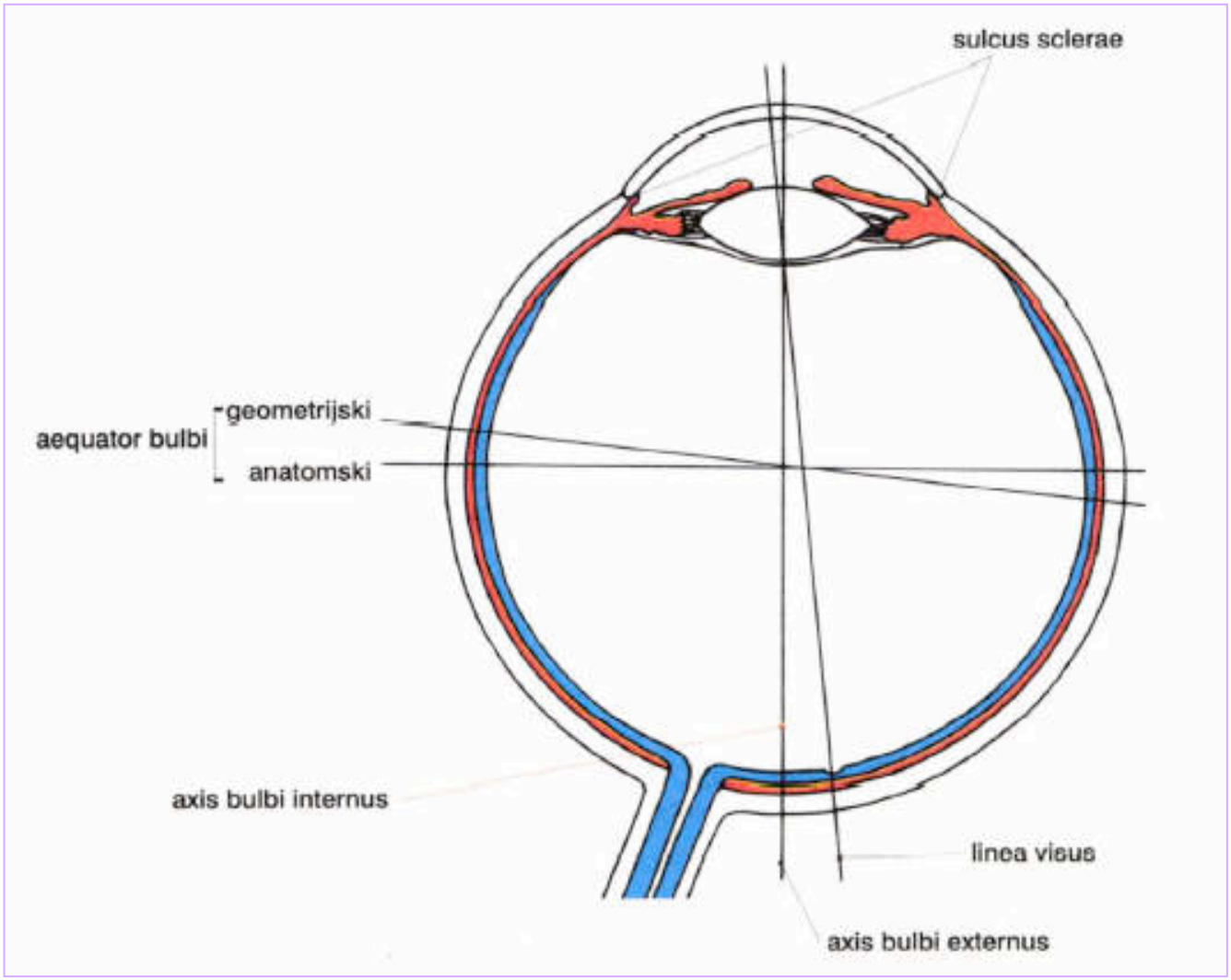
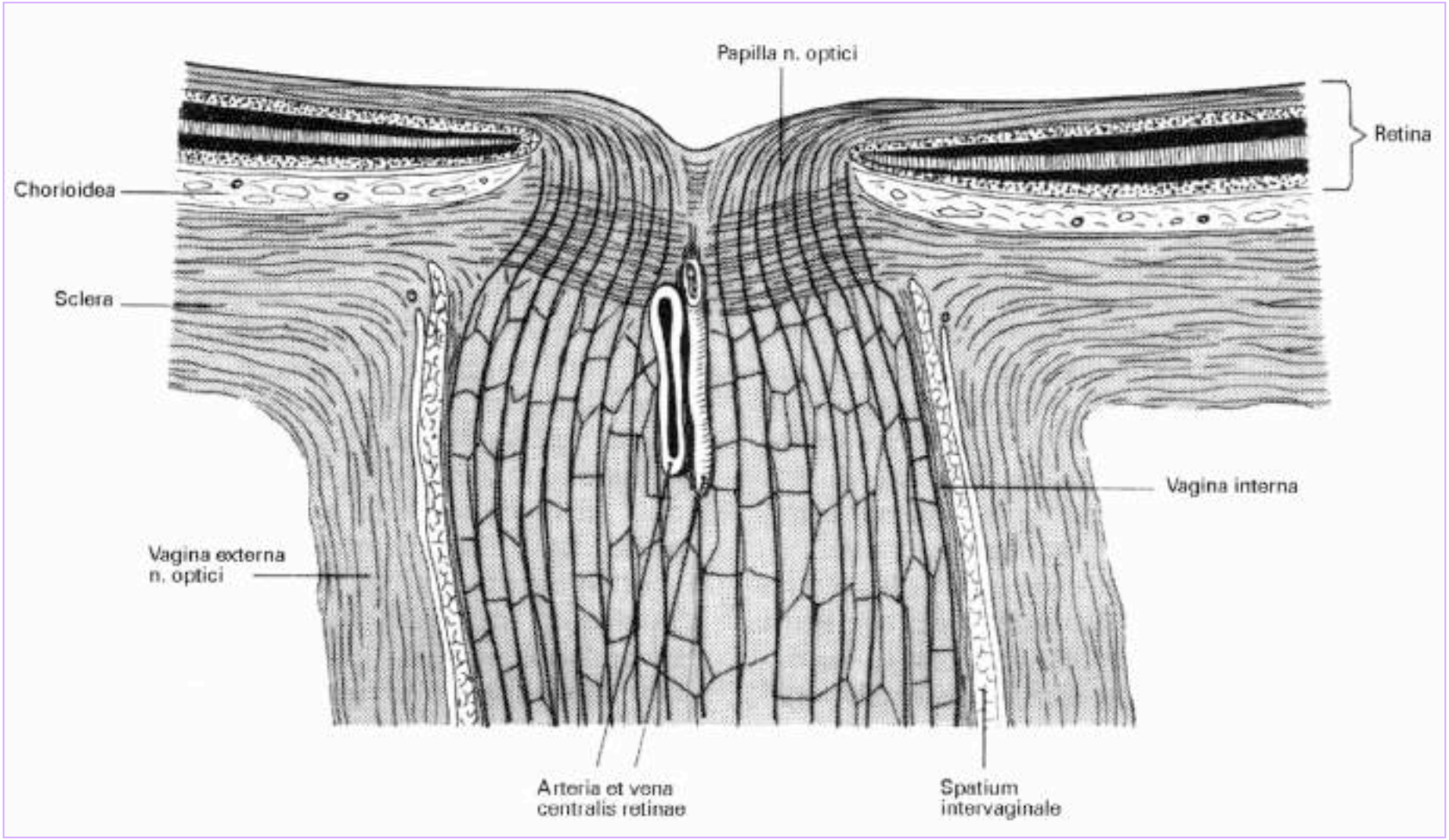
Eye physiology and phototransduction

Zoran Đogaš

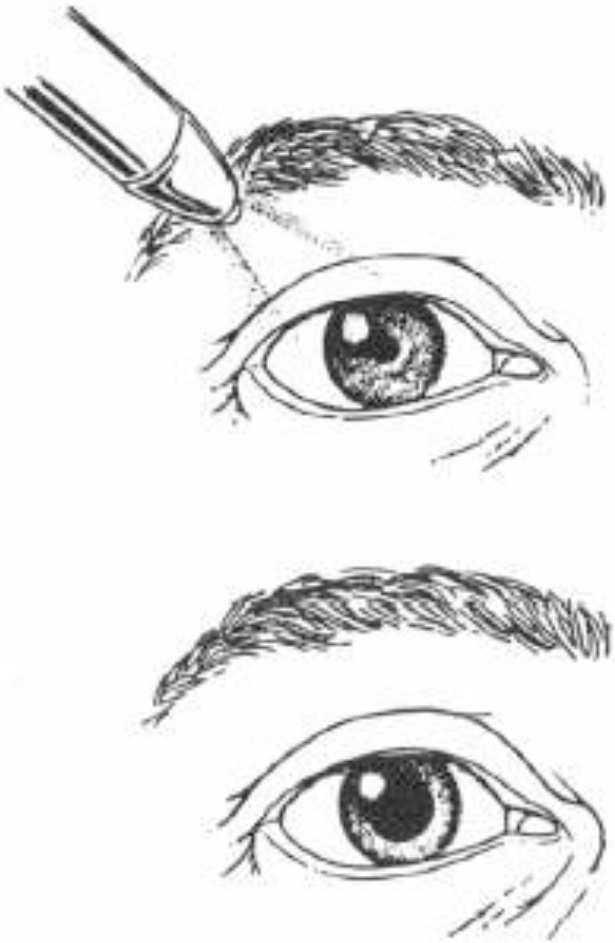
Eye geometry



Nervus opticus

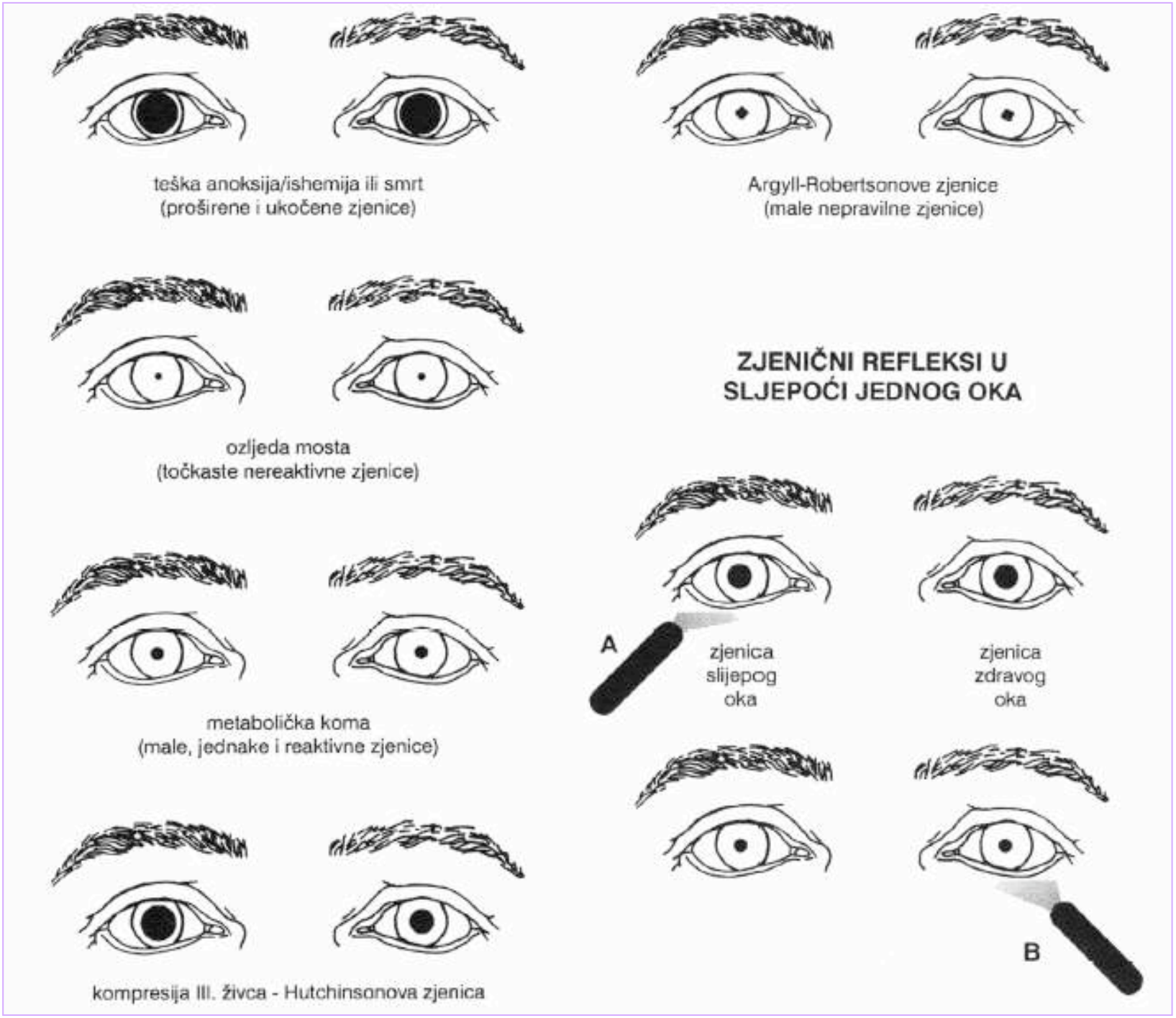


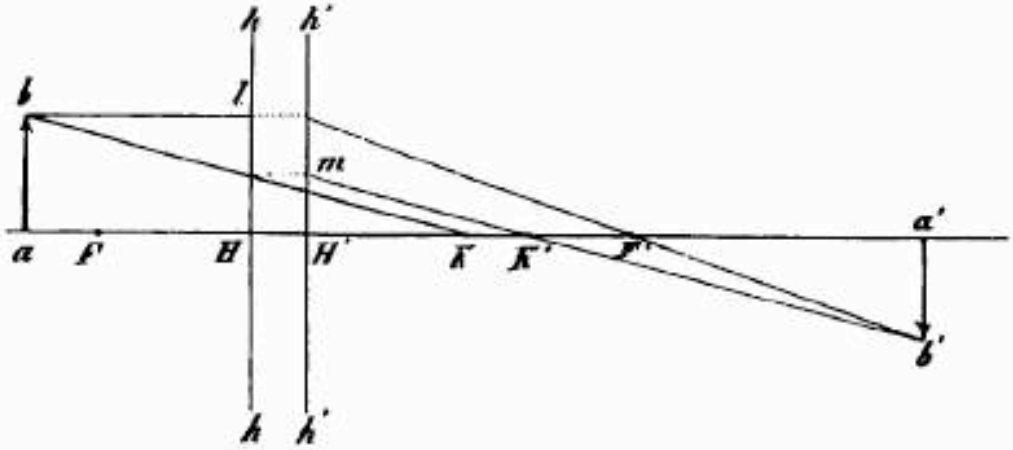
Pupillary reflex and accommodation

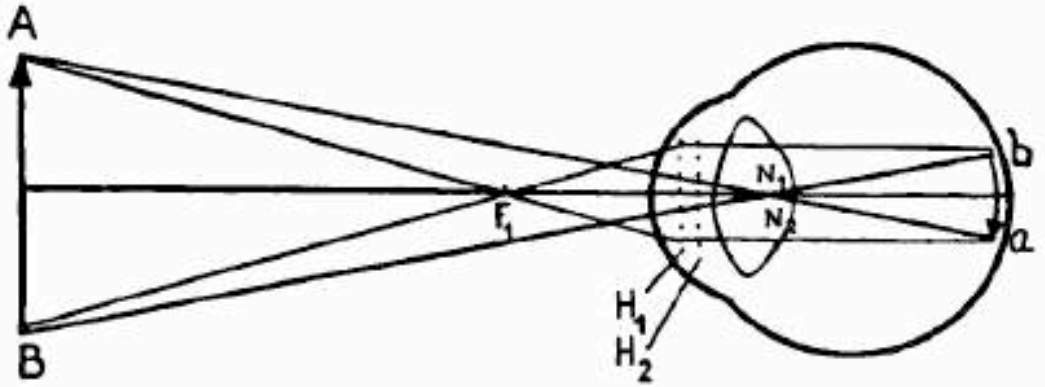


Slika 27-3. Zjenični refleks i refleks akomodacije. **Gore:** Zjenica je sužena (*miosis*) kad je izložena svjetlu ili kad promatramo bliski predmet. **Dolje:** Zjenica je proširena (*mydriasis*) kad smo u polumraku ili mraku ili kad gledamo udaljeni predmet.

Clinical Sy

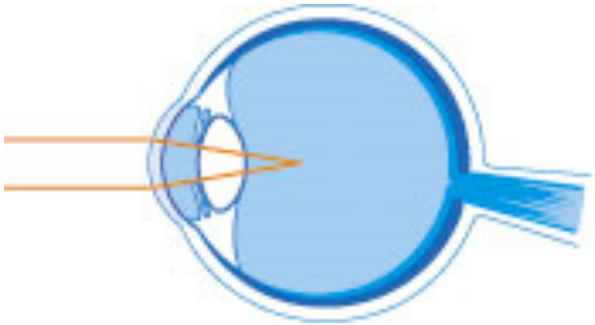

teška anoksija/ishemija ili smrt
(proširene i ukočene zjenice)
Argyll-Robertsonove zjenice
(male nepravilne zjenice)
ozljeda mosta
(točkaste nereaktivne zjenice)
ZJENIČNI REFLEKSI U
SLJEPOĆI JEDNOG OKA
A
zjenica
slijepog
oka
zjenica
zdravog
oka
metabolička koma
(male, jednake i reaktivne zjenice)
B
kompresija III. živca - Hutchinsonova zjenica

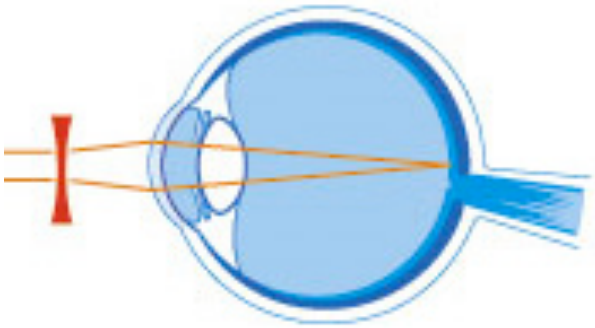


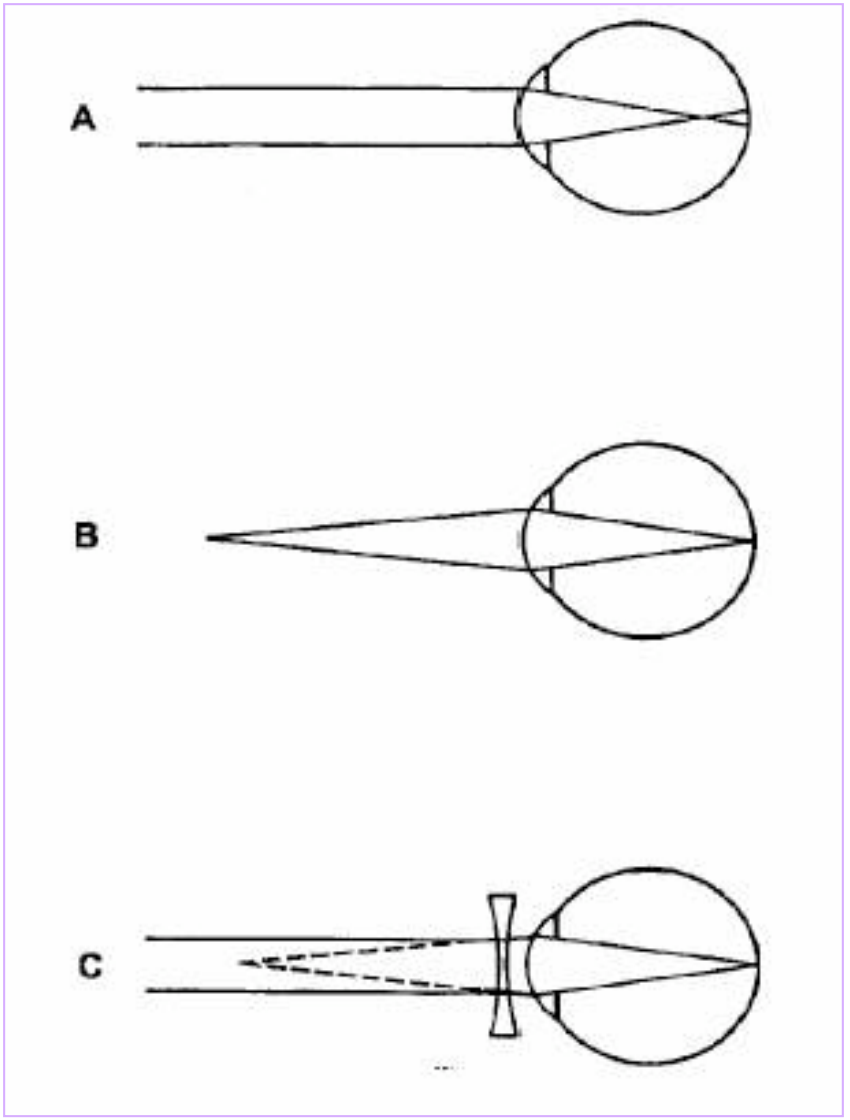


Slika 27-7. Gornji dijagram prikazuje kardinalne točke centriranog optičkog sustava sukladno Gaussovom teoremu: F,F' = prednja i stražnja žarišna točka (žarište, tj. fokus); H,H' = prednja i stražnja glavna točka; K,K' = prednja i stražnja čvorna točka; strelica a-b = gledani predmet; strelica a'-b' = slika predmeta; b-l = zraka što nakon loma prolazi kroz stražnje žarište; b-K = zraka što nakon loma postaje m-K'; h-h = prednja glavna ravnina; h'-h' = stražnja glavna ravnina.
Donji dijagram prikazuje nastanak realne, smanjene i obrnute slike gledanog predmeta u shematskom ljudskom oku. Strelica A-B = gledani predmet; strelica a-b = slika na mrežnici; F_1 = prednje žarište; H_1,H_2 = prednja i stražnja glavna ravnina; N_1, N_2 = prednja i stražnja čvorna točka (za praktične svrhe, možemo pretpostaviti da se obje spajaju u zajedničku čvornu točku). Kut ABN je tzv. vidni kut.

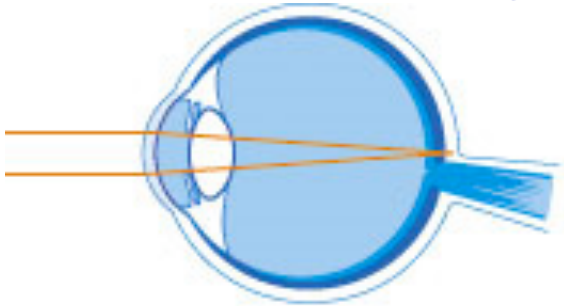
Myopia

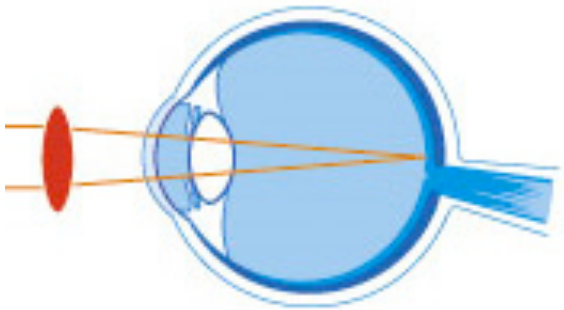


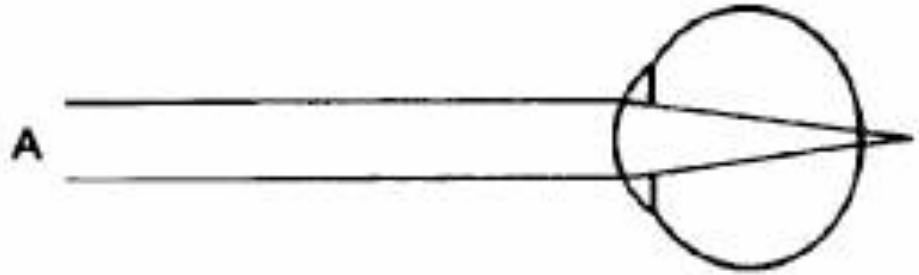


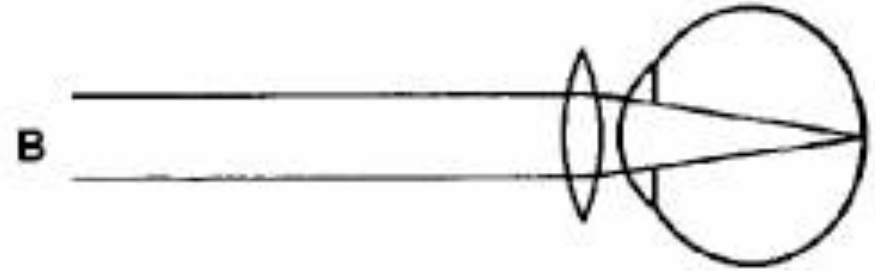


Hypermetropia



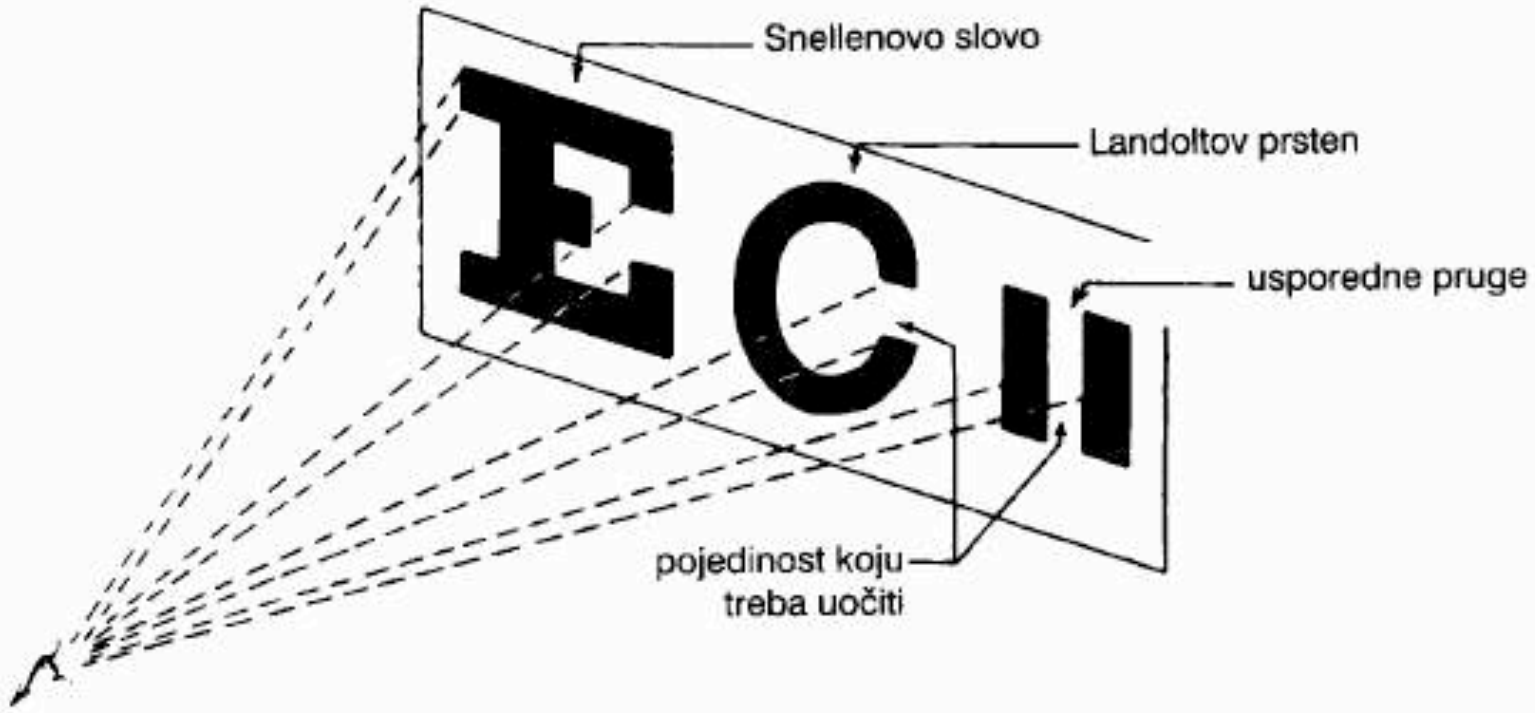




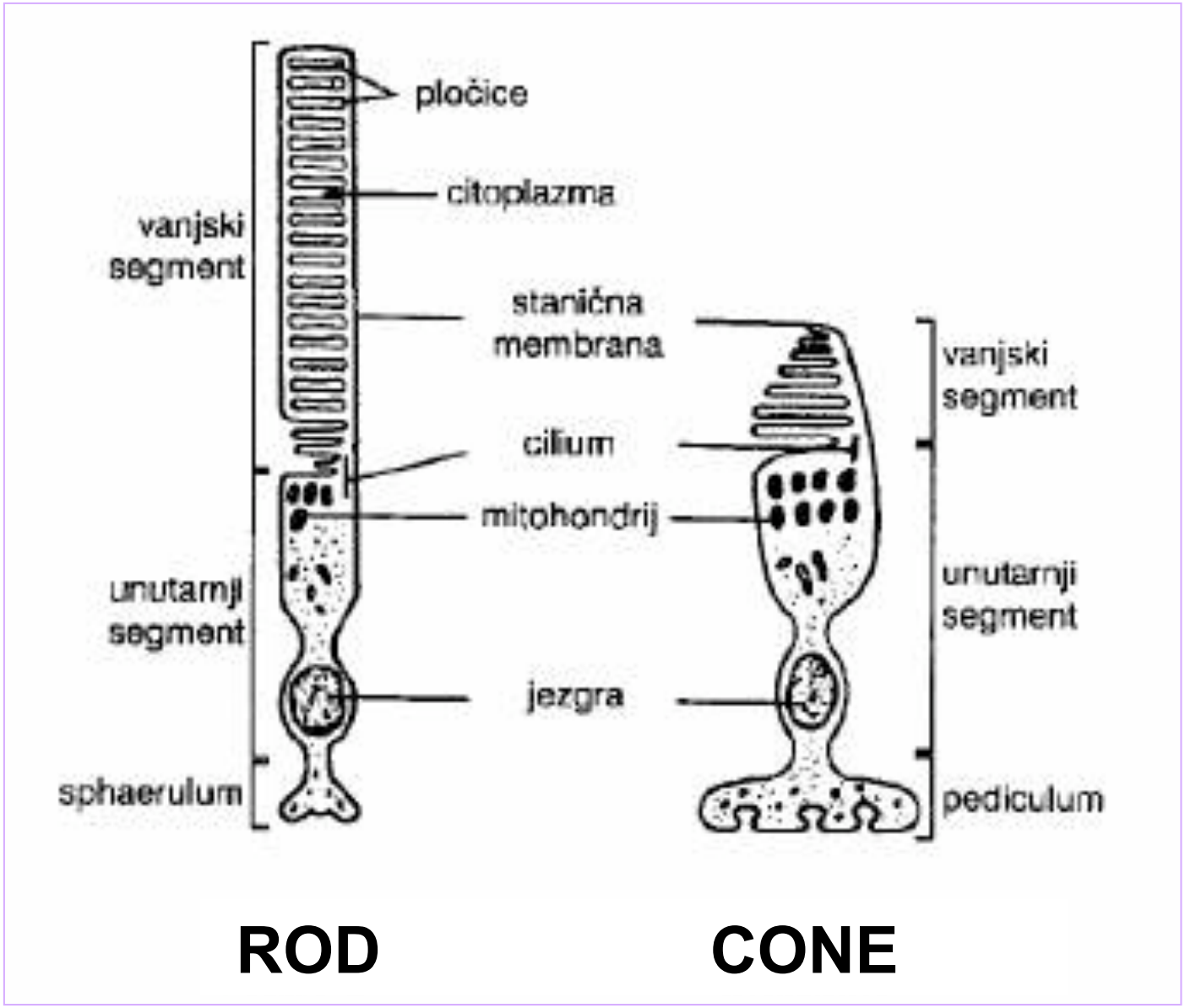


Slika 27-8. Dalekovidno oko (*hypermetropia*). Zrake s udaljenog predmeta sijeku se iza ravnine mrežnice (**A**). Tu refrakcijsku anomaliju ispravljamo naočalama što imaju bikonveksne (+) leće (**B**).

ČETIRI VRSTE OŠTRINE VIDA: DETEKCIJSKA OŠTRINA
LOKALIZACIJSKA (VERNIER) OŠTRINA
OŠTRINA RAZLUČIVANJA
OŠTRINA PREPOZNAVANJA



Photoreceptors



Photoreceptors

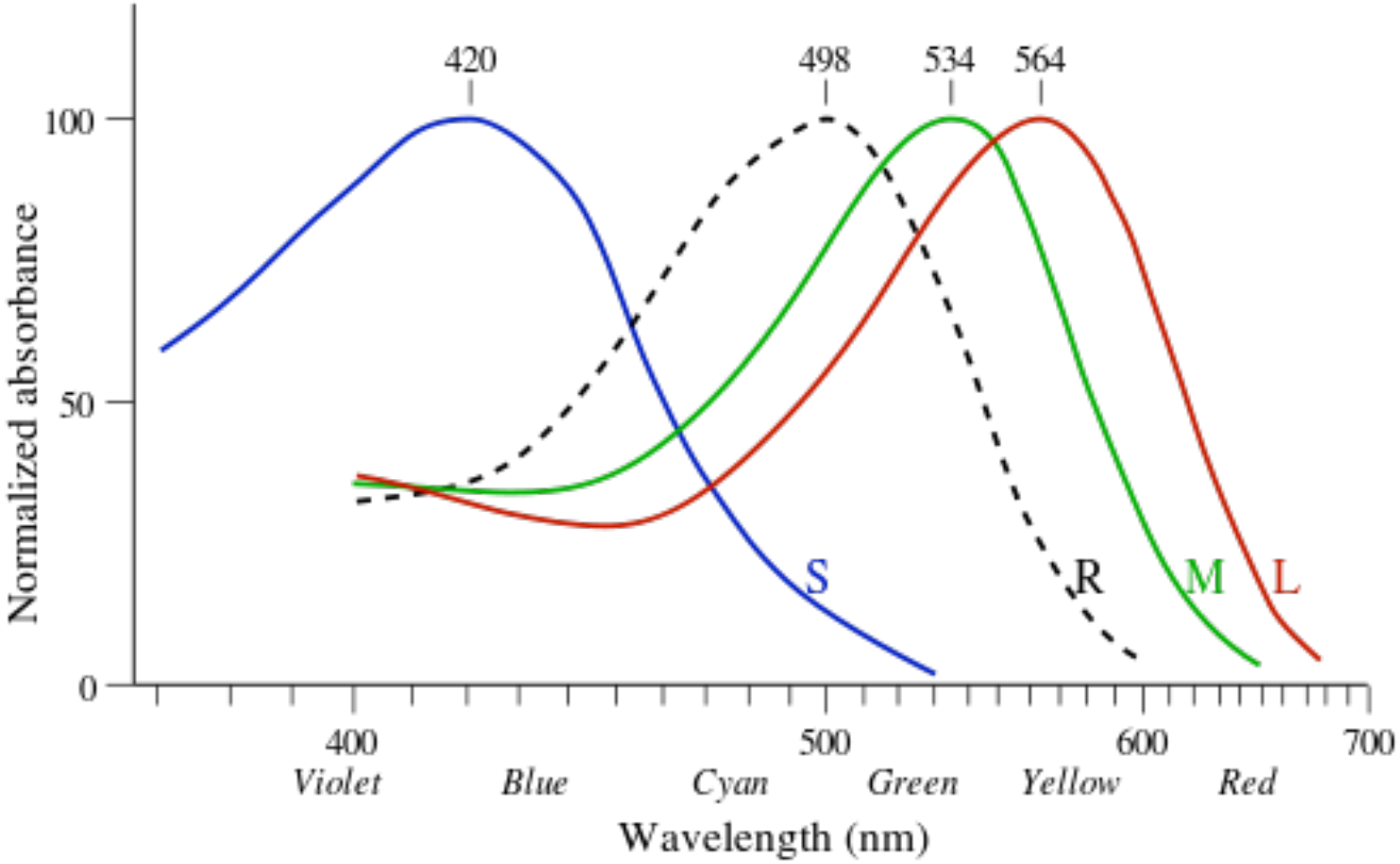
- The photoreceptor cells involved in vision are the rods and cones.
- These cells contain a chromophore (11-cis retinal, the aldehyde of Vitamin A1 and light-absorbing portion) bound to cell membrane protein, opsin.
- Rods deal with low light level and do not mediate color vision.
- Cones, on the other hand, can code the color of an image through comparison of the outputs of the three different types of cones.
- Each cone type responds best to certain wavelengths, or colors, of light because each type has a slightly different opsin.

Photoreceptors

- The three types of cones are L-cones, M-cones and S-cones that respond optimally to long wavelengths (reddish color), medium wavelengths (greenish color), and short wavelengths (bluish color) respectively.

- Humans have a trichromatic visual system consisting of three unique systems, rods, mid and long-wavelength sensitive (red and green) cones and short wavelength sensitive (blue) cones.

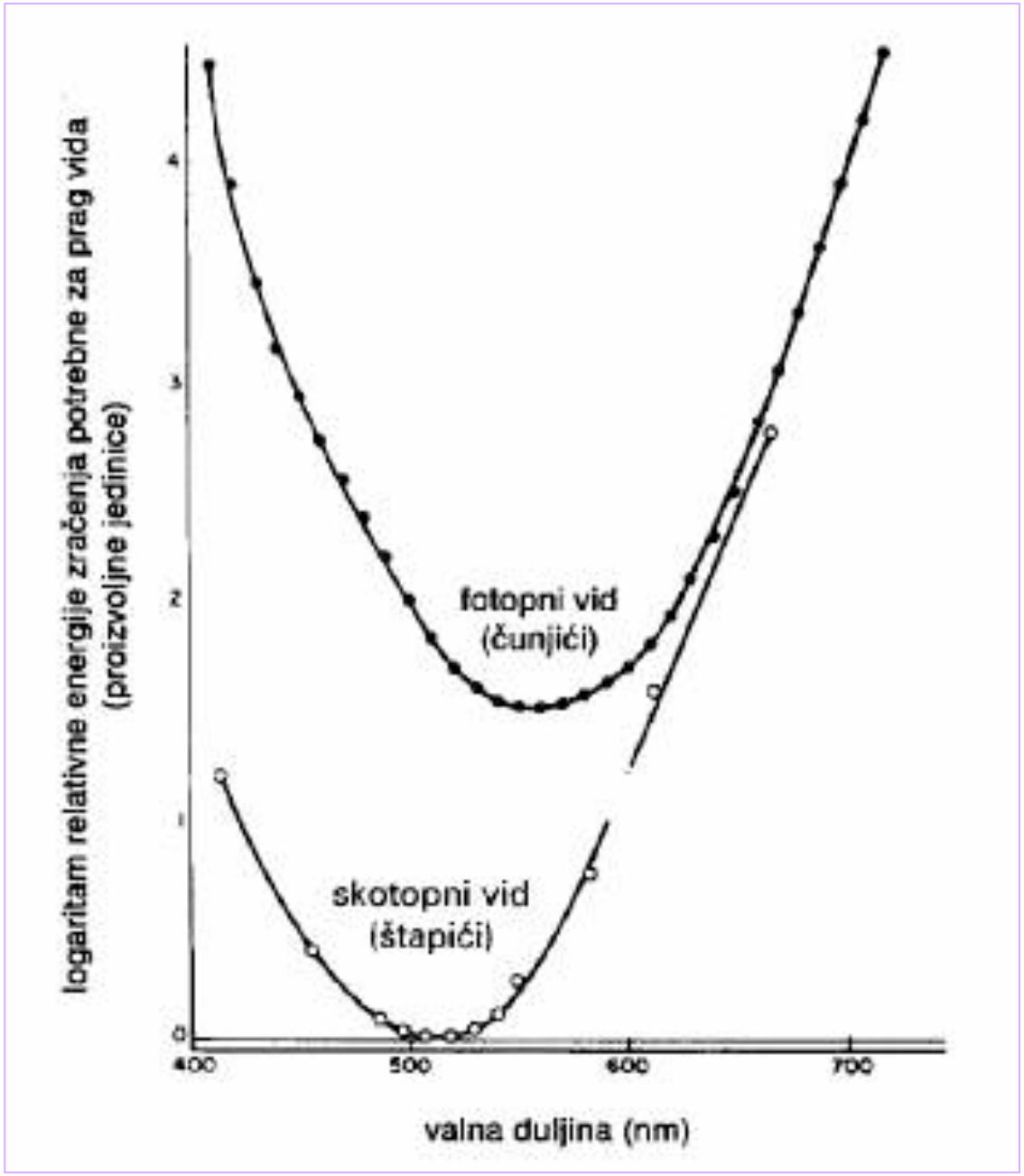
Spectral absorption curves of the short (S), medium (M) and long (L) wavelength pigments in human cone and rod (R) cells



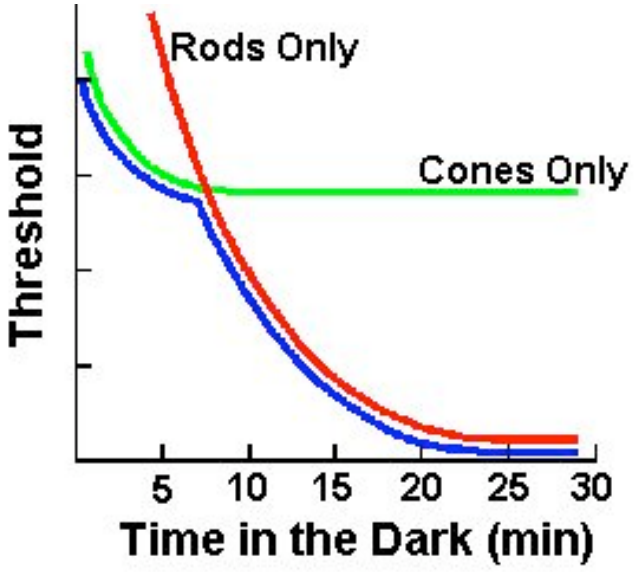
Comparison of human rod and cone cells, from Eric Kandel et al. in *Principles of Neural Science*

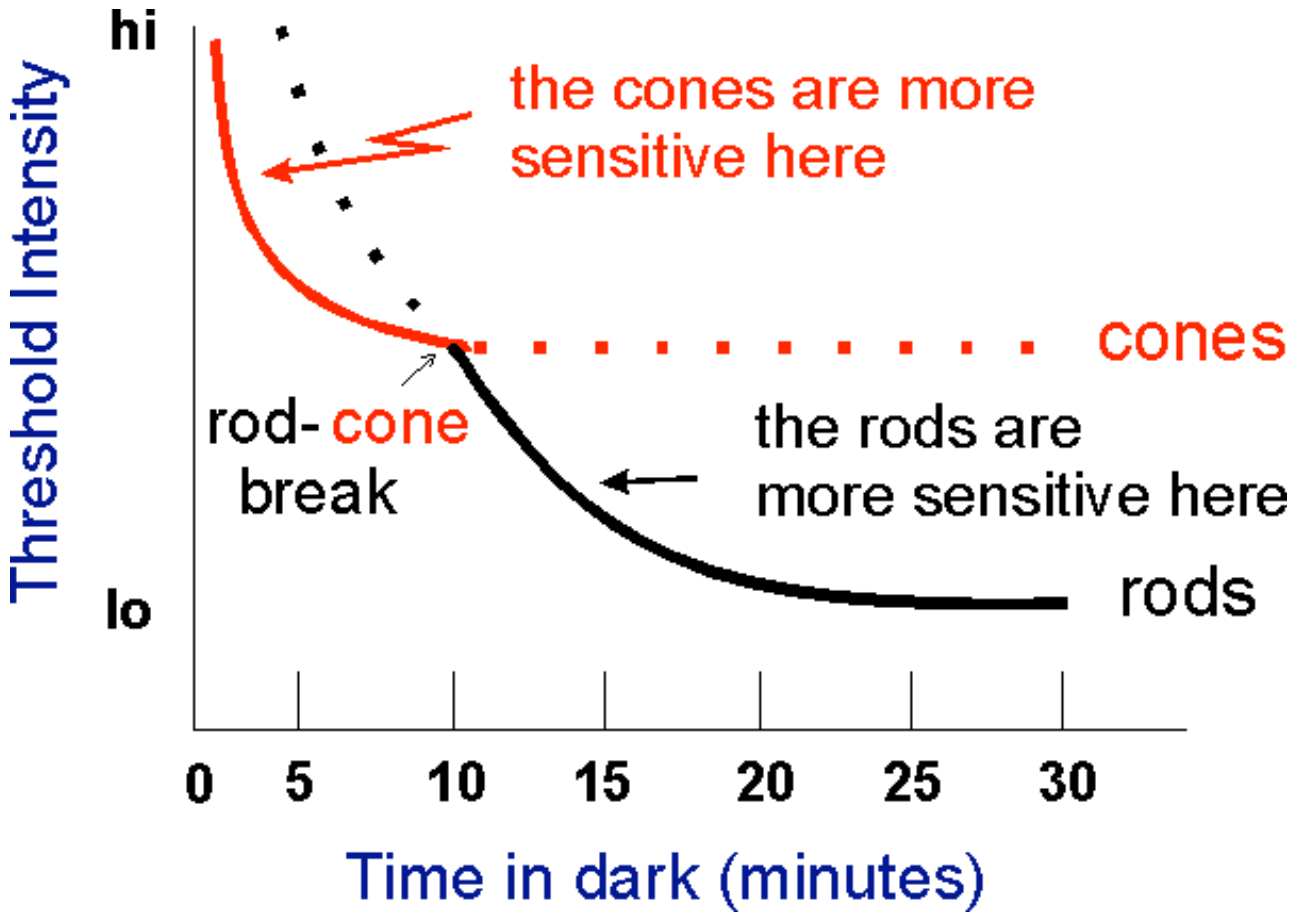
Rods	Cones
Used for scotopic vision (vision under low light conditions)	Used for photopic vision (vision under high light conditions)
Very light sensitive; sensitive to scattered light	Not very light sensitive; sensitive to only direct light
Loss causes night blindness	Loss causes legal blindness
Low visual acuity	High visual acuity; better spatial resolution
Not present in fovea	Concentrated in fovea
Slow response to light, stimuli added over time	Fast response to light, can perceive more rapid changes in stimuli
Have more pigment than cones, so can detect lower light levels	Have less pigment than rods, require more light to detect images
Stacks of membrane-enclosed disks are unattached to cell membrane directly	Disks are attached to outer membrane
About 120 million rods distributed around the retina	About 6 million cones distributed in each retina
One type of photosensitive pigment	Three types of photosensitive pigment in humans
Confer achromatic vision	Confer color vision

Photopic and scotopic vision



Dark Adaptation

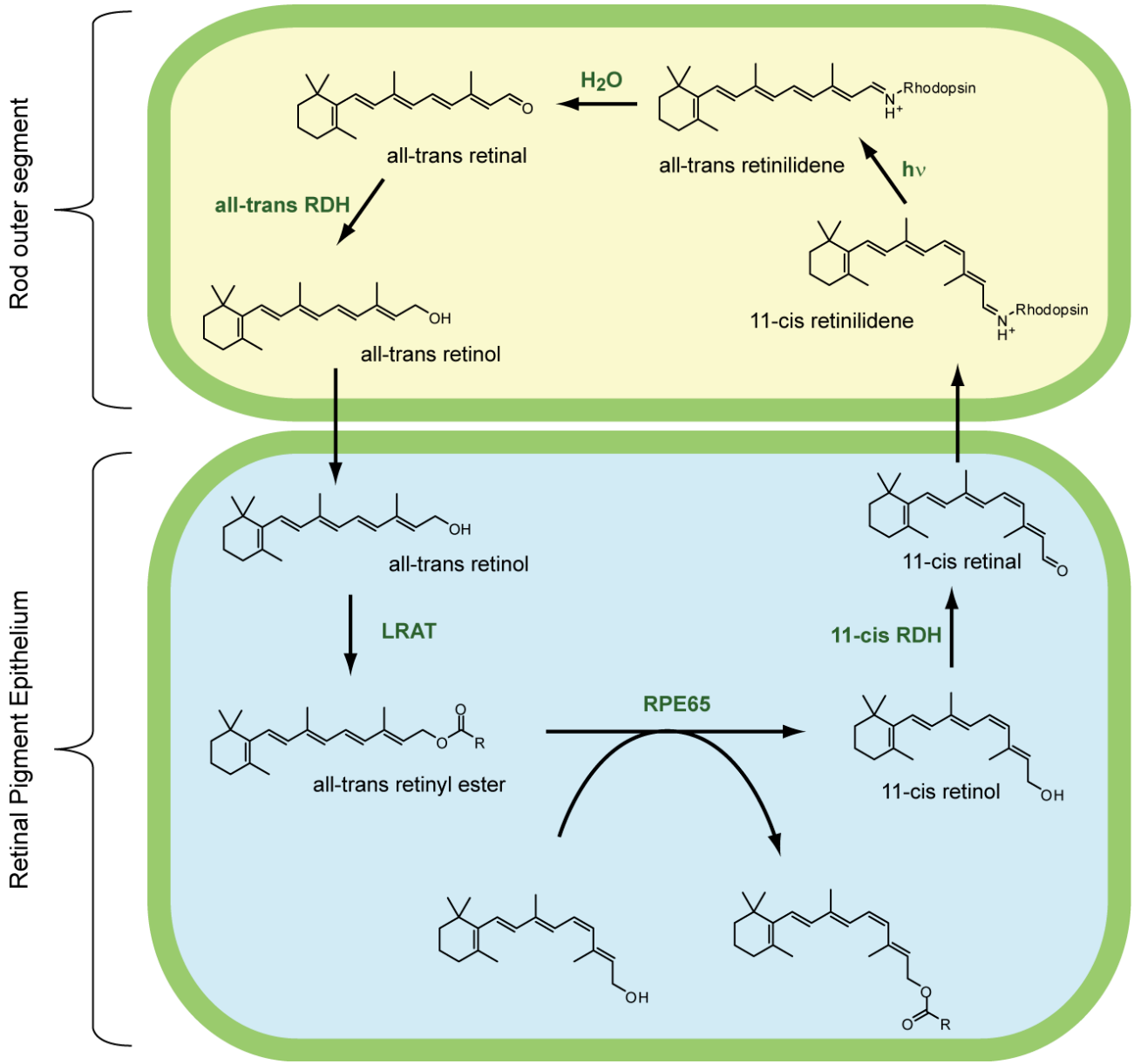




Visual phototransduction

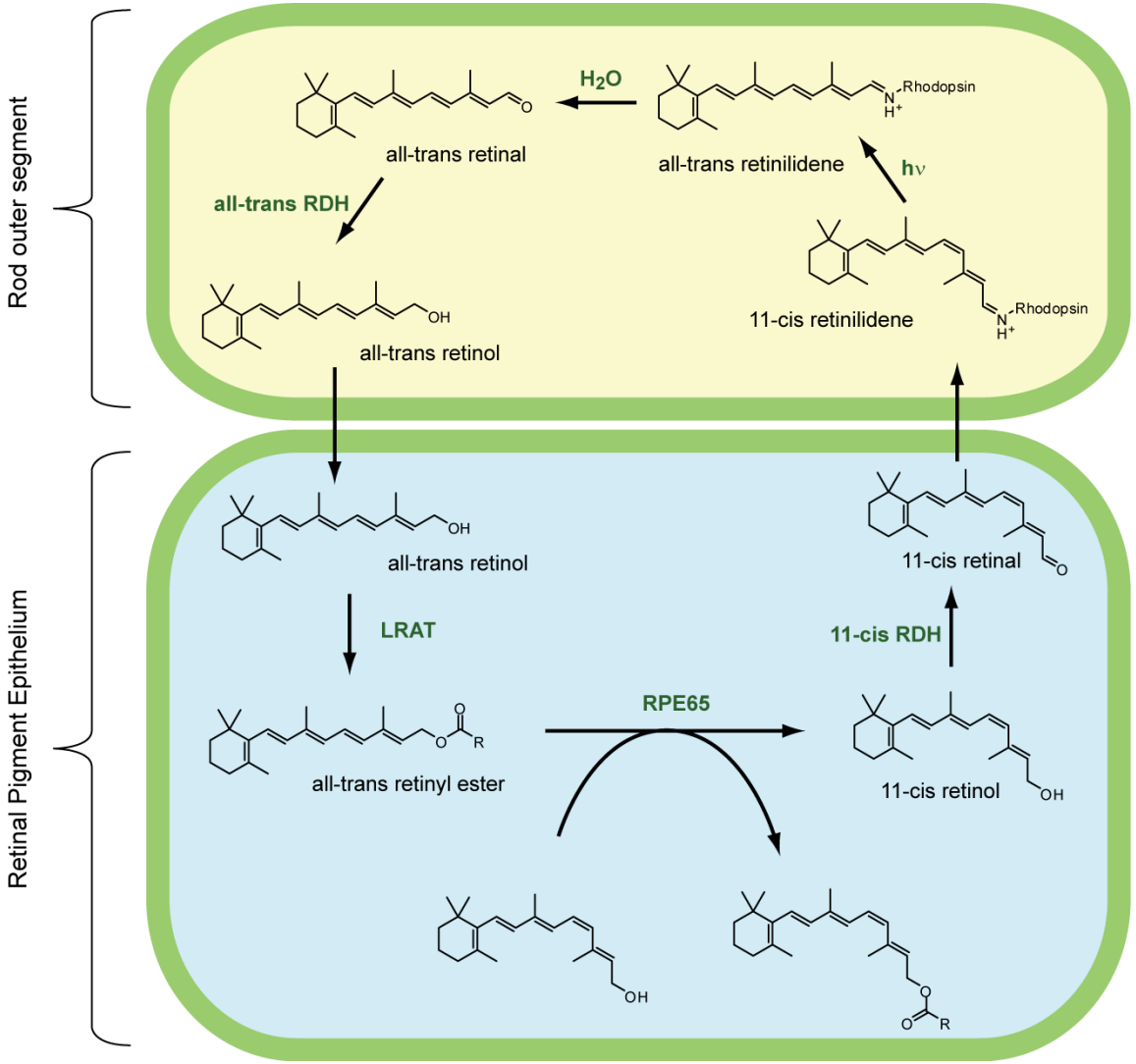
- It is a process by which light is converted into electrical signals in the rod cells, cone cells and photosensitive ganglion cells of the retina of the eye.
- The visual cycle is the biological conversion of photon into an electrical signal in the retina. This process occurs via G-protein coupled receptors called opsins

Visual phototransduction



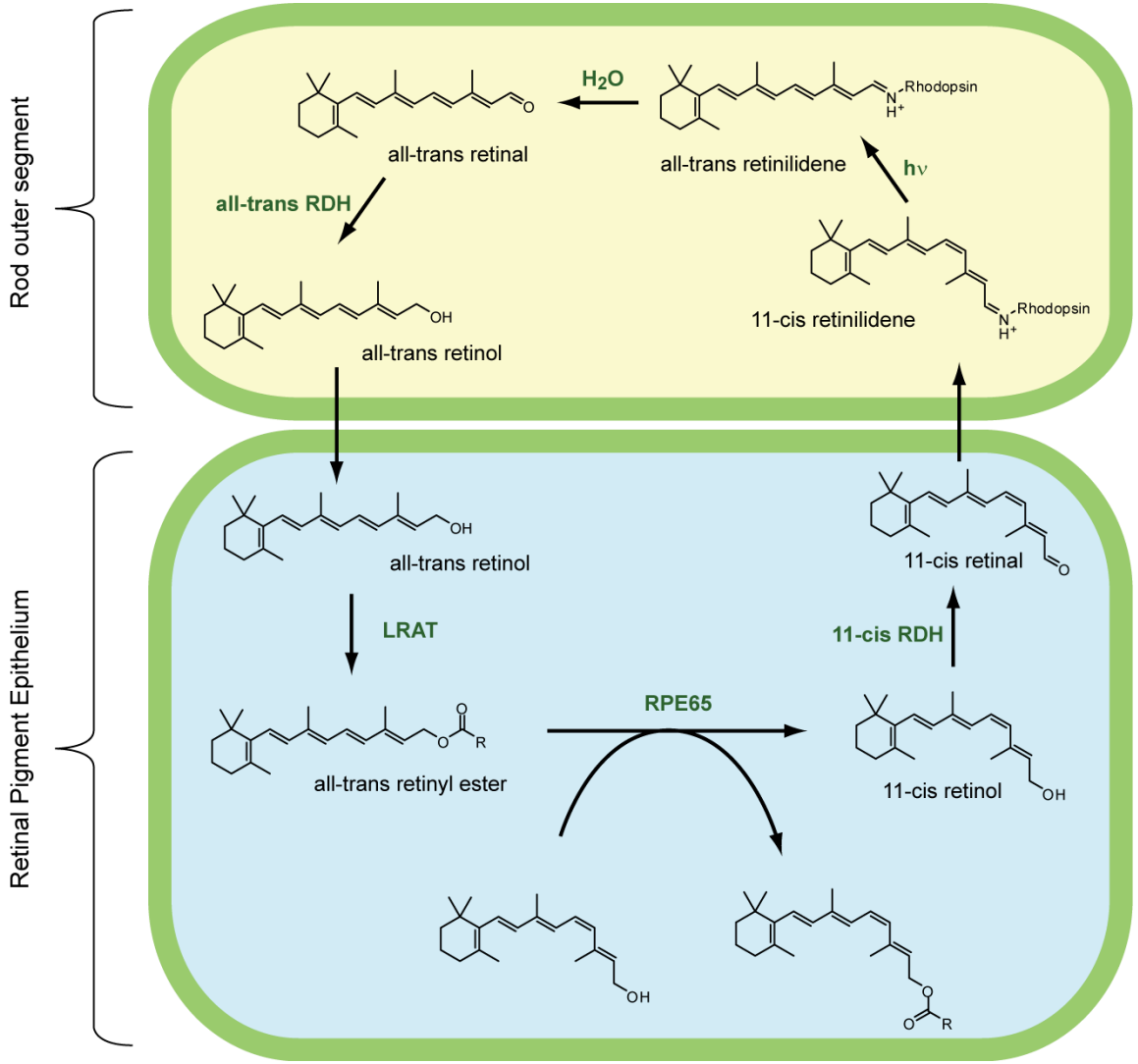
Visual phototransduction

- Opsins contain the chromophore 11-cis retinal. 11-cis retinal is covalently linked to the opsin receptor via Schiff base forming retinylidene protein. When struck by photon, 11-cis retinal undergoes photoisomerization to all-trans retinal.



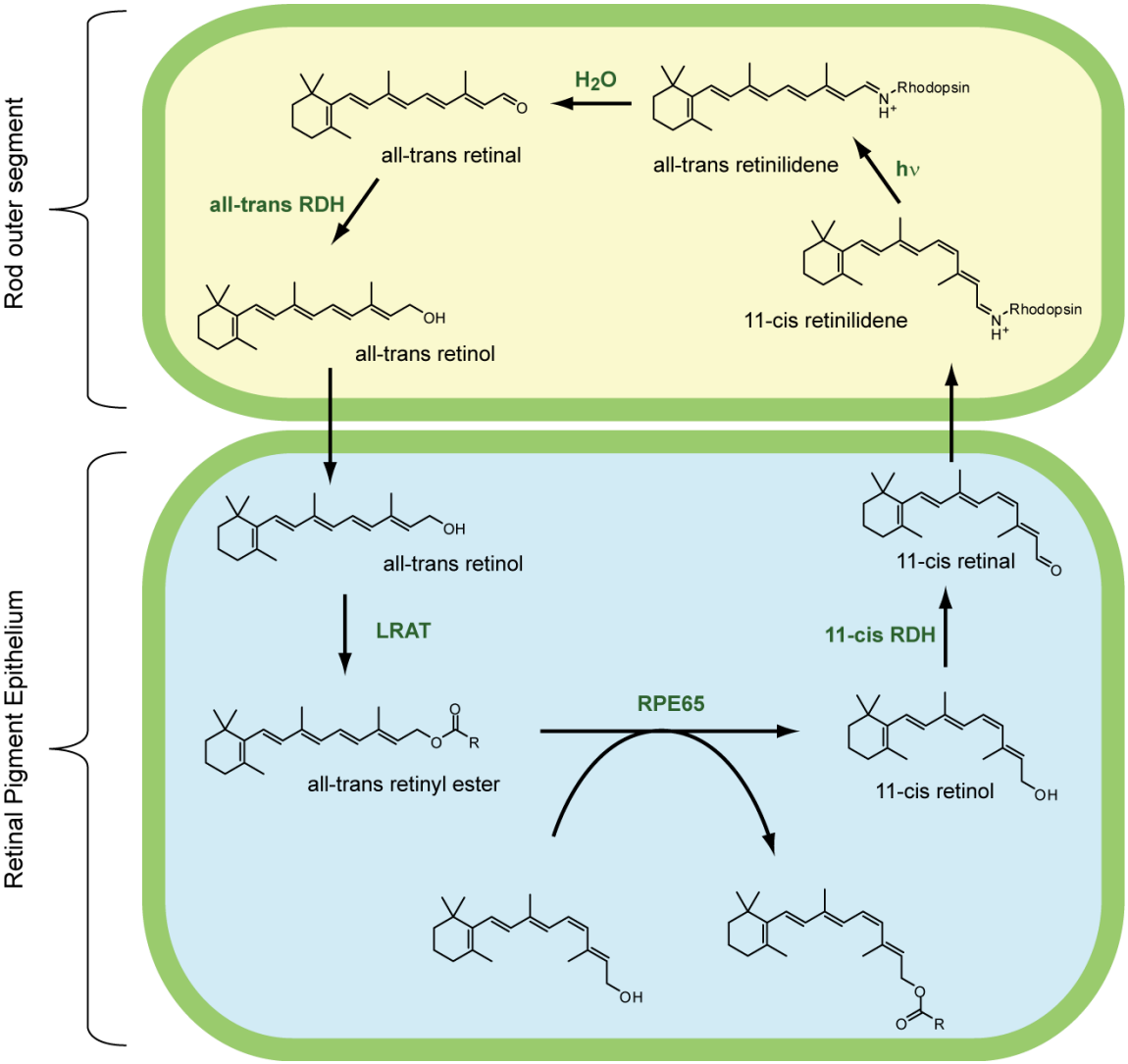
Visual phototransduction

- All-trans retinal changes the conformation of the opsin GPCR leading to signal transduction cascades which causes closure of cyclic GMP-gated cation channel, and hyperpolarization of the photoreceptor cell.



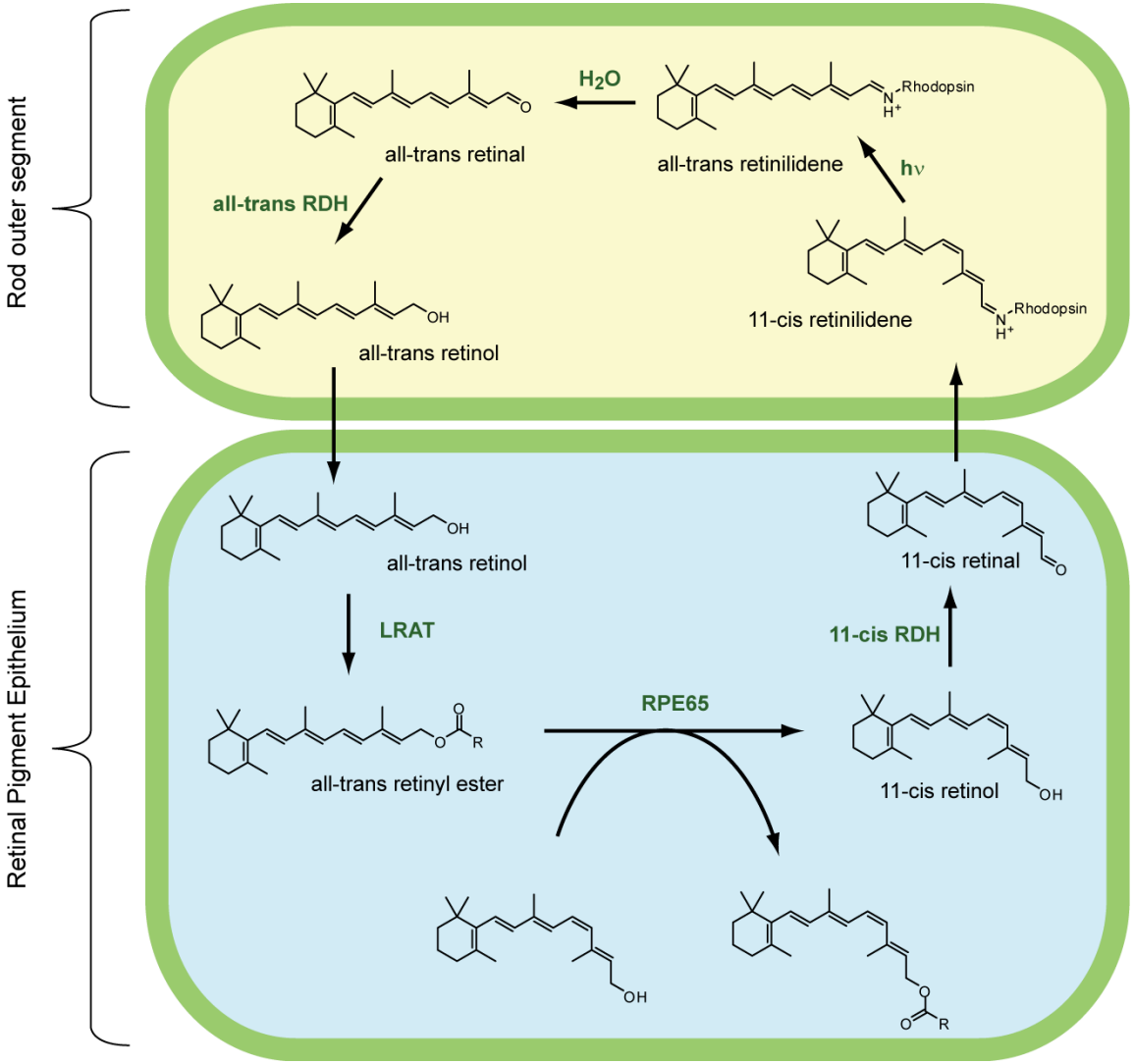
Visual phototransduction

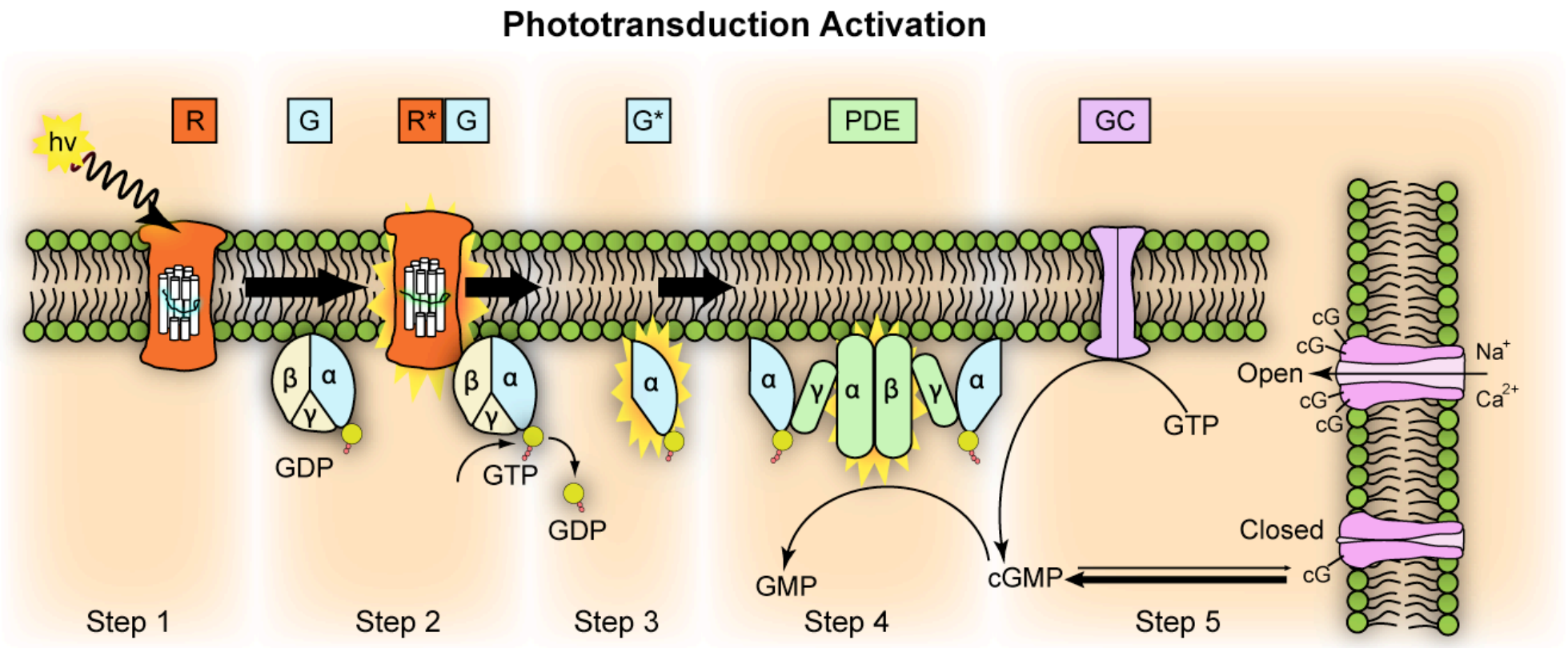
- Following isomerization and release from the opsin protein, all-trans retinal is reduced to all-trans retinol and travels back to the retinal pigment epithelium to be "recharged". It is first esterified by lecithin-retinol acyltransferase (LRAT) and then converted to 11-cis retinol by the isomerohydrolase RPE65.



Visual phototransduction

- The isomerase activity of RPE65 has been shown; it is still uncertain whether it also acts as hydrolase. Finally, it is oxidized to 11-cis retinal before traveling back to the rod outer segment where it is again conjugated to an opsin to form new, functional visual pigment (rhodopsin).





Representation of molecular steps in photoactivation (modified from Leskov et al., 2000). Depicted is an outer membrane disk in a rod. Step 1: Incident photon (hv) is absorbed and activates a rhodopsin by conformational change in the disk membrane to R*. Step 2: Next, R* makes repeated contacts with transducin molecules, catalyzing its activation to G* by the release of bound GDP in exchange for cytoplasmic GTP. The α and γ subunits Step 3: G* binds inhibitory γ subunits of the phosphodiesterase (PDE) activating its α and β subunits. Step 4: Activated PDE hydrolyzes cGMP. Step 5: Guanylyl cyclase (GC) synthesizes cGMP, the second messenger in the phototransduction cascade. Reduced levels of cytosolic cGMP cause cyclic nucleotide gated channels to close preventing further influx of Na+ and Ca2+.

In the dark

- Photoreceptor cells are strange cells because they are depolarized in the dark, meaning that light hyperpolarizes and switches off these cells, and it is this 'switching off' that activates the next cell and sends an excitatory signal down the neural pathway.
- In the dark, cGMP levels are high and keep cGMP-gated sodium channels open allowing a steady inward current, called the dark current. This dark current keeps the cell depolarized at about -40 mV.

In the dark

- The depolarization of the cell membrane opens voltage-gated calcium channels.
- An increased intracellular concentration of Ca^{2+} causes vesicles containing glutamate to releasing the neurotransmitter into the synaptic cleft.

In the dark

In the cone pathway glutamate:

- Hyperpolarizes ON-center bipolar cells. Glutamate that is released from the photoreceptors in the dark binds to metabotropic glutamate receptors (mGluR6), which, through a G-protein coupling mechanism, causes non-specific cation channels in the cells to close, thus hyperpolarizing the bipolar cell.
- Depolarizes OFF-center bipolar cells. Binding of glutamate to ionotropic glutamate receptors results in an inward cation current that depolarizes the bipolar cell.

In the light

1. A light photon interacts with the retinal in a photoreceptor cell. The retinal undergoes isomerisation, changing from the 11-cis *to* all-trans *con*figuration.
2. Retinal no longer fits into the opsin binding site.
3. Opsin therefore undergoes a conformational change to metarhodopsin II.
4. Metarhodopsin II is unstable and splits, yielding opsin and all-trans retinal.
5. T*he op*sin activates the regulatory protein transducin. This causes transducin to dissociate from its bound GDP, and bind GTP, then the alpha subunit of transducin dissociates from the beta and gamma subunits, with the GTP still bound to the alpha subunit.
6. The alpha subunit-GTP complex activates phosphodiesterase.

In the light

1. Phosphodiesterase breaks down cGMP to 5'-GMP. This lowers the concentration of cGMP and therefore the sodium channels close.
2. Closure of the sodium channels causes hyperpolarization of the cell due to the ongoing potassium current.
3. Hyperpolarization of the cell causes voltage-gated calcium channels to close.
4. As the calcium level in the photoreceptor cell drops, the amount of the neurotransmitter glutamate that is released by the cell also drops. This is because calcium is required for the glutamate-containing vesicles to fuse with cell membrane and release their contents.
5. A decrease in the amount of glutamate released by the photoreceptors causes depolarization of On center bipolar cells (rod and cone On bipolar cells) and hyperpolarization of cone off-center bipolar cells.

Deactivation of the phototransduction cascade

- GTPase Activating Protein (GAP) interacts with the alpha subunit of transducin, and causes it to hydrolyse its bound GTP to GDP, and thus halts the action of phosphodiesterase, stopping the transformation of cGMP to GMP.
- Guanylate Cyclase Activating Protein (GCAP) is a calcium binding protein, and as the calcium levels in the cell have decreased, GCAP dissociates from its bound calcium ions, and interacts with Guanylate Cyclase, activating it. Guanylate Cyclase then proceeds to transform GTP to cGMP, replenishing the cell's cGMP levels and thus reopening the sodium channels that were closed during phototransduction.

Deactivation of the phototransduction cascade

- Finally, Metarhodopsin II is deactivated.
- Recoverin, another calcium binding protein, is normally bound to Rhodopsin Kinase when calcium is present.
- When the calcium levels fall during phototransduction, the calcium dissociates from recoverin, and rhodopsin kinase is released, when it proceeds to phosphorylate metarhodopsin II, which decreases its affinity for transducin.
- Finally, arrestin, another protein, binds the phosphorylated metarhodopsin II, completely deactivating it.

Deactivation of the phototransduction cascade

- Thus, finally, phototransduction is deactivated, and the dark current and glutamate release is restored.
- It is this pathway, where Metarhodopsin II is phosphorylated and bound to arrestin and thus deactivated, which is thought to be responsible for the S2 component of dark adaptation.
- The S2 component represents a linear section of the dark adaptation function present at the beginning of dark adaptation for all bleaching intensities.

Deactivation of the phototransduction cascade

- All-*trans* retinal is transported to the pigment epithelial cells to be reduced to all-*trans* retinol, the precursor to 11-*cis* retinal.
- This is then transported back to the rods. All-*trans* retinal cannot be synthesised by humans and must be supplied by vitamin A in the diet.
- Deficiency of all-*trans* retinal can lead to night blindness. This is part of the bleach and recycle process of retinoids in the photoreceptors and retinal pigment epithelium.