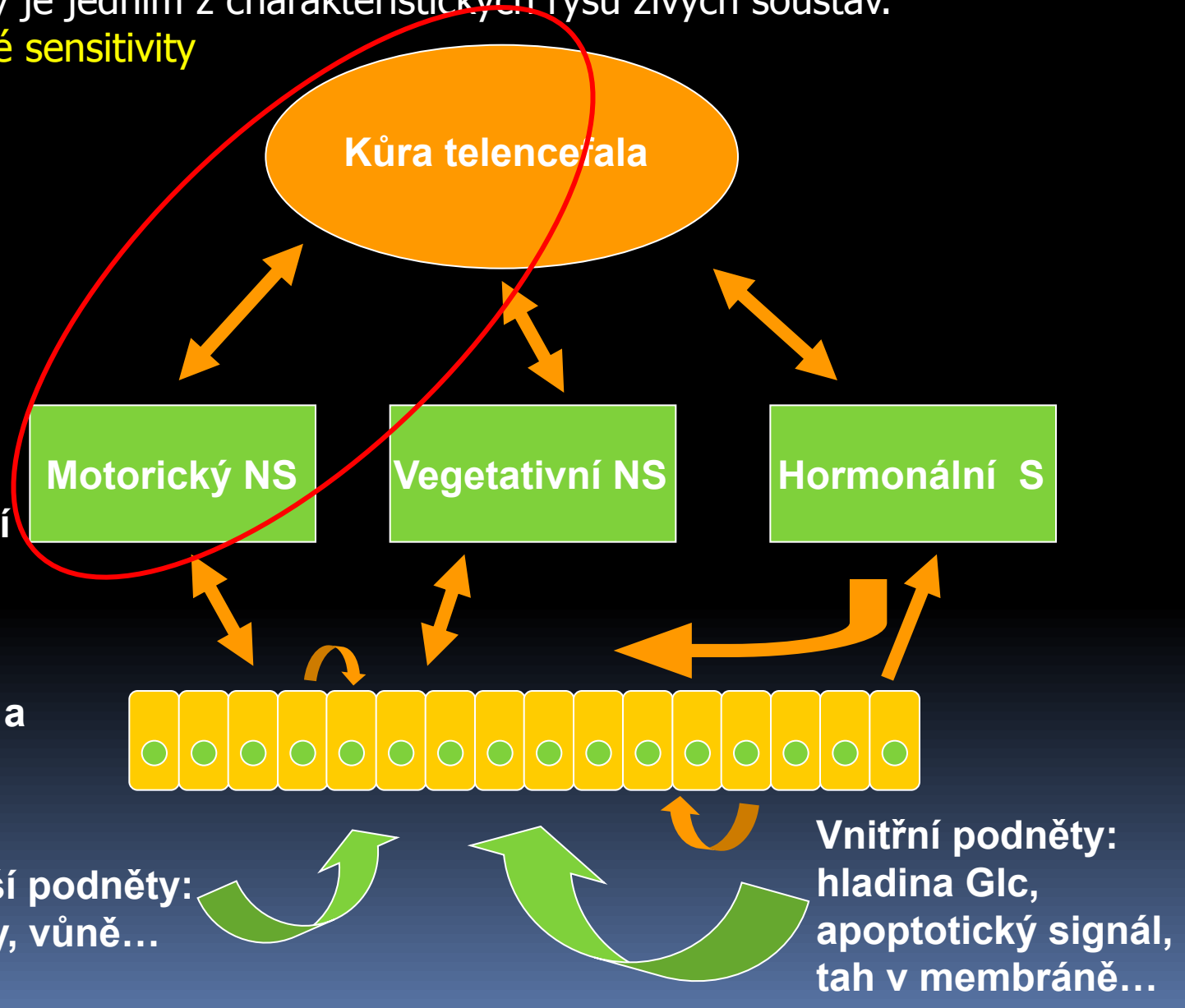
CHEMORECEPCE

Všechny buňky a všichni živočichové jsou citliví na chemické složení jejich životního prostředí. To je důležité nejen při rozeznávání potravy, ale i při páření, vztazích matka-mládě, značení teritoria a při dalších případech sociálního chování. Citlivost na chemické signály je jedním z charakteristických rysů živých soustav.

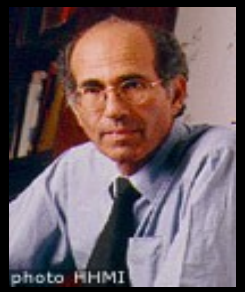
Využití membránové sensitivity ve službách celku:



Čich

The Nobel Prize in Physiology or Medicine 2004

"for their discoveries of odorant receptors and the organization of the olfactory system"



Richard Axel

1/2 of the prize

USA

Columbia University New York, NY, USA; Howard Hughes Medical Institute

b. 1946

Linda B. Buck

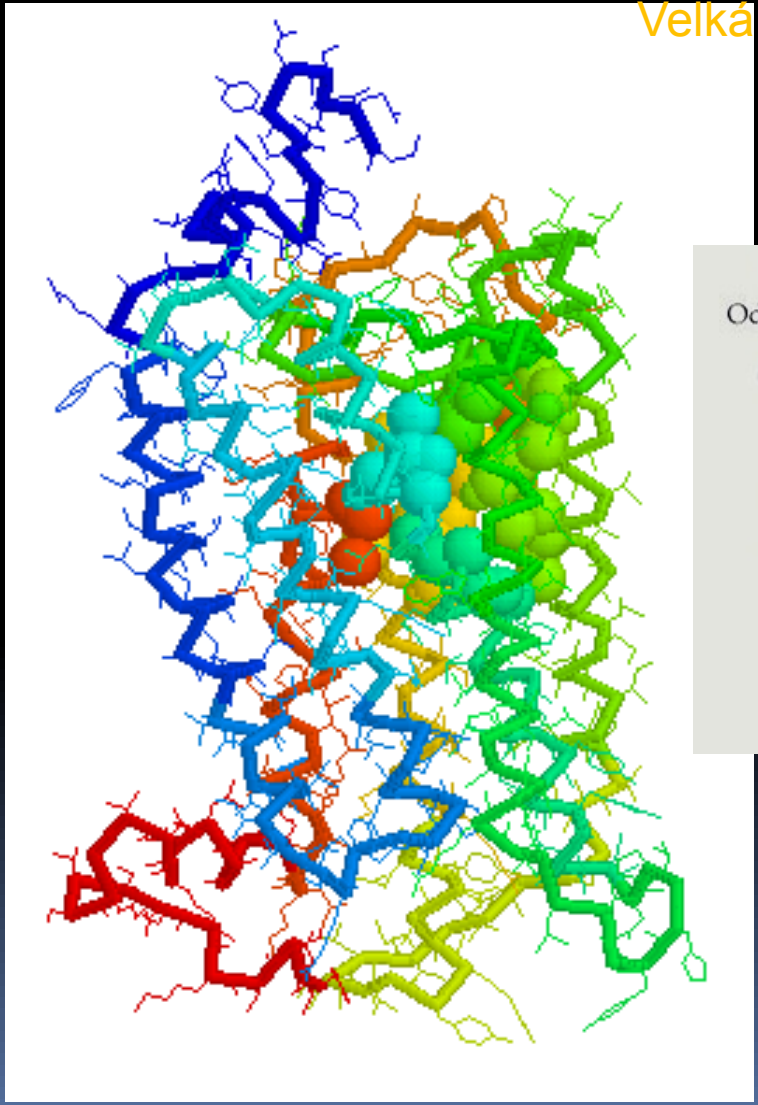
1/2 of the prize

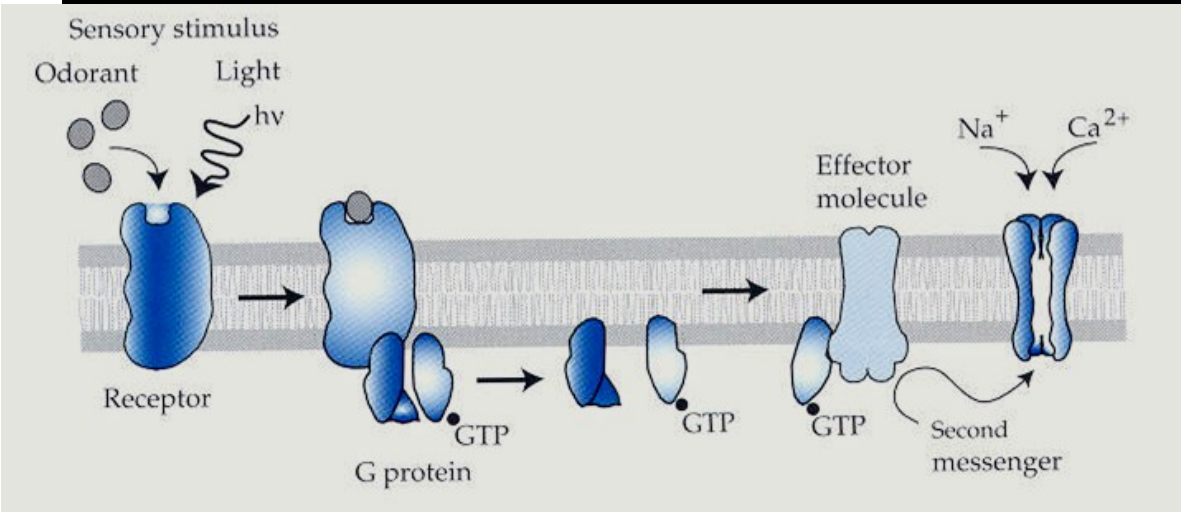
USA

Fred Hutchinson Cancer Research Center Seattle, WA, USA; Howard Hughes Medical Institute

b. 1947

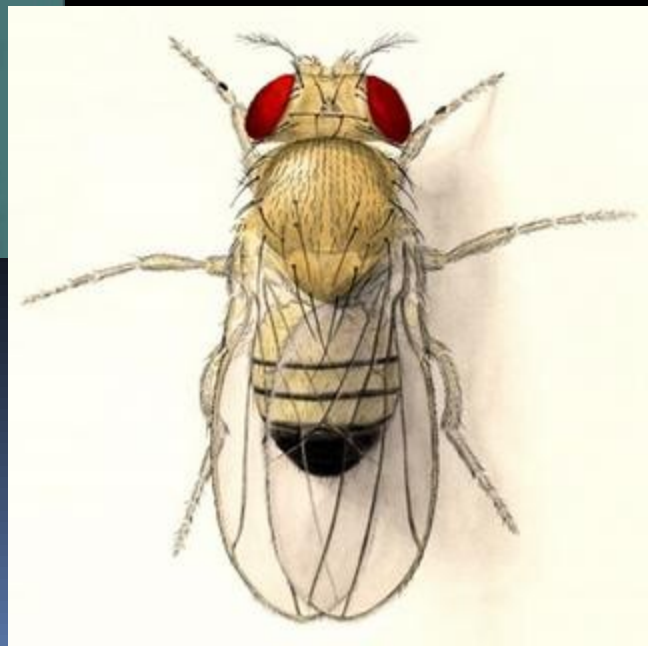
Čich - Distanční chemorecepce
Modelový objekt pro mnoho dalších signálových drah
7TM receptory
Metabotropní signalizace prostřednictvím G proteinů
Otevřený systém podobný imunitnímu
Velká část (4%) genomu věnovaná čichovým receptorům



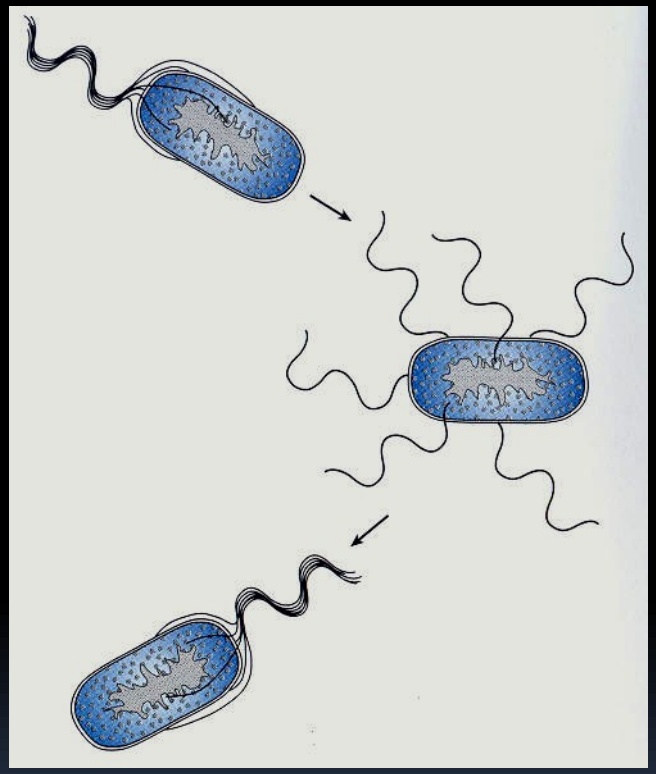


Savci: 1000 genů pro čichové receptory – největší genová rodina
Člověk: 350 funkčních genů
Drosophila: 62

Háďátko 1500 GPCR –
– G prot. coupled rec.
1031 buněk
302 neuronů



Už u prokaryot chemosensitivita E.coli



Repelent a atraktant roztáčí flagelární motor na opačné strany, jako lodní šroub.

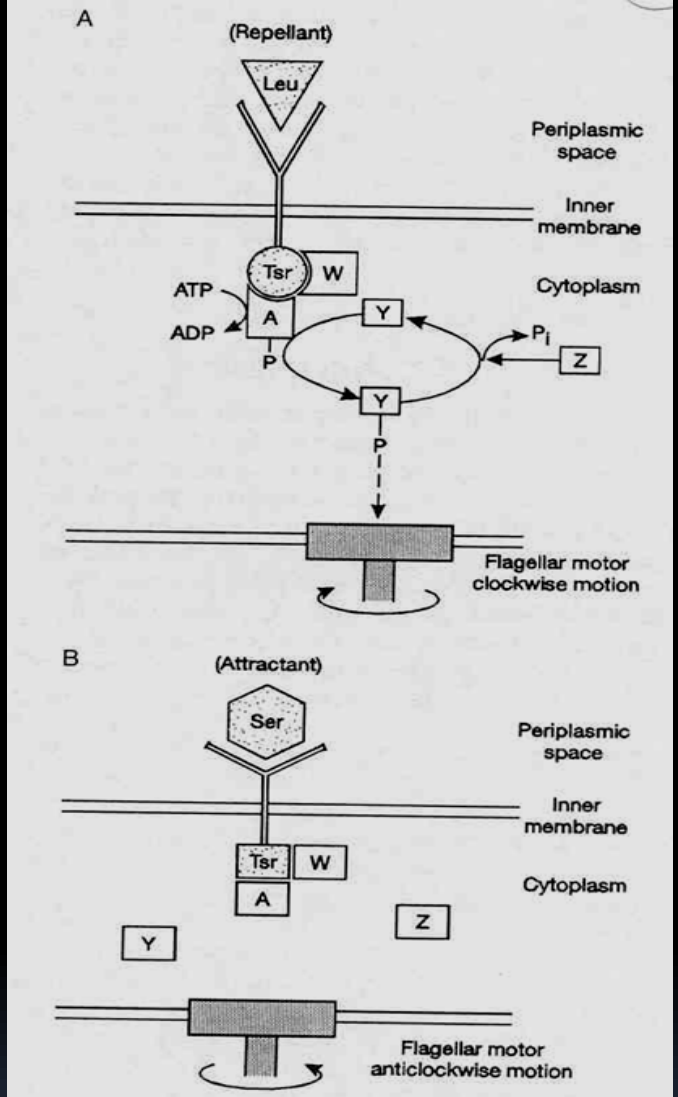
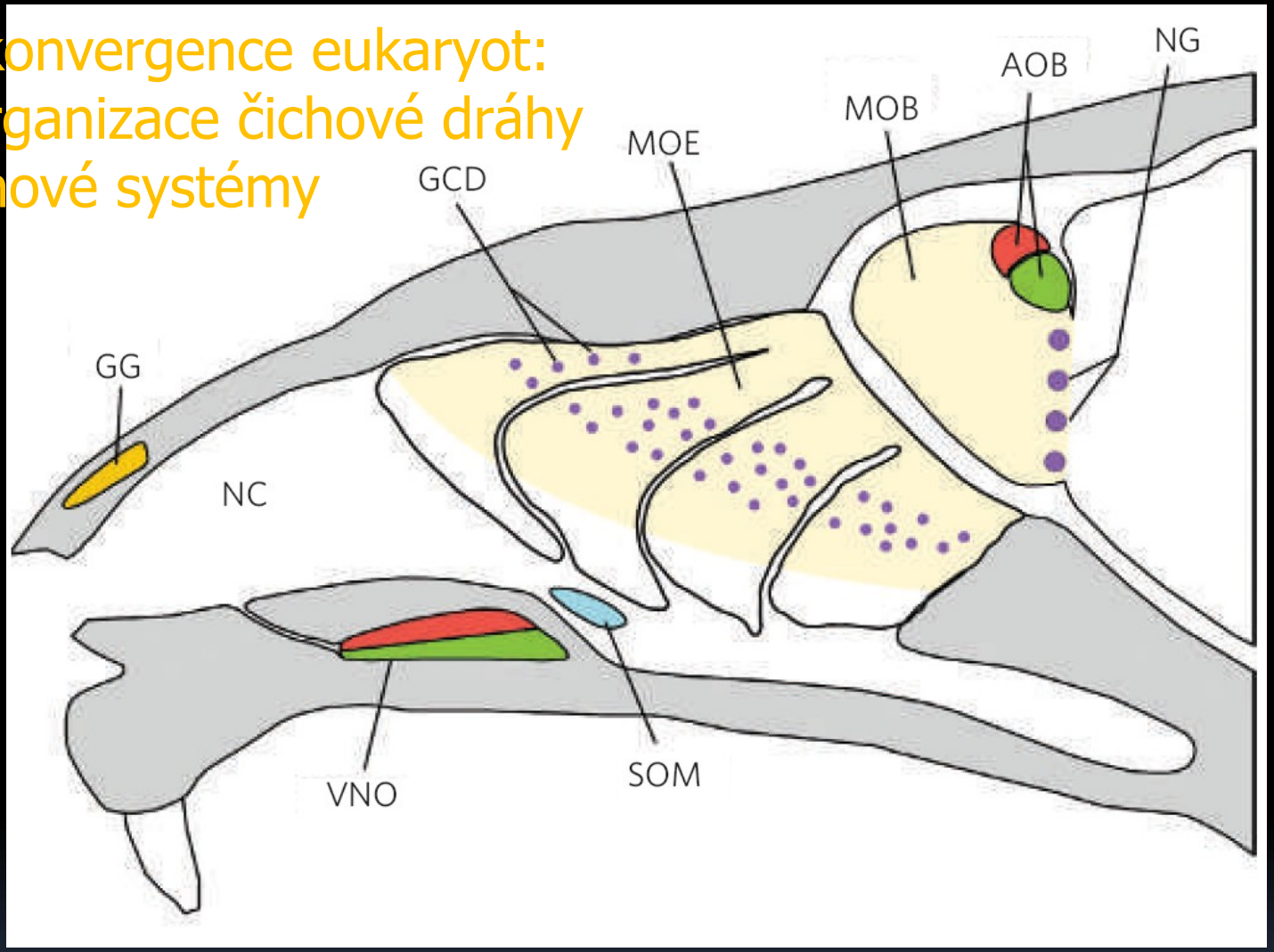


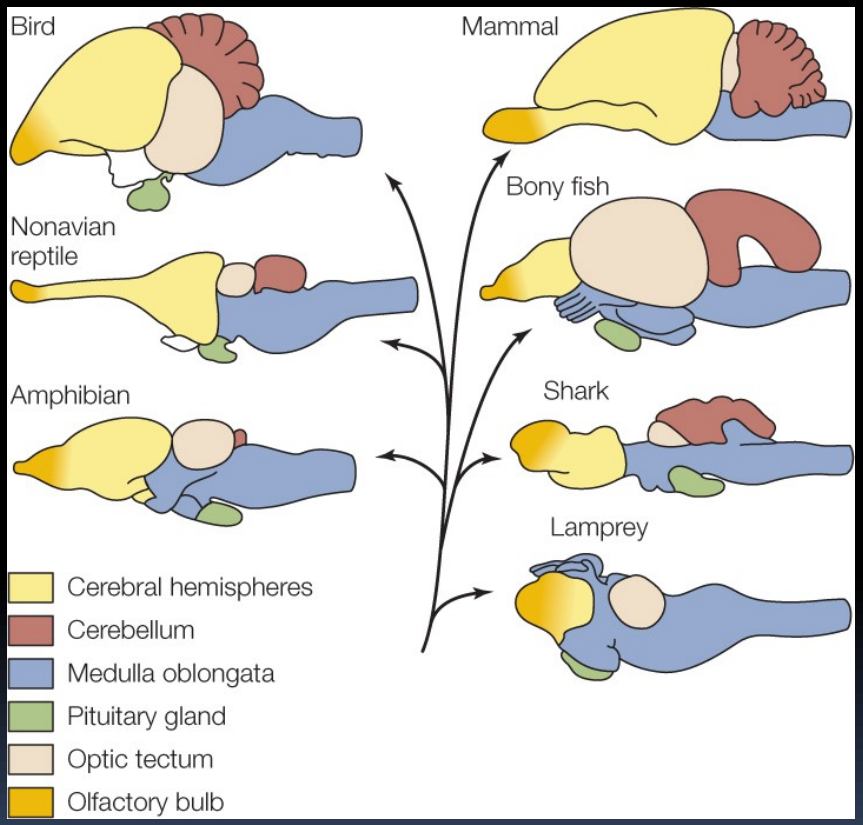
Figure 10.6 Molecular signalling in the *E. coli* chemosensory system. (a) The Tsr receptor-transducer protein accepts a repellant molecule (Leu). CheW and CheA are activated. CheA accepts phosphate from ATP and passes it on CheY. CheY diffuses to the flagellar motor and induces a clockwise rotation and hence tumbling. CheY is eventually dephosphorylated by CheZ. (b) The Tsr receptor-transducer accepts an attractant molecule (Ser). The consequent conformational change inactivates CheA and CheW so that CheY remains unphosphorylated and consequently inactive. The flagellum resumes its anticlockwise motion and the bacterium swims smoothly forward. A = CheA; W = CheW; Y = CheY; Z = CheZ. Data from Bourrett, Borkovich and Simon, 1991

Pozoruhodná konvergence eukaryot: Transdukce, organizace čichové dráhy 2 paralelní čichové systémy



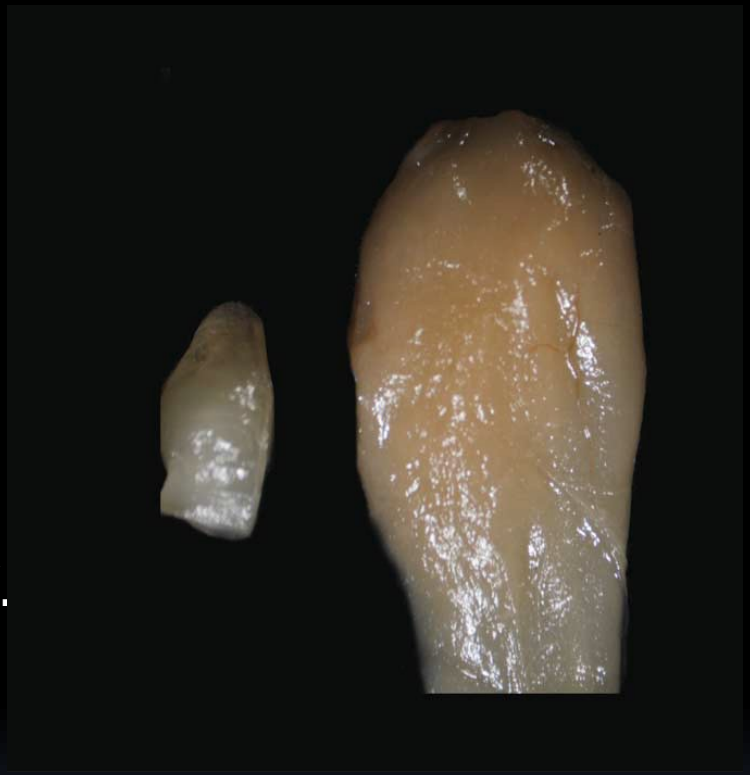
Vomeronasální orgán pro vnitrodruhovou komunikaci a čichový systém pro ostatní pachy.

Neuroanatom 19. století Paul Broca označil lidi jako anosmické, protože věřil, že rozvoj čelních laloků telencefala spojený s uvažováním a osobností na úkor čichových laloků, vedl ke ztrátě důležitosti čichu.



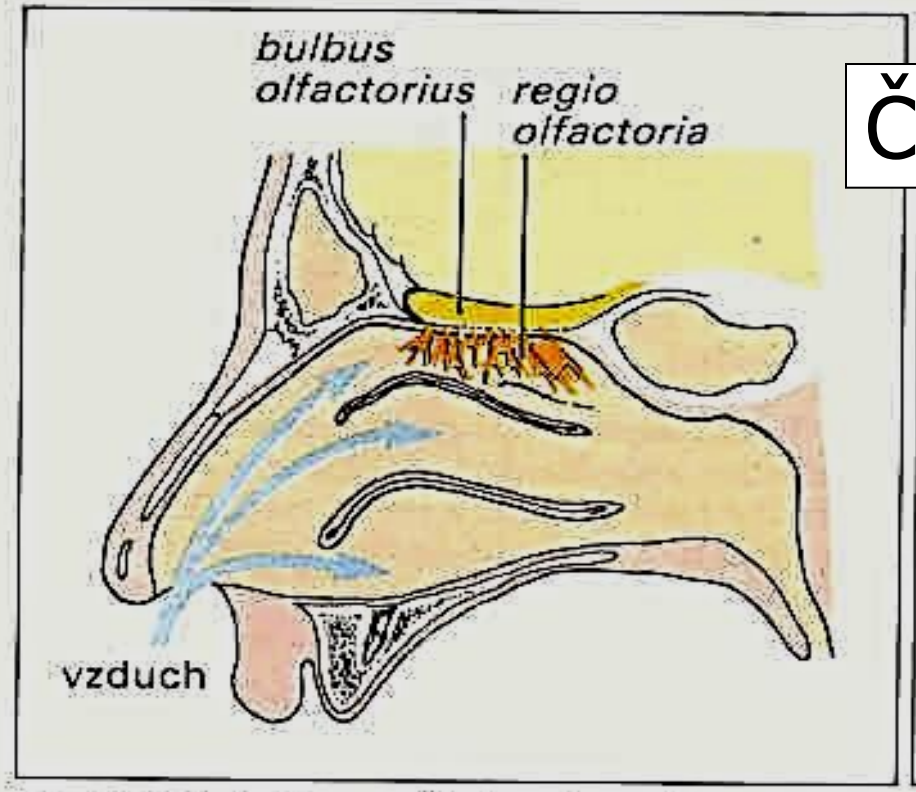
McGann, Science 356, 597 (2017) 12 May 2017

Ale: ačkoliv je čichový lalok relativně menší, má stejně neuronů jako u myši a je mnohem větší absolutně.
Srovnávají-li se výkony, velmi záleží na volbě dané vůně. Zřejmě kvůli existenci různé výbavě receptory. Pro některé vůně lidé předstihnou myš i psa. Množství vůní je i u lidí obrovské a i člověk dokáže sledovat pachovou stopu.
Pachová komunikace existuje i mezi lidmi a nese informaci o příbuzenství, stresu, reprodukčním stavu, i když často podvědomě.
Jde o vysoce dynamický smysl spojený s pamětí. emočním doprovodem a okolnostmi.
Poruchy čichu mohou informovat o postupující neurodegenerativní chorobě.

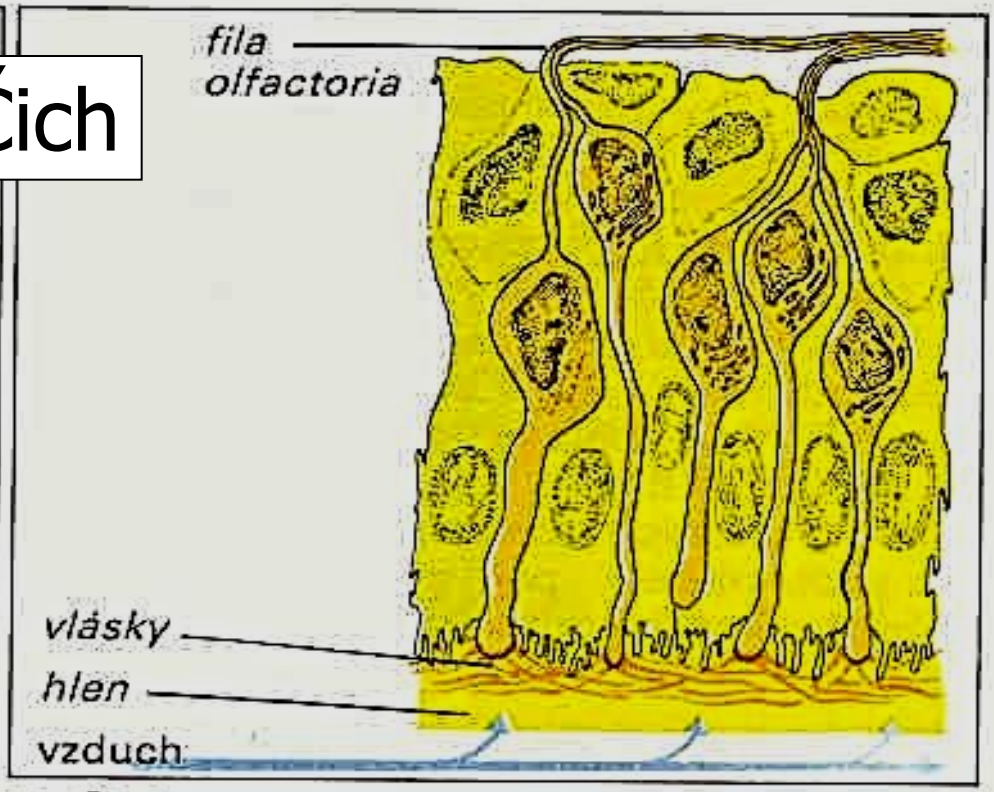


McGann, Science 356, 597 (2017) 12 May 2017

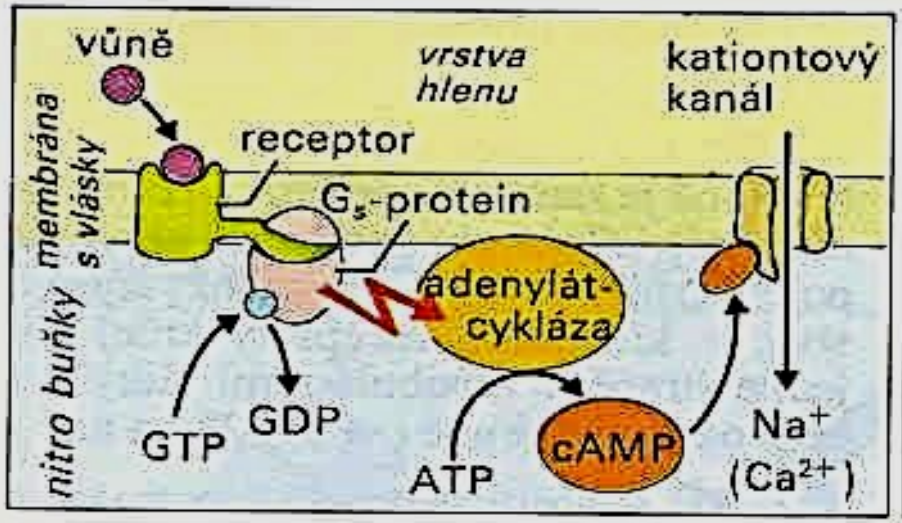
Čich



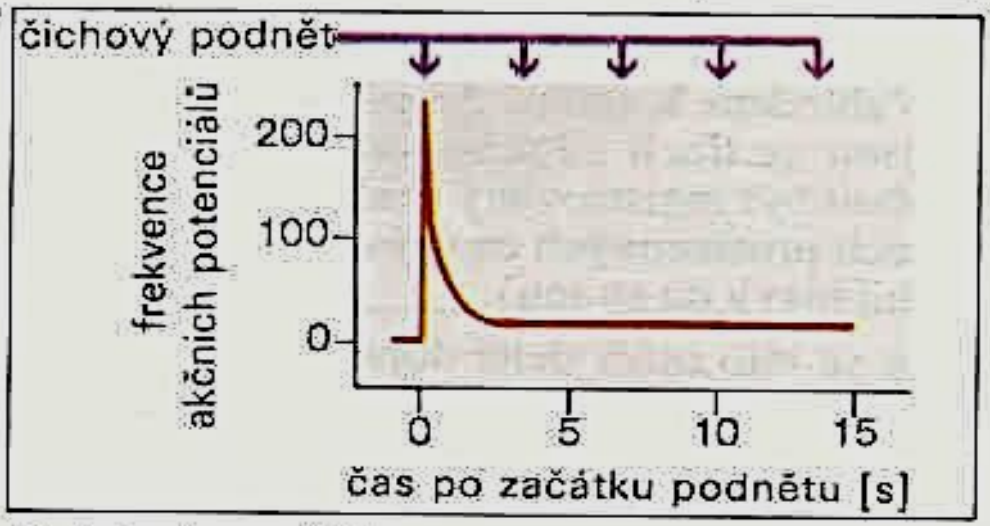
A. Nosní dutina a čichový orgán



B. Čichový epitel (podle Andrese)



C. Transdukce čichového podnětu

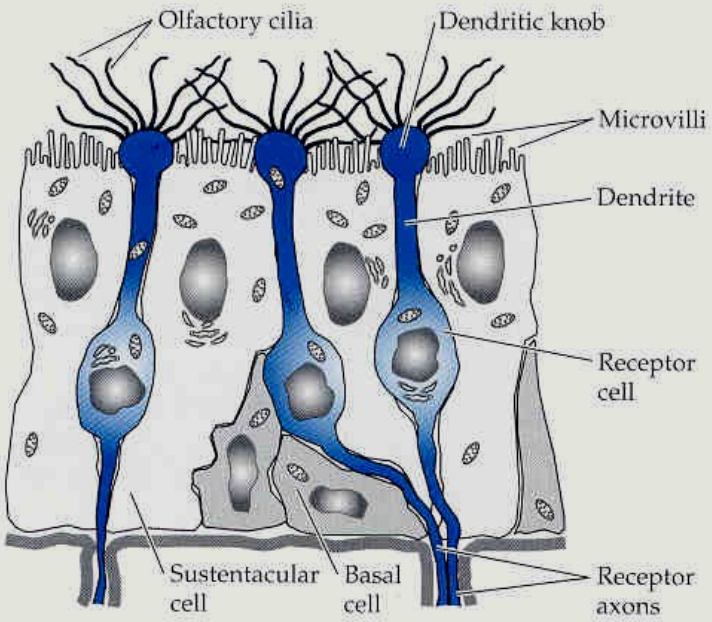


D. Adaptace čichu

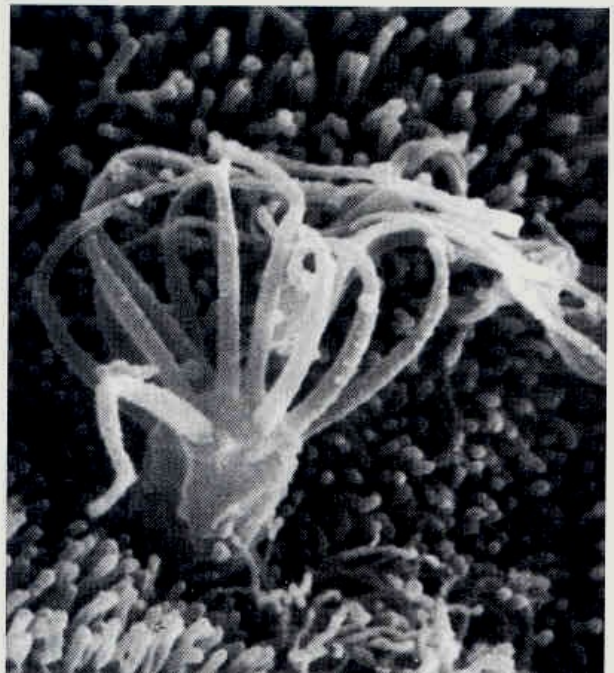
Čichové buňky savců jsou bipolární, primární r., je jich 6-10 milionů, dendrit má na konci 5-20 vlásků - cilií, řasinek.

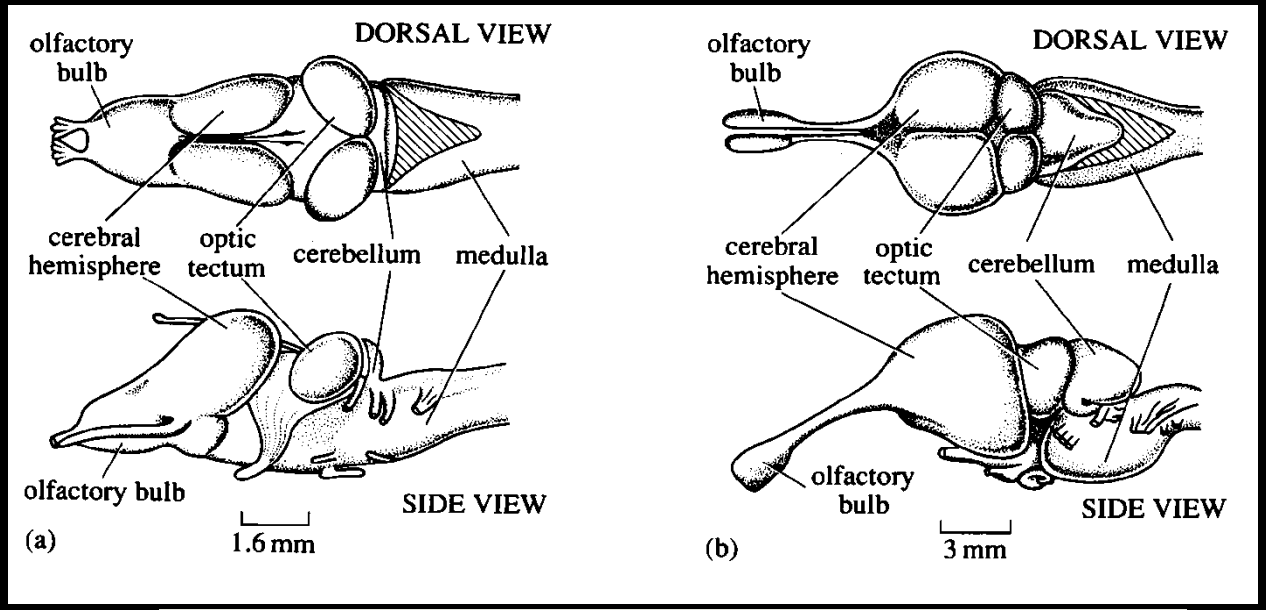
Figure 7.7
Olfactory epithelium (A) Schematic cross section of olfactory epithelium. (B) Scanning micrograph of a dendritic knob and dendrites of a human olfactory receptor neuron. Magnification: 18,500×. (From Morrison and Costanzo, 1990.)

(A)



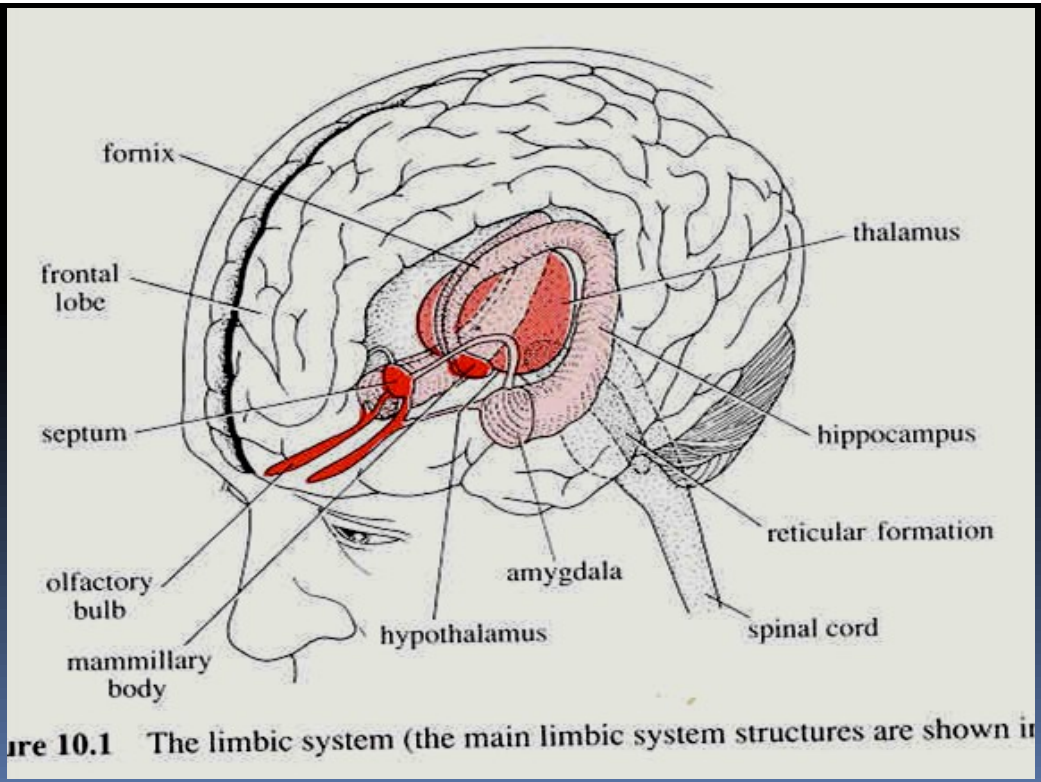
(B)





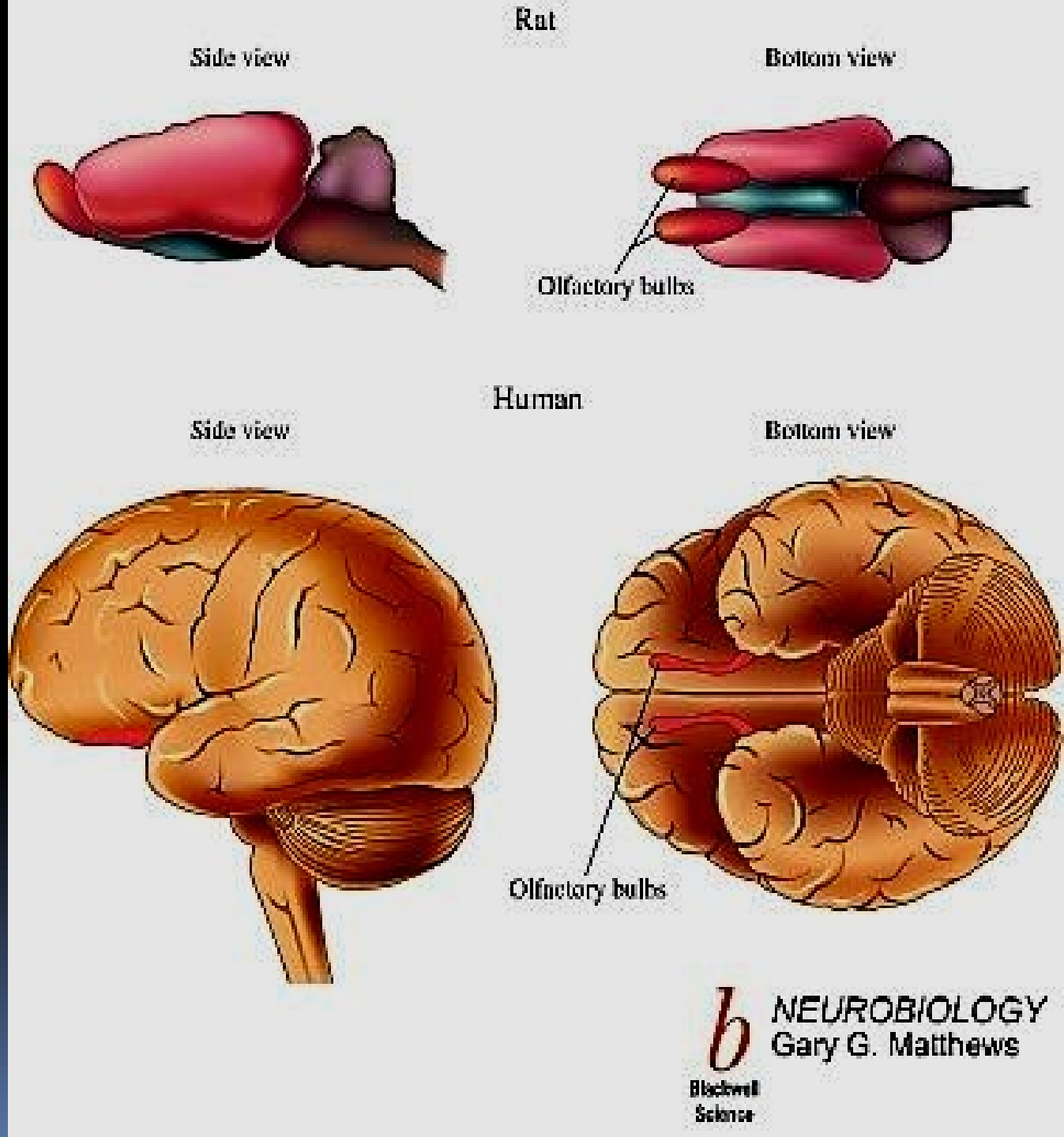
Čichový lalok – součást koncového mozku

Začátek nervové trubice se formoval jako čichové centrum.



ure 10.1 The limbic system (the main limbic system structures are shown i

Čichový lalok – součást koncového mozku



Univerzální receptor G prot. signální dráhy
7TM a-helix receptor
Čichové receptory tvoří největší rodinu GPCR – G prot. coupled rec.
s jedinou zvláštností: velmi dlouhou druhou extracelulární smyčkou.
Možná nejzajímavější je hypervariabilní oblast na 3., 4. a 5. transmembránové doméně.
Na prostorových modelech se tyto oblasti přikládají k sobě a vytváří jakousi kapsu. Ta je pravděpodobným místem pro vazbu těkavých ligandů .

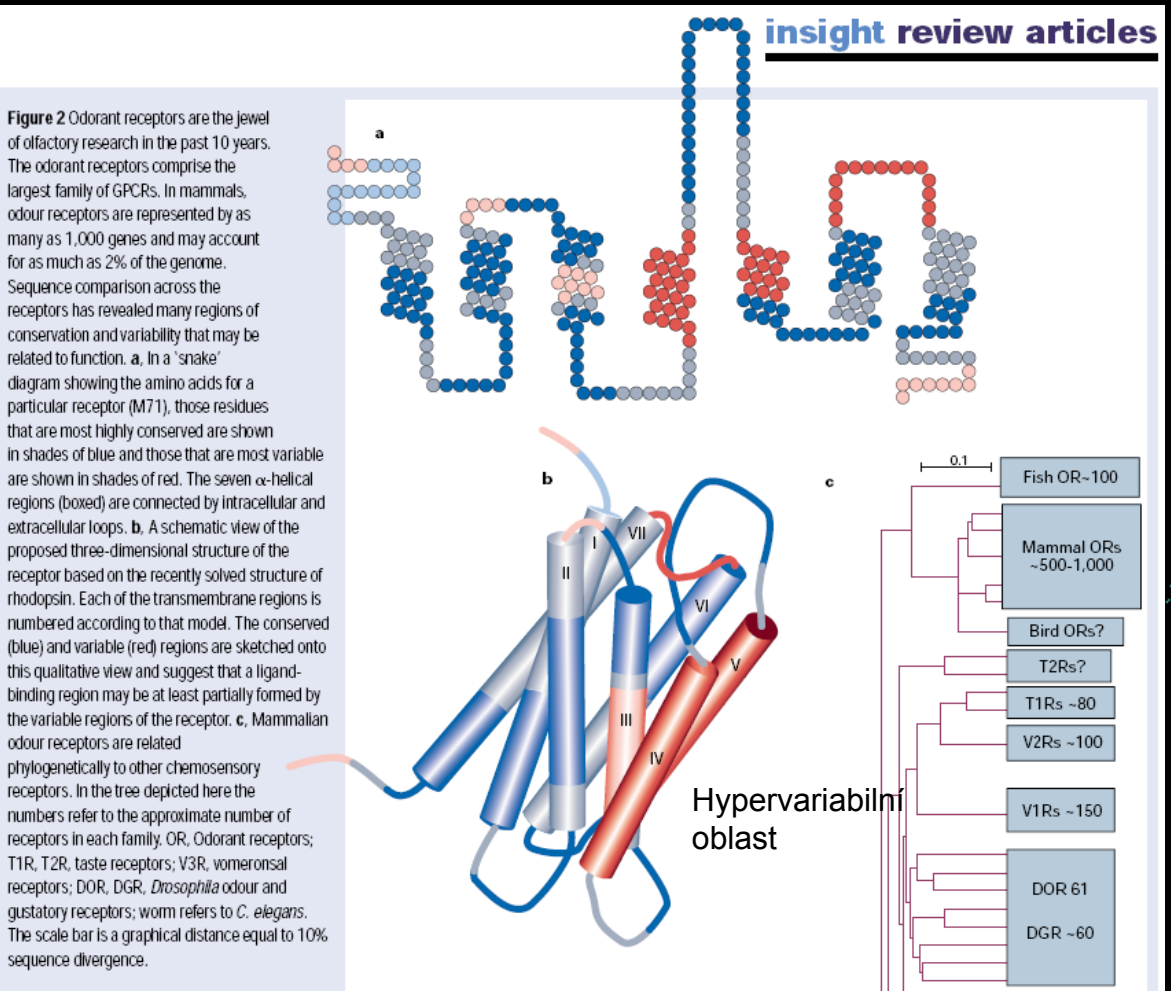
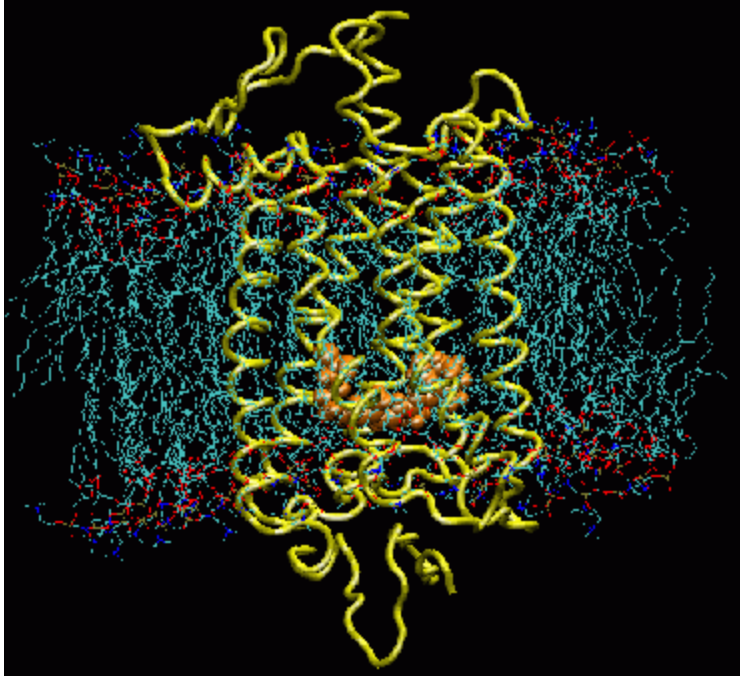
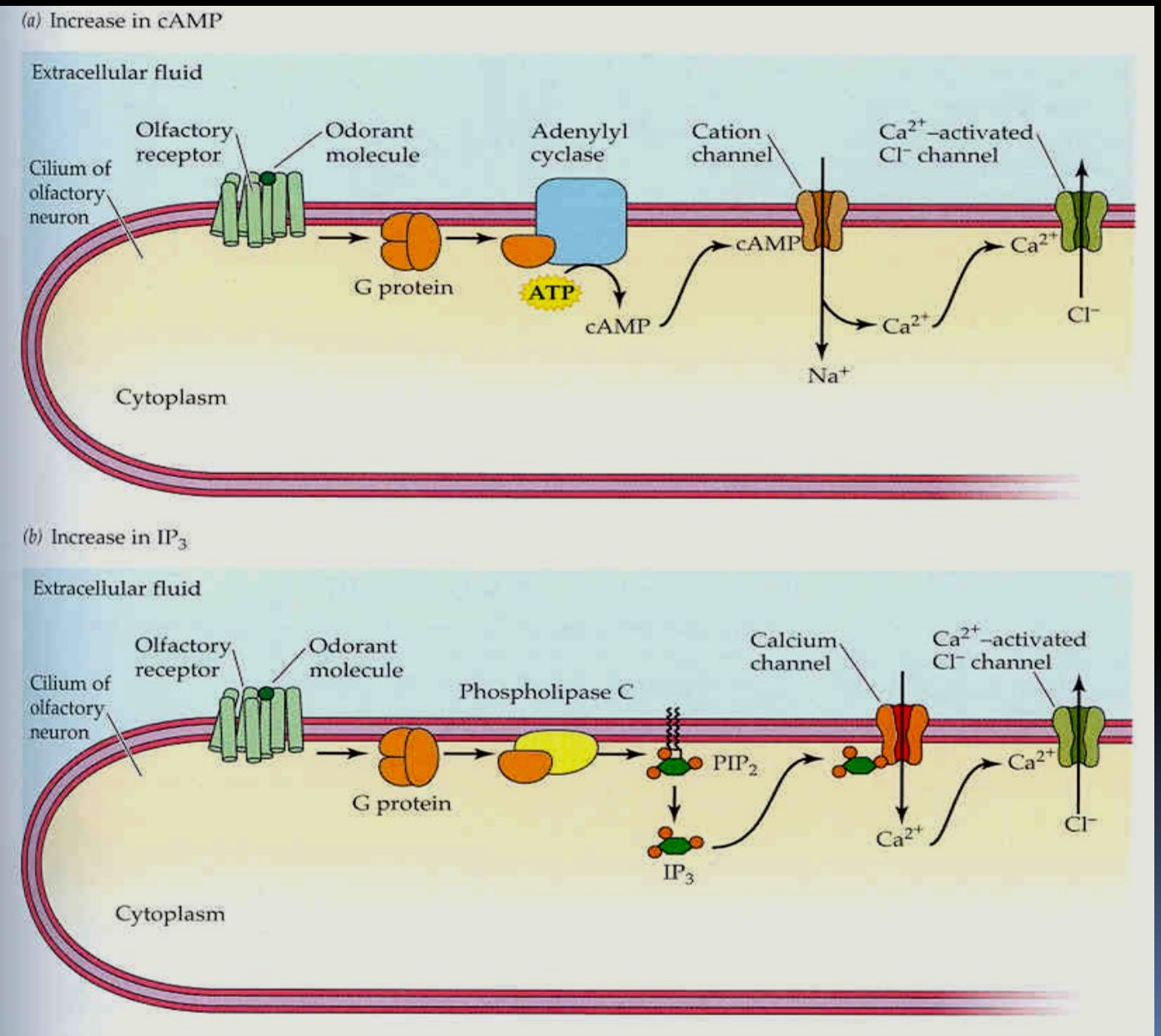


Figure 2 Odorant receptors are the jewel of olfactory research in the past 10 years. The odorant receptors comprise the largest family of GPCRs. In mammals, odour receptors are represented by as many as 1,000 genes and may account for as much as 2% of the genome. Sequence comparison across the receptors has revealed many regions of conservation and variability that may be related to function. **a**, In a 'snake' diagram showing the amino acids for a particular receptor (M71), those residues that are most highly conserved are shown in shades of blue and those that are most variable are shown in shades of red. The seven α-helical regions (boxed) are connected by intracellular and extracellular loops. **b**, A schematic view of the proposed three-dimensional structure of the receptor based on the recently solved structure of rhodopsin. Each of the transmembrane regions is numbered according to that model. The conserved (blue) and variable (red) regions are sketched onto this qualitative view and suggest that a ligand-binding region may be at least partially formed by the variable regions of the receptor. **c**, Mammalian odour receptors are related phylogenetically to other chemosensory receptors. In the tree depicted here the numbers refer to the approximate number of receptors in each family. OR, Odorant receptors; T1R, T2R, taste receptors; V3R, vomeronsal receptors; DOR, DGR, *Drosophila* odour and gustatory receptors; worm refers to *C. elegans*. The scale bar is a graphical distance equal to 10% sequence divergence.



Univerzální mechanismy transdukce



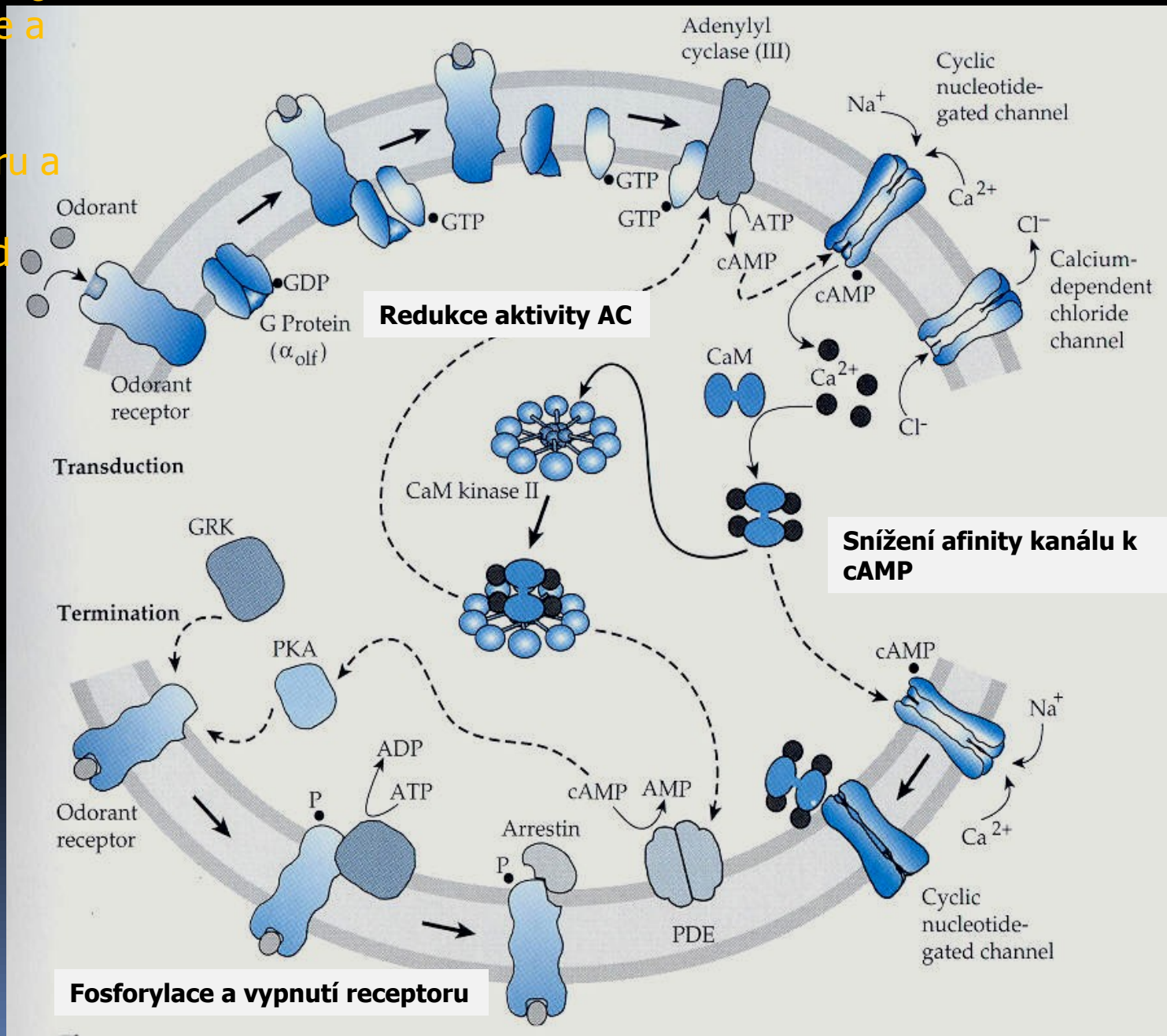
Cl ionty také depolarizují – výjimka kvůli vysoké koncentraci uvnitř

Ca ionty mají i adaptační význam

Aktivace
Zesílení, max. 4.10^{-15}g/l
Adaptace, terminace a modulace

Fosforylace receptoru a navázání Arestinu
GRK-G prot. coupled rec. Kináza

Vše závisí na Ca



Obecný mechanismus vypínání metabotropního receptoru

Nejen aktivace G prot., ale i vystavení Ser a Thre zbytků blízko C konce a usnadní navázání G protein coupled receptor kinázy (GRK). Ta katalyzuje připojení fosfátové skupiny z ATP na am.kys. GPCR. Fosforylovaný receptor váže arestin, který zasahuje do vazebného místa receptoru pro G protein a brání jeho další aktivaci. Tím ukončuje aktivitu receptoru.

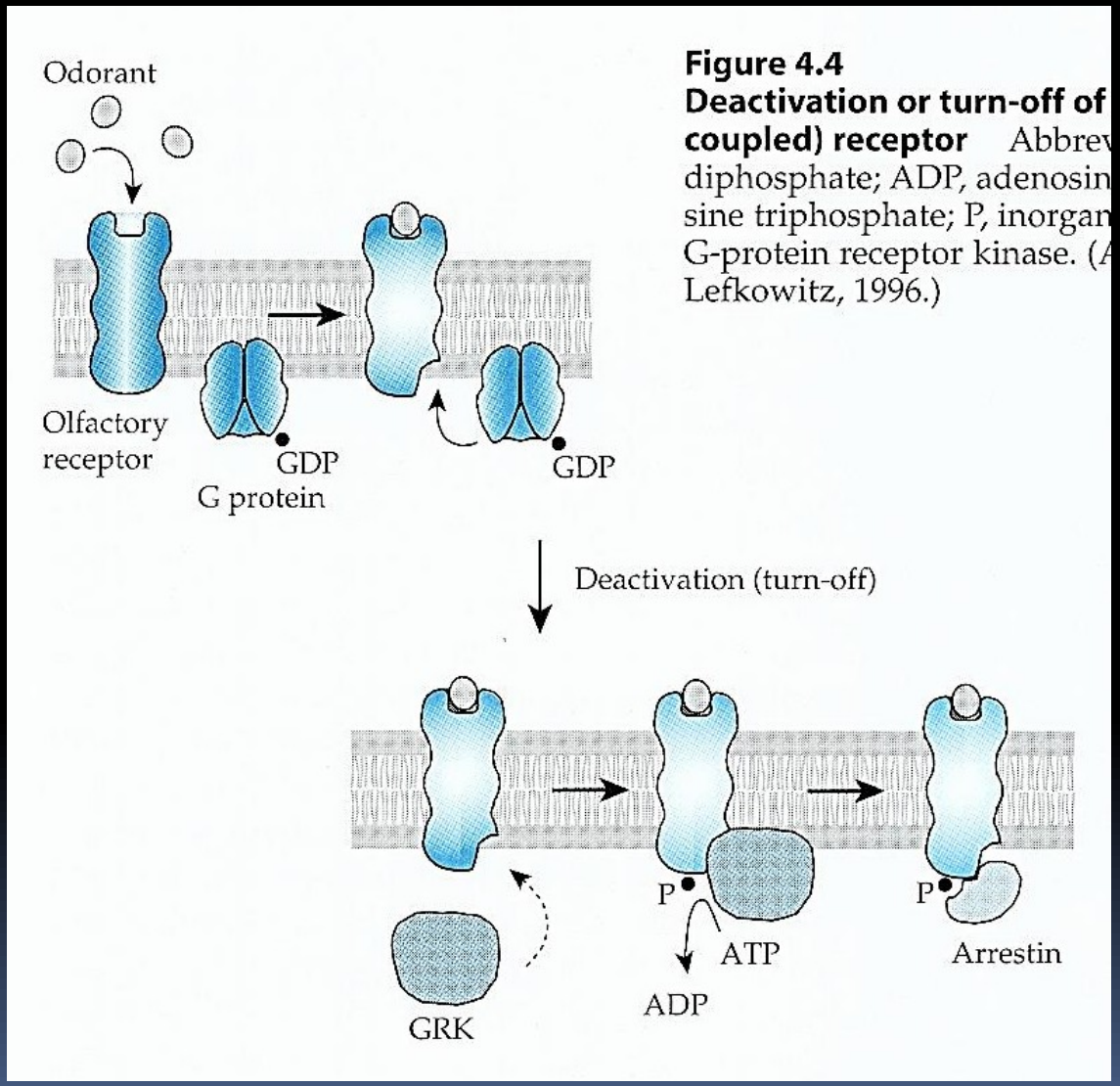


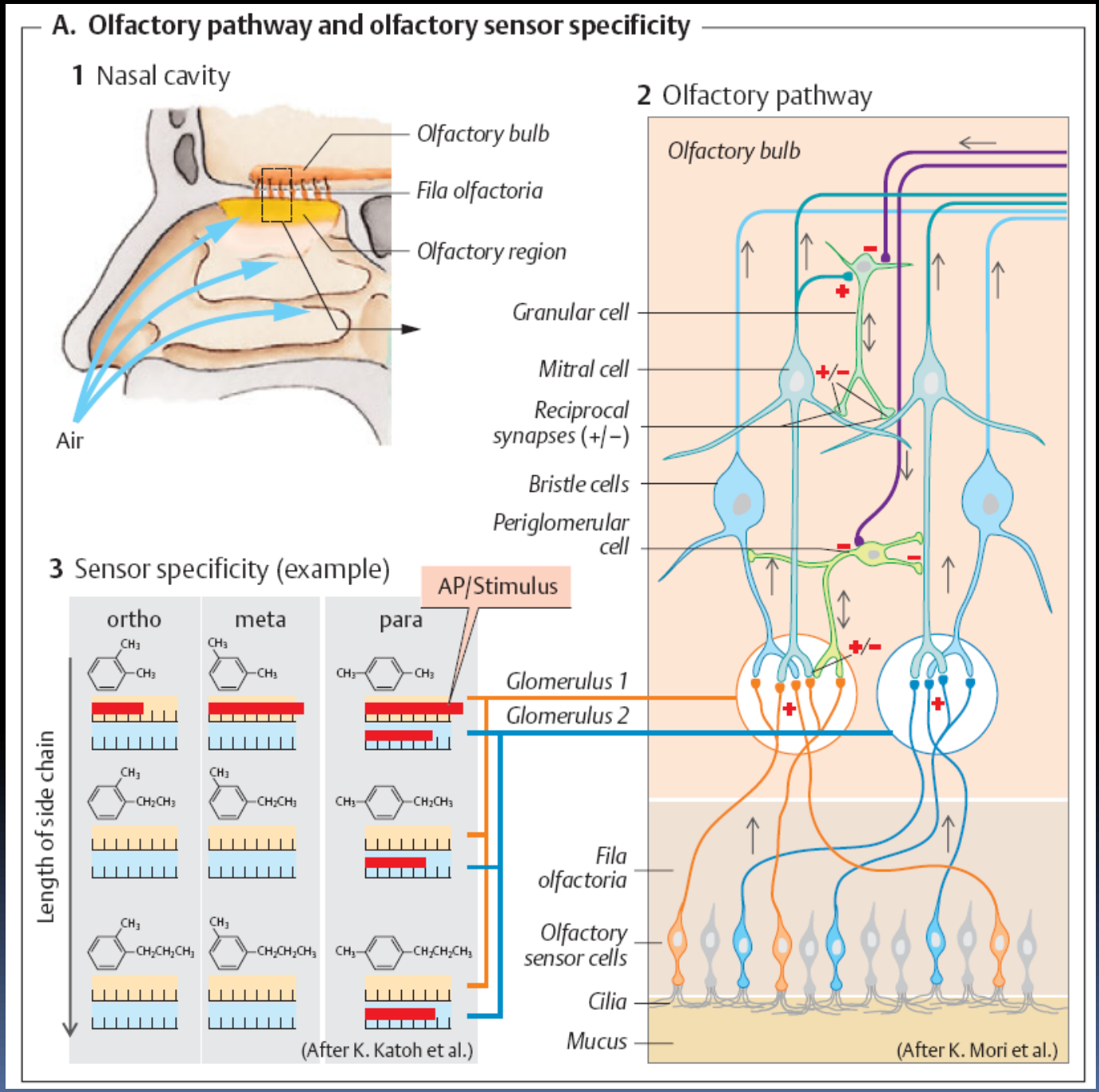
Figure 4.4
Deactivation or turn-off of coupled) receptor Abbrev diphosphate; ADP, adenosin sine triphosphate; P, inorgan G-protein receptor kinase. (A Lefkowitz, 1996.)

Periferie
čichové dráhy

Rozlišování chem.
Struktury podle:
a) pozice skupin
b) Délky řetězce

Laterální inhibice
Kontrastování

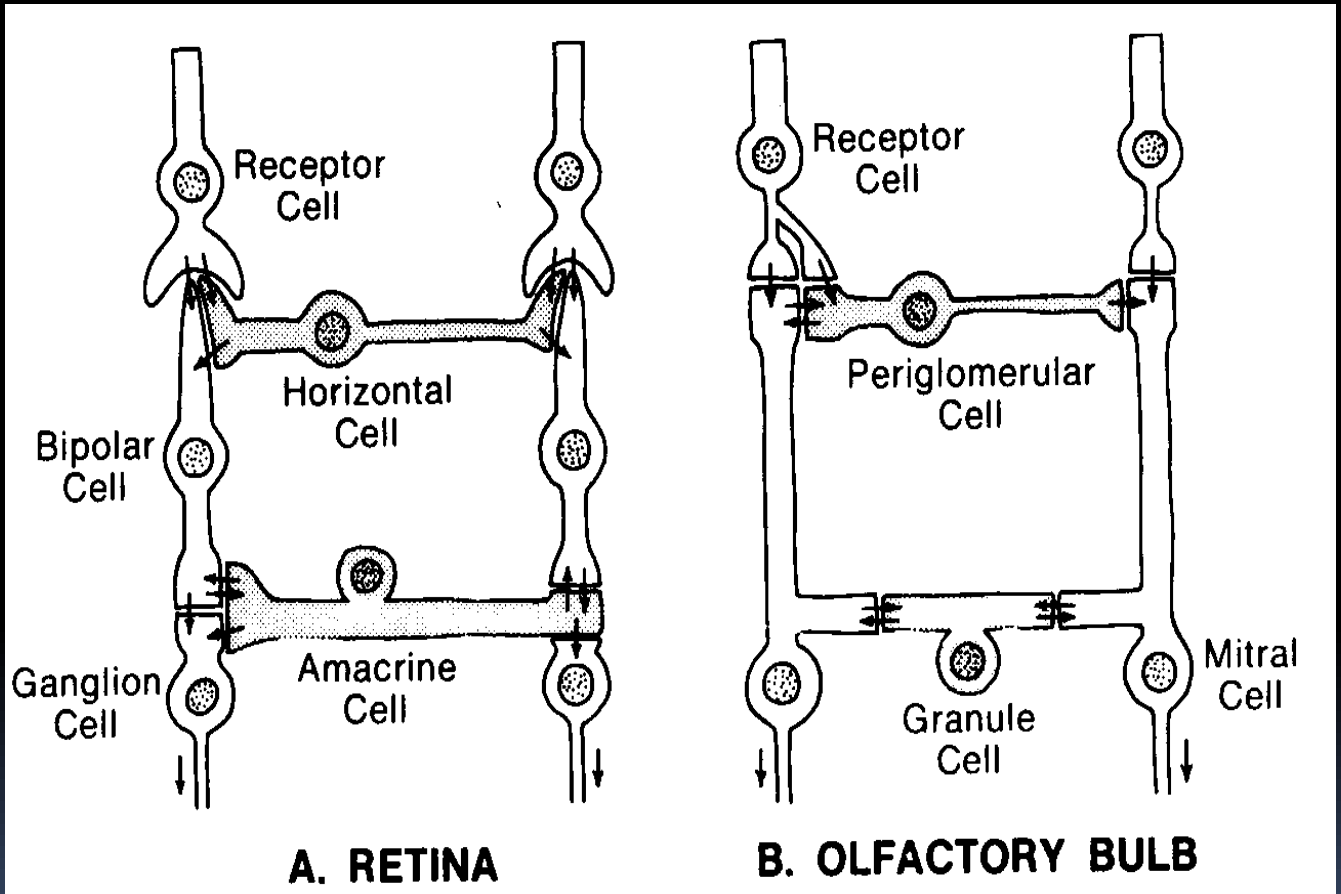
Eferentní inhibice



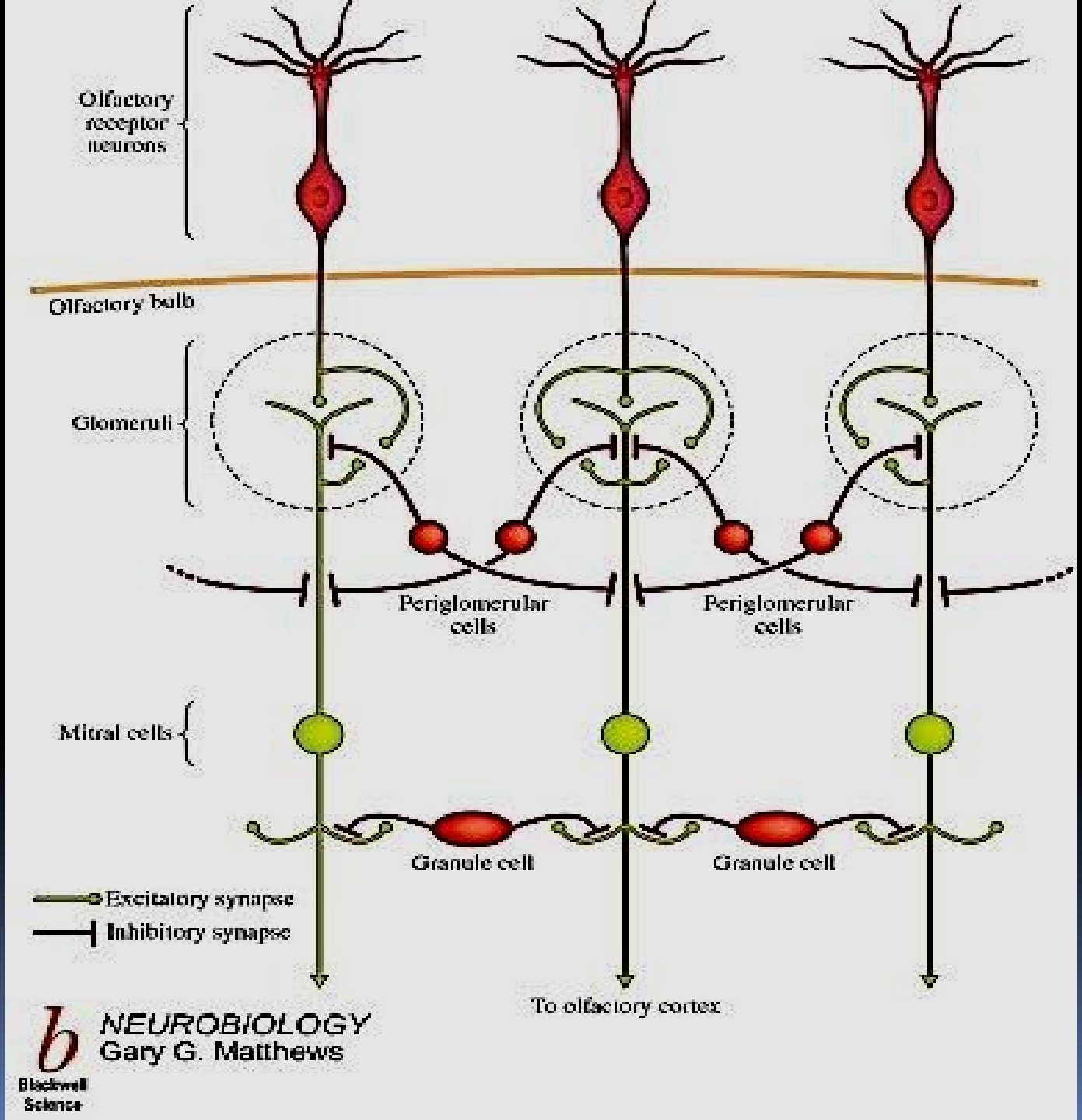
Všechny neurony exprimující určitý receptor, bez ohledu na to, kde je umístěn na sliznici, konvergují na jedno jediné místo na čichovém laloku. Těmito místy jsou glomeruly, kulovité shluky šedé hmoty, asi 50-1000 mikrometrů, sestávající z přicházejících axonů z receptorů a z dendritů mitrálních buněk. V jednom zvlášť extrémním případě konverguje několik tisíc smyslových neuronů na asi 10 mitrálních buněk, což je v nervovém systému rekord.

https://oup-arc.com/access/content/sensation-and-perception-5e-student-resources/sensation-and-perception-5e-14-1-olfactory-anatomy?previousFilter=tag_chapter-14

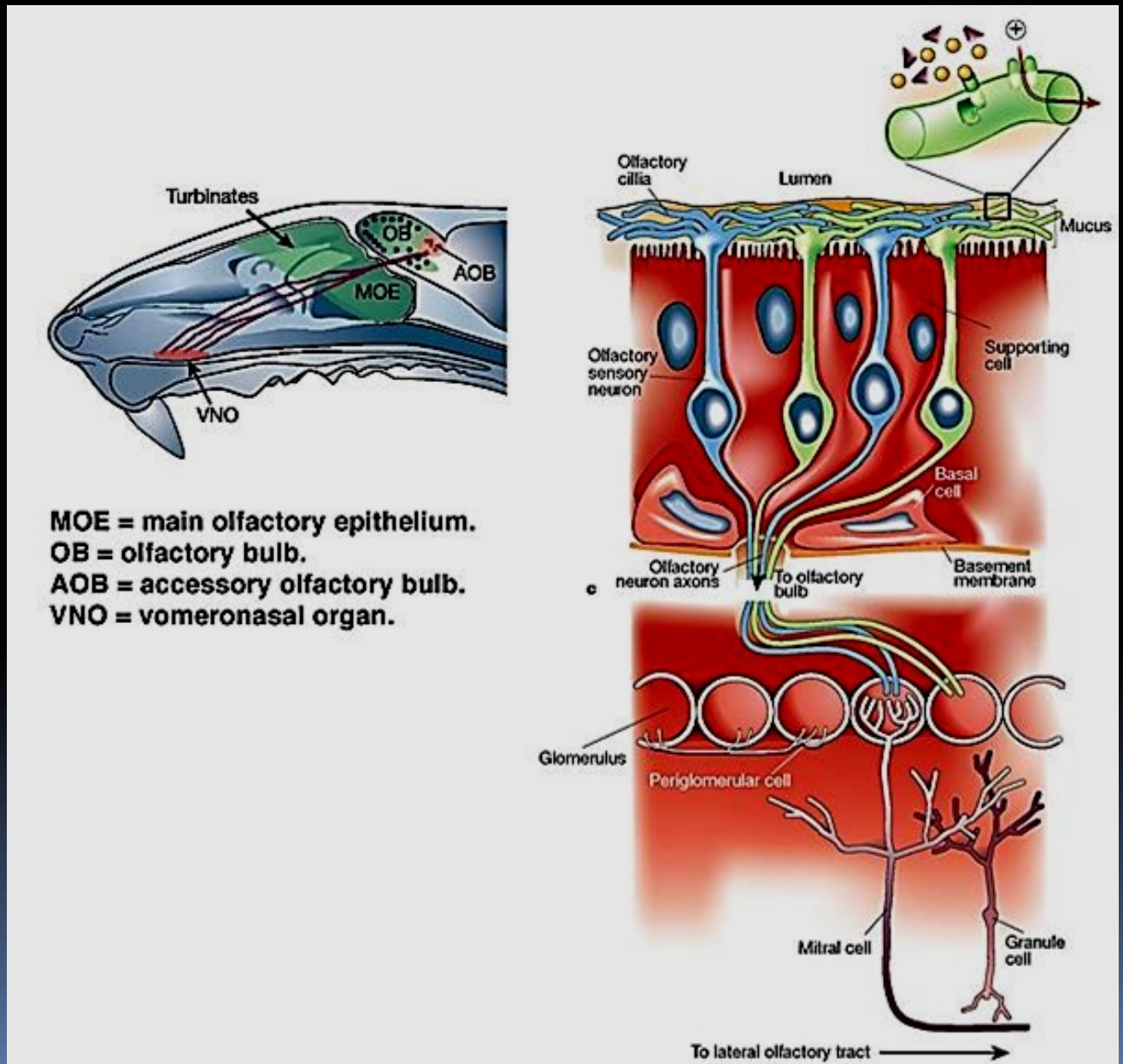
Podobnost architektury sensorických obvodů a drah



Comparison between simplified basic circuit diagrams of the vertebrate r
bulb. (After Shepherd, 1978)

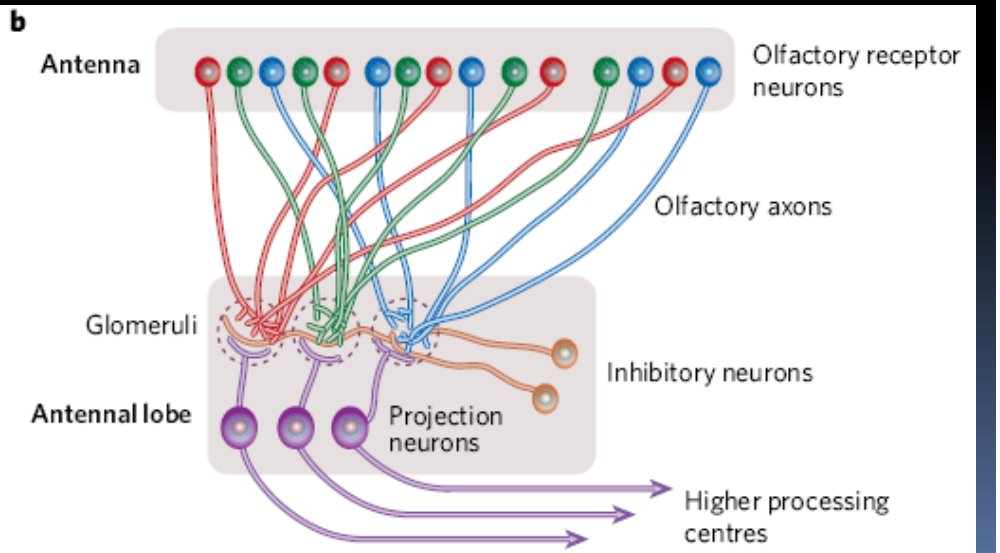

Olfactory receptor neurons
Olfactory bulb
Glomeruli
Periglomerular cells
Periglomerular cells
Mitral cells
Granule cell
Granule cell
Excitatory synapse
Inhibitory synapse
To olfactory cortex
NEUROBIOLOGY
Gary G. Matthews
Blackwell Science

Konvergence na příslušný glomerulus (100 - 1000/1)



Může tak vzniknout „mapa vůní“ – vzorec aktivovaných glomerulů čichového laloku. Specifická „mozaika“ aktivace pro konkrétní vůni

Jde tak o konvergenci neprostorového parametru na prostorový



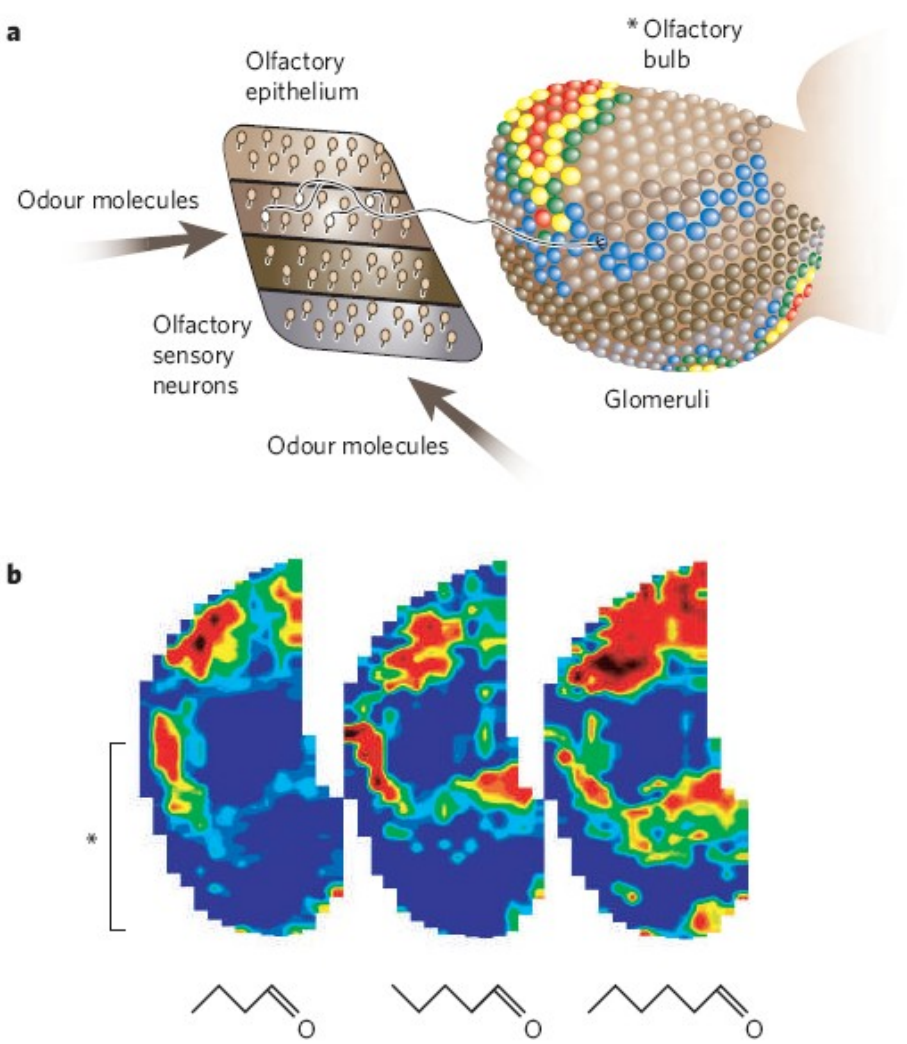
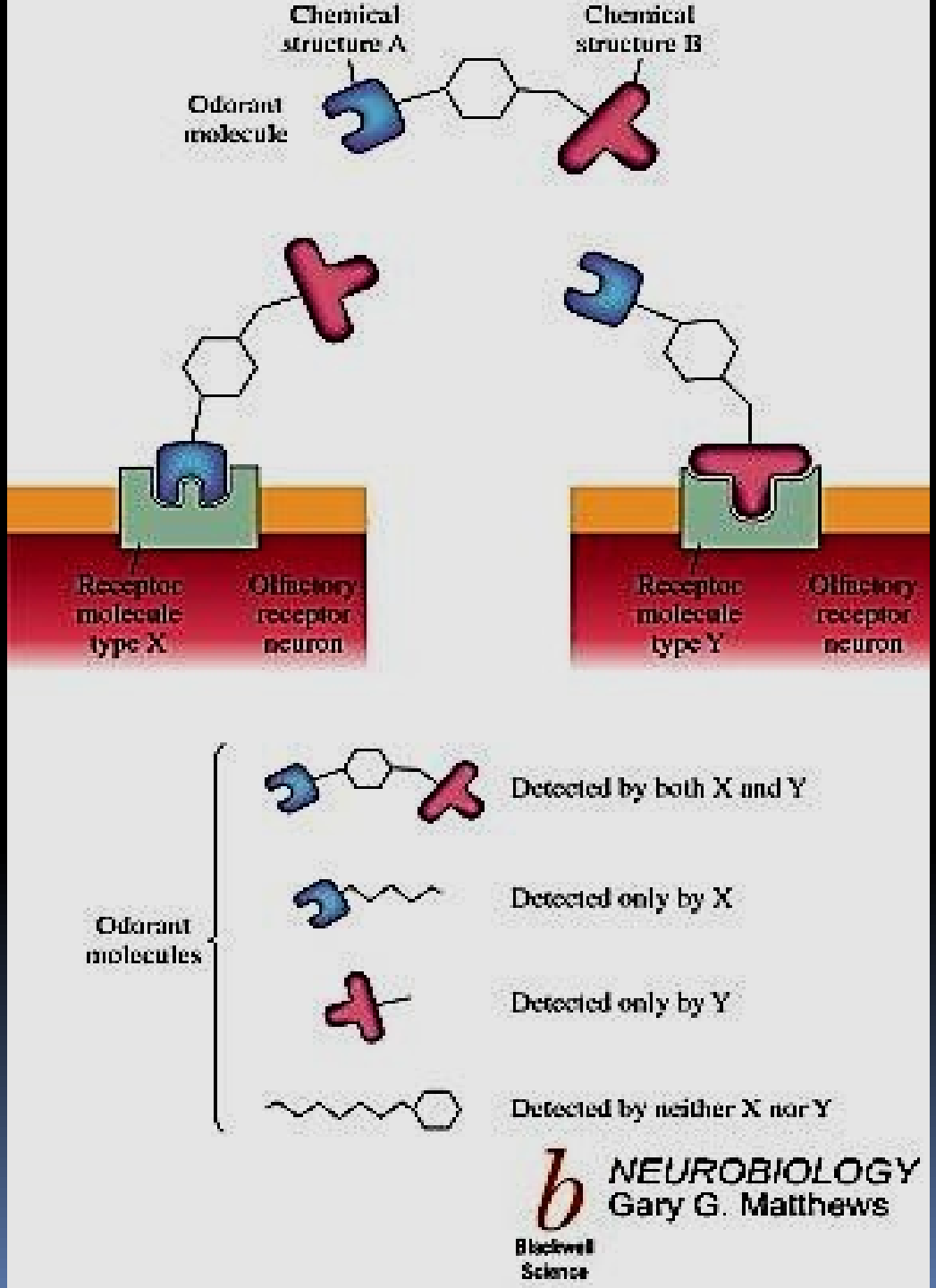


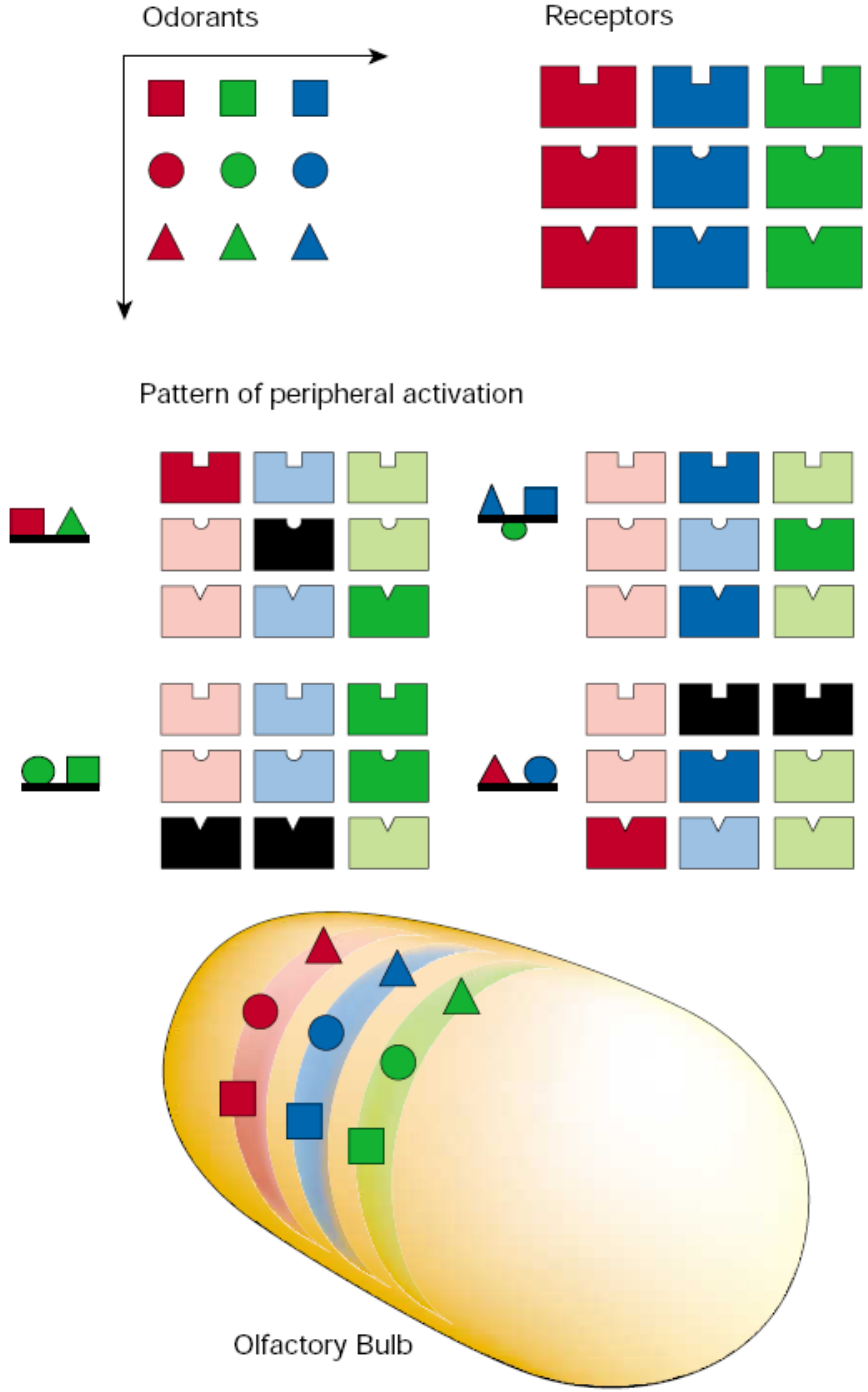
Figure 1 | Odour images in the olfactory glomerular layer. **a**, Diagram showing the relationship between the olfactory receptor cell sheet in the nose and the glomeruli of the olfactory bulb[53]. **b**, fMRI images of the different but overlapping activity patterns seen in the glomerular layer of the olfactory bulb of a mouse exposed to members of the straight-chain aldehyde series, varying from four to six carbon atoms. The lower part of the image in the left panel corresponds to the image on the medial side of the olfactory glomerular layer as shown in **a** (see asterisk). (Image in **a** adapted, with permission, from ref. 53; image in **b** adapted, with permission, from ref. 10.)

Specializace receptorů
Kombinace cca 350 receptorů
3.000-100.000 vůní (?)

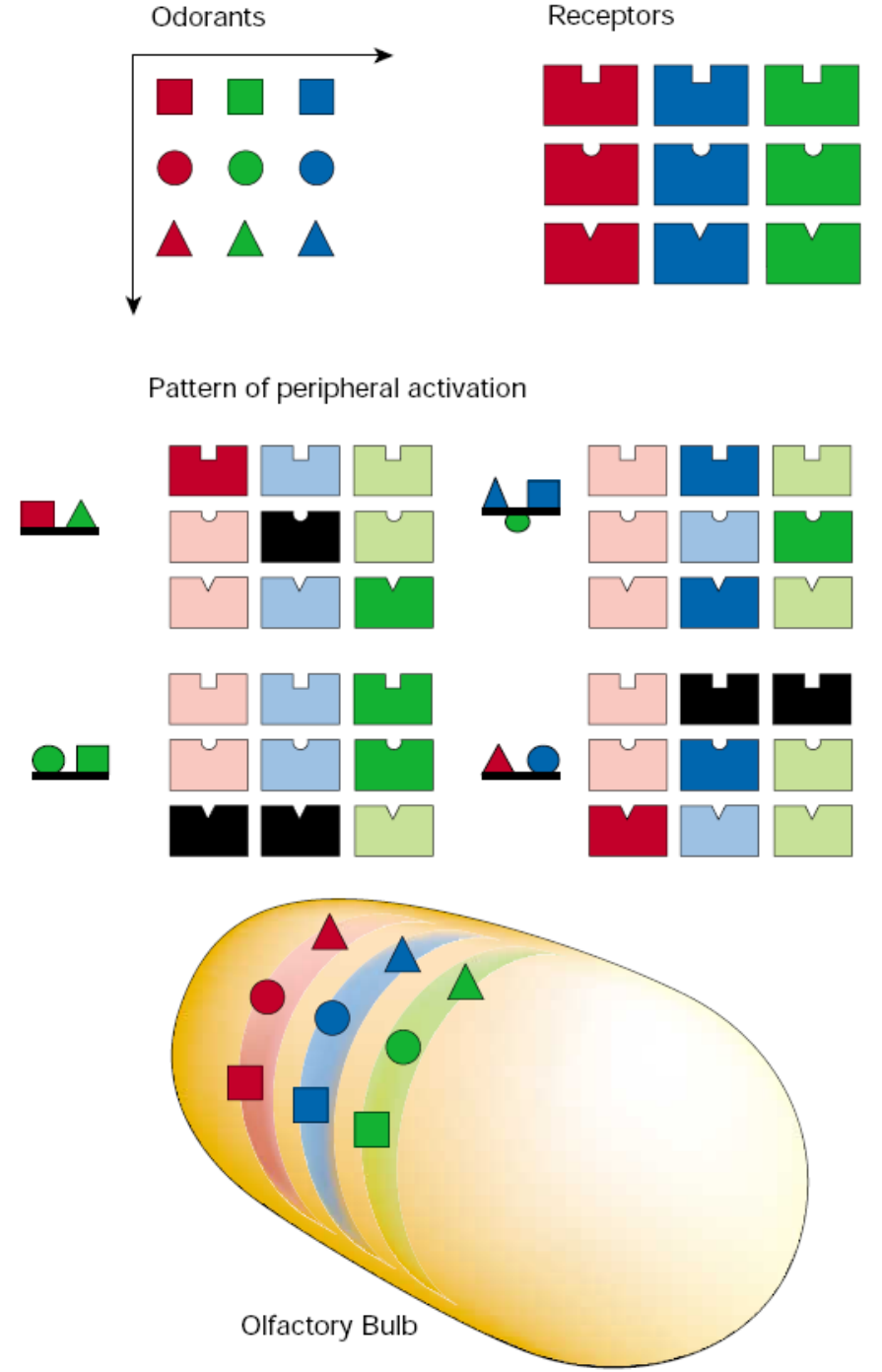
Ale: 21 MARCH 2014 VOL 343 SCIENCE
10^{12} – trilion vůní

Rozeznává tisíce hlavně nízkomolekulárních organických látek, kterým říkáme pachy nebo vůně. Jsou to alifatické nebo aromatické molekuly s různými uhlovodíkovými bočními větvemi a vazebnými skupinami., aldehydy, estery, ketony, alkoholy, aminy, karboxylové kyseliny, atd.





Although there are some 1,000 ORs, detecting the enormous repertoire of odours requires a combinatorial strategy. Most odour molecules are recognized by more than one receptor (perhaps by dozens) and most receptors recognize several odours, probably related by chemical property. The scheme in the figure represents a current consensus model. There are numerous molecular features, two of which are represented here by colour and shape. Receptors are able to recognize different features of molecules, and a particular odour compound may also consist of a number of these 'epitopes' or 'determinants' that possess some of these features. Thus the recognition of an odorant molecule depends on which receptors are activated and to what extent, as shown by the shade of colour (black represents no colour or shape match and thus no activation). Four odour compounds are depicted with the specific array of receptors each would activate. Note that there are best receptors (for example, red square), but also other receptors that are able to recognize some feature of the molecule (for example, any square) and would participate in the discrimination of that compound. In the olfactory bulb there seem to be wide areas of sensitivity to different features (for example, functional group or molecular length). This model is based on current experimental evidence, but is likely to undergo considerable revision as more data become available.



Většina vůní je rozeznávána více než jedním typem receptoru a většina receptorů rozeznává více vůní. Informace o určité vůni je kódována vzájemným poměrem vzruchových aktivit jednotlivých výstupů různě specializovaných čichových buněk.

Vůně jsou v reálném světě ve směsích a smícháním více kvalit vzniká nová kvalita (jako barvy u zraku). Rozeznáme dvě směsi, ale ne komponenty v nich (na rozdíl od chuti nebo sluchu). Čich je syntetickým smyslem. Smícháním desítek (různých) vůní vzniká vjem „olfactory white" vůně. Tak jako u barev a zraku.

Zajímavé je, že určité vůně jsou stále stejně cítit při 5 řádovém rozdílu intenzit – přitom se přece zapojují i ne úplně naladěné receptory a tedy i receptory pro jiné vůně! Řešení je možná v neuronech specializovaných jen na koncentrace vyšších pater dráhy.

Podobnost architektury sensorických obvodů a drah zraku a čichu nebude náhodná

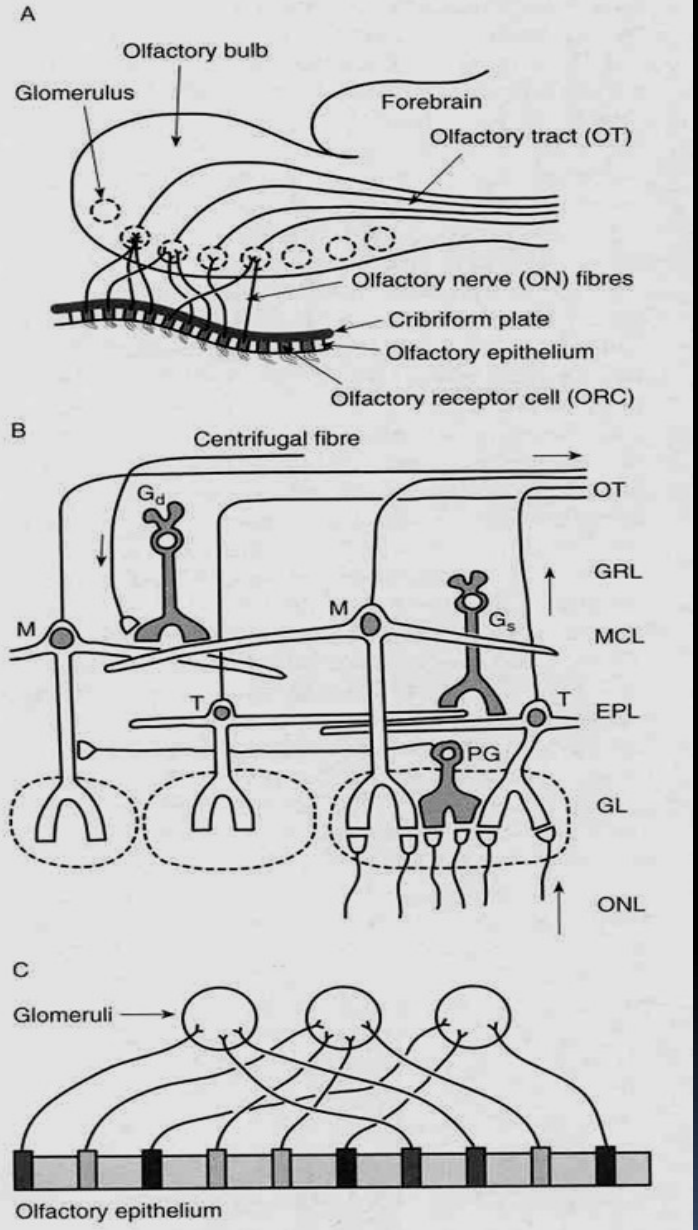
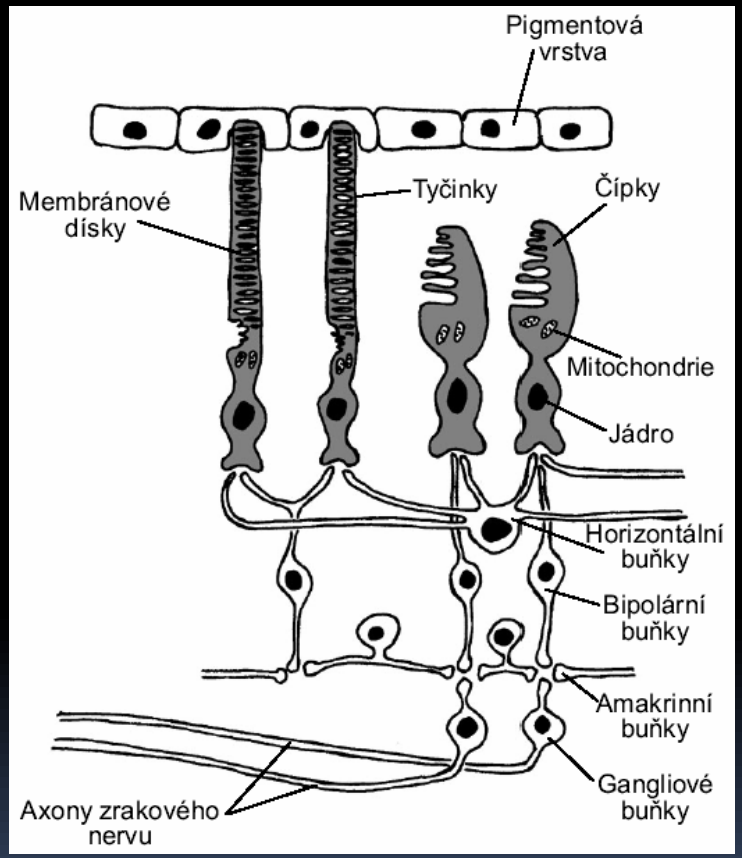


Figure 13.7 Olfactory bulb. (a) The figure shows olfactory axons passing through the cribriform plate to end in glomeruli in the olfactory bulb. (b) Basic circuit of the mammalian olfactory bulb. Layers: EPL = external plexiform layer; GL = glomerular layer; GRL = granule cell layer; OT = olfactory tract; MCL = mitral cell layer. Cells: G_d = deep granule cell; G_s = superficial granule cell; M = mitral cell; PG = periglomerular cell; T = tufted cell. Inhibitory cells stippled. Simplified from



Podobnost architektury sensorických obvodů a drah zraku a čichu nebude náhodná

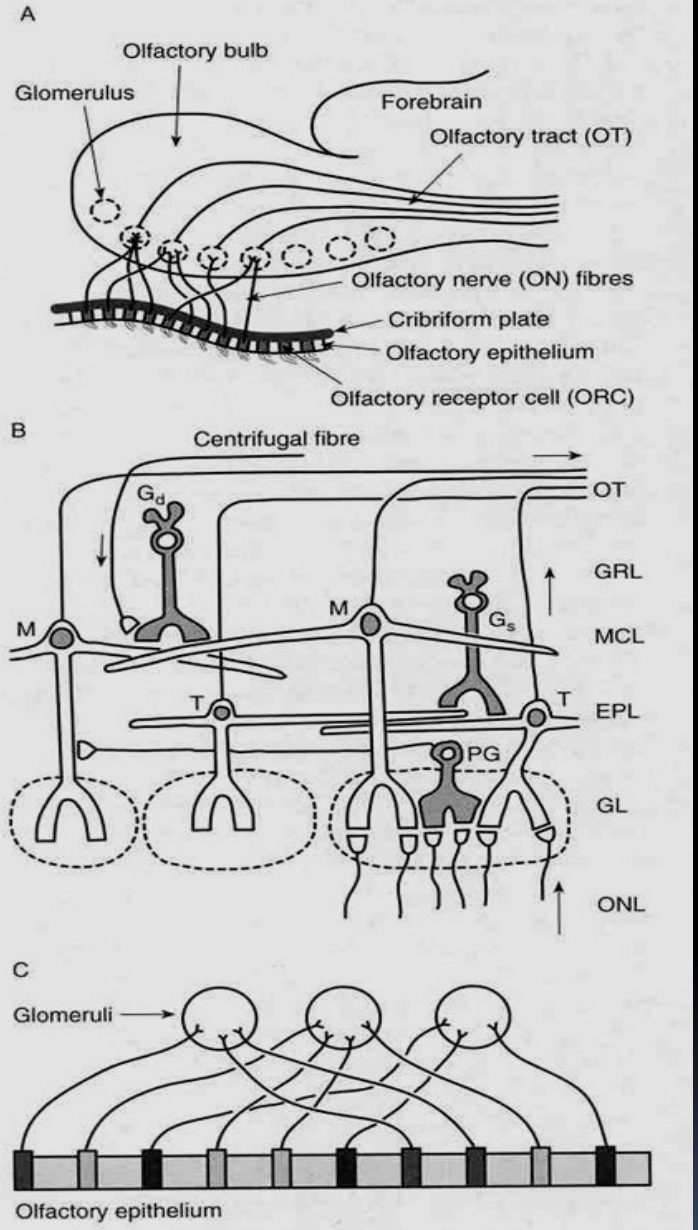
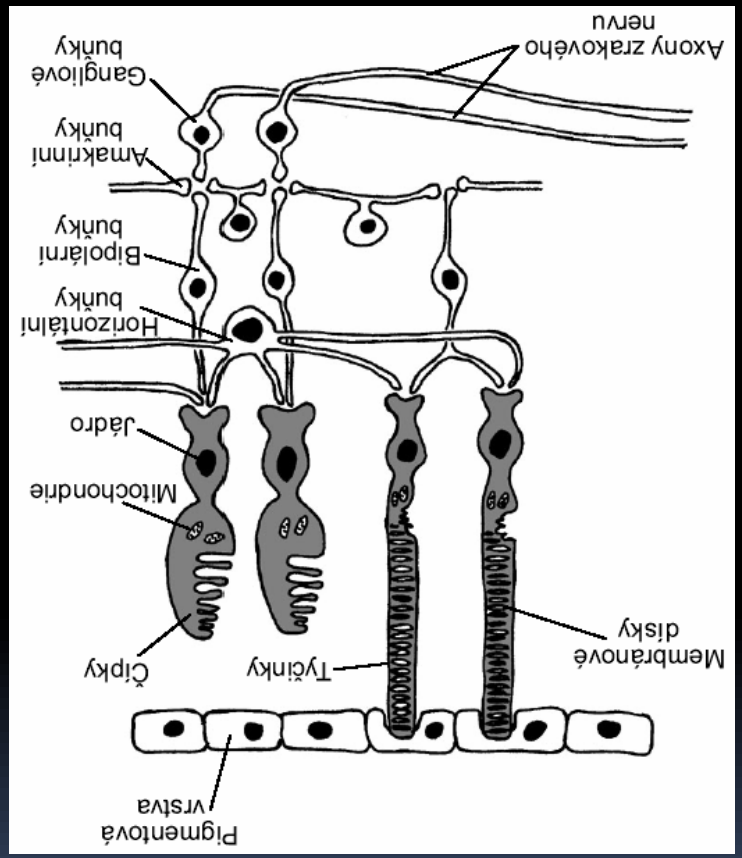
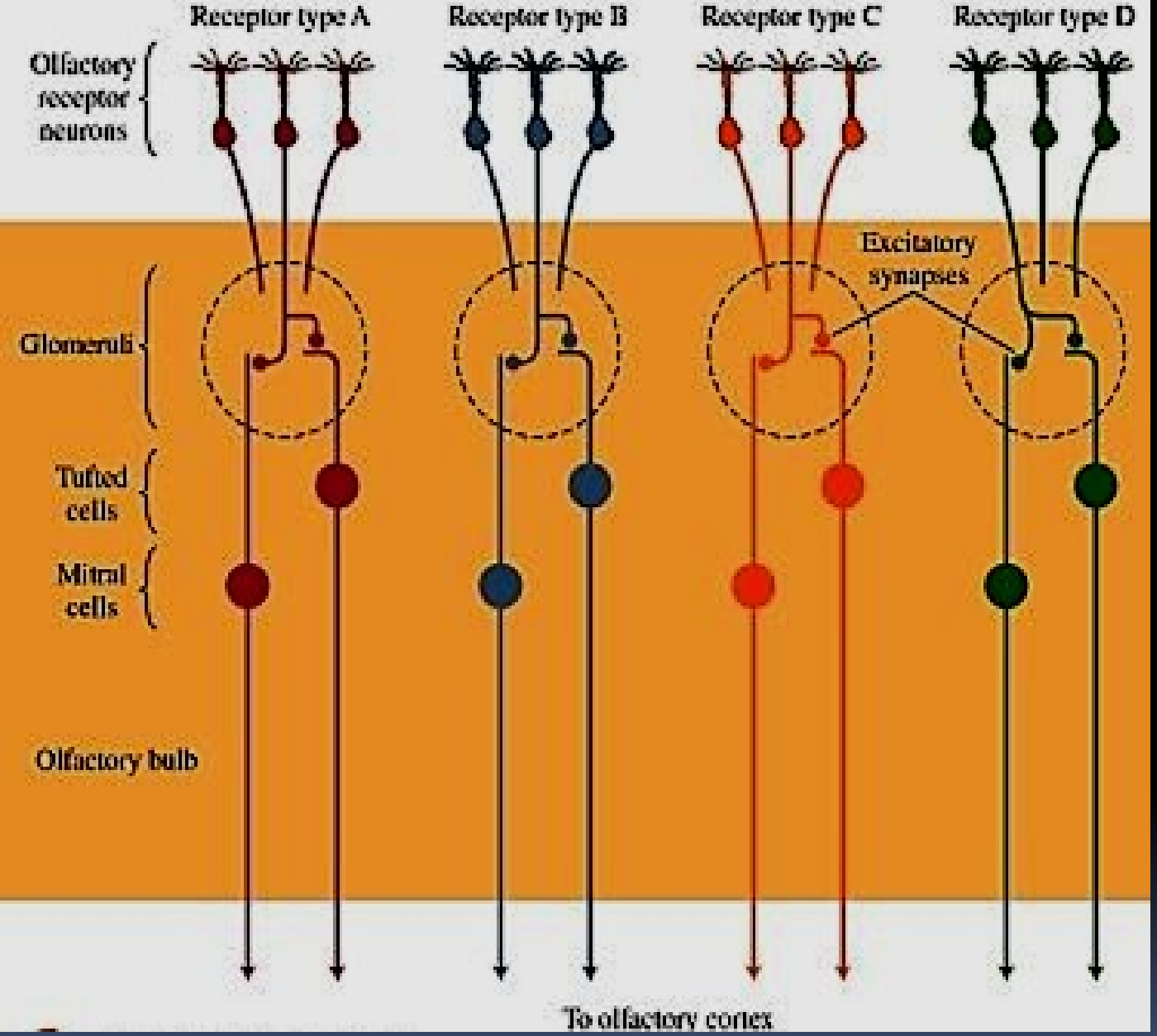
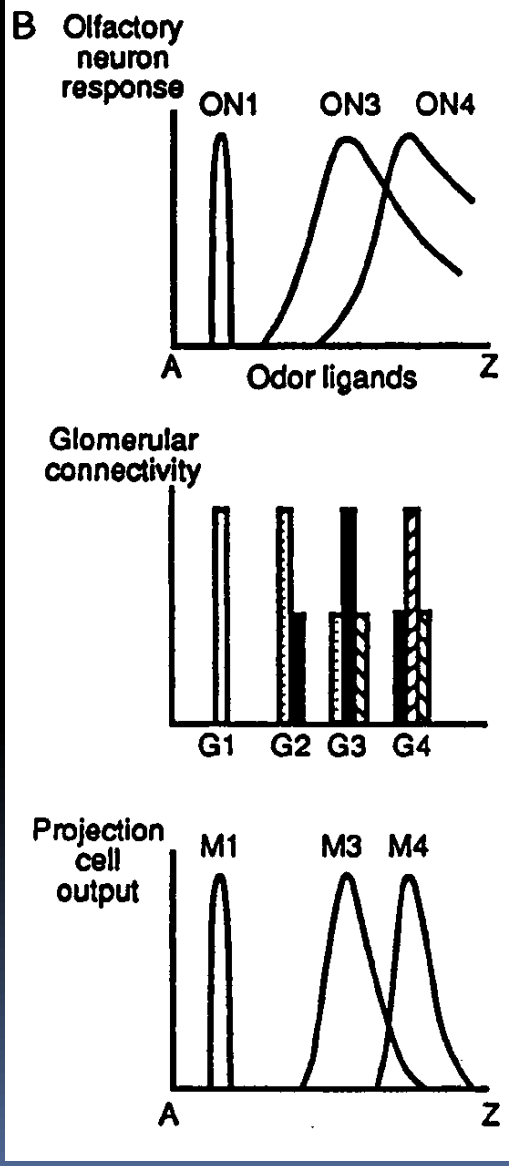


Figure 13.7 Olfactory bulb. (a) The figure shows olfactory axons passing through the cribriform plate to end in glomeruli in the olfactory bulb. (b) Basic circuit of the mammalian olfactory bulb. Layers: EPL = external plexiform layer; GL = glomerular layer; GRL = granule cell layer; OT = olfactory tract; MCL = mitral cell layer. Cells: G_d = deep granule cell; G_s = superficial granule cell; M = mitral cell; PG = periglomerular cell; T = tufted cell. Inhibitory cells stippled. Simplified from





Překryv



Laterální inhibice: „Zostření“ ladění ve vyšších patrech dráhy

Adaptace a habituace: Některé receptorové buňky reagují trvale nebo jen s malou adaptací na trvalé dráždění. To je ale v kontrastu se zkušeností velmi rychlé adaptace nebo i inhibice subjektivního počitku. Příčina je ve vyšších neurálních obvodech čichové dráhy.

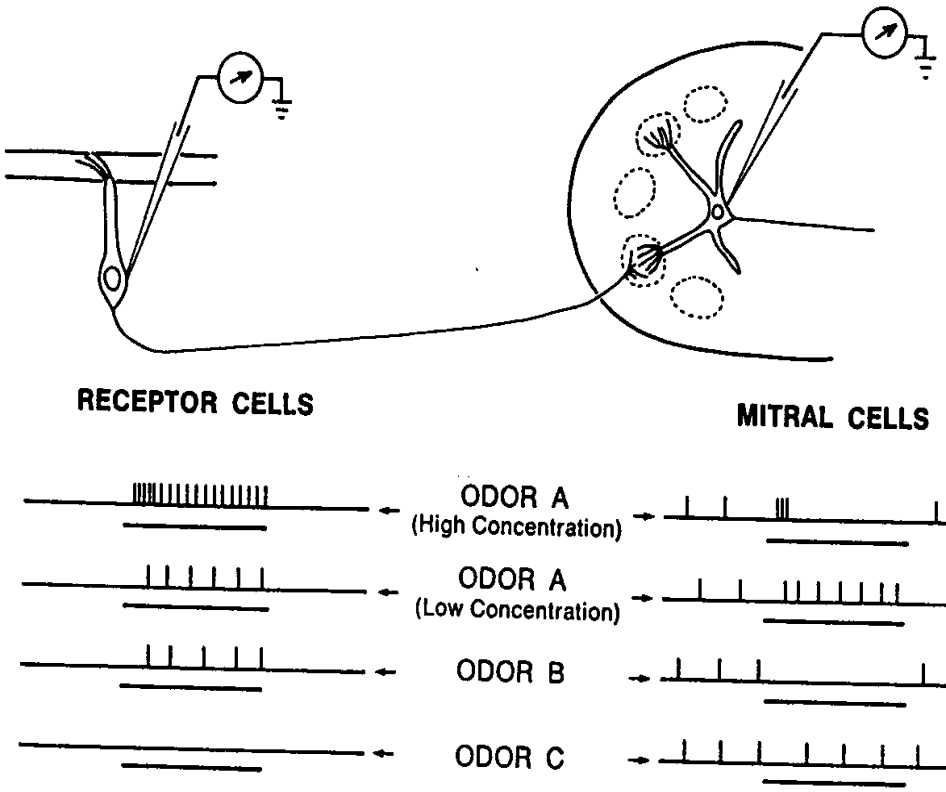


Fig. 11.11 Extracellular single-unit recordings of responses to odors of receptor cells *(left)* and mitral cells *(right)* in the salamander, showing different types of responses and different temporal patterns of activity. (After Kauer, 1974, and Getchell and Shepherd, 1978)

Citlivost: Práh čichové citlivosti může být u živočichů podle behaviorálních pokusů dokonce nižší než u jednotlivých receptorů elektrofyziologicky měřený. Jedním důvodem je právě konvergence na glomerulární buňky, dovolující mitrálním buňkám sbírat vstupy z velké populace identicky naladěných primárních neuronů a posílajících tak i velmi slabé signály do mozku. Systém také někdy zvyšuje citlivost na úkor rychlosti (časového rozlišení), která u čichu nehraje tak životně důležitou roli jako u zraku nebo sluchu.

Časové parametry čichání – řešení problému identity a koncentrace?

At the level of the olfactory bulb (OB) odor information is contained in the spike patterns of mitral/tufted (M/T) cells. Today it is generally assumed that in addition to the identity of the activated M/T cells, the temporal patterns of their responses are important for olfactory coding.

In mammals, every sniff evokes a precise, odour-specific sequence of activity across olfactory neurons.

Distributed representations reflecting different features of a stimulus can therefore occur in the same circuit at different epochs of a response.
Spatial coding and temporal coding are not mutually exclusive, and may instead exhibit synergy in numerous ways. We speculate that time comparisons across *glomeruli* give a concentration-invariant readout for odour *identity*, whereas temporal comparison to an *internal representation* of the sniff yields information about odour *concentration*. Such a coding scheme can rapidly resolve ambiguities that arise as odour identity and intensity change. Extracting both parameters on a sniff-by-sniff basis may help animals locate and identify odour sources in natural olfactory scenes.

Smear, M., Shusterman, R., O'connor, R., Bozza, T., & Rinberg, D. (2011). Perception of sniff phase in mouse olfaction. *Nature, 479*(7373), 397.

Lateralizace čichu

- With the smells that were either neutral or ones that dogs liked (food, lemon, vaginal secretion and cotton swab), the first time dogs sniffed them, they did so with their right nostrils. However, as time went on and they encountered the smells more, they then switched to their left nostrils

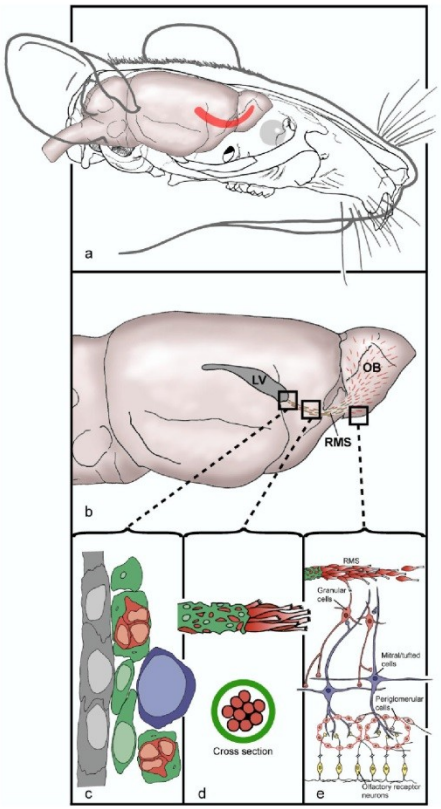
- The fact that dogs smell with their right nostril first implies that the right side of the brain is involved first. This is thought to be because the right-hand side of the brain deals with novel information (in this case, a new smell), and then once the dog has become accustomed to the smell the left side of the brain takes over more, as this side handles more familiar stimuli.

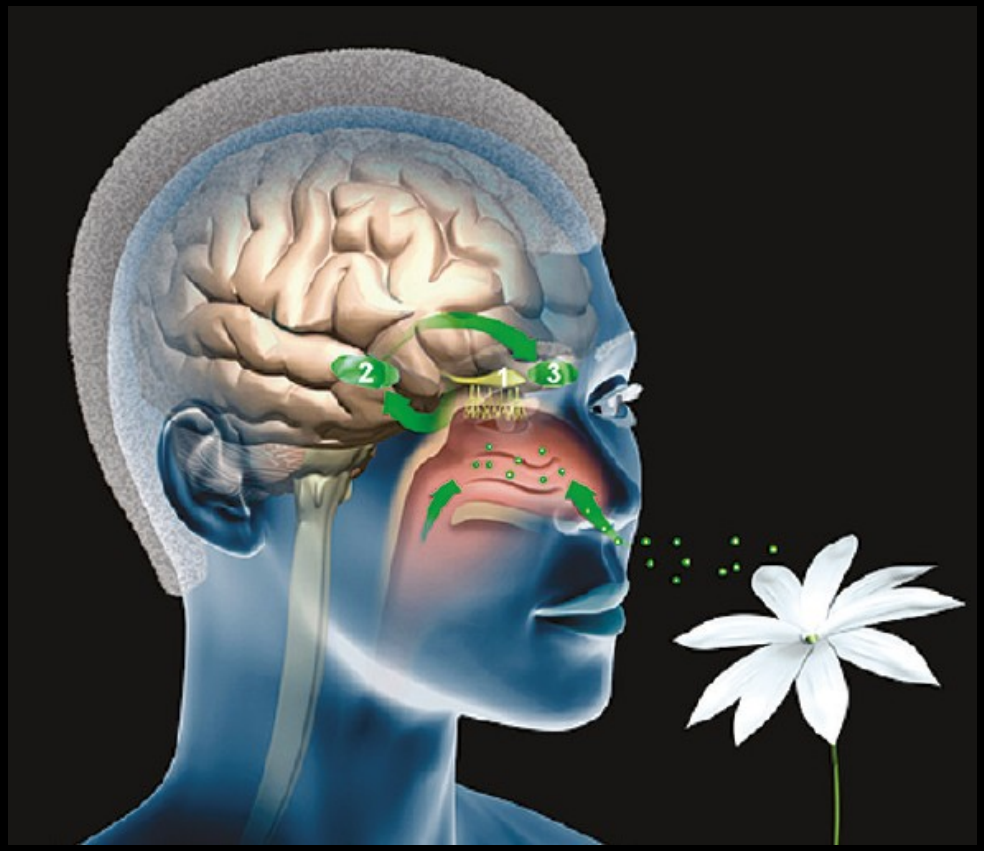
- However, for the other two smells (the vet's sweat and adrenaline), that perhaps may not be quite as welcome to a dog, the dogs always smelled them with their right nostril. Even though the smell of the vet would be as familiar to the dogs as perhaps dog food or the smell from a female dog, it must have been more stressful to the dogs (as any person who owns a dog knows, taking it to the vet's generally isn't a relaxing event for anyone involved). The fight-or-flight response is mainly dealt with by the right side of the brain. Therefore, even though these smells became as familiar as the other ones did, they elicited enough strong emotions like fear to continue being processed by the right-side of the brain (and therefore the right nostril).

- doi:10.1016/j.anbehav.2011.05.020

Rostral migratory stream

- The **rostral migratory stream** (RMS) is a specialized migratory route found in the brain of some animals along which neuronal precursors that originated in the subventricular zone (SVZ) of the brain migrate to reach the main olfactory bulb(OB). The importance of the RMS lies in its ability to refine and even change an animal's sensitivity to smells, which explains its importance and larger size in the rodent brain as compared to the human brain, as our olfactory sense is not as developed. When the neurons reach the OB they differentiate into GABAergic interneurons as they are integrated into either the granule cell layer or periglomerular layer.
- Although it was originally believed that neurons could not regenerate in the adult brain, neurogenesis has been shown to occur in mammalian brains, including those of primates. However, neurogenesis is limited to the hippocampus and SVZ, and the RMS is one mechanism neurons use to relocate from these areas.

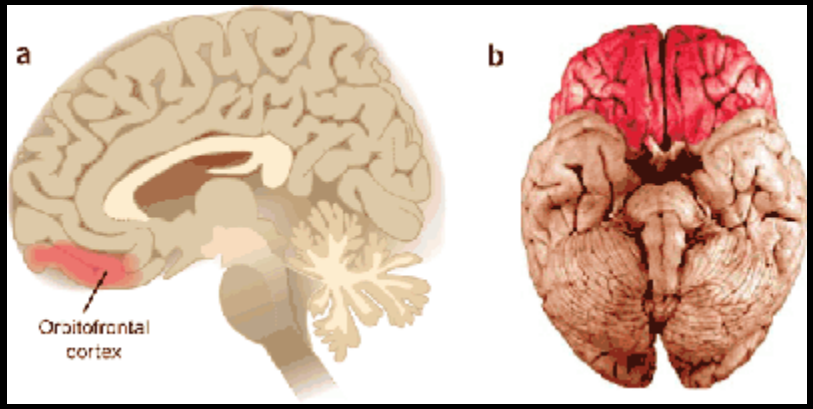




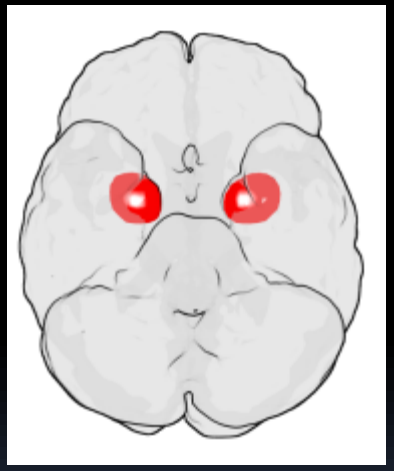
Centrální části čichové dráhy

1. Čichový lalok
2. Piriformní kůra
3. Orbitofrontální kůra

Figure 1. Schematic overview of the basic steps of the central processing of odorous stimuli. Odorants are first detected by receptors at the top of the nasal cavity, and from there, the signal travels to the olfactory bulb (1). This signal is then routed to the piriform cortex (2) and subsequently to the orbitofrontal cortex (3), among other structures. Note the dual route that odorants can take to reach the receptors at the top of the nasal cavity. The route via the nostrils is known as orthonasal olfaction, whereas the route via the back of the throat is known as retronasal olfaction. See the text for

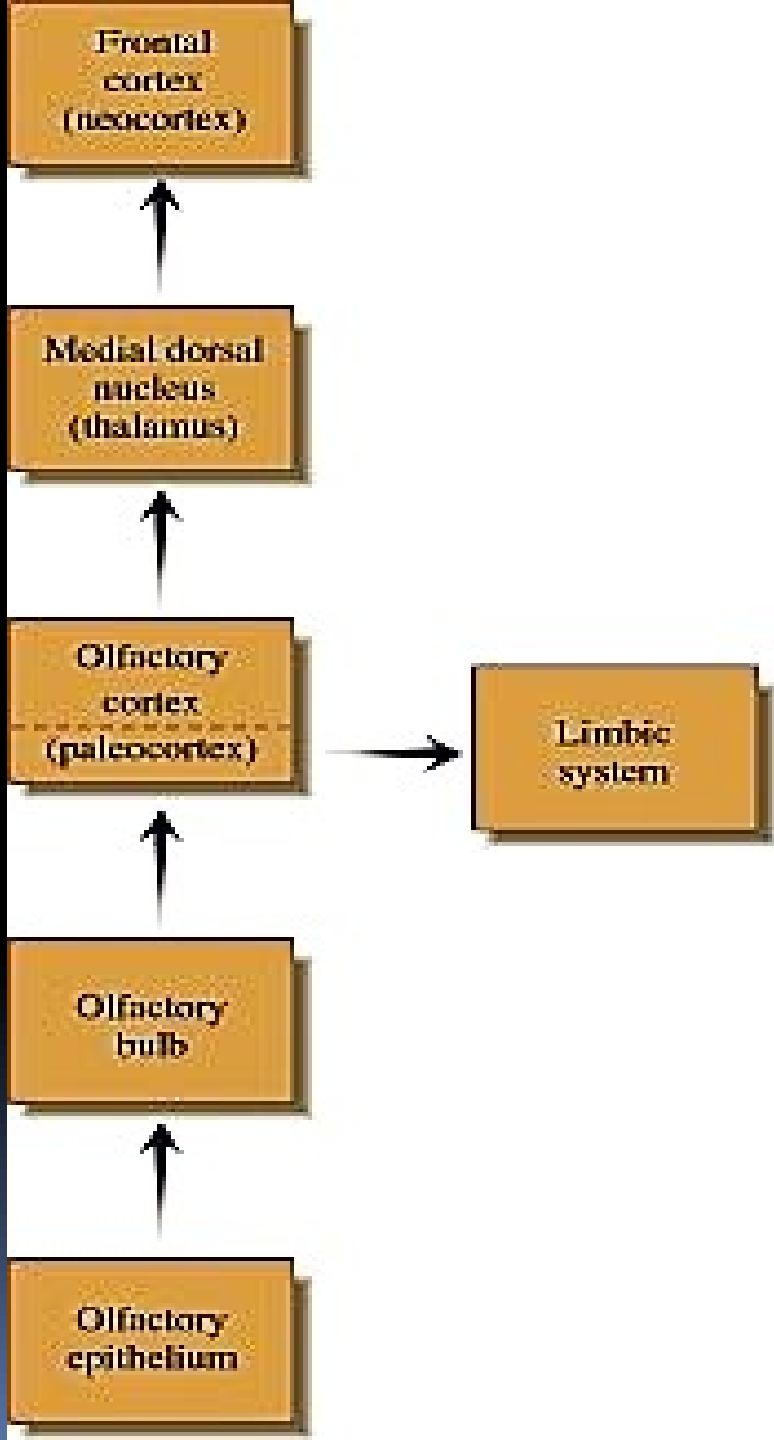


Orbitofrontální kůra neokortexu



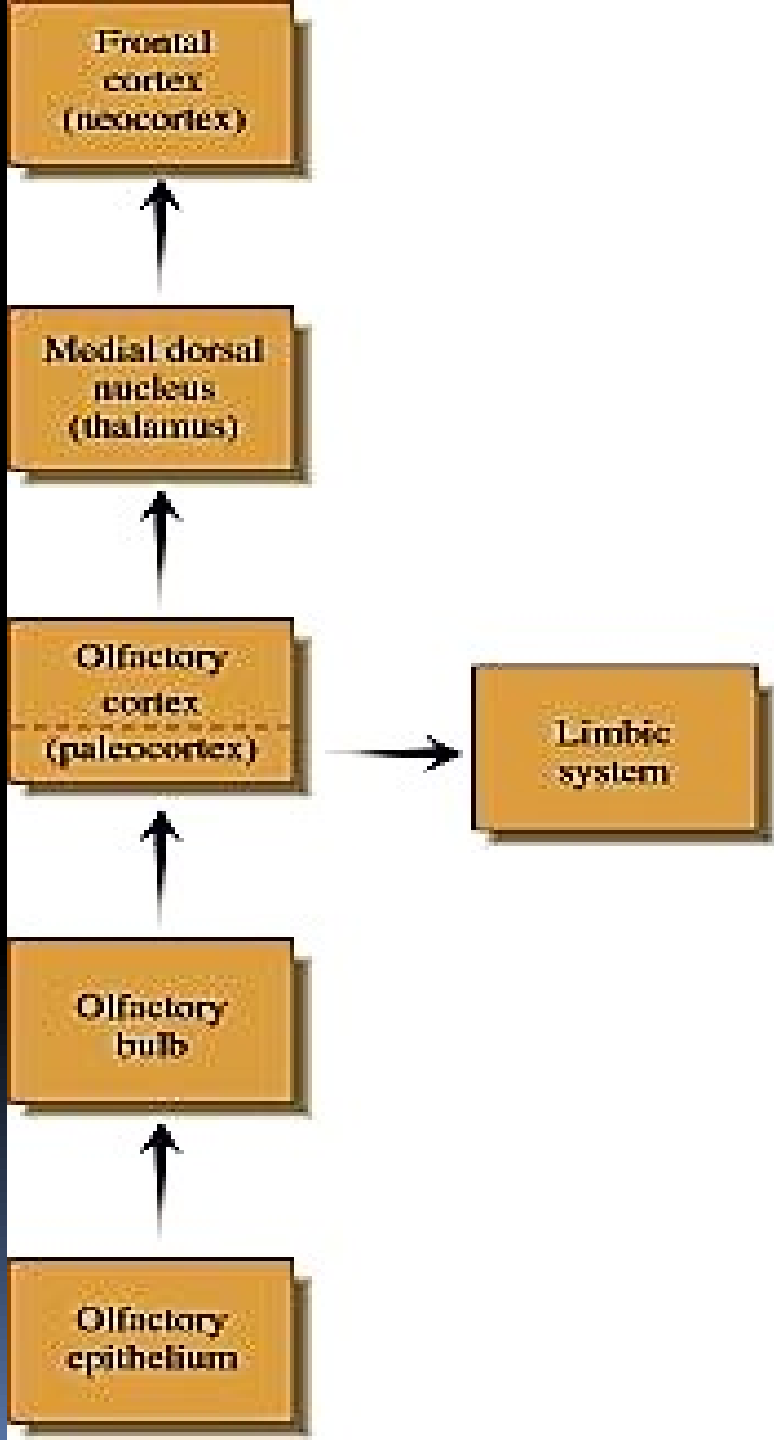
Piriformní kůra zahrnuje kortikální amygdalu (paleokortex)

Anosmie doprovází úrazy hlavy či neurodegeneraci ve stáří.



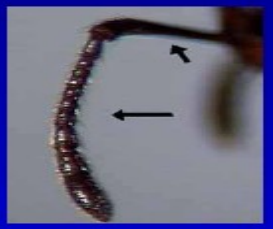
Lingvistické, deklarativní schopnosti jsou odděleny od čichu – je těžké pojmenovat a popsat čichové počitky.

Má vztah k silné emocionální složce čichových vjemů a ukládání paměťových stop. Antabus. Aromaterapie. Vzpomínky.
Emoční, hedonická hodnota vždy automaticky přítomná. Je většinou naučená, ne vrozená.

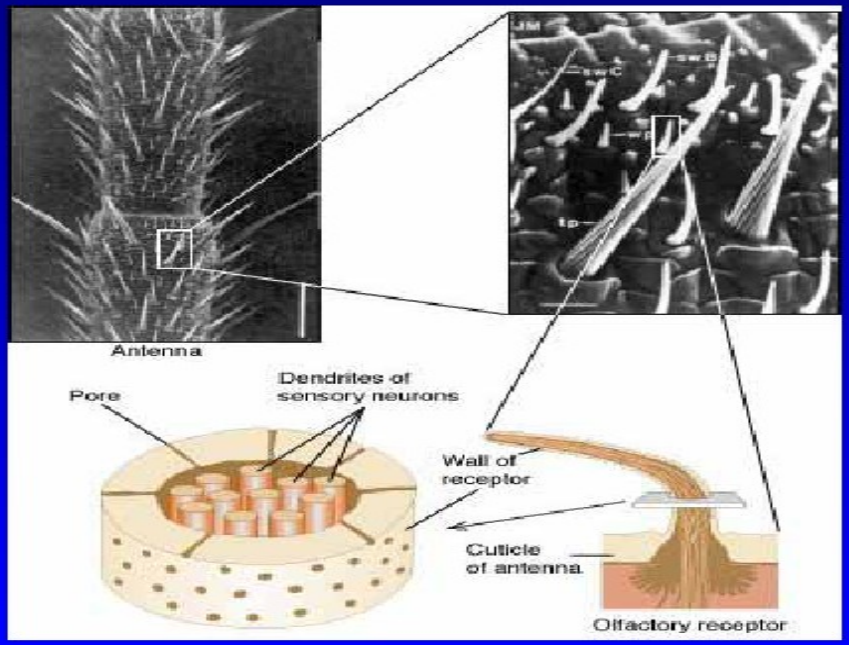


A co hmyz ?

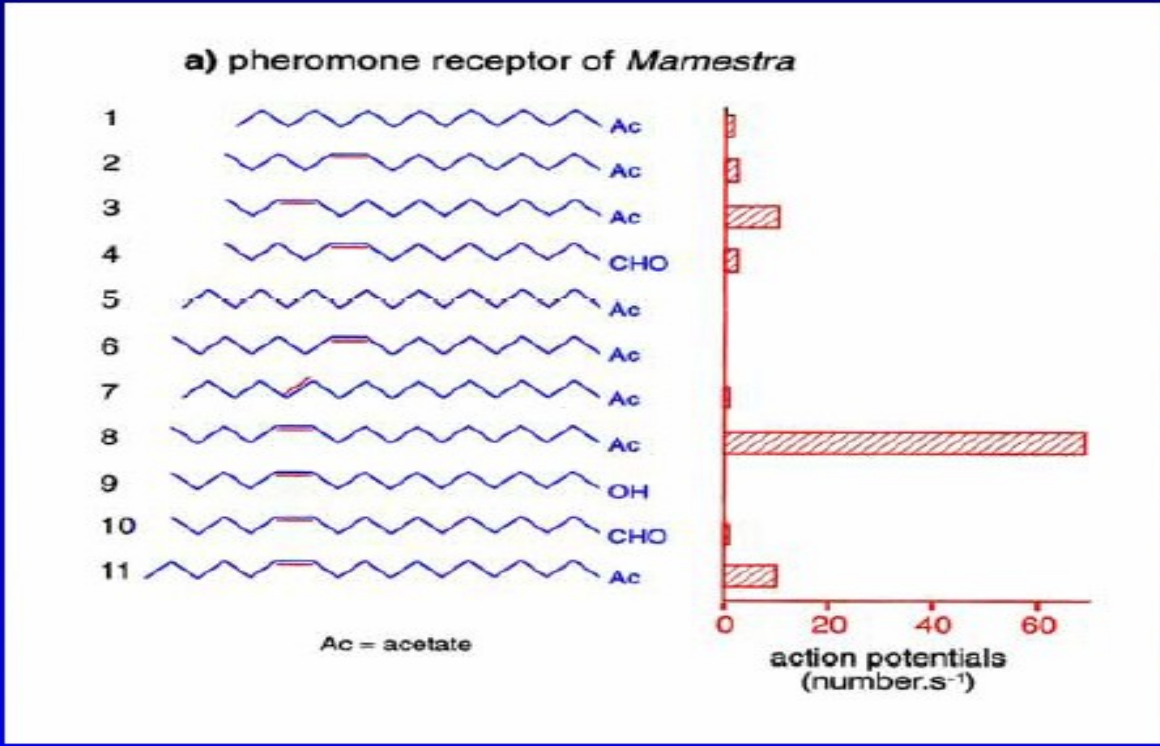
Antennal morphology diversity



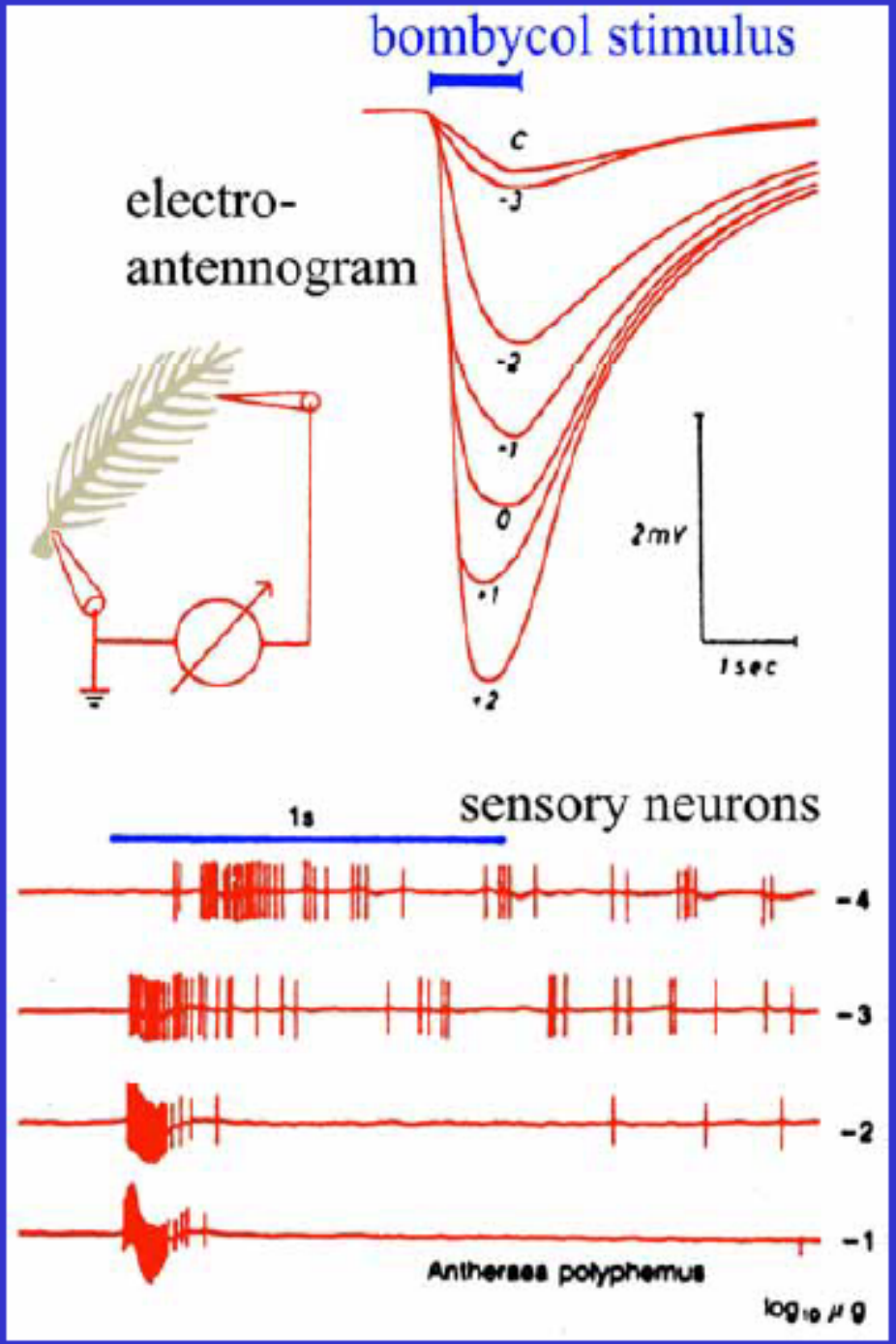
Anatomy of an antennal sensilla



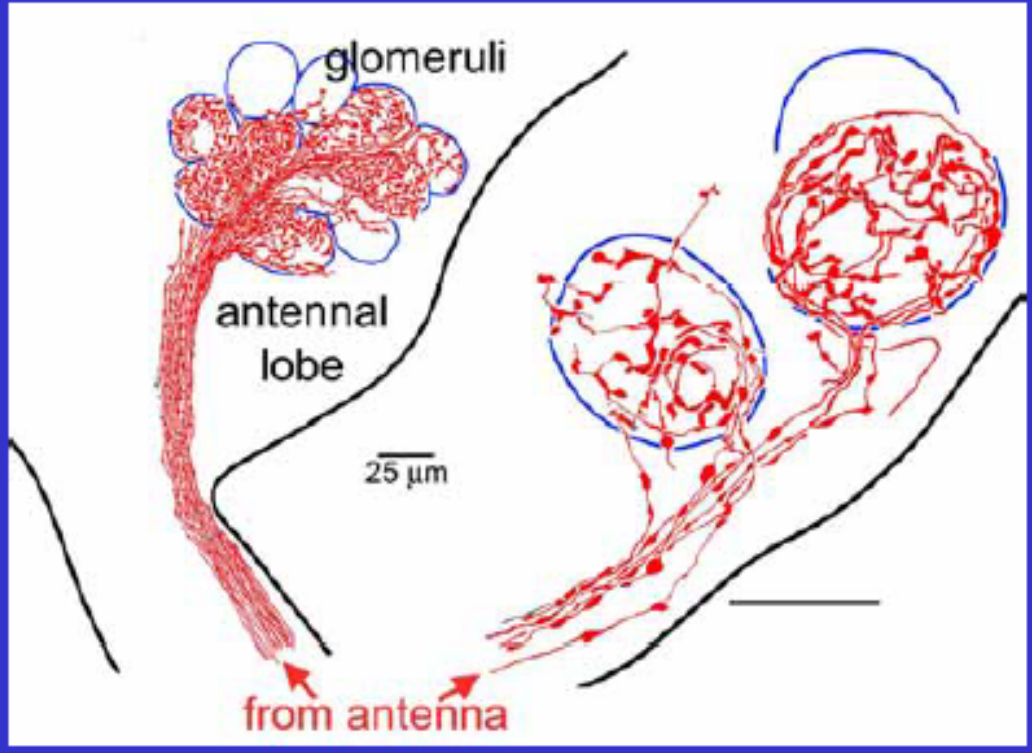
Response specificity to size and composition of odorant molecule

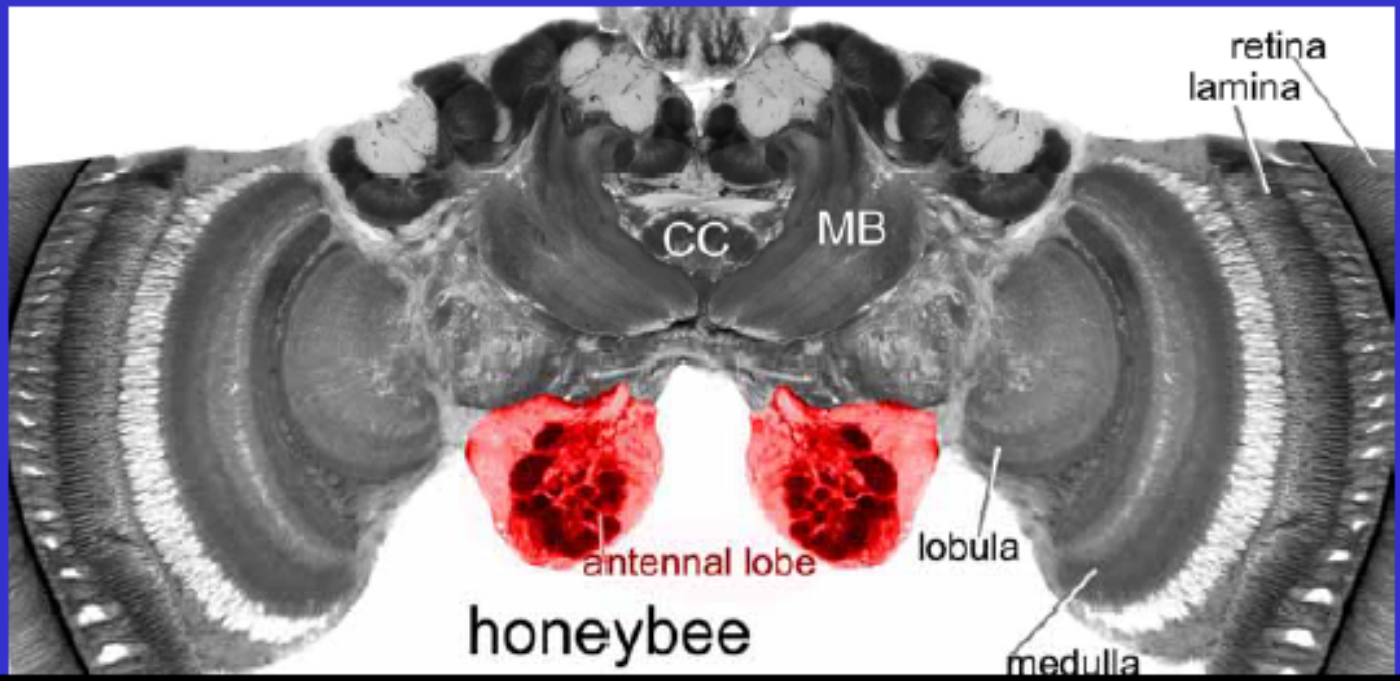


Olfactory receptor neurons respond to odorants

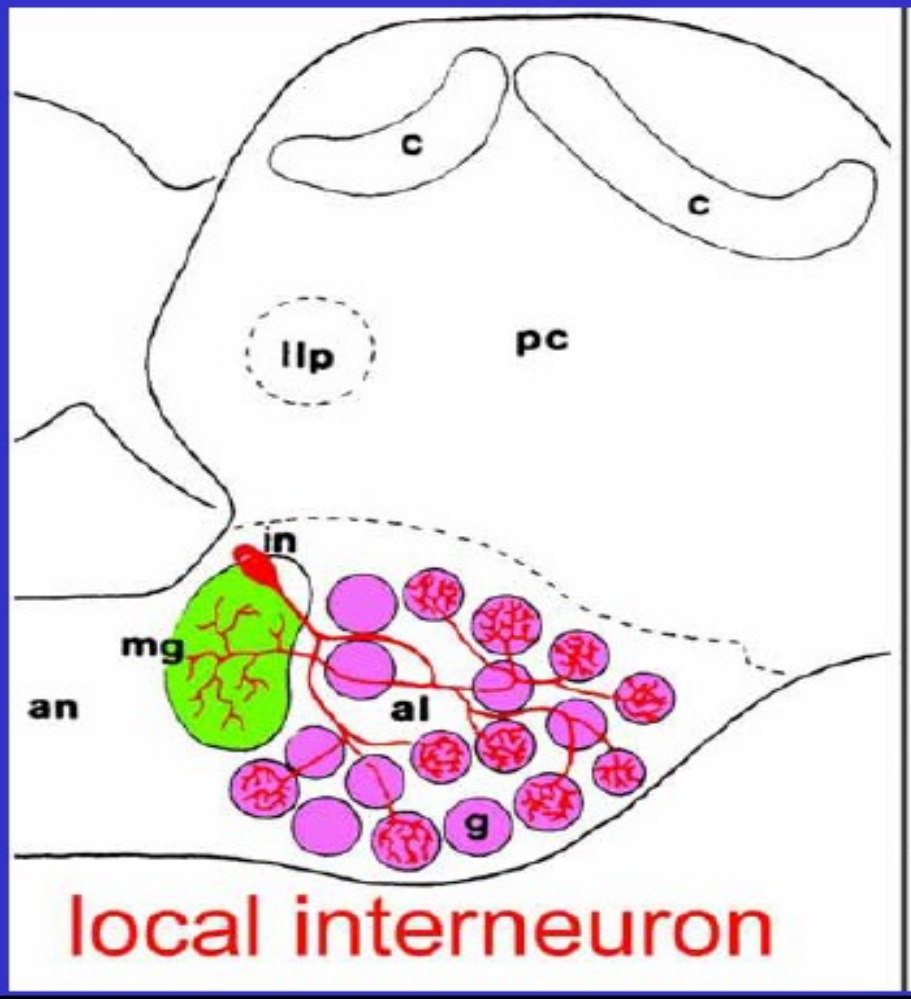


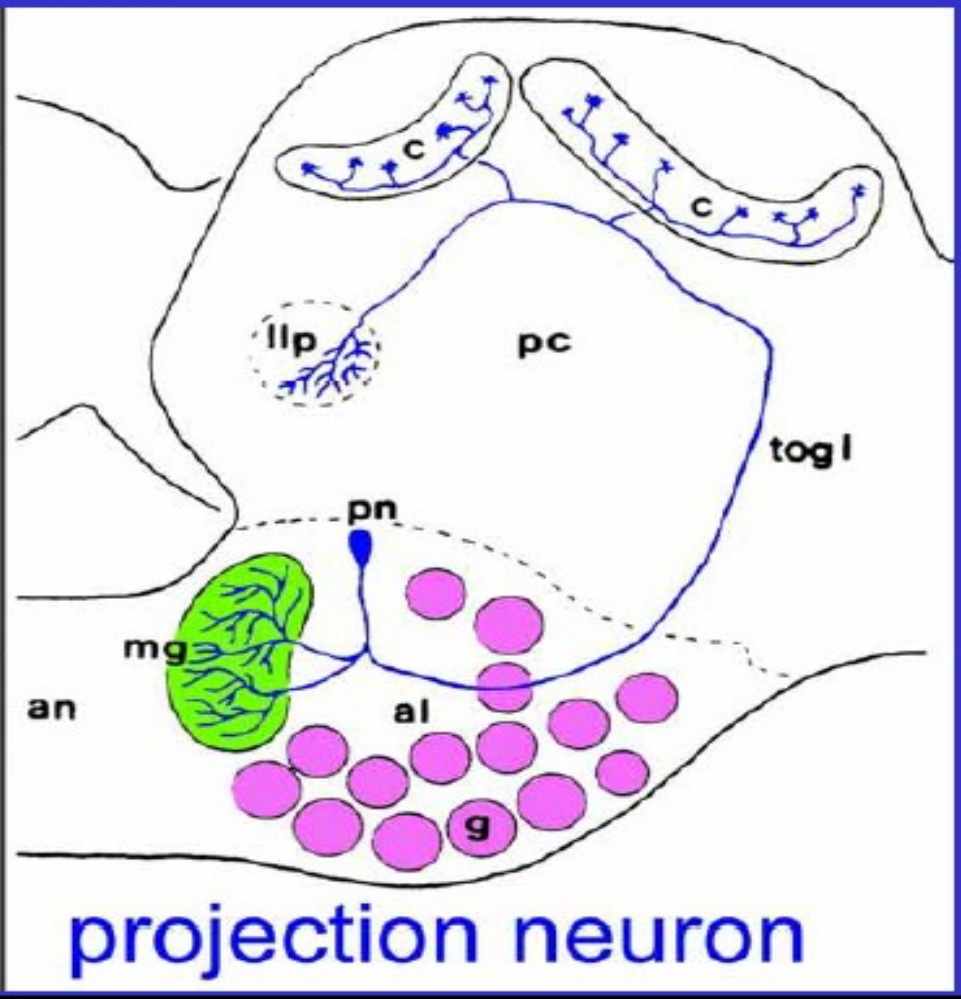
Antennal olfactory receptor neurons terminate in antennal lobe **glomeruli**





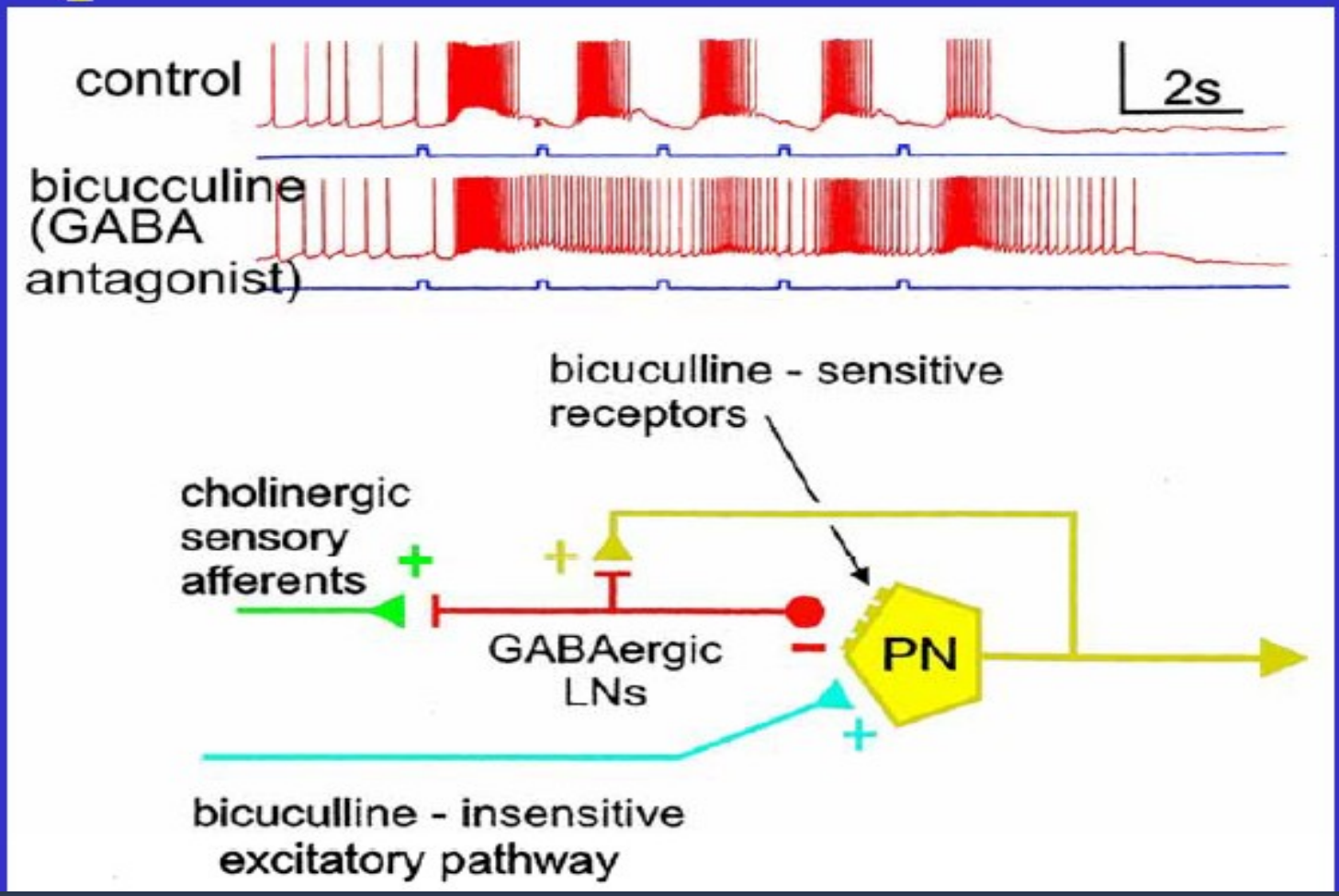
Antennal lobe: two major classes of neurons





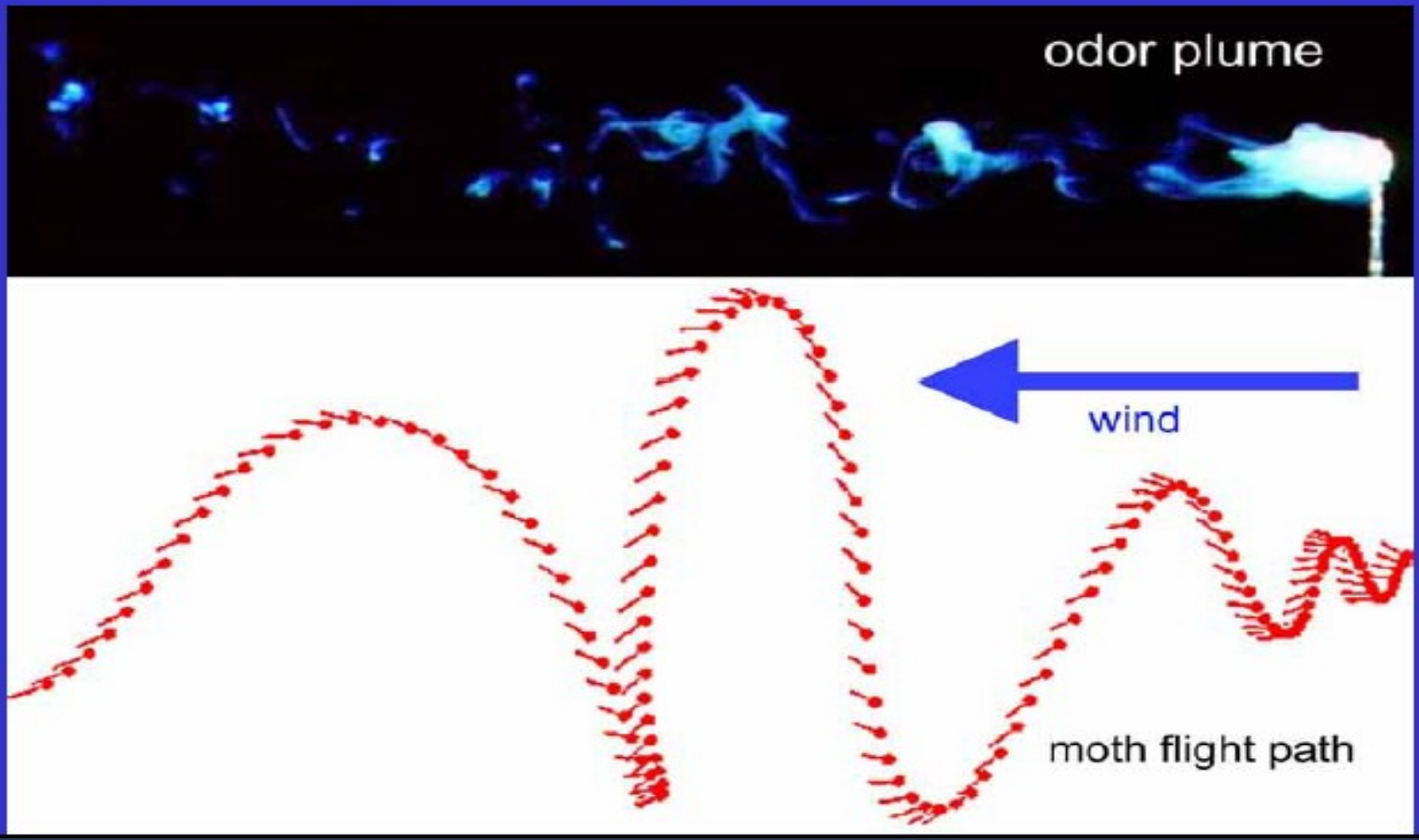
Projekce do tzv. houbových tělísek, ty zajišťují paměť a naučené chování

Inhibition ‘sharpens’ the PN response (temporal and odor discrimination)



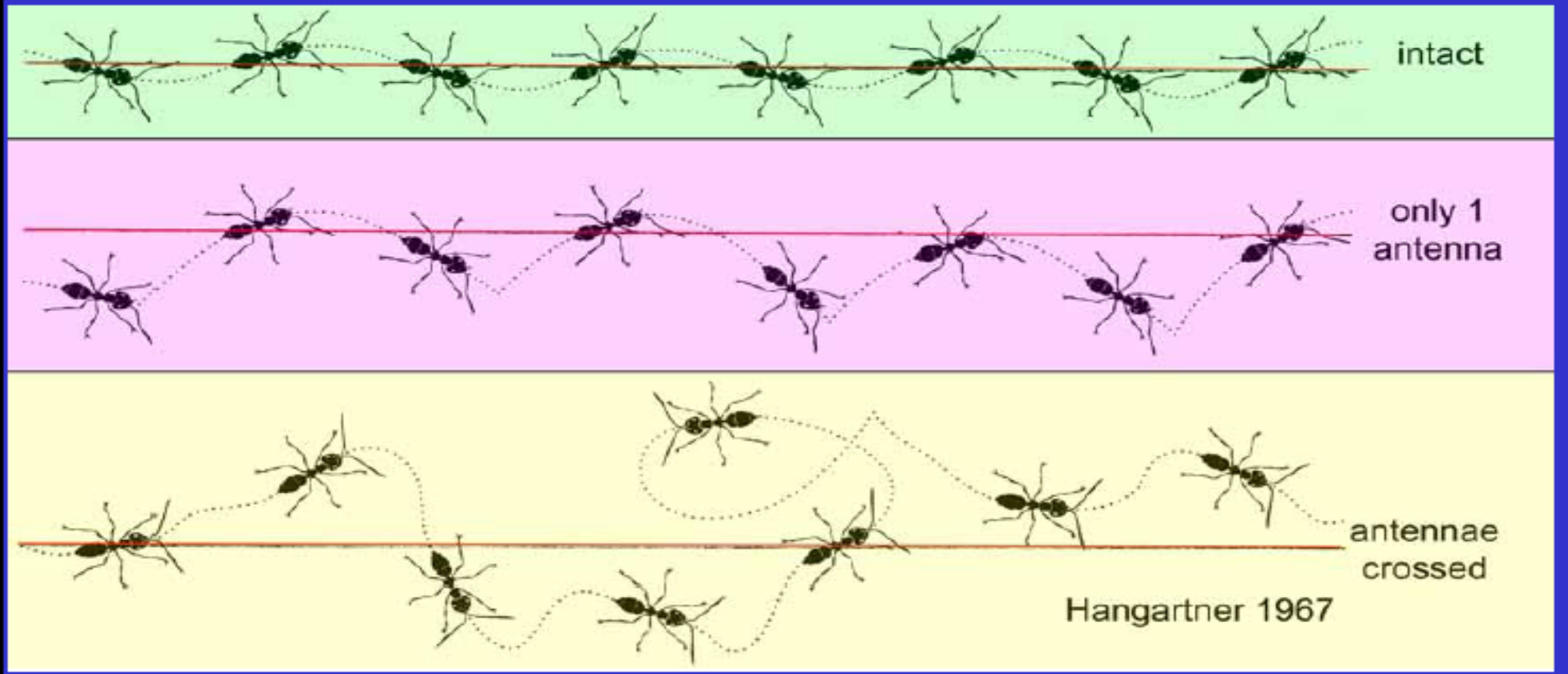
Terminace odpovědi nezbytná pro časovou rozlišitelnost signálů. Ta je nezbytná pro sledování pachové stopy. Inhibice GABAergním neuronem nutná pro časové rozlišení. Při vyřazení splývají časově oddělené podněty do jednoho.

Odor is discontinuously distributed in air

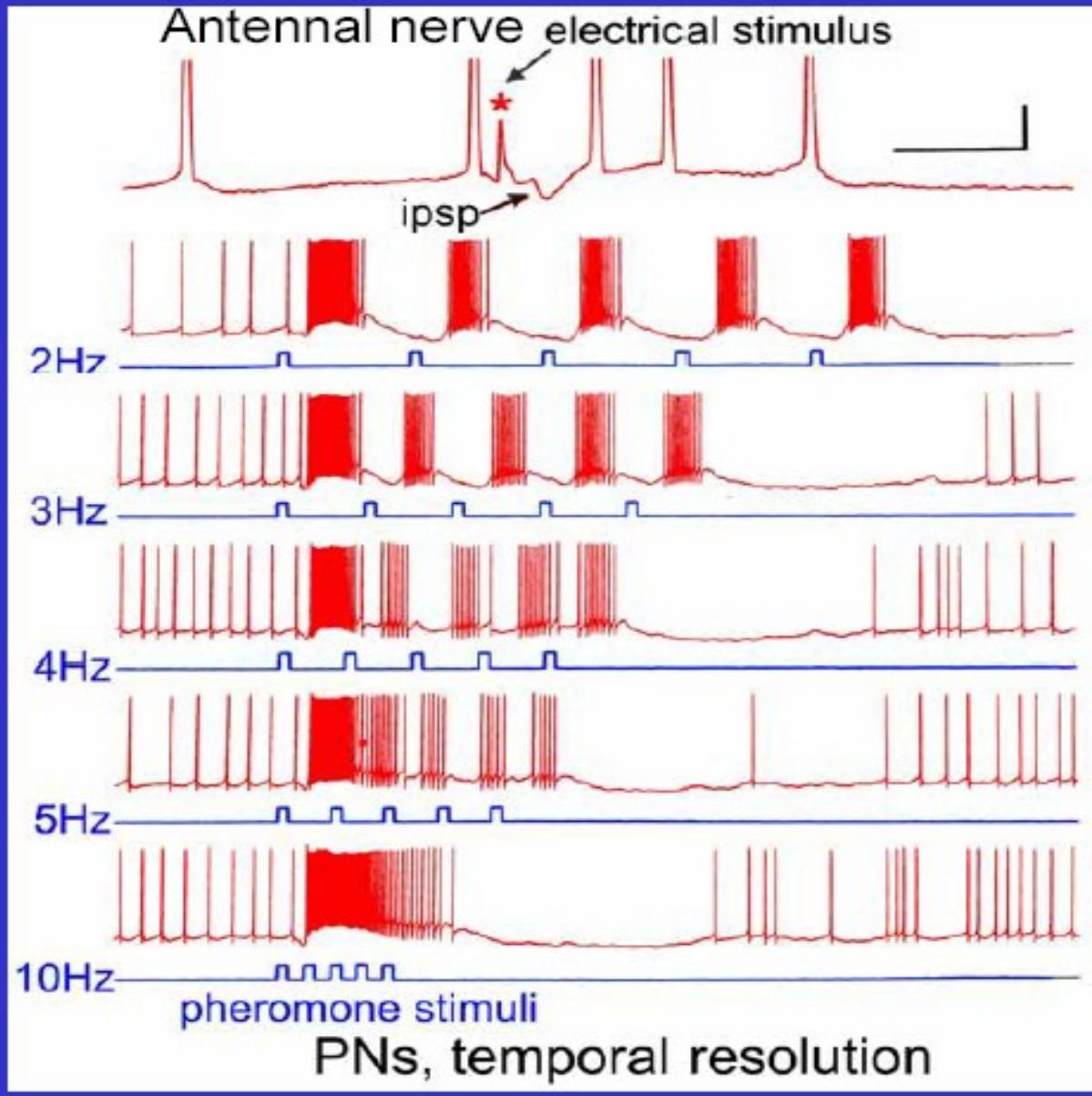


Časové parametry čichu jsou pro sledování voňavé stopy důležité. Pach netvoří kontinuálním gradient, ale sérií obláčků.

Even when following an odor trace, perception is discontinuous



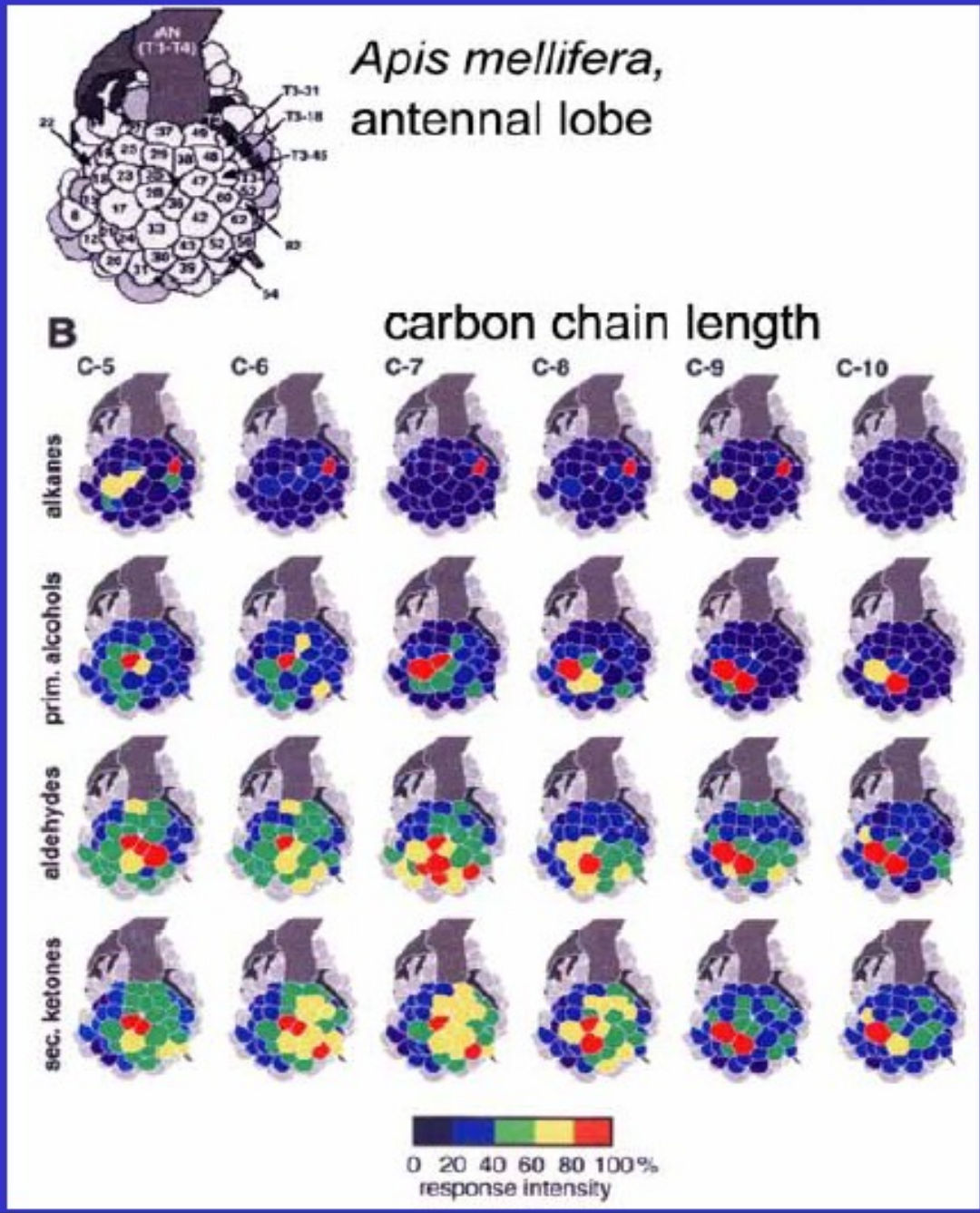
Temporal resolution is limited



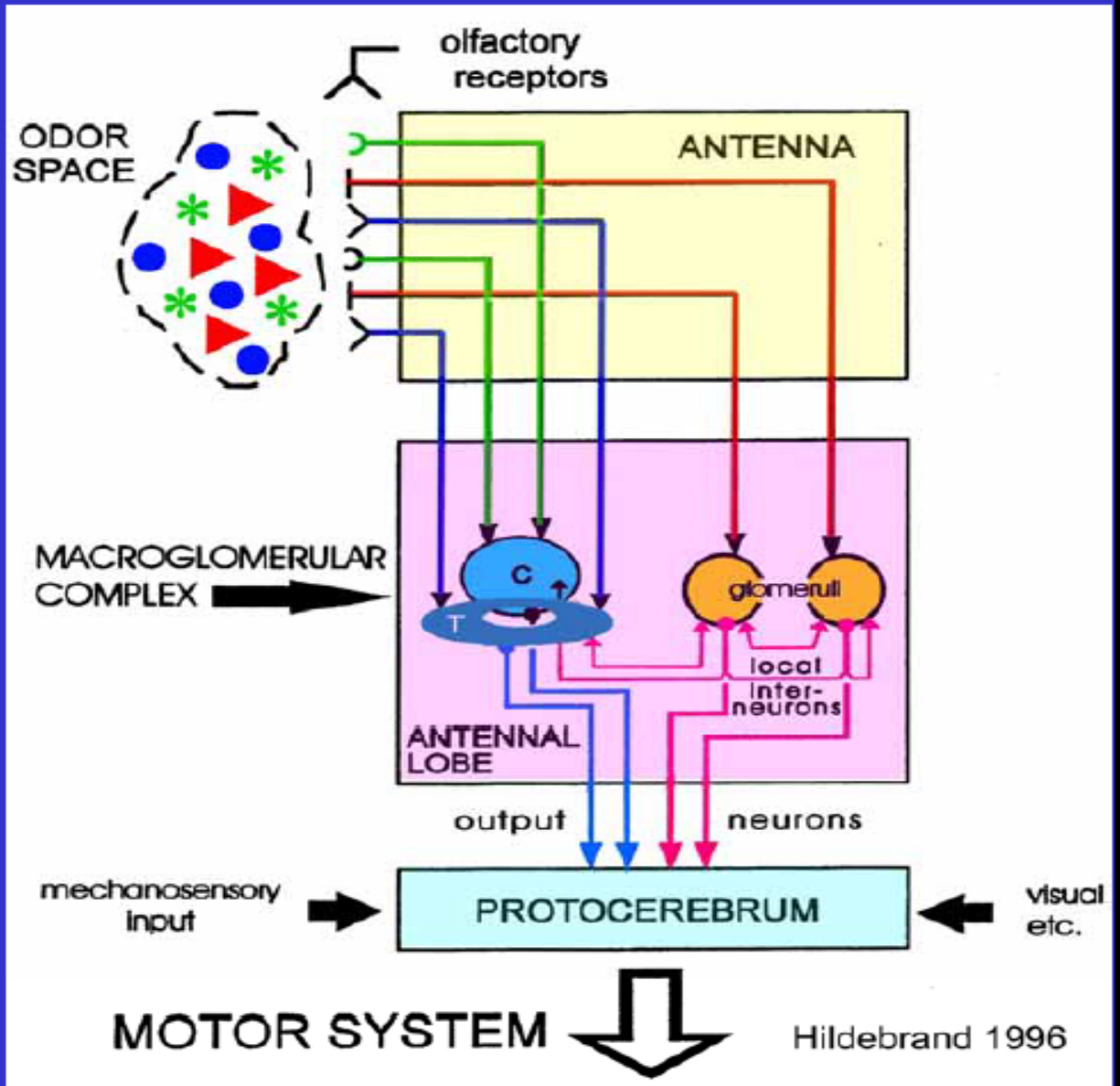
Časové rozlišení má hranici mezi 5 a 10 Hz.

Glomeruli responses reflect odorants' structural properties (chain length, residues, polarity etc.):

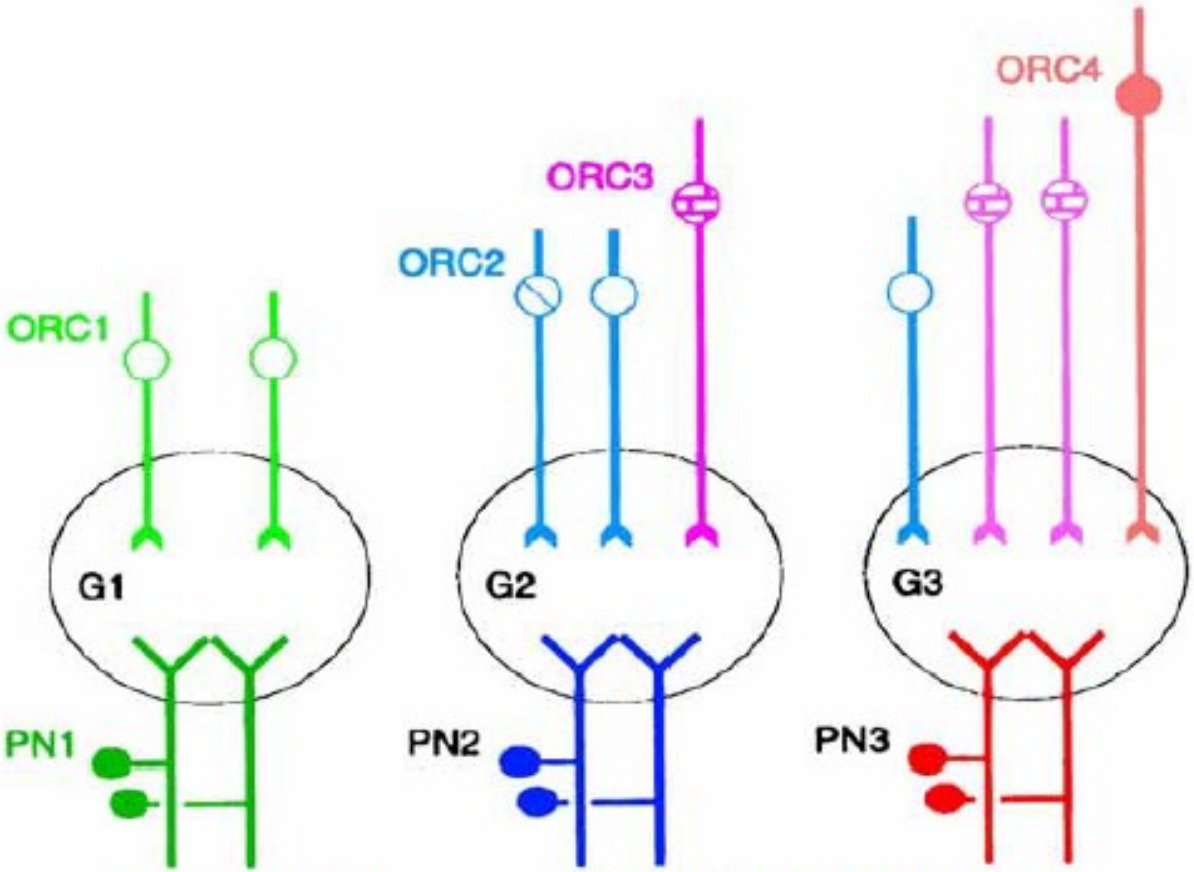
odor map



(sex) pheromones and 'ordinary' odors are processed by two different pathways

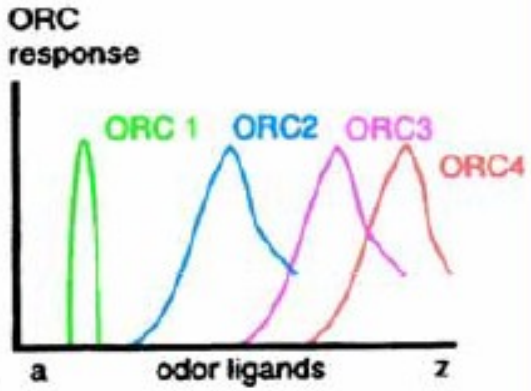


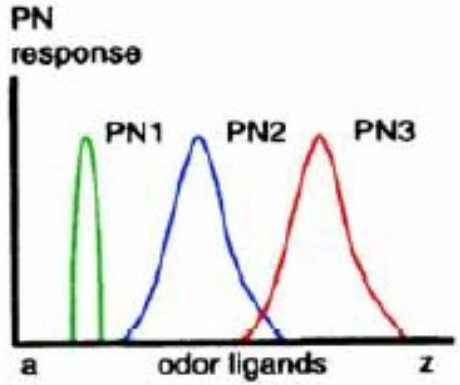
PNs may have narrower response spectra than receptor neurons



specialist
(e.g. pheromone)

'ordinary' PNs





J.G. Hildebrand 1996

Podobnost mezi hmyzem a obratlovci jen omezená

Table 2 | **Commonalities and differences of olfactory receptors in vertebrates and insects**

Characteristic	Vertebrates	Insects
Class	GPCR	Non-GPCR
Repertoire	Large, variable	Smaller, constant
Topology	Heptahelical	Inverse heptahelical
Activation	Metabotropic	Ionotropic
Pseudogene fraction	High	None to low
Stoichiometry	Monomers	Heteromers
One receptor–one neuron rule	Yes	Yes*
Gene selection	Stochastic	Deterministic
Expression pattern	Zonal and random	Zonal and random
Instructive role	Yes	Unknown
Ectopic expression	Yes	Unknown
Inhibitory action of odorants	Rare	Common
Convergence of axons to glomeruli	Yes	Yes
Glomeruli per receptor type	Variable, ≤2 up to 20	~1

GPCR, G protein-coupled receptor. *There are notable exceptions to this rule, which have been excluded from this table for clarity.

Box 1 | **Amplification and sensitivity of olfactory signalling**

Vertebrates

In general, G protein-coupled receptor (GPCR) signalling, such as that mediated by photoreceptors, amplifies a signal[138]. However, the principles governing olfactory signalling are quite different. Owing to the relatively low binding affinity of many odorants (micromolar range), the lifetime of the receptor–ligand complex is brief. Consequently, the probability that a receptor–ligand complex will meet a G protein and catalyse GDP–GTP exchange is low[72]. Why do most olfactory neurons not require high amplification at the receptor level? At micromolar odorant concentrations, more than 20 million odorant molecules arrive at a cilium every second[139]. Thus, although the probability that a single odorant molecule will activate the signalling pathway is minuscule, it is likely that a few odorant molecules will successfully evoke a response. By contrast, at low light levels, at which only a few photons reach the eye, amplification allows rod photoreceptors to detect and respond to single photons.

In the vomeronasal organ, concentrations of pheromone molecules above 0.1 pM can elicit a response[140,141]. At these low concentrations, only a few molecules per second are captured by a cilium. What are the biophysical requirements for such exquisite sensitivity? Receptors must bind the ligand with high affinity, increasing the lifetime of the ligand–receptor complex (seconds to minutes). During this time, the receptor may activate many hundreds of G proteins. However, active mechanisms are required to disable such stable ligand–receptor complexes. Receptor phosphorylation and β-arrestin capping may be an important route for response termination. In other cases, there may be no need for rapid inactivation, because temporal coding of successive stimuli does not matter.

Insects

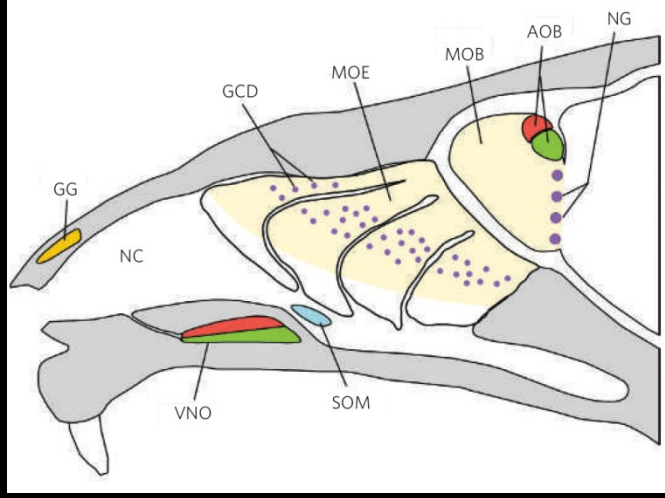
Similar to vertebrate neurons, insect olfactory receptor neurons (ORNs) can be very sensitive, responding to the binding of a single molecule of a sex pheromone[142]. Insect ORNs, which have an ionotropic mechanism of action, also lack the amplification provided at the receptor and G protein level. How then can a single pheromone molecule activate an insect neuron? The open probability (P_o) of a ligand-gated channel is determined by its affinity for the ligand and, for nanomolar binding affinities, may reach unity on a timescale of seconds. Depending on the single-channel conductance, a single channel may readily carry currents in the order of a few picoamperes. The input resistance of vertebrate ORNs is high (2–8 GΩ) and a few picoamperes of inward current produce a voltage response that is sufficient to reach the threshold for triggering an action potential[143]. Similar mechanisms are seen in rod photoreceptors and sperm, which detect single photons and single molecules, respectively[108,144,145].

Feromony u obratlovců

Interindividuální komunikace
-Spouštěče: vyvolávají okamžitý behaviorální projev
-Primery: pomalejší změny vývoje nebo metabolismu
-Modulátory (?): ovlivňující emoce, náladu (u lidí)

Chemické složení: velikost, polarita, těkavost:
Atraktanty nebo poplachové feromony – malé a těkavé (alkoholy)
Individuální feromony – netěkavé (proteiny)

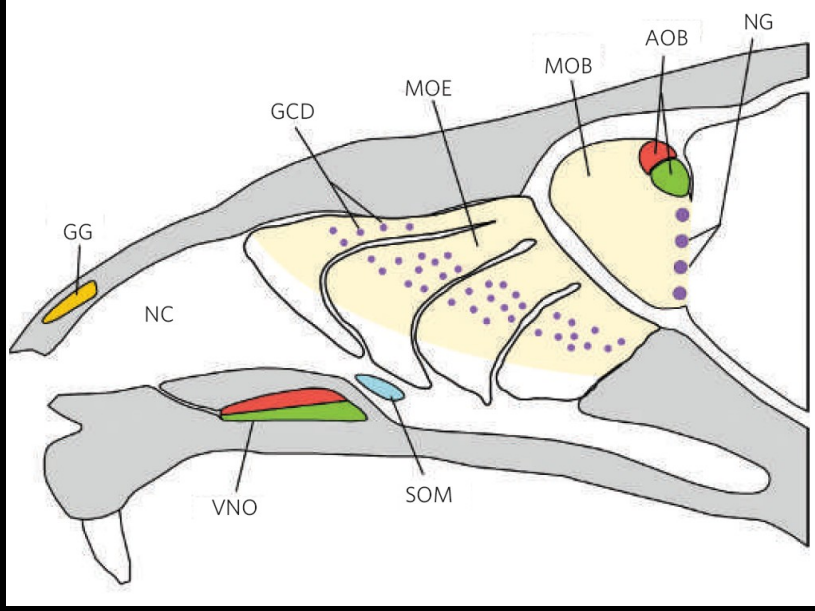
Dva chemosensitivní systémy savců



Hlavní čichový epitel (MOE):
Těkavé látky, ciliátní čichové buňky
Projekce do čichového laloku
Každá buňka exprimuje jediný typ receptoru (1300 u myši)
Proud vzduchu při nadechování (a vydechování)
Identifikace potravy, kořisti, predátora, značení teritoria
Otevřený systém vybudovaný na předpokladu, že není možné předvídat, se kterou molekulou se potká.

Vomeronasální orgán (VNO):
Slepá dutinka pod hlavní čichovou sliznicí
Mikrovilární morfologie
Projekce do přídavného čichového laloku (AOB)
2 třídy receptorů (G protein, ale málo příbuzné čichovým asi 200 celkem), velmi citlivé a specifické
Vzduch přichází „pumpováním" při vzrušení (také přímým kontaktem)
Nezbytný pro paletu chování spojených s pohlavím a rozmnožováním, výchovou potomstva, nástupu pohl. dospívání, blokování těhotenství, obrany a rozeznávání mláďat, mateřského chování, páření a vnitrodruhové agrese.

Vomeronasální orgán (VNO):



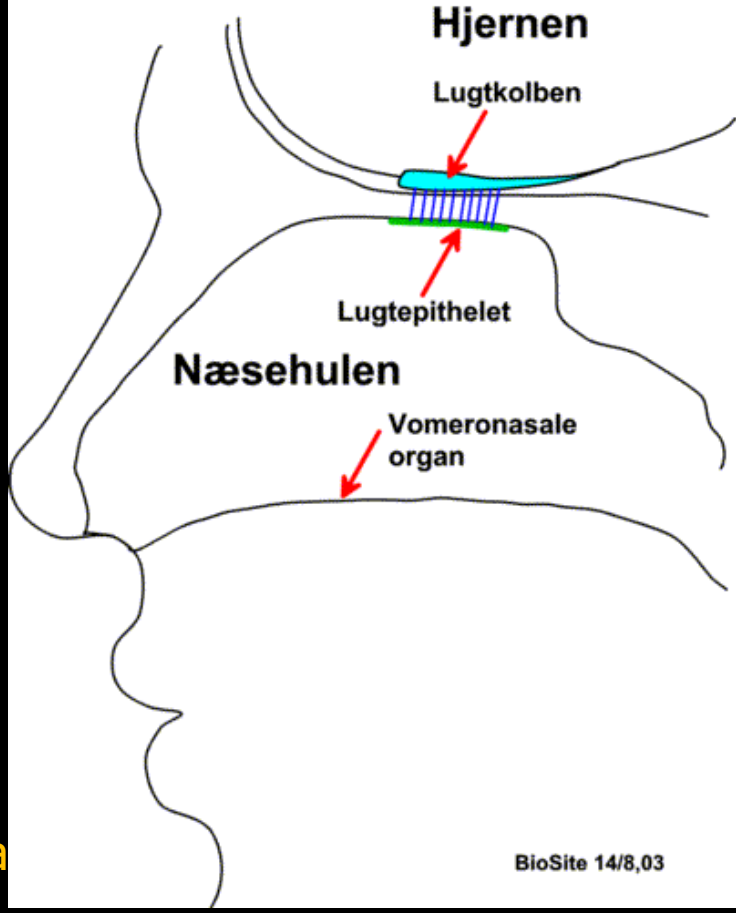
Citlivost je vysoká, pro feromony myši až 10^{-10}M. Axony jsou mezi čichovými laloky a vstupují do přídatných čichových laloků. Zde najdeme podobně jako v hlavní dráze specificky naladěné glomeruli (přijímají vstupy jen z buněk exprimujících jeden typ receptoru). Projekce pak nevedou ani tak do čichového kortexu, ale spíše do amygdaly a hypotalamu limbického systému, kde vyvolávají nevědomé odpovědi.

U člověka také?

AOB u dospělců nenalezen, ani inervace ne.

Experimentální izolace dvou feromonů:
Mužského z potu, ženského z moči
MRI a PET ukázaly „rozsvícení" čichové kůry
žen u ženského f. a hypotalamu u mužského f.
Muži reagovali opačně.
Gayové jako ženy.

MHC nepříbuznost detekovaná čichem?
MHC molekuly ovlivňují složení těkavých látek moči a
Potu = Individualita na dálku
Volba partnera, afrodiziaka, parfémy…



Aroma, příchuť jídla – kromě orthonasálního ještě i retronasální olfaktorický vjem

FIGURE 14.1 Molecules released into the air inside our mouths as we chew and swallow food travel up through the retronasal passage into the nose, where they then move upward and contact the olfactory epithelium.

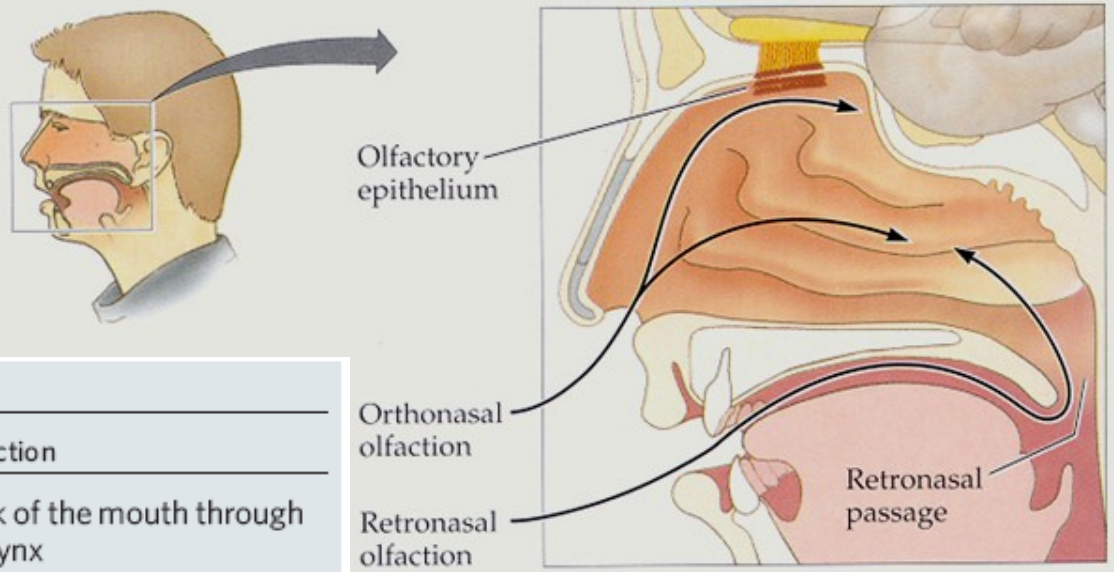
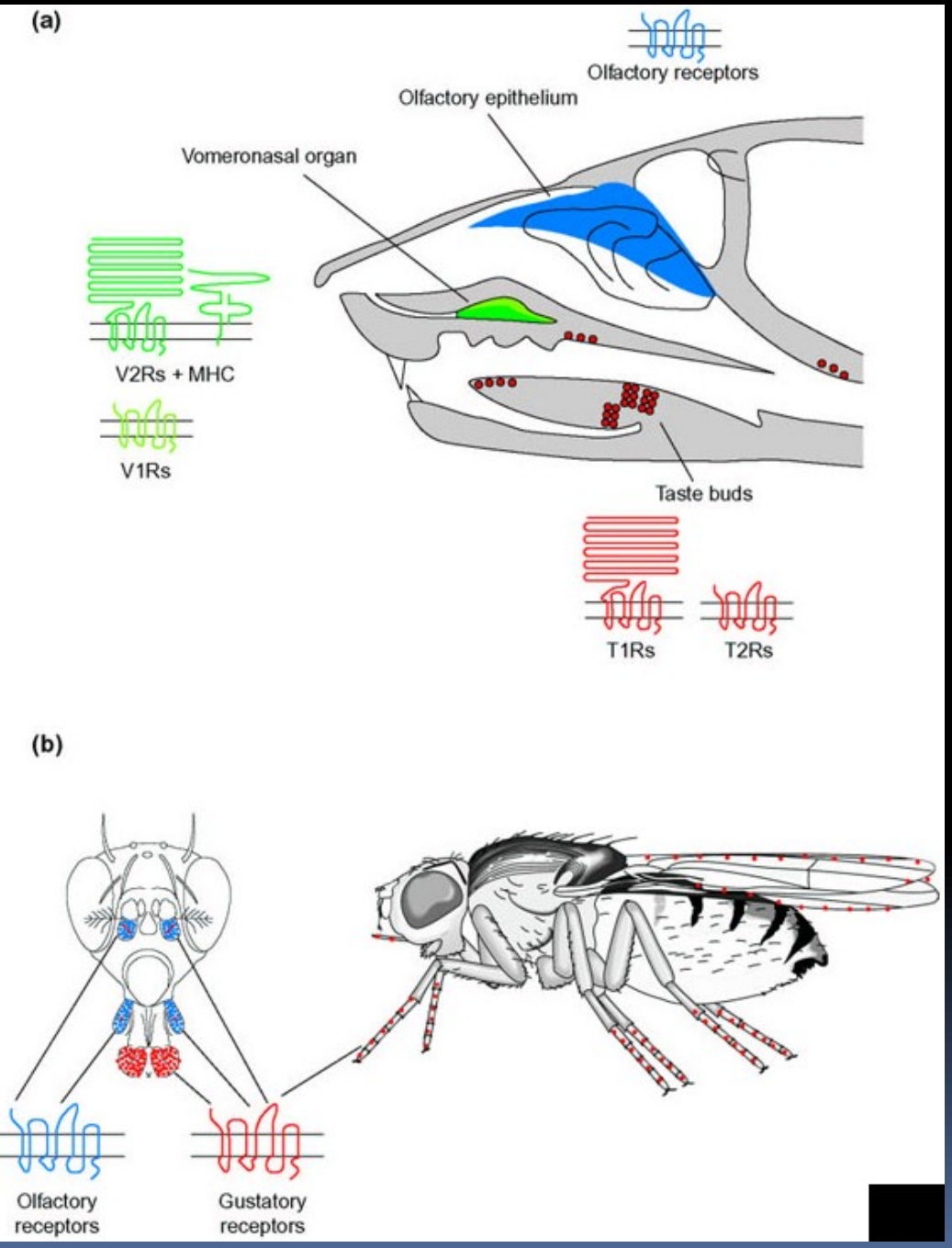


Table 1 | The dual olfactory system

Operations	Orthonasal olfaction	Retronasal olfaction
Stimulation route	Through the external nares	From the back of the mouth through the nasopharynx
Stimuli	Floral scents Perfumes Smoke Food aromas Prey/predator smells Social odors Pheromones MHC molecules	Food volatiles
Processed by	Olfactory pathway influenced by the visual pathway	Olfactory pathway combined with pathways for taste, touch, sound and active sensing by proprioception form a 'flavour system'

Note the interesting contrast, that orthonasal olfactory perception involves a wide range of types of odors processed through only the olfactory pathway, in comparison with retronasal olfactory perception which involves only food volatiles but processed in combination with many brain pathways.



The location of chemosensory organs in the mouse and *Drosophila*. **(a)** A sensory neuron in the olfactory epithelium of mice expresses one of about 1,000 olfactory receptors. Neurons in the apical and basal layers of the vomeronasal organ express distinct, unrelated classes of G-protein-coupled pheromone receptors (V1Rs in the apical and V2Rs in the basal layer). In addition, a small family of MHC class I-like molecules is coexpressed with V2Rs in neurons of the basal layer. The taste cells in the tongue, palate and pharynx express other classes of GPCRs, one encoding sweet-taste receptors (T1Rs) and one encoding receptors for bitter compounds (T2Rs). Note that V1Rs and T2Rs are related to each other, as are V2Rs and T1Rs, respectively. **(b)** The olfactory neurons of *Drosophila* are located in two pairs of appendages in the head, the third antennal segment and the maxillary palps, and each neuron expresses very few, possibly just one, of the 61 olfactory receptor genes identified so far. The gustatory or taste sensory neurons are located in numerous organs, including the two labial palps on the head, internal sensory clusters in the pharynx (not shown), all the legs and the anterior wing margin. Each neuron expresses a few, possibly just one, gustatory receptor gene. A few gustatory receptor genes are also expressed in olfactory neurons of the antenna and maxillary palps.

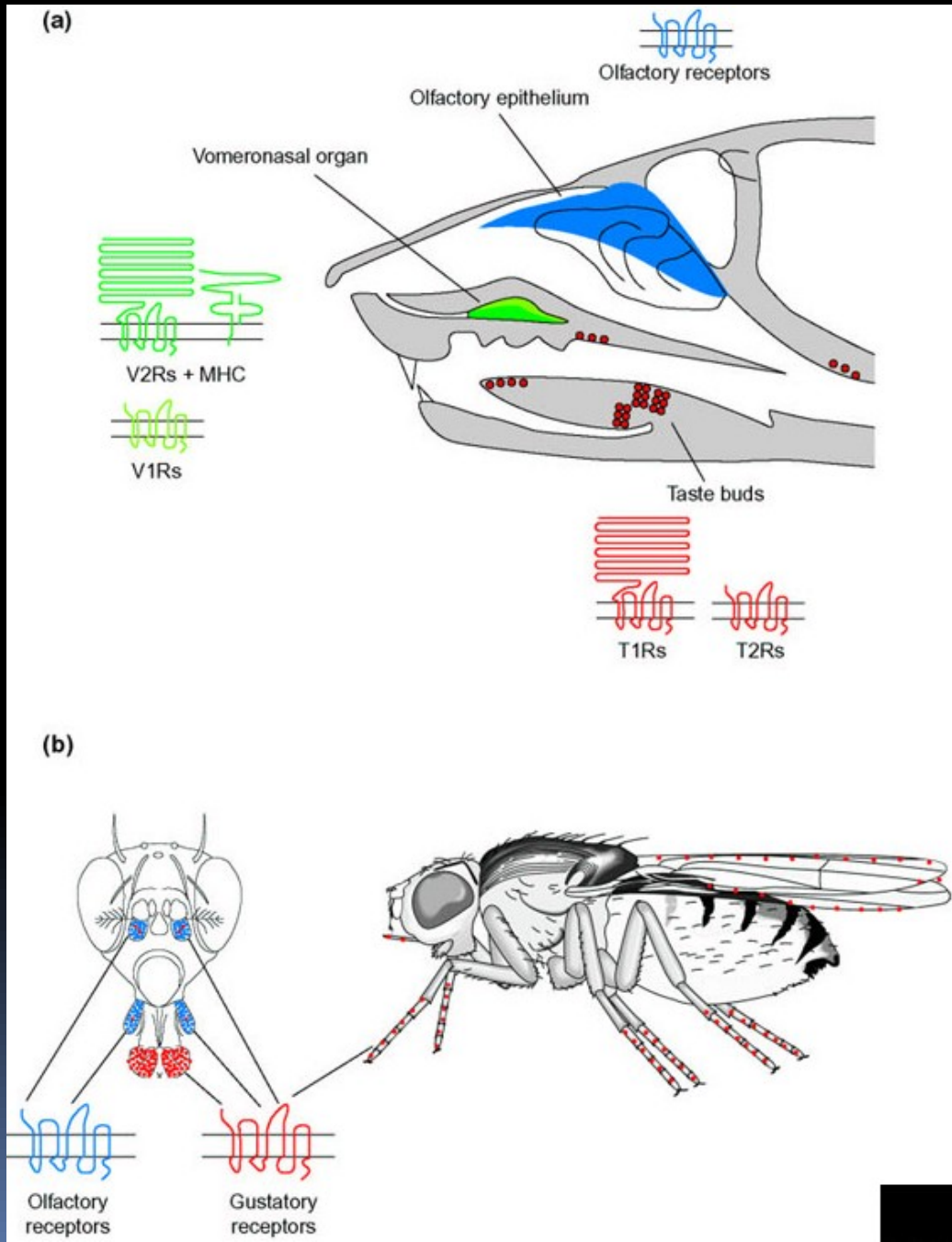
Čich a chuť spolupracují

Chuť

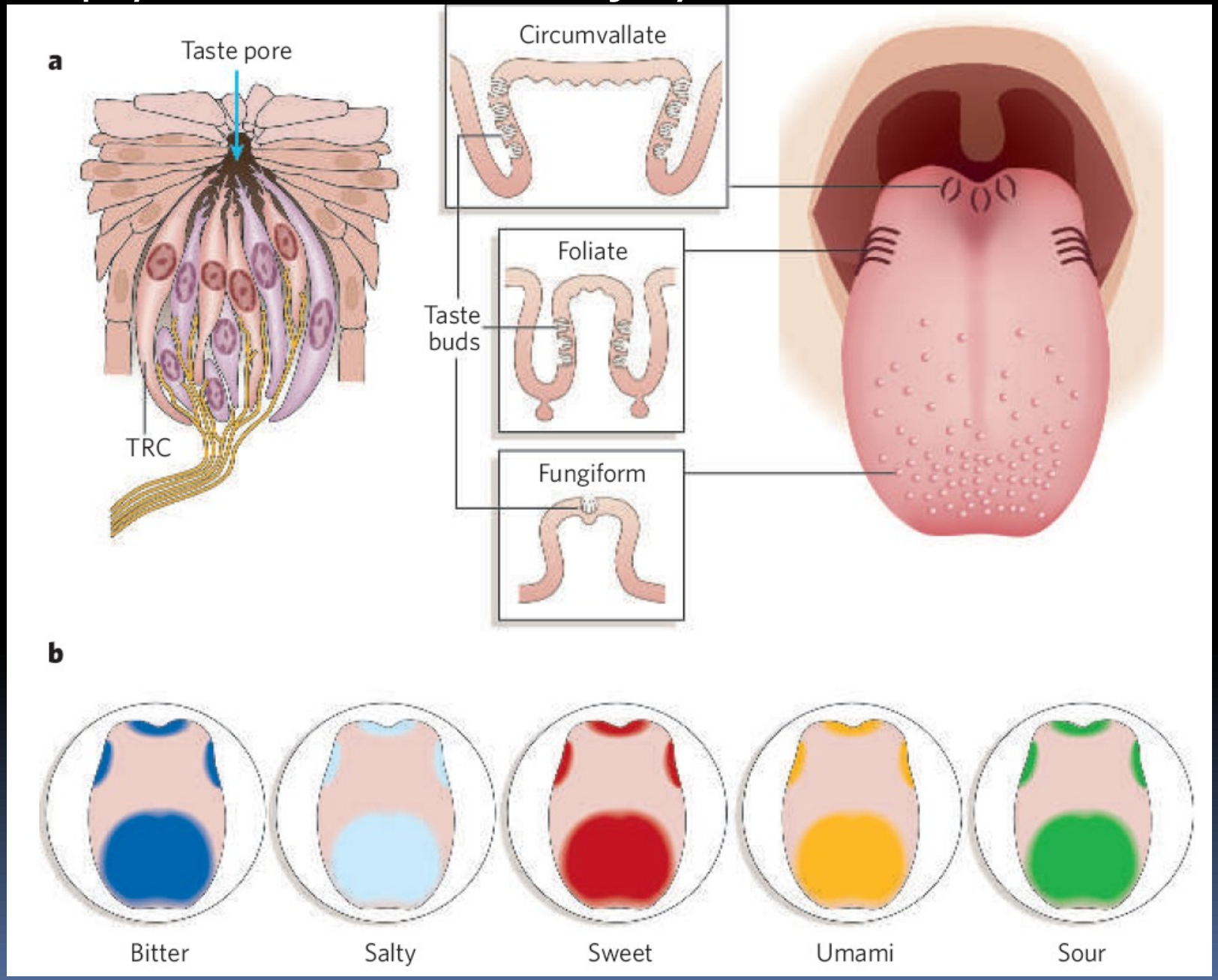
Chuť

Na rozdíl od čichu je to smysl, kontaktní, méně citlivý, má mnohem méně typů receptorů, ale překvapivě různá transdukční schémata.

Čich často rozeznává plynnou fázi, chuť vždy kapalnou.



Papily a distribuce chutí na jazyku



Scientific Legend—The Tongue Map

One of the "facts" that experts have been unable to purge from many textbooks is the notion that sweet is perceived at the tip of the tongue, bitter at the back, sour on the sides, and salty all over. In the case of this myth, we know roughly when it began and we have some idea about what has maintained it in the face of determined efforts by experts to stamp it out.

The origin is most likely a book written by Harvard University's Edwin Boring in 1942. Boring, in addition to his own work, chronicled the history of sensation and perception. He described a study conducted by Hänig in the laboratory of Wilhelm Wundt in 1901 (Hänig, 1901). Hänig wanted to show that the four basic tastes were mediated by different receptor mechanisms (something we take for granted today). He reasoned that if taste thresholds varied with tongue locus, then one would have to conclude that the receptor mechanisms varied as well. Hänig selected points on the oval distribution of taste buds around the perimeter of the tongue and laboriously measured thresholds for substances representing each of the four basic tastes. The variation in thresholds was small but the patterns across the four tastes were different; Hänig had made his point. Boring apparently misunderstood the concentration units in Hänig's study and failed to appreciate just how small the variations in thresholds really were. Thus, Hänig's result that sweet thresholds were slightly lower on the front of the tongue and bitter thresholds were slightly lower on the back was misconstrued and turned into the notion that we taste sweet on the front of our tongues, bitter on the back, etc.

Since the tongue map became a common laboratory demonstration, generations of students have had reason to doubt the map. Asked why they could not observe it, one group of students said that they "must have done the experiment wrong." It is worth remembering that textbooks are not always correct. But you can believe us here: receptors for all four of the basic tastes are distributed over the entire tongue.

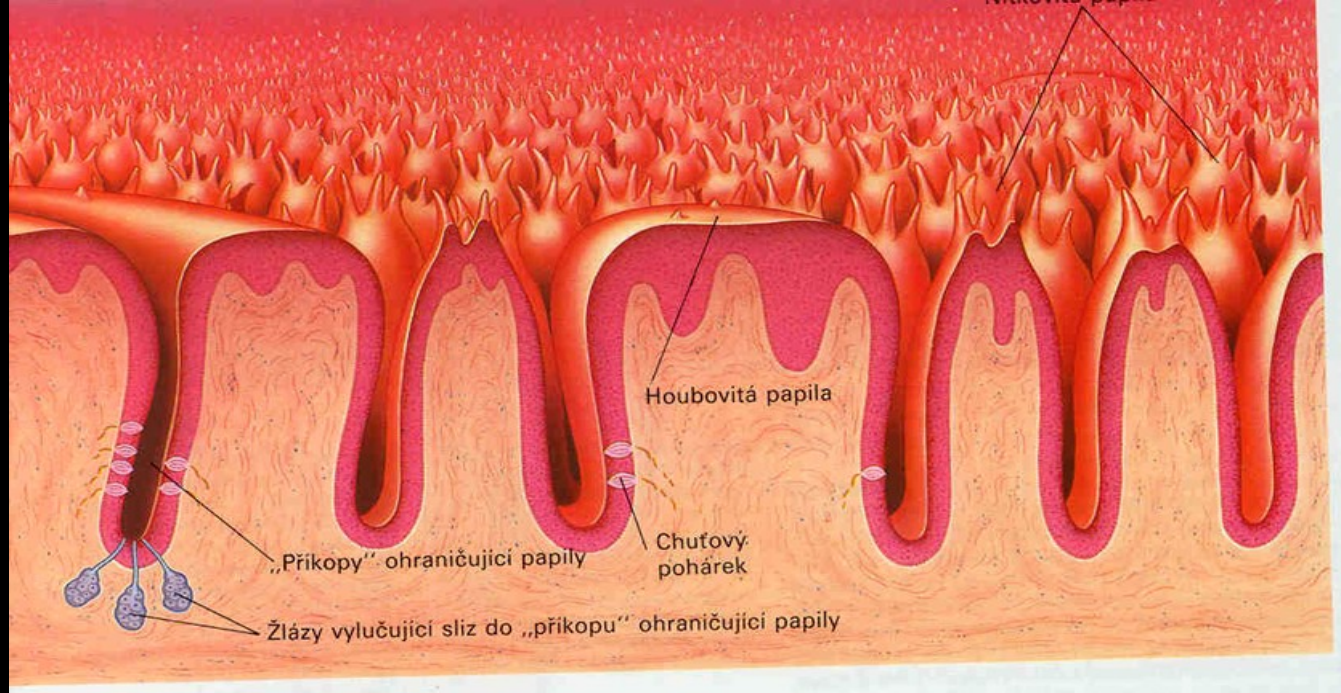
References

Boring, E. G. (1942). *Sensation and Perception in the History of Experimental Psycho* Appleton-Century-Crofts.

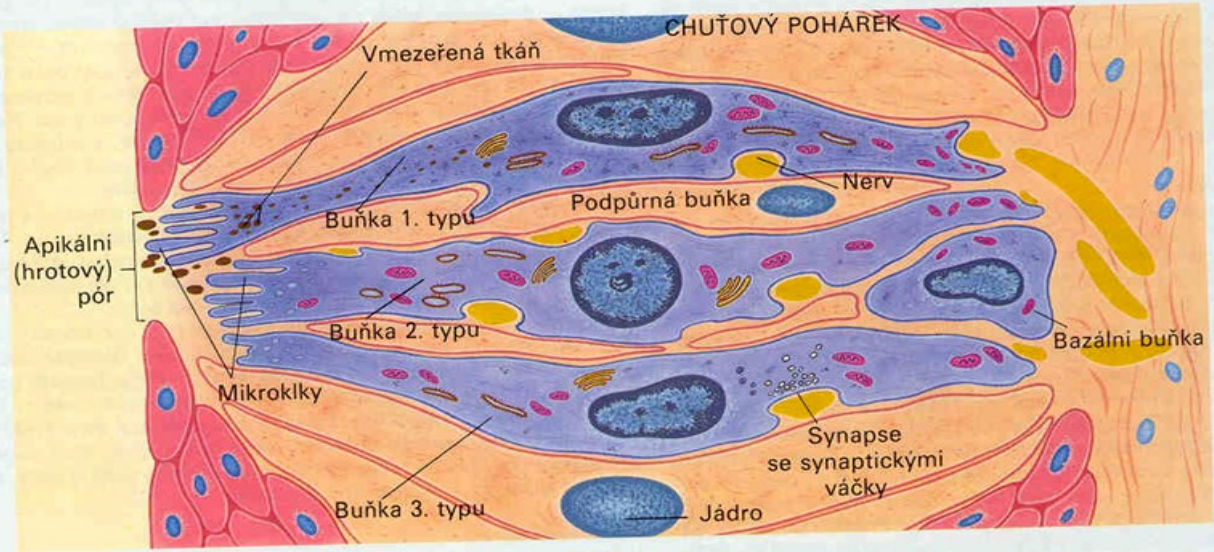
Hänig, D. P. (1901). Zur Psychophysik des Geschmackssinnes.*Philosophische Studien*

Chandrashekar, J., Hoon, M. A., Ryba, N. J. P., & Zuker, C. S. (2006). *The receptors and cells for mammalian taste. Nature, 444(7117), 288–294.*doi:10.1038/nature05401

Receptory nejsou neurony, vznikají z epitelu pokožky, sekundární. Opatřené mikrovilli.
Chuťové, podpůrné a bazální .



v „příkopech" obklopujících jejich centrální val, reagují na chutě hořké. Mezery mezi papilami zvlhčuje sliz, vylučovaný žlázami umístěnými na bázi těchto mezer. Chuťové molekuly se musí v tomto vlhkém prostředí nejprve rozptýlit, a teprve poté je mohou chuťové pohárky detekovat.



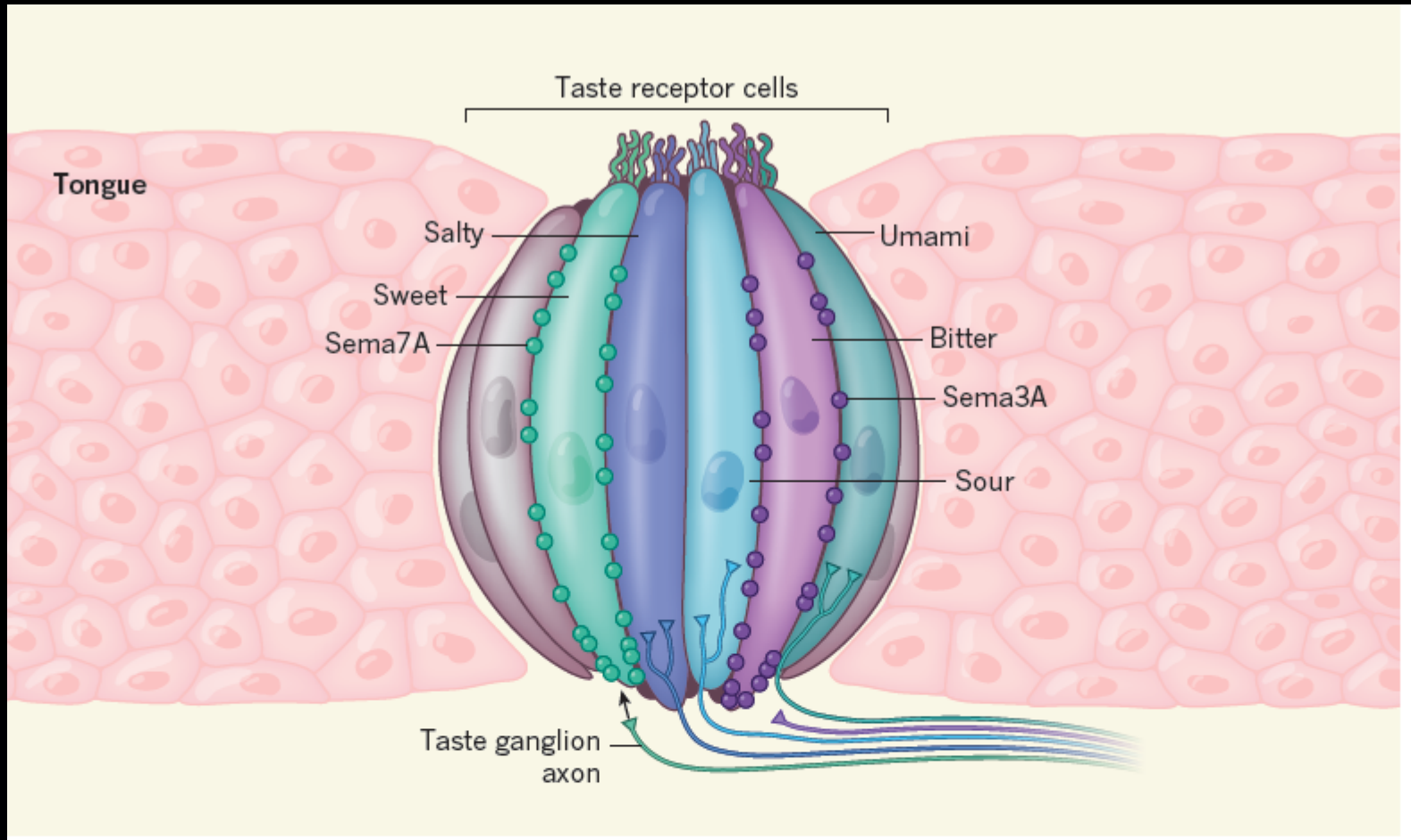
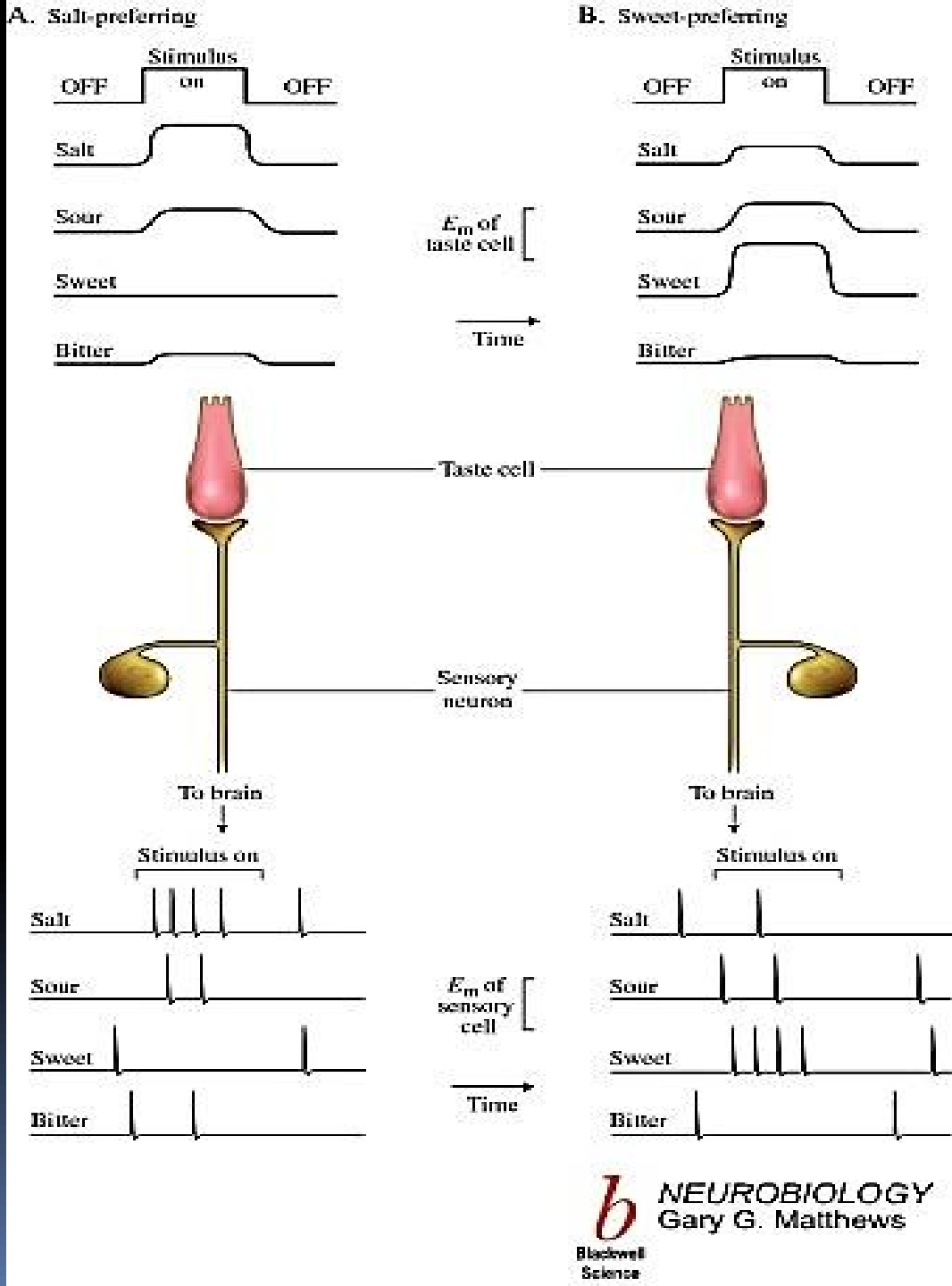


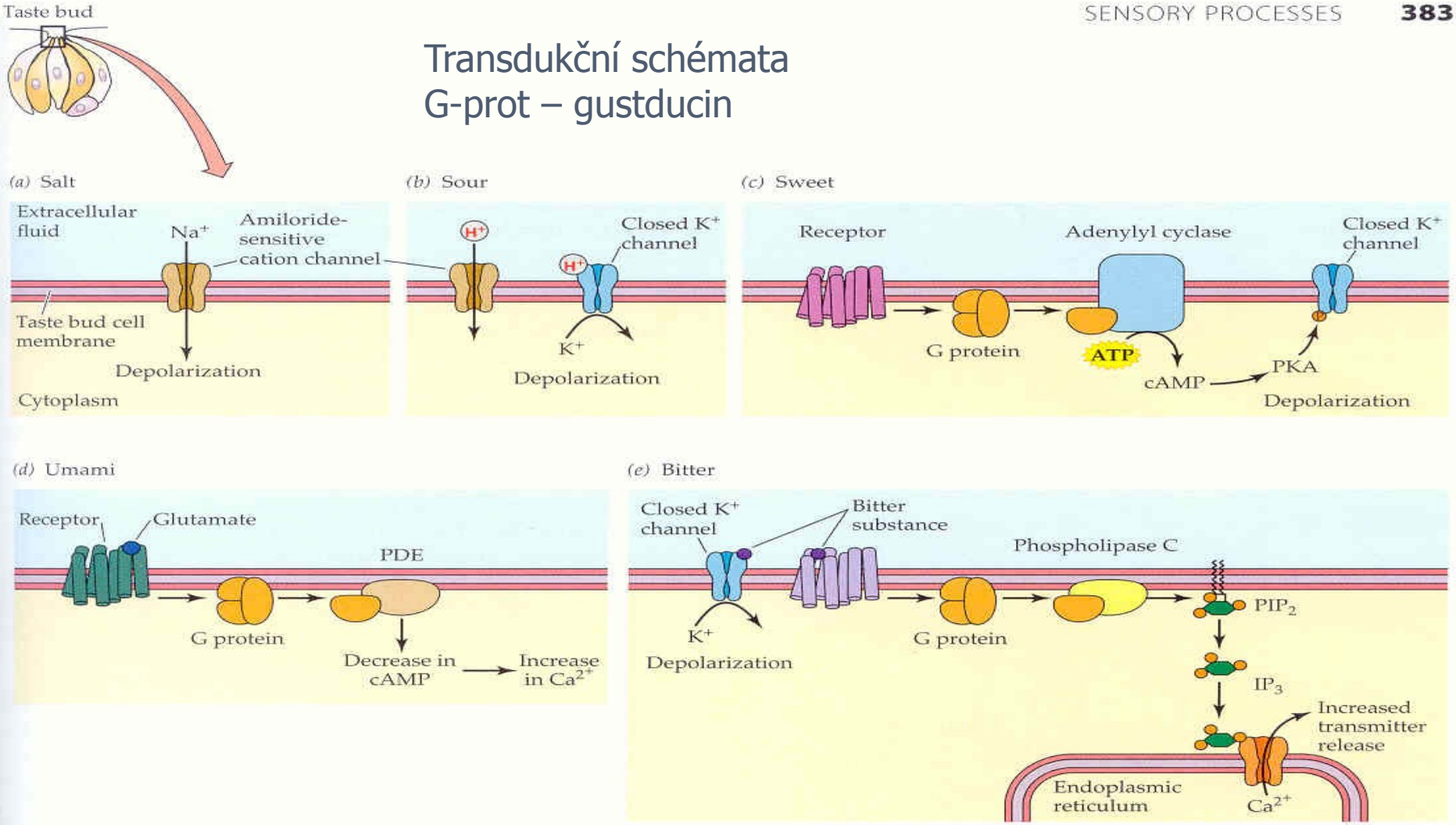
Figure 1 | Wiring the taste system in mice. Each taste bud of the tongue harbours dozens of taste receptor cells (TRCs), most of which are receptive to only one of the five taste qualities — bitter, sweet, sour, salty and umami. In mice, TRCs connect to neuronal projections called axons that originate from clusters of neurons called ganglia in the head that relay taste information, mostly in a type-specific manner (type-specific axons are colour-coded to match TRCs). For example, TRCs that respond to sweet tastes connect to axons from sweet-responsive ganglion neurons. Lee *et al.*[1] have shown that two proteins from the semaphorin family guide this pattern of wiring. Sema3A, produced by bitter TRCs, guides connections with bitter ganglion neurons. Sema7A has the same role but in the sweet taste pathway.

Selektivita omezená.

Člověk může rozlišit asi 100 chuťových kvalit, přičemž jde asi o skládání 5 základních kvalit: sladké, slané, kyselé, hořké a UMAMI. Jedna chuťová buňka může reagovat na všechny čtyři základní chuťové kvality, ale na jeden typ odpovídá maximálním generátorovým potenciálem. Některé jsou více specialisté jiné generalisté.



Transdukční schémata
G-prot – gustducin

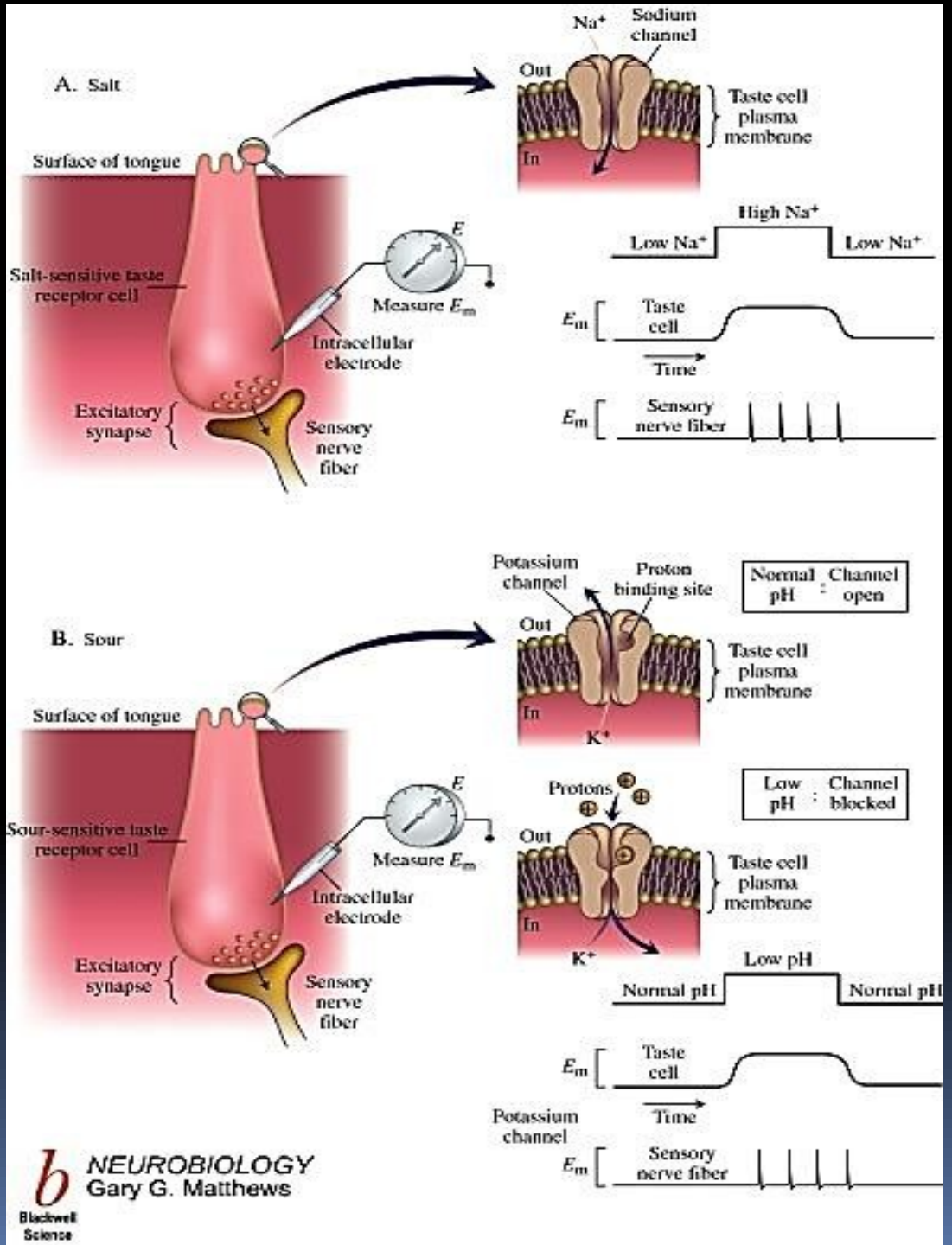


igure 13.34 Taste-transduction mechanisms differ for different aste qualities All transduction mechanisms except the IP_3 action in e) lead to *depolarization*, which spreads to the basal end of the cell nd opens voltage-gated Ca^{2+} channels to allow Ca^{2+} entry and trans-nitter release. *(a)* For salt taste, sodium ions enter a taste bud cell hrough amiloride-sensitive cation channels, directly depolarizing the ell. *(b)* In sour taste, either H^+ ions enter the cell through amiloride-ensitive cation channels, or they close K^+ channels to produce depo-arization. *(c)* Sweet taste is most commonly mediated by the binding f sugars to a G protein–coupled receptor, which acts via a G protein to ctivate adenylyl cyclase and produce cyclic AMP. Cyclic AMP then acti-ates protein kinase A (PKA) to close a K^+ channel (by phosphorylating it), producing depolarization. *(d)* The amino acid glutamate (monosodi-um glutamate, MSG) stimulates the taste quality umami (a savory or meaty quality). Glutamate binds to a G protein–coupled receptor (related to synaptic metabotropic glutamate receptors) to activate a phosphodiesterase (PDE) and decrease the concentration of cAMP. The decrease in cAMP leads to an increase in intracellular Ca^{2+} concentra-tion. *(e)* Bitter taste mechanisms can involve a G protein–coupled receptor for bitter substances that acts via a G protein and phospholi-pase C to produce IP_3. IP_3 liberates Ca^{2+} ions from intracellular stores, eliciting transmitter release without requiring depolarization. Other bitter substances bind to K^+ channels and close them to depolarize the cell.

Transdukční schémata

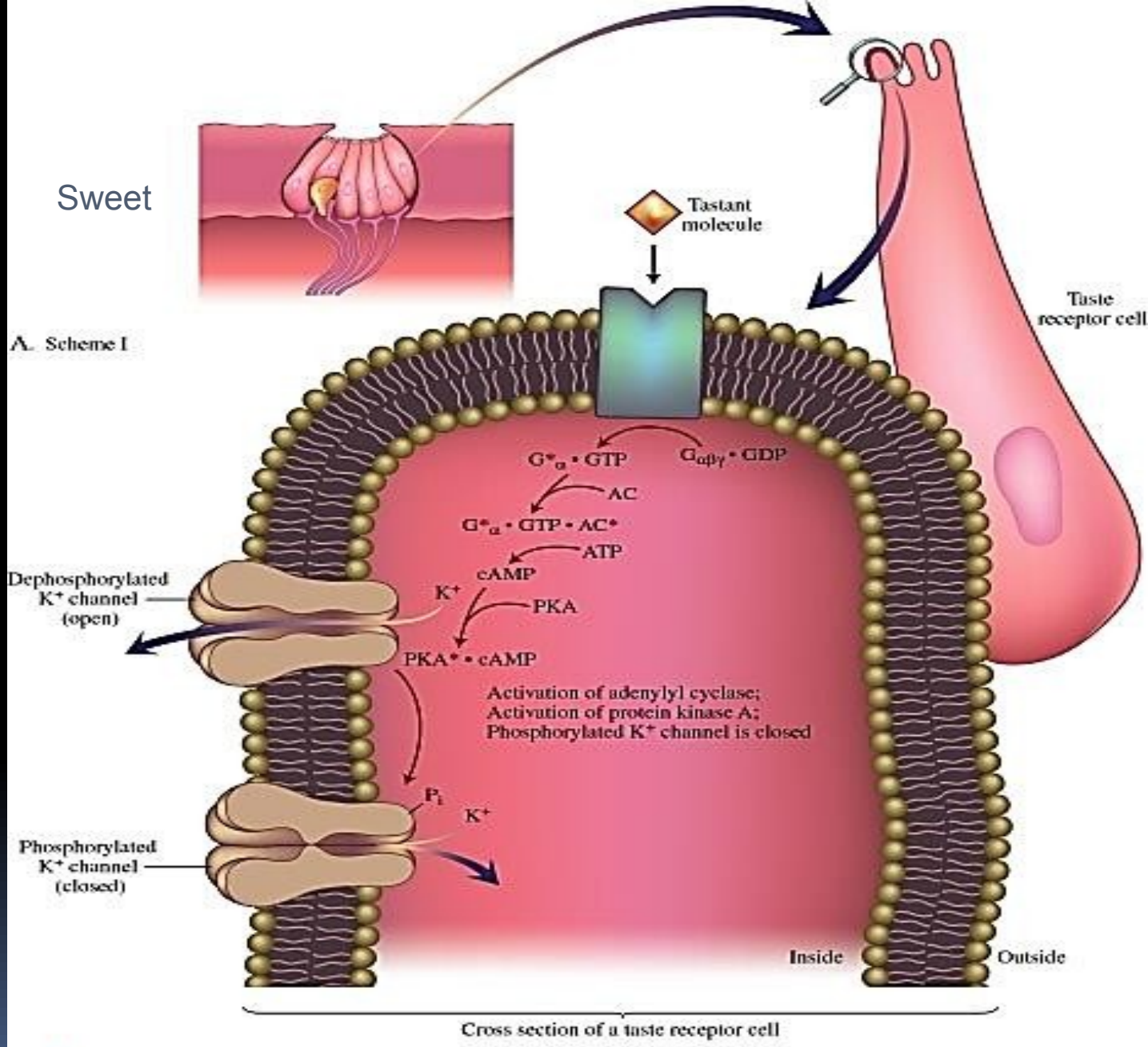
Kanál vůbec nemusí měnit propustnost – slané

Nebo je citlivý na pH - kyselé



Transdukční schémata pro sladké
Varianta I

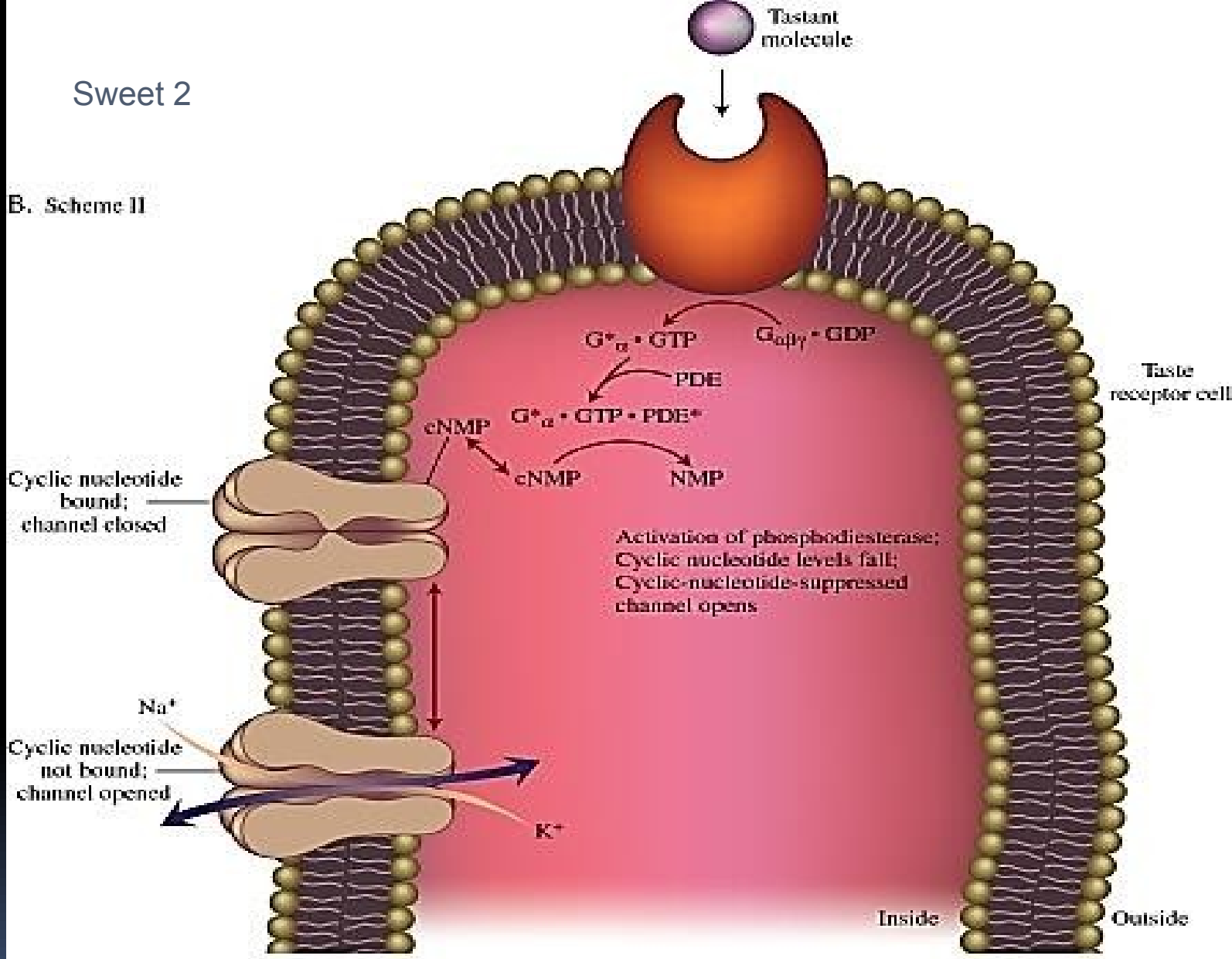
Uzavření K kanálu fosforylací



Transdukční schémata pro sladké Varianta II

Neselektivní kationtový kanál se otevírá

Sweet 2



Hořká chuť

Velká řada ligandů
Různí druzí poslové

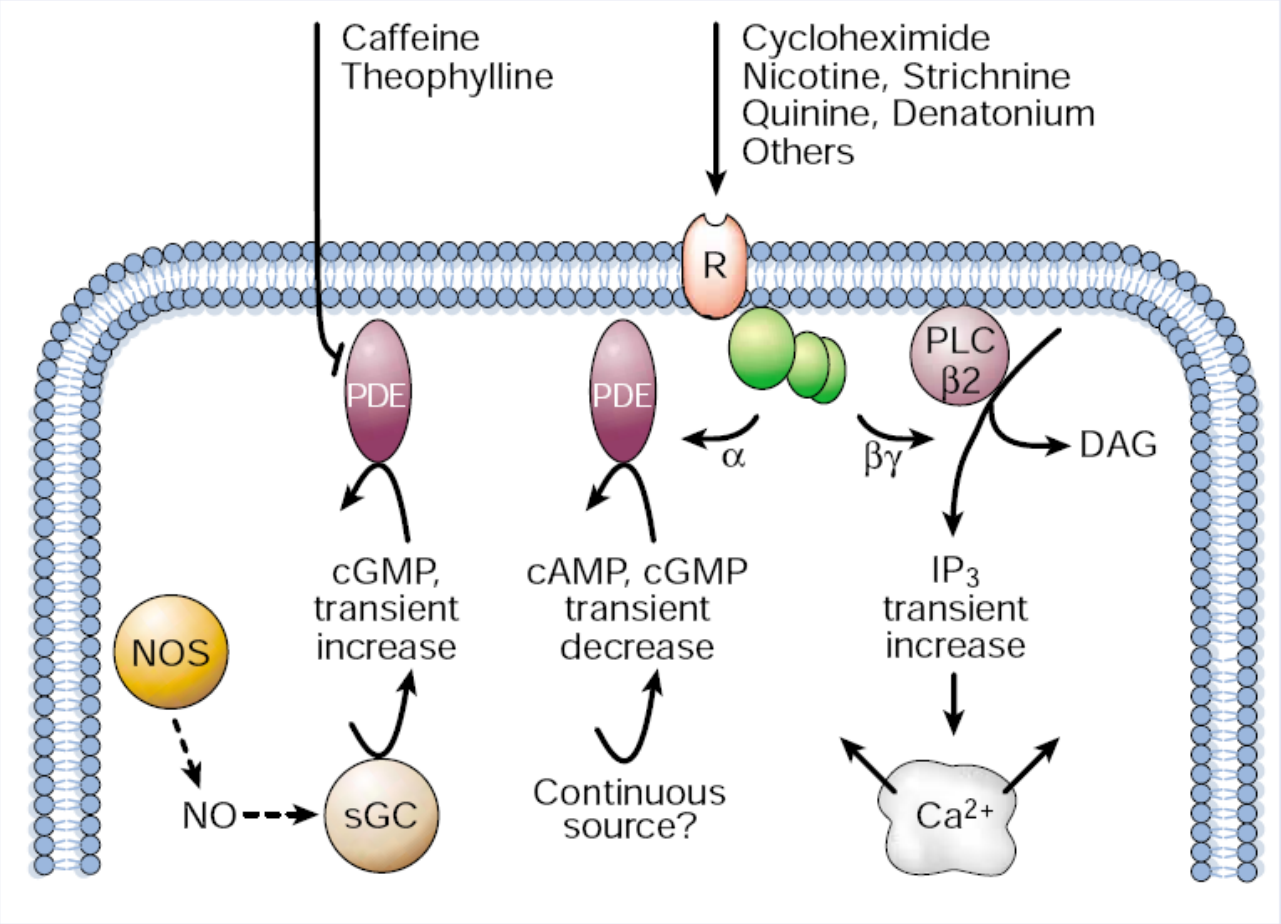
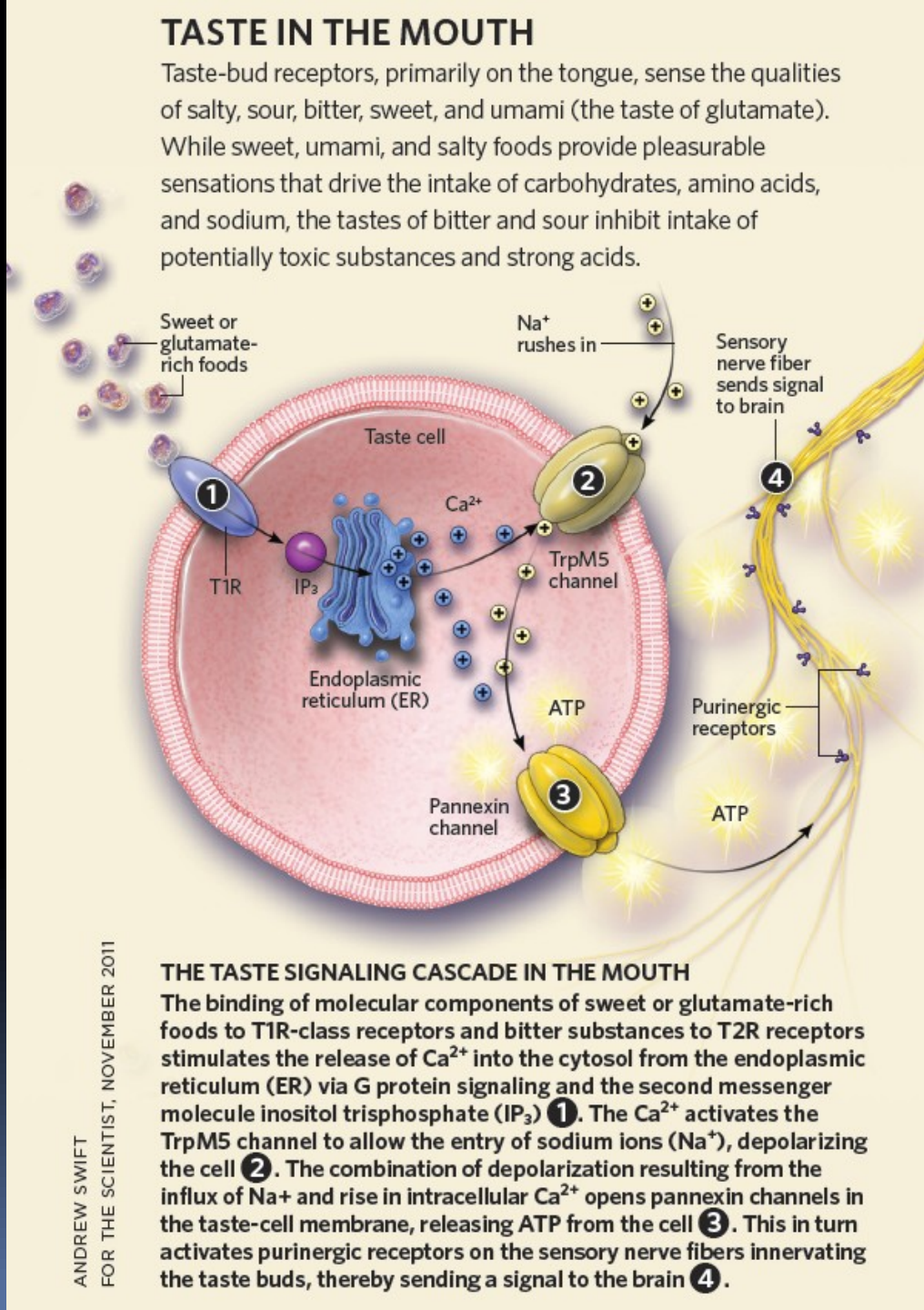


Figure 3 Transduction of bitter taste as elicited by a variety of ligands. Rs, multiple GPCRs of the T2R family, coupled to the G protein gustducin[47–49]; α, α-subunit of gustducin[6,57]; βγ, G-protein subunits β3 and γ13 (refs 60–62); PLCβ2, phospholipase C subtype[61]; Ins(1,4,5)P_3, inositol-1,4,5-trisphosphate[59]; PDE, taste-specific phosphodiesterase[58]; cAMP, cyclic adenosine monophosphate[59]; cGMP, cyclic guanosine monophosphate[59]; sGC, soluble guanylate cyclase[55]; NO, nitric oxide[55]; NOS, NO synthase[56]. For second-messenger kinetics, see refs 55,59,63,64.

ATP jako mediátor purinergní signalizace.



Chuť ve střevě?

Stejné receptory a podobné dráhy řídí reflexní reakce na potravu

Zatímco sladká, umami, slaná (a tučná) chuť poskytují příjemné vjemy, hořká a kyselá chrání před příjmem potenciálně toxických látek a silných kyselin.

TASTE IN THE GUT

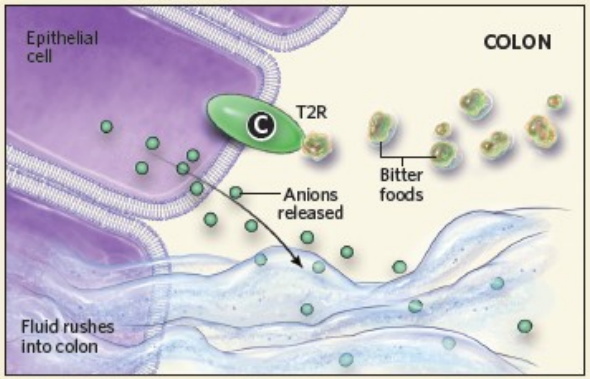
In contrast to taste receptors in the mouth, T1R and T2R receptors in the gut do not induce sensations of taste, but rather initiate molecular pathways that help guide the digestion or rejection of food substances traveling through the intestines. The underlying pathways, however, have many similarities.

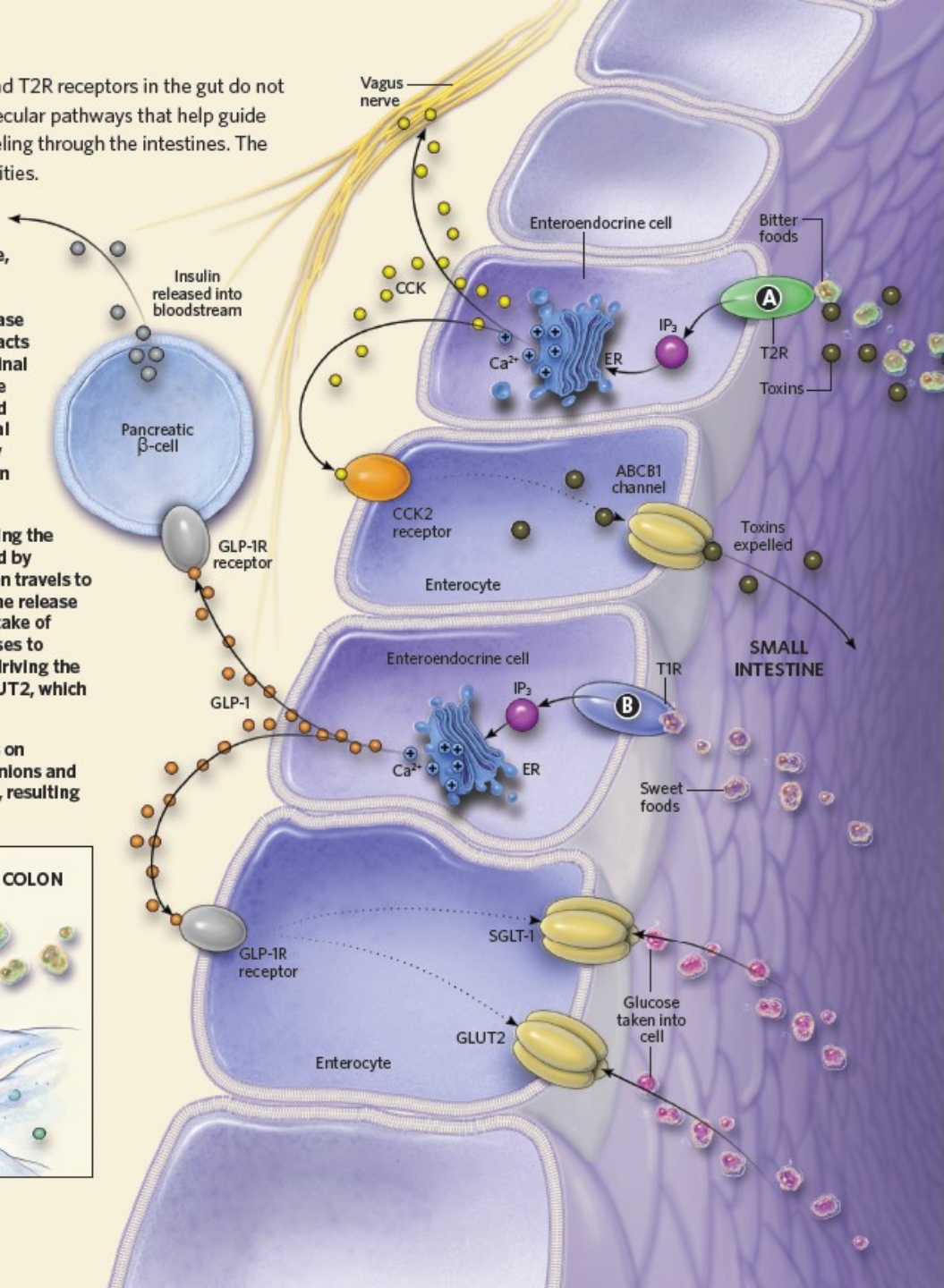
FOODS IN THE GUT

A Specialized endocrine cells of the small intestine, known as enteroendocrine cells, display T2R bitter receptors on their cell membranes. When bitter compounds bind to the T2R receptors, the cells release the peptide hormone cholecystokinin (CCK), which acts on CCK2 receptors located on enterocytes, or intestinal absorptive cells. This increases the expression of the transporter ABCB1, which pumps toxins or unwanted substances out of the cell and back into the intestinal lumen. CCK also binds to CCK1 receptors on sensory fibers of the vagus nerve, sending signals to the brain to cease food intake.

B T1R-class receptors on enteroendocrine cells lining the small intestine detect sweet substances and respond by secreting the glucagon-like peptide GLP-1. GLP-1 then travels to the pancreas via the bloodstream, where it boosts the release of insulin from pancreatic β-cells, promoting the uptake of glucose by diverse tissues. Additionally, GLP-1 diffuses to neighboring enterocyte cells in the small intestine, driving the insertion of the glucose transporters SGLT-1 and GLUT2, which facilitates the uptake of glucose from the intestines.

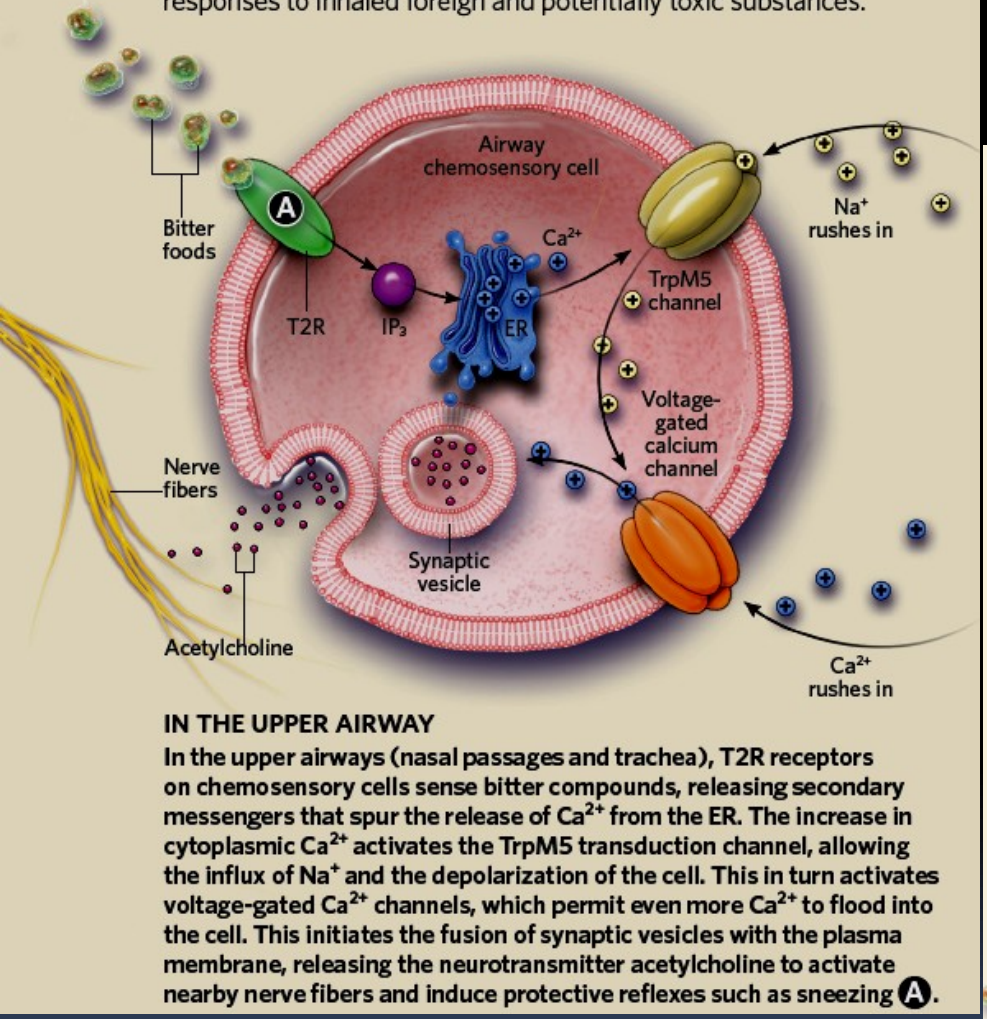
C In the colon, bitter ligands bind to T2R receptors on epithelial cells, where they induce the secretion of anions and water, which leads to fluid rushing into the intestine, resulting in diarrhea that flushes out the colon.

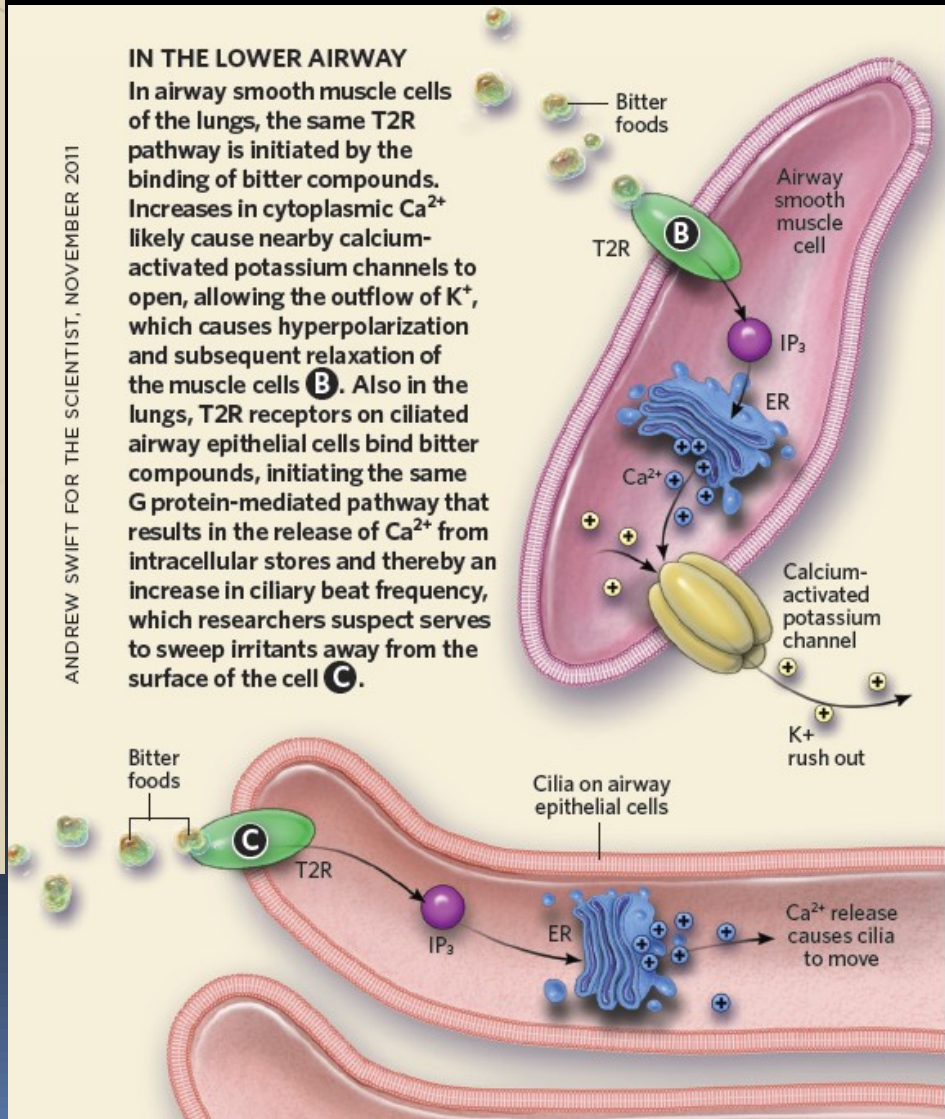




Potenciálně toxické (hořké) substance
T2R receptor
Kýchání, relaxace dých. cest, pohyb řasinek

Plíce – dolní c.d.



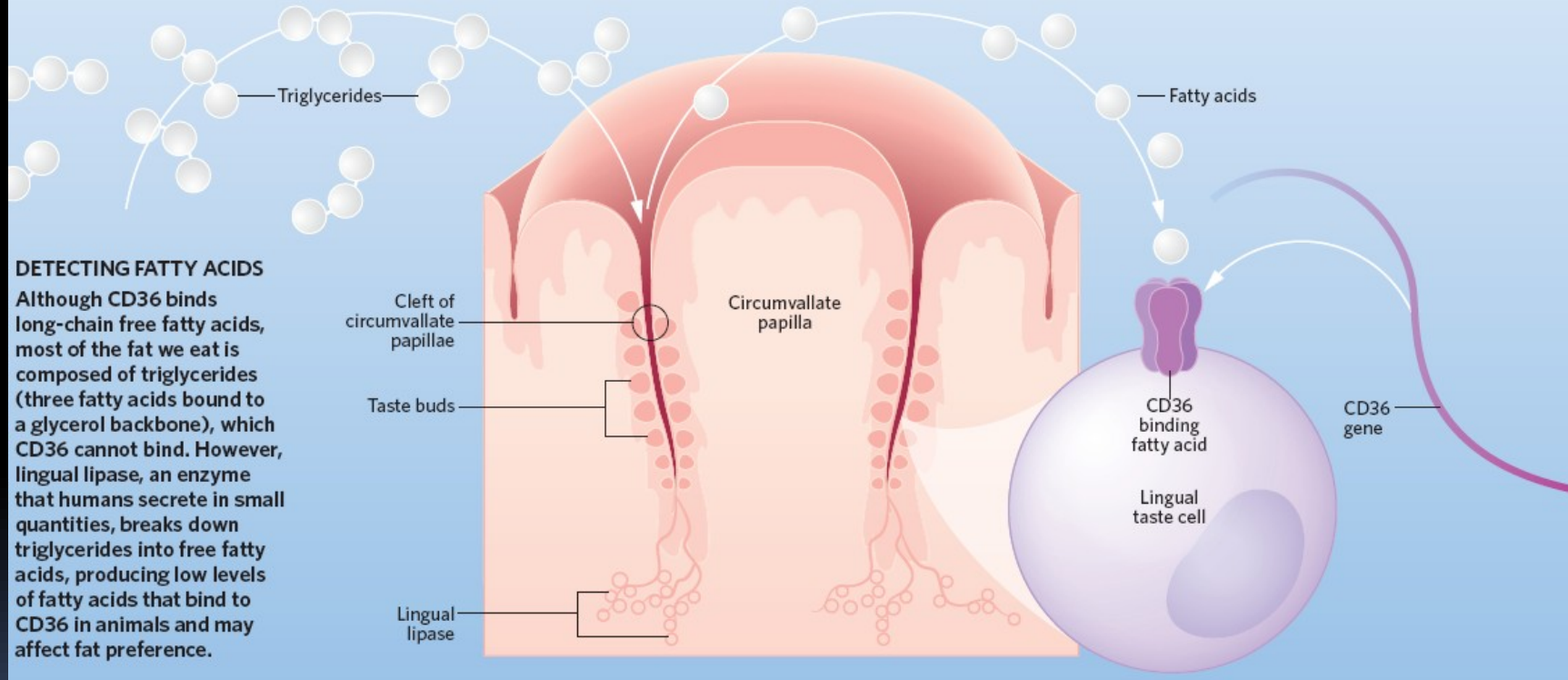


Nosohltan a trachea – horní c.d.

Sensing fat?

CAN WE TASTE FATS?

Although *gustin* and *TAS2R38* contribute to the supertaster phenotype and may contribute to the perception of fat texture, researchers are still looking for a receptor directly triggered by fat. One promising candidate is the protein CD36, which binds long-chain fatty acids in mice, and is expressed on taste buds. The mechanism by which the CD36 carrier protein initiates a neural signal is poorly understood. CD36 may serve as a carrier protein that transfers the fatty acid to another receptor or it may activate an ion channel that alters the excitability of taste cells.



DETECTING FATTY ACIDS

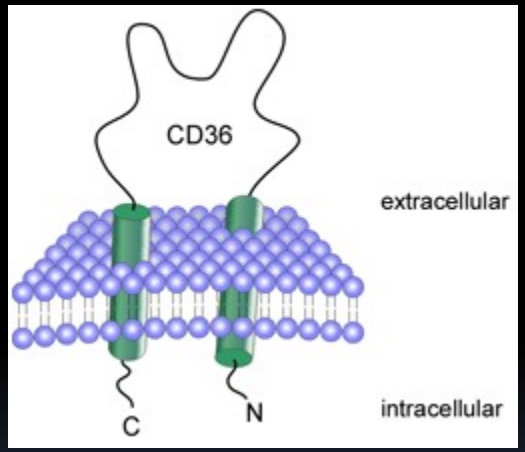
Although CD36 binds long-chain free fatty acids, most of the fat we eat is composed of triglycerides (three fatty acids bound to a glycerol backbone), which CD36 cannot bind. However, lingual lipase, an enzyme that humans secrete in small quantities, breaks down triglycerides into free fatty acids, producing low levels of fatty acids that bind to CD36 in animals and may affect fat preference.

HOW DOES THIS LEAD TO OBESITY?

Recent work has shown that people who had a particular single nucleotide difference in their CD36 gene perceived high levels of creaminess in foods regardless of the fat level. These individuals, showed high preferences for creamy, usually fattier, foods. Although the mechanism remains unclear, this finding raises the possibility that disruptions in this gene lead to both persistently high responsiveness to the oral sensation of fat and an elevated preference for fat which could lead to obesity over time.

Chuť na tučné

- CD36 – receptor na lipidy (?), scavenger receptor, uplatňuje se v metabolismu lipidů, zánětu, hemostáze, ateroskleróze, řízení tlaku, při malárii sekvestrace Ery ve slezině



http://www.scientificamerican.com/article.cfm?id=potential-taste-receptor

2 názory na kódování chutí:

A) labeled lines (analogie sluchu) – jeden nerv, jedna nemíchaná chuť, nepřekrývají se ani buňky ani dráhy, nebo:

B) specifické vzorce aktivity (analogie b.vidění nebo čichu – jeden receptor o výsledné kvalitě nic neříká a až směs dvou dává třetí kvalitu)

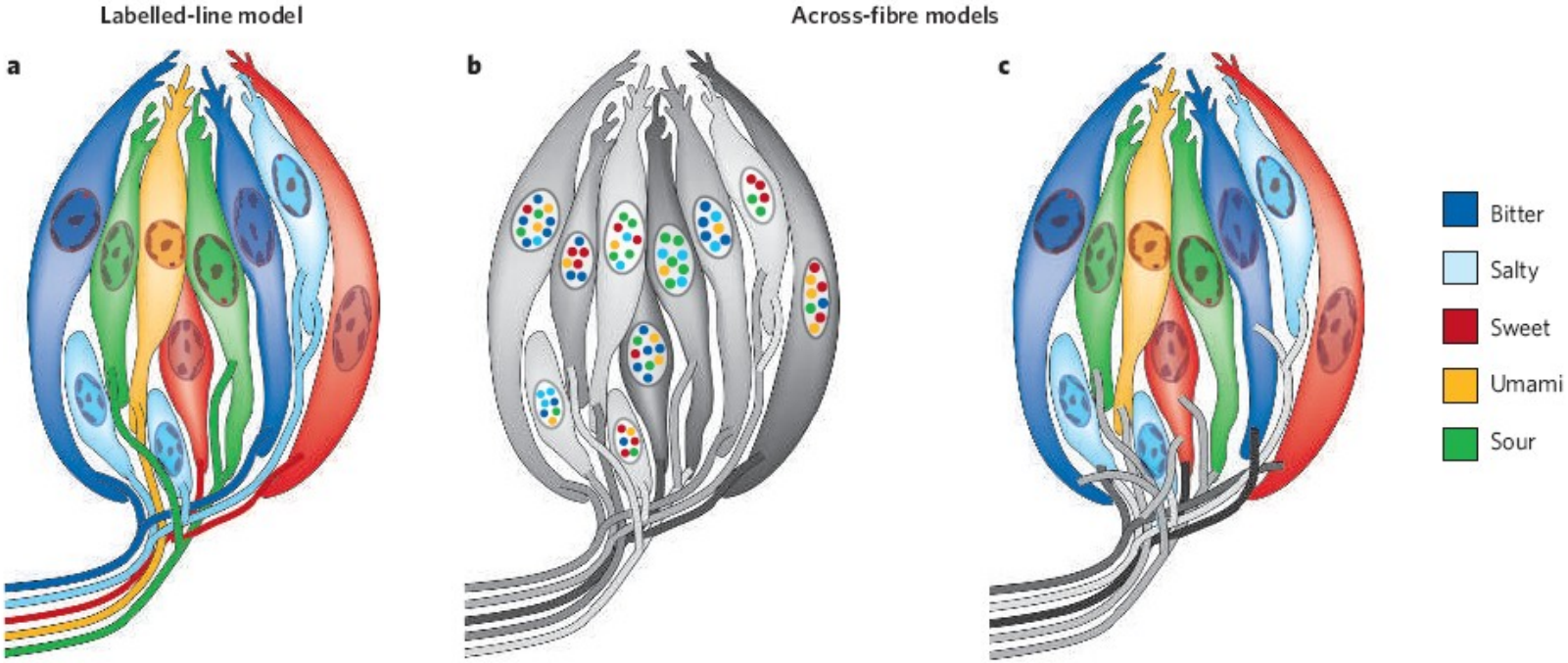
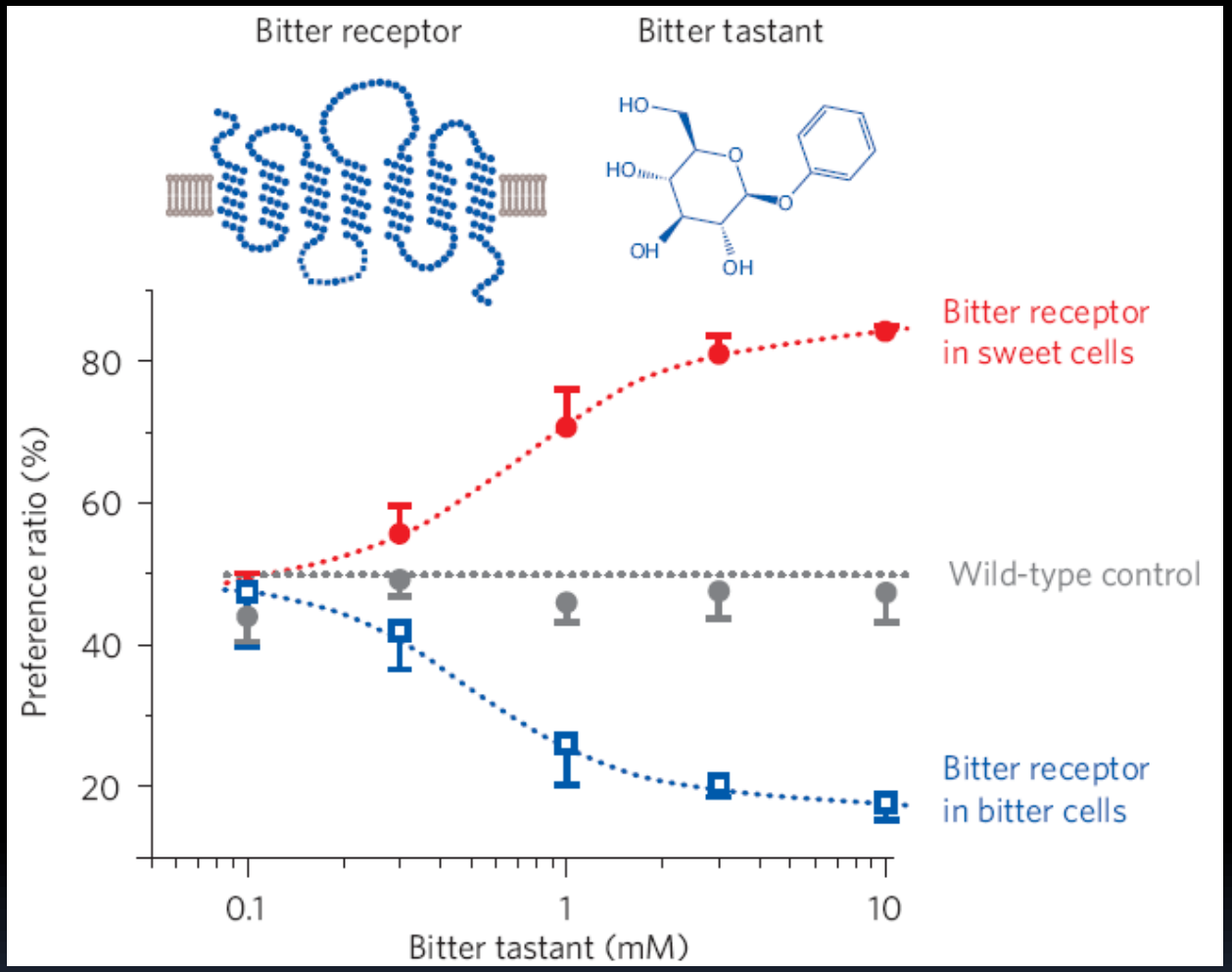


Figure 2 | Encoding of taste qualities at the periphery. There are two opposing views of how taste qualities are encoded in the periphery. **a**, In the labelled-line model, receptor cells are tuned to respond to single taste modalities — sweet, bitter, sour, salty or umami — and are innervated by individually tuned nerve fibres. In this case, each taste quality is specified by the activity of non-overlapping cells and fibres. **b**, **c**, Two contrasting models of what is known as the 'across-fibre pattern'. This states that either individual TRCs are tuned to multiple taste qualities (indicated by various tones of grey and multicoloured stippled nuclei), and consequently the same afferent fibre carries information for more than one taste modality (**b**), or that TRCs are still tuned to single taste qualities but the same afferent fibre carries information for more than one taste modality (**c**). In these two models, the specification of any one taste quality is embedded in a complex pattern of activity across various lines. Recent molecular and functional studies in mice have demonstrated that different TRCs define the different taste modalities, and that activation of a single type of TRC is sufficient to encode taste quality, strongly supporting

Transgenní myši s přehozenými receptory



Vnímání sladkého nebo hořkého odráží aktivaci jen určitých receptorových buněk bez ohledu na vlastnosti receptoru nebo chuťových molekul

Jayaram Chandrashekar, Mark A. Hoon, Nicholas J. P. Ryba & Charles S. Zuker. *Nature* **444**, 288-294(16 November 2006) doi:10.1038/nature05401.

Závěr: Každou jednotlivou chuť rozeznáme i ve směsi chutí – ochrana. Mícháním chutí se tedy nevytváří chuť (kvalita) zcela nová. Chuť je analytickým smyslem.

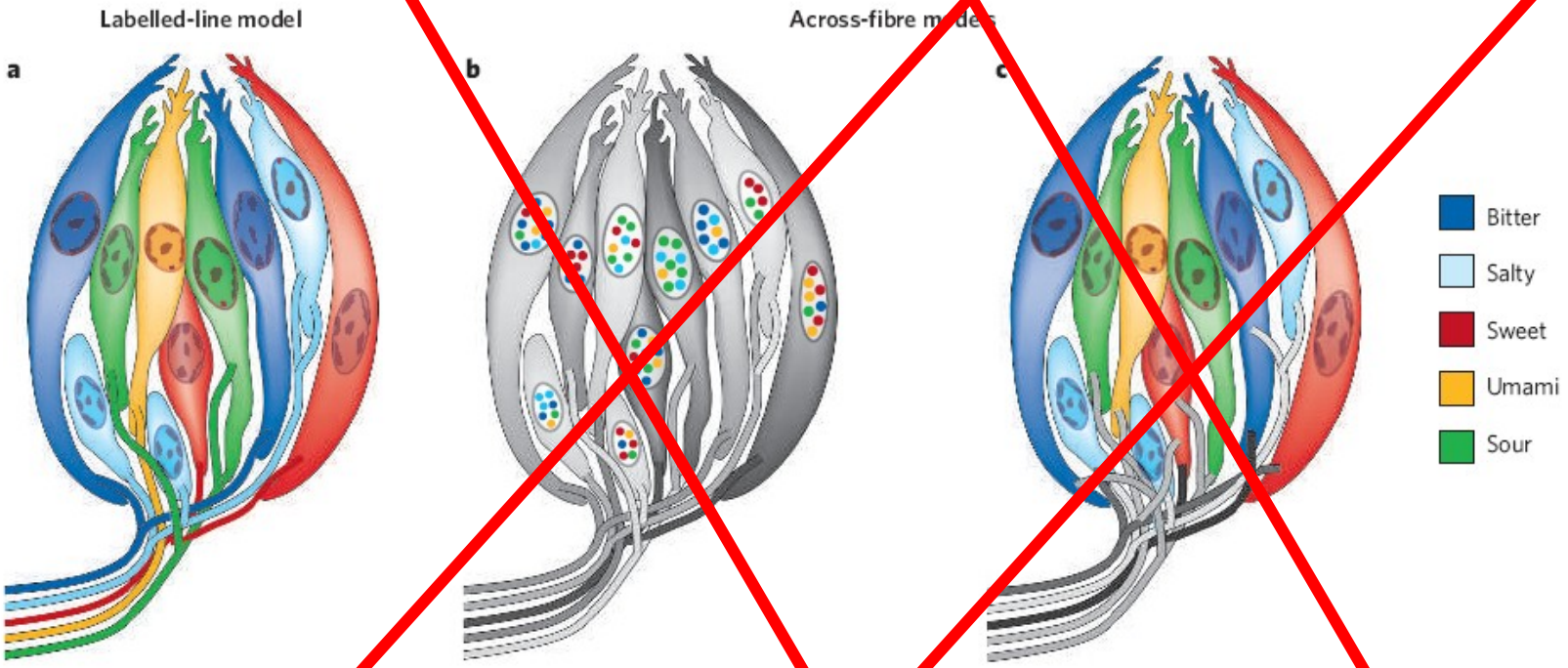
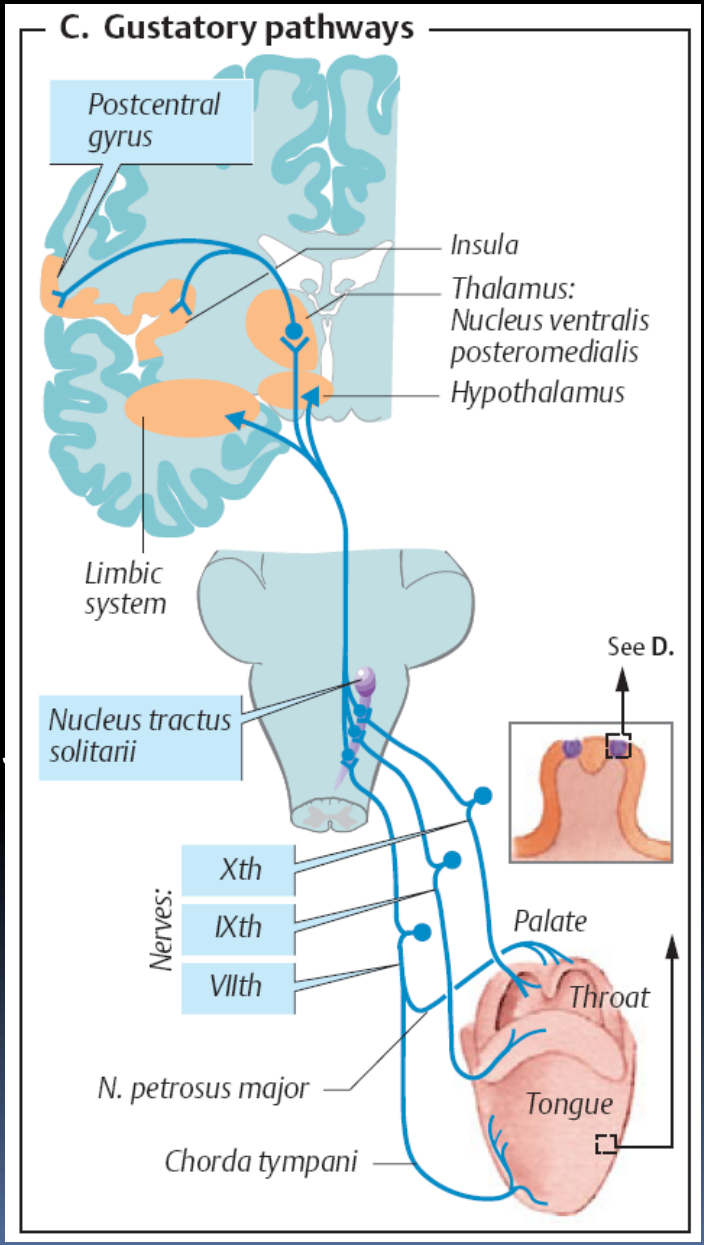
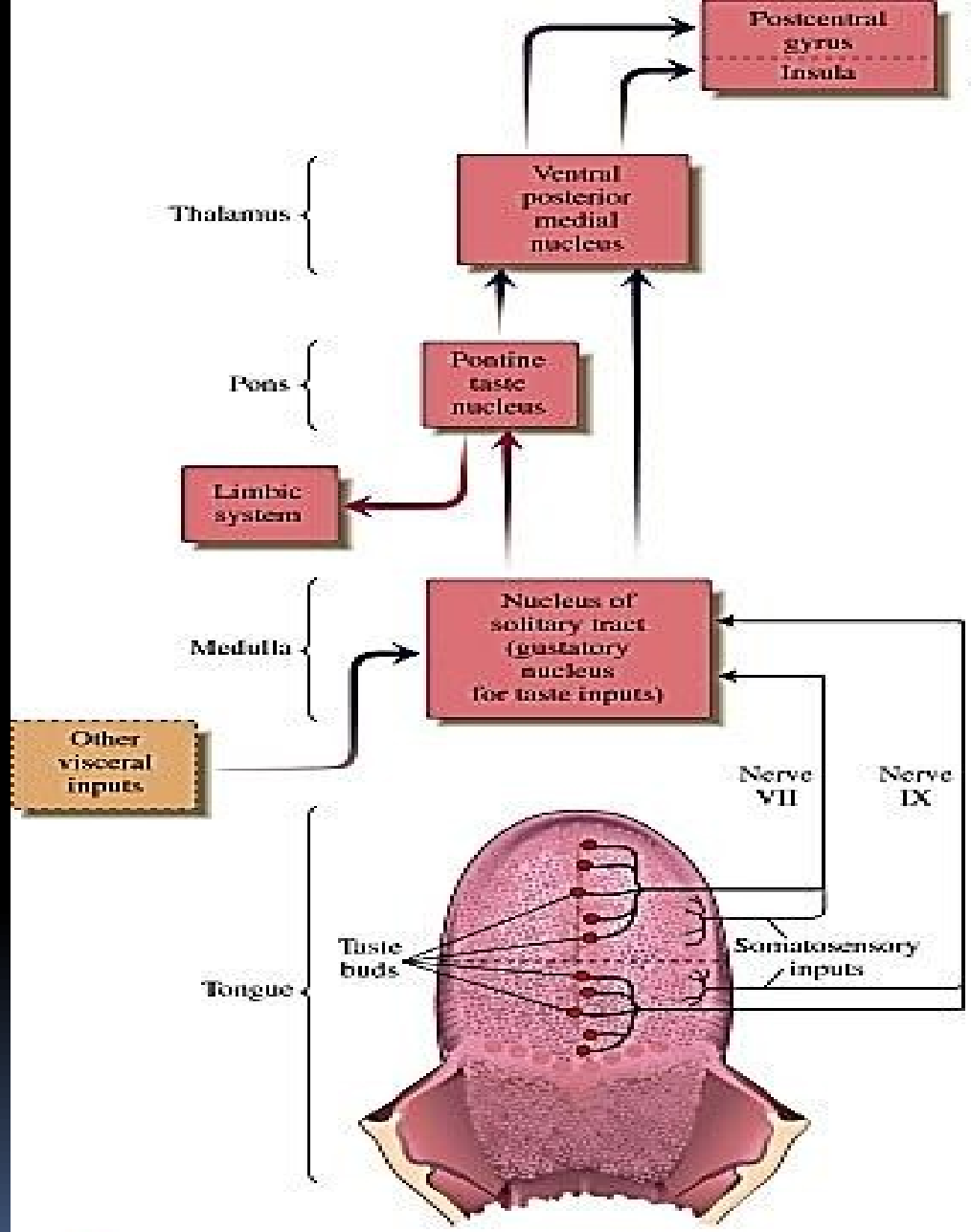


Figure 2 | Encoding of taste qualities at the periphery. There are two opposing views of how taste qualities are encoded in the periphery. **a**, In the labelled-line model, receptor cells are tuned to respond to single taste modalities — sweet, bitter, sour, salty or umami — and are innervated by individually tuned nerve fibres. In this case, each taste quality is specified by the activity of non-overlapping cells and fibres. **b**, **c**, Two contrasting models of what is known as the 'across-fibre pattern'. This states that either individual TRCs are tuned to multiple taste qualities (indicated by various tones of grey and multicoloured stippled nuclei), and consequently the same afferent fibre carries information for more than one taste modality (**b**), or that TRCs are still tuned to single taste qualities but the same afferent fibre carries information for more than one taste modality (**c**). In these two models, the specification of any one taste quality is embedded in a complex pattern of activity across various lines. Recent molecular and functional studies in mice have demonstrated that different TRCs define the different taste modalities, and that activation of a single type of TRC is sufficient to encode taste quality, strongly supporting the labelled-line model.

Chuťová dráha





NEUROBIOLOGY
Gary G. Matthews
Blackwell Science

Chuťová dráha

Axony patří pseudounipolárním neuronům, jejichž těla leží v gangliích VII., IX. a X. hlavového nervu. Přes nižší mozková centra (hypotalamus, talamus) můžeme sledovat cestu chuťové informace ke dvěma korových chuťovým oblastem (postcentrální závit a insula).

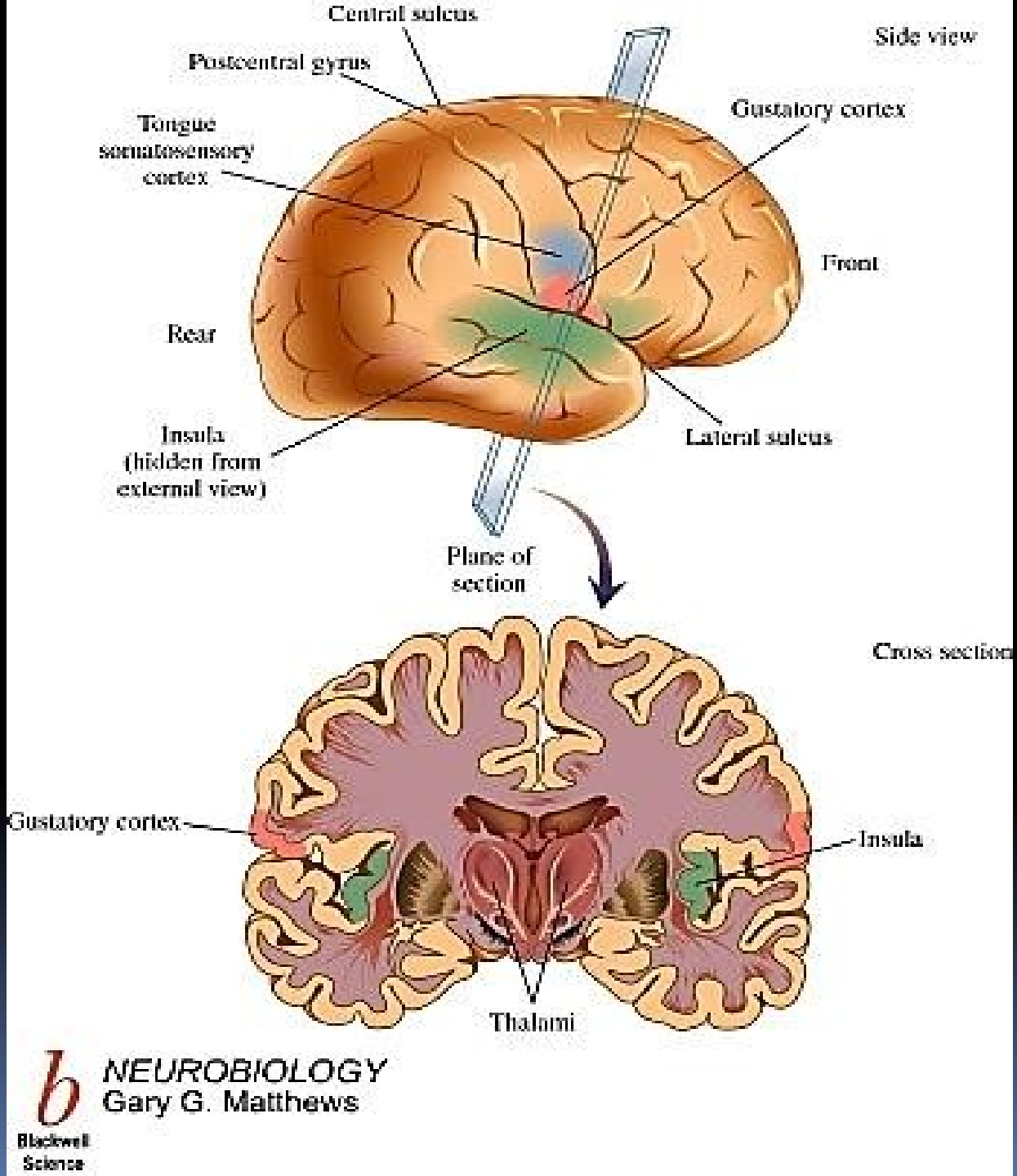
První asi hraje roli při vnímání prostorového rozmístění chuťových počitků na jazyku a druhá je zodpovědná za vnímání vlastní kvality chuti.

Najdeme také významnou projekci do limbického systému a hypotalamu.

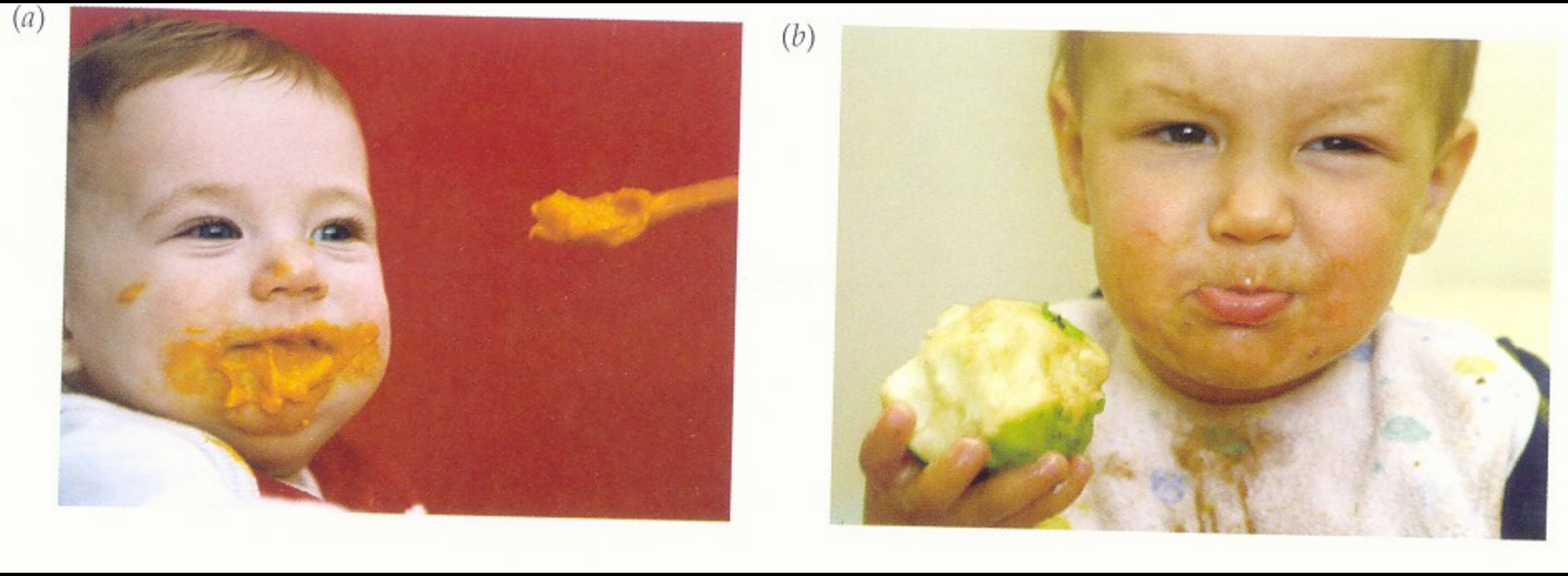
Uvedené spoje jsou morfologickým substrátem významné emocionální komponenty, která vždy doprovází určitý chuťový vjem a pojí se paměťovými stopami – rozlišování vhodné a nevhodné potravy už od mládí. Zřejmě také zprostředkovávají autonomní reflexní reakce při příjmu potravy (sekrece slin, žaludeční šťávy apod.).

Chuťová kůra

Insula – lat. část mozkové kůry ležící v hloubi postranní brázdy mozkové sulcus lateralis, je překrytá čelním, temenním a spánkovým lalokem.
lat. ostrov



http://lekarske.slovniky.cz/pojem/insula



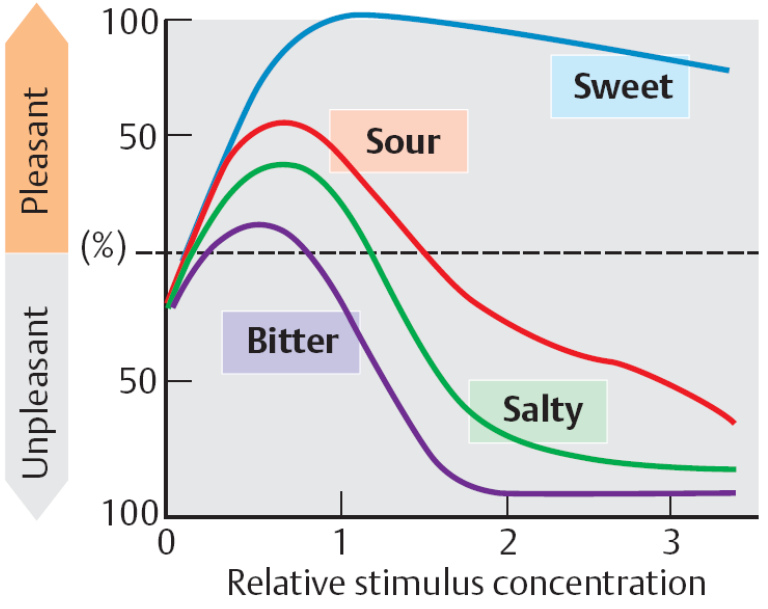
Potěšení z chutí - vrozené prospěšné reflexy. Zvýšená chuť na chybějící složku.

Příjemné tóny sladkého a umami signalizují kalorické stravitelné jídlo. Hořká chuť má nízký práh při vyvolávání dávivého reflexu, jde o varování před obvykle jedovatými látkami.

(a)

(b)

E. Evaluation of taste stimuli



(After Pfaffmann)

Spolupráce s čichem a dalšími smysly při kontrole příjmu potravy.

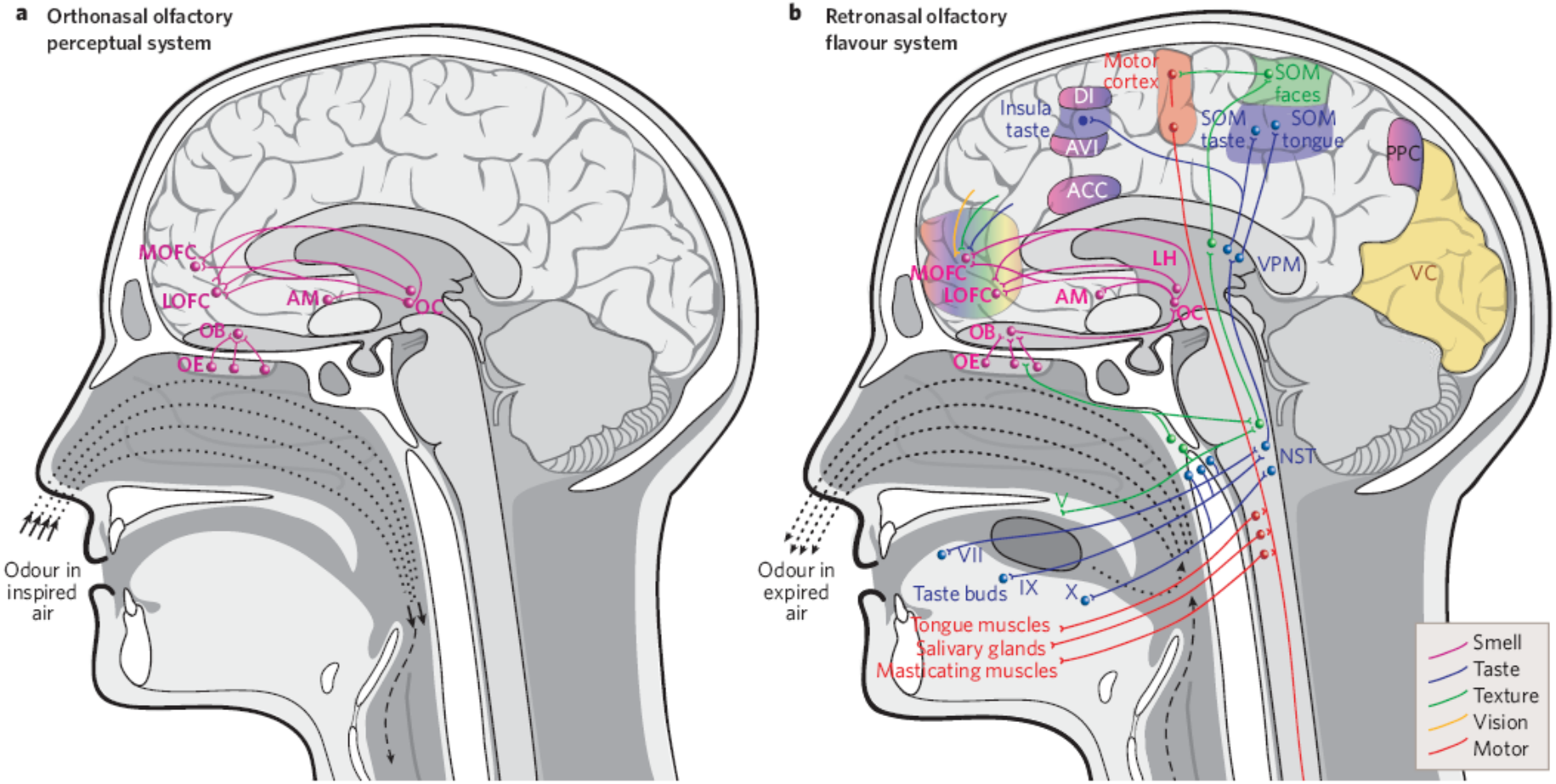


Figure 2 | The dual olfactory system. **a**, Brain systems involved in smell perception during orthonasal olfaction (sniffing in). **b**, Brain systems involved in smell perception during retronasal olfaction (breathing out), with food in the oral cavity. Air flows indicated by dashed and dotted lines; dotted lines indicate air carrying odour molecules. ACC, accumbens; AM, amygdala; AVI, anterior ventral insular cortex; DI, dorsal insular cortex; LH, lateral hypothalamus; LOFC, lateral orbitofrontal cortex; MOFC, medial orbitofrontal cortex; NST, nucleus of the solitary tract; OB, olfactory bulb; OC, olfactory cortex; OE, olfactory epithelium; PPC, posterior parietal cortex; SOM, somatosensory cortex; V, VII, IX, X, cranial nerves; VC, primary visual cortex; VPM, ventral posteromedial thalamic nucleus.

Spolupráce s čichem a dalšími smysly a emocemi při kontrole příjmu potravy – komplex řídící potravní chování. Chuť úzce navázána na emoce, motivace, žádost. Důležité téma současnosti.

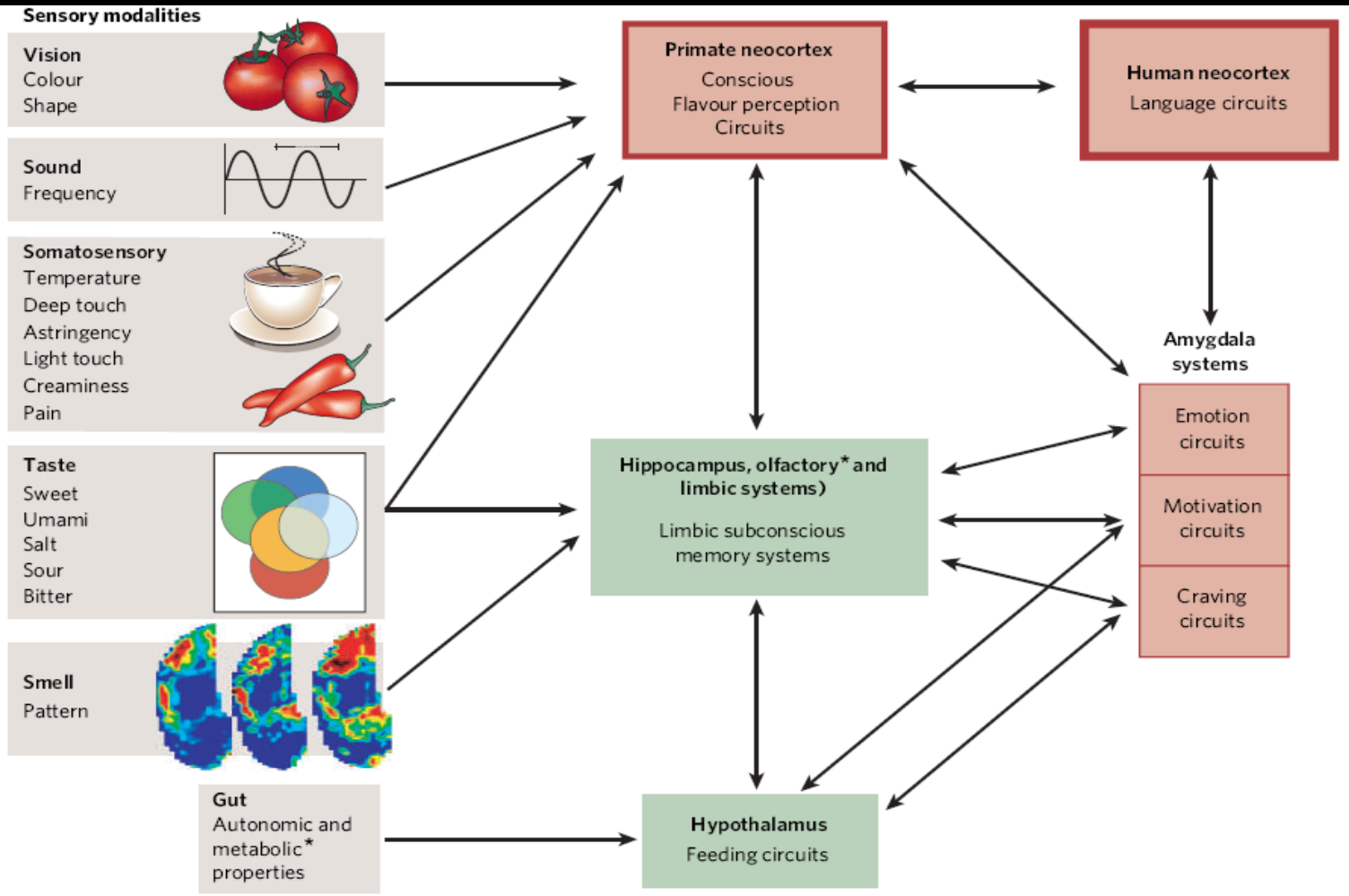
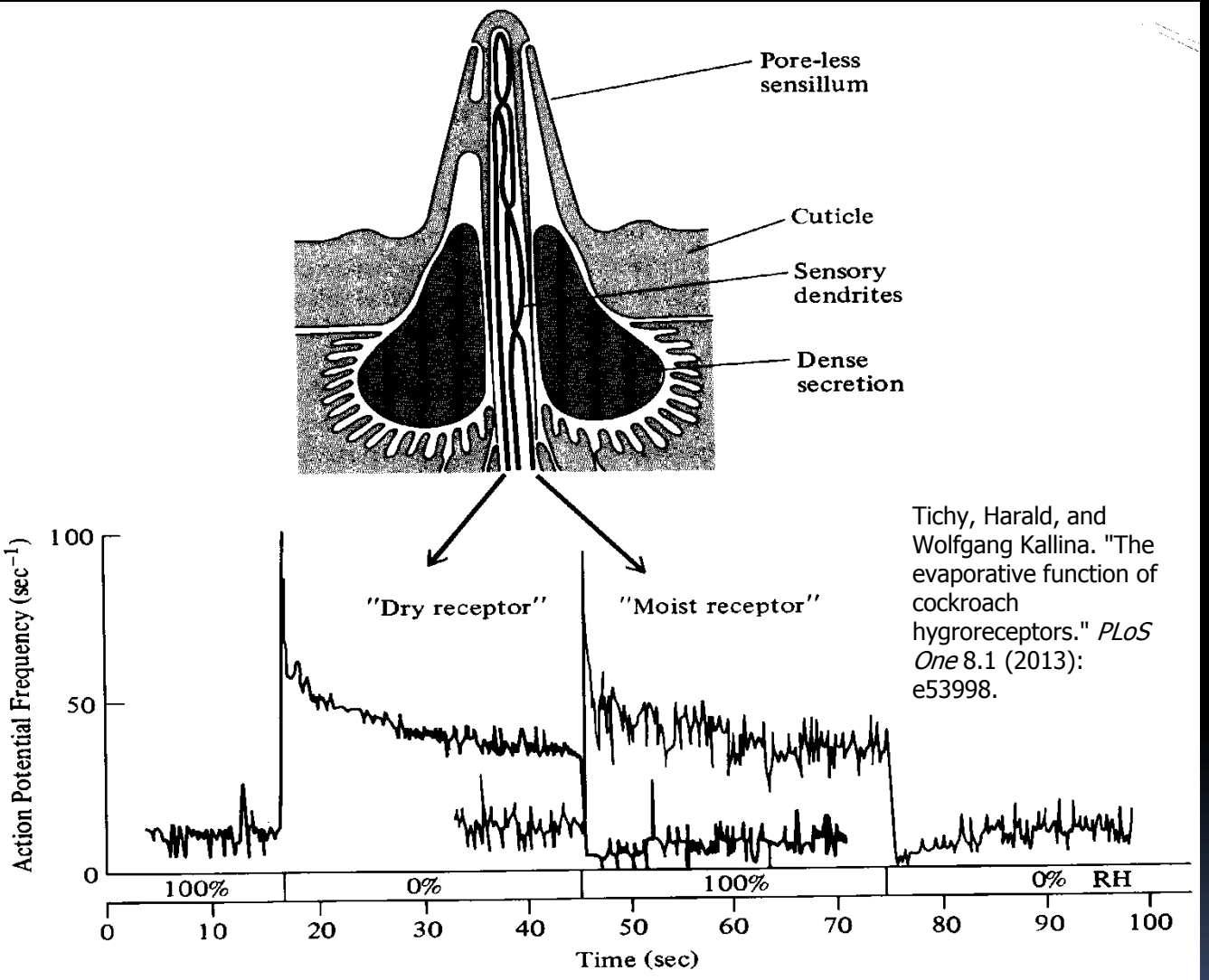


Figure 3 | The human brain flavour systems that evaluate and regulate food intake. The diagram shows the areas involved in the perceptual, emotional, memory-related, motivational and linguistic aspects of food evaluation mediated by flavour inputs[32,41,54,55]. Left, different sensory modalities and submodalities that contribute to flavour perception. Middle and right, brain flavour system that evaluates and regulates food intake. Red regions mediate conscious sensory perception; thicker outlines indicate their greater importance in humans and other primates. Green regions mediate subconscious feeding regulation. Deficiencies in essential amino acids are sensed by the anterior olfactory cortex (asterisk).

Hygrorecepce

Vnímání vlhkosti u hmyzu. Podstatné pro život. Mechanismus neznámý: 1) mechanical hygrometers, 2) evaporation detectors 3) psychrometers.

Mechanical hygrometers are assumed to respond to the relative humidity, evaporation detectors to the saturation deficit and psychrometers to the temperature depression (the difference between wet-bulb and dry-bulb temperatures).

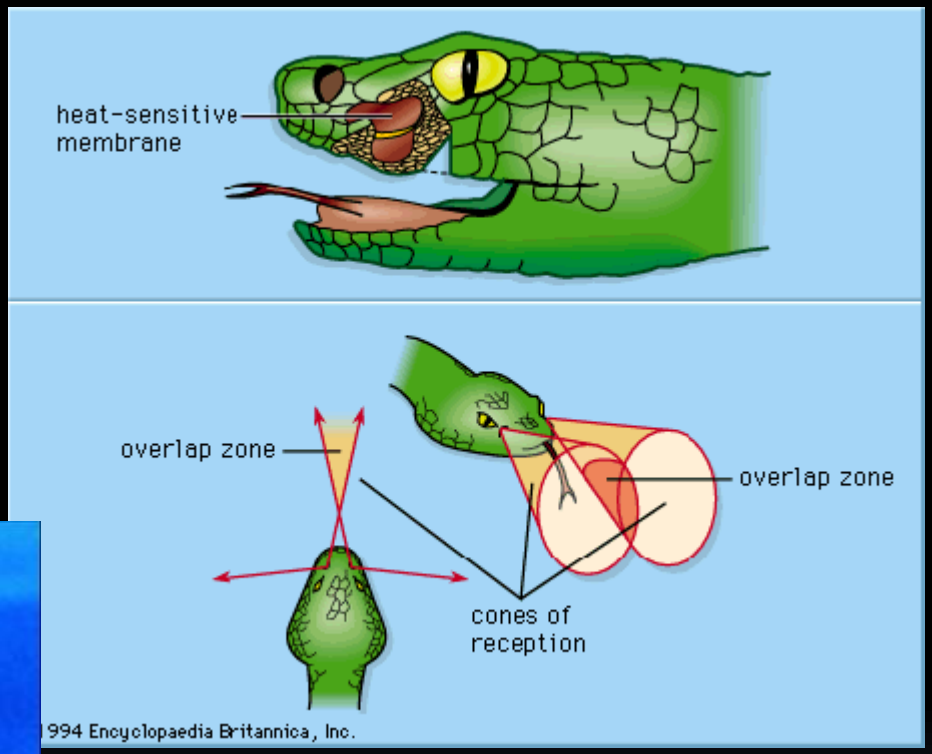


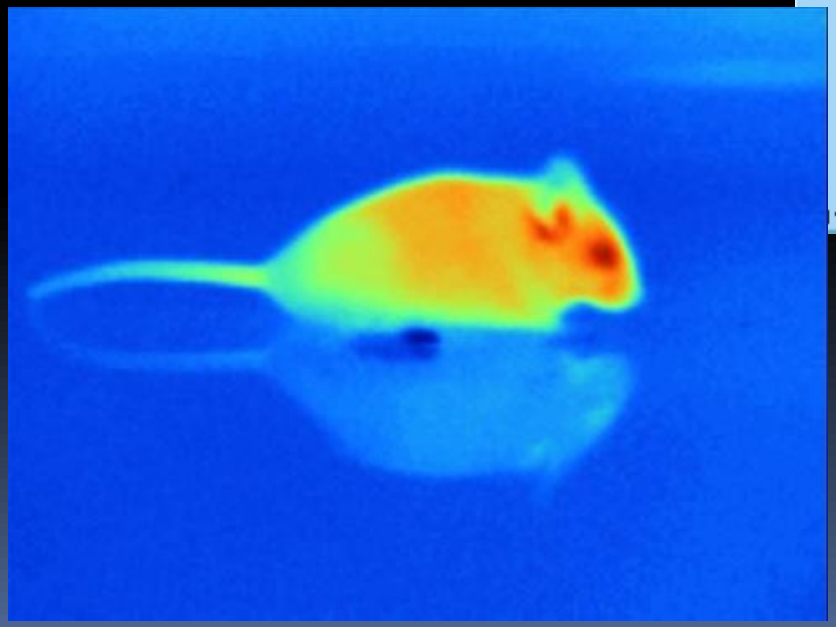
Tichy, Harald, and Wolfgang Kallina. "The evaporative function of cockroach hygroreceptors." *PLoS One* 8.1 (2013): e53998.

FIGURE 7–18 The "cold-moist-dry" triad sensory sensillum of the cockroach contains three bipolar sensory neurons; one neuron of the hygroreceptor responds to high humidity ("moist" receptor) and one to low humidity ("dry" receptor). The receptor cavity of the poreless sensillum is filled with a dense secretion. *(Modified from Yokohari and Tateda 1976; Schaller 1978.)*

Termorecepce

U některých zvířat spíše Infračervená recepce – elektromagnetické vlny.





Termorecepce

U některých zvířat spíše Infračervená recepce – elektromagnetické vlny.

Mechanismus transdukce ale není příbuzný zraku (fotochemická reakce). Jde o citlivou termorecepci – změna teploty otevírá kanál. Extrémně citlivé (0.001°C)

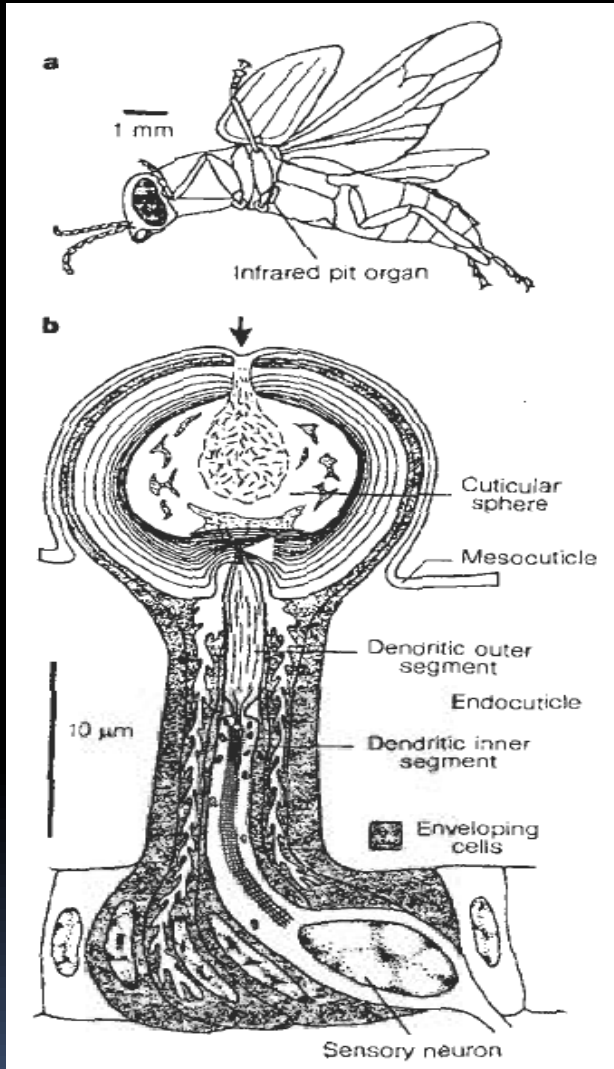


Figure 1 a, Diagram of *Melanophila* (body length 10 mm). The infrared pit organs, situated next to the coxae of the middle legs, are completely exposed during flight. b, An infrared sensillum, redrawn from ref. 3.

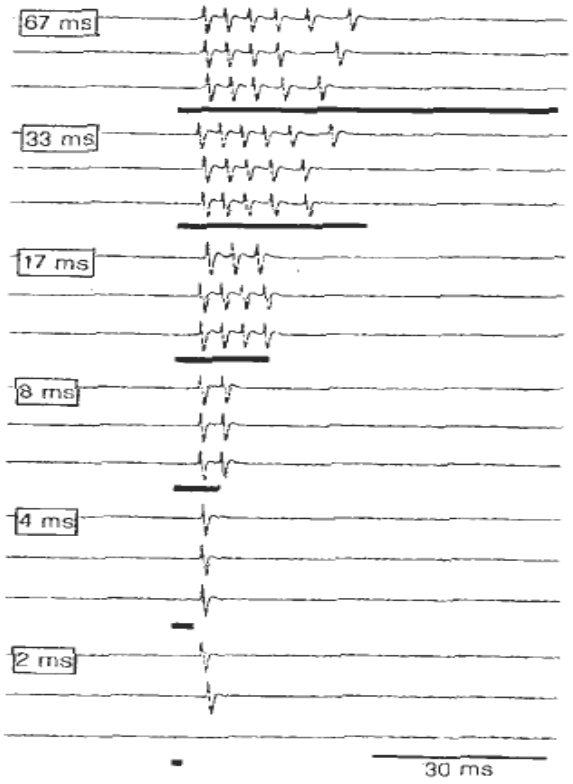


Figure 2 The responses of a neuron, recorded from the pit organ, to various infrared stimuli. Each trace shows the original response to one stimulus. Horizontal bars indicate exposure times. Each trial was repeated three times. The number of action potentials decreases with decreasing stimulus duration; 2 ms was sufficient to generate a response. If the mirror was covered, no response was recorded at any of the infrared intensities and shutter speeds tested.

pass infrared filter (50% cut-on at 1.8 µm) and neutral-density filters. At a radiation intensity of 24 mW cm^{-2} single neurons

Termorecepce

Kožní termorecepce. Chladově a na horko specializované receptory v kůži.

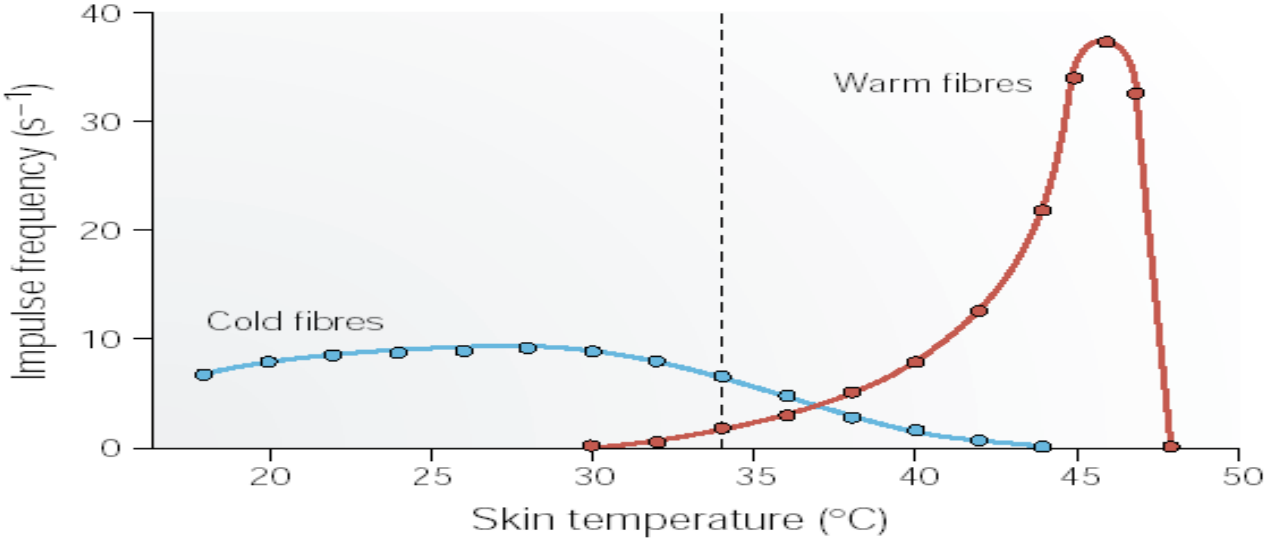


Figure 2 | **Average discharge frequency of individual cold- and warm-sensitive fibres in response to changes in skin temperature.** The dotted line indicates the normal skin temperature (33°C). Cold-sensitive fibres respond only to cooling, whereas warm-sensitive fibres respond to warming. Neither type of fibre responds to mechanical stimulation. Adapted, with permission, from REF. 13 © (1969) The Physiological Society.

Termorecepce a nocicepce v kůži spolupracují

TRPV (transient receptor potential) kanály jsou univerzálními sensory.

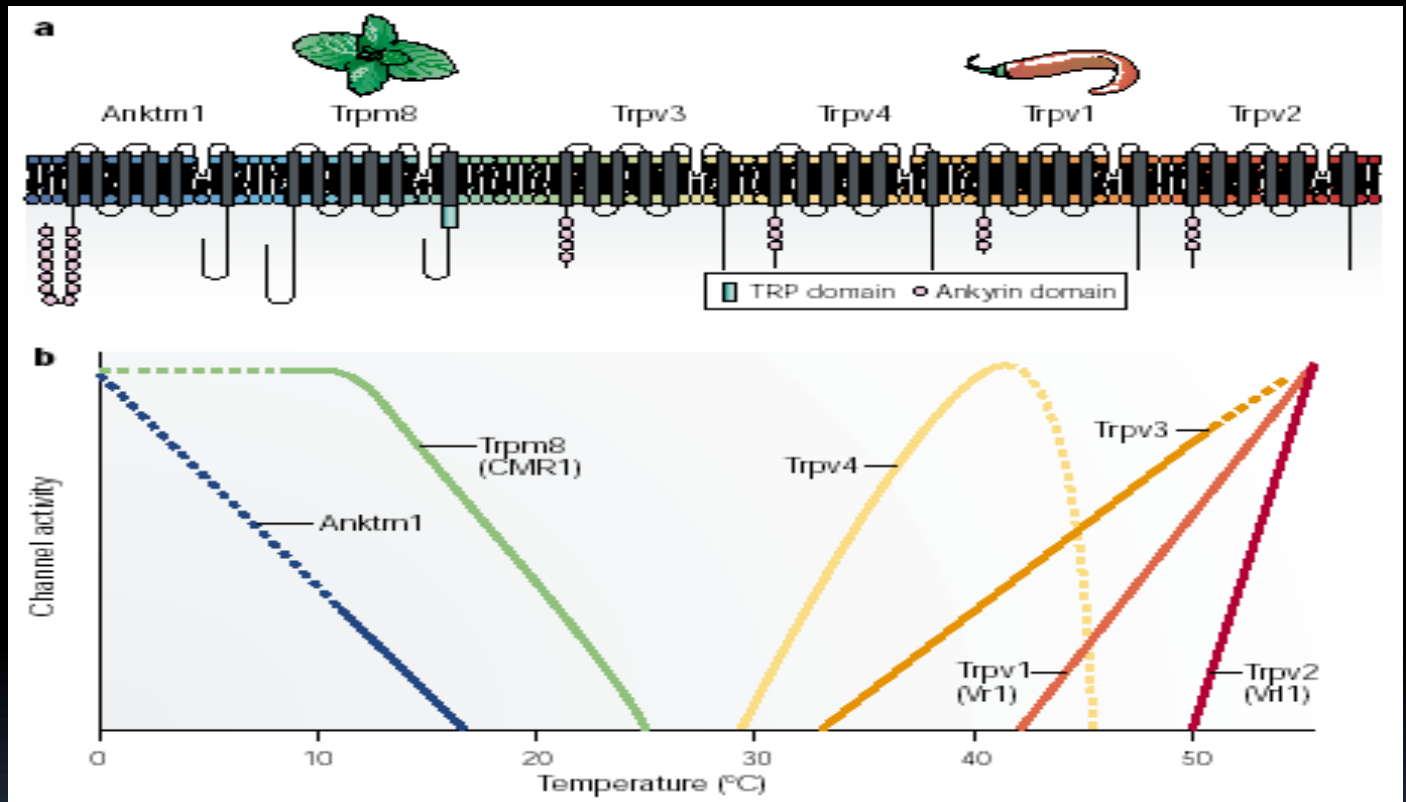
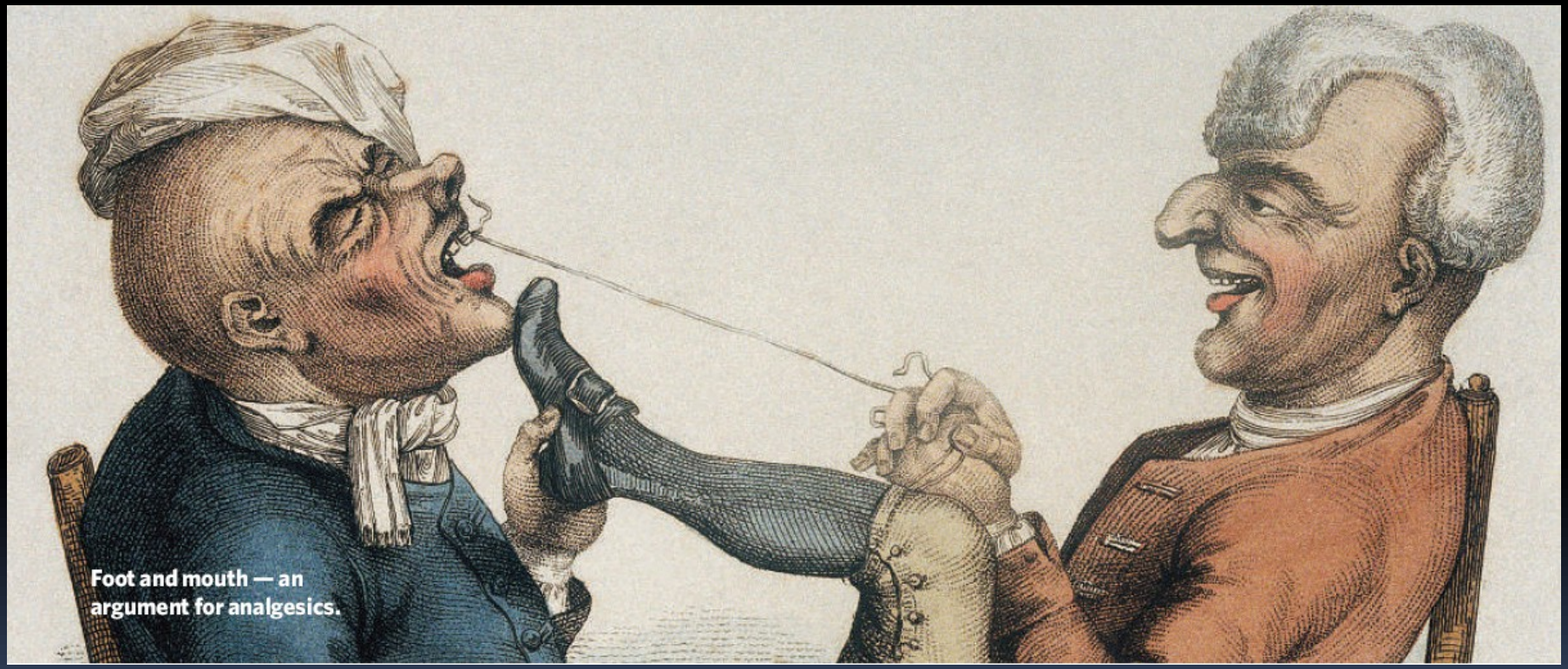


Figure 3 | **Domain organization and temperature thresholds of temperature-activated transient receptor potential ion channels (thermoTRPs).** a | TRP channels are composed of six putative membrane-spanning units and cytoplasmic amino and carboxyl termini. Some TRPs also have variable numbers of ankyrin repeats at the amino terminus, or a conserved TRP domain of 25 amino acids after the transmembrane regions. b | Temperatures ranging from noxious heat to noxious cold activate several members of the TRP family. The cooling compound menthol and capsaicin (the hot ingredient of chilli pepper) act as non-thermal activators of Trpm8 and Trpv1, respectively. The thresholds of activation and maximal activation are based on activity of these channels in heterologous systems; some of these thresholds are averaged values from different studies. Dashed lines indicate an uncertainty in the exact slope of the lines.

Nocicepce – vnímání bolesti



V případě zraku nebo čichu potřebují primární neurony jediný druh stimulu. Nocicepce je jiná v tom, že primární neurony dráhy bolesti mají schopnost detekovat širokou škálu modalit včetně chemické a fyzikální povahy. Musí být tedy vybavena rozmanitým repertoárem transdukčních zařízení.

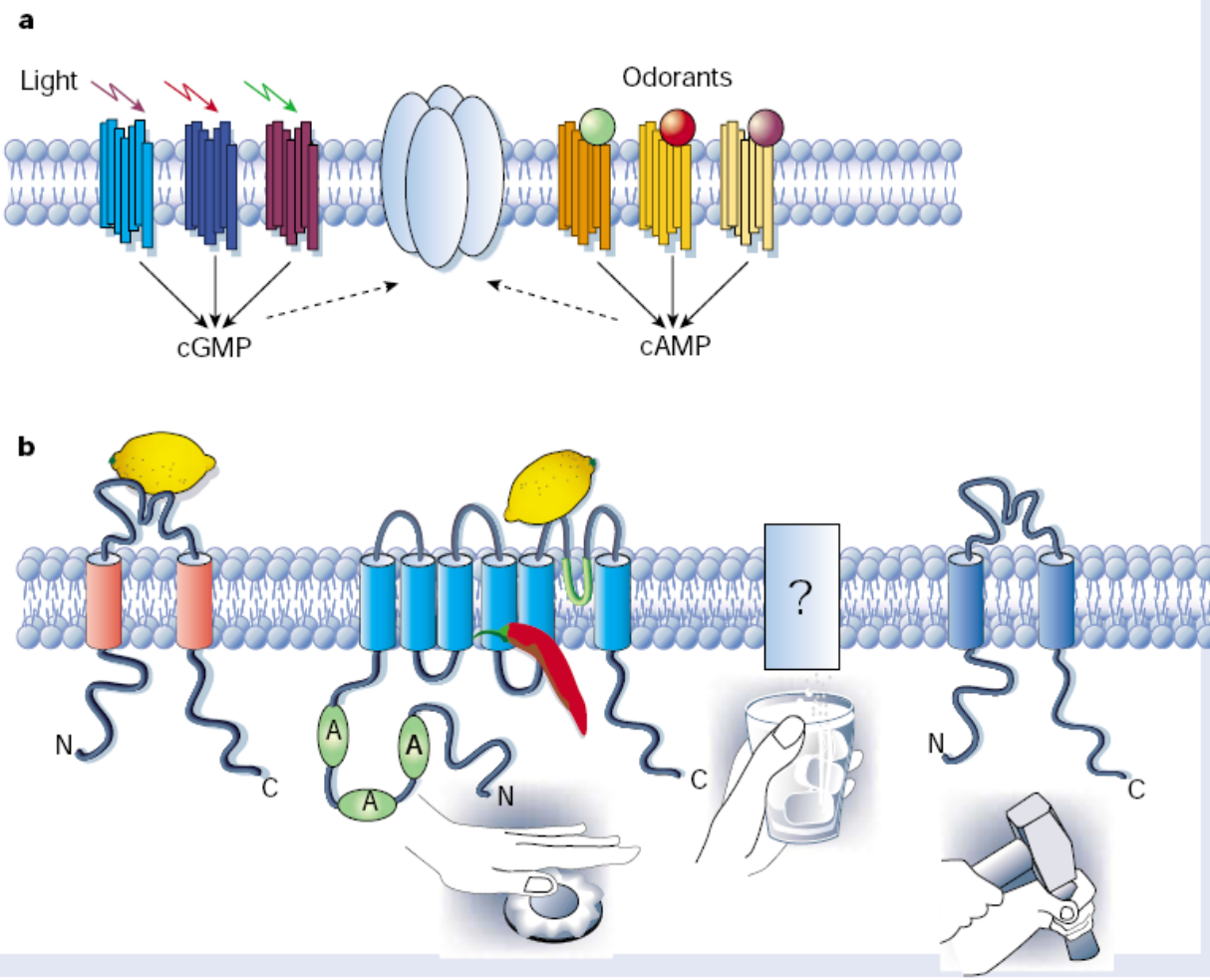
Na rozdíl od zraku chuti nebo čichu nejsou nervová zakončení pro bolest lokalizována v nějaké anatomické struktuře, ale jsou rozptýlena po celém těle, v kůži, svalech, kloubech vnitřních orgánech.

Jsou různé typy vláken, o kterých se předpokládá, že vedou různou rychlostí a zprostředkovávají akutní, ostrou prudkou bolest a jiná difúzní, pozdní bolest tupou.

Receptory jsou obvykle polymodální, odpovídající jak na teplotu, tak na mechanické a chemické stimuly a na poranění tkáně. Odpověď na horko je jednou z nejprostudovanějších bolestivých odpovědí.

Na rozdíl od čichu nebo fotorecepce polymodalita nociceptorů – chemické, fyzikální i teplotní stimuly
Receptory jsou rozptýleny po celém těle

Figure 2 Polymodal nociceptors use a greater diversity of signal-transduction mechanisms to detect physiological stimuli than do primary sensory neurons in other systems. **a**, In mammals, light or odorants are detected by a convergent signalling pathway in which G-protein-coupled receptors modulate the production of cyclic nucleotide second messengers, which then alter sensory neuron excitability by regulating the activity of a single type of cation channel. **b**, In contrast, nociceptors use different signal-transduction mechanisms to detect physical and chemical stimuli. Recent studies suggest that TRP-channel family members (VR1 and VRL-1) detect noxious heat, and that ENaC/DEG-channel family detect mechanical stimuli. Molecular transducers for noxious cold remain enigmatic. Noxious chemicals, such as capsaicin or acid (that is, extracellular protons) may be detected through a common transducer (VR1), illustrating aspects of redundancy in nociception. At the same time, a single type of stimulus can interact with multiple detectors, as shown by the ability of extracellular protons to activate not only VR1, but also ASICs, which are also members of the ENaC/DEG-channel family.



Jste li u zubaře a necháte-li si aplikovat anestezi, anestetika blokují všechny napěťově řízené sodíkové kanály. To zablokuje jakékoliv čití a i motorické funkce. Nyní však byly objeveny sodíkové kanály, které jsou pouze v neuronech vnímajících bolest. To je výzva pro farmaceutické laboratoře, aby našly „kouzelnou kulku“ selektivně na ně.

TRPV1 kanál, který je otevírán kapsaicinem, nebo teplotami nad 42°C se vyskytuje pouze na nociceptorech! Takže jeho blokáda způsobí anestezii bez paralýzy.

Shepherd, Smell…