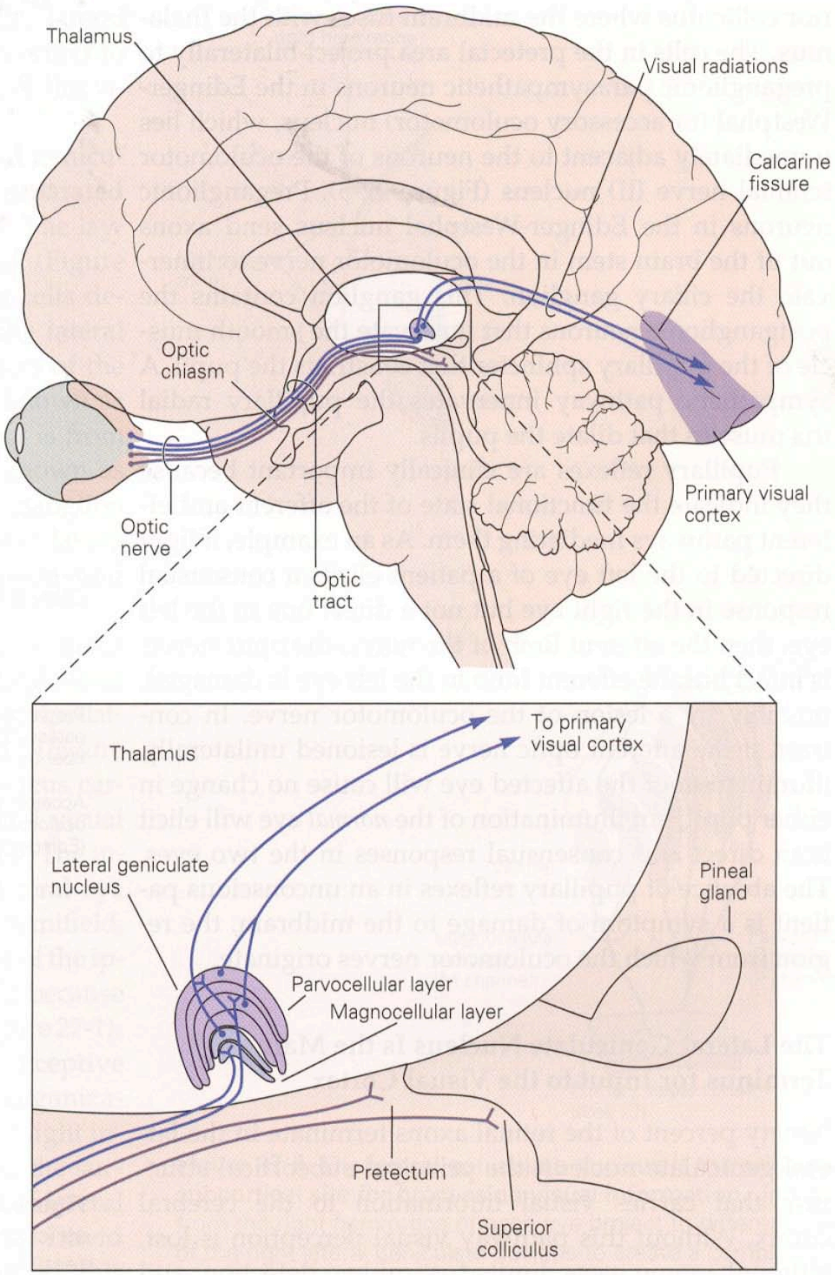
Bi150 (2004)

Vision I: Retina and LGN

10/25/04

Reading: Chs. 25-27 (26 is most important for this lecture; 25 and 27 are more relevant to the next 2 lectures).

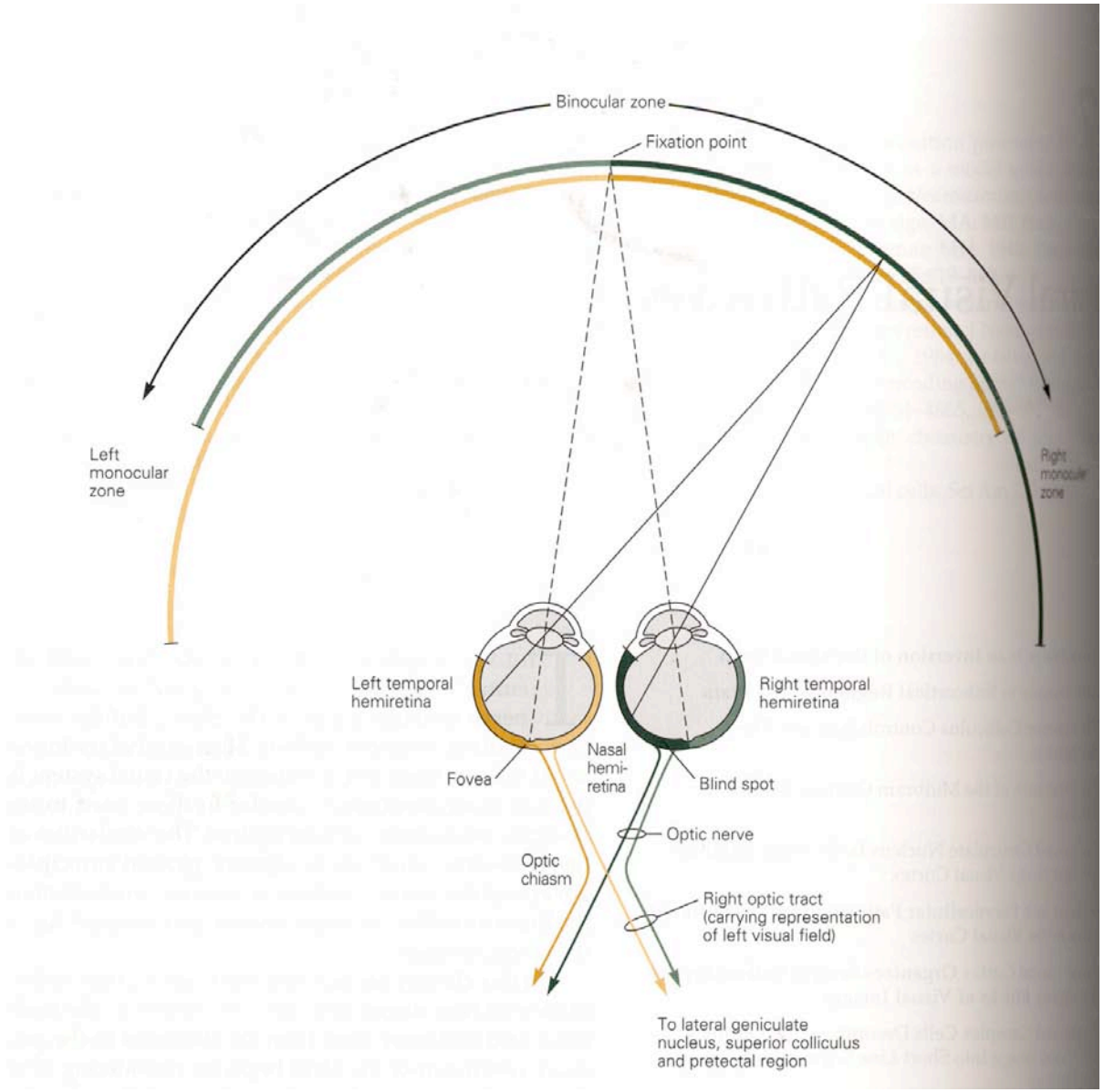


Organization of the visual pathways in the human brain

- Retinal ganglion cells (RGCs) project to the lateral geniculate nucleus (LGN), as well as to the superior colliculus (SC),which controls eye movements.
- The LGN relays visual information to cortex.

The visual field

- The visual field has binocular and monocular zones.
- The right optic nerve carries input from the right half of each eye, so it transmits a representation of the left visual field.
- The nasal half of each retina projects to the contralateral LGN, while the temporal half projects ipsilaterally.



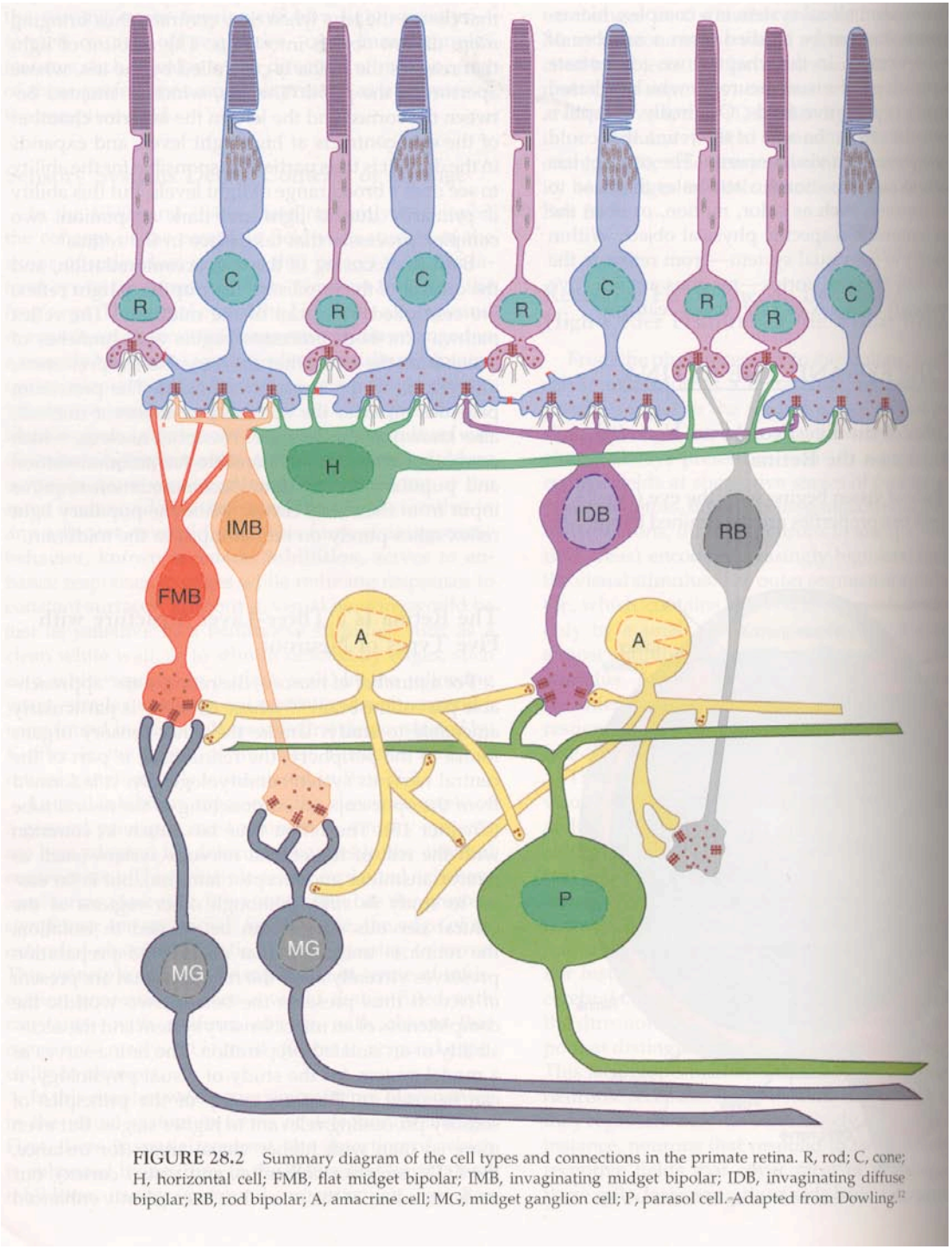
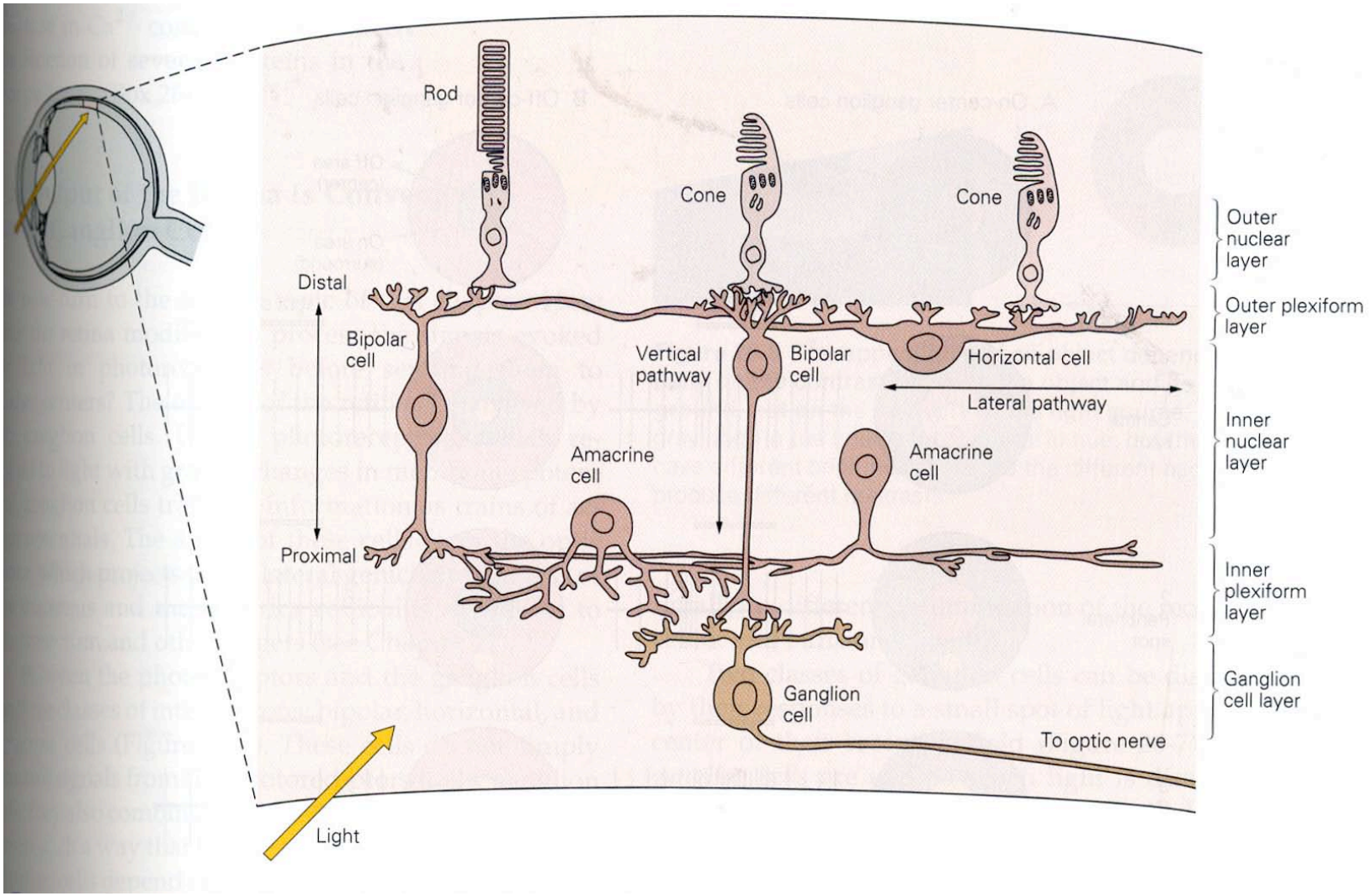


FIGURE 28.2 Summary diagram of the cell types and connections in the primate retina. R, rod; C, cone; H, horizontal cell; FMB, flat midget bipolar; IMB, invaginating midget bipolar; IDB, invaginating diffuse bipolar; RB, rod bipolar; A, amacrine cell; MG, midget ganglion cell; P, parasol cell. Adapted from Dowling.[12]

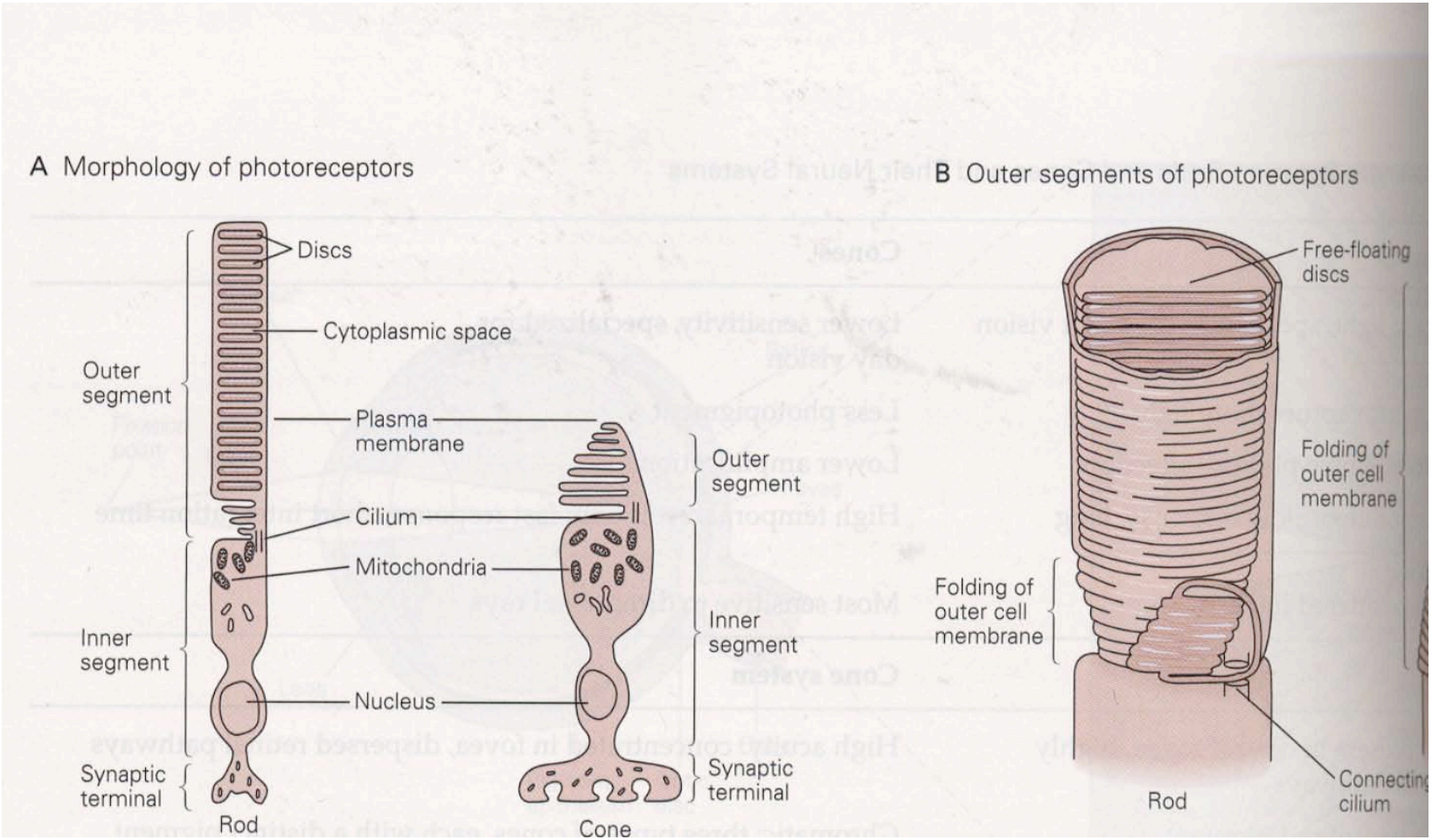
Cells of the primate retina

- The retina is a layered structure (from top: photoreceptor outer segment layer, outer nuclear layer (ONL), outer plexiform (neuronal processes) layer (OPL), inner nuclear layer (INL), inner plexiform layer (INL), ganglion cell layer (GCL)).

A simplified diagram of retinal circuits



Photoreceptor morphology



Characteristics of rods and cones

- Rods have high sensitivity to light, can do single photon detection, used for night vision.
- Rods use rhodopsin as their sole photopigment.
- Rod vision is low acuity and has poor temporal resolution.
- Rods are located in the peripheral region of the retina.
- Cones have lower sensitivity, used for high-acuity day (color) vision.
- Cones have one of three types of photopigment, each most sensitive to a different part of the spectrum.
- Cones are concentrated in fovea.

Light absorption by rhodopsin

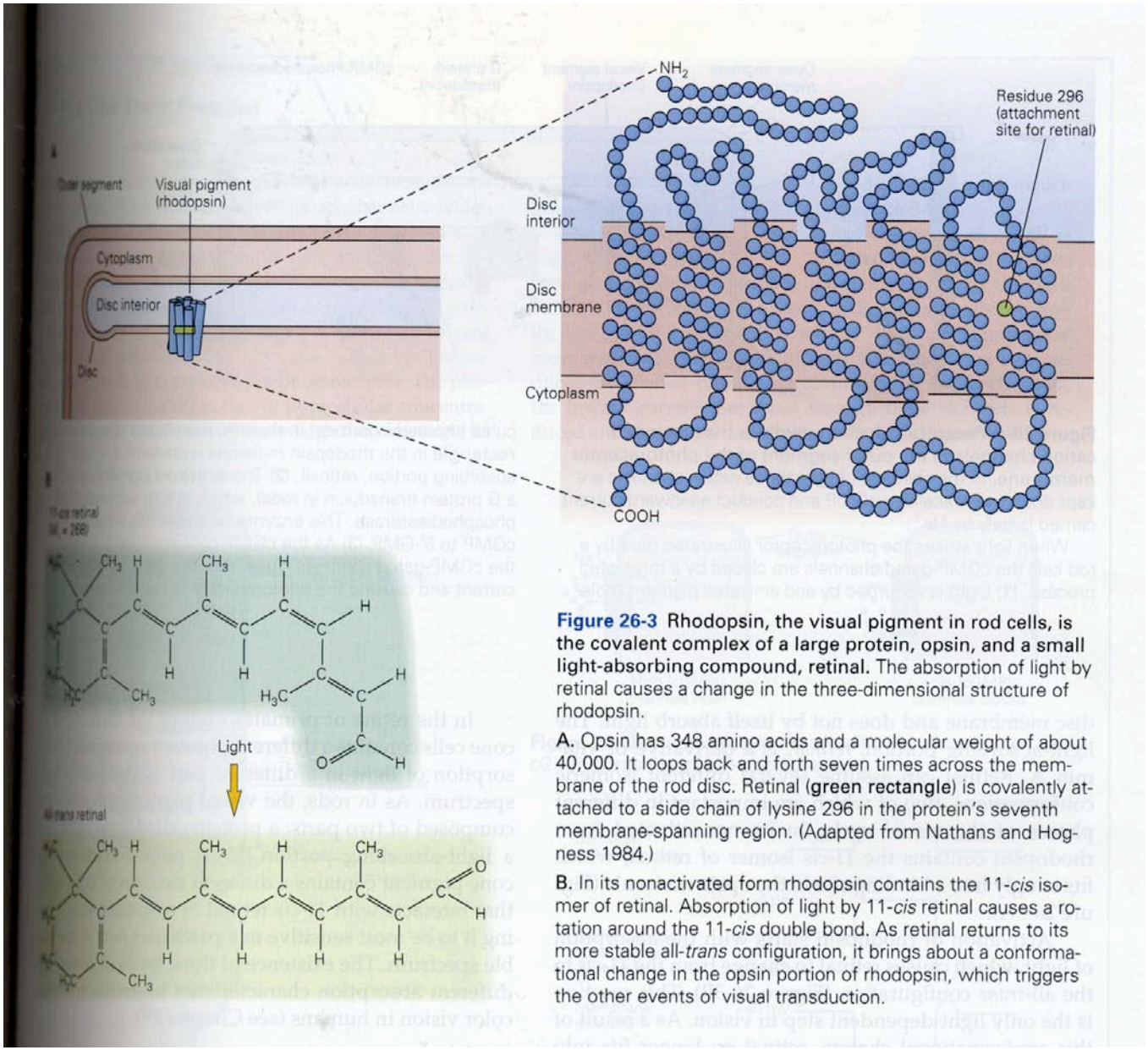


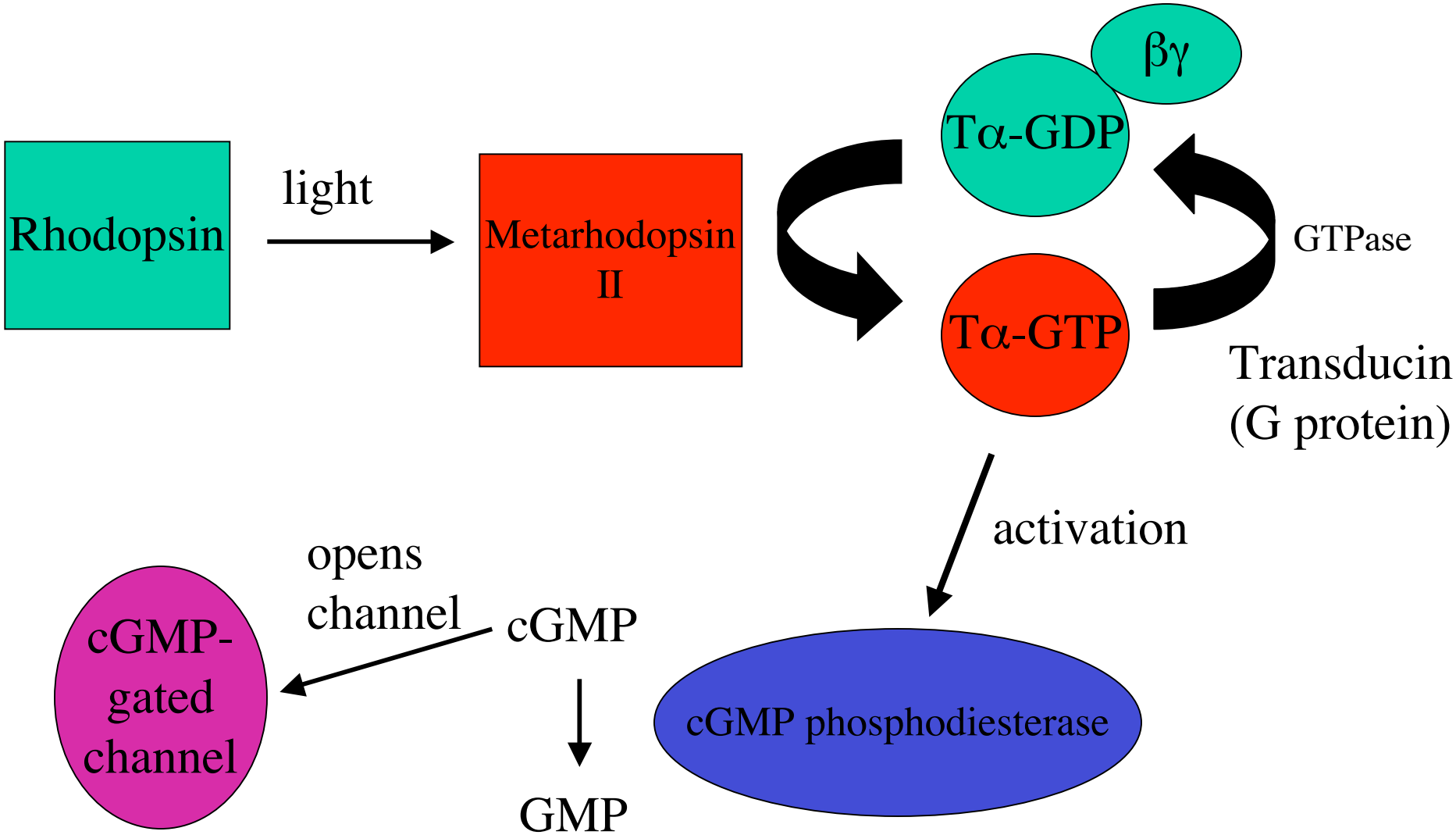
Figure 26-3 **Rhodopsin, the visual pigment in rod cells, is the covalent complex of a large protein, opsin, and a small light-absorbing compound, retinal.** The absorption of light by retinal causes a change in the three-dimensional structure of rhodopsin.

A. Opsin has 348 amino acids and a molecular weight of about 40,000. It loops back and forth seven times across the membrane of the rod disc. Retinal (**green rectangle**) is covalently attached to a side chain of lysine 296 in the protein's seventh membrane-spanning region. (Adapted from Nathans and Hogness 1984.)

B. In its nonactivated form rhodopsin contains the 11-*cis* isomer of retinal. Absorption of light by 11-*cis* retinal causes a rotation around the 11-*cis* double bond. As retinal returns to its more stable all-*trans* configuration, it brings about a conformational change in the opsin portion of rhodopsin, which triggers the other events of visual transduction.

- Rhodopsin is a 7-transmembrane protein in rod outer segments with a covalently bound retinal chromophore that absorbs visible light.
- Light converts 11-cis retinal to all-trans retinal and causes a conformational change in opsin protein.

Visual signal transduction



- The components of the signaling pathway are located in the outer segment.
- Rods and cones are passive and do not fire action potentials.
- Rod and cone signaling are similar, but cones use cone photopigments rather than rhodopsin.

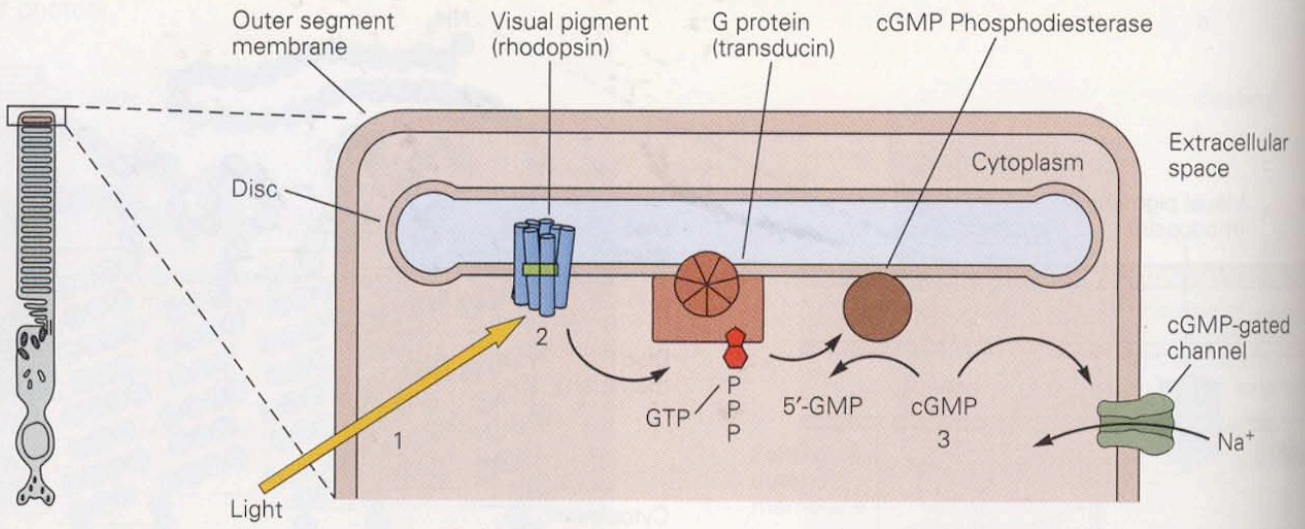


Figure 26-4 **Phototransduction involves the closing of cation channels in the outer segment of the photoreceptor membrane.** In the absence of light these cation channels are kept open by intracellular cGMP and conduct an inward current, carried largely by Na^+.

When light strikes the photoreceptor (illustrated here by a rod cell) the cGMP-gated channels are closed by a three-step process. (**1**) Light is absorbed by and activates pigment molecules (rhodopsin in rods) in the disc membrane (the green **rectangle** in the rhodopsin molecule represents the light-absorbing portion, retinal). (**2**) The activated pigment stimulates a G protein (transducin in rods), which in turn activates cGMP phosphodiesterase. This enzyme catalyzes the breakdown of cGMP to 5′-GMP. (**3**) As the cGMP concentration is lowered, the cGMP-gated channels close, thereby reducing the inward current and causing the photoreceptor to hyperpolarize.

Electrical response to light

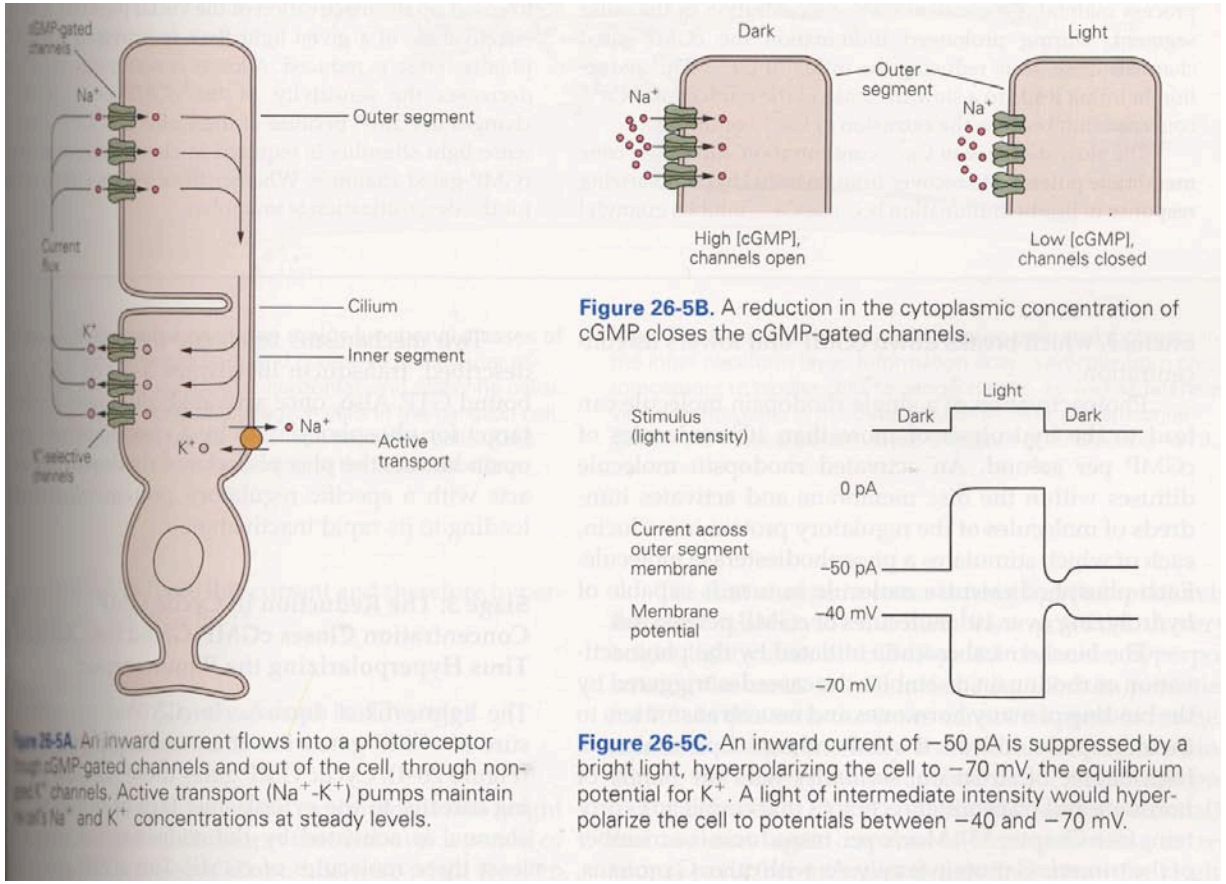


Figure 26-5B. A reduction in the cytoplasmic concentration of cGMP closes the cGMP-gated channels.

Figure 26-5A. An inward current flows into a photoreceptor through cGMP-gated channels and out of the cell, through non-gated K^+ channels. Active transport (Na^+-K^+) pumps maintain the cell's Na^+ and K^+ concentrations at steady levels.

Figure 26-5C. An inward current of −50 pA is suppressed by a bright light, hyperpolarizing the cell to −70 mV, the equilibrium potential for K^+. A light of intermediate intensity would hyperpolarize the cell to potentials between −40 and −70 mV.

- cGMP opens a CNG channel that allows Na^+ into the cell, producing the constitutive dark current and depolarizing the cell to -40 mV.
- Light activates PDE, reducing cGMP, closing the channel.
- K^+ leak channels hyperpolarize the PR toward -70.

Amplification

- One metaII can catalyze formation of hundreds of T-GTPs during its lifetime.
- Each T-GTP activates one PDE.
- Each PDE breaks down >1K cGMP/sec.
- Thus absorption of one photon by a rod --> closing of 300 cGMP-gated channels, or 3% of total, producing hyperpolarization of 1 mV.
- Net amplification: ~10^7 ions/photon.

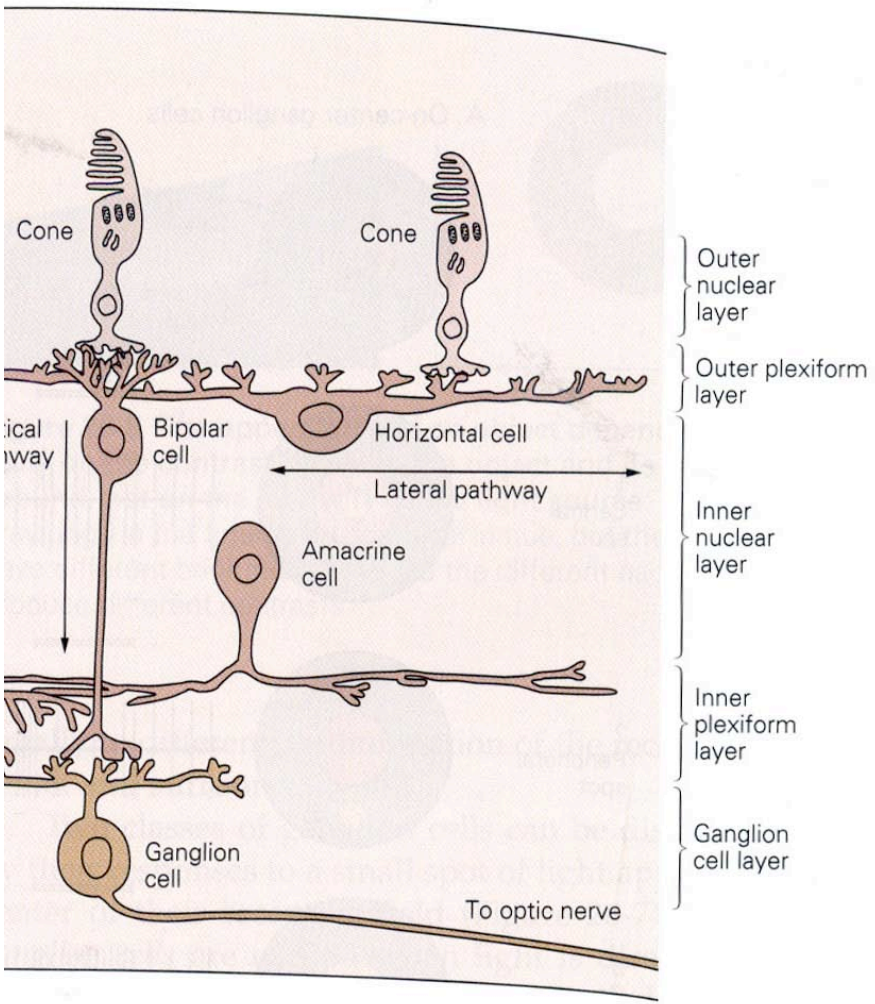
Adaptation

- Vision can work over a 10^{12} -fold range in light intensity. This is partially due to a switchover between rods and cones, to pupillary contraction,and other factors.
- However, a single PR can respond over a 10^{5}-fold range in light intensity even though it has only a 30 mV response window and each photon can hyperpolarize it by 1mV.
- Ca^{2+} can enter through channel; this inhibits guanylate cyclase, which makes cGMP from GTP, so as channels close Ca^{2+} decreases, increasing GC levels, increasing cGMP, so channels reopen.
- Rhodopsin kinase is activated by light and phosphorylates rhodopsin, making it bind less well to transducin.

Signal termination

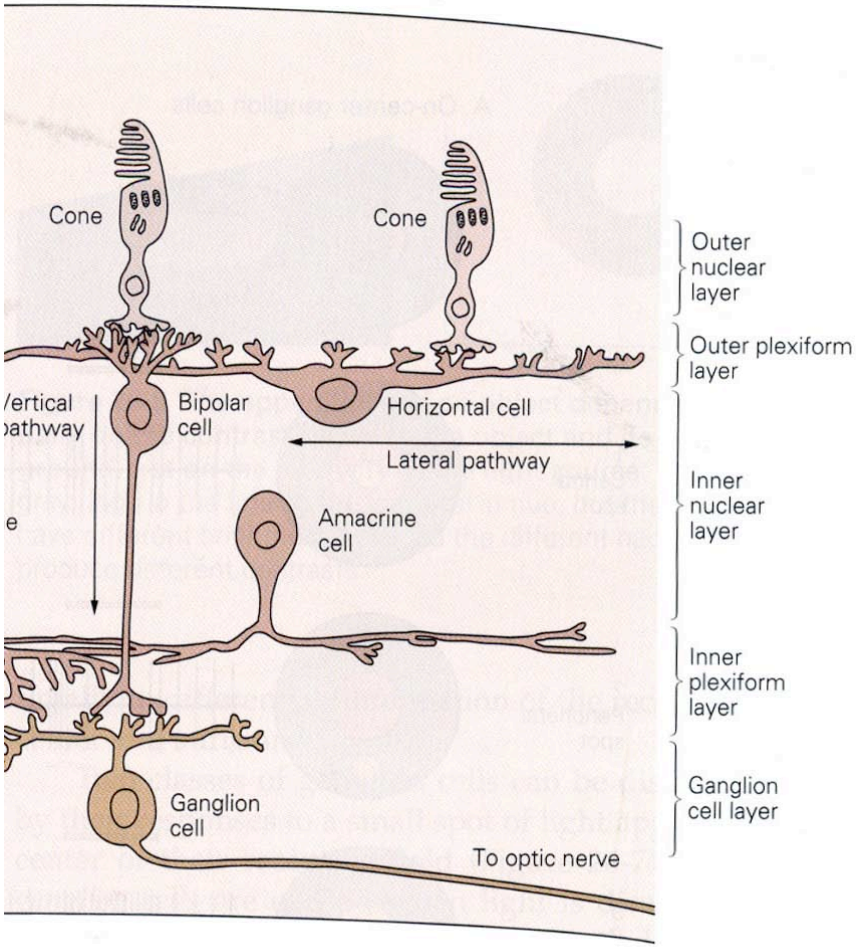
- Arrestins and Rh kinase work together to deactivate metaII.
- PDE acts as a GAP, increasing the intrinsic GTP hydrolysis rate of Tα-GTP and thus deactivating it more rapidly.

Bipolar cells



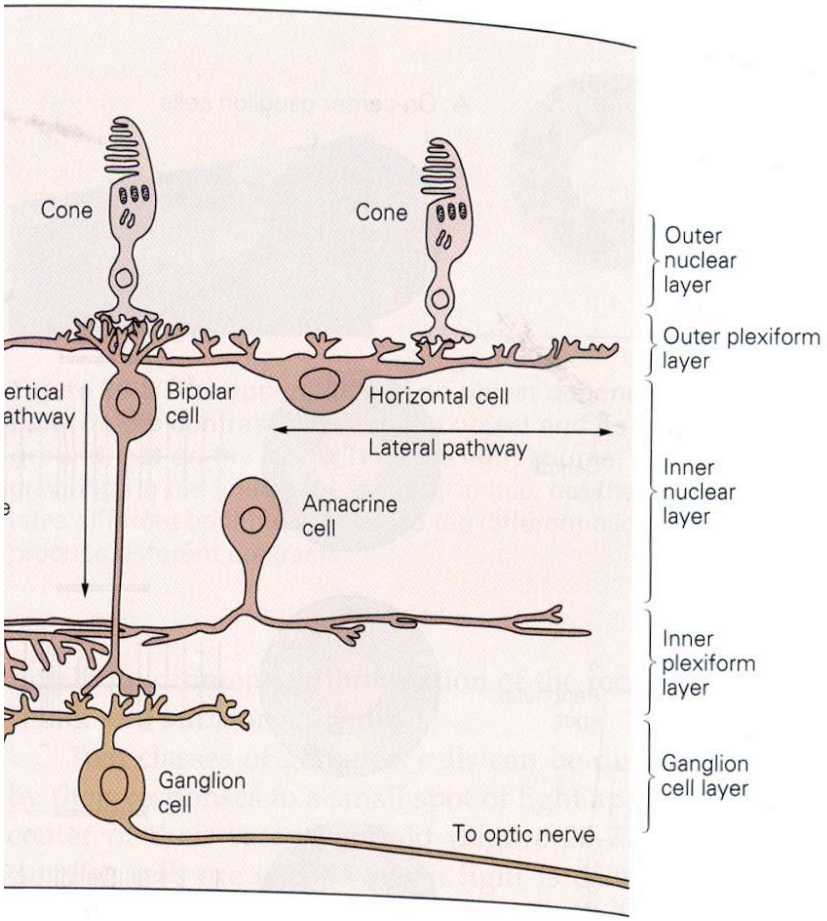
- Cones release transmitter (glu) onto bipolar cells.
- Because they are depolarized in the dark they constantly release glu.
- Bipolars are also passive; they connect cones to RGCs.
- 2 types: depolarizing and hyperpolarizing.

Bipolar cells II

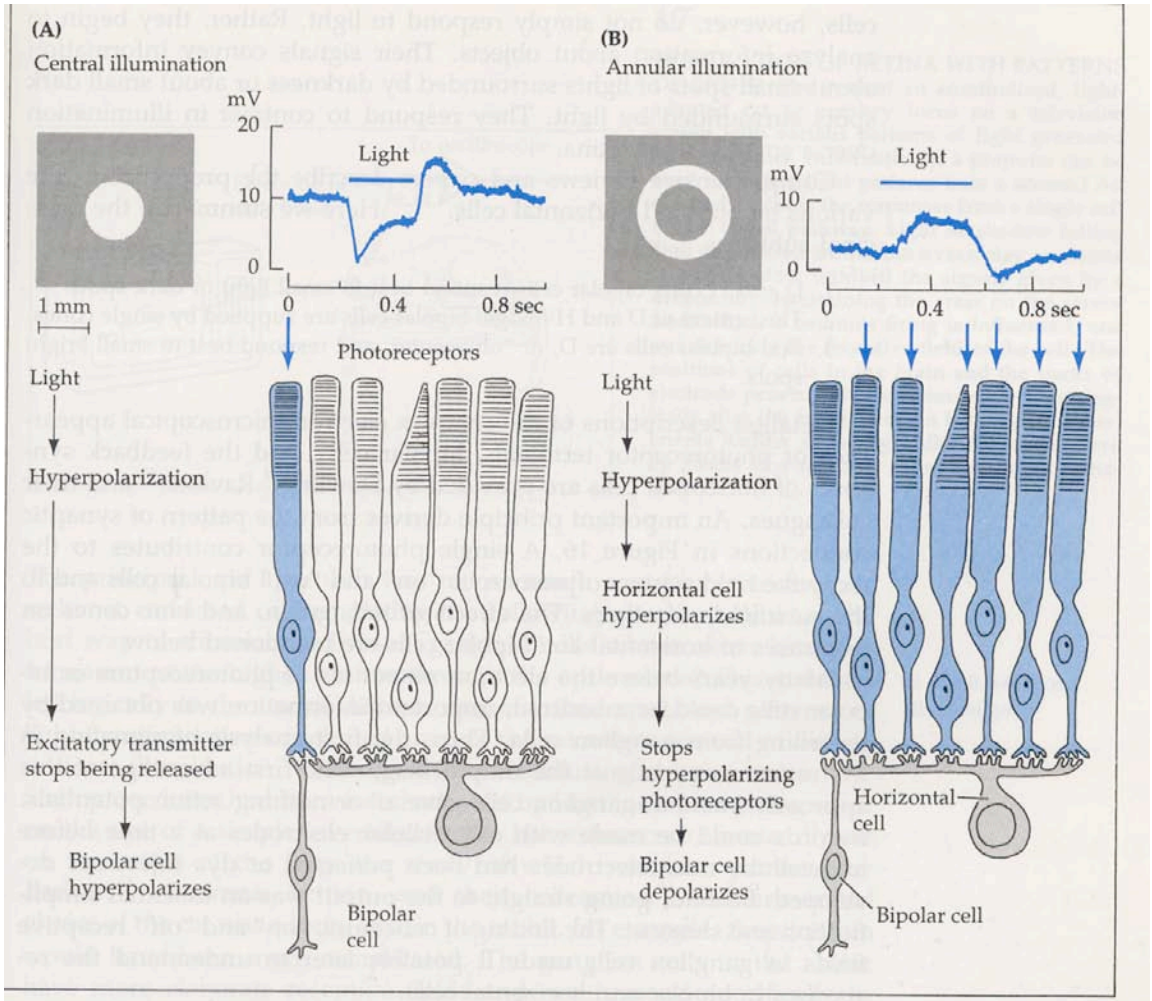


- H bipolars have ionotropic GluRs, and are thus depolarized by transmitter released from depolarized cones in the dark.
- When cone hyperpolarizes in the light it reduces glu release onto H-bp, hyperpolarizing it.
- This in turn reduces H-bp glu release onto RGC, causing its (net) hyperpolarization and reducing its probability of firing.

Bipolar cells III



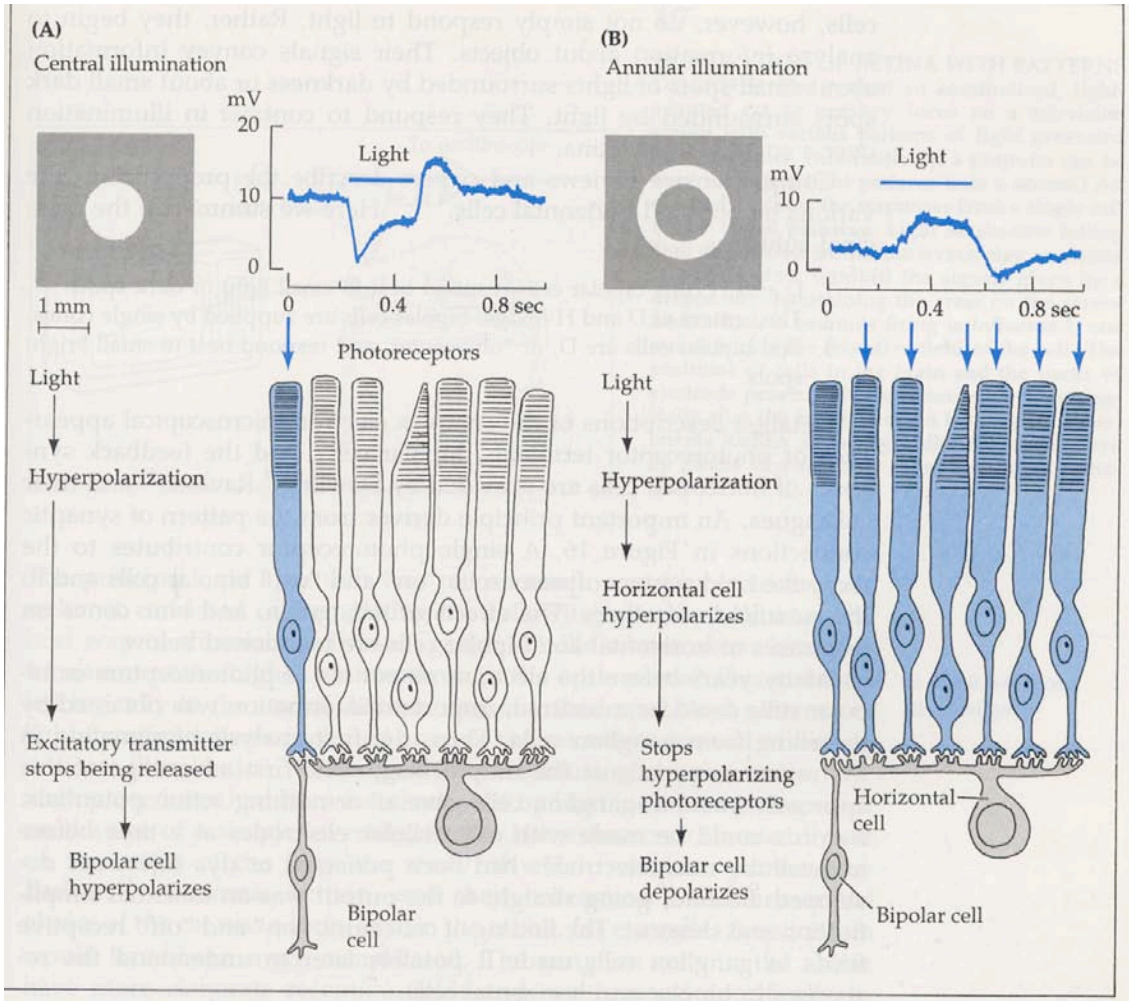
- D bps have the opposite electricaal response to glu: they have a metabotropic GluR that activates a G protein which activates PDE, decreasing ion flux through a CNG channel as in PRs.
- Thus reduction in glu release from cone in light causes a decrease in PDE activity, increasing cGMP, opening channels, and depolarizing the cell.
- The D-bp then releases more glu onto the RGC in the light, increasing its firing probability.



16 RESPONSES AND CONNECTIONS OF BIPOLAR CELL. Records show the receptive field of a bipolar cell in a goldfish retina responding by hyperpolarization (H) to illumination of its center and by depolarization to a ring of light. Other bipolar cells (D) respond in the opposite way (depolarization with central illumination); neither type of bipolar cell generates impulses. The diagrams illustrate connections required to elicit these responses. This is a difficult series of interactions to understand because in one part of the circuit the "stimulus" (light) stops transmitter release, while at another synapse it indirectly causes an increase in transmitter release. (A) Light falling on the photoreceptor causes hyperpolarization. As a result, excitatory transmitter stops being released and the bipolar cell becomes hyperpolarized. (B) Light falling on the surrounding area again prevents transmitter from being released by photoreceptors; as a result, horizontal cells become hyperpolarized. This hyperpolarization prevents the horizontal cell from releasing its inhibitory transmitter onto the photoreceptor. The photoreceptor therefore becomes depolarized and starts to release its excitatory transmitter once again. The bipolar cell becomes depolarized. (Bipolar cell records from Kaneko, 1970.)

Horizontal cells

- Also passive,but inhibitory (GABAergic).
- Light on cones that connect to HC reduces glu release onto HC, hyperpolarizing it and reducing its release of GABA onto cone synapse with bp.
- Thus HC hyperpolarization in light reduces inhibition of glu release from cone.



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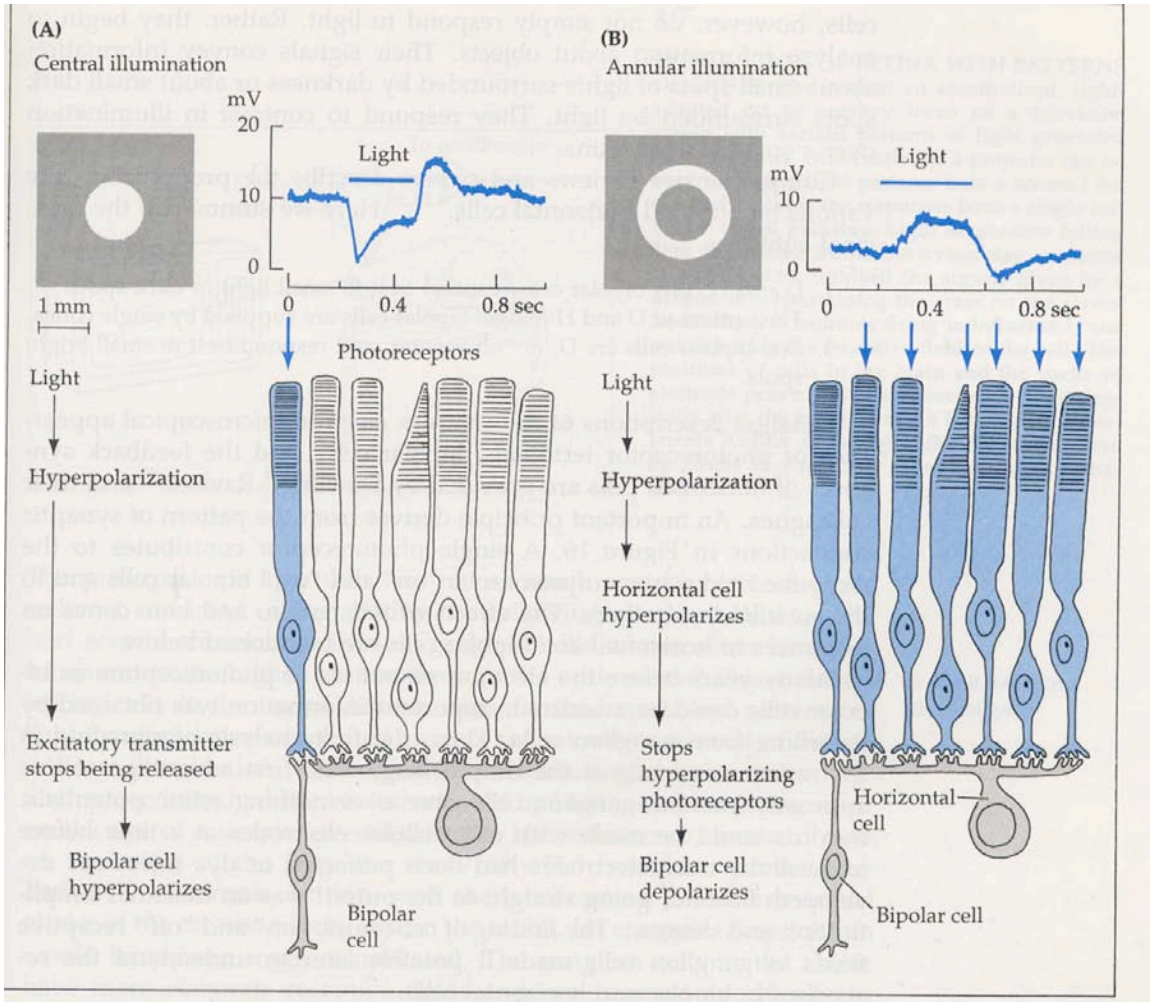
Horizontal cells II

- Light in the surround will cause depolarization of an H-bp through inhibition of HC.
- Conversely, it will cause hyperpolarization of a D-bp.
- Thus the responses of bps to light in the surround are opposite to those to light in the center.



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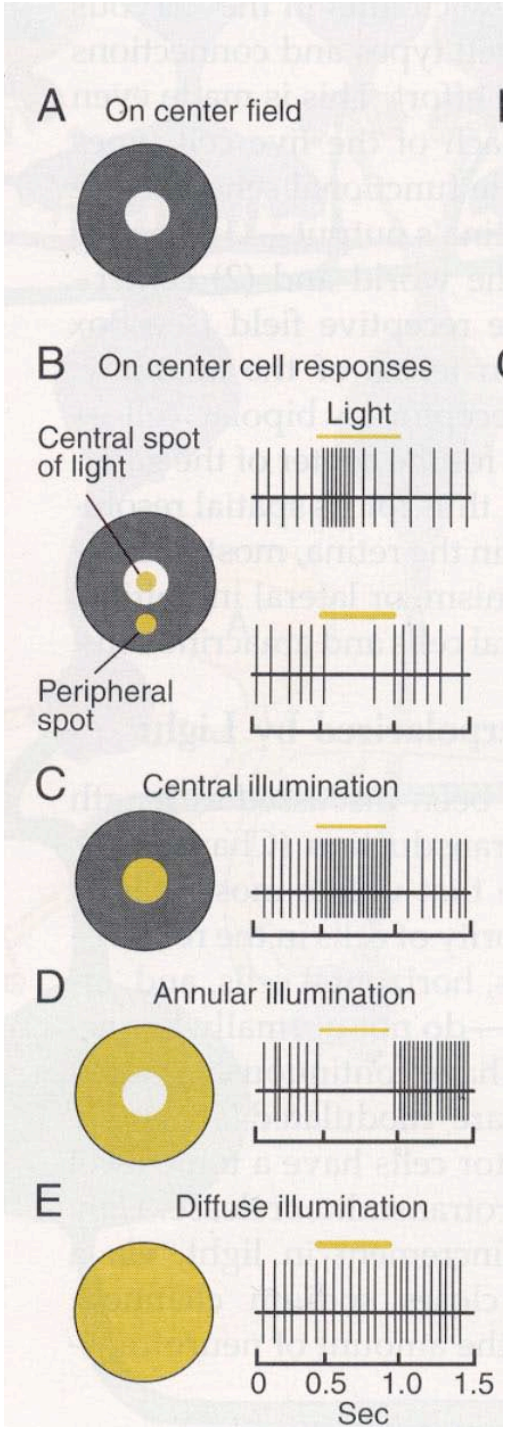
Horizontal cells III

- Circuit diagram means that bp responses to diffuse light are weak.
- Strong bipolar responses (hyperpolarizing or depolarizing) are seen to central illumination or annular illumination.
- This is the first example of a *receptive field*.

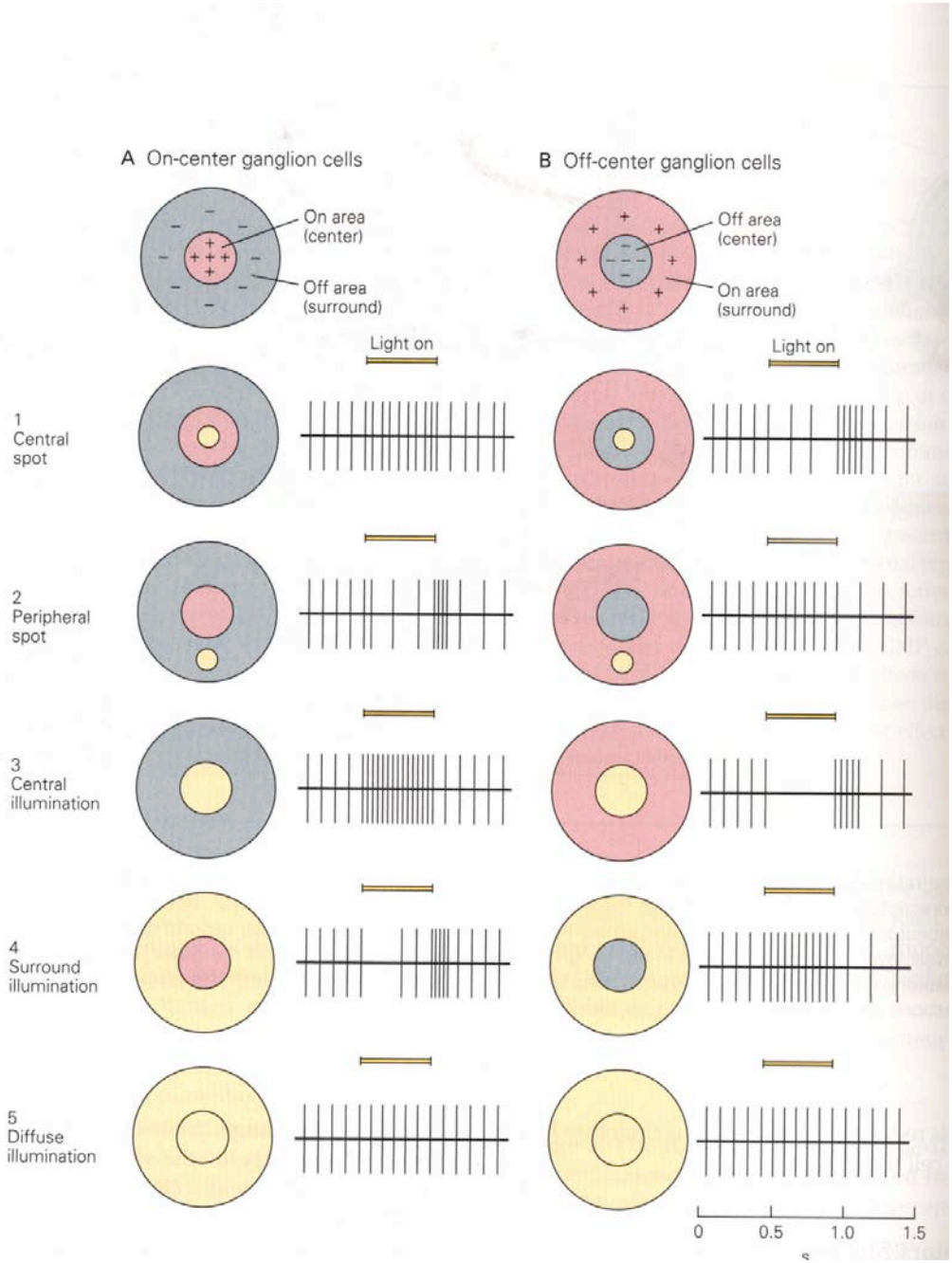
Ganglion cells

- RGCs are connected to bps, and also have center-surround receptive fields.
- RGCs are the outputs of the retina, and fire action potentials.
- An on-center RGC is connected to a D (on-center) bp, and thus depolarizes (fires more spikes) when the D-bp is depolarized.
- This occurs when light is in the center of the D-bp's receptive field.
- Light in the surround hyperpolarizes the D-bp and inhibits the on-center RGC.

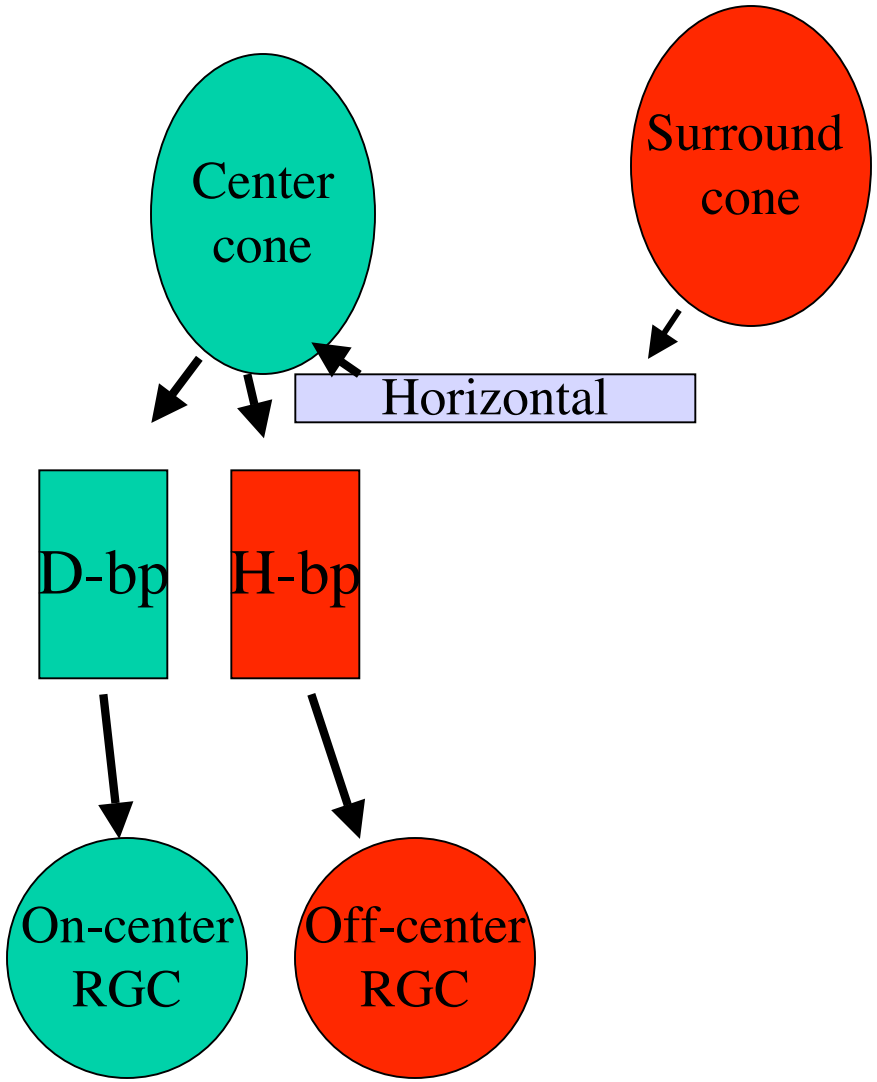


Ganglion cells II

- By the same logic, off-center RGCs are connected to H (off-center) bps, so they hyperpolarize with light in the center of the bp's receptive field.
- Light in the surround depolarizes the H-bp, depolarizing the off-center RGC and increasing its firing rate.

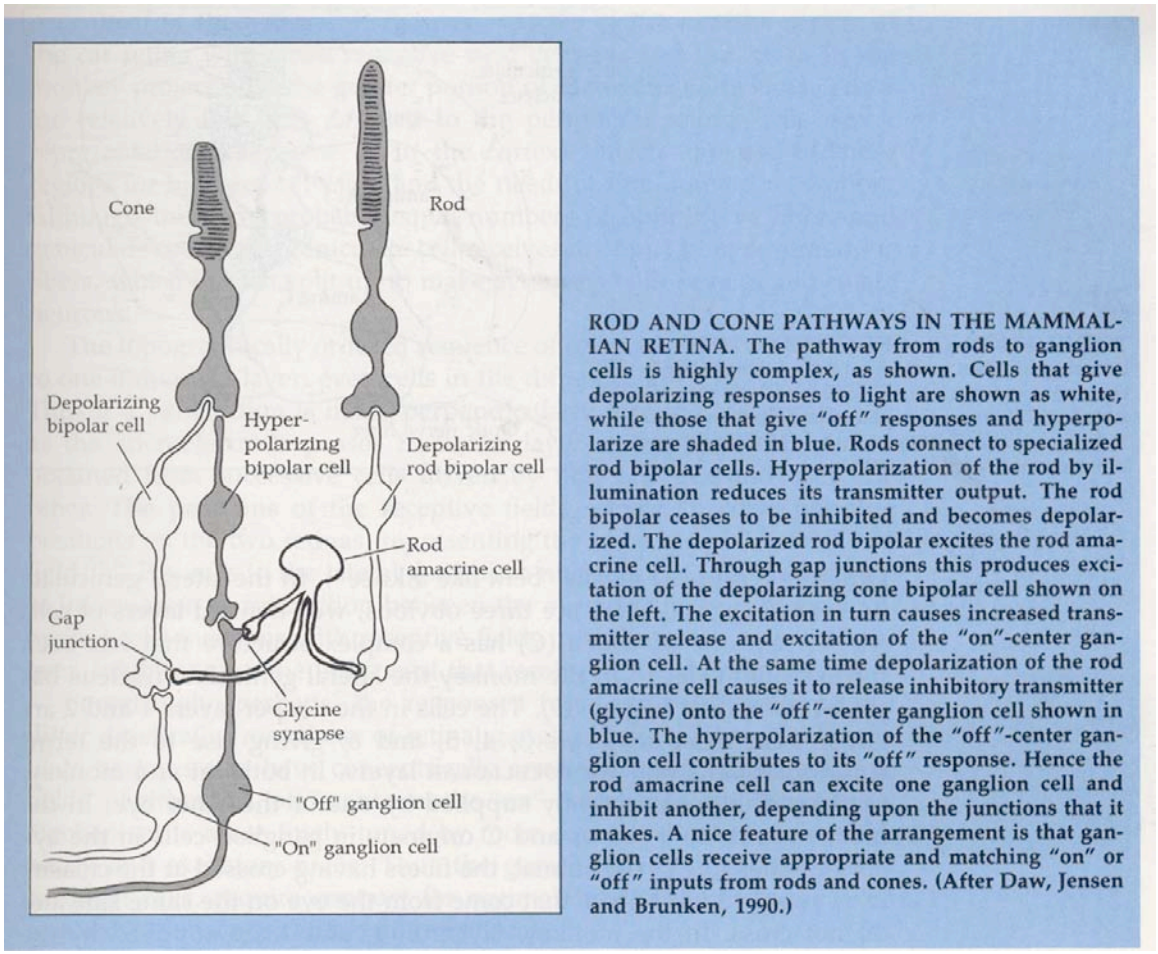


Simplified diagram of the basic retinal circuit



- Light in center: hyperpolarizes center cone. Surround cone is more depolarized-->HC releases more GABA and inhibits center cone, further hyperpolarizing it. D-bp becomes depolarized, switching on on-center RGC. H-bp is hyperpolarized and switches off off-center RGC.
- Light in surround: Center cone depolarized; light hyperpolarizes surround cone--->HC is hyperpolarized, releases less GABA, so center cone is more depolarized. D-bp hyperpolarizes, switching off on-center RGC;H-bp depolarizes, switching on off-center RGC.

Amacrine cells

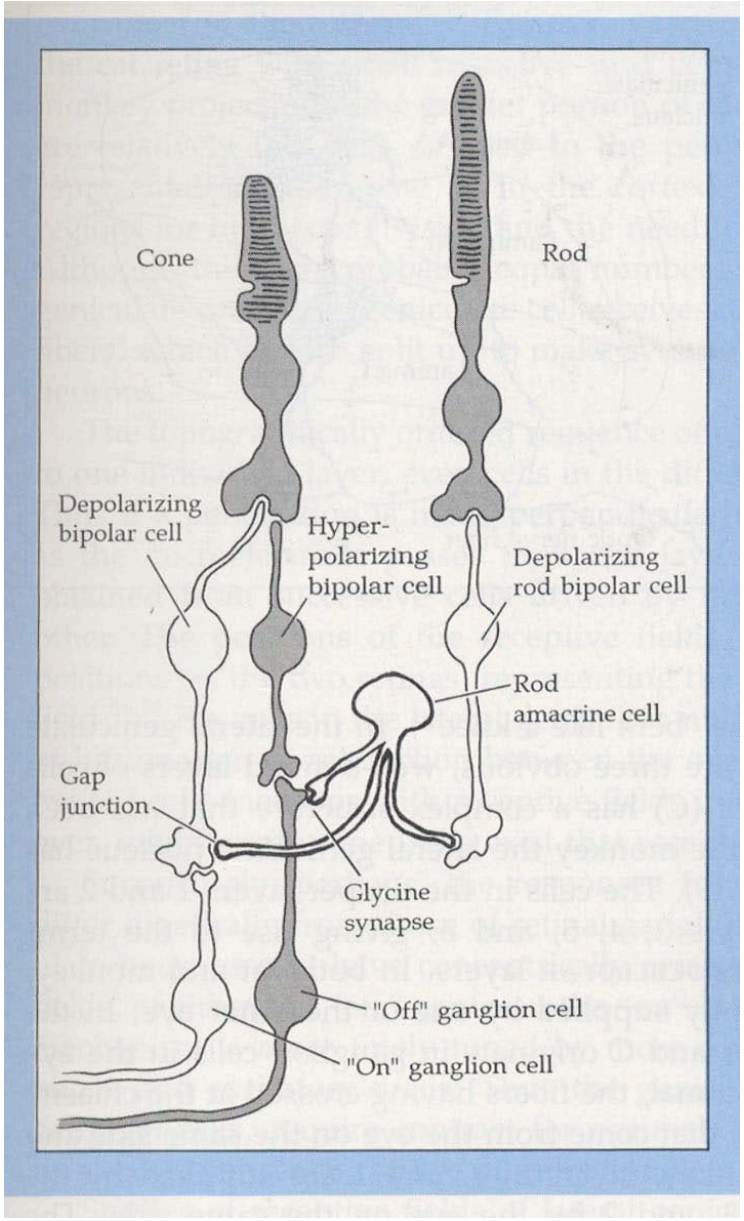


ROD AND CONE PATHWAYS IN THE MAMMALIAN RETINA. The pathway from rods to ganglion cells is highly complex, as shown. Cells that give depolarizing responses to light are shown as white, while those that give "off" responses and hyperpolarize are shaded in blue. Rods connect to specialized rod bipolar cells. Hyperpolarization of the rod by illumination reduces its transmitter output. The rod bipolar ceases to be inhibited and becomes depolarized. The depolarized rod bipolar excites the rod amacrine cell. Through gap junctions this produces excitation of the depolarizing cone bipolar cell shown on the left. The excitation in turn causes increased transmitter release and excitation of the "on"-center ganglion cell. At the same time depolarization of the rod amacrine cell causes it to release inhibitory transmitter (glycine) onto the "off"-center ganglion cell shown in blue. The hyperpolarization of the "off"-center ganglion cell contributes to its "off" response. Hence the rod amacrine cell can excite one ganglion cell and inhibit another, depending upon the junctions that it makes. A nice feature of the arrangement is that ganglion cells receive appropriate and matching "on" or "off" inputs from rods and cones. (After Daw, Jensen and Brunken, 1990.)

- Amacrine cells make horizontal connections like HCs, but fire action potentials.
- Very complex- over 20 types.
- A2 (rod) amacrines connect rods to RGCs.
- Light on rod depolarizes the rod D-bp, exciting the A2 cell.

Amacrine cells II

- A2 cell makes an excitatory (gap junction) synapse onto neighbouring cone D-bp, exciting it and increasing firing rate of on-center RGC connected to it.
- A2 also makes inhibitory synapse onto off-center RGC connected to cone H-bp, inhibiting it.
- This preserves RGC receptive field organization, and ensures matching of dim light (rod) and bright light (cone) responses.



M and P cells

- RGCs are of two types: parvocellular (P) and magnocellular (M).
- P cells connect to few cones, have small receptive fields, and are color-sensitive.
- M cells connect to more cones, have larger receptive fields, are not color-sensitive, have faster response times.
- The M and P cells connect to separate layers of the LGN and on to separate circuits in visual cortex.
- These are called the M and P pathways, and are used to process different features of the image (P-->color vs. M-->motion).

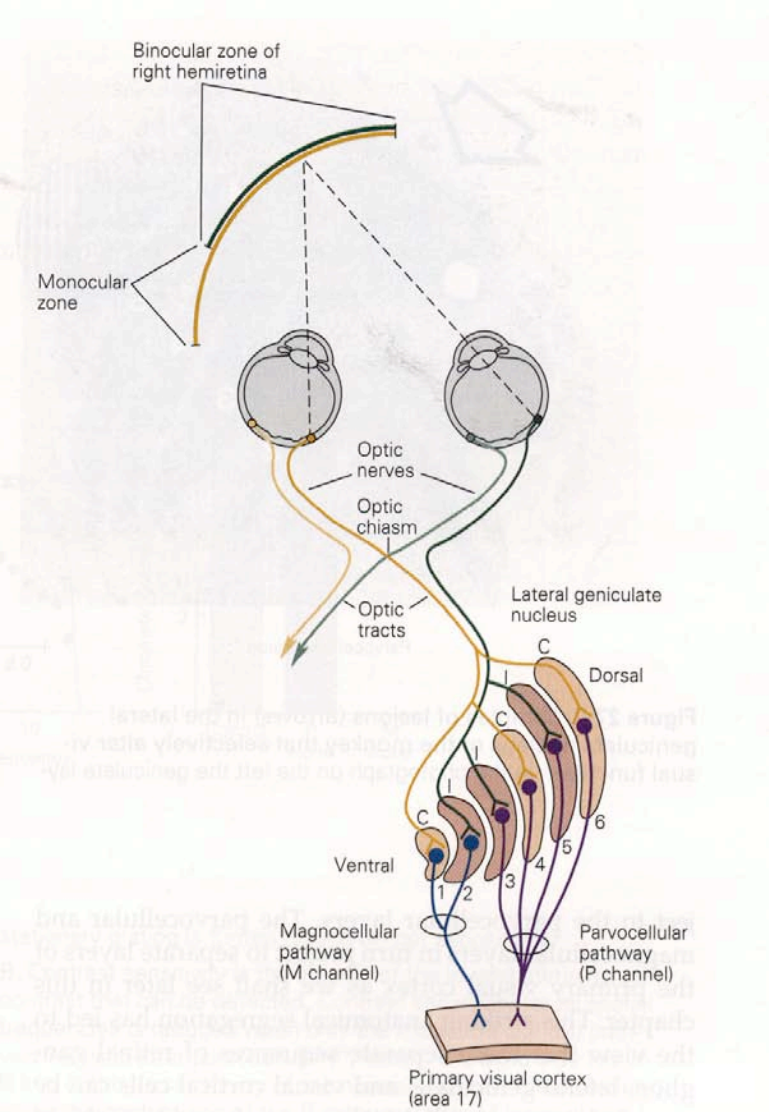
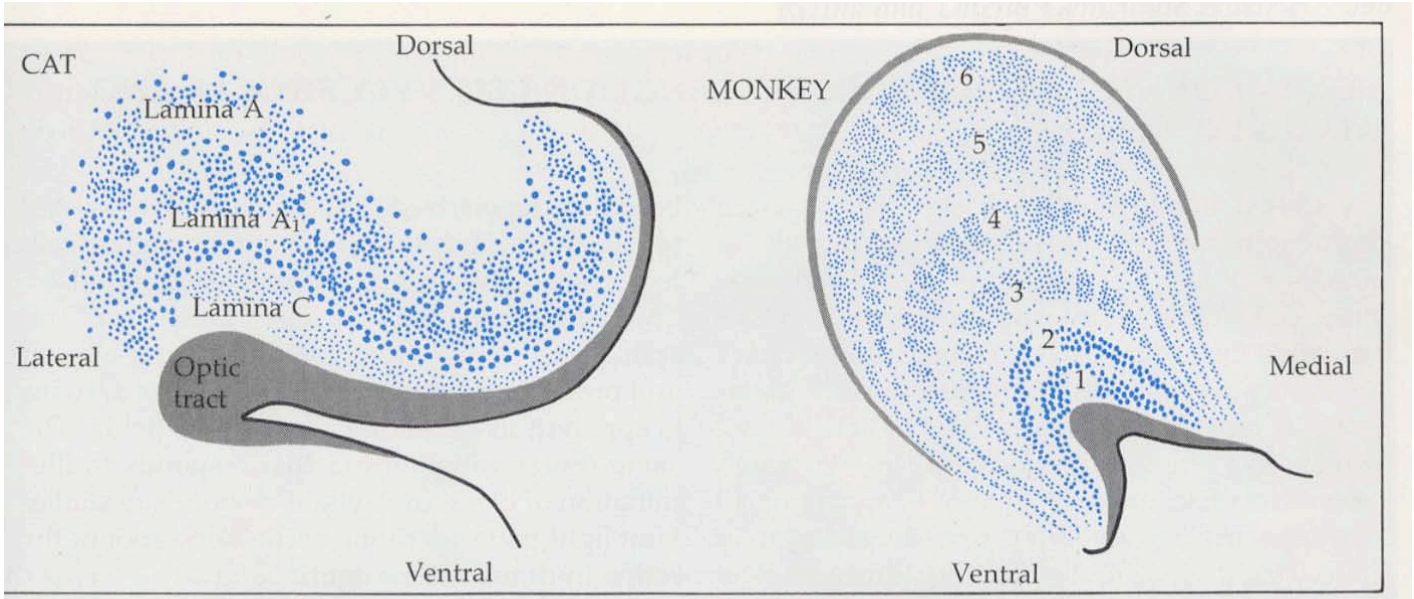


Figure 27-6 **The lateral geniculate nucleus is the principal subcortical site for processing visual information.** Inputs from the right hemiretina of each eye project to different layers of the right lateral geniculate nucleus to create a complete representation of the left visual hemifield. Similarly, fibers from the left hemiretina of each eye project to the left lateral geniculate nucleus (not shown). The temporal crescent is not represented in contralateral inputs (see Figure 27-1). Layers 1 and 2 comprise the magnocellular layers; layers 3 through 6 comprise the parvocellular layers. All of these project to area 17, the primary visual cortex. (C = contralateral input; I = ipsilateral input.)

Connections to LGN

- The right halves of each retina are connected to the right LGN and process the left visual field.
- The right and left (ipsi and contra) eyes connect to different LGN layers.
- M and P RGCs also connect to different LGN layers.
- LGN cells also have center-surround receptive fields.
- LGN acts as a separator of M and P pathways and as a relay to visual cortex.

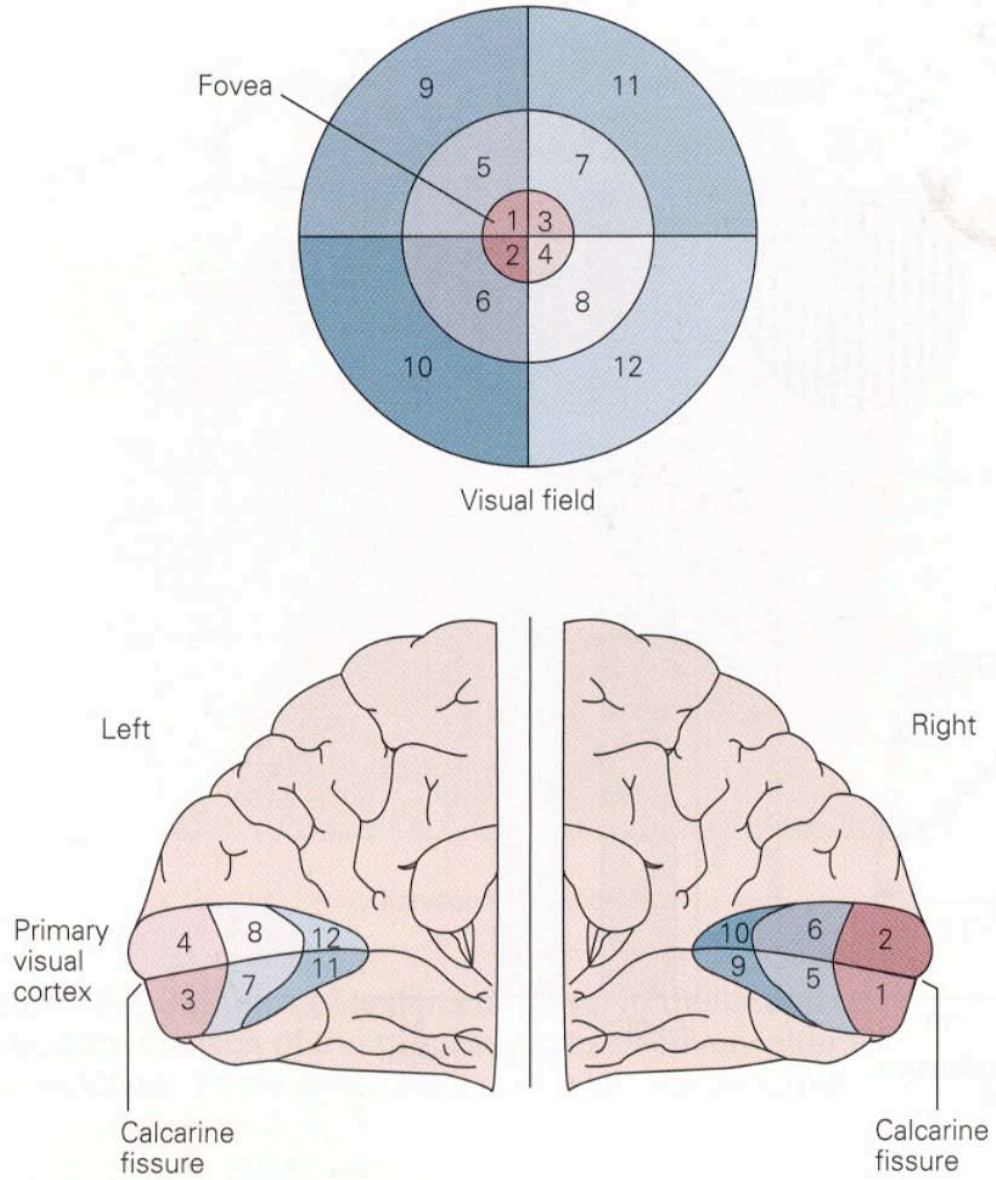
LGN II



19 LATERAL GENICULATE NUCLEUS. (A) In the lateral geniculate nucleus of the cat, there are three layers of cells: A, A_1, and C. (B) In the monkey, the lateral geniculate nucleus has six layers. In the four dorsal layers (3, 4, 5, 6; parvocellular), the cells are smaller than in layers 1 and 2 (magnocellular). In both animals, each layer is supplied by only one eye and contains cells with specialized properties. (From Szentágothai, 1973.)

- LGN is not just a relay;there are ~10X more back-connections from visual cortex to LGN than forward connections from LGN to visual cortex.
- The roles of these corticothalamic back-connections are not well understood.

Representation of the visual field in retina and visual cortex.



- 50% of visual cortex is used to process input from the foveal region, which is 4% of retinal area.