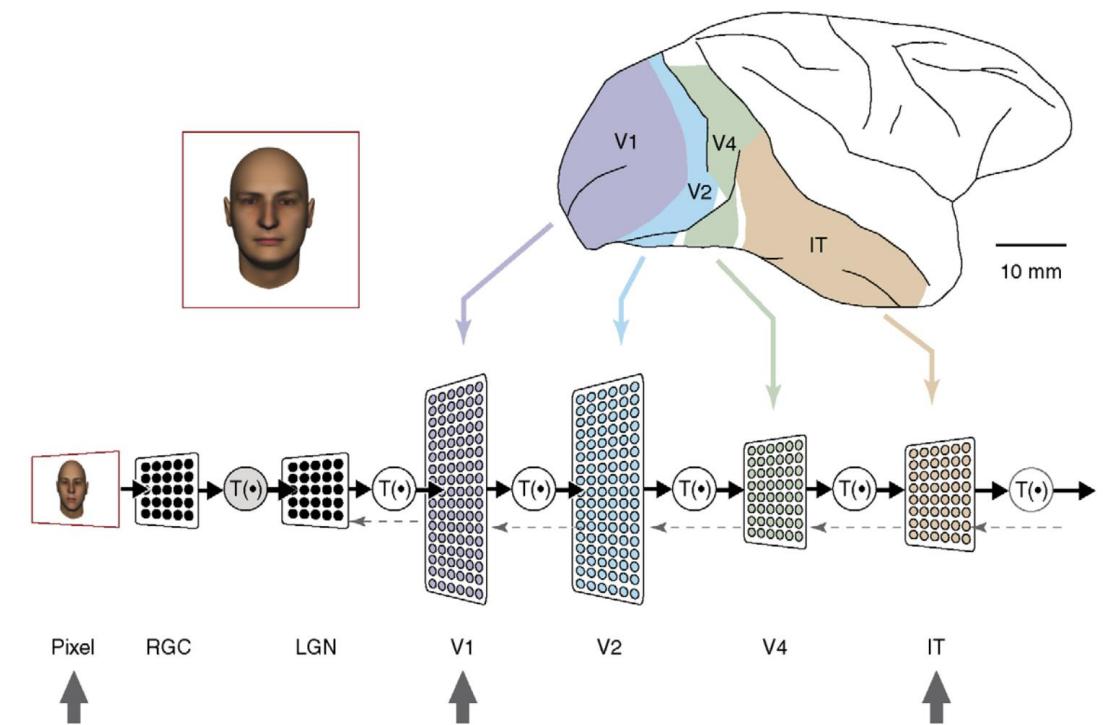
Olfactory representation v.s. Visual representation

1. Spatial Organization and Mapping:

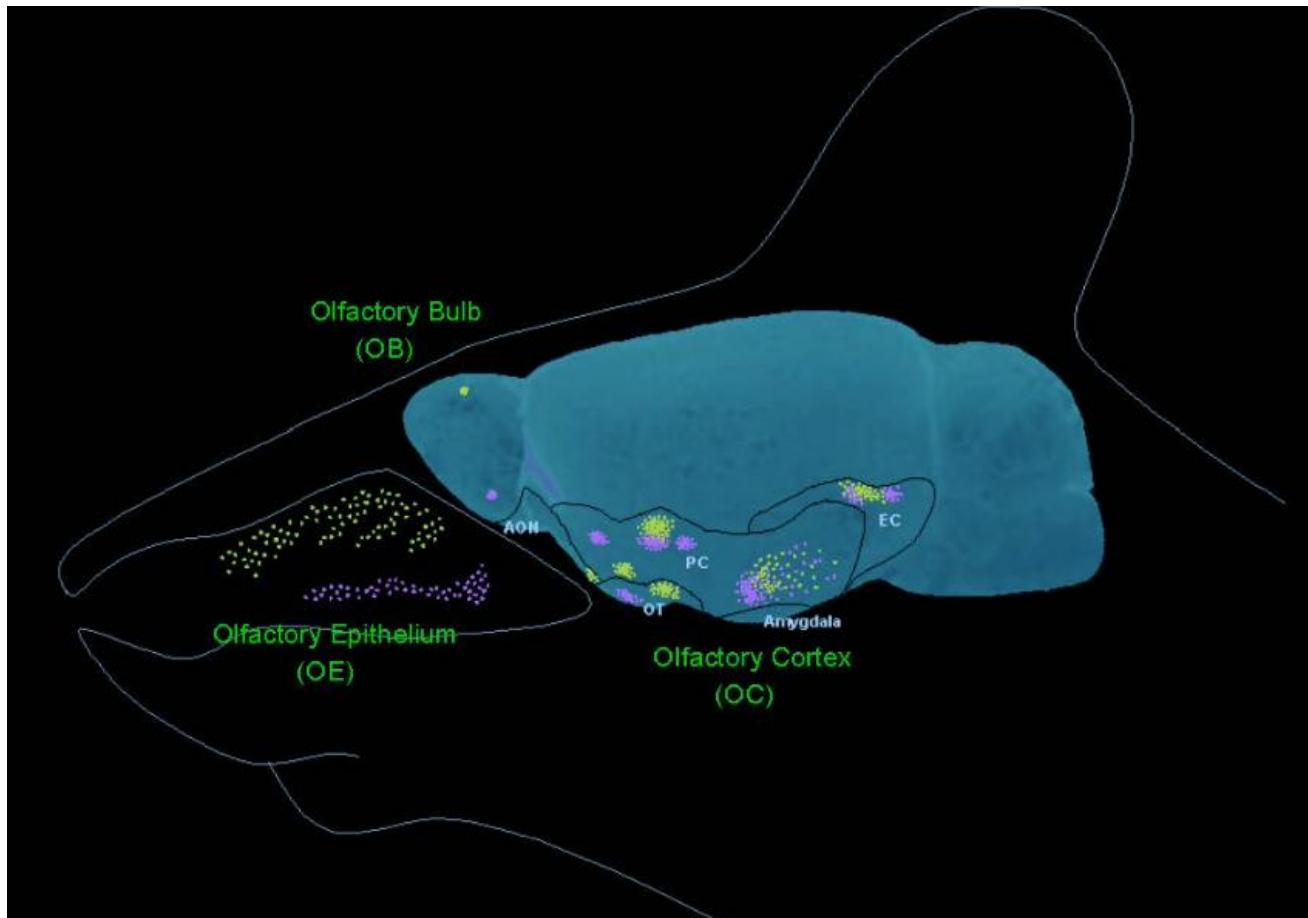
- The visual system uses a highly organized, retinotopic map where adjacent neurons in the visual cortex correspond to adjacent regions on the retina, creating a structured, spatially ordered representation. This hierarchy progresses from simple edge detection in the primary visual cortex (V1) to complex object recognition in higher visual areas like the inferotemporal cortex [MDPI](#).
- In contrast, olfactory information does not use a clear topographic map in the same way. Odorants are initially detected by olfactory receptor neurons in the olfactory epithelium, which respond selectively to molecular features of odorants. These signals converge in the olfactory bulb, forming spatial activity patterns called *glomeruli*, but from here, information is relayed to the olfactory cortex without the same degree of spatial organization seen in vision. Instead, olfactory processing is more distributed and involves a pattern-based representation where different odors correspond to unique combinations of activated neurons rather than spatial maps [MDPI](#).

2. Processing Pathways and Hierarchies:

- Visual processing follows a more defined hierarchical pathway, with feedforward and feedback loops progressing from primary sensory input to complex interpretations, such as faces or scenes, in higher cortical regions. This ordered pathway allows for detailed spatial and contextual integration.
- The olfactory system has a more direct pathway, where signals from the olfactory bulb are transmitted to the olfactory cortex, the amygdala, and other limbic areas involved in emotion and memory. This structure allows olfactory signals to rapidly evoke memory and emotional responses. The direct link with the limbic system highlights olfaction's connection to instinctive and affective processing, unlike the more compartmentalized visual system [MDPI](#) temporal vs. Spatial Encoding**:
- Visual representations rely heavily on spatial encoding, where location and patterns on the retina translate to spatial information in the cortex.
- Olfactory representations, on the other hand, rely more on temporal encoding, where the timing and sequence of neural activations contribute to odor recognition. Temporal patterns help discriminate between odors over time, which is especially useful for distinguishing complex mixtures of odorants. This temporal aspect of olfactory coding is less prominent in visual processing, where spatial detail is primary .

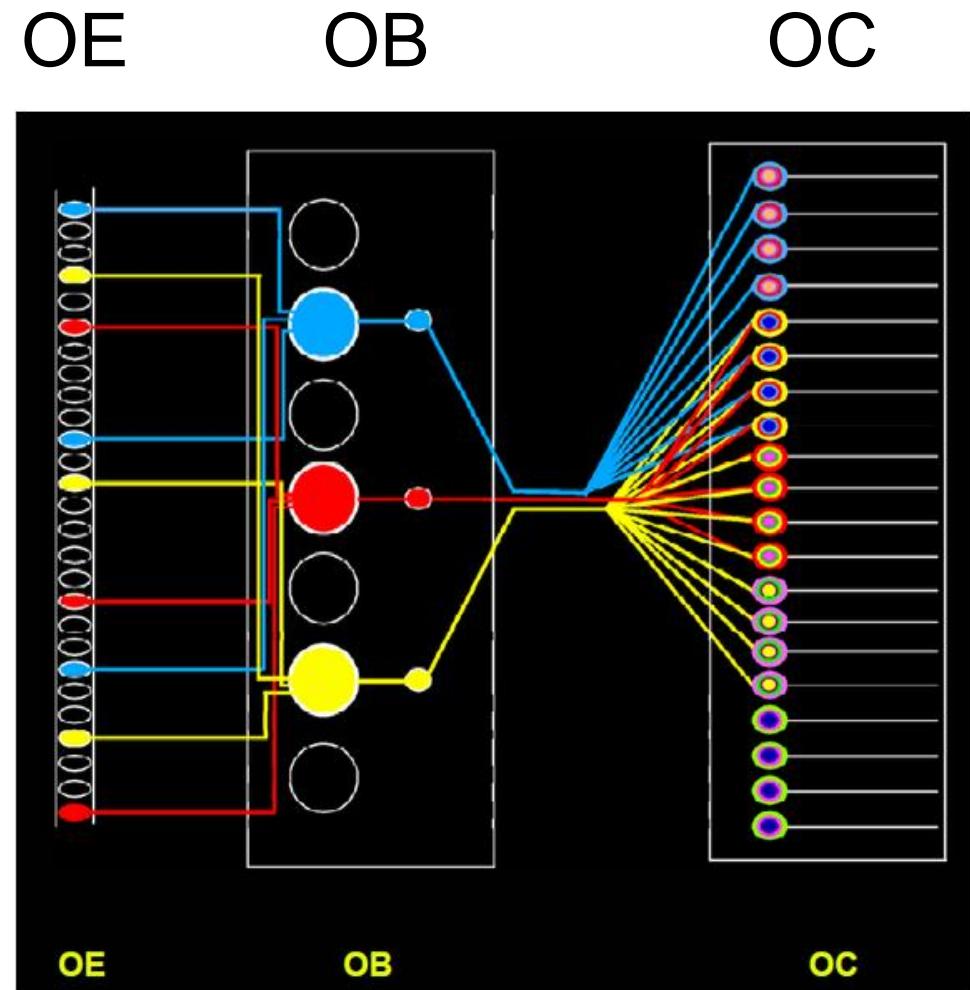


Dimensionality Expansion in the Olfactory Cortex

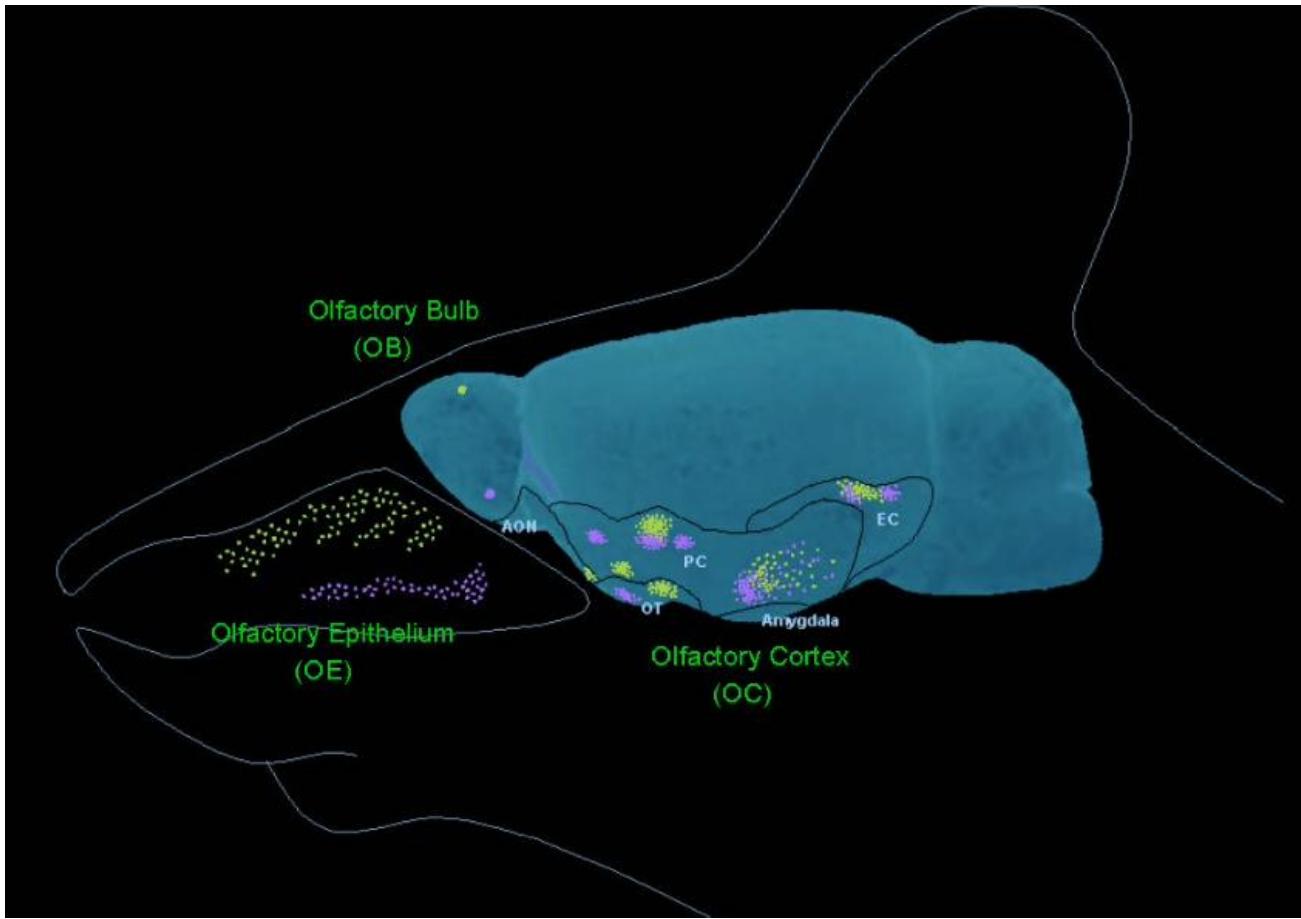


Stereotyped map in the olfactory cortex.

Signals of the same type of olfactory receptor (marked with the same color) project to multiple spots in the cortex.

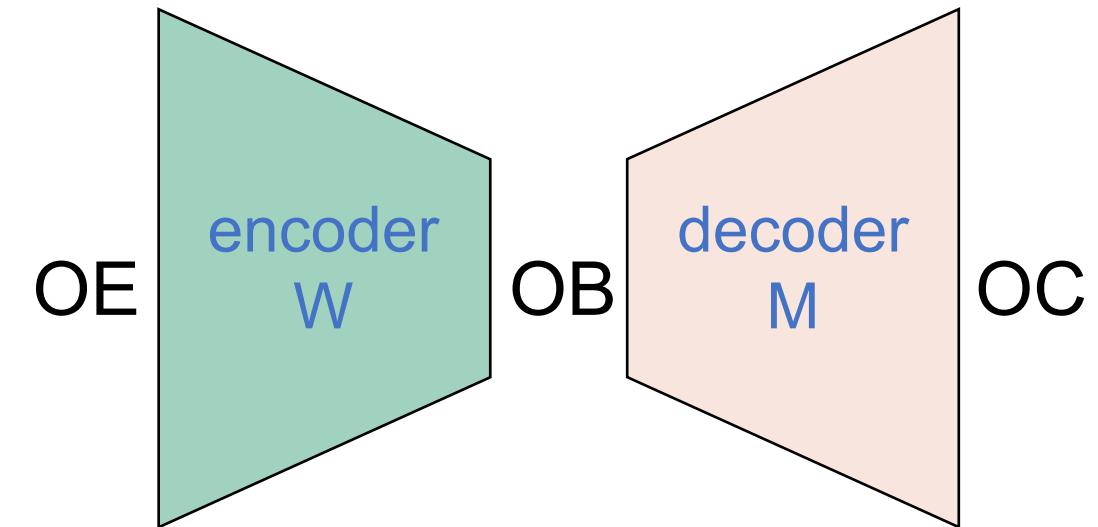


Dimensionality Expansion in the Olfactory Cortex



Stereotyped map in the olfactory cortex.

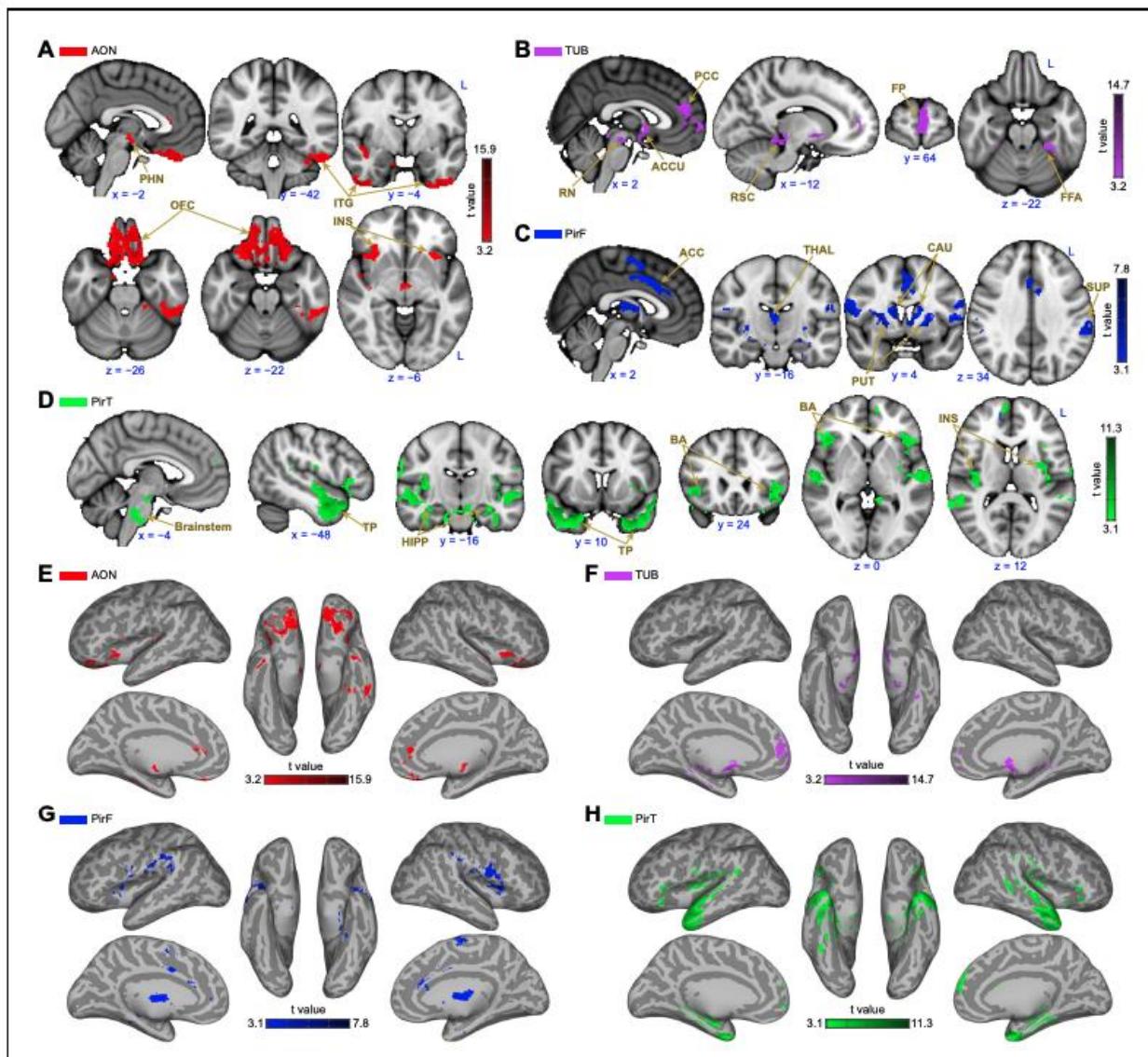
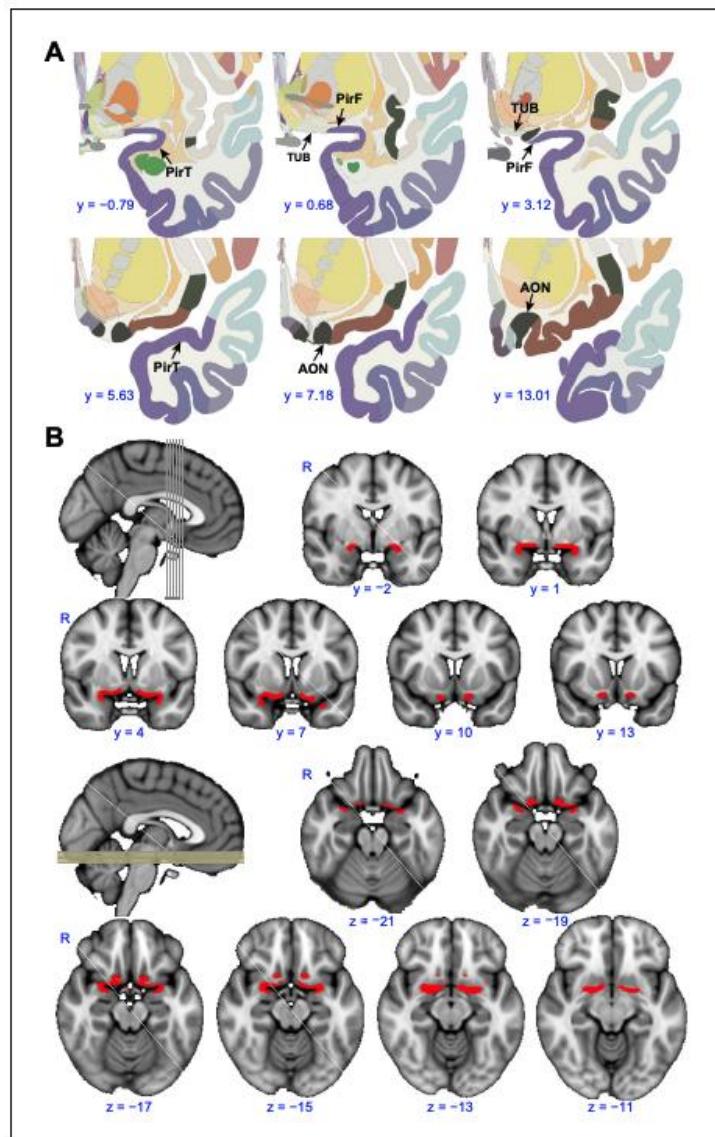
Signals of the same type of olfactory receptor (marked with the same color) project to multiple spots in the cortex.



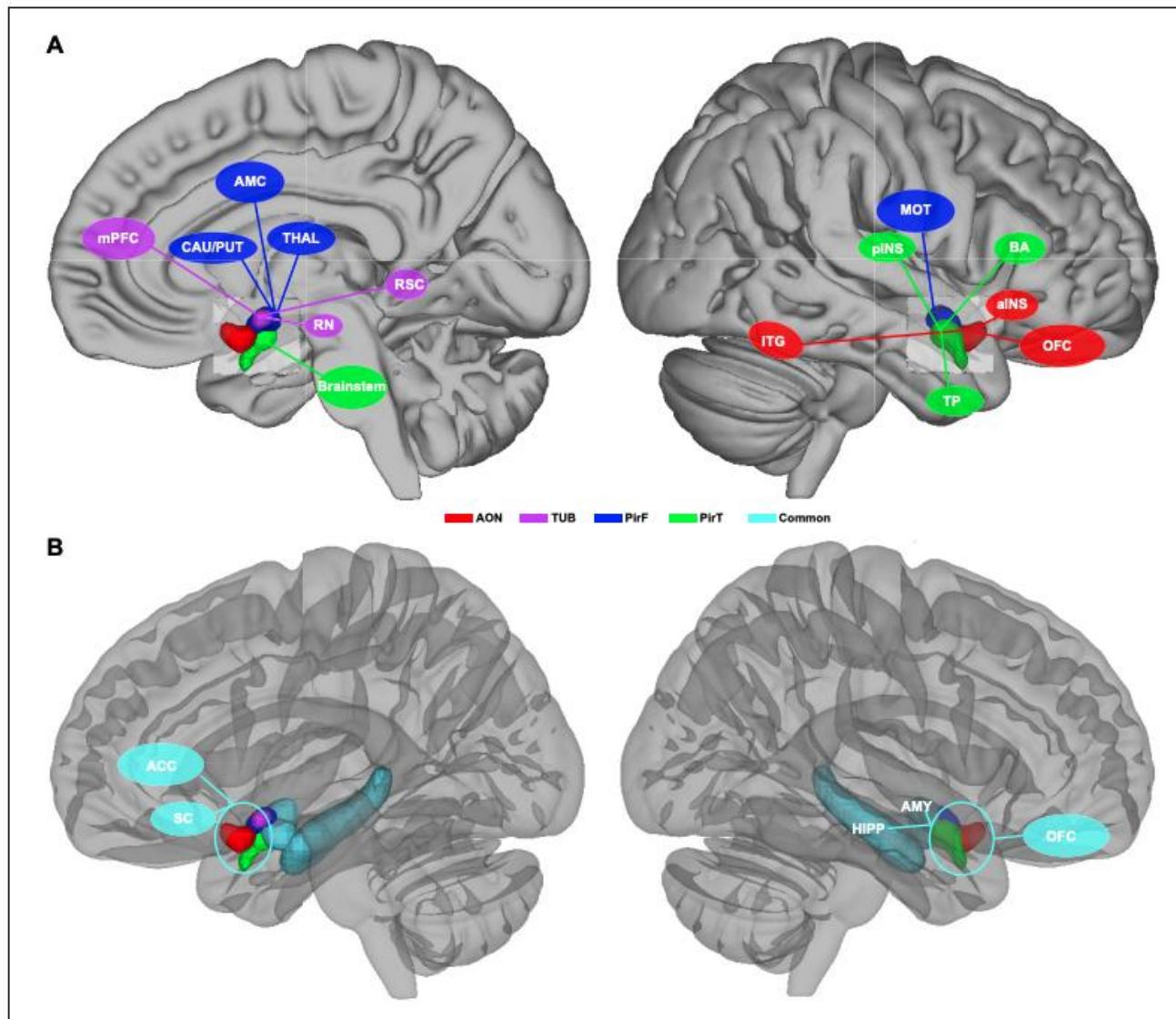
Sparse Coding with Overcomplete Basis Functions

$$\min_{W,M} |x - \hat{x}|^2$$

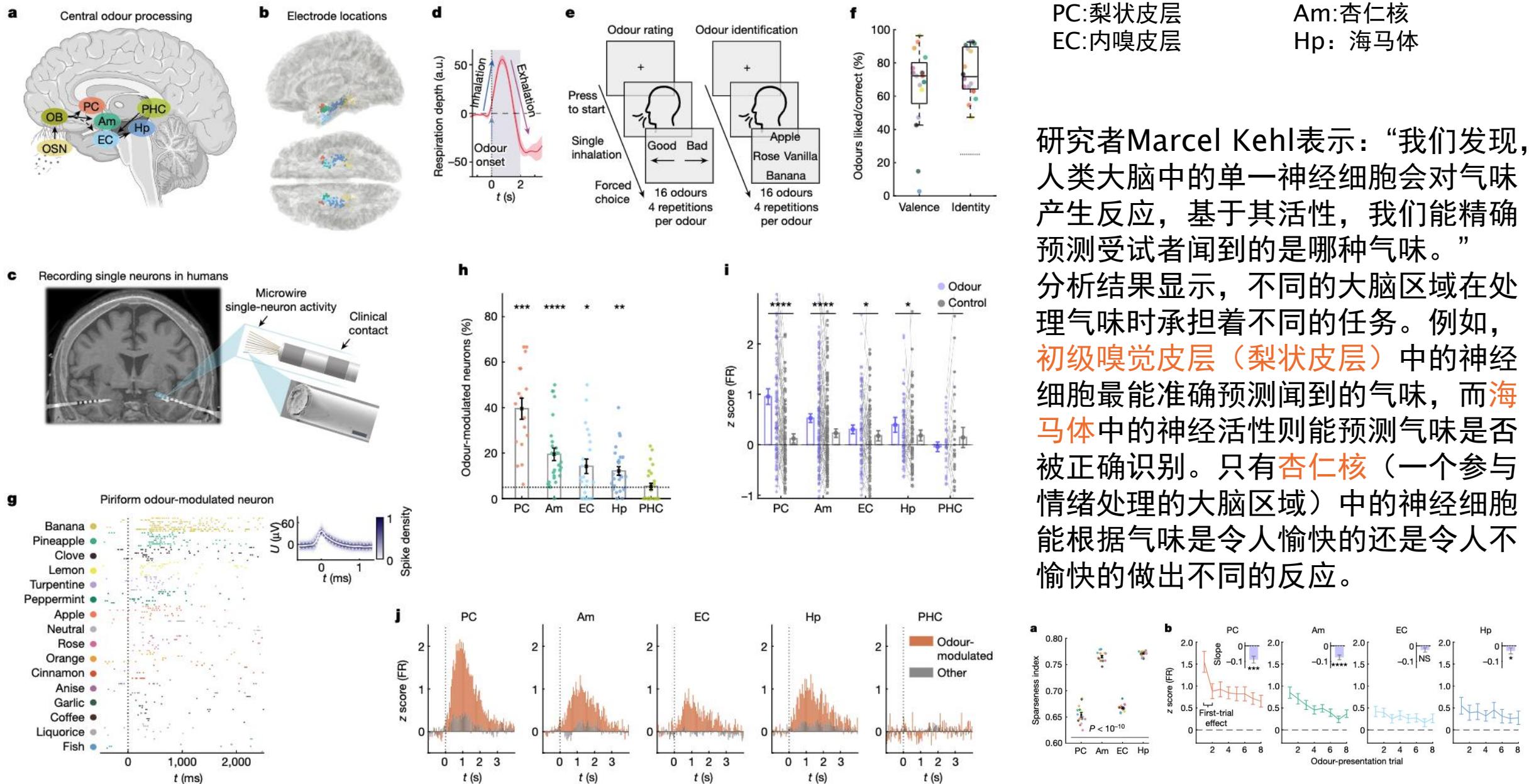
Functional pathways of the human olfactory system



Functional pathways of the human olfactory system



嗅觉皮层与情绪(Amygdala)和
记忆(Hippocampus)相关脑区有重叠。

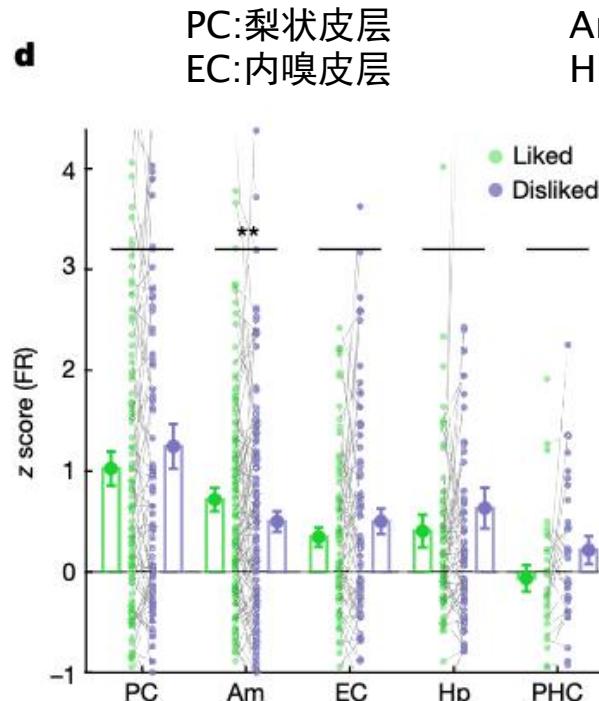
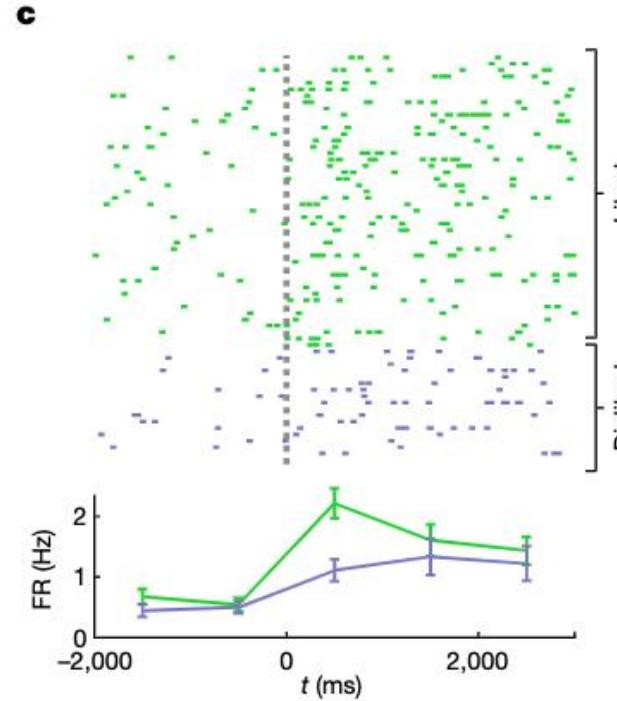
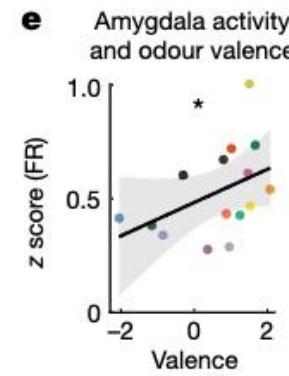
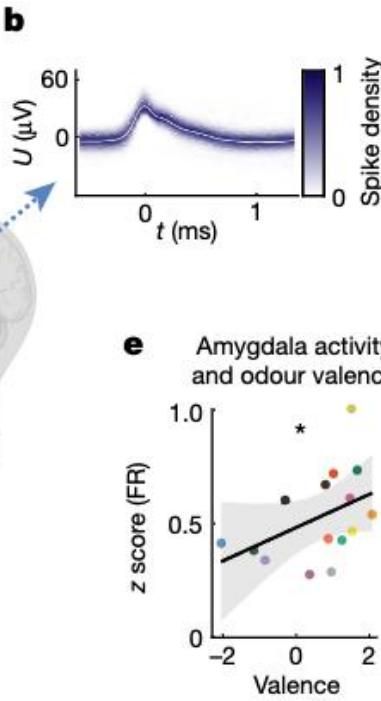
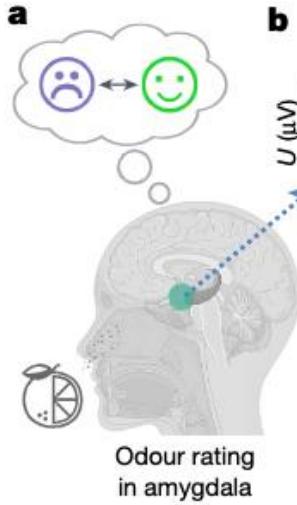


PC:梨状皮层
EC:内嗅皮层

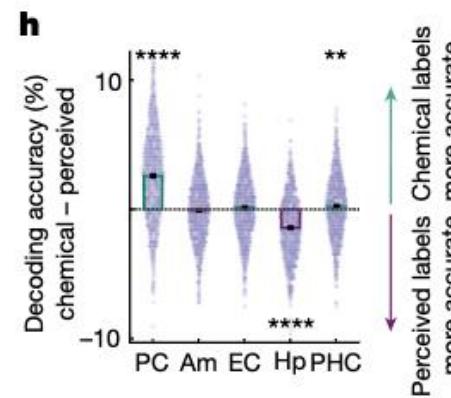
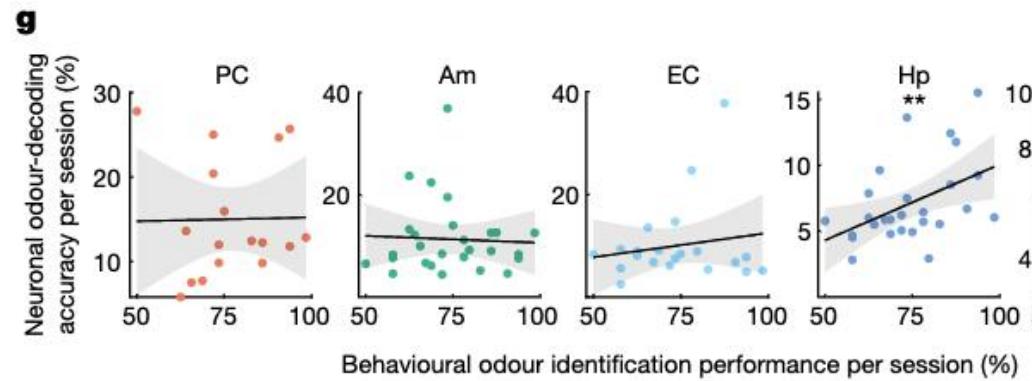
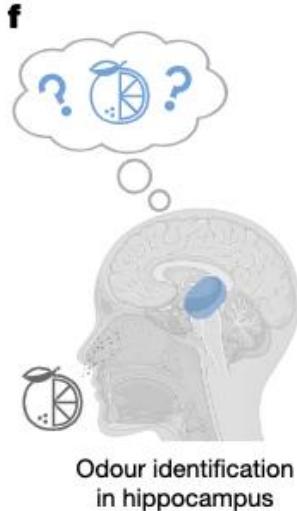
Am:杏仁核
Hp: 海马体

研究者Marcel Kehl表示：“我们发现，人类大脑中的单一神经细胞会对气味产生反应，基于其活性，我们能精确预测受试者闻到的是哪种气味。”

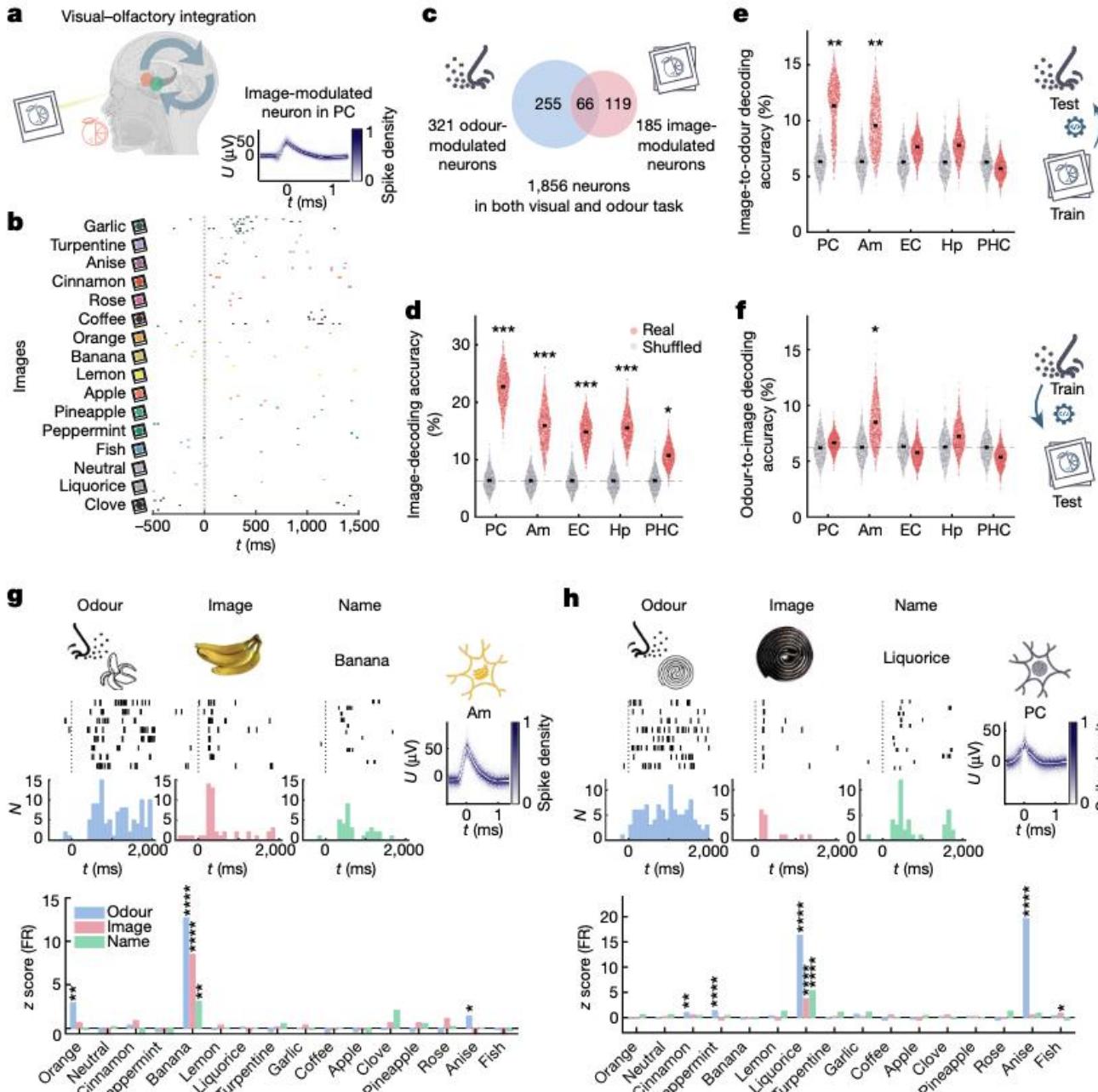
分析结果显示，不同的大脑区域在处理气味时承担着不同的任务。例如，**初级嗅觉皮层（梨状皮层）**中的神经细胞最能准确预测闻到的气味，而**海马体**中的神经活性则能预测气味是否被正确识别。只有**杏仁核**（一个参与情绪处理的大脑区域）中的神经细胞能根据气味是令人愉快的还是令人不愉快的做出不同的反应。



杏仁核神经元
编码气味的
valence
(喜欢or不喜欢)



海马预测行为
气味识别表现



研究人员探讨了**气味感知和图像感知之间的关联**。

他们向参与者展示了每种气味的匹配图像，比如气味和香蕉的照片，然后分析了神经元的反应。令人惊讶的是，**初级嗅觉皮层中的神经细胞不仅对气味有反应，对图像也有反应**。

这表明，人类嗅觉皮层的任务远远超出了单纯的气味感知。

研究人员发现，**单个神经细胞能对气味、图像和文字（如“香蕉”）产生特定的反应**。这一发现表明，**语义信息（即与气味相关的概念和意义）在人类嗅觉处理的早期阶段就已经被处理了**。

这一结果不仅证实了动物研究的结论，还揭示了不同大脑区域在特定人类气味处理功能中的作用。

Olfactory habituation & adaptation

与善人居，如入芝兰之室，久而不闻其香，即与之化矣。

与不善人居，如入鲍鱼之肆，久而不闻其臭，亦与之化矣。

Olfactory habituation

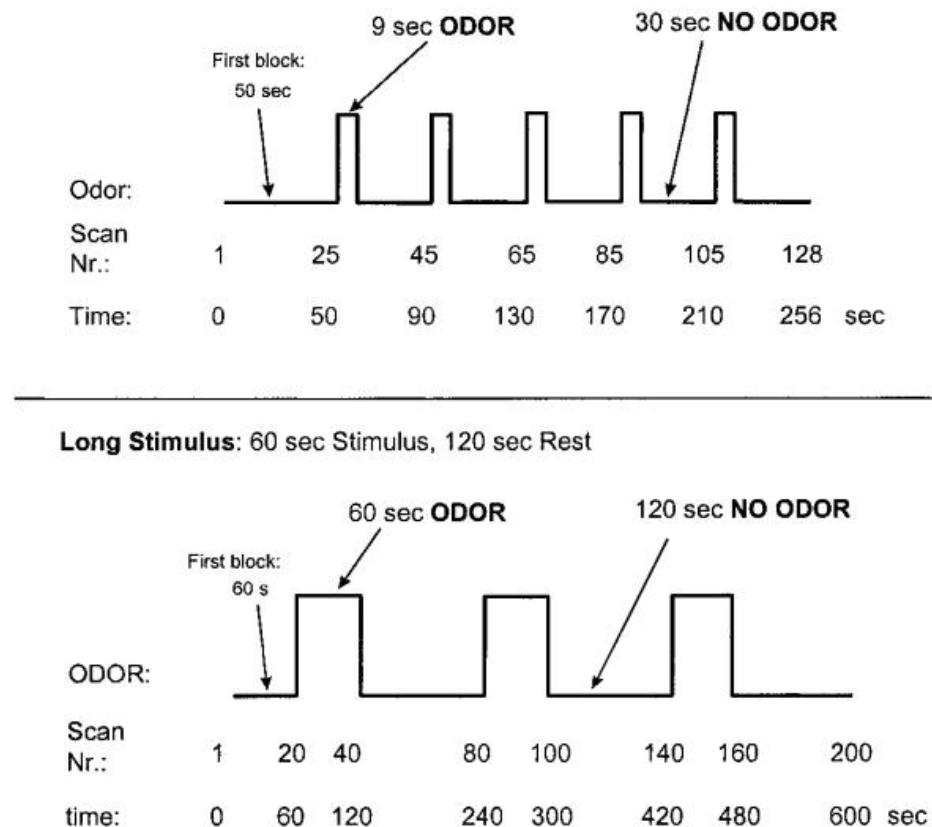
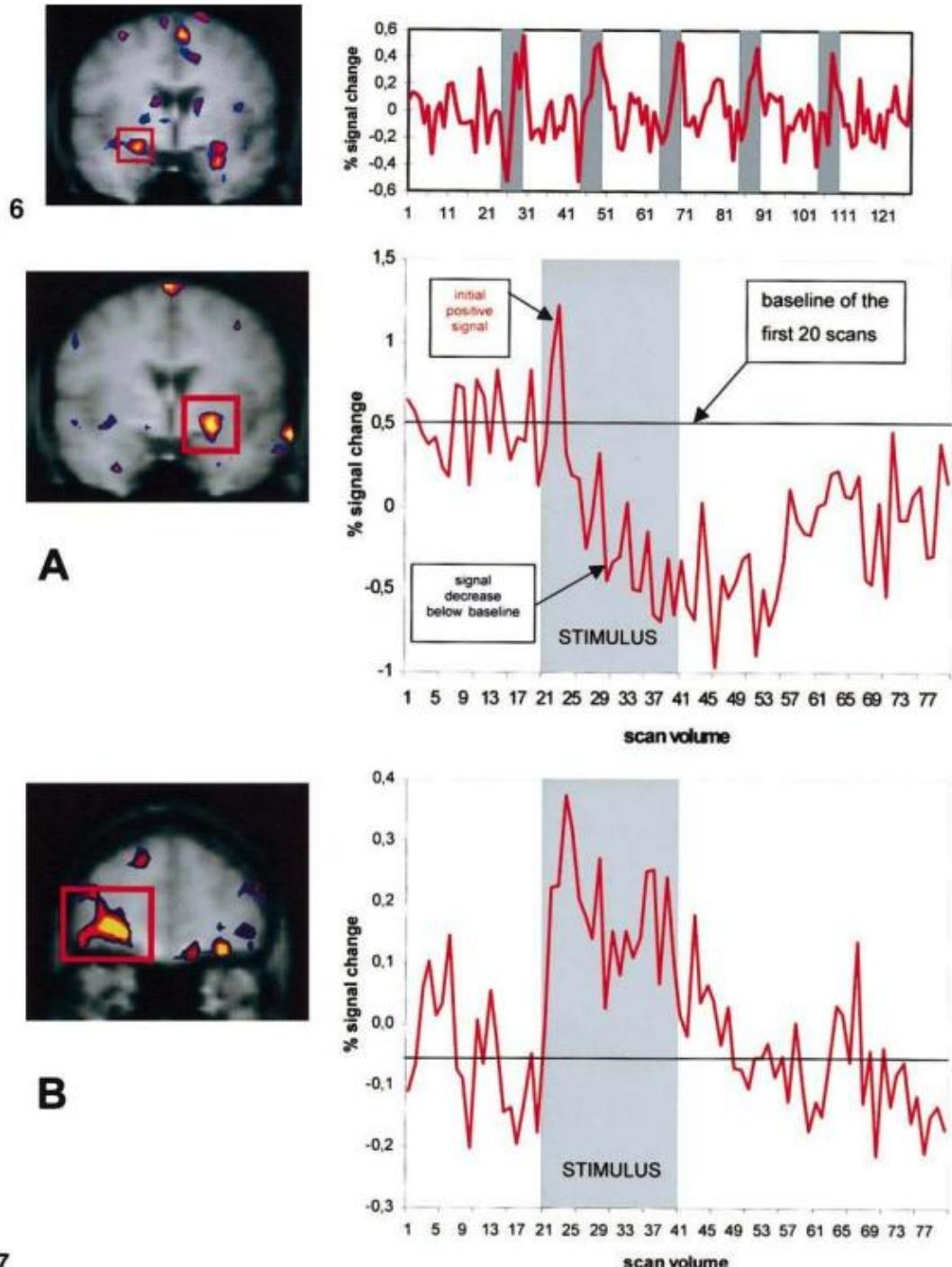


FIG. 1. Olfactory paradigms for the short runs (9 s stimulation) and the long runs (60 s stimulation).



Poellinger, A., Thomas, R., Lio, P., Lee, A., Makris, N., Rosen, B. R., & Kwong, K. K. (2001). Activation and habituation in olfaction—an fMRI study. *Neuroimage*

Olfactory habituation vs Olfactory adaption

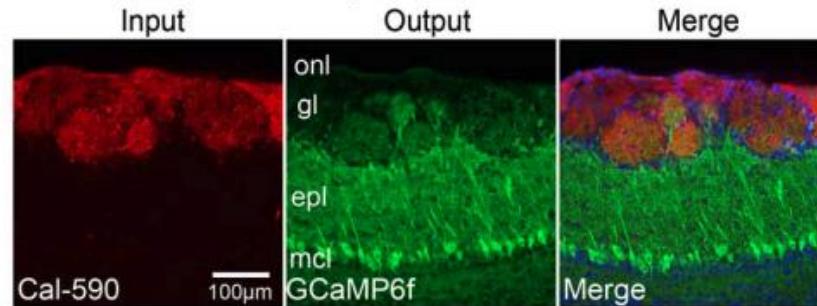
According to Rankin, “*habituation* is defined as a behavioral response decrement that results from repeated stimulation and that **does not** involve sensory adaptation/sensory fatigue or motor fatigue.”

This definition comes from traditional animal studies where observed behaviors were reduced, and does not encompass underlying processes that create such behavioral changes, as a decrease of a perception or of a sensation.

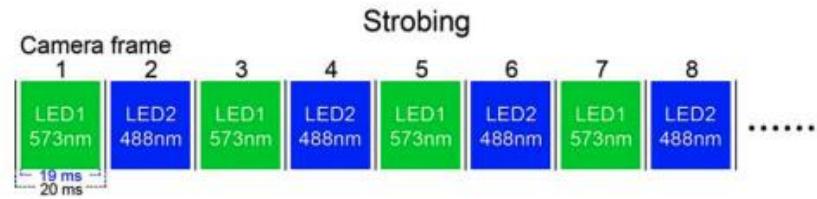
Olfactory adaptation

Figure 1: Targeting input and output

a Location of the activity sensors

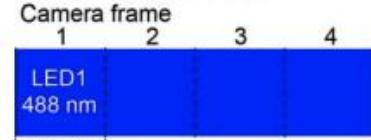


b Near-simultaneous imaging from input and output



c Imaging paradigm

Continuous



d Signal time-course

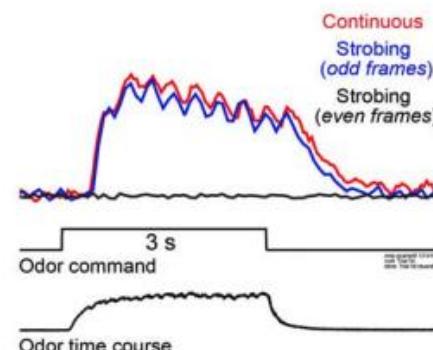
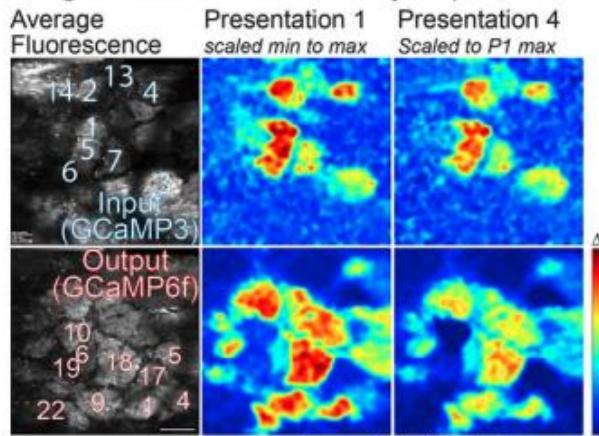
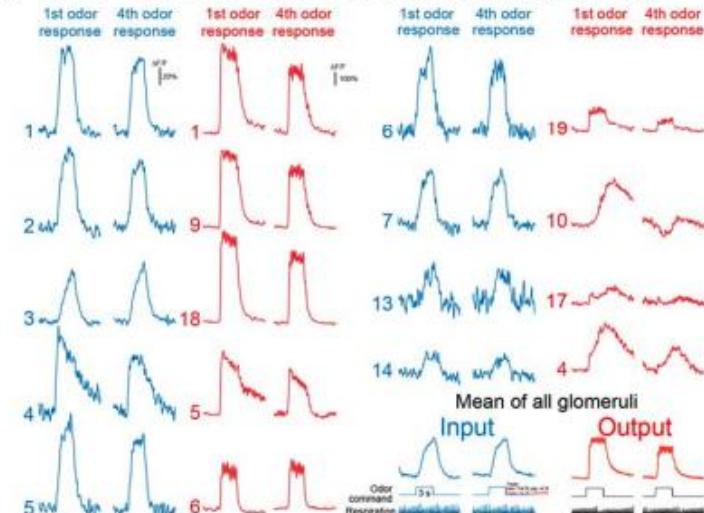


Figure 4: 2-photon imaging from input and output in different, anesthetized preparations

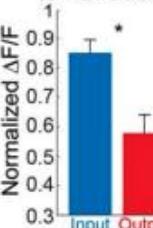
a Average fluorescence and activity maps



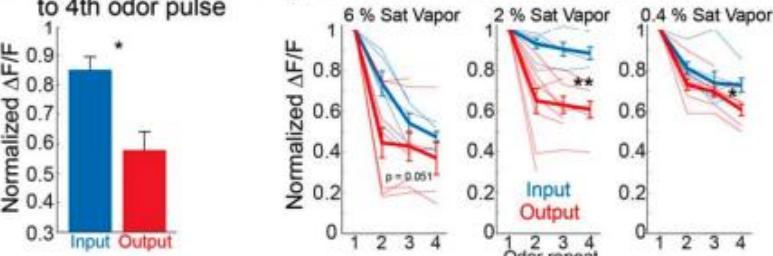
b Fluorescence time course from individual glomeruli



c Normalized response to 4th odor pulse



d Adaptation at different concentrations



Scent stimulation is too tedious to set up.

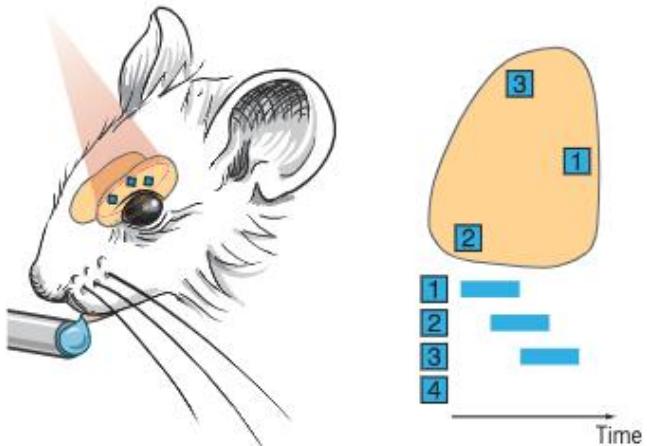
How about using optogenetic stimulation to OB?

Storage, Douglas A., and Lawrence B. Cohen. "The olfactory bulb contributes to the adaptation of odor responses: the input-output transformation." *BioRxiv* (2019).

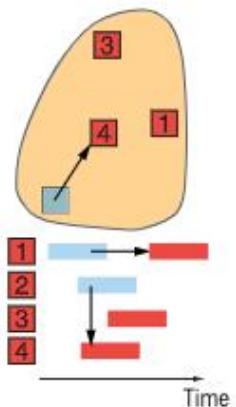
能否直接刺激神经元，产生嗅觉感受？

Manipulating synthetic optogenetic odors

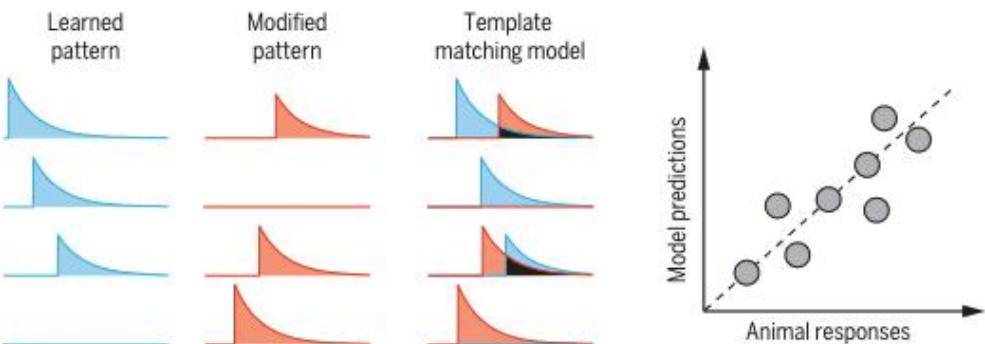
A Mice were trained to recognize "synthetic odor" pattern



B Changes in recognition patterns were measured as trained pattern was modified



C Template matching model explains olfactory perception



Probing olfactory perception with synthetic odors. (A) We trained mice to recognize synthetic odor patterns: artificially stimulated neural activity in the olfactory bulb. Patterns were defined in space (top right) and time (bottom right). (B) Perceptual responses were measured across systematic modifications of trained patterns. (C) Template-matching model of pattern activity (left) accounts for perceptual responses (right).

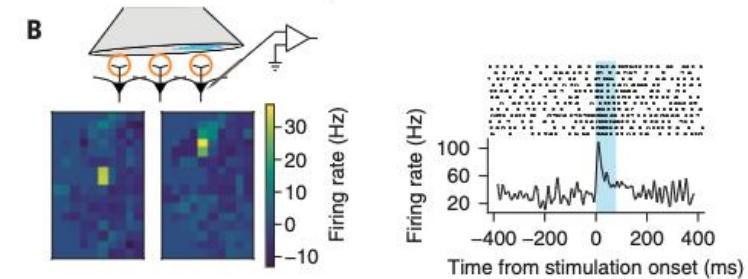
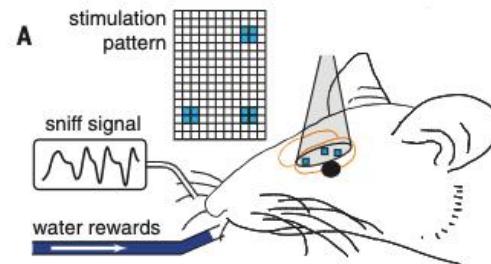


Fig. 1. Optogenetic stimulation as synthetic odors. (A) Schematic of the

a stimulation grid. Target patterns comprised six spots, initialized randomly but fixed

Chong, Edmund, et al. "Manipulating synthetic optogenetic odors reveals the coding logic of olfactory perception." *Science* 368.6497 (2020).

Hyperbolic geometry of the olfactory space

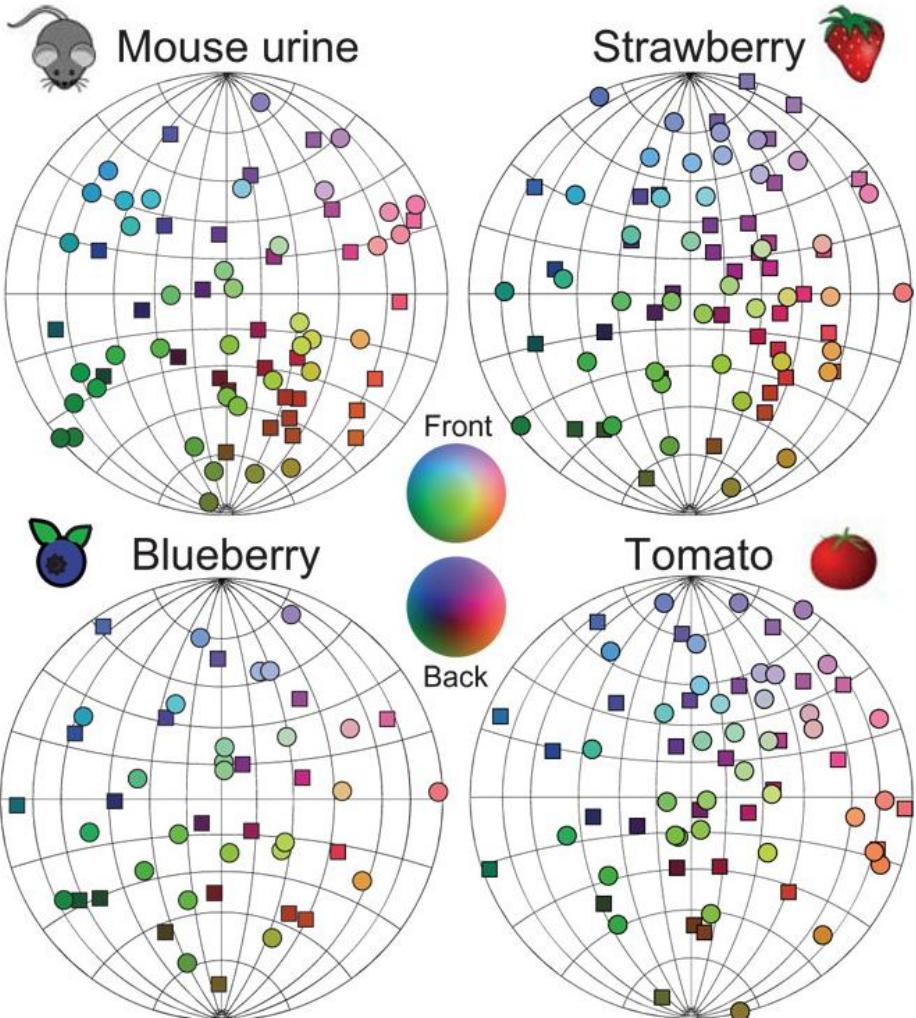


Fig. 3 Visualization of the natural olfactory space using nonmetric MDS.

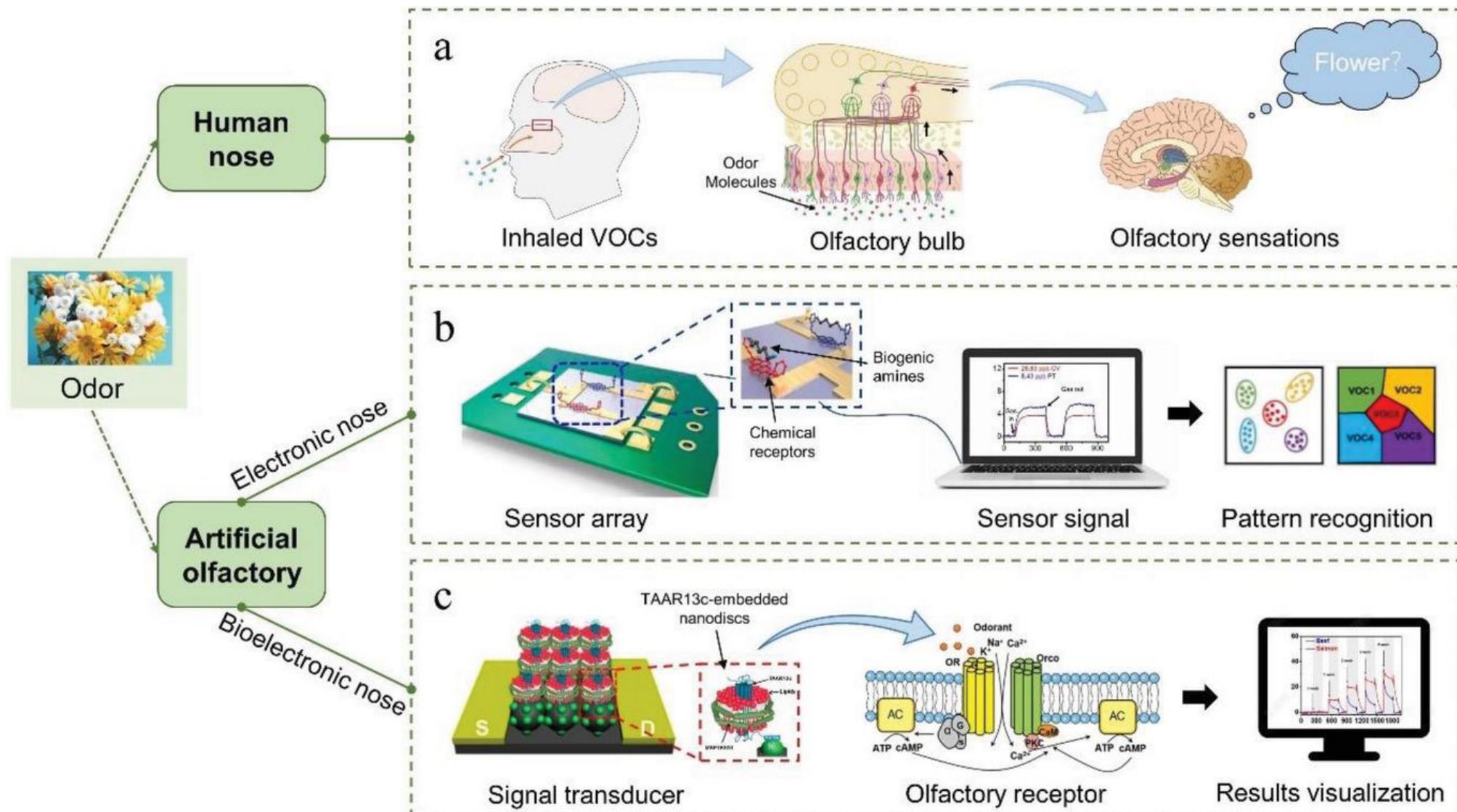
Because the variation in radius is small, data points are shown on the surface of a sphere with circles/rectangles for points falling on the near/far side of the sphere. The RGB color scales were proportional to the XYZ coordinates of points.

Salk Institute scientists discovered a new way to organize **odor molecules** based on **how often they occur together in nature**, and were then able to map this data to discover regions of odor combinations humans find most **pleasurable**.

Zhou, Y., Smith, B. H., & Sharpee, T. O. (2018). Hyperbolic geometry of the olfactory space. *Science advances*, 4(8), eaaq1458.

嗅觉系统启发的电子鼻

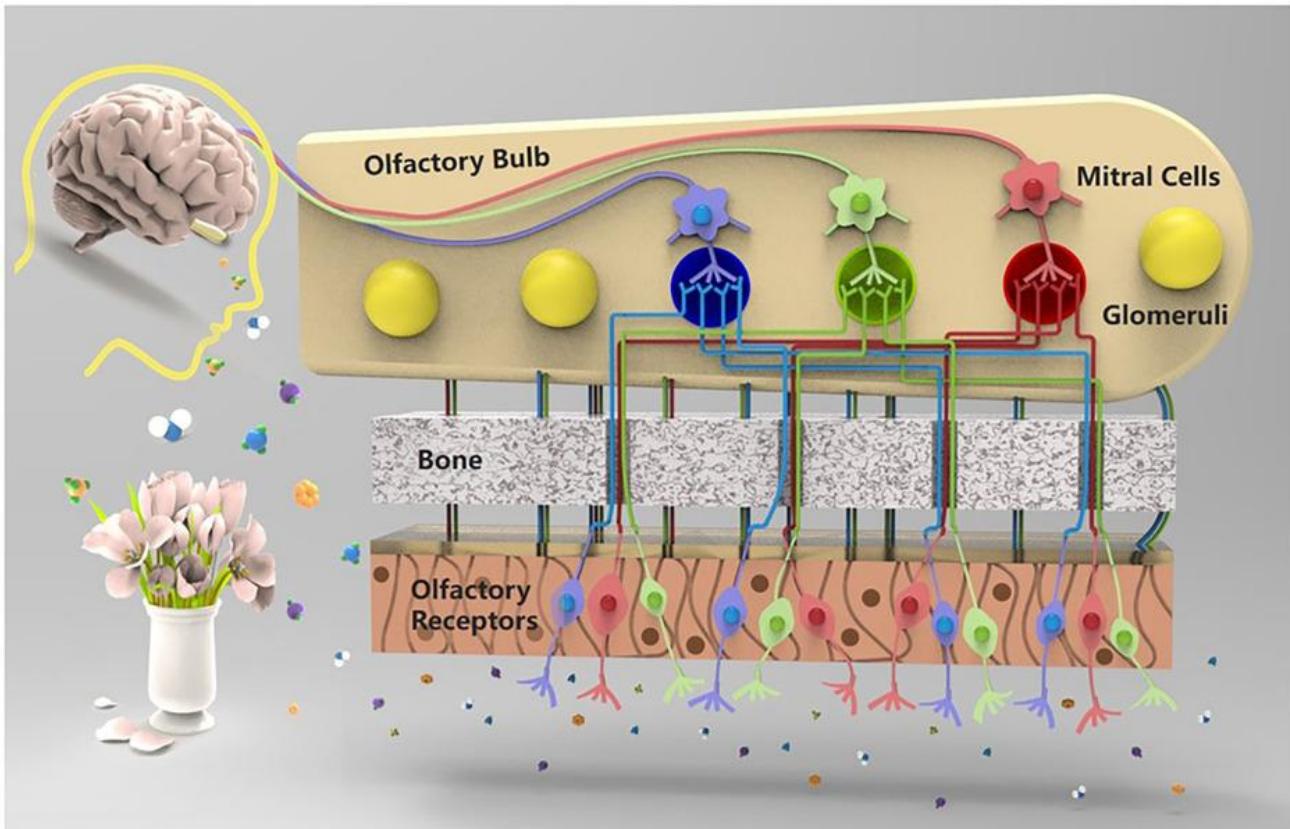
Artificial Olfactory Biohybrid System



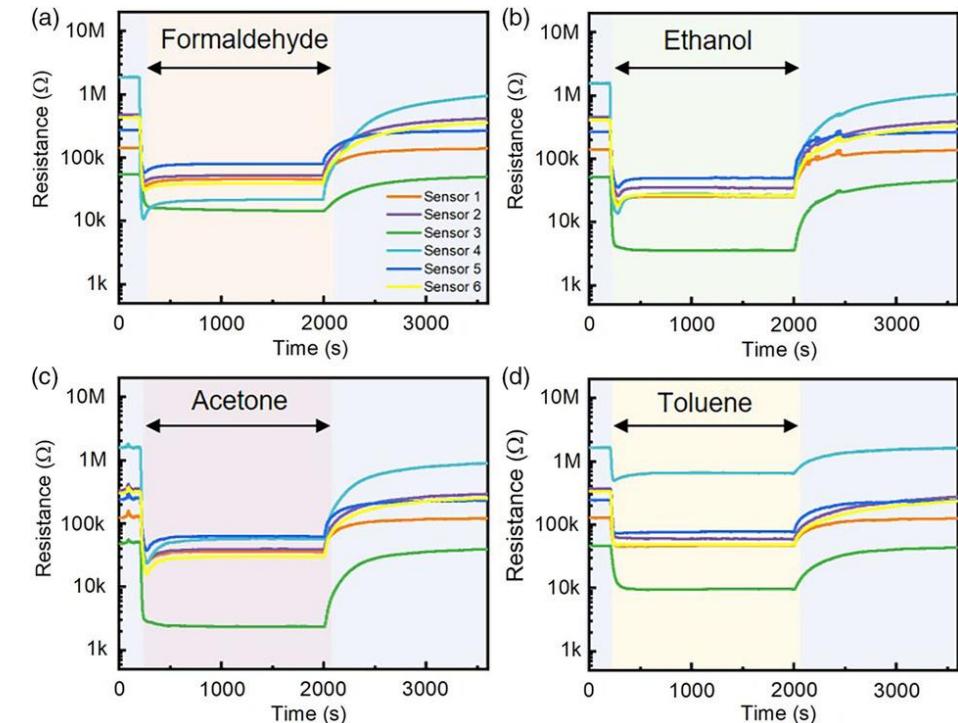
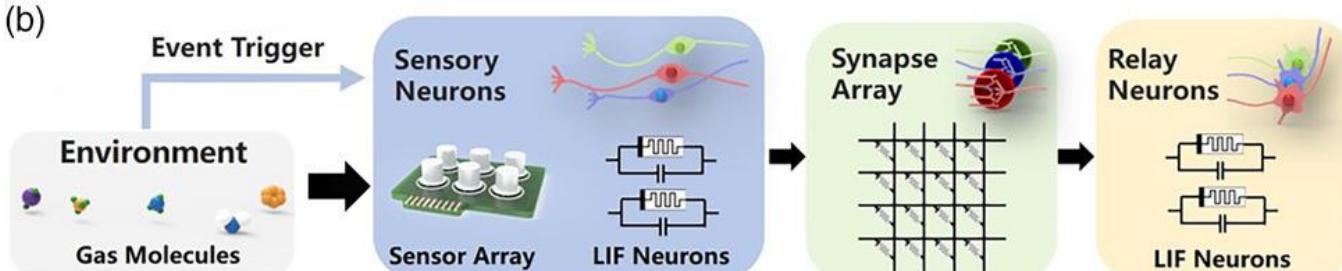
Qin, Chuanting, Yi Wang, Jiawang Hu, Ting Wang, Dong Liu, Jian Dong, and Yuan Lu. "Artificial Olfactory Biohybrid System: An Evolving Sense of Smell." *Advanced Science* (2023)

A bio-inspired neuromorphic sensory system

(a)

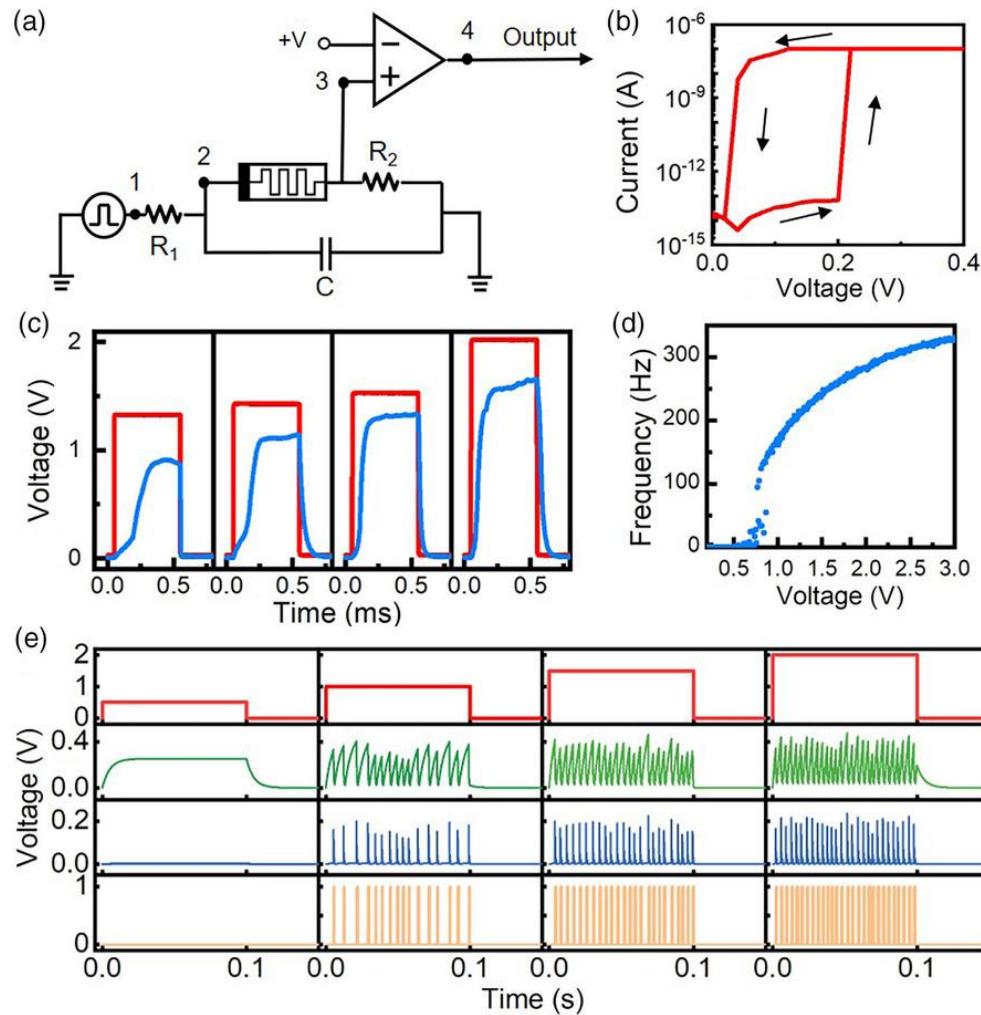


(b)



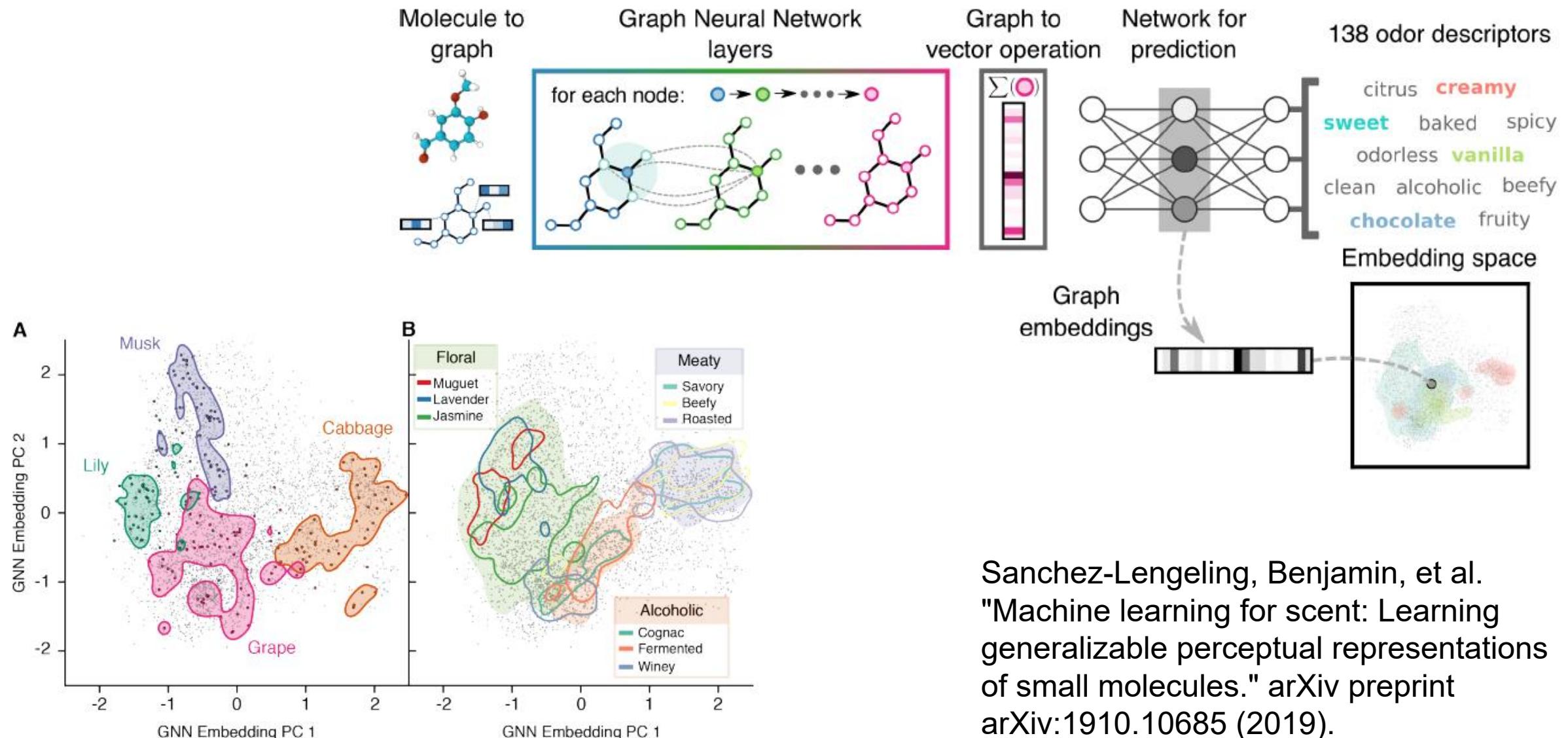
A sensor array of **six** commercial sensors (TGS2611, TGS2600, TGS2602, TGS2603, TGS2610, TGS2620) were used to detect **four** kinds of gases (formaldehyde, ethanol, acetone, toluene).

A bio-inspired neuromorphic sensory system



- a) **Leaky integrate-and-fire (LIF) neuron** based on the memristive device Pt/Ag/TaO_x/Pt ($R_1 = 108 \Omega$, $R_2 = 106 \Omega$, $C = 0.1 \text{ nF}$).
- b) **I–V curve** and c) **delay time** of the memristive device Pt/Ag/TaO_x/Pt.
- d) Output frequency of the LIF neuron.
- e) Sampling voltages from points 1 to 4 in the LIF neuron. A larger input signal (red lines) results in a shorter capacitor charging time (green lines), a quicker device switching (blue lines), and a higher output frequency (orange lines).

Machine learning for scent detection



Principal odor map (POM)

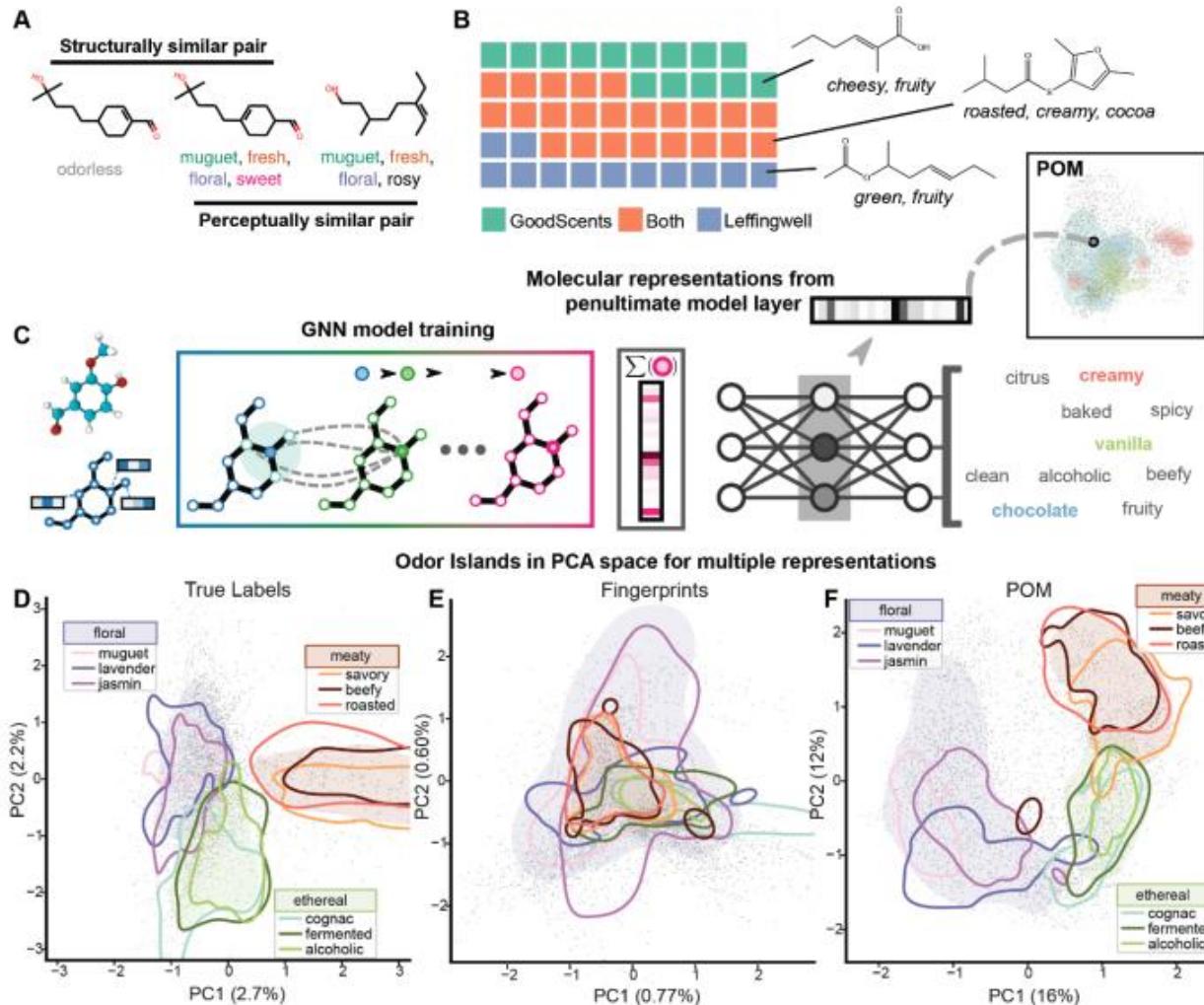


Fig. 1. POM preserves the structure of odor perceptual space. (A) Example triplet of molecules in which the structurally similar pair is not the perceptually similar pair. (B) The GNN was trained on a curated dataset of ~5000 semantically labeled molecules drawn from GoodScents (13) and Leffingwell (14) flavor and fragrance databases; one square represents 100 molecules; three example training set molecules and their odor descriptions are shown: 2-methyl-2-hexenoic acid (top), 2,5-dimethyl-3-

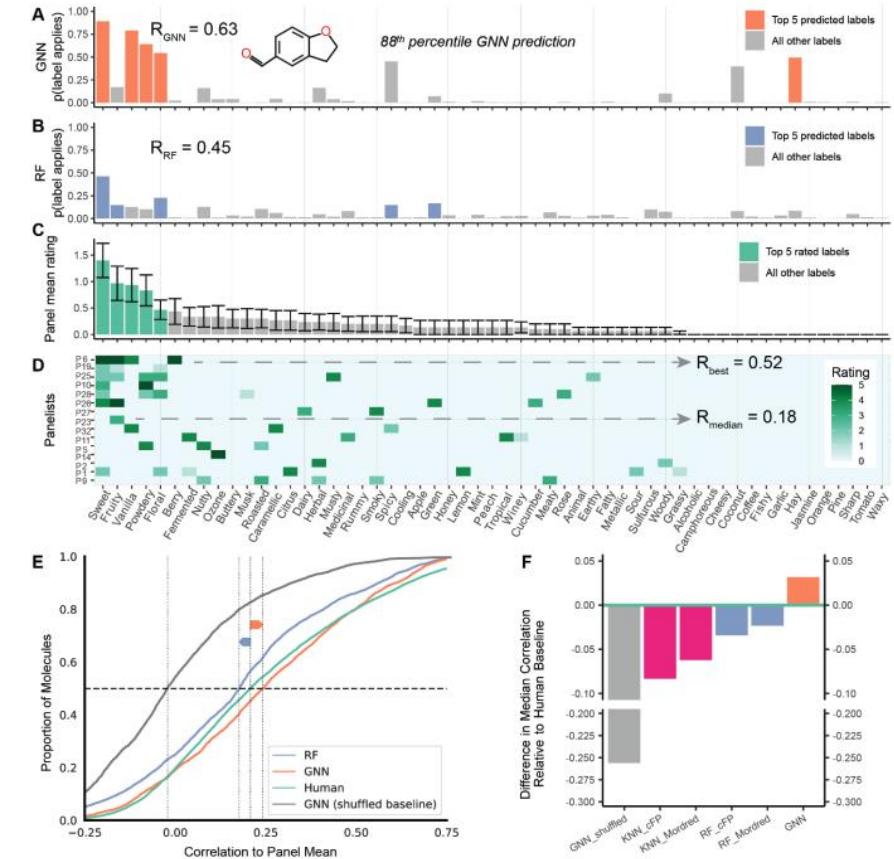


Fig. 2: GNN model displays human-level odor description performance. (A) GNN model label predictions, (B) random forest (RF) model label predictions, (C) panel mean ratings with standard error bars, and (D) individual panelist ratings, averaged over 2 replicates, for the molecule 2,5-dihydrobenzofuran-5-carboxaldehyde. In panels A-C, the top 5 ranked descriptors are in orange (GNN),

Lee, Brian K., et al. "A principal odor map unifies diverse tasks in olfactory perception." *Science* 381.6661 (2023): 999-1006.

调香师

调香师是如何训练出来的?



调香师的培养过程结合了科学训练和艺术感悟，通常需要经历长时间的训练、经验积累以及对气味的敏锐感知。成为专业调香师往往需要以下几个步骤：

1. 化学基础和感官训练

- 学习化学知识：调香涉及复杂的化学反应和分子结构，调香师需要了解香料的分子构成和挥发性特性，以及如何安全处理这些化合物。
- 嗅觉训练：调香学校和香水公司会提供系统的嗅觉训练，让学员熟悉数百种甚至数千种原料的气味。学员需要学会区分不同类型的香气（如花香、果香、木香）以及气味的不同层次和持续时间。
- 嗅觉记忆：调香师必须建立庞大的“嗅觉记忆库”，这种记忆力的训练有助于在创作时准确找到符合需求的香料组合。

2. 专业教育和实践经验

- 调香学校：例如，法国的ISIPCA (Institut Supérieur International du Parfum, de la Cosmétique et de l'Aromatique Alimentaire) 和意大利的Mane等学校提供专门的调香课程。这些课程通常包括香料化学、香水历史、市场趋势和品牌定位等方面的学习。
- 学徒制度：一些著名香水品牌会设立学徒项目，学员通过与资深调香师的合作来获得实际经验。资深调香师会教导学员如何搭配香料、调整比例、以及处理不同香调层次（如前调、中调和后调）之间的平衡。

3. 创意与艺术修养

- 艺术欣赏与灵感：调香师的灵感常来自于文学、艺术、自然风光等。培养艺术感知能力对调香创作至关重要，有助于调香师将情感和主题融入香水设计。
- 市场需求理解：调香师还需要理解消费者的需求，追踪市场流行趋势，并在香水设计中融入品牌理念和个性。

4. 不断更新和创新

- 持续学习新原料：调香师需不断尝试新兴香料，探索不同的香料组合方式。
- 实验与反馈：每种新香型都需要多次实验、调试以及专家和客户的反馈，以达到最终的最佳香味平衡。

成为调香师需要在科学知识和艺术创作之间找到平衡，这种职业既是技术性的，又具备高度的艺术性和创造性。



让AI进行调香？？

- 表征学习（气味表征）
- 生成模型（气味混合生成）
- 强化学习（学习人类偏好）

AI调香师

如何让AI学习多种气味的表征空间，然后优化气味的混合进行调香，打造AI调香师？请设计研究思路。



要打造一个AI调香师，需要设计一个能学习多种气味的表征空间并优化混合方式的研究框架。以下是一个可行的研究思路：

1. 数据收集与表征学习

- **收集气味数据：**使用电子鼻（e-nose）设备或其他气体传感器获取各种气味的原始数据。气味通常由多种挥发性有机化合物（VOCs）组成，通过传感器检测到的化学信号可以用于建立气味的原始特征。
- **数据预处理：**收集到的原始信号需要标准化、降噪等预处理步骤，保证模型能从干净、规范的数据中学习。
- **表征空间的学习：**使用深度学习方法（如变分自编码器VAE、生成对抗网络GAN等）来学习气味的高维表征空间。可以采用迁移学习或对比学习方法，通过这些非监督学习模型捕捉气味的潜在特征。

2. 气味表征空间的优化

- **表征空间的解释性：**为了生成具有预期香气的混合气味，气味表征空间应具备一定的解释性。这可以通过对气味数据进行主成分分析（PCA）或使用多模态学习方法，使特定的气味特征（如花香、果香）在空间中具有可识别的特定位置。
- **气味特征因子的控制：**在表征空间中，气味的特征因子（如甜度、浓度）可以通过模型微调来实现精细控制。例如，通过使用基于先验知识的约束或正则化，使模型在生成气味时能够有目的地调节这些特征因子。

3. 生成模型的训练

- **生成气味组合：**利用生成对抗网络（GAN）或变分自编码器（VAE）生成气味组合。在训练过程中，可以通过优化目标函数来控制生成的气味混合物符合特定的香气调性或风格。
- **风格迁移与样式优化：**在生成模型中，利用风格迁移（Style Transfer）技术来控制香味的基调和风格。例如，可以从不同的香水样本中提取风格特征，将其作为生成气味混合物的目标特征。可以通过调香专家提供的偏好标签进行有监督训练，使AI生成符合人类偏好的气味。

4. 人类偏好与反馈优化

- **基于偏好的强化学习：**通过人类用户的反馈数据，利用强化学习（如PPO算法）优化调香过程。反馈信号可以包含用户的满意度评分，从而引导模型在表征空间中寻找更受欢迎的香味组合。
- **模拟气味扩散：**建立气味分子的扩散模型以模拟调香后香味的实际效果。通过在虚拟环境中测试气味扩散特性，优化香气在空气中的传播效果，使生成的调香方案更具实际应用价值。

5. 验证与应用

- **嗅觉测试与评估：**在实验室中进行盲测实验，使用调香专家的评价来验证AI生成的香味效果。可以将AI生成的气味样本与现有香水进行对比，分析其相似度和创新性。
- **实际应用与生产优化：**在商业化生产中，通过模型的可调参数对不同气味浓度进行微调，以满足不同市场需求。可以应用于定制化香水、空气清新剂等产品，为用户提供个性化的香气方案。

这种方法可以通过深度学习、生成建模和强化学习等技术，使AI能够学习和生成符合用户偏好的气味组合，从而实现智能调香师的设计和应用。

设计一种动态变化的香氛能维持长期的愉悦感

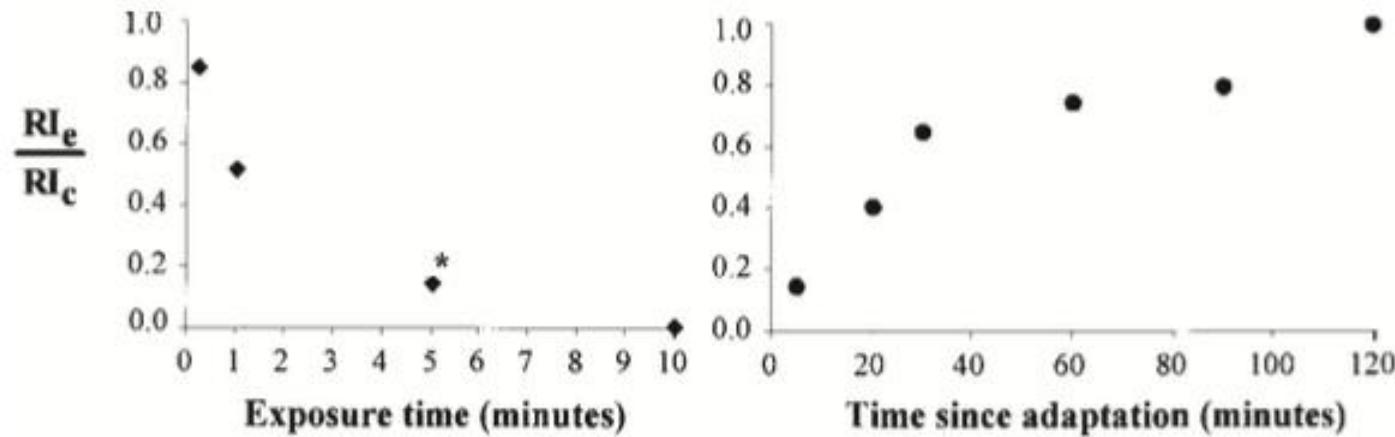


Figure 1 The effect of pre-exposure duration to the odorant on the degree of adaptation among *Drosophila* larvae. The response index (RI) was calculated by subtracting the number of larvae that crawled to the blank disk from the number of larvae that crawled to the odorant disk and dividing by the number of larvae that moved from the starting position. Increasing durations of pre-exposure to the odorant greatly reduced the number of larvae that responded to the odorant disk during a 5 min test period. Adapted from (Wuttke, 1999).

Dalton, P. (2000). Psychophysical and behavioral characteristics of olfactory adaptation. *Chemical senses*, 25(4), 487-492.

5分钟之后，已经适应味道。

40分钟之后，才恢复对味道敏锐度。

应该怎么设计动态香氛的开关？

Online course

<https://www.bilibili.com/video/BV1L34y1p7a7/>

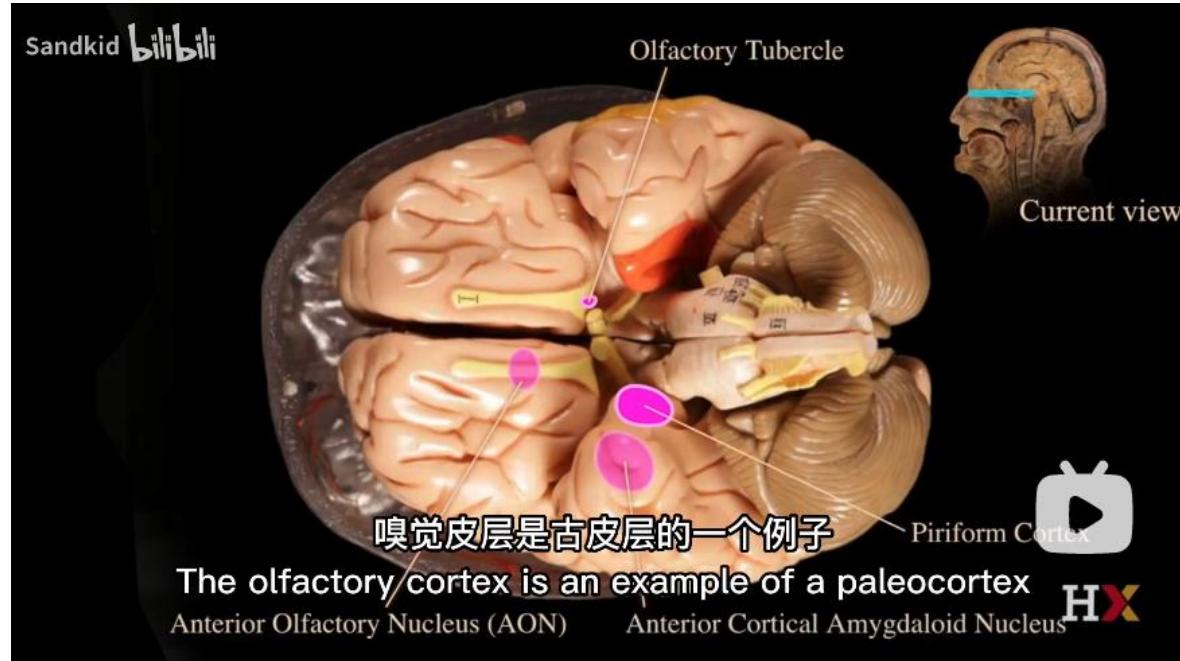
【哈佛大学】嗅觉受体——花香未必香

<https://www.bilibili.com/video/BV1vN4y1M7rM>

【哈佛大学】嗅觉通路——我们闻到香味的分子通路

<https://www.bilibili.com/video/BV1xr4y1u75w>

【哈佛大学】嗅觉系统的解剖解释



Interesting videos

<https://www.bilibili.com/video/BV1if4y1J7qU/>

【纪录片】寻香之旅 Nose (2021)

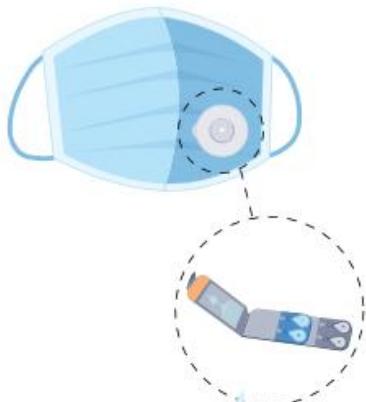
<https://www.bilibili.com/video/BV1PL411b7sc>

职业调香师出道前要修炼多少年？

Wearable breath analysis

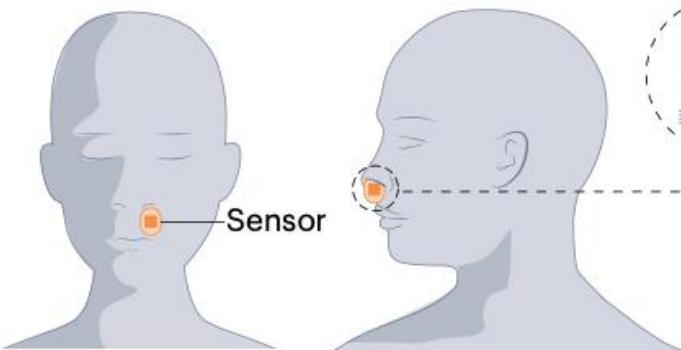
20世纪70年代，首次通过色谱法对呼吸进行分析，证明了呼出气中存在有机物质。从那时起，在呼吸中已经发现了3000多种挥发性有机成分（VOC），这些成分检查可以帮助疾病诊断。

Disposable face masks



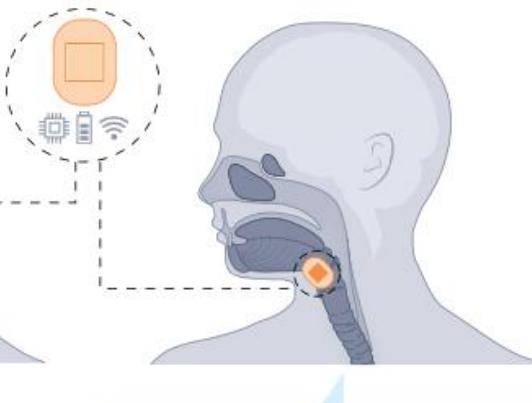
Sampling, sample preparation and sensing modules integrated into a face mask

In- or under-nose patches



Continuous monitoring through exhaled breath by in- or under-nose patches

In-trachea patches



Patch placed in the trachea for self-powered monitoring using existing metabolites (lactate and/or glucose)

Vaping devices

