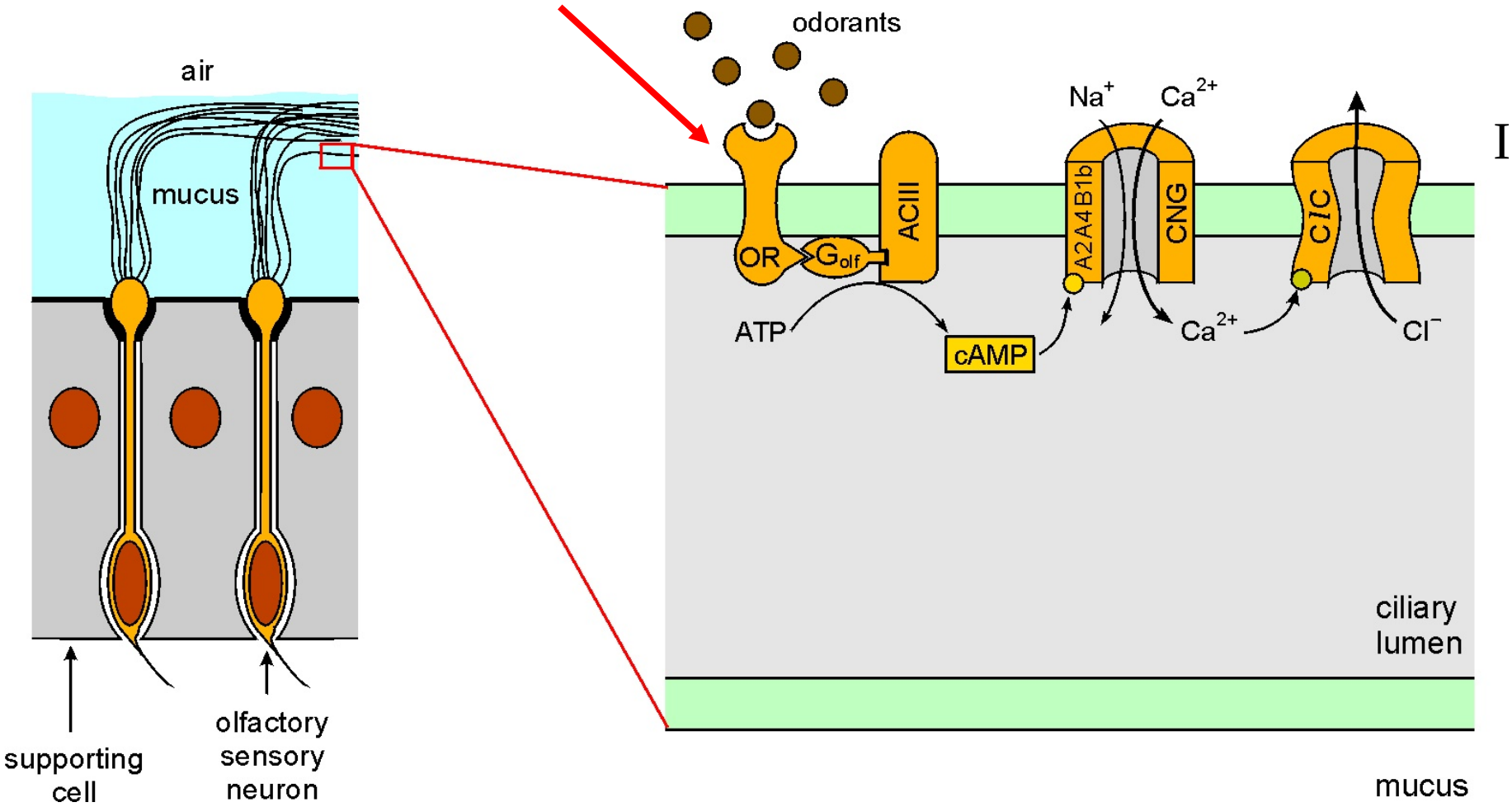
Properties of the

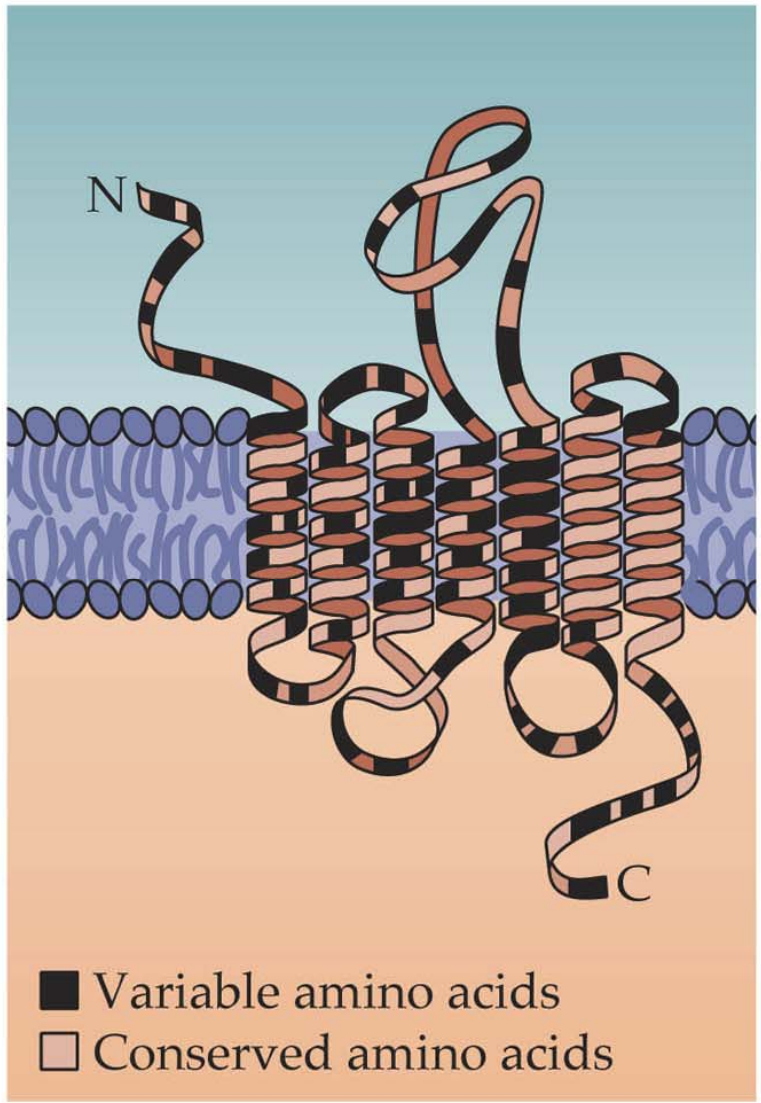
molecular components

of the olfactory signalling cascade

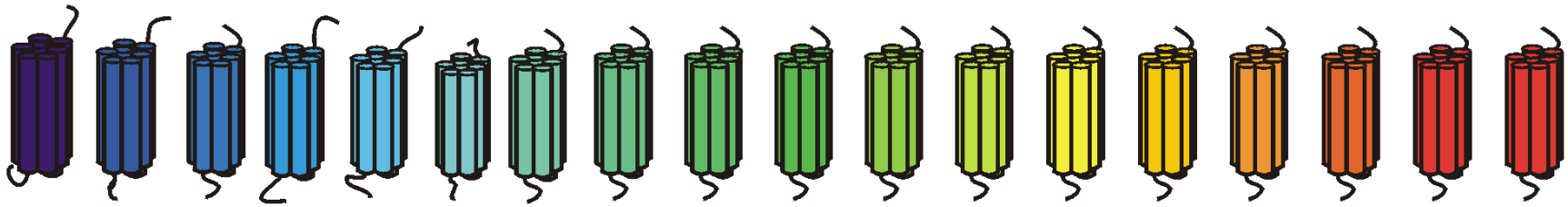
Olfaction


air
mucus
supporting cell
olfactory sensory neuron
odorants
OR
G_{olf}
ACIII
ATP
cAMP
Na^+
Ca^{2+}
A2A4B1b
CNG
Ca^{2+}
ClC
Cl^-
ciliary lumen
mucus

Odorant receptor



Signal transduction



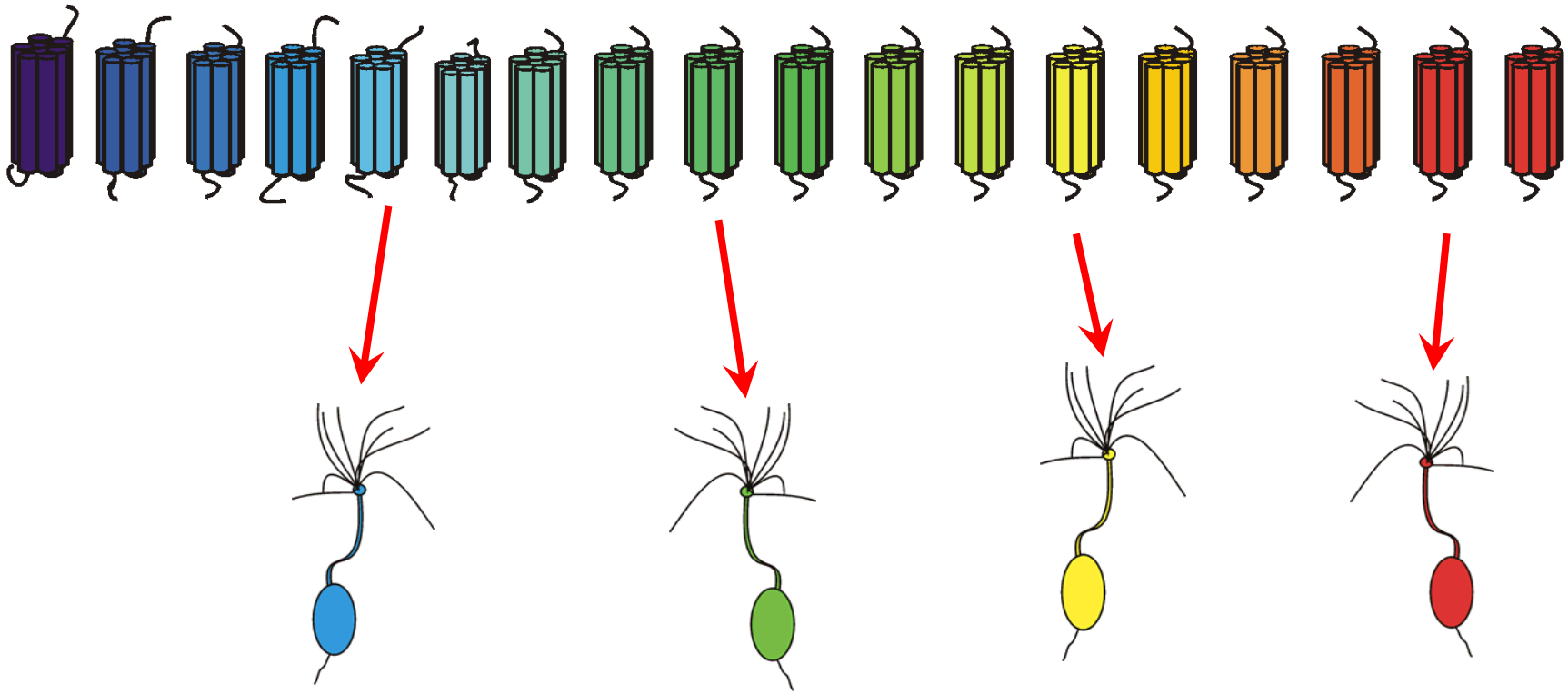
Large number of different odorant receptors.

Odorant receptors belong to the gene family of G-protein coupled receptors (→rhodopsin).

Mouse genome: approx. 1300 genes encode odorant receptors; 30% are pseudo-genes.

Human: approx. 1000 genes encode odorant receptors; 65% are pseudo-genes.

Odorant receptors

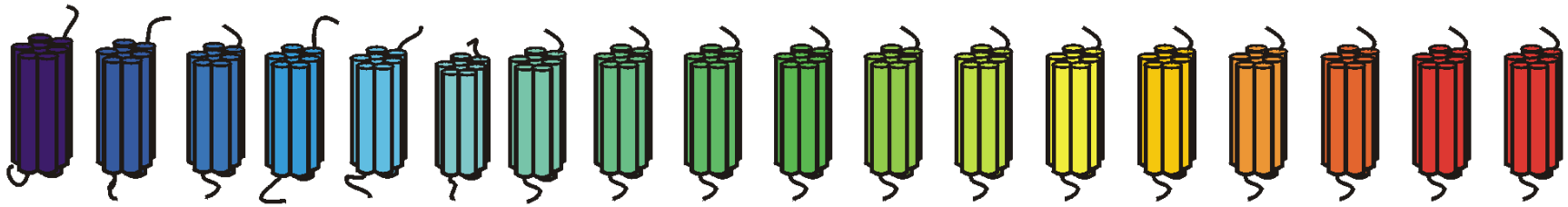


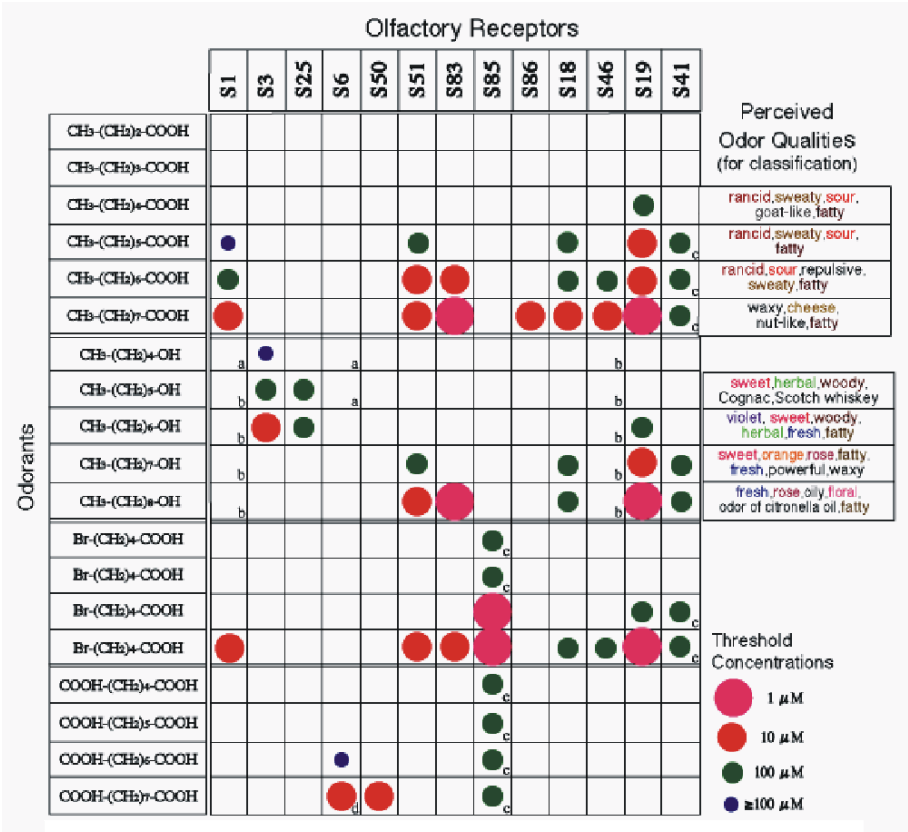
Each olfactory neuron expresses one single type of odor. receptor

Each cell expresses only one allele of the gene (allelic exclusion)

15.000 - 30.000 olfactory neurons express the same allele

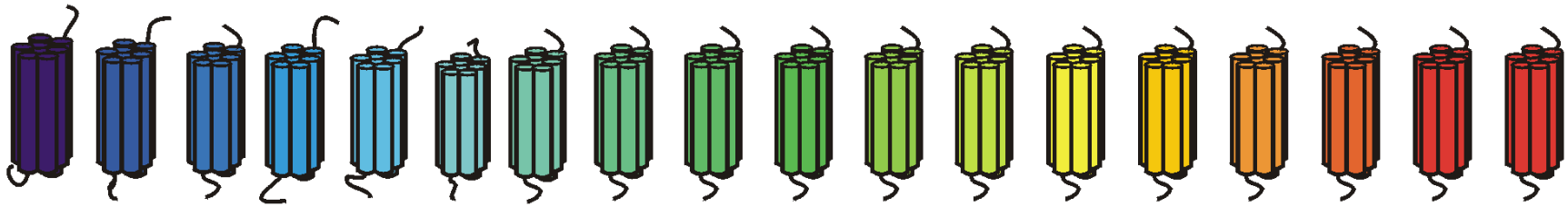
Signal transduction

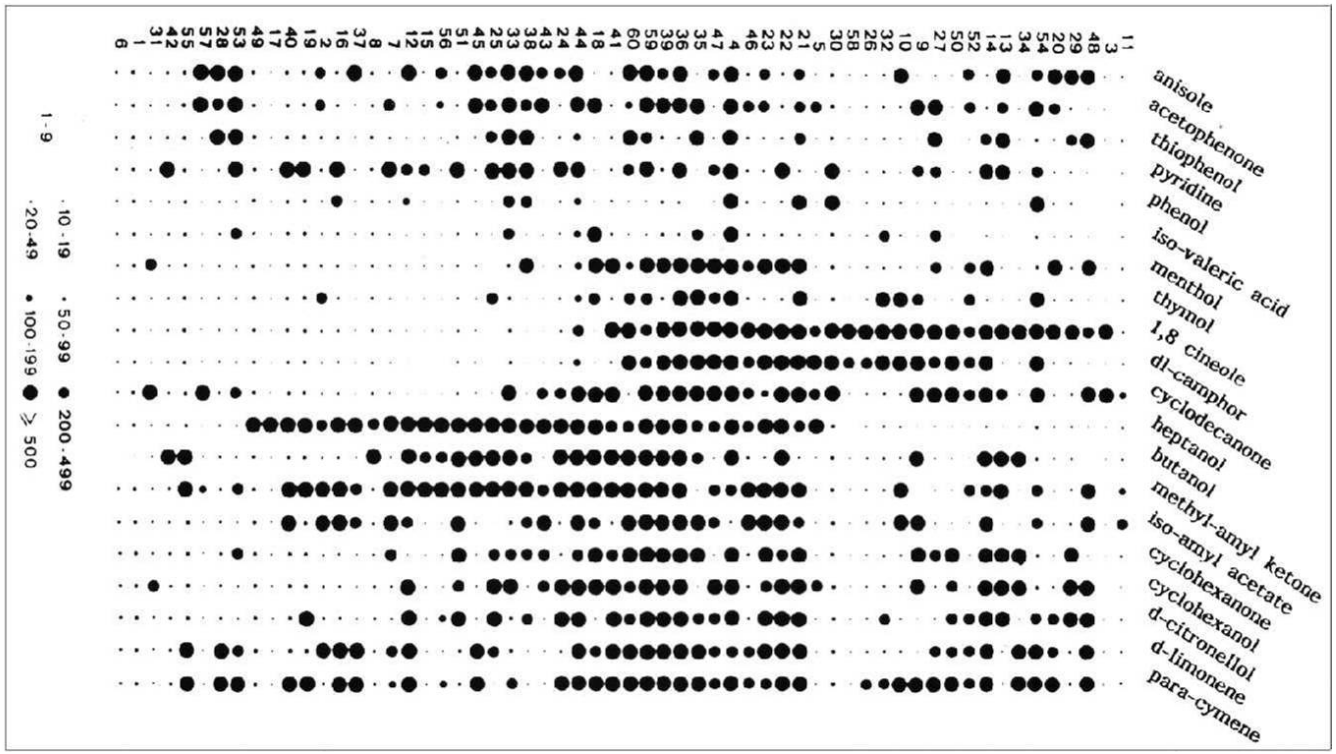




Ligand-specificity of olfactory receptors is low

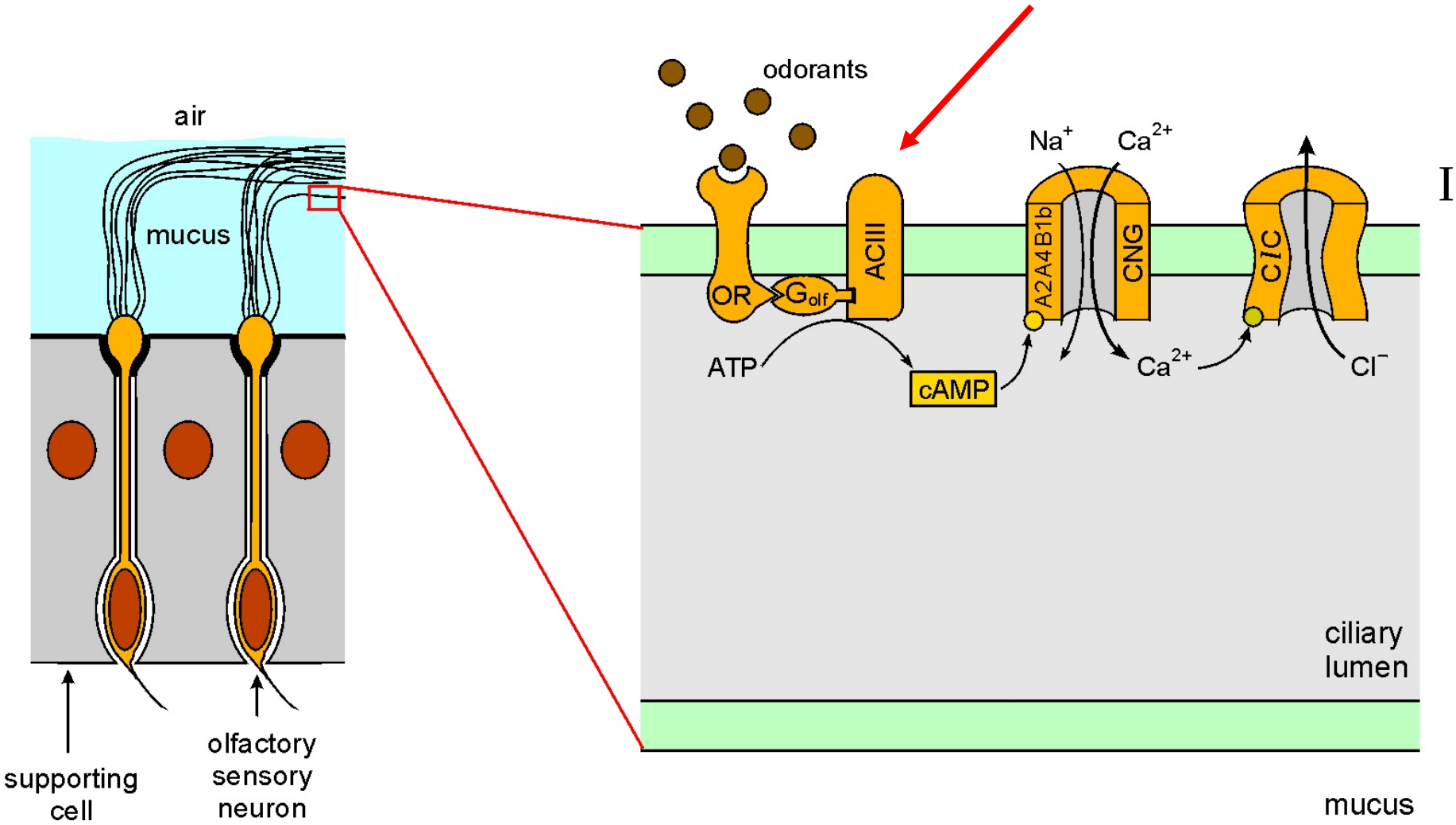
Signal transduction





Ligand-specificity of olfactory receptors is low

Olfaction


air
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ACIII
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cAMP
Na^+
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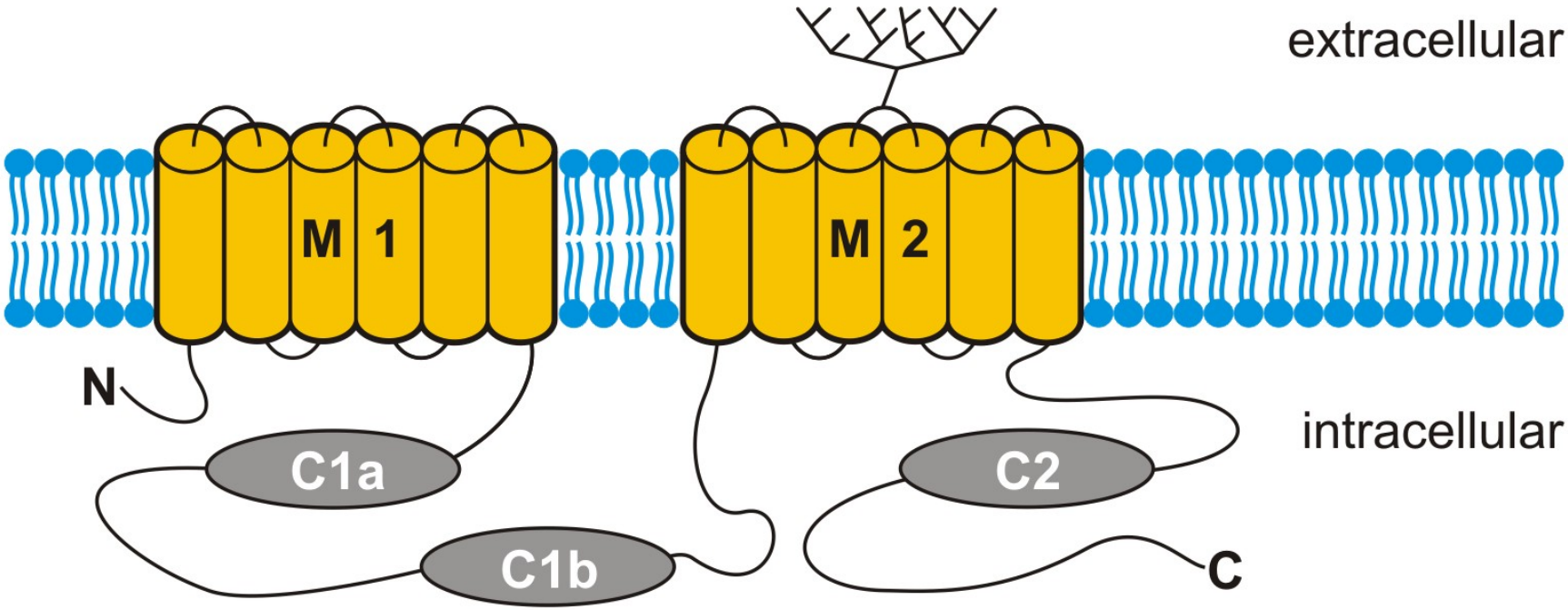
CNG
Ca^{2+}
ClC
Cl^-
ciliary lumen
mucus

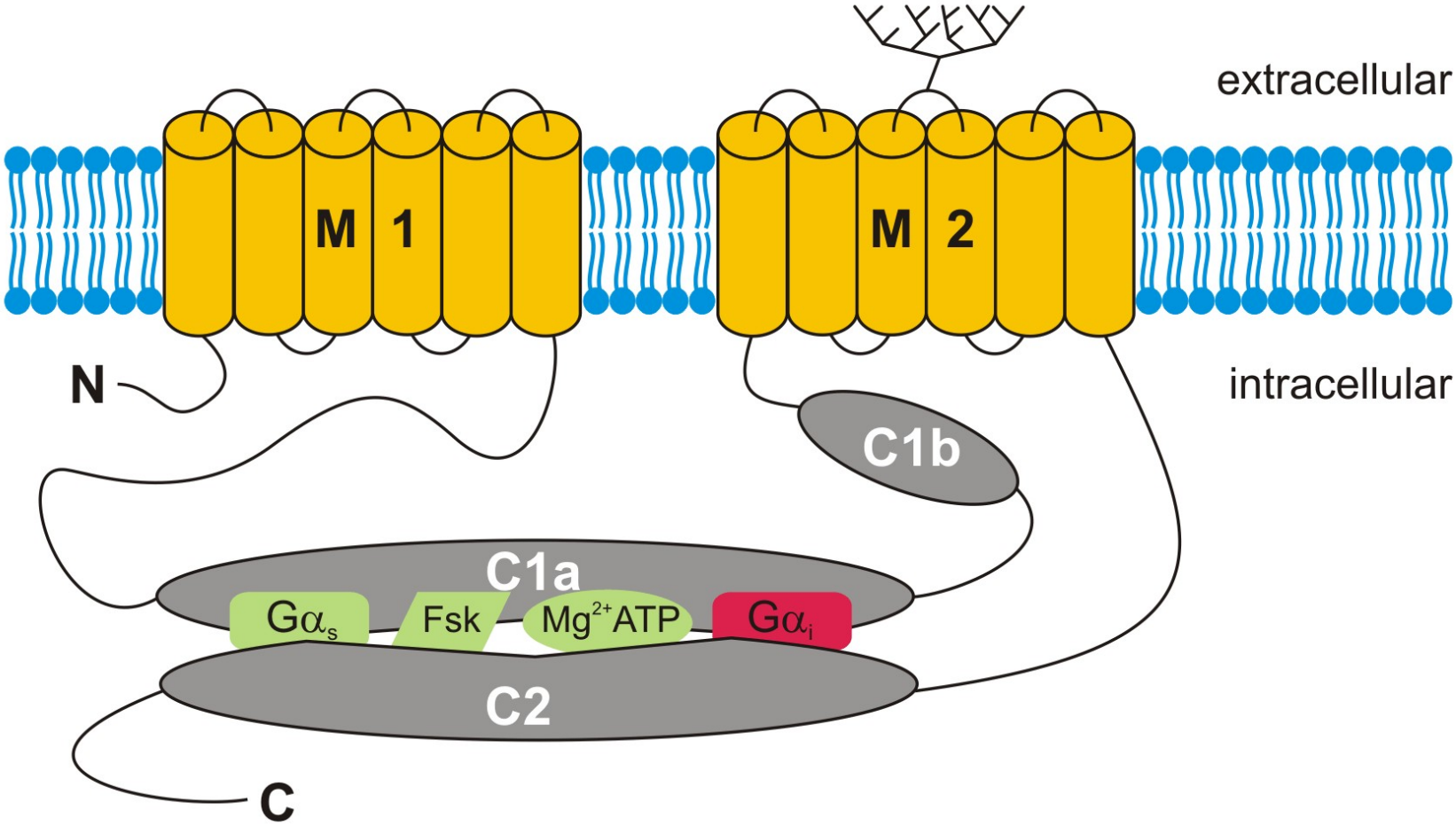
Adenylyl cyclase



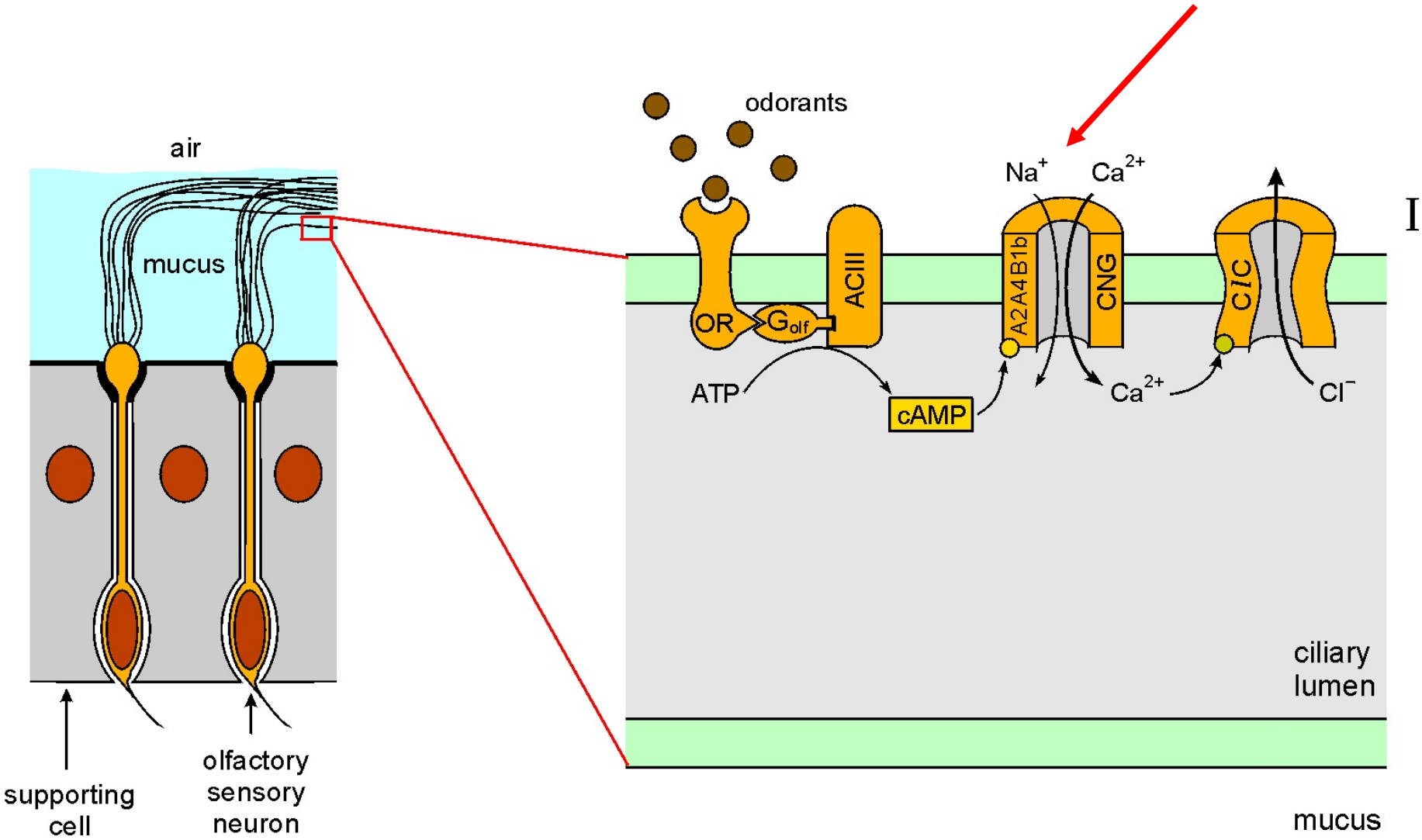
AC = integral membrane protein (9 genes identified)

AC soluble (1 gene identified)

Adenylyl cyclase



Olfaction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ClC
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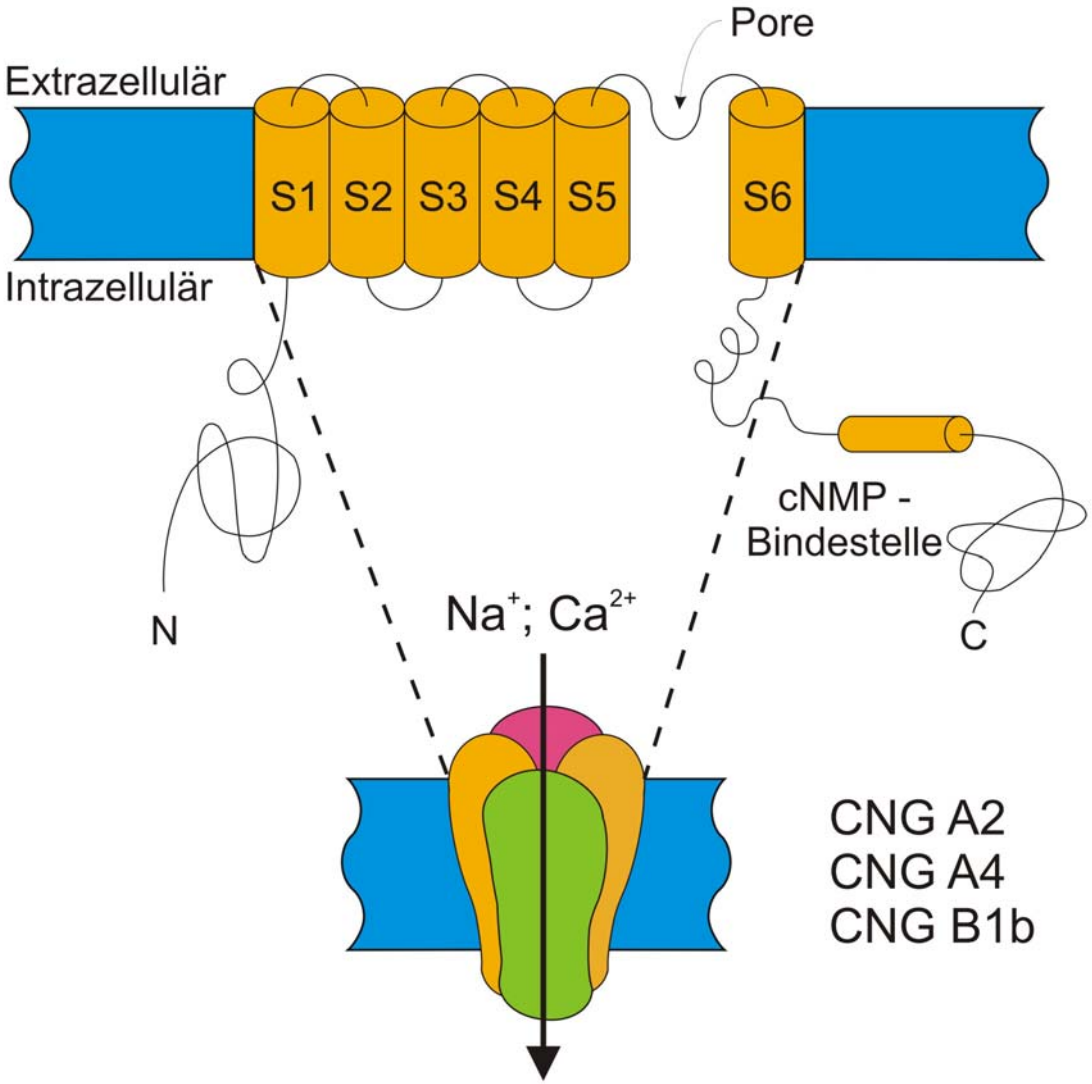
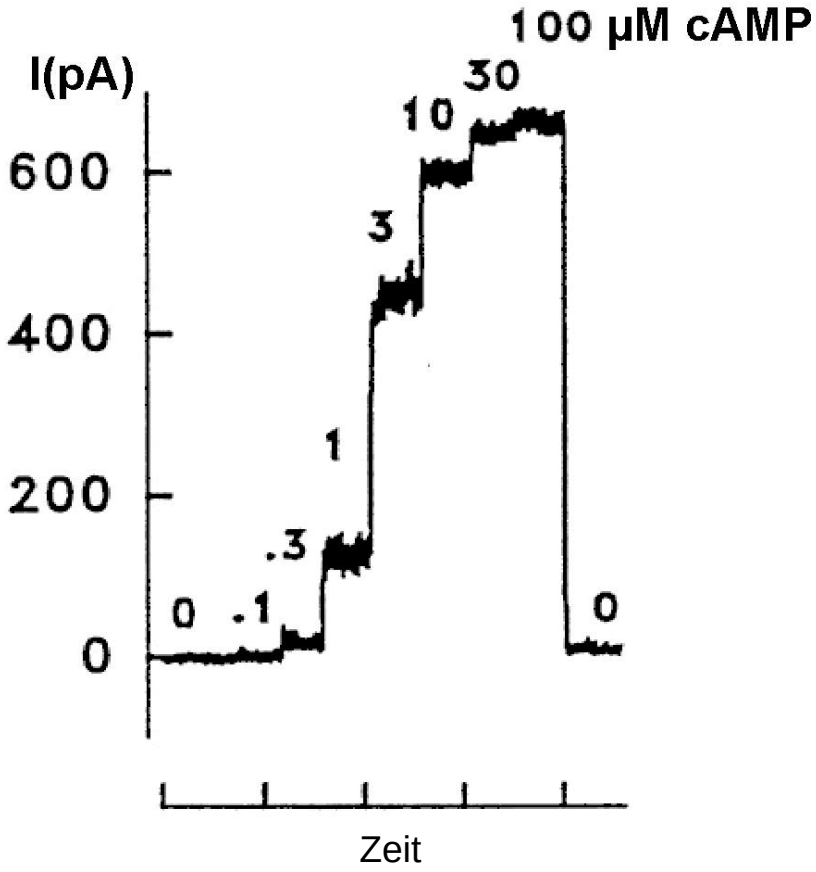
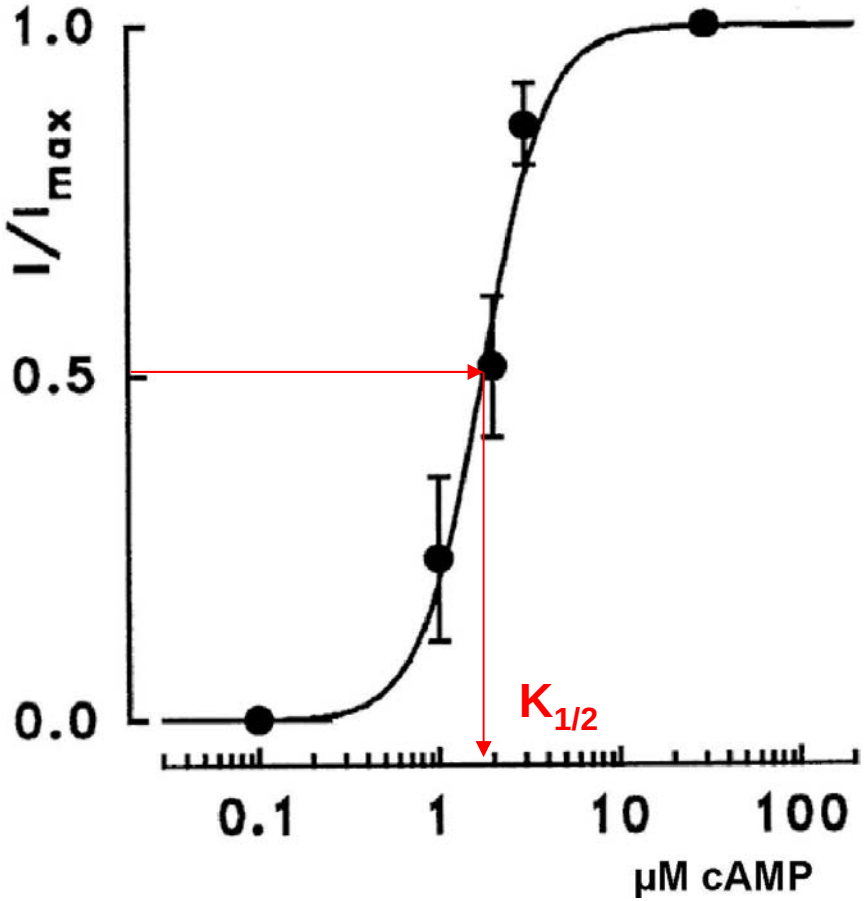
ciliary lumen
mucus

Cyclic nucleotide-gated ion channels



Cyclic nucleotide-gated ion channels

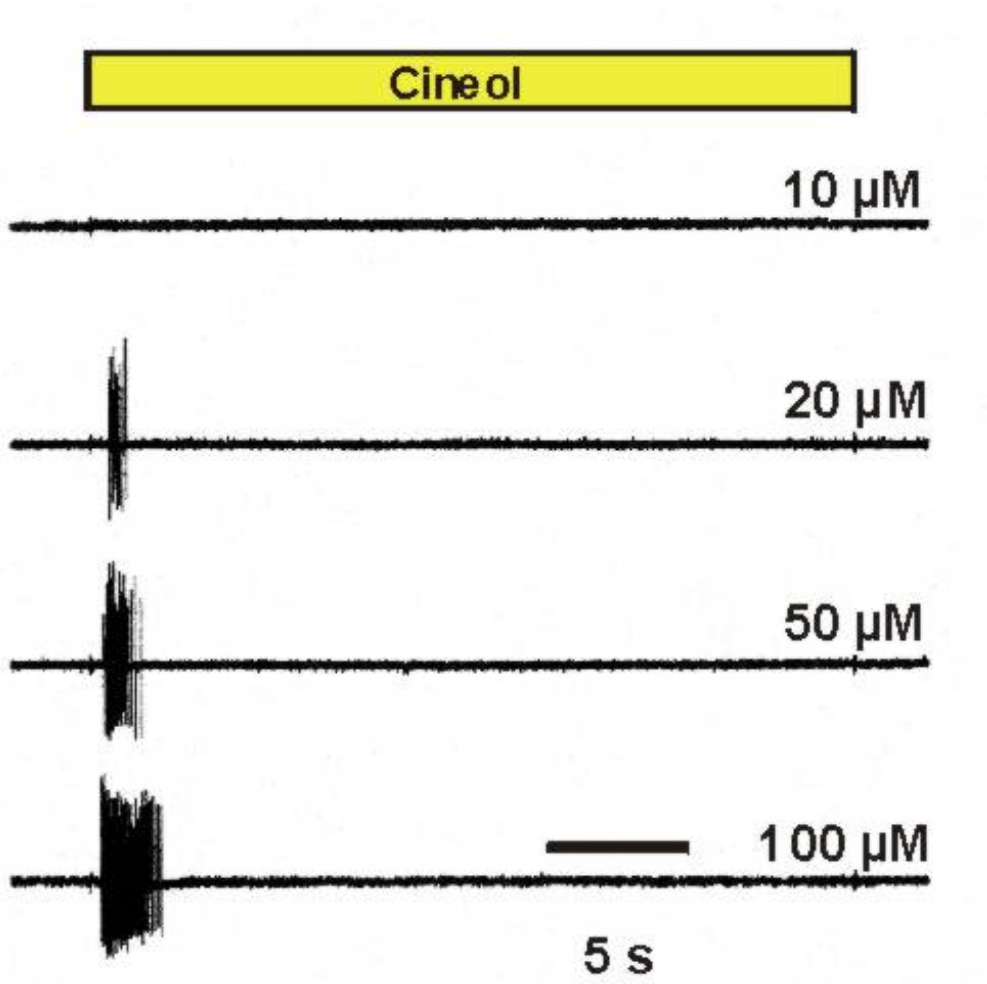




Hill equation: $I/I_{max} = C^n/(C^n + K_{1/2}^n)$; $K_{1/2}$ = EC50, n = Hill coefficient

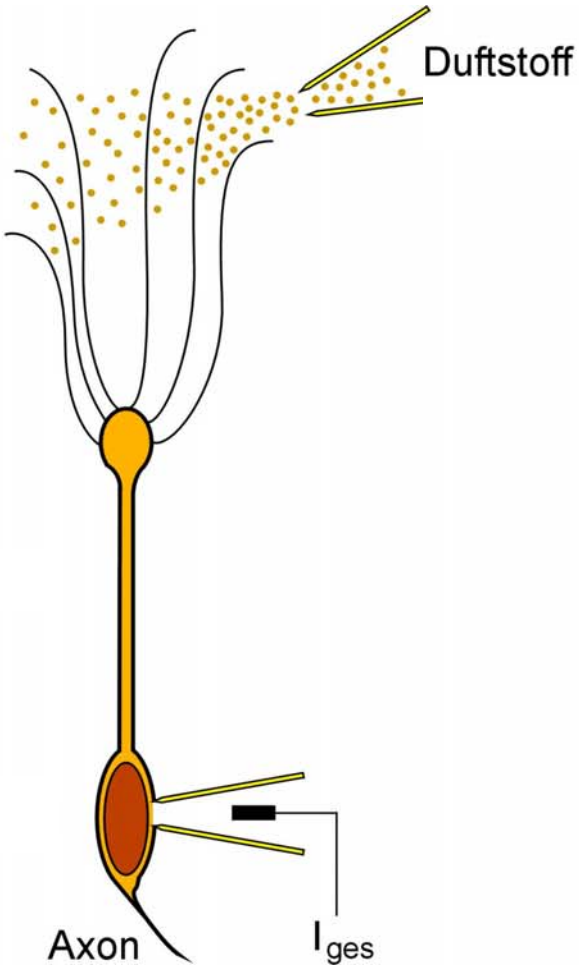
Adaptation

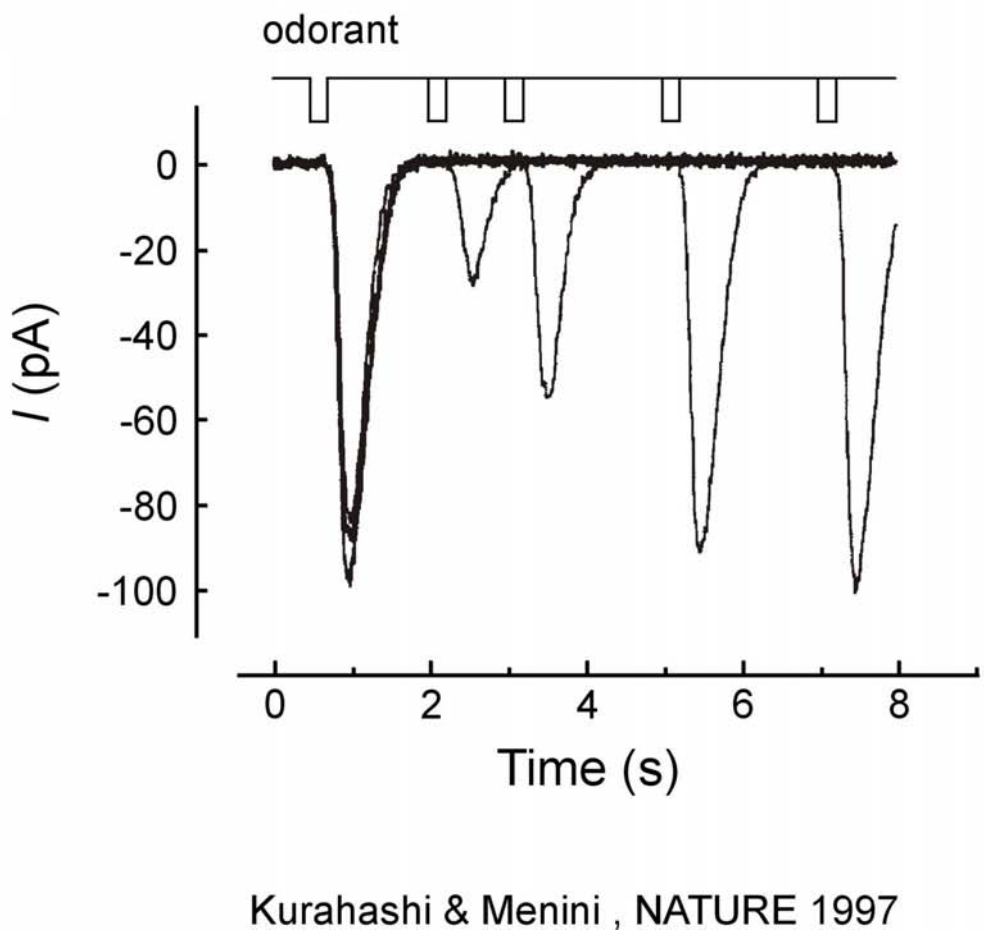
Signal transduction



Olfactory neurons adapt to long lasting odorant stimulation

Signal transduction



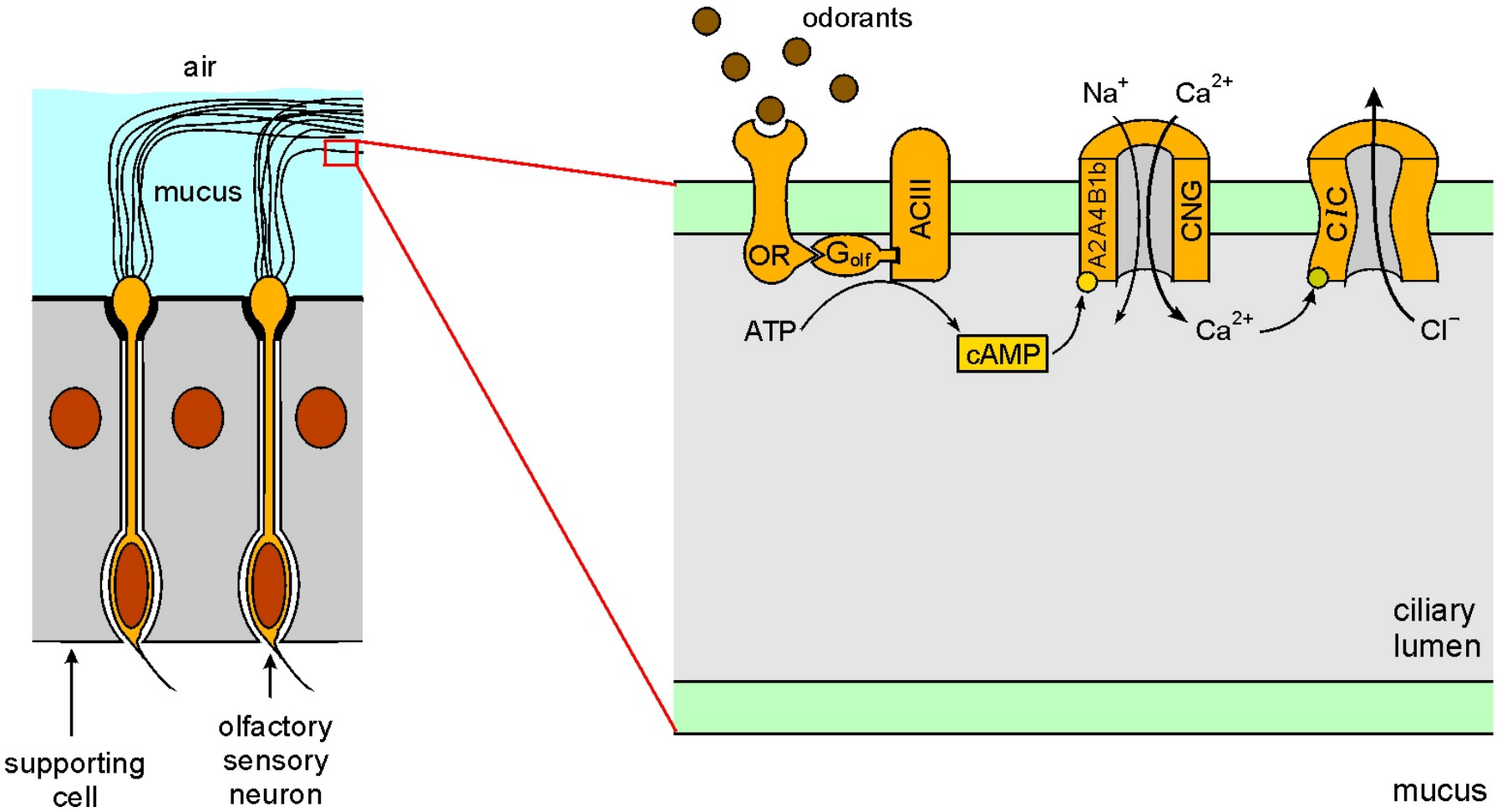


Kurahashi & Menini , NATURE 1997

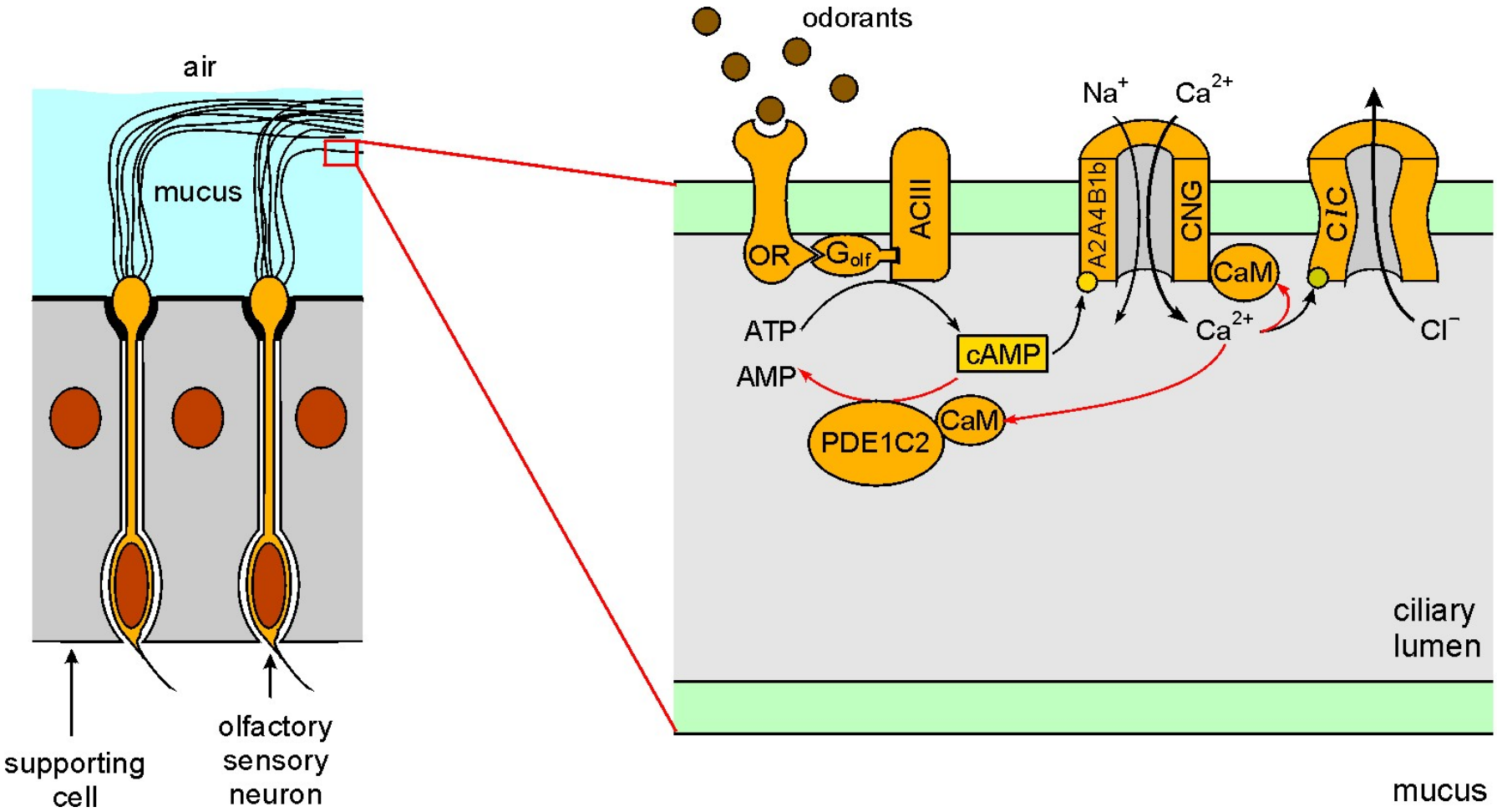
Adaptation lasts for several seconds

Signal transduction

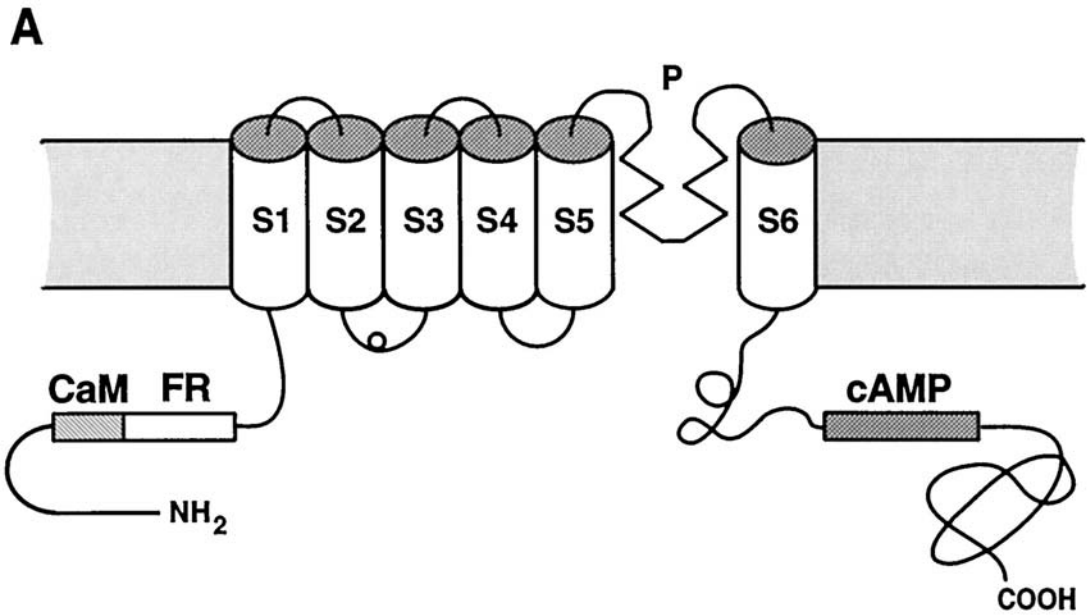
Ca^{2+} is the messenger of adaptation

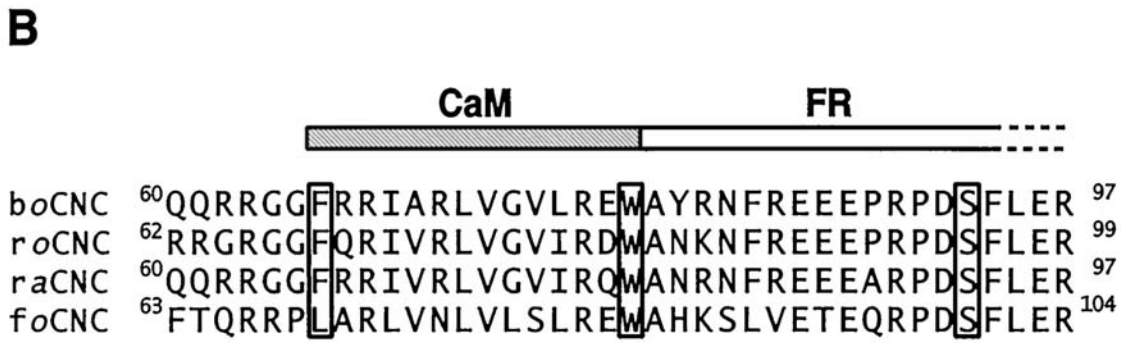


Ca^{2+}/Calmodulin and adaptation



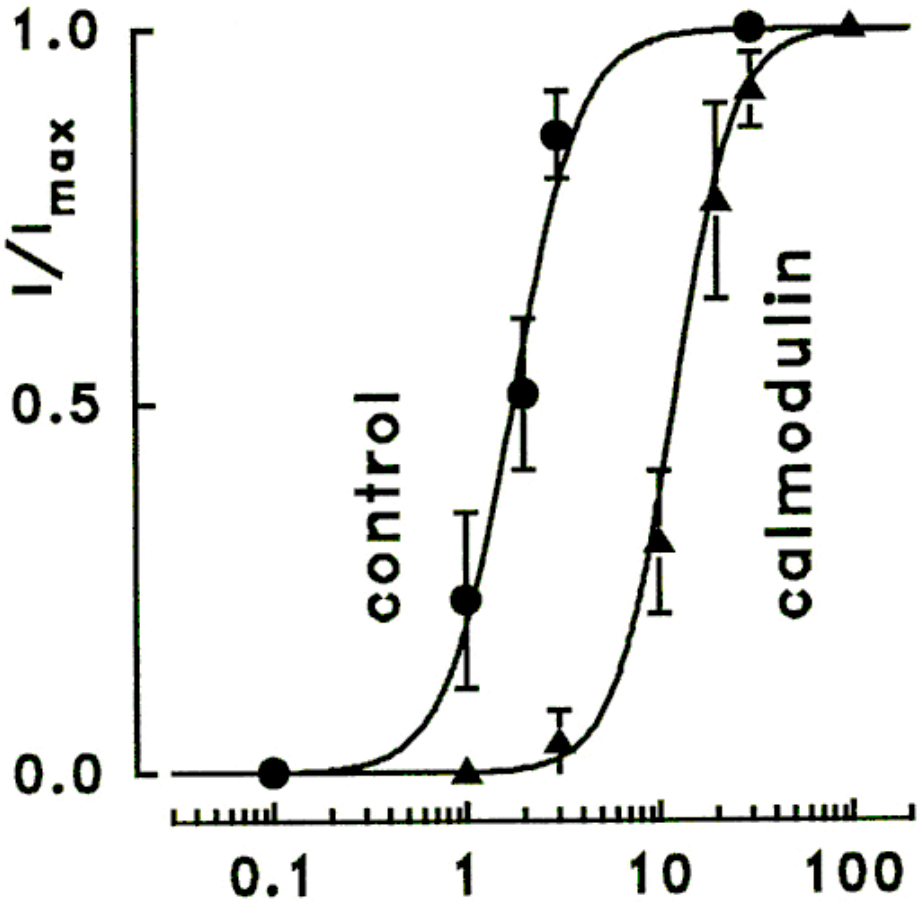
A2-subunit contains a CaM binding site





CaM reduces cAMP sensitivity of CNG channel

negative feedback - adaptation!



Summary

Olfactory neurons utilize a G-protein coupled signalling cascade. cAMP is the messenger of olfaction.

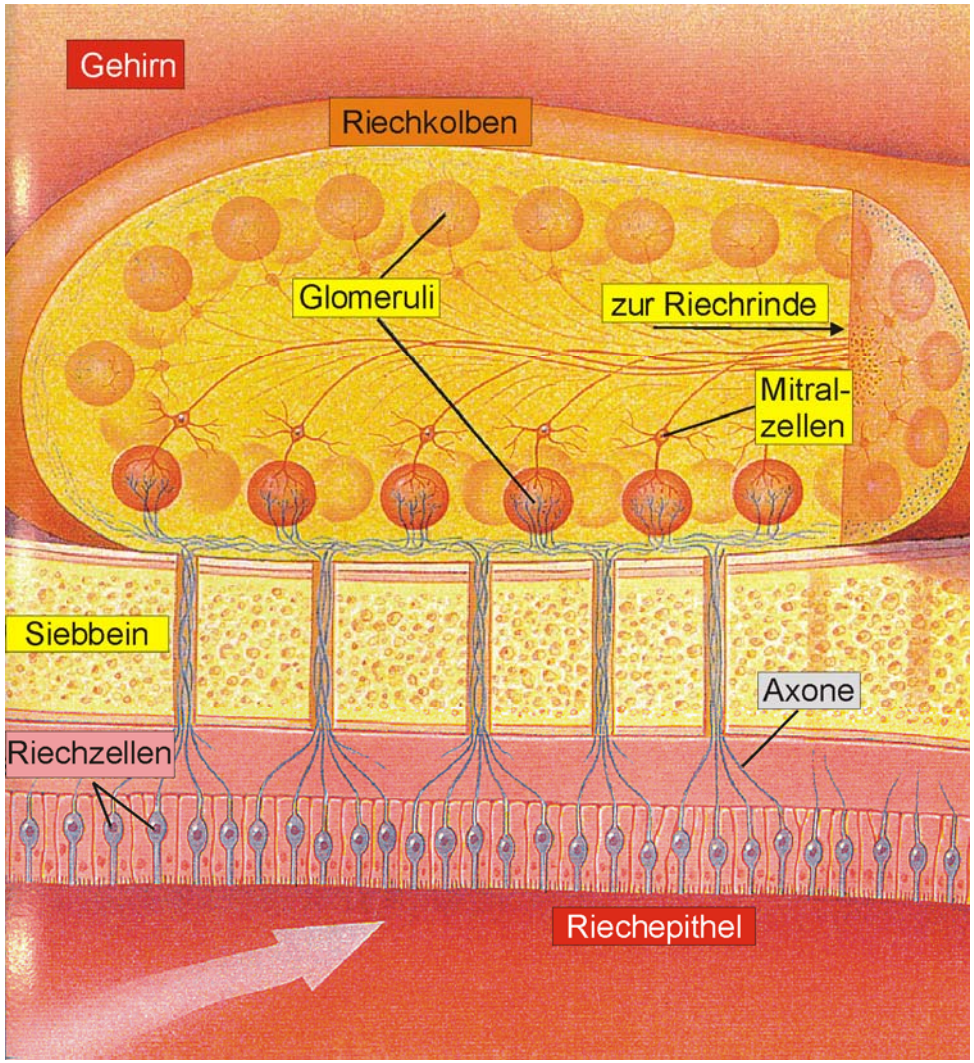
Receptor potential / amplification: opening of CNG- and Ca^{2+}-activated chloride channels.

Each olfactory neuron expresses a single olfactory receptor gene.

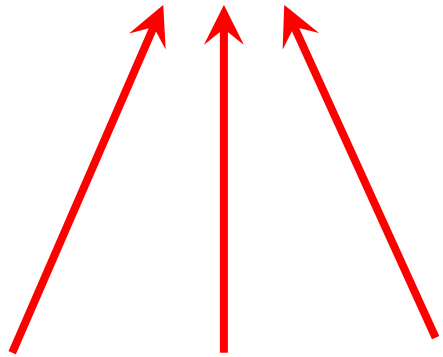
Olfactory receptors are rather unspecific and bind to several odorants. The „smell“ of an odorant is decoded from the activity pattern of cell ensembles.

Ca^{2+}-dependent negative feedback processes terminate the receptor current and the neurons activity within a few seconds.

Signal propagation



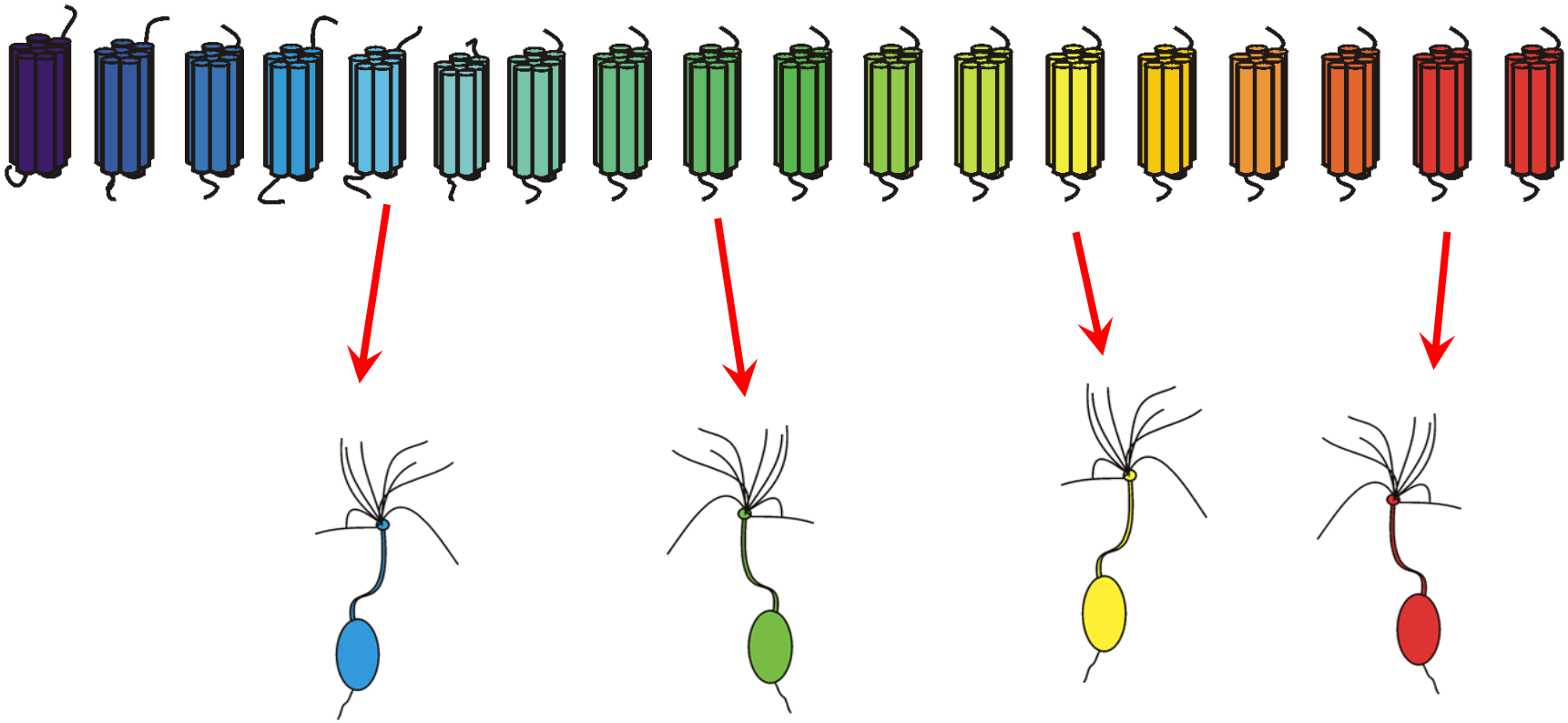
4000 glomeruli



10 million olfactory neurons

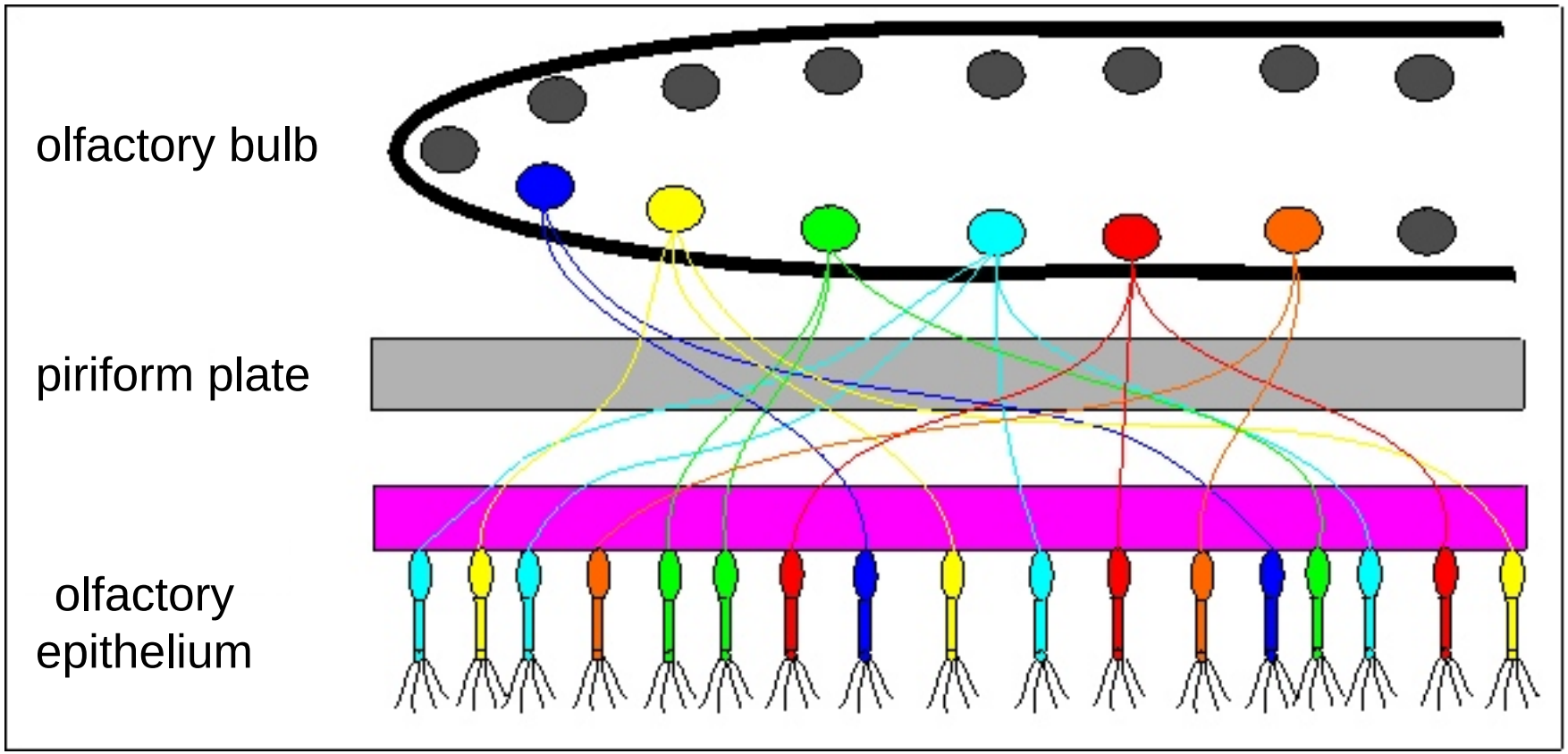
Axel, R. Spektrum der Wissenschaft, Dezember 1995

Projection of olfactory neurons to olfactory bulb

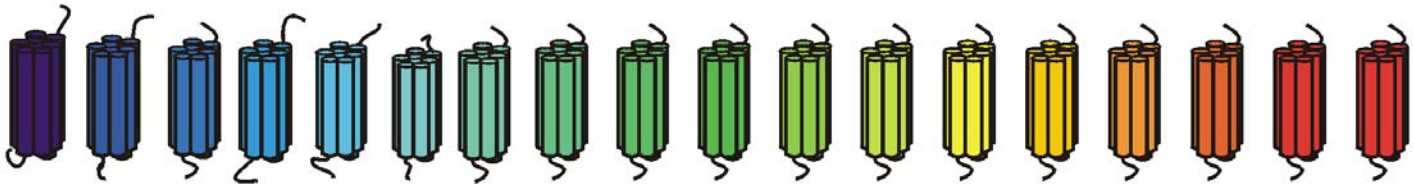


Conservation of olfactory neuron specificity
in the olfactory bulb

The „olfactory map“



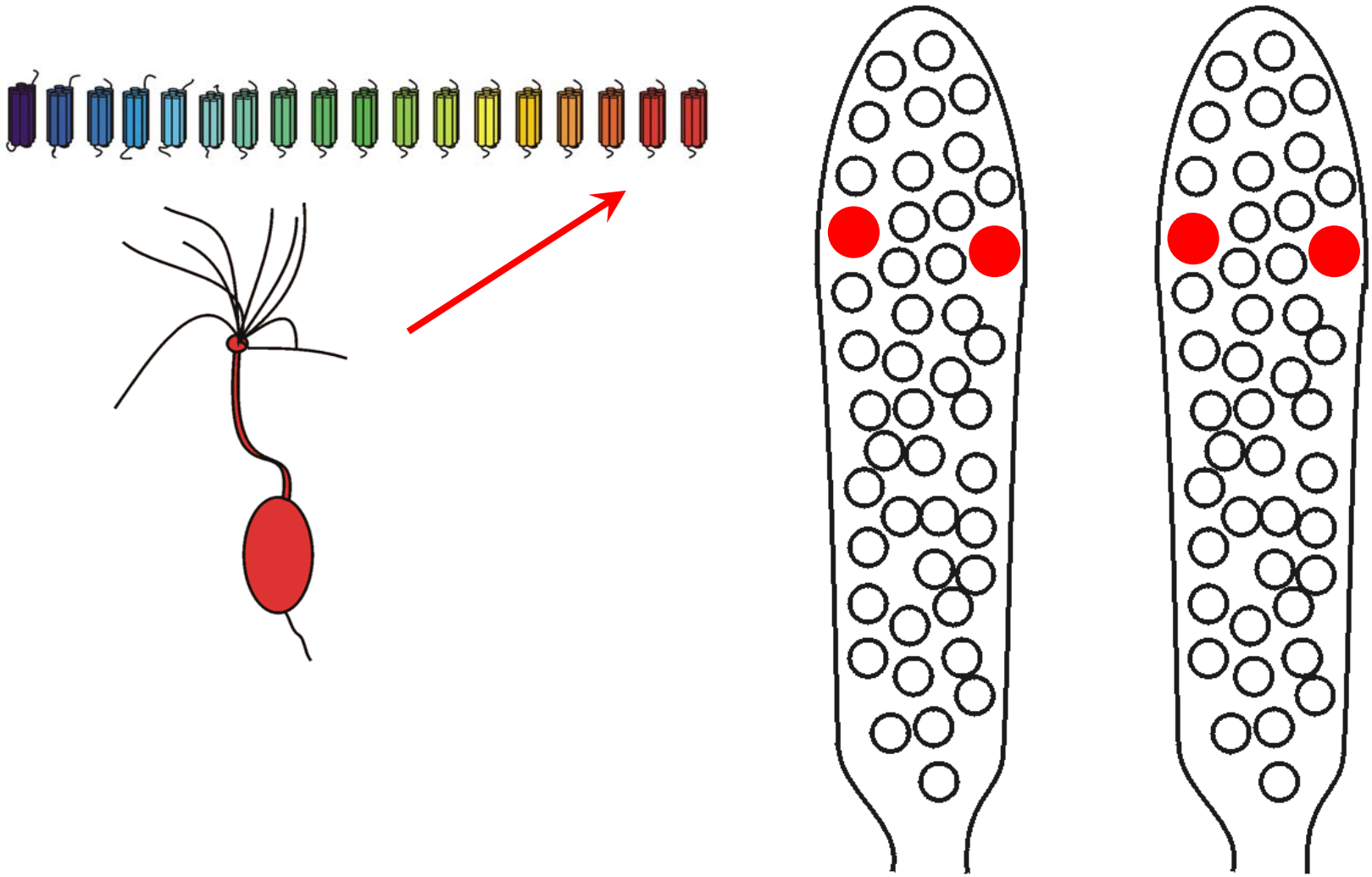
Representation in the olactory bulb



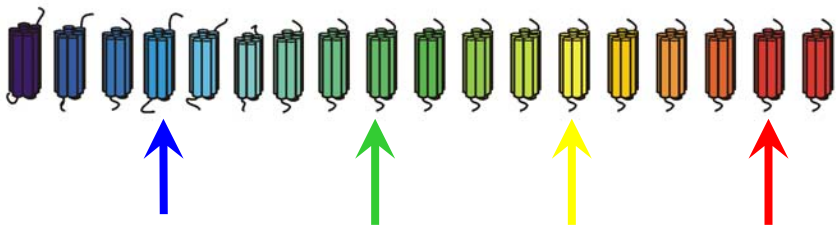
All olfactory neurons that converge onto the same glomerulus express identical olfactory receptors.

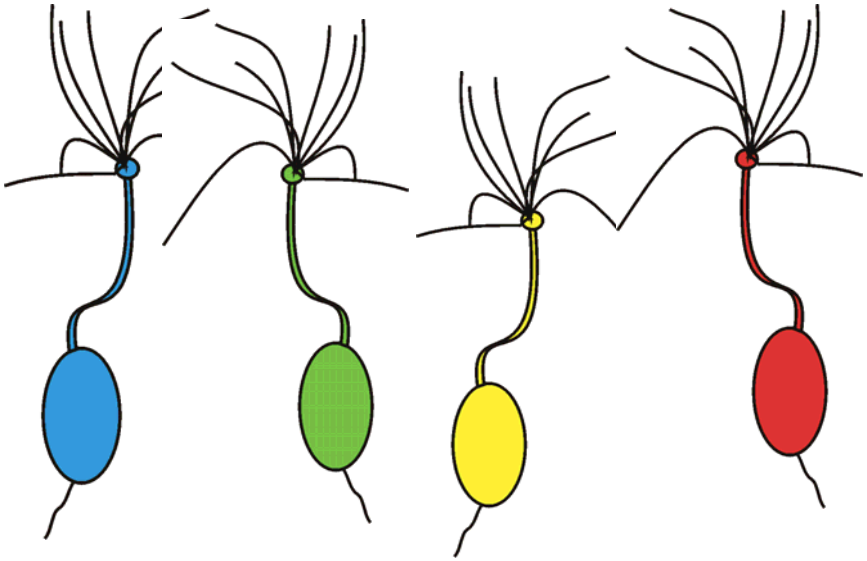
There are 1 - 4 (mostly 2) glomeruli for each olfactory receptor in both halves of the bulbus.

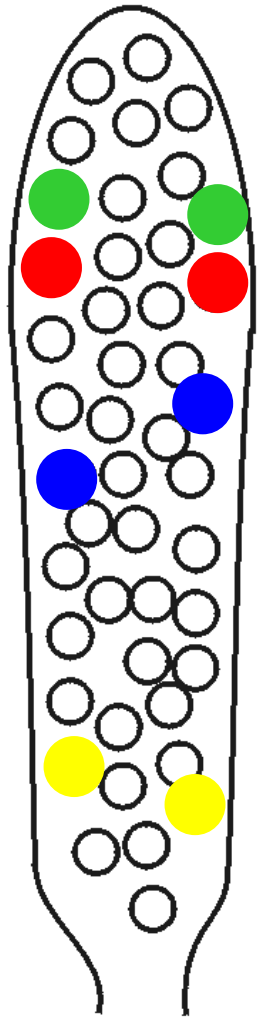
Activity pattern

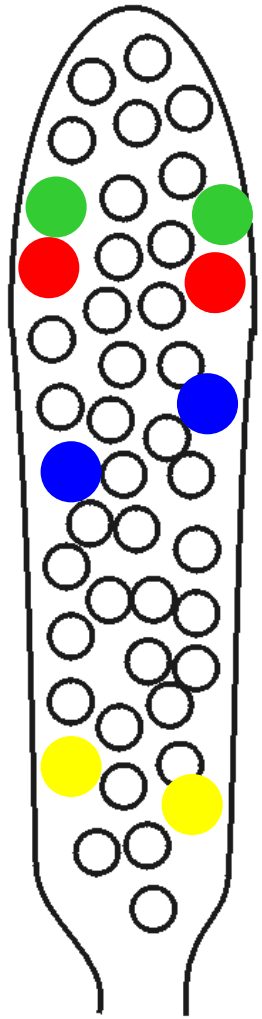


Activity pattern

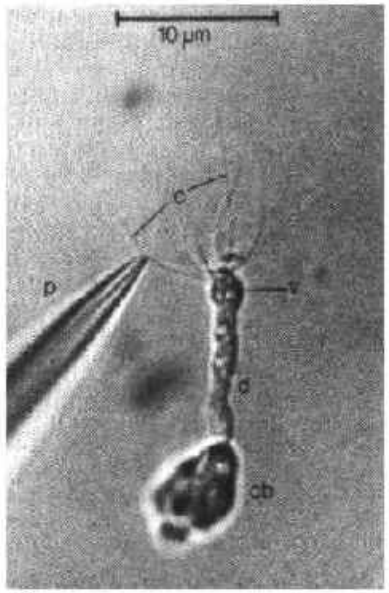


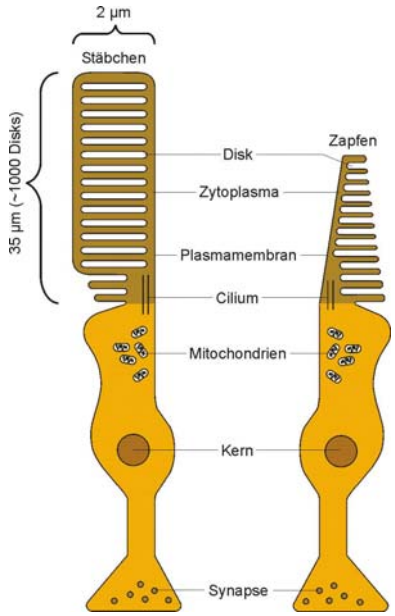


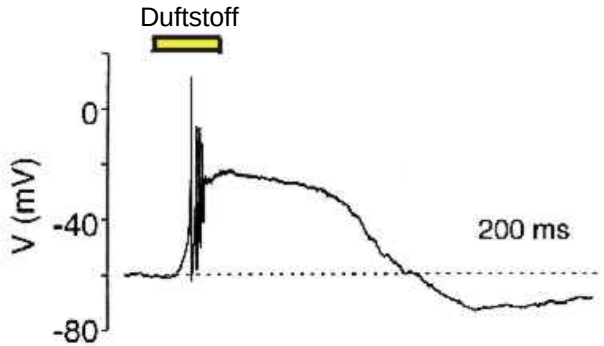


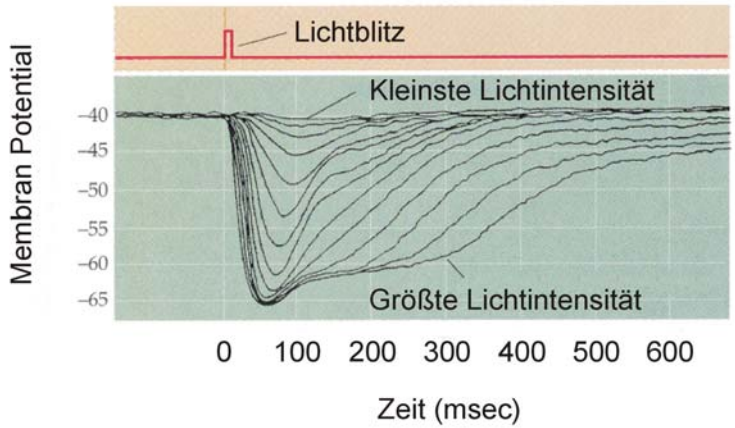


Signal transduction









Depolarisation

Hyperpolarisation