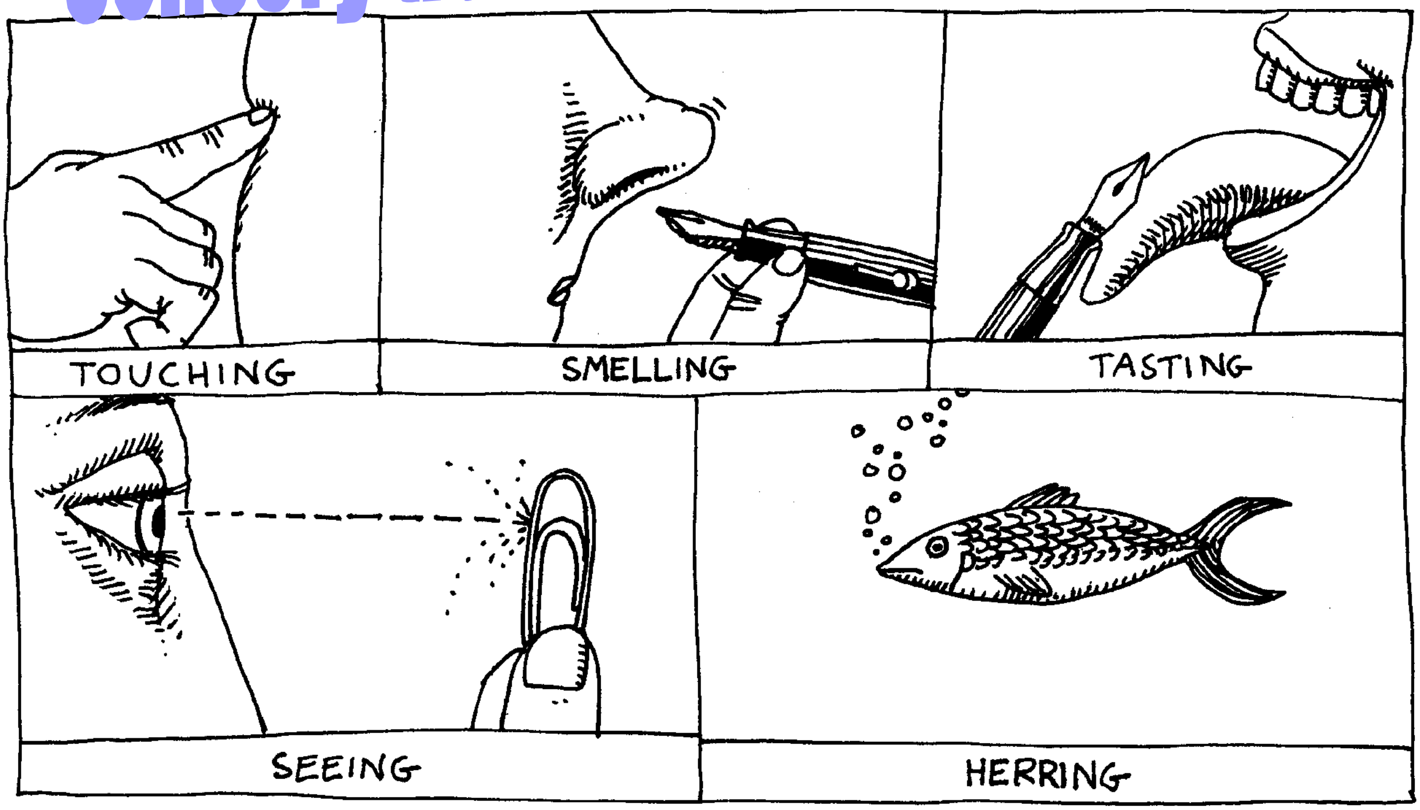
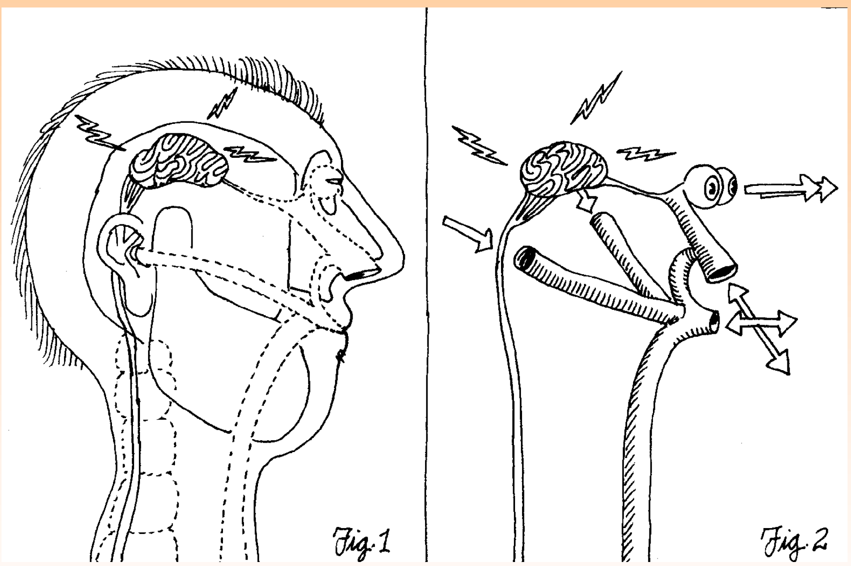
Sensory transduction*



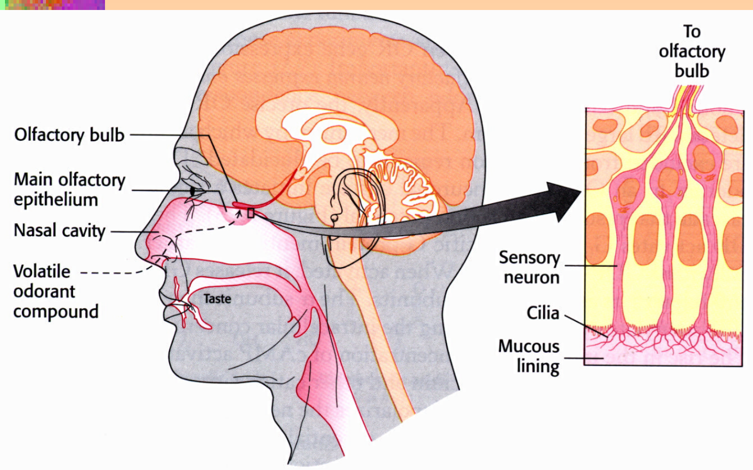
*besides vision!

Sensory “connections”

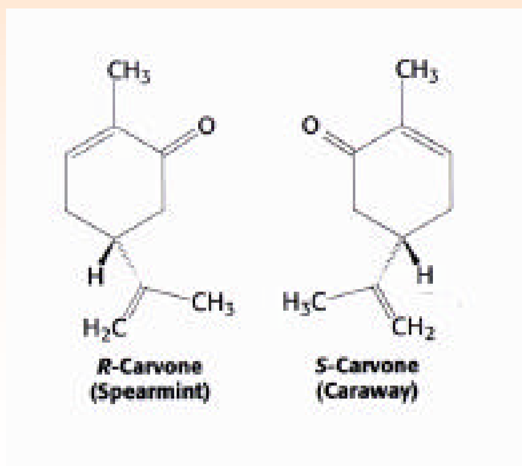


- Olfaction
- Taste
- Hearing
- Touch

Olfaction



- Extremely discriminating-even between odorant enantiomers

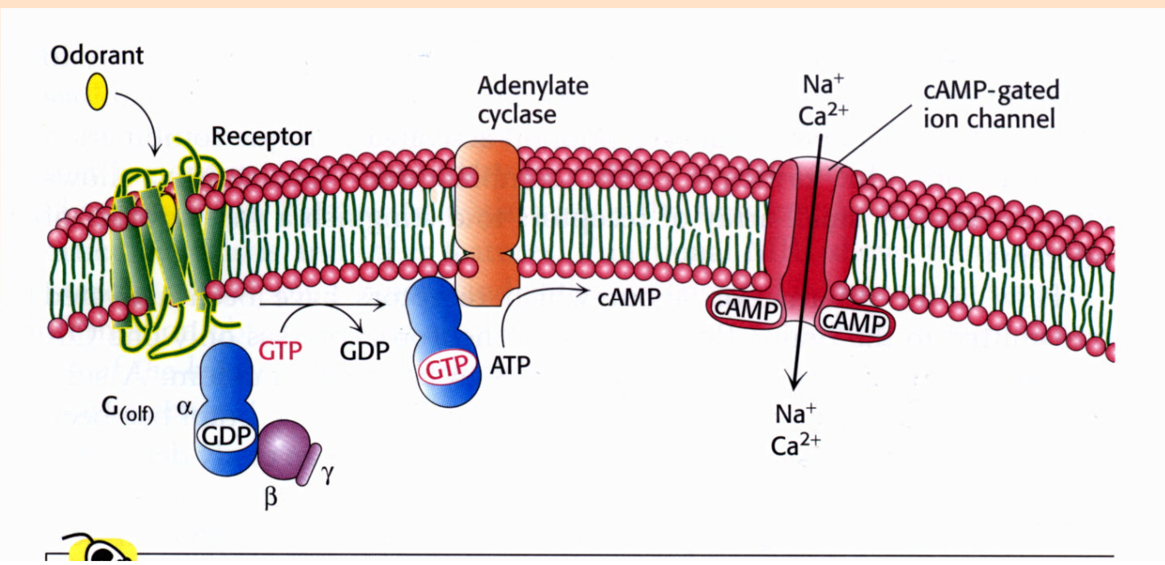


Olfaction

- In late 80's odorant receptors were cloned from cilia
- These were 7TM helix G-protein receptors (OR) stimulating a unique Gα protein, G_{olf}
- Human OR genes number 500 but only about 30 are not pseudogenes!

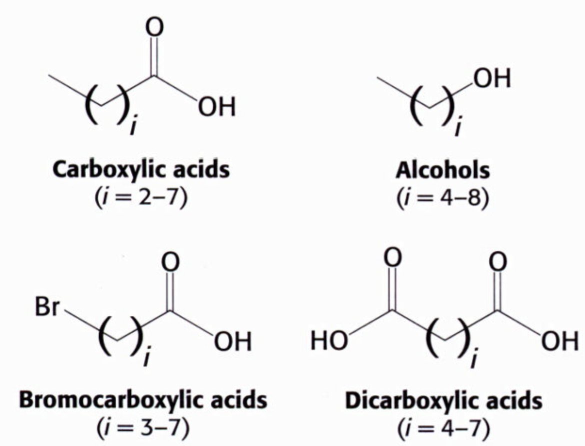
Olfaction

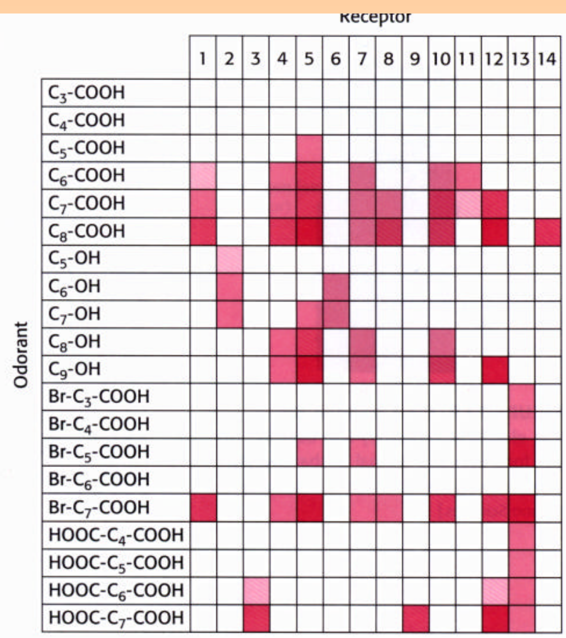
- Each neuron expresses only 1 OR
- G_{olf} stimulates Ad. Cyclase
- cAMP opens cation channels;depolarization occurs; action potential propagates



Olfaction

- **Decoding of olfactory stimuli -in mouse suggests a combinatorial mechaism**





Olfaction

- All neurons expressing a given OR converge on a discrete area in the olfactory bulb
- The spatial pattern of OR stimulation is somehow transformed to a unique scent.

FIGURE 32.8 Converging olfactory neurons. This section of the nasal cavity is stained to reveal processes from sensory neurons expressing the same olfactory receptor. The processes converge to a single location in the olfactory bulb. [From P. Mombaerts, F. Wang, C. Dulac, S. K. Chao, A. Nemes, M. Mendelsohn, J. Edmondson, and R. Axel. *Cell* 87(1996):675–689.]

Taste

- More limited scope of possible tastes
- Olfaction contributes to complex tastes

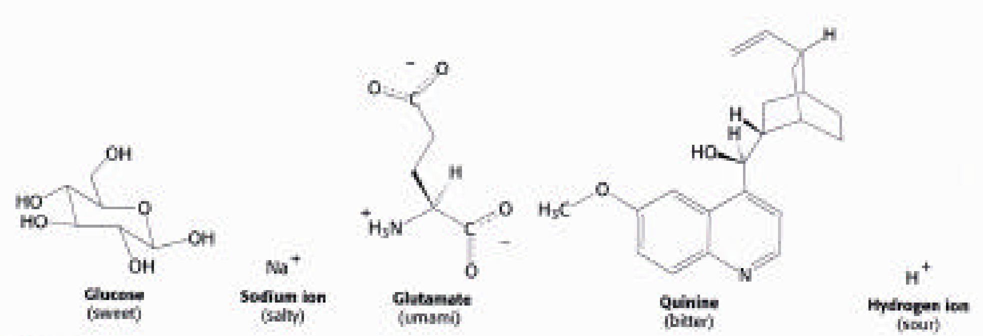
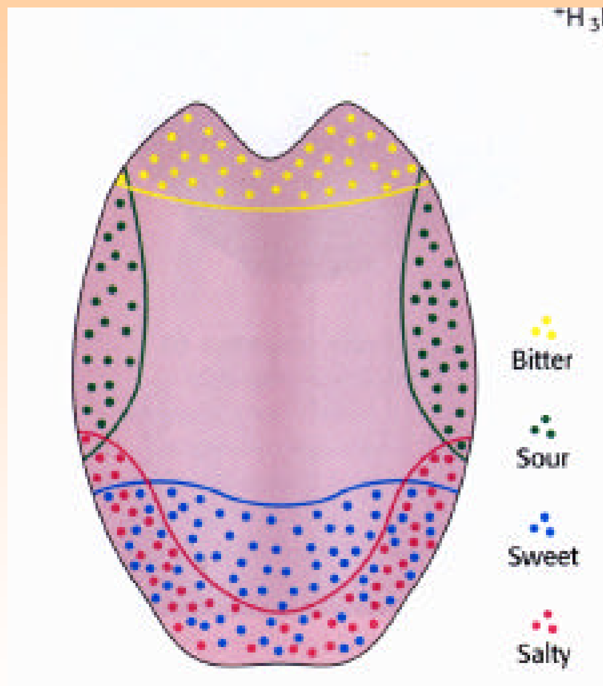


FIGURE 32.11 Examples of tastant molecules. Tastants fall into five groups: sweet, salty, umami, bitter, and sour.

Taste

- Gustation receptors are located in different areas
- In taste buds (~150 cells w/ sensory neurons) in papillae (big knobs)



Taste-Bitter

- So far only bitter receptors (G-protein Receptors) with Gα, gustducin have been found
- There are 50-100 genes (for bitter?) in the genome but they are mixed on taste buds

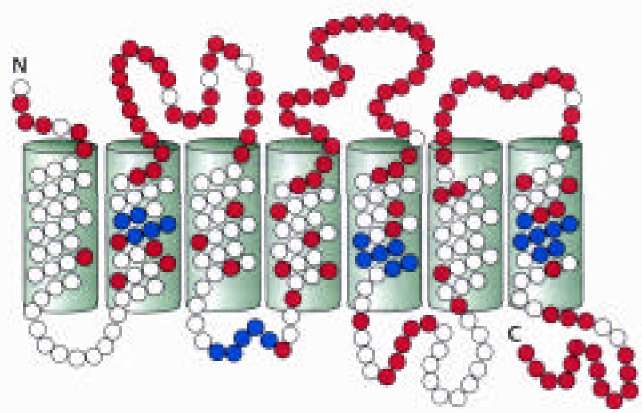


FIGURE 32.14 Conserved and variant regions in bitter receptors. The bitter receptors are members of the 7TM receptor family. Strongly conserved residues characteristic of this protein family are shown in blue, and highly variable residues are shown in red.

Taste

- **Bitter receptors ? Stimulation by specific bitter substance of mT2R**
- **But different ones get mixed up in brain**

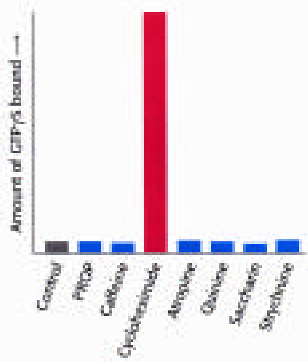


FIGURE 32.15 Evidence that T2R proteins are bitter taste receptors. Cycloheximide uniquely stimulates the binding of the GTP analog GTPγS to gustducin in the presence of the mT2R protein. [Adapted from J. Chandrashekar, K. L. Mueller, M. A. Hoon, E. Adler, L. Feng, W. Guo, C. S. Zuker, and N. J. Ryba. *Cell* 100(2000):703.]

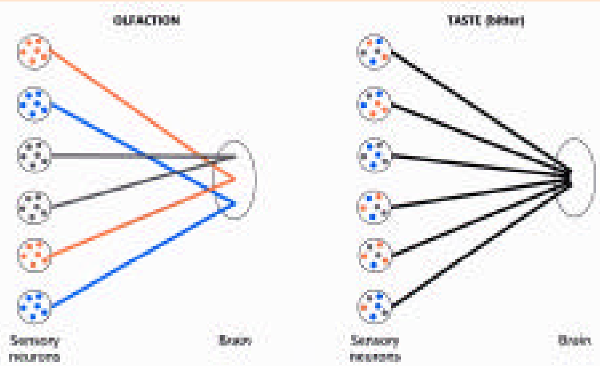
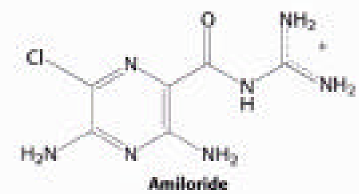


FIGURE 32.16 Differing gene expression and connection patterns in olfactory and bitter taste receptors. In olfaction, each neuron expresses a single OR gene, and the neurons expressing the same OR converge to specific sites in the brain, enabling specific perception of different odorants. In gustation, each neuron expresses many bitter receptor genes, so the identity of the tastant is lost in transmission.

Taste-Salty

- Salt receptors ? Direct sensation by Na+ ion channels blocked by Amiloride
- Analogous to the 4 subunit type channels (like K+)



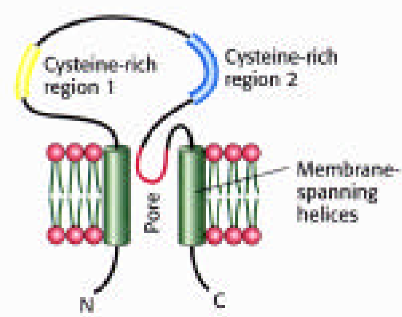
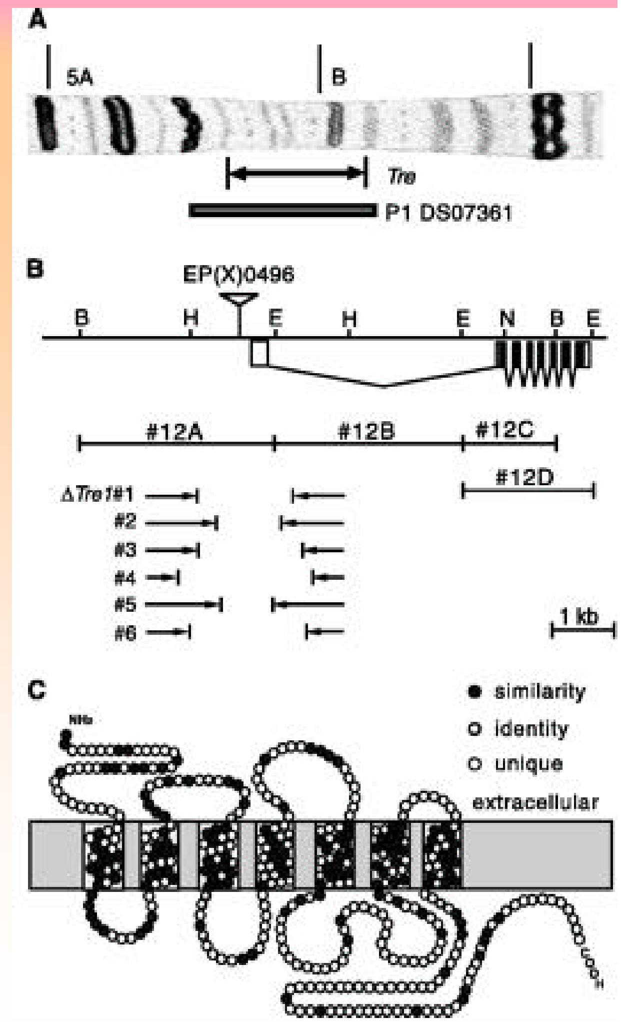


FIGURE 32.17 Schematic structure of the amiloride-sensitive sodium channel. Only one of the four subunits that constitute the functional channel is illustrated. The amiloride-sensitive sodium channel belongs to a superfamily having common structural features, including two hydrophobic membrane-spanning regions, intracellular amino and carboxyl termini; and a large, extracellular region with conserved cysteine-rich domains.

Taste-Sweet

- Not isolated in humans but likely G-protein since gustducin knock-out mice can't taste sweet substances
- Tre 1, a sugar responsive GPR has been found in flies



Taste-Umami

- Japanese-Deliciousness
- Lots in protein rich foods like soy sauce, roasted meat and and vegemite!
- Na+ Glutamate is the key (1903-Kikunae Ikeda)
- A GPR sensitive to glutamate in the brain is clipped by 309 amino acids in the buds to give low affinity umami receptor.

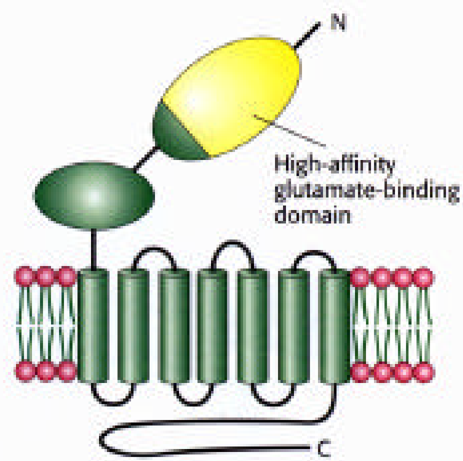
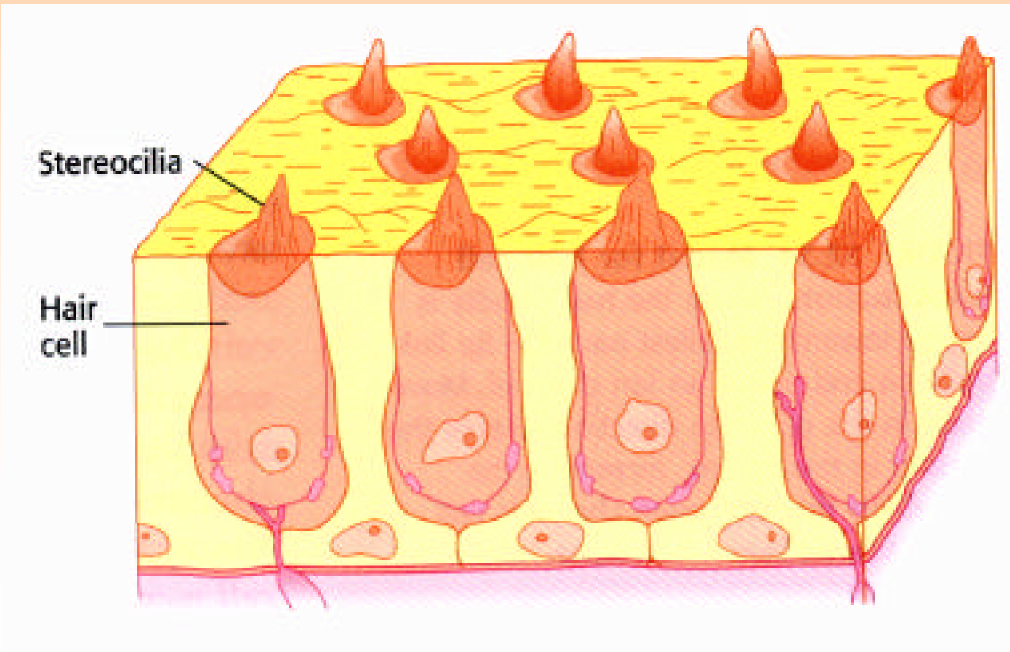


FIGURE 32.18 Schematic structure of a metabotrophic glutamate receptor. The umami receptor is a variant of a brain glutamate receptor. A substantial part of the high-affinity glutamate-binding domain (shown in yellow) is missing in the form expressed in the tongue.

Hearing

- Mechanical stimulation of hair cells in cochlea is the key
- Hair cells are specialized neurons



Hearing

- **Displacement of bundle by 3 Å results in a measurable membrane potential change (like 1 inch movement at the top of the Empire State building)**

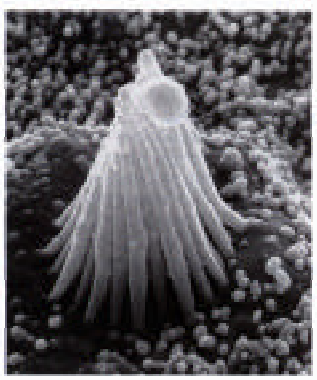


FIGURE 32.31 An electron micrograph of a hair bundle. [Courtesy of A. Jacobs and A. J. Hudspeth.]

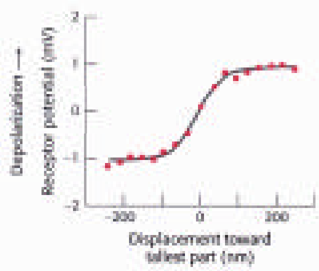


FIGURE 32.32 Micromanipulation of a hair cell. Movement toward the tallest part of the bundle depolarizes the cell as measured by the microelectrode. Movement toward the shortest part hyperpolarizes the cell. Lateral movement has no effect. [Adapted from Hudspeth, A. J. Nature 341(1989):397.]

FIGURE 32.33 Electron micrograph of tip links. The tip link between two hair fibers is marked by an arrow. [Courtesy of A. Jacobs and A. J. Hudspeth.]

Hearing

- Tip link seems to pull open an ion "hatch"; a mechanosensory channel
- Back and forth flow induces an oscillating ion current

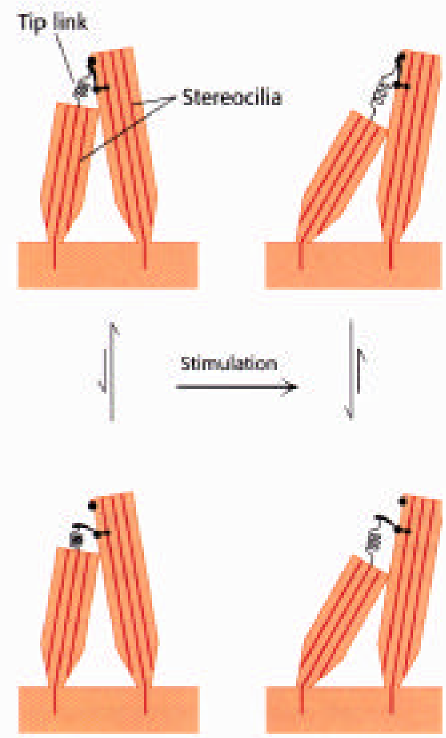


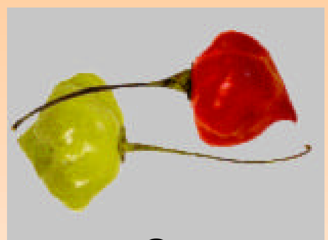
FIGURE 32.34 Model for hair-cell transduction. When the hair bundle is tipped toward the tallest part, the tip link pulls on and opens an ion channel. Movement in the opposite direction relaxes the tension in the tip link, increasing the probability that any open channels will close. [Adapted from A. J. Hudspeth. *Nature* 341 (1989):397.]

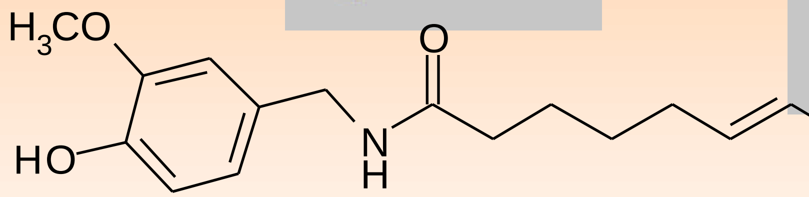
Touch

- Hot, Cold
- Pressure
- Capsaicin/hot receptor
- Cold/menthol receptor

Capsaicin and friends

Capsicum (chili pepper)





capsaicin

Touch

- Example: Capsaicin
- Capsaicin/hot receptor
- Reacts to noxious stimuli (heat, acid]
- Also involved in taste

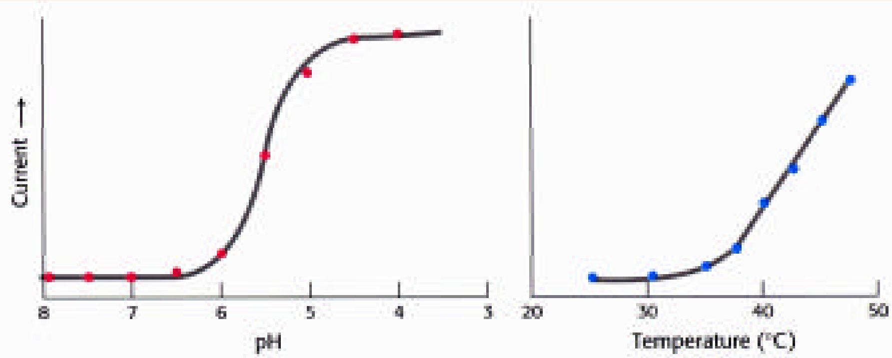


FIGURE 32.37 Response of the capsaicin receptor to pH and temperature. [Adapted from Tominaga, M., Caterina, M. J., Malmberg, A. B., Rosen, T. A., Gilbert, H., Skinner, K., Raumann, B. E., Basbaum, A. I., and Julius, D. *Neuron* 21(1998):531.]

Touch-Capsaicin

- The receptor, VR1, is involved in nociception (pain sensation) as well.
- Used medicinally to alleviate pain by the principle of counterirritation
- How does this work?

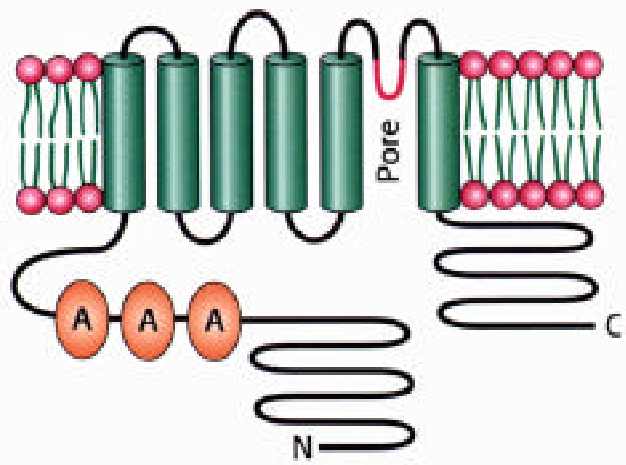


FIGURE 32.36 The membrane topology deduced for VR1, the capsaicin receptor. The proposed site of the membrane pore is indicated in red, and the three ankyrin (A) repeats are shown in orange. The active receptor comprises four of these subunits. [Adapted from Caterina, M. J., Schumacher, M. A., Tominaga, M., Rosen, T. A., Levine, J. D., and Julius, D. *Nature* 389 (1997):816.]

UCSF Study Suggests Capsaicin Significantly Reduces Debilitating Nerve Pain. Mice without it don’t experience pain from heat (Science,2000).