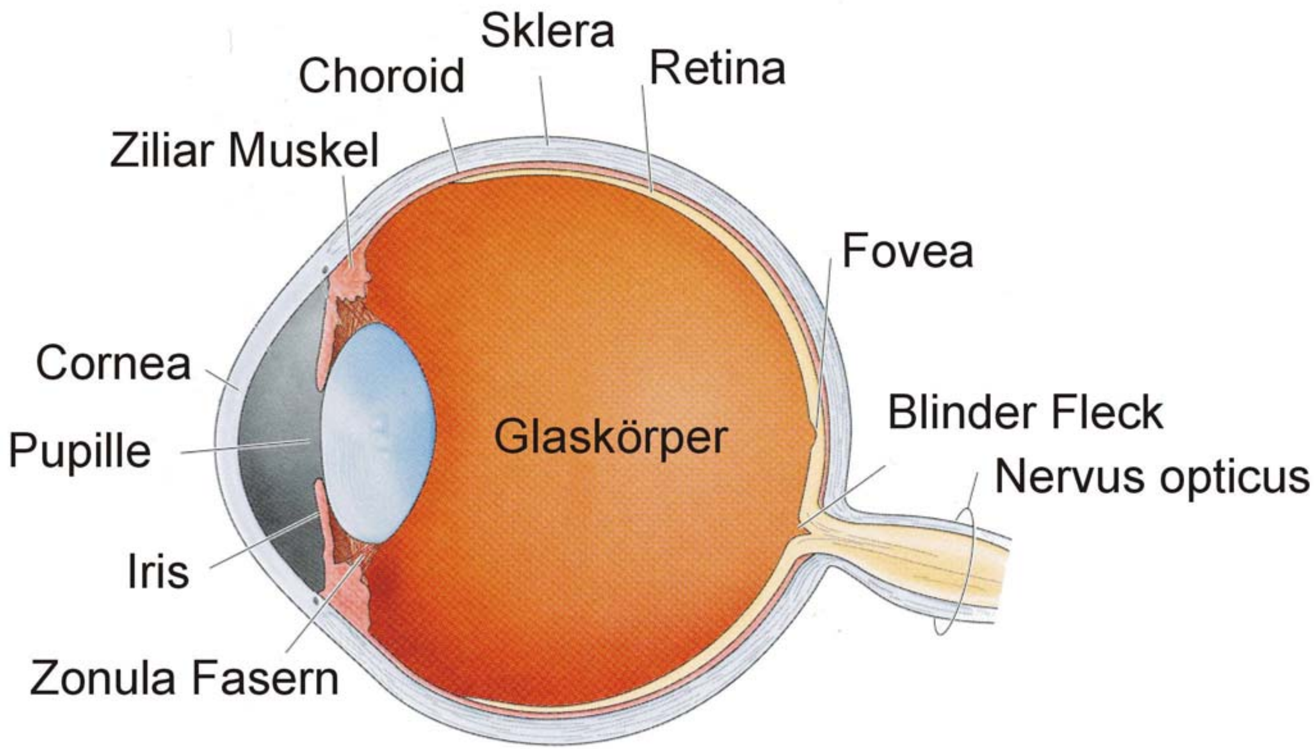
Vision -

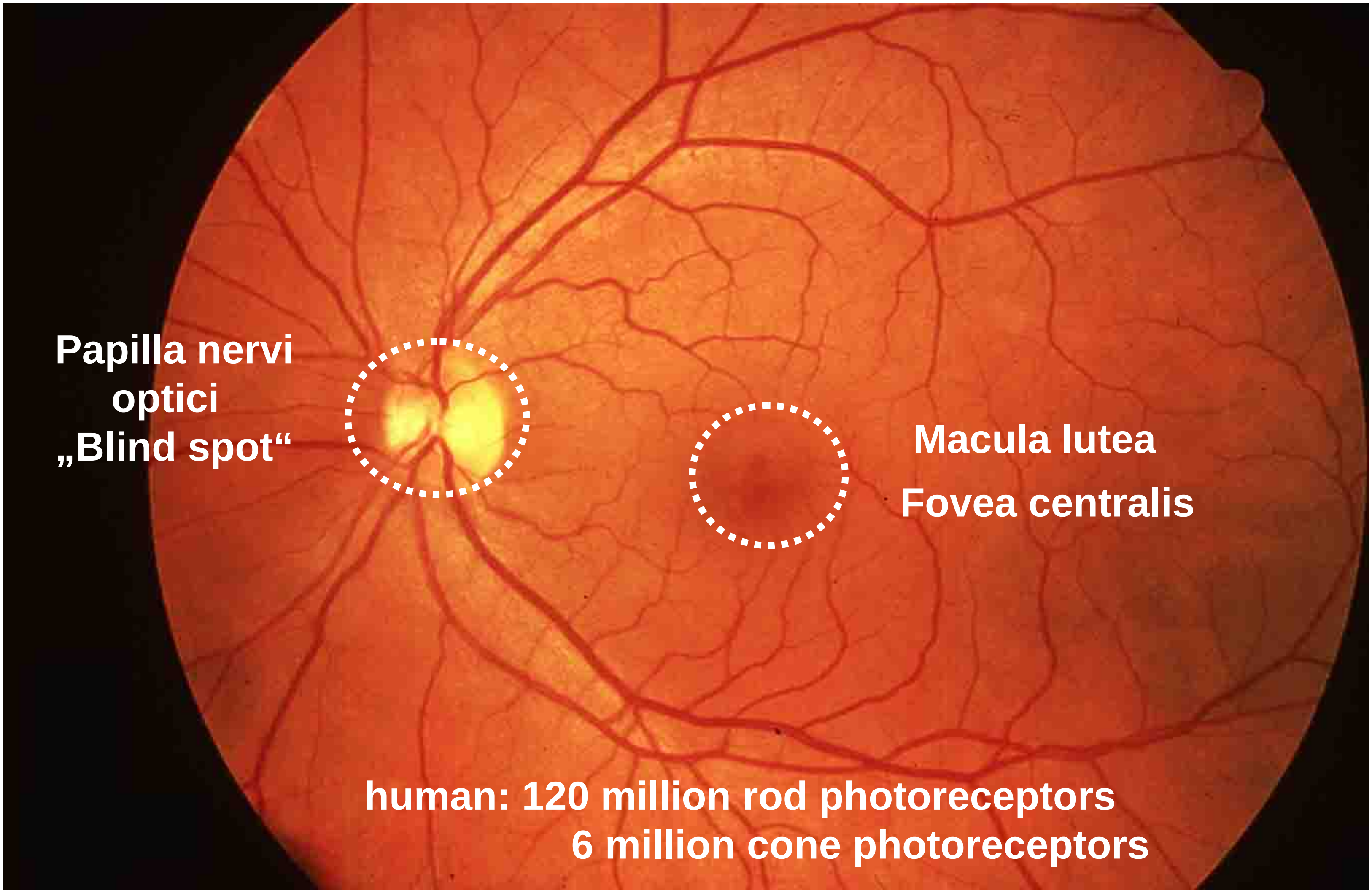
an example of a

GPCR-regulated signalling cascade

Morphology of the vertebrate eye



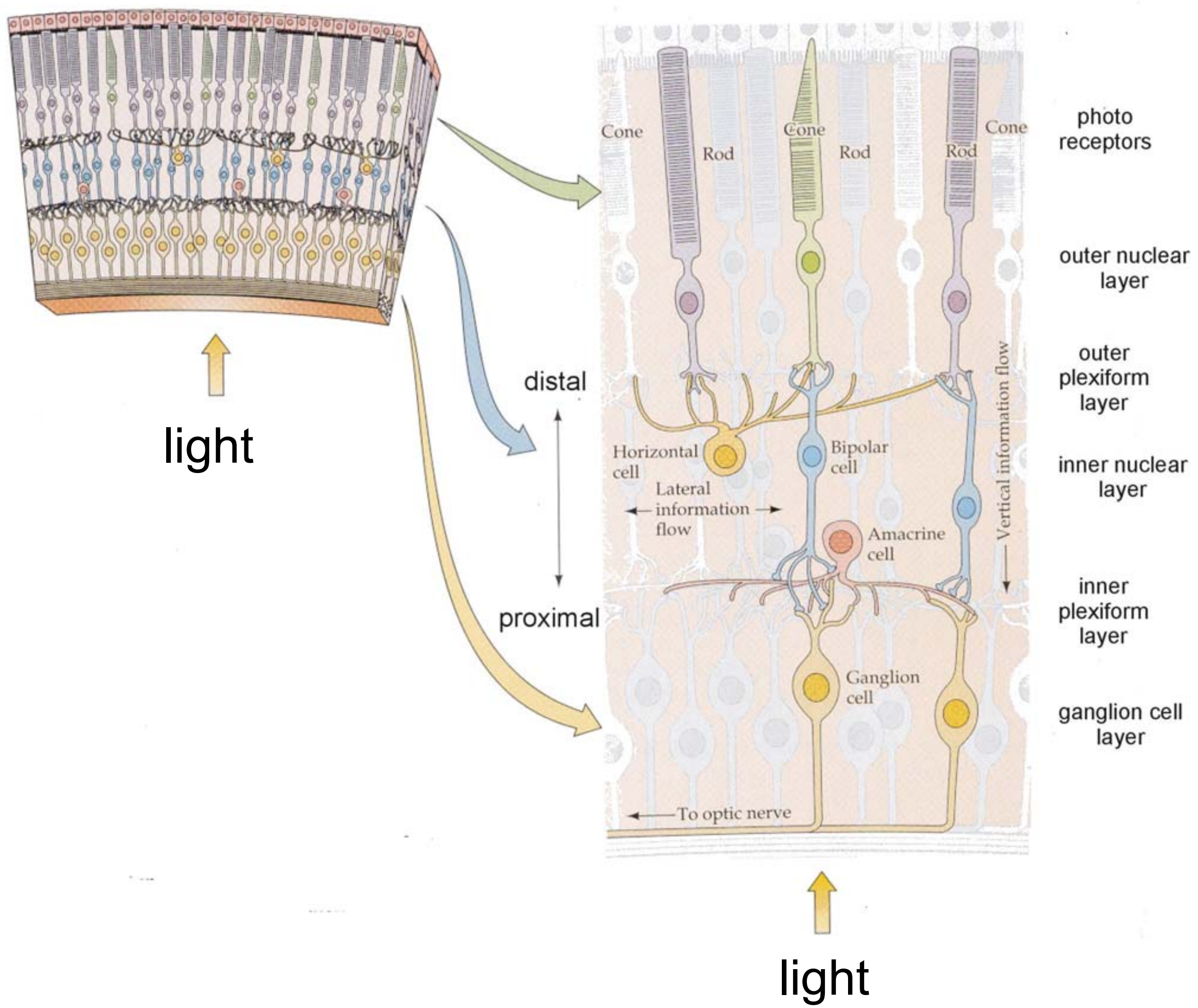
Signal transduction



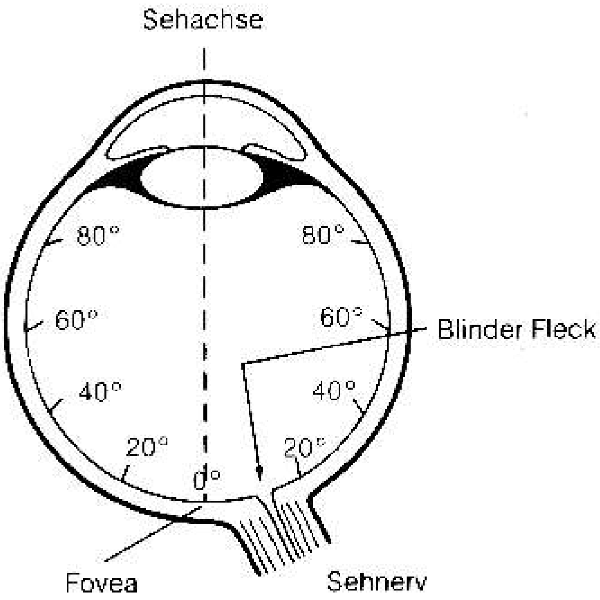
http://www.penneye.com/html/retina_vitreous.html

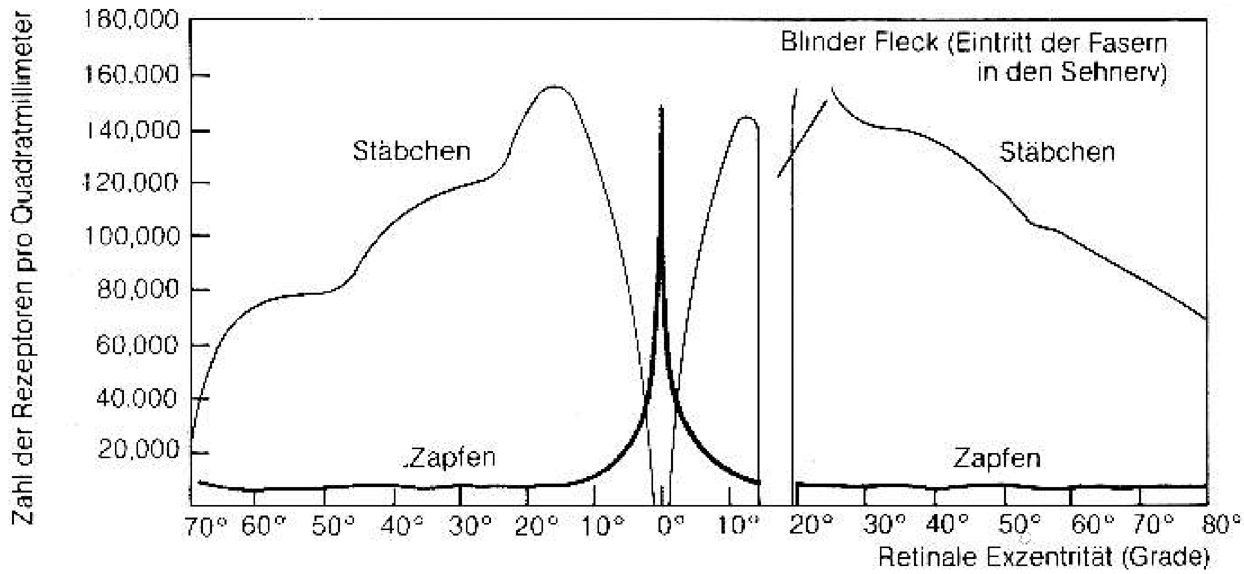
Kepler

Signal transduction



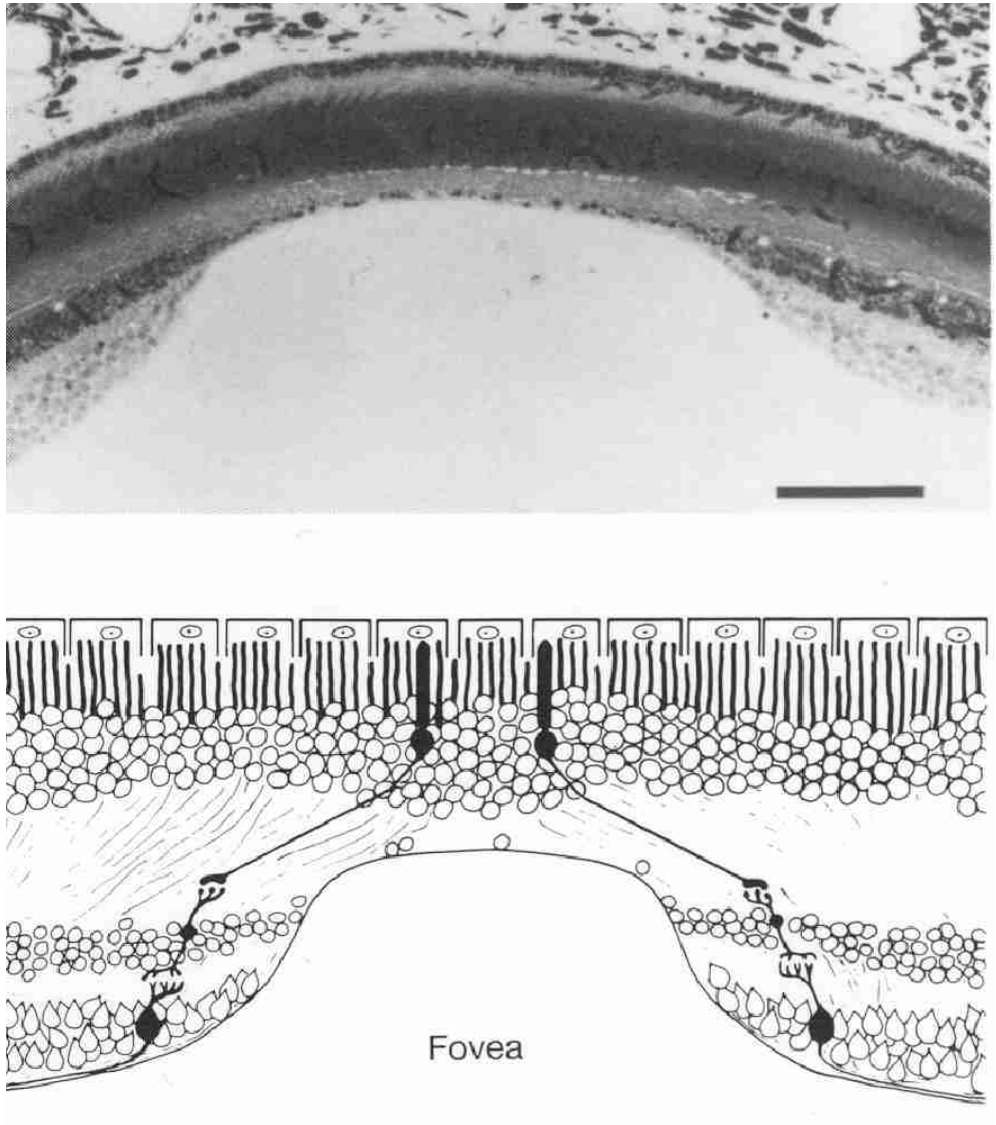
Signal transduction

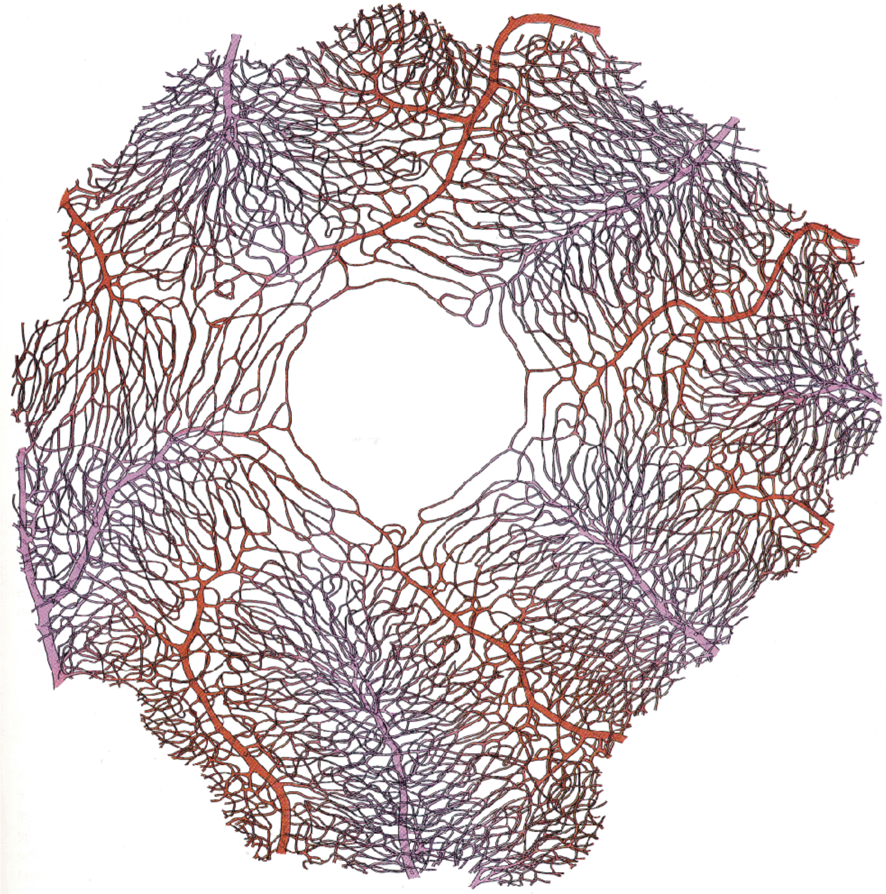




Photoreceptor cells are not evenly distributed!

Signal transduction



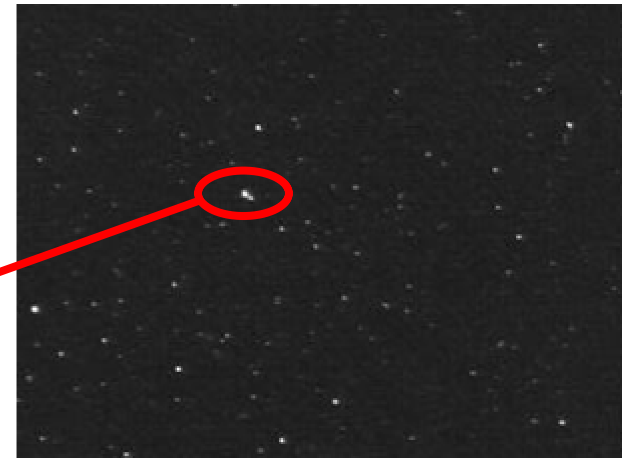


Fovea is free of blood vessels

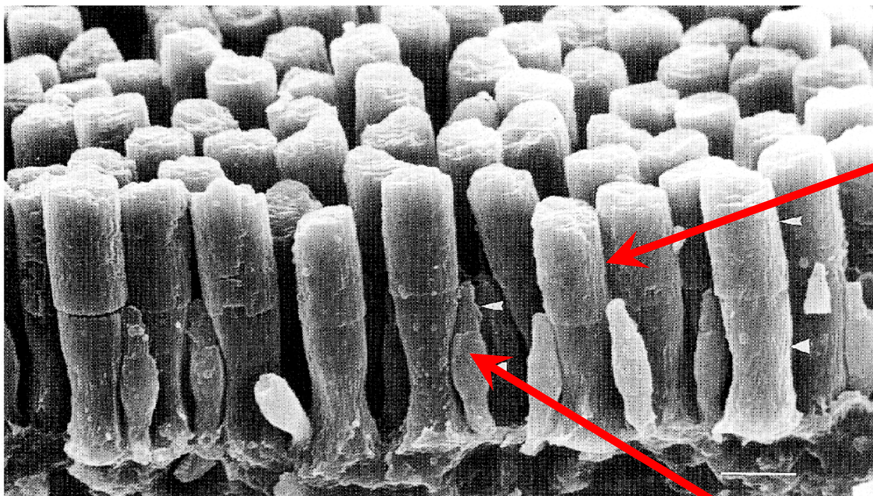
Rodieck, R.W. (1998) The first steps in seeing. Sinauer Ass.

Signal transduction

rods



< 10 to approx. 500 photons / s

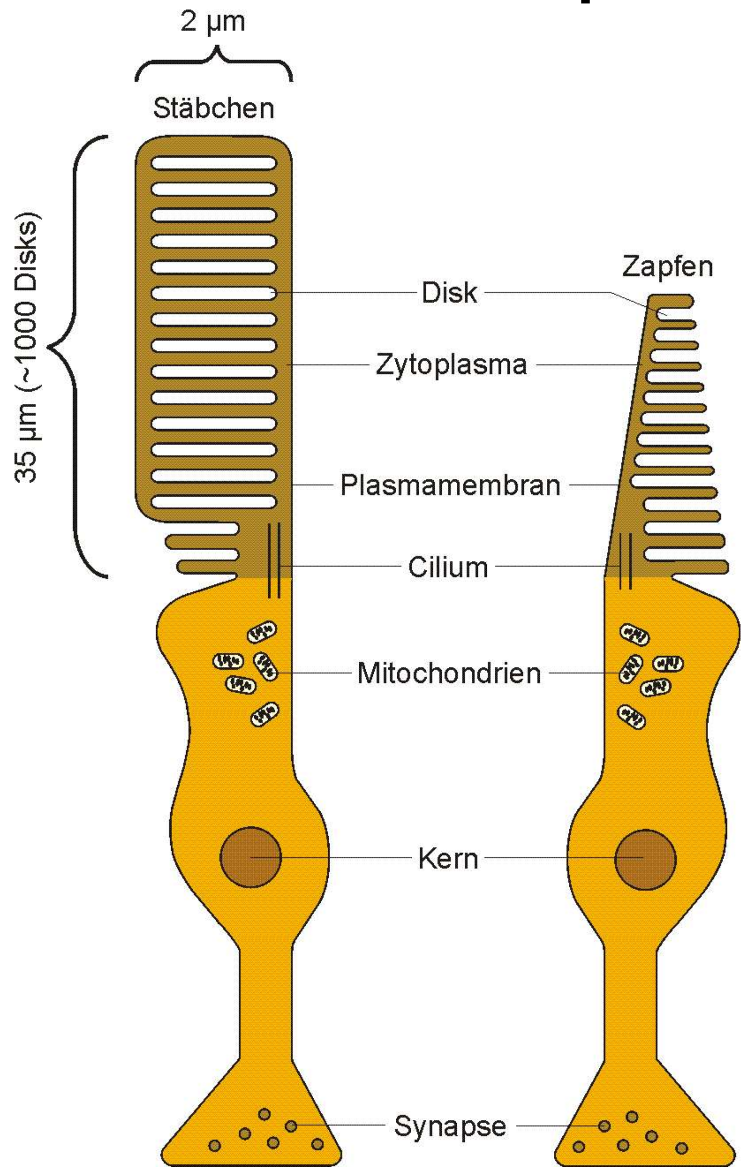


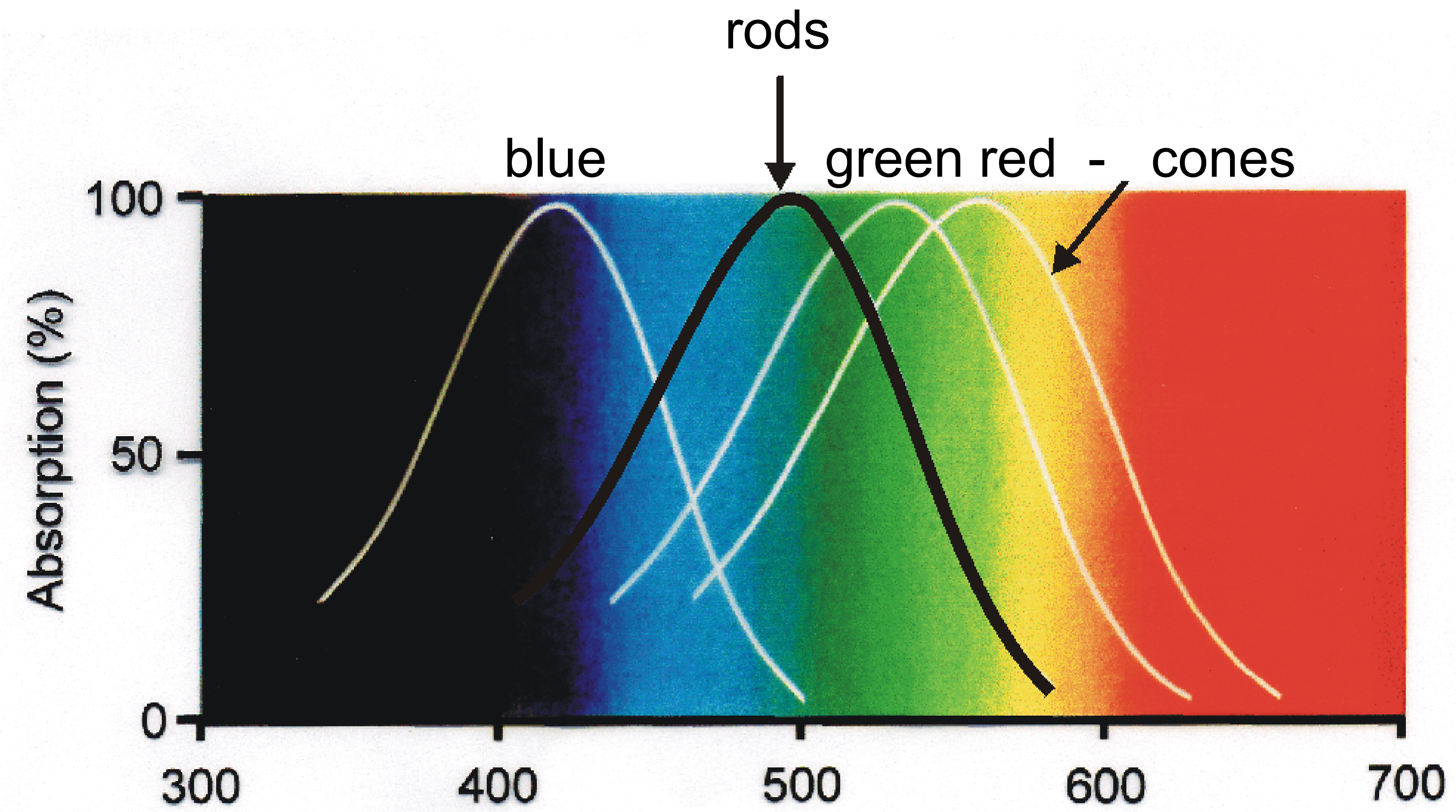
cones

**approx.
30 to 1.000.000
photons / s**

Wehner, R. & Gehring, W (1995) Zoologie. Thieme Verlag, Stuttgart

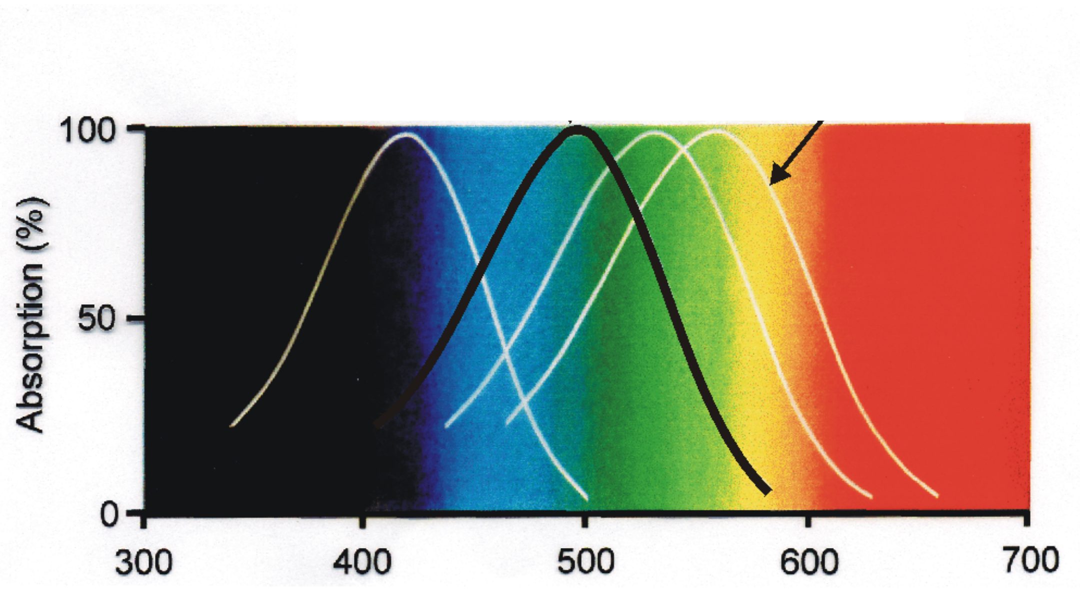
Photoreceptors





Absorption spectra of visual pigments

Signal transduction



photopigments

rods: rhodopsin

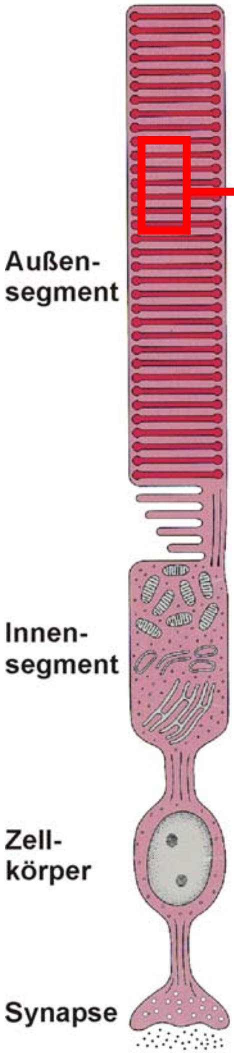
cones: blue, green, red opsin

Light response

The outer segment of a photoreceptor cell contains all components to

- absorp light,
- amplify the signal
- generate an electrical cellular response.

Signal transduction

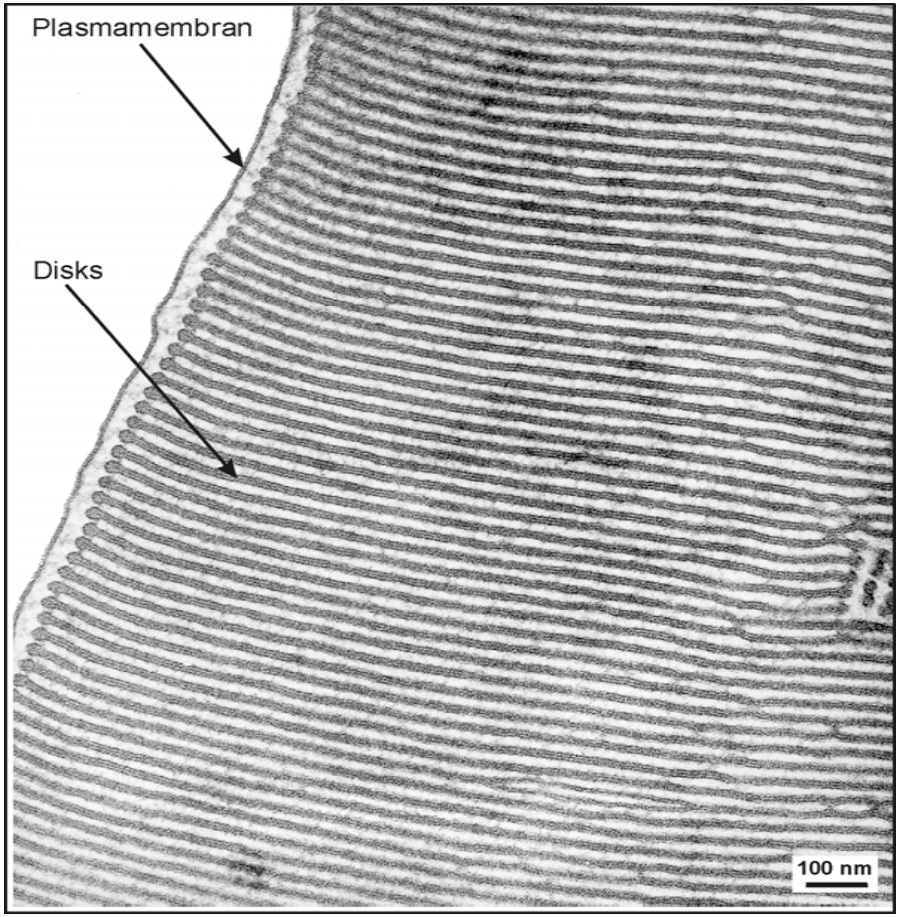


800 disks / outer segment

30.000 rhodopsins / µm^2

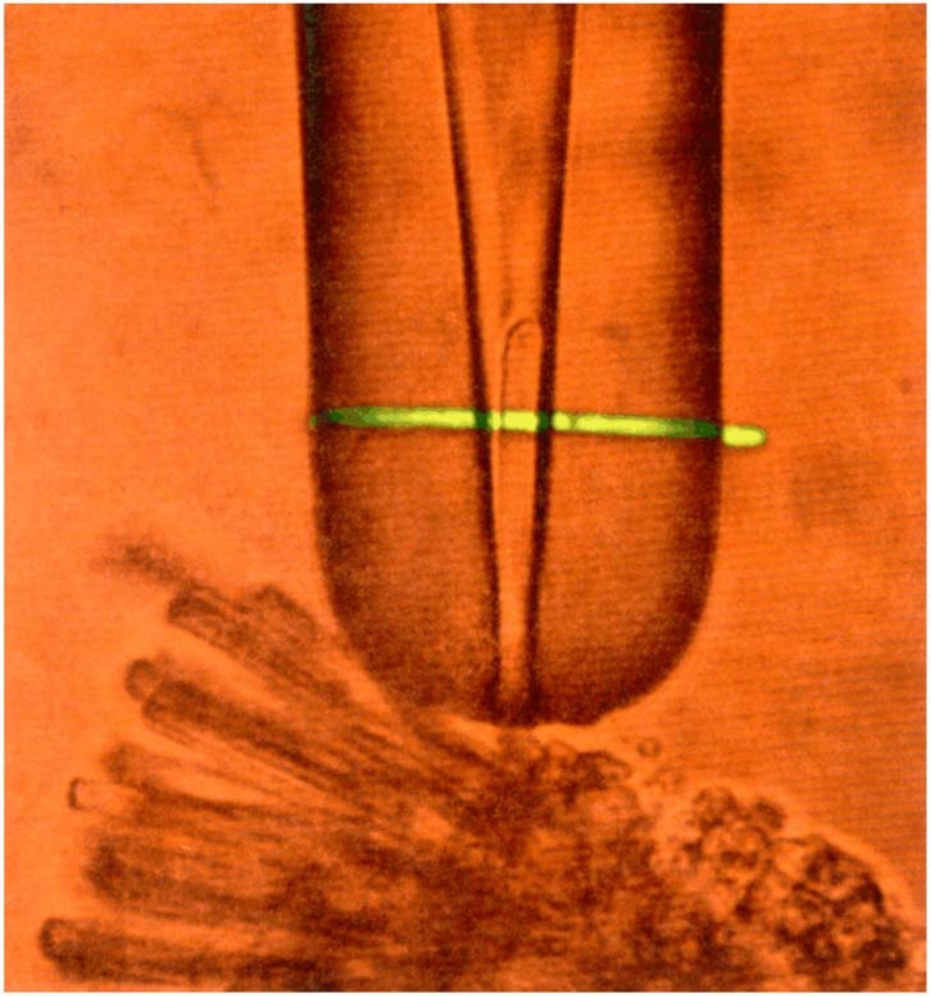
Total no. 50 million rhodopsin molecules

Maximal reactivity when 0.001% of rhodopsins have absorbed light

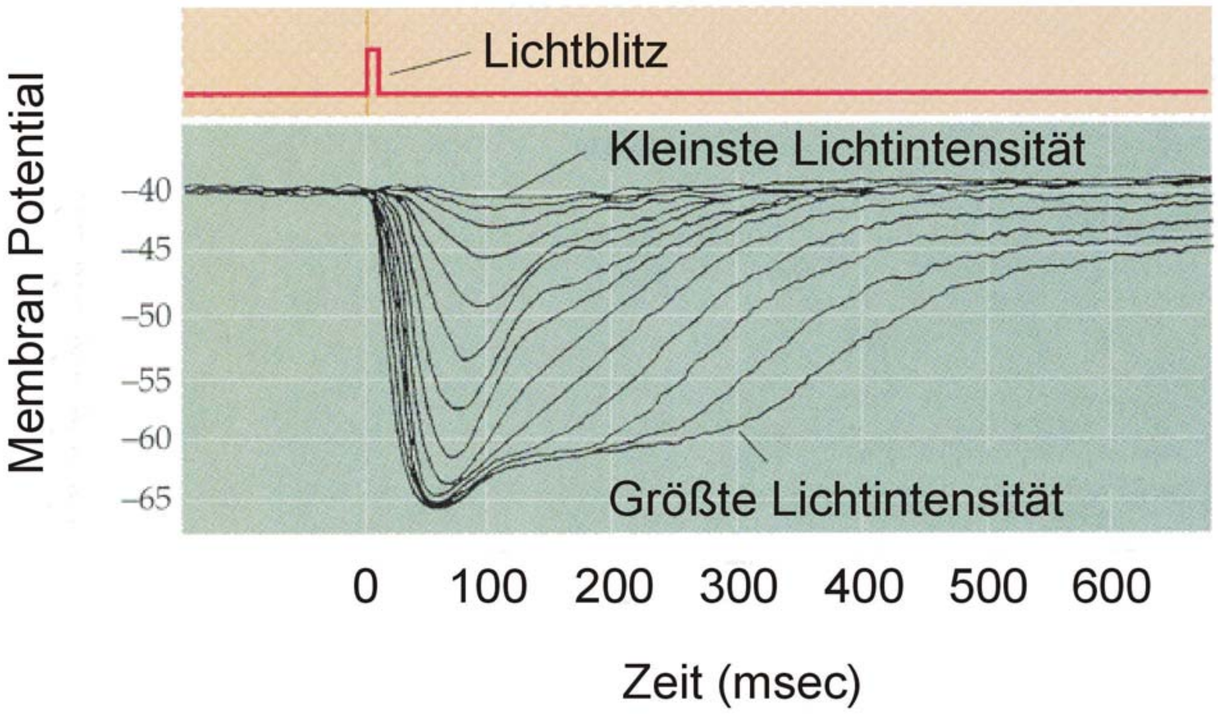


Walter Schröder
Forschungszentrum Jülich

Recording the dark current with a suction electrode



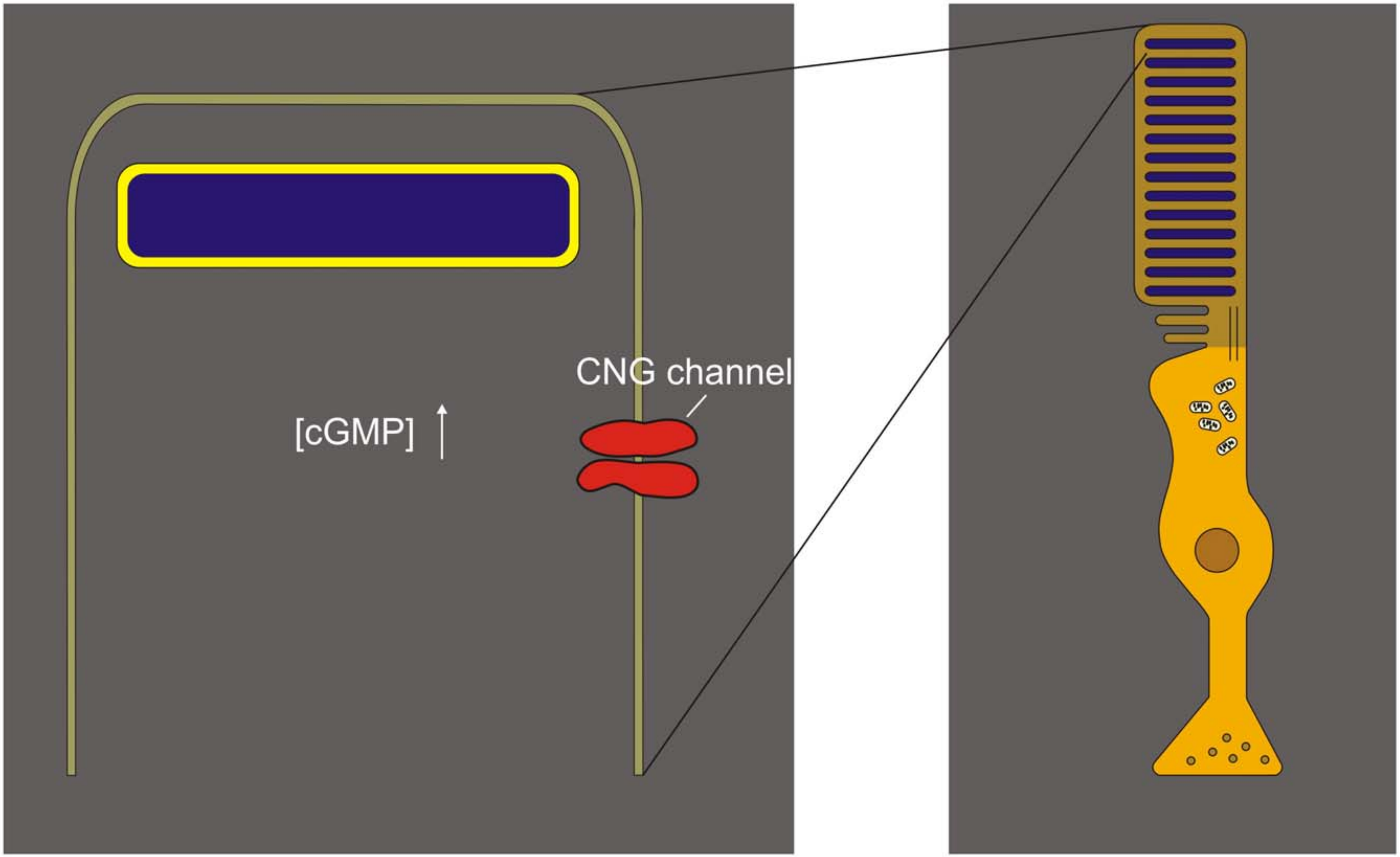
Schnapf & Baylor (1987)



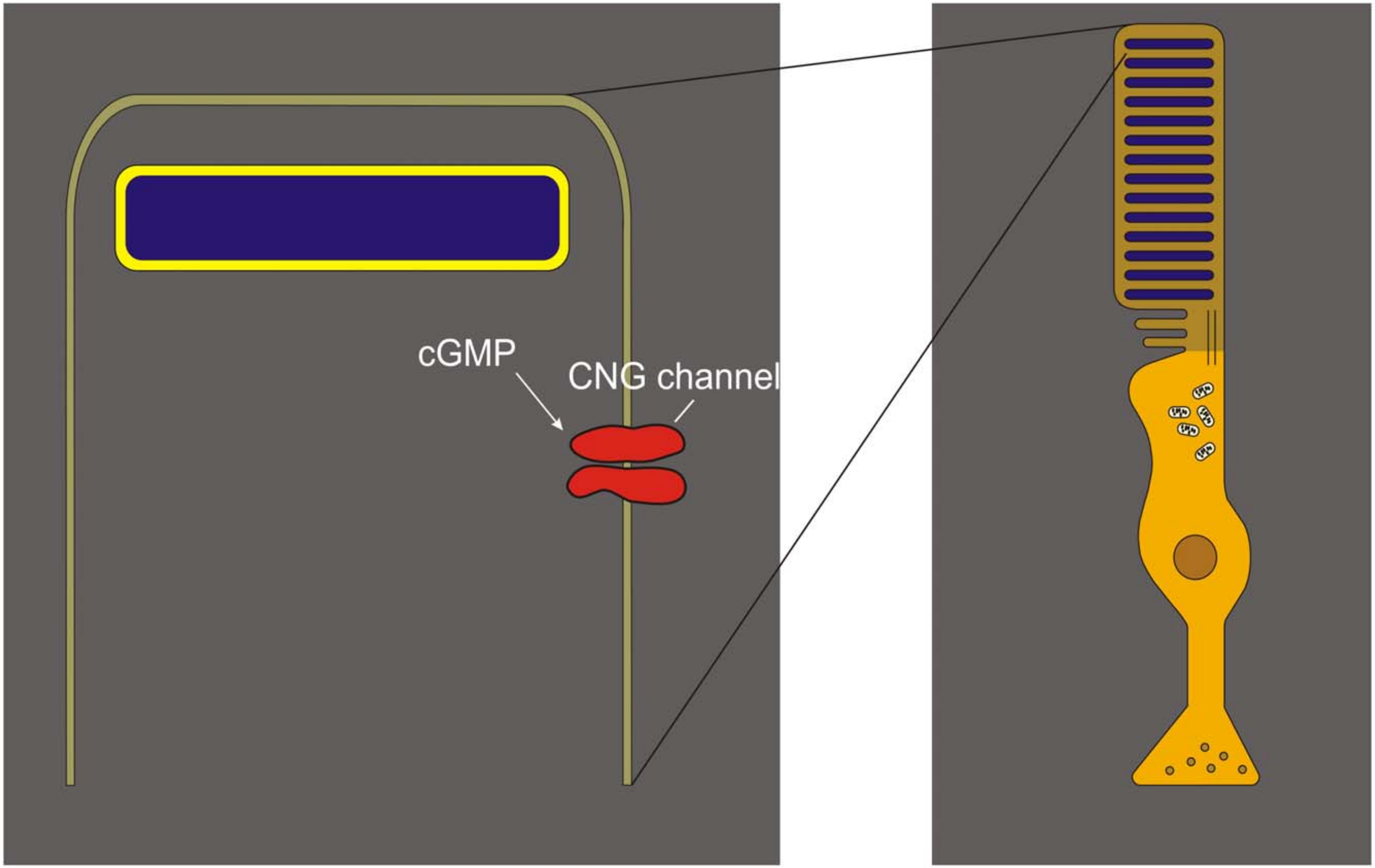
Light response of a photoreceptor cell

The light response at the molecular level

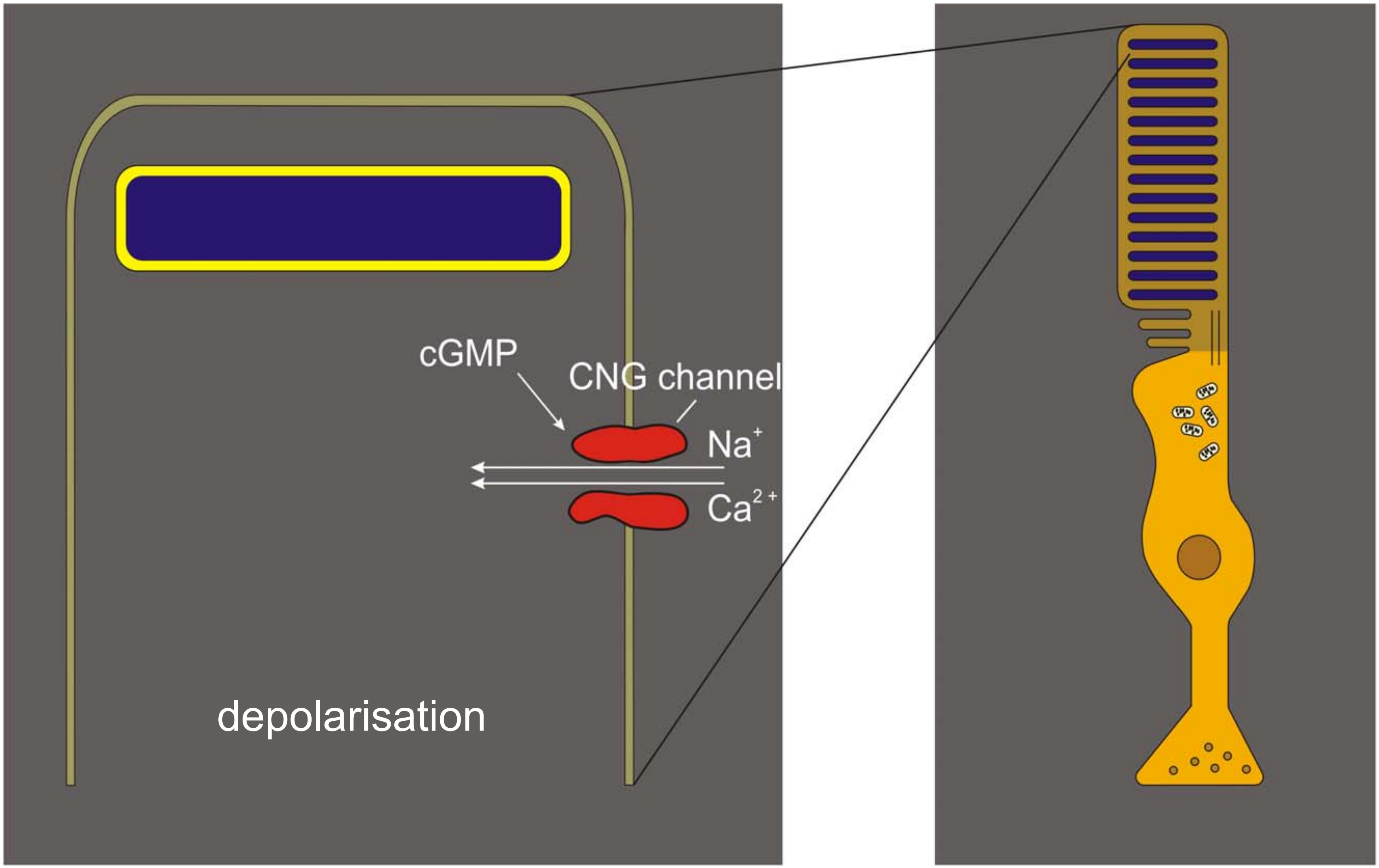
Dark state



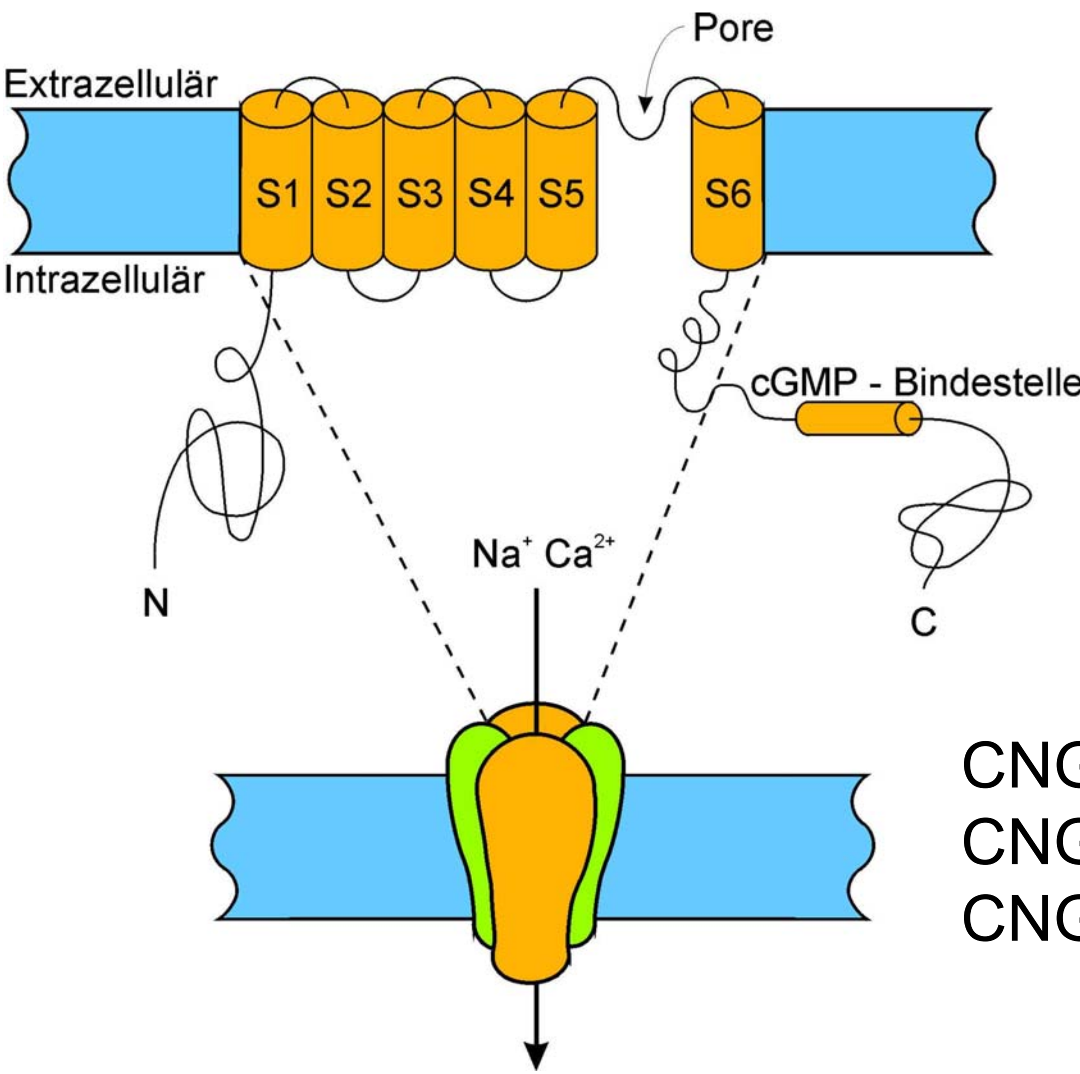
Dark state



Dark state

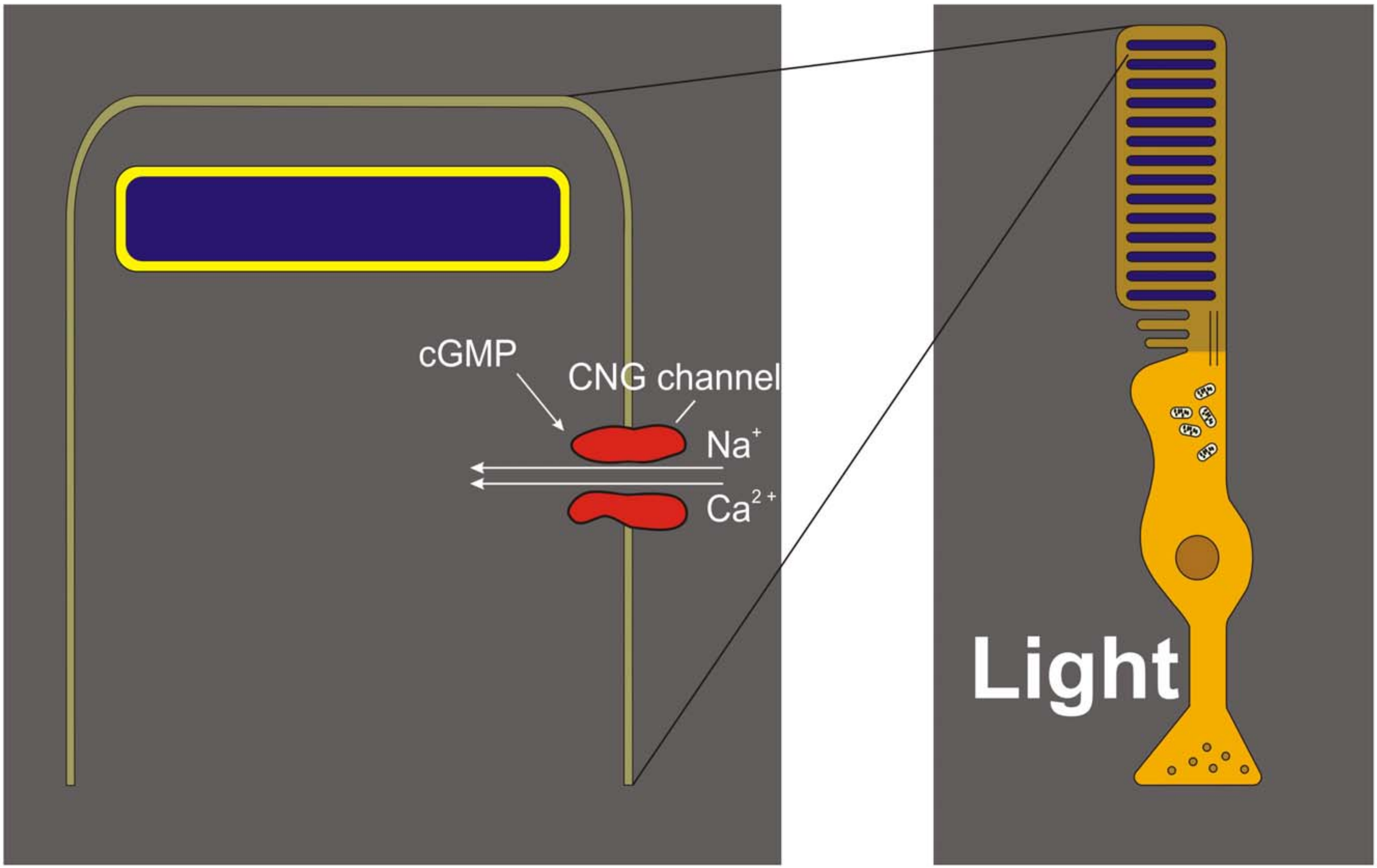


Cyclic nucleotide-gated ion channels

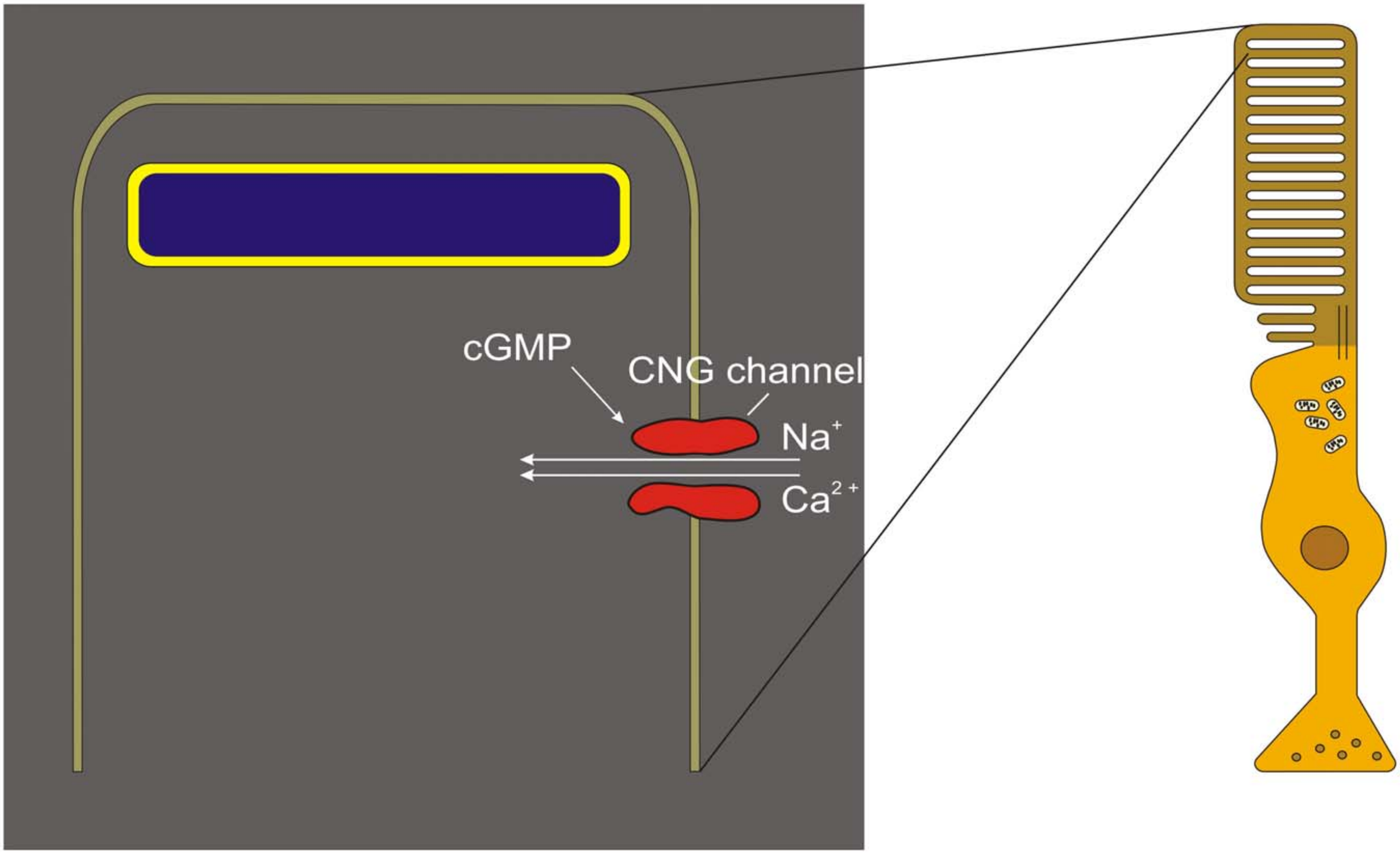


CNG A1 rod
CNG A3 cone
CNG B1a/3 rod/cone

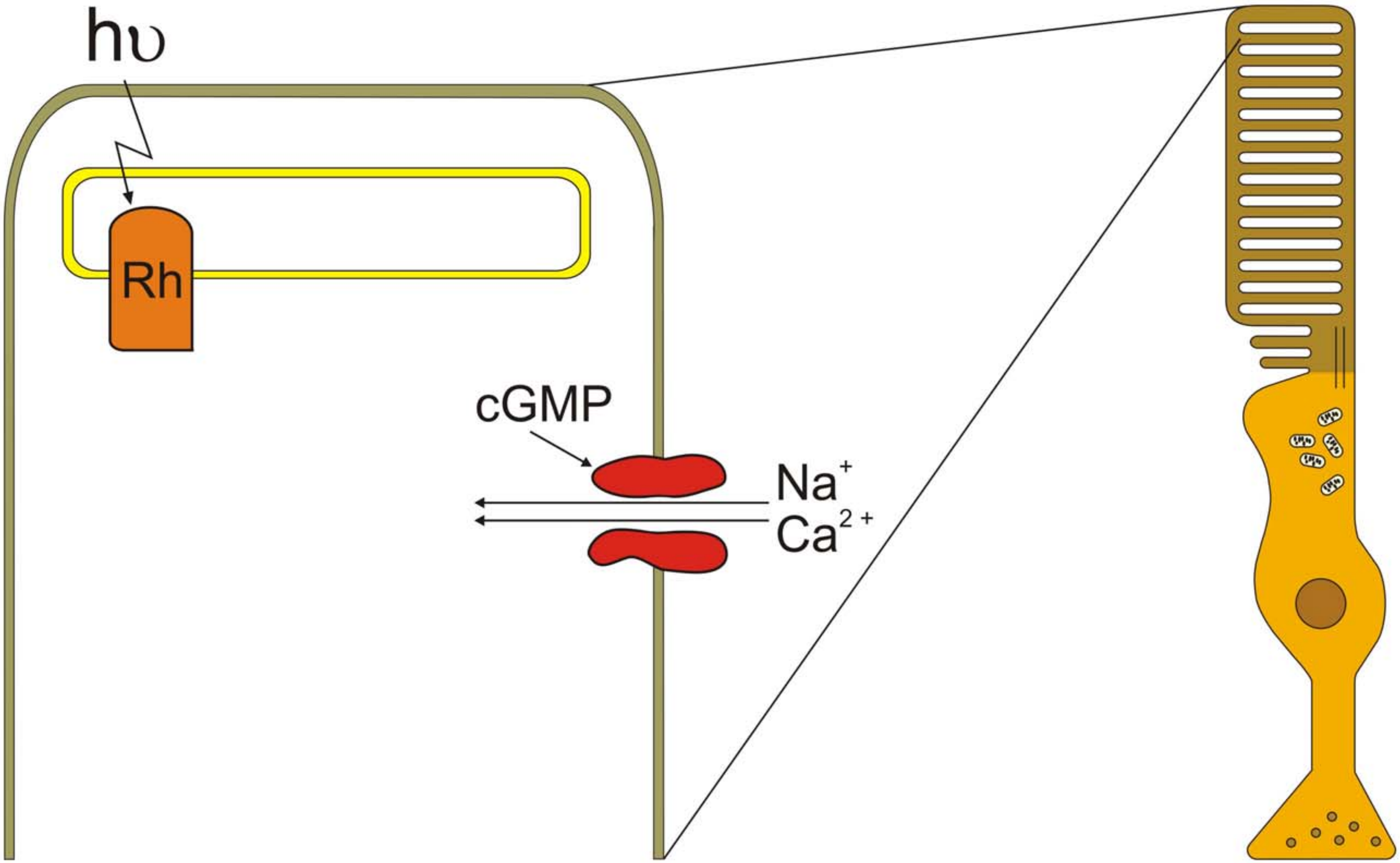
Dark state



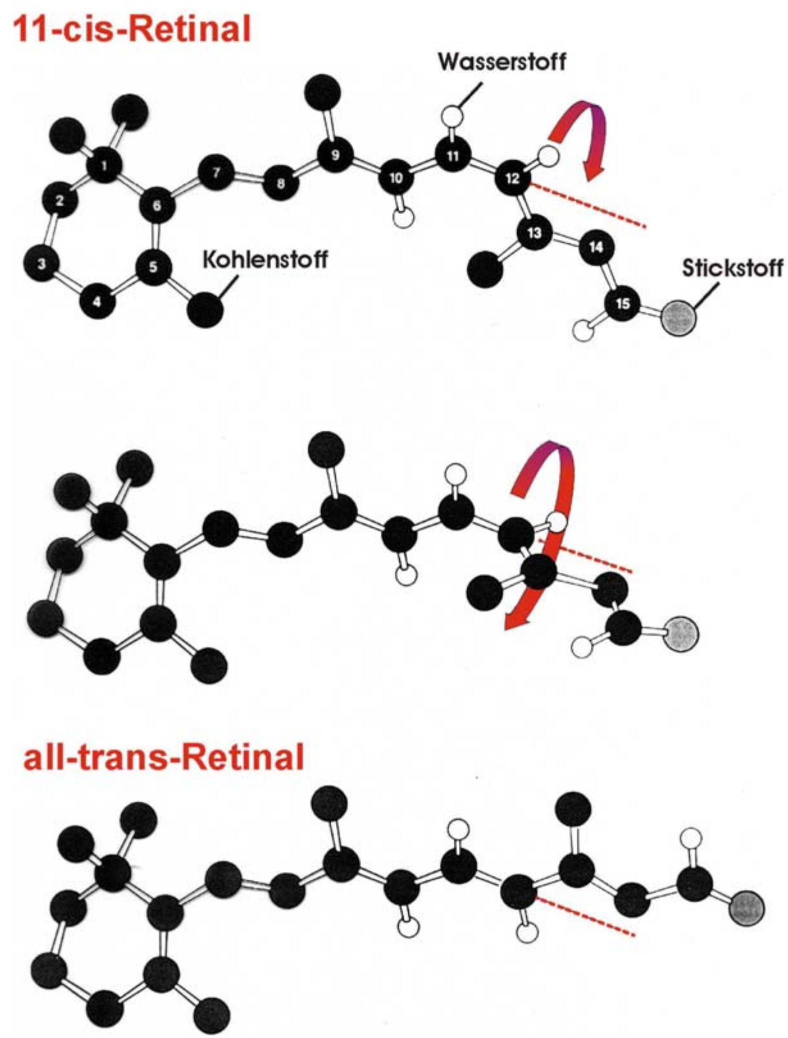
Illumination



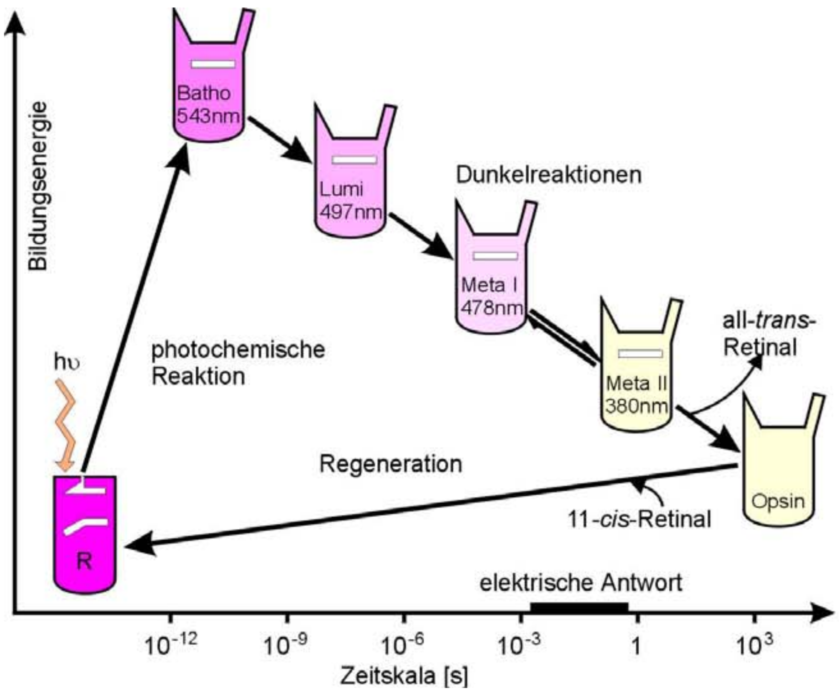
Illumination

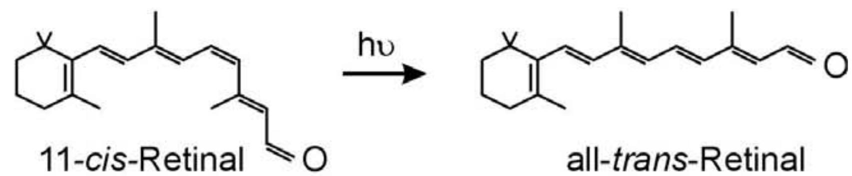


Photoisomerisation of retinal

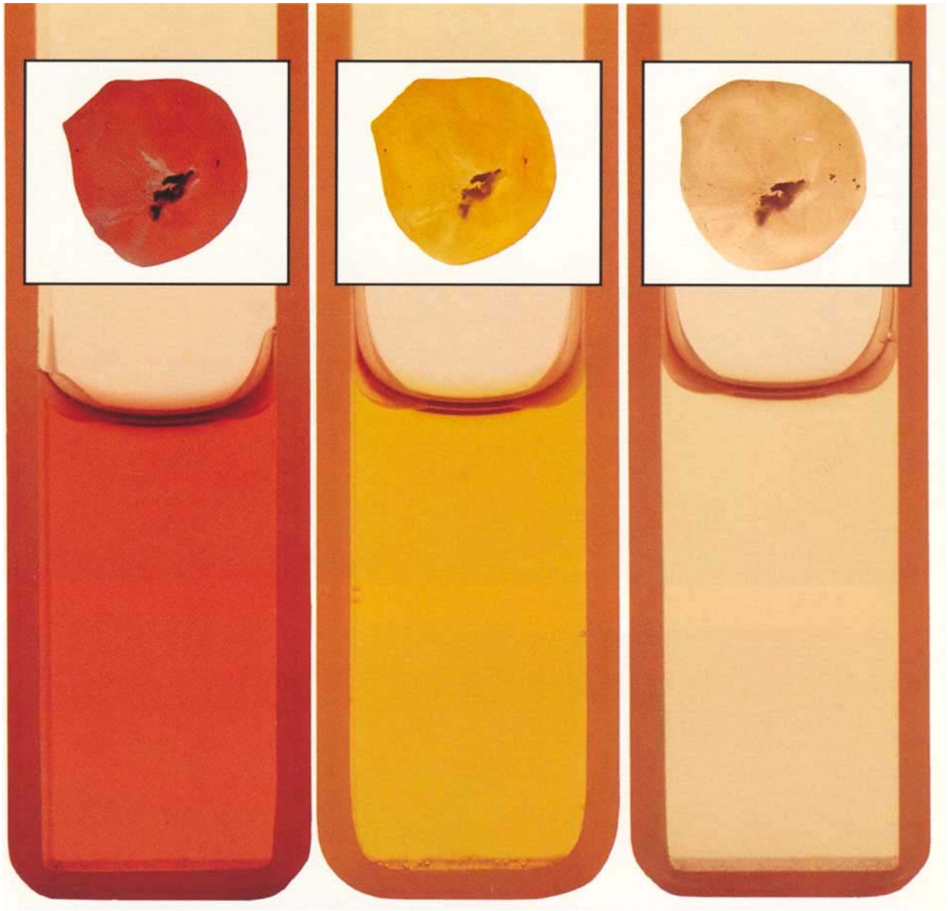


Photocycle of rhodopsin



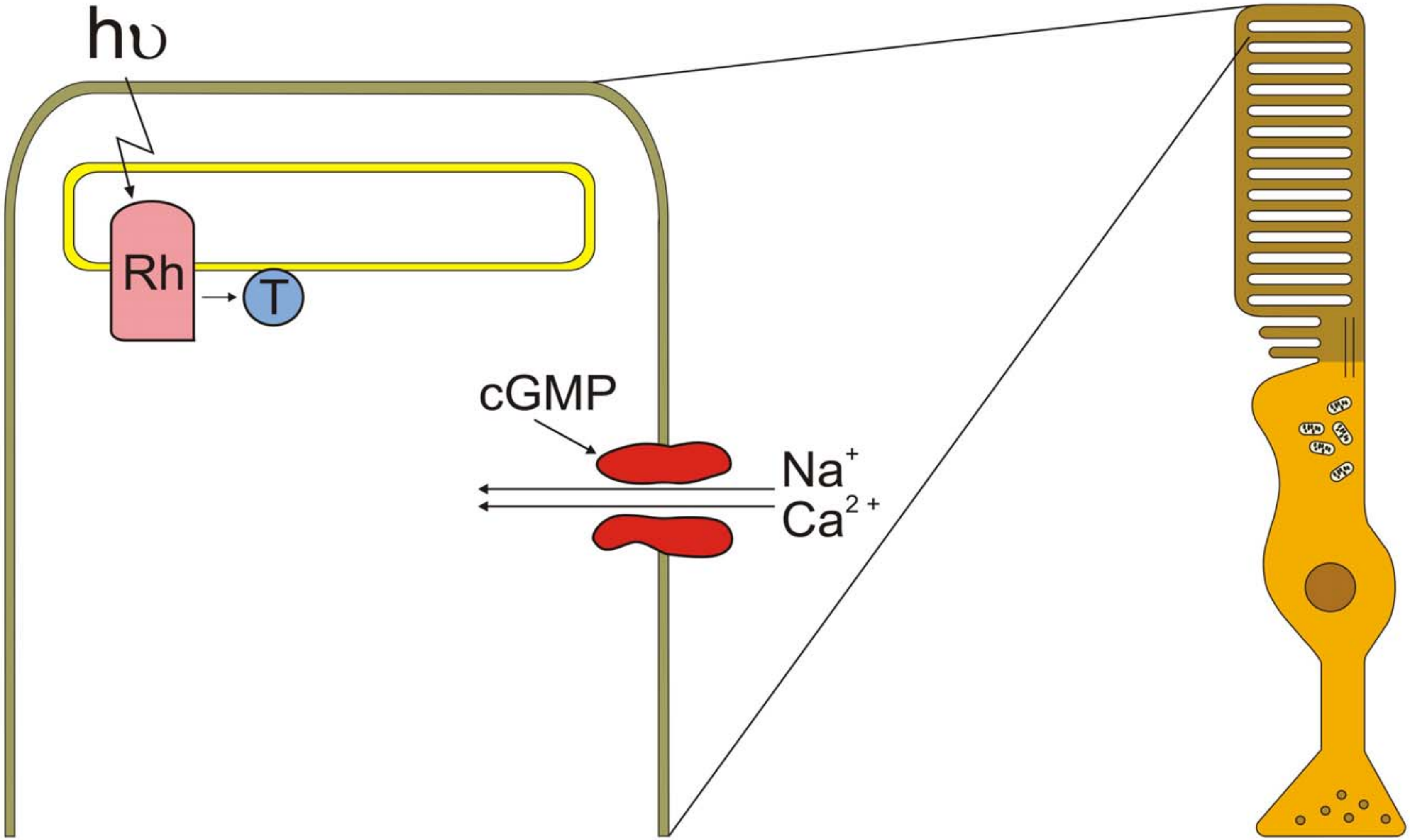


Signal transduction

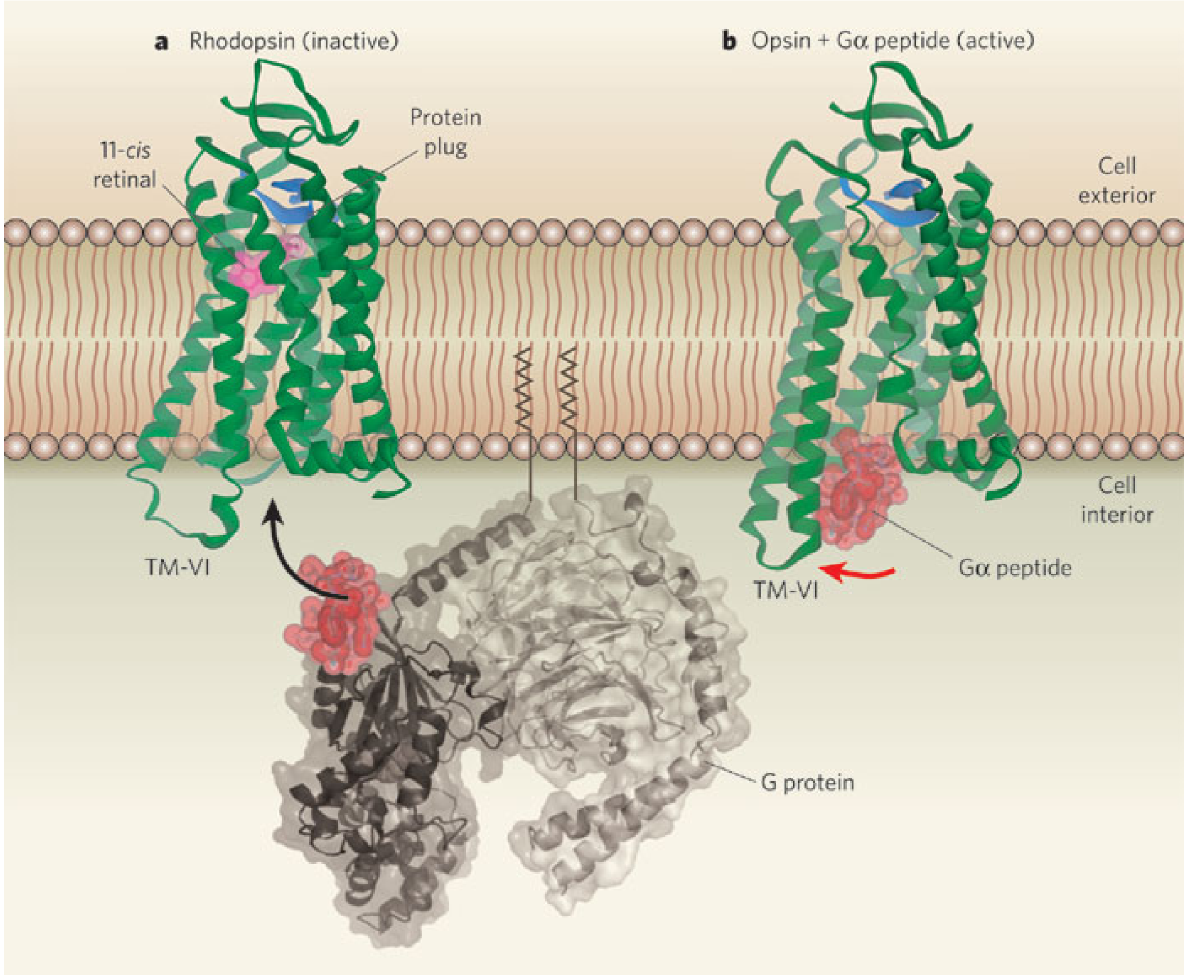


Rhodopsin is bleached by light.
Once bleached it no longer can absorb light!

Illumination

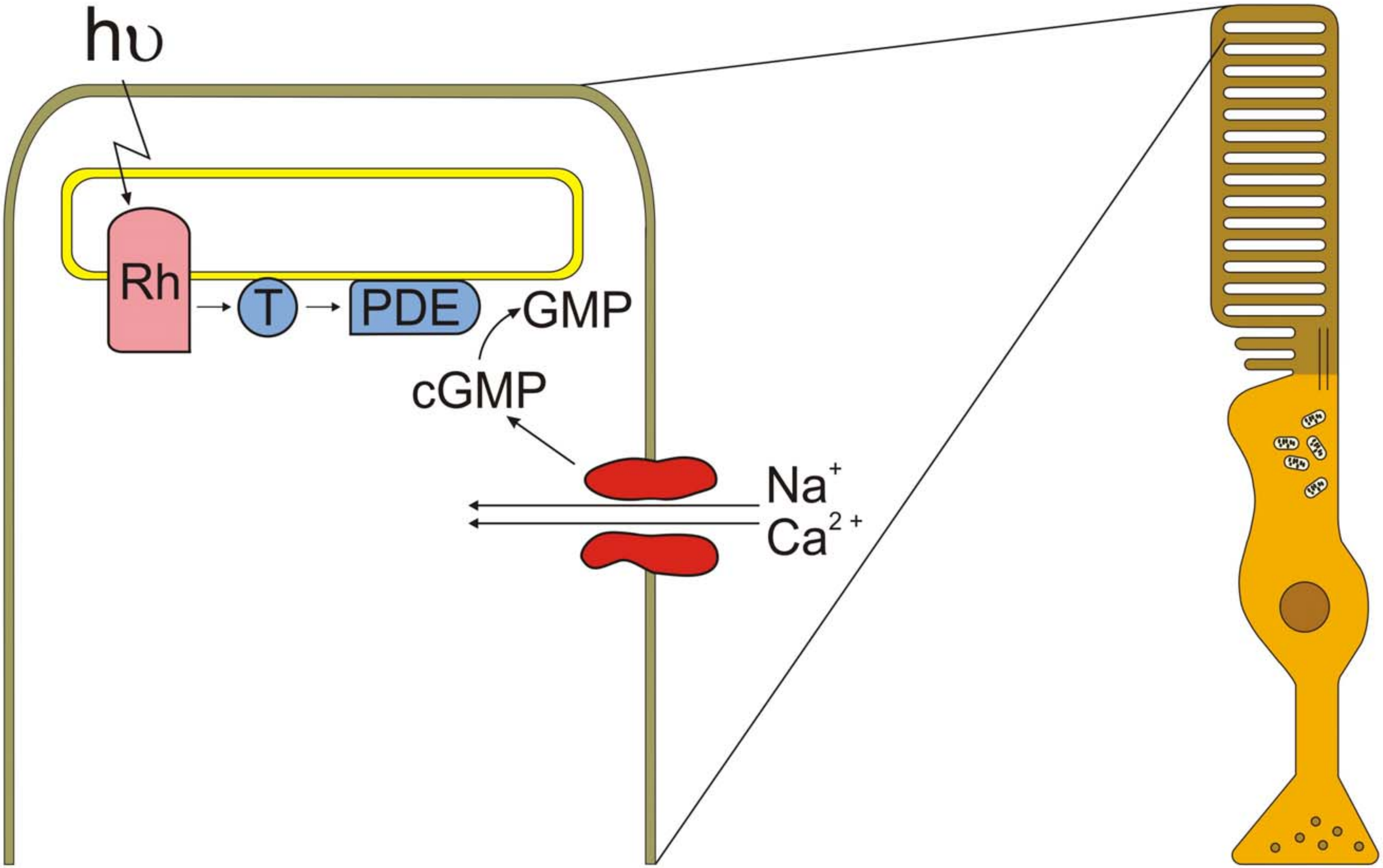


Illumination



Schwartz, T. W. & Hubbell, W. L. (2008) Nature **455**, 473-474

Illumination



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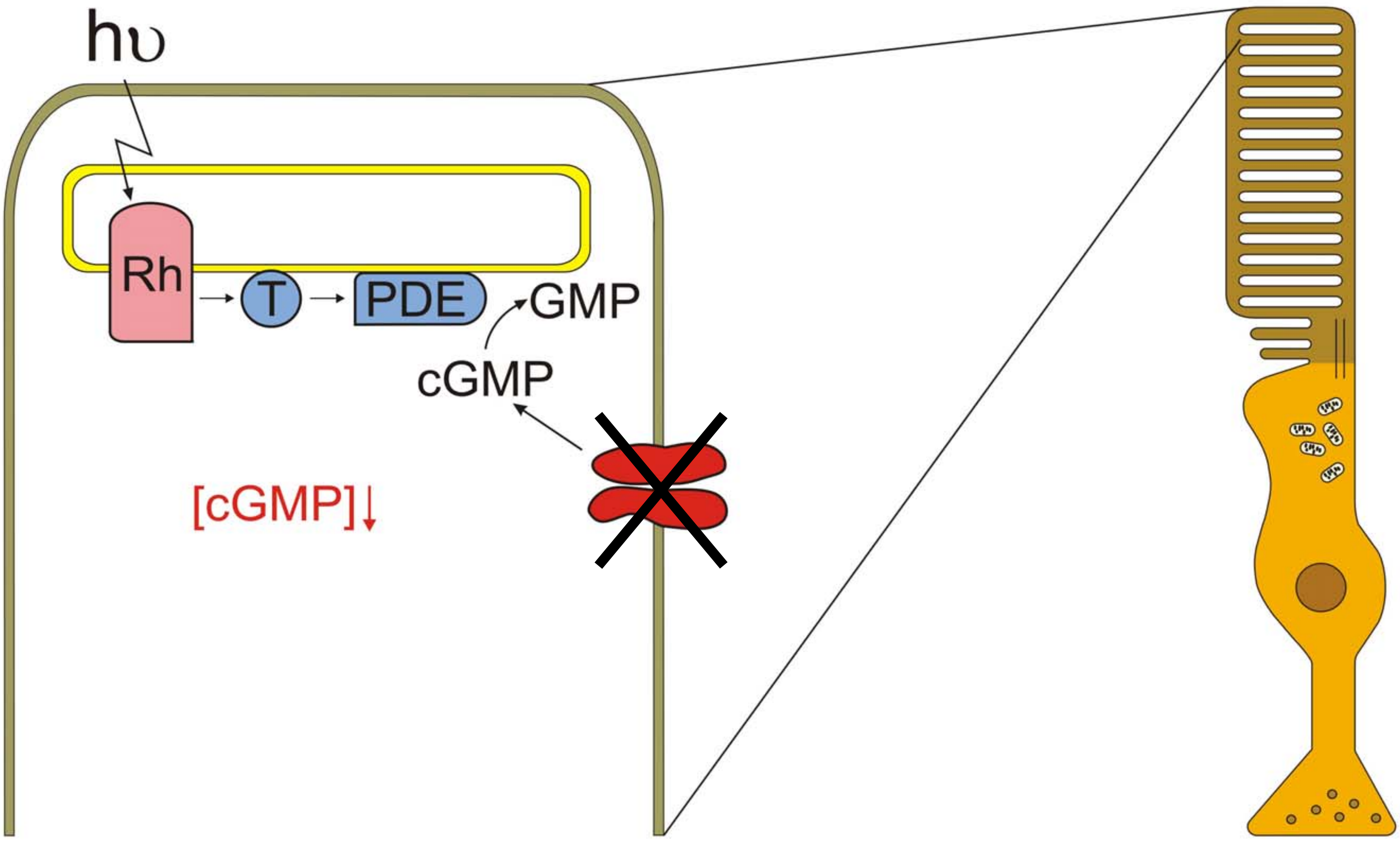

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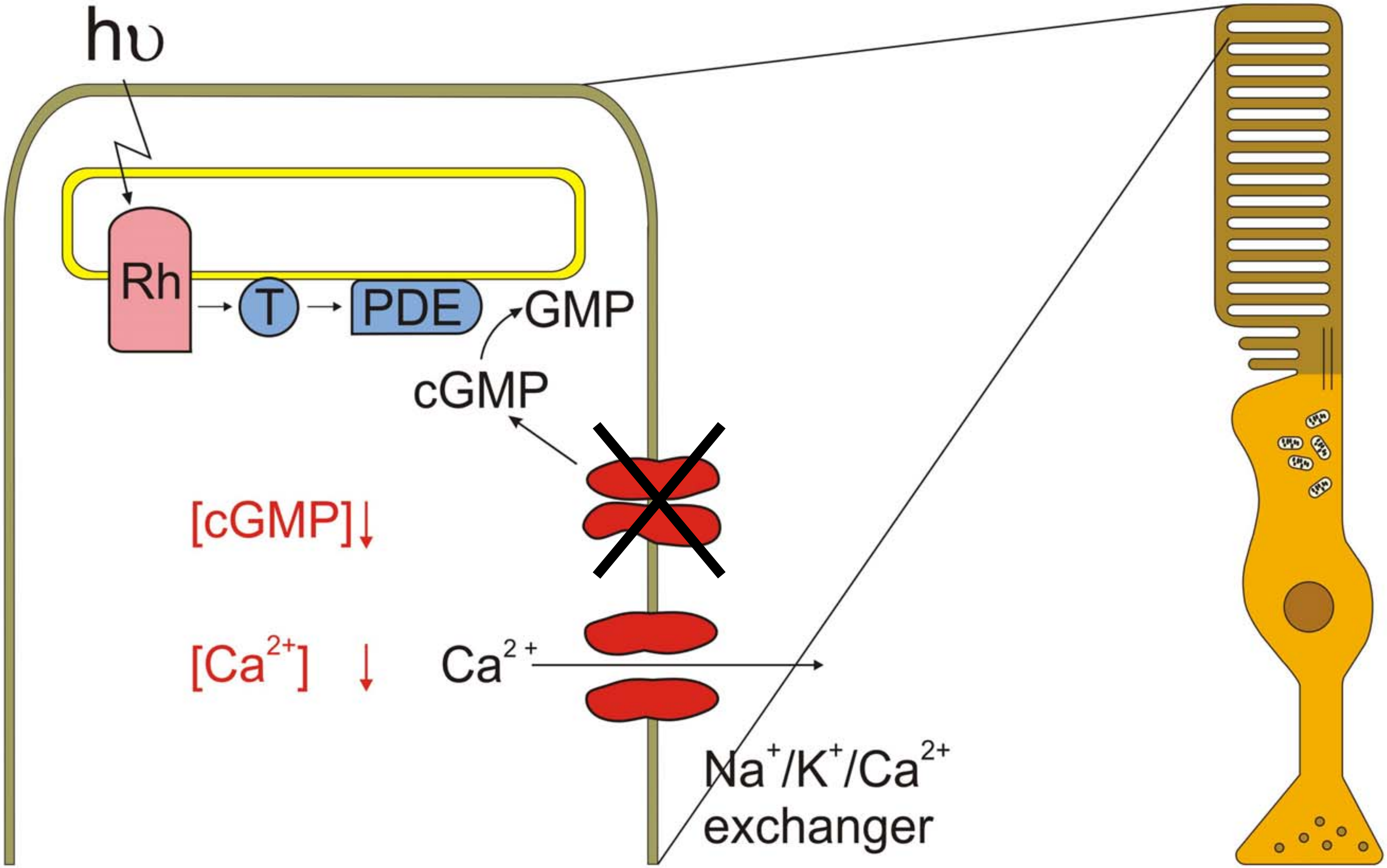
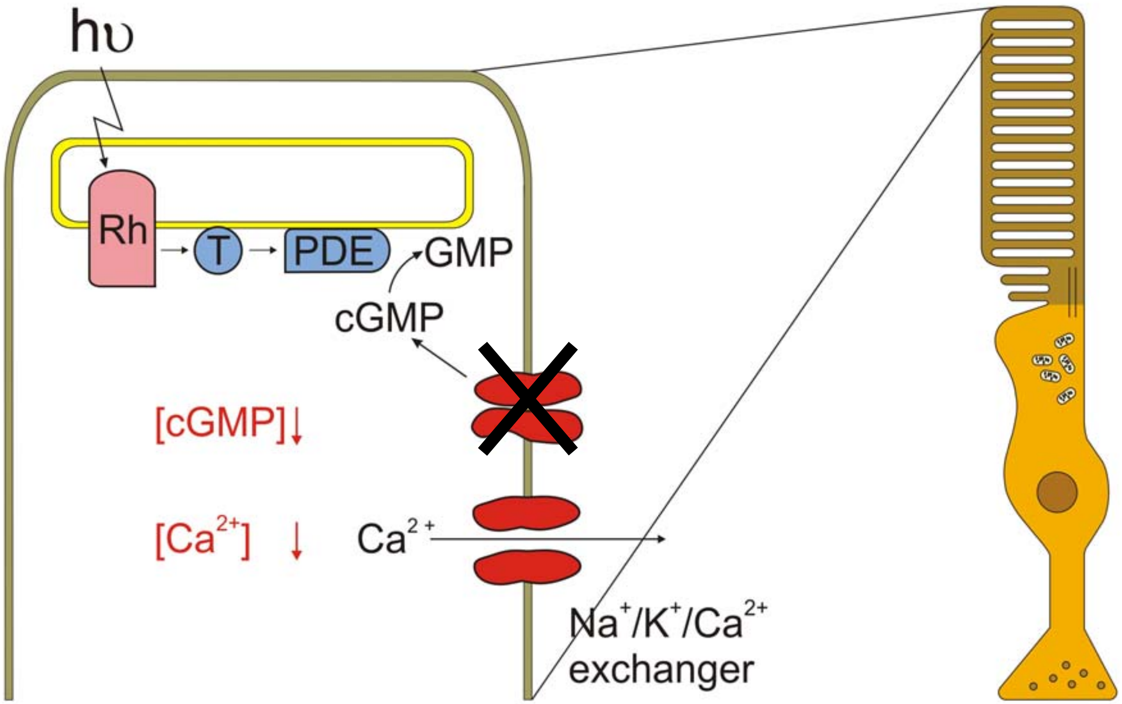


Illumination



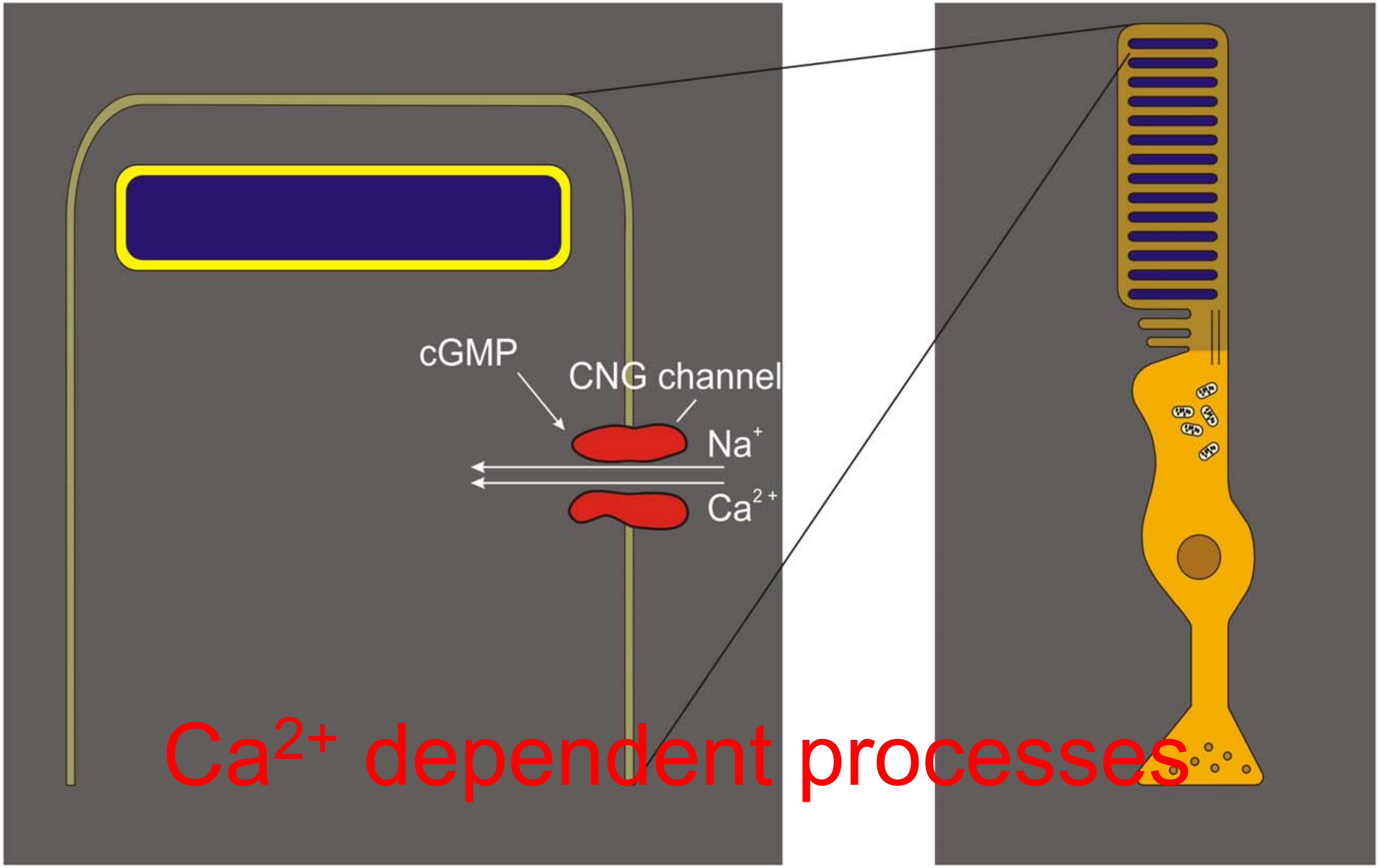
Hyperpolarisation

Amplification

1 photon / 1 rhodopsin → ≥ 100 transducins → PDE (~4000 cGMP/sec)

~500.000 – 1.000.000

Recovery of the dark state



Ca^{2+} dependent processes

Recovery of the dark state

1. phosphorylation of rhodopsin by rhodopsin kinase
2. binding of arrestin to phosphorylated rhodopsin
3. intrinsic GTPase activity of transducin (α-subunit)

   $\rightarrow$inhibition of PDE
4. re-synthesis of cGMP by guanylyl cyclase
5. (re-)opening of CNG channel

Summary

The vertebrate retina can adapt to light intensities ranging over 9 – 10 orders of magnitude.

Rod photoreceptors can detect single photons.
Cone photoreceptors allow vision at day light.

Phototransduction utilizes a highly amplifying, GPCR-activated enzymatic cascade.

Summary

cGMP is the cellular messenger of phototransduction.

Receptorpotential / amplification: hydrolysis of cGMP and closing of CNG channels.

Rods and cones express celltype specific opsin genes with distinct absorption properties.

Ca^{2+}-dependent cellular processes re-establish the dark state of photoreceptors.