ity that is progressively lost in older nymphs or adults. Bees reared in UV are less sensitive to light of longer wavelengths; terminals of photoreceptors that peak in the green, in which the bees were deprived, also have fewer synapses. Other examples of structural plasticity are reported. In flies, lamina feedback synapses are more numerous in young dark-reared adults, and during subjective night in flies held under constant darkness; these synapses also exhibit reactive synaptogenesis after losing their targets, R1–R6. Photoreceptor input synapses are not fixed synaptic sites: fly tetrads can both form and disappear rapidly in the adult, in minutes, especially in response to functional reversals (light exposure after dark rearing; warm recovery after cold exposure). Central optic lobe neurons sprout after congenital deprivation of their visual inputs, procured either by lesion or mutation. The volume of the optic neuropils increases in *Drosophila* reared under "enriched" conditions, relative to solitary rearing, and with various other rearing conditions. At the cellular level, L1 and L2 change the calibre of their lamina axons during a cycle of day/night changes.

4. The morphogenetic interdependence of eye and visual centers

Development in the visual centers generally exhibits some dependence on innervation from the eye, but this is quantitatively variable; eye development is usually autonomous. In *Drosophila*, clones of mutant tissue with perturbed organization generated in either the eye or optic lobe reveal that abnormal pattern is communicated from the retina to the lamina, but not in the opposite direction. This confirms the coarser effects of deafferentation in many species. More central neuropils are volumetrically less affected by deafferentation. In congenitally eyeless mutant *Drosophila*, second-order neurons in the lamina never differentiate but some medulla neurons grow axons, albeit their morphogenesis is abnormal, whereas many lobula neurons look quite normal and establish a regular array of neuropil columns. Tangential cells of all neuropils show complete autonomy from centripetal innervation. Qualitatively similar results follow lesions in the embryonic *Daphnia* eye. Differentiation in the fly's lamina and medulla is largely unaffected by the absence of target cells on the lobula, indicating the relative absence of retrograde influences of central visual neuropils upon distal ones. On the other hand, ommatidia eventually degenerate after disconnection from the lamina, indicating that the optic lobe has a retrograde influence on the long-term maintenance of the retina.

References

Ali MA, ed. (1984): *Photoreception and Vision in Invertebrates*. NATO ASI Serie A, Vol. 74, New York: Plenum Press

Dickson B, Hafen E (1993): Genetic dissection of eye development in *Drosophila*. In: *The Development of Drosophila melanogaster*, Bate M, Martinez Arias A, eds. Plainview, NY: Cold Spring Harbor Laboratory Press, pp. 1327–1362

Krämer H, Cagan RL, Zipursky SL (1991): Interaction of *bride of sevenless* membrane-bound ligand and the *sevenless* tyrosine-kinase receptor. *Nature* 352:207–212

Macagno E (1984): Formation of ordered connections in the visual system of *Daphnia magna*. *BioScience* 34:308–312

Meinertzhagen IA (1973): Development of the compound eye and optic lobe of insects. In: *Developmental Neurobiology of Arthropods*, Young D, ed. Cambridge: Cambridge University Press, pp. 51–104

Meinertzhagen IA (1990): Development of the squid's visual system. In: *Squid as Experimental Animals*, Gilbert DL, Adelman Jr WJ, Arnold JM, eds. New York: Plenum Press, pp. 399–419

Meinertzhagen IA, Hanson TE (1993): The development of the optic lobe. In: *The Development of Drosophila melanogaster*, Bate M, Martinez Arias A, eds. Plainview, NY: Cold Spring Harbor Laboratory Press, pp. 1363–1491

Quiring R, Walldorf U, Kloter U, Gehring WJ (1994): Homolgy of the *eyeless* gene of *Drosophila* to the *Small eye* gene in mice and *Aniridia* in humans. *Science* 265:785–789

Schneider T, Reiter C, Eule E, Bader B, Lichte B, Nie Z, Schimansky T, Ramos RGP, Fischbach K-F (1995): Restricted expression of the irreC-rst protein is required for normal axonal projections of columnar visual neurons. *Neuron* 15:259–271

Selleck SB, Gonzalez C, Glover DM, White K (1992): Regulation of the G1-S transition in postembryonic neuronal precursors by axon ingrowth. *Nature* 355:253–255

Wolff T, Ready DF (1993): Pattern formation in the *Drosophila* retina. In: *The Development of Drosophila melanogaster*, Bate M, Martinez Arias A, eds. Plainview, NY: Cold Spring Harbor Laboratory Press, pp. 1277–1325

Zipursky SL, Rubin GM (1994): Determination of neuronal cell fate: Lessons from the R7 neuron of *Drosophila*. *Annu Rev Neurosci* 17:373–397

See also Fly, visual system; Visual transduction; Pioneer neurons; Photoreceptors and photoreceptor dysfunctions; Genes and behavior in *Drosophila*; Neuroscience, comparative; Identified neurons and behavioral determinism; Neural development, genetics; Fly, neuronal control of visual orientation

Update (April 1998)

Details of the molecular characterization of *Pax-6* genes and transcripts, the patterns of their expression, and of the phenotypic characterization of their mutants, supports the view that *Pax-6* is universally associated with the developing eyes in diverse animal groups, and that it is a master regulator for eye development, at least in *Drosophila*.

Callaerts P, Halder G, Gehring WJ (1997): *Pax-6* in development and evolution. *Annu Rev Neurosci* 20:483–532

Visual system, organization

John Allman

In most animals the eyes are directed laterally and the visual field is nearly panoramic, which enables them to detect the approach of potential predators from nearly all directions. In a few animals such as primates, cats and owls, the eyes are directed frontally, and the visual field is thus constricted. It has often been suggested that frontally directed eyes in primates provide these creatures with a large binocular field, thus enabling them to make stereoscopic depth judgments when leaping from branch to branch. However, many prodigious branch leapers such as squirrels have laterally directed eyes. An alternative explanation offered by M. Cartmill is that ancestral primates, like cats and owls, were visual predators. Indeed the living primates that most resemble ancestral primates, the tarsiers, are predators. As I have noted elsewhere, cats, owls and tarsiers have more in common than just being predators; they are also nocturnal, and it is highly probable that ancestral

primates were nocturnal as well. Because of bilateral symmetry, all predators tend to position themselves so their prey lie straight ahead of them when they prepare to strike. Thus, the portion of the visual field straight ahead is particularly important to the predator as it observes the prey's defenses. The neural representations in the brain of the portion of the visual field straight ahead are commensurately expanded. However, in the dimly illuminated world of the nocturnal predator, the optical clarity of the retinal image also plays an important role. In the eye of the predator, as in most optical systems, the clearest image is created by the rays near the rotational axis of the system. Thus, for an animal with laterally directed eyes the retinal image for objects straight ahead will be somewhat compromised. In a brightly illuminated environment this image degradation can be minimized by stopping down the pupil and thus restricting the off axial rays, but this option is not available to the nocturnal predator. Thus, optimal retinal image quality for the portion of the visual field straight ahead would provide a selective advantage to nocturnal predators with frontally directed eyes. Frontally directed eyes offer several additional advantages to nocturnal predators. Binocular correlation of the retinal images might facilitate the detection of camouflaged prey, and binocular summation might facilitate the detection of prey under low light conditions.

Predatory primates use their hands to seize their prey. This behavior presumably is linked to the development of neural mechanisms for eye–hand coordination. The meticulous manual grooming of the fur, including the removal of minute ecto-parasites, may be a relic in higher primates of the predatory behavior of earlier primates.

R.D. Martin has suggested that the ancestral primate adaption was to the "fine branch niche". Ancestral primates were small creatures who used their prehensile hands and feet to grasp the fine terminal branches of tropical trees, a niche rich in insect and small vertebrate prey. This is a particularly complex environment in which to move about since the fine branches provide an unstable platform, thus placing greater demands on the orienting functions of the visual system.

The fossils of Eocene primates more than 50 million years old possessed expanded bony orbits that in life encircled large eyes and cranial endocasts that reveal a commensurate expansion of the occipital and temporal lobes. The organization of the cerebral cortex in early primates cannot, of course, be determined directly, but it is possible to arrive at a number of inferences on the basis of what is known of the physiology and anatomy of the cortex in living primates. Figure 1 illustrates the organization of the cortex in the owl monkey, macaque monkey and human. The occipital, much of the temporal, and even some of the parietal and frontal lobes are devoted to the processing of visual input. Since the last common ancestor of owl monkeys, macaque monkeys and humans lived no more recently than the Eocene and since there is fossil evidence for occipital and temporal lobe expansion in that period, it is likely that early primates possessed an extensive array of cortical areas.

The main source of visual input to the cerebral cortex arrives via the geniculostriate system which contains two principal ascending pathways originating in the retina. The first is a fast conducting pathway that is relayed by neurons in the magnocellular laminae of the lateral geniculate nucleus to layer 4C-alpha of V1, then to layer 4B in V1, then to MT. The neurons in layer 4B of V1 and in MT are usually highly sensitive to the direction of stimulus motion. Findings by J.A. Movshon and his collaborators show that some MT neurons respond to the apparent direction of motion of complex patterns, whereas V1 neurons respond to the actual direction of motion of the components of the stimulus, which can be quite different from the apparent direction of motion of the whole pattern. Thus, the properties of MT neurons more nearly match perception and constitute a significant elaboration of function beyond that found in V1.

F. Miezin, E. McGuinness, and I have found that the total receptive field (TRF) for most MT neurons is much larger than the classical receptive field (CRF) that is mapped with a single stimulus against a featureless background. As illustrated in Figure 2, we first mapped the CRF and determined its preferred direction to a pattern of moving dots. We then found that the second set of dots moving entirely outside the CRF profoundly and selectively influenced the response to stimuli presented simultaneously within the CRF. We also found that the velocity of movement in the surround influenced the response from the CRF (see Figure 3). The detection of differential shearing motion by these neurons could be the basis of depth perception through motion parallax. The areas of the surrounds were 50 to 100 times that of the CRF and thus included much of the visual field. MT neurons thus make a simultaneous comparison between the direction and velocity of movement of objects occurring locally within their CRFs and globally over nearly the whole visual field. There is increasing evidence that neurons at many levels in the visual system make analogous local–global comparisons. The brain contains many maps of the visual field as revealed by the topographic organization of CRFs, but the TRFs for many neurons in these maps may extend throughout much of the visual field. The TRFs would provide mechanisms of local–global comparisons embedded in visiotopic matrices that may serve as the basis for many functions in vision, such as perceptual constancies and figure–ground discrimination.

The second major ascending pathway is slower conducting and is relayed from the retina by the neurons in the parvocellular laminae of the lateral geniculate nucleus to layer 4C-beta in V1, then to layer 3 in V1, then to V2, then to DL, then to inferotemporal cortex. This system appears to be devoted in part to the analysis of form. S. Petersen, J. Baker, and I have found that DL neurons are highly selective to the size and shape of visual stimuli irrespective of their exact position within the CRF. R. Desimone and collaborators have found striking evidence for shape selectivity for neurons in inferotemporal cortex. Infero-temporal cortex is also strongly implicated in the ability to learn to discriminate visual shapes. There is evidence in macaque monkeys that a distinct subsystem within this pathway may be devoted to the analysis of color. There are also ascending pathways from V2 to DM, M and VP.

Why are there so many cortical visual areas? In attempting to develop computer analogs to visual perception, D. Marr enunciated the principle of modular design. Marr stated that any large computation should be broken down into a collection of small modules as independent as possible from one another. Otherwise, "the process as a whole becomes extremely difficult to debug or improve, whether by a human engineer or in the course of natural evolution, because a small change to improve one part has to be accompanied by many simultaneous changes elsewhere". The formation of modules may have been produced by the replication of visual areas in evolution. The replication of existing structures appears to have been a fundamental mechanism in evolution. The paleontologist W. Gregory proposed that a common mechanism of evolution is the replication of a body part due to a genetic mutation in a single generation, which is then followed in subsequent generations by the gradual divergence of structure and functions of the duplicated parts. S. Ohno has theorized that duplicated genes escape the pressures of natural selection operating on the original gene and thereby can accumulate mutations that enable the replicated gene to encode for a novel protein capable of assuming new functions, and, indeed, there exist many examples of DNA sequence homologies in replicated genes. The same evolutionary advantages that hold for the replication of genes may also hold for the replication of visual areas.

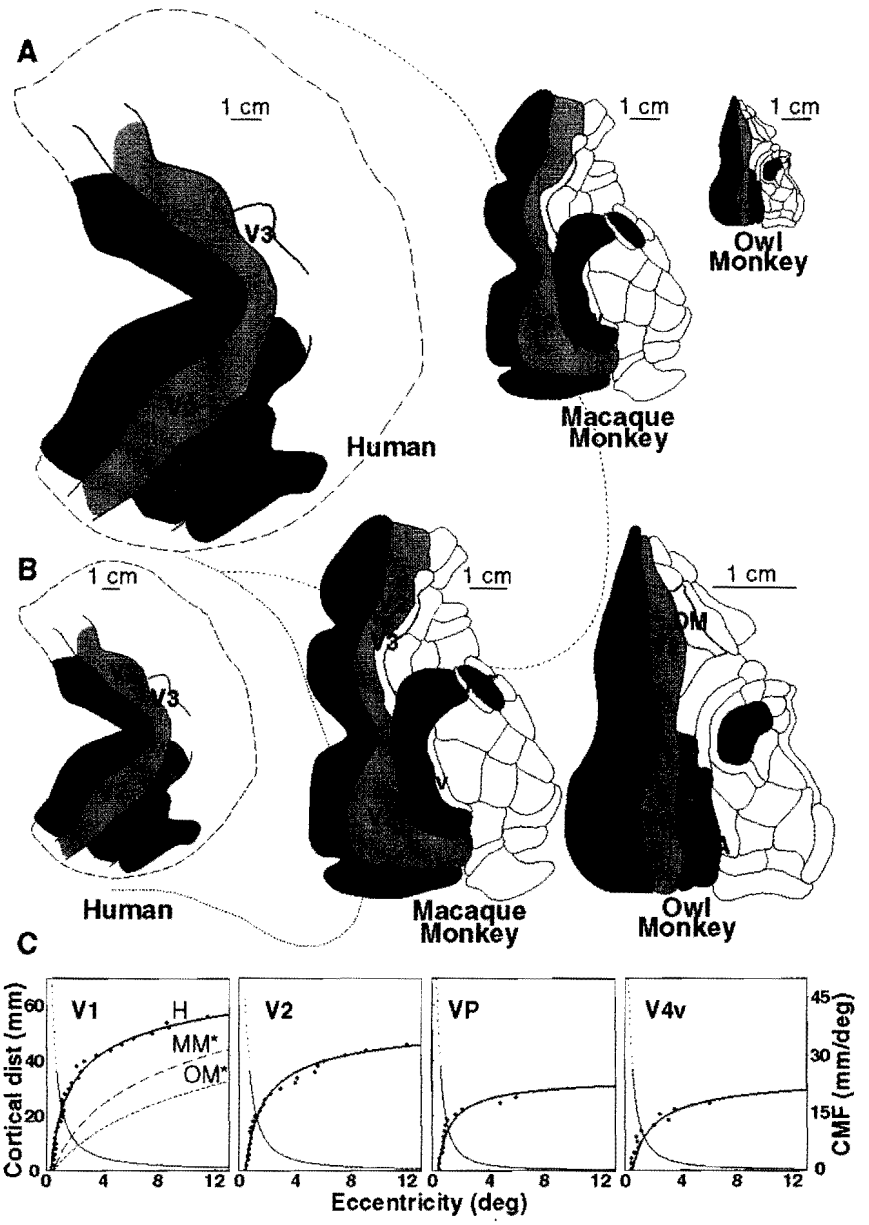

Figure 1. Schematic summary of retinotopic visual areas in the owl monkey, the macaque monkey, and the human at the same scale (A) and approximately normalized by the area of V1 (B). (Human V1 is twice the area of macaque V1, with larger ocular dominance columns and cytochrome oxidase blobs, but a similar number of cells.) Visual areas in humans show a close resemblance to visual areas originally defined in monkeys. The anterior border of the visual cortex in humans was estimated by using the superior temporal sulcus and intraparietal sulcus as landmarks. In (C), the mapping functions (heavy lines; scale is on the left axis) and magnification factor functions (light lines; scale is on the right axis) are shown for the upper field representations of human V1, V2, VP and V4. The V1 mapping functions for owl monkeys (OM*, dotted) and macaque monkeys (MM*, dashed) shown at the left were scaled up to match the overall size of human V1. An increased emphasis on the center-of-gaze in human V1 is evident. CMF, cortical magnification factor.

Finally, to return to the ecological and behavioral theme, the restricted visual field of animals with frontally directed eyes increases their vulnerability to attack. This limitation appears to have been compensated by good sound-localizing ability in owls, cats and some prosimian primates. Another solution is to recruit extra sets of eyes by living in social groups. Thus, the restricted visual field resulting from frontally directed eyes may have provided a selective pressure favoring the development of social organization in primates. In most mammals olfaction plays an important role in social communication. Olfactory cues define territorial boundaries and express sexual receptivity. The amygdala receives major olfactory input and is reciprocally connected with the neuroendocrine control centers of the hypothalamus, and thus is likely to mediate the linkage between olfactory cues and behavior. In higher primates, the olfactory system is much reduced and the amygdala receives its main sensory input from the neocortex, particularly from the highest levels of visual and auditory processing in the temporal cortex. Portions of the amygdala also project back onto the border between layers 1 and 2 in cortical visual areas. These connections may activate long-term memory processes in the neocortex. In higher primates, social communication is mediated largely

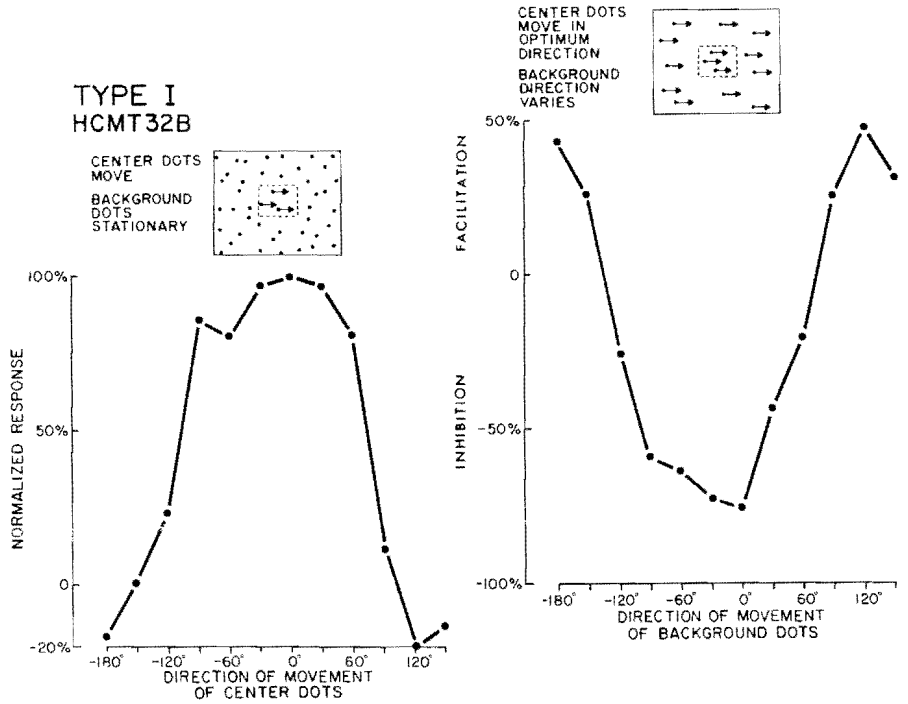

Figure 2. Direction-selective neuron with an antagonistic direction-selective surround recorded from the middle temporal visual area (MT) in an owl monkey. The left graph depicts the response of the cell to 12 directions of movement of an array of random dots within an area coextensive with its classical receptive field (CRF), the small dashed line rectangle. The response is normalized so that 0% is equal to the average level of spontaneous activity sampled for 2-s periods before each presentation. Negative percentages in the left graph indicate inhibition relative to spontaneous activity. In the left graph, the response to the optimum direction in 100%. The right depicts the response of the cell to different directions of background movement while the CRF was simultaneously stimulated with an array of dots moving in the cell's preferred direction. In the right graph, the CRF was stimulated by the array moving in the optimum direction during the 2-s sample periods preceding background movement, and thus a response of 100% in the left graph is equivalent to 0% in the right graph. The stimulus conditions are depicted schematically above each graph. In the actual experiment, the dots were 50% dark, 50% light, and the background was much larger relative to the center than is depicted schematically. (Reproduced from Allman et al., 1985, with permission of Annual Reviews, Inc.)

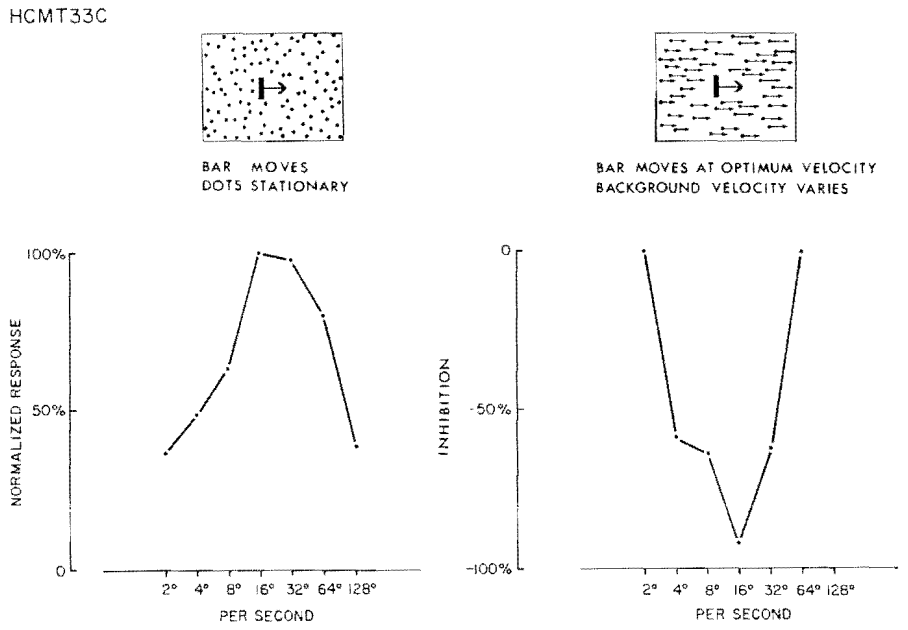

Figure 3. The effect of center and background velocity on a neuron recorded from the middle temporal visual area (MT) in an owl monkey. The left graph is a velocity tuning curve for a bar moving in the preferred direction with a stationary random dot background. The right graph is a velocity tuning curve for background movement while simultaneously presenting the bar moving at the optimum velocity (16° per second). Note the strong suppression of the response by movement in the surround at the preferred velocity for movement within the CRF. (Reproduced from Allman et al., 1985, with permission of Annual Reviews, Inc.)

through visual and acoustic channels, which have much greater information-carrying capacities than olfactory cues. Neurons in the depths of the superior temporal sulcus in monkeys are selectively responsive to faces, and neurons in the amygdala respond selectively to particular facial expressions. Thus, during the course of primate evolution there has been a transformation of social communication from pheromones and olfaction to facial expression and vision.

Reference

Allman JM, Miezin F, McGuinness E (1985): Stimulus specific responses from beyond the classical receptive field: Neurophysiological mechanisms for local–global comparisons in visual neurons. In: *Annual Review in Neuroscience, vol. 8*, Cowan WM, Shooter EM, Stevens CF, Thompson RF, eds. Palo Alto, CA: Annual Reviews, pp. 407–430

Further reading

Allman JM (1977): Evolution of the visual system in the early primates. In: *Progress of Psychobiology and Physiological Psychology, vol. 7*, Sprague JM, Epstein AN, eds. New York: Academic Press, pp. 1–53

Allman J, McGuinness E (1988): Visual cortex in primates. *Comp Primate Biol* 4:279–326

Amaral DG, Price JL (1984): Amygdalo-cortical projections in the monkey (*Macaca fascicularis*). *J Comp Neurol* 230:465–496

Cartmill M (1974): Rethinking primate origins. *Science* 184:436–443

Desimone R, Albright TD, Gross CG, Bruce C (1984): Stimulus-selective properties of interior temporal neurons in the macaque. *J Neurosci* 4:2051–2062

Marr D (1976): Early processing of visual information. *Phil Trans R Soc Land* B275:483–519

Martin RD (1990): *Primate Origins and Evolution*. London: Chapman & Hall

Movshon JA, Adelson EH, Gizzi MS, Newsome WT (1986): The analysis of moving visual patterns. In: *Pattern Recognition Mechanisms*, Gattass R, Gross C, eds. New York: Springer, pp. 117–151

Sereno MI, Dale AM, Reppas JB, Kwong KK, Belliveau JW, Brady TJ, Rosen BR, Tootall RBH (1995): Borders of multiple visual areas in human revealed by functional magnetic resonance imaging. *Science* 268:889–893

Sereno MI, MacDonald CT, Allman JM (1994): Analysis of retinotopic maps. *Cereb Cortex* 6:601–620

Stephan H, Andy OJ (1970): The allocortex in primates. In: *The Primate Brain*, Noback CR, Montagna W, eds. New York: Appleton

See also Visual development; Evolution of vertebrate brains; Neuroscience, comparative; Visual field; Retina, vertebrate; Vision, extrageniculostriate; Visual cortex, extrastriate; Striate cortex

Visual transduction

Gordon L. Fain and John E. Lisman

Figure 1A is a schematic representation of the salient structural features of the vertebrate rod cell. As indicated, the cell has two distinct anatomical regions, the inner and outer segment. The inner segment contains the subcellular organelles required for the usual metabolic processes of cells and terminates in a synaptic foot. The outer segment is specialized for phototransduction and is densely packed with a highly ordered stack of flattened membrane saccules generally referred to as disks, whose membranes contain a high concentration of the protein rhodopsin. The rims of the disks have an exceedingly small radius of curvature and are specialized structures containing specialized proteins (including rim protein and peripherin), which hold the disk in shape and keep adjacent disks in register. Adjacent disk membranes lie in close apposition, resulting in an intradiskal spacing of only 3 nm and a highly regular spacing between adjacent disks of approximately 15 nm. The cytoskeletal network contributed by rim protein and other disk proteins, including interconnecting filamentous structures between adjacent disks and between the disks and the plasma membrane, is mostly responsible for the structural rigidity of the outer segment.

Although the disk and plasma membrane systems are structurally connected, they are functionally separate and in rods show no membrane continuity except at the base of the outer segment, where a few new disks are in the process of formation by invagination of the plasma membrane. In the other type of vertebrate photoreceptor, the cones (not shown), the disks are continuous with the plasma membrane everywhere along the outer segment, and the inside of the disk is open to the extracellular space. Despite the nearly crystalline appearance of the disk array, the membranes themselves are highly fluid and support a rapid rotational and translational diffusion of rhodopsin and other proteins necessary for transduction.

Figure 1B shows the anatomy of a representative invertebrate photoreceptor cell, in this case from the squid. The rhodopsin molecules are located in cylindrical microvillar structures which (as for the disks of cones) are continuous with the plasma membrane. The rhodopsin molecules are rotationally restricted, providing for differential sensitivity to different polarizations of incident radiation.

Rhodopsin consists of a protein moiety, called opsin, and a chromophore, which in most vertebrates and invertebrates is 11-*cis* retinal. Freshwater fish and aquatic reptiles and amphibians use a closely related chromophore, 11-*cis* dehydroretinal, or a combination of retinal and dehydroretinal. Rhodopsin is formed by the covalent linkage of retinal to the protein opsin, via a Schiff base linkage of the retinal aldehyde to the ε-amino group of a lysine (lysine-296 in bovine opsin).

Opsins have been cloned and sequenced from many species and are a member of the family of G-protein receptors. Opsins from rods and cones, and from vertebrates and invertebrates are all thought to have a similar structure, with about half of the protein within 7 transmembrane domains and the rest about equally divided between the cytoplasmic and intradiskal (or extracellular) space. As a result, four of the "loop" regions interconnecting the transmembrane domains face the cytoplasm, as does the carboxy terminal; three loop regions and the amino terminal face the intradiskal (or extracellular) space. The chromophore is thought to be positioned within the transmembrane domains of the protein, nearly in the middle of the membrane.

The absorption of light by rhodopsin causes a photoisomerization of the chromophore from 11-*cis* to all-*trans* retinal, which produces a pigment intermediate called photoactivated meta II (or Rh^*), whose conformation is subtly different from that of the dark-adapted pigment. This change in conformation is sufficient in vertebrates to facilitate the binding of Rh^* to a G-protein called transducin, which facilitates the exchange of GTP