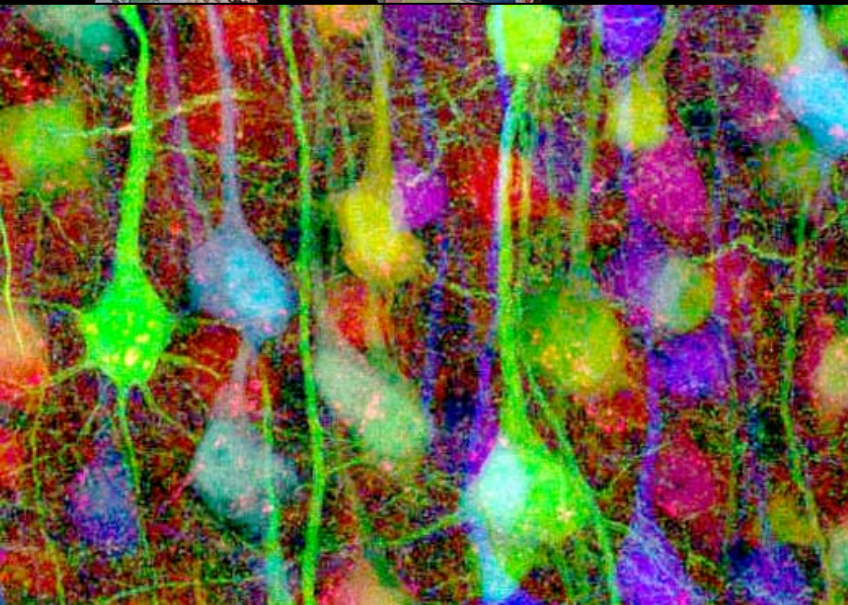


Les sens chimiques

Prof. Alan Carleton

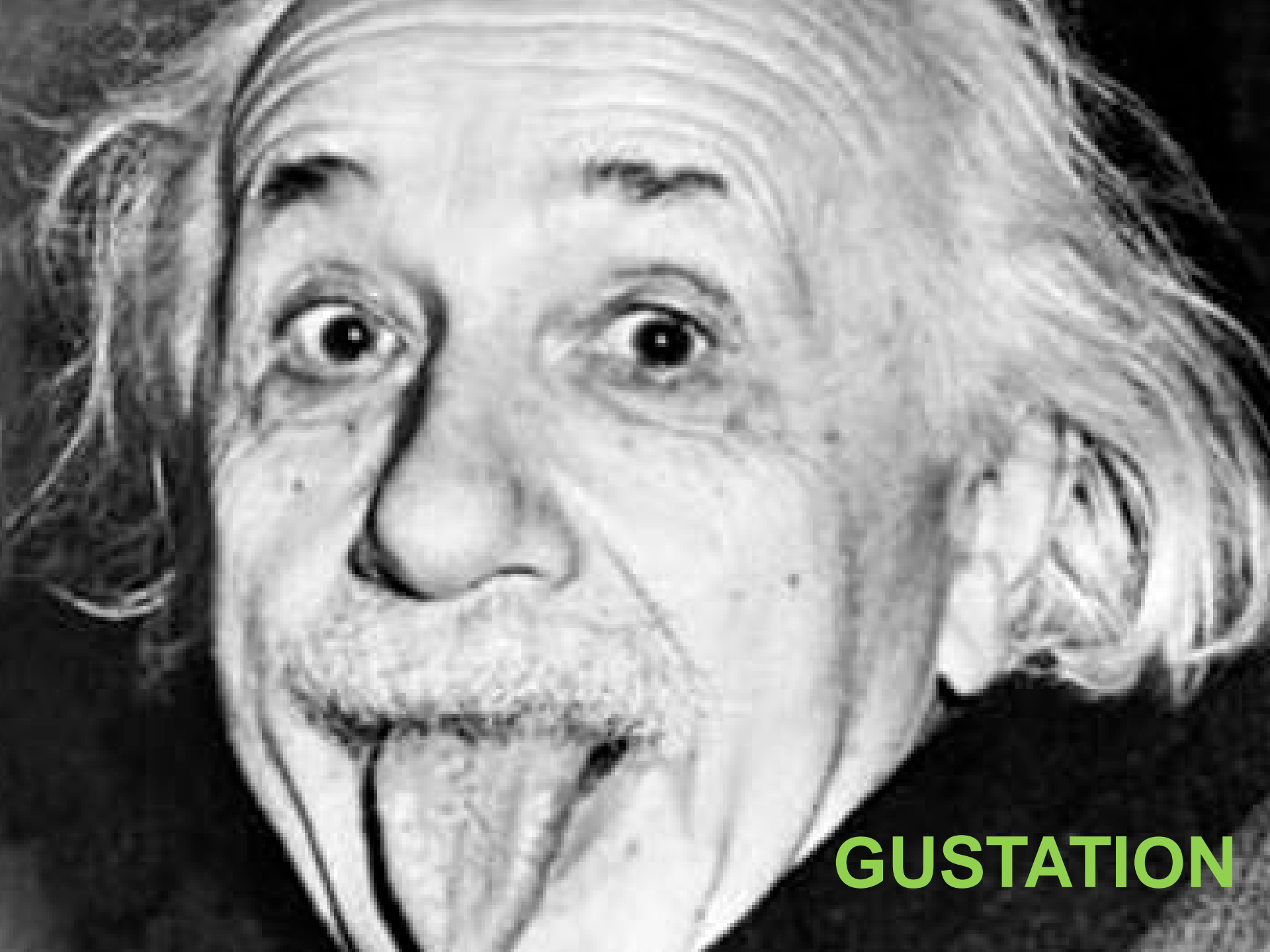
Département de Neurosciences Fondamentales



Les sens chimiques

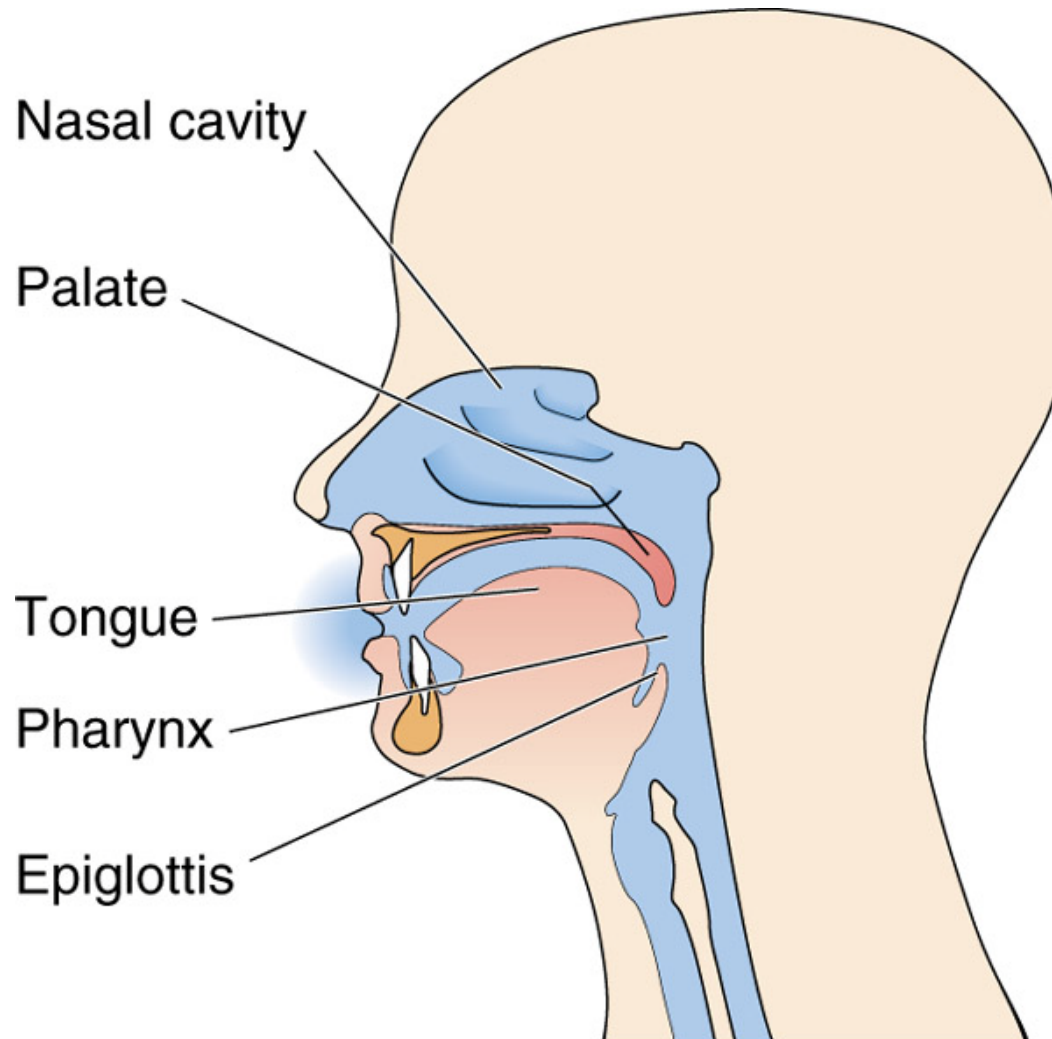
- Le système olfactif principal
- Organe voméronasal et détection des phéromones
- La perception des goûts



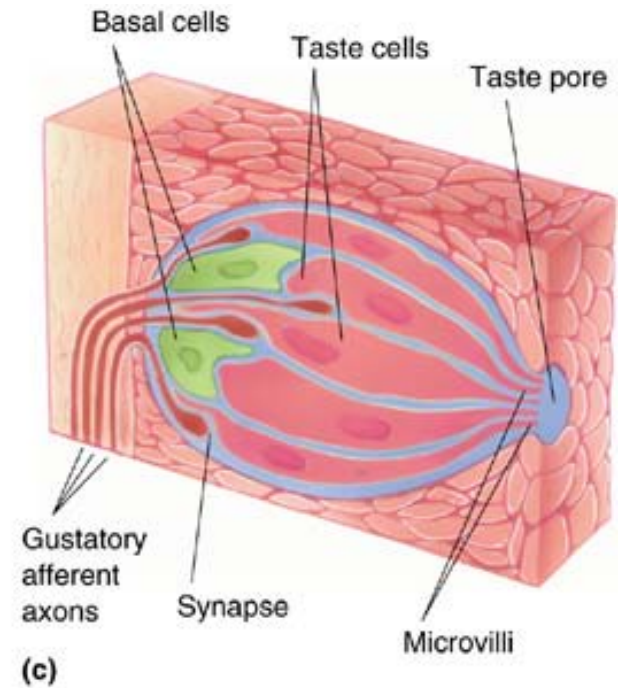
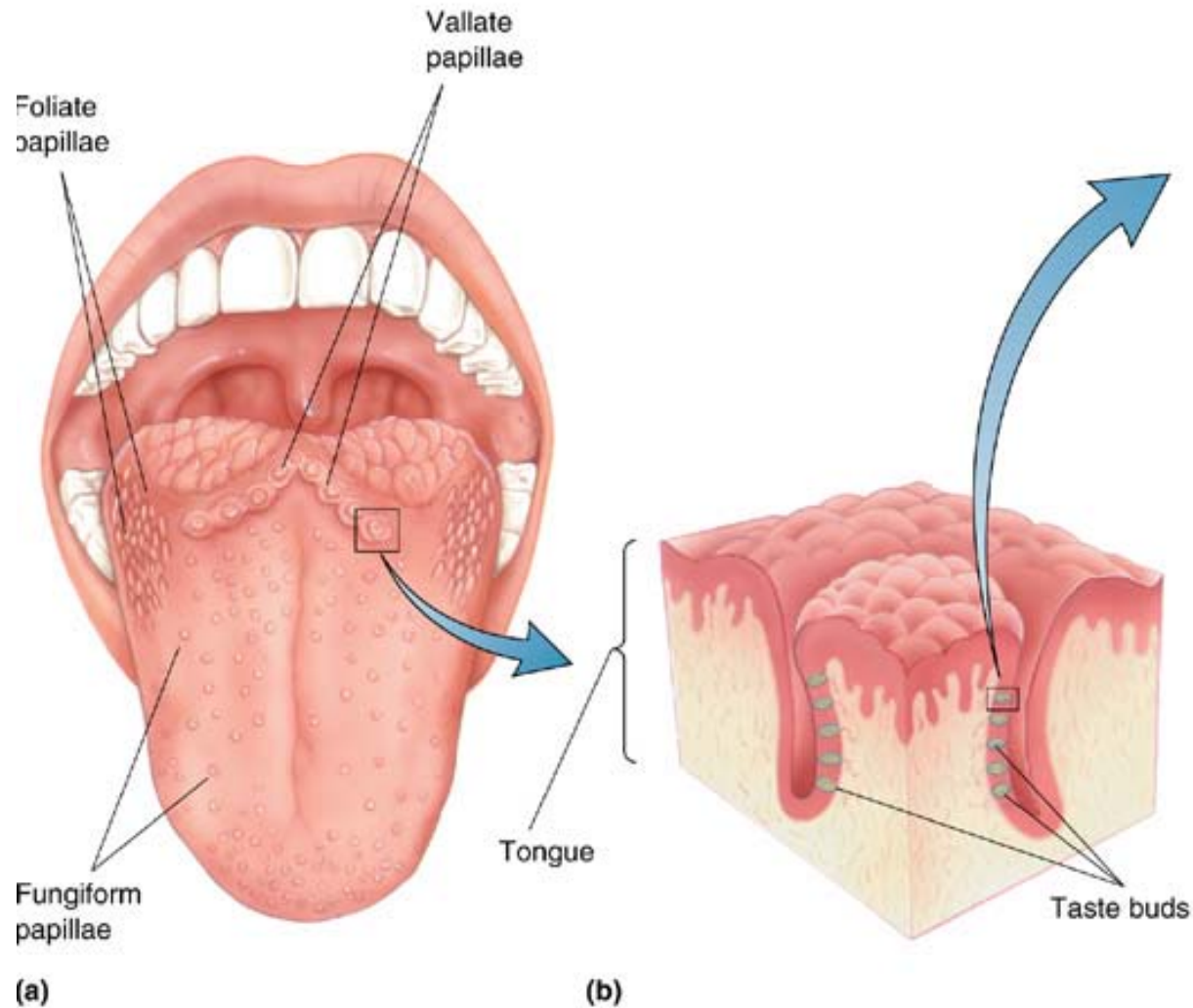


GUSTATION

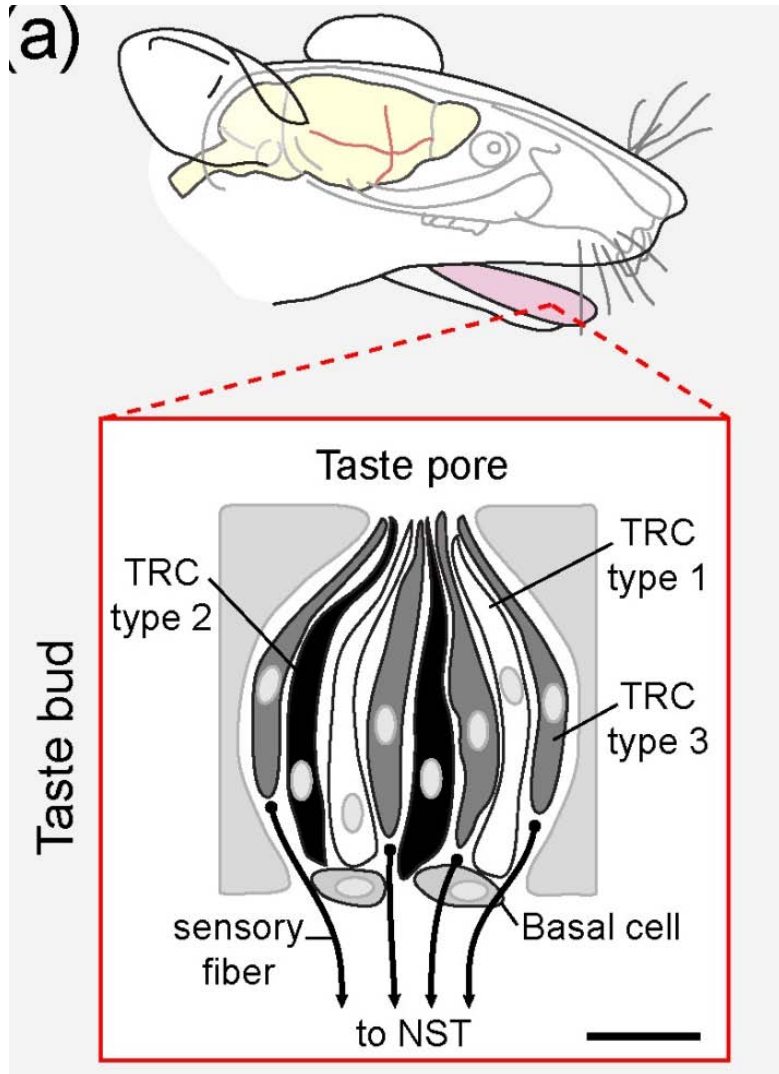
Organisation anatomique de la perception du goût



Les bourgeons du goût et papilles gustatives



Organisation des bourgeons du goût

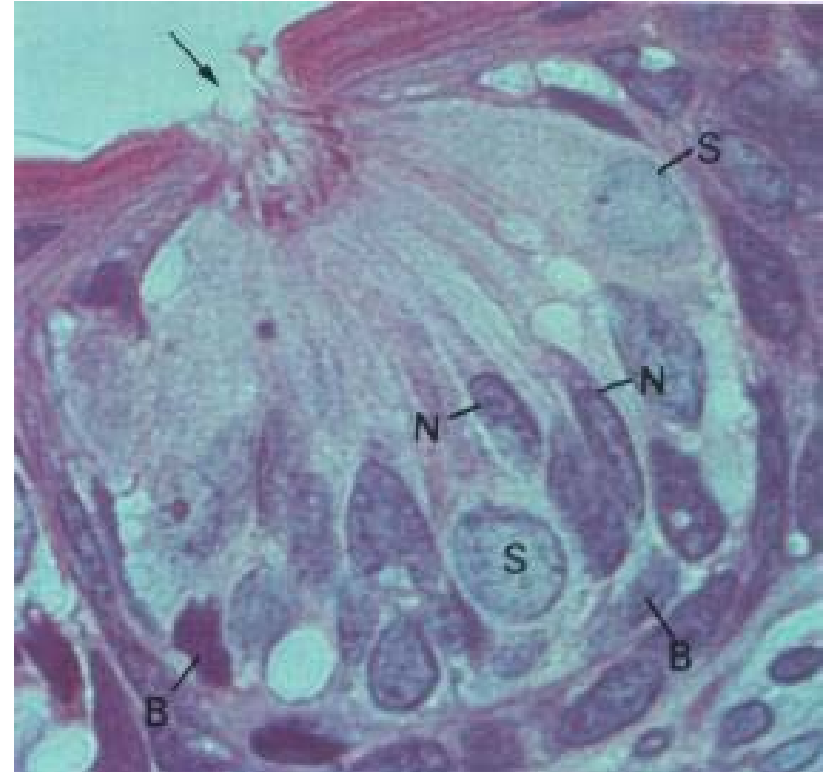


Bourgeons du goût:

Homme (10000)

Rat (1000)

500 CV



20 μ m

Les saveurs du goût

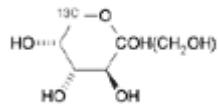
Salé

NaCl

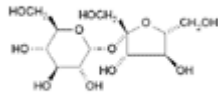
KCl

Sucré

Fructose



Sucrose



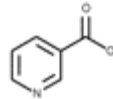
Artificial Sweeteners

Acide

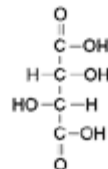
HCl

Citric Acid

Nicotinic Acid

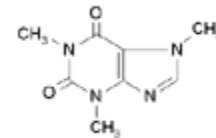


Tartaric Acid

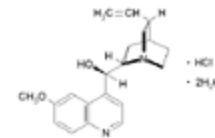


Amer

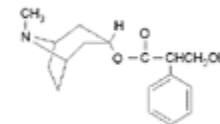
Caffeine



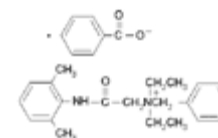
Quinine-HCl



Atropine



Denatonium



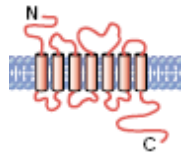
Umami

MSG



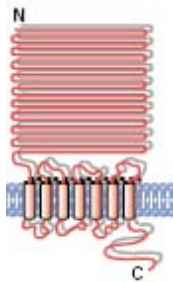
Les receptors du goût

Bitter



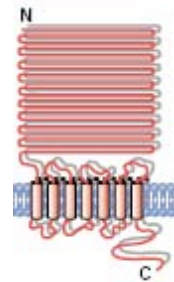
40 T2Rs

Sweet



T1R2/T1R3

Umami



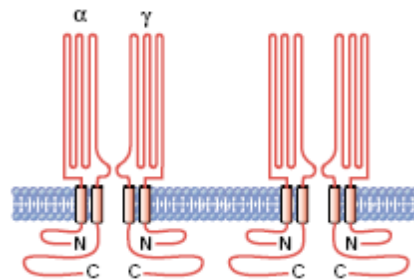
T1R1/T1R3



GPCRs

Salt

Sour



ENAC
Epithelial Na Chan.

Pkd2l1



Ion channels

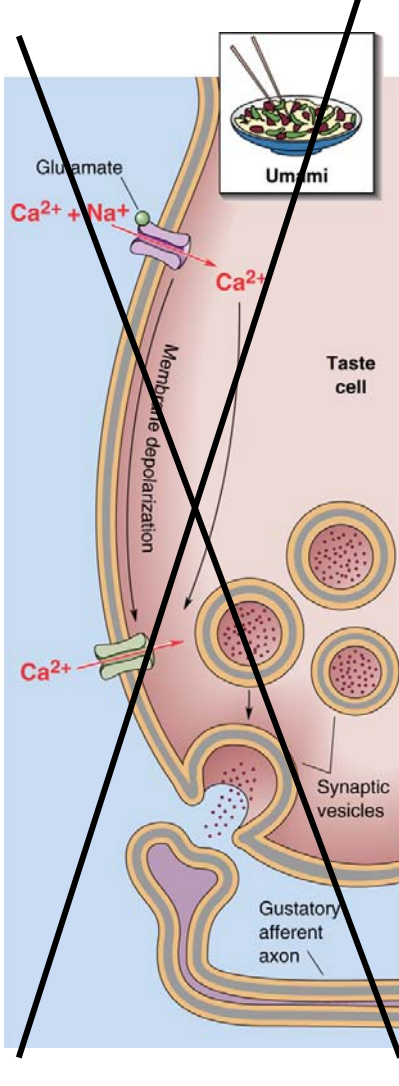
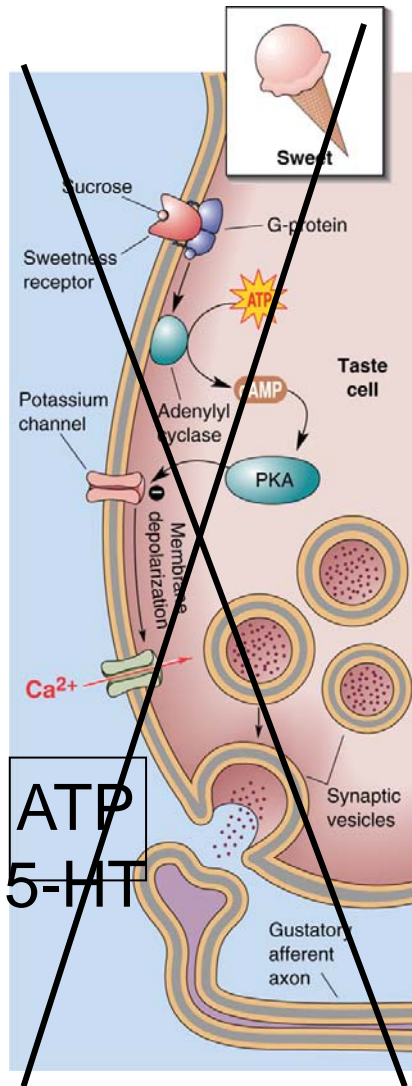
Transduction

T1R2-T1R3

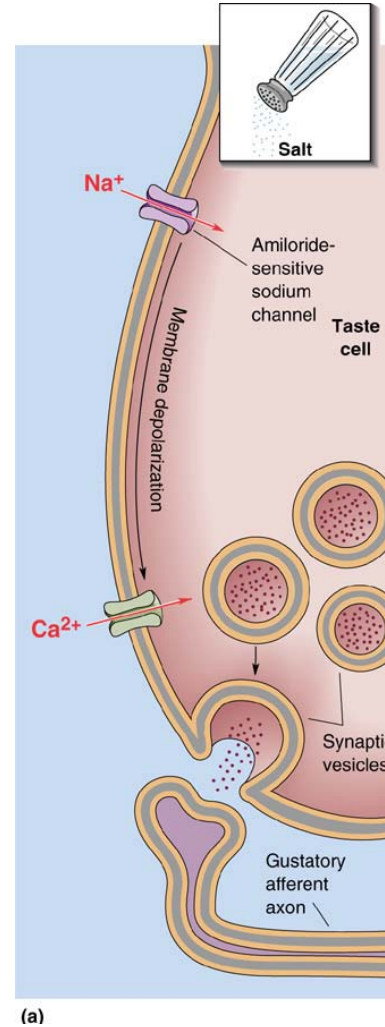
T1R1-T1R3

ENAC

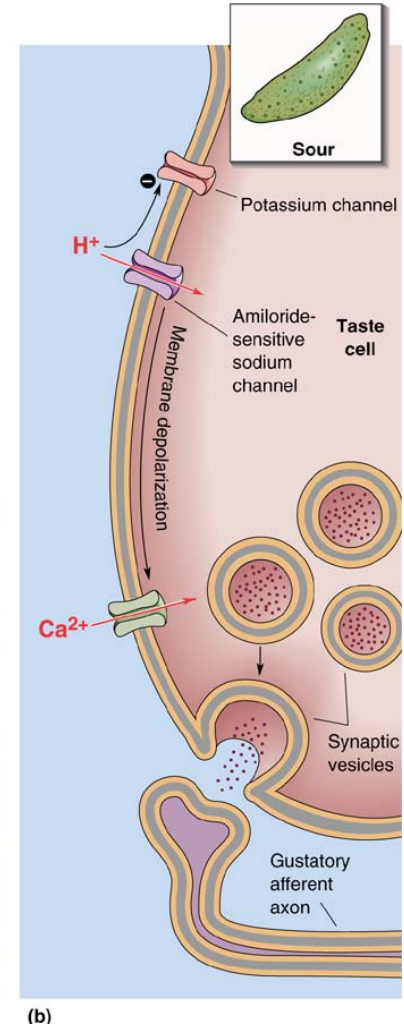
PKD2L1



Epithelial Na Chan.

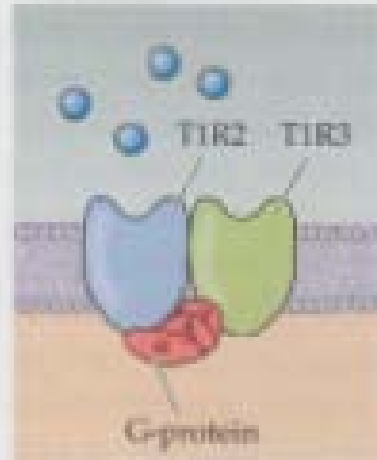


TRP channel

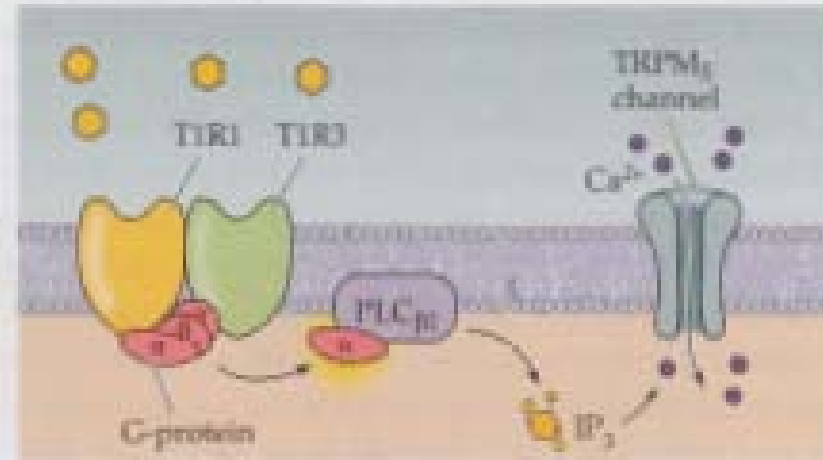


Transduction

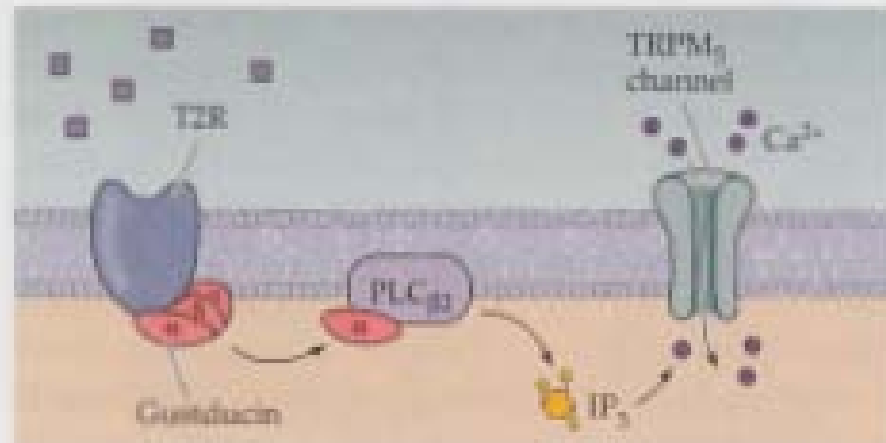
(C) Sweet



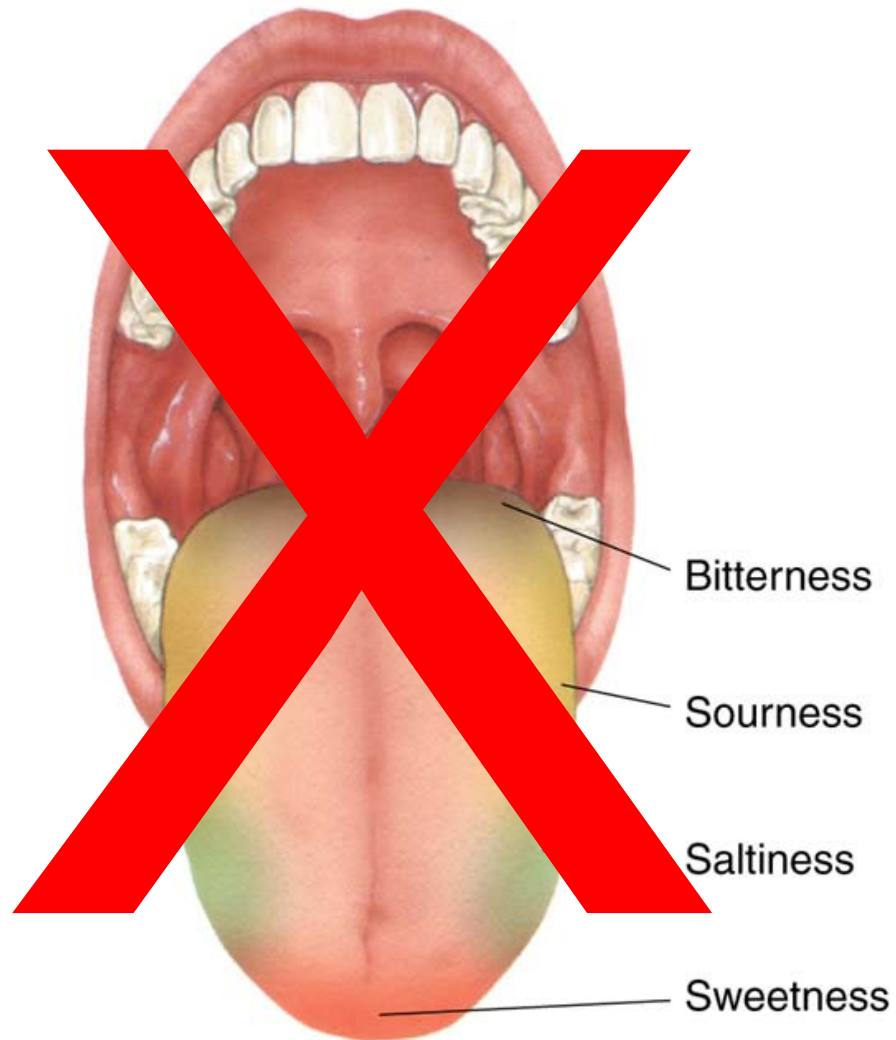
(D) Amino acids (umami)



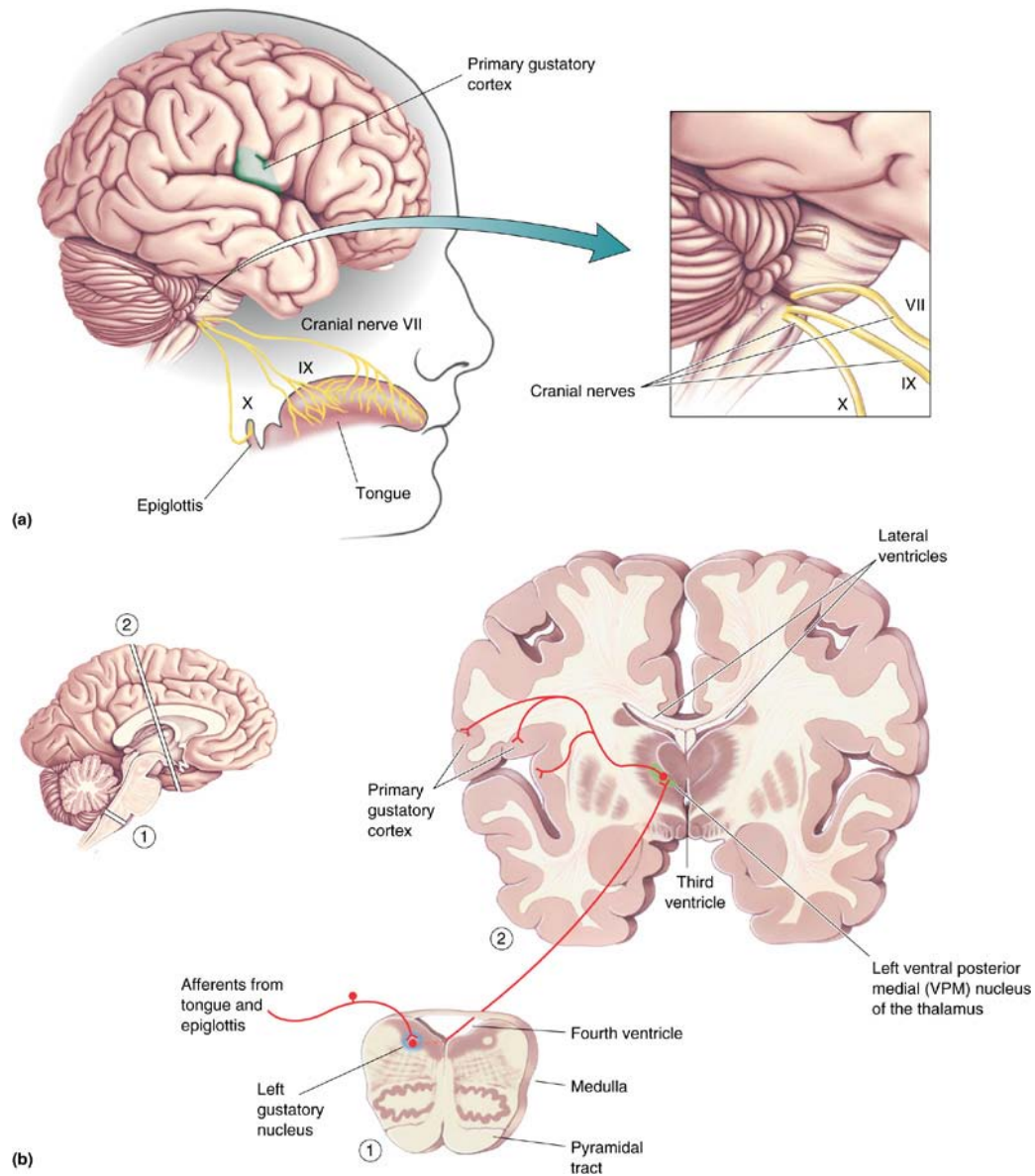
(E) Bitter



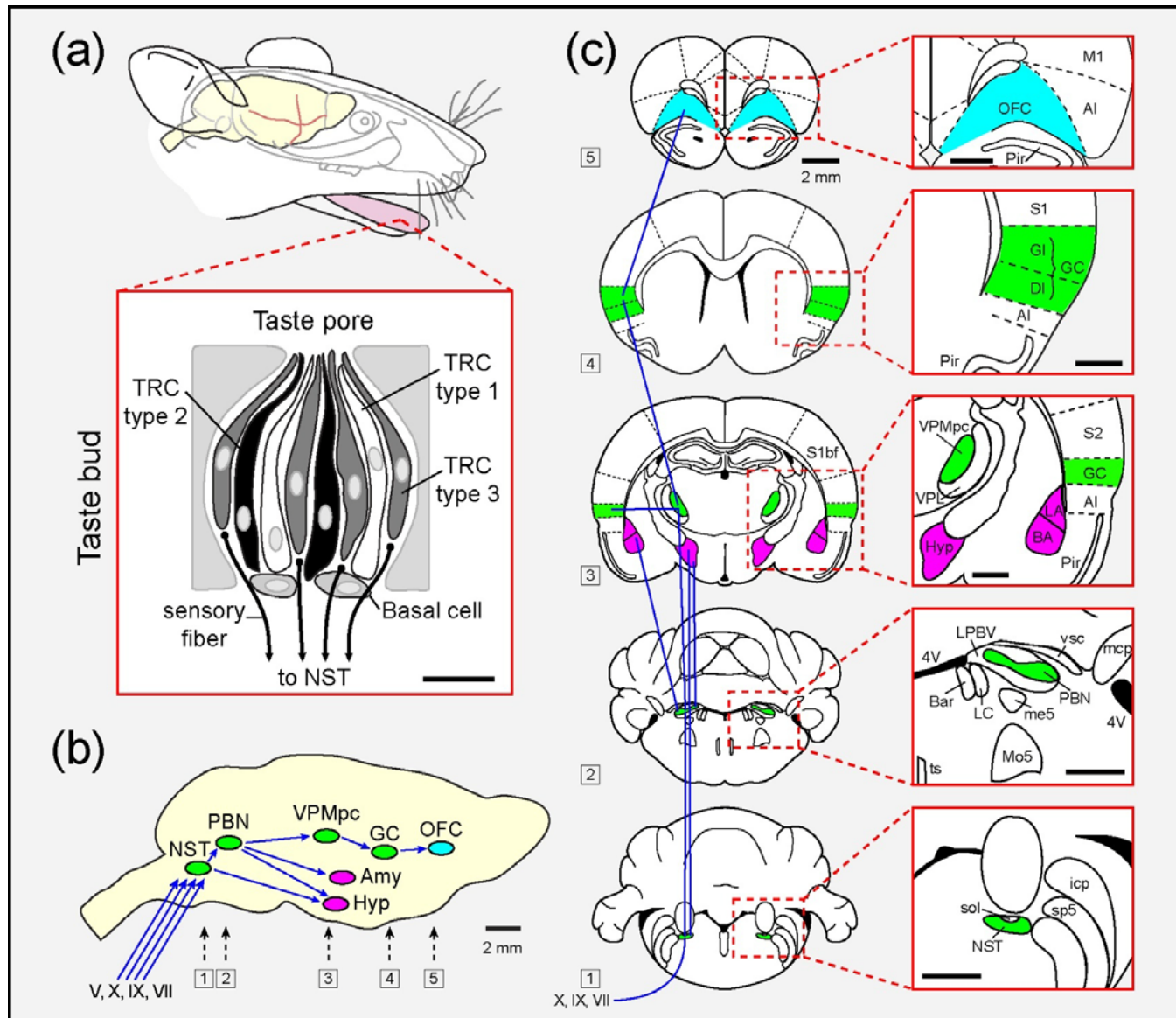
Representation sensorielle sur la langue



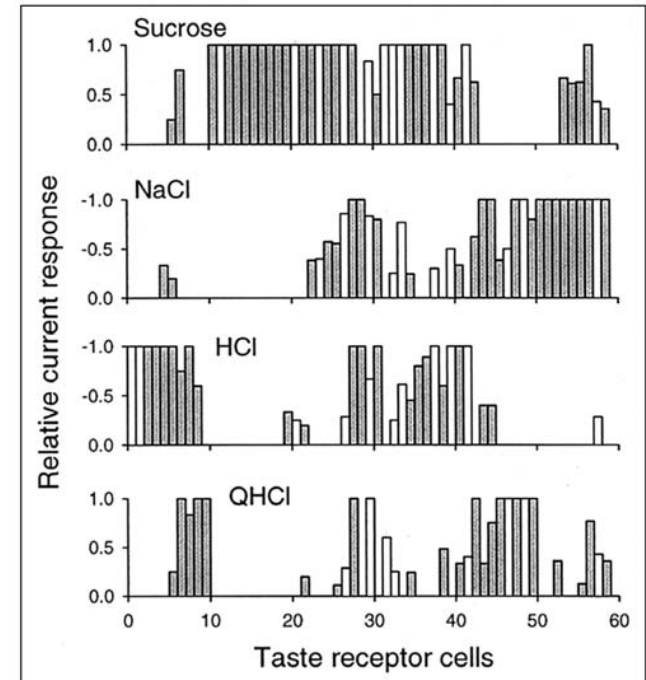
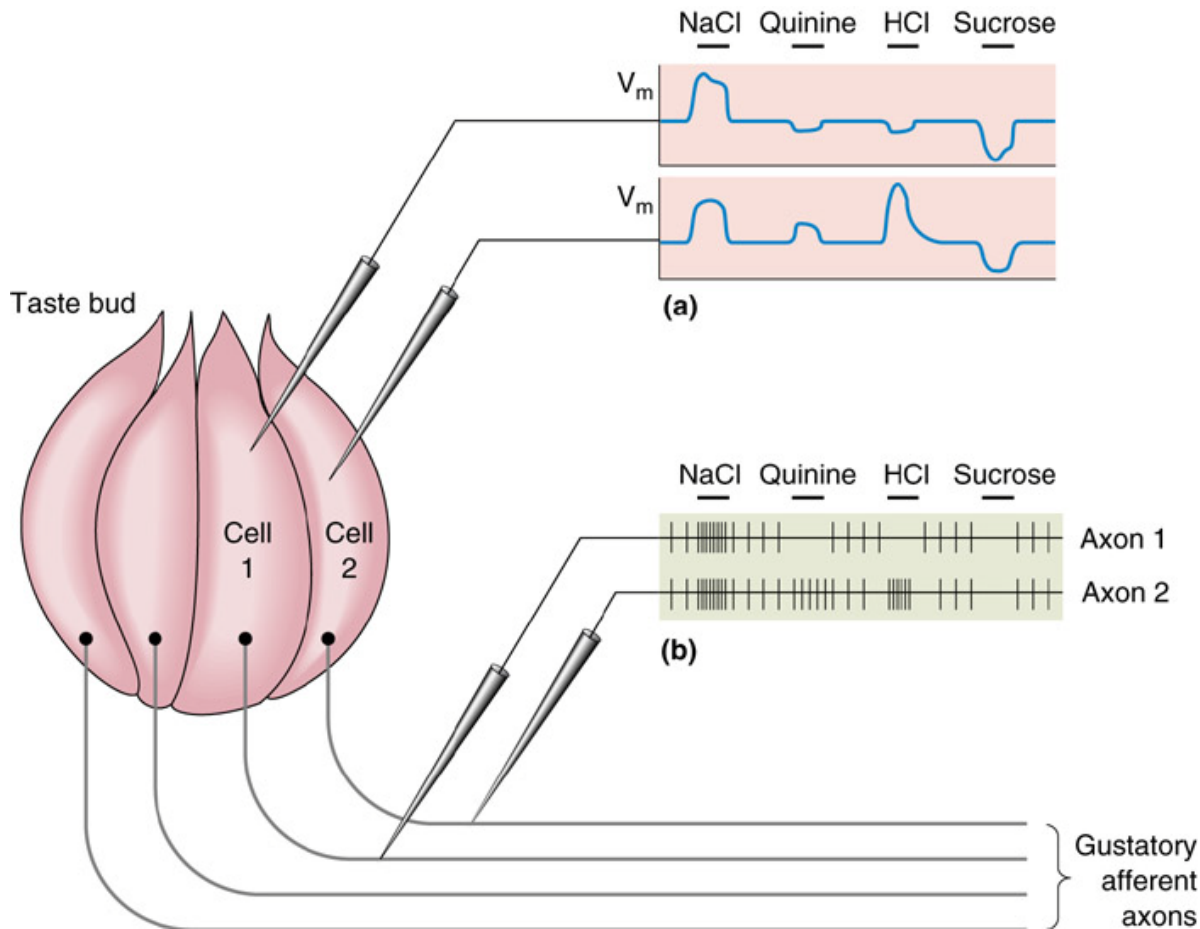
Gustatory pathways in the human brain



Gustatory pathways in the rodent brain

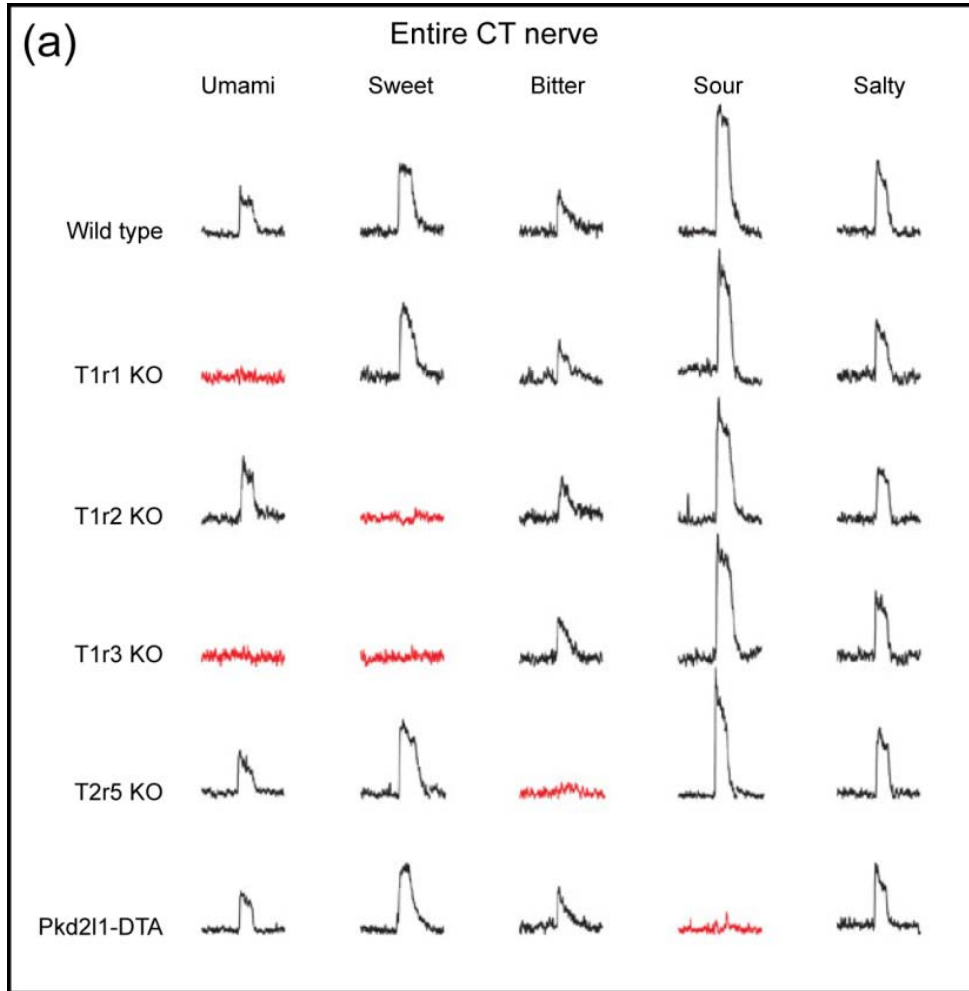


Codage de l'information sensorielle

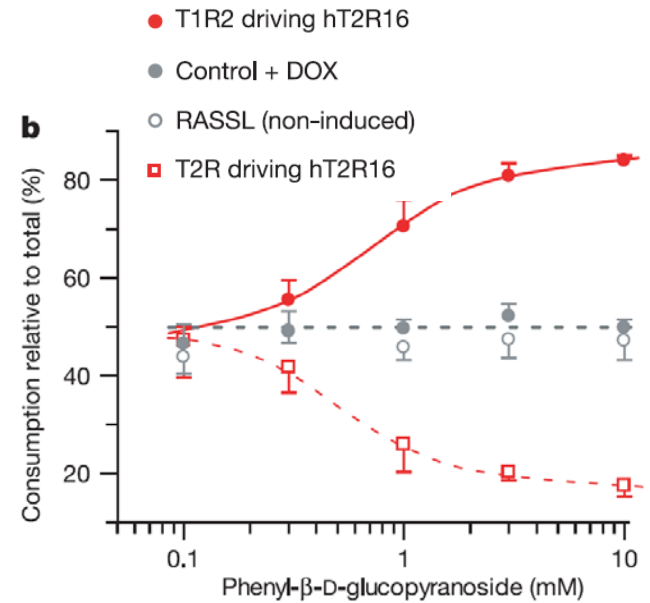
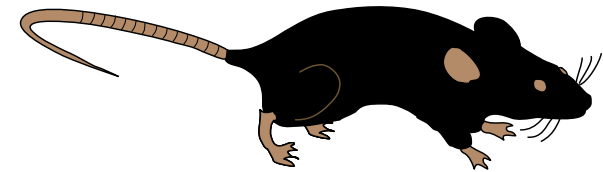


Gilbertson et al. J Neurosci (2001)

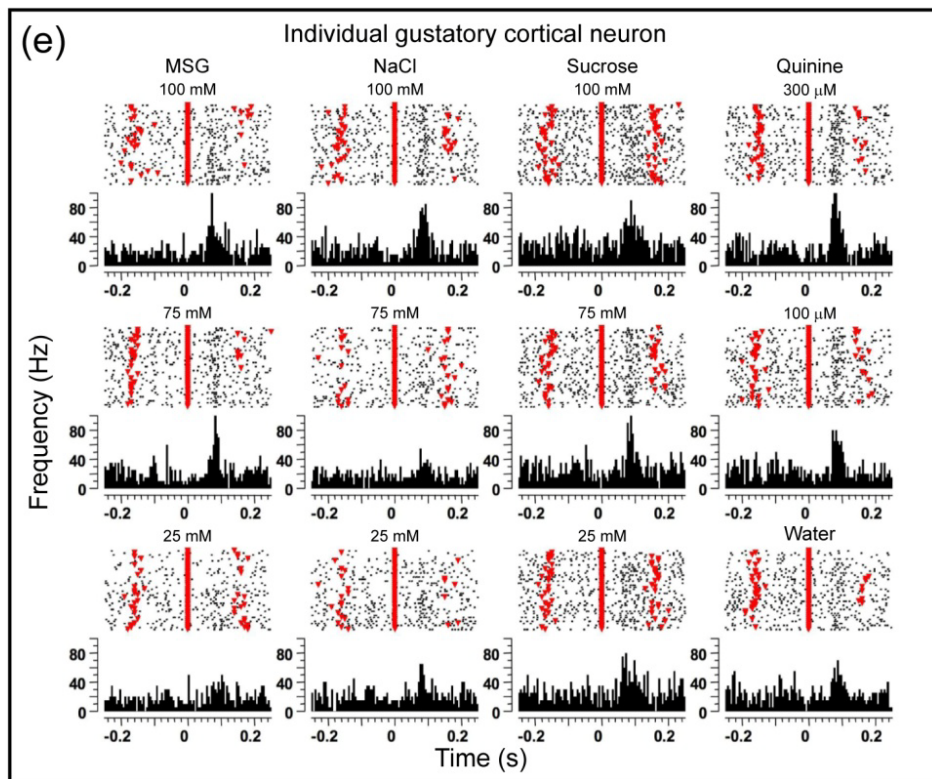
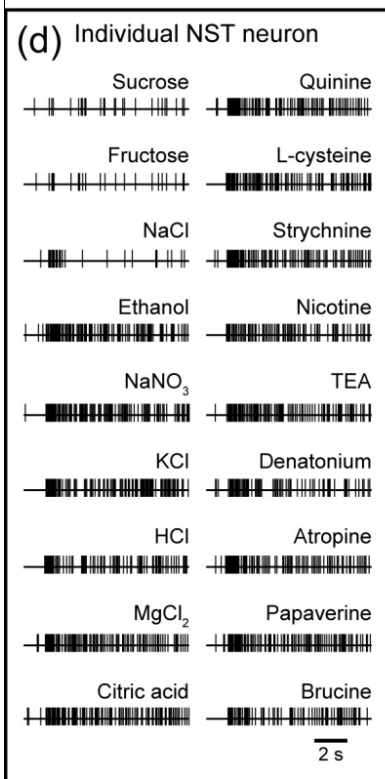
Codage de l'information sensorielle



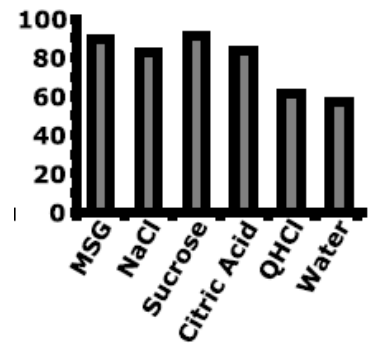
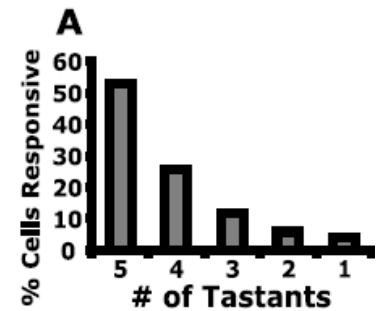
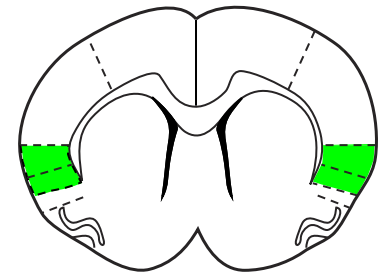
Mouse behaviour



Codage de l'information sensorielle

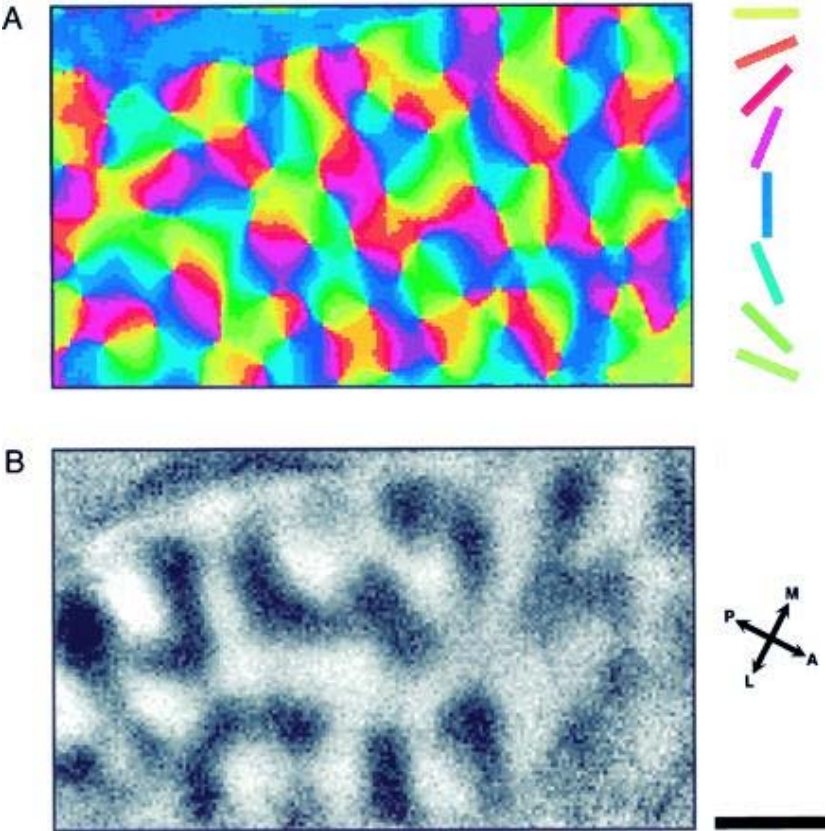


Cortical neurons

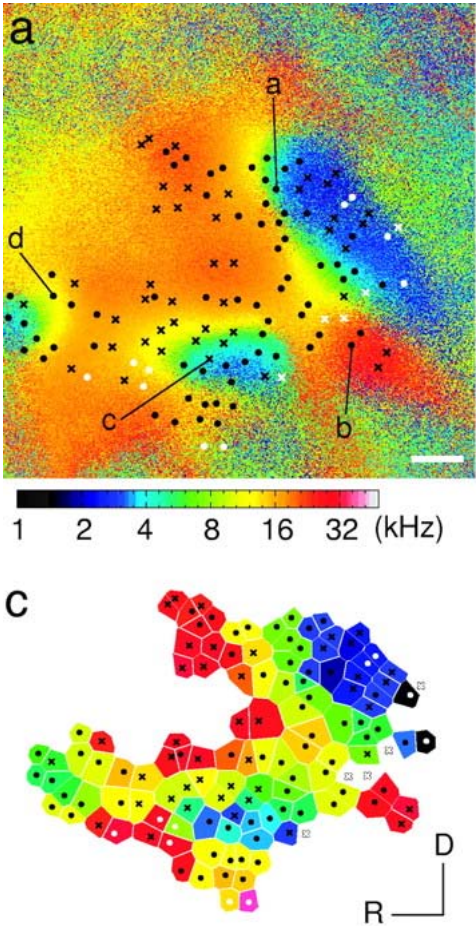


Représentation sensorielle dans le cortex

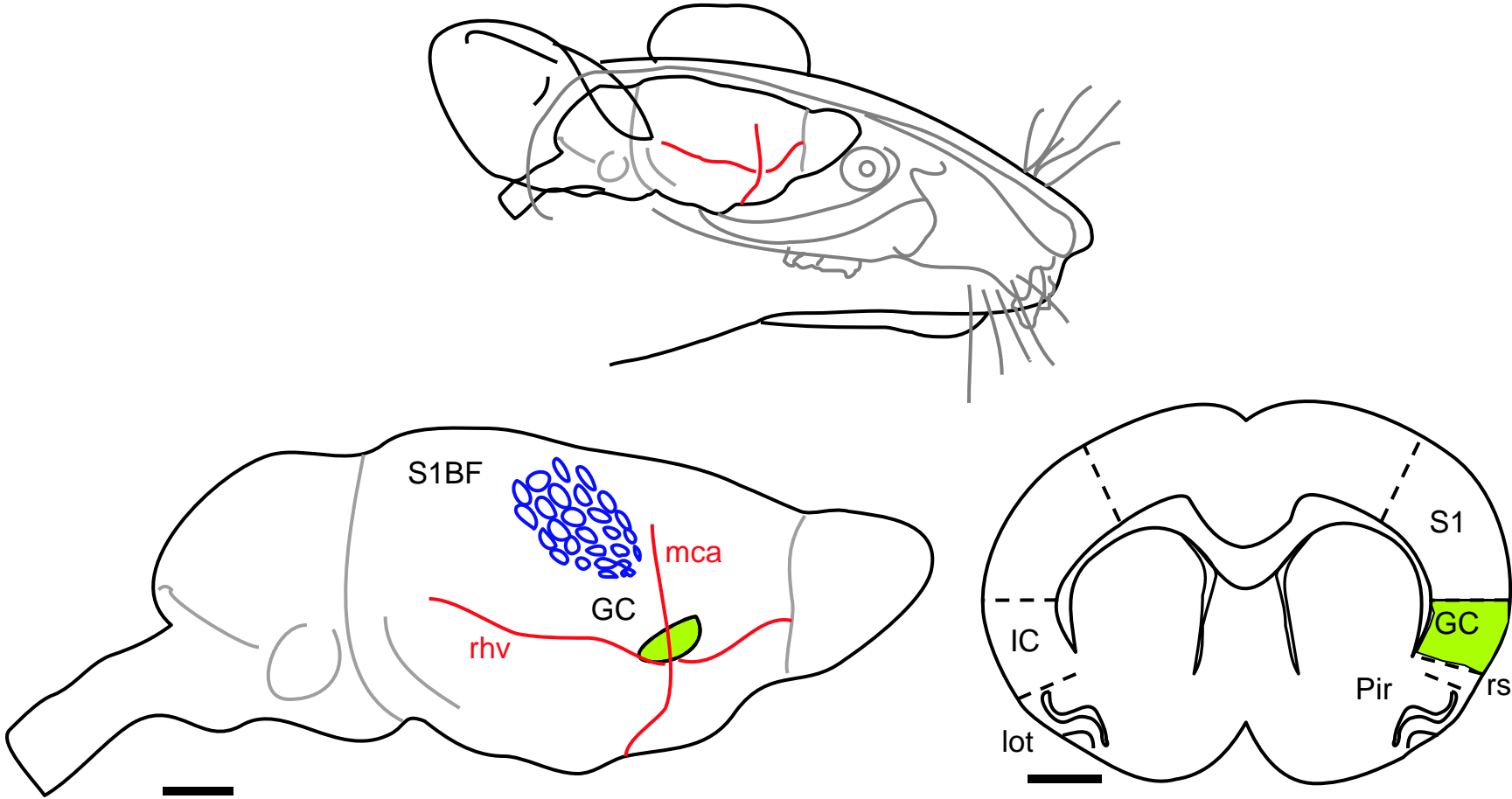
Vision



Audition

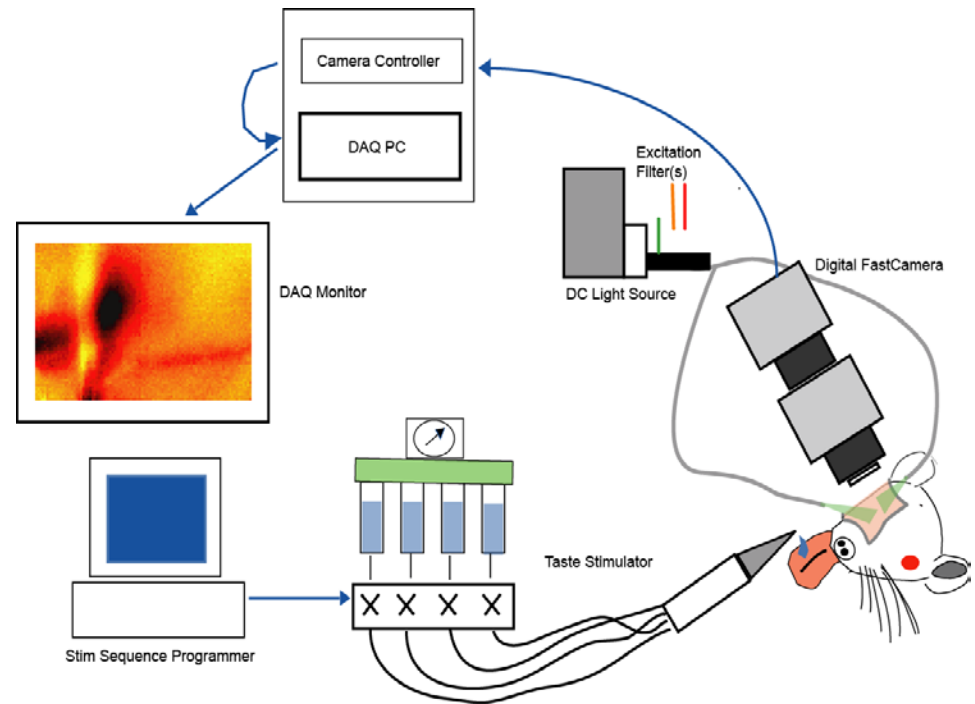


Location of the gustatory cortex in the rodent brain



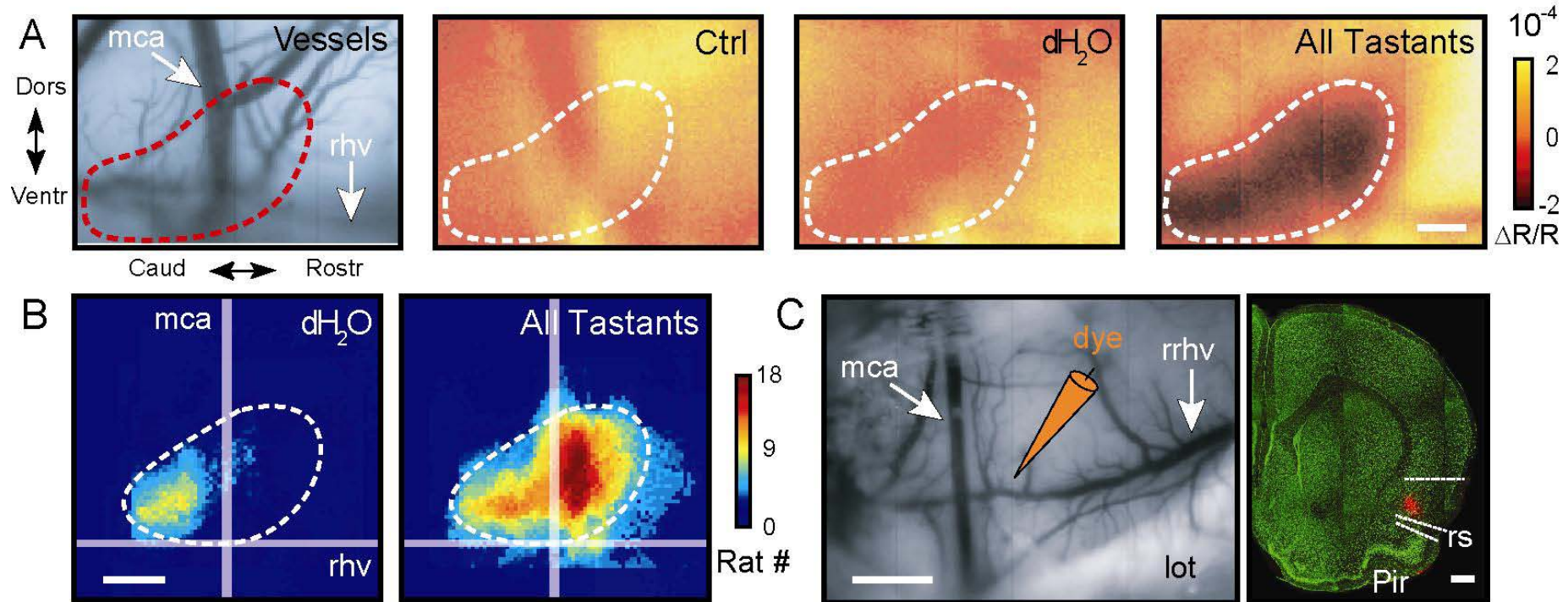
Methods – Intrinsic imaging

- Changes in Reflectance upon activation
- Functional Population Activity
- Good Spatial Resolution

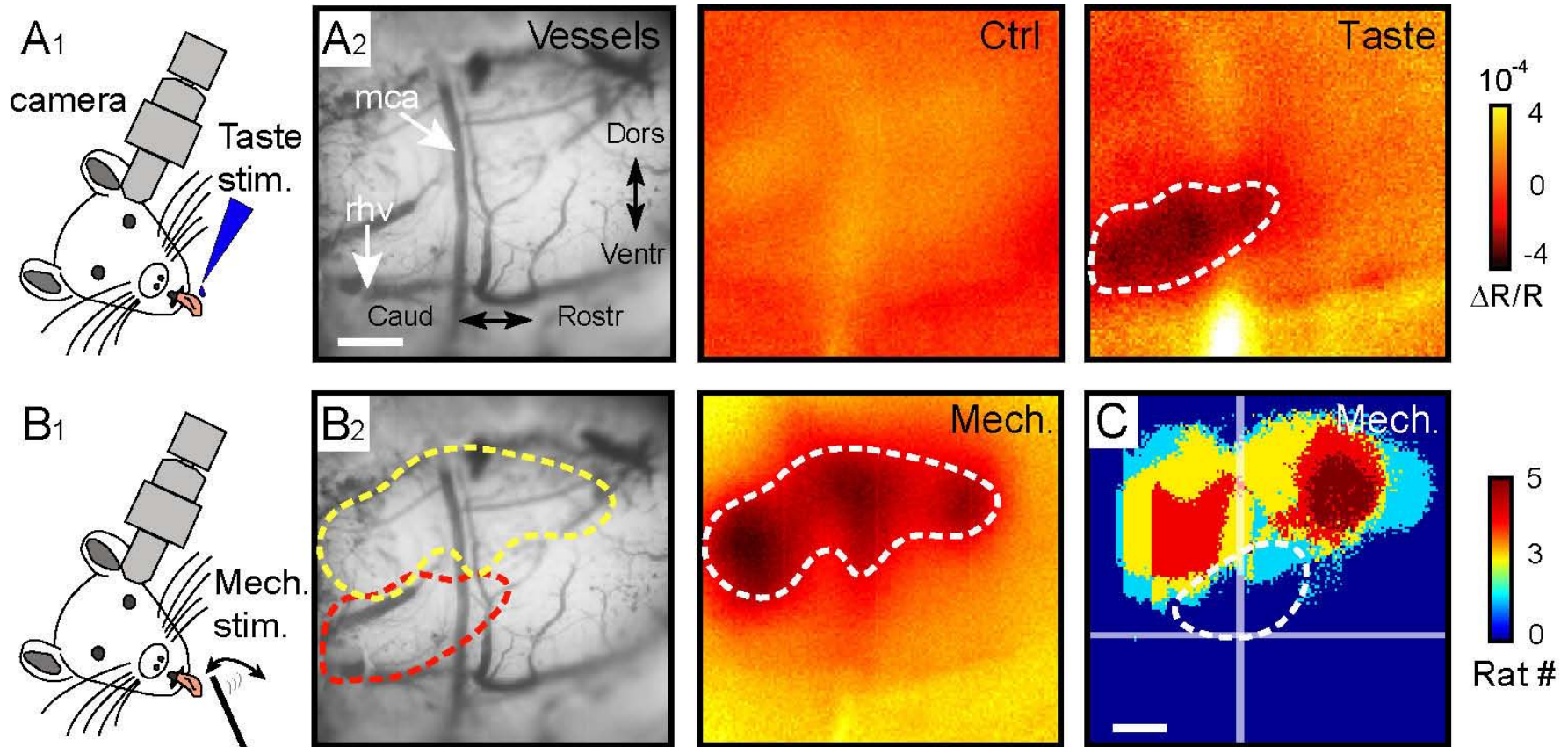


- Successfully used to establish spatial organization of other sensory areas

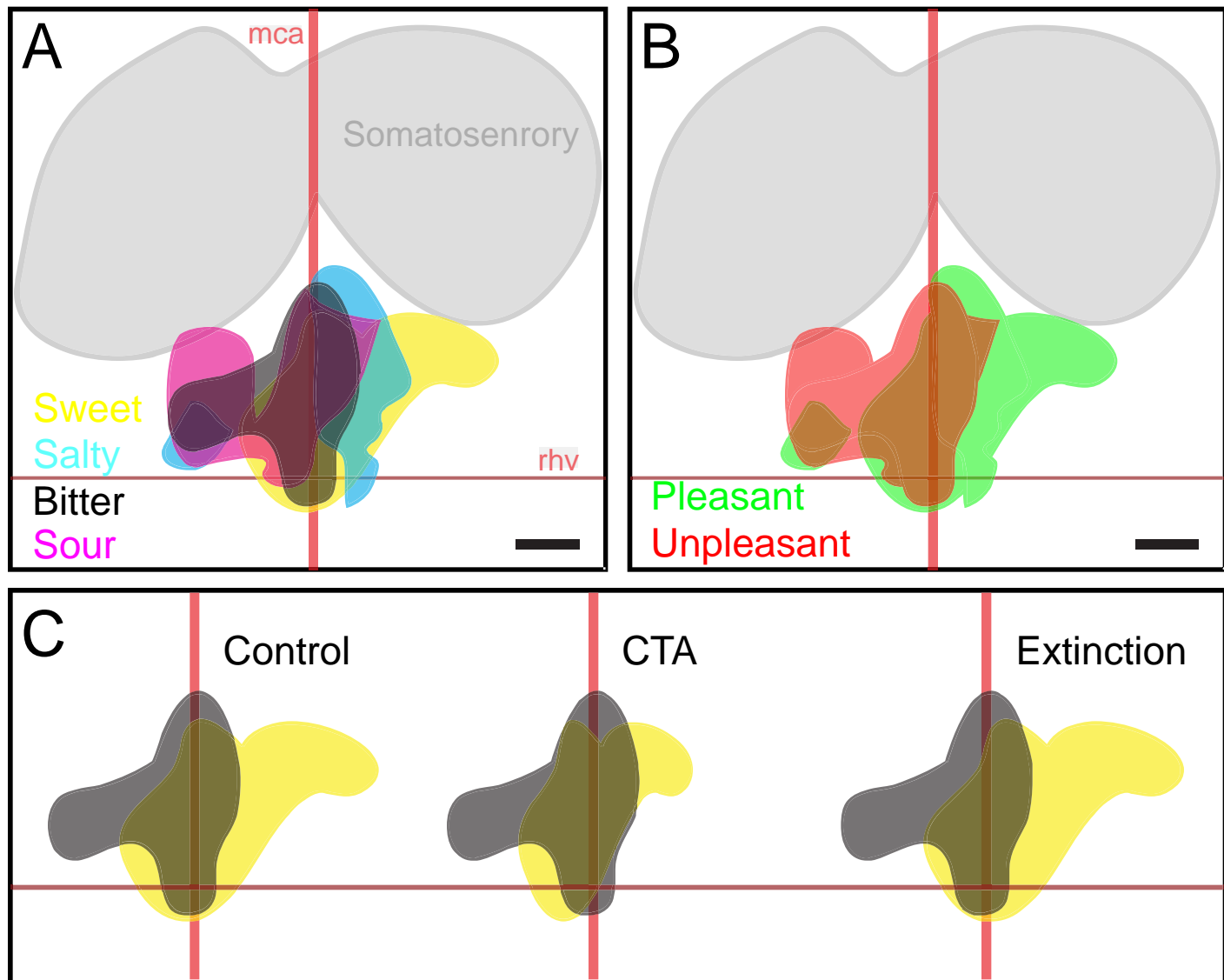
Functional localization of the gustatory cortex



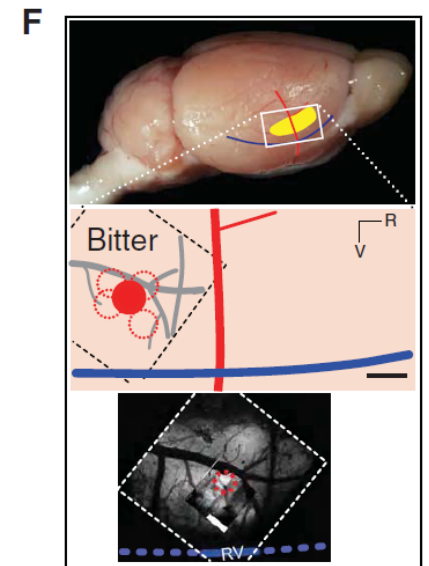
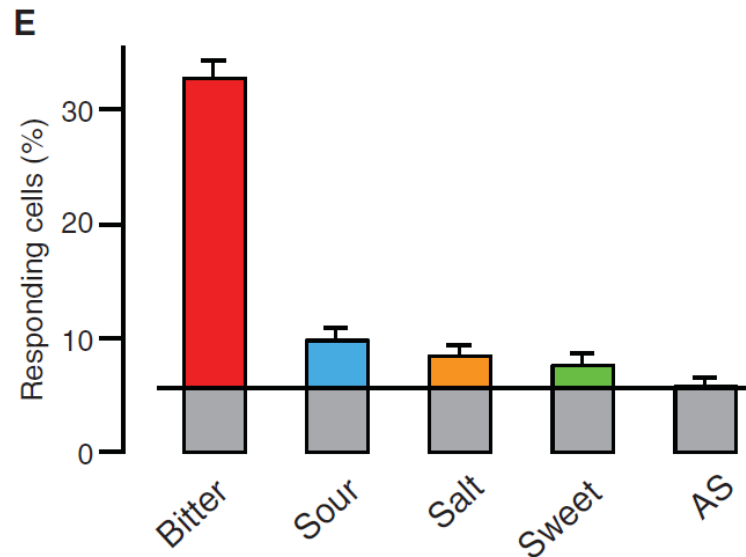
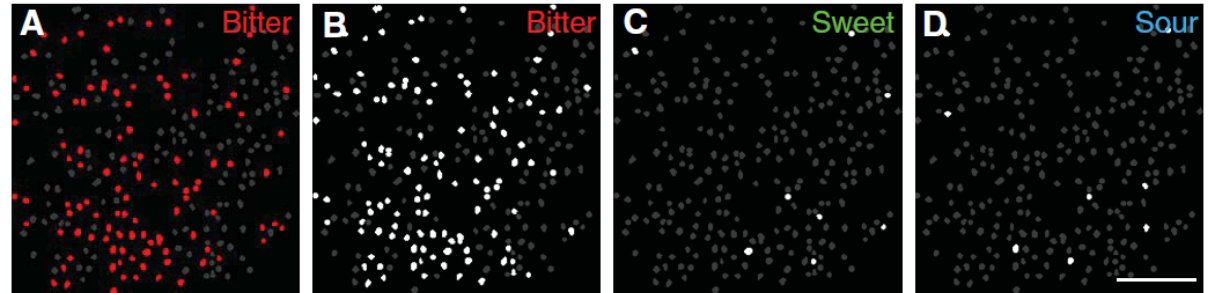
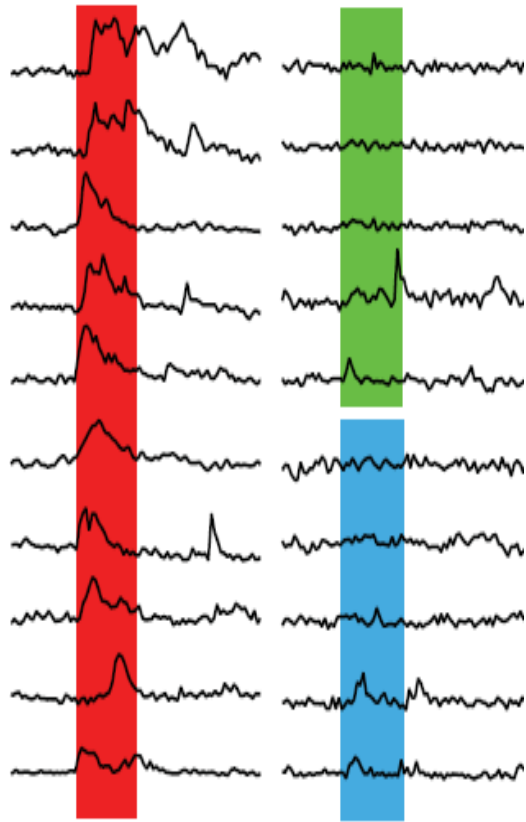
Signals are taste specific



Representation des goûts dans le cortex



Gustotopic map in the taste cortex

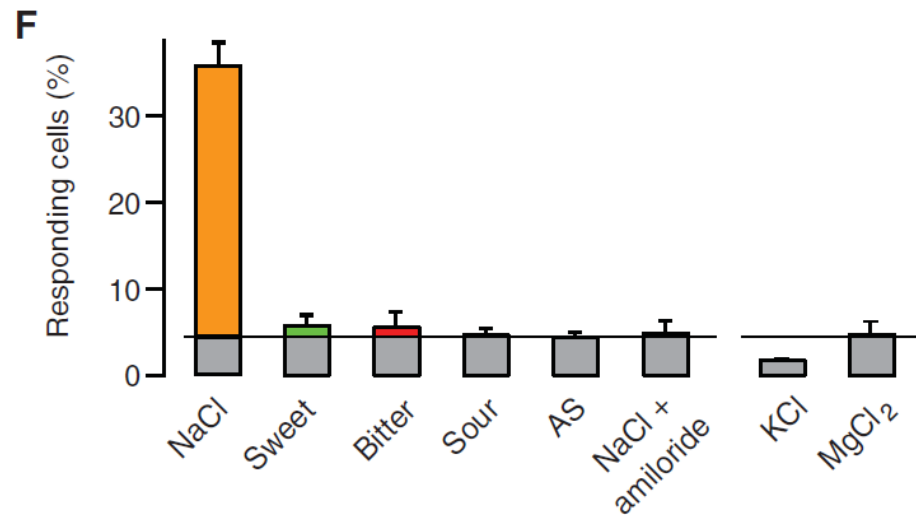
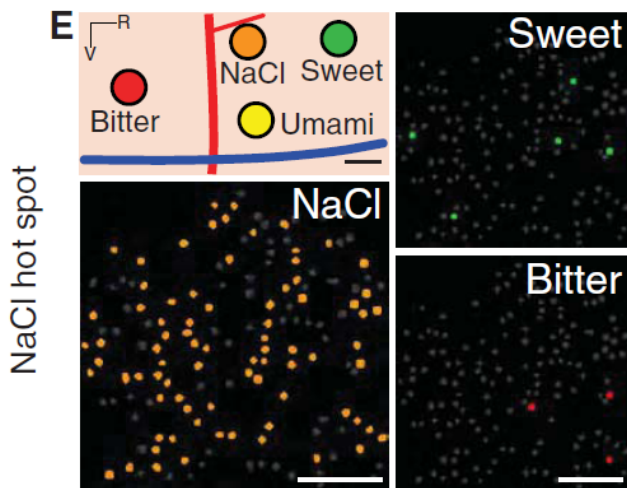
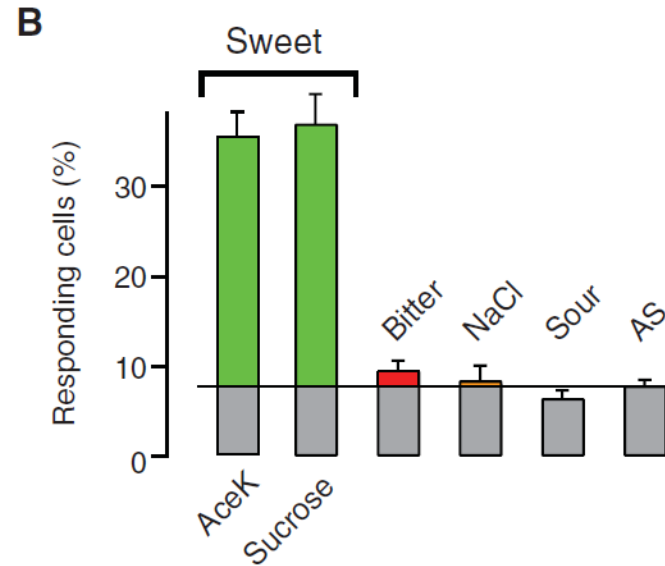
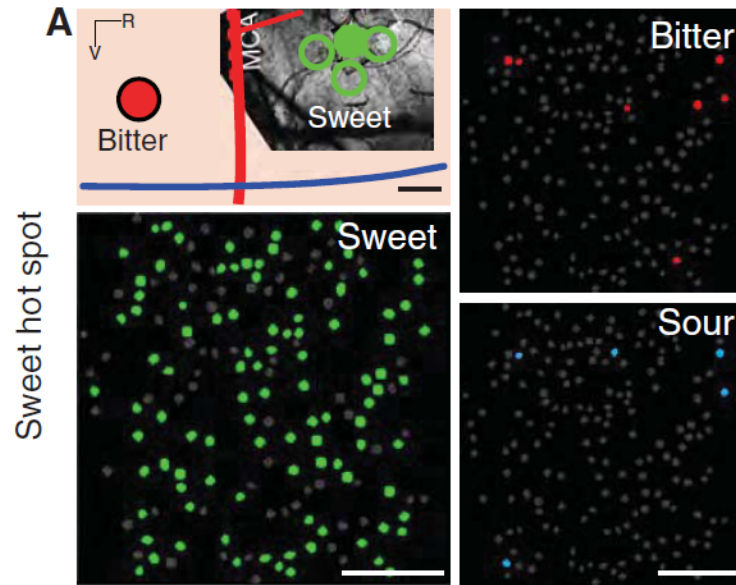


A Gustotopic Map of Taste Qualities in the Mammalian Brain

Xiaoke Chen,¹ Mariano Gabitto,¹ Yueqing Peng,¹ Nicholas J. P. Ryba,² Charles S. Zuker^{1,3*}

2 SEPTEMBER 2011 VOL 333 SCIENCE

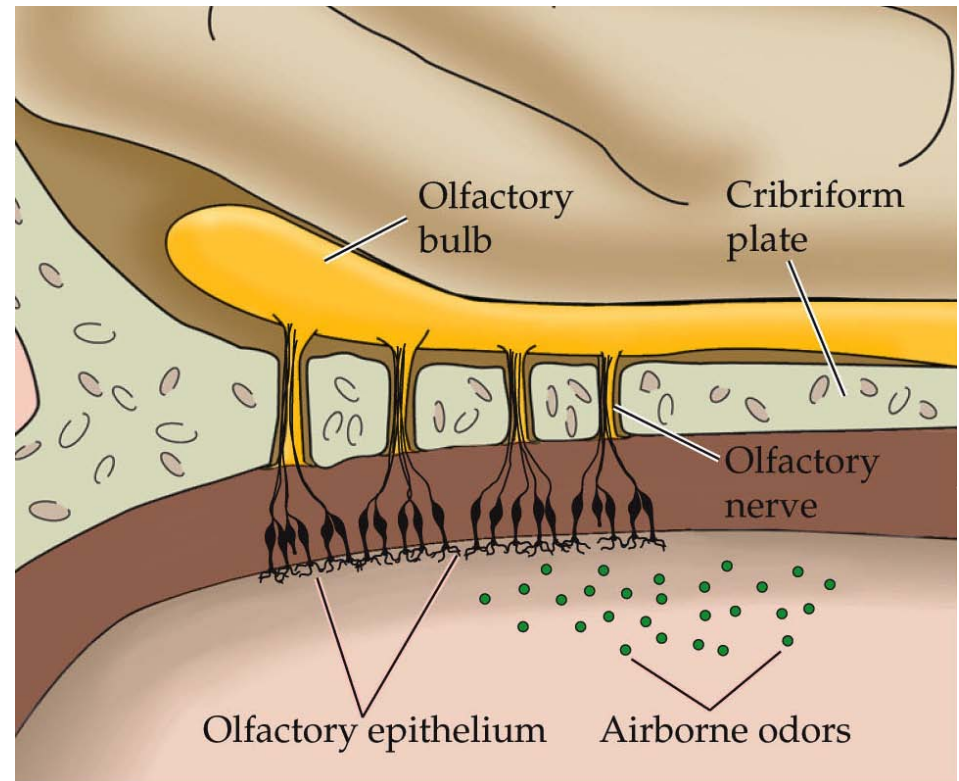
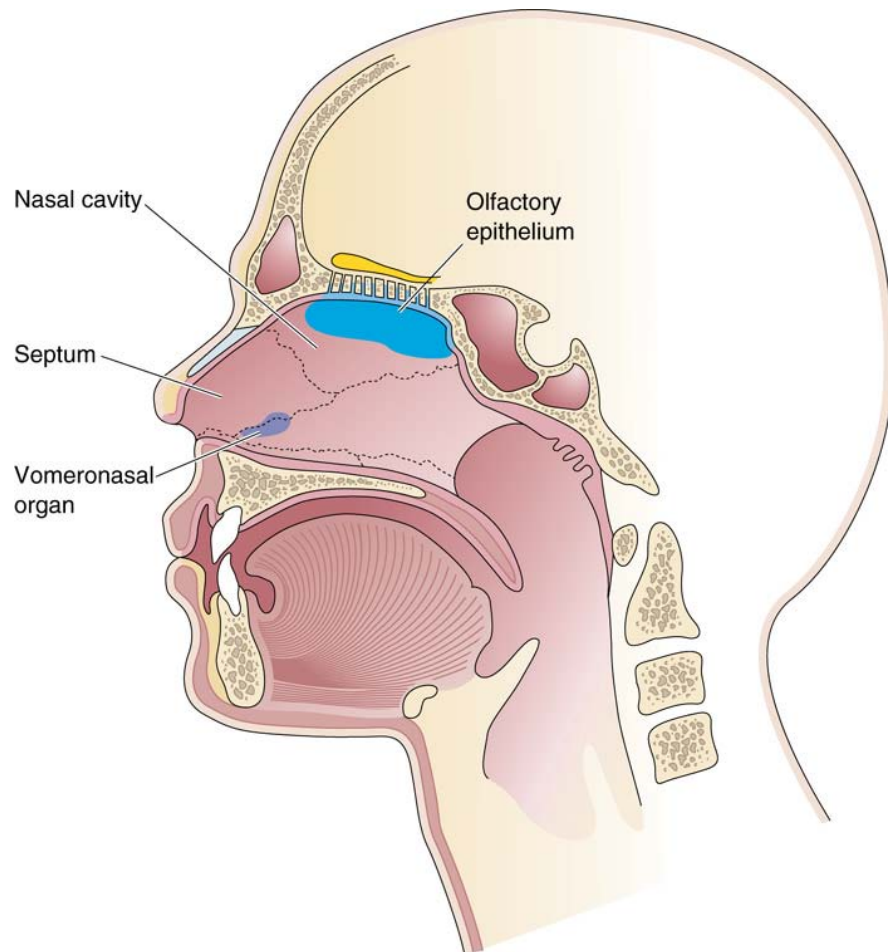
Gustotopic map in the taste cortex



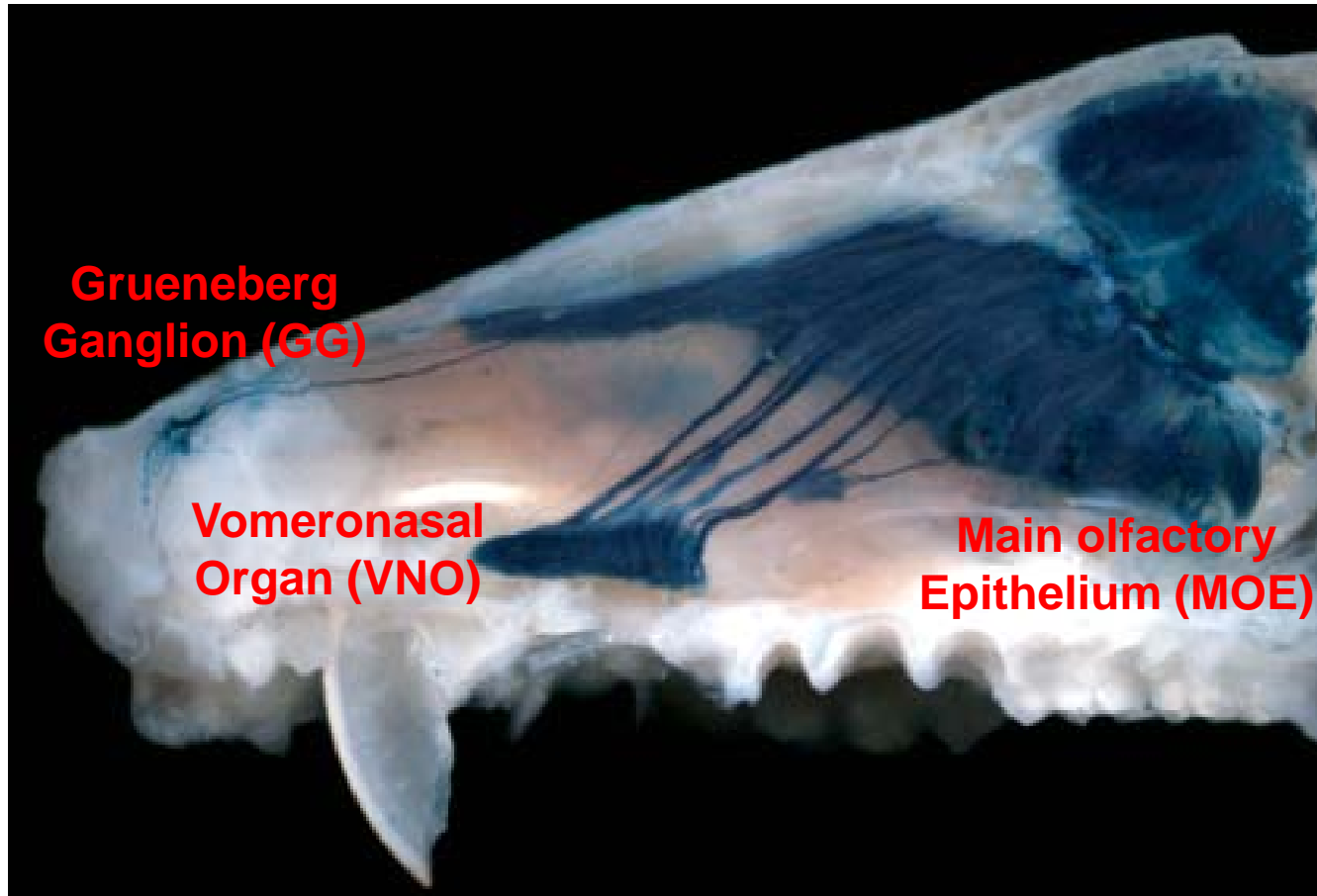
OLFACTION



Organization of the human olfactory system



Organization of the olfactory systems



**Grueneberg
Ganglion (GG)**

**Vomeronasal
Organ (VNO)**

**Main olfactory
Epithelium (MOE)**

**Olfactory
Bulb (OB)**

(Omp-TauLacZ) Tg mouse

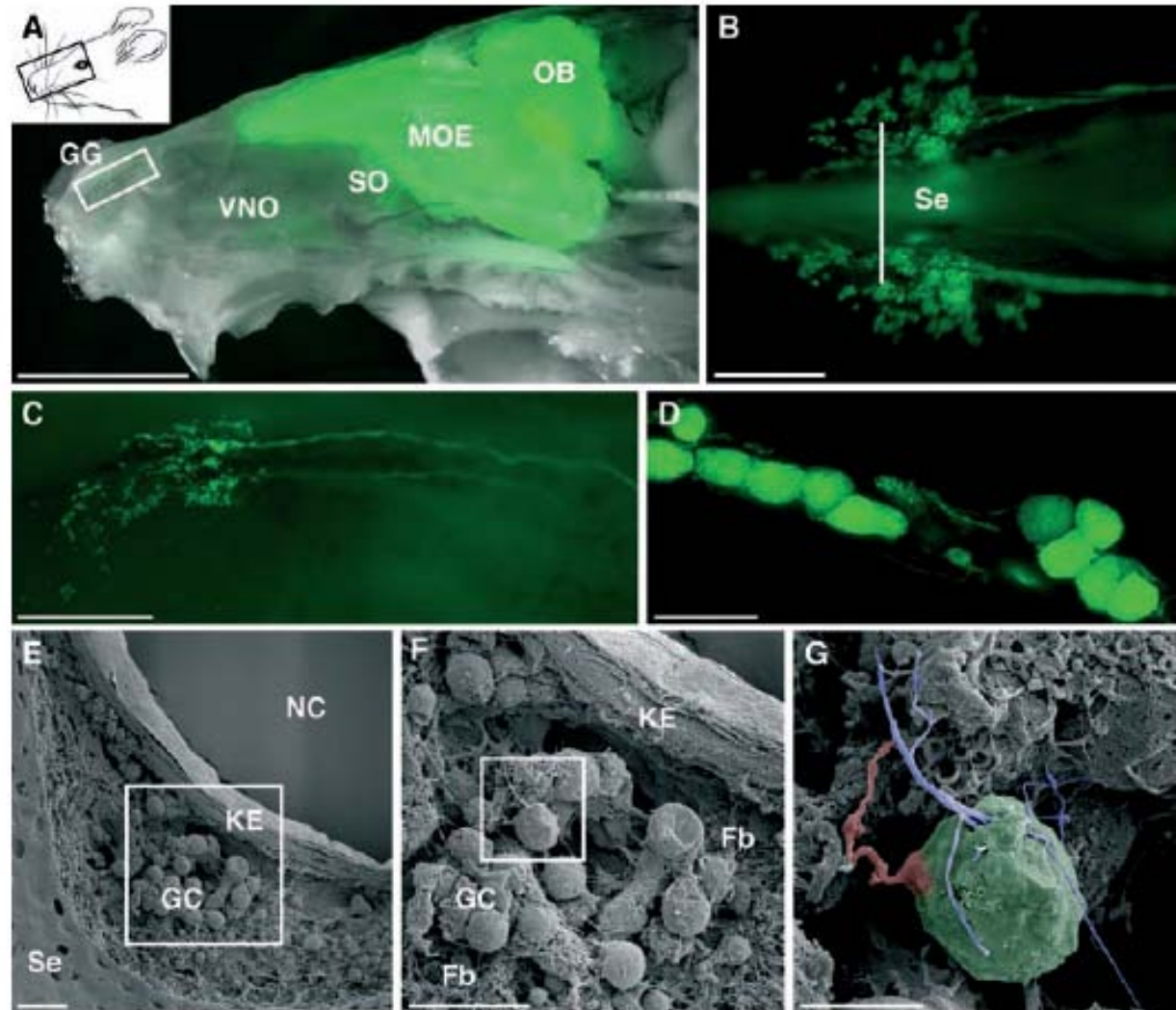
Photo: courtesy of Prof. Rodriguez (UNIGE)

Grueneberg ganglion

Grueneberg Ganglion Cells Mediate Alarm Pheromone Detection in Mice

Julien Brechbühl, Magali Klaey, Marie-Christine Broillet*

22 AUGUST 2008 VOL 321 SCIENCE

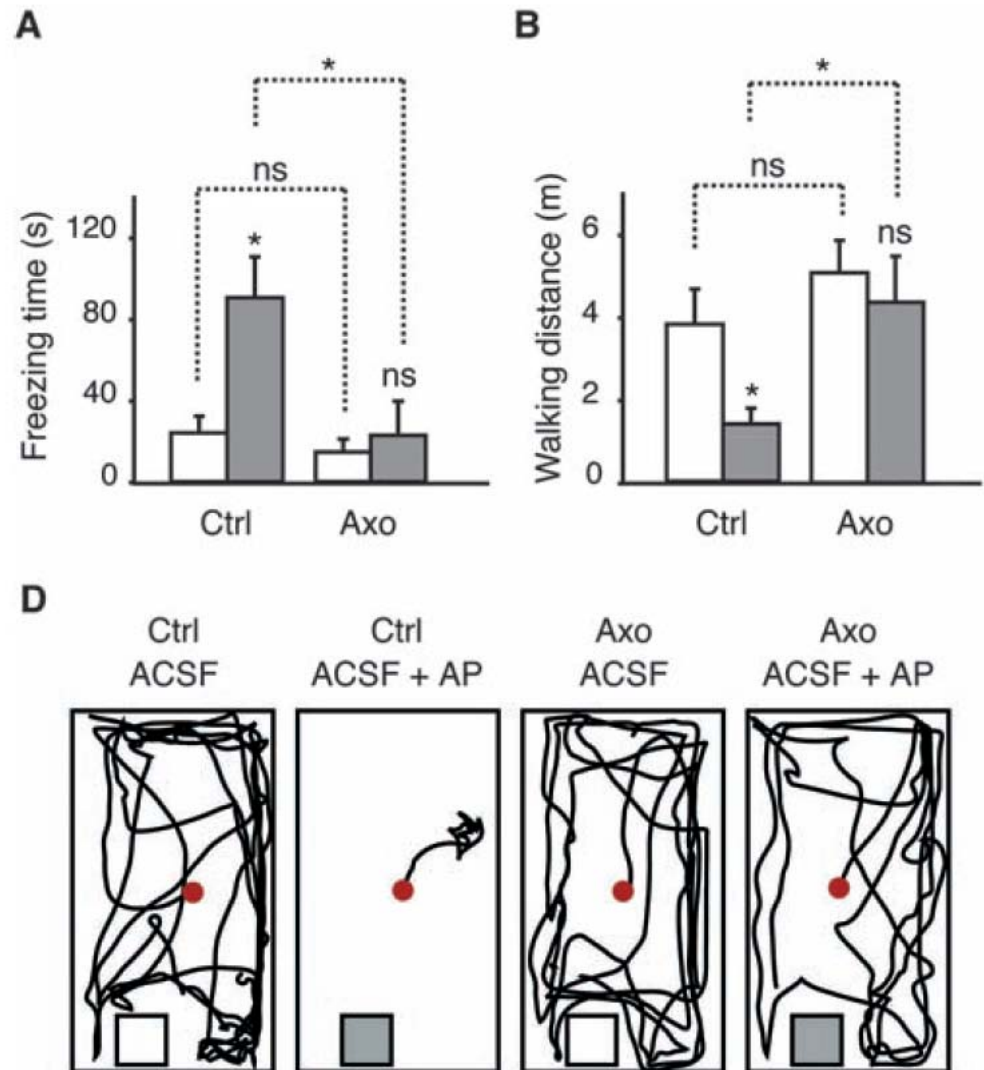


Grueneberg ganglion

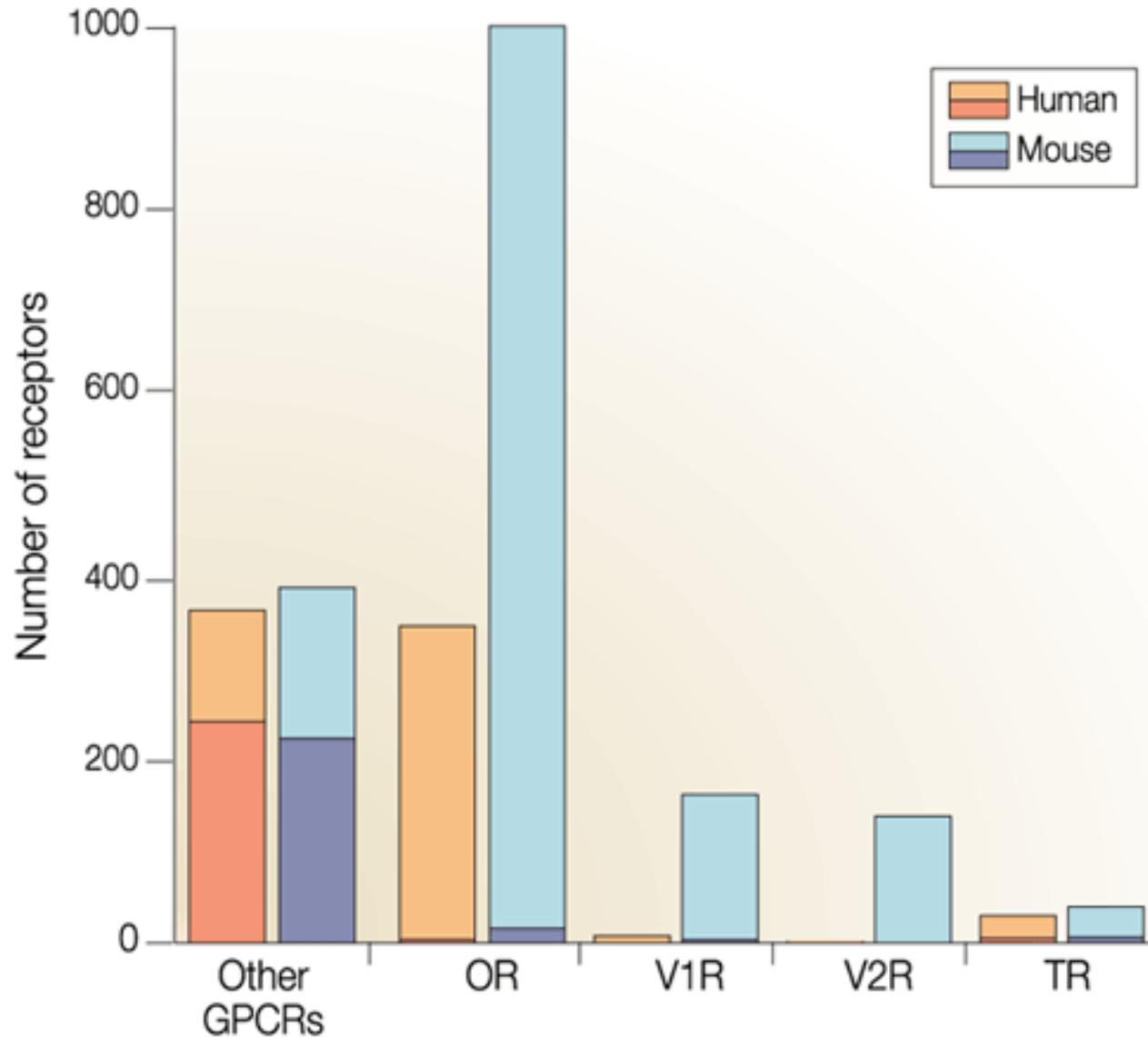
Grueneberg Ganglion Cells Mediate Alarm Pheromone Detection in Mice

Julien Brechbühl, Magali Klaey, Marie-Christine Broillet*

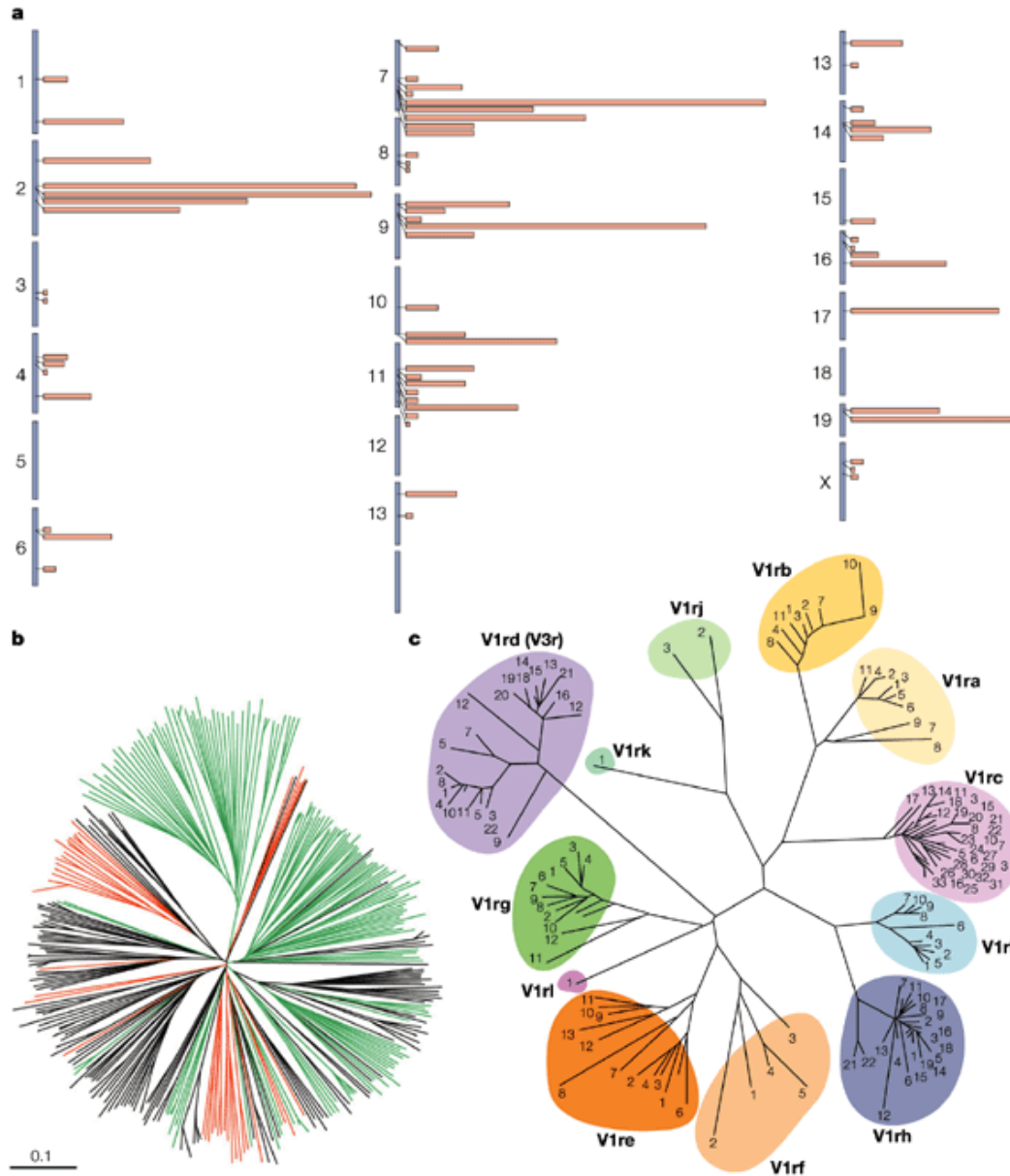
22 AUGUST 2008 VOL 321 SCIENCE



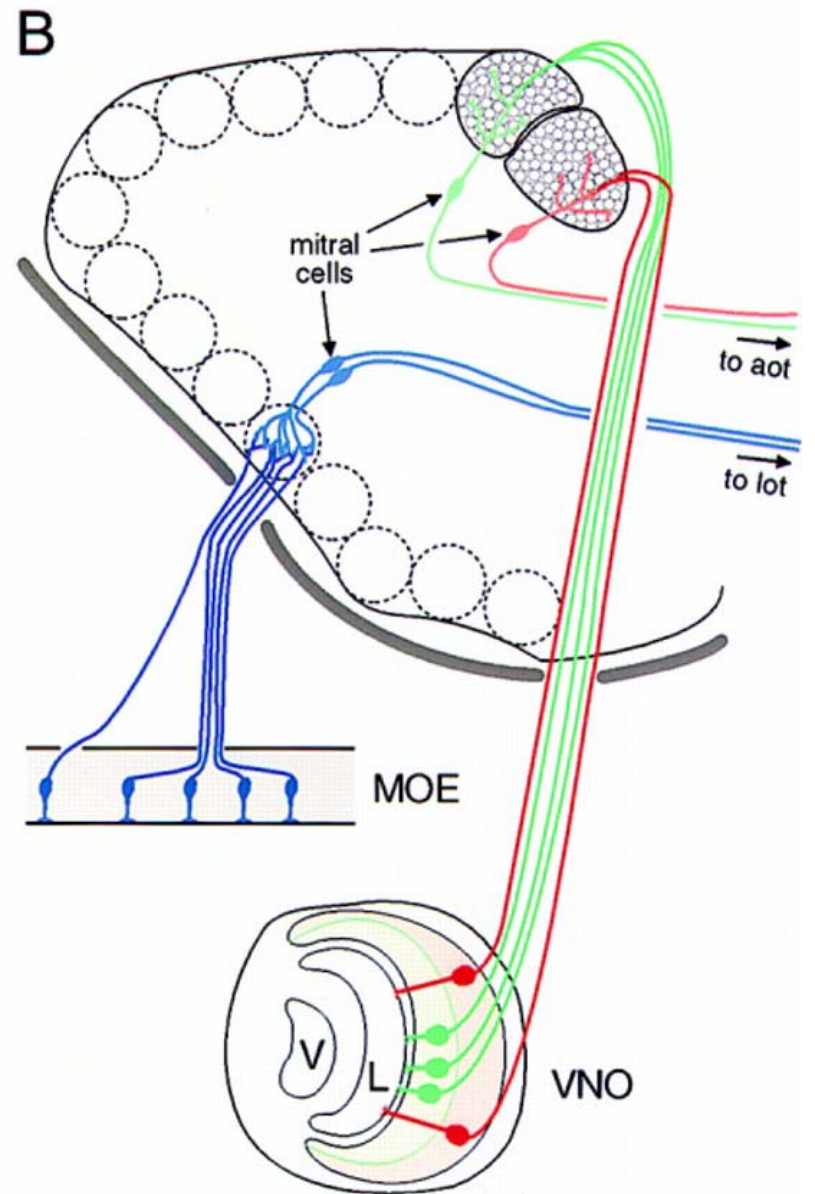
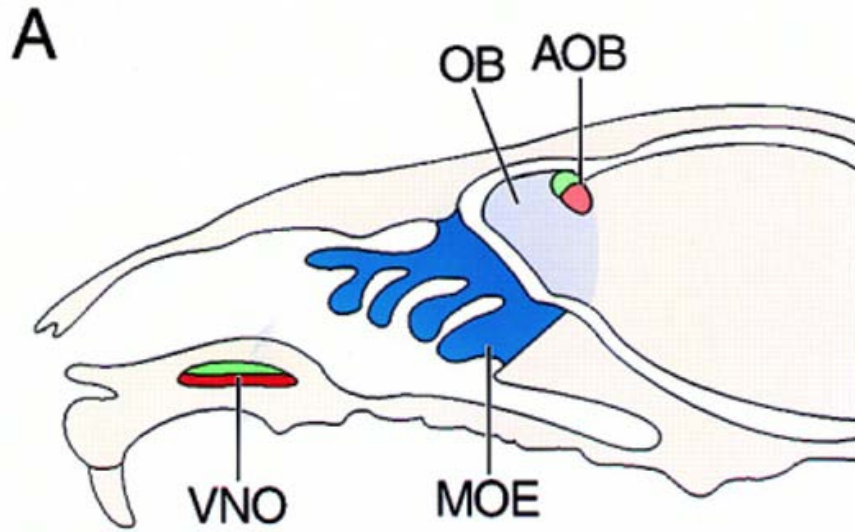
Chemical senses receptors



Vomerinal receptors



Organization of the olfactory systems



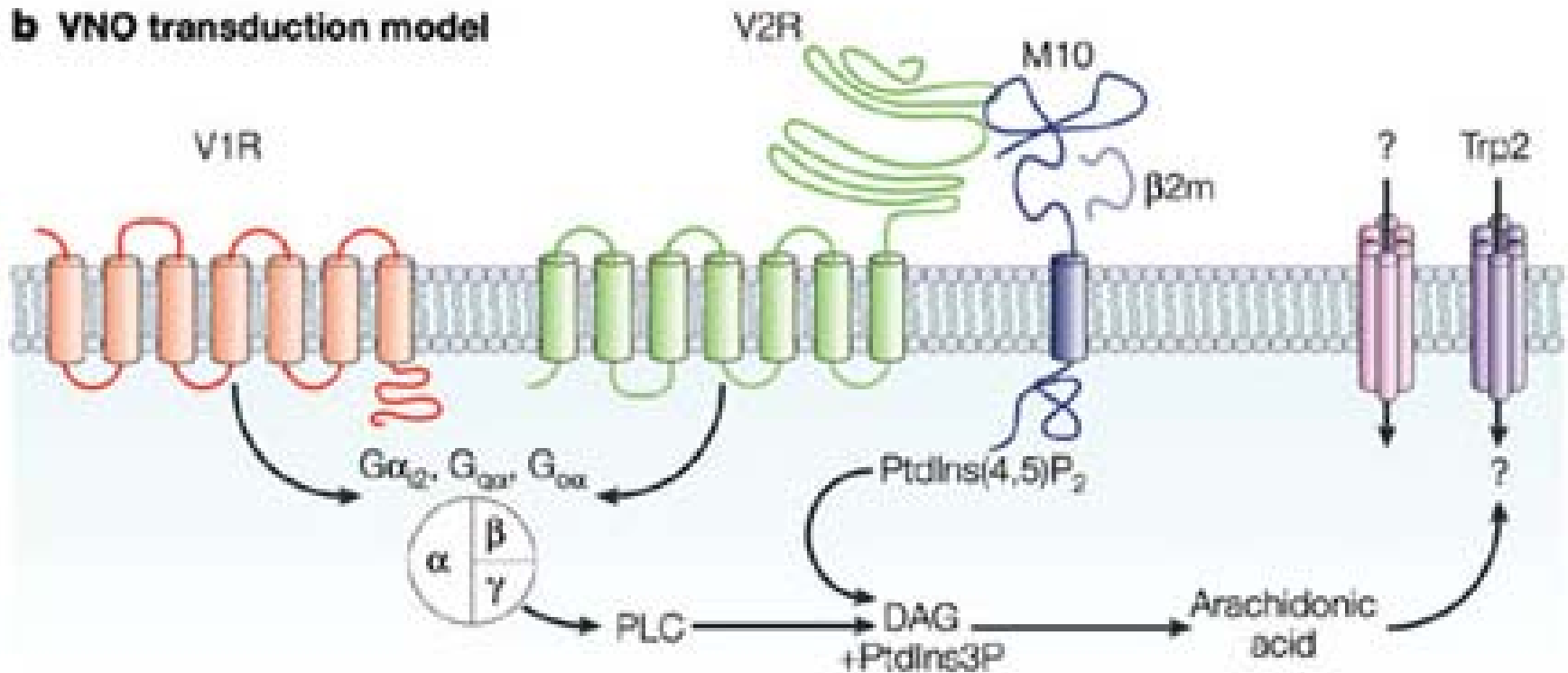
OR

V2R

V1R

Transduction in the VNO

b VNO transduction model

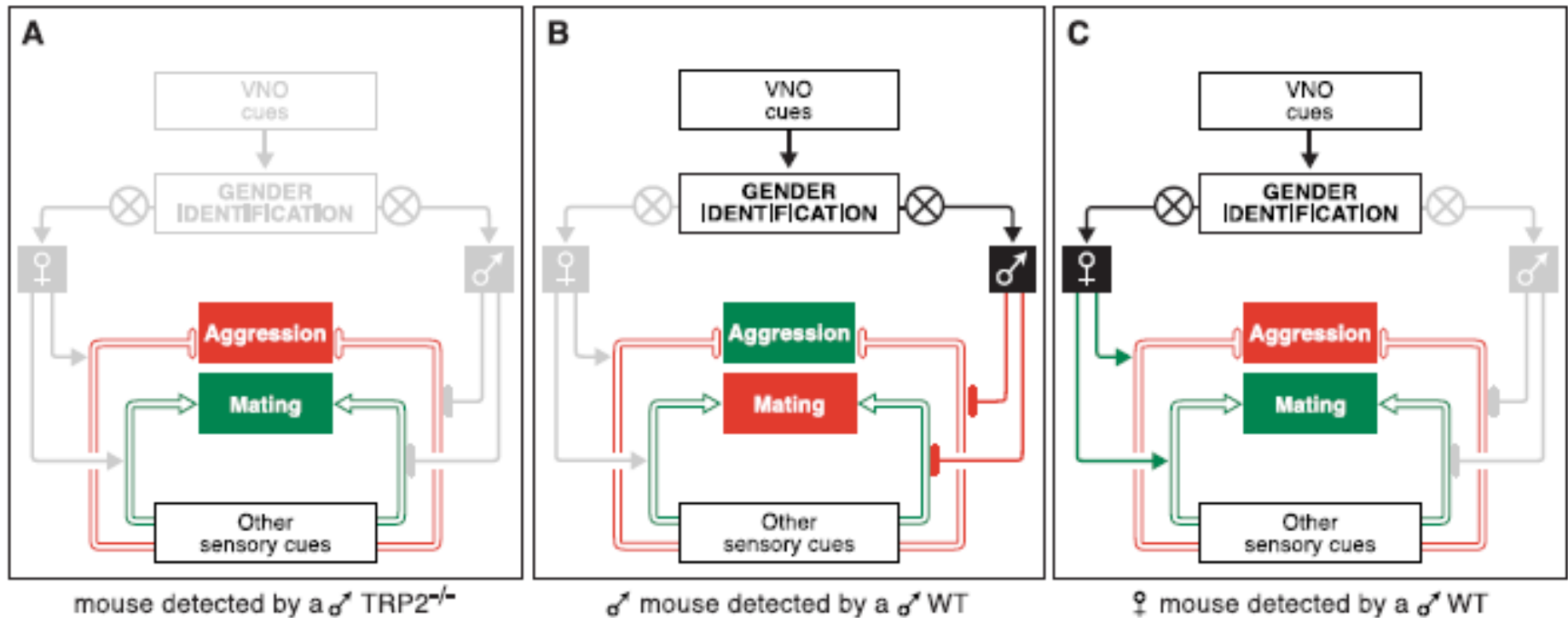


Sexual behavior controlled by the vomeronasal organ

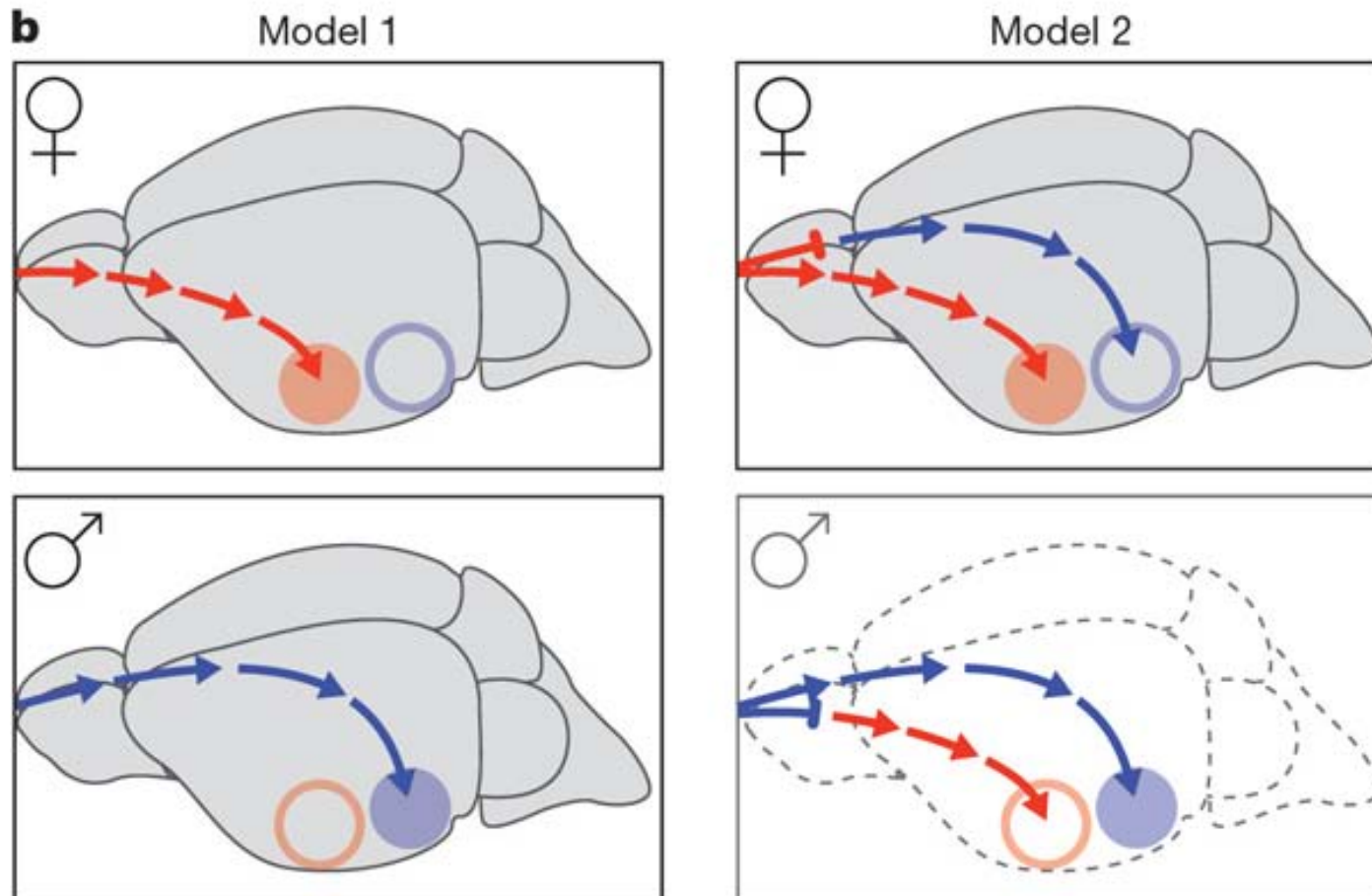
Loss of Sex Discrimination and Male-Male Aggression in Mice Deficient for TRP2

Lisa Stowers,¹ Timothy E. Holy,^{2*} Markus Meister,²
Catherine Dulac,^{1†} Georgy Koentges^{1‡}

SCIENCE VOL 295 22 FEBRUARY 2002

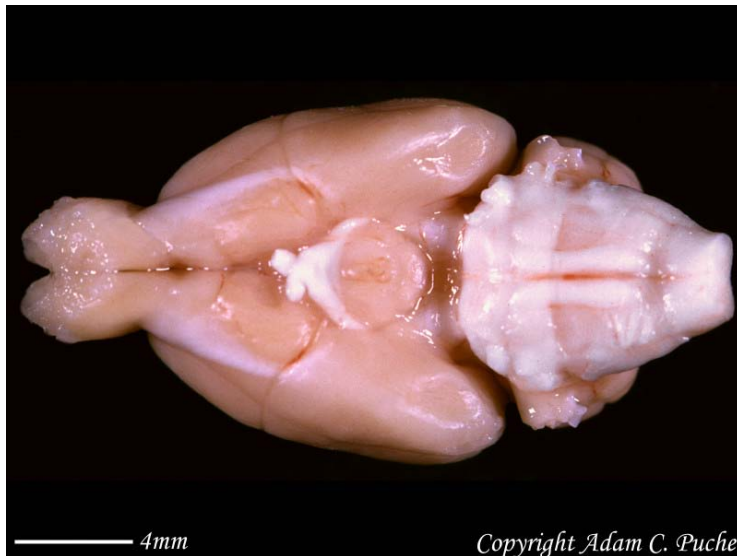
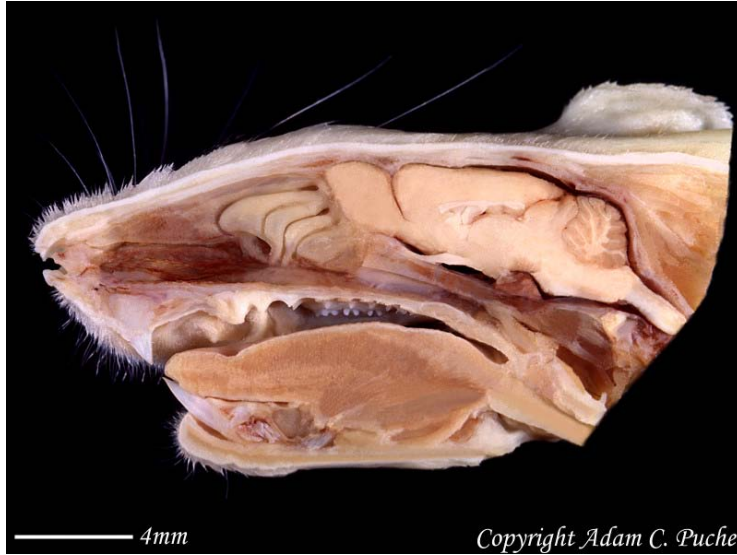


Sexual behavior controlled by the vomeronasal organ

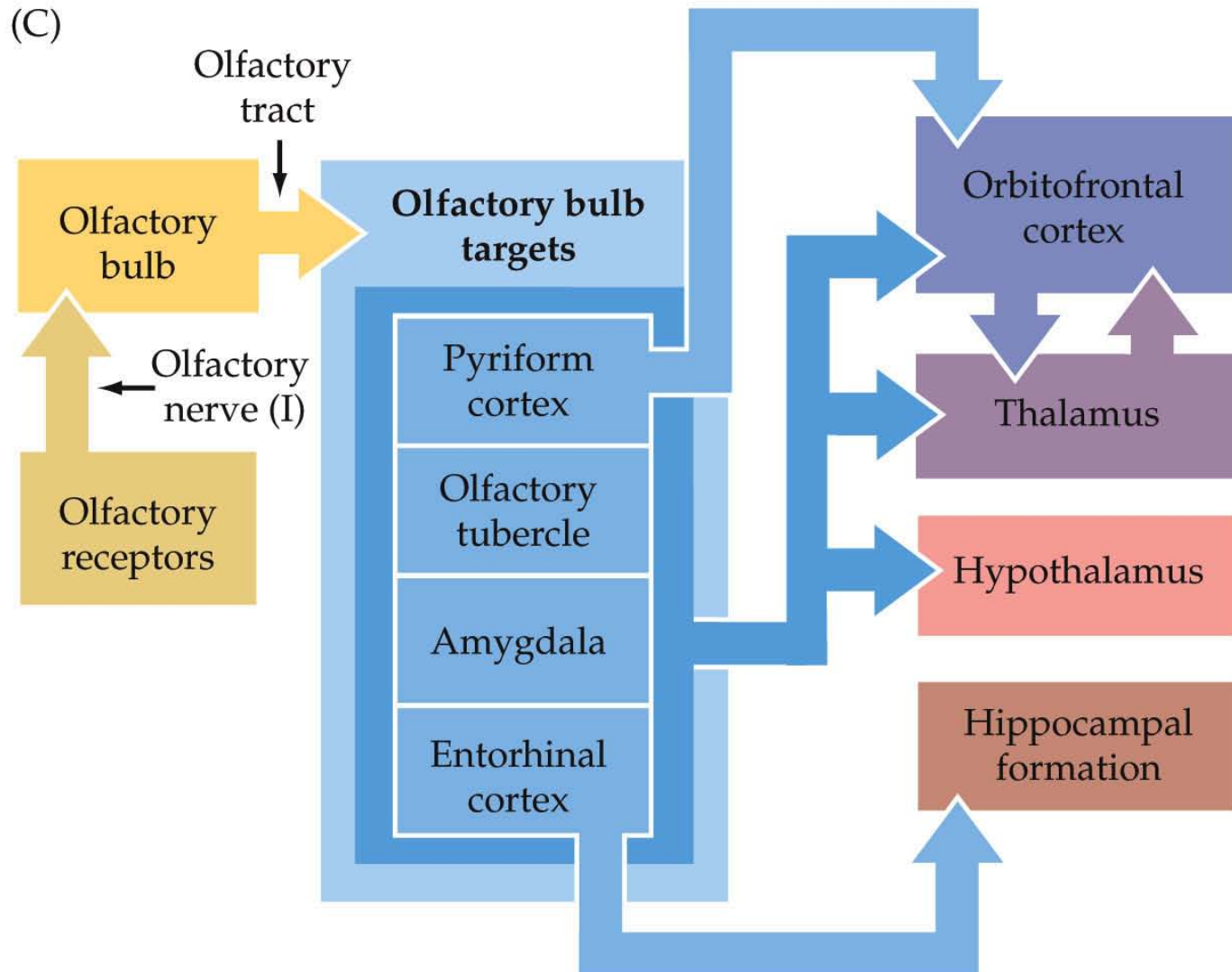


A functional circuit underlying male sexual behaviour in the female mouse brain
Tali Kimchi, Jennings Xu & Catherine Dulac
Nature **448**, 1009-1014 (2007)

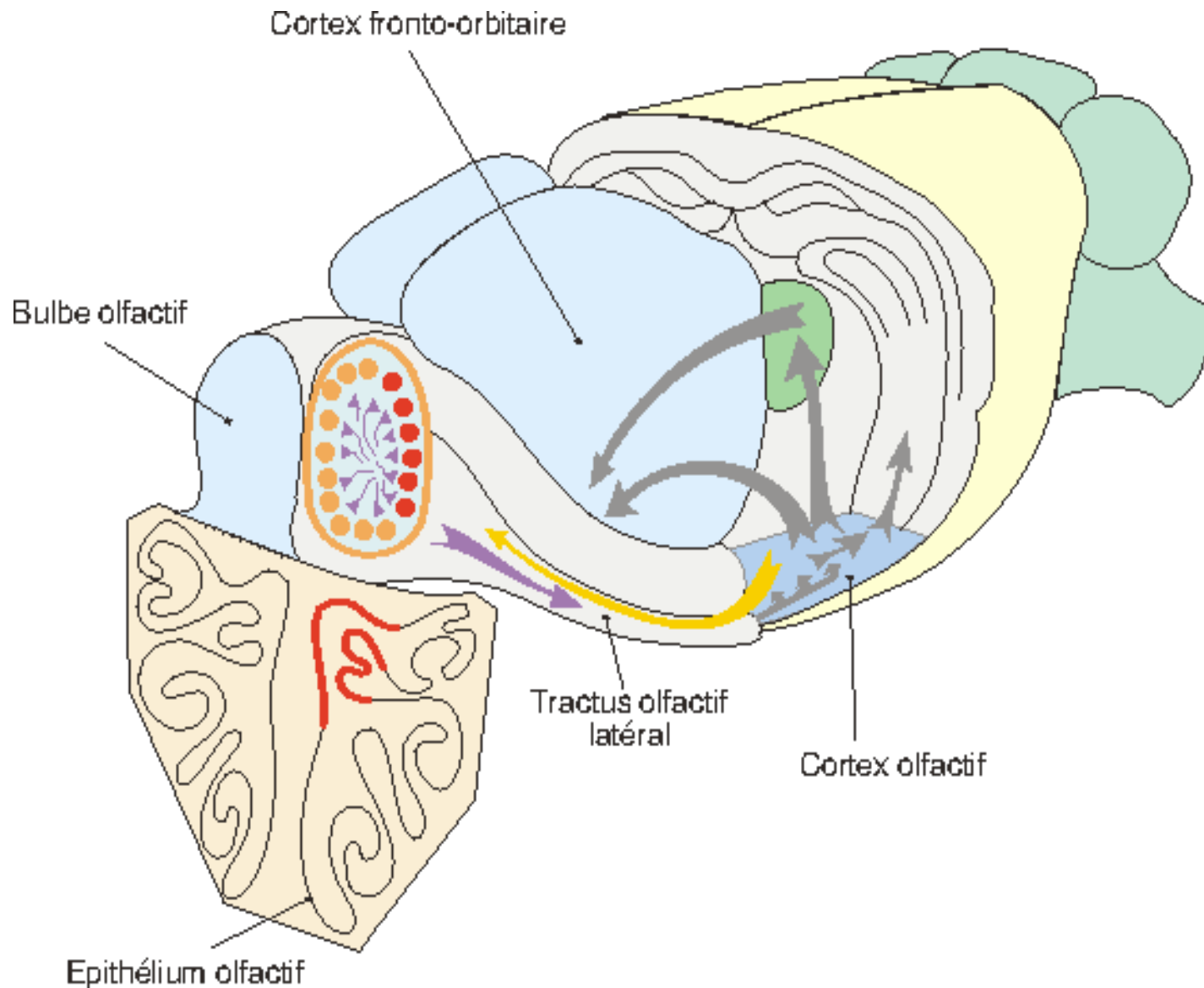
Organization of the olfactory system



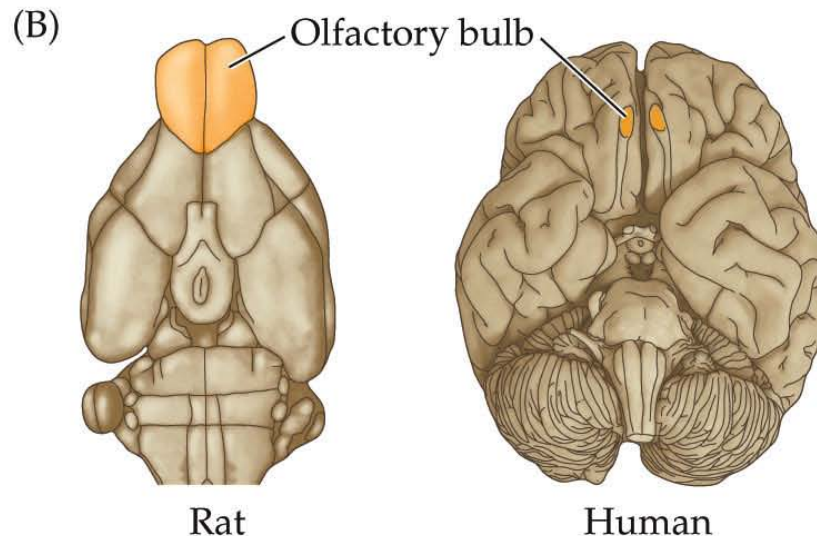
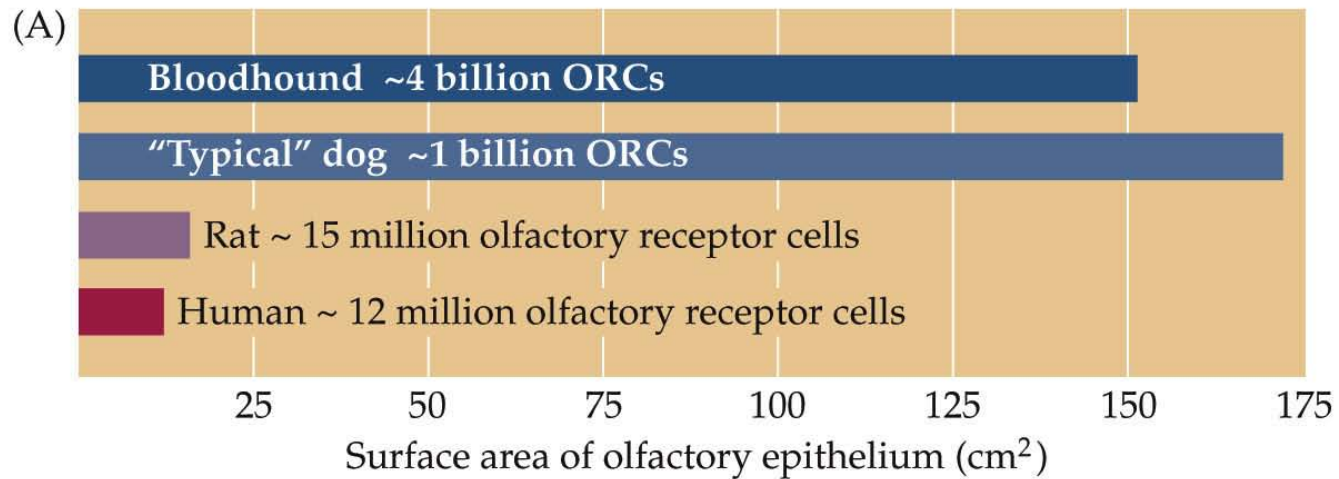
Organization of the main olfactory system



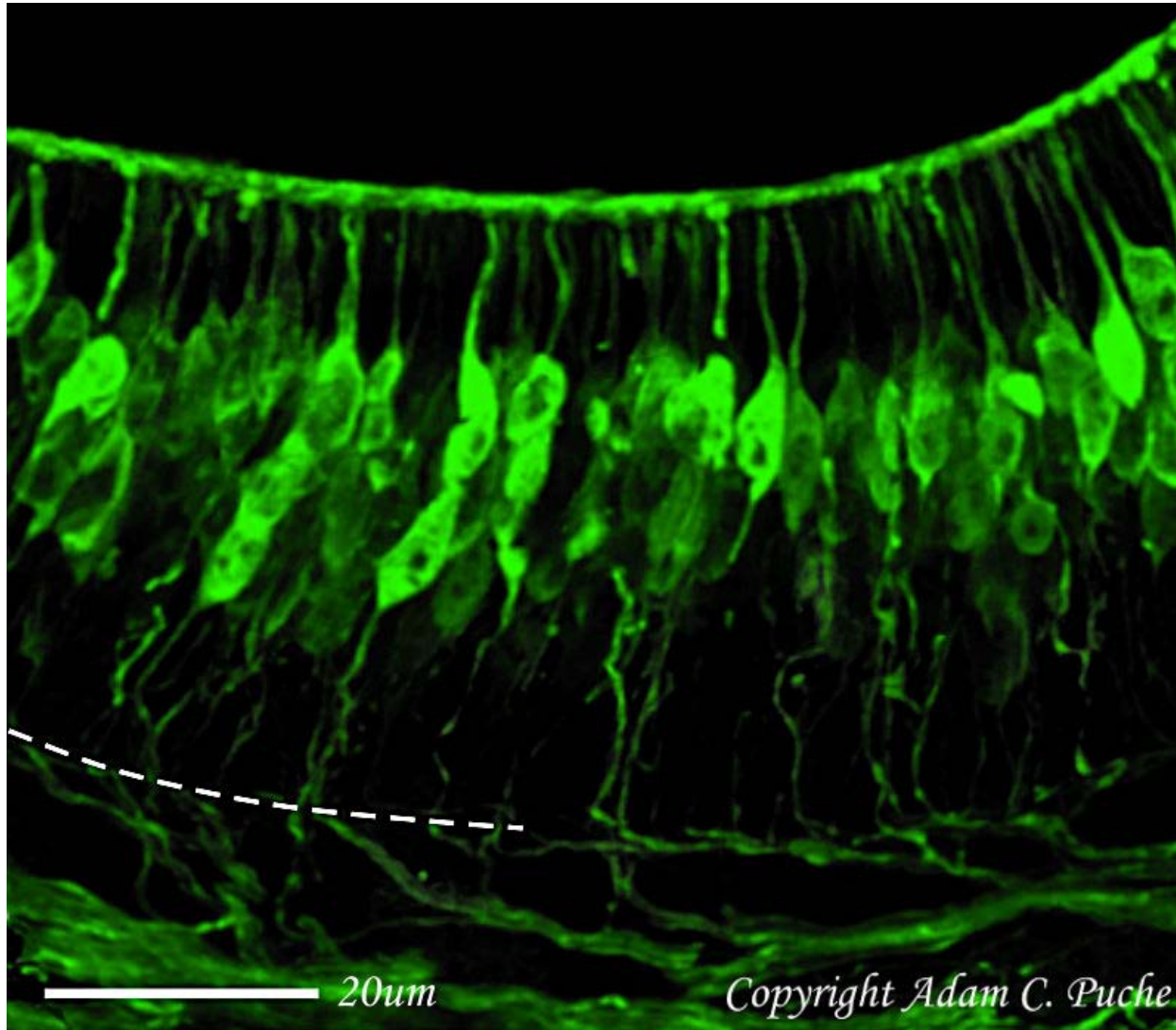
Organization of the main olfactory system



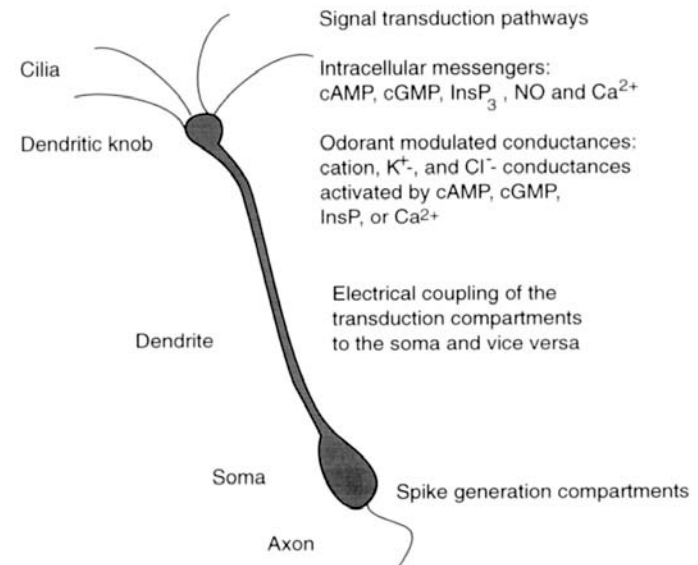
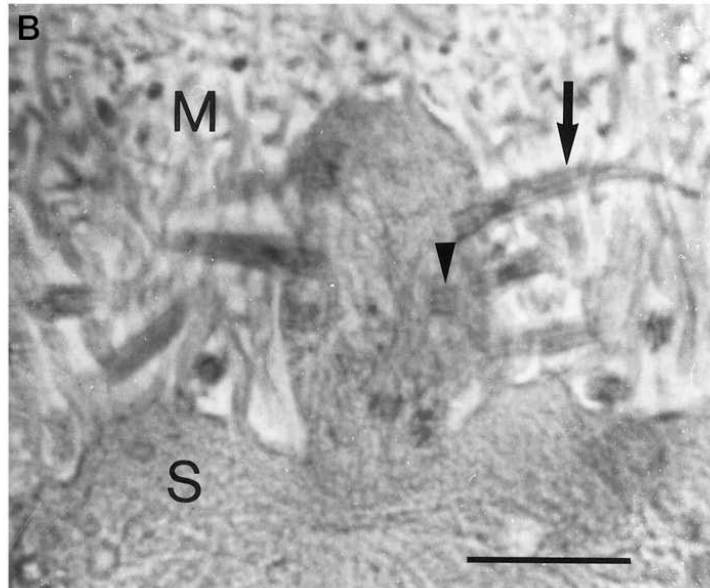
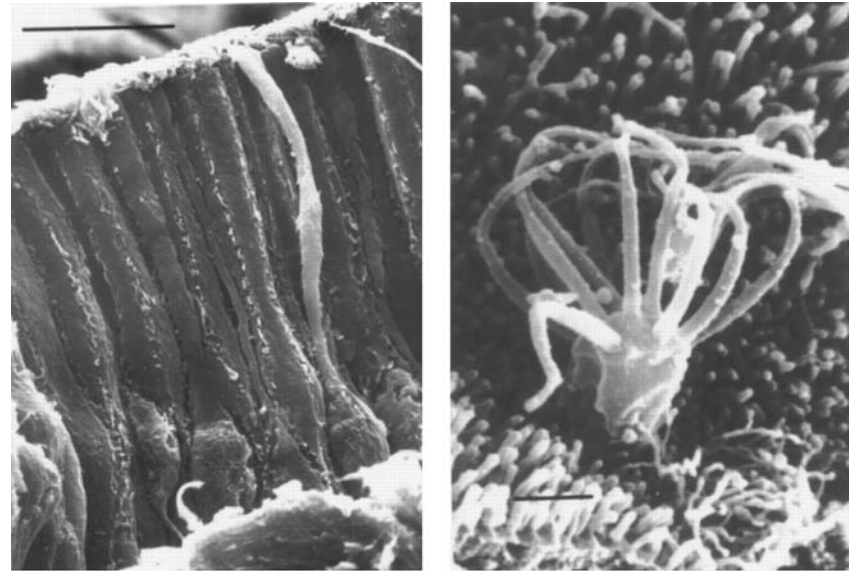
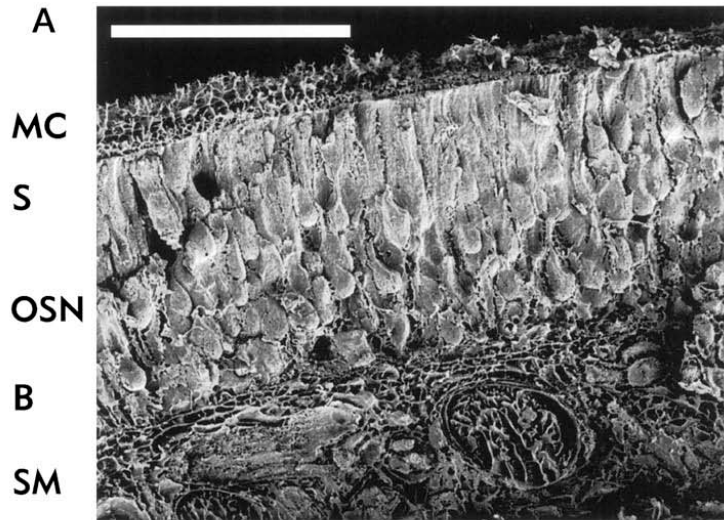
The main olfactory epithelium



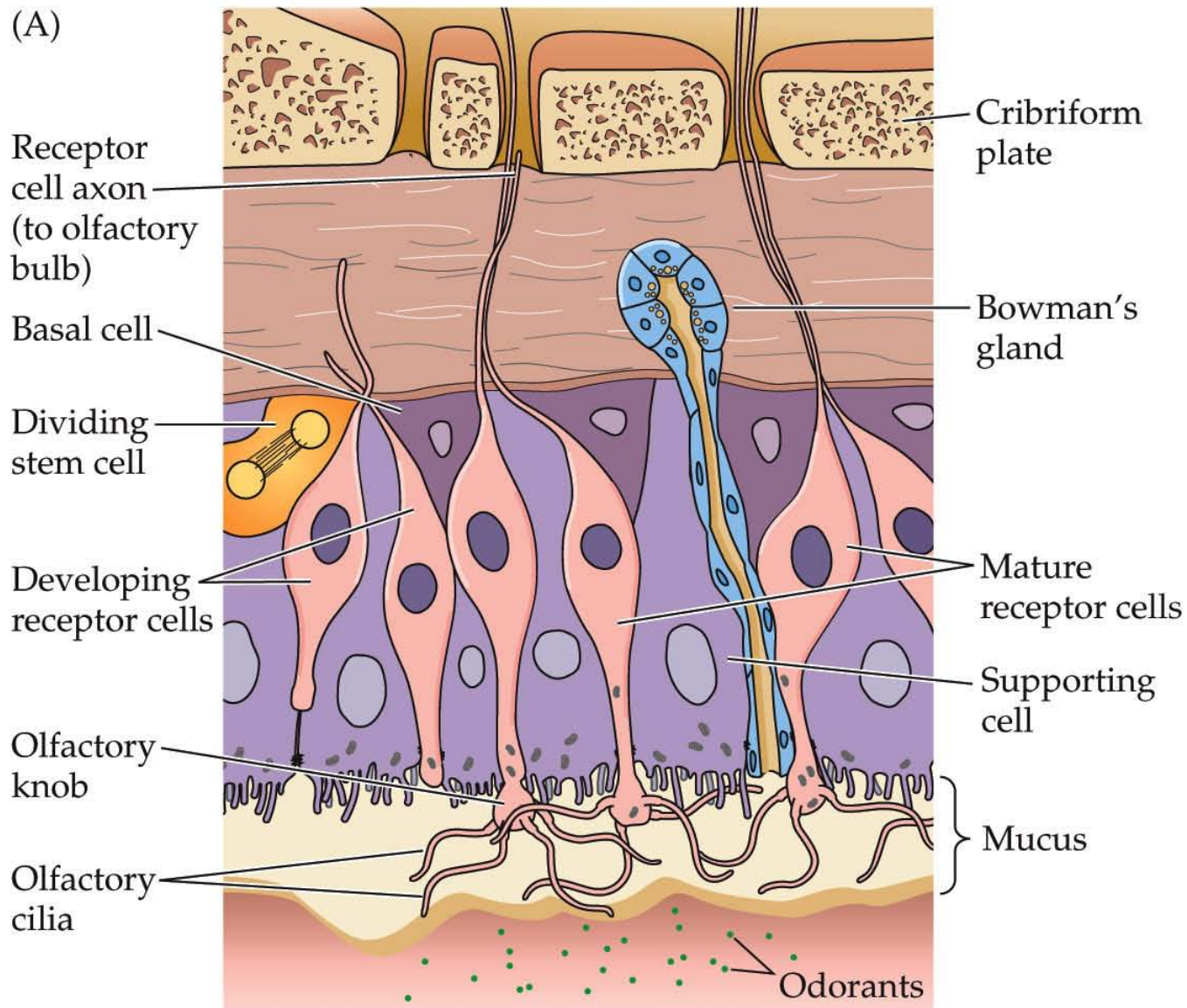
Sensory neurons in the main olfactory epithelium



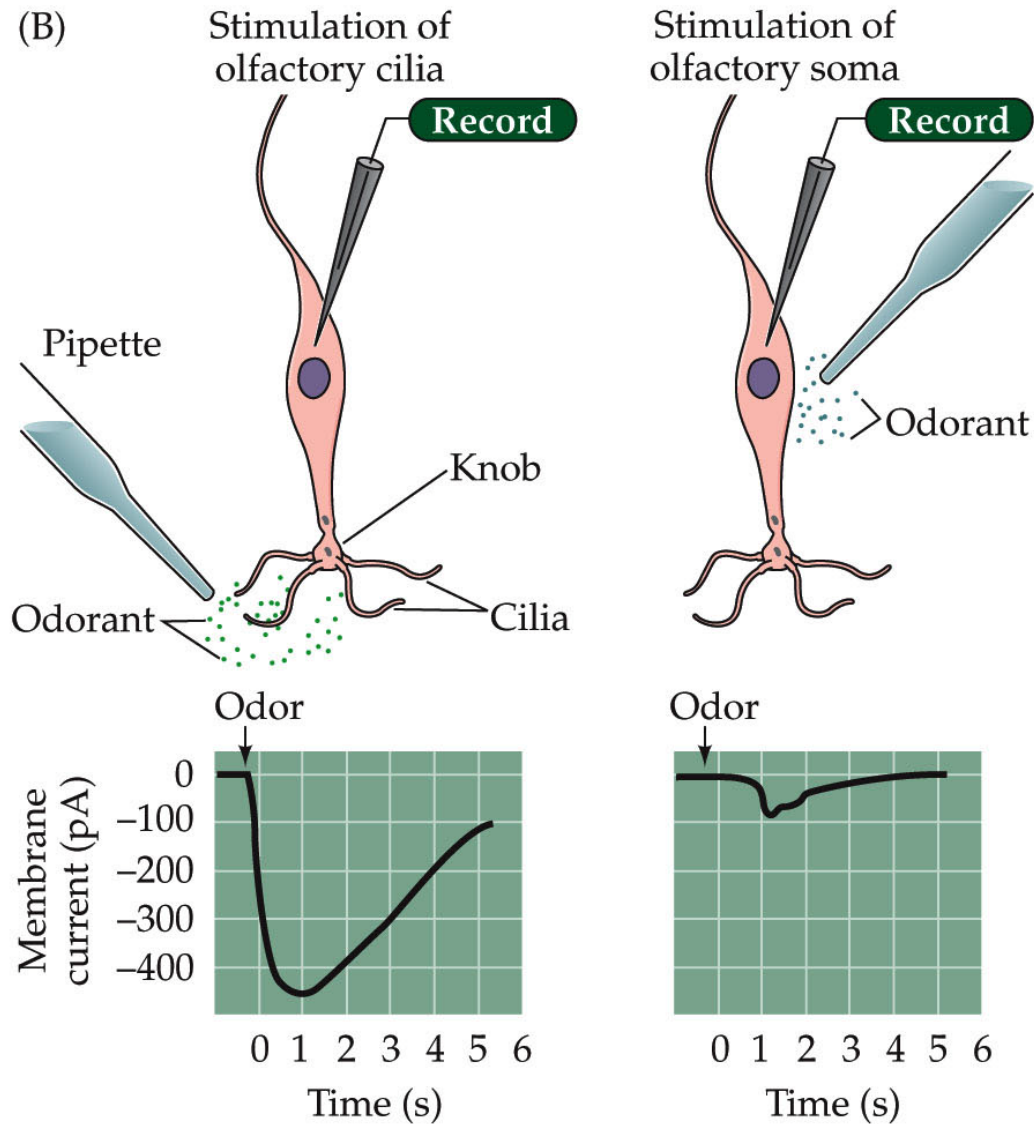
Sensory neurons in the main olfactory epithelium



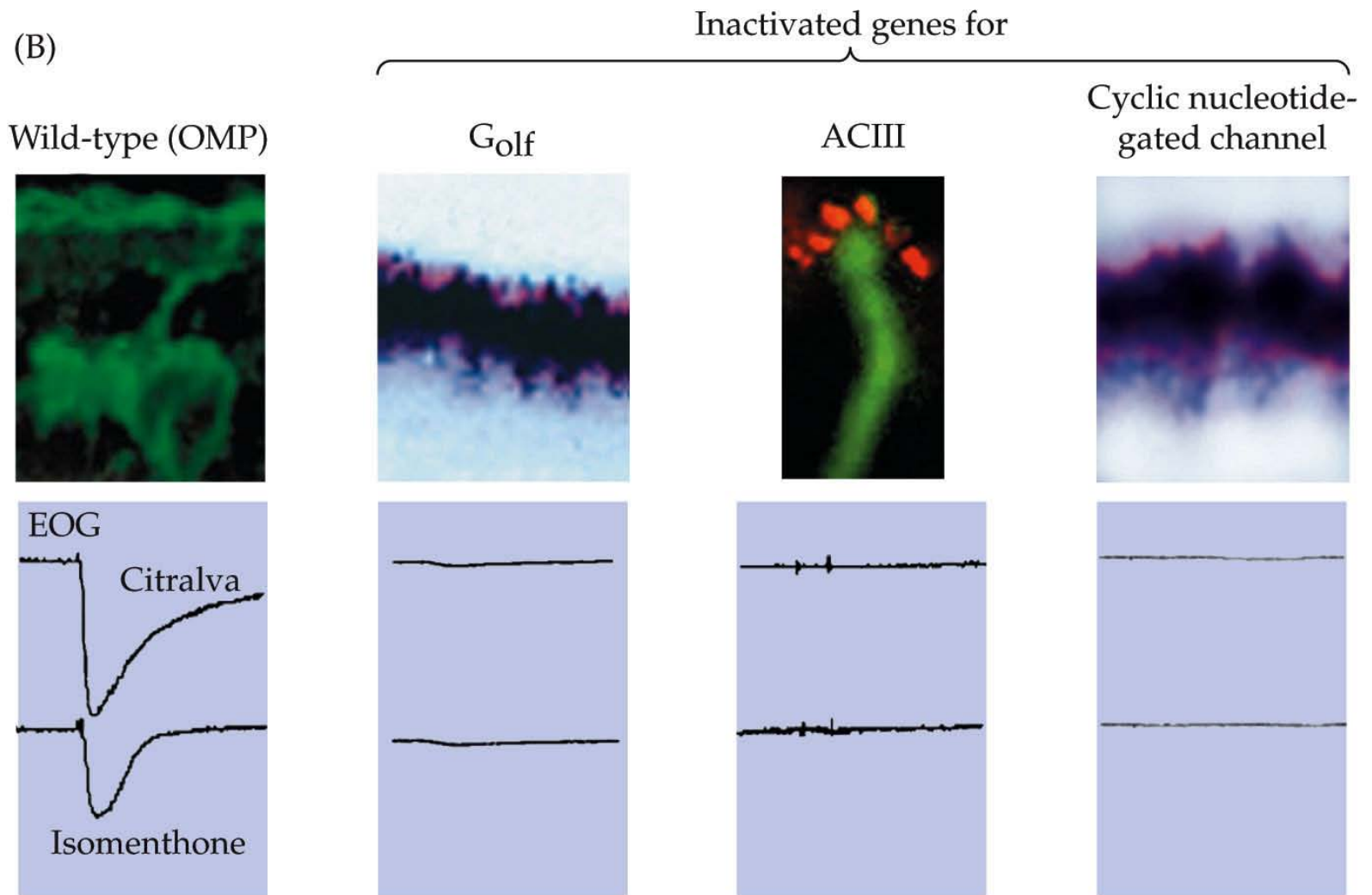
Organization of the main olfactory epithelium



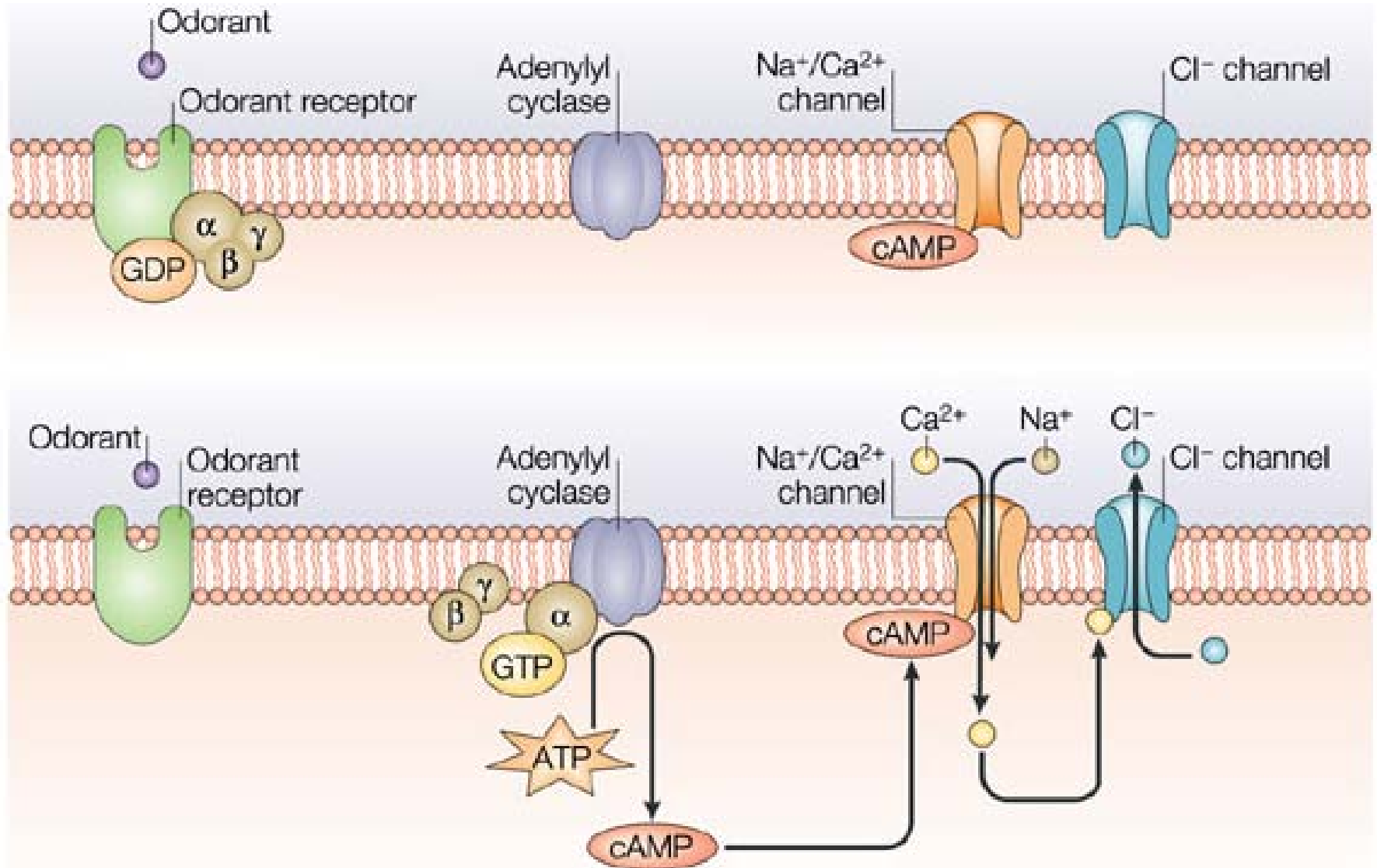
Transduction in the MOE



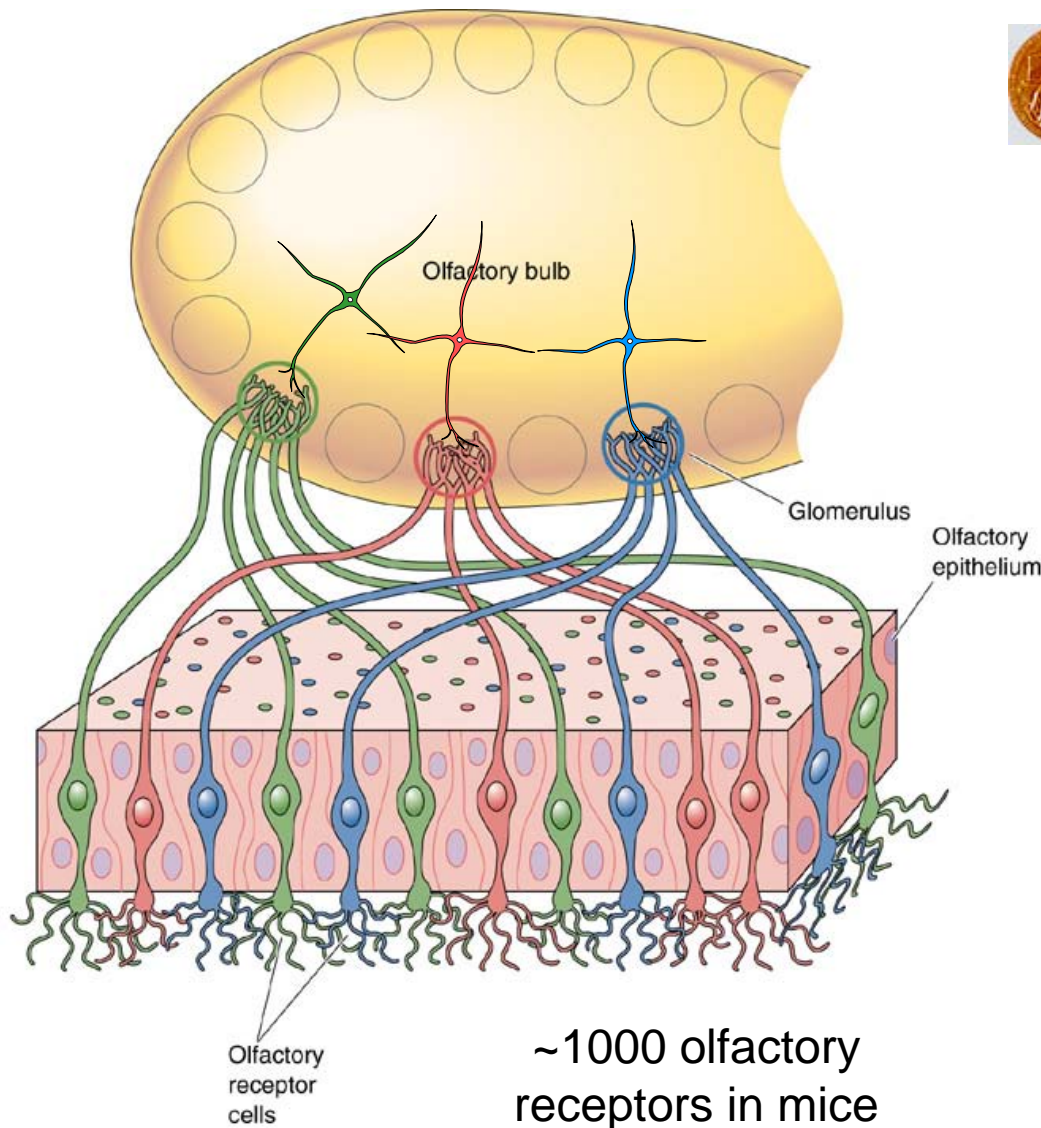
Transduction in the MOE



Transduction in the MOE



Organization of the olfactory system



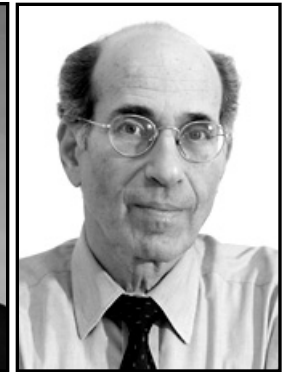
~1000 olfactory receptors in mice



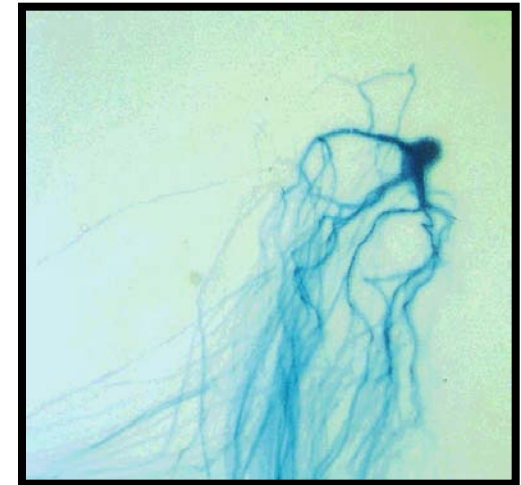
The Nobel Prize in Physiology or Medicine 2004



L. Buck

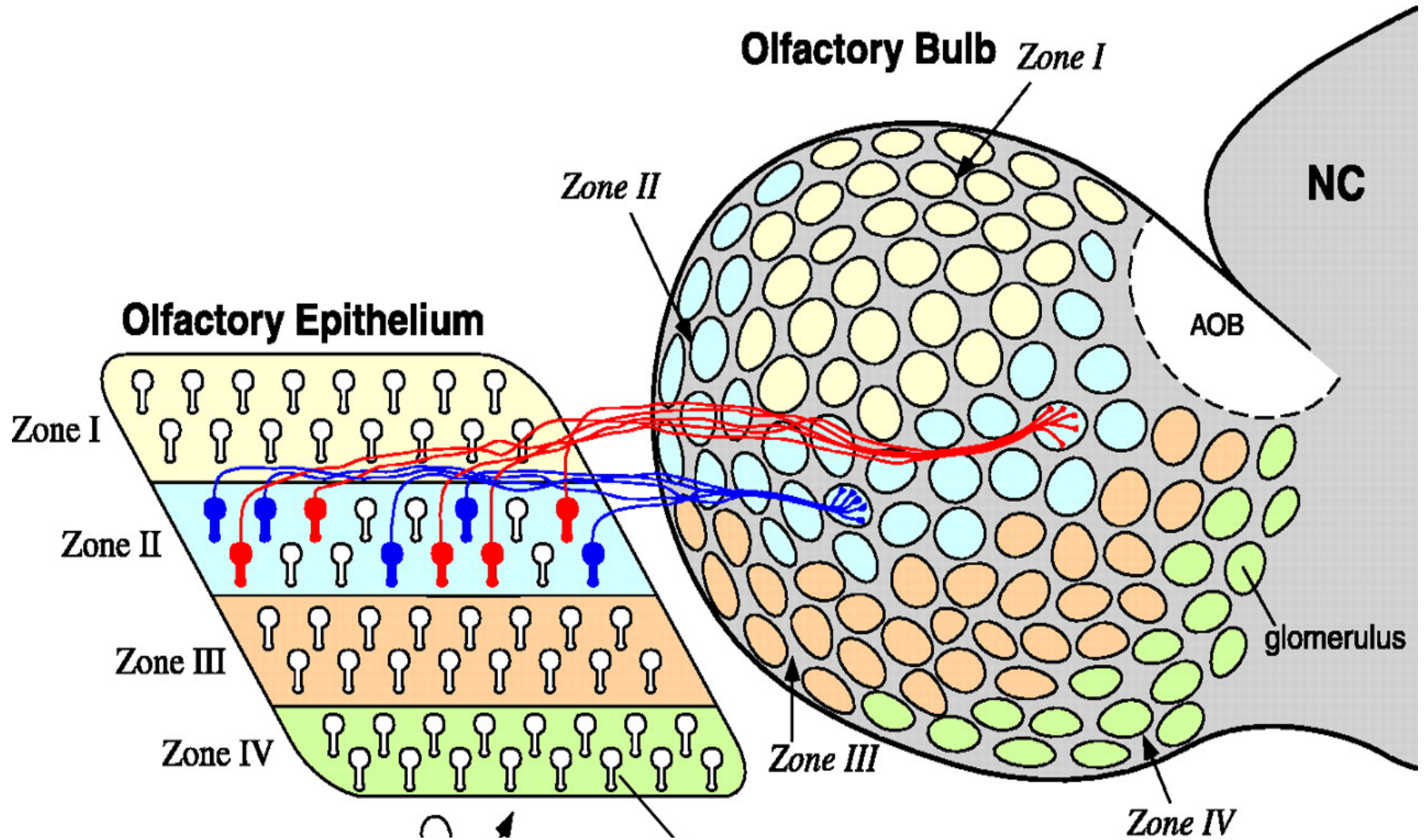


R. Axel



(M50-TauLacZ) Tg mouse

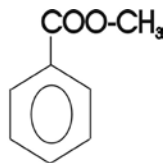
Zonal organization



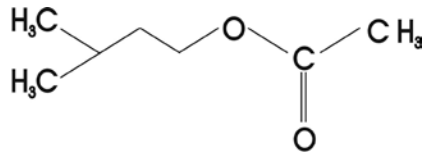
Simplex and complex odors



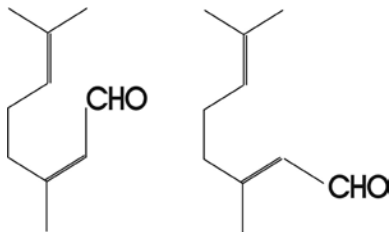
Butanal



Methyl Benzoate

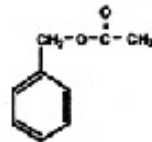


Iso-Amylacetate



Citral

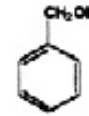
Jasmine



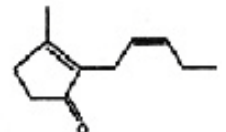
benzyl acetate
(major component)



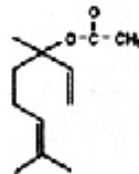
d-linalool



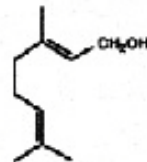
benzyl alcohol



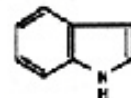
jasmine
(peculiar component)



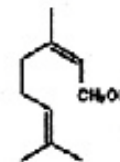
linalyl acetate



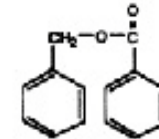
geraniol



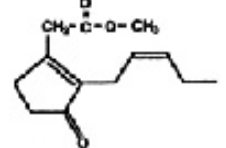
indole



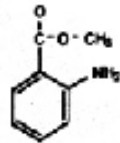
nerol



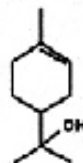
benzyl benzoate



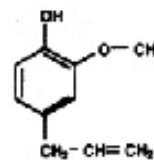
methyl jasmonate
(peculiar component)



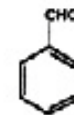
methyl anthranilate



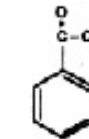
α -terpineol



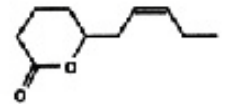
eugenol



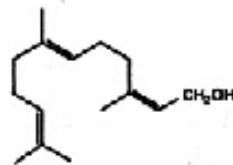
benzaldehyde



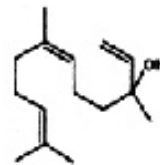
benzoic acid



jasmine lactone
(peculiar component)



farnesol



nerolidol



p-cresol



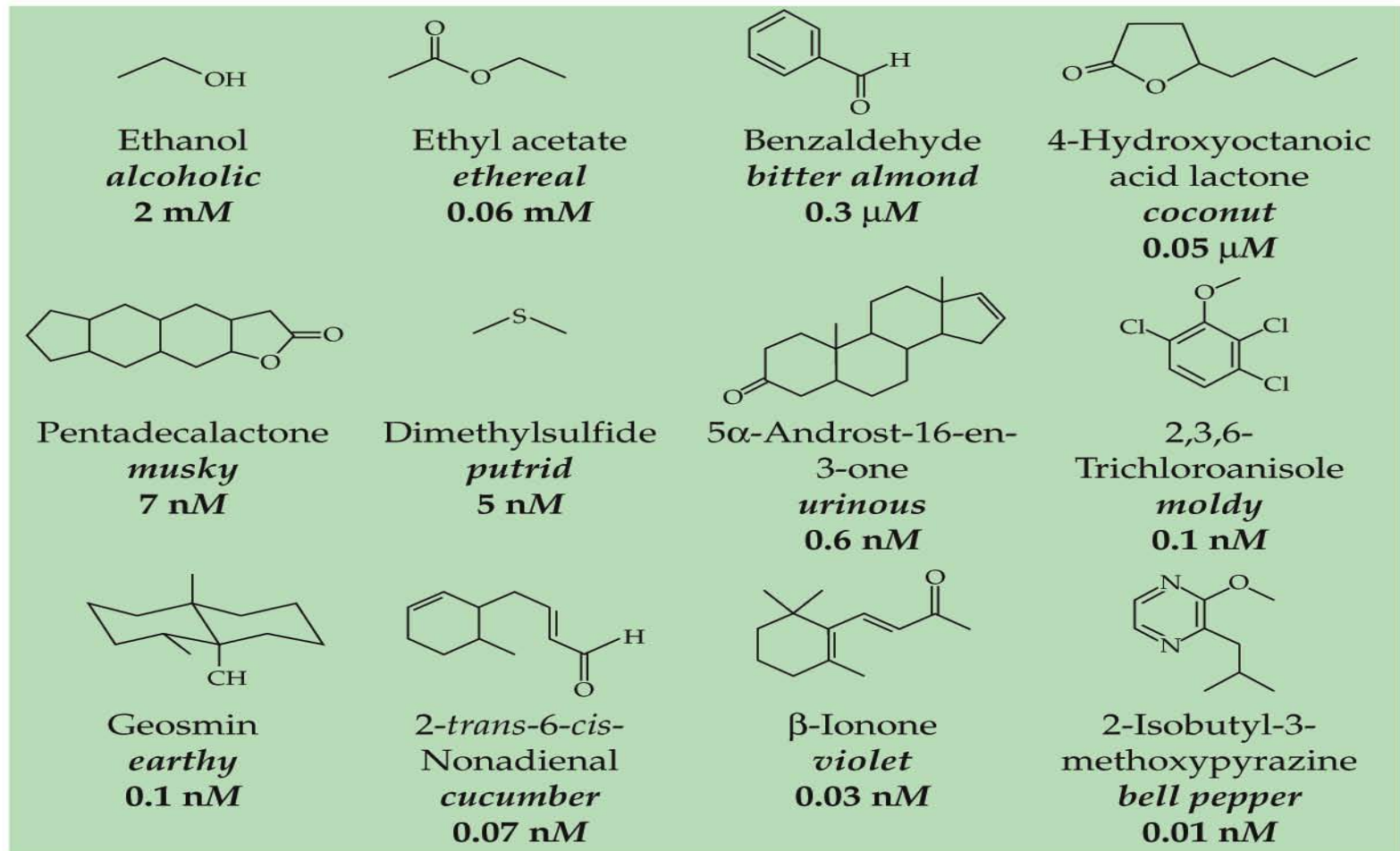
nonadiene - 2, 6 - ol

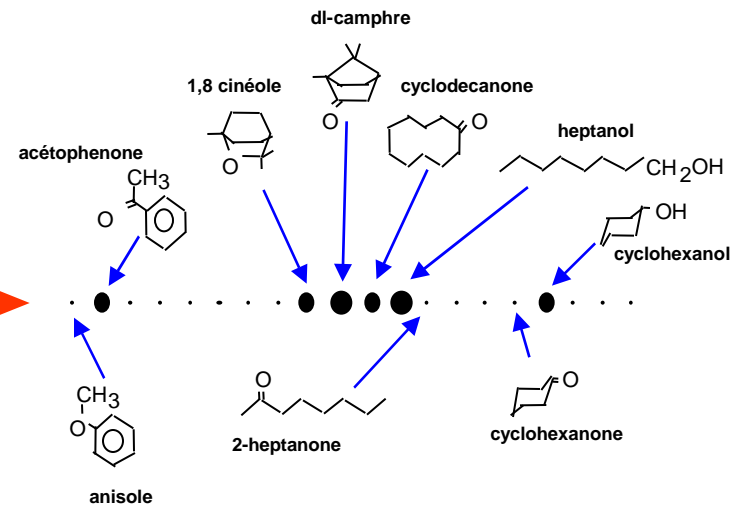
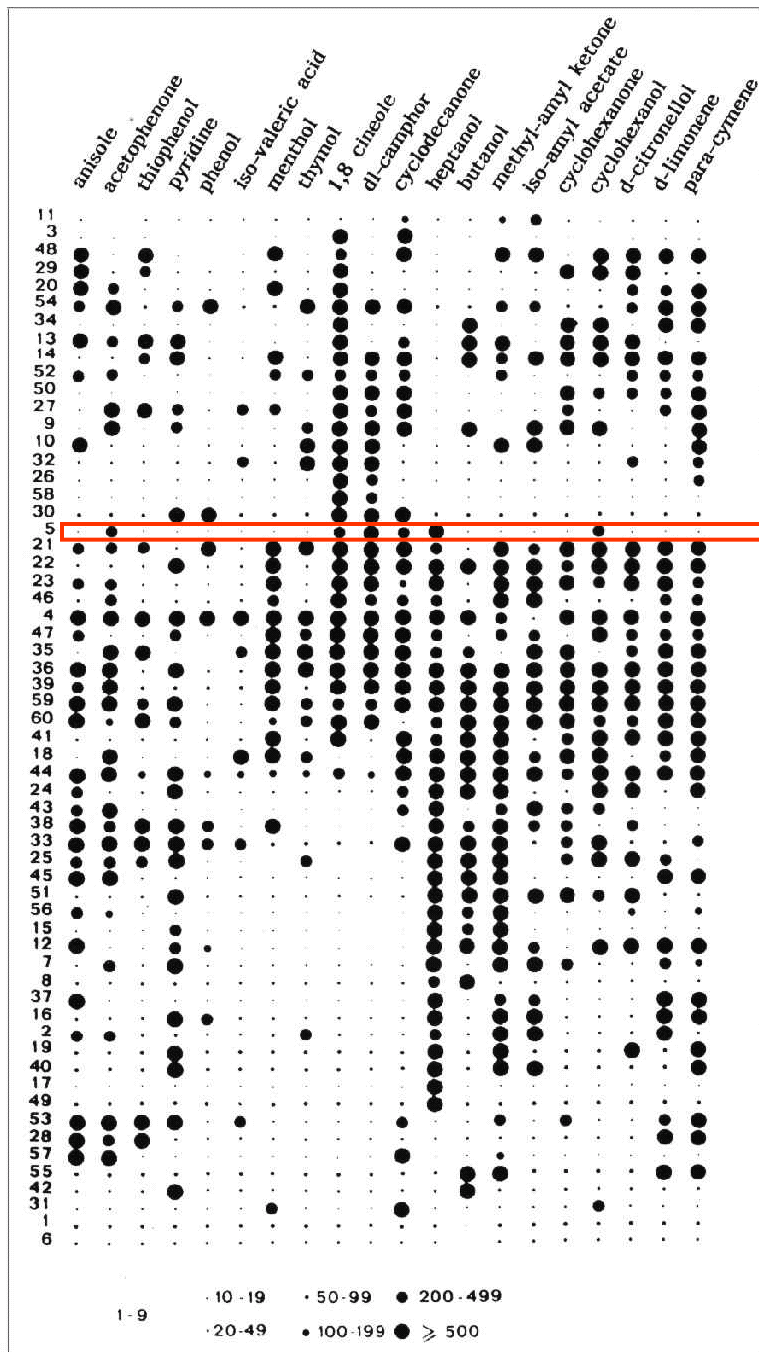


nonadiene - 2, 6 - al

Odor detection in mammals

(C)

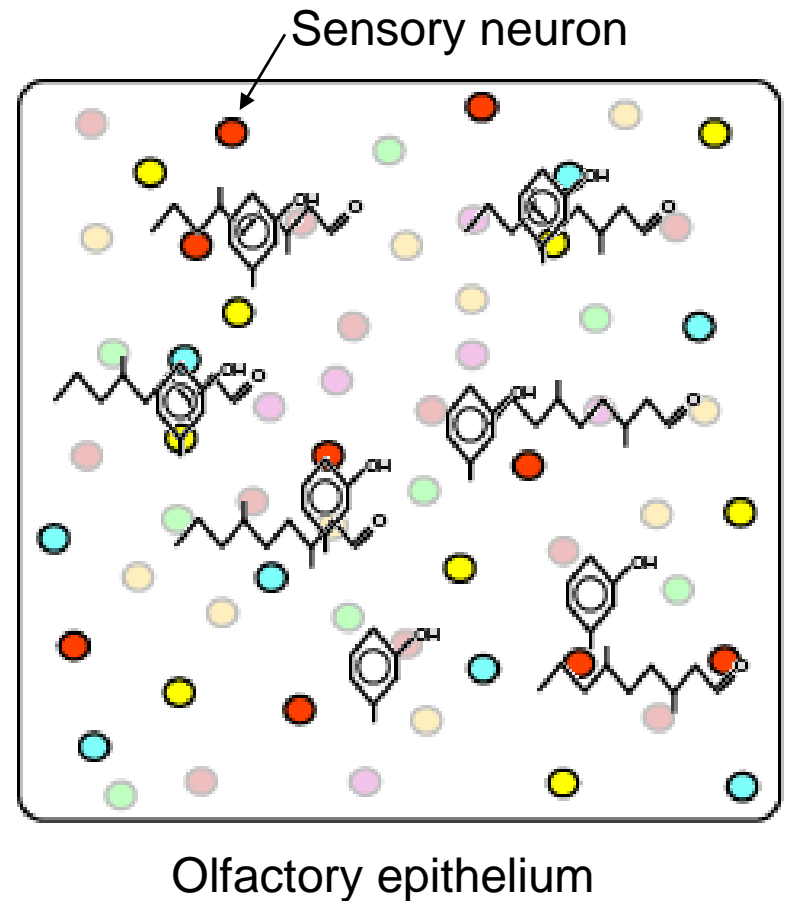




Sicard, G. and Holley, A. (1984). Receptor cell responses to odorants: similarities and differences among odorants. *Brain Research*, 292, (2), 283-96.

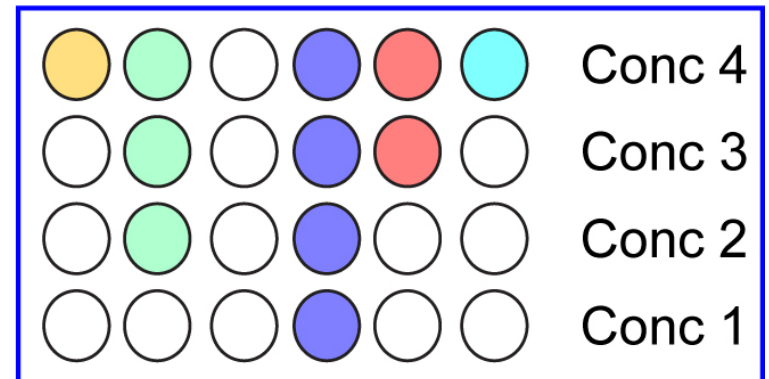
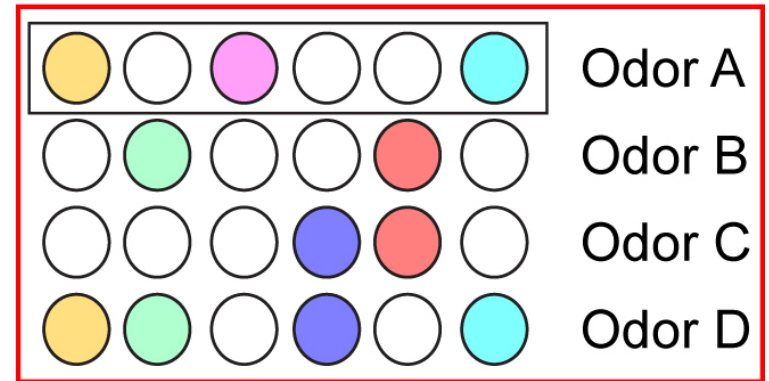
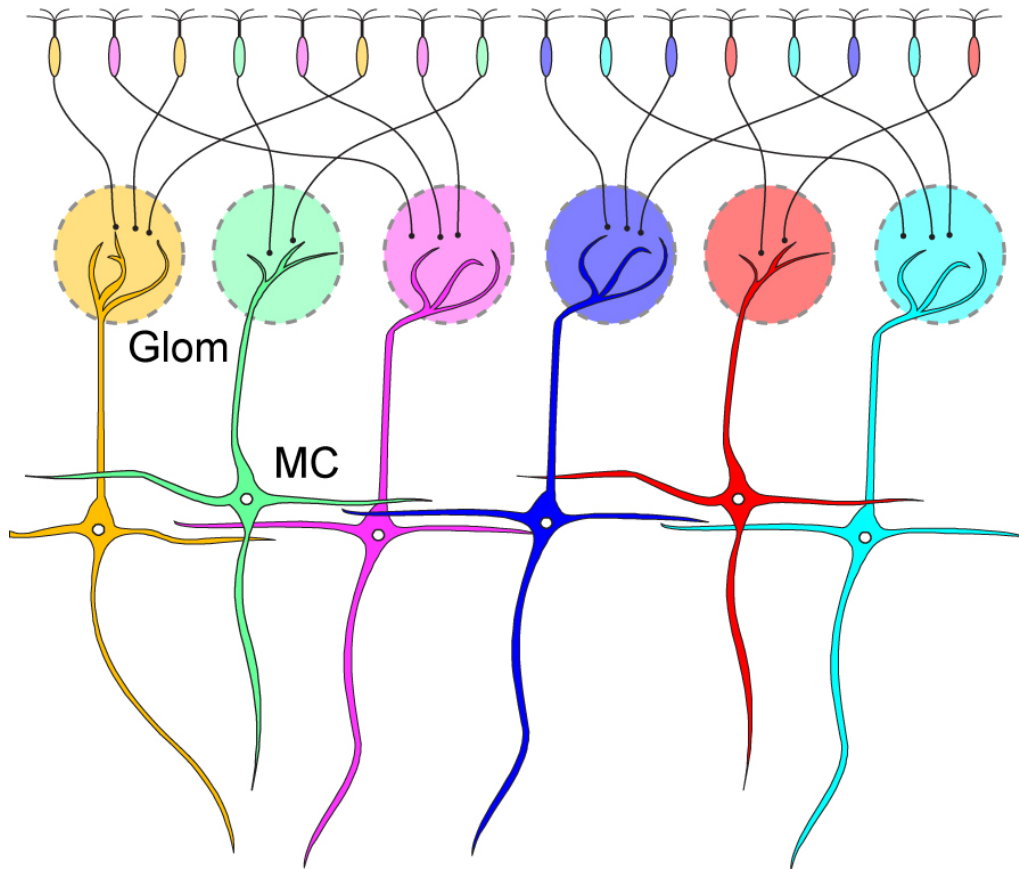
Chemodetection

- **One receptor is not specific of a single molecule**
- **Different odors are detected by different sets of receptors**

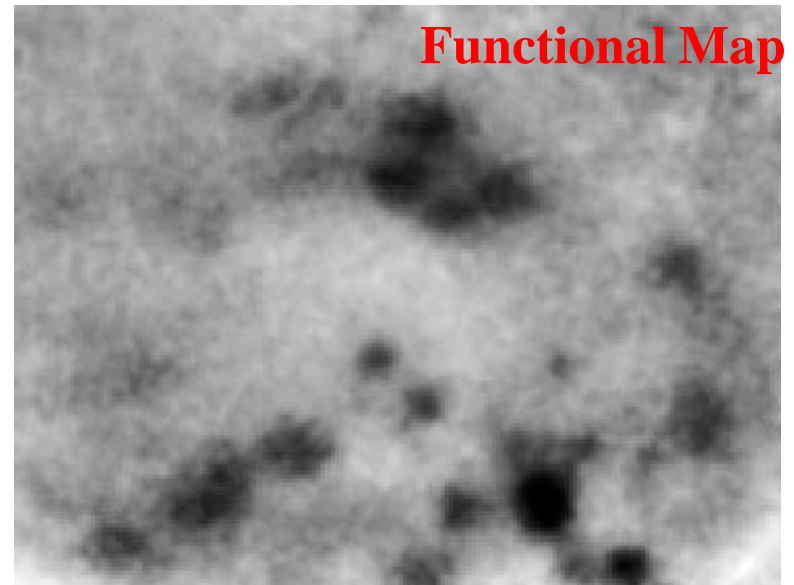
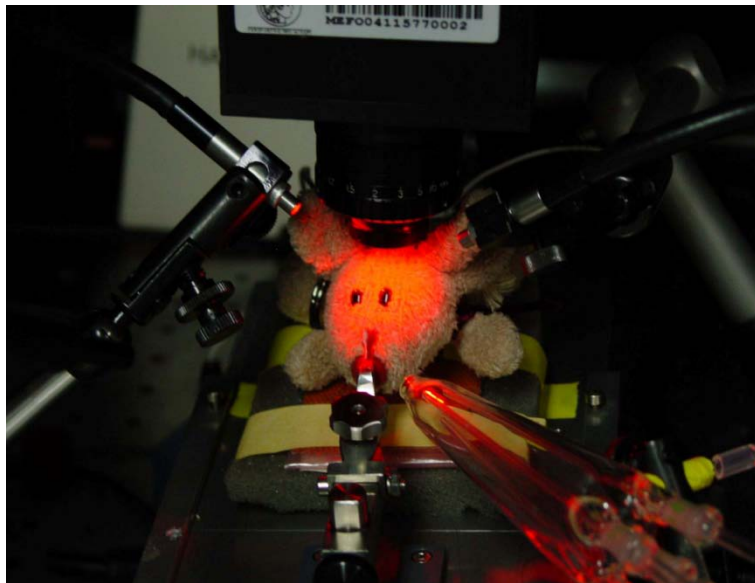
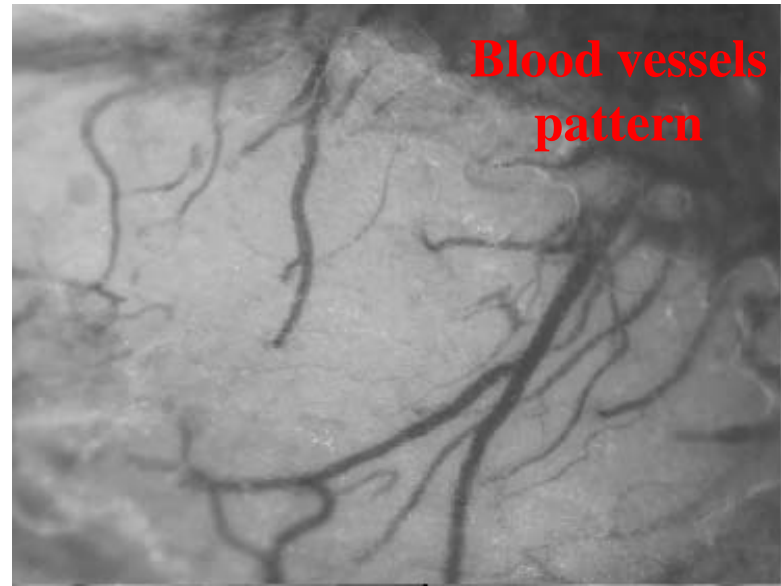
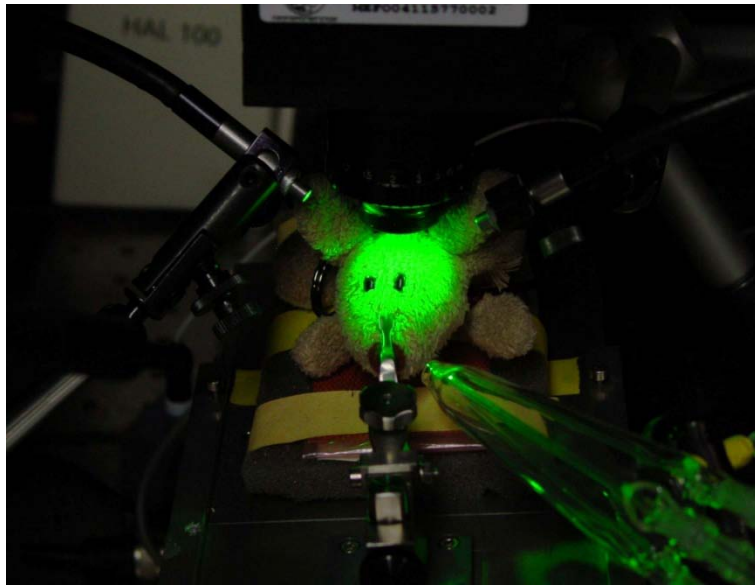


Odor coding = Combinatorial coding

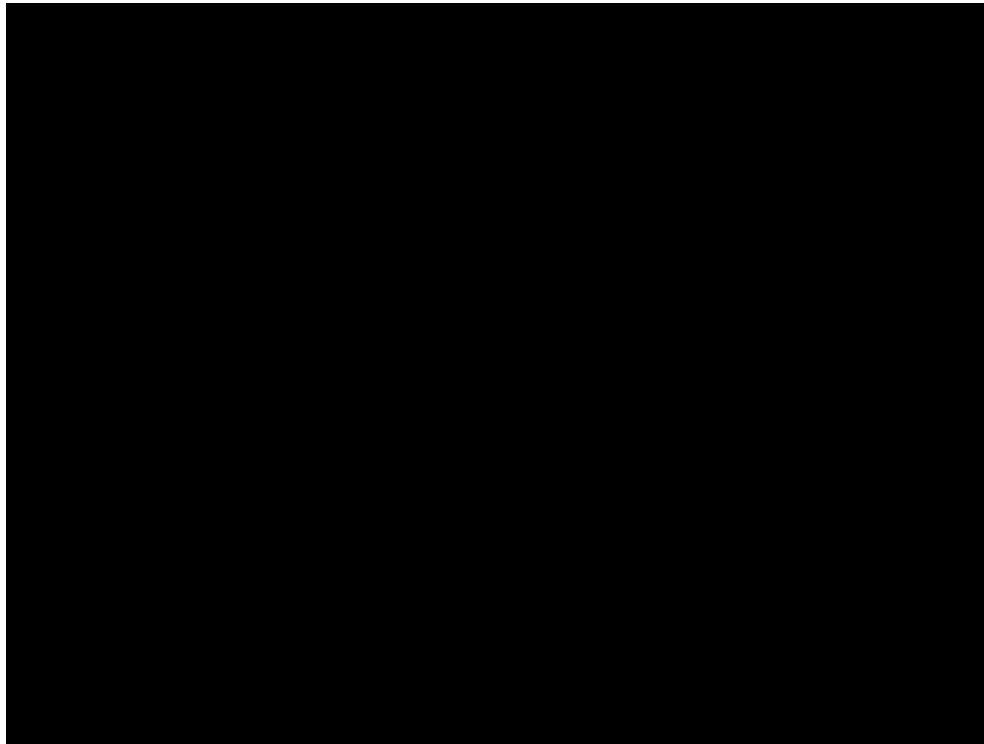
Sensory neurons



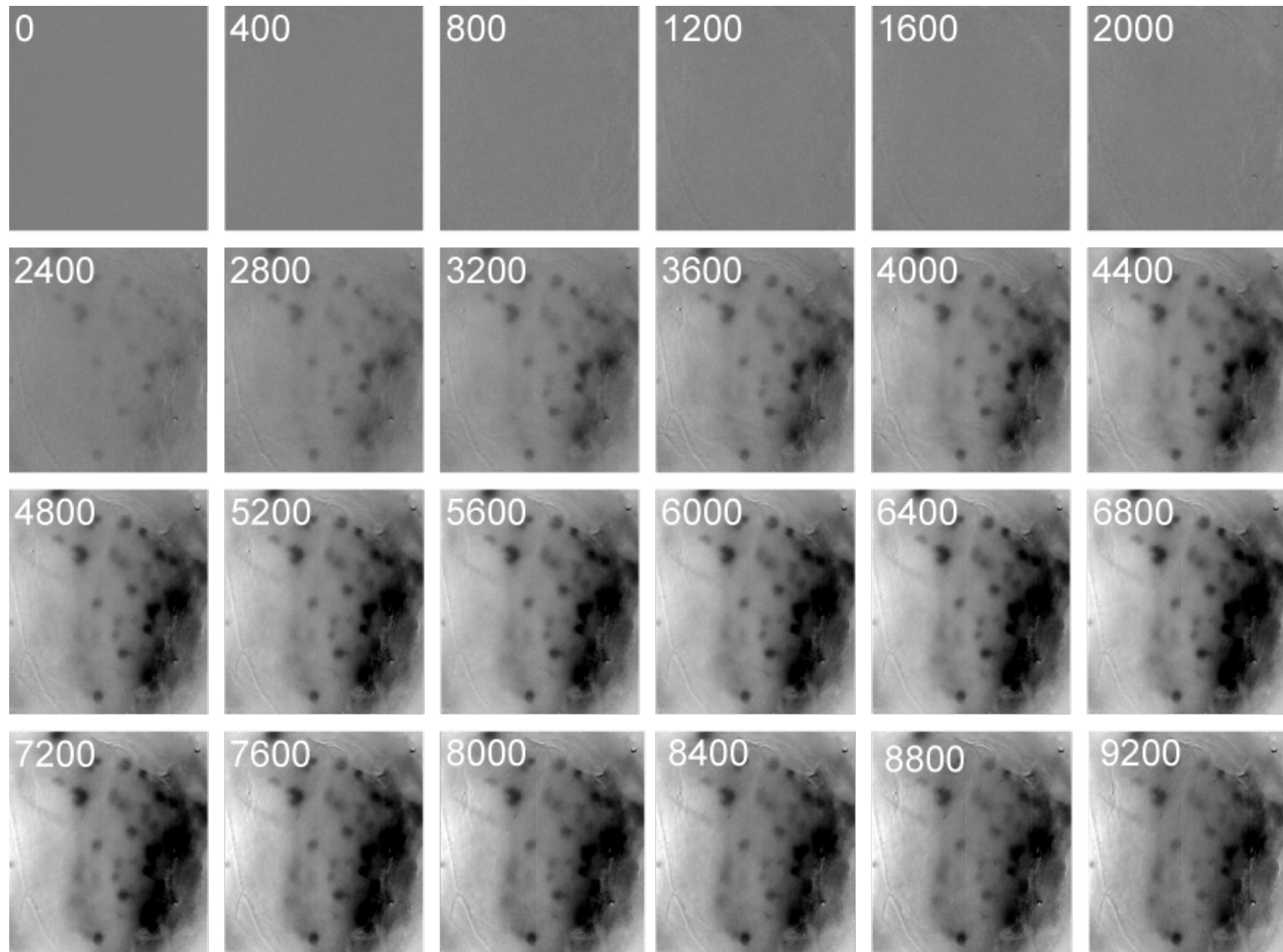
Imaging odor maps



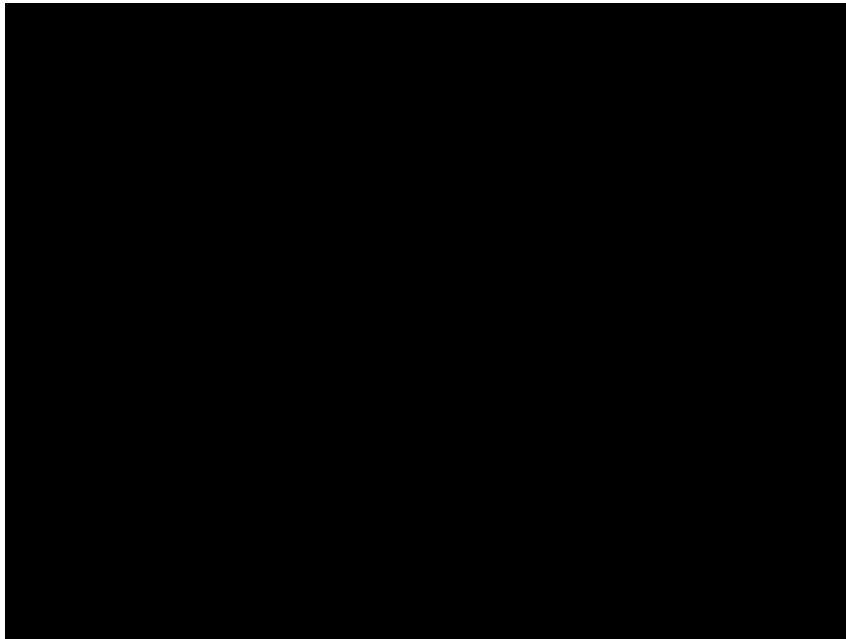
IOS imaging of odorant evoked activity in the olfactory bulb



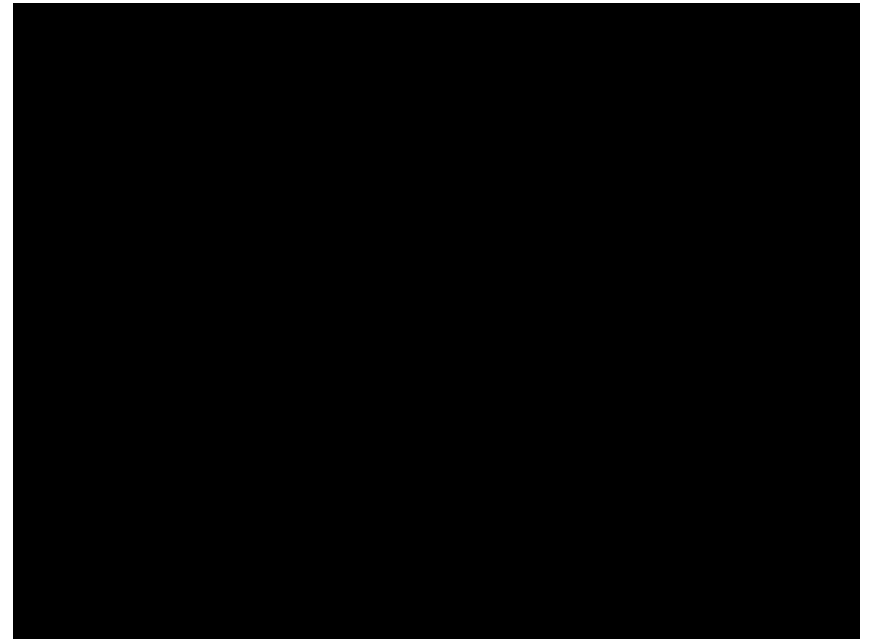
Functional organization of cortical regions



IOS imaging of odorant evoked activity in single trials

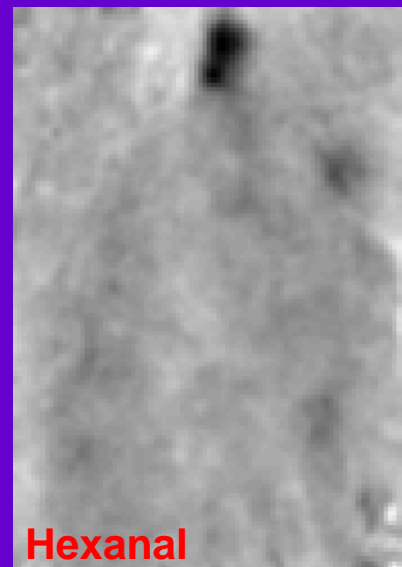
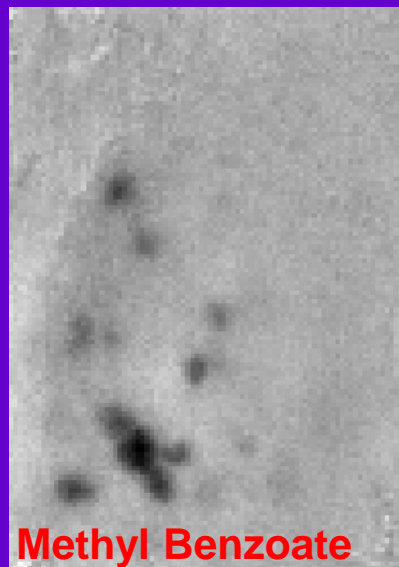
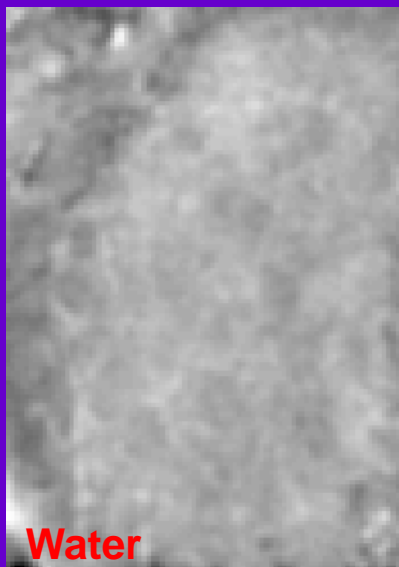
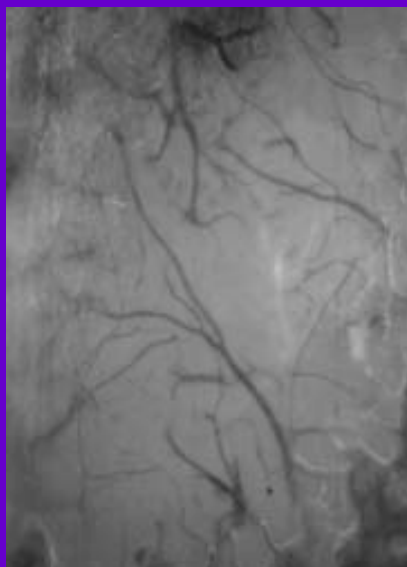


**Amyl
acetate**



**Ethyl
Butyrate**

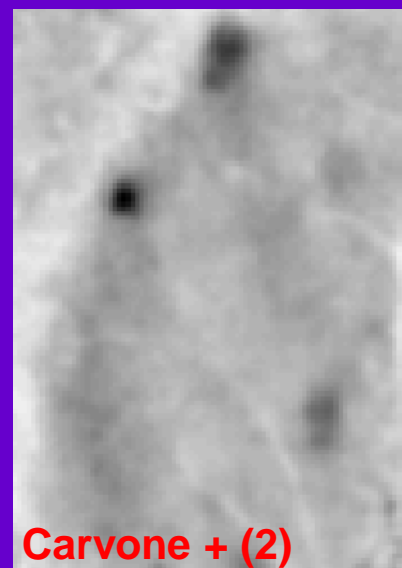
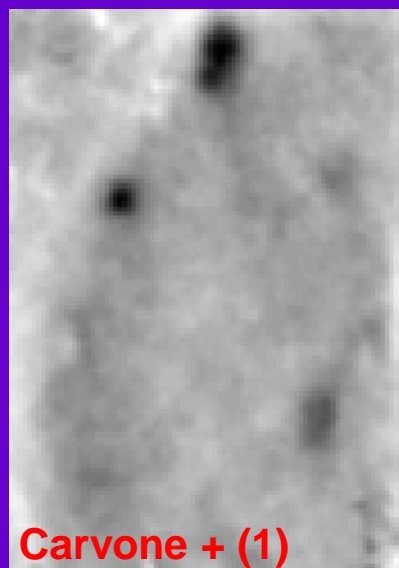
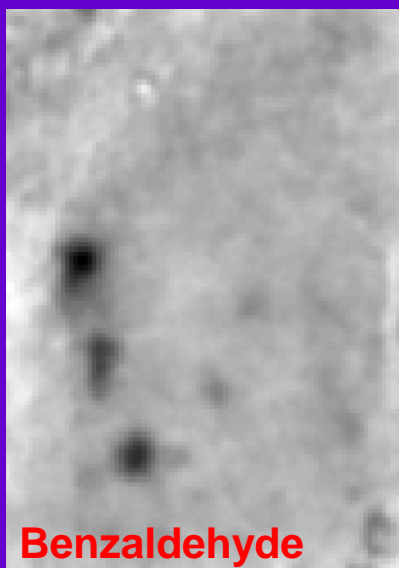
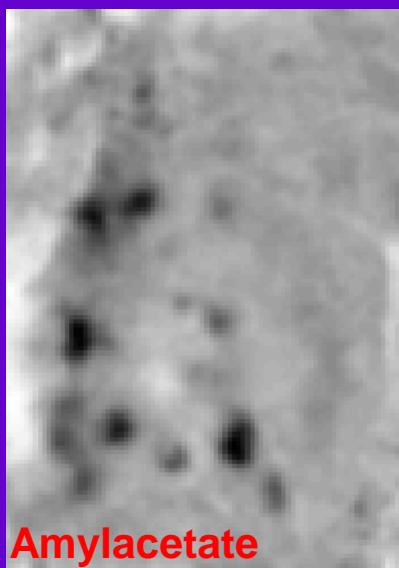
Odor maps



Water

Methyl Benzoate

Hexanal



Amylacetate

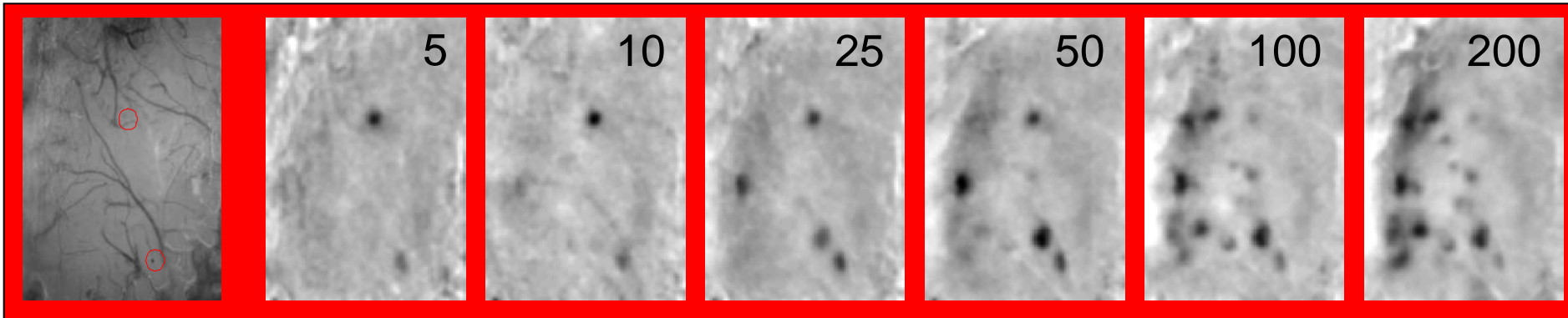
Benzaldehyde

Carvone + (1)

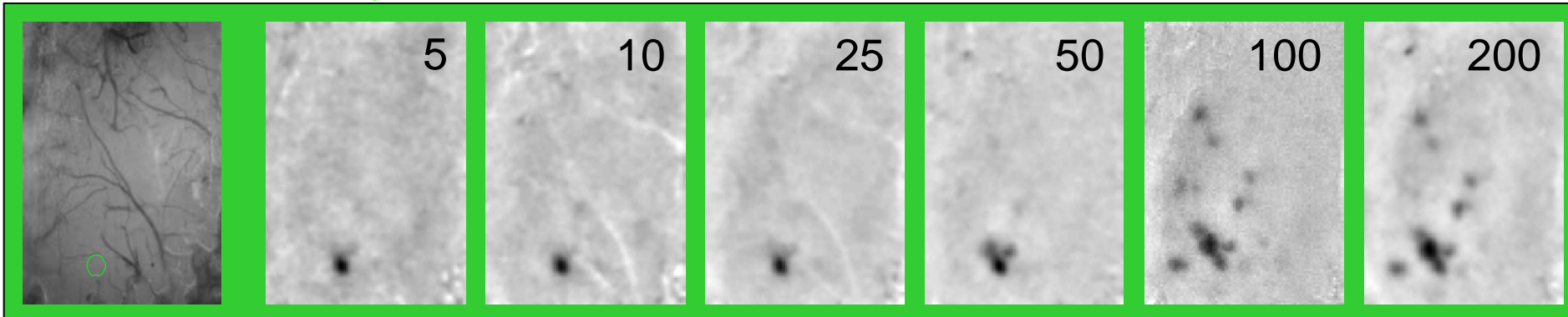
Carvone + (2)

Odor evoked glomeruli maps

Amylacetate



Methyl Benzoate

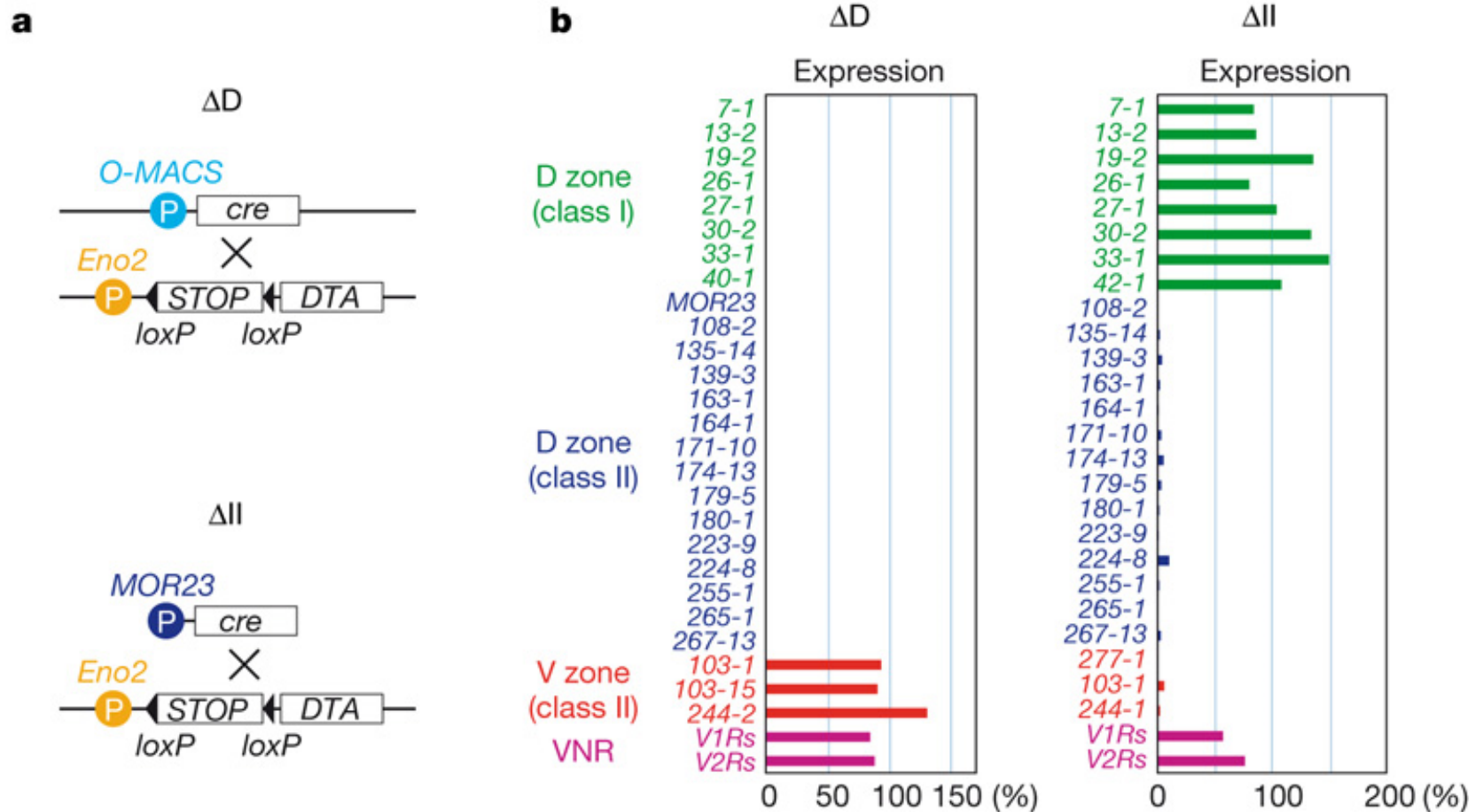


Olfactory mediated behavior

Innate versus learned odour processing in the mouse olfactory bulb

Vol 450 | 22 November 2007 | doi:10.1038/nature06281

Ko Kobayakawa^{1*}, Reiko Kobayakawa^{1*}, Hideyuki Matsumoto², Yuichiro Oka¹, Takeshi Imai¹, Masahito Ikawa³, Masaru Okabe³, Toshio Ikeda⁴, Shigeyoshi Itohara⁴, Takefumi Kikusui⁵, Kensaku Mori² & Hitoshi Sakano¹

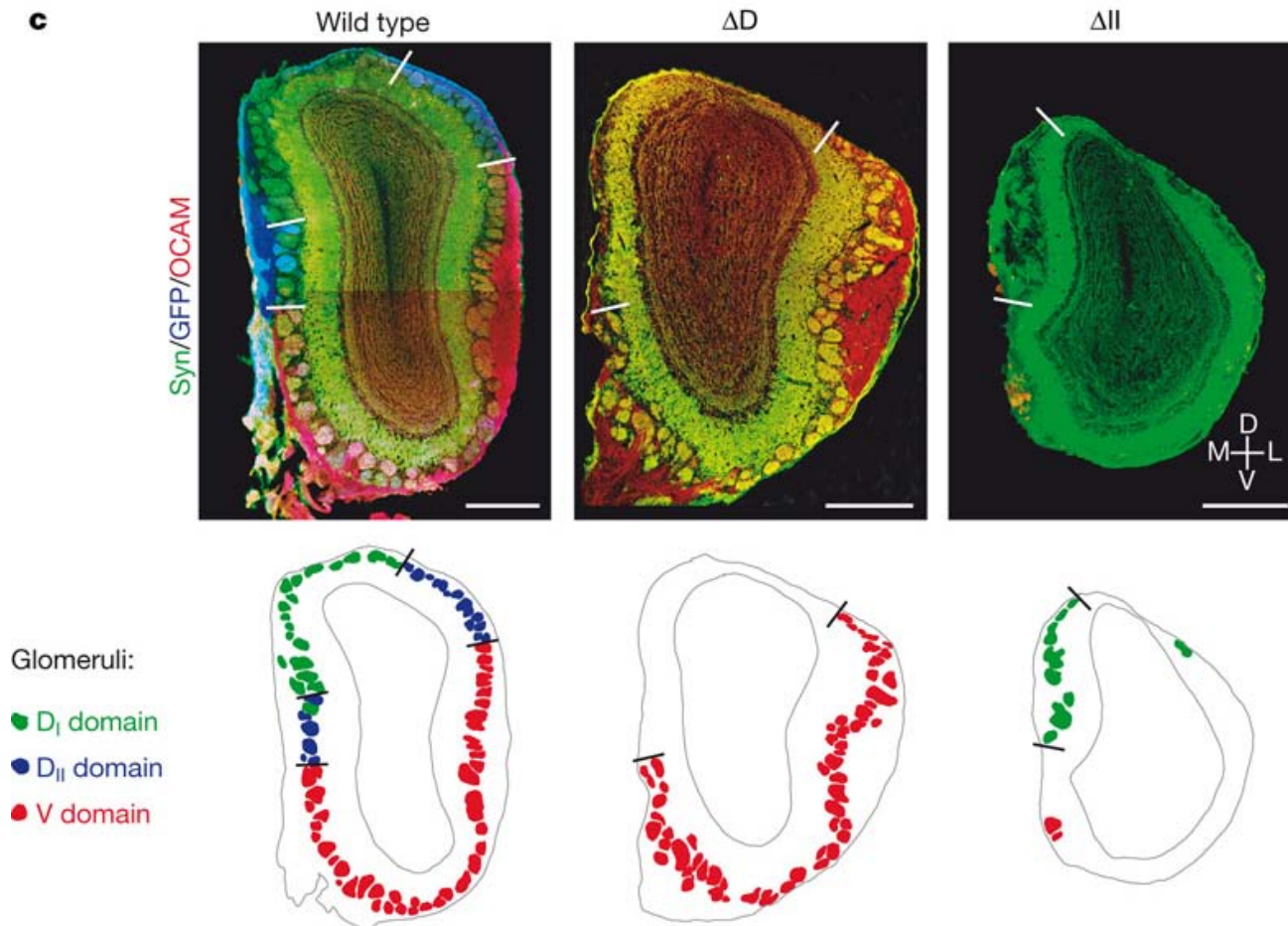


Organization of the olfactory system

Innate versus learned odour processing in the mouse olfactory bulb

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Ko Kobayakawa^{1*}, Reiko Kobayakawa^{1*}, Hideyuki Matsumoto², Yuichiro Oka¹, Takeshi Imai¹, Masahito Ikawa³, Masaru Okabe³, Toshio Ikeda⁴, Shigeyoshi Itohara⁴, Takefumi Kikusui⁵, Kensaku Mori² & Hitoshi Sakano¹



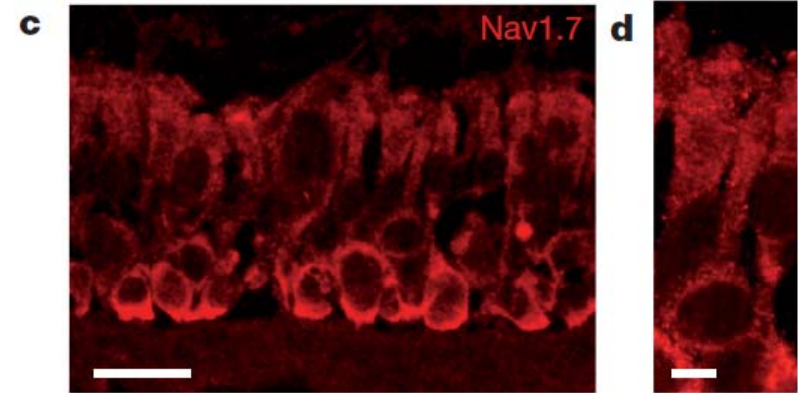
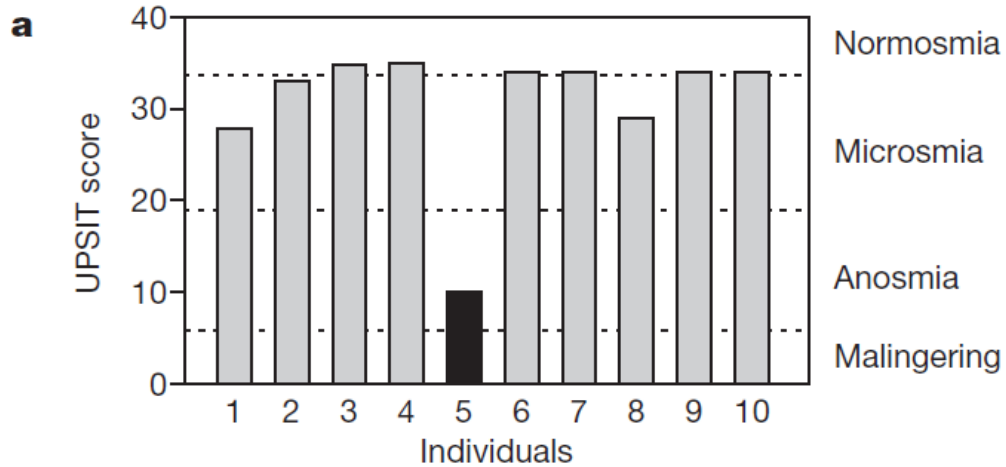
Loss-of-function mutations in sodium channel $\text{Na}_v1.7$ cause anosmia

Jan Weiss^{1*}, Martina Pyrski^{1*}, Eric Jacobi¹, Bernd Bufe¹, Vivienne Willnecker², Bernhard Schick², Philippe Zizzari³, Samuel J. Gossage⁴, Charles A. Greer⁵, Trese Leinders-Zufall¹, C. Geoffrey Woods⁶, John N. Wood^{4,7} & Frank Zufall¹

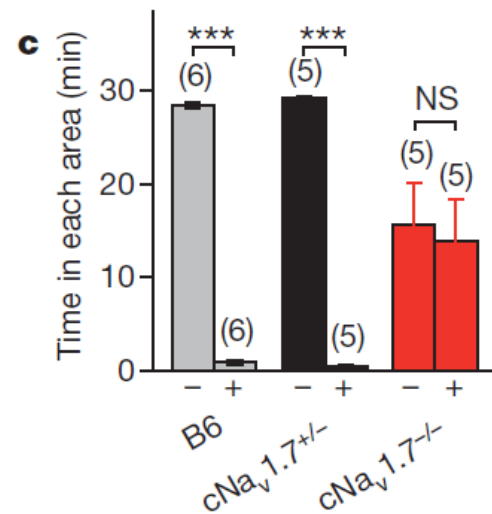
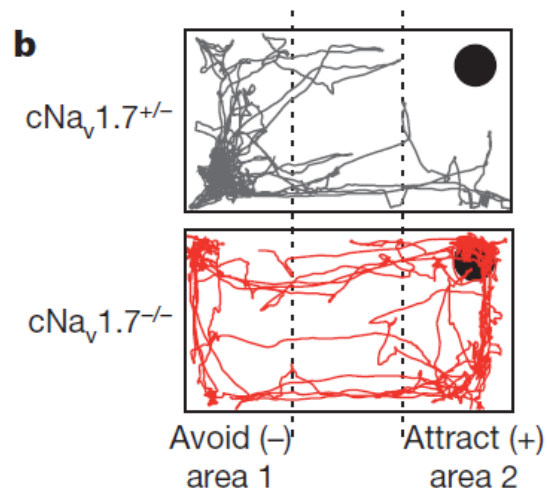
Loss of function of the gene *SCN9A*, encoding the voltage-gated sodium channel $\text{Na}_v1.7$, causes a congenital inability to experience pain in humans. Here we show that $\text{Na}_v1.7$ is not only necessary for pain sensation but is also an essential requirement for odour perception in both mice and humans. We examined human patients with loss-of-function mutations in *SCN9A* and show that they are unable to sense odours. To establish the essential role of $\text{Na}_v1.7$ in odour perception, we generated conditional null mice in which $\text{Na}_v1.7$ was removed from all olfactory sensory neurons. In the absence of $\text{Na}_v1.7$, these neurons still produce odour-evoked action potentials but fail to initiate synaptic signalling from their axon terminals at the first synapse in the olfactory system. The mutant mice no longer display vital, odour-guided behaviours such as innate odour recognition and avoidance, short-term odour learning, and maternal pup retrieval. Our study creates a mouse model of congenital general anosmia and provides new strategies to explore the genetic basis of the human sense of smell.

Anosmia: loss of the sense of smell

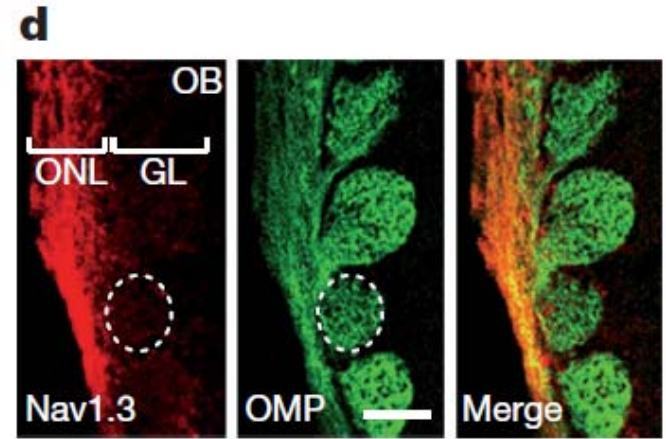
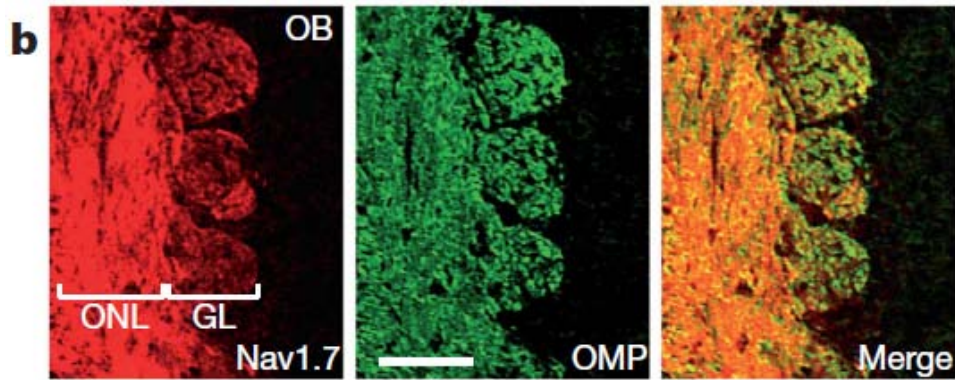
Human



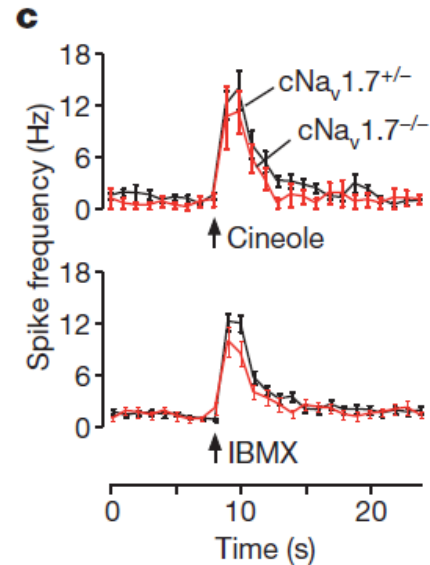
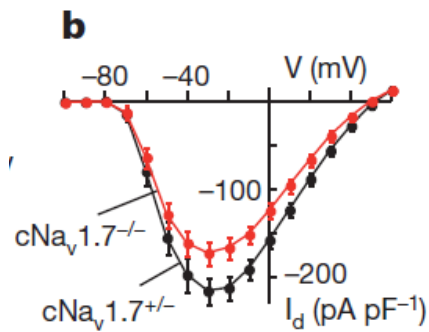
Mouse



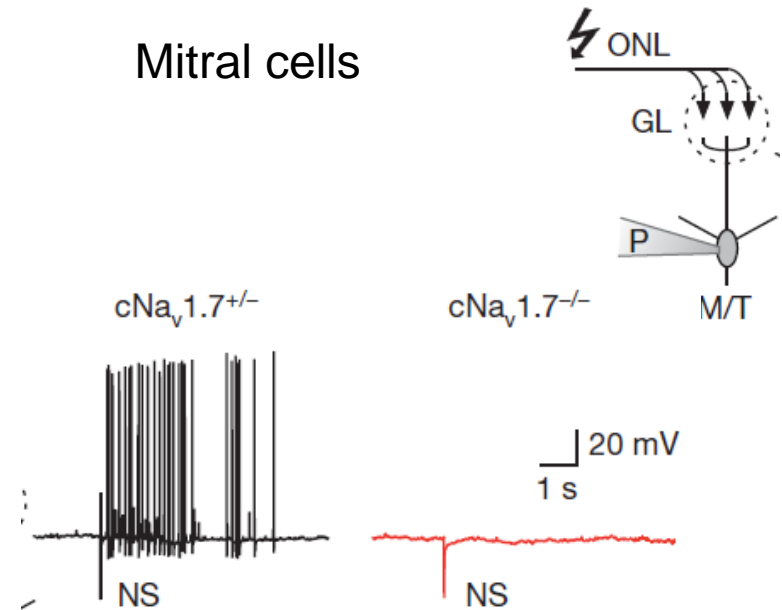
Anosmia: loss of the sense of smell



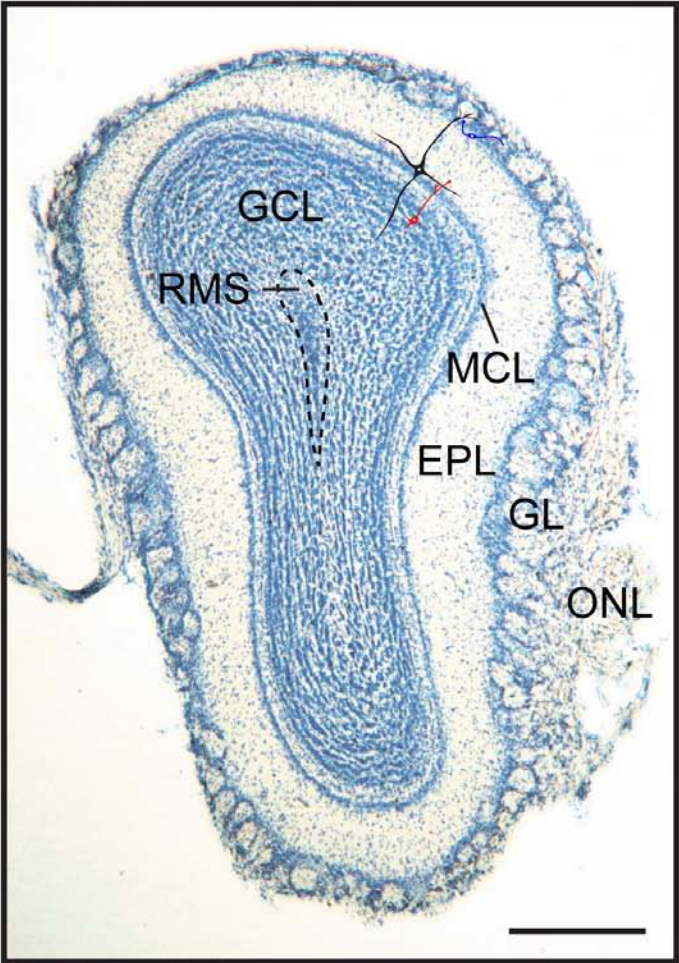
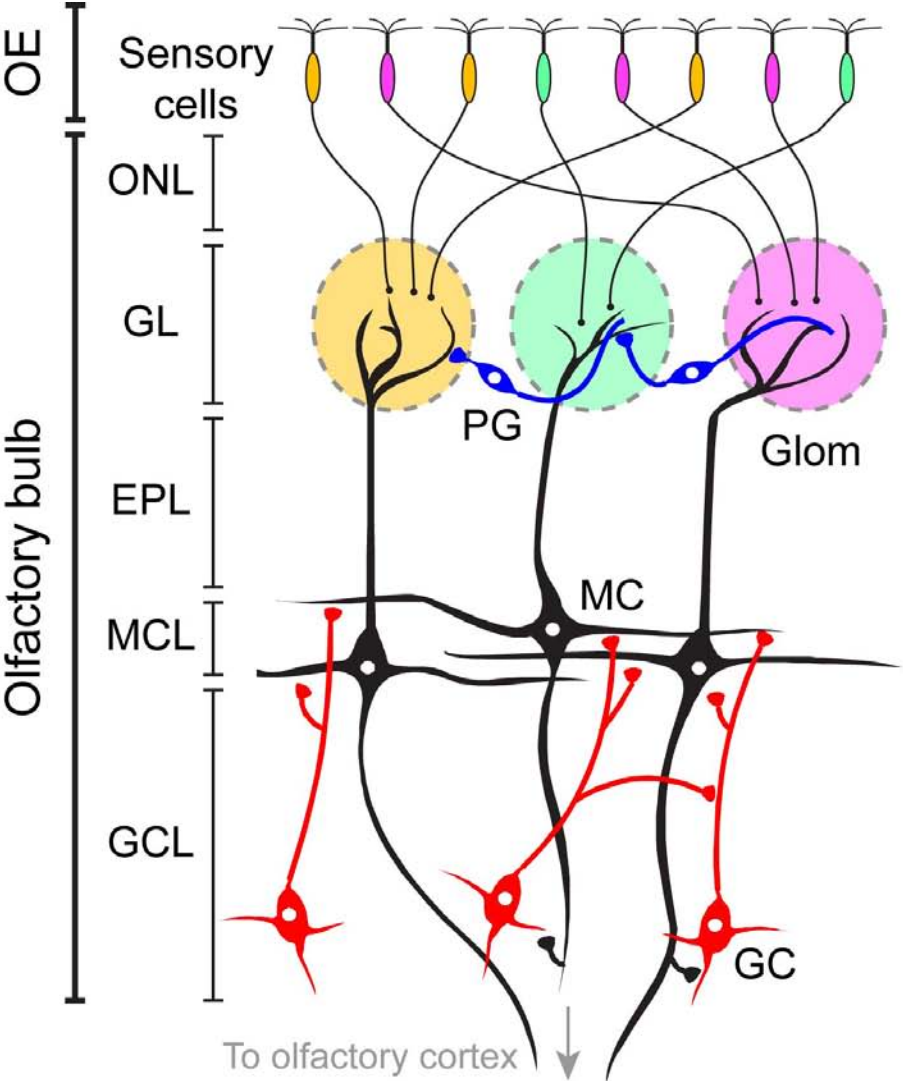
Sensory neurons



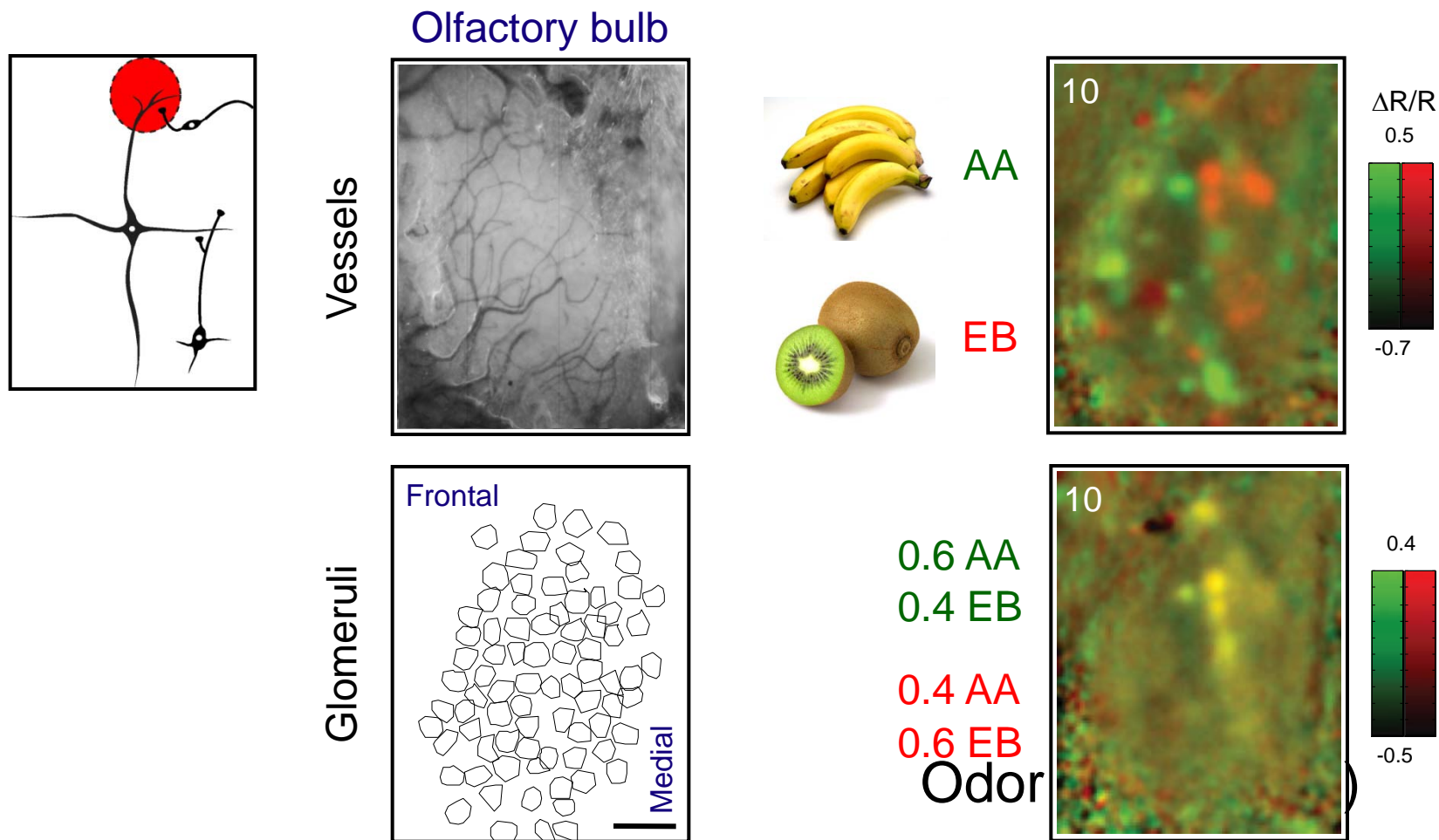
Mitral cells



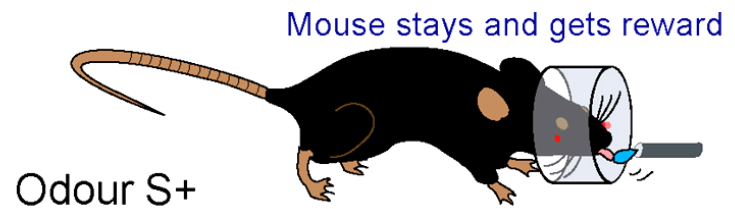
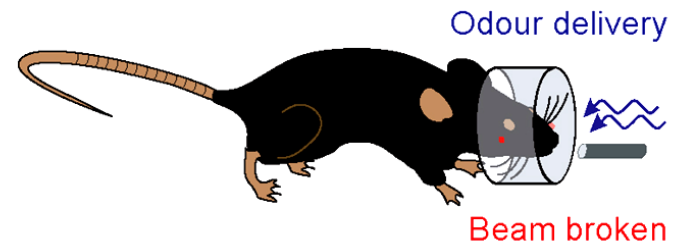
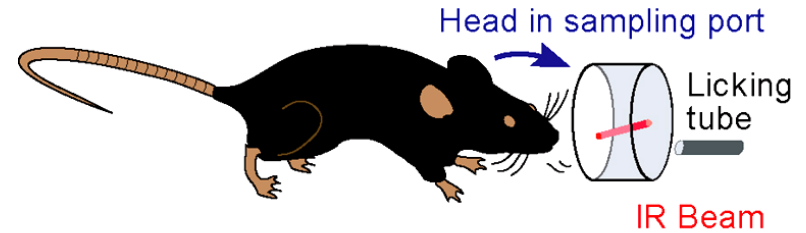
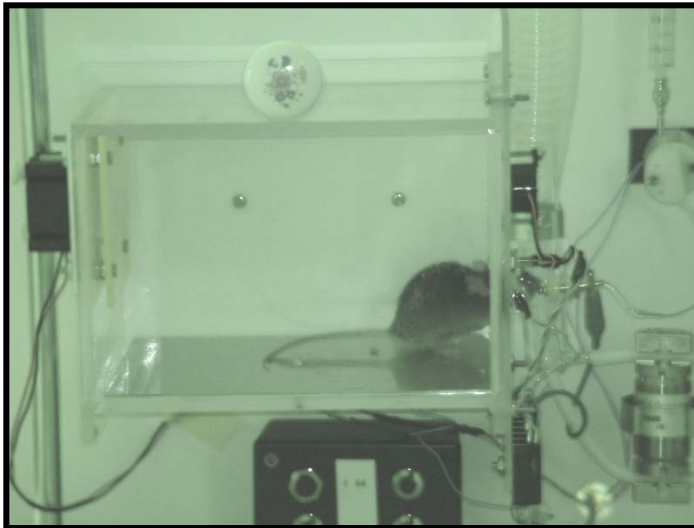
Olfactory bulb circuitry



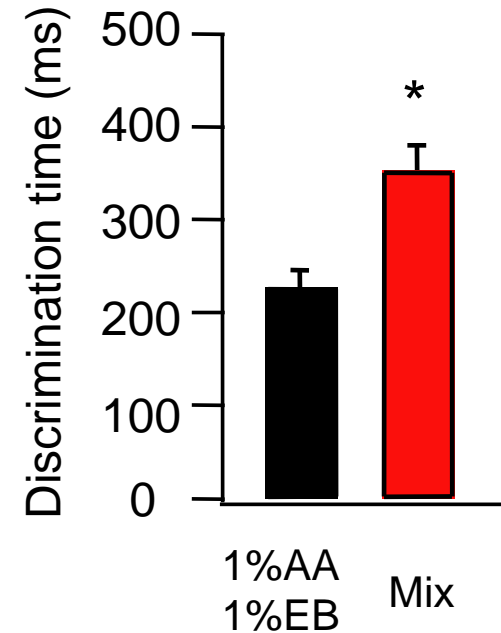
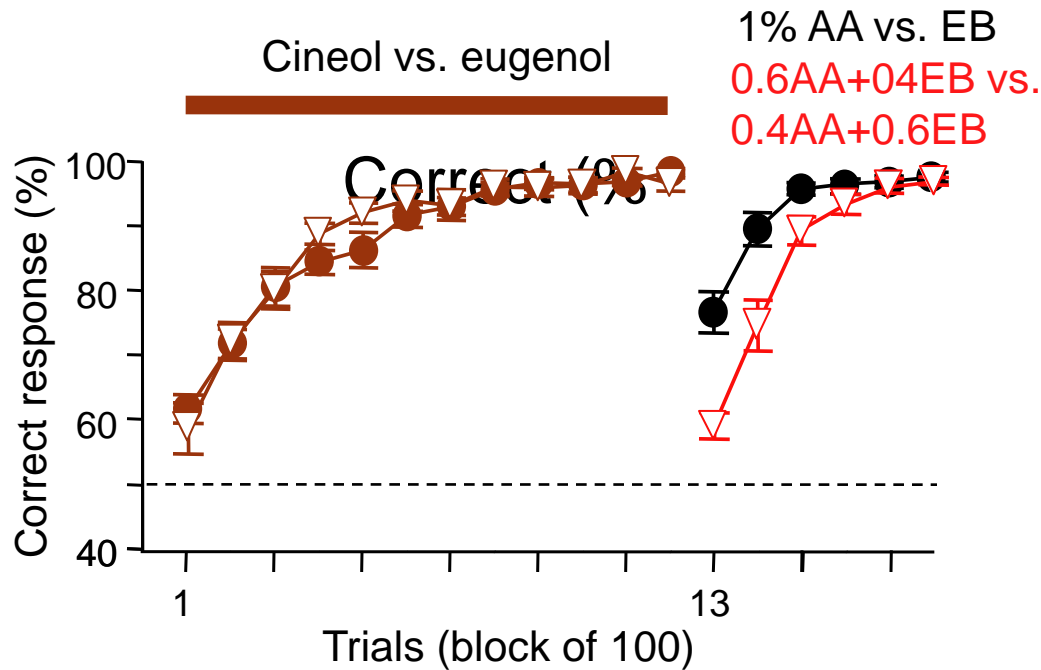
Spatial patterns of odor mixtures measured by intrinsic Imaging are highly similar in trained mice



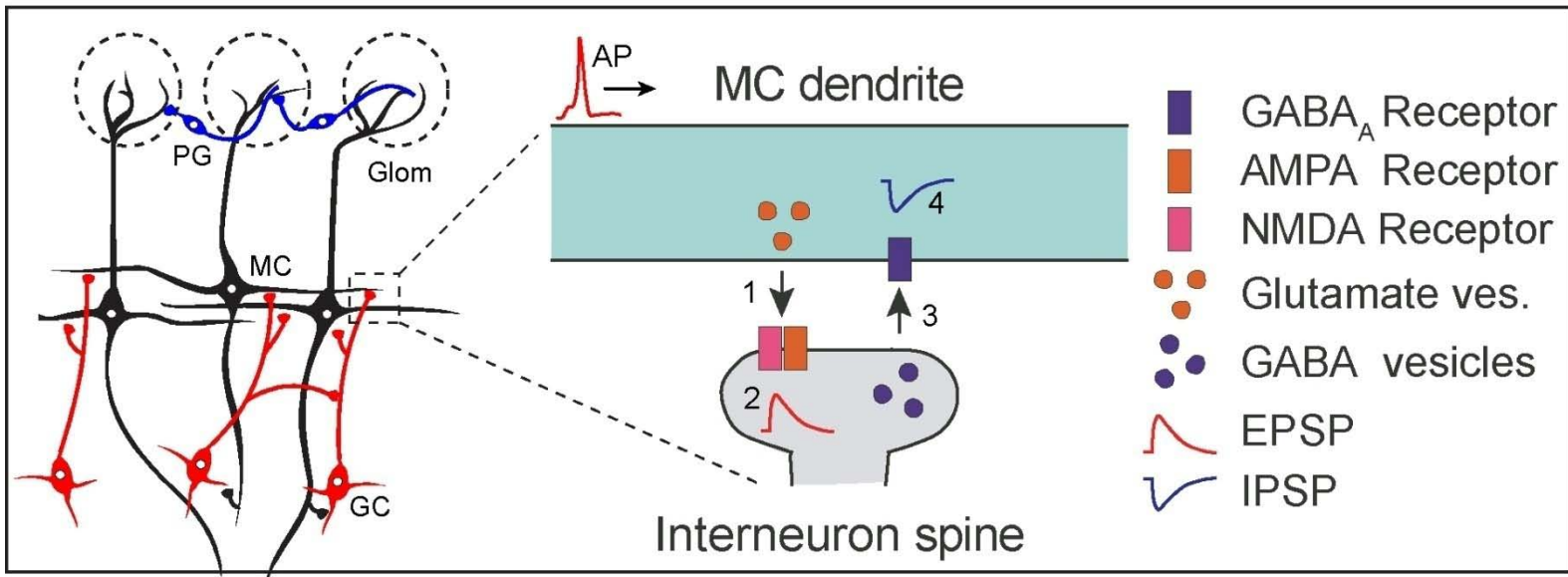
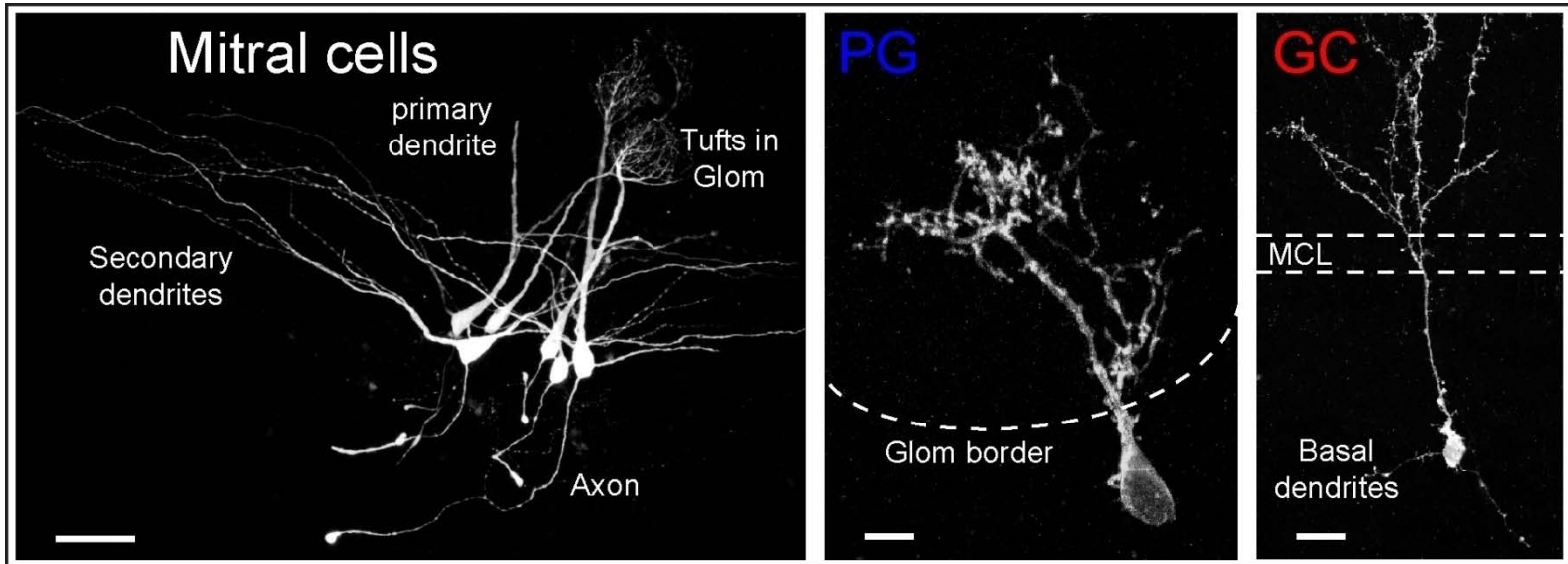
Behavioural assessment of olfactory performances



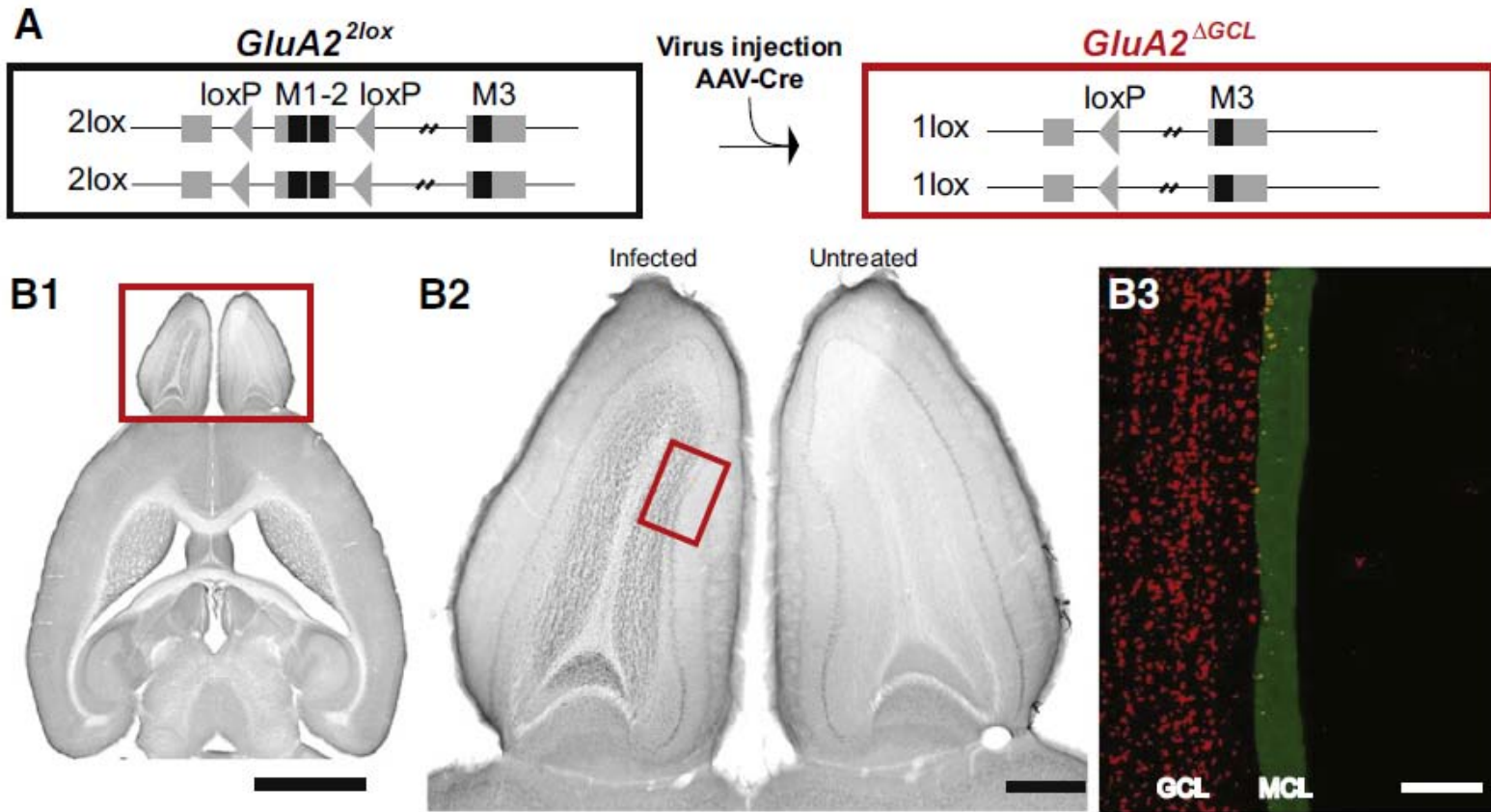
Mice can discriminate odors in a single sniff



Olfactory bulb circuitry



Genetic manipulation of granule cell inhibition



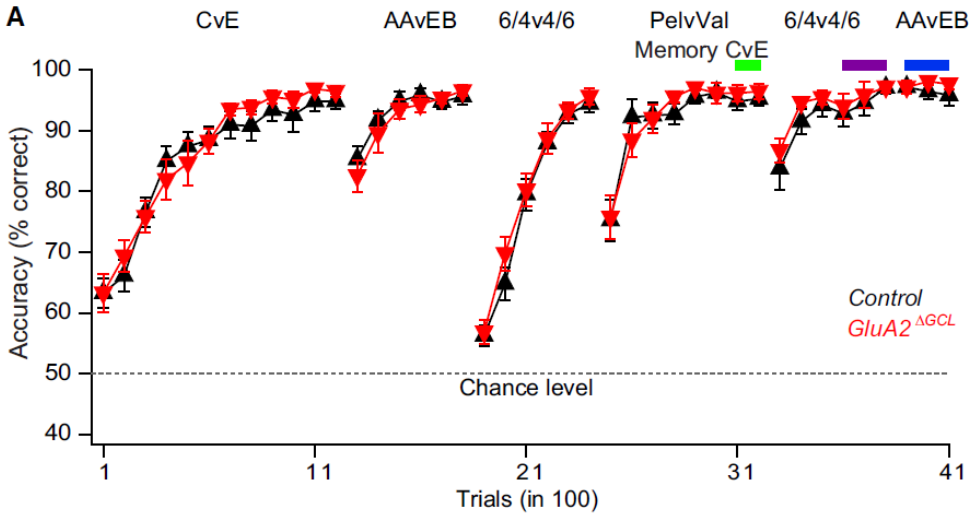
Synaptic Inhibition in the Olfactory Bulb Accelerates Odor Discrimination in Mice

Nixon M. Abraham,^{1,2} Veronica Egger,⁵ Derya R. Shimshek,³ Robert Renden,¹ Izumi Fukunaga,⁴ Rolf Sprengel,³ Peter H. Seeburg,³ Matthias Klugmann,^{6,8} Troy W. Margrie,⁷ Andreas T. Schaefer,^{2,4,7,*} and Thomas Kuner^{1,2,*}

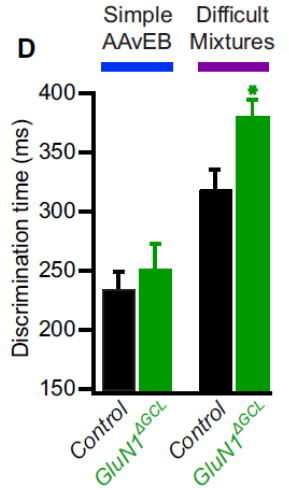
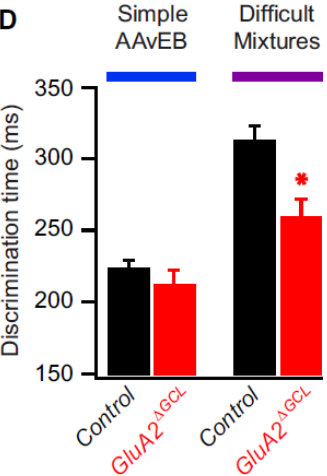
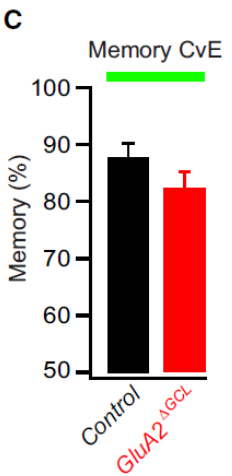
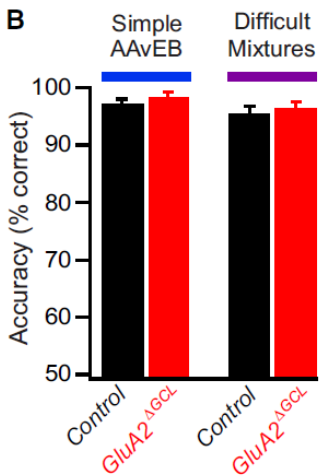
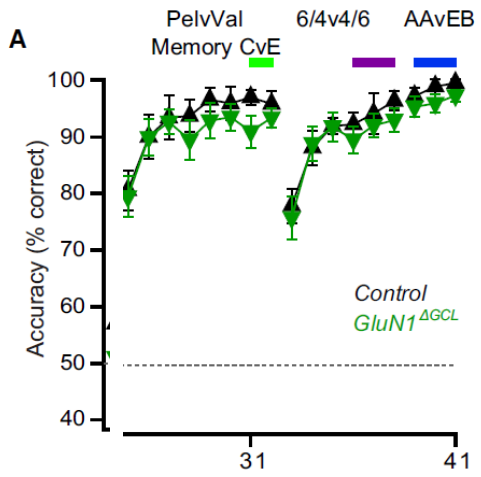
Neuron 65, 399–411, February 11, 2010

Granule cell inhibition modulate odor discrimination

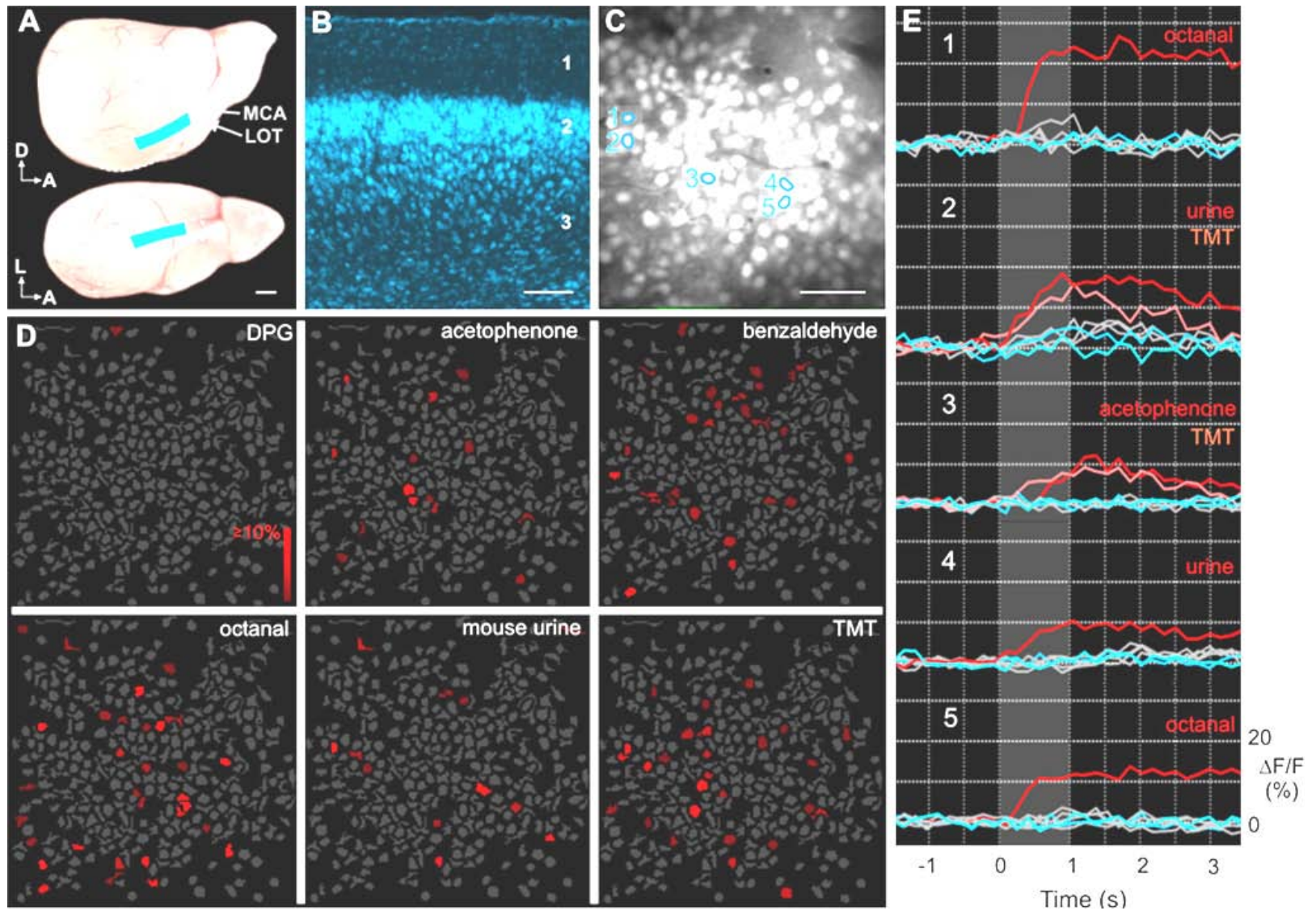
More inhibition



Less inhibition



Odor representation in the olfactory cortex



Odor representation in the olfactory cortex

