Chemosensory System

Spring 2013

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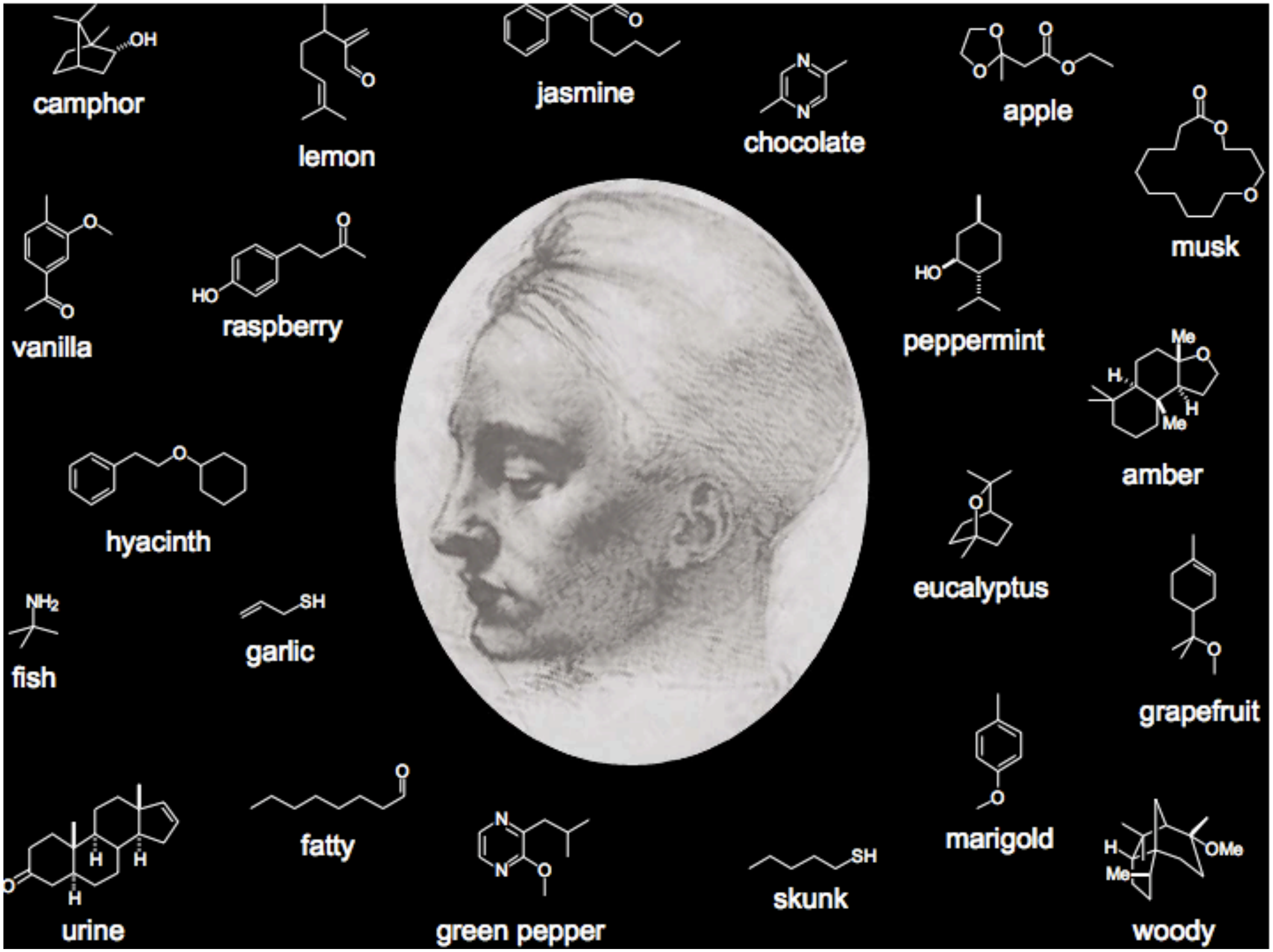
Reading: Chapter 15, Neuroscience by Purves et al; Fifth edition (Sinauer Publishers)

Learning Objectives

- Anatomical and functional organization of the olfactory system
- Salient expression characteristics of olfactory receptor genes
- Organization of odorant receptor inputs in the olfactory epithelium and olfactory bulb
- Molecular mechanisms of odorant transduction
- Common and unique features of the gustatory system

Odorants are very diverse chemical compounds (humans can detect ~10,000 different smells)



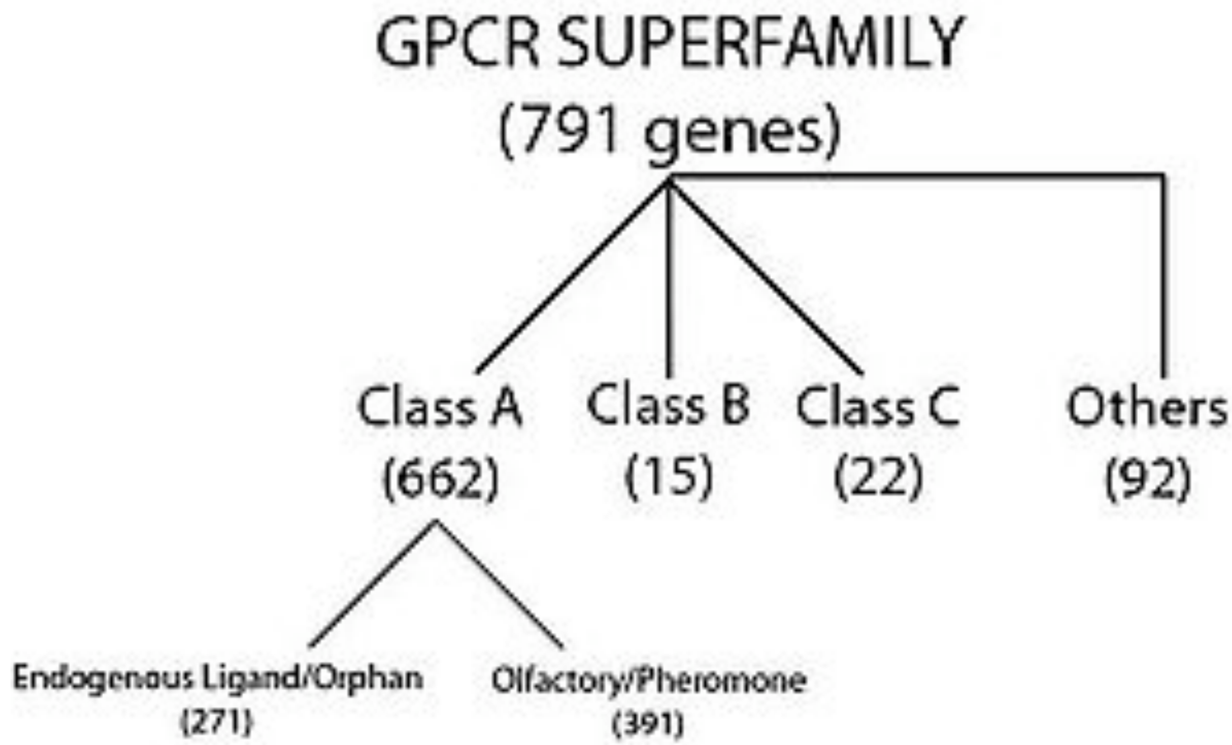
From Linda Buck's Nobel Prize Lecture

The Enigma of Smell

- A particular chemical compound can evoke a distinct smell

- That smell can also be evoked by a different compound or mixture of compounds

- What is the receptor(s) in the nose that conveys this information to the brain?

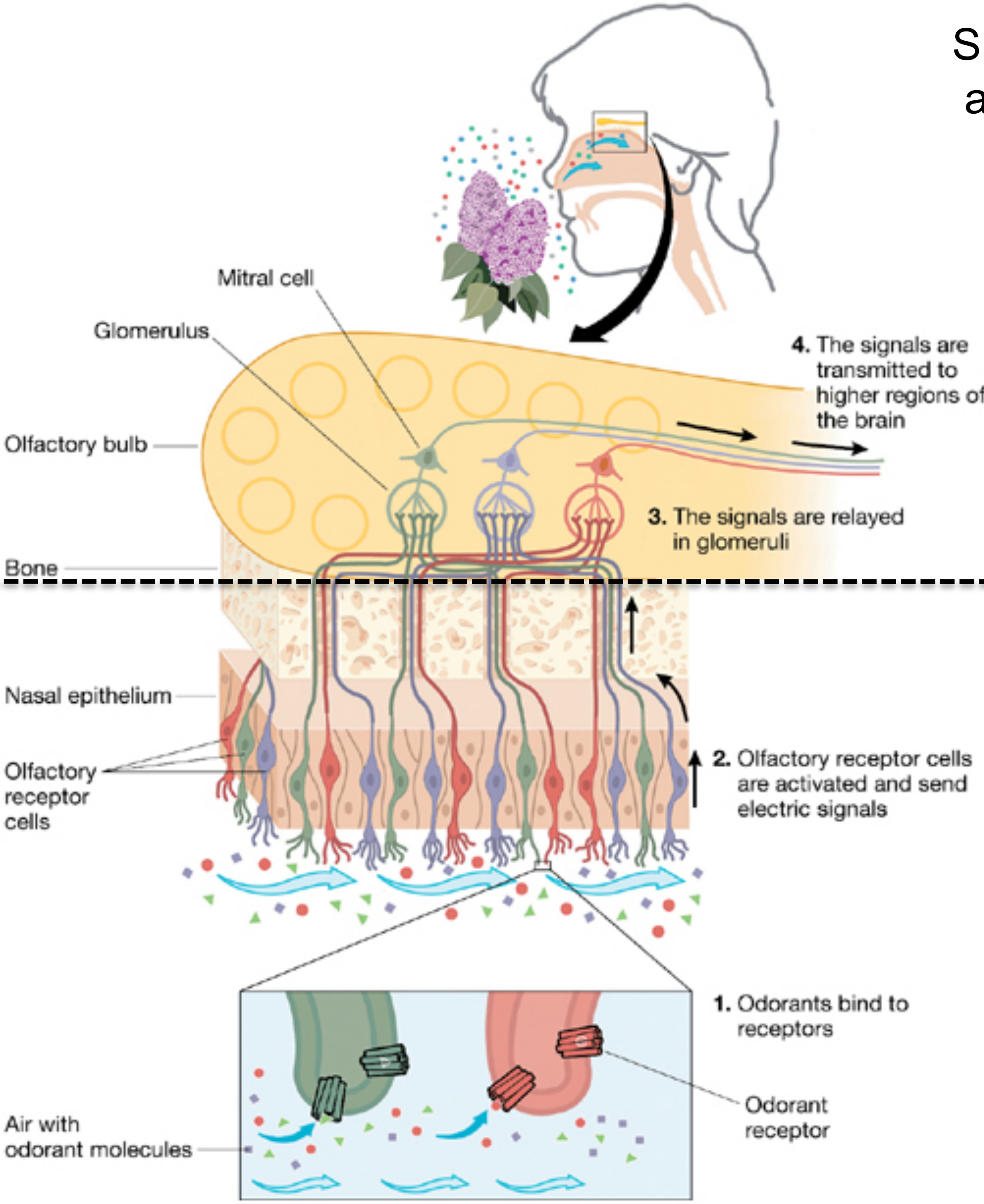


Classification Scheme of GPCRs.
Class A (Rhodopsin-like)
Class B (Secretin-like)
Class C (Glutamate Receptor-like)
Others (Adhesion (33), Frizzled (11), Taste type-2 (25), unclassified (23))

Why study the olfactory system?

- Largest group and most diverse of the GPCR family
- Olfactory system re-innervates its connections to the brain from the PNS every month
- Nose is very accessible for experimentation
- Olfactory neurons are also regenerated after injury (*model of nervous system repair, e.g. spinal cord trauma*)
- *Stem cells regenerate these lost neuron*
- *Smell therapy may offer new insight into the limbic system, e.g. PTSD and neuro-economics*

Smell begins at the nose and ends in the brain



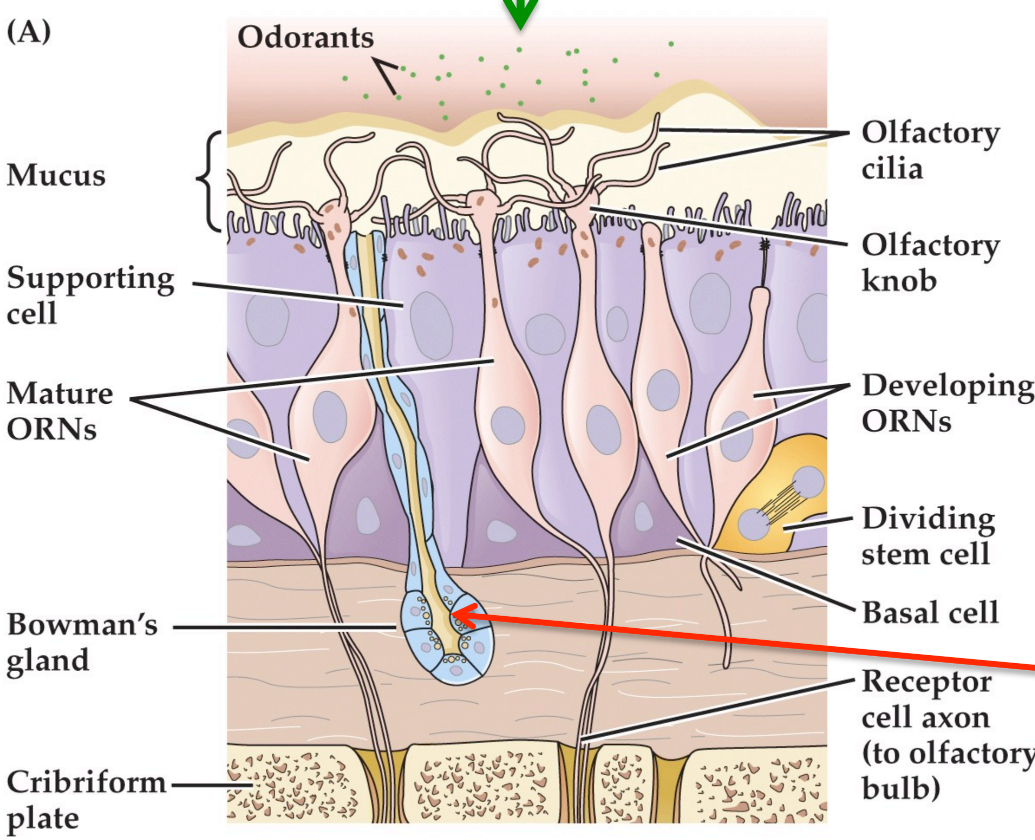
Inside the brain

Inside the nose

EMBO reports (2007) ***8*, 629 - 633**

The olfactory epithelium of the nose

"odorant release"



Mucus producing gland

NEUROSCIENCE 5e, Figure 15.7 (Part 1)

To the brain

Odorants dissolve in mucus

Concentration of odorant matters

Olfactory receptor neurons fire **action potentials**

Small diameter, non-myelinated neurons

Odorant receptor (OR) proteins

Humans have 340 functional Receptors; many pseudogenes

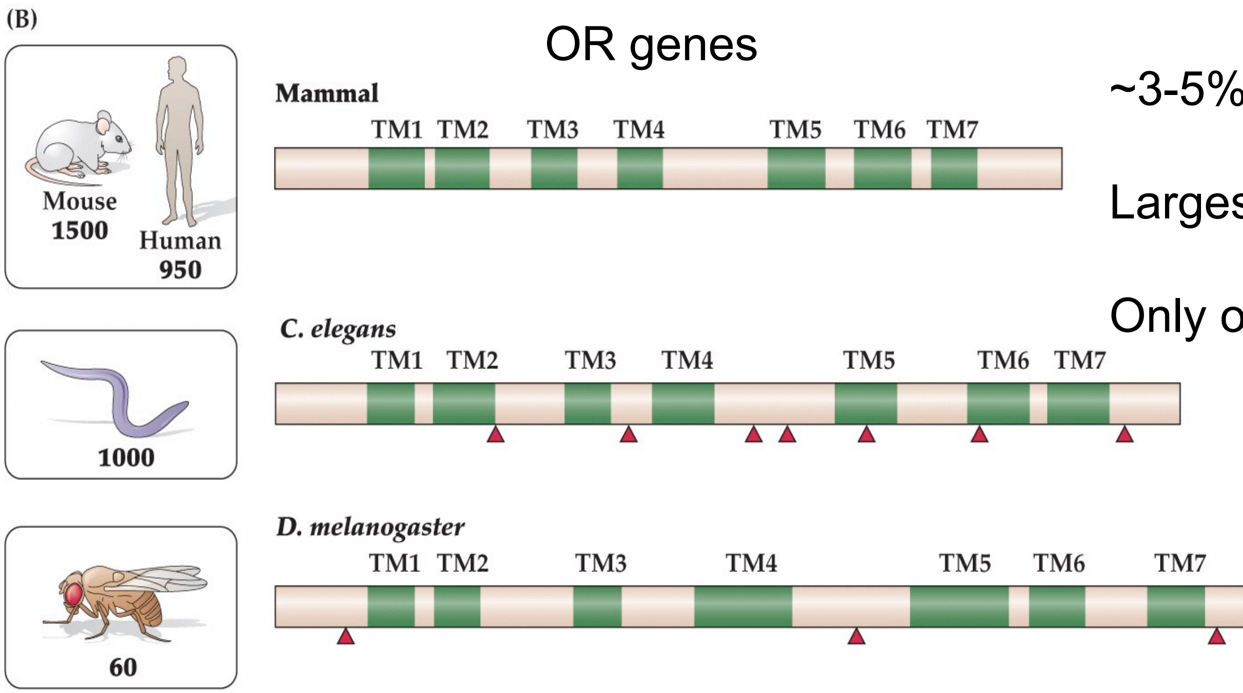
One receptor gene: One neuron

~3-5% of total mammalian genome

Largest gene family

Only one allele is expressed

OR genes



NEUROSCIENCE 5e, Figure 15.9 (Part 2)

Characteristics of OR genes

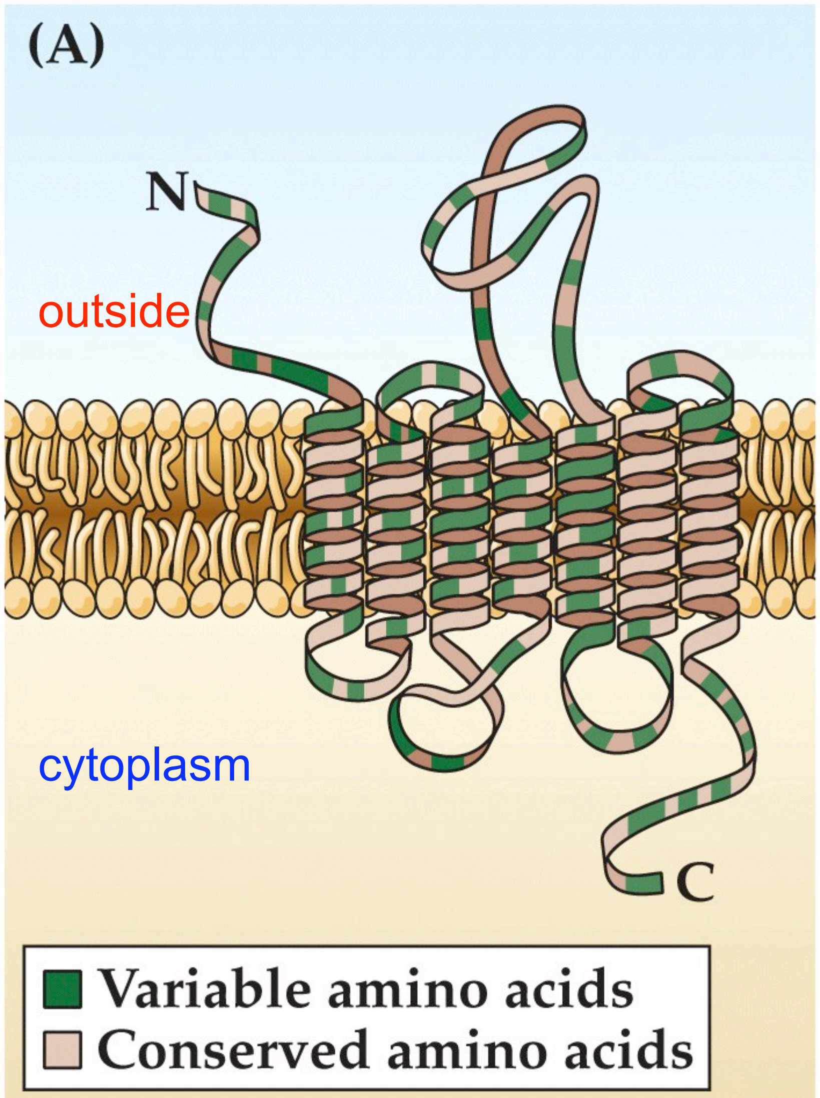
One OR gene expressed per neuron – pseudogenes [no AUG start; premature STOPs] initially expressed, replaced by functional one

Expression of receptor genes around olfactory epithelium is mostly stochastic –topographic by place in epithelium
-exceptions shown in mice for certain gene families

Human olfactory receptor genes found on many chromosomes, in clusters (families)

55 ORs respond to octanol

Structure of odorant receptor



NEUROSCIENCE 5e, Figure 15.9 (Part 1)

7-helix transmembrane receptor protein

GTP-binding protein coupled receptor (GPCR)

ORN replaced every 6-8 weeks

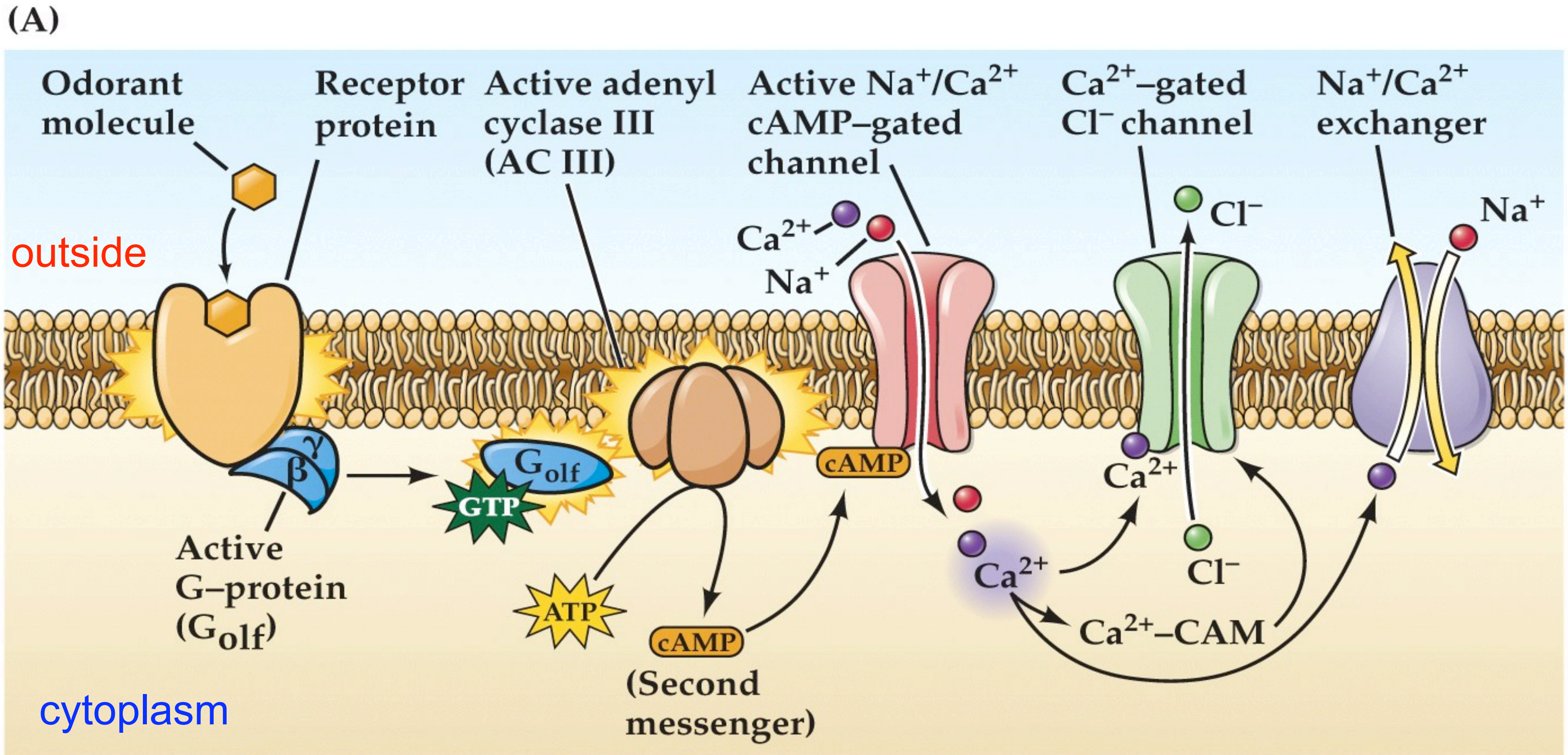
We lose smell perception with age

Anosmias: loss of particular smell sensation

Transient anosmia: stuffy nose; drug induced

Smell dysfunction: Alzheimer's disease

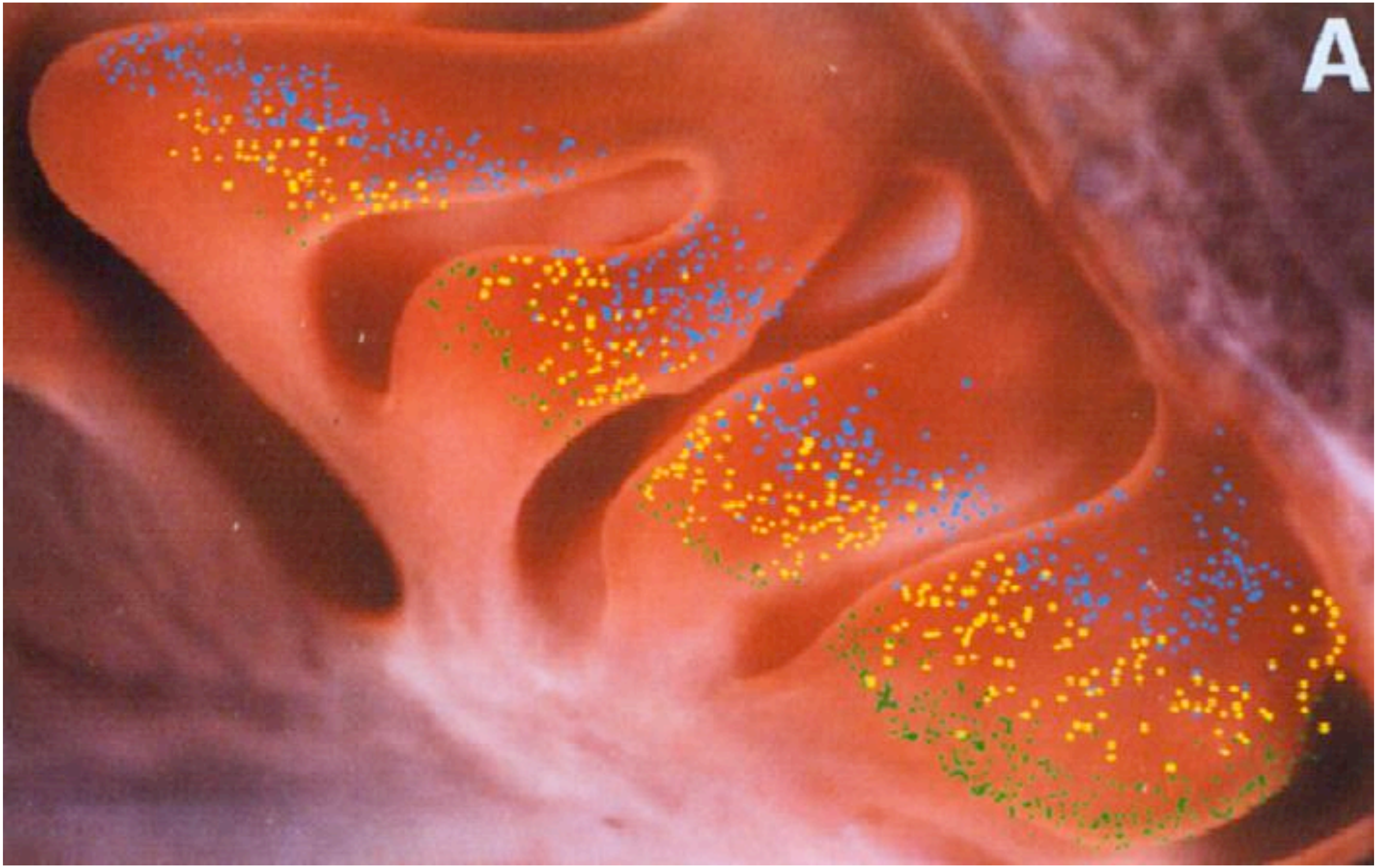
Molecular mechanisms of odorant transduction



NEUROSCIENCE 5e, Figure 15.11 (Part 1)

Olfactory transduction starts with odorant binding to the GPCR and involves both second messengers (cAMP) and ionic currents (Ca^{2+}, Na^{+})

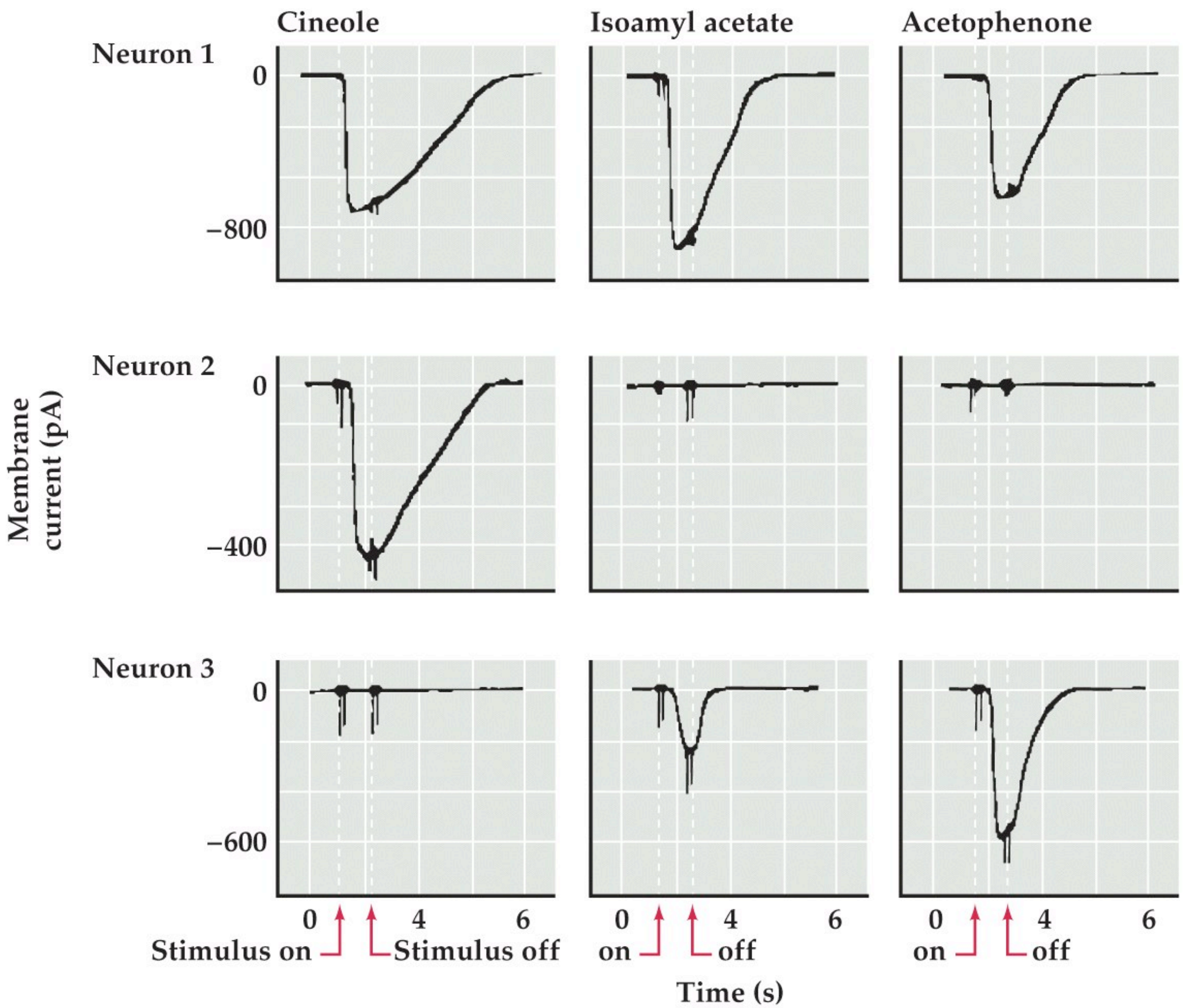
Very strong adaptation to smells – one of the senses that is strongly or fast adapting



3 distinct zones: odorant receptors or receptor subfamilies are expressed.
Green: F12, F23, I7 I8, and J2; Yellow: F3 and F5; Blue: F6, J7, and J14.

Cell 74: 309-18

Responses of receptor neurons to selected odorants



The optimal odorant is very difficult to find.

NEUROSCIENCE 5e, **Figure 15.12**

Organization of the mammalian olfactory bulb

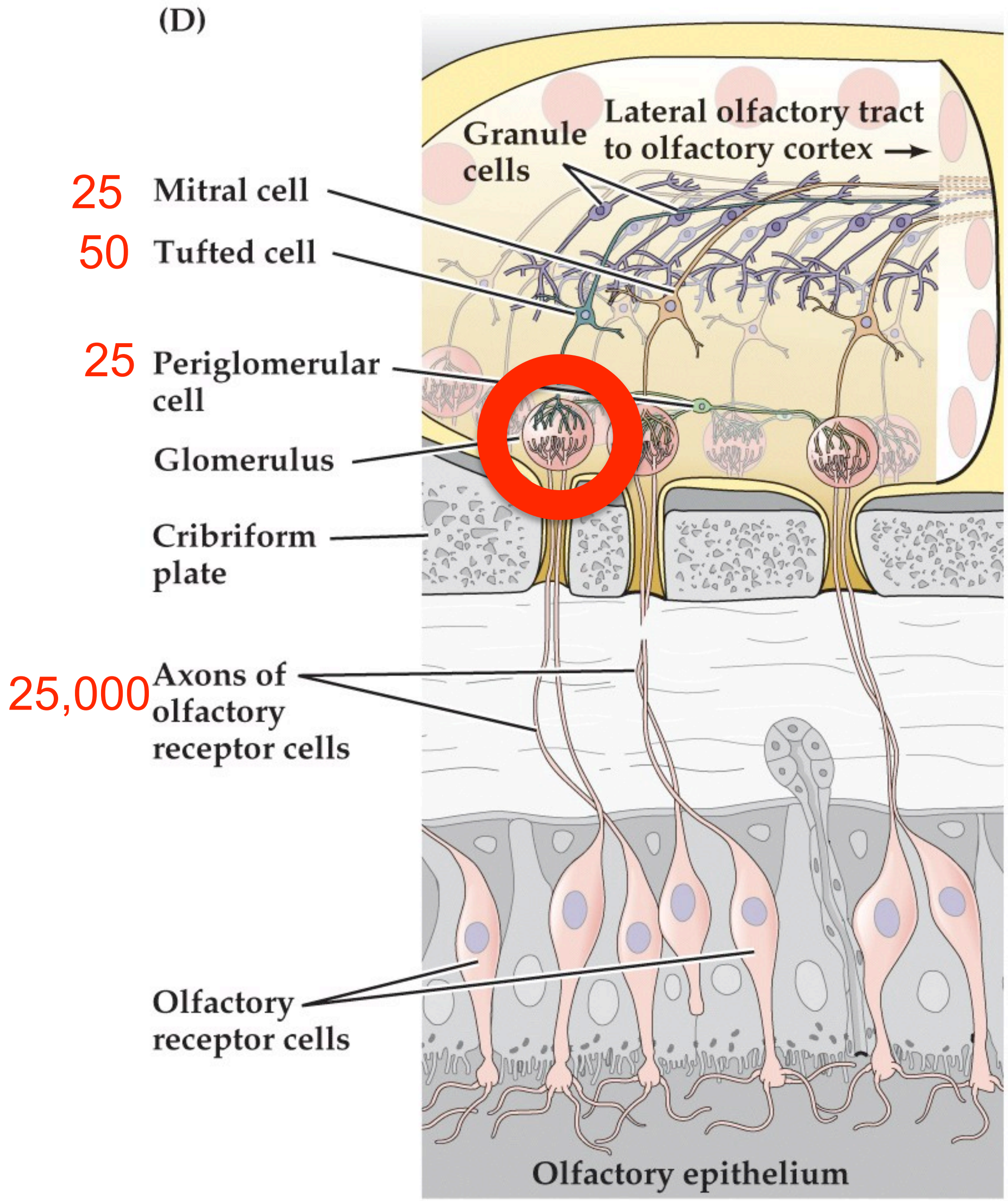
Mitral & tufted cell dendrites in glomerulus with axons projecting to pyriform cortex, amygdala & entorhinal cortex

Reinnervation of the glomerulus;specific for 1 receptor type

Axons grow through cribriform plate

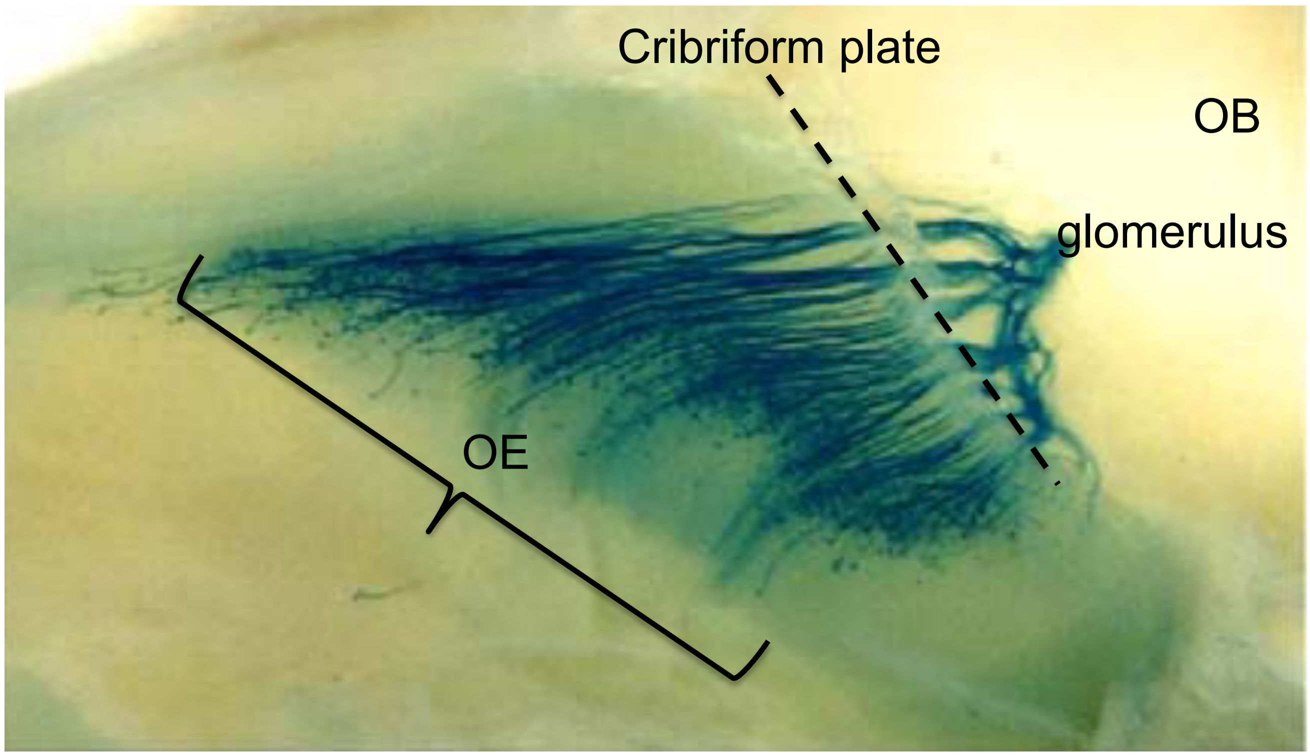
Neurons replaced every few weeks

Olfactory cilia are up to 30 micrometer long



***NEUROSCIENCE 5e*, Figure 15.14 (Part 4)**

Transgenic mouse nasal cavity and brain showing olfactory epithelium (OE) and olfactory bulb (OB) from a single olfactory receptor (OR) labeled with lacZ and stained with X-gal



ORs are widely distributed in the OE

Olfactory sensory neurons converge on a single glomerulus

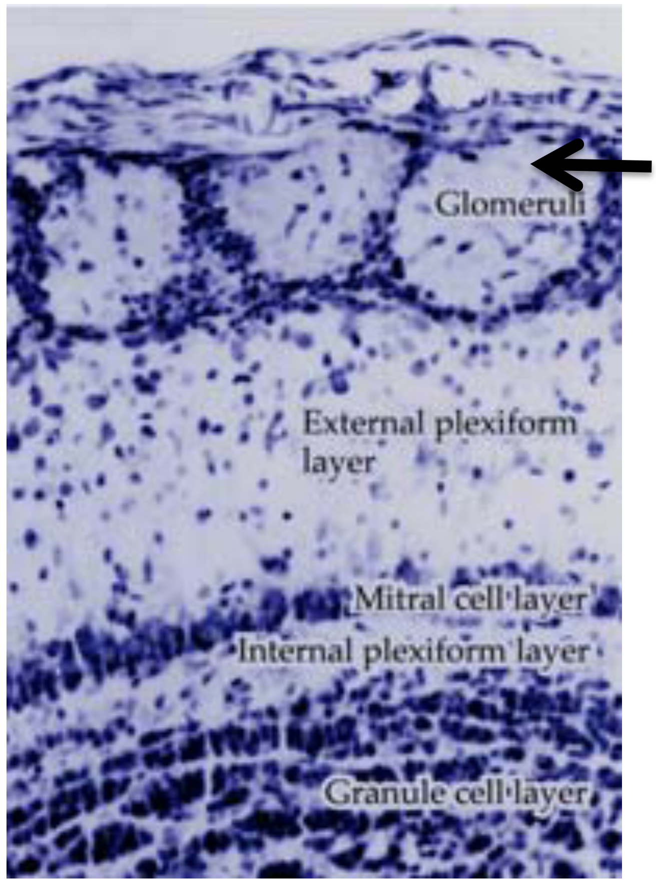
Organization of the mammalian olfactory bulb

25,000 ORN inputs/ glomerulus

1,000 ORN inputs/ mitral/tufted cell

100 intrinsic neurons (periglomerular, granule) = interneurons / mitral or tufted cell

MANY glomeruli / mitral cell; MANY Mitral cells/glomerulus



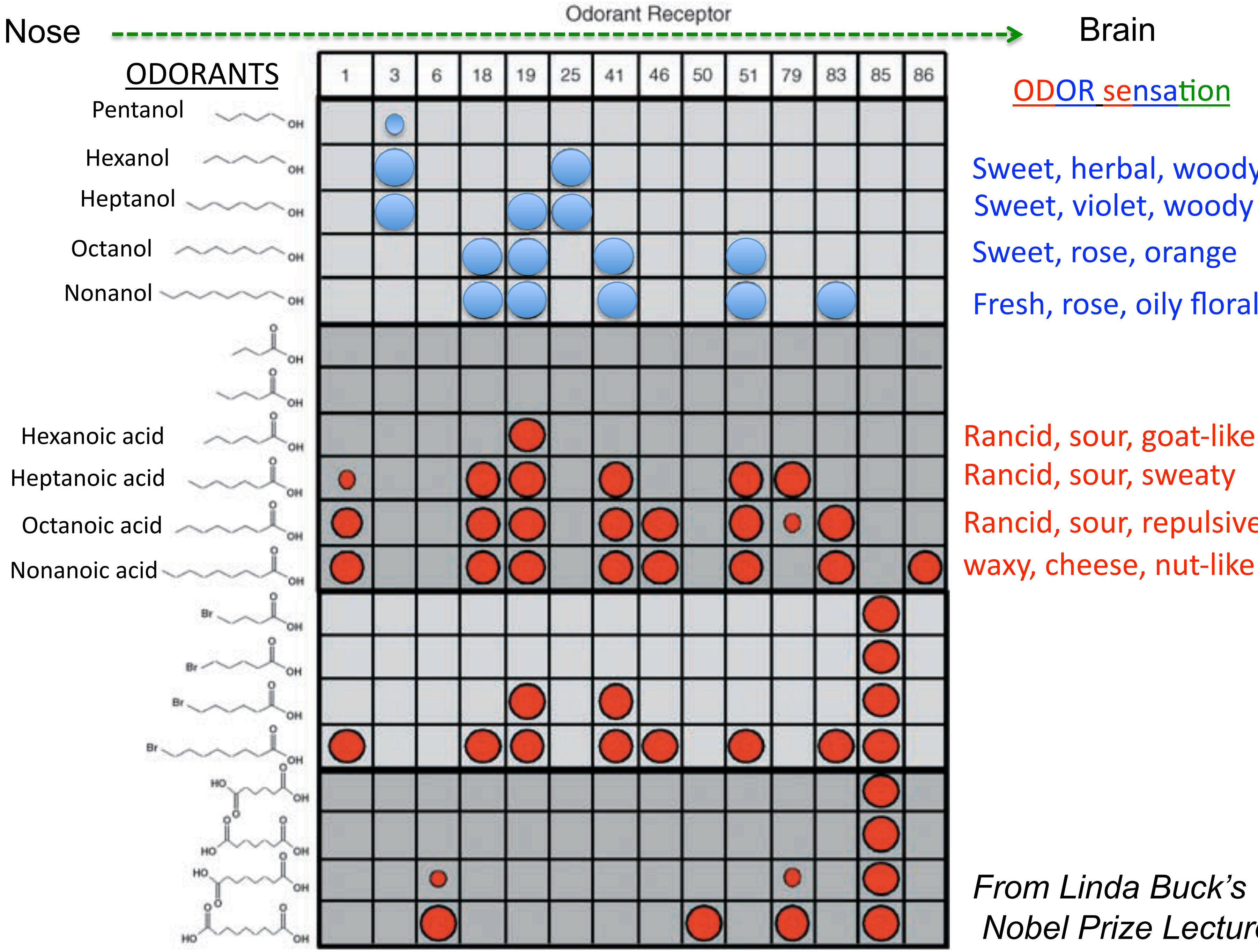
Inputs; much "sharpening" of signal here; mitral cell tufts = dendrites

Output to cortex

interneurons

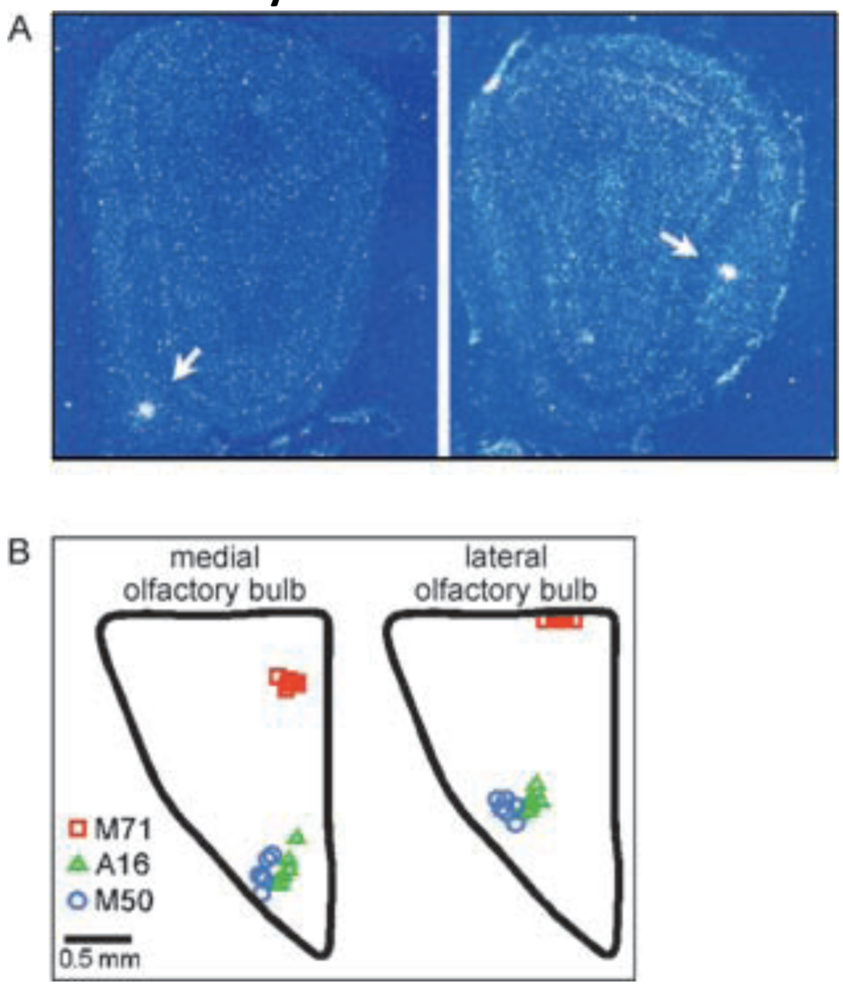
Increasing odorant conc. Increases activity of glomeruli and the #s activated

Distinct odorants can activate one or few glomeruli



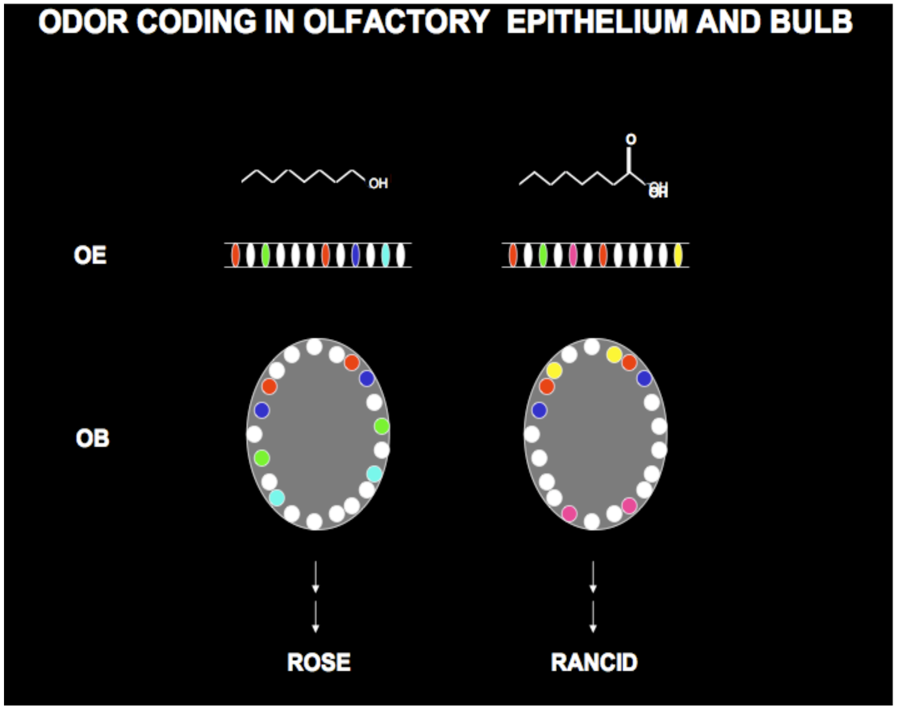
From Linda Buck's Nobel Prize Lecture

Axons of neurons of the same OR converge In the olfactory bulb



A). A single OR gene probe hybridized to sensory axons in 1 or 2 glomeruli on either side of the olfactory bulb

B). Different OR probes hybridized to different glomeruli and those glomeruli had similar locations in six different bulbs.



OE: Inputs from different ORs are indicated by different colors; dispersed ensemble of neurons

OB: Specific combination of glomeruli whose spatial arrangement is similar among individuals. Partially overlapping combinations of OR inputs generate distinct odor perceptions

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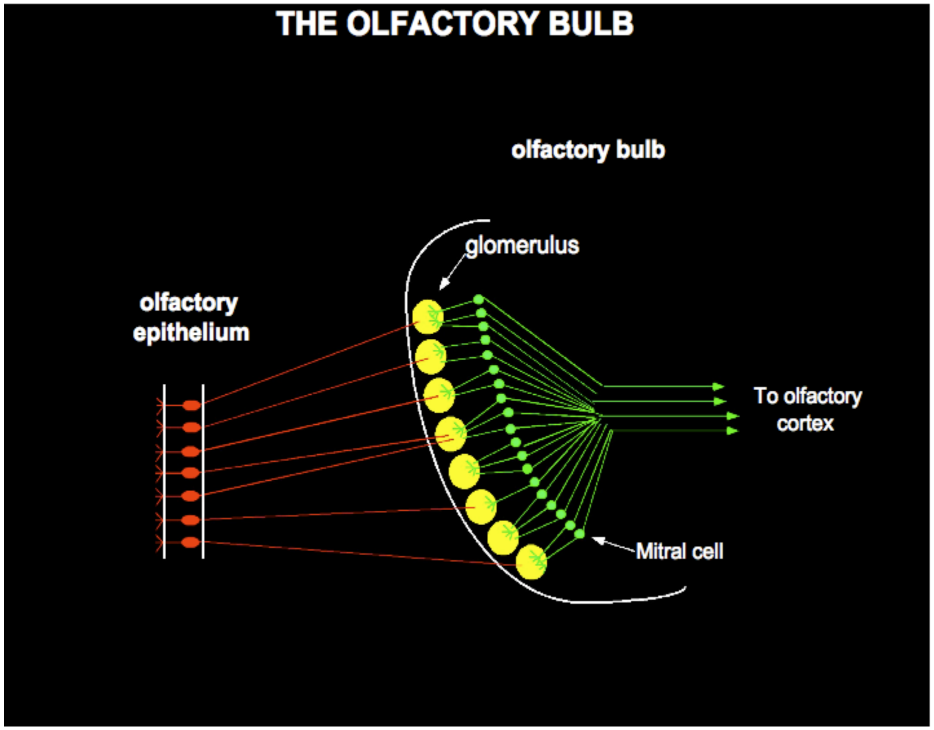
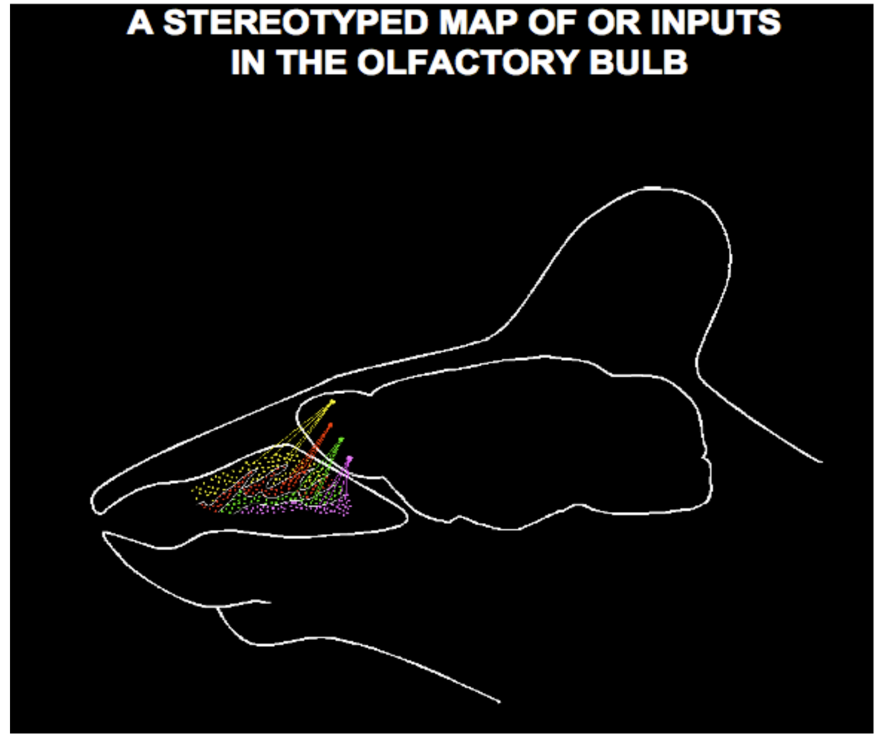
Schematic diagram showing the organization of odorant receptor inputs in the olfactory epithelium and olfactory bulb





Inputs from different ORs are segregated in different neurons and glomeruli in the OE and OB.

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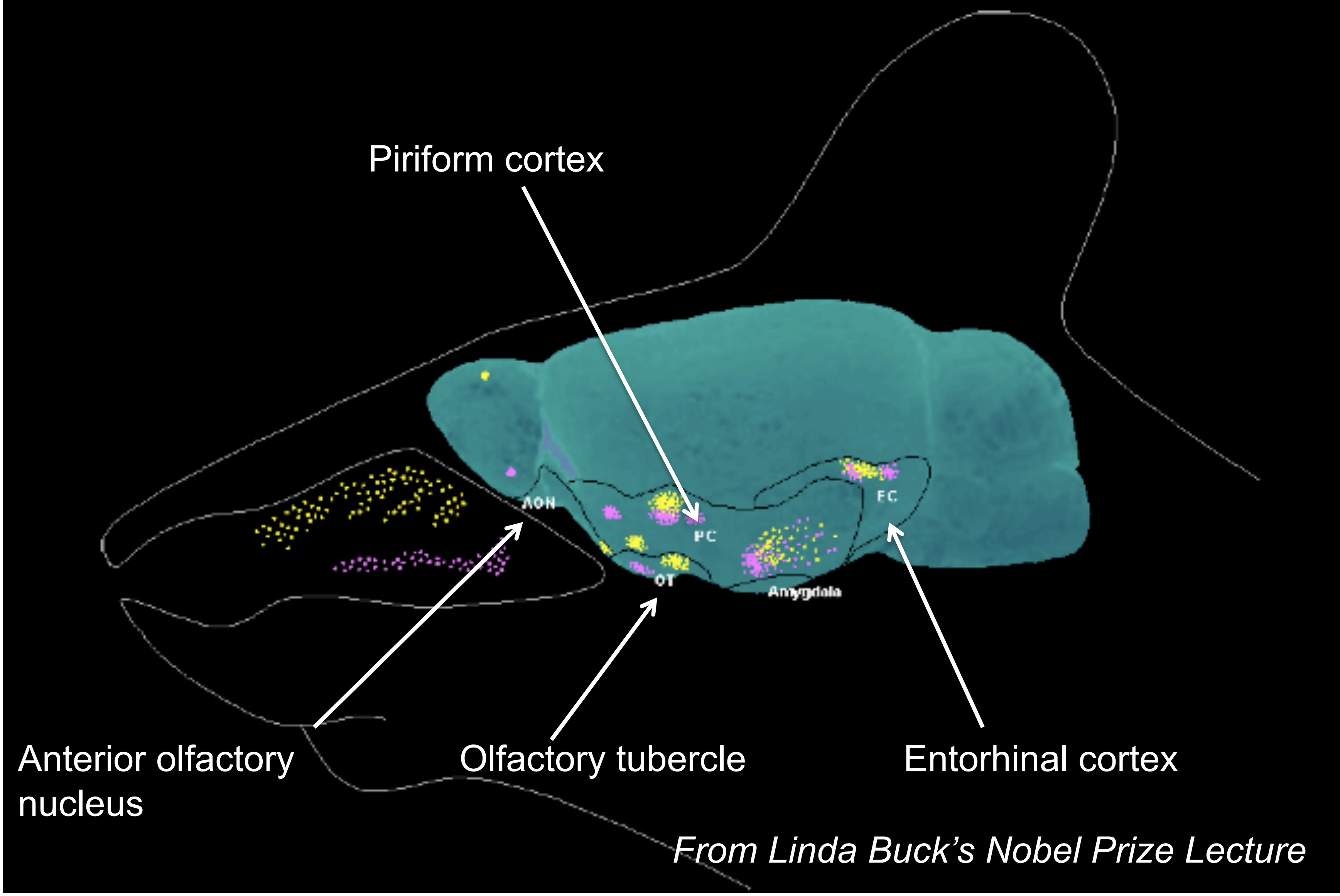
A STEREOTYPED MAP OF OR INPUTS IN OLFACTORY CORTEX



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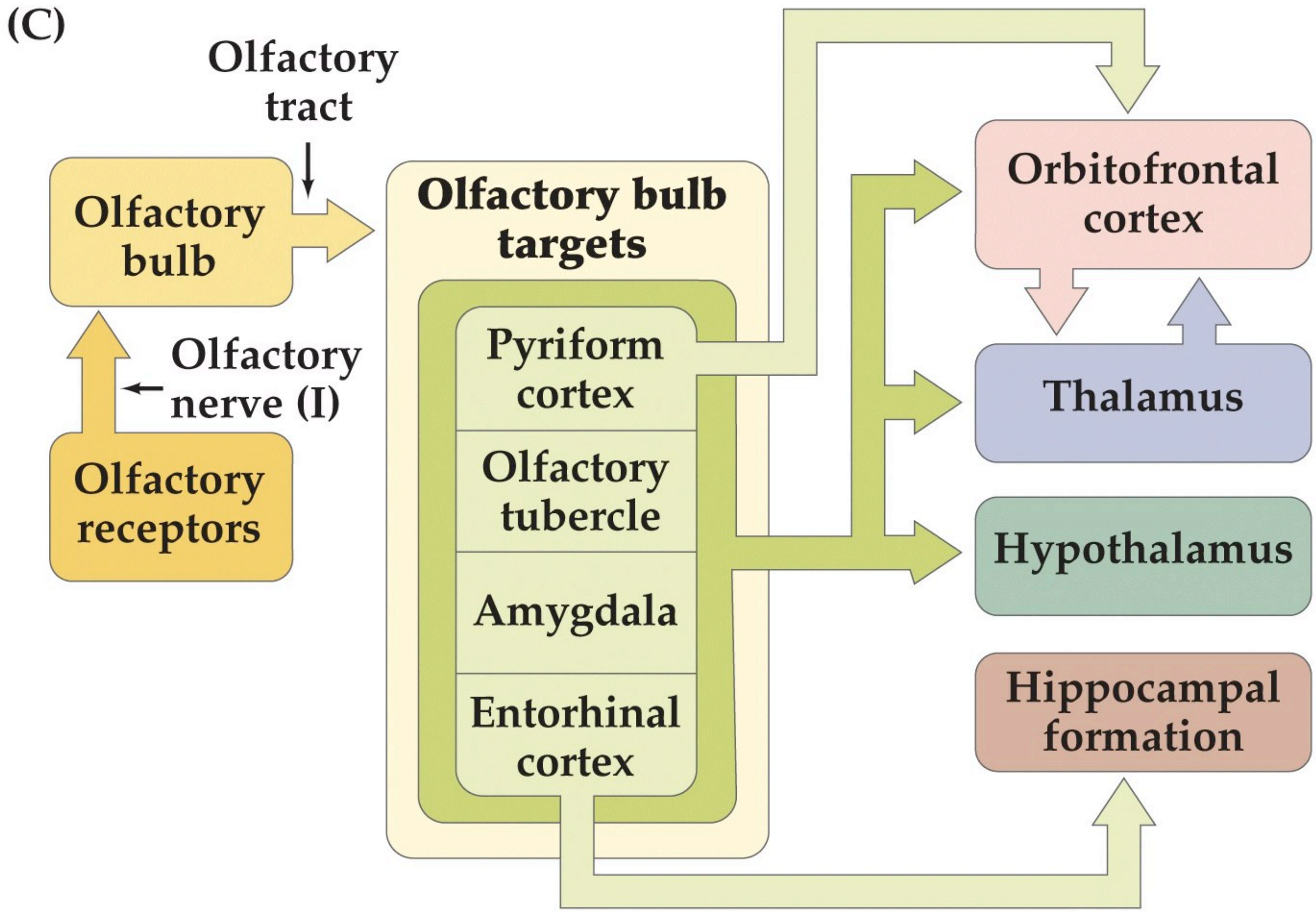
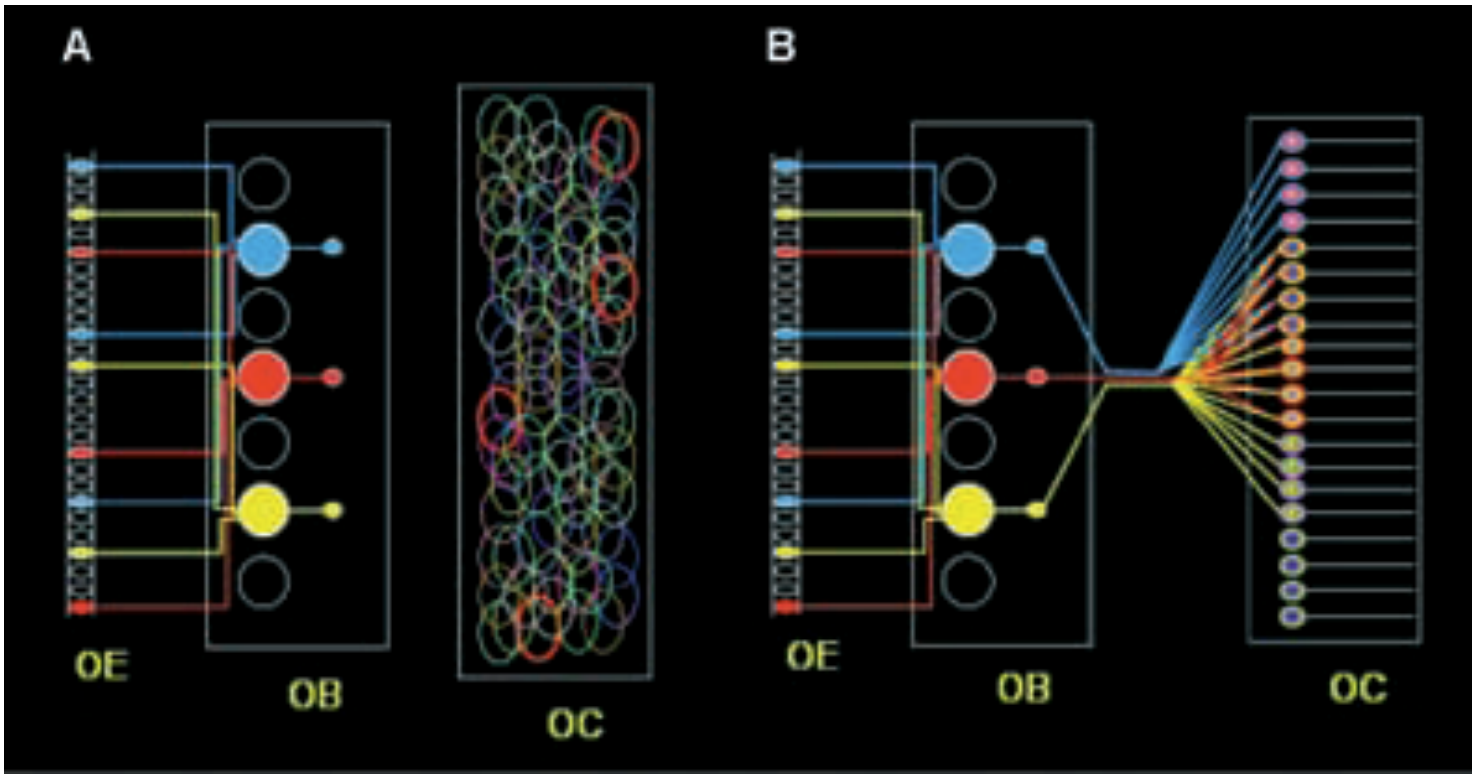


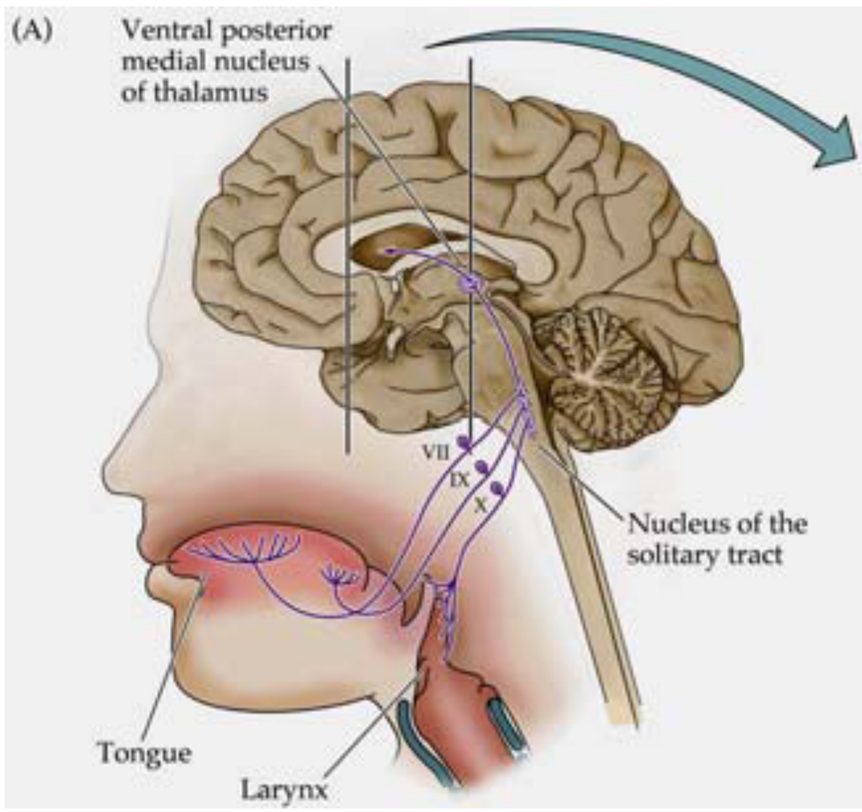
NEUROSCIENCE 5e, **Figure 15.1 (Part 2)**

Schematic diagrams showing the organization of odorant receptor inputs in the olfactory epithelium (OE), olfactory bulb (OB), and olfactory cortex (OC)



Inputs from different ORs are segregated in different neurons and glomeruli in the OE and OB. In contrast, it appears that different receptor inputs overlap extensively in the OC (A) and that single cortical neurons receive signals from a combination of receptors (B)

The human taste system

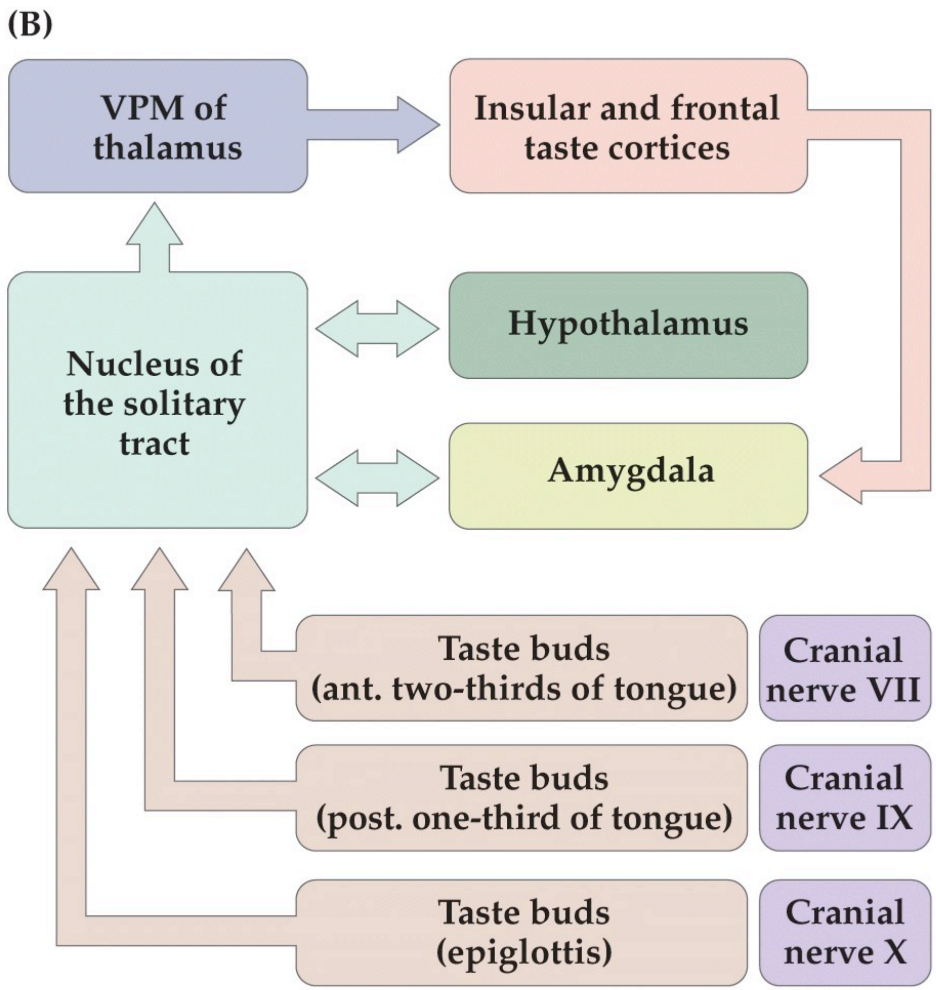


Cortical processing unclear

All converge to NTS, then thalamus

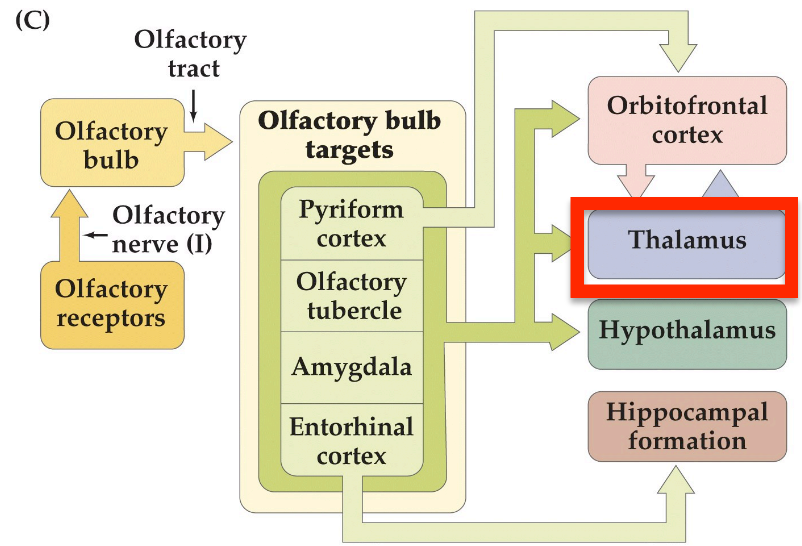
Nerves VII, IX, X from different regions of the mouth

The human taste system



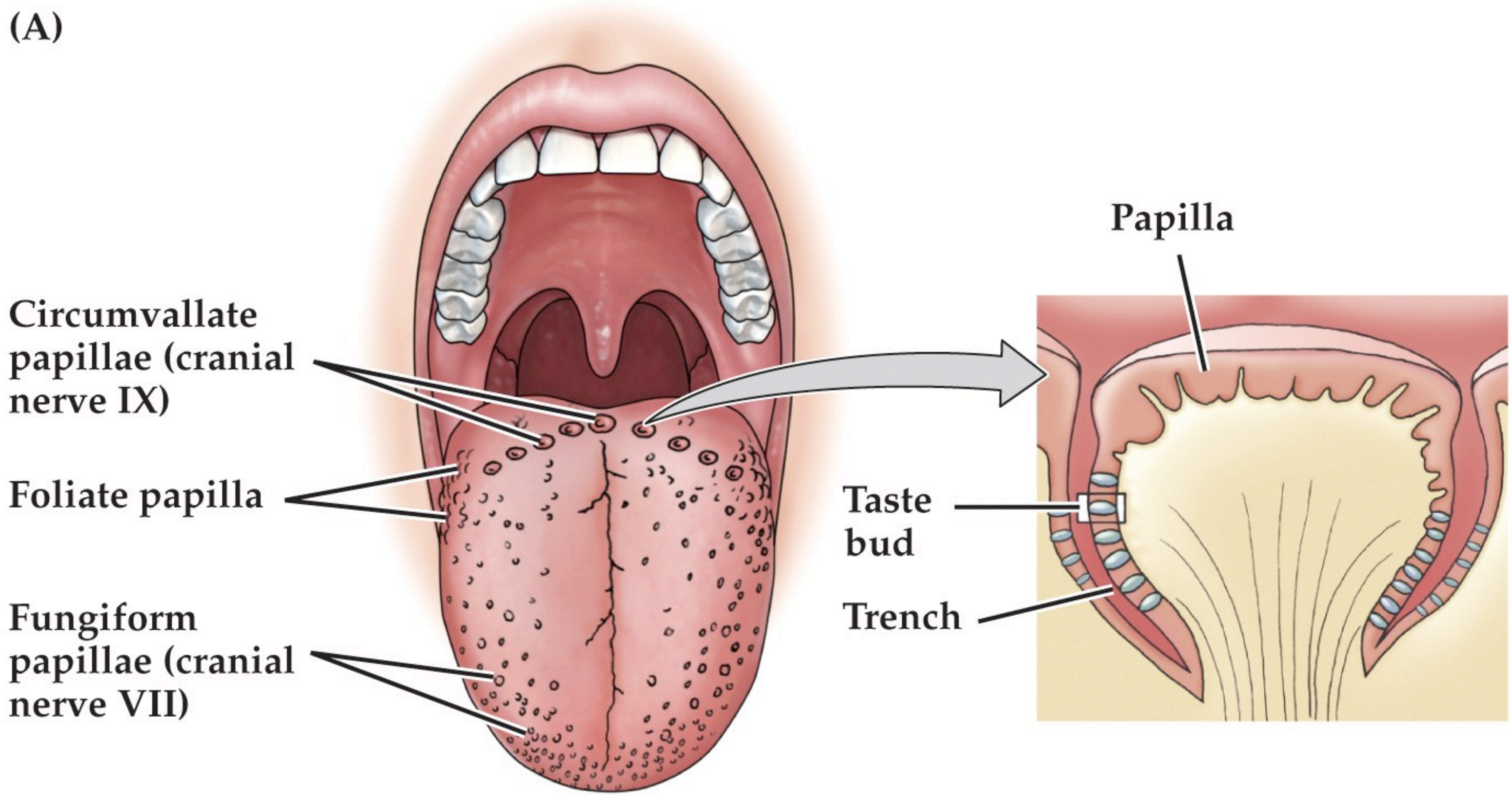
NEUROSCIENCE 5e, **Figure 15.17 (Part 2)**

Human Olfactory System



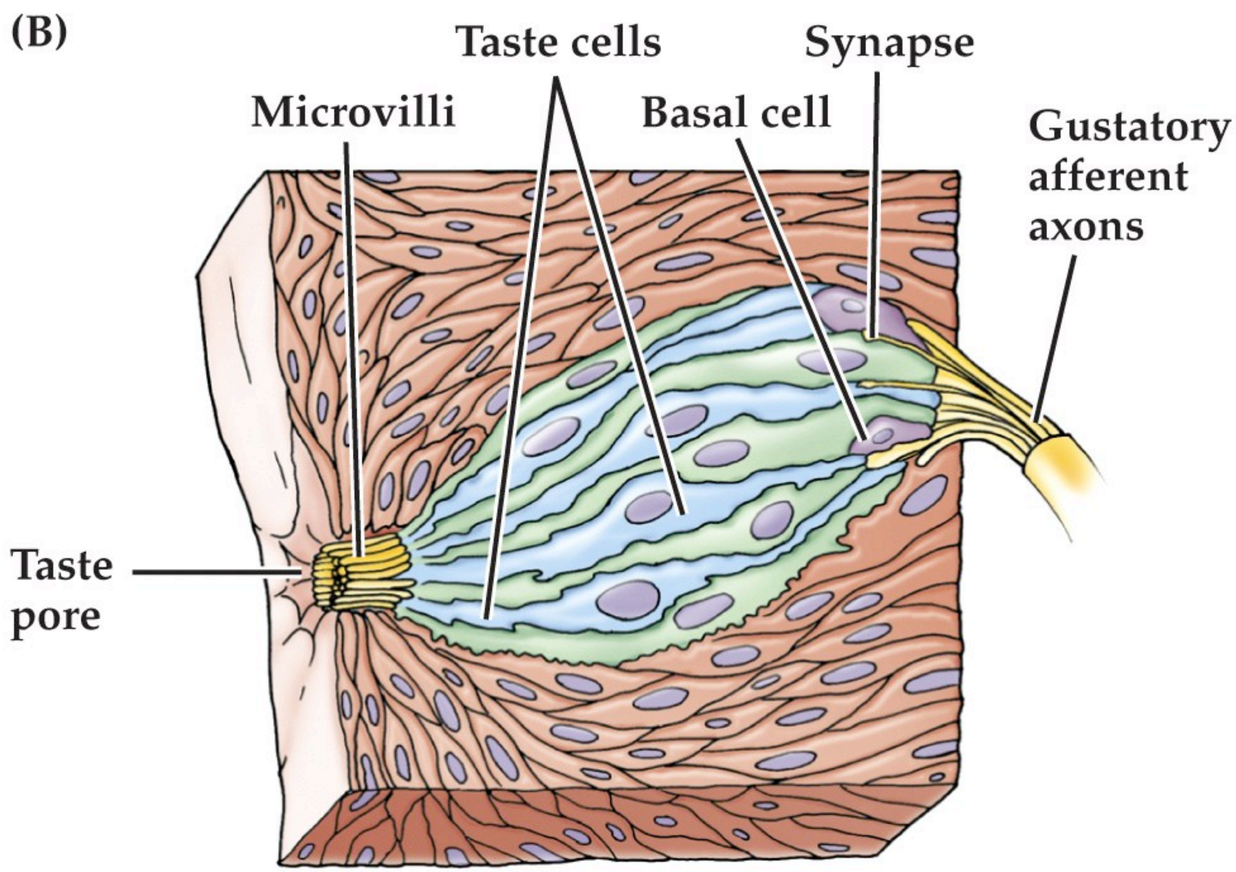
NEUROSCIENCE 5e, **Figure 15.1 (Part 2)**

Taste buds and taste papillae



NEUROSCIENCE 5e, **Figure 15.18 (Part 1)**

Taste buds and taste papillae



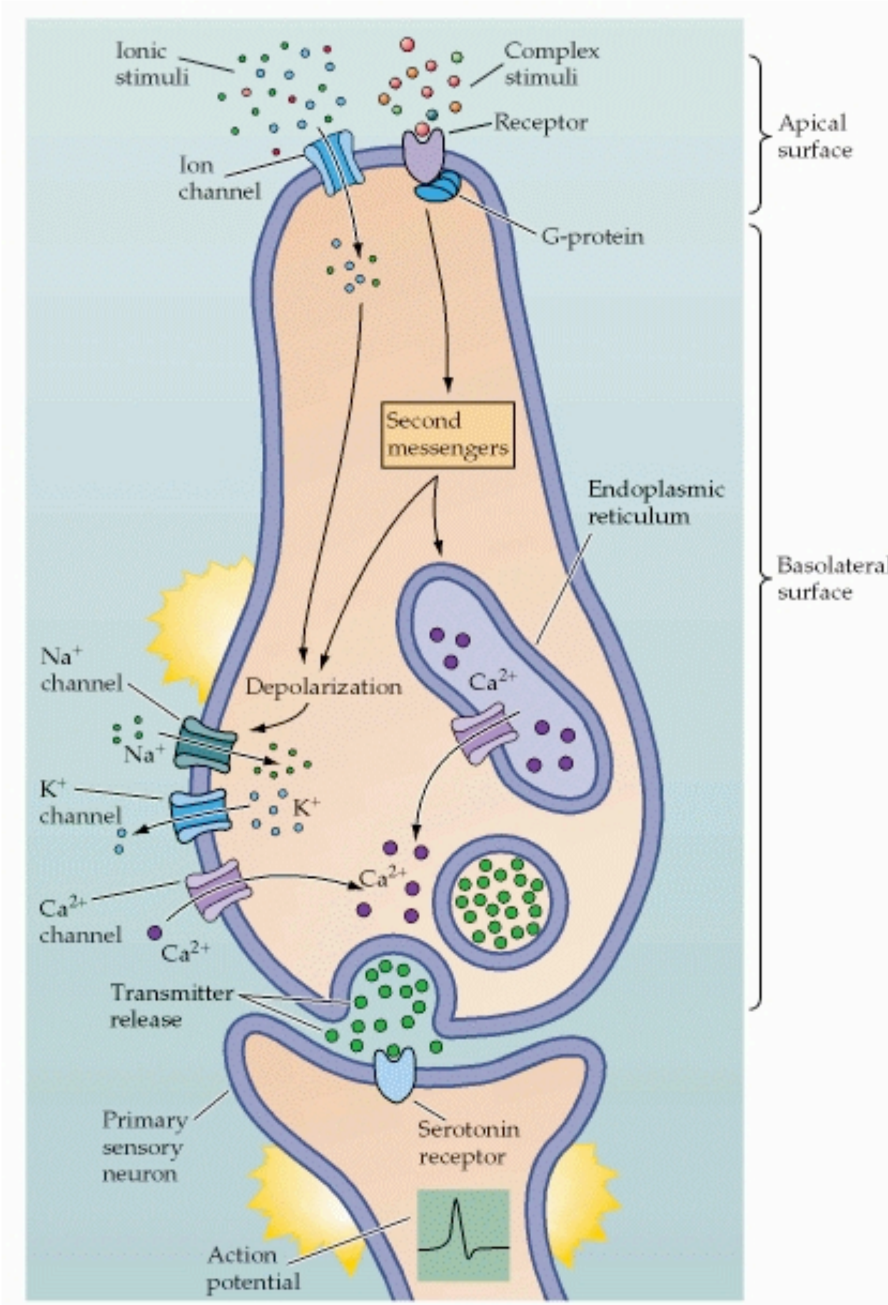
NEUROSCIENCE 5e, Figure 15.18 (Part 2)

50-100 receptor cells in bud; renew every 10 days or so 5-20 axons leave the bud; integration must be happening !!

Salty, acidic, sweet, amino acid, bitter ALL represented by cells in the bud

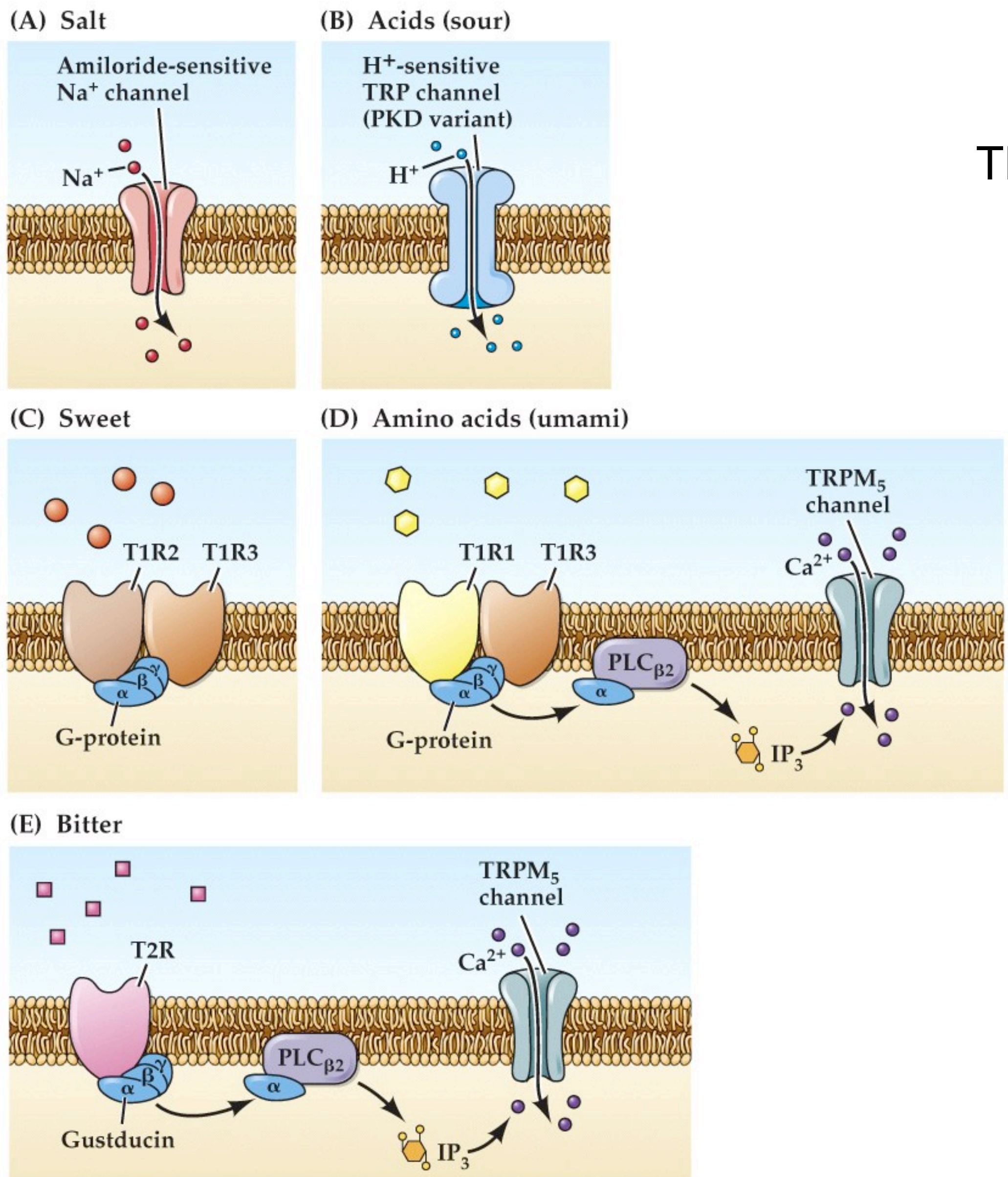
Bitter cells do not directly contact nerve – indirect through sweet and amino acid cells

Salty, acidic, sweet, amino acid, bitter ALL represented by cells in the bud



Transduction mechanism in a typical taste cell

Taste receptors are both ion channels and GPCRs



***NEUROSCIENCE 5e*, Figure 15.21**

TRP: transient receptor potential

T1R2: Taste receptor 1 member 2

TRPM: TRP melastatin;
No-ankyrin repeat domain