The Neurology of Vision

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Linus D. Sun

It is estimated that nearly half of the brain's neurons are connected directly to the retina and involved in the processing of vision, attesting to the paramount importance of vision in brain functioning. For more than a century, scientists have investigated the visual system through studies of its complex anatomy, biochemistry, and physiology. Although we are still at the early stages of understanding vision, great progress is being made toward deciphering how the brain interprets shapes, objects, movement, location, and facial recognition.

The optical system of the cornea and lens projects focused images of the external world onto the retina, but experiencing and interpreting conscious, visual phenomena involve structures deep within the brain's cortex and brain stem. Scientists have only begun to decode and build neural network models to simulate and explain how what we experience as vision is processed and interpreted by the brain.

Visual experience begins in the retina. There are approximately 120 million photoreceptors (7 million cones and 110 million rods) in each retina that receive images from the external world. Rod receptors respond to low light; cone receptors are less sensitive to low light but are specialized to distinguish color, which rods are incapable of doing. While peripheral vision is represented in the outer retina, the highest density of photoreceptors, and thus high-resolution vision, is in the center of the macula known as the fovea. Cone receptors are most densely packed in the fovea, where there are few rods, and hence, the central retina is less sensitive to dim light but exquisitely responsive to color discrimination. This anatomic organization has been known by astronomers for many years, using a technique known as "averted vision": stars that are too dim to be detected directly by the fovea may become visible when the observer looks adjacent to the star, placing it on the low-light receptive, black and white (scotopic) portion of the retina, rather than the central, color-specialized fovea (photopic). This phenomenon occurs because of higher rod density in parafoveal areas, which enhances low-light visual acuity.

Highly accurate acuity and color vision is best appreciated in the fovea, where 20/20 or better vision is possible. Foveal color cones are densely packed, approximately 50 per square micrometer, compared to approximately 12 in parafoveal areas. The majority of cone cells respond to red light and a smaller amount to green light; very few actually respond to blue light, which results in vision more heavily weighted toward the yellow-green spectrum. It is this central retinal area that is most sensitive to disruption by calcification (drusen) or fluid collection in macular degeneration.

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D. S. Casper, G. A. Cioffi (eds.), *The Columbia Guide to Basic Elements of Eye Care*,
https://doi.org/10.1007/978-3-030-10886-1_38

Vision is enabled by proteins located within photoreceptor cells (rhodopsin, also known as "visual purple," in rods and photopsin in cones), which are activated by light, initiating a biochemical pathway that produces an electrical signal. Rhodopsin and photopsin are part of a group of proteins known as opsins. This group also includes melanopsin, a blue light-sensitive visual pigment that is found in ganglion cells, but not photoreceptor cells, and is involved in pupillary reflex and circadian rhythm activities, rather than conscious visual perception. The photoreceptor cell's electrical signal, through neural transmission, is processed by retinal ganglion cells and inhibitory interneurons. Ultimately, through the retinal ganglion cells this signal is transmitted to the brain for visual perception.

The retina is able to detect and processes light, dark, motion, contrast, and edges. It can sense total light input and adjust its sensitivity to the wide range of light levels we experience. Because the ratio of photoreceptors to ganglion cells is approximately 100:1, a major component of image processing involves compression of signal information as it proceeds toward the inner retina. Color and light are first acquired in the deepest (outer) retinal layer (Fig. 38.1): this information is processed initially via photoreceptors and, subsequently, through a parallel series of interactions between bipolar cells (within the inner nuclear layer), inhibitory amacrine interneurons, and laterally connected inhibitory horizontal cells, which act to suppress surrounding photoreceptors. Final output is through the gan-

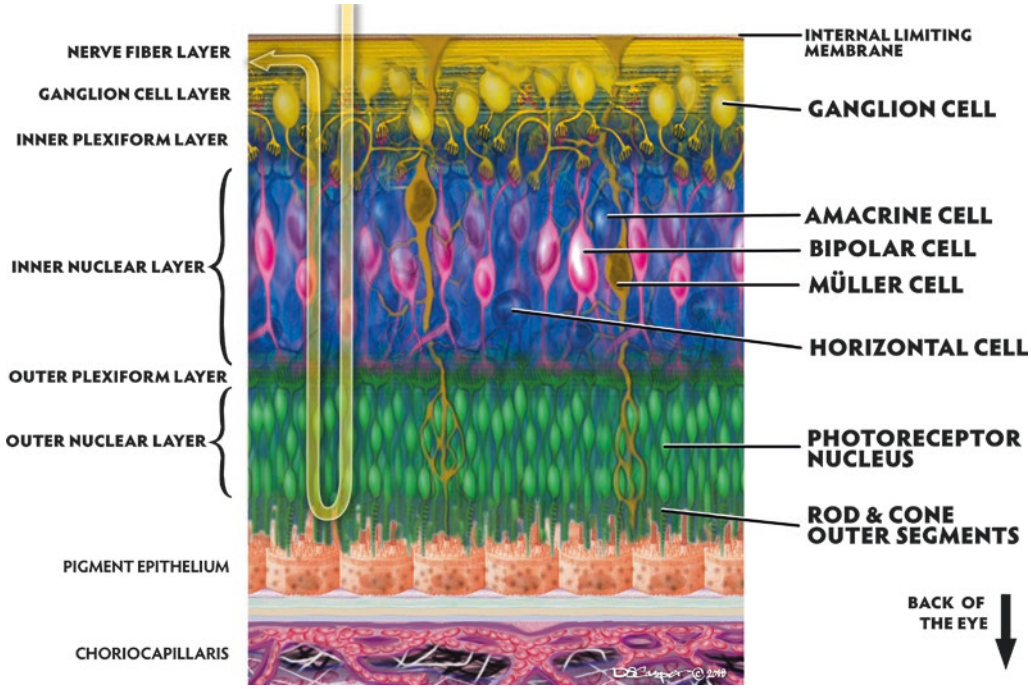


Fig. 38.1 Retinal microanatomy and image processing (long arrow represents the path of information through the retina to the ganglion cell axon). Light enters from the top of the illustration and traverses the transparent retina to reach the posteriorly located rod and cone photoreceptors. There, light is converted to neural signals which are then processed in a chain-like fashion from deep ("outer") retinal structures (bottom) to the superficial ("inner") layers. In the ganglion cell layer, information is organized and output via the nerve fibers, which converge at the optic nerve, which then exits the eye (see Chap. 1). The pigment epithelium layer absorbs excess light which helps to reduce scatter and improve the image, as well as provide nutrients to the photoreceptor cells.

glion cells, whose axons form the retinal nerve fibers that travel radially across the superficial (inner) retinal surface and converge to form the optic nerve, which exits the eye and enters the central nervous system. Through electrophysiological studies, we know that patches of photoreceptors are connected to individual retinal ganglion cells (RGCs) whose activity is referred to as receptive fields. Individual ganglion cells respond to small columns of photoreceptors of the same color, while surrounding photoreceptors inhibit the ganglion cell response. This is known as the "center-surround" receptive field and this type of signal processing is propagated throughout all neurons in the visual system. Thus there is a one-to-one connection between microscopic portions of the retina and individual, visually responsive neurons that exist throughout the brain's visual pathway.

Five classes of retinal ganglion cells have been identified, each of which plays a specific role in visual processing:

- *Midget retinal ganglion cells* comprise 80% of all RGCs and have small receptive fields that are color sensitive, have slower conduction velocities, and project to the *"What" color detail selective layers (or parvocellular pathway)* of the lateral geniculate nucleus (LGN). Some scientists refer to these cells as the P-cell for its connection.
- *Parasol retinal ganglion cells* represent 10% of all RGCs, are connected to more rod and cone cells (thus having larger receptive fields), have faster conduction velocities, and project to the *"Where" motion selective layers (or magnocellular pathway)* of the LGN. They are sometimes referred to as the M-cell for it's connection.
- The *bistratified cell* is intermediate in receptive field size and sensitivities ("on" to blue cone input but "off" to green and red), have large receptive fields, and may be participate in *color vision perception*.
- As mentioned above, a population of *specialized photosensitive ganglion cells* respond to light due to their melanopsin photopigment; they have large receptive fields and are thought to *modulate circadian rhythms* directly via the suprachiasmatic nucleus and control the pupillary light reflex via the Edinger-Westphal nucleus.
- *A specific group of visually sensitive retinal ganglion* cells bypasses the cortical visual processing system. They project directly to the *saccade-driving* superior colliculus in the brain stem and thus subconsciously elicit the fastest reaction time eye movement to a visual stimulus (90–120 ms); if the slower conscious motor-vision network is engaged, the latencies are longer and are typical for human reaction times (170–230 ms).

After exiting the posterior globes and orbits, the optic nerves merge in the optic chiasm, just above the pituitary stalk, and segregate based on vertical hemifields (see Chap. 36). Post-chiasmal optic tracts continue posteriorly to the lateral geniculate bodies of the thalamus, where the majority of the brain's initial visual processing begins (Fig. 38.2).

The lateral geniculate nucleus (LGN) of the thalamus has distinct layers, defined by which eye from which it receives input. Thalamic structures are considered "way stations" for sensory information collected from peripheral organs. There are also extensive connections between the cortex and thalamic nuclei – only about 5% of inputs into the LGN originate in the retina. The remaining 95% are reciprocal connections with the visual cortex, superior colliculus, pretectum, thalamic reticular nuclei, and local LGN interneurons. This suggests that the LGN plays a significant role in visual perceptual processing, which includes stereoscopic vision, vergence to an object of regard, motion, eye positioning, and attention. LGN output travels through the optic radiations in the retrolenticular limb of the internal capsule to what is known as the striate cortex (primary visual cortex, V1). Input arrives in layer 4 of V1, which sends feedforward connections to higher visual areas (V2, V3, V4, V5) in the occipital cortex. Layer 6 in V1 sends its output back to the LGN to complete the feedback circuit. LGN neurons are not "tuned" for detecting edges; the primary visual cortex performs this task.

Each hemi-primary visual cortex receives contralateral visual field input from both eyes (i.e., the right primary visual cortex receives left visual field input from both eyes and vice versa; see Fig. 38.2). Hubel and Wiesel (1960s) received the Nobel Prize in part for their discovery that primary V1 neurons have receptive fields that respond to light edge stimuli oriented at a specific angle. It is highly instructive to witness their original mapping experiments, which are available online (https://youtu.be/KE952yueVLA). Remarkably, millimeter-wide stripes in V1 appear as "columns" in cross-section; these are organized by which eye provides input to those neurons in a particular column (Fig. 38.3). Within a group of several neurons, the orientation preference of adjacent neurons is not random but continuously and topographically organized into a "pinwheel"-like arrangement. While it is thought that early stereopsis is processed in area V2, it is likely that motion, shadow, and vergence cues are combined throughout the brain to produce full stereo vision. This is an area of active investigation in vision neuroscience.

Visual information is first processed in the striate cortex and then streams from V1 to other cortical areas that are concerned with "What" things are and "Where" those things are located

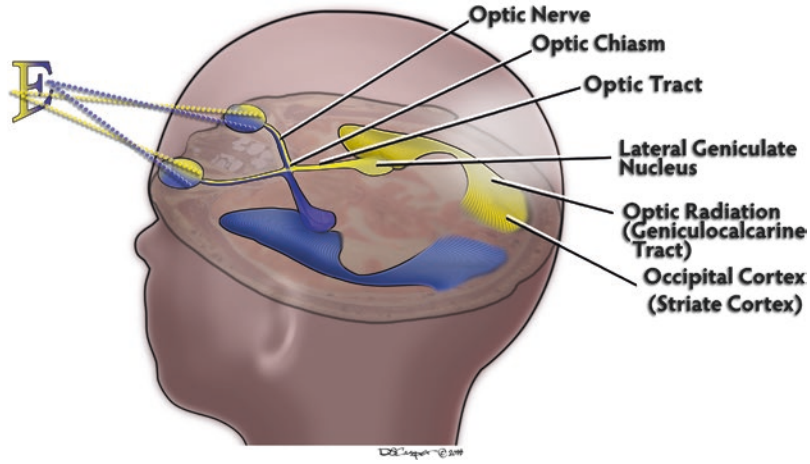
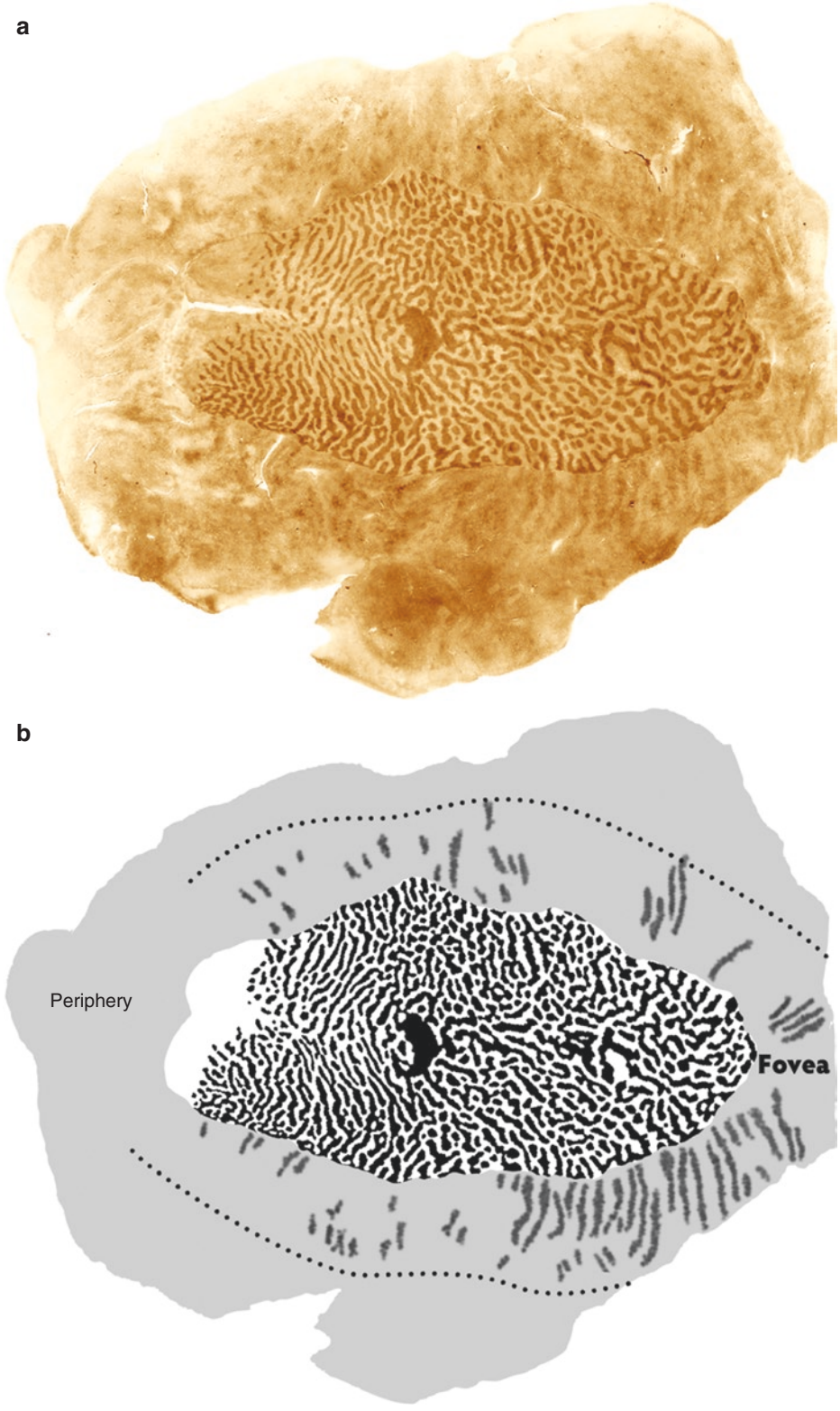


Fig. 38.2 A schematic view of the visual pathway from object to the visual cortex. Image projections are separated along the retinal vertical medians and travel together. Combined nasal and temporal nerve fibers enter the middle cranial fossa as the optic nerves but segregate out into separate temporal and nasal retinal information at the optic chiasm (note that the yellow, left half of the image contributes only to the right visual path intracranially, while the purple, or right side of the image, becomes the left; this is accomplished by temporal fibers remaining on the ipsilateral side, while nasal fibers cross over at the chiasm). Segregated right and left retinal information continues posteriorly in the optic tracts, is further processed in the lateral geniculate nuclei, and then reaches the visual cortex via the optic radiations. Not shown are optic tract fibers which leave the visual pathway prior to the lateral geniculate nuclei and terminate at the Edinger-Westphal nucleus, hypothalamic nuclei, and the superior colliculi to enable pupillary, circadian, and saccadic processing

Fig. 38.3 The complete pattern of ocular dominance columns in the human brain. (**a**) Cytochrome oxidase (CO) activity in layer 4 Cβ montage of the right primary visual cortex after loss of the right eye. The CO pattern in V2 is a montage compiled from three sections passing through layer 4. (**b**) Ocular dominance columns rendered by high-pass Fourier filtering of the image in (**a**). Columns are absent in the blind spot and monocular crescent regions. (From Adams DL, Sincich LC, Horton JC. Complete pattern of ocular dominance columns in human primary visual cortex. J Neurosci. 2007;27(39):10391–403, with permission)


a
b
Periphery
Fovea

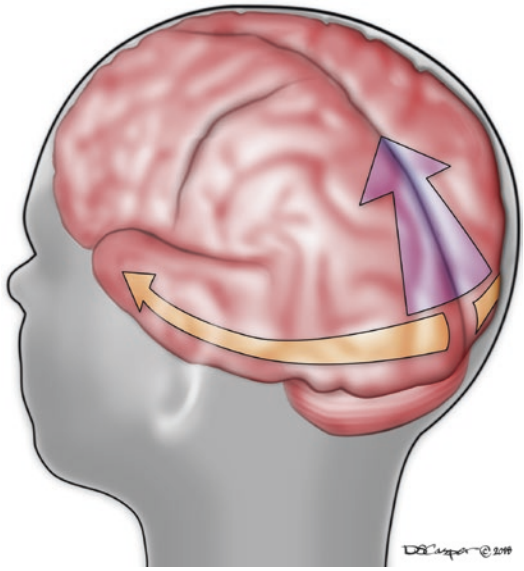


Fig. 38.4 V1 neurons project to two functional pathways: (1) the "What" pathway (horizontal arrow) where slow, color-sensitive parvocellular lateral geniculate nucleus (LGN) neurons project to V1, V2, and V4 and then project ventrally to the inferior temporal cortex; and (2) the "Where" pathway (vertical arrow), where fast magnocellular LGN neurons project to V1, V2, and V3 and then to the medial temporal cortex (MT) for motion processing and to the posterior parietal cortex for attention, localization, and action. (Data from the image found at https://en.wikipedia.org/wiki/Visual_cortex (https://commons.wikimedia.org/wiki/File:Ventral-dorsal_streams.svg) under the GNU Free Documentation License, version 1.2)

(Fig. 38.4). The "Where" pathway runs dorsally, projecting to area V5/MT (medial temporal cortex in humans) and the posterior parietal cortex. This is a specialized pathway where speed and motion in vision are processed. MT lesions (through trauma, neurodegenerative disease, or medication effects) lead to the perception that motion is frozen (akinetopsia) or that objects leave a trail of afterimages (palinopsia). However, these patients maintain the ability to identify objects.

The ventral "What" pathway appears to be involved in conscious identification of objects and features. For example, lesions to areas associated with V4 can cause loss of color vision (cerebral achromatopsia). Associated with V4, and nearby in the inferior temporal cortex, is the fusiform gyrus. Lesions in this area produce an inability to recognize faces, even familiar ones like the patient's parents and siblings (prosopagnosia). In a monkey model, neuroscientists have discovered that facial features are broken down into a series of information nodes that work together as a network to encode memory traces (engrams) of individually recognized faces.

Lesions to the right parietal cortex through large strokes in the middle cerebral artery territory can produce a particularly debilitating condition referred to as the contralateral hemispatial-neglect syndrome. In this condition, patients with a right unilateral parietal cortical defect are "blind" to stimuli in their contralateral left visual field, in either visual or personal sensory space. This can be tested with double simultaneous visual or tactile stimulation of the patient. For example, a patient with a right parietal lesion may forget to put their left arm into a sleeve, or to shave the left side of their face, or, negelct to eat food off the left side of their plate. Navigation and independent living are severely limited in these patients, much more so than in patients with verbal aphasias or hemiparesis. Right sided hemispatial neglect is rare because it is redundantly encoded in the brain bilaterally. While the left side of the world is predominantly encoded in the right hemisphere for most right-handed (left dominant) brains.

Hemispatial neglect (the absence of awareness) should not be confused with hemianopsia. Conscious awareness of vision requires intact visual processing areas located within the temporal-parietal cortex. Lesions to the optic tracts, LGN, and optic radiations, which spare the temporal and parietal cortex (see Chap. 36), result in a hemianopsia. Patients are fully aware of this specific type of visual scotoma, particularly if it is acquired later in life. Over time, however, patients may fill in empty regions by a perceptual illusion that replaces the blind area with the surround.

Suggested Reading

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