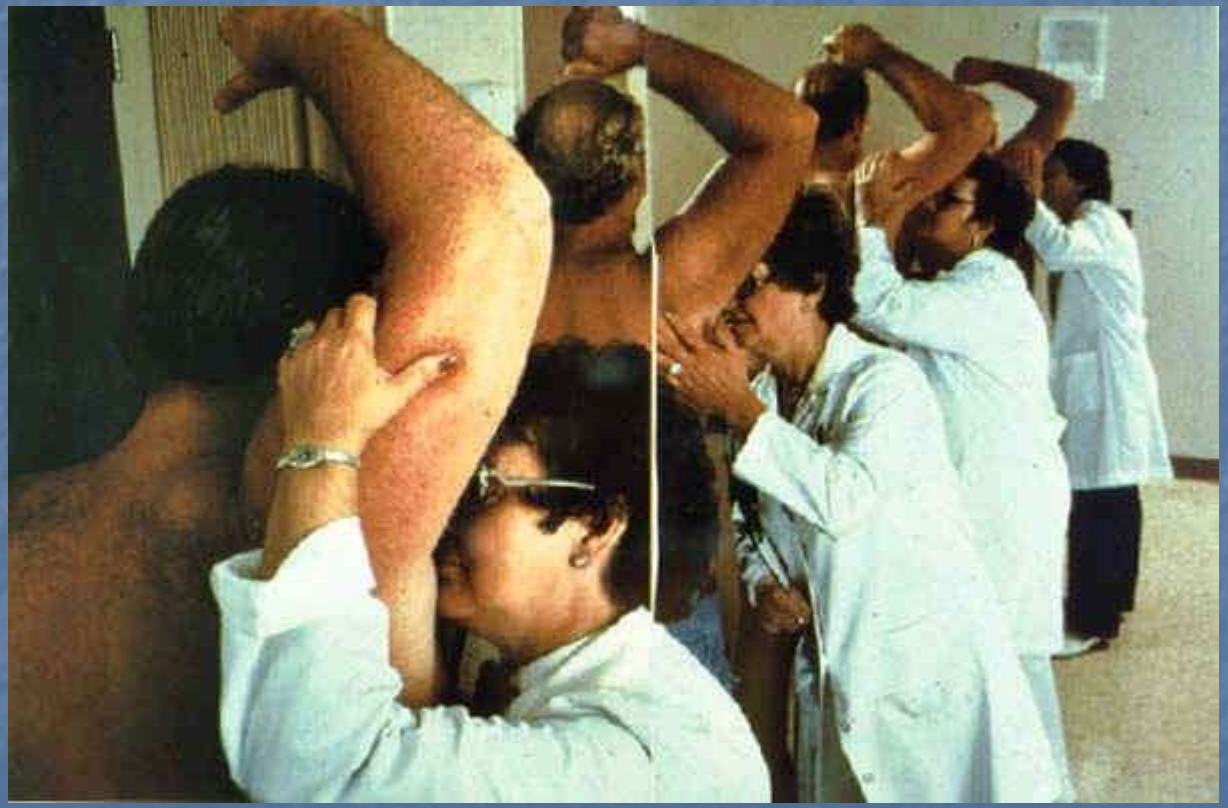
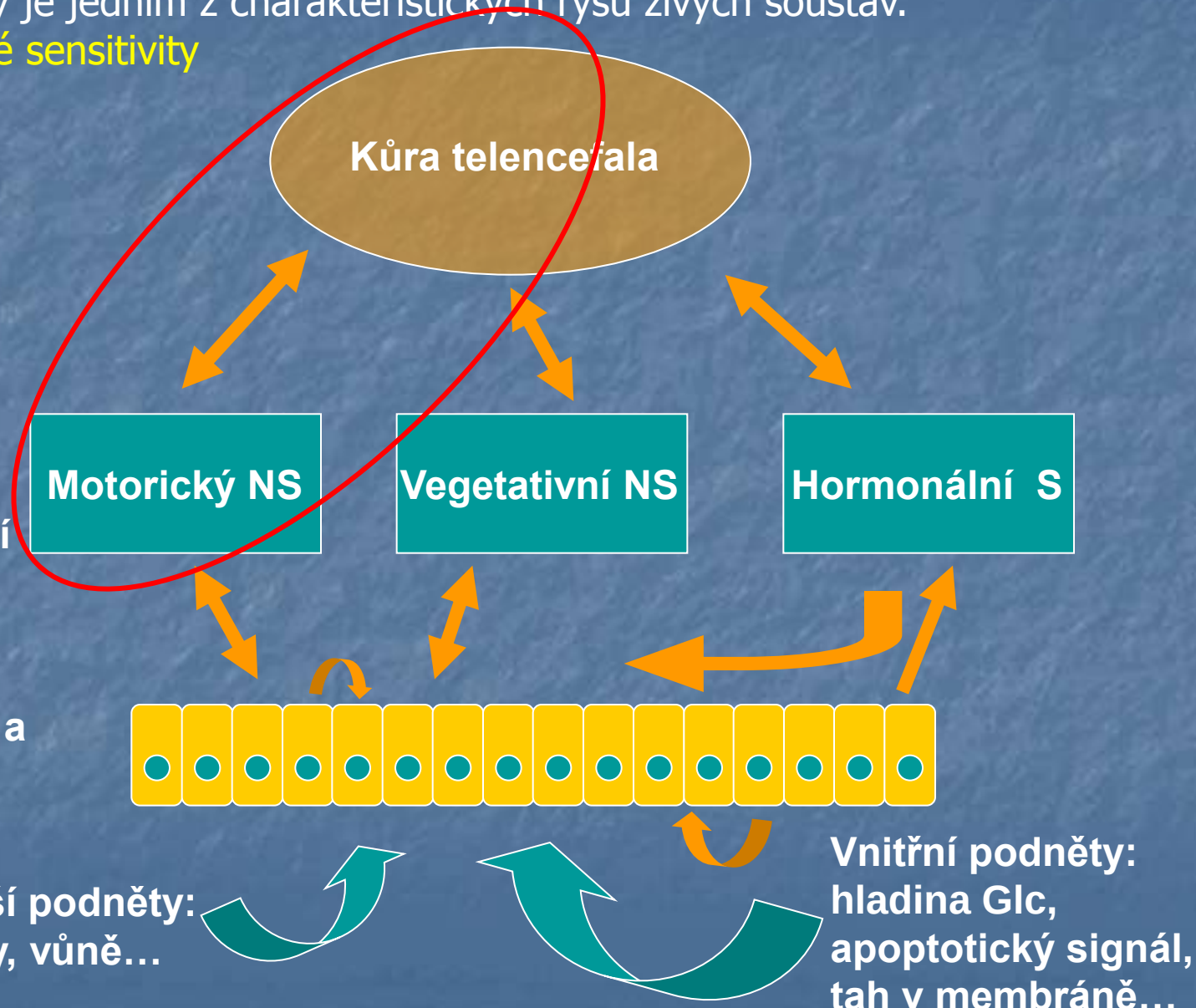
Chemorecepce



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.

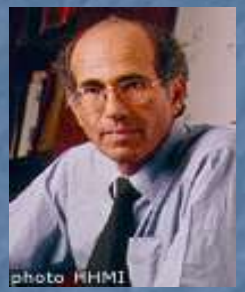
Využití membránové sensitivity ve službách celku:



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

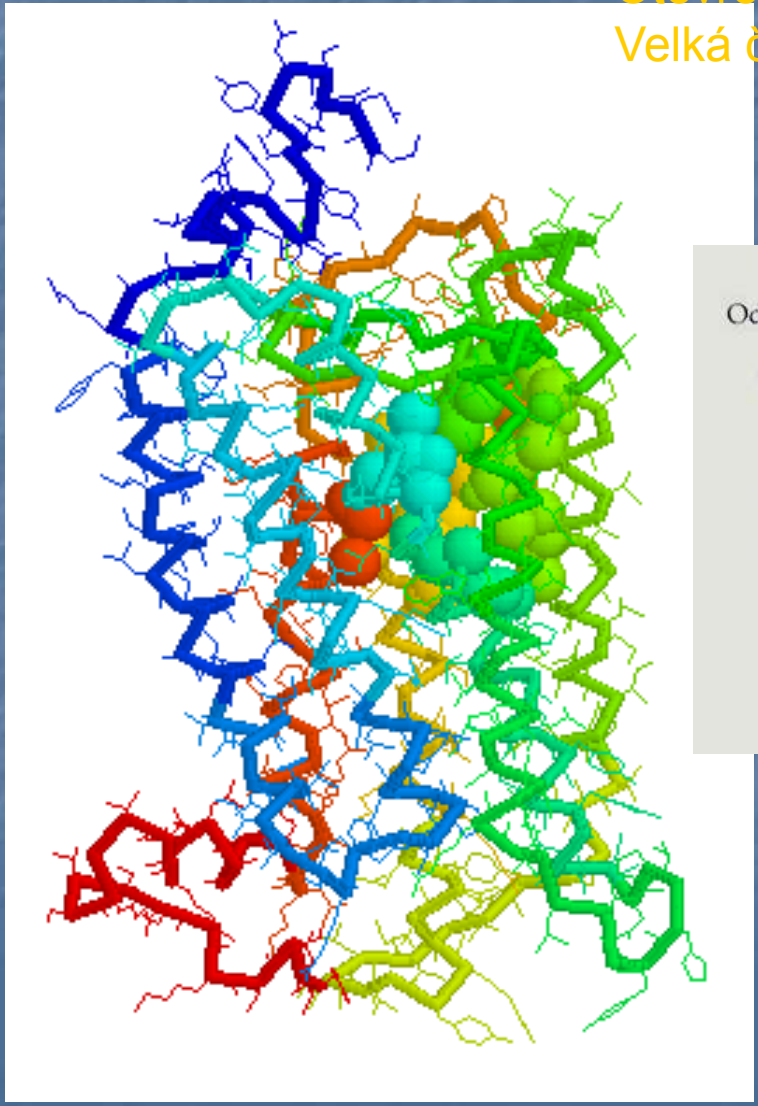
1/2 of the prize

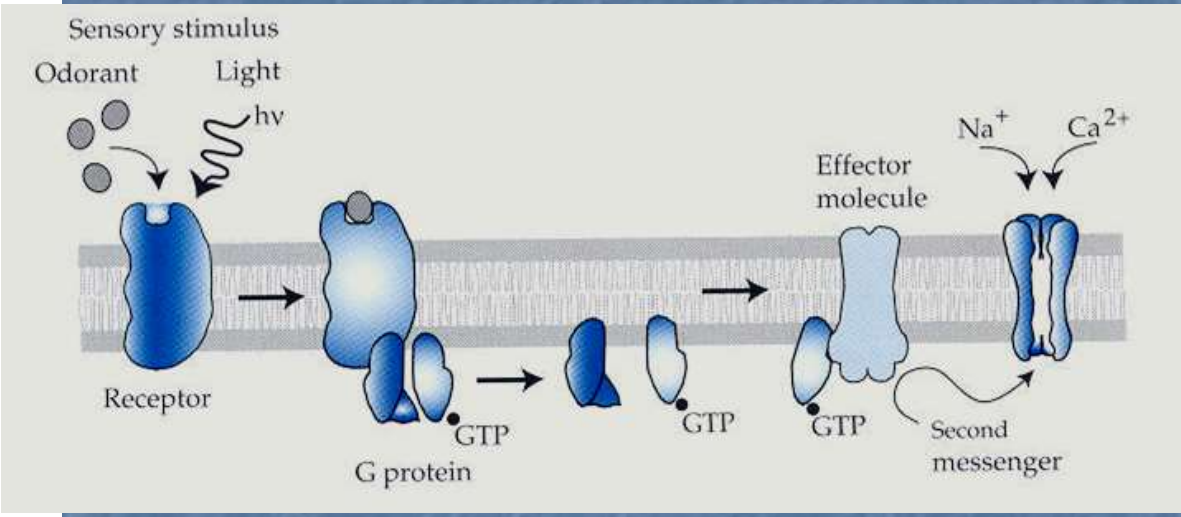
USA

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

b. 1947

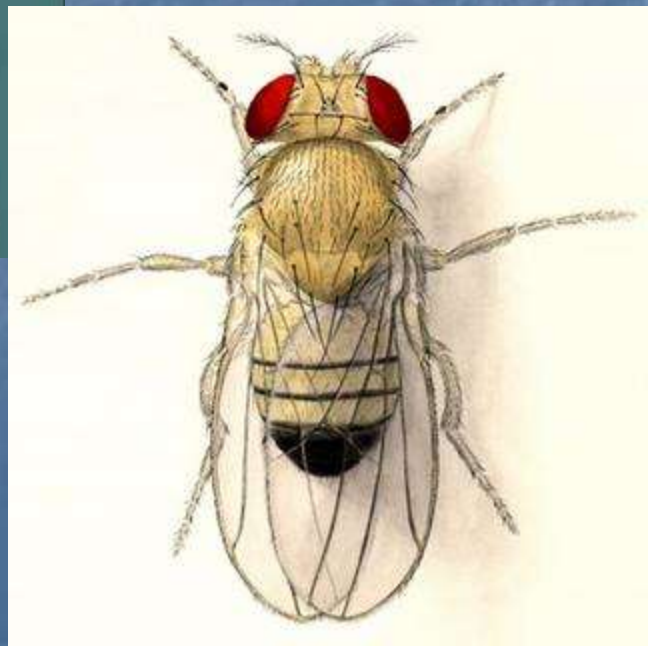
Čich - Distanční chemorecepce
Modelový objekt pro mnoho dalších signálových drah
7TM receptory
Metabotropní signalizace prostřednictvím G proteinů
Otevřený systém podobný imunitnímu
Velká část (4%) genomu věnovaná čichovým receptorům



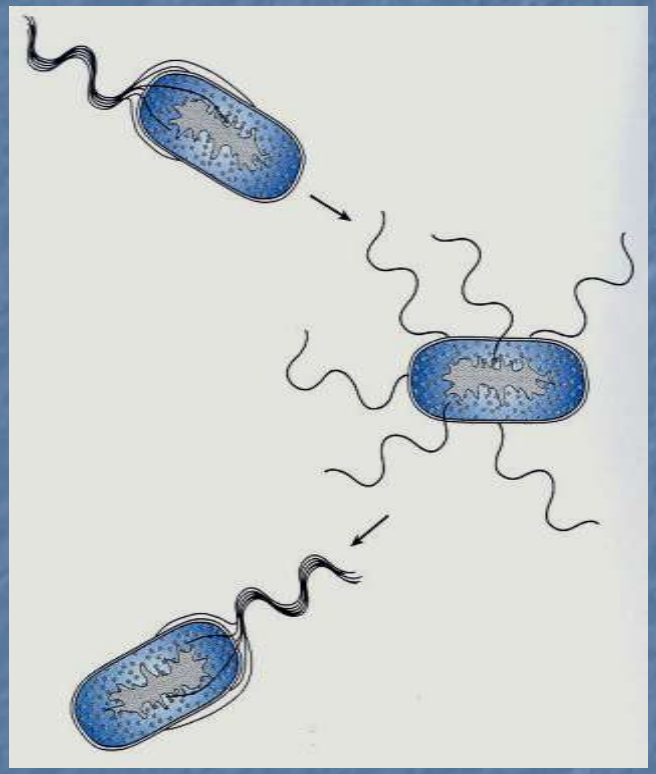


Savci: 1000 genů pro čichové receptory – největší genová rodina
Člověk: 350 funkčních genů
Drosophila: 62

Háďátko 1500 GPCR –
– G prot. coupled rec.



Už u prokaryot chemosensitivita E.coli



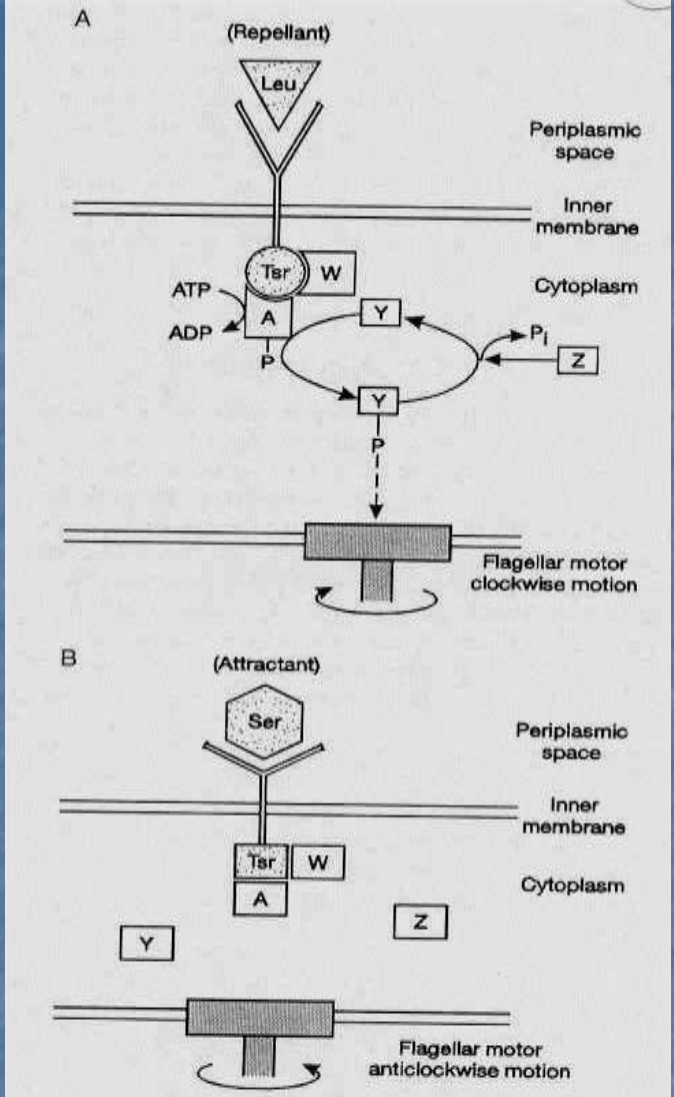
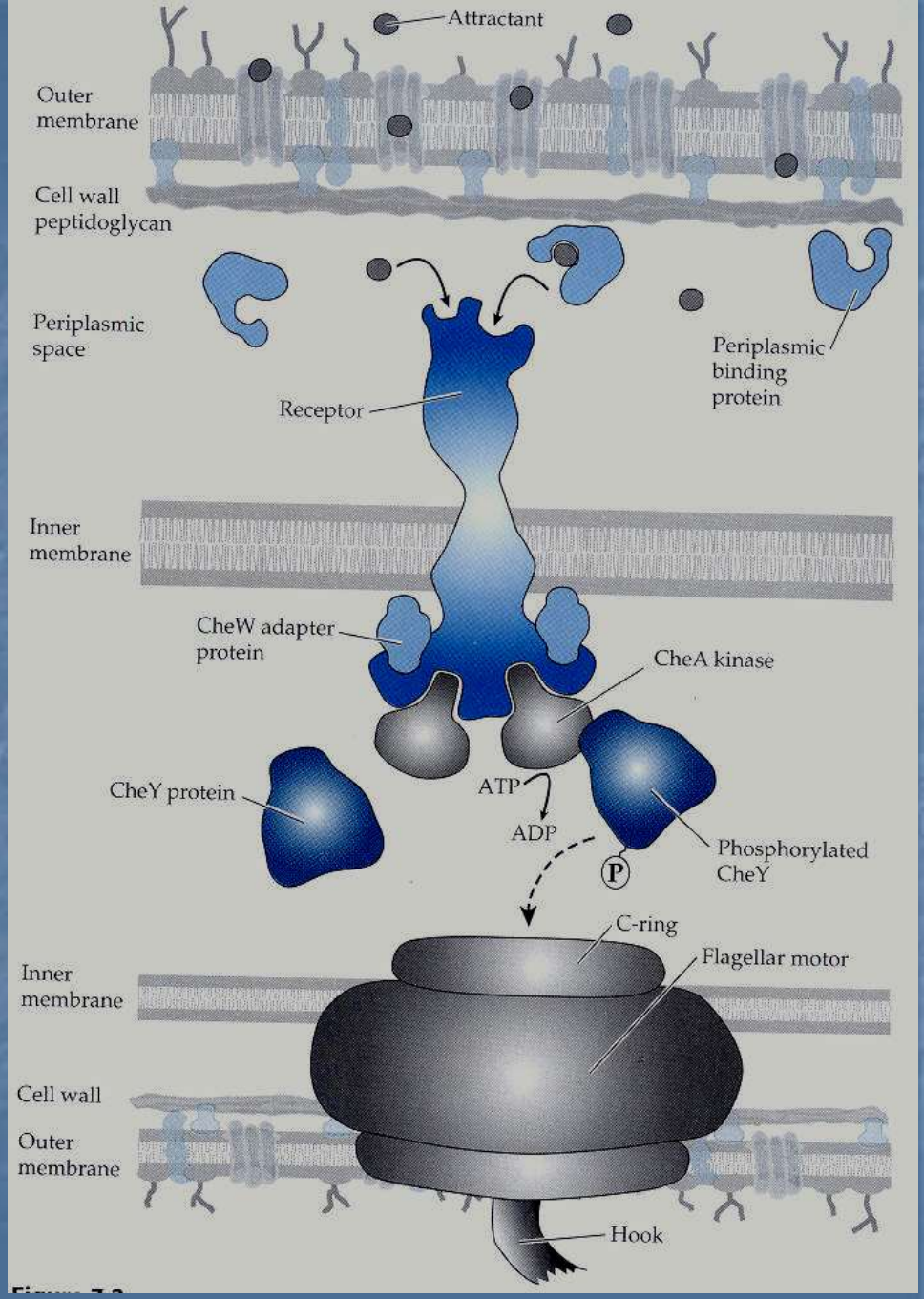


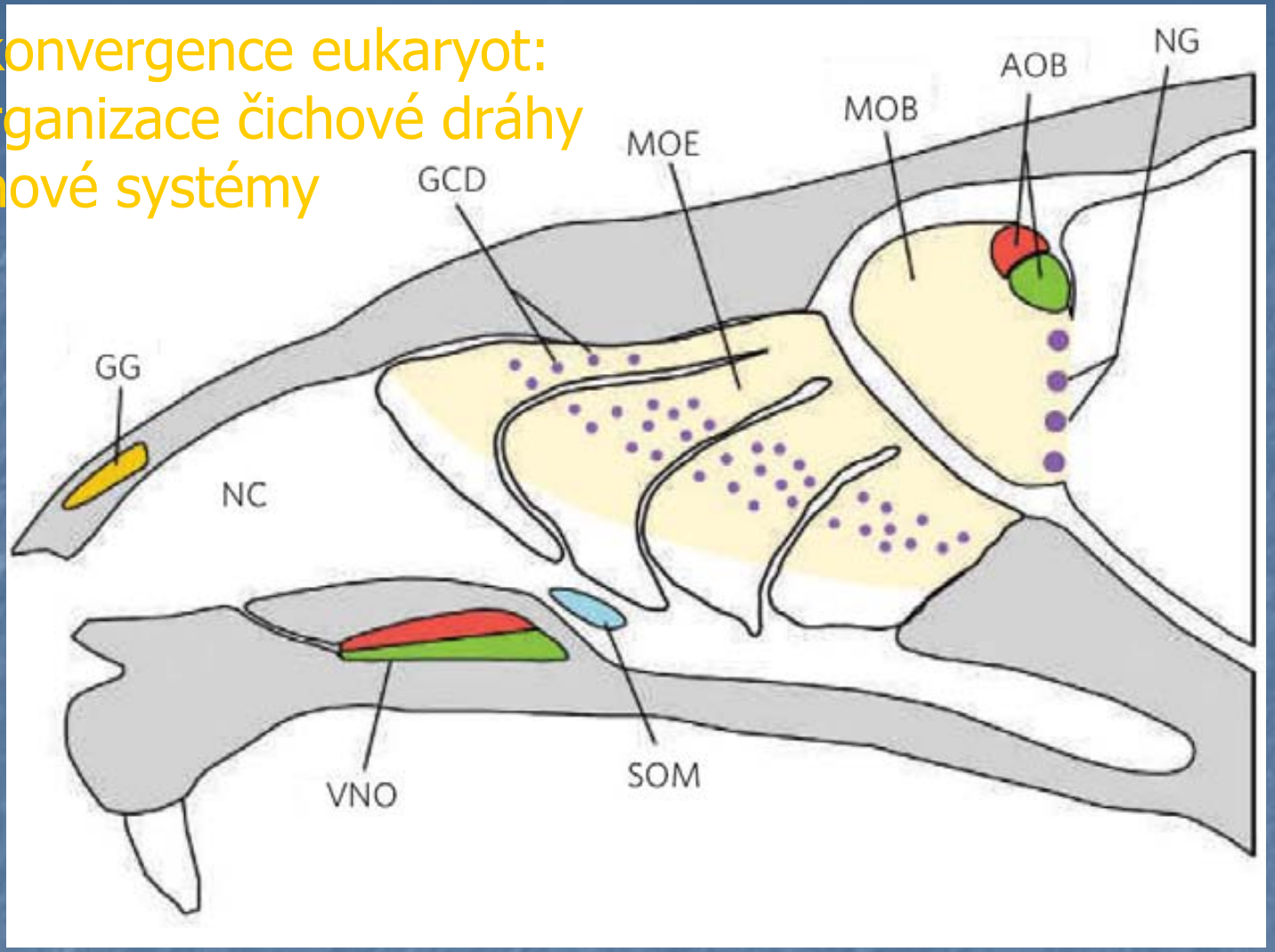
Figure 10.6 Molecular signalling in the *E. coli* chemosensory system. (a) The Tsr receptor-transducer protein accepts a repellant molecule (Leu). CheW and CheA are activated. CheA accepts phosphate from ATP and passes it on CheY. CheY diffuses to the flagellar motor and induces a clockwise rotation 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

E.coli

Zatímco u obratlovců jde o posuny filament proti sobě, u baktérií jde asi o jediný známý biologický případ rotačního pohybu. Konec bičíku na straně buňky rotuje asi 100x za vteřinu mechanismem poháněným transmembránovým gradientem vodíku

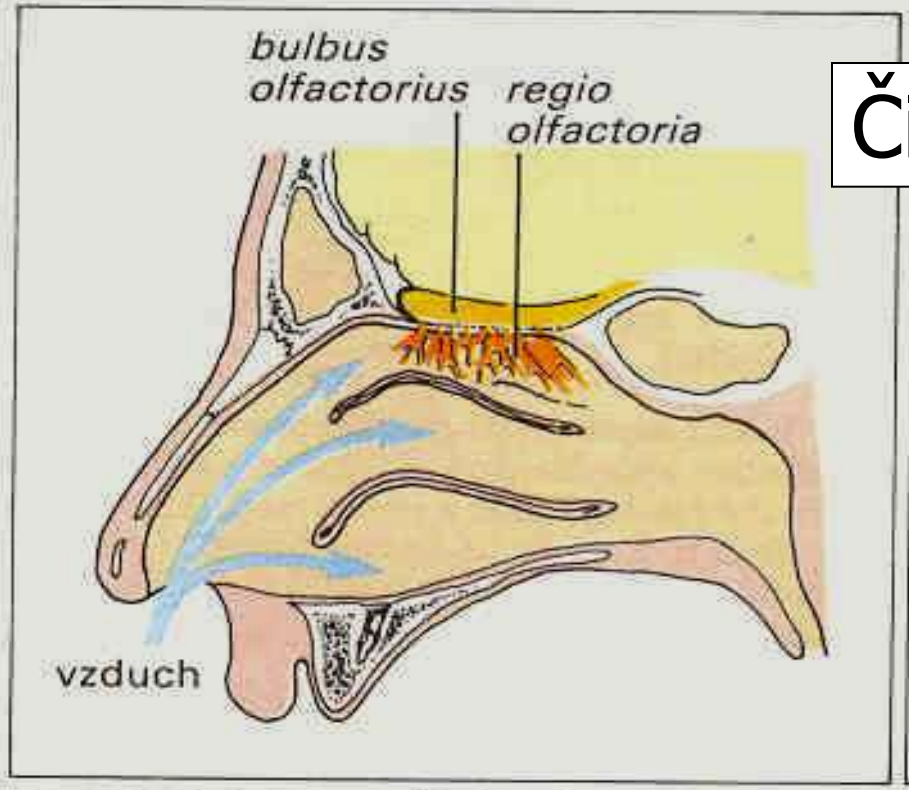


Pozoruhodná konvergence eukaryot: Transdukce, organizace čichové dráhy 2 paralelní čichové systémy

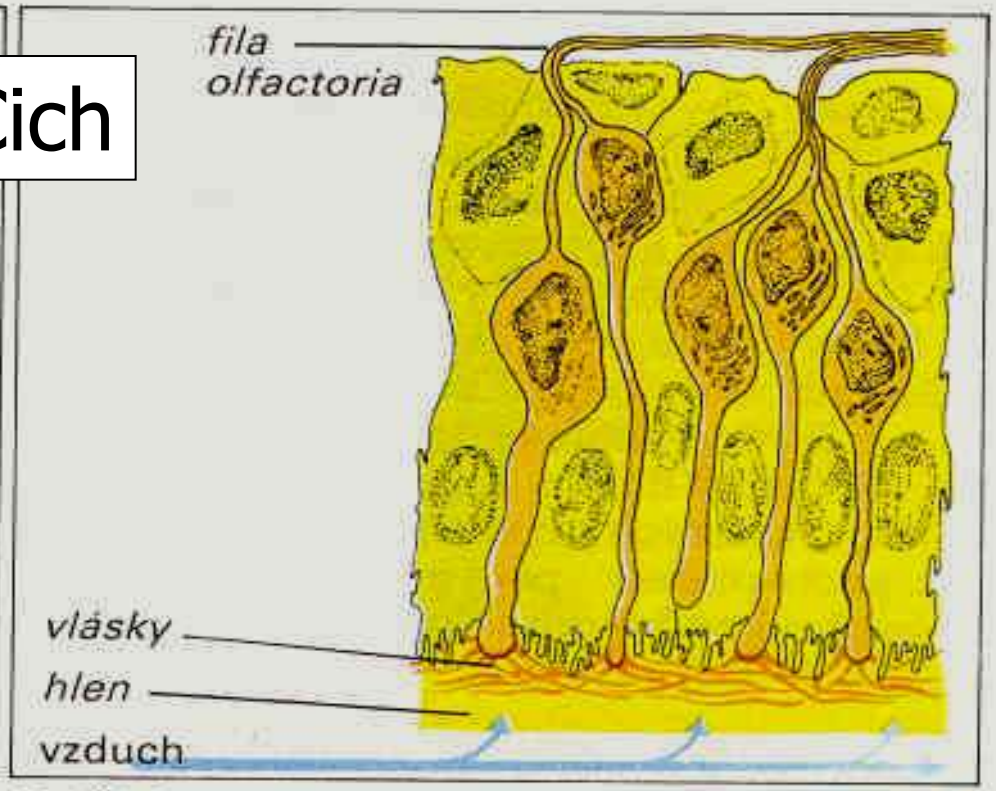


accessory olfactory bulb (AOB).
vomeronasal organ (VNO)
main olfactory epithelium (MOE) consists predominantly of ciliated olfactory sensory neurons (OSNs), which project to the main olfactory bulb (MOB)

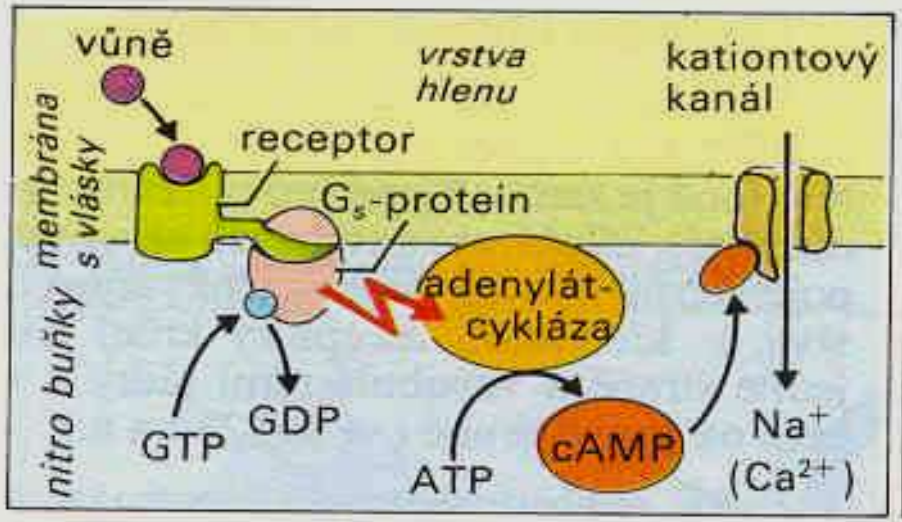
Čich



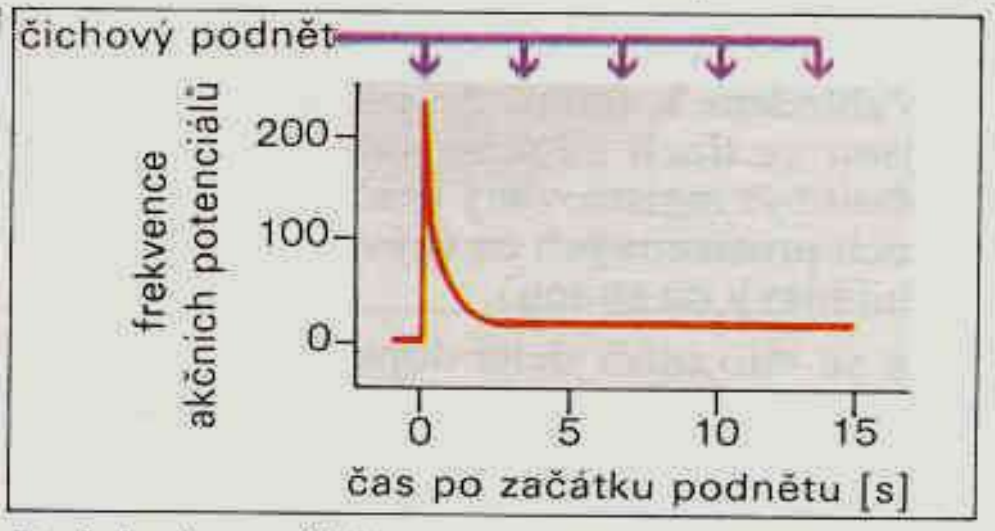
A. Nosní dutina a čichový orgán



B. Čichový epitel (podle Andrese)



C. Transdukce čichového podnětu

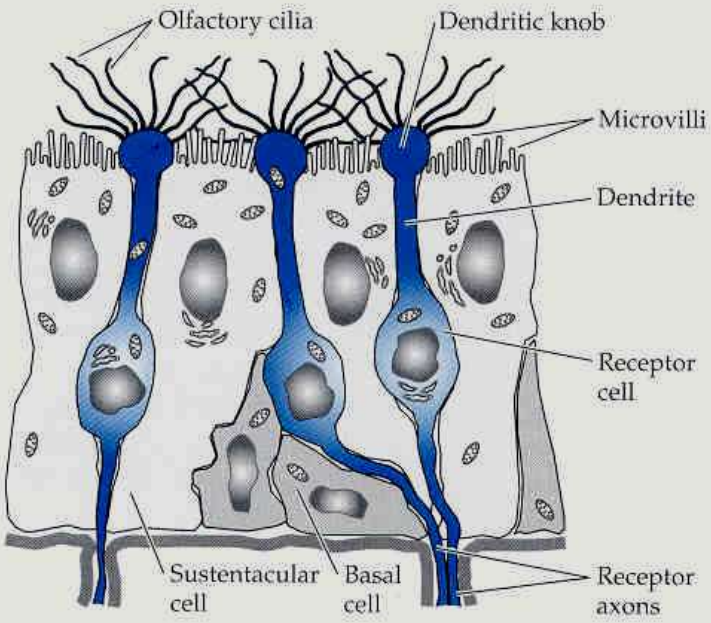


D. Adaptace čichu

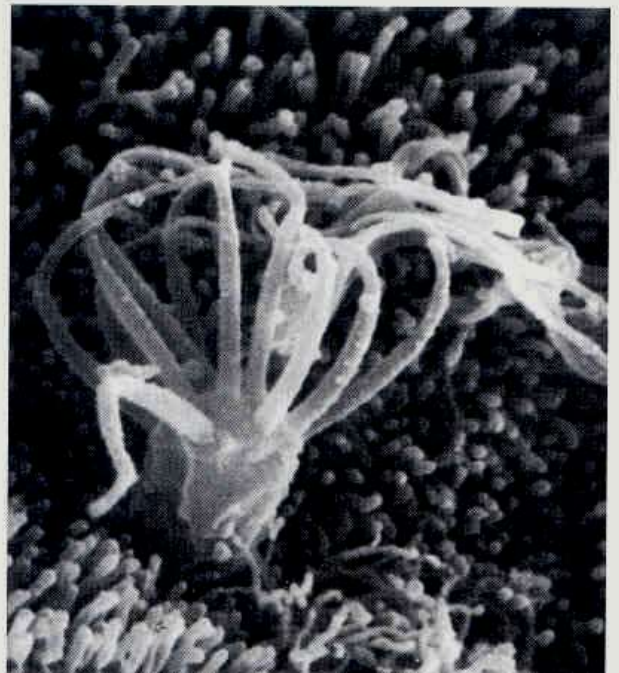
Čichové buňky savců jsou bipolární, primární r., je jich 6-10 milionů, dendrit má na konci 5-20 vlásků - cilií, řasinek.

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.)

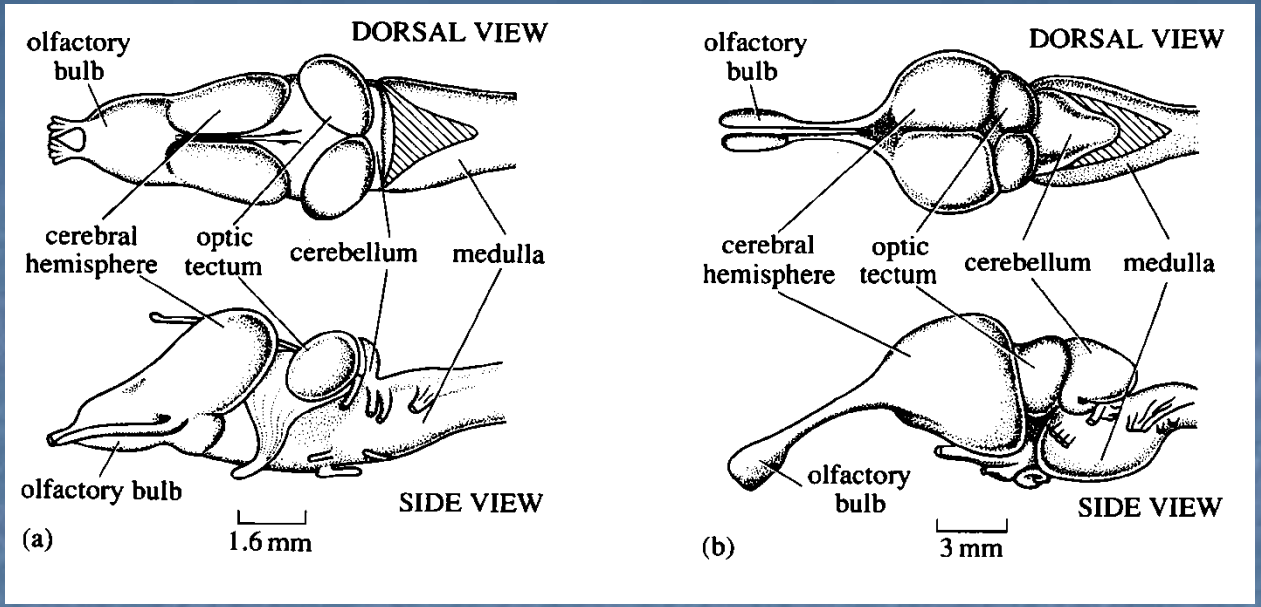
(A)

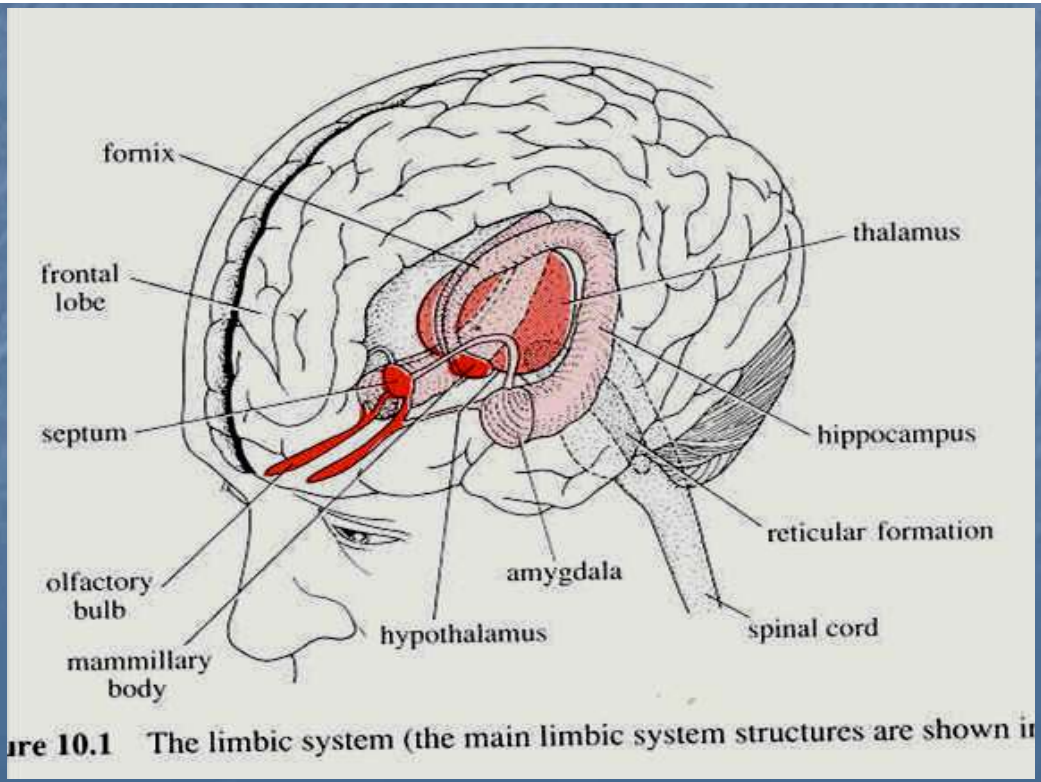


(B)



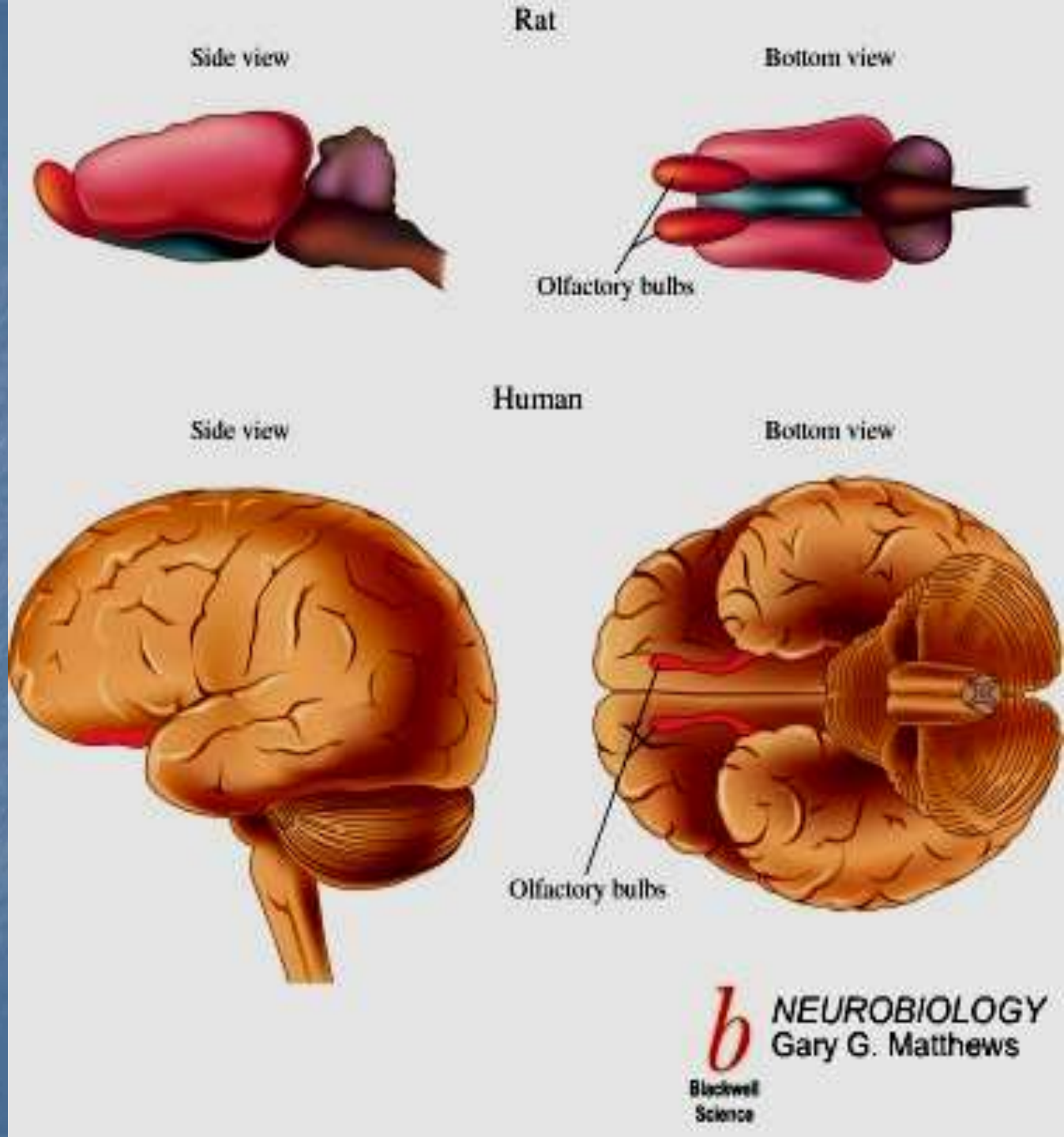
Čichový lalok – součást koncového mozku





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
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 .

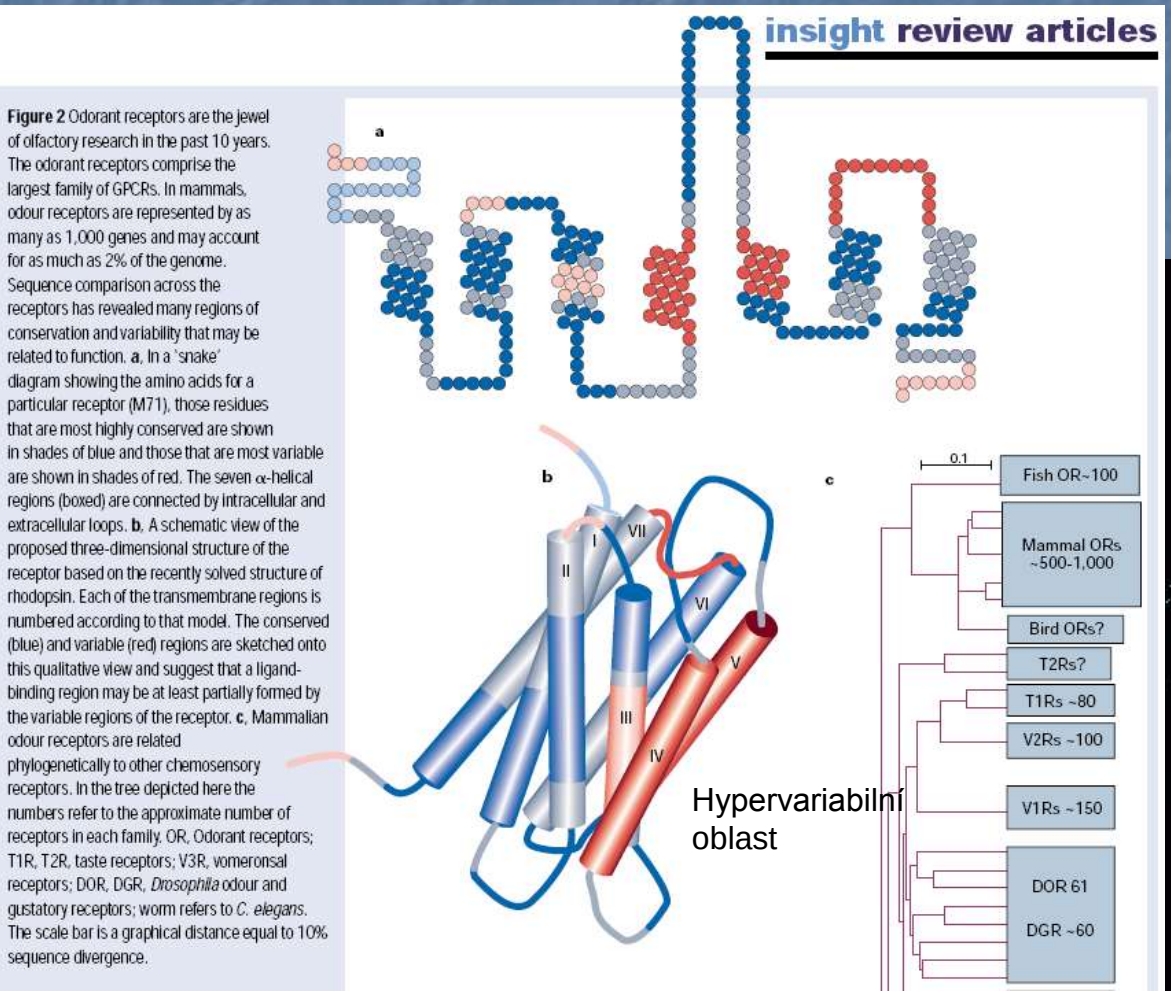
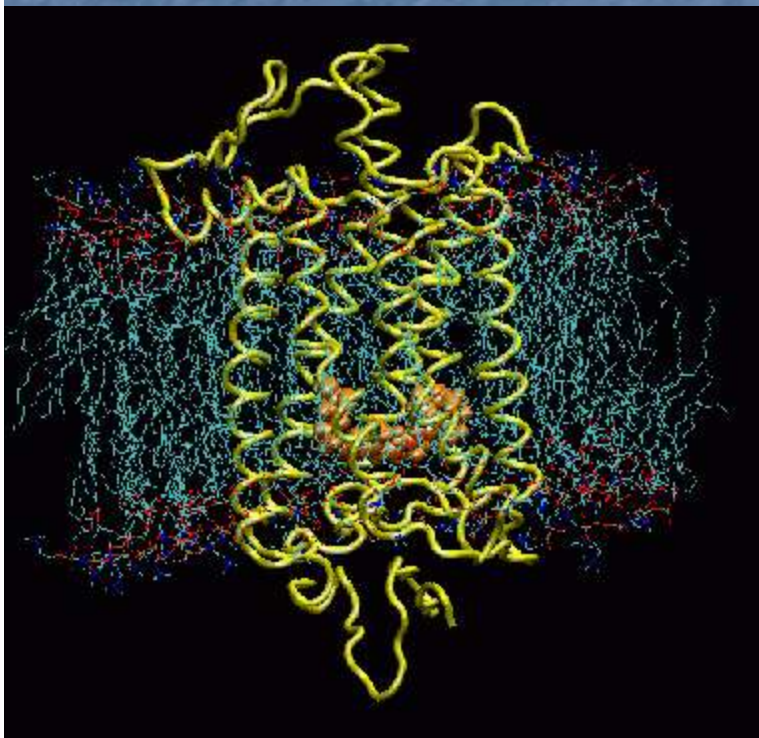
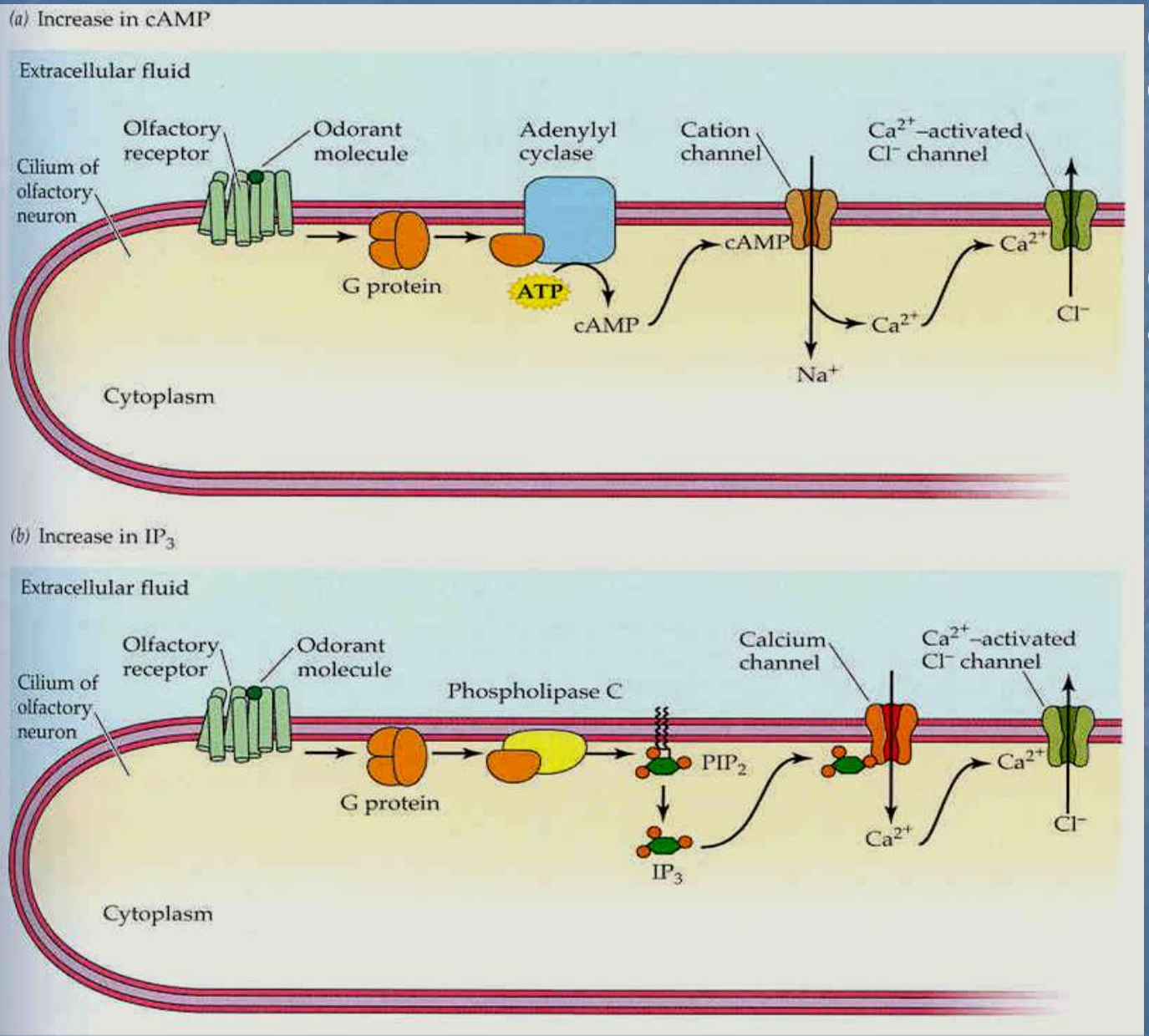


Figure 2 Odorant receptors are the jewel of olfactory research in the past 10 years. The odorant receptors comprise the largest family of GPCRs. In mammals, odour receptors are represented by as many as 1,000 genes and may account for as much as 2% of the genome. Sequence comparison across the receptors 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.

Hypervariabilní oblast



Univerzální mechanismy transdukce



Cl ionty také depolarizují – výjimka kvůli vysoké koncentraci uvnitř

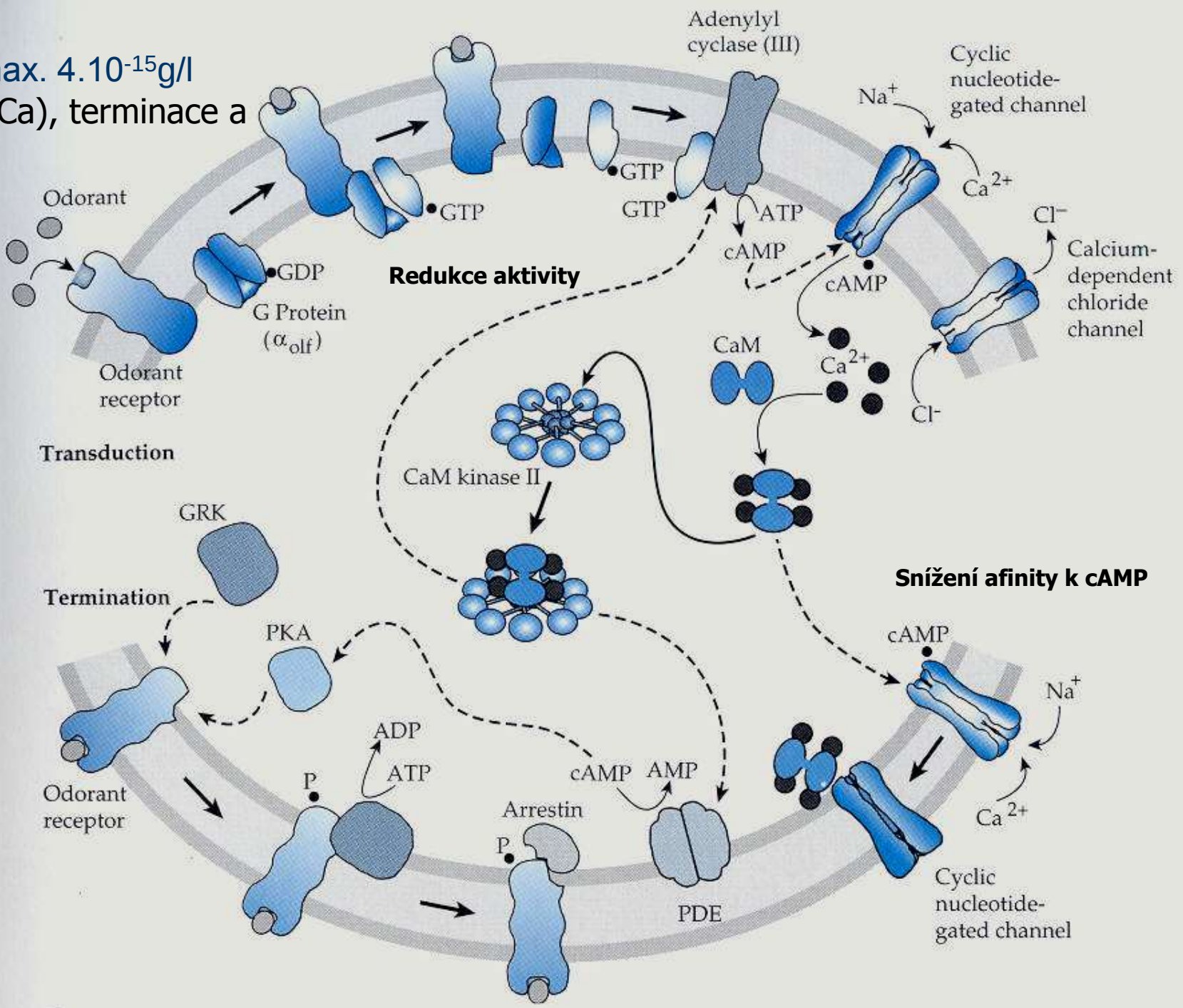
Ca ionty mají i adaptační význam

Aktivace

Zesílení, max. 4.10^{-15}g/l

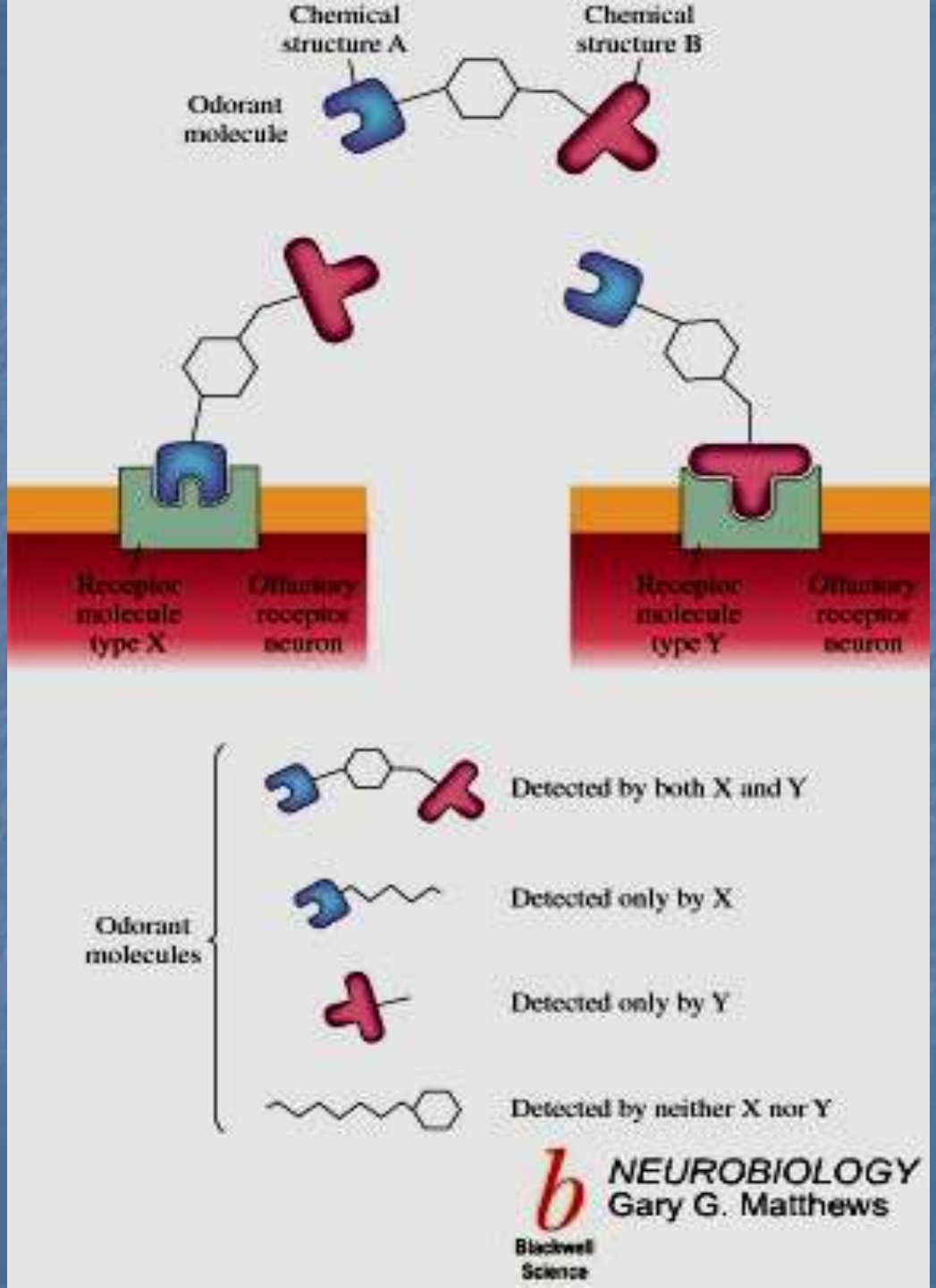
Adaptace (Ca), terminace a modulace

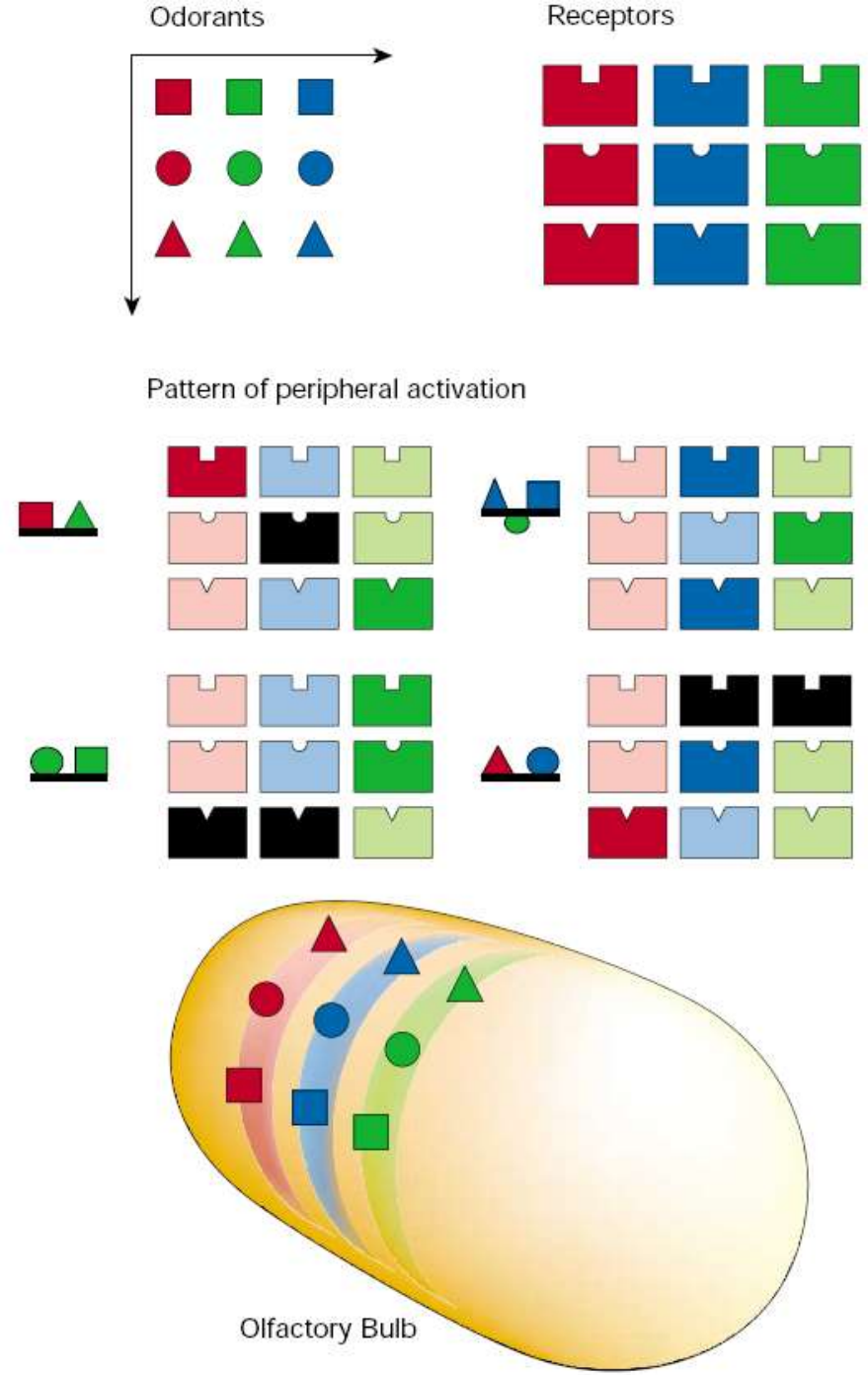
Arestin



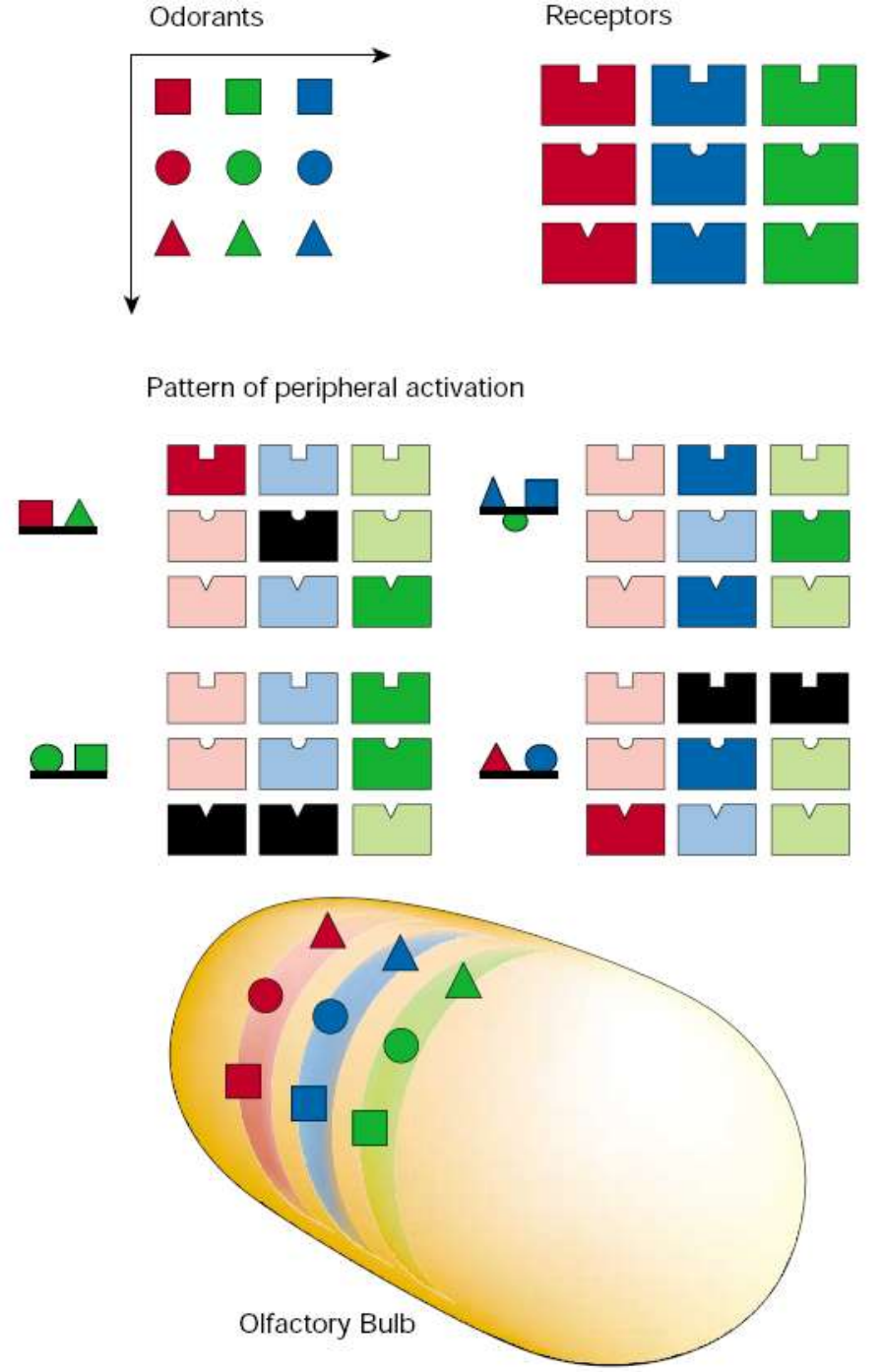
Specializace receptorů
Kombinace cca 350 receptorů
3.000-100.000 vůní (?)

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.



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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.

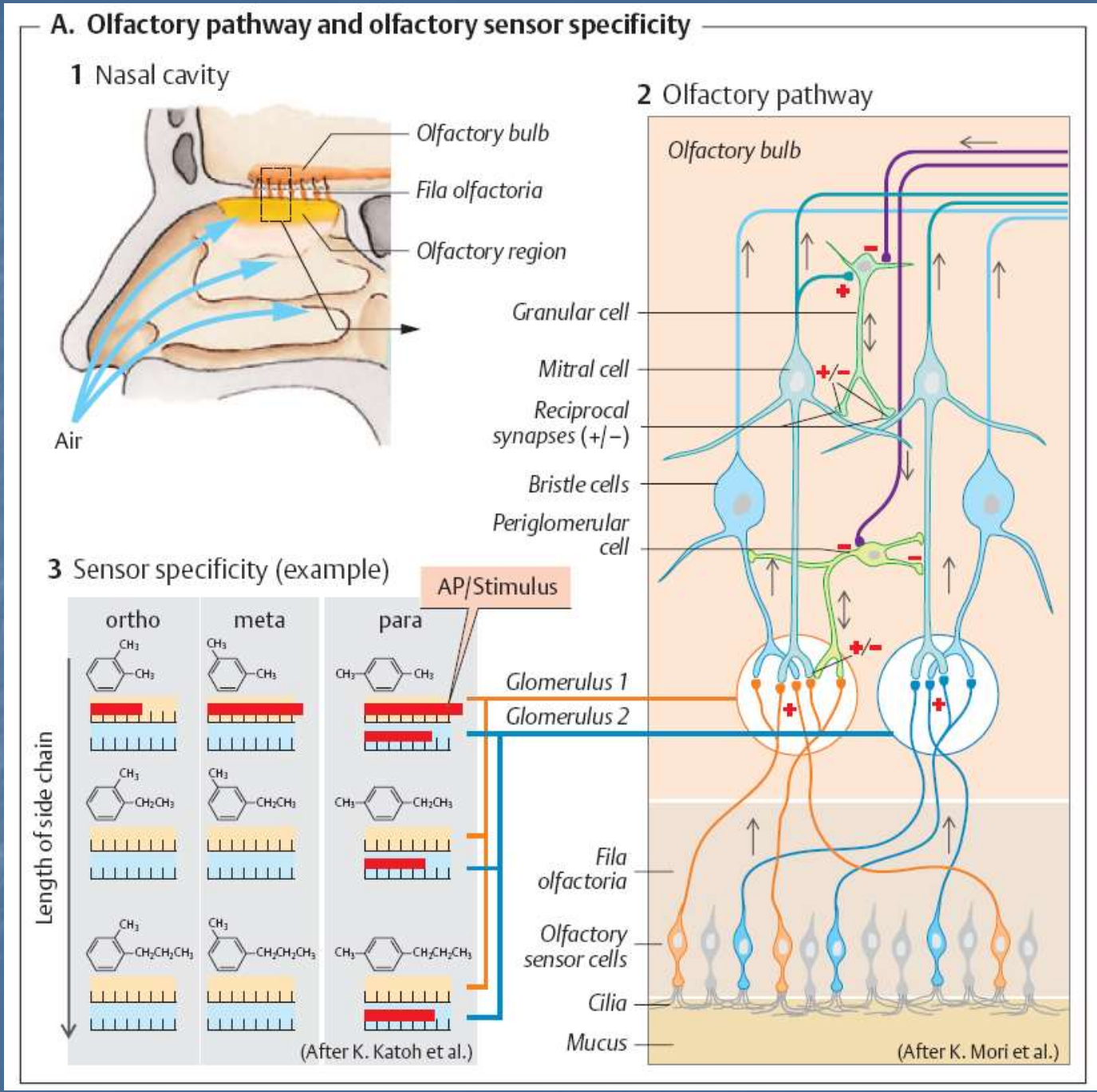
Zajímavé je, že určité vůně jsou stále stejně cítit při 5 řádovém rozdílu intenzit – přitom se přece zapojují i ne úplně naladěné receptory a tedy i receptory pro jiné vůně. Patrně budou existovat široce naladěné receptory měřící pouze intenzitu.

Periferie
čichové dráhy

Rozlišování chem.
Struktury

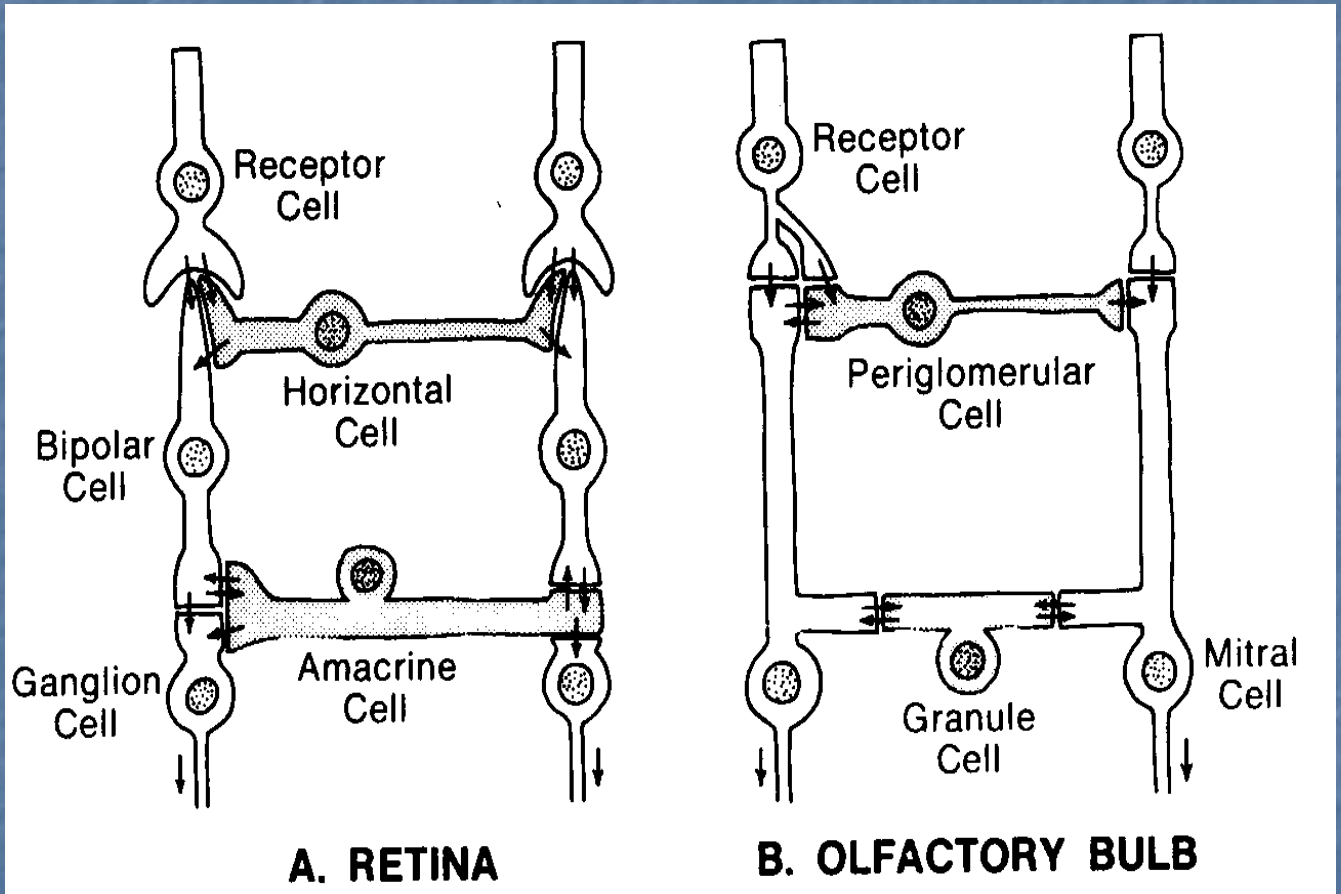
Laterální inhibice
Kontrastování

Eferentní inhibice

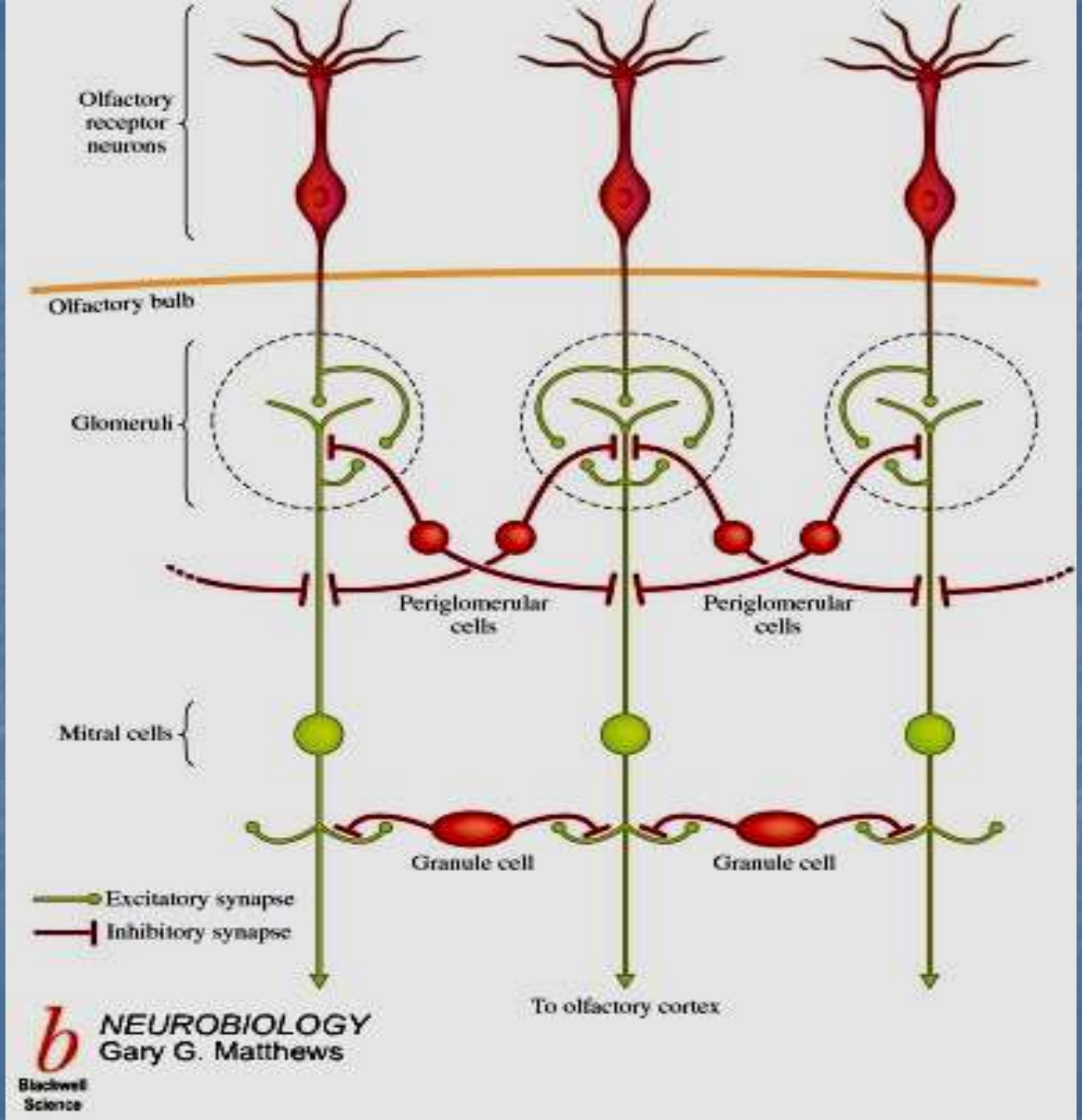


Všechny neurony exprimující určitý receptor, bez ohledu na to, kde je umístěn, na sliznici konvergují na jeden jediné místo na čichovém laloku. Těmito místy jsou glomeruly, kulovité shluky šedé hmoty, asi 50-1000 mikrometrů, sestávající z přicházejících axonů z receptorů a z dendritů mitrálních buněk.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

Podobnost architektury sensorických obvodů a drah



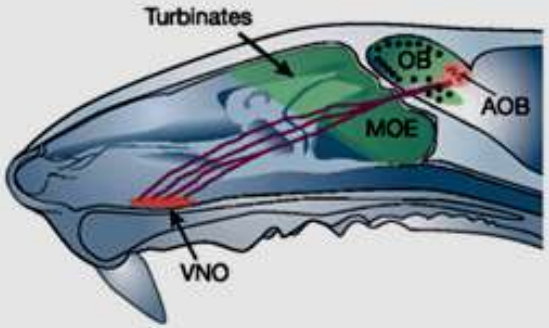
Comparison between simplified basic circuit diagrams of the vertebrate r
bulb. (After Shepherd, 1978)



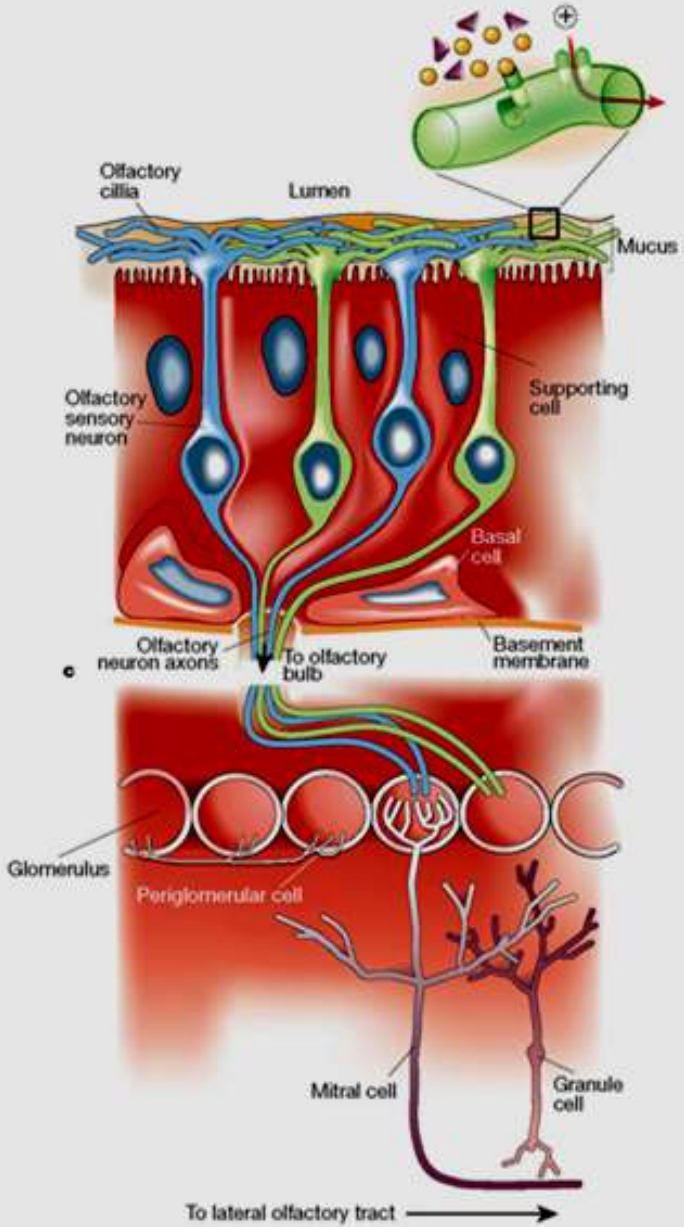
NEUROBIOLOGY
Gary G. Matthews

Blackwell Science

Konvergence na příslušný glomerulus (100 - 1000/1)

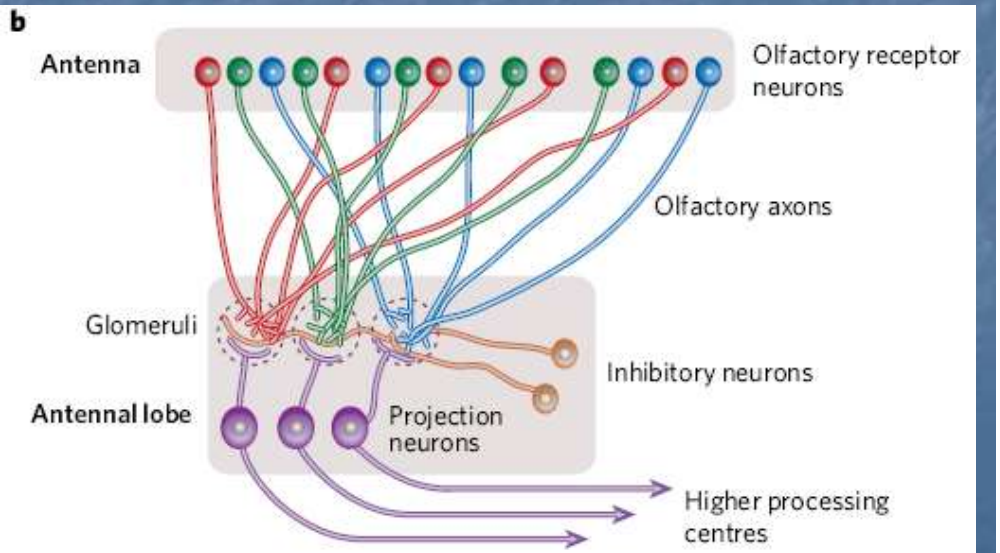


MOE = main olfactory epithelium.
OB = olfactory bulb.
AOB = accessory olfactory bulb.
VNO = vomeronasal organ.



Mapa vůní – vzorec aktivovaných Glomerulů čichového laloku
Specifická „mozaika" aktivace pro konkrétní vůni

Konvergence neprostorového parametru na prostorový



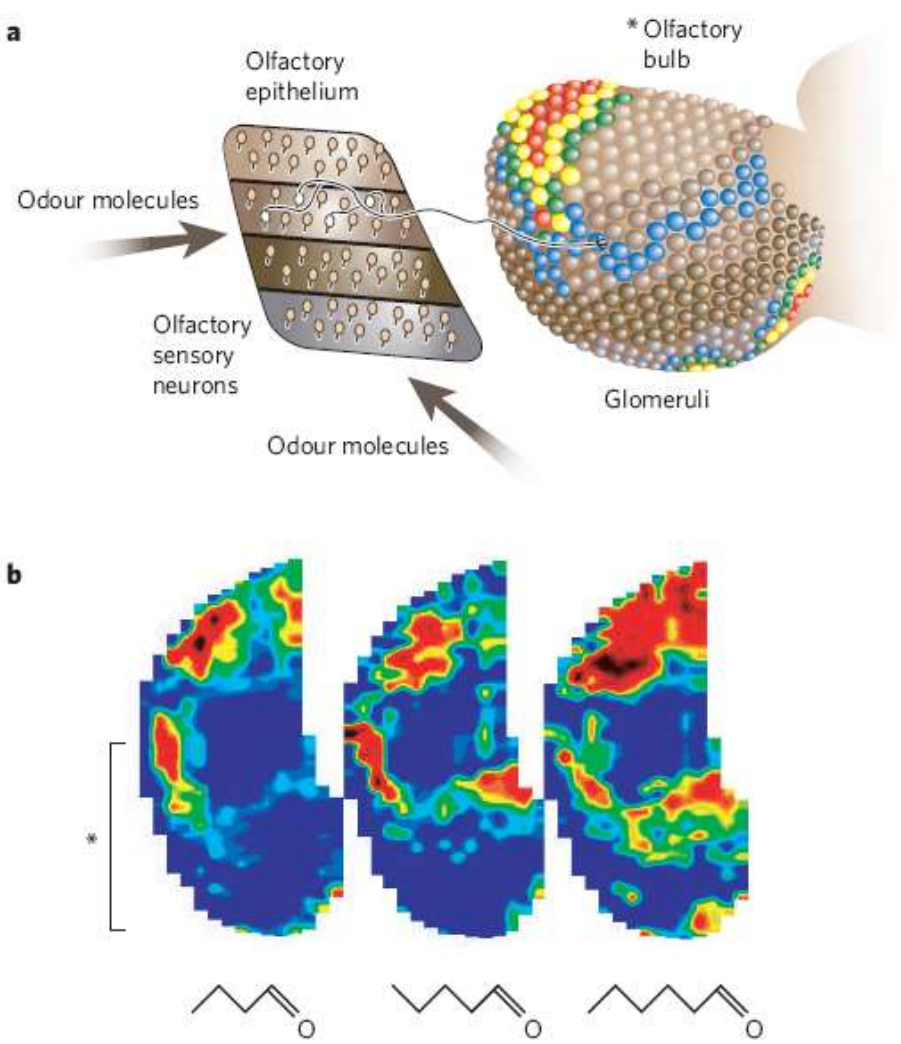


Figure 1 | Odour images in the olfactory glomerular layer. **a**, Diagram showing the relationship between the olfactory receptor cell sheet in the nose and the glomeruli of the olfactory bulb[53]. **b**, fMRI images of the different but overlapping activity patterns seen in the glomerular layer of the 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.)

Podobnost architektury sensorických obvodů a drah

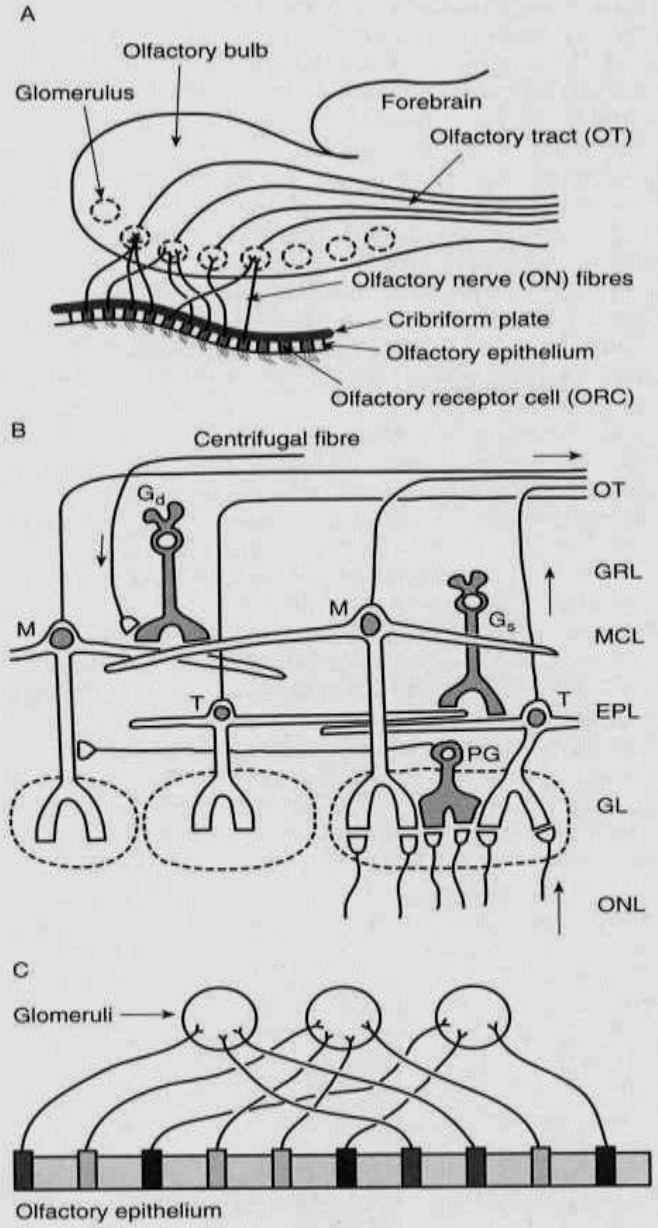
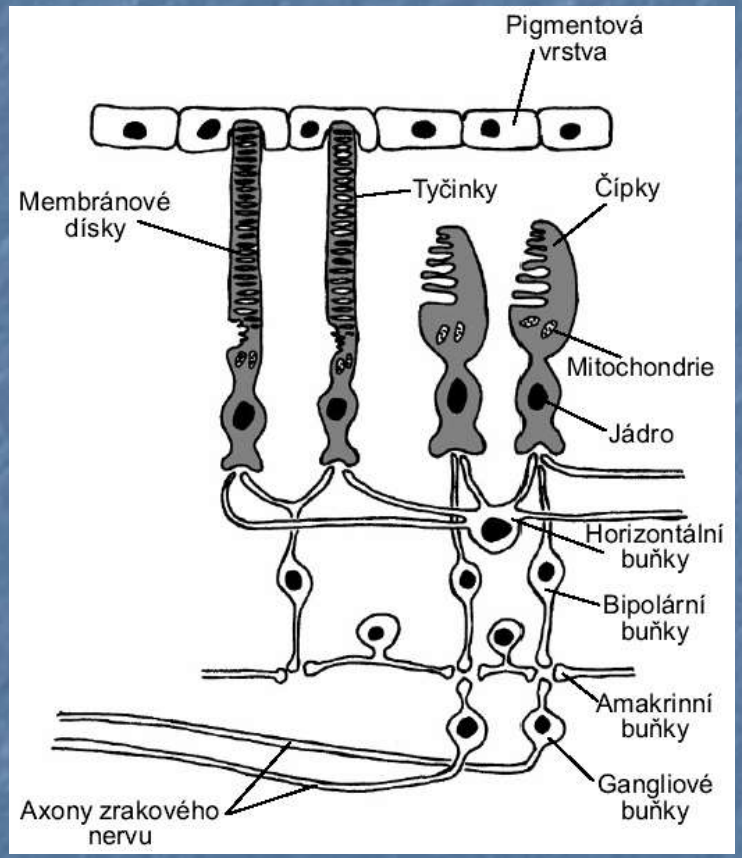


Figure 13.7 Olfactory bulb. (a) The figure shows olfactory axons passing through the cribriform plate to end in glomeruli in the olfactory bulb. (b) Basic circuit of the mammalian olfactory bulb. Layers: EPL = external plexiform layer; GL = glomerular layer; GRL = granule cell layer; OT = olfactory tract; 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

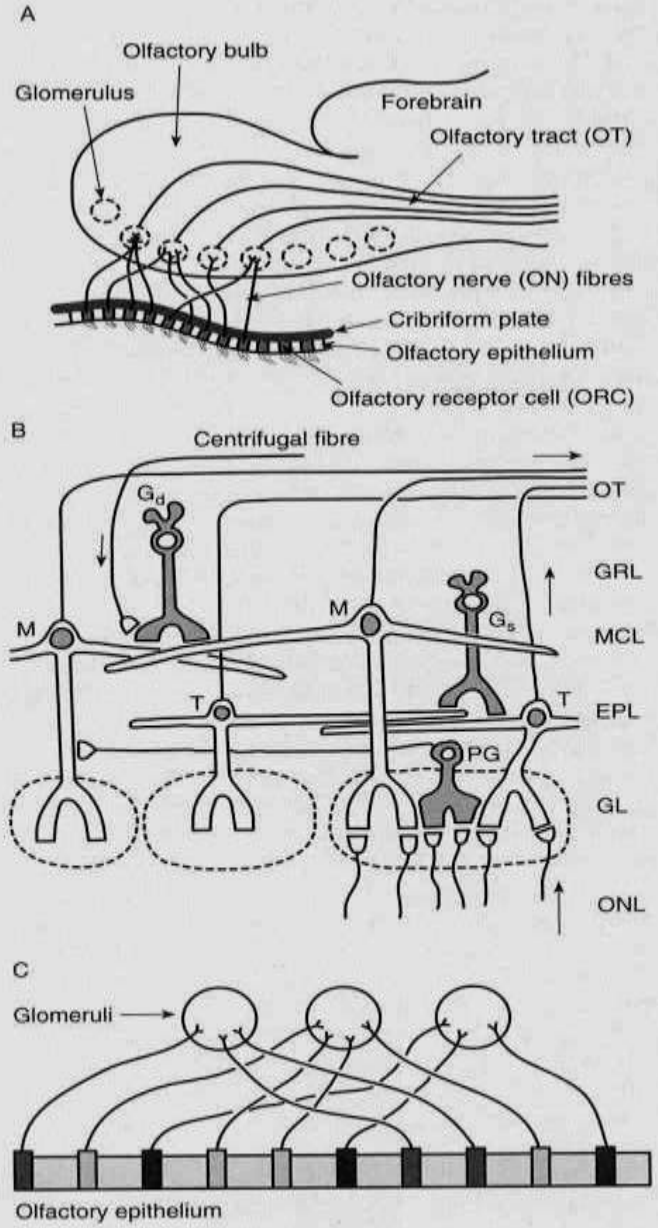
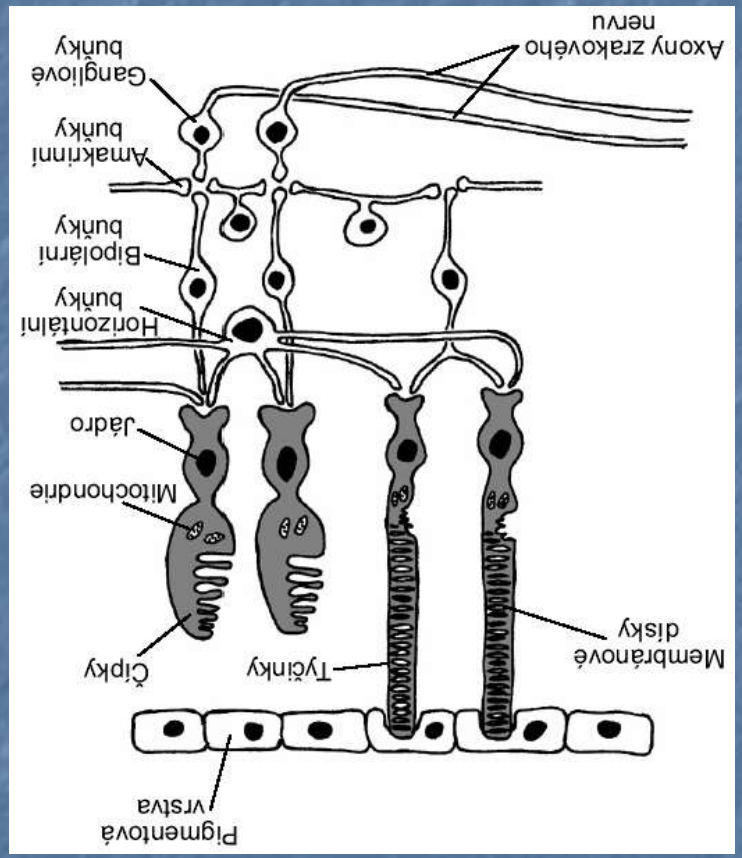
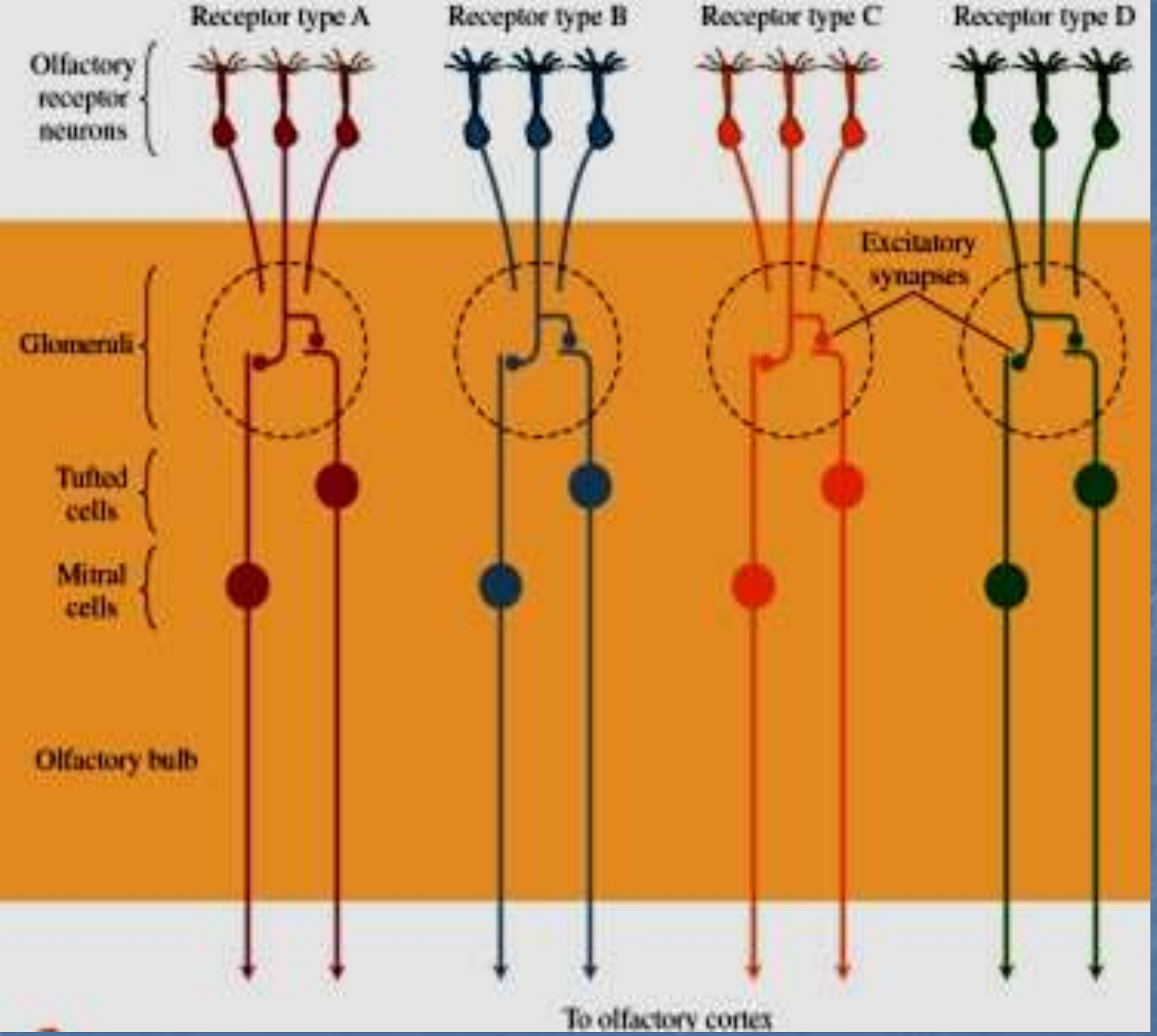


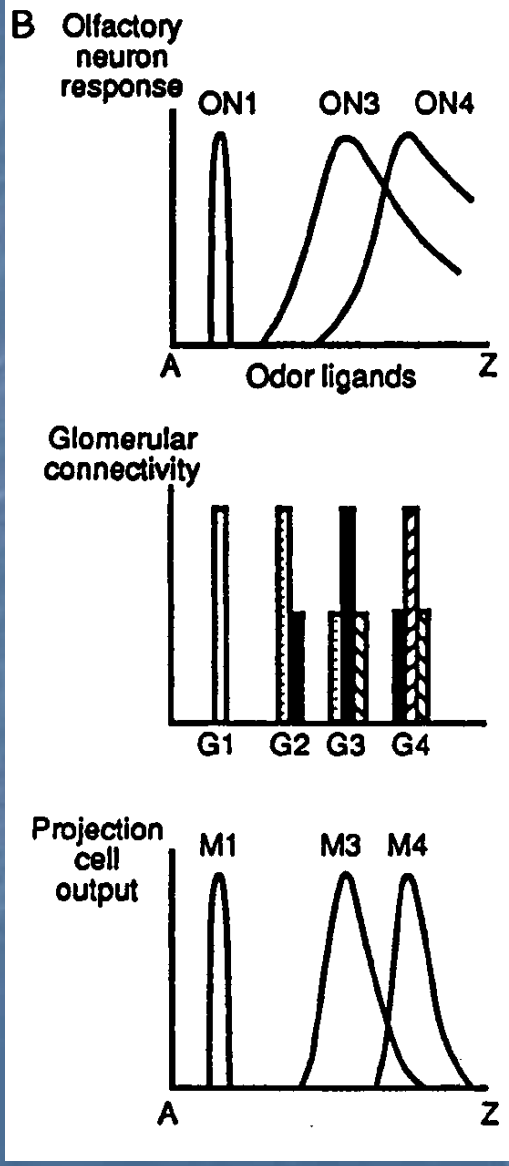
Figure 13.7 Olfactory bulb. (a) The figure shows olfactory axons passing through the cribriform plate to end in glomeruli in the olfactory bulb. (b) Basic circuit of the mammalian olfactory bulb. Layers: EPL = external plexiform layer; GL = glomerular layer; GRL = granule cell layer; OT = olfactory tract; 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





Laterální inhibice: „Zostření“ ladění ve vyšších patrech dráhy

Překryv



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

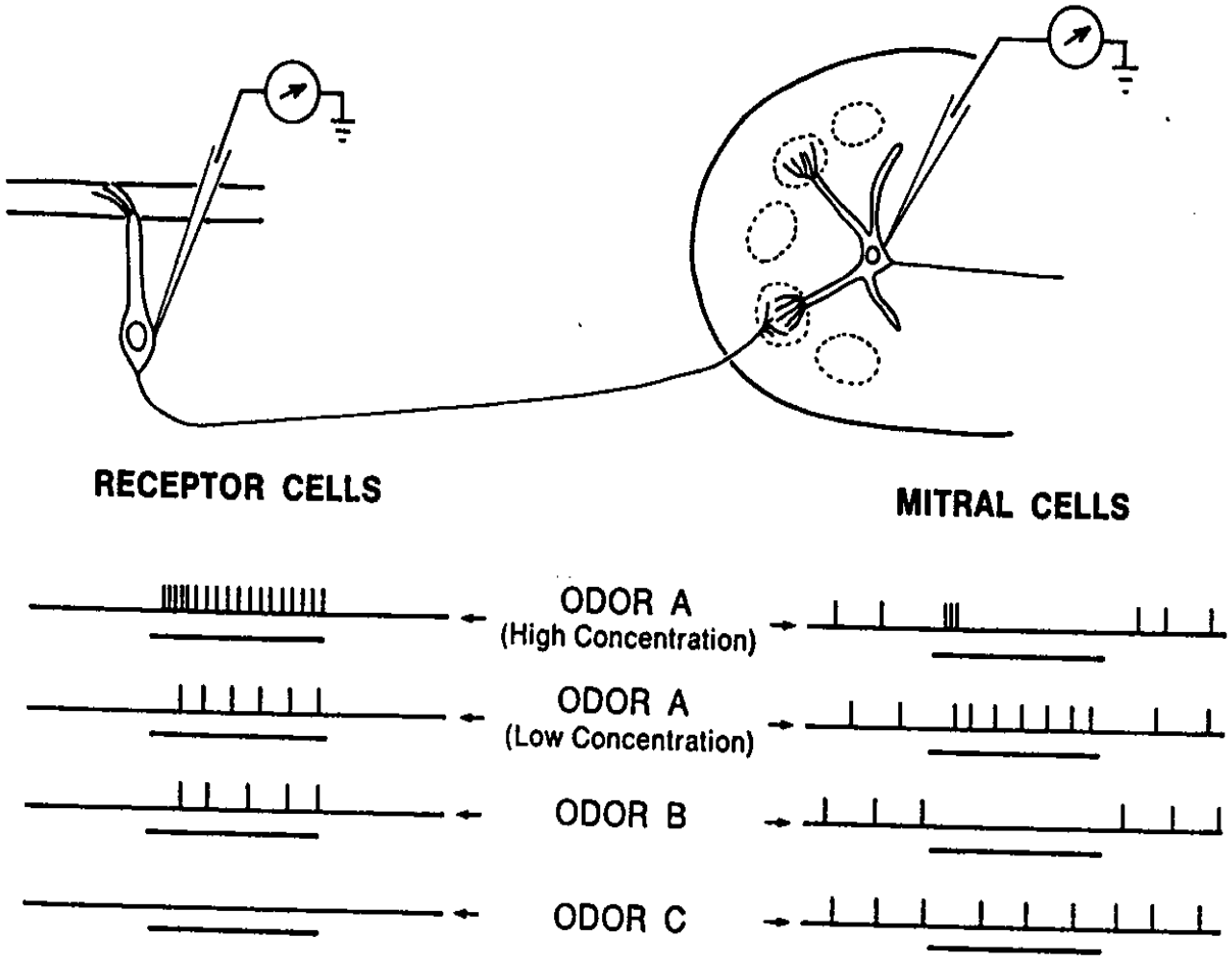


Fig. 11.11 Extracellular single-unit recordings of responses to odors of receptor cells *(left)* and mitral cells *(right)* in the salamander, showing different types of responses and different temporal patterns of activity. (After Kauer, 1974, and Getchell and Shepherd, 1978)

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

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 (Friedrich and Laurent, 2001; Laurent et al., 2001; Schaefer and Margrie, 2007).

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.
doi:10.1038/nature10521

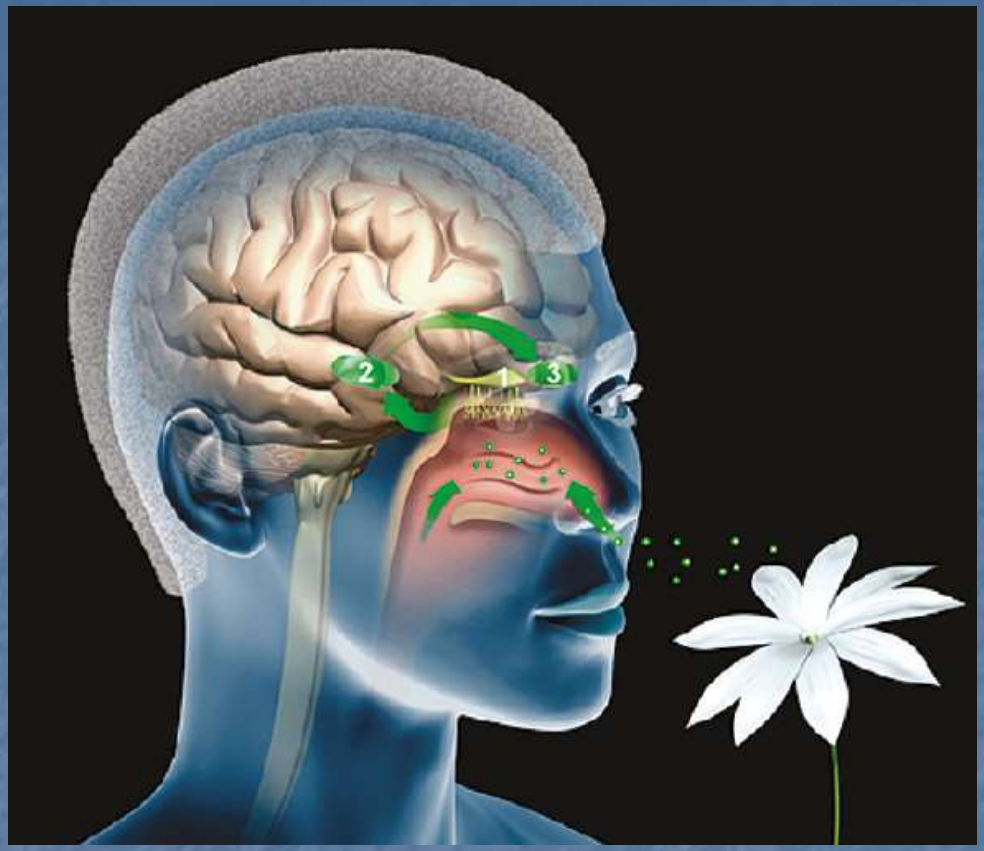
Lateralizace čichu

- 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).

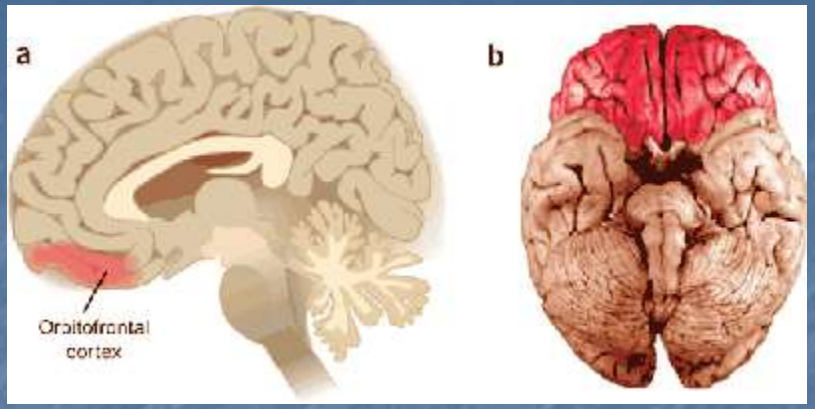
- doi:10.1016/j.anbehav.2011.05.020



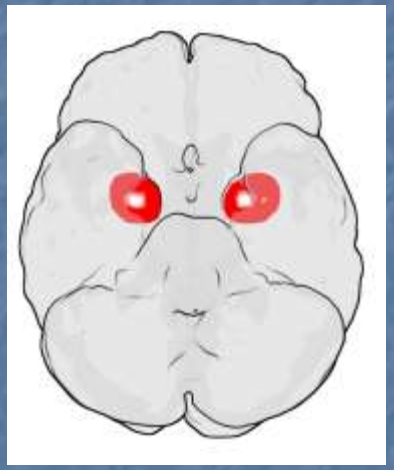
Centrální části čichové dráhy

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

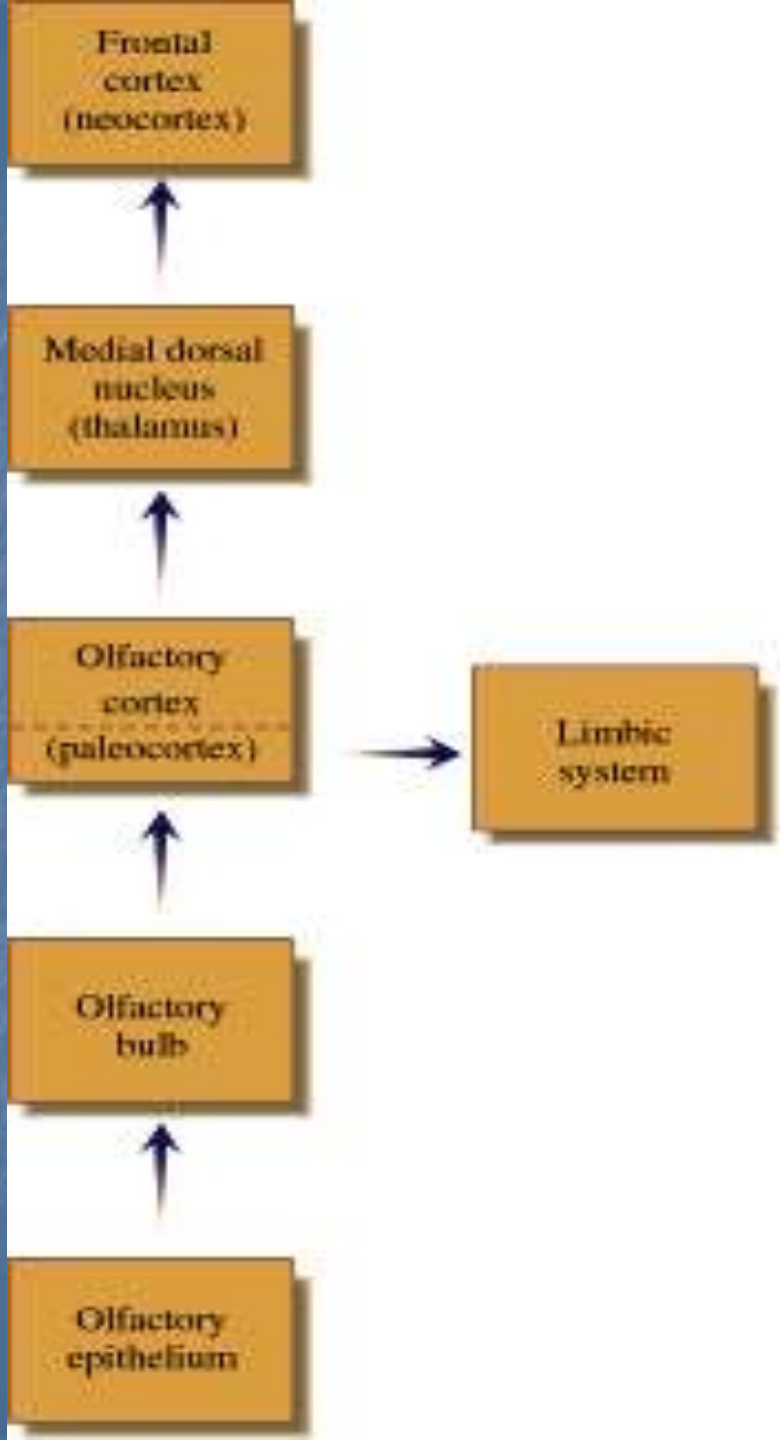


Orbitofrontální kůra



Piriformní kůra

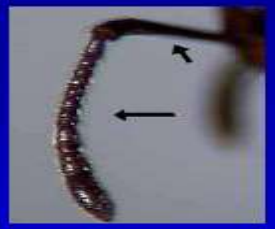
Má vztah k silné emocionální složce čichových vjemů a ukládání paměťových stop.



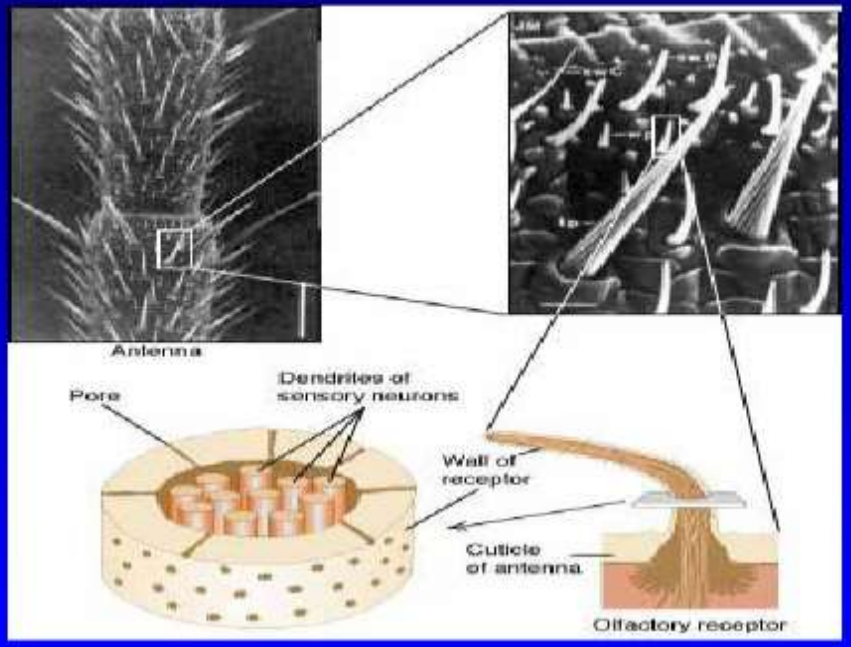
A co hmyz ?

Antennal morphology diversity

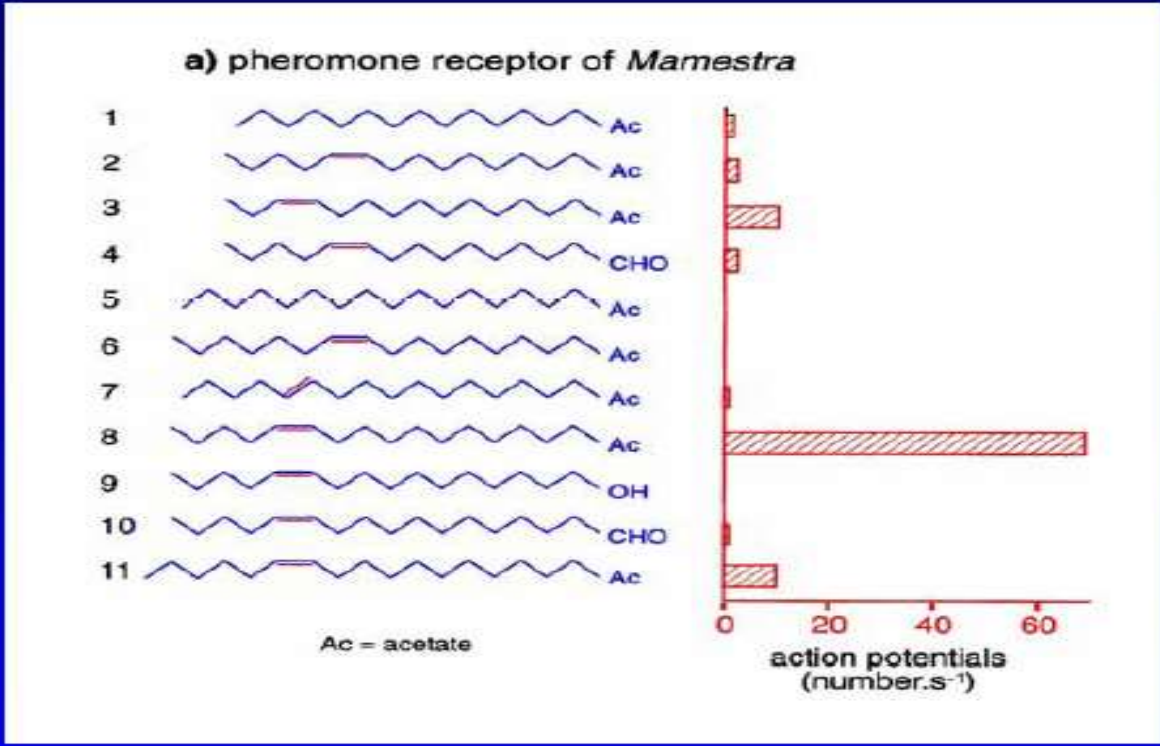




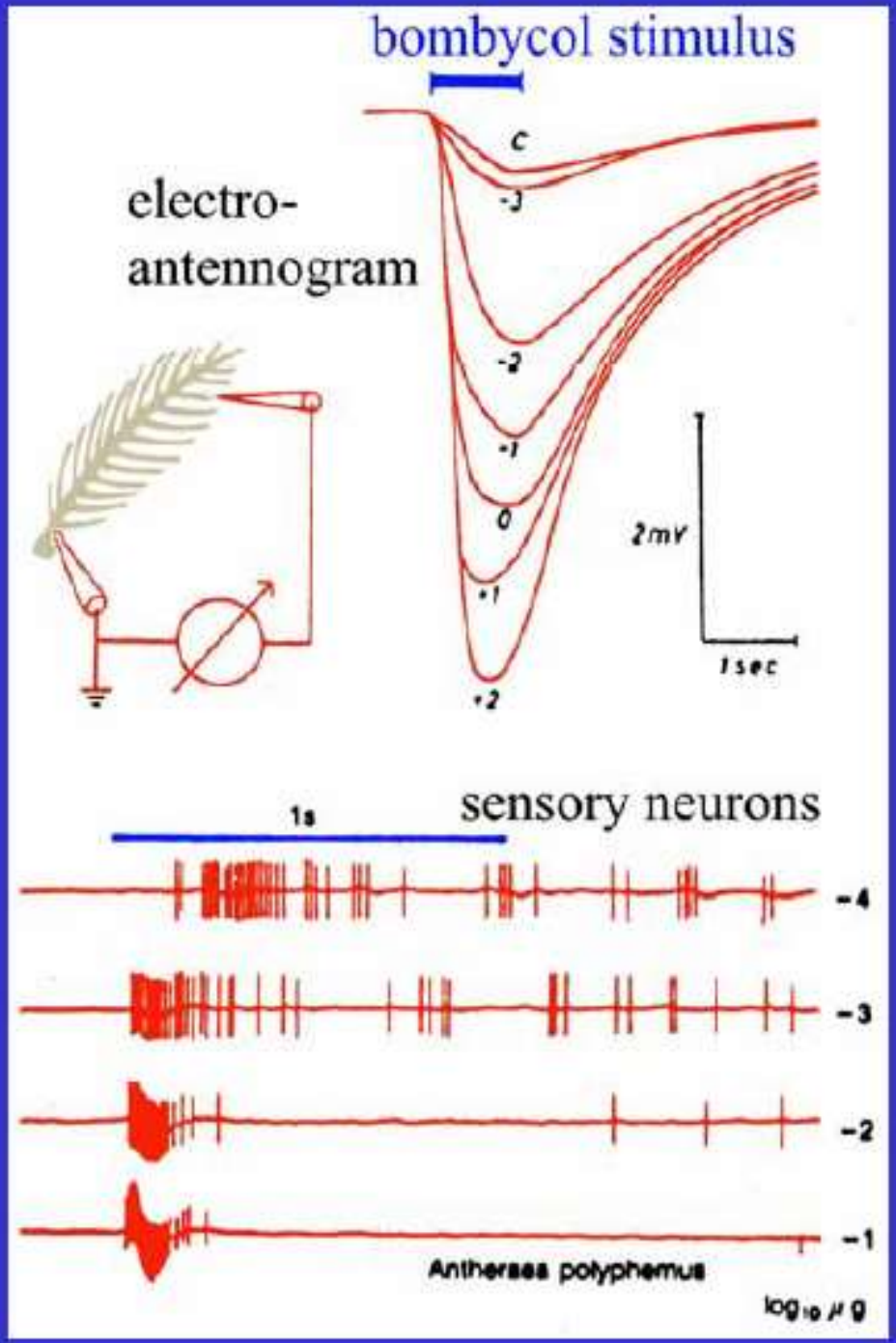

Anatomy of an antennal sensilla



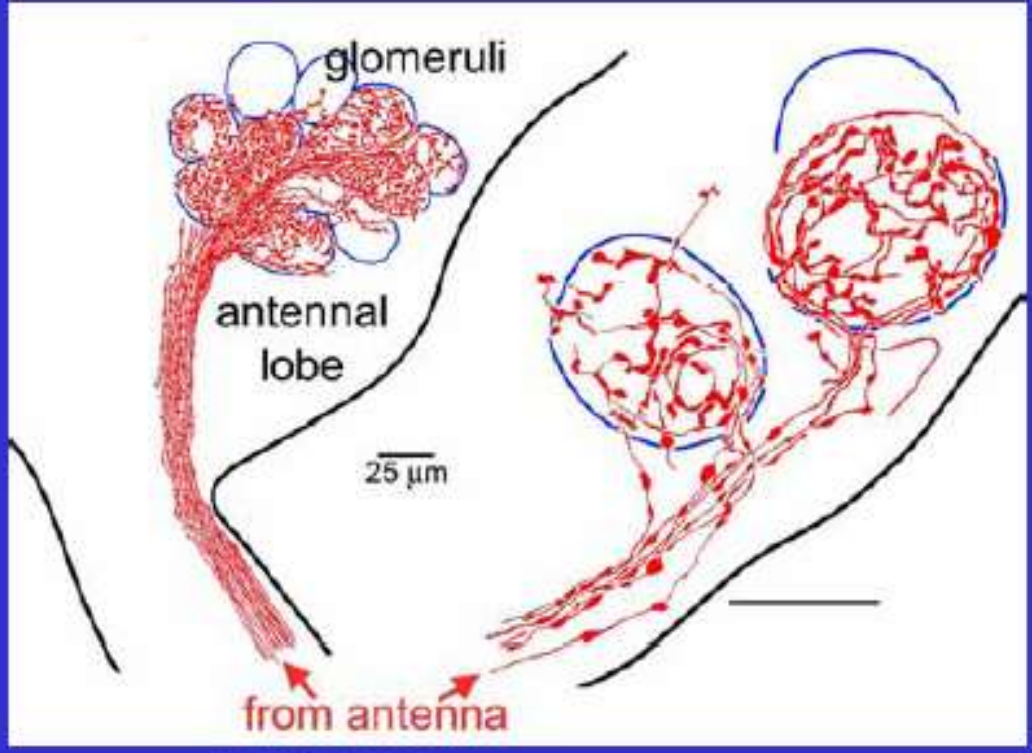
Response specificity to size and composition of odorant molecule

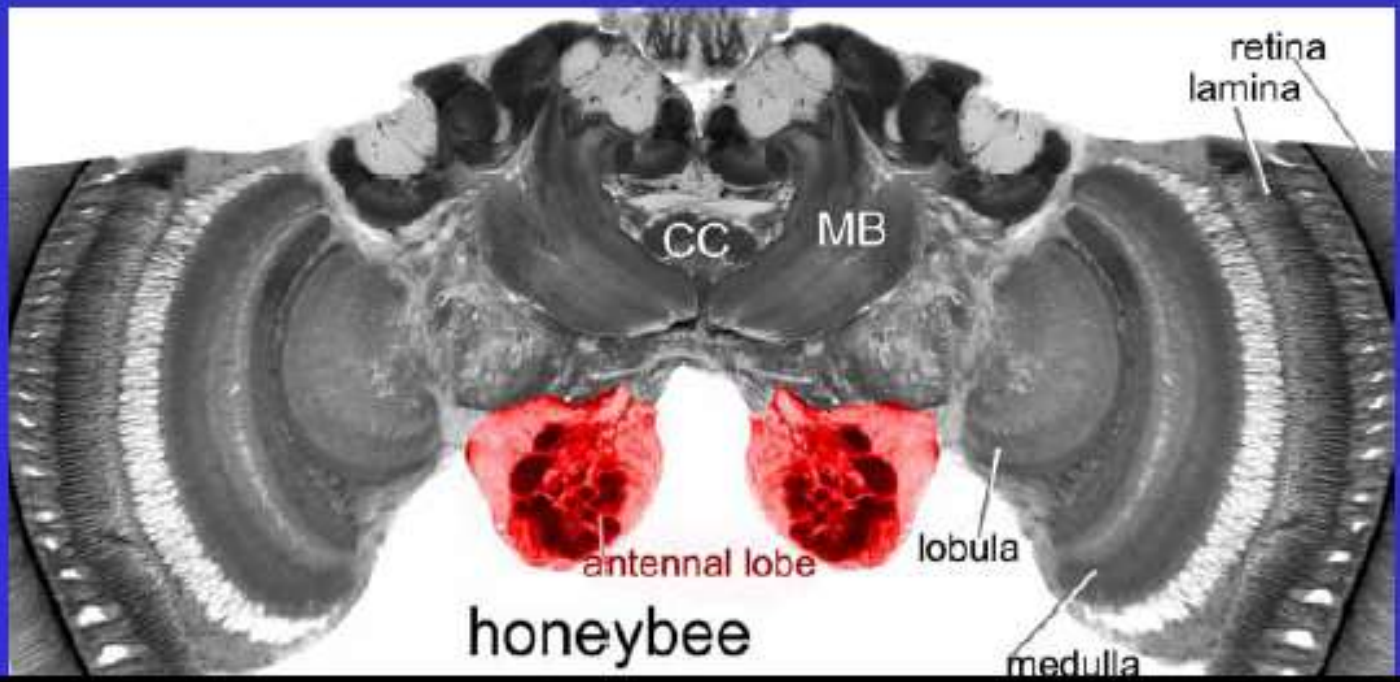


Olfactory receptor neurons respond to odorants

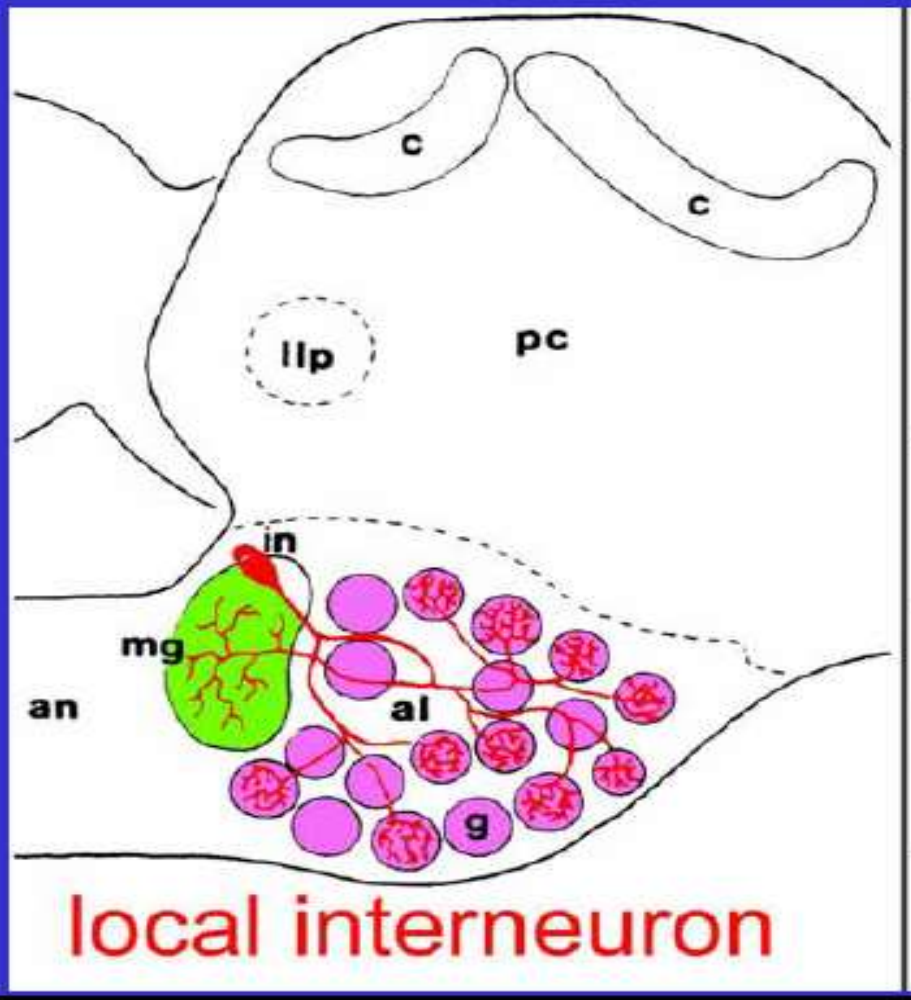


Antennal olfactory receptor neurons terminate in antennal lobe **glomeruli**

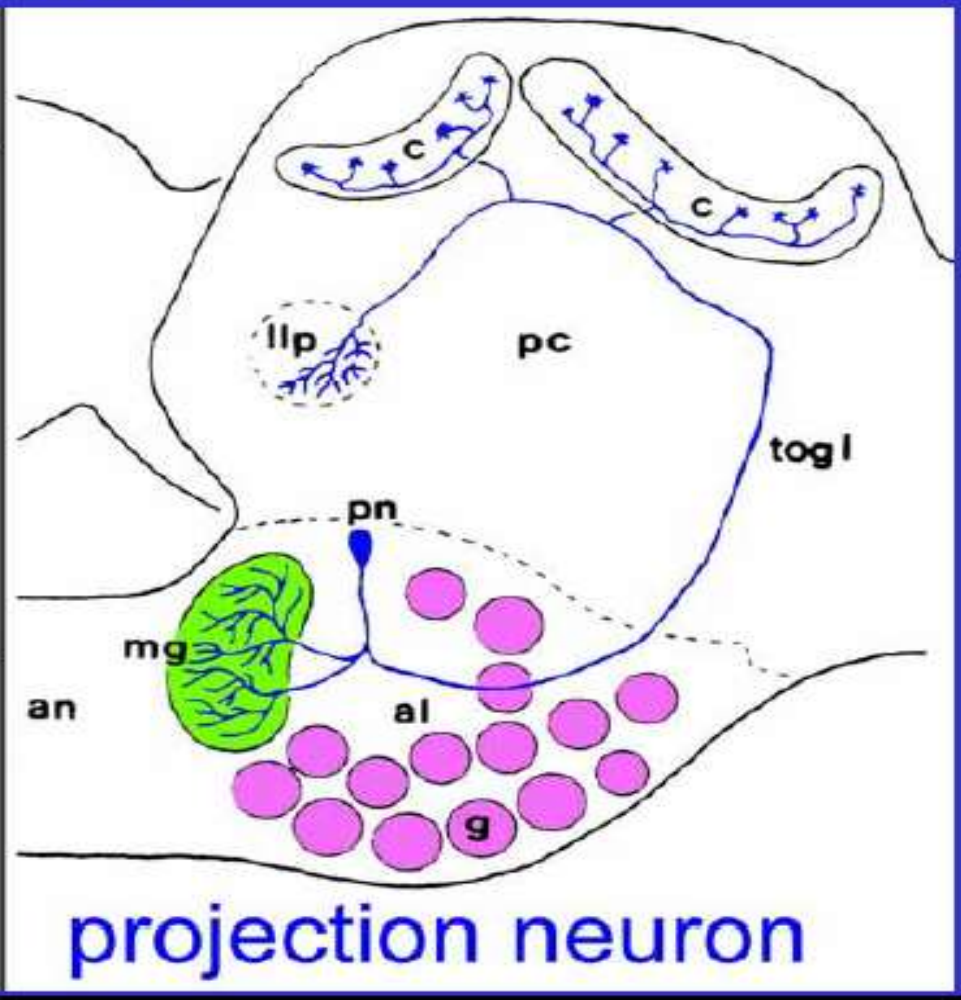




Antennal lobe: two major classes of neurons

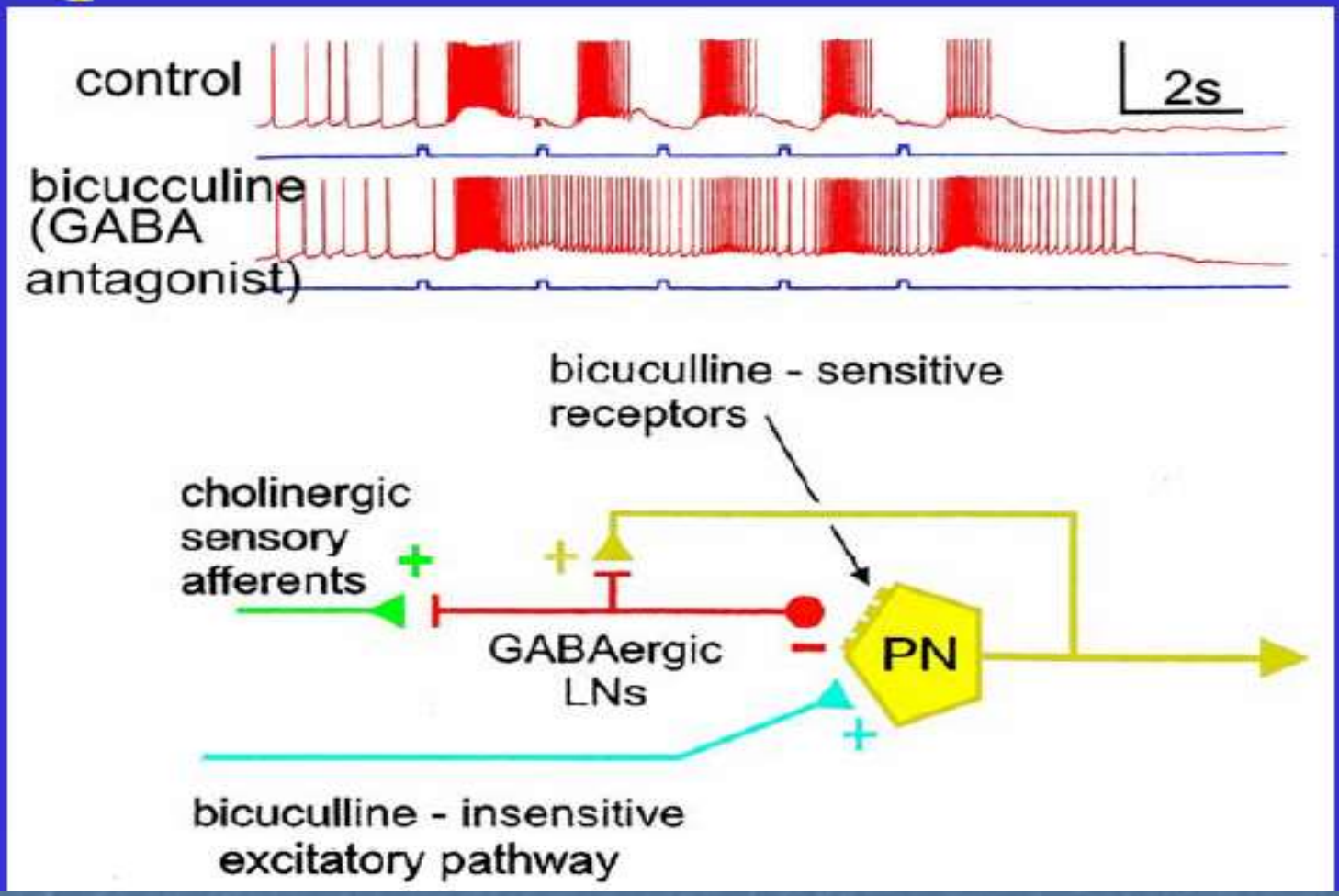


local interneuron



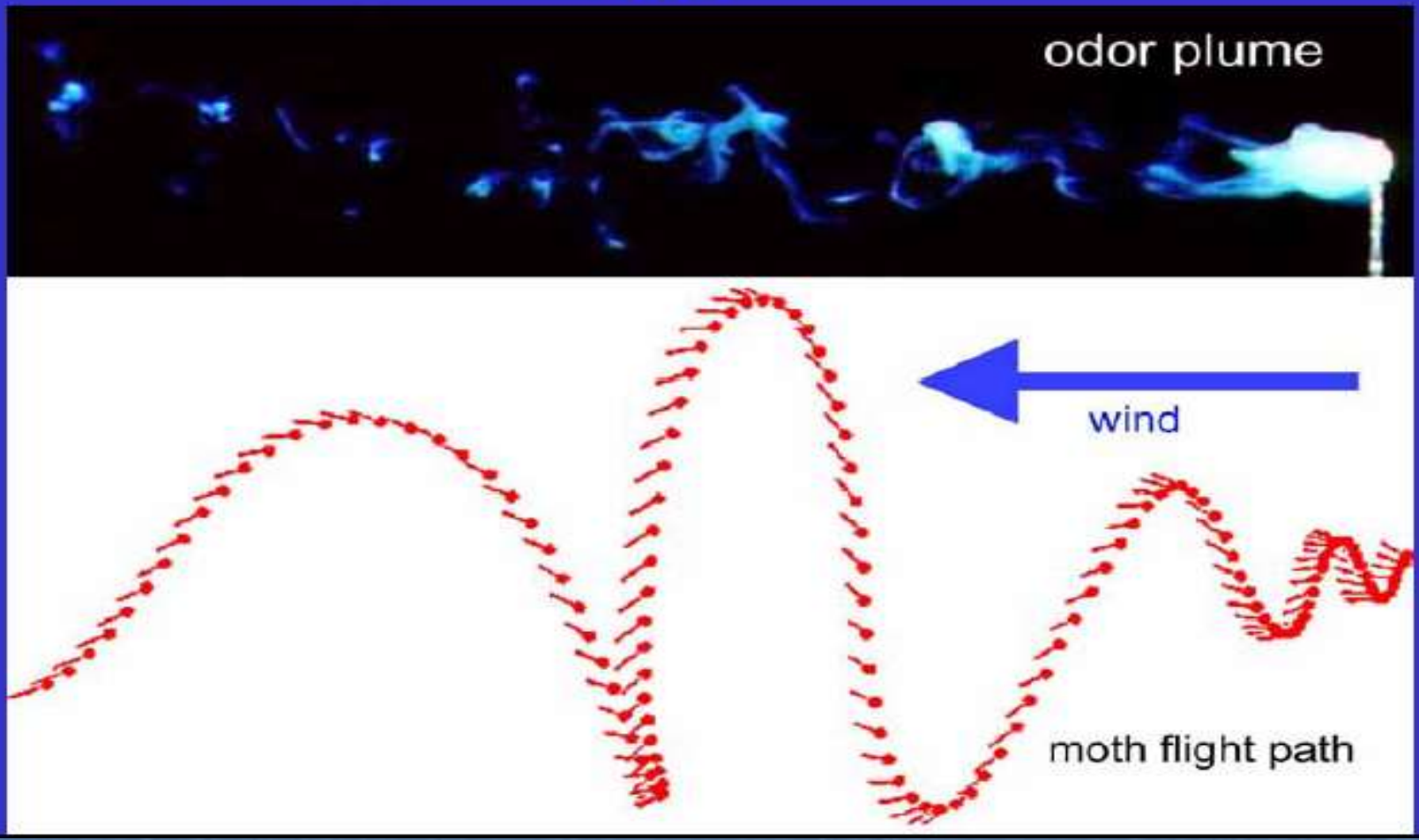
projection neuron

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

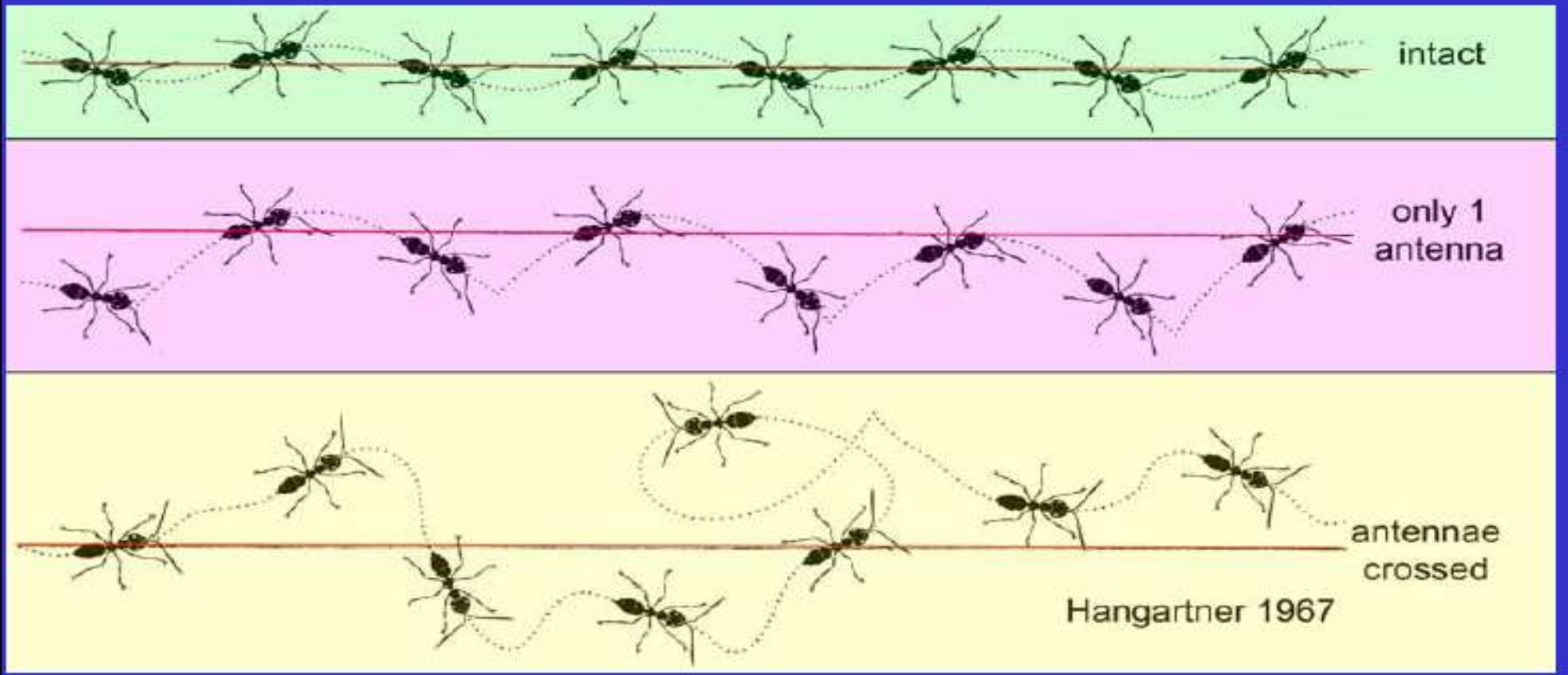


Terminace odpovědi nezbytná pro časovou rozlišitelnost signálů.

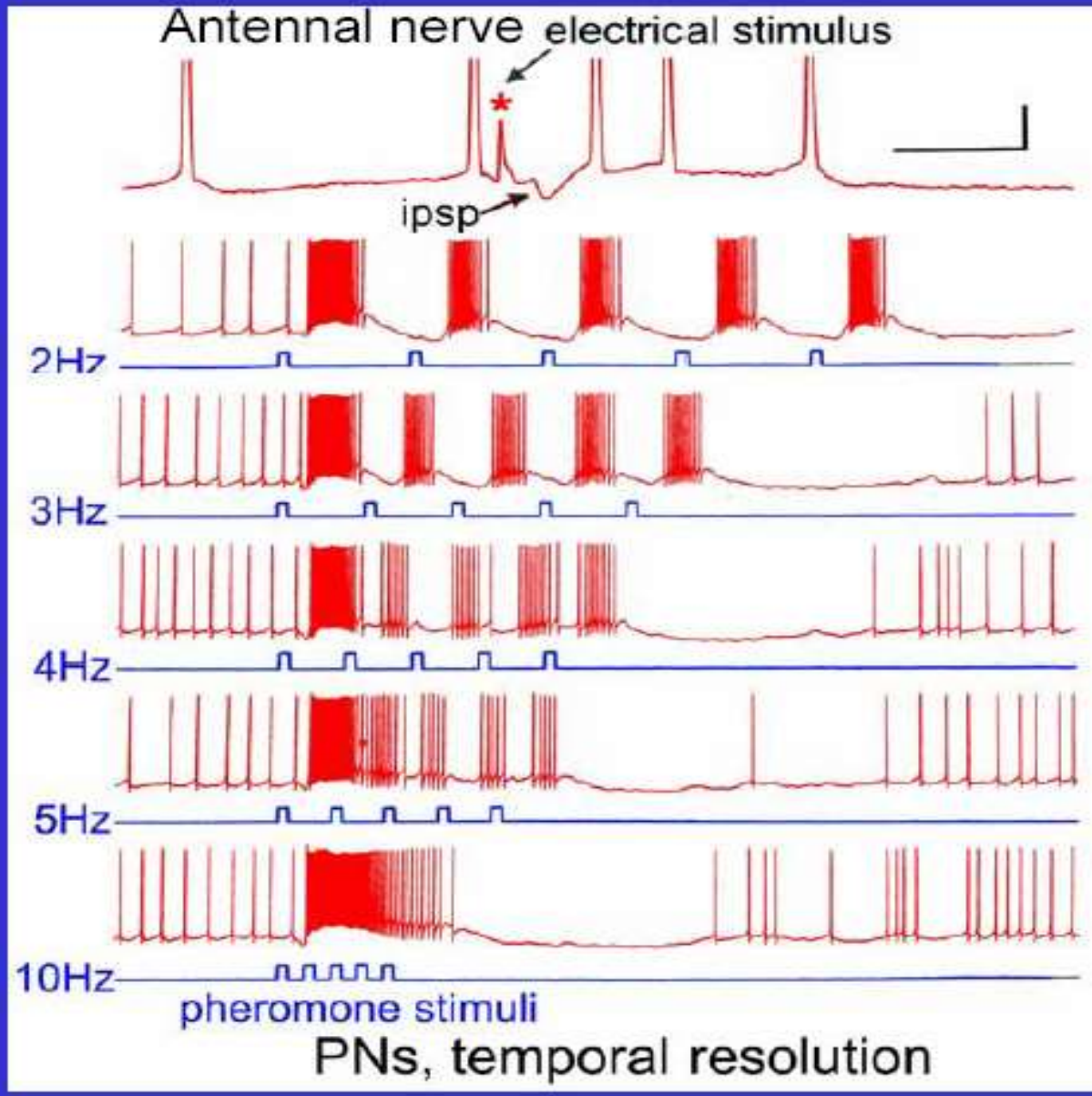
Odor is discontinuously distributed in air



Even when following an odor trace, perception is discontinuous

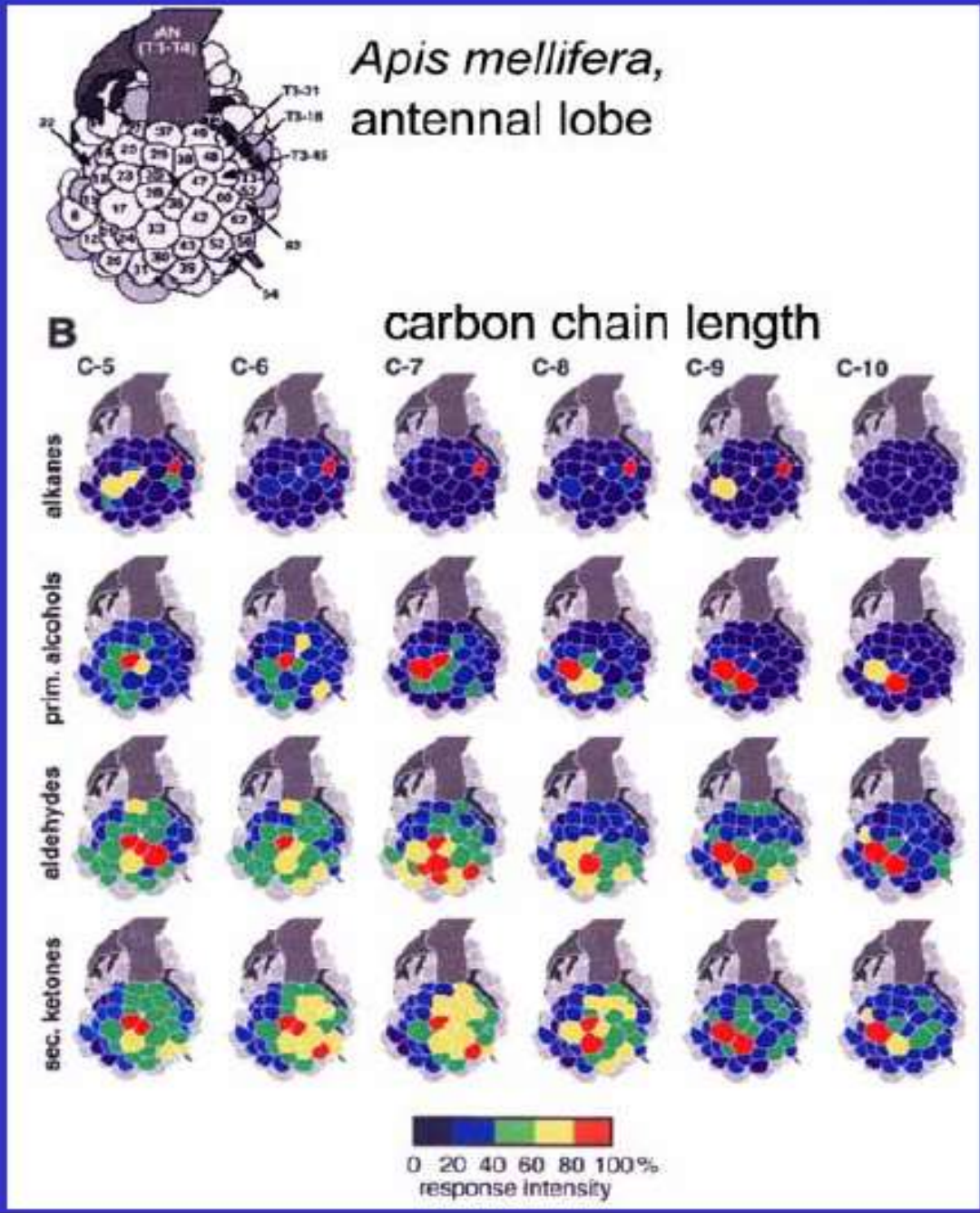


Temporal resolution is limited

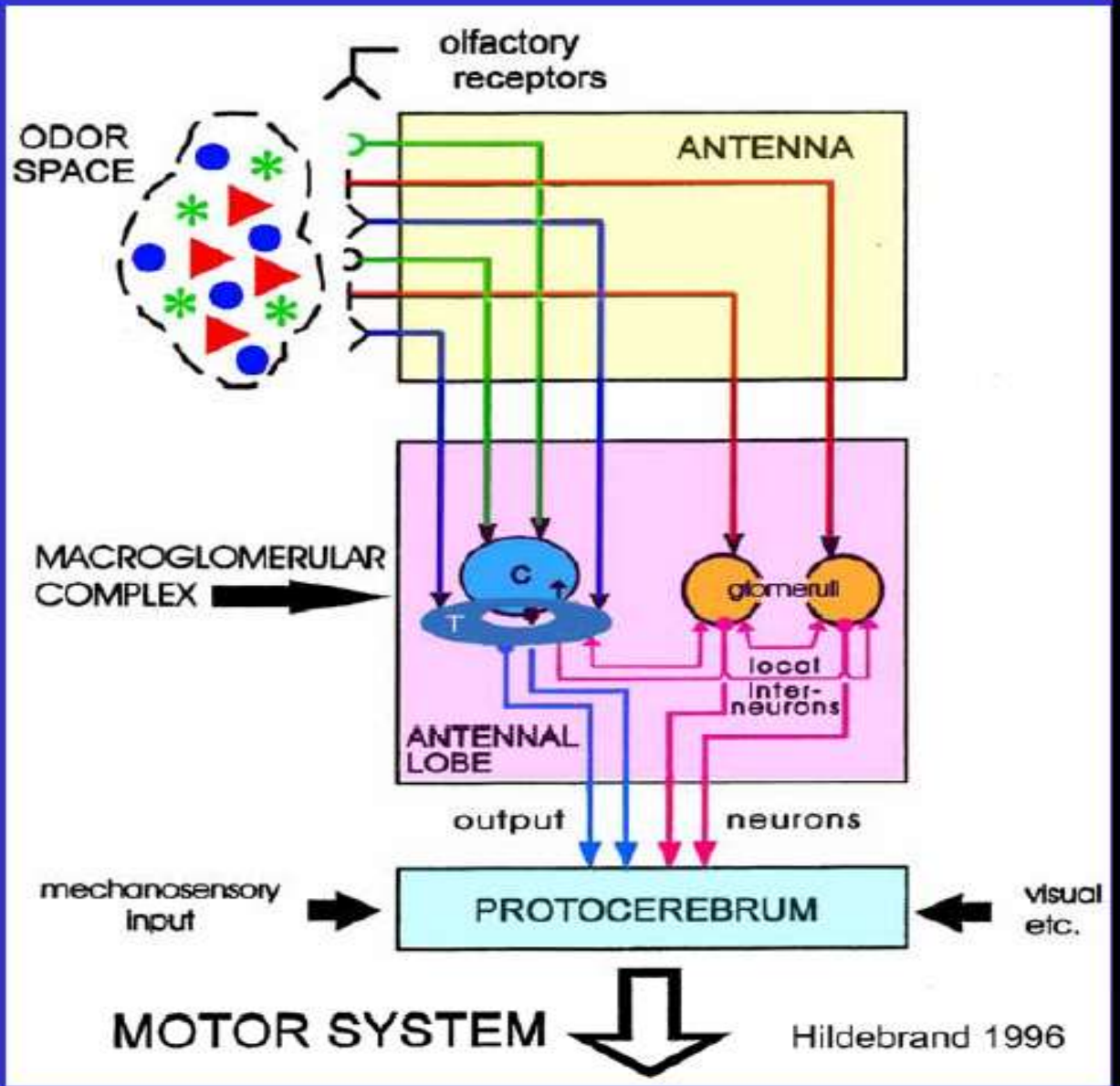


Glomeruli responses reflect odorants' structural properties (chain length, residues, polarity etc.):

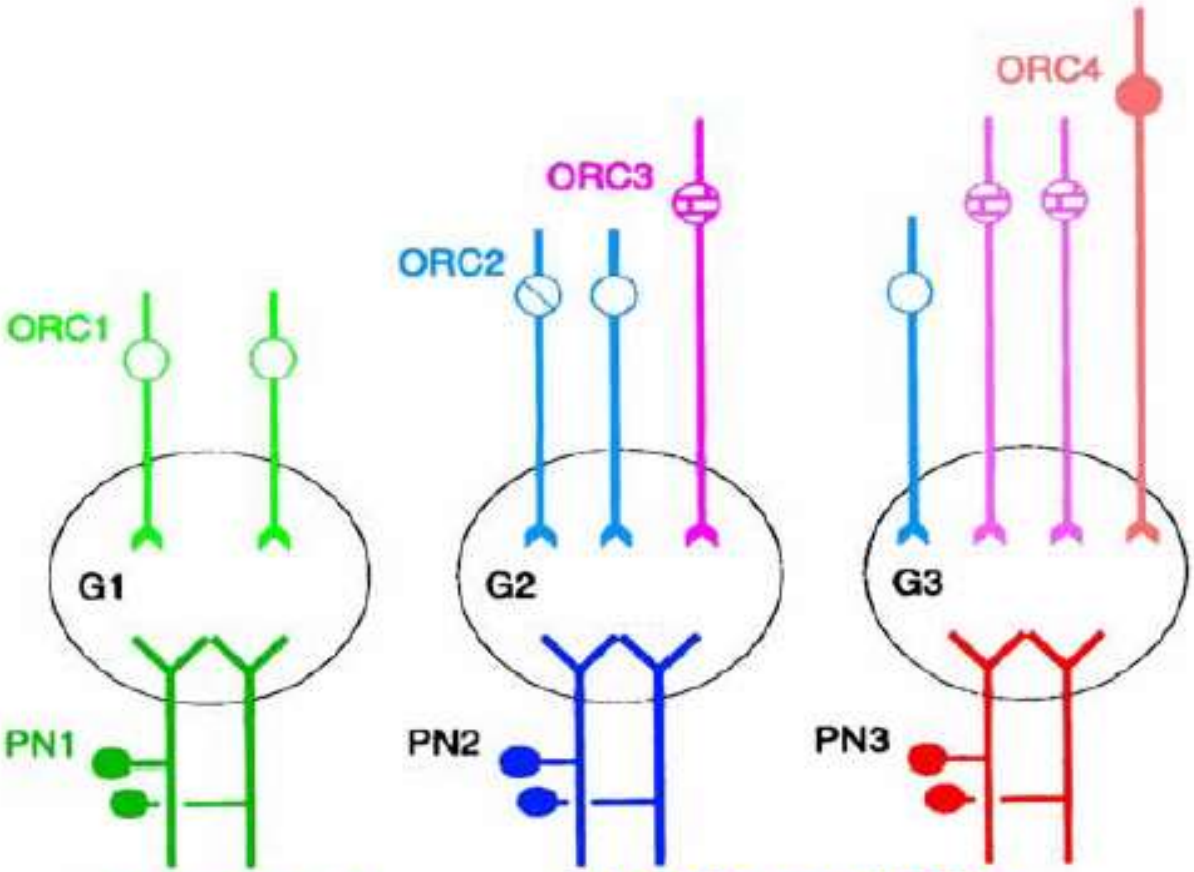
odor map

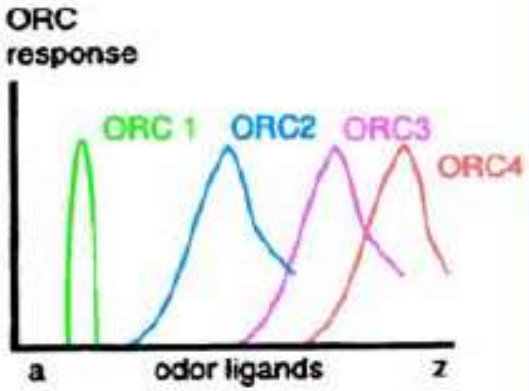


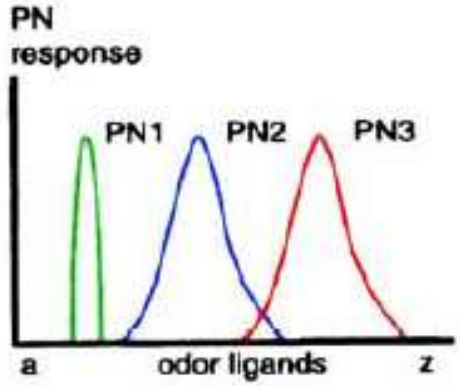
(sex) pheromones and 'ordinary' odors are processed by two different pathways



PNs may have narrower response spectra than receptor neurons







J.G. Hildebrand 1996

Podobnost mezi hmyzem a obratlovci přece jen omezená

Class	Receptors	Ligands	Oligomeric state	Localization
Vertebrates				
GPCRs	OR	Odours	Monomer	Main olfactory epithelium, Grüneberg ganglion, vomeronasal organ and exogenic expression
	TAAR	Amines	Monomer	Main olfactory epithelium and Grüneberg ganglion
	FPR	Pathogen- and inflammation-related compounds	Unknown	Apical layer of vomeronasal organ
	V1R	Small, volatile molecules and sulphated steroids	Monomer	Apical layer of vomeronasal organ and main olfactory epithelium
	V2R	Peptides (ESP1 and MHC peptides), MUPs and sulphated steroids	Monomer and heteromer with H2-Mv proteins and B2M	Basal layer of vomeronasal organ and Grüneberg ganglion
Monotopic receptors (RTK type)	GCD	Extracellular: uroguanylin and guanylin Intracellular: bicarbonate, Ca^{2+} and neurocalcin-δ	Dimer	Main olfactory epithelium
	GCG	Unknown	Unknown	Grüneberg ganglion
Insects				
Ionotropic '7-TM' receptors	OR	Food odours and pheromones	Heterodimer (OrX–Or83b)	Antenna (basiconic, trichoid and coeloconic sensilla) and maxillary palp
	GR	CO_2	Heterodimer (Gr21a–Gr63a)	Antenna (basiconic sensilla)
Ionotropic 'glutamate' receptors	IR	Ammonia, amines, water vapour and alcohols	Multimeric	Antenna (coeloconic sensilla)

B2M, β2 microglobulin; ESP1, exocrine gland-secreting peptide 1; FPR, formyl peptide receptors; GCD and GCG, guanylate cyclase type D and G; GPCR, G protein-coupled receptor; GR, gustatory receptor; Gr21a and Gr63a, *Drosophila melanogaster* gustatory receptors 21a and 63a; H2-Mv, non-classical class I major histocompatibility genes; IR, ionotropic receptor; MHC, major histocompatibility complex; MUP, major urinary protein; OR, odorant receptor; RTK, receptor tyrosine kinase; OrX–Or83b, heteromeric *D. melanogaster* odorant receptor composed of Or83b and another OR (OrX); TAAR, trace amine-associated receptor; 7-TM, seven-transmembrane; V1R and V2R, vomeronasal receptors type 1 and 2.

Podle: Čich hmyz a obratlovci, 2010

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

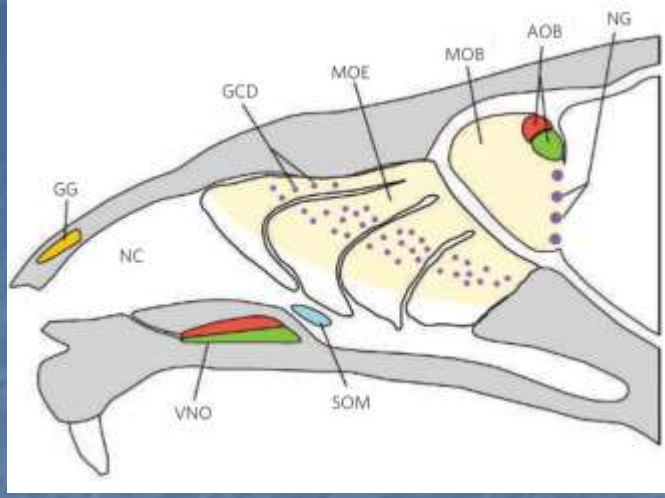
Similar to vertebrate neurons, insect olfactory receptor neurons (ORNs) can be very sensitive, responding to the binding of a single molecule of a sex pheromone[142]. Insect ORNs, which have an ionotropic mechanism of action, also lack the amplification provided at the receptor and G protein level. How 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 lidí

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

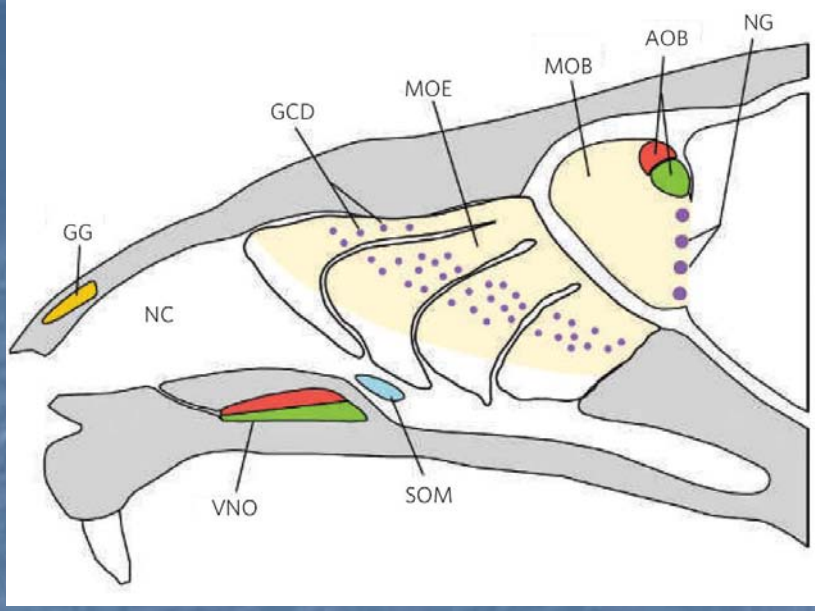
Dva chemosensitivní systémy savců



Hlavní čichový epitel (MOE):
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 (spíše 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):



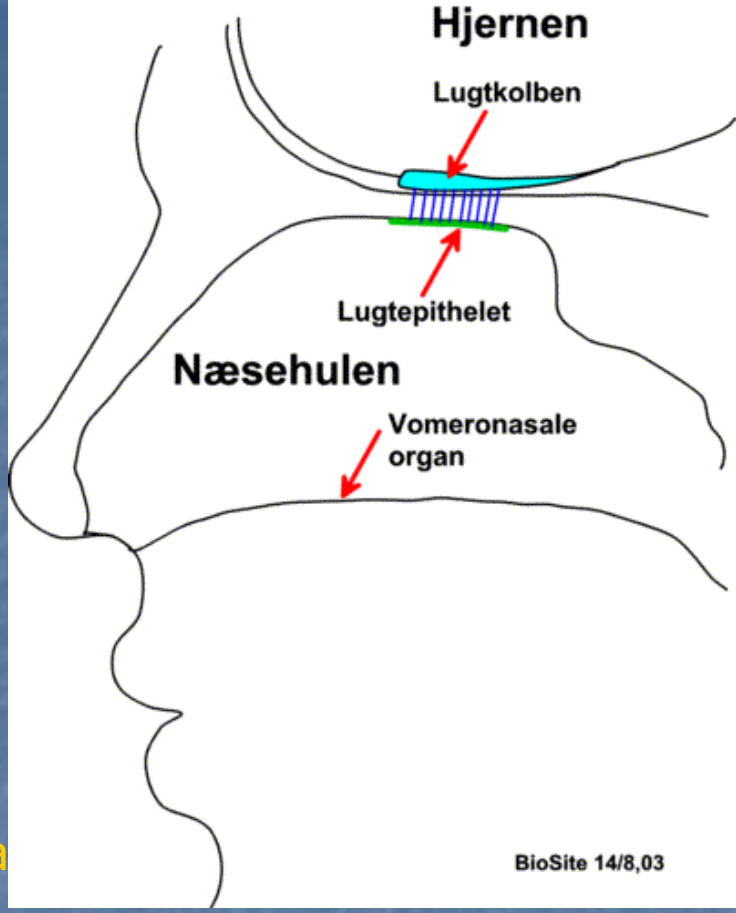
Citlivost je vysoká, pro feromony myši až 10-10M. Axony jsou mezi čichovými laloky a vstupují do přídatných čichových laloků. Zde najdeme podobně jako v hlavní dráze specificky naladěné glomeruli (přijímají vstupy jen z buněk exprimujících jeden typ receptoru). Projekce pak nevedou ani tak do čichového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

U člověka také?

AOB u dospělců nenalezen, ani inervace ne.

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 – 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.

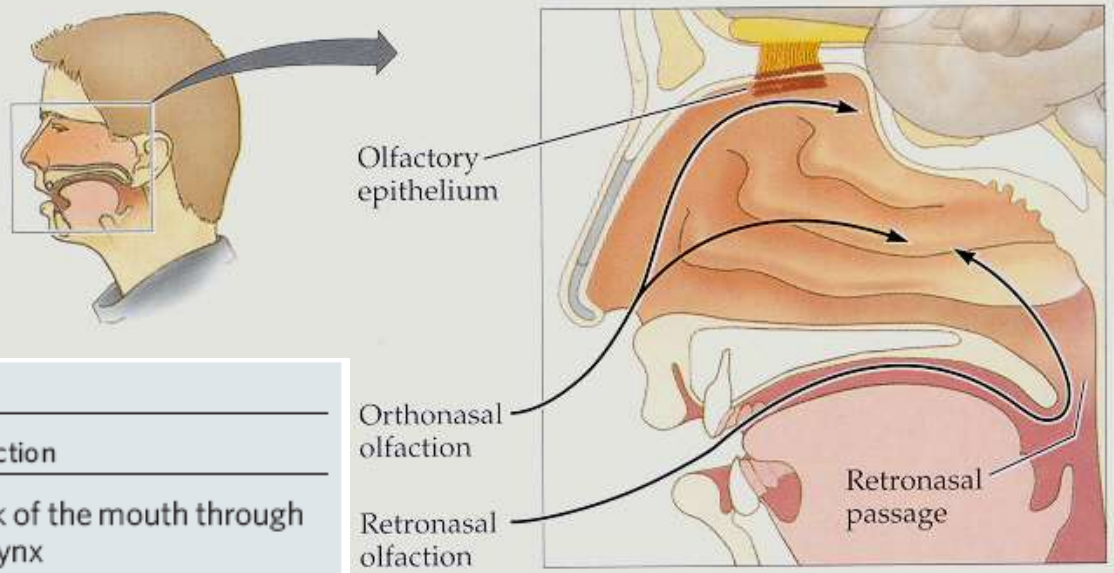
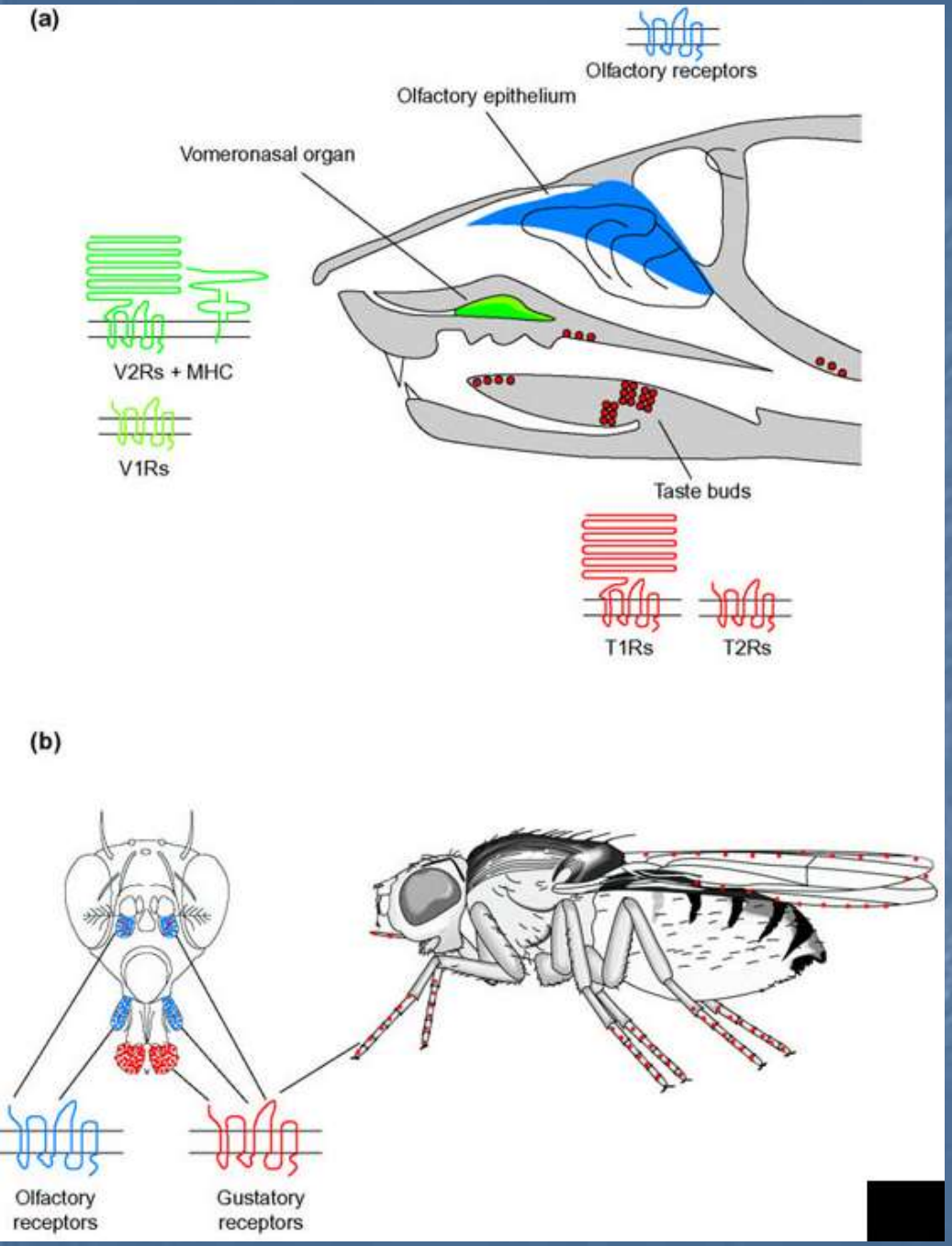


Table 1 | The dual olfactory system

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.

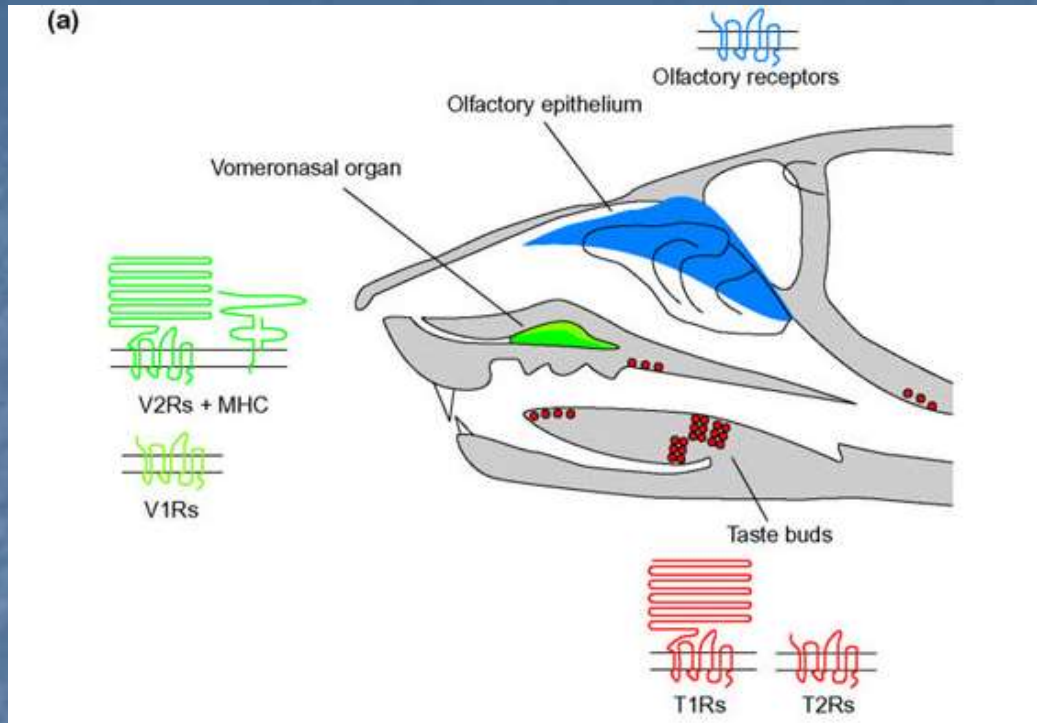
Čich a chuť spolupracují

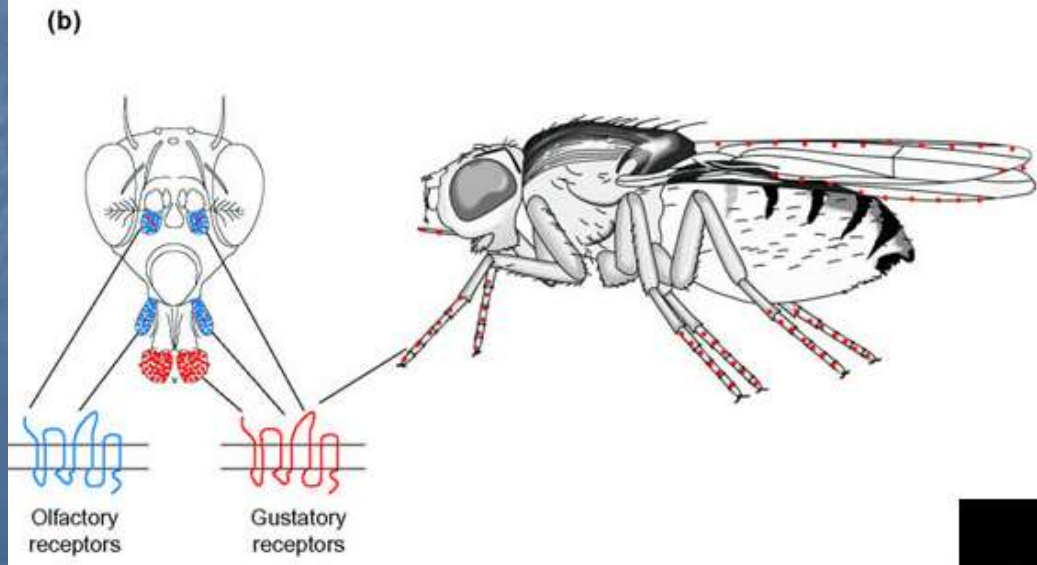
Chuť

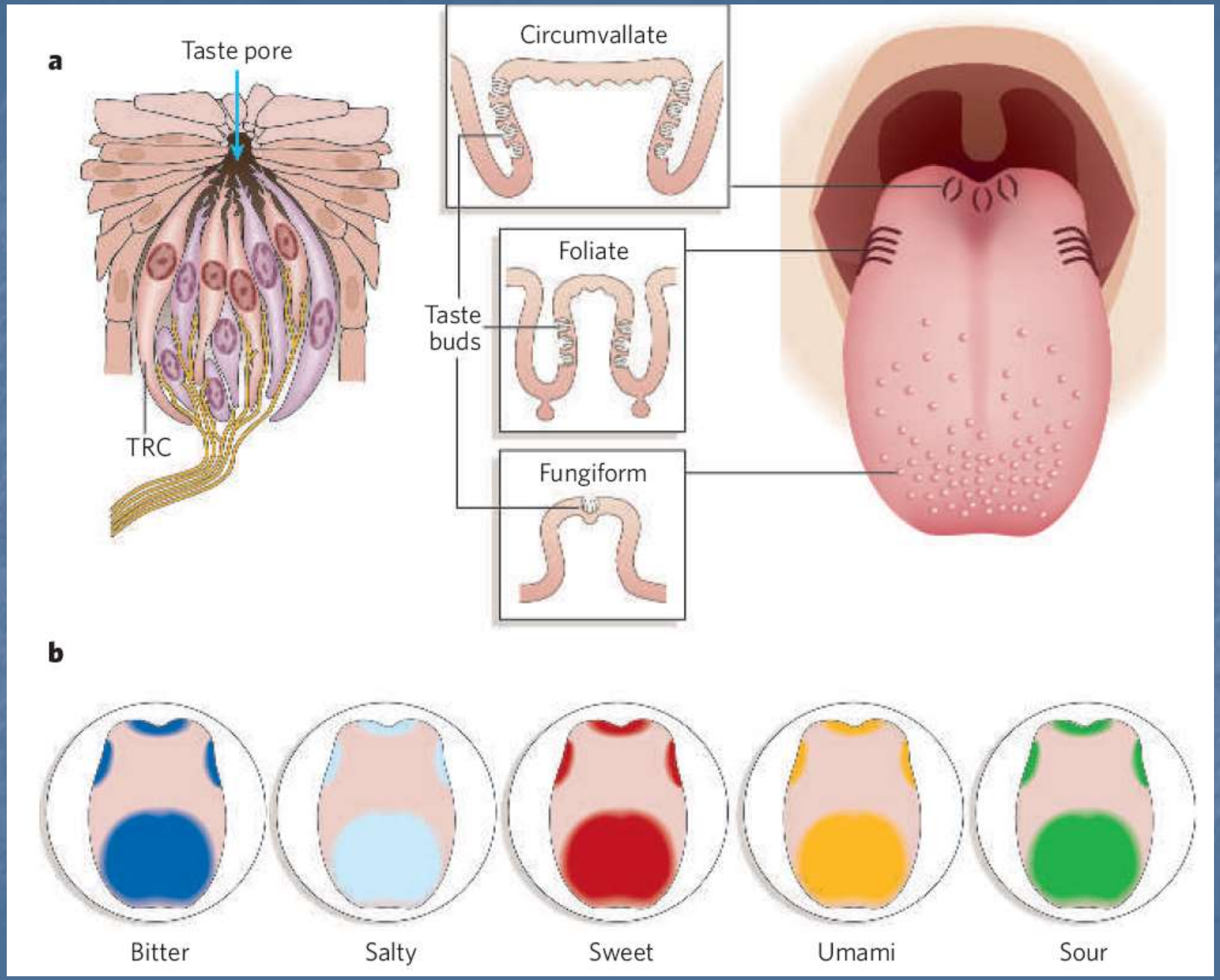
Chuť

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

Čich rozeznává kapalnou fázi, chuť kapalnou.






a
Taste pore
TRC
Circumvallate
Foliate
Taste buds
Fungiform
b
Bitter
Salty
Sweet
Umami
Sour

15.1 Scientific Urban Legend—The Bogus 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.

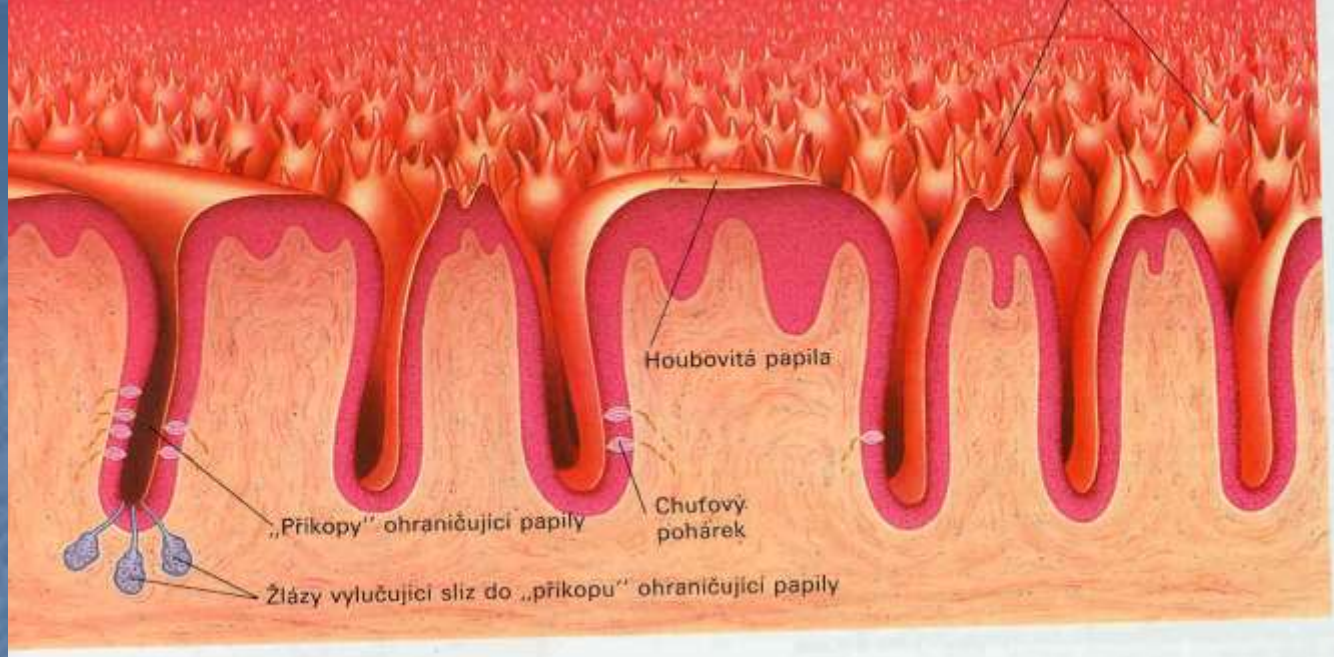
The origin is most likely a book written by Harvard University's Edwin Boring in 1942. Boring, in addition to his own work, chronicled the history of sensation and perception. He described a study conducted by Hänig in the laboratory of Wilhelm Wundt in 1901 (Hänig, 1901). Hänig wanted to show that the 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.

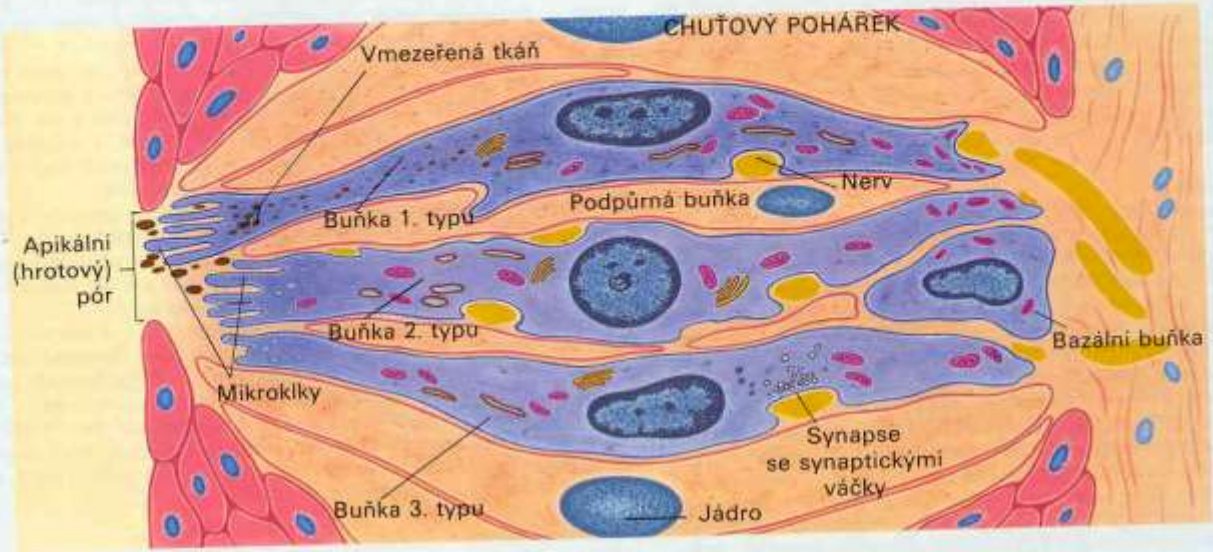
References

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*

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

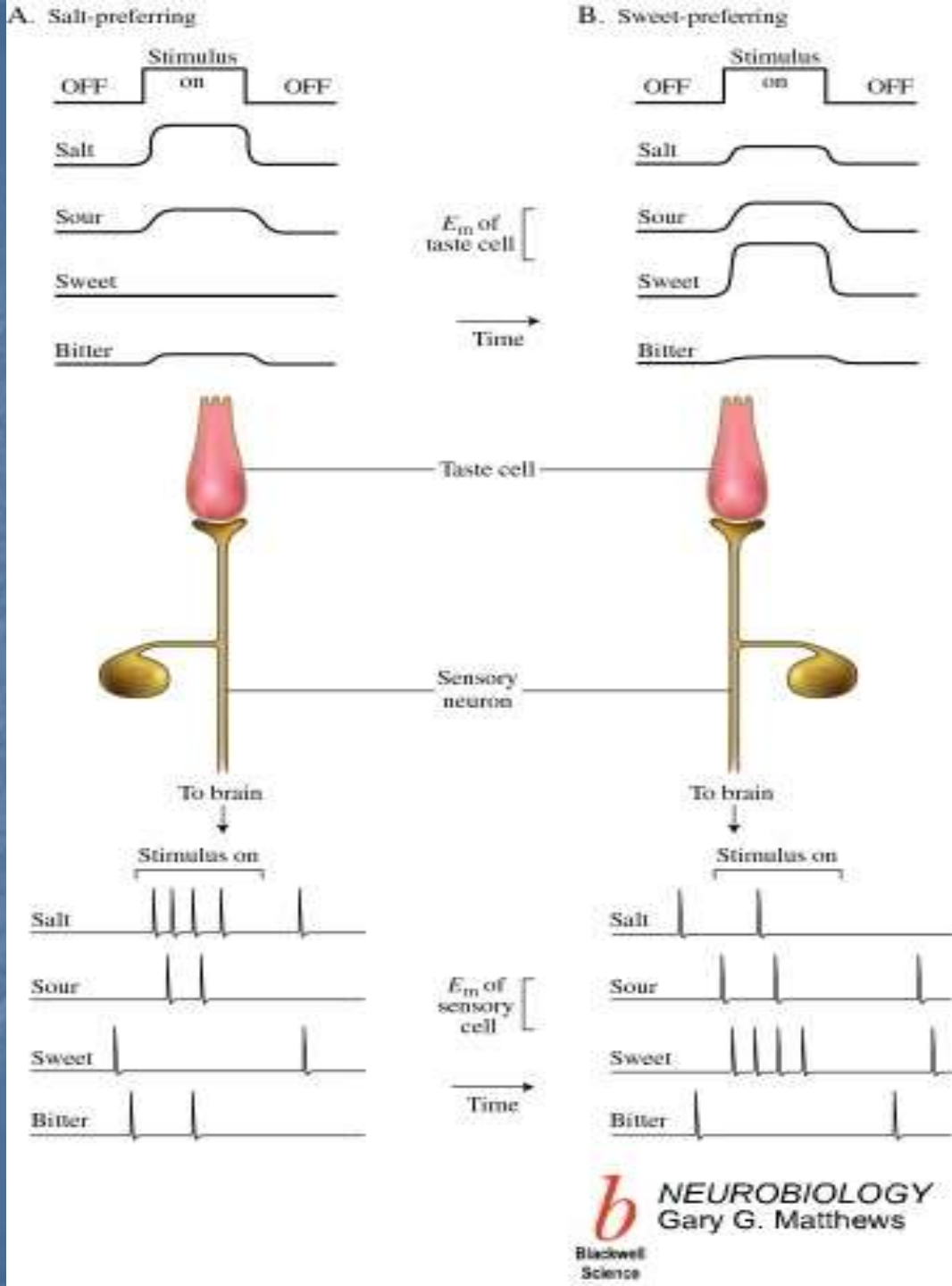


v „přikopech" obklopujících jejich centrální val, reagují na chutě hořké. Mezery mezi papilami zvlhčuje sliz, vylučovaný žlázami umístěnými na bázi těchto mezer. Chuťové molekuly se musí v tomto vlhkém prostředí nejprve rozptýlit, a teprve potě je mohou chuťové pohárky detekovat.

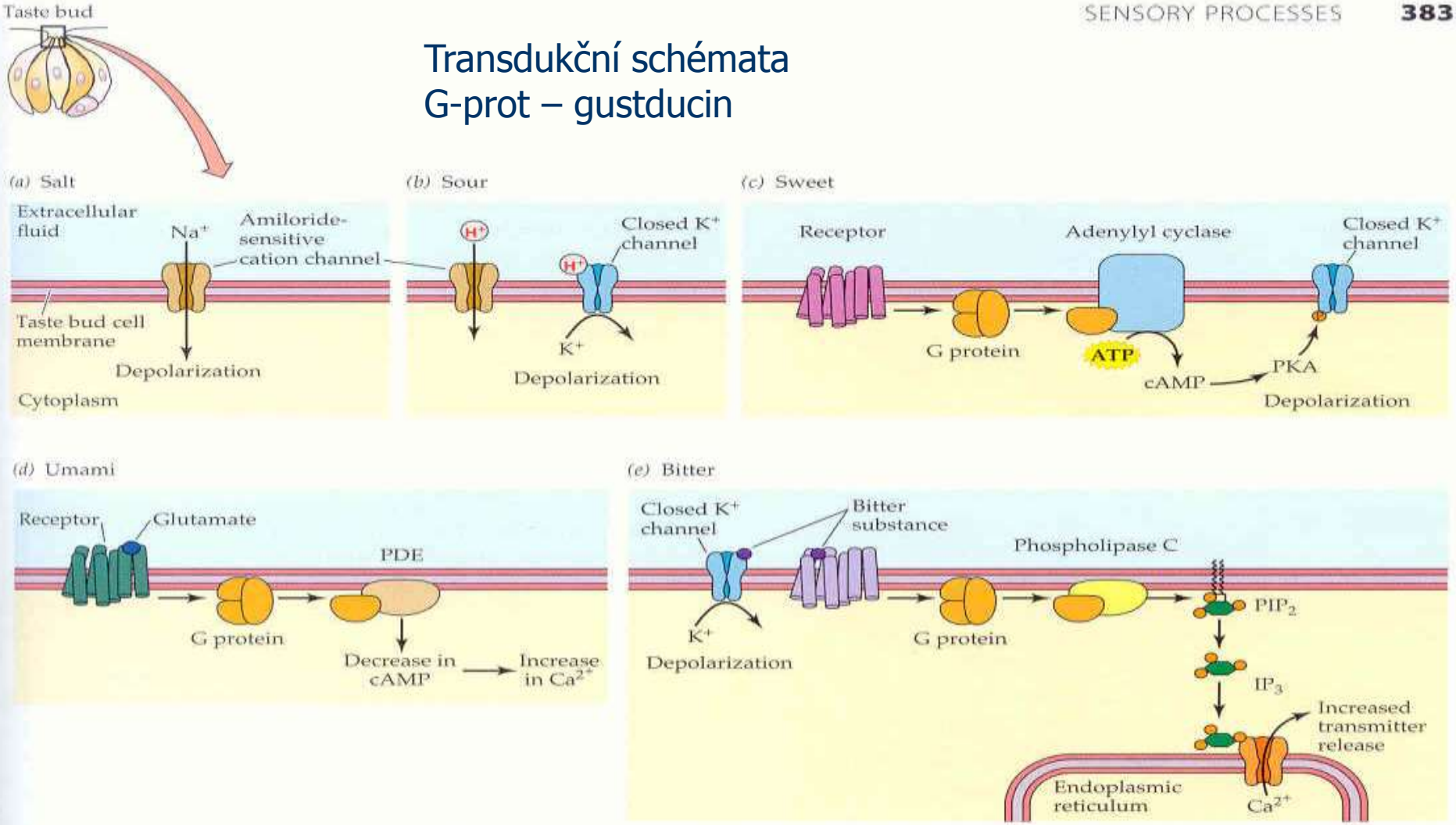


Selektivita omezená.

Člověk může rozlišit 100 chuťových kvalit, přičemž jde asi opět 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.

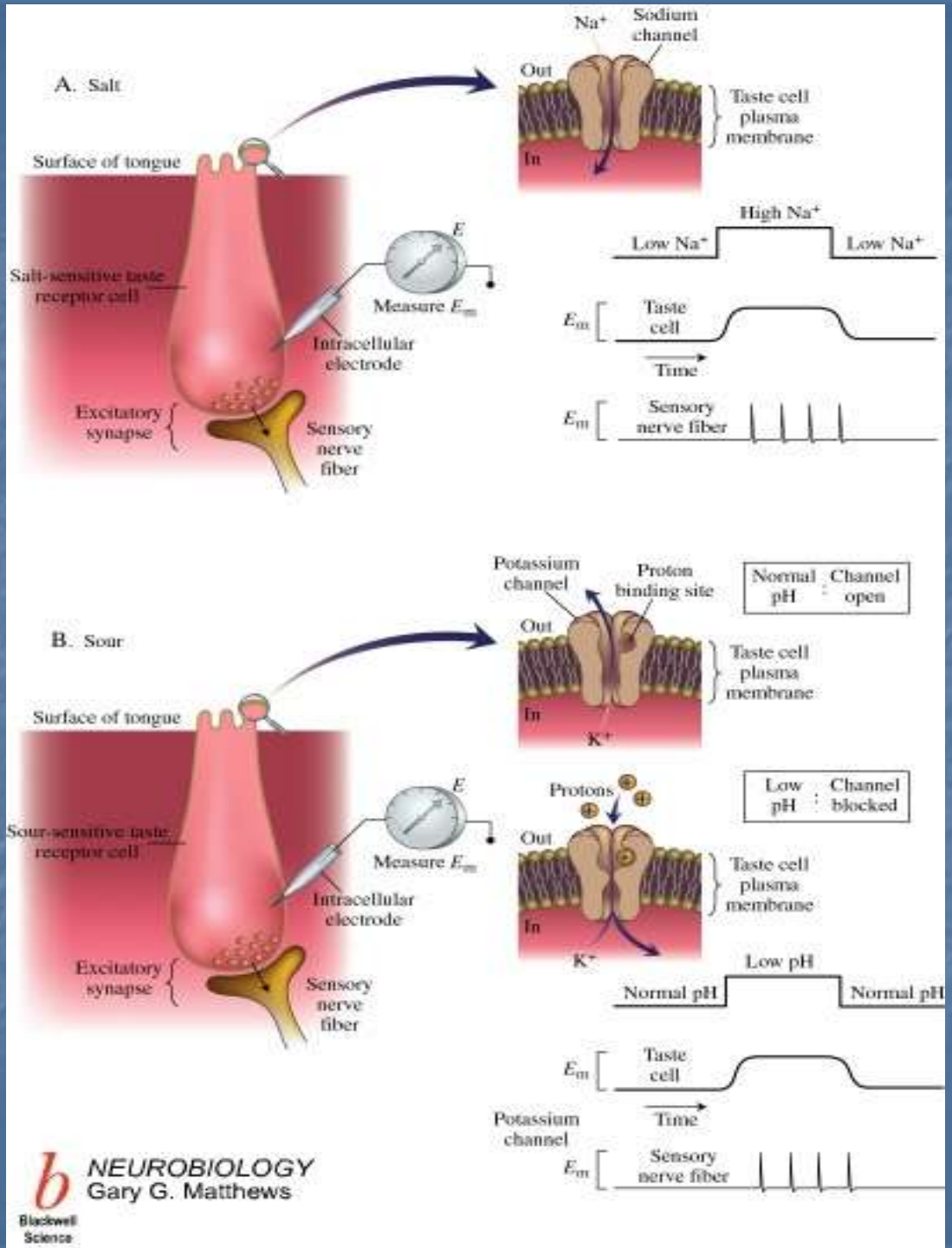


Transdukční schémata
G-prot – gustducin



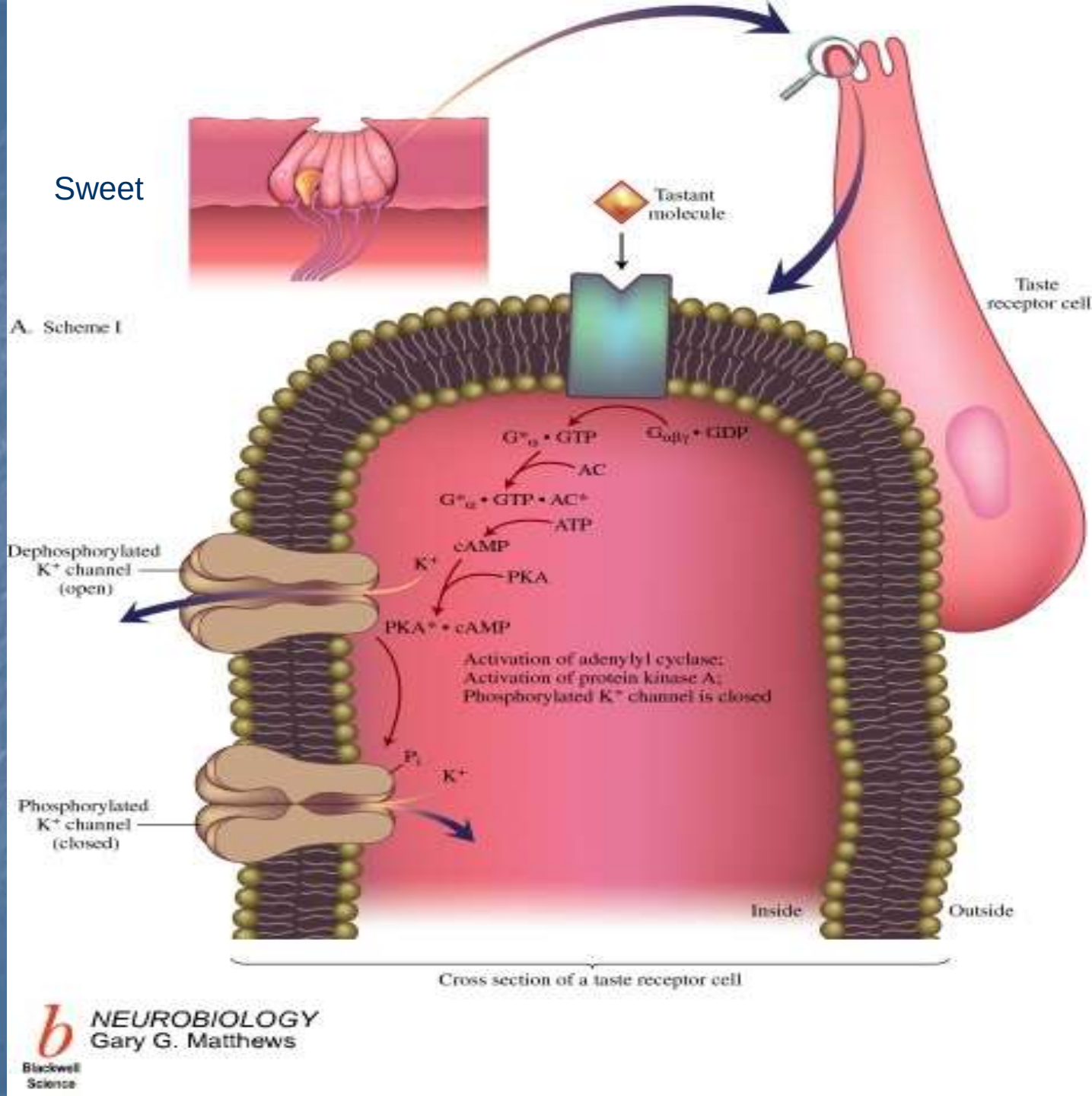
igure 13.34 Taste-transduction mechanisms differ for different aste qualities All transduction mechanisms except the IP_3 action in e) lead to *depolarization*, which spreads to the basal end of the cell nd opens voltage-gated Ca^{2+} channels to allow Ca^{2+} entry and trans-nitter release. *(a)* For 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



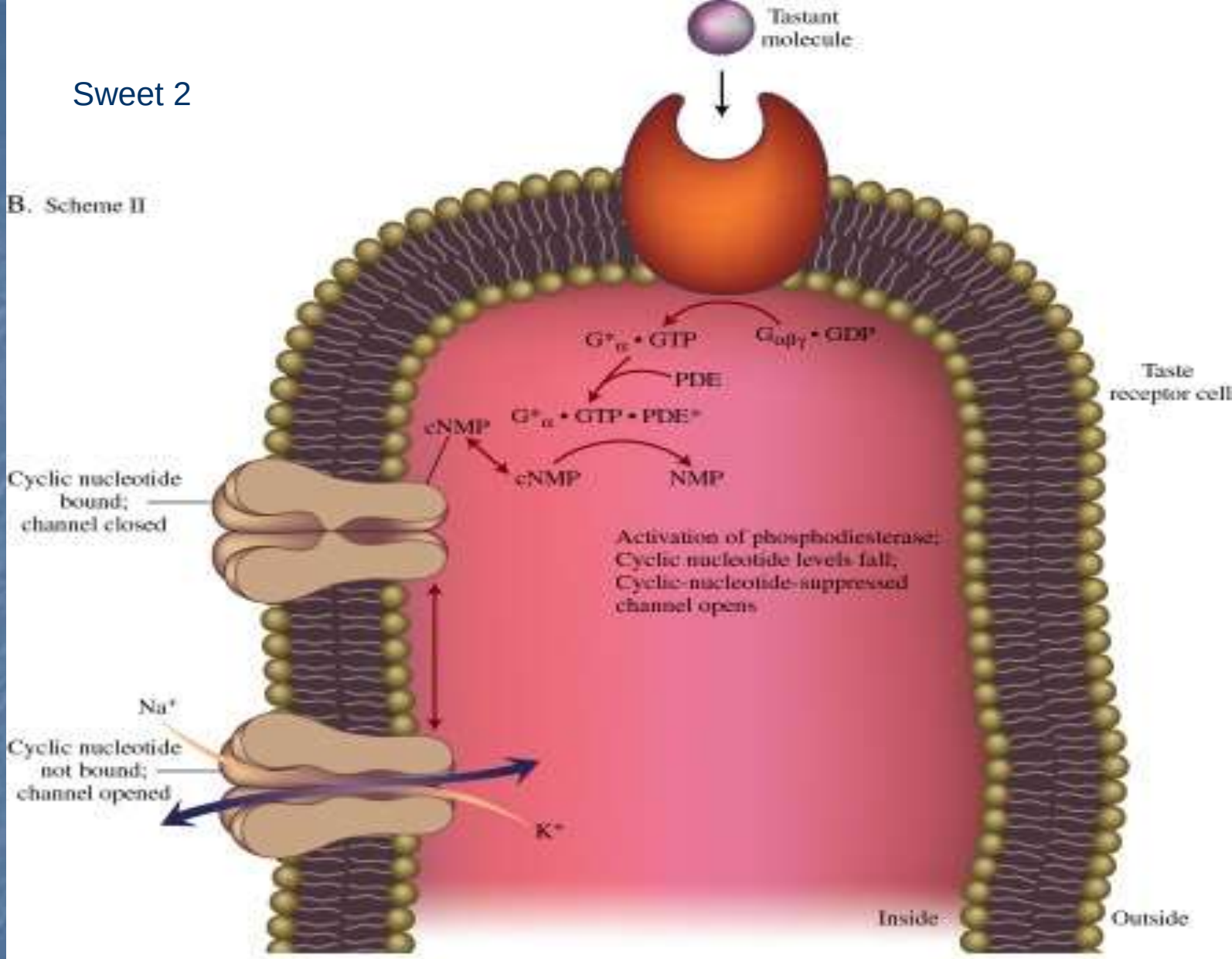
Transdukční schémata

Uzavření K kanálu



Neselektivní kationtový kanál se otevírá

Sweet 2



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Hořká chuť

Velká řada ligandů

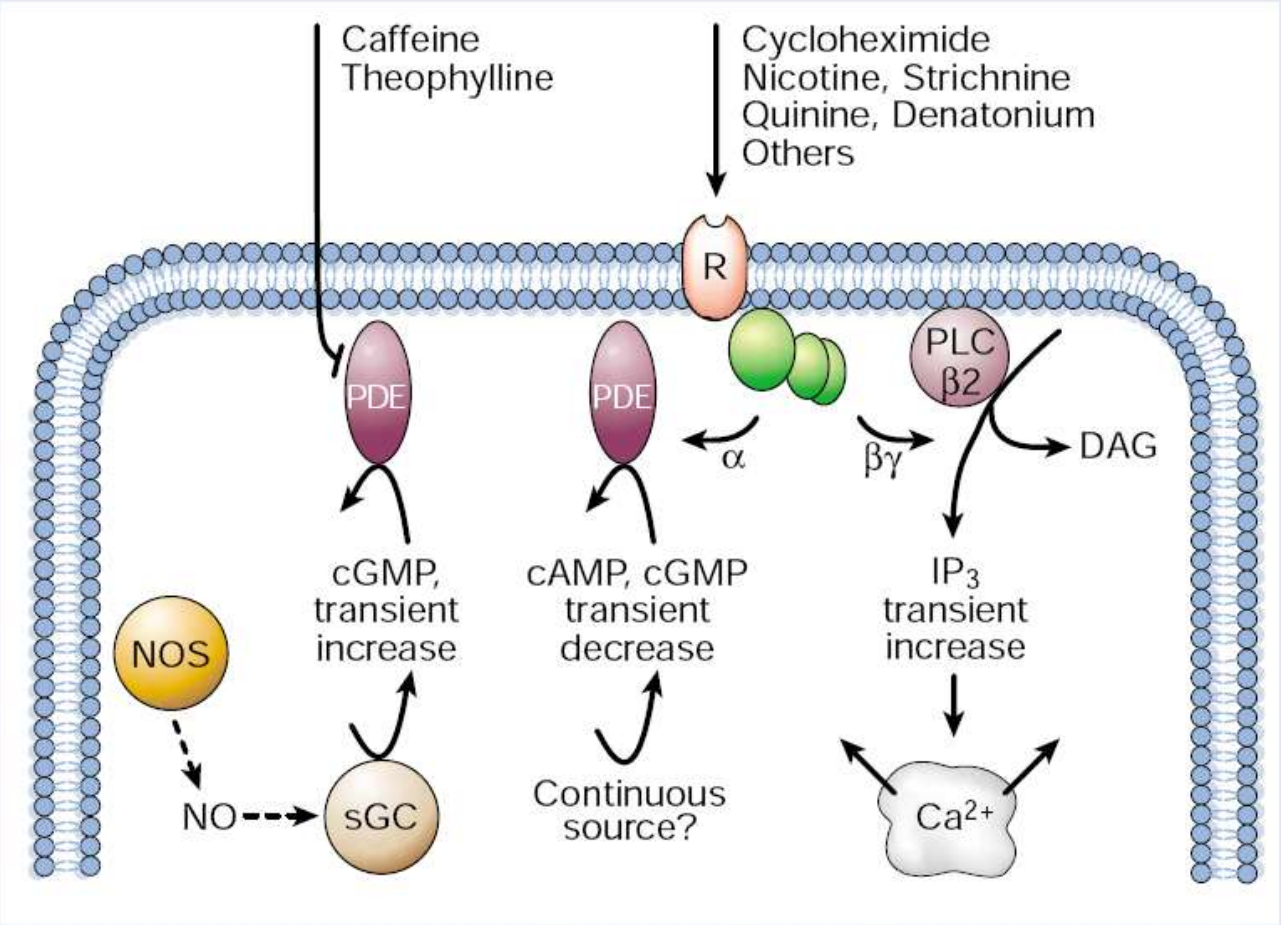
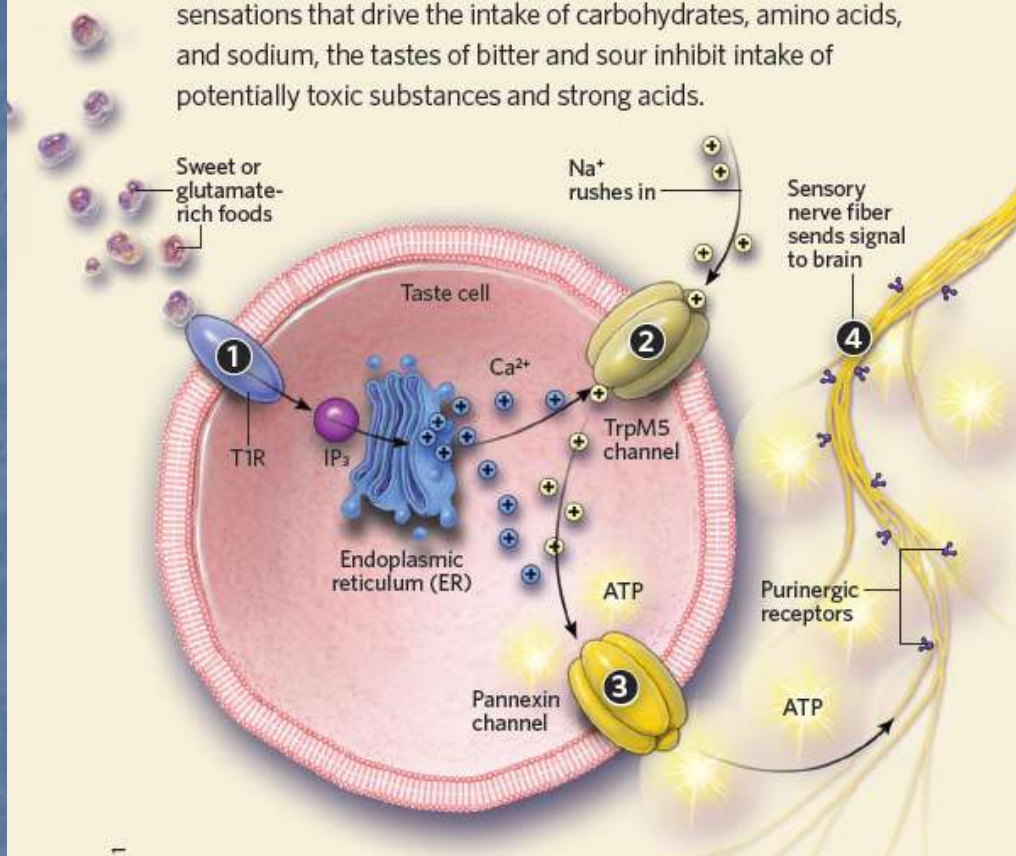


Figure 3 Transduction of bitter taste as elicited by a variety of ligands. Rs, multiple GPCRs of the T2R family, coupled to the G protein gustducin[47–49]; α, α-subunit of gustducin[6,57]; βγ, G-protein subunits β3 and γ13 (refs 60–62); PLCβ2, phospholipase C subtype[61]; Ins(1,4,5)P_3, inositol-1,4,5-trisphosphate[59]; 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.

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

ATP jako mediátor



THE TASTE SIGNALING CASCADE IN THE MOUTH

The binding of molecular components of sweet or glutamate-rich foods to T1R-class receptors and bitter substances to T2R receptors stimulates the release of Ca^{2+} into the cytosol from the endoplasmic reticulum (ER) via G protein signaling and the second messenger molecule inositol trisphosphate (IP_3) ❶. The Ca^{2+} activates the TrpM5 channel to allow the entry of sodium ions (Na^+), depolarizing the cell ❷. The combination of depolarization resulting from the influx of Na+ and rise in intracellular Ca^{2+} opens pannexin channels in the taste-cell membrane, releasing ATP from the cell ❸. This in turn activates purinergic receptors on the sensory nerve fibers innervating the taste buds, thereby sending a signal to the brain ❹.

Chuť ve střevě?

TASTE IN THE GUT

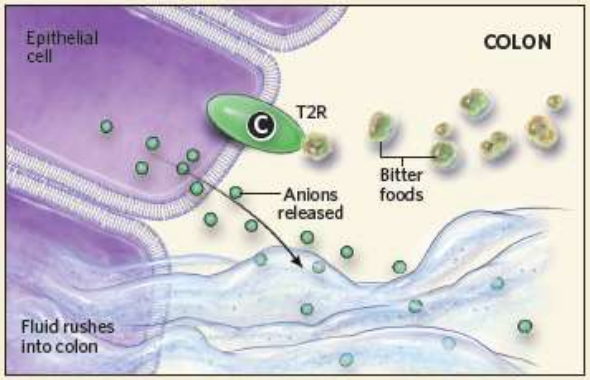
In contrast to taste receptors in the mouth, T1R and T2R receptors in the gut do not induce sensations of taste, but rather initiate molecular pathways that help guide the digestion or rejection of food substances traveling through the intestines. The underlying pathways, however, have many similarities.

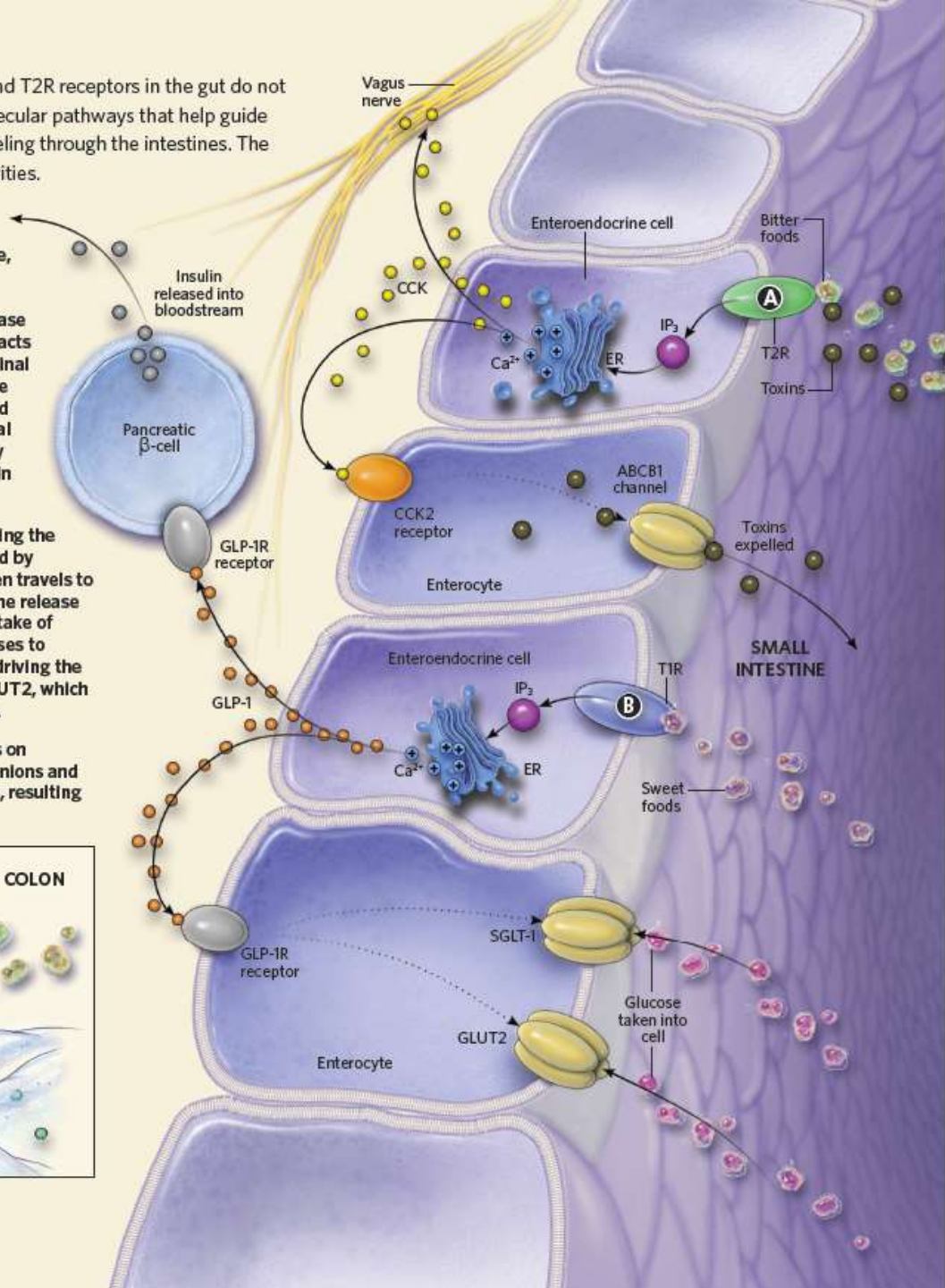
FOODS IN THE GUT

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.





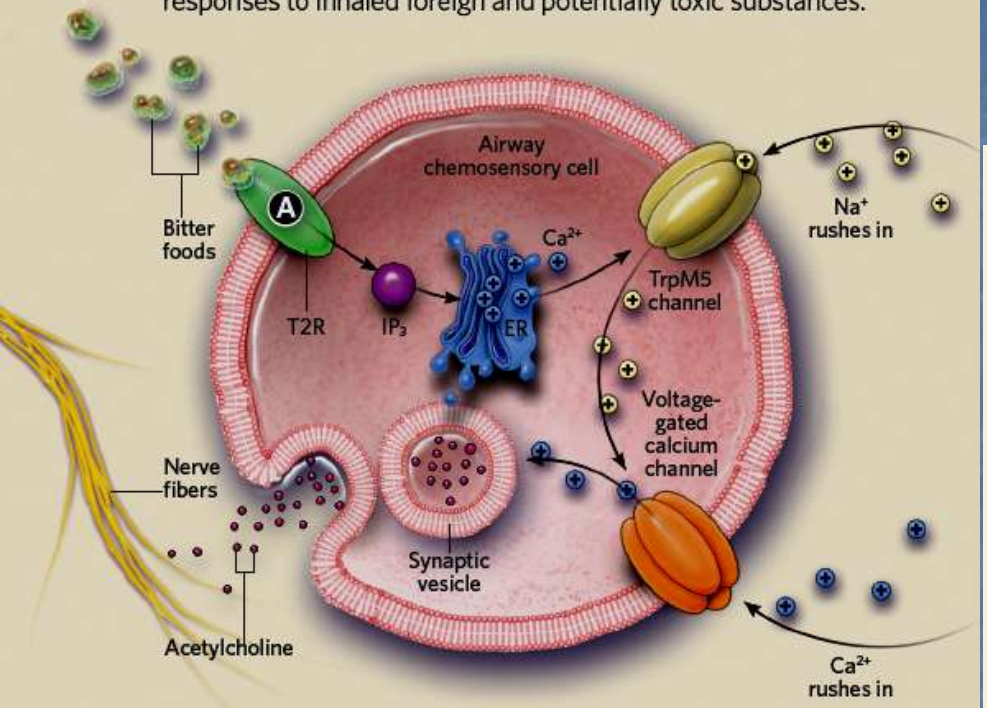
Potenciálně toxické (hořké) substance
T2R receptor
Kýchání, pohyb řasinek

Plíce – dolní c.d.

Nosohltan a trachea – horní c.d.

TASTE IN THE AIRWAYS

Scientists have also recently identified the existence of taste pathways in human airway cells, where they likely mediate defensive responses to inhaled foreign and potentially toxic substances.

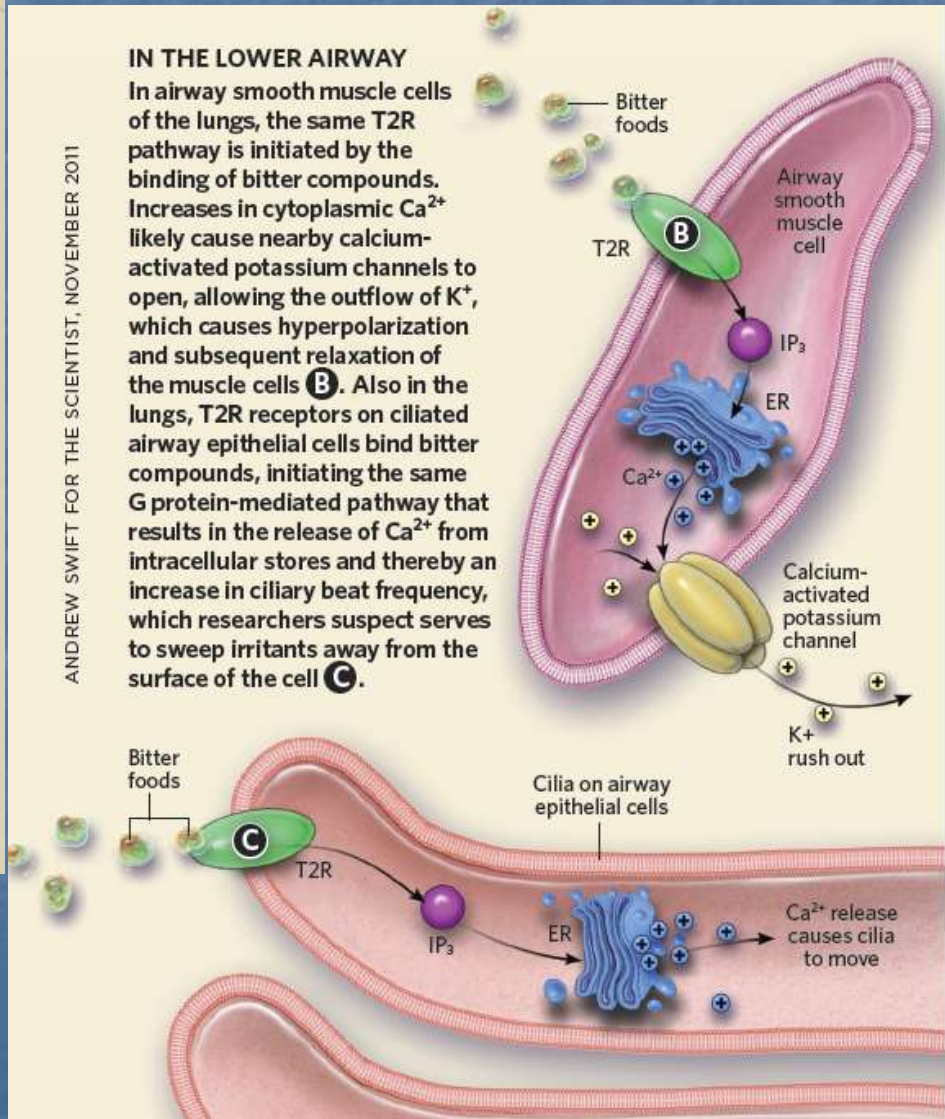


IN THE UPPER AIRWAY

In the upper airways (nasal passages and trachea), T2R receptors on chemosensory cells sense bitter compounds, releasing secondary messengers that spur the release of Ca^{2+} from the ER. The increase in cytoplasmic Ca^{2+} activates the TrpM5 transduction channel, allowing the influx of Na^{+} and the depolarization of the cell. This in turn activates voltage-gated Ca^{2+} channels, which permit even more Ca^{2+} to flood into the cell. This initiates the fusion of synaptic vesicles with the plasma membrane, releasing the neurotransmitter acetylcholine to activate nearby nerve fibers and induce protective reflexes such as sneezing A.

IN THE LOWER AIRWAY

In airway smooth muscle cells of the lungs, the same T2R pathway is initiated by the binding of bitter compounds. Increases in cytoplasmic Ca^{2+} likely cause nearby calcium-activated potassium channels to open, allowing the outflow of K^{+}, which causes hyperpolarization and subsequent relaxation of the muscle cells B. Also in the lungs, T2R receptors on ciliated airway epithelial cells bind bitter compounds, initiating the same G protein-mediated pathway that results in the release of Ca^{2+} from intracellular stores and thereby an increase in ciliary beat frequency, which researchers suspect serves to sweep irritants away from the surface of the cell C.

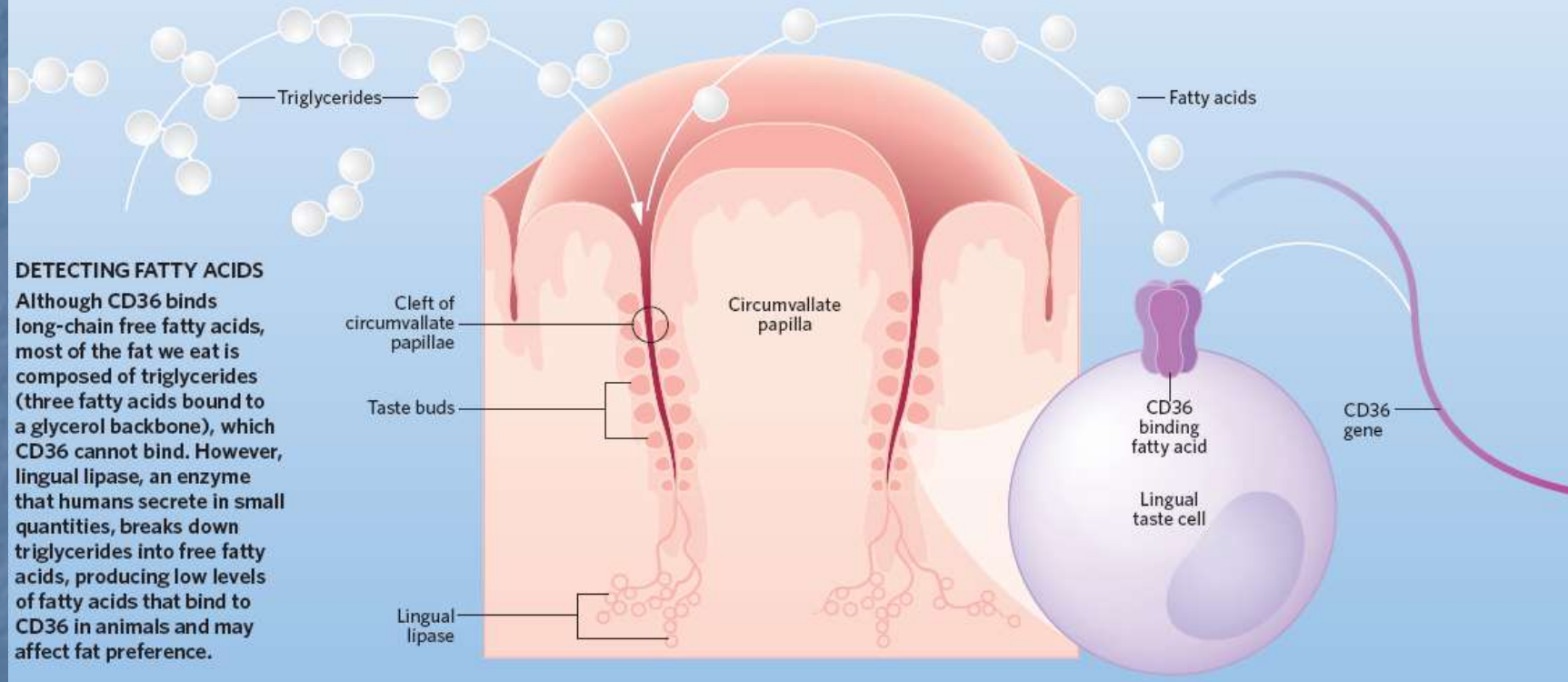


ANDREW SWIFT FOR THE SCIENTIST, NOVEMBER 2011

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.

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)

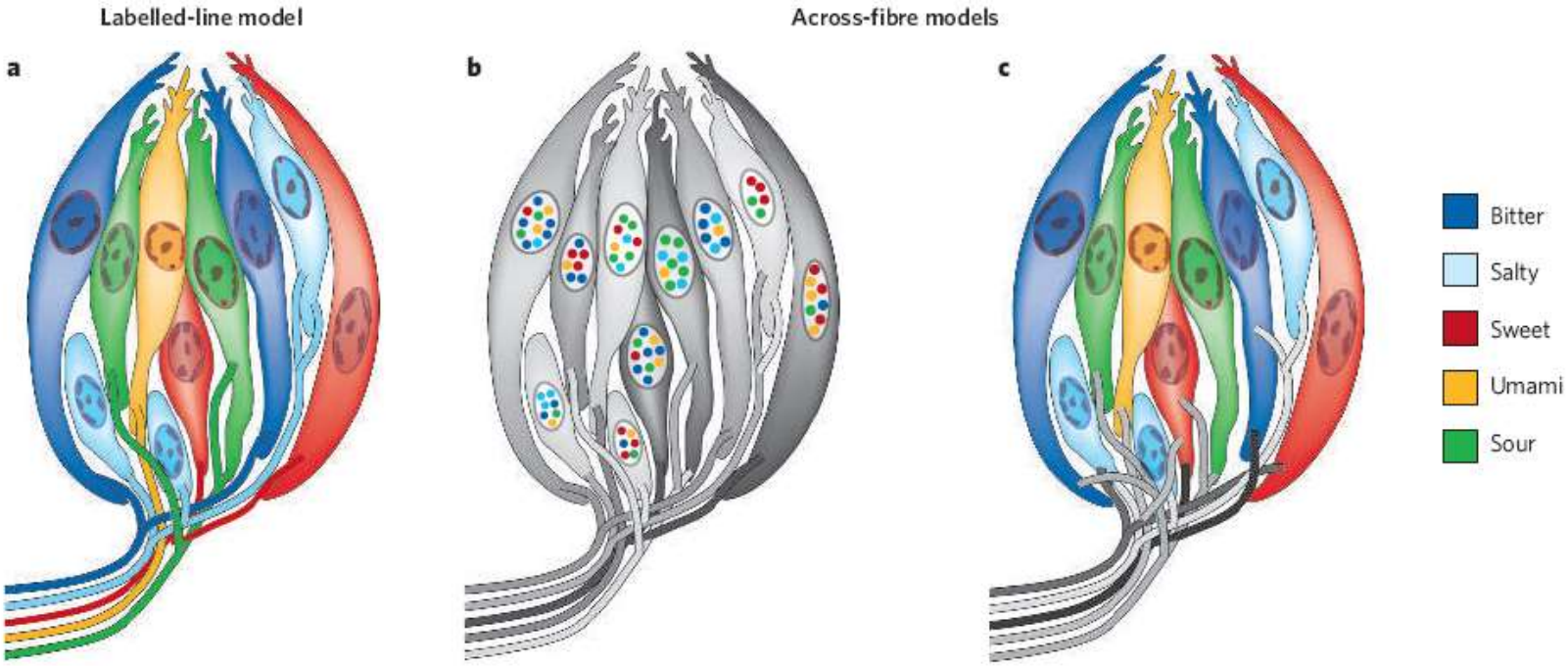
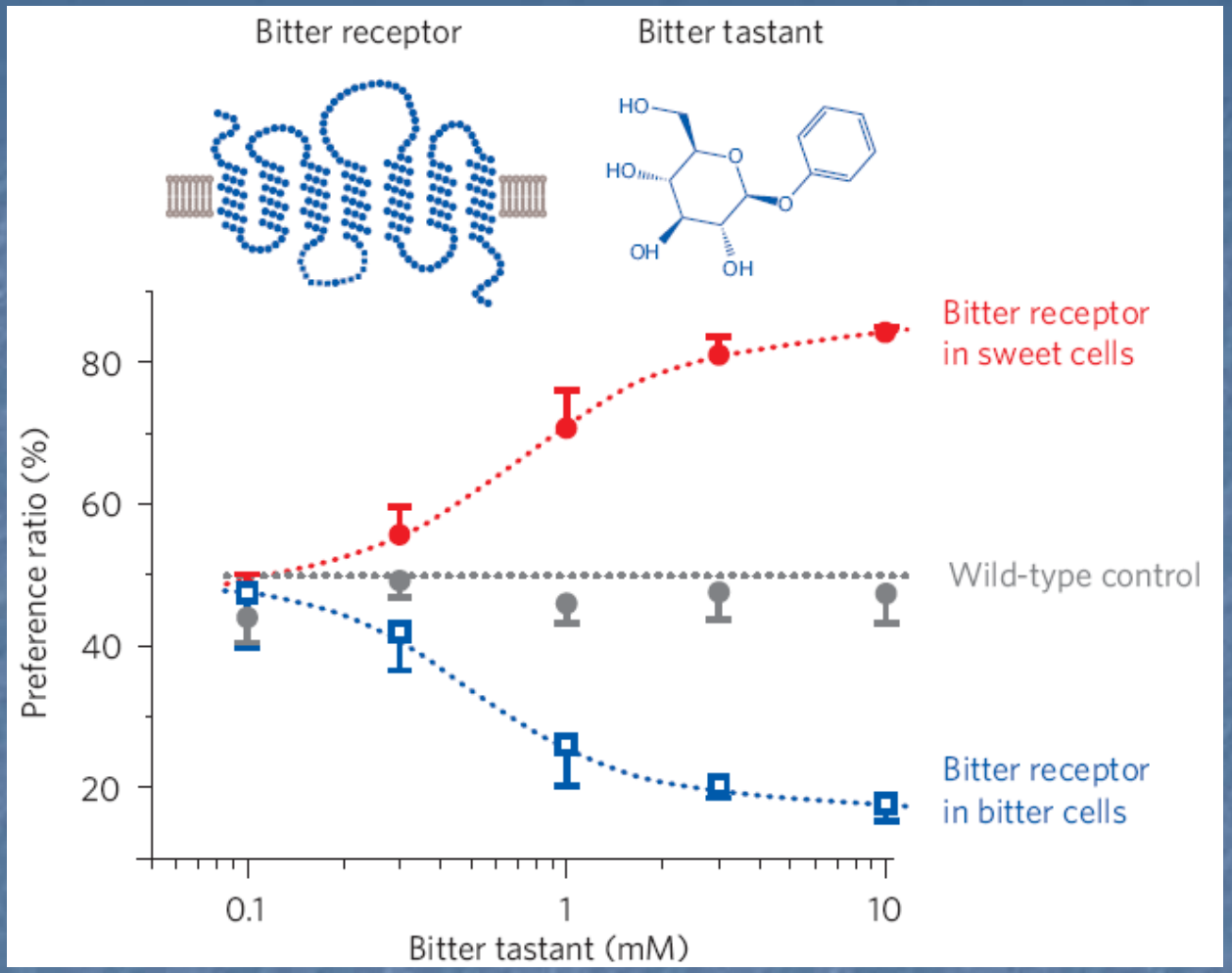


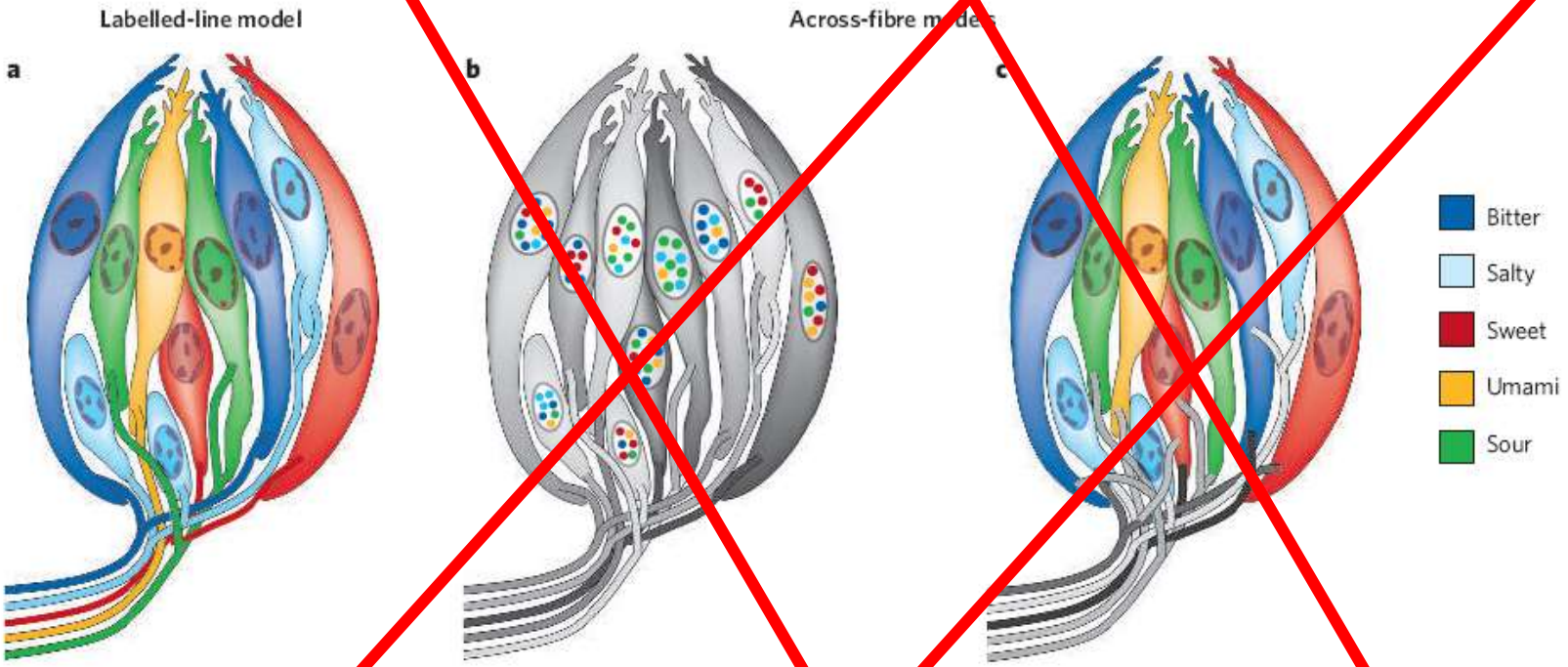
Figure 2 | Encoding of taste qualities at the periphery. There are two opposing views of how taste qualities are encoded in the periphery. **a**, In the labelled-line model, receptor cells are tuned to respond to single taste modalities — sweet, bitter, sour, salty or umami — and are innervated by individually 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 the labelled-line model.

Transgenní myši s přehozenými receptory



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

Každou jednotlivou chuť rozeznáme i ve směsi chutí – ochrana.
Nevytváří se tedy mícháním chutní chuti nové.



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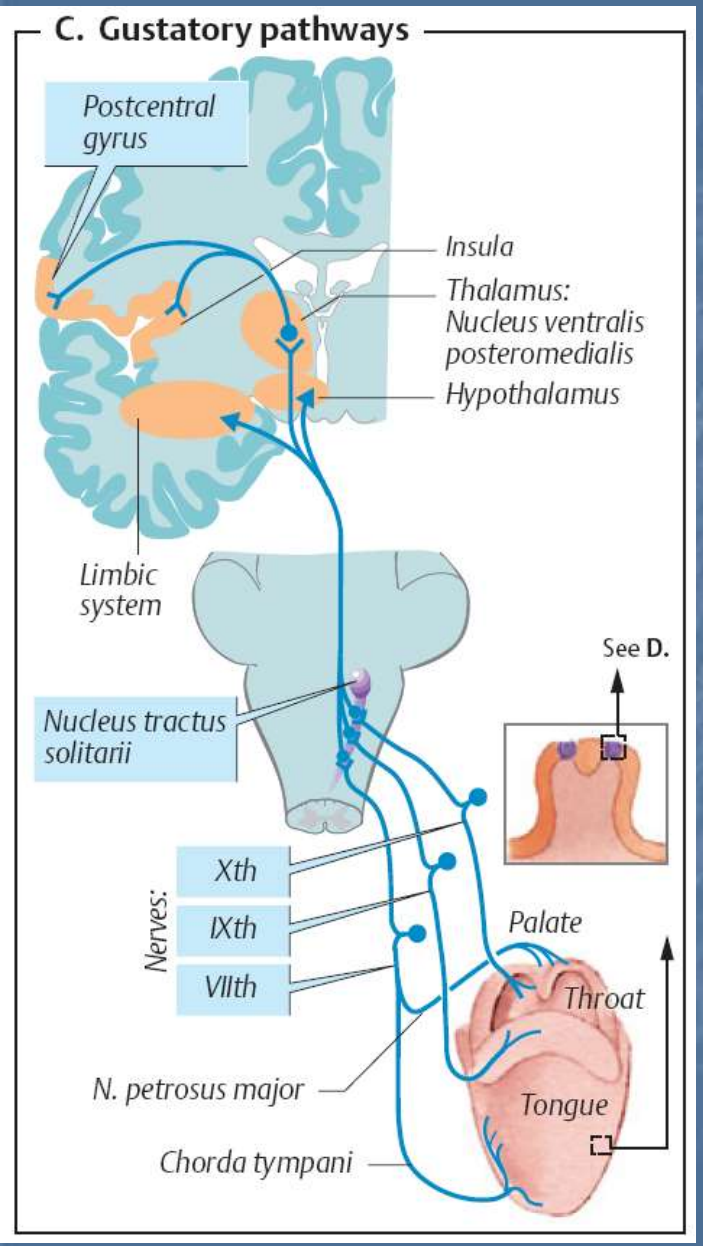
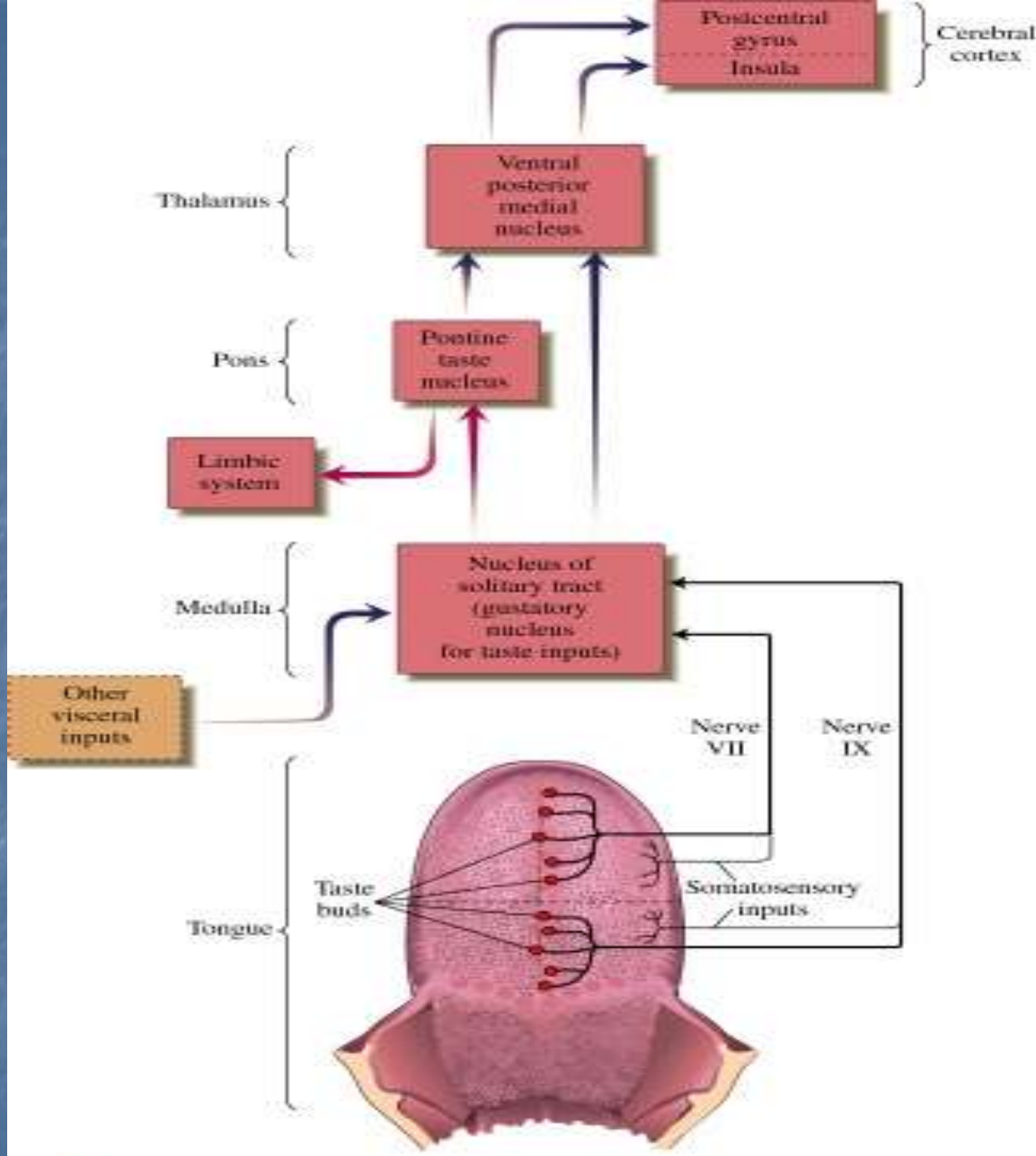
Axony patří pseudounipolárním neuronům, jejichž těla leží v gangliích VII., IX. a X. hlavového nervu. Přes nižší mozková centra můžeme sledovat cestu chuťové informace ke dvěma korových chuťovým oblastem.
První asi hraje roli při vnímání prostorového rozmístění chuťových počitků na jazyku a druhá je 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.).

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.





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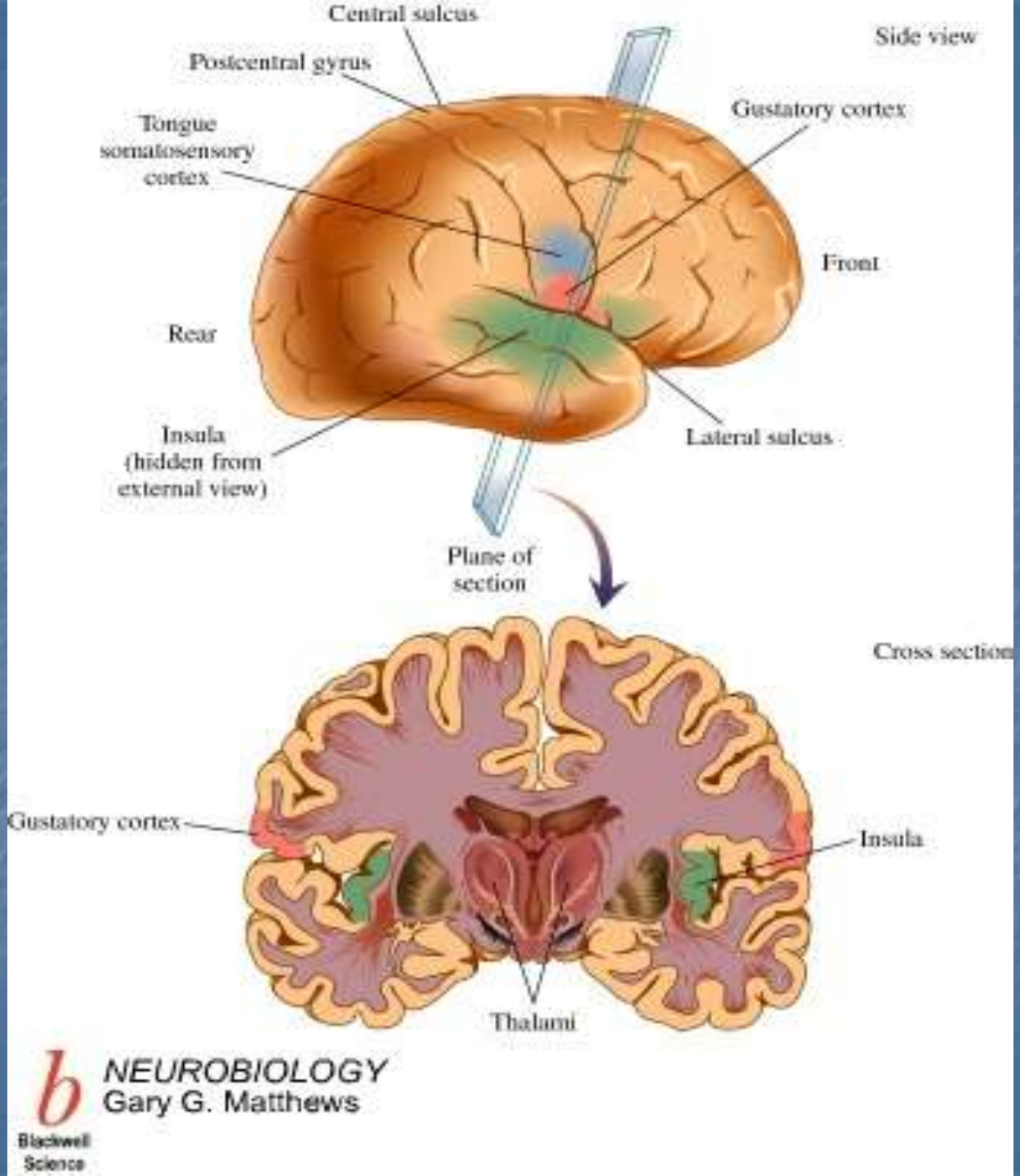

NEUROBIOLOGY
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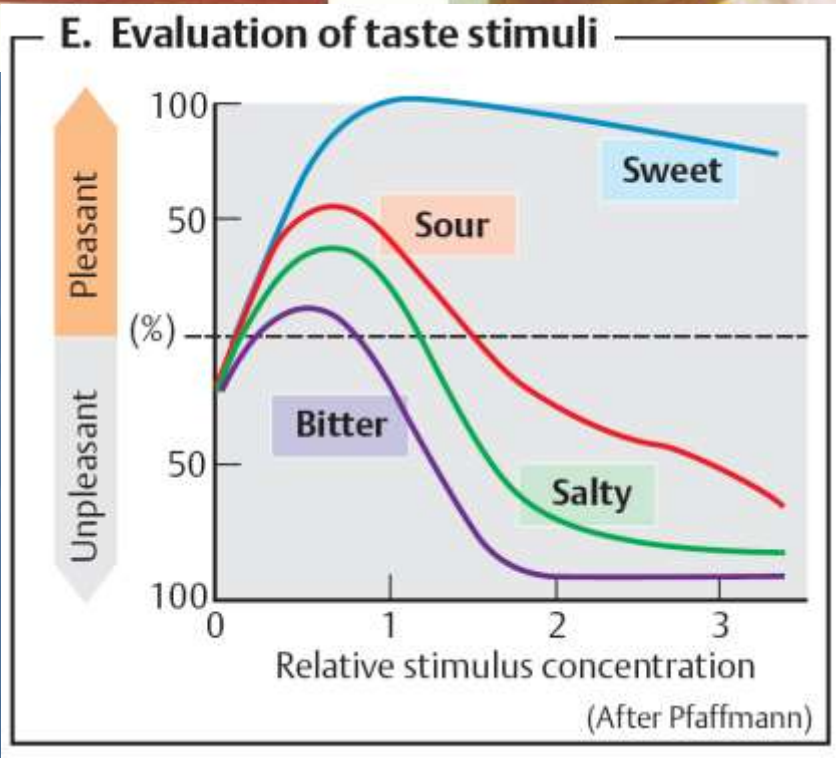
Potěšení z chutí - vrozené prospěšné reflexy. Zvýšená chuť na chybějící složku.

(a)

(b)



Hygrorecepce

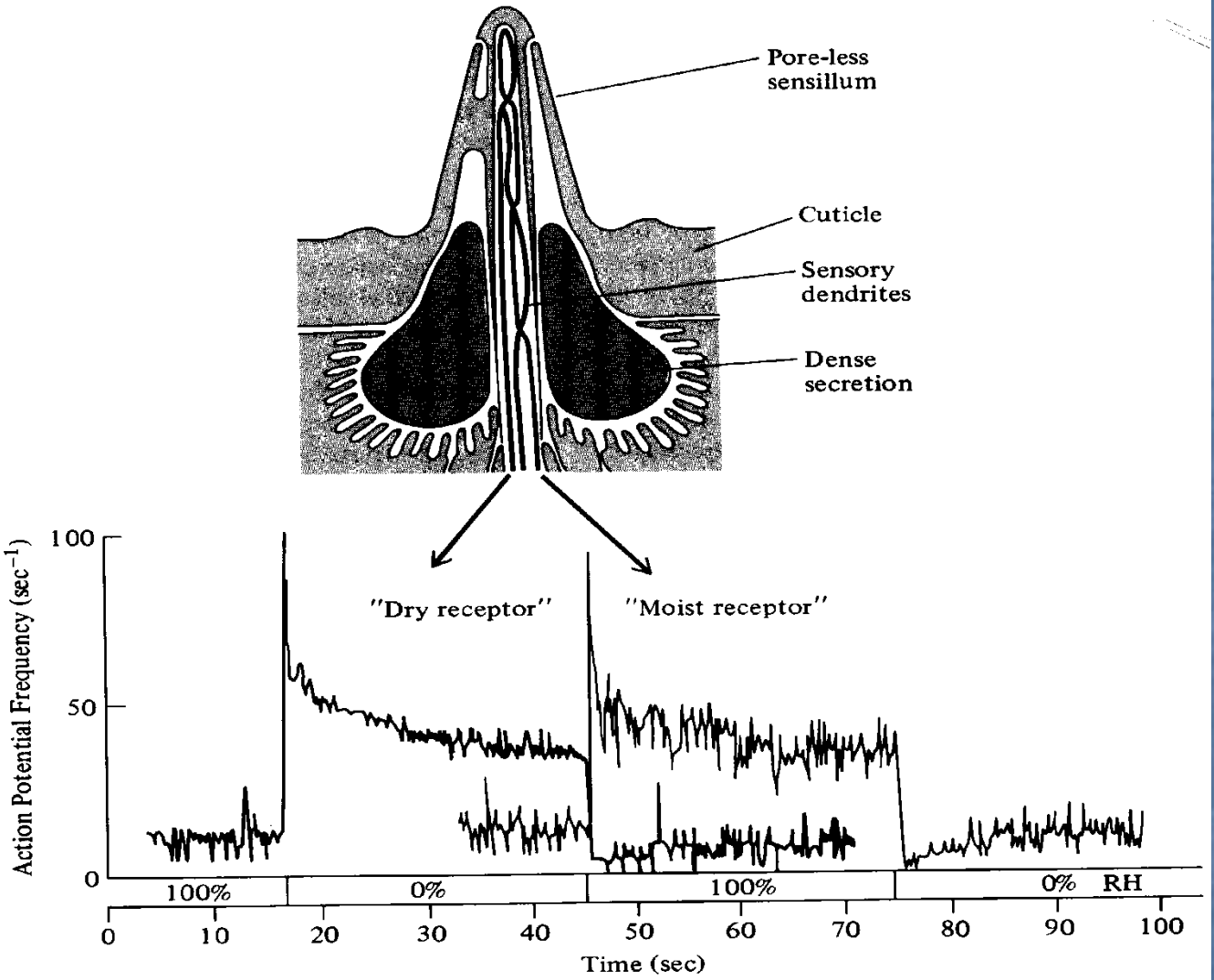


FIGURE 7–18 The "cold-moist-dry" triad sensory sensillum of the cockroach contains three bipolar sensory neurons; one neuron of the hygroreceptor responds to high humidity ("moist" receptor) and one to low humidity ("dry" receptor). The receptor cavity of the poreless sensillum is filled with a dense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

Termorecepce

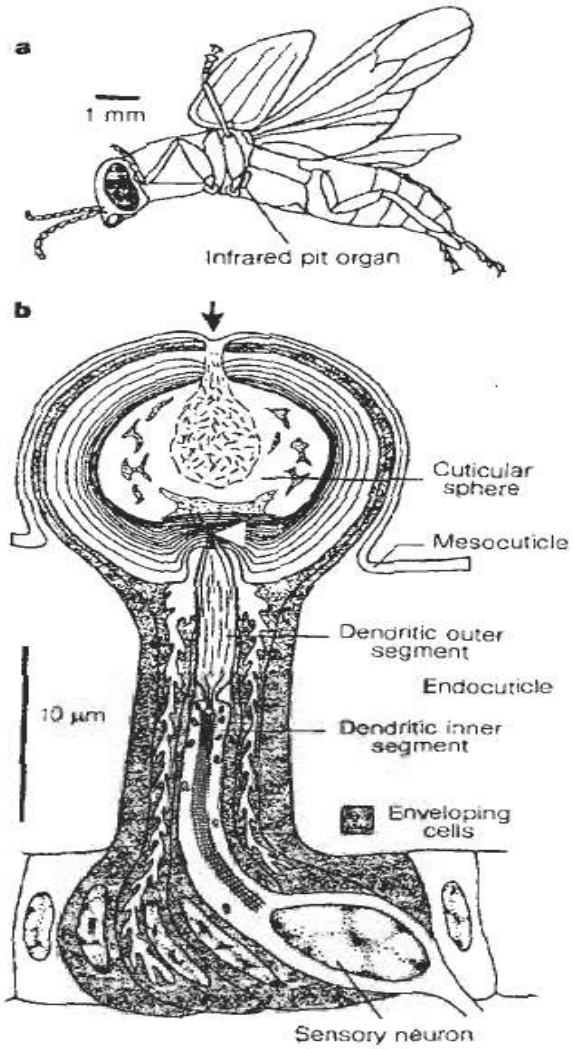


Figure 1 a, Diagram of *Melanophila* (body length 10 mm). The infrared pit organs, situated next to the coxae of the middle legs, are completely exposed during flight. b, An infrared sensillum, redrawn from ref. 3.

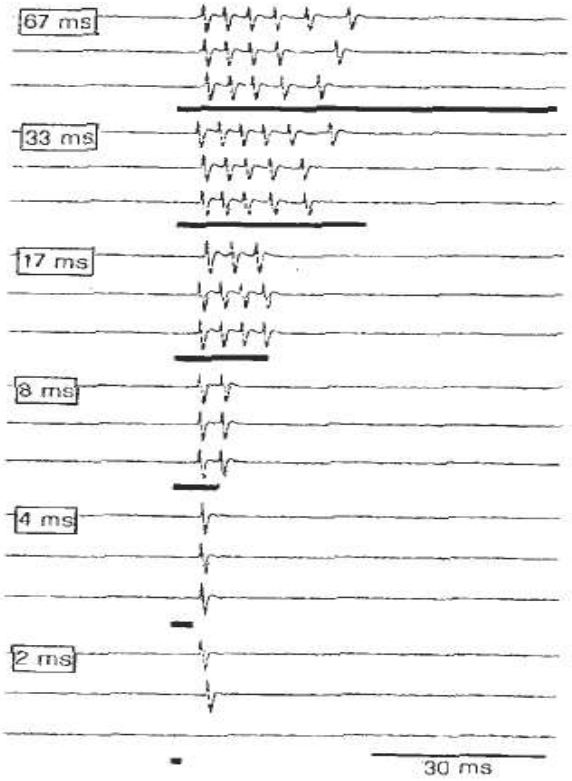


Figure 2 The responses of a neuron, recorded from the pit organ, to various infrared stimuli. Each trace shows the original response to one stimulus. Horizontal bars indicate exposure times. Each trial was repeated three times. The number of action potentials decreases with decreasing stimulus duration; 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

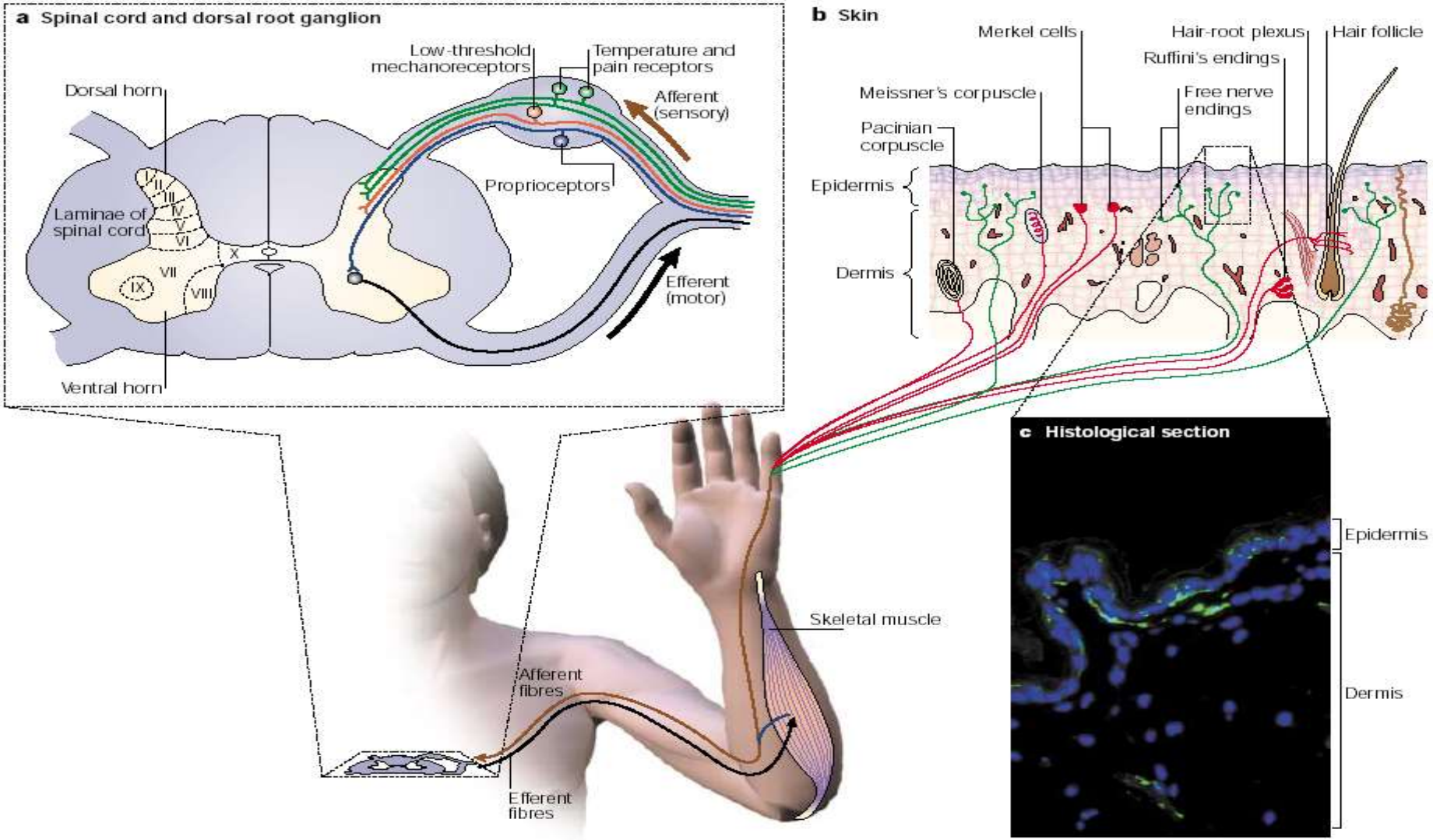


Figure 1 | **Anatomic and functional organization of touch. a** | Spinal nerves formed by the joining of afferent (sensory) and efferent (motor) roots provide peripheral innervation to skin, skeletal muscle, viscera and glands. Arrows denote the direction of incoming sensory and outgoing motor impulses. The cell bodies of motor neurons are located within the ventral horn (laminae VII–IX) of the spinal cord. Cell bodies of sensory neurons are located in the dorsal root ganglia (DRG). Within the DRG there are subclasses of sensory neurons known as proprioceptive (blue), low-threshold mechanosensitive (red) and temperature- and pain-sensing neurons (green). These neurons project centrally to dorsal horn interneurons (laminae I–VI of the spinal cord) and peripherally to target tissues. Proprioceptive neurons (blue fibre) project to specialized structures within target tissues such as muscle, and sense muscle stretch. **b** | Low-threshold mechanosensitive neurons (red fibres) project to end organs that transmit mechanical stimuli. Five types of mechanosensitive assemblies have been described and are illustrated in the figure. Temperature and pain sensing neurons (green) do not project to specialized end organs; instead they terminate as free nerve endings in all layers of the skin, and near blood vessels and hair follicles. **c** | Section of skin showing free nerve endings (green fibres) stained with the pan-neuronal marker PGP9.5. The nuclei of skin cells are stained (blue) with 4,6-diamidino-2-phenylindole (DAPI). Free nerve endings are found in both the epidermal and dermal layers.

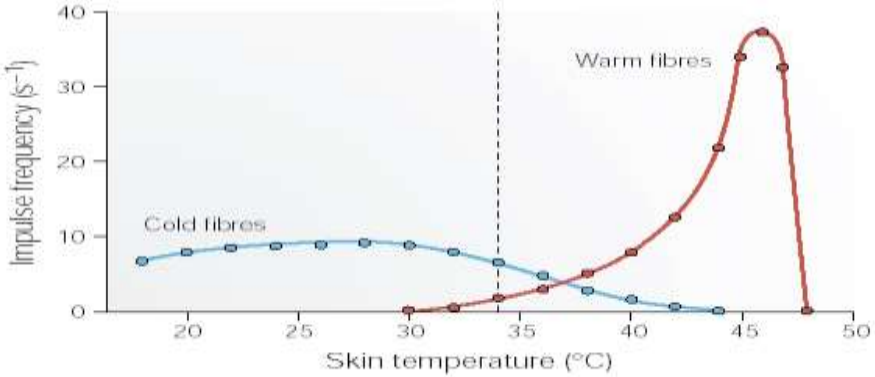


Figure 2 | **Average discharge frequency of individual cold- and warm-sensitive fibres in response to changes in skin temperature.** The dotted line indicates the normal skin temperature (33°C). Cold-sensitive fibres respond only to cooling, whereas warm-sensitive fibres respond to warming. Neither type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

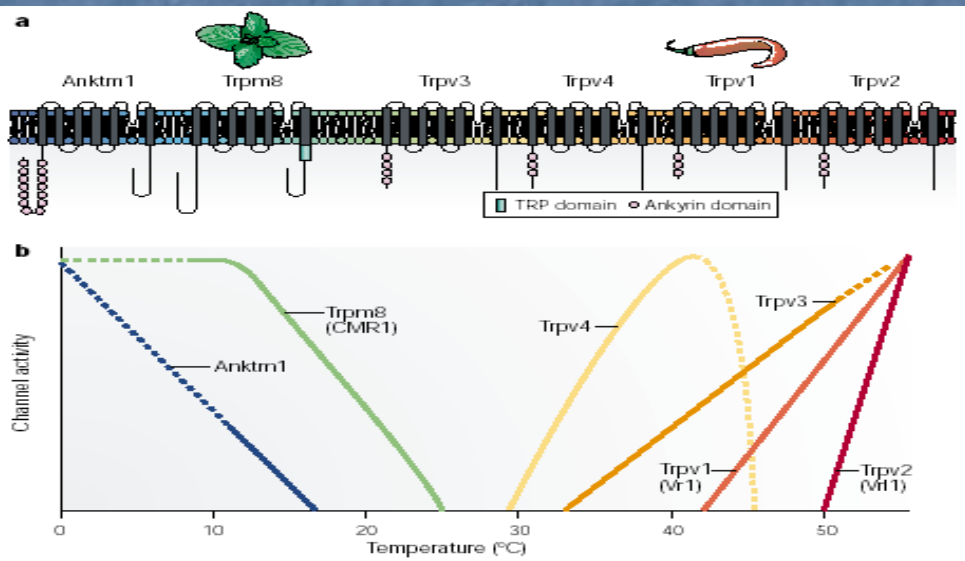


Figure 3 | **Domain organization and temperature thresholds of temperature-activated transient receptor potential ion channels (thermoTRPs).** a | TRP channels are composed of six putative membrane-spanning units and cytoplasmic amino and carboxyl termini. Some TRPs also have variable numbers of ankyrin 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.

Shepherd, Smell…

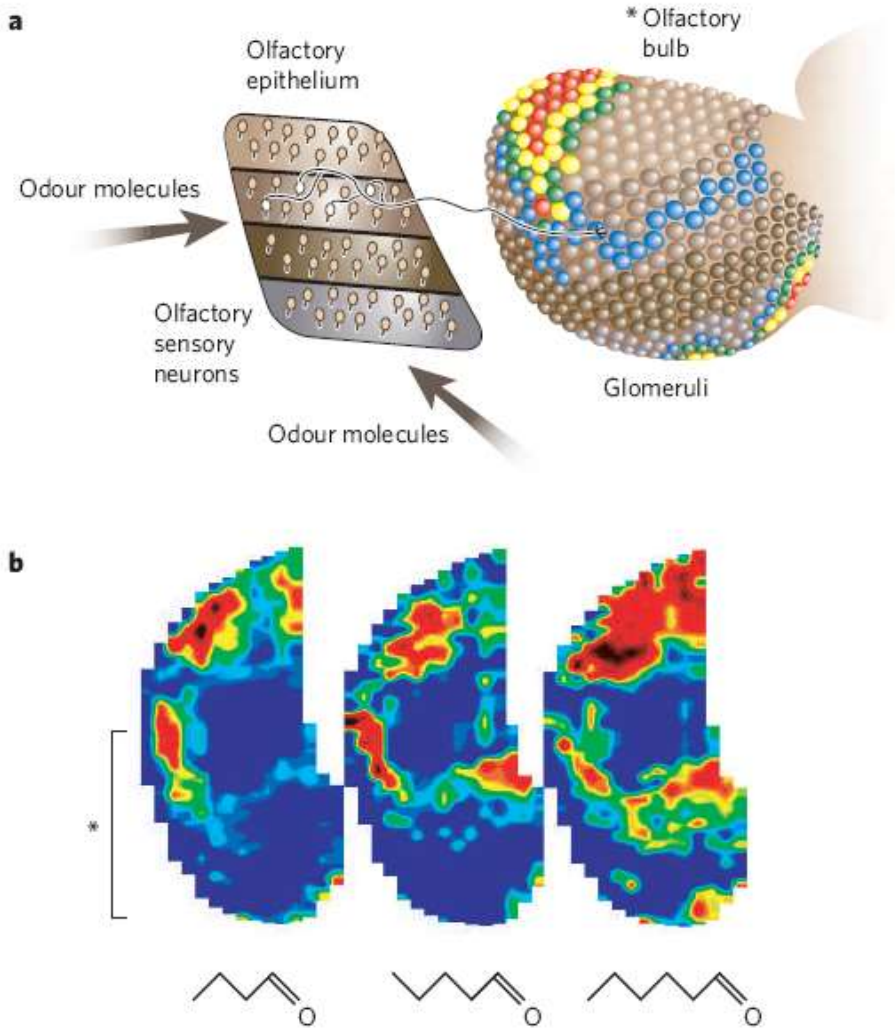


Figure 1 | Odour images in the olfactory glomerular layer. **a**, Diagram showing the relationship between the olfactory receptor cell sheet in the nose and the glomeruli of the olfactory bulb[53]. **b**, fMRI images of the different but overlapping activity patterns seen in the glomerular layer of the 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.)

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.

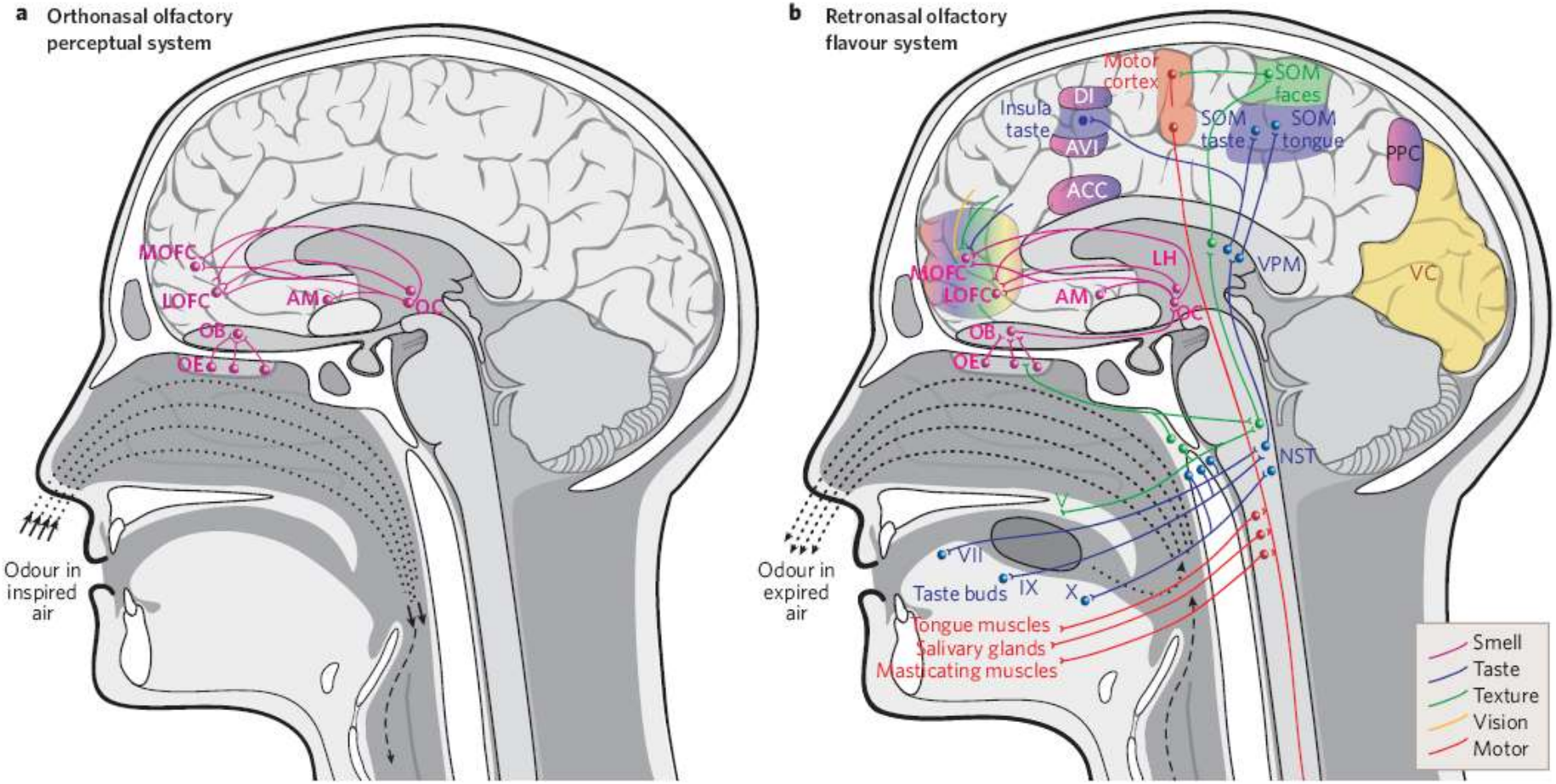


Figure 2 | The dual olfactory system. **a**, Brain systems involved in smell perception during orthonasal olfaction (sniffing in). **b**, Brain systems involved in smell perception during retronasal olfaction (breathing out), with food in the oral cavity. Air flows indicated by dashed and dotted lines; 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.

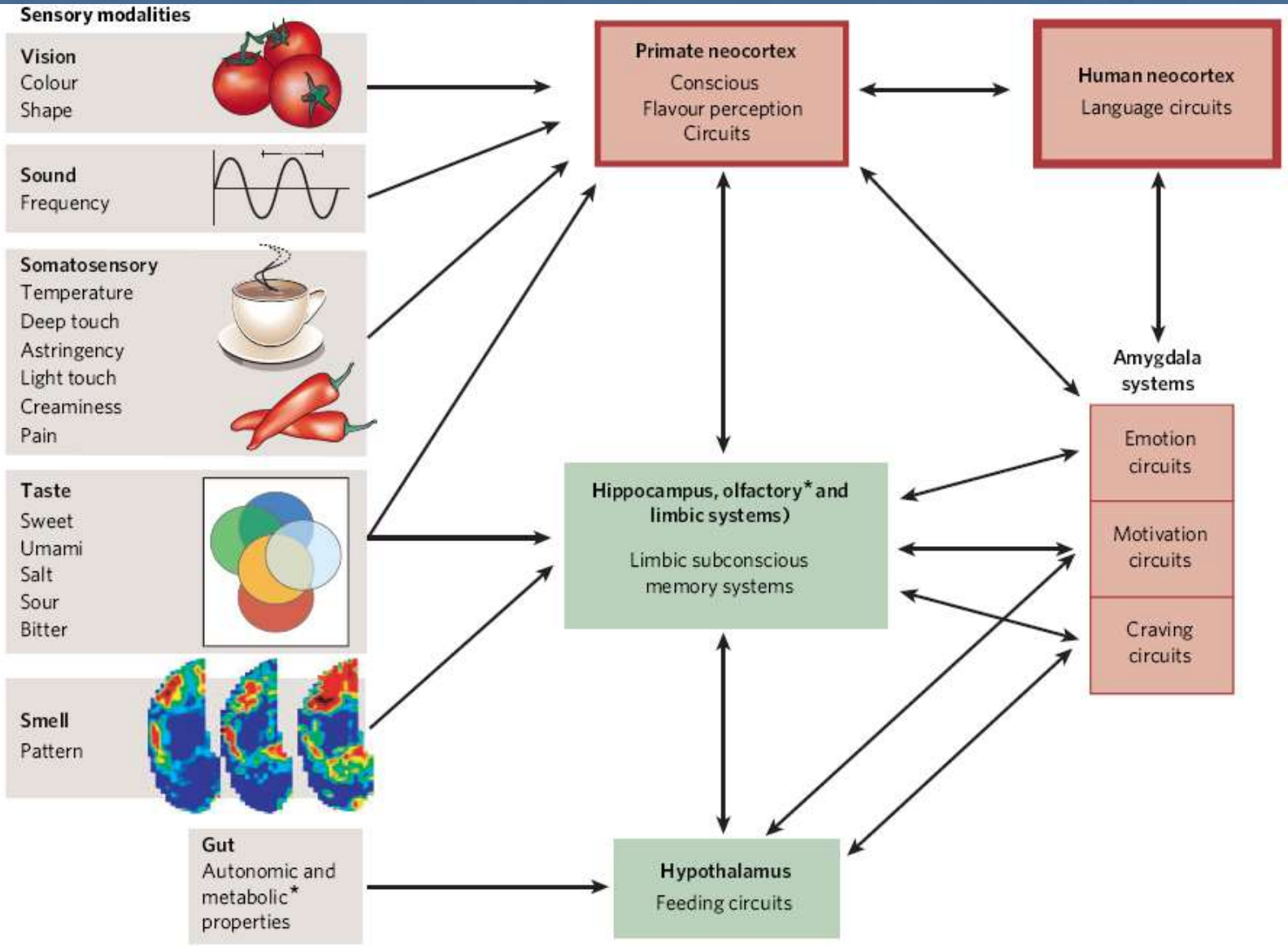


Figure 3 | The human brain flavour systems that evaluate and regulate food intake. The diagram shows the areas involved in the perceptual, emotional, memory-related, motivational and linguistic aspects of food evaluation mediated by flavour inputs[32,41,54,55]. Left, different sensory modalities and 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).