Cellular Biophysics – Sensory systems: The visual system as an example

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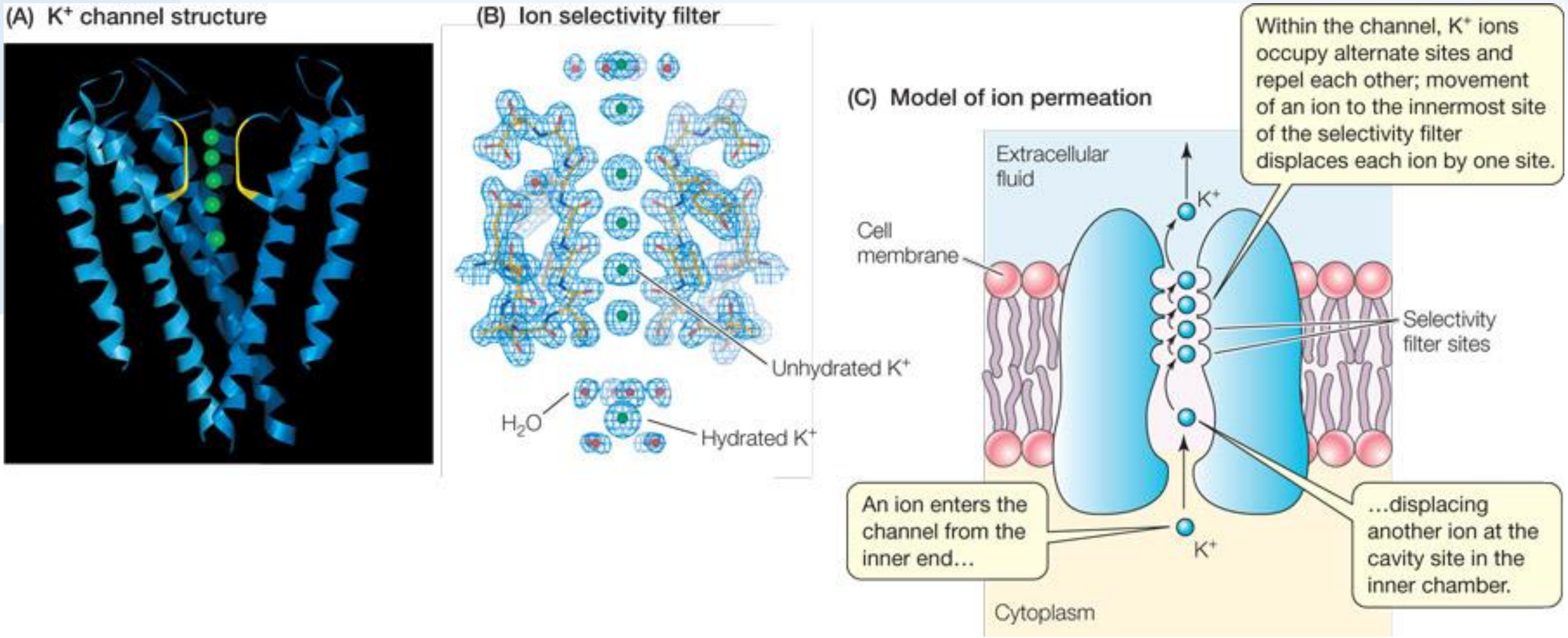
Contents of the lecture

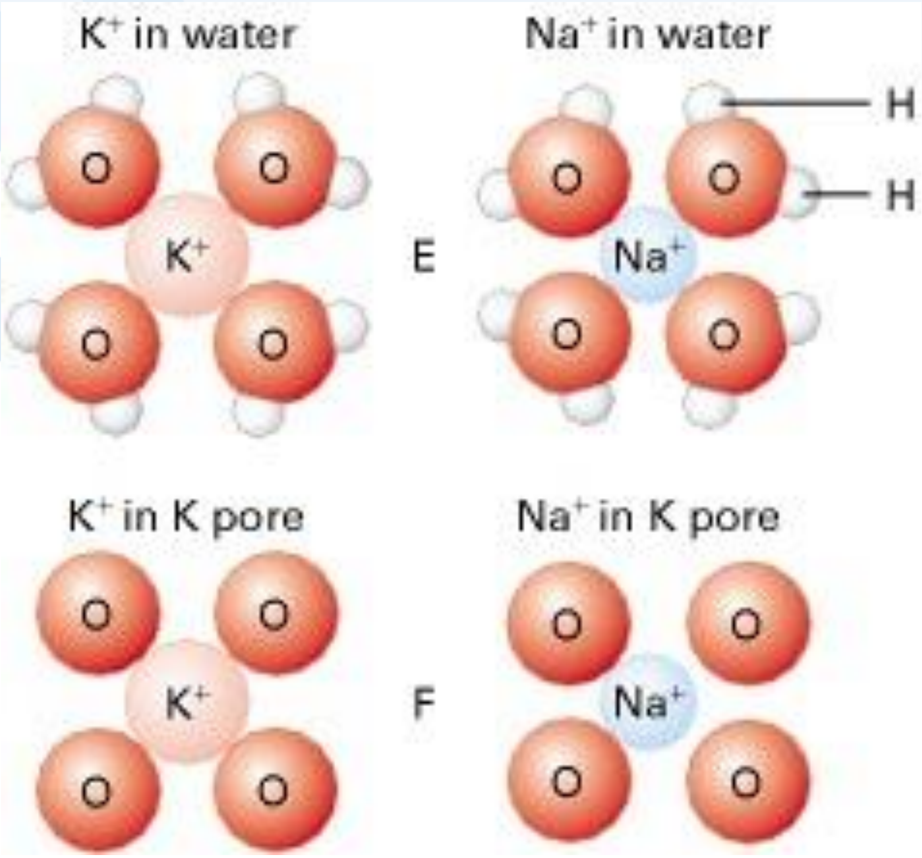
- Few points to answer questions from last lecture
- Sensory systems
  - Example: visual system

Ion selectivity in voltage-gated K⁺ channel



Animal Physiology, 4th ed

Ion channel selectivity

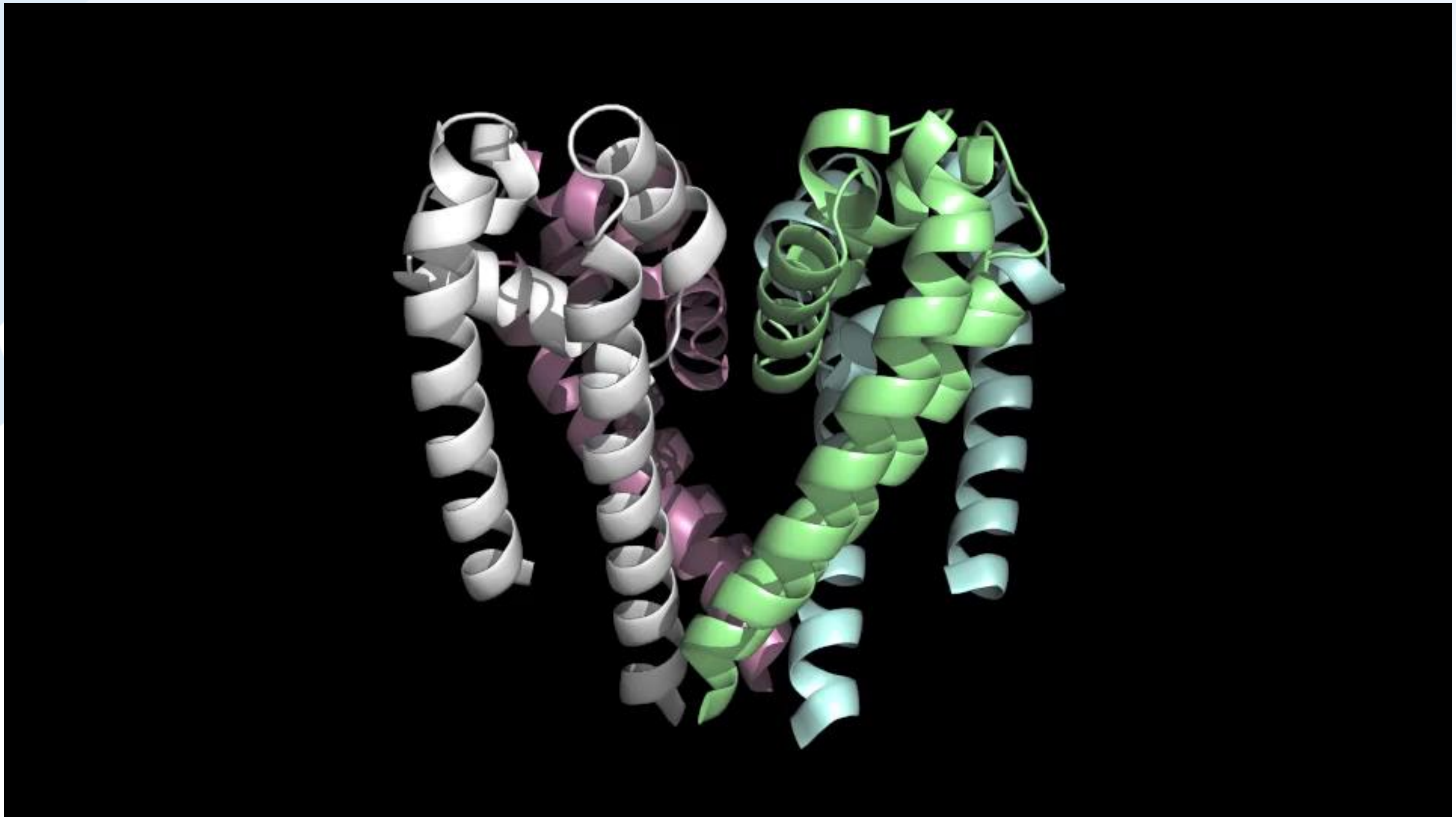


K^+ ions (hydrated in solution) lose their bound water molecules as they pass through the selectivity filter and become coordinated to four backbone carbonyl oxygens in the channel-lining loop of each P segment.

Na^+ ions, being smaller, cannot perfectly coordinate with these oxygens. They pass through the channel only rarely.

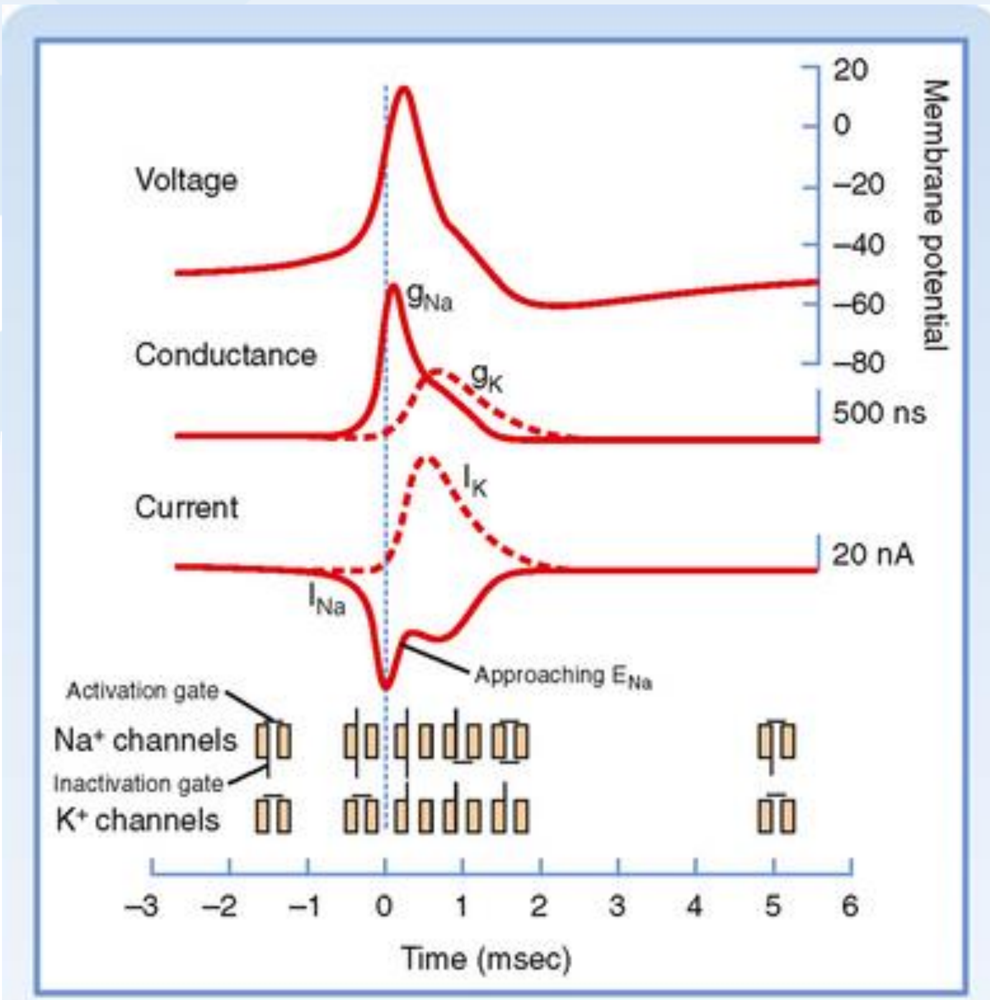
Molecular Cell Biology. 4th ed.

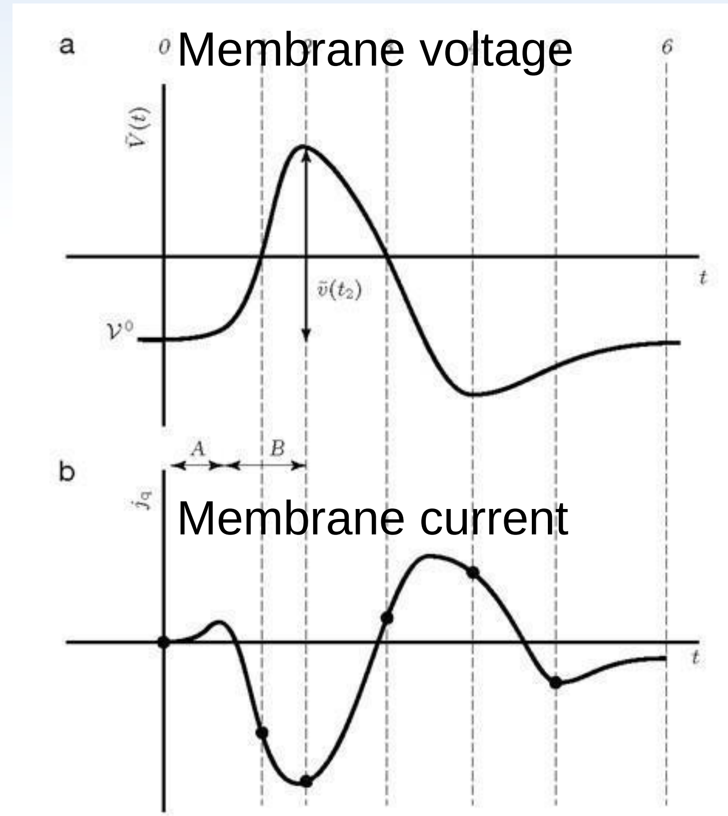
Opening and closing of voltage-gated Na^+ channels



Bagneris et al. JGP, DOI: 10.1085/jgp.201411242

Action potential: Changes in membrane voltage vs. current





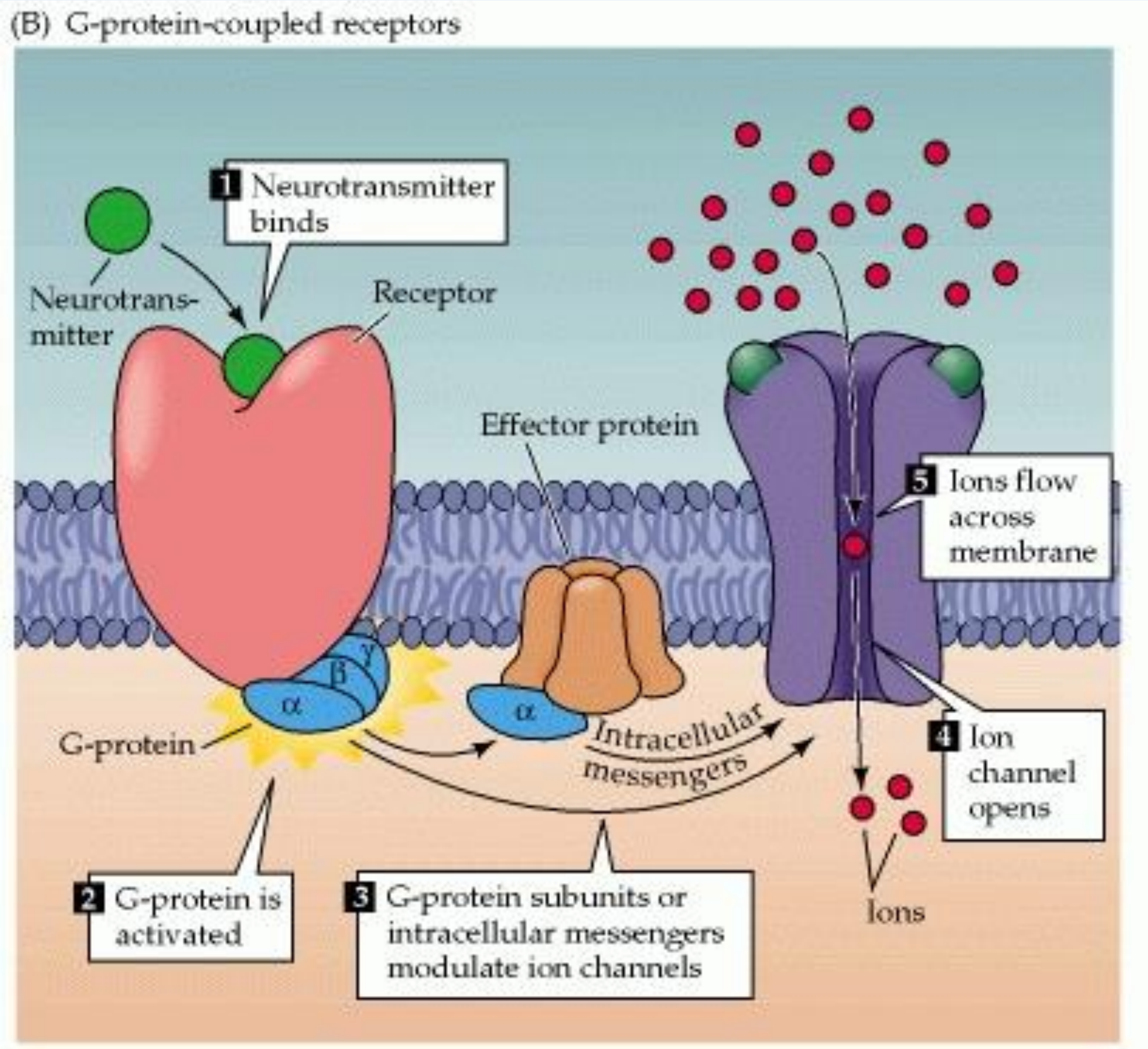
Squires et al: Fundamental Neuroscience, 2nd ed. San Diego, CA, Academic Press, 2002.

Second messengers

- Intracellular signaling molecules released by the cell to trigger physiological changes

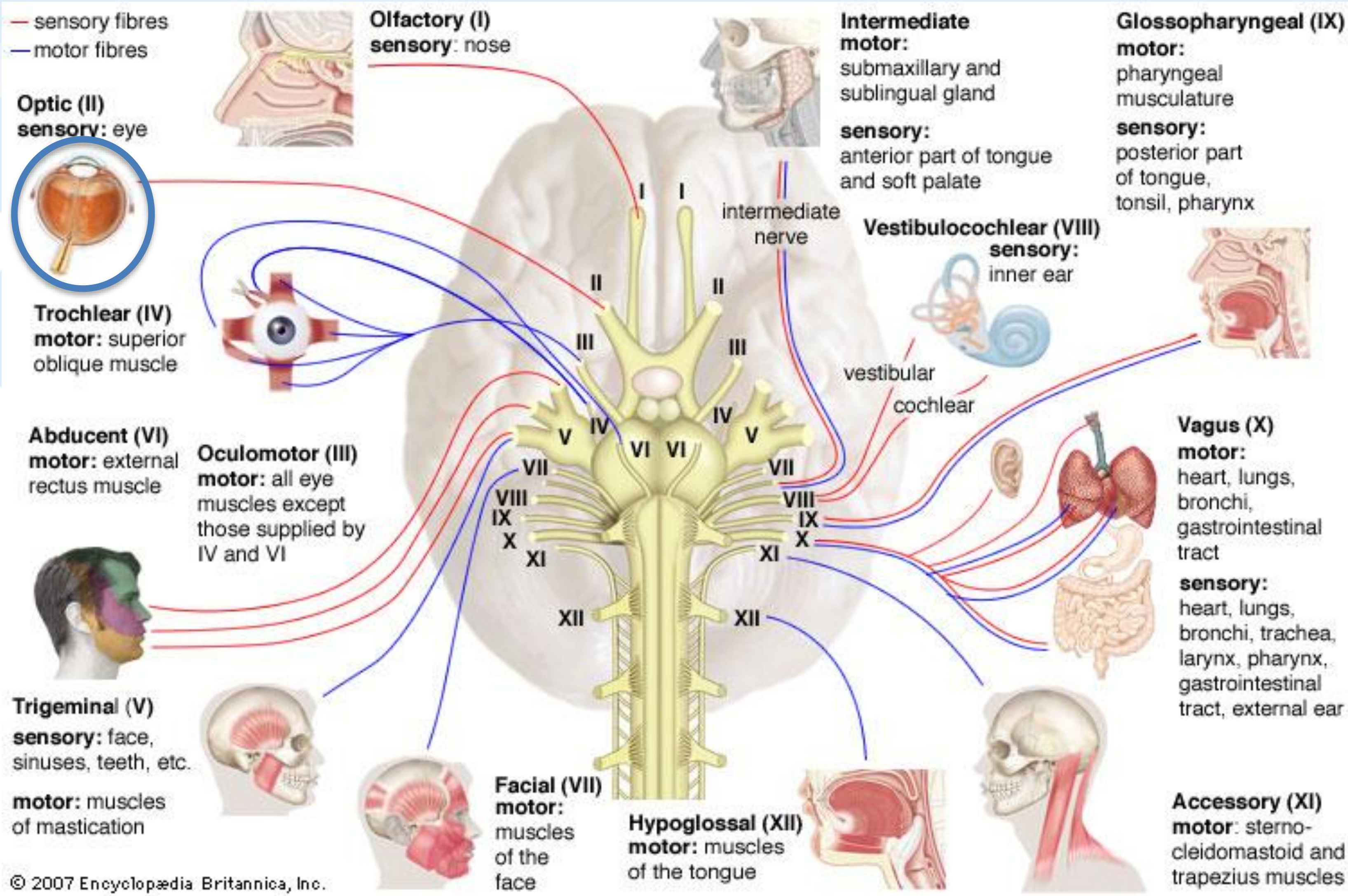
  => initiating components of intracellular signal transduction cascades
- Examples: cyclic AMP, cyclic GMP, Ca^{2+}
- Released in response to extracellular signaling molecules - the first messengers
- First messengers typically extracellular factors, e.g. hormones or neurotransmitters
- G-protein cascade a typical example

Metabotropic receptor and G-protein cascade



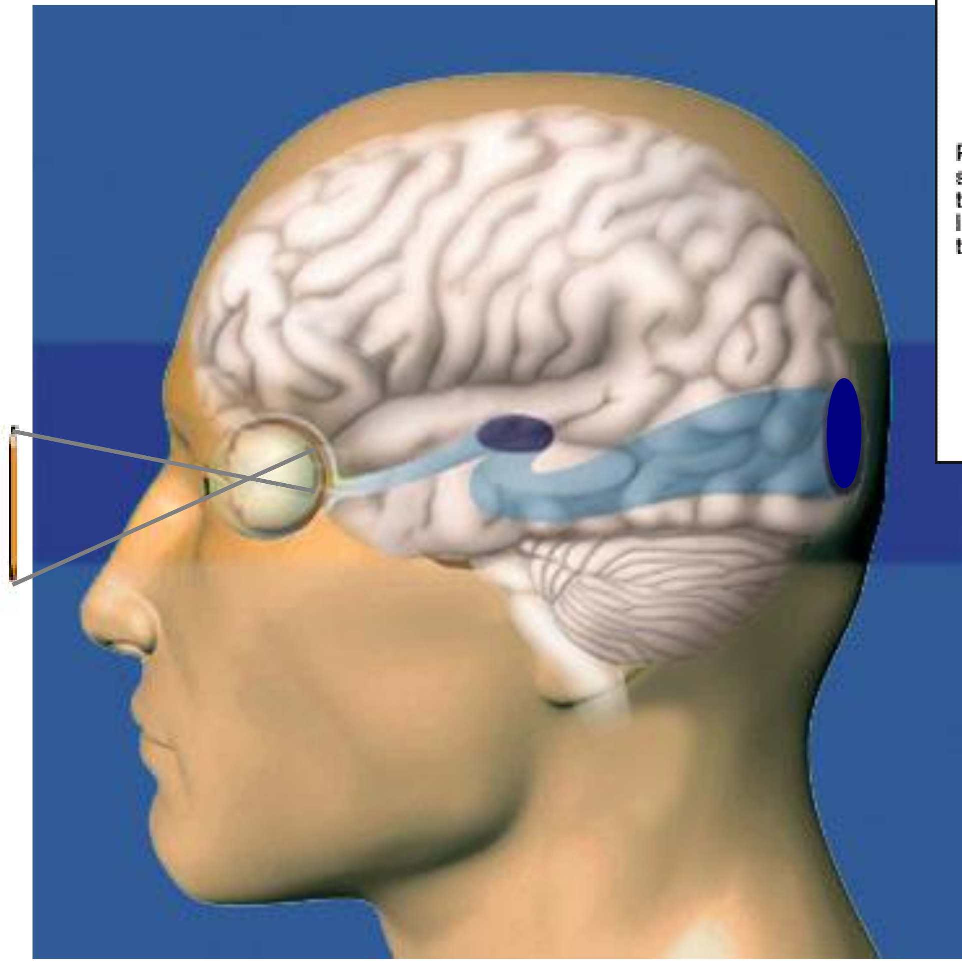
Purves (Ed.), Neuroscience

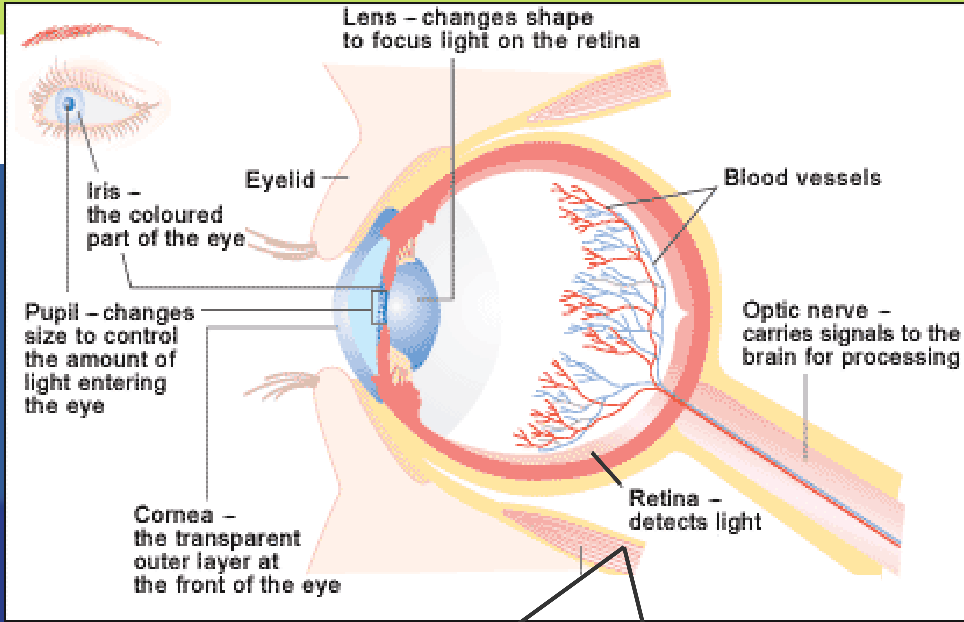
Sensory and motor systems

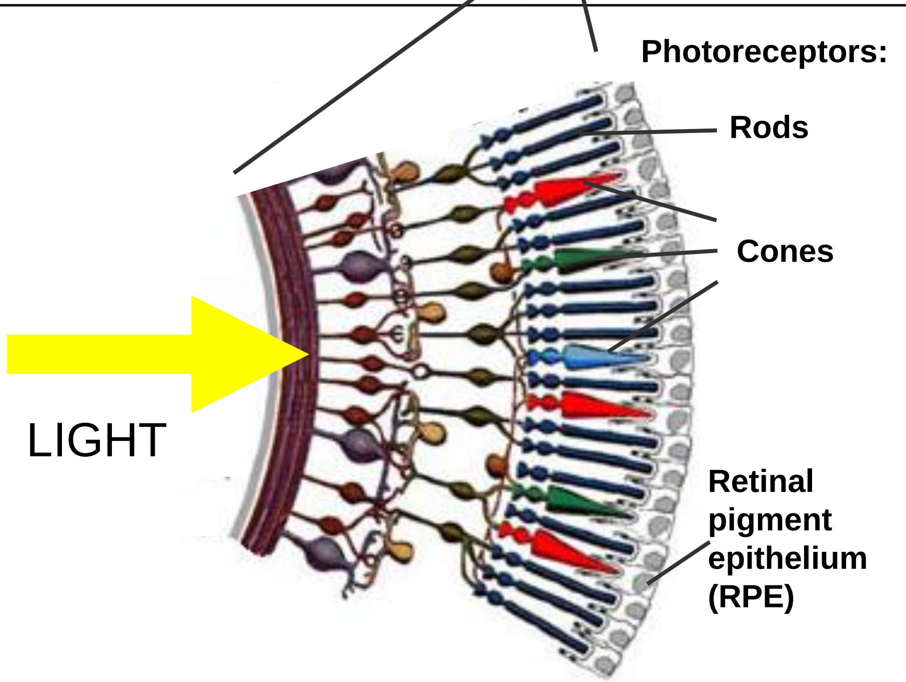


http://media-2.web.britannica.com/eb-media/44/54244-004-892C5169.jpg

Sensory functions - vision

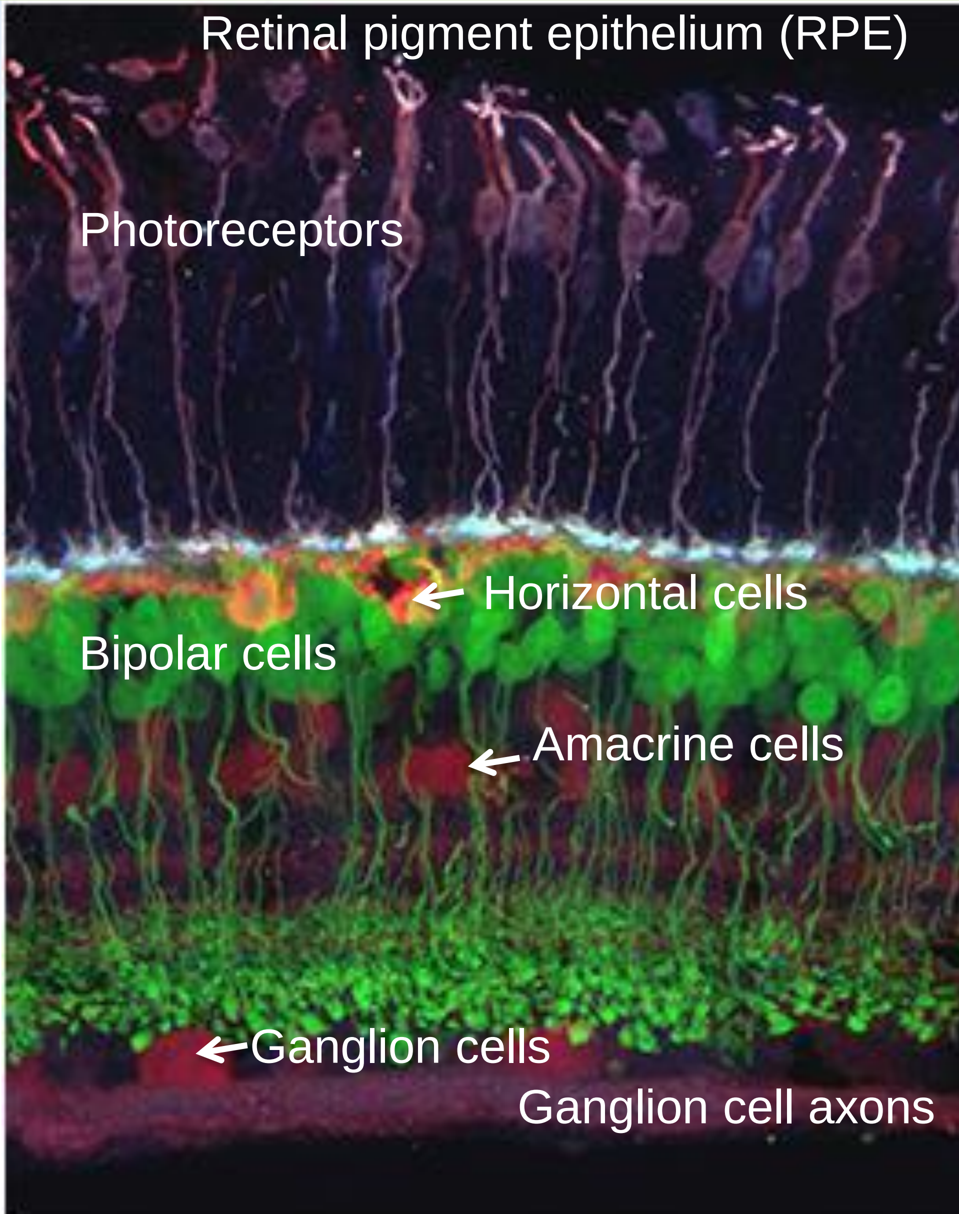






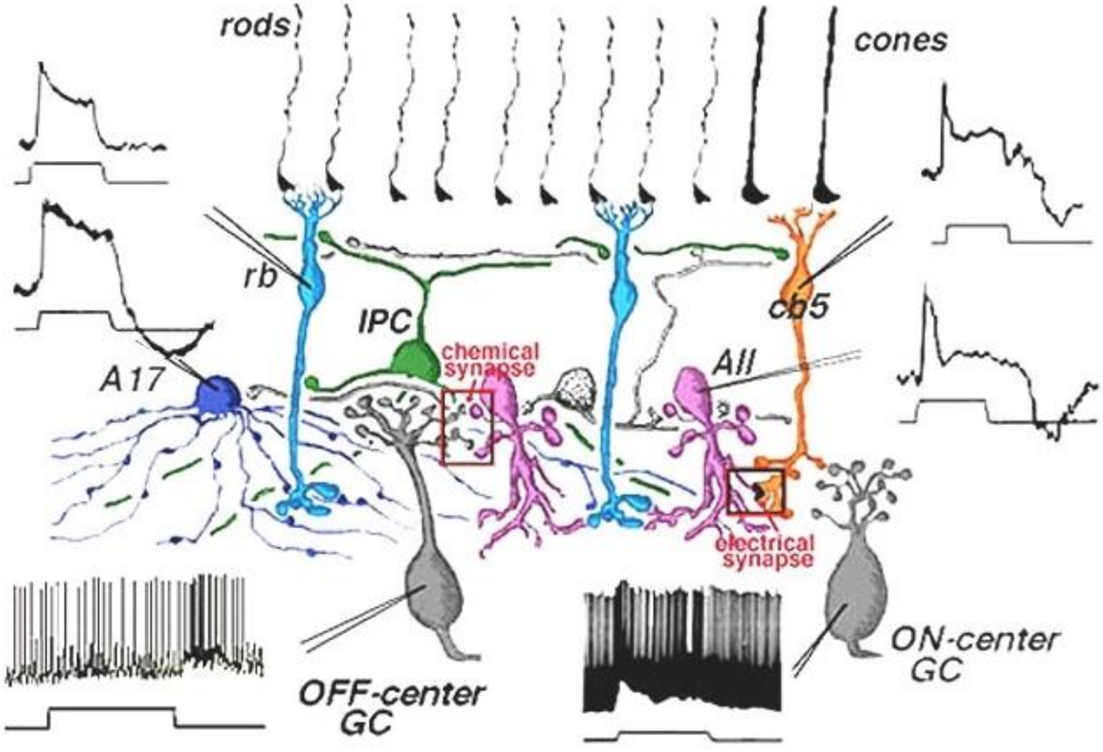
Sensory functions - vision

- Vision is based on light sensitive neural tissue – the retina
- Many types of neurons organized to form a complex neural tissue – comparable to brain tissue
- Layered structure with lots of information processing



Vision and retinal signaling

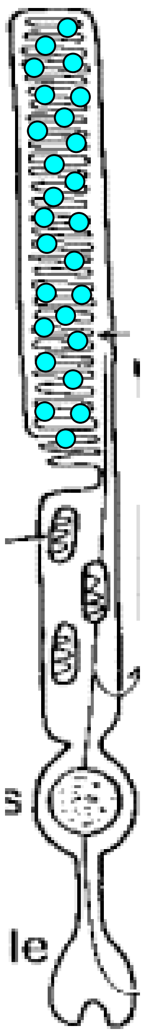
- Retinal photoreceptors (rods and cones) transform the light signal into an electrical signal
- This electrical signal is then passed via a complex retinal circuitry to ganglion cells
- Ganglion cells generate action potentials and send this information to brain for further processing



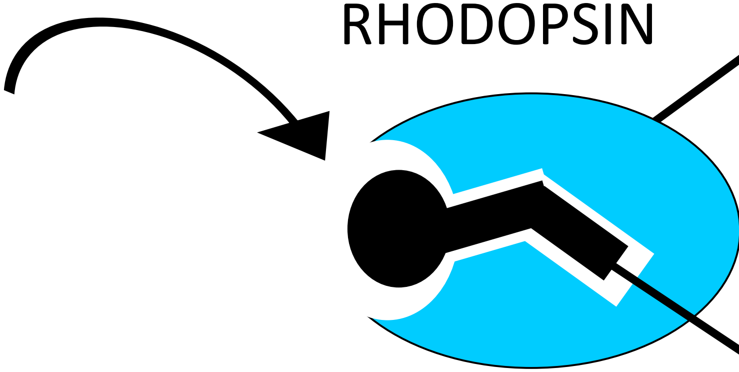
Light sensing in retina and its photoreceptors, rod and cones

- Structure of the light sensitive visual pigment

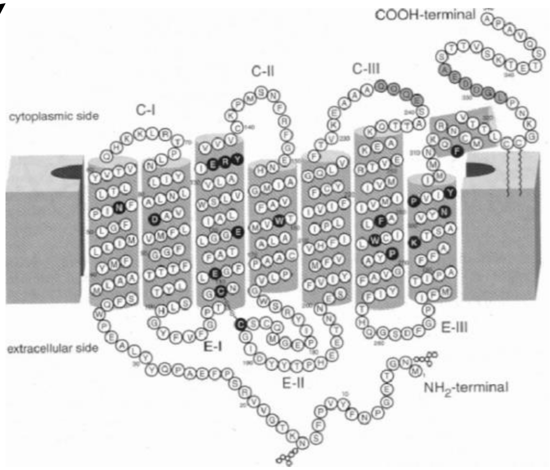
ROD



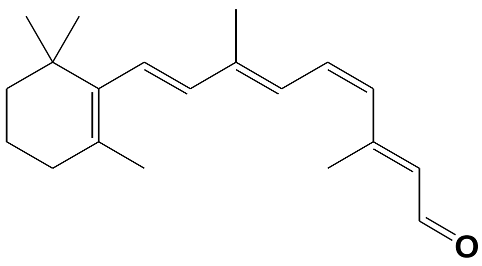
RHODOPSIN



Opsin Protein



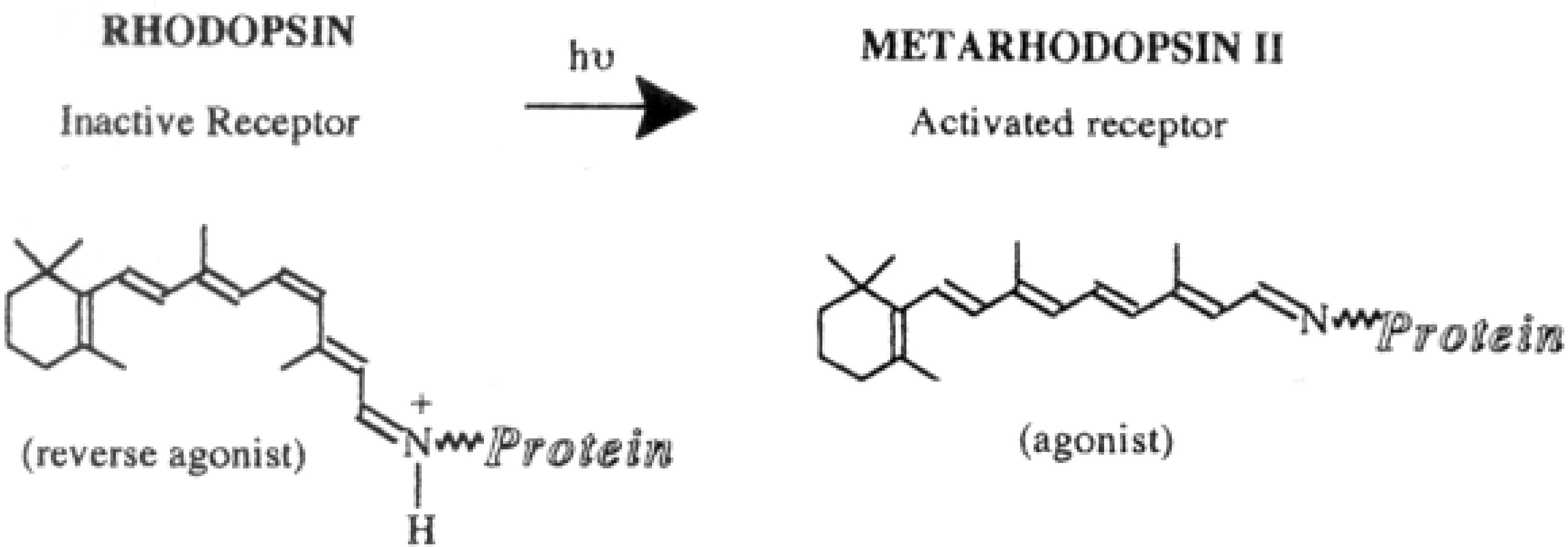
11-*cis* retinal



In the dark, 11-*cis* retinal is bound to opsin by a covalent bond which maintains the pigment in an inactive configuration

Light does one and only one thing....

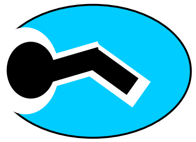
Photoisomerization



11-*cis* retinal

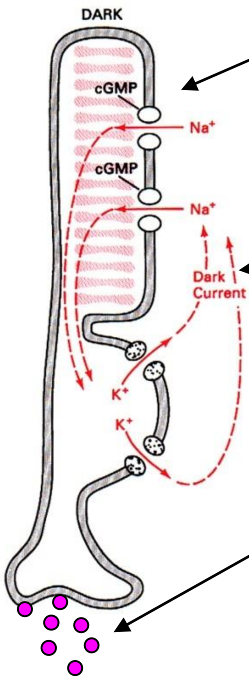
All-*trans* retinal

DARK:



Inactive Rhodopsin

11-*cis*

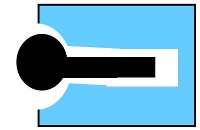


cGMP-gated channels OPEN

Dark current

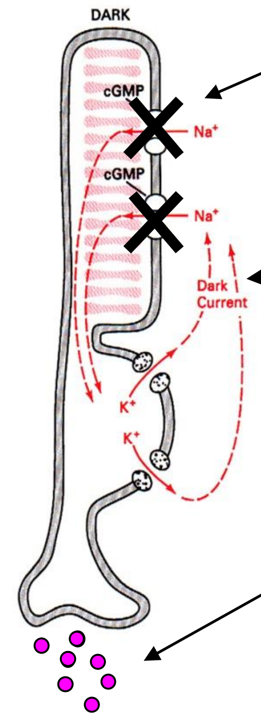
Continuous glutamate neurotransmitter secretion

LIGHT:



Activated Rhodopsin

all-*trans*



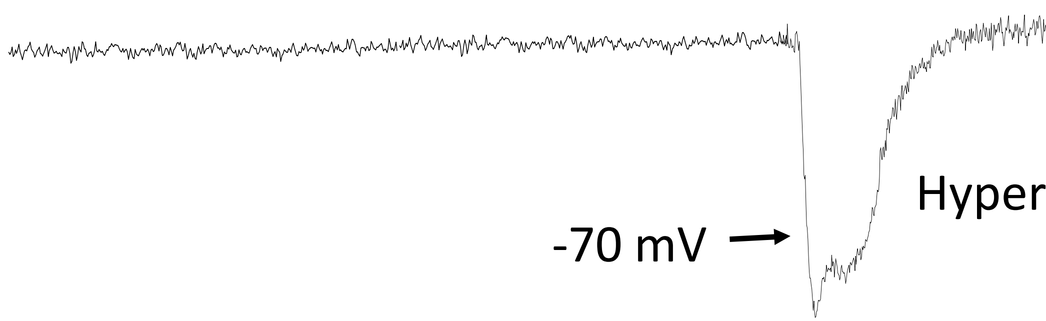
cGMP-gated channels CLOSE

Dark current declines

Reduction of glutamate secretion

Cell continuously depolarized

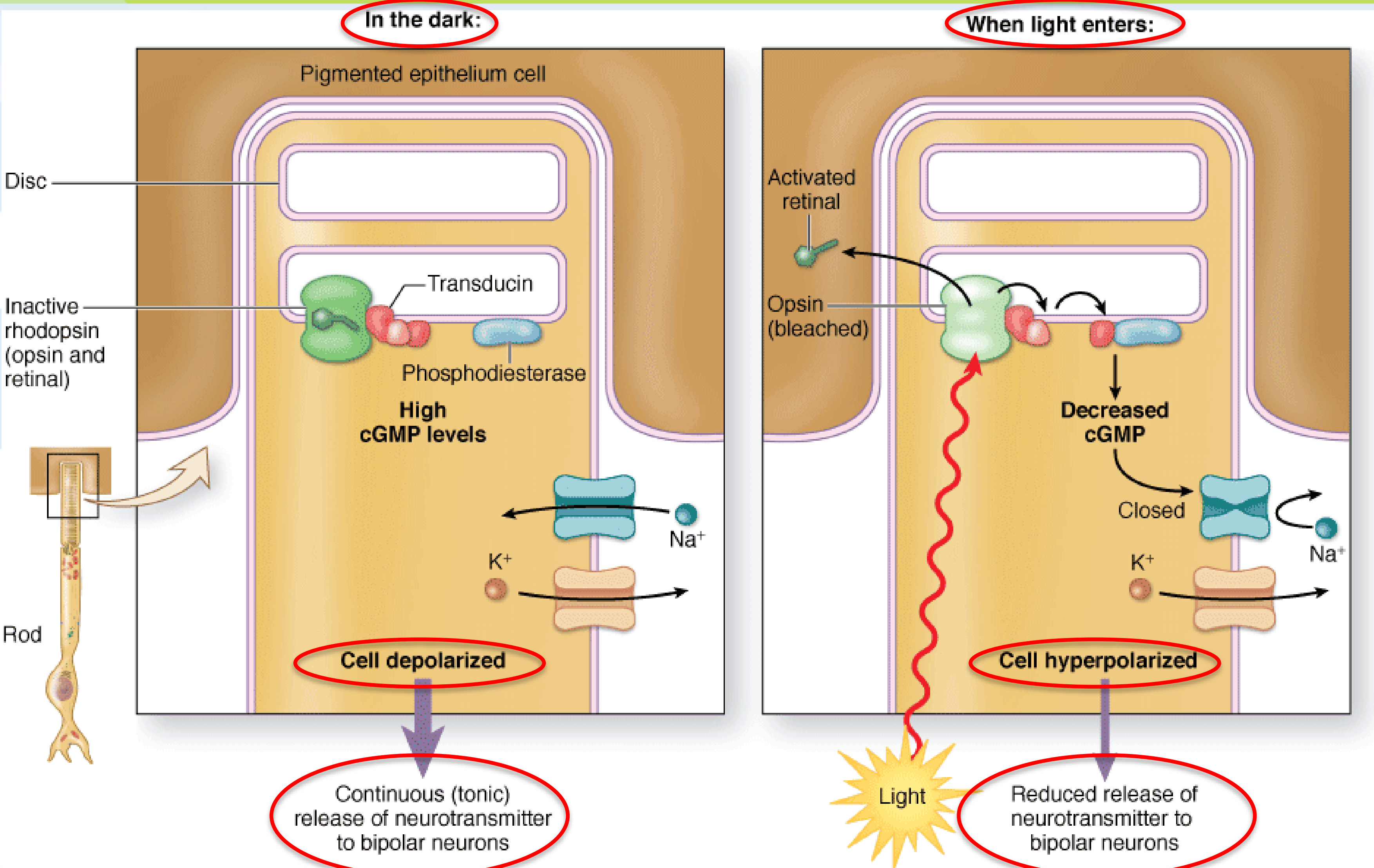
V_m = -35 mV



Hyperpolarized

-70 mV

Phototransduction – conversion of light signal into electrical signal

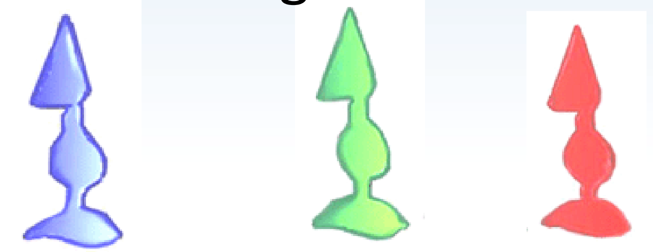


Source: Mescher AL: *Junqueira's Basic Histology: Text and Atlas, 12th Edition*: http://www.accessmedicine.com

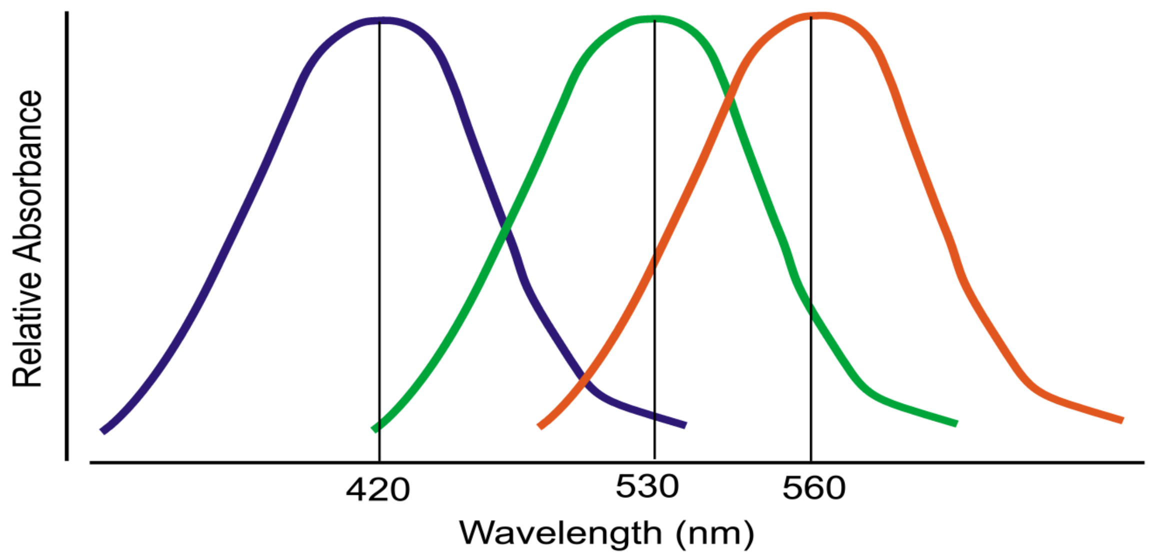
How do we see color?

- We have 3 cone types
- Each cone has a different opsin type.
- Each opsin has a different spectral sensitivity curve

blue green red



s-opsin m-opsin l-opsin

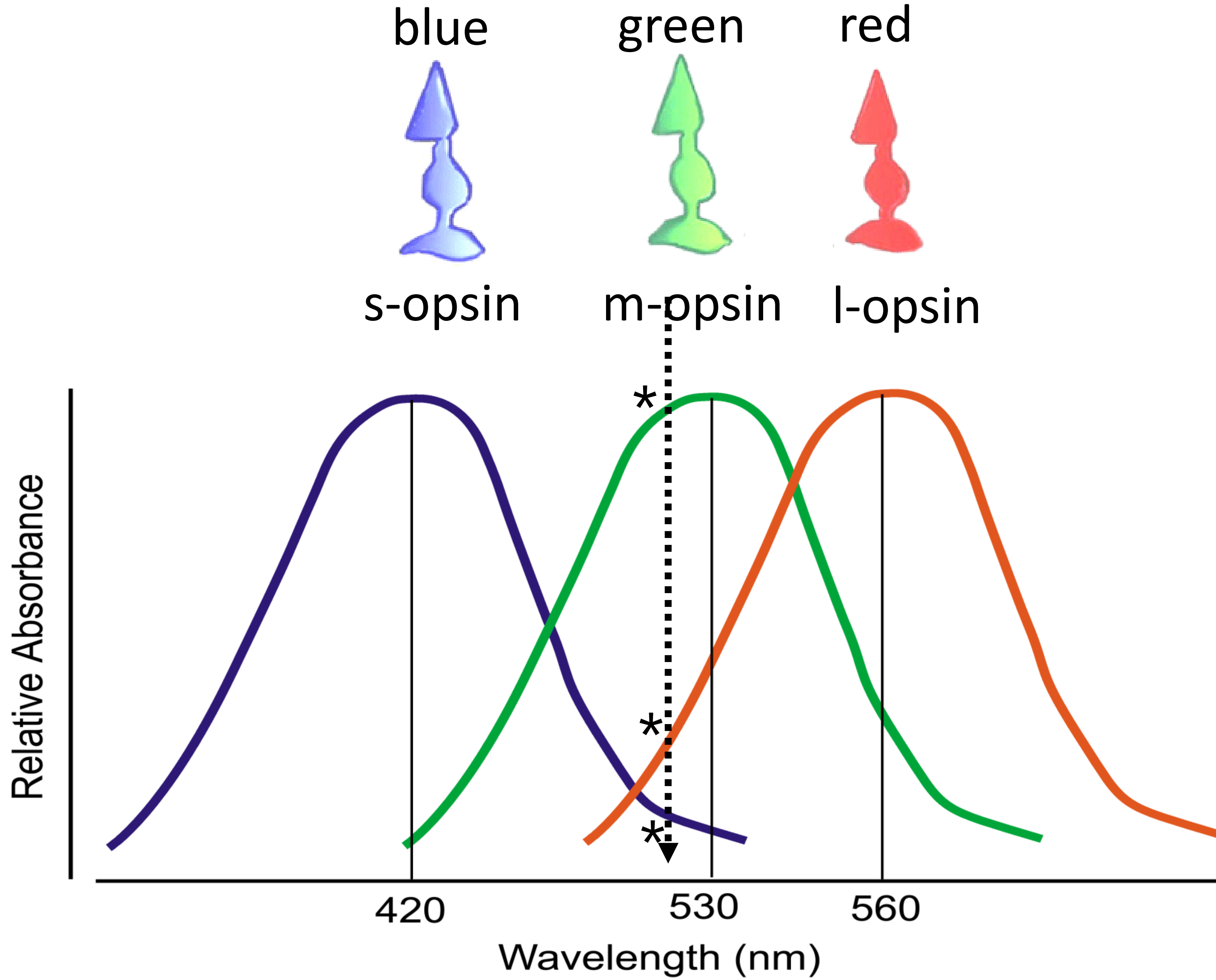


Why do we need more than one cone type for color vision?

RUSHTON'S PRINCIPLE:

The receptor potential of a photoreceptor depends upon its quantum catch, but not upon *what* quanta are caught.

Translation: The response of each photoreceptor depends upon the number of photons absorbed (and subsequent visual pigment molecules photoisomerized) but not upon the wavelength.



The human visual system extracts color information by *comparing* the output of the three different cone types.

The more opsin types, the better the color discrimination

1 Monochromatic

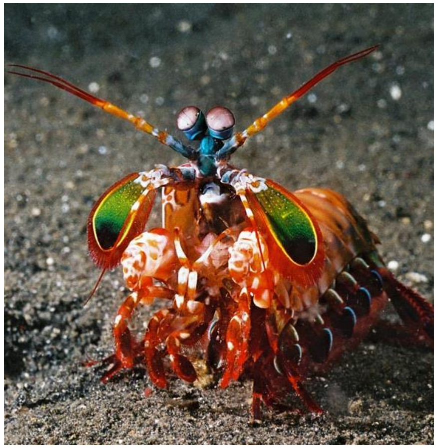
2 Dichromatic

3 Trichromatic

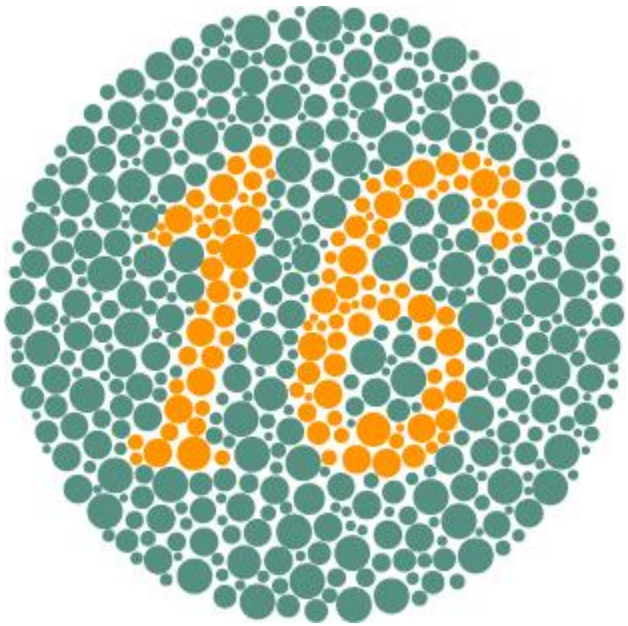
4 Tetrachromatic

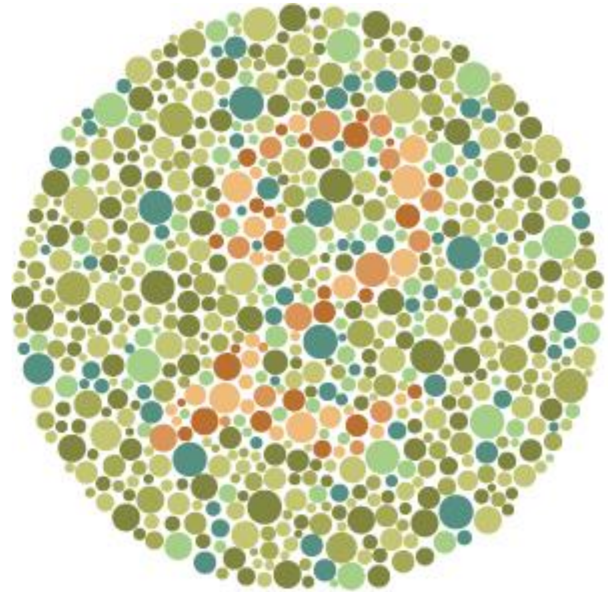
6 Hexachromatic

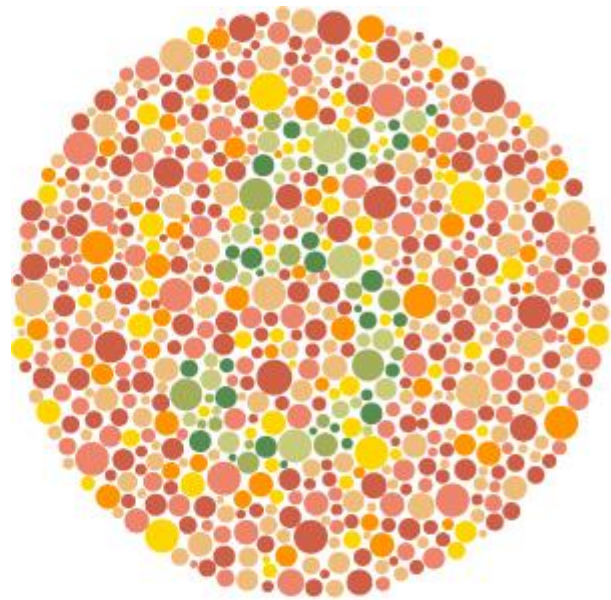
12 Dodecachromatic



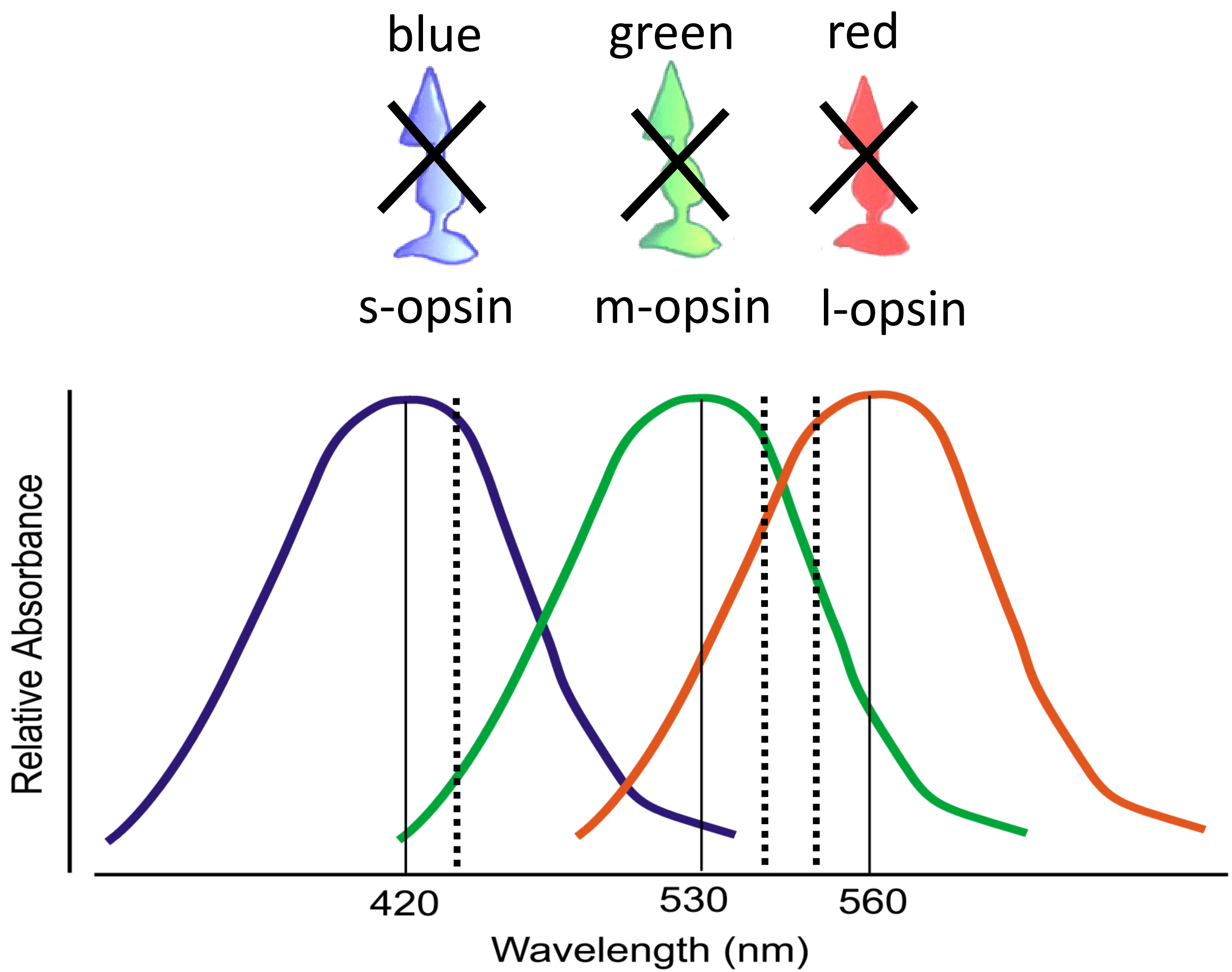
Color vision test





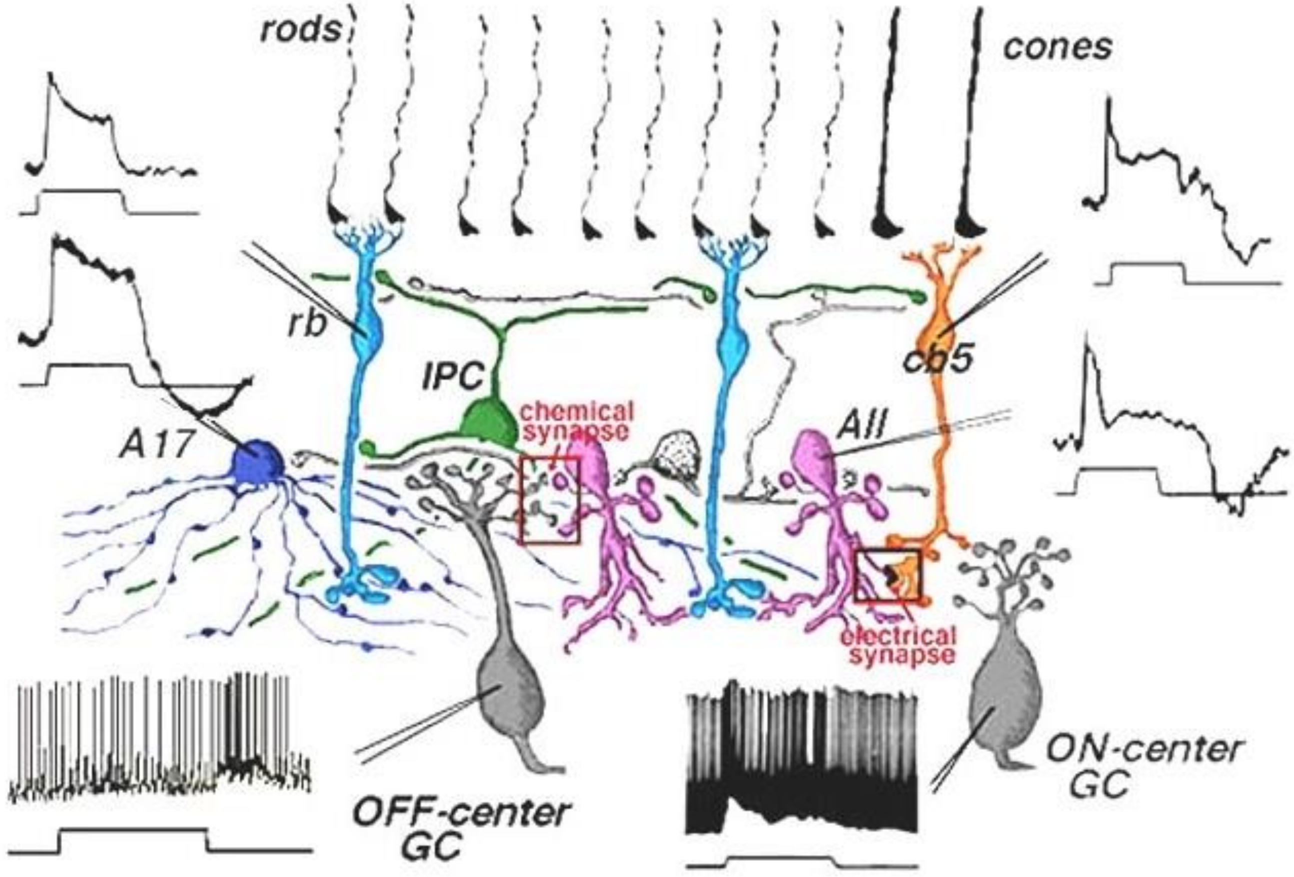


Color blindness



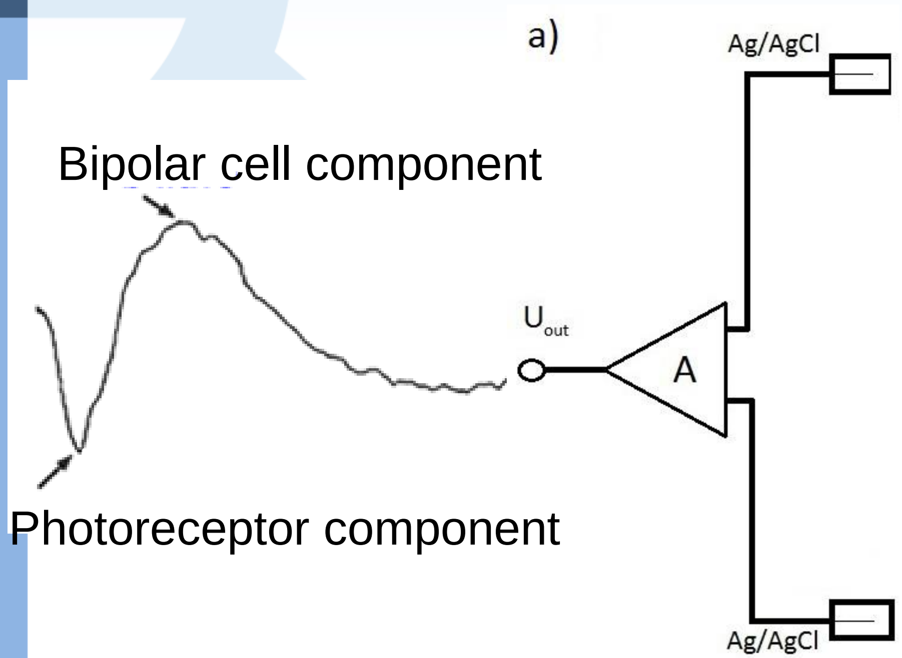
Retinal electrical signals

- Graded potentials: receptor neurons (photoreceptors, absorb light), bipolar cells, amacrine cells, horizontal cells
- Action potentials: ganglion cells (send long axons to brain)



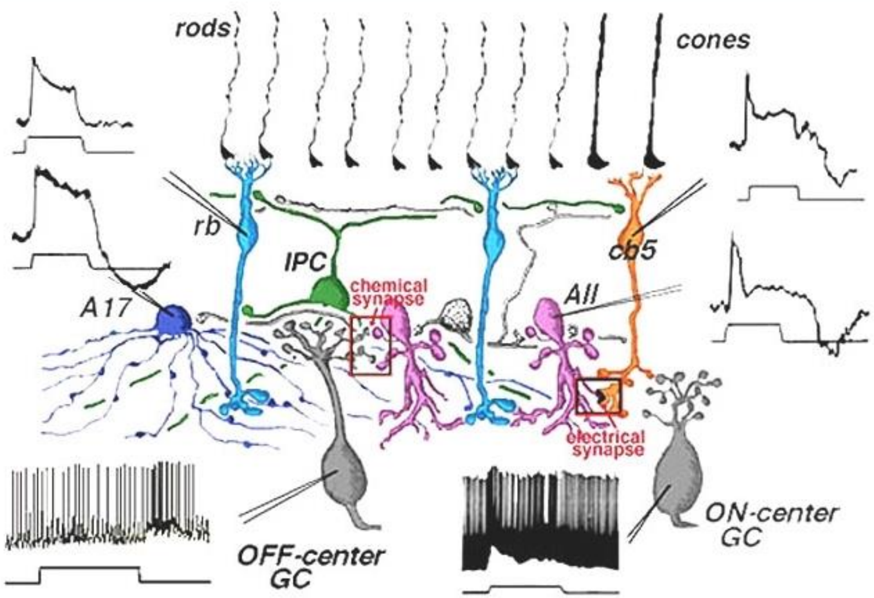
Retinal recordings *in vitro*

- Outside the tissue:



Electroretinogram (ERG)

- Inside the tissue:



Patch clamp

ERG *in vivo*

some corneal ERG electrodes

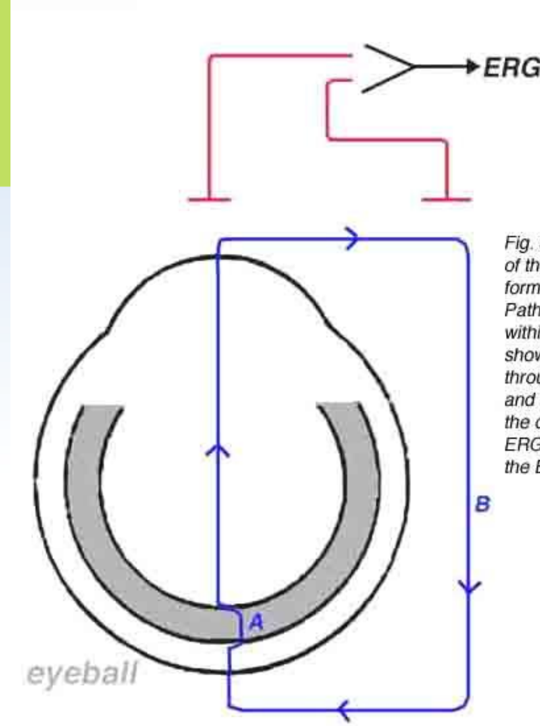
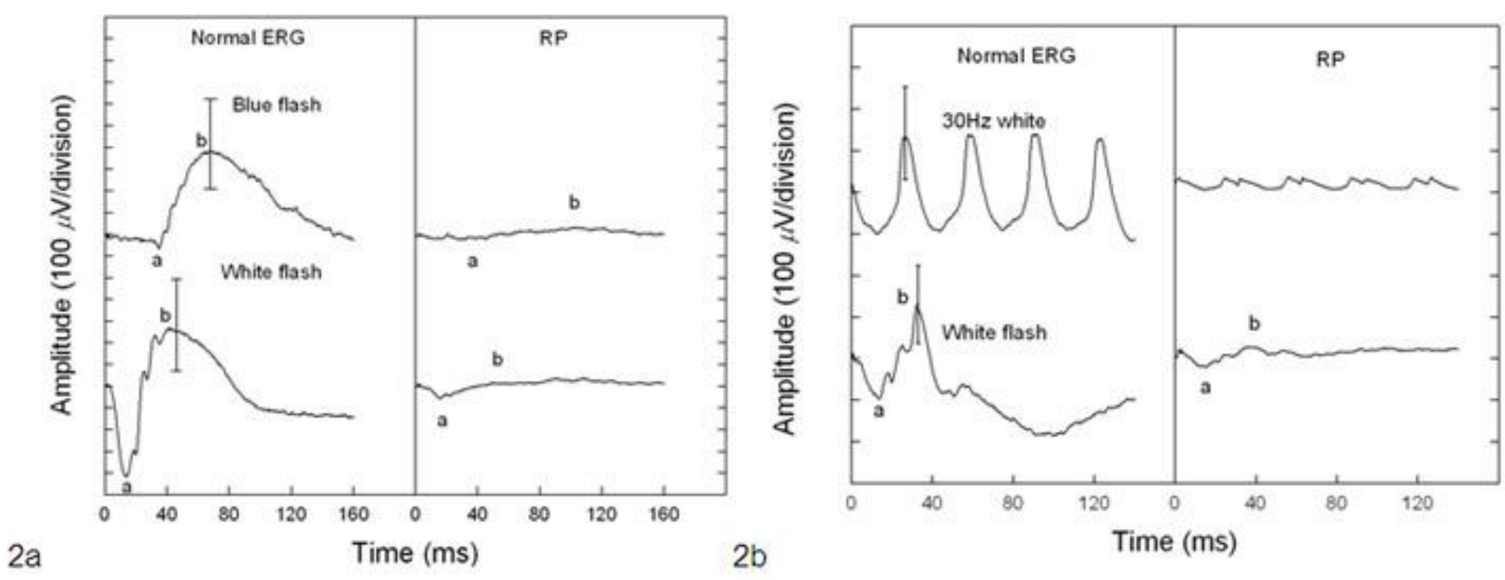
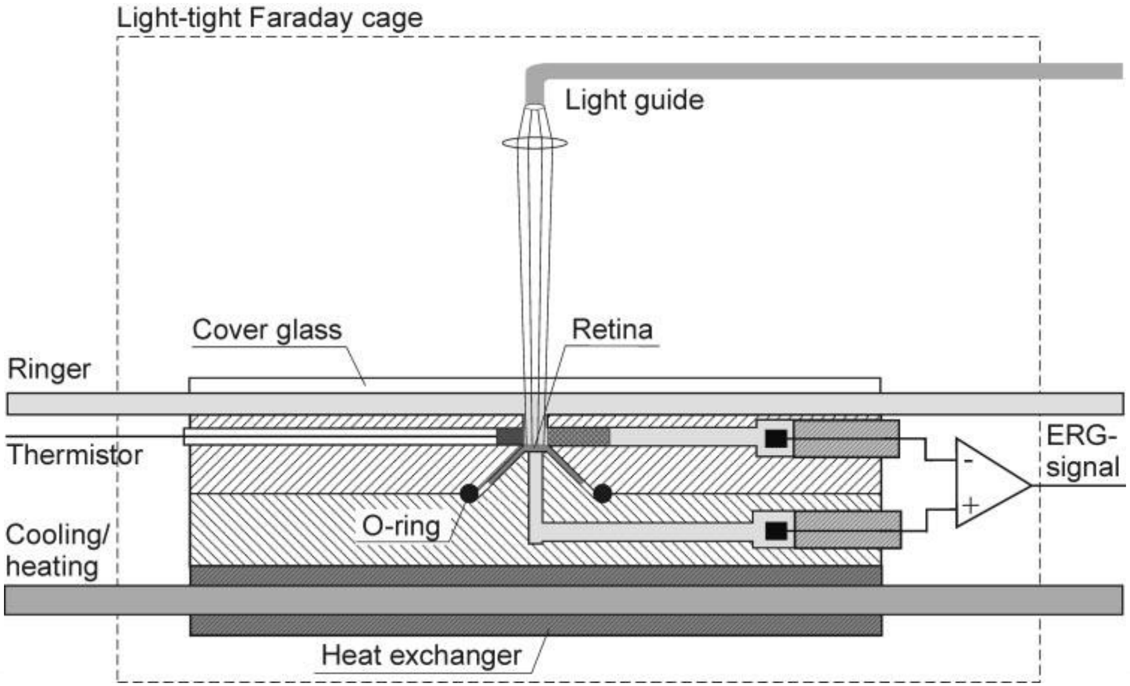


Fig. 3a. A schematic representation of the extracellular currents that are formed following light stimulation. Pathway A represents local currents within the retina, while pathway B shows the currents leaving the retina through the vitreous and the cornea and returning to the retina through the choroid and the pigment epithelium. ERG recording in human is done along the B path.



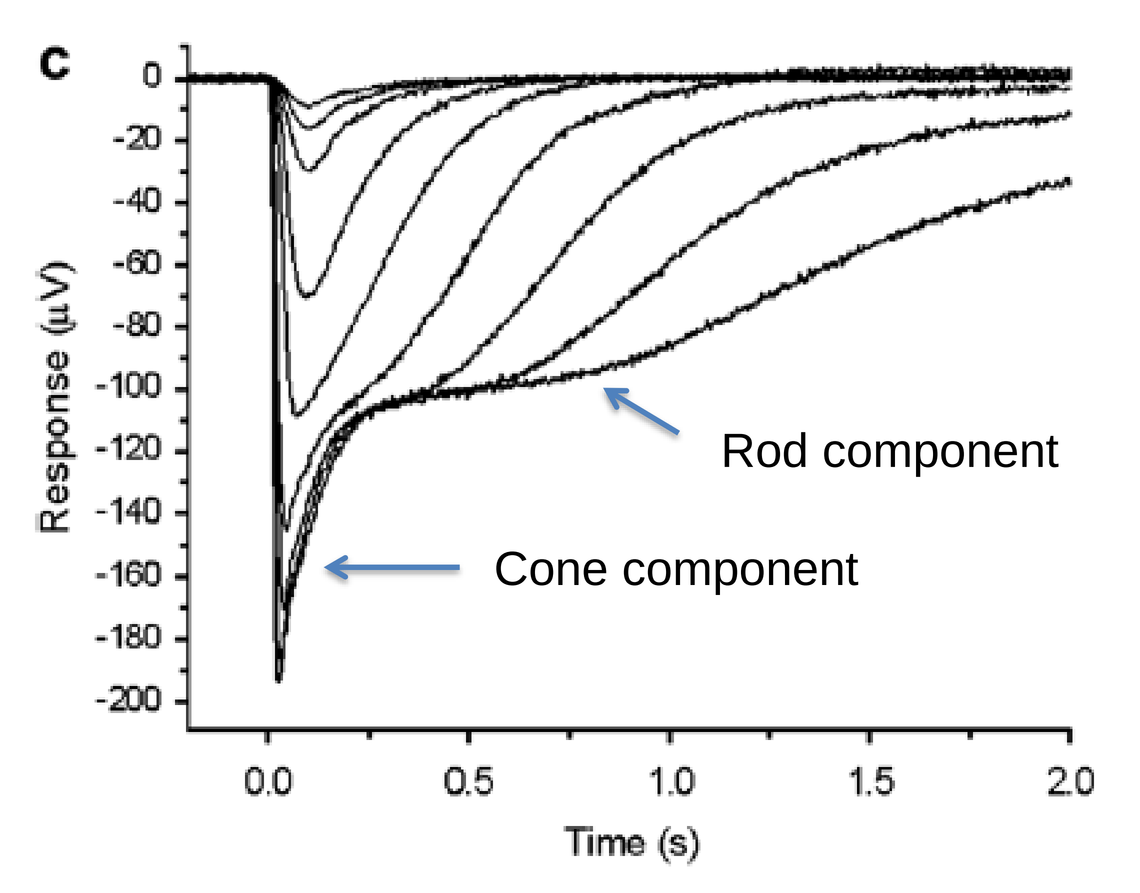
Field potential recordings

- Electroretinogram (ERG) is a field potential
- Field potentials can be recorded by placing electrodes outside the recordable tissue
- Wire electrodes and pellet electrodes common

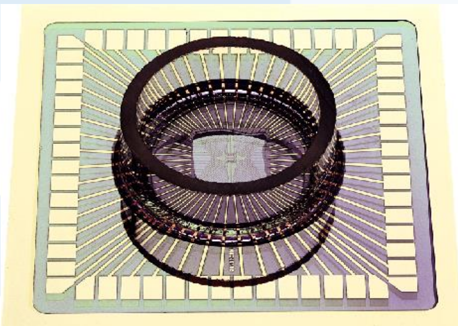


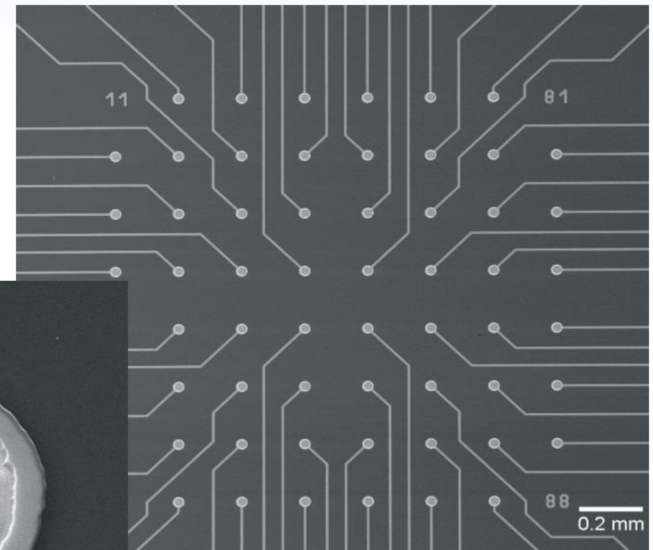
ERG recordings from mouse retina

- Photoreceptor responses, other signal components blocked by pharmacological compounds

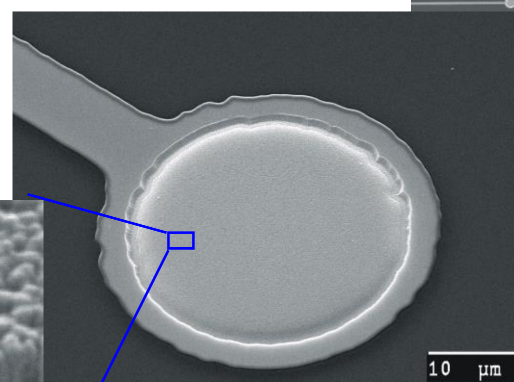


Microelectrode array (MEA) technique

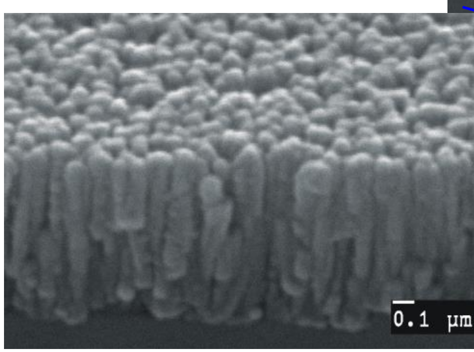




100 or 200 µm grid



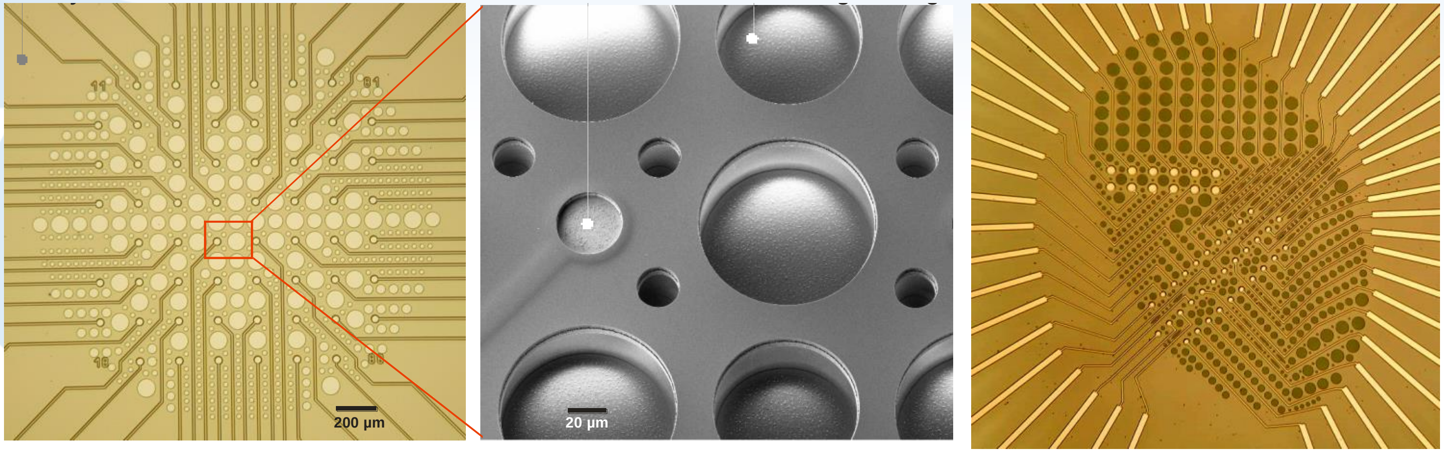
10-30 µm electrode diameter

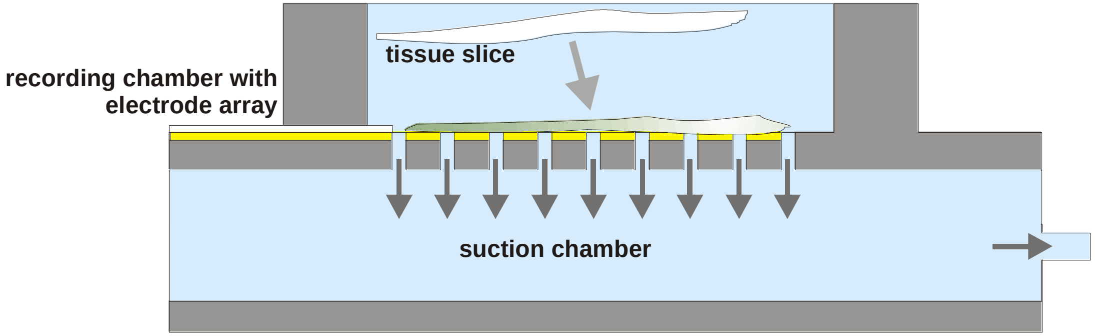


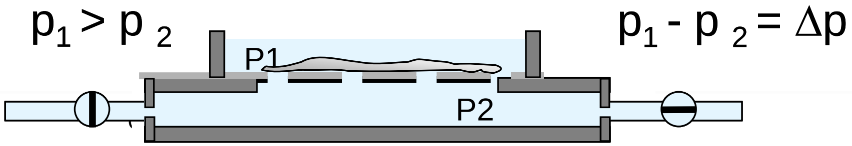
impedance: 30-300 kΩ

Egert et al. 1998

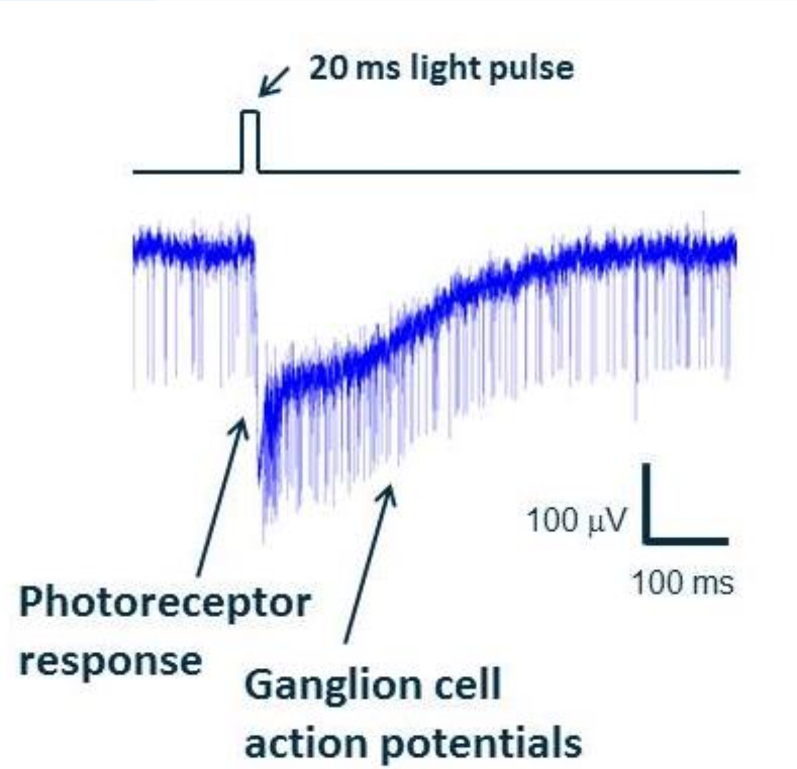
Perforated MEAs

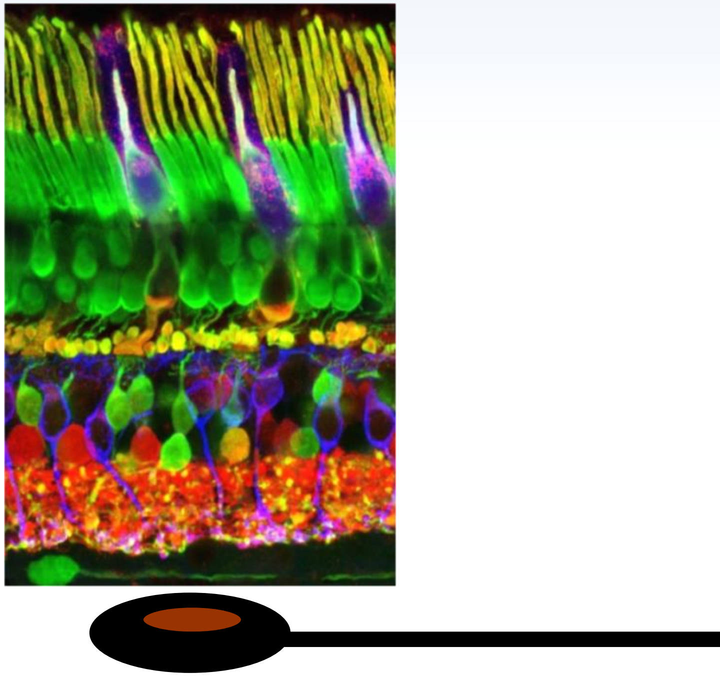






Retinal recordings with MEA





Microelectrode array (MEA)

MEA recordings – retinal action potentials