# Anatomical Organization of Retinotopic Motion-Sensitive Pathways in the Optic Lobes of Flies

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*KEY WORDS* anatomical organization; retinotopic neurons; directional selectivity; Insecta; motion vision

*ABSTRACT* Anatomical methods have identified conserved neuronal morphologies and synaptic relationships among small-field retinotopic neurons in insect optic lobes. These conserved cell shapes occur across many species of dipteran insects and are also shared by Lepidoptera and Hymenoptera. The suggestion that such conserved neurons should participate in motion computing circuits finds support from intracellular recordings as well as older studies that used radioactive deoxyglucose labeling to reveal strata with motion-specific activity in an achromatic neuropil called the lobula plate. While intracellular recordings provide detailed information about the motion-sensitive or motion-selective responses of identified neurons, a full understanding of how arrangements of identified neurons compute and integrate information about visual motion will come from a multidisciplinary approach that includes morphological circuit analysis, the use of genetic mutants that exhibit specific deficits in motion processing, and biomimetic models. The latter must be based on the organization and connections of real neurons, yet provide output properties similar to those of more traditional theoretical models based on behavioral observations that date from the 1950s. *Microsc. Res. Tech. 62:132–150, 2003.* 

## INTRODUCTION: STRUCTURE AS A PREDICTOR OF FUNCTION

Neuroanatomy not only provides the organic context for physiological studies, it traditionally suggests that specific functions might be ascribed to identified brain areas or systems of nerve cells. Although fundamentally erroneous, Franz Gall's interpretations of the folds and fissures of the cerebral cortex in the early 1800s represent the first objective attempt to interpret the significance of brain structure in terms of functional attributes. In the 1850s, Félix Dujardin's first neuroanatomical descriptions of insects similarly attributed functions, such as industriousness and sociality, to surface folds of the bee's brain. An empirical approach to correlating structure with function first gained respect after 1861 with Broca's report of the localization of a functional brain area in humans and by the first electrophysiological experiments, performed on dogs by Fritsch and Hitzig in 1870, showing participation by the cerebral cortex in motor actions (Young, 1990). Already by the end of the 19th century, Ramon y Cajal's penetrating interpretations of Golgi-impregnated neurons in the mammalian retina were vanguards of functional investigations at the level of definable circuits.

Our understanding of the insect visual system also began with anatomical observations and from them speculations about functional organization. In the early 1900s, Paul Vigier correctly predicted neural superposition (Vigier, 1909) from observing how photoreceptor axons from several ommatidia converge onto single target neurons, the large monopolar cells (LMCs) of the fly lamina. The optical properties and corresponding receptor projections of the superposition eye were finally demonstrated by Kirschfeld and Braitenberg in 1967 (Kirschfeld, 1967; Braitenberg, 1967), who showed that six receptors sharing the same optical alignment in six different ommatidia send their axons to the same second-order neurons in the lamina (Fig. 1A). In 1915, Cajal and Sánchez proposed specific analogies between the cellular organization in insect optic lobes and organization in the mammalian visual system, and it is now recognized that synaptic connections beneath the compound eye, among photoreceptor endings, amacrines, and interneurons (Strausfeld and Campos-Ortega, 1977) bear comparison with synaptic connections in the primate external plexiform layers (Dowling and Boycott, 1966). Cajal and Sánchez also pioneered in demonstrating similarities between specific retinotopic neurons across evolutionarily divergent insect taxa, suggesting the possibility of their common function.

Anatomically identified systems of horizontally and vertically oriented tangential neurons in the fly's lobula plate (Fig. 1B) were anticipated to encode horizontal and vertical motion (Braitenberg, 1970), a prediction later confirmed, in general, by intracellular recordings and dye filling (Hausen, 1981; Hengstenberg, 1982). Columnar neurons that characterize the lobula (Fig. 1B) were predicted to encode local stimuli, such as

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Received 20 April 2002; accepted in revised form 9 December 2002

Contract grant sponsor: NIH; Contract grant number: R01 RR08688; Contract grant sponsor: ONR; Contract grant number: N68936-00-2-0002.

DOI 10.1002/jemt.10367

Published online in Wiley InterScience (www.interscience.wiley.com).

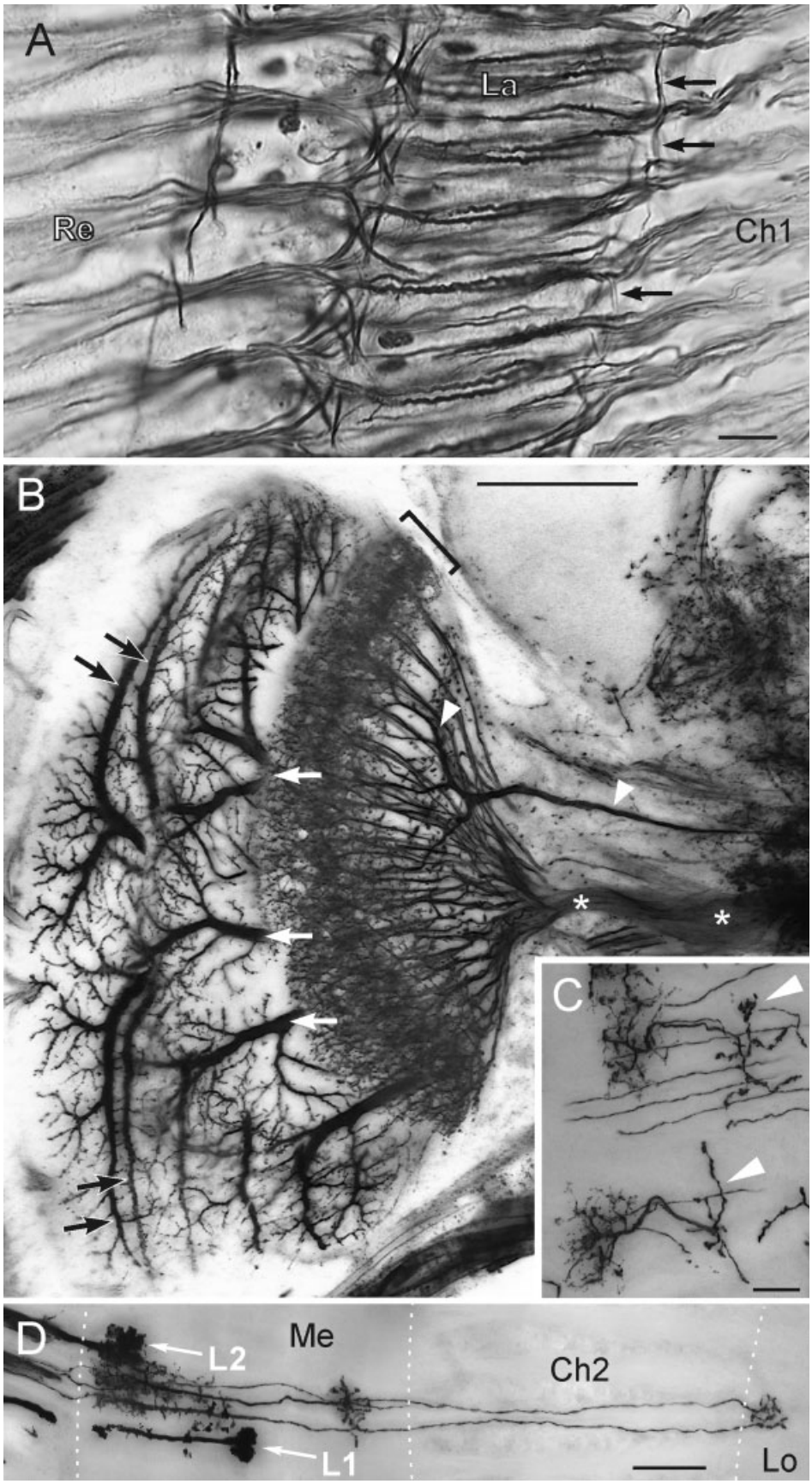


Fig. 1. Components of retinotopic motion processing pathways to wide-field lobula plate tangential cells. **A:** Block Cajal reduced silver preparation of the lamina, illustrating the neural superposition architecture that is characteristic of insects with open-rhabdom retinas. Axons of receptors R1-R6 in each ommatidium of the retina (Re) diverge to adjacent optic cartridges in the lamina (La), where outputs from receptors that share the same optical axis end in the same cartridge. L4 collaterals (arrows) provide a network of tangential connections just distal to the edge of the first optic chiasma (Ch1). **B:** Cobalt-filled and silver-intensified neurons in the optic lobe of *Musca domestica*, showing the dendrites of wide-field HS and VS tangential cells (white and black arrows, respectively) in the lobula plate. Palisades of columnar neurons characterize the lobula. Each species of columnar neuron has its dendrites in a characteristic level of the neuropil (bracketed). Axons from such an isomorphic assembly of columnar neurons project coherently (asterisks) into the lateral protocerebrum. Also visible is a unique species of neuron (white arrowheads) that sends its axon directly into the ventral nerve cord. **C:** Two Golgi-impregnated T5 neurons showing their dendrites in the superficial layer of the lobula and their terminals in the lobula plate (arrowheads). **D:** Golgi impregnation showing two Tm1 cells in adjacent retinotopic columns and their layer relationships to the terminals of the large monopolar cells (LMCs) L1 and L2 in the outer medulla (Me). The axons of the Tm1 cells cross the second optic chiasma (Ch2) to terminate side by side in the superficial layer of the lobula (Lo). A and B are from *Musca domestica;* C and D, *Phaenicia sericata*. Scale bars in A and C = 10 μm, 50 μm in B, and 25 μm in D.

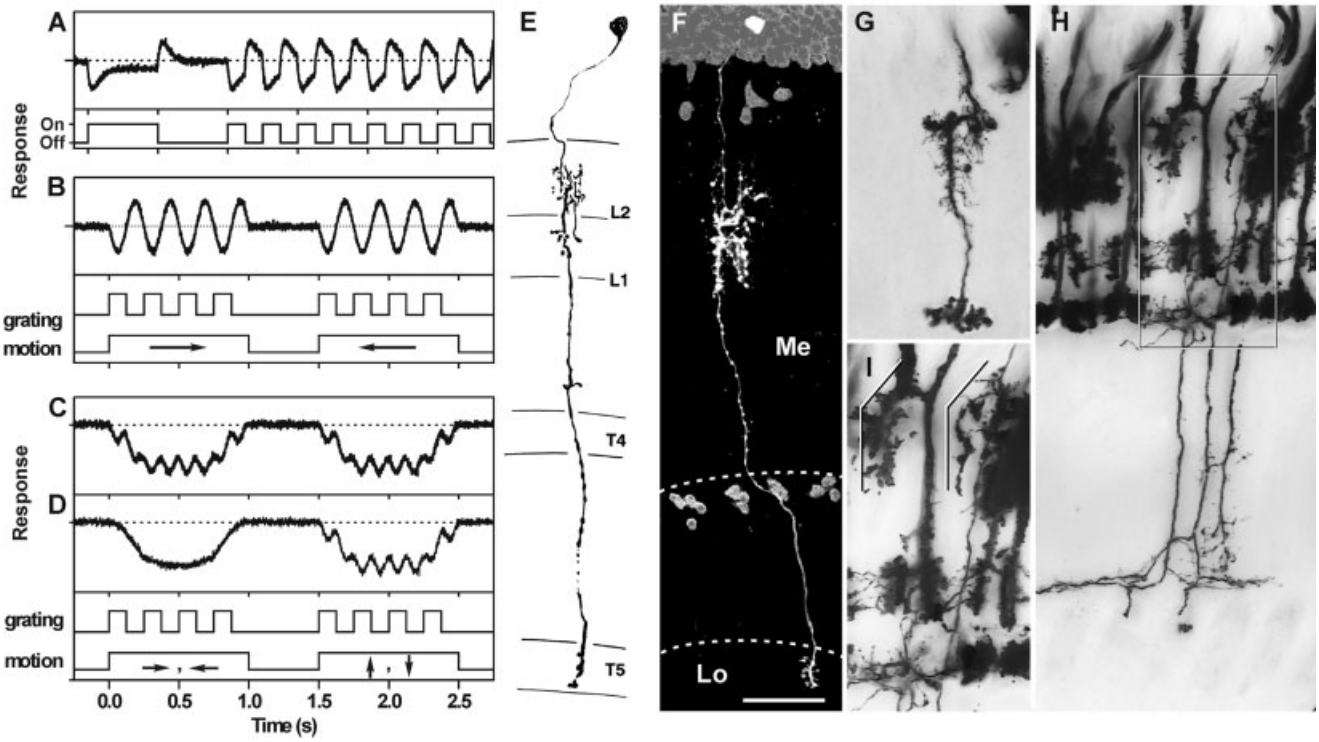


Fig. 2. Idealized intracellular responses in fly visual interneurons to flicker and motion stimuli (A–D), with examples of identified neurons that exemplify these response types (E–I, all from *Phaenicia sericata*). In the intracellular response plots, lower traces indicate (A) flicker On and Off times, (B–D, grating), times when brighter and darker edges of a grating motion stimulus cross a cell's receptive field center, and (B–D, motion) the durations and example directions (arrows) of grating motion. **A:** Responses to a wide-field flicker stimulus presented at 1 and 4 Hz. Nonspiking ON-hyperpolarizations (often with sustained hyperpolarizing plateaus at low flicker frequencies) and OFF-depolarizations are characteristic of LMC cells L1, L2, and L3 (not shown), and also have been observed in transmedullary neurons including Tm1 and Tm1b. Tm1 (**E**) is shown here with its relationship to the medullary strata corresponding to L2 and L1 endings and T4 dendrites, as well as the T5 dendritic layer in the outer lobula. **B:** Motion-sensitive, yet flicker-like responses to motion of a striped grating have been observed in several small-field transmedullary neurons including Tm9 (**F**) and Tm1b (not shown), as well as in lamina monopolar cells L1, L2, and L4. **C:** Responses that are motion-selective, in that they differ from flicker responses at the same contrast frequency, have been observed in many cell types including L5 (ending shown in **G**). **D:** Motion-selective responses that are also orientation-selective, have been observed in the centrifugal neuron C2 (**H,I**). H illustrates palisades of monopolar cell endings L1, L3, and L2 from the lamina, terminating in the outer layer of the medulla. These are shown with centrifugal C2 neurons, the dendrites of which are at the inner surface of the medulla, and at the bilobed endings of L1 cells. Centrifugal neurons also have a recurved varicosity superficially in the medulla, that matches the curvature (bracketed in I) of L2 terminals. The boxed area is shown enlarged in I. (E, after Douglass and Strausfeld 1995; F, modified from Douglass and Strausfeld 1998.) Lo, lobula; Me, medulla. Scale bar in F (also applies to E, G–I) = 20 μm.

positional, textural, or chromatic properties (Gilbert and Strausfeld, 1992; Hertel, 1980). Unique tangential neurons serving the upper frontal eye region were hypothesized to encode the direction of small objects moving in the frontal visual field (Collett and Land, 1978), a prediction since supported by intracellular recordings (Gilbert and Strausfeld, 1991). More recently, a subset of small retinotopic neurons (Fig. 1C,D), which are conserved across species (Buschbeck and Strausfeld, 1996, 1997), was anticipated to constitute cardinal elements in an achromatic system of motion-analyzing circuits supplying wide-field tangential neurons in the lobula plate (Bausenwein et al., 1992; Strausfeld and Lee, 1991). This account focuses on the neuroanatomical context and functional attributes of these small interneurons, which are now recognized as providing motion-sensitive inputs to lobula plate tangentials (Douglass and Strausfeld, 1995, 1996). A general background on the functional organization of dipterous visual systems is provided by several symposium volumes (Ali, 1984; Autrum, 1981; Horridge, 1975; Stavenga and Hardie, 1989; Zanker and Zeil, 2001).

## WHAT IS VISUAL MOTION?

Movement of an image across the retina is characterized by local fluctuations in light intensity that occur successively across arrays of photoreceptors. A great many neurons in the fly visual system can respond equally well to such motion-associated fluctuations, or to a non-motion flicker stimulus (Fig. 2A,B). If a neuron's responses to flicker and motion stimuli having the same contrast frequency are essentially indistinguishable, the neuron can be considered to be flicker and motion-sensitive (Fig. 2B), but not selectively sensitive to movement (motion-*selective*).

No specialized circuitry is required for motion sensitivity, but it is for motion specificity. Whereas all photoreceptors, their postsynaptic lamina monopolar cells, as well as many neurons that lie deeper within the optic lobes, are at least motion-sensitive, only a subset

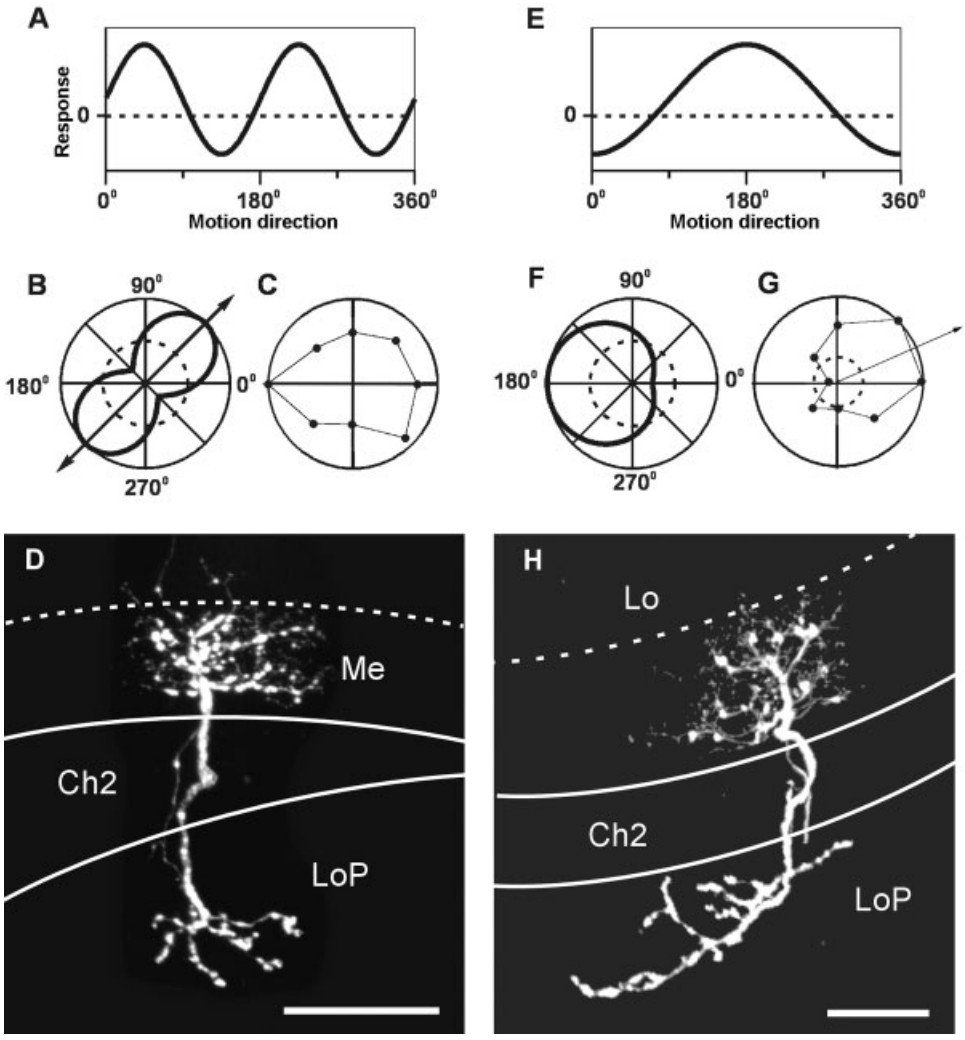


Fig. 3. Orientation-selective (OS) and direction-selective (DS) responses of dipterous visual interneurons to unidirectional grating motion, accompanied by confocal reconstructions of identified neurons that exhibit these distinct forms of motion selectivity. Dotted lines (**A,E**) and dotted circles (**B,F,G**) indicate zero response levels. The idealized response plots illustrate basic response characteristics as viewed by using both Cartesian (A,E) and polar (B,F) coordinates. OS responses (A,B) have two maxima, two minima, and symmetry about the preferred axis of orientation (B, arrowed line), whereas DS responses (E,F) define a single maximum, single minimum, and preferred excitatory and inhibitory (or null) response directions (here, at 180° and 0°, respectively). Plots obtained from actual intracellular recordings (**C** and G, respectively) show intracellular responses from the bushy T cells T4 (**D**) and T5 (**H**) during grating motion. The T4 showed responses suggestive of very weak orientation-selectivity with a nearly horizontal preferred axis, whereas T5 was strongly direction-selective to slightly upward, progressive (rightward) motion (arrow shows vector sum of responses). (C and D after Douglass and Strausfeld, 1996; G and H, modified from Douglass and Strausfeld, 1995). Scale bars in D and H = 20 μm.

of motion-sensitive cells is motion-*selective*, meaning that some component or components of the neuron's responses to motion differs from its responses to flicker (e.g., Fig. 2C,D). In the search for neurons that participate in elementary motion detector circuits, here referred to as EMDs, cells that are motion-*sensitive* may be good candidates as intrinsic elements of such circuits, whereas motion-*selectivity* reveals the presence of an additional level of processing. Thus, the neurons that constitute the most preliminary stage of an EMD circuit need not themselves be motion-selective: motion selectivity is most likely to emerge only from some interaction within the neuronal architecture that is mediated by synaptic connections among motion-sensitive neurons (see below and Fig. 9).

Motion-selective cells, without any other attributes, can inform the nervous system that motion is present within a specific spatiotemporal receptive field. More restricted information is provided by neurons that respond selectively to motion along a specific orientation in the visual field, or in one direction along this orientation. Such neurons are called *orientation-selective* or *direction-selective* neurons, implying additional levels of sophistication in the underlying neural circuitry. Orientation selectivity is characterized by bidirectional responses tuned to a preferred axis across the retina (Fig. 3A,B), whereas direction selectivity typically involves unidirectional tuning to a preferred direction along a preferred axis (Fig. 3E–G). It should be noted that the demonstration of a particular type of motion responsiveness in a given neuron establishes its minimum capability, but does not preclude the presence of additional motion-tuning properties that could be revealed under different experimental conditions. For example, all motion-selective neurons, if tested at different motion speeds, will turn out to be selective for some combination of contrast frequency, spatial frequency, and velocity.

## REPRESENTATION OF VISUAL SPACE IN RETINOTOPIC NEUROPILS

Retinotopic organization among a succession of relay neurons is a cardinal feature of visual systems that support more than mere phototactic responses. Flies are no exception, having unusually complex optic lobes

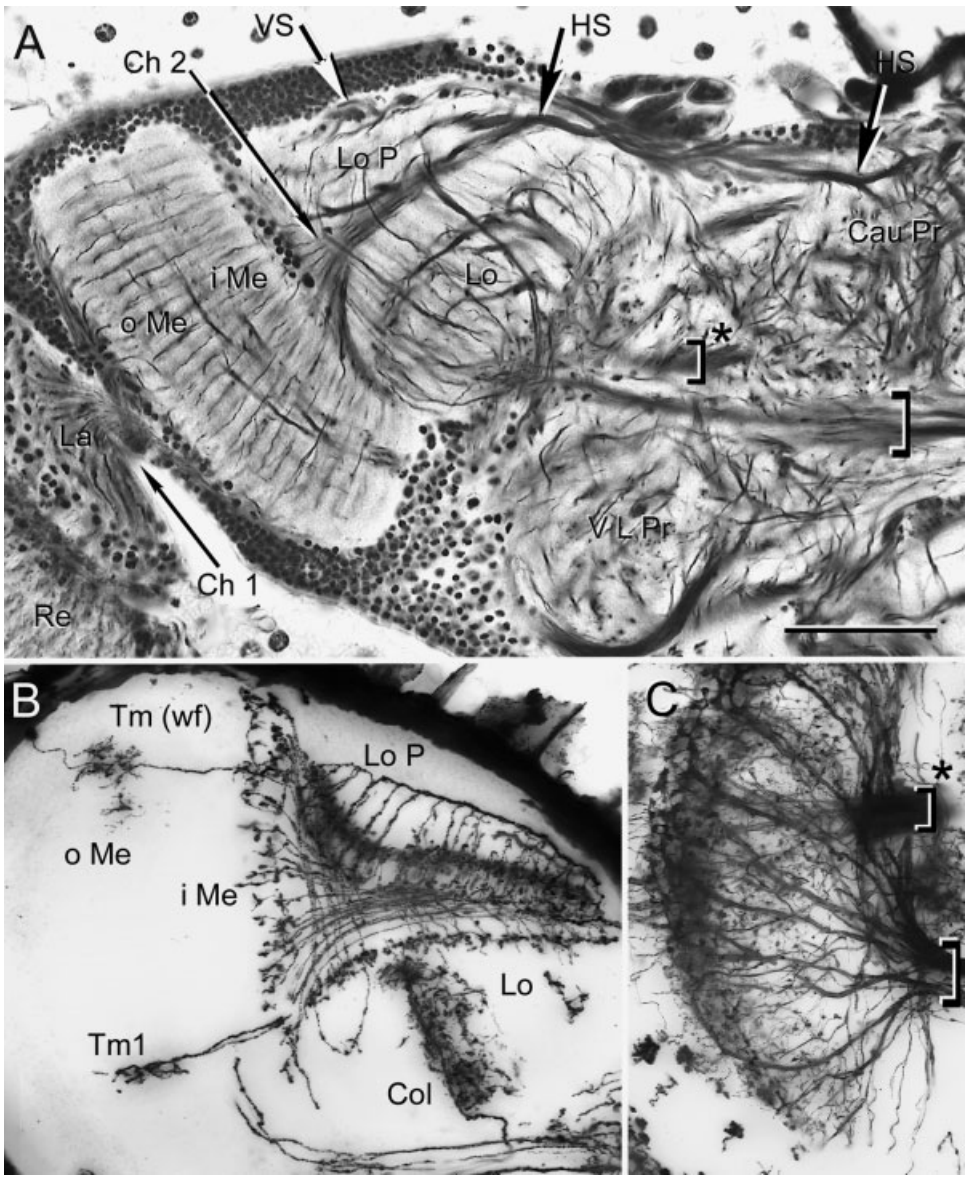


Fig. 4. Some architectural features of the optic lobes of *Drosophila melanogaster*. **A:** Horizontal section of a reduced silver preparation showing part of the retina (Re) and the five retinotopic neuropils of the optic lobe. These are the lamina (La), outer and inner medulla (o Me and i Me, respectively), lobula plate (LoP), and lobula (Lo). Chiasmata link the lamina to the medulla (Ch1), and link the inner medulla to the lobula and lobula plate (Ch2). The lobula complex (LoP and Lo) sends tracts of efferent neurons to circumscribed regions of the lateral protocerebrum (bracketed). Two giant-fiber systems of the lobula plate are indicated (VS and HS), the terminals of HS neurons shown ending in the caudal protocerebrum (Cau Pr). Also shown is a lobe of the ventrolateral protocerebrum (VL Pr). **B:** Golgi preparation showing a wide-field (Tm (wf)) and small-field (Tm1) transmedullary cell in the medulla. The lobula (Lo) is shown with an impregnated columnar efferent neuron (Col). Layers in the medulla, lobula, and lobula plate associated with the T4 and T5 pathways are here shown invaded by terminal varicosities all of which arise from an axon reaching the posterior face of the lobula plate. **C:** Assemblies of lobula columnar neurons providing bundles of axons into two tracts that correspond to those shown in A (bracketed with and without asterisk). Scale bar in A (also applies to B and C) = 50 μm.

that comprise five retinotopic neuropils (Fig. 4). These are the lamina, the outer and inner medullas, and the lobula and lobula plate, the latter two collectively known as the lobula complex.

Information processing begins at the level of the compound eye and retina, which are composed of many hundreds of units, called ommatidia. In dipterous insects, each ommatidium accommodates a set of eight photoreceptors (called R1-R8) that are optically isolated from their neighbors by screening pigments. The eight receptors are capped by a single corneal lens and crystalline cone, both of which focus light onto their tips (Franceschini, 1975). Six of the photoreceptors (R1-R6) are both UV- and blue-green-sensitive ($\lambda_{max}$ = 480 nm, see below), and can operate across an approximately four-$\log_{10}$-unit range of intensities depending on their state of light adaptation (Laughlin, 1981). Each ommatidium is "wall-eyed" because its six R1-R6 receptors have diverging optical alignments such that they look at six different points in space. Their axons diverge to six *different* retinotopic columns (called optic cartridges) in the lamina. Retinotopy is nevertheless established between the retina and lamina because those R1-R6 photoreceptors sharing the same optical alignment are distributed among six different ommatidia and send their axons to the *same* optic cartridge (Braitenberg, 1967; Kirschfeld, 1967). Such assemblages have been called visual sampling units (VSUs) by Franceschini (1975), a term that applies equally well to columns in the medulla because each represents, at a deeper level, an optic cartridge. The seventh and eighth photoreceptors within each ommatidium (called R7 and R8) have a narrower working range and are sensitive to ultraviolet (UV) or blue. Each pair of these "long visual fiber" axons passes down alongside the optic cartridge that receives the six optically equiv-

alent short photoreceptor axons. Long visual fiber axons project into the medulla in parallel with the axons of relay neurons, called large monopolar cells (LMCs), that are postsynaptic to the six short photoreceptor terminals. Thus, the retina is mapped sampling point for sampling point, first into the lamina by short receptor axons, and then into the medulla by long visual fibers and accompanying LMCs (Campos-Ortega and Strausfeld, 1972a; Horridge and Meinertzhagen, 1970). A fly's eye consisting of 3,000 facets, for example, will provide receptor axons to 3,000 optic cartridges in the lamina and 3,000 columns in the medulla. From there, systems of relay neurons map each medulla column into the lobula, while other systems relay retinotopic maps into the lobula plate. As will be summarized below, the lobula plate map derives initially from a type of LMC called L2 that receives its numerous inputs from the short photoreceptors R1-R6, and that terminates on small-field relays in the medulla. The lobula map initially derives its inputs from a second type of LMC, called L1, that terminates on neurons that end deep in the lobula. Another parallel pathway to the lobula is initially provided by pairs of long visual fibers (called R7 and R8) and a monopolar cell, called L3, that accompanies each pair and has fewer synaptic connections with R1-R6 than does L2. Together, the peripheral elements R7, R8, and L3 provide a trichromatic pathway that operates at higher light intensities than does the L2 pathway (see below).

Efferents from the optic lobes, as well as retinotopic neurons that constitute the optic lobes, possess characteristically shaped dendritic fields. For any particular cell type, its dendrites (and terminal branches) extend among a characteristic number and arrangement of retinotopic columns, each of which represents a discrete area of the visual hemisphere. Thus, by mapping the optical alignments of photoreceptors, the extent of any dendritic tree within the map of retinotopic columns can provide a first approximation of its physiological receptive field (Gilbert and Strausfeld, 1991; Strausfeld, 1991), although this may turn out to be physiologically somewhat larger or smaller than originally estimated from the morphology. Mapping of such relationships is useful when considering the possible roles of small motion-selective neurons, the dendrites of which have characteristic extents and orientations within the retinotopic map.

In addition to their columnar organization, each of the four retinotopic neuropils beneath the lamina is divided tangentially into numerous strata (Campos-Ortega and Strausfeld, 1972b; Strausfeld, 1970). These are defined by dendritic trees of retinotopic neurons, tangential processes of wide field efferent or afferent neurons and, crucially, laminar arrangements of amacrine cells that provide local interactions among the retinotopic columns. This arrangement is exemplified by the organization of local circuits among optic cartridges provided by amacrine cells and a class of centripetal cells called T1 neurons (Campos-Ortega and Strausfeld, 1973). As will be described below, these associations may also play a crucial role in motion detection.

## THE SEGREGATION OF OPTIC LOBE OUTPUTS INTO THREE PATHWAYS

A number of distinct and uniquely identifiable neural arrangements provide parallel pathways that are assumed to be specialized for reconstructing specific attributes of the visual world. These include: the discrimination of colors, the detection and relationship of contours and corners (and hence form vision), motion direction, motion orientation, velocity, and relative motion.

A large variety and number of neurons send axons from the medulla, lobula, and lobula plate to circumscribed neuropils of the ipsi- and/or contralateral midbrain. For example, in the lobula complex, each palisade of small-field columnar neurons that branch among larger tangentially arrayed neurons (Fig. 5A) consists of many hundreds of similarly shaped elements (Fig. 5C). These neurons send bundles of axons to the midbrain, where they contact local interneurons (Fig. 5D,E). These neuropils further integrate visual information with other modalities. The final output of integrated visual data is carried by long-axoned neurons that extend from the brain to neuropils of the thoracic and abdominal ganglia (Gronenberg and Strausfeld, 1991; Strausfeld and Gronenberg, 1990). Although little is known about efferent neurons from the fly medulla, intracellular studies on the similarly organized moth *Manduca sexta* show that wide-field neurons encoding perimeter length extend from the medulla to the midbrain, whereas neurons that encode looming or receding stimuli comprise centrifugal neurons that originated in the midbrain and extend back out to the medulla (Wicklein and Strausfeld, 2000). The dendrites of these latter neurons originate in discrete neuropils that receive terminals from wide-field horizontal and vertical motion selective neurons of the lobula plate, and from a class of small-field columnar neurons from the lobula (see below). This arrangement reveals that processing of complex visual motion can occur deeper than in the optic lobes, in neuropils that are analogous in function to the middle temporal cortical area of primates (Geesaman and Anderson, 1996).

The lobula and lobula plate are distinguished from each other by their efferent neuron organization. The lobula contains numerous ensembles of columnar neurons, the axons of which are spaced one per nine retinotopic columns (Braitenberg, 1970). Their oval dendritic fields spread through between six and nine columns vertically, and between four and six horizontally. Sixteen anatomically distinct ensembles of columnar neurons have been identified, each of which sends its axons coherently to a specific target neuropil in the midbrain (Douglass and Strausfeld, 1998; Strausfeld and Bassemir, 1985; Strausfeld and Gilbert, 1992; e.g., Fig. 5D). However, certain ensembles of columnar cells extend across only part of the retinotopic neuropil and thus subtend only a specific segment of the visual hemisphere. For example, a palisade of columnar neurons serving the frontal area of binocular overlap connects the two lobulas (Fig. 5B), at least in males (Strausfeld, 1979). In male calliphorids and sarcophagids, the upper frontal area of the retina is served by an area of the lobula containing several restricted populations of columnar neurons in addition to a set of

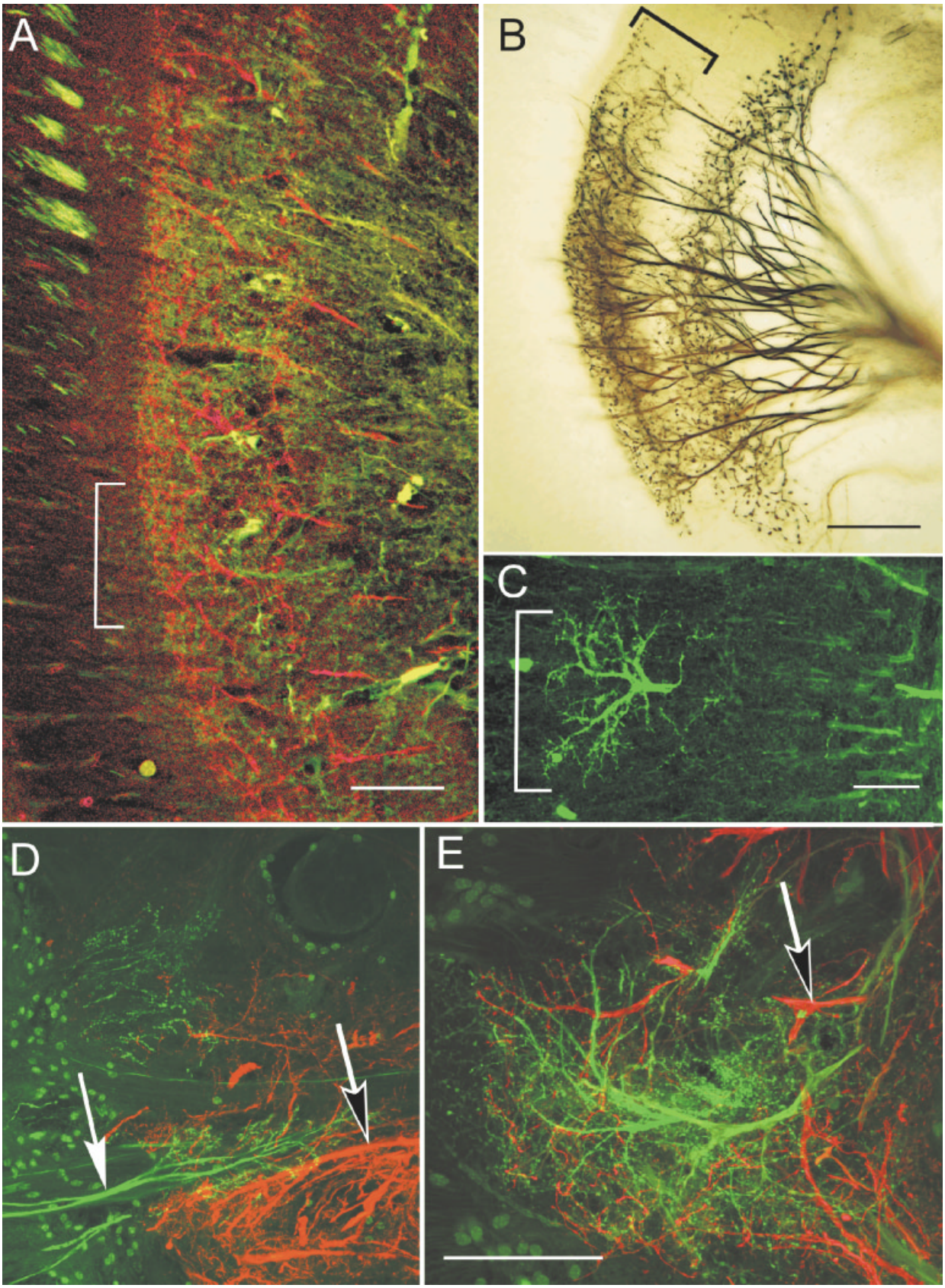


Fig. 5. Columnar organization of the lobula. **A:** Confocal image showing double labeling of palisades of small-field columnar neurons stained with Texas Red and Lucifer Yellow among the wider spacing of large-diameter profiles of a wide-field tangential neuron also stained with Lucifer Yellow. **B:** Two strata of afferent endings in the lobula filled with cobalt chloride that has been intensified with silver. The outer layer of terminals (bracketed) is the columnar endings of a palisade of columnar neurons that originates at a corresponding location in the contralateral lobula. These arrangements between the two lobulas might provide a basis for crude binocular vision. **C:** Confocal image of one of the dendritic trees of the palisade of columnar neurons shown in A. (Brackets indicate equivalent dendritic spreads). **D:** Lucifer Yellow-filled bundles of axons from lobula efferents (white arrow) terminate in the lateral deutocerebrum but suggest little direct contact with the dendritic trees of descending neurons (filled arrow, Texas Red-filled profiles). **E:** Overlap between the dendrites of Texas Red-filled descending neurons (filled arrow) and the terminal arborization of an interneuron originating from optic foci in the contralateral protocerebrum. Scale bars in A–C =25 μm; D and E, 50 μm.

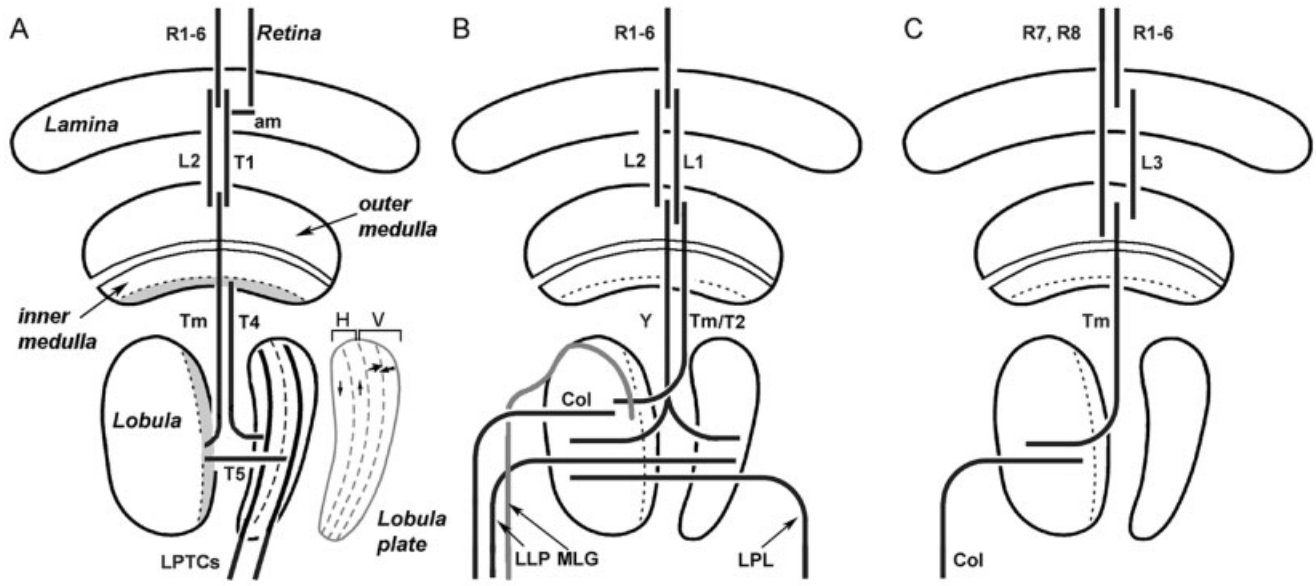


Fig. 6. Schematic overview of the five identified parallel retinotopic pathways through the dipteran optic lobe, shown in horizontal section. **A:** Achromatic pathway delivering information about the orientation and direction of motion to four direction-specific layers in the lobula plate. In the gray outline of the lobula plate (right inset), the arrows from left to right indicate preferred motion directions, respectively, corresponding to progressive and regressive horizontal motion in the H [horizontal] layers, and upward and downward motion in the V [vertical] layers. R1-R6, photoreceptors from the retina terminating in the lamina; L2 and T1, the type 2 LMC accompanied by the type T1 bushy T-cell terminating in the outer medulla. L2 is directly provided with inputs from R1-R6. Amacrine cells (am) provide relays from adjacent R1-R6 to T1. Tm, transmedullary cells terminating in a specialized superficial layer (shaded gray) over the outer lobula that contains the dendrites of T5 bushy T-cells. These occur as quartets representing each VSU. Their endings segregate to four layers in the lobula plate. LPTCs, wide-field lobula plate tangential cells, the dendrites of which invade one or more of the four direction-specific layers. Quartets of T4 bushy T-cells originate from a deep stratum in the inner medulla (shaded). **B:** Achromatic, non-direction-sensitive pathways originating with R1-R6 are proposed to provide three more parallel channels via the two LMCs, L1 and L2. One channel involves transmedullary Y cells that supply both the lobula plate and the lobula , targeting columnar neurons (LPL and LLP cells; Strausfeld and Gilbert, 1992) shared by these neuropils. Certain other types of transmedullary cells (Tm) supply columnar neurons (col) and directionally selective motion sensitive tangential neurons (MLG: male specific giant neurons) in the lobula with information about motion. T2 cells (T2), associated with L1 terminals, are thought to provide information about contour orientation to the lobula (Douglass and Strausfeld, 2003). **C:** R7 and R8 receptors, in parallel with L3 relaying from R1-R6, provide inputs to a fifth parallel channel, which serves color vision and may involve transmedullary cell relays from R7,8 and L3 to columnar neurons in the lobula.

tangentially arranged dendrites of uniquely identifiable neurons called male lobula giants (MLGs: Hausen and Strausfeld, 1980; Strausfeld, 1980, 1991). Together, these elements are thought to underlie object detection and, via descending pathways, contribute to indirect flight motor systems that allow target pursuit and interception (Collett and Land, 1978; Gronenberg and Strausfeld, 1991).

This subset of tangential neurons in the lobula, which are directional motion- and/or orientation-selective (Gilbert and Strausfeld, 1991) is reminiscent of tangential neurons in the thin tectum-like region known as the lobula plate. This neuropil contains four distinct levels of tangential processes that collate and integrate information about directional motion, relaying to descending pathways associated with thoracic circuits mediating flight (see Borst and Egelhaaf, 1989; Krapp et al., 1998). The lobula and lobula plate also share populations of columnar neurons that arborize in both regions, and whose axons terminate in discrete mid-brain neuropils associated with descending neurons of the flight control system (Strausfeld and Gronenberg, 1990; Strausfeld and Gilbert, 1992).

Thus, the peripheral retinotopic map of the lamina (Fig. 1A) and medulla (Figs. 1D, 4A) is represented by *five* major systems of efferents from the two deep retinotopic neuropils: systems of tangential neurons from the lobula plate that collate information about motion (Fig. 1B, Fig. 6A, LPTCs); at least two classes of columnar neurons from the lobula (Fig. 1B, Fig. 6B,C, col), one of which is expected to encode orientation, the other color; systems of object motion selective tangential cells in the male lobula (Fig. 6B, MLG) that are involved with target detection and pursuit (Gilbert and Strausfeld, 1991; Gronenberg and Strausfeld, 1991); and systems of small-field columnar neurons (Gilbert and Strausfeld, 1992) that have dendrites in both the lobula and the lobula plate (Fig. 6B, LPL and LLP;) and which respond to local visual cues (Douglass and Strausfeld, 1998).

## PARALLEL ACHROMATIC AND CHROMATIC PATHWAYS

Achromatic systems (Fig. 6A,B) are supplied by R1-R6, all of which share the same visual pigment with an $\lambda_{max}$ at 490 nm (blue-green) and an antenna pigment that absorbs in the UV range (Hardie, 1986; Smakman and Stavenga, 1986). These pigments, along with the optical properties of the photoreceptors and their screening pigments, result in a dual-peaked (McCann

and Arnett, 1972) but functionally achromatic spectral sensitivity in R1-R6. The axons of R1-R6 are presynaptic onto pairs of wide-diameter second-order neurons, the L1 and L2 large monopolar cells (LMCs). As the inputs to L1 and L2 arise exclusively from R1-R6 (Boschek, 1971; Meinertzhagen and O'Neil, 1991), the spectral sensitivities of R1-R6 and of L1 and L2 are expected to be quite similar. The available physiological recordings from lamina neurons, however, are inconclusive on this point. In intracellular recordings from the *Calliphora* lamina, the spectral sensitivity of small receptive field interneurons interpreted to be large monopolar cells (Laughlin and Hardie, 1978) closely resembled that of R1-R6, as expected. Without anatomical correlates, however, the precise morphological identities of these units are uncertain. In a separate study of *Calliphora* that included intracellular staining and identification of neurons, Moring (1978) found two classes of large monopolar cells. One class exhibited spectral tuning roughly like that of R1-R6, whereas the other showed only a single sensitivity maximum in the UV, with just a weak shoulder near 490 nm. Each spectral class was reported to include both L1 cells and L2 cells, as well as a few monopolar neurons that could not be further identified. Unfortunately, no anatomical illustration was provided that might have helped resolve a potentially intriguing finding. Although Moring's (1978) data seem to suggest that some subset of lamina monopolar cells receives inputs dominated by purely UV-sensitive R7 cells, there is no additional evidence in support of such a hypothesis. To date, the only R7 cells known to have output terminals in the lamina occur in the male-specific acute zone, where both R7 and R8 are endowed with R1-R6 visual pigments (see below).

Thus, available evidence indicates that L1 and L2 receive achromatic inputs from R1-R6. In the medulla, L1 and L2 provide inputs to two parallel streams of retinotopic neurons. L1 is associated with orientation-selective neurons (T2 cells, described below) supplying the lobula (Douglass and Strausfeld, 2003), whereas L2 is associated with a succession of neurons that eventually supply the lobula plate with information about directional motion to its wide-field tangential neurons (see below).

Achromatic inputs might also supply some members of another class of medulla efferent neurons known as Y cells (Fig. 6B). These neurons have bifurcating axons supplying both the lobula and lobula plate, terminating at dendrites belonging to columnar efferent neurons shared by these two neuropils. These latter efferent neurons possibly constitute the second of two color insensitive systems of optic lobe efferents and, judging from the responses of their input neurons in the lobula and lobula plate (Douglass and Strausfeld, 1998; Gilbert and Strausfeld, 1991; Gronenburg and Strausfeld, 1991), might encode information about object location, textures, or orientations. A fourth achromatic pathway to the lobula is implicit from responses of male-specific neurons (Gilbert and Strausfeld, 1991), which are directional motion selective and are presumably supplied by small-field afferents carrying information about directional motion. These afferents are distinct from those supplying the lobula plate.

A fifth pathway (Fig. 6C) carries wavelength-specific information and originates from the R7 and R8 photoreceptors. The spectral sensitivity of R7 shows a single $\lambda_{max}$ at 340–60 nm (UV), whereas two types of R8s (R8p and R8y in *Musca* and *Calliphora*) have their $\lambda_{max}$ at 440 (blue) and 540 nm (green), respectively (Hardie, 1979; Smola and Meffert, 1979), with R8y having small peaks in the near-UV (Hardie and Kirschfeld, 1983). There are exceptions to these typical sensitivities of R7 and R8 (reviewed by Hardie, 1986). In the polarized light-sensitive dorsal rim area, R7 and R8 are exclusively UV-sensitive, and both still have their output terminals in the medulla. In the high-acuity zone of male flies, R7 and R8 end in the lamina, and both contain the R1-R6 photopigment. These local specializations, however, do not detract from a general role for R7 and R8 in color vision.

The R7 and R8 pairs terminate deep in the outer medulla, where they provide dichromatic channels to each medulla column. Trichromacy is thought to be made possible at this level by the addition of inputs from the brush (L3) monopolar cells, whose dendrites in the lamina are postsynaptic to the achromatic R1-R6 receptors (Boschek, 1971; Meinertzhagen and O'Neil, 1991; Strausfeld and Campos-Ortega, 1973b). It has been suggested that because L3 has only about a quarter to a fifth of the number of postsynaptic sites that L1 or L2 has, its response threshold must be higher (Anderson and Laughlin, 2000). It is activated only by high-intensity illumination of the R1-R6 photoreceptors and thus provides a high-intensity blue-green (+UV) channel to the medulla in parallel with the R7 and R8 receptors, which are also active at high light intensities (Anderson and Laughlin, 2000). Thus, one working hypothesis (Fig. 6C) is that R7, R8, and L3 inputs to the medulla, coding for UV alone, green, and UV+blue-green, respectively, supply color-opponent retinotopic neurons that end in deep layers of the lobula. Color-opponent responses have not yet been demonstrated electrophysiologically in flies, although there is evidence for them in honey bees (Hertel, 1980). However, there is good behavioral evidence for color vision in the flies *Lucilia* and *Drosophila* (Fukushi, 1990; Hernández de Salomon and Spatz, 1983; Menne and Spatz, 1977; Tang and Guo, 2001).

## EVIDENCE THAT MOTION PROCESSING IS ACHROMATIC, MEDIATED BY R1-R6 AND LMCs

In both calliphorid and drosophilid flies, optomotor behaviors and the responses of lobula plate tangential neurons to grating motion exhibit a dual-peaked spectral sensitivity that closely resembles that of photoreceptors R1-R6 (Kaiser, 1975). This was interpreted as evidence that the achromatic R1-R6 photoreceptors and their immediately postsynaptic relays provide the main input to direction-selective motion processing pathways. If major inputs included R7 or R8, specific differences in the spectral sensitivity curves would be expected in these experiments. A possible counterargument could have been made, however, that a simple additive input from R7 and/or R8 might be overwhelmed by the more numerous R1-R6 inputs. Another challenge came from optomotor experiments on a *Drosophila* mutant (*Vam, vacuolar medulla*) that suffers

from degeneration of LMCs L1 and L2 (and possibly of other lamina cells as well, Coombe et al., 1989). This mutant was named, however, for its severe degeneration in the outer medulla, which appears almost immediately upon eclosion, before much of the LMC degeneration is complete (Coombe and Heisenberg, 1986). Coombe et al. (1989) cited a poor correlation between LMC degeneration and optomotor responses as evidence that L1 and L2 might not be essential for this behavior. But as the optomotor responses in *Vam* are already greatly reduced within 1 hour of eclosion, and also could easily be affected by damage to the medulla, the implications for LMC function are ambiguous. A more convincing and interesting exception to achromatic motion processing occurs in honey bees (*Apis*) and their dipterous Batesian mimic, *Eristalis*. Both species show evidence that more than one spectral type of photoreceptor mediates their optomotor pathways (Srinivasan and Guy, 1990), suggesting that the clear advantages of excluding spectral information from motion processing pathways (Srinivasan, 1985) are not evolutionarily invariant.

Experiments with *Drosophila* mutants strongly support the achromatic nature of direction-sensitive motion processing in flies. $Ort^{1}$ $ninaE^{1}$ (formerly designated $ora^{JK84}$ or *outer rhabdoms absent*) is a visual mutant in which optomotor behavior is much diminished, and the only anatomical abnormality appears to be that R1-R6 are reduced to mere rudiments (Bülthoff, 1982a,b; Harris et al., 1976; Heisenberg and Buchner, 1977; Koenig and Merriam, 1977). In a more recent mutant strain $ninaE^{17}$, characterized by complete suppression of the photopigment specific to R1-R6, the same severe defects in optomotor behaviors are observed, though object fixation is affected only moderately (Strauss et al., 2001). Deoxyglucose activity labeling of $ort^{1}$ $ninaE^{1}$ shows a complete loss of both motion- and flicker-specific labeling in the optic lobes (Bülthoff, 1986; also see Neuroanatomical Evidence for a Specialized Motion-Sensitive Pathway). If flicker responses mediated by R7 or R8 served as major inputs to EMD circuits supplying the lobula plate, one would expect at least some flicker-induced or motion direction-selective activity to remain intact in this neuropil. In the mutant *retinal degeneration* ($rdgB^{KS222}$) light-induced degeneration of R1-R6 abolishes responses to visual motion, although R7 and R8 remain intact (Heisenberg and Buchner, 1977).

*Drosophila* mutants have also been used to examine the roles of specific neuropils or neurons in the optomotor response and to examine flicker- and motion-induced activity within the brain (Heisenberg and Wolf, 1984). For example, the mutant *optomotor blind* ($omb^{H31}$) has reduced optomotor turning responses that are ascribed to the absence of giant tangential neurons in the lobula plate. The *no on-transient* mutant $nonA^{H2}$ lacks the electroretinogram's (ERG) evoked "on"-"off" transients that are ascribed to LMCs, and shows specific impairment in its response to progressive motion of vertical gratings. $NonC^{P37}$, which similarly lacks evoked ERG transients, has an impaired optomotor response and reduced spatial resolution.

Enhancer trap techniques that express transgenes that either suppress (Keller et al., 2002) or report neuron activity (Ng et al., 2002) are opening up new possibilities for a genetic dissection of *Drosophila* sensory systems. In one recent report (Keller et al., 2002), expression of tetanus toxin (TNT) was used to block evoked synaptic vesicle release in specific visual interneurons, including the L1 and L2 monopolar cells. In one line in which LMCs and layers in the lobula plate and outer lobula were inactivated, flies showed no response to optomotor stimuli that normally induce walking, head movements, or landing responses, although the flies could fixate stationary objects (Keller, 2002). In another TNT construct, using a Gal4 line expressing only in L2 monopolar cells, optomotor responses were suppressed, whereby the range of contrast frequencies able to elicit a strong turning response was diminished (Keller, 2002). The implications of these experiments for motion processing are still rather unclear but both suggest that of the LMCs, L2 is likely to be a major player in elementary motion detection.

## NEUROANATOMICAL EVIDENCE FOR A SPECIALIZED MOTION-SENSITIVE PATHWAY

Golgi studies have suggested that there might be as many as forty distinct morphological types of retinotopic neurons in the medulla of the hoverfly *Eristalis* (Strausfeld, 1970). A similar number was suggested from Golgi studies of the housefly *Musca domestica* (Strausfeld, 1970) and the fruitfly *Drosophila melanogaster* (Fischbach and Dittrich, 1989). Among all these cell types, how might it be possible to identify candidates for involvement in motion computation?

Two experimental strategies have narrowed the search to just a few neurons. The first line of evidence comes from functional imaging studies using activity-dependent incorporation of deoxyglucose, a sugar that accumulates in metabolically active neurons because it cannot be metabolized (Bausenwein and Fischbach, 1992; Buchner et al., 1984).

These experiments support the idea that LMCs from the lamina and columnar neurons in the medulla are associated with the T4 and T5 "bushy" T-cells, the terminals of which end in the lobula plate. After flies were fed radioactive deoxyglucose, prolonged stimulation of the flies' visual fields with horizontal motion of vertical gratings resulted in deoxyglucose accumulation at the level of LMC endings in the medulla, and in the inner medulla at a proximal level corresponding to the dendrites of T4 cells (see Fig. 6 for schematic illustration of optic lobe neuropils and levels). Accumulation also occurred in the T5 dendritic layer over the lobula. Most significantly, this experiment selectively revealed two outer strata in the lobula plate (Fig. 6A). One of these was labeled after prolonged stimulation with front-towards-back (progressive) motion. The other was labeled after prolonged stimulation with back-towards-front (regressive) motion. Stimulation with vertical motion of horizontal gratings revealed the same accumulations in the medulla and over the lobula, but now labeled two other, inner strata in the lobula plate, one corresponding to upward motion, the other to downward motion. Stimulation with flicker again revealed deoxyglucose accumulation in both the outer and inner medulla and the T5 layer in the lobula, but, significantly, not in the lobula plate. The identification of these four directional motion-selective layers

in the lobula plate was especially interesting because both the T4 and T5 neurons (Strausfeld and Lee, 1991) occur as quartets in each medulla column. Thus, each VSU is represented by eight bushy T-cells, with four axons from each quartet segregating to one of the four "activity" levels in the lobula plate.

A second line of evidence identifies those retinotopic medulla neurons, which connect LMCs with dendritic trees of T4 and T5 neurons supplying the lobula plate (Figs. 3D,H, 6). This evidence derives from comparative studies of evolutionarily recent as well as basal Diptera where, despite taxon-specific stratifications in the medulla, the layer relationships among a subset of retinotopic neurons are highly conserved (Buschbeck and Strausfeld, 1996). Additionally, this conserved set of neurons has also been identified in Hymenoptera (Cajal and Sánchez, 1915; Strausfeld, 1976) and in sphingid moths (Strausfeld and Blest, 1970; Wicklein and Strausfeld, 2000). Comparisons across different species show that T4 dendrites are always visited by the varicose terminals of a characteristic form of retinotopic neuron, called the intrinsic transmedullary cell (iTm), the dendrites of which are constrained to a single column in the outer medulla where they overlap with the level of L2 endings from the lamina (Buschbeck and Strausfeld, 1996; Fischbach and Dittrich, 1989; Strausfeld, 1970). Comparative studies also demonstrate that the T5 cell dendrites are visited by the endings of a second and characteristic type of narrow-field transmedullary cell called Tm1, the dendrites of which coincide with L2 endings and those of a second lamina efferent neuron, the basket cell T1 (Strausfeld, 1970). These observations, along with the finding that T4 and T5 neurons are presynaptic to lobula plate tangential neurons (Strausfeld and Lee, 1991), suggest that these relay neurons connect the R1-R6 photoreceptors, via very few intervening synapses, to lobula plate tangential neurons that respond selectively to motion direction and orientation. However, apart from the T4 and probably T5 dendritic trees, these retinotopic neurons do not allow connections between retinotopic channels, which is a requirement for a circuit that can compute the direction of motion across two neighboring visual sampling units. Thus, a crucial question that must be addressed is: at what level and by which neurons are such cross connections supplied, if not by the T4 and T5 neurons themselves?

## IDENTIFIED RETINOTOPIC NEURONS IMPLICATED IN MOTION PROCESSING

Extracellular recordings from fly and moth optic lobes (Collett, 1971, 1972; McCann and Dill, 1969; Mimura, 1970, 1971) demonstrated the presence of motion-sensitive cells and provided the first evidence for direction-selective responses in the medulla and lobula complex. The development of intracellular methods, dye filling, and confocal microscopy have since provided quite detailed information about the identities and filtering properties of some of the smallest neurons in the fly visual system, which the anatomical studies summarized above predicted should carry information about motion direction to the lobula plate.

### Lamina Monopolar Cells and T1

Five monopolar cells are associated with each optic cartridge but only three receive first order inputs from R1-R6 (Boschek, 1971; Meinertzhagen and O'Neil, 1991). L1 and L2 receive direct inputs from R1-R6 onto rows of postsynaptic dendrites through the entire lamina. L3 has dendrites only in the outer two-thirds of the lamina and receives about one third to one fifth as many synapses from R1-R6 (Strausfeld and Campos-Ortega, 1973b). The small monopolar cells L4 and L5 are likely to have the status of local interneurons, as neither is directly postsynaptic to photoreceptor terminals. L4 is postsynaptic to amacrine cell processes that are themselves postsynaptic to photoreceptor endings. L4 also provides axon collaterals in an inner layer of the lamina where they are presynaptic to the axon hillocks of the L1 and L2 neurons of L4's own optic cartridge, and of the L1 and L2 neurons in two neighboring cartridges posterior to it (Meinertzhagen and O'Neil, 1991; Strausfeld and Campos Ortega, 1973a). L5 receives inputs from wide-field tangential processes in the lamina, possibly amacrine in nature. A sixth efferent neuron extends from each optic cartridge. This is the basket cell T1, the dendrites of which receive inputs indirectly from photoreceptors via the processes of amacrine cells (Campos-Ortega and Strausfeld, 1973). It is this last system of connections that provides the most peripheral and systematic network of connections among VSUs (see Fig. 9a).

Although numerous recordings have been attributed to L1 and L2, based either on intracellular staining (Järvilehto and Zettler, 1971, 1973) or on functional criteria (Laughlin, 1981), few experiments have tested visual motion with subsequent identification by intracellular staining. When this has been done (Gilbert et al., 1991), the responses of L1 and L2 to motion and flicker are indistinguishable at equivalent contrast frequencies. Thus, L1 and L2 are not motion-specific. Typically, their nonspiking responses consist of an ON-hyperpolarization, sustained hyperpolarization during illumination, and a transient OFF-depolarization, with variations dependent on details of the stimulus conditions and the state of light adaptation (Laughlin, 1981). In the only published recording from L3, its responses to flicker and motion were similar to those of L1 and L2 (Gilbert et al., 1991). Douglass and Strausfeld (1995) described a single nonspiking recording from L4 that showed essentially similar flicker and motion responses, except for a direction-dependent phase shift in the timing of DC depolarizations during grating motion. Because L4 exhibits a mirror symmetric, but not radially symmetric arrangement of lateral connections to neighboring columns at the proximal surface of the lamina (Burkhardt and Braitenberg, 1976; Strausfeld and Braitenberg, 1970), a role in elementary motion detection has sometimes been discussed for this monopolar cell. A possible role for T1 has also been suggested (Douglass and Strausfeld, 1995), because its terminals in the medulla interpose between each L2 terminal and the dendrites of the corresponding Tm1 cell, suggesting a possible source of the asymmetrical "delay" or low-pass filtering required by models of elementary motion detection (see below). A single T1 recording showed motion responses without clear depo-

larizations, whereas the flicker responses included the usual ON-hyperpolarizations and OFF-depolarizations (Douglass and Strausfeld, 1995). These response amplitudes were quite weak, and can only be considered suggestive of motion selectivity. To date, the clearest evidence for motion *selectivity* in a lamina monopolar cell is provided by a recording from L5 that showed sustained hyperpolarization during motion (Fig. 2C), contrasting with its fairly typical LMC-like ON/OFF responses to flicker (Douglass and Strausfeld, 1995). However, if L5 receives inputs from centrifugal feedback arising in the medulla, any L5 motion selectivity may have an origin deep in the system. In summary, L1 and L2 are clearly not motion-specific while T1 shows a motion-specific amplitude modulation. However, as emphasized earlier in this report, there is no requirement for any of the peripheral elements of the EMD circuit to exhibit motion selectivity.

### Retinotopic Neurons of the Medulla: Tms, iTm, and C2

The medulla consists of two concentric neuropils: an outer two thirds that receives afferents from the lamina, and a separate inner third that lies beneath the serpentine layer (Figs. 4A, 6A). The latter carries tangential sheets of axons destined for the mid-brain or contralateral medulla. Transmedullary (Tm) cells are retinotopic neurons that originate from cell bodies above the medulla and send their axons through these two layers (Fig. 1D). Most Tm cells send their axons to deep layers of the lobula, with the notable exception of the smallest transmedullary cell Tm1, and similarly shaped cells (Tm1a, Fischbach and Dittrich, 1989; Tm1b, Douglass and Strausfeld, 1998), all of which terminate in the superficial T5 dendritic layer covering the lobula. A second class of transmedullary neurons, called intrinsic transmedullary cells, connects the outer to the inner medulla. A third class, called transmedullary Y-cells, sends bifurcating axons to both the lobula plate and deep layers of the medulla (Strausfeld, 1976).

Of the many morphological types of Tm neurons (Fischbach and Dittrich, 1989; Strausfeld, 1976; Strausfeld and Nässel, 1980), only a fraction has yielded intracellular recordings followed with identification by dye filling. The type 1 transmedullary cell (Tm1) and the intrinsic transmedullary neuron (iTm) are notable: both have narrow fields of dendrites that appear to be restricted to their parent retinotopic column, and their dendrites are thought to be postsynaptic to at least the L2 terminal ending in the same column, possibly in conjunction with the ending of T1 neurons.

A single recording from a Tm1 neuron (Douglass and Strausfeld, 1995) shows a subtle, though unambiguous change in the frequency of depolarizations during regressive (rightward) vs. progressive motion. This recording provides some evidence for directional selectivity in a retinotopic medullary neuron. However, compared with higher-order neurons deeper in the visual system that show obvious excitation by preferred-direction motion and inhibition by motion in the opposite, or "null," direction, Tm1's directional selectivity is subtle at best. On the other hand, its targets, the T5 neurons, show fully fledged directionally selective motion responses (see below). This suggests that the more obvious forms of directional selectivity may develop by stages, through collaboration of such input neurons at the T5 dendritic trees (Douglass and Strausfeld, 1995). Two additional small-field transmedullary cells, Tm1a and Tm9, also terminate in the layer over the lobula. These were first described from *Drosophila melanogaster* (Fischbach and Dittrich, 1989), and have since been identified in *Phaenicia sericata* (Tm9 and a possible Tm1a homologue, termed Tm1b by Douglass and Strausfeld, 1998). In recordings from Tm9 and Tm1b, neither showed evidence for motion selectivity (Douglass and Strausfeld, 1998).

The medulla also gives rise to retinotopic neurons that project back out to the lamina. These are the centrifugal neurons, C2 and C3, which provide feedback from their dendrites in the inner medulla to the lamina. C2 provides GABA-immunoreactive boutons that are presynaptic to L1 and L2 above the level of their dendrites (Datum et al., 1986; Meyer et al., 1986). C3 has GABA-immunoreactive boutons (Sinakevitch et al., 2003) that are presynaptic to L1 and L2 along the length of their dendritic segments. Intracellular recordings from C2 (Douglass and Strausfeld, 1995) revealed motion-specific but non-directionally selective DC hyperpolarizations, similar to those of L5, but also showing a clear orientation-selective difference between vertical and horizontal motion (see Fig. 2D). Because C2 is presynaptic only to L1 and L2, hyperpolarizations of L5 during motion appear to arise independently of C2.

### Delivery of Direction- and Orientation-Selective Information to the Lobula Complex: Tm Cells, Bushy T Cells, and Y Cells

Retinotopic pathways from the medulla to deeper levels in the lobula are provided by many types of transmedullary cells, most of which have dendritic trees spreading through several neighboring retinotopic columns. These Tm cells have dendrites within the outer two thirds of the medulla, and may have additional dendritic or axon collateral processes within the inner medulla layer, beneath the serpentine layer. Transmedullary cells originate from cell bodies that lie distal to the outer medulla. So too, does the class of transmedullary Y cells that provide bifurcating axons supplying both the lobula plate and deep layers of the lobula.

All of these transmedullary cells are distinct from another morphological class of retinotopic neurons that originate from cell bodies either lying beneath or lateral to the inner medulla, or behind the lobula plate. The first of these derives from cell bodies that lie lateral to the medulla, and which give rise to two types of T-cells (T2 and T3), so-called because the neurite from the cell body makes a T-like bifurcation to form a functional axon. There are four well-documented types of T-cells: T2, T3, T4, and T5. T2 neurons, which end deep in the lobula, have dendritic trunks that extend outwards through the inner and then outer medulla to reach the deep terminals of L1 monopolar cells (Campos-Ortega and Strausfeld, 1972b). Recordings from T2 demonstrate its orientation selectivity, suggesting that L1 provides a parallel pathway to the lobula via T2 (Douglass and Strausfeld, 2003). T3 neurons are re-

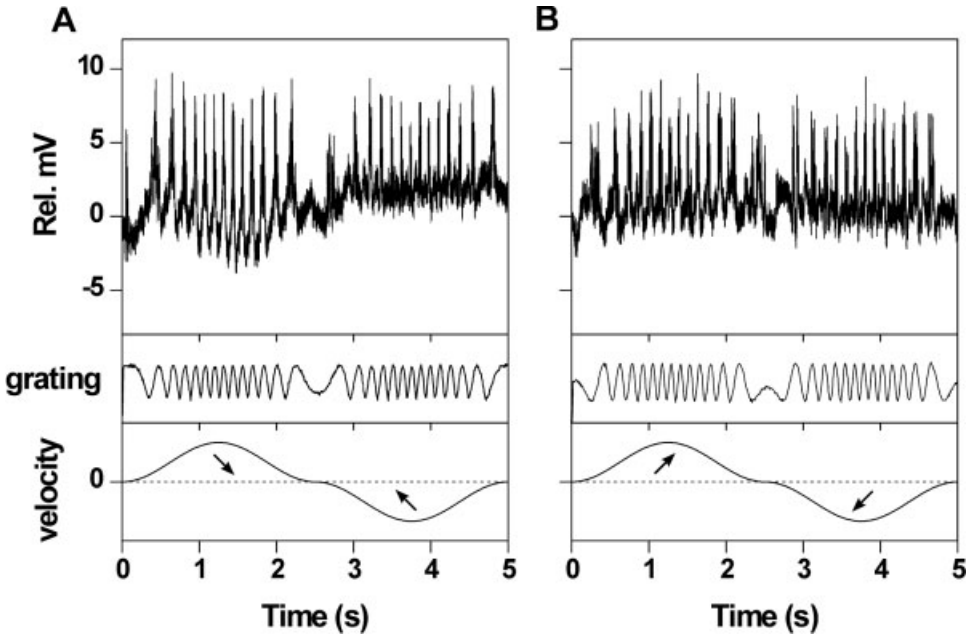


Fig. 7. Intracellular responses of a T4 cell in *Phaenicia sericata* (top traces) to directional motion stimulation, showing bursts of spike-like depolarizations that follow the grating contrast frequency across a range of motion speeds. Responses were zeroed to the pre-stimulus baseline level (**A**, downward progressive and upward regressive motion; **B**, upward progressive and downward regressive motion). Middle traces record the passage of bright and dark grating stripes, monitored by projecting an image of the center of the stimulus CRT onto a photodiode. Bottom traces indicate the grating velocity, which was varied sinusoidally from 0 to 12 and back to 0 Hz (0°–93°–0°/s) before each change in motion direction (arrows). The recordings were obtained from the T4 cell illustrated in Figure 3D, and represent a portion of the raw data used to compute the response *vs*. direction data plotted in Figure 3C.

stricted to the inner medulla where their dendrites extend through all its strata. T3 neurons have terminals in the lobula beneath the T5 dendritic layer. Their responses to visual stimuli are as yet unknown. T4 and T5 cells both arise from a dense population of cell bodies that lies behind the lobula plate. Neurites extend from these cell bodies through the lobula plate to reach the underside of the medulla (T4 neurons) or the outermost layer over the lobula (T5 neurons). At both locations, each neurite gives rise to a flattened bush-like dendritic tree from which an axon extends back into the lobula plate. As described above, these neurons have long been considered prime candidates for participation in the processing of directional motion information because of their close anatomical relationships with retinotopic neurons that are assumed to relay information from the terminals of LMCs (Strausfeld and Lee, 1991). T4 and T5 cells occur as quartets and the terminals of individual T4 and T5 neurons from each quartet segregate to the four levels in the lobula plate strata corresponding to the four direction-selective levels revealed by deoxyglucose activity staining (Strausfeld and Lee, 1991).

Intracellular recordings from T4 and T5 neurons show that both cell types are motion-selective, but in different ways. In two recordings from T4 cells (Douglass and Strausfeld, 1996), the responses to wide-field flicker consisted of (1) transient ON-depolarizations that often were followed by additional spike-like transients during light ON, and (2) slower, smaller OFF-depolarizations. Responses to directional grating motion (Fig. 7) resembled the flicker ON responses, but with bursts of depolarizations phase-locked to the contrast frequency of the grating stripes and generally lacking intervening OFF responses. Moreover, small variations in the amplitude of these depolarizations were correlated with motion orientation, with larger average spike amplitudes during horizontal motion in either direction (Fig. 3C).

To date, two recordings have been obtained from neurons that dye fills revealed to be T5 cells (Douglass and Strausfeld, 1995). One of these neurons exhibited quite small (up to approximately 1 mV) voltage fluctuations, which are thought to have resulted from impalement of the cell near the base of its dendritic tree. Unlike the T4 recordings, this T5 cell exhibited more "typical" flicker responses consisting of an ON-hyperpolarization, a sustained hyperpolarizing plateau, and an OFF-depolarization (cf. Fig. 2A). In response to motion, the frequency of miniature excitatory potentials in this neuron changed in a direction-dependent manner, with maximal excitation by progressive, slightly upward motion and inhibition by regressive motion (Fig. 3G). The second T5 neuron showed larger-amplitude responses, which probably resulted from impalement of the axon. This cell showed sustained direction-dependent depolarizations or hyperpolarizations to motion (Fig. 8) that closely resemble the characteristic DC shifts of HS and VS cells to wide-field grating motion, but with the additional presence of fluctuations matching the contrast frequency. Although this recording was too brief to permit the construction of a complete polar plot of directional selectivity, the data clearly show strong depolarizations during progressive (0°)

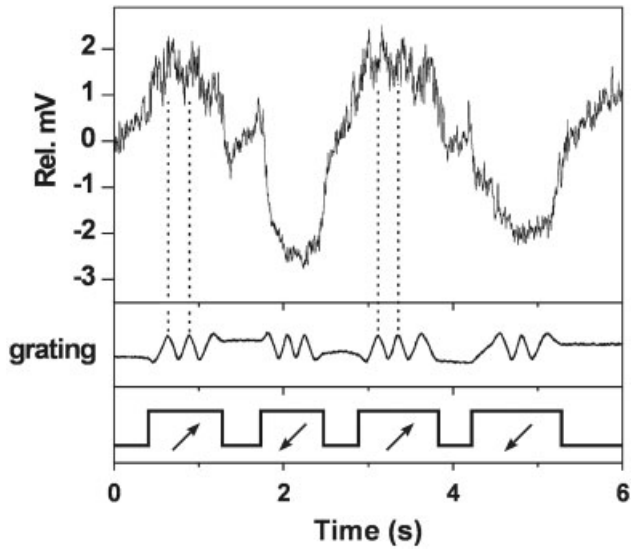


Fig. 8. Intracellular responses of a *Phaenicia sericata* T5 cell to unidirectional grating motion, formatted as in Figure 7, but with approximately constant-velocity motion. Bottom: The stimulus durations and the directions (arrows) of grating motion. This record illustrates direction-selective excitatory and inhibitory responses. Sustained depolarizations occurred during upward-progressive motion, and hyperpolarizations during downward-regressive motion. The vertical dotted lines illustrate the phase-locking of small-amplitude voltage fluctuations to the grating frequency, which occurred only during the depolarizations. This recording was obtained from the T5 cell illustrated in Figure 3H. [See Douglass and Strausfeld (1995) for this cell's responses to horizontal motion.]

and upward-progressive (45°) motion, whereas hyperpolarizations were induced by regressive (180°) and downward-regressive (225°) motion. Both T5 cell recordings thus show directional sensitivity, with excitation to a preferred direction (approximately horizontal progressive motion in both cases), and inhibition to a null direction.

In summary, the recordings from T4 show excitatory responses and a weak form of orientation-selectivity, whereas T5 exhibits strong directional selectivity resulting from both excitatory and inhibitory responses. It is still unknown whether the distribution of T5 preferred directions is grouped into four cardinal directions (up, down, progressive, and regressive), as suggested by their aforementioned architectural relationships with the four direction-selective layers in the lobula plate. Modeling of the mechanisms that generate optic flow sensitivity in dipterous suggests that a minimum of only three such cardinal directions is needed to generate robust optic flow sensitivity in wide-field neurons that receive their inputs from arrays of small-field, T5-like direction-selective neurons (Douglass and Strausfeld, 2000). Thus, it is still something of a puzzle why there are two sets of bushy T-cell quartets disposed at two separate levels in the optic lobes. One possibility that is consistent with the physiological recordings is that only the T5 cells deliver direction-sensitive information to the lobula plate, whereas T4 may serve as a channel for non-direction sensitive, yet motion-specific information (Douglass and Strausfeld, 1996). In general, nondirectional motion information could be used in circuits that analyze motion speed (see e.g. Ibbotson, 2001), and can be useful for other types of motion analysis such as range estimation (Sobel, 1990; Srinivasan et al., 1991) and male-specific visual tracking and pursuit (Gronenberg and Strausfeld, 1991). To date, however, there is no evidence linking T4 cells to the pathways that mediate these behaviors.

The last type of retinotopic neuron to be considered here comprises cells that originate from cell bodies beneath the medulla, but have bifurcating axons to the lobula and lobula plate. Branches of these Y cells extend through the inner medulla, some invading deep strata of the outer medulla. The extent to which their branches in the medulla function as terminals or dendrites is still unclear, and such neurons may represent a class of centrifugal cells, with dendrites in the lobula plate and terminals in both the medulla and lobula.

## AT WHAT LEVEL IN THE SYSTEM IS MOTION COMPUTED?

The recordings from the medulla indicate that motion might first be computed within its outer layer, or possibly distally in the lamina. What is certain is that considerable motion processing has occurred by the time retinotopic neurons reach the lobula plate, where motion information is parsed among, and further integrated by, the lobula plate's wide-field tangential neurons. These tangentials provide information about visual flow field properties (Hausen, 1984; Hengstenberg, 1982; Krapp and Hengstenberg, 1997; Krapp et al., 1998), relative motion of objects against background (Egelhaaf, 1985), and binocular motion using integrated information from both eyes via heterolateral connections between the left and right lobula plates (Hausen, 1981; Krapp et al., 2001; Strausfeld et al., 1995; Strausfeld, 1997).

The lobula plate is not the only center that integrates retinotopic motion information. The lobulas of many species of flies have high-acuity zones, such as in both sexes of robber flies (Asilidae; Buschbeck and Strausfeld, 1997) and in the upper frontal retina of the males of several species, as well as in the upper part of the turban eyes of bibionids (Zeil, 1983). In sarcophagid flies, such high-acuity regions are served by motion direction- and/or orientation-selective neurons in a corresponding region of the lobula (Gilbert and Strausfeld, 1991). But where do these neurons acquire their motion information? It cannot come from T4 or T5 cells, as these neurons project only to the lobula plate. The question then is: does the lobula acquire its motion-specific inputs from a ubiquitous EMD circuit that also supplies relays to T4 and T5 neurons? Or, might the lobula receive direction- and orientation-selective relays from the lobula plate itself, or even from EMD circuits that exclusively supply the lobula?

Recordings from neurons that supply the lobula provide clues as to which alternative is correct. Recordings from one species of retinotopic Y cell that supplies both the lobula and lobula plate (the Y18 neuron; Strausfeld, 1976) show that it depolarizes to upward motion and hyperpolarizes to downward motion (Douglass and Strausfeld, 1998). Its bistratified outputs in the lobula are at the level of the direction-selective male lobula giant tangential neurons MLG1 and MLG2 (homo-

logues of these neurons occur in female flies; Strausfeld, unpublished data). A long-lasting recording from the type 1 Y1 cell, a small-field columnar neuron, also revealed its motion-selectivity within a restricted receptive field, but no evidence for orientation or direction selectivity to either grating or single bar motion (Douglass and Strausfeld, 1998). Columnar neurons in the lobula, which share levels of the Y1 endings, responded similarly to motion, but showed no direction or orientation specificity (Douglass and Strausfeld, 1998; Gilbert and Strausfeld, 1991).

A few recordings have been obtained from transmedullary neurons that penetrate deep into the lobula. A recording from the type Tm2 neuron (Douglass and Strausfeld, 1998) showed fluctuations at the grating contrast frequency but no evidence for motion selectivity, whereas some transmedullary cell recordings (Gilbert et al., 1991) were at least suggestive of motion selectivity. Together, these data would seem to suggest that neurons that receive their inputs in the medulla, and which terminate in the deep lobula, provide motion-sensitive, but not motion-selective information. An important exception, however, is the type T2 neuron. As noted above, T2 is Tm-like, but has its cell body lateral to the medulla, and shows clear evidence of orientation selectivity (Douglass and Strausfeld, 2003).

In summary, because the lobula receives direction-selective inputs from at least one Y cell, and orientation-selective inputs via T2, there is no need to invoke an EMD circuit that is specific to the lobula in order to explain directional selectivity in this neuropil. It is more reasonable to suppose that a single peripheral array of EMD circuits supplies different subsets of retinotopic motion-selective neurons. These subsets diverge from the medulla to reach higher-level motion-selective elements, such as the male-specific tangential cells in the lobula, and, in the lobula plate, systems of wide-field neurons involved in the visual stabilization of flight.

An additional system of motion-sensitive elements is composed of columnar neurons that are shared between the lobula plate and lobula. These neurons have bistratified dendritic trees, with a system of dendrites in both neuropils (Strausfeld and Gilbert, 1991). Several of these neurons respond to motion stimuli and differentiate them from flicker (Douglass and Strausfeld, 1998; Gilbert and Strausfeld, 1992). They are thus motion-selective, and one (called LPL-67) is even direction-selective (*Sarcophaga bullata*: Gilbert and Strausfeld, 1991, *P. sericata*: Douglass and Strausfeld, 1998). It is unknown whether the dendrites of these neurons receive motion-selective inputs at the level of the lobula, lobula plate, or both. In any case, it is of considerable interest that motion-selective columnar neurons shared between the lobula and lobula plate send their axons to neuropils of the mid-brain that also receive terminals or collaterals of direction-selective tangential neurons from the lobula plate (Strausfeld and Gronenberg, 1990). Like recordings from centrifugal looming-selective neurons that extend out to the sphingid medulla (Wicklein and Strausfeld, 2000), this last observation again suggests that further integration of motion information must occur at deeper levels of the brain. Thus, the analysis of information about looming and receding objects, and possibly other complex visual phenomena, is provided by the integration of various higher-order motion primitives that are combined at levels deeper than the retinotopic neuropils of the optic lobes.

## CIRCUITS UNDERLYING ELEMENTARY MOTION DETECTION

Since 1956, one model has been invoked to account for the results of behavioral and electrophysiological experiments involving motion detection. This model, devised by Hassenstein and Reichardt (1956) from observations of optomotor responses by the beetle *Chlorophanus* (Hassenstein and Reichardt, 1956), comprised a simple correlation circuit that is selective for motion direction. The outputs of this circuit and its subsequent refinements correctly predict both behavioral responses to motion stimuli, and electrophysiological responses of wide-field motion-selective tangential cells in the lobula plate (reviews; Borst and Egelhaaf, 1989; Egelhaaf and Borst, 1993). While the Hassenstein-Reichardt circuit is perhaps the most robust of such models in the neurosciences, without reference to the anatomical organization and function of retinotopic neurons it is limited as a template for developing ideas about how motion is actually computed in the optic lobes. A circuit based on real neurons, yet that still provides outputs that are consistent with physiology and behavior, is highly desirable as an alternative to the convenient, but artificial view that lobula plate tangential cells are supplied by arrays of virtual Reichardtian cross correlators.

What, then, are the most likely identities and arrangements of neurons that could provide a "universal" motion detector circuit? A synthesis of the anatomical and physiological findings reviewed in this report suggests plausible solutions to this question. A basic search image has been provided by the identification of small field retinotopic neurons peripheral to the lobula plate that are common across taxa (Buschbeck and Strausfeld, 1996), and by intracellular recordings from these neurons (Douglass and Strausfeld, 1995, 1996). These neurons and their properties cannot all be shoehorned into a Hassenstein-Reichard-type circuit (Fig. 9, upper right). Instead, configurations must be considered that are both consistent with this search image and provide "Reichardtian" outputs. One such circuit is now particularly attractive because it meets these criteria, and also takes into account even broader commonalities in the organization of the laminas of insects and other arthropods possessing compound eyes (Strausfeld, unpublished data). The model (Higgins et al., 2001) defines a tiered architecture that first computes non-directional motion, then motion orientation, and, finally, motion direction. In this neuron-based model, lamina amacrine cells, which in flies provide relays from receptor endings to T1 neurons, play a major role in the reconstruction of motion selectivity. Activity of T1 cells is motion-selective, but insensitive to motion orientation or direction. These latter properties emerge at deeper levels involving Tm1 and T5 cells, respectively. Just as in a conventional Hassenstein-Rechardt circuit, elaborations upon this basic scheme, such as feedback and the modulation of synaptic strengths and spatial extent, can be used to account for motion adaptation as well as spatial pooling

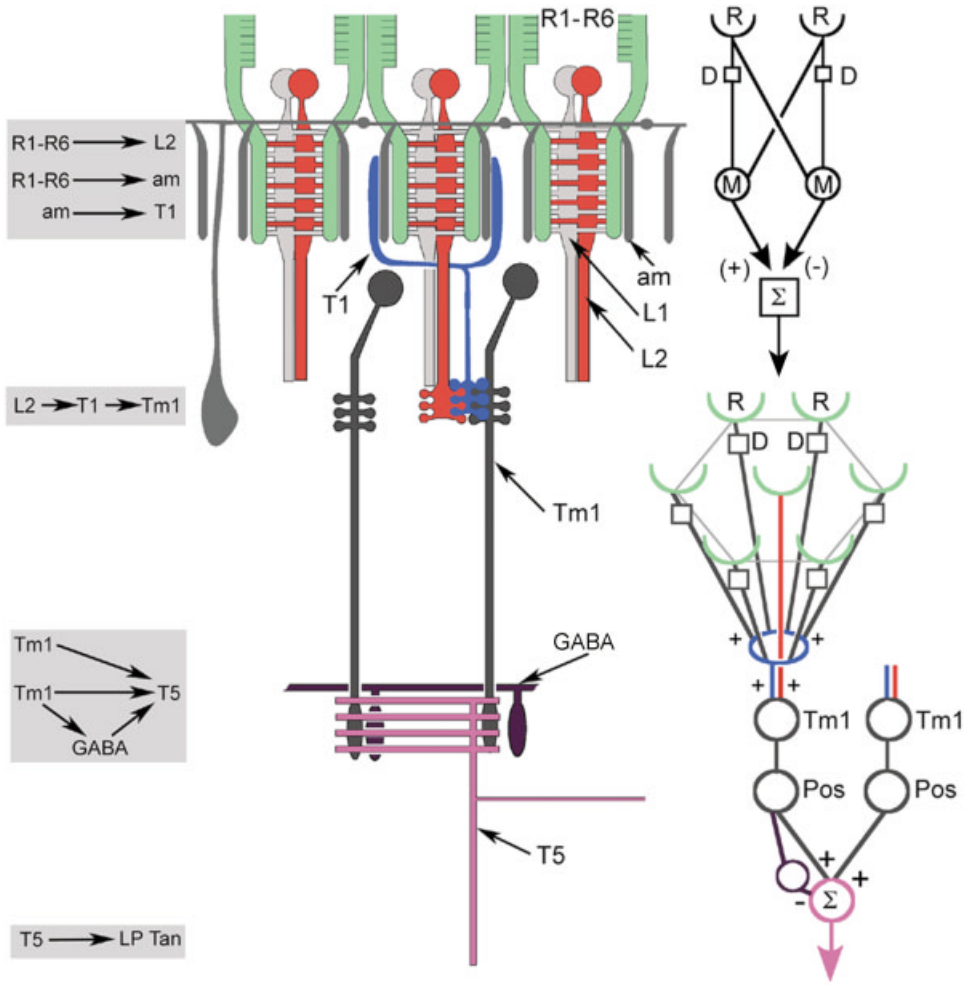


Fig. 9. Types of neurons shared across the Diptera and found in other insect and crustacean taxa provide necessary and sufficient elements for an EMD circuit. This neuron-based circuit differs in some crucial steps from the Hassenstein-Reichardt theoretical motion detection circuit (top right). Neurons that probably participate in elementary motion detection are receptors (R1-6), lamina amacrines (am), the L2 lamina monopolar cell (shown here with its partner L1, but the latter without its endings), the T1 basket cell, the type 1 transmedullary cell (Tm1), the bushy type 5 T-cell (T5), and a wide-field GABAergic neuron that provides local specializations among T5 dendrites over the entire lobula. T1 basket dendrites derive their inputs from R1-6 via amacrine cell processes. Inputs to Tm1 from L2 are thought to be via the intervening terminal of T1. The theoretical correlation-type EMD circuit (top right) has two unidirectional EMDs combining at a "subtraction stage" to yield fully opponent preferred-direction (excitatory) and null-direction (inhibitory) responses at the summation stage (Σ), with selectivity for contrast frequency (Borst and Egelhaaf, 1990). Motion inputs arrive sequentially at each receptor (R), and are combined at an integrator stage (M), via lateral connections between adjacent channels, with an asymmetrical delay or low-pass filter operation (D) in one input relative to the other. The neuron-based model (bottom right, colored as in main figure) provides inputs from a hexagonal surround of VSUs (green, R: their geometrical arrangement indicated by gray lines) via amacrines to a T1 lying alongside an L2 neuron that derives its input from R1-6 of the central VSU. Amacrines provide the necessary delay (low pass filters) between VSUs and T1. Convergence of T1 with the parallel channel L2 occurs at the Tm1 dendrites. This arrangement allows motion detection by Tm1 but does not provide direction or orientation selectivity. These selectivities are hypothesized to arise by the convergence (+) and differential weighting of adjacent Tm1 neurons, representing neighboring VSUs, onto T5. The asymmetric inputs at this level are provided by the wide-field GABAergic local interneuron (−). The model requires that for each VSU, there should be a pair of Tm1-like neurons, one of each pair associated with the inhibitory interneuron. Partial rectification (POS) is postulated to occur at synapses between Tm1 and T5. Current integration occurs in the T5 dendritic tree (Higgins et al., 2001).

of EMD inputs under dim ambient light conditions (Pick and Buchner, 1979; Schuling et al., 1989; Srinivasan and Dvorak, 1980), or to produce selectivity for motion speed (Zanker et al., 1999).

## CONCLUSIONS

Neuroanatomical studies have predicted functional attributes of many of the elements that are now known to be involved either in motion computation or the integration of information about motion. Braitenberg's (1970) anatomical survey of the optic lobe's retinotopic organization, and Pierantoni's (1976) description of lobula plate neurons both predicted that this neuropil provides horizontal and vertical motion-selective efferents to the mid-brain. Recordings from these neurons proved the anatomists correct. Likewise, cross-taxonomic studies of retinotopic neurons predicted that a specific subset of medulla and centrifugal neurons

should be involved in early processing of motion stimuli (Buschbeck and Strausfeld, 1996). Intracellular recordings have again supported the anatomical predictions.

What must still be experimentally substantiated is the level at which the first cross-correlation occurs between neighboring receptor channels to provide the first element of motion detection: activity that is tuned to a sequential intensity change occurring between two neighboring visual sampling points. Does this occur in the lamina, by means of amacrine processes shared among several VSUs? Or might it be a function of connections between neighboring retinotopic columns within the outer medulla, such as provided for by tangential elements at the level of LMC terminals? If so, might movement information recorded from lamina neurons merely reflect feedback from the outer levels of the medulla? Further anatomical and functional studies are required to resolve these important questions. What is clear, however, is that any motion-detecting circuit that is based on the structural and functional organization of real neurons must also be consistent with the types of outputs that are produced by wide-field efferents from the lobula plate, and by the Reichardt and Hassenstein model. This challenge reflects on the fact that a robust model, originally invoked to explain a simple behavior of a beetle, still drives the search for its organic basis.

## ACKNOWLEDGMENTS

The proposed elementary motion detecting circuit described here abstracts joint studies with Dr. Charles Higgins, which will be published in full elsewhere. We thank Dr. Higgins for helpful discussions and suggestions in the writing of the present study.

## REFERENCES

Ali MA, editor. 1984. Photoreception and vision in invertebrates. New York: Plenum Press. 858 p.

Anderson JC, Laughlin SB. 2000. Photoreceptor performance and the co-ordination of achromatic and chromatic inputs to the fly visual system. Vision Res 40:13–31.

Autrum H, editor. 1981. Comparative physiology and evolution of vision in invertebrates. Handbook of Sensory Physiology VII/6B. Berlin: Springer.

Bausenwein B, Fischbach K-F.1992. Separation of functional pathways in the fly's medulla: combination of 2-deoxyglucose studies with anatomical fine analysis. In: Singh RN, editor. Nervous systems: principles of design and function. Bombay: Wiley Eastern. p 223–240.

Bausenwein B, Dittrich APM, Fischbach K-F. 1992. The optic lobe of *Drosophila melanogaster*. II. Sorting of retinotopic pathways in the medulla. Cell Tissue Res 267:17–28.

Borst A, Egelhaaf M. 1989. Principles of visual motion detection. Trends Neurosci 12:297–306.

Borst A, Egelhaaf M. 1990. Direction selectivity of blowfly motion-sensitive neurons is computed in a two-stage process. Proc Natl Acad Sci USA 87:9363–9367.

Boschek CB. 1971. On the fine structure of the peripheral retina and the lamina of the fly, *Musca domestica*. Z Zellforsch Mikrosk Anat 110:336–349.

Braitenberg V. 1967. Patterns of projection in the visual system of the fly. I. Retina-lamina projections. Exp Brain Res 3:271–298.

Braitenberg V. 1970. Ordnung unt Orientierung der Elemente im Sehsystem der Fliege. Kybernetik 7:235–242.

Buchner E, Buchner S, Bülthoff I. 1984. Deoxyglucose mapping of nervous activity induced in *Drosophila* brain by visual movement. J Comp Physiol A 155:471–483.

Bülthoff H. 1982a. *Drosophila* mutants disturbed in visual orientation. I. Mutants affected in early visual processing. Biol Cybern 45:63–70.

Bülthoff H. 1982b. *Drosophila* mutants disturbed in visual orientation. II. Mutants affected in movement and position computation. Biol Cybern 45:71–77.

Bülthoff H. 1986. Deoxyglucose mapping of nervous activity induced in *Drosophila* brain by visual movement. III. Outer rhabdomeres absent$^{JK84}$, small optic lobes$^{KS58}$ and no object fixation E$^{B12}$, visual mutants. J Comp Physiol A 158:195–202.

Burkhardt W, Braitenberg V. 1976. Some peculiar synaptic complexes in the first visual ganglion of the fly, *Musca domestica*. Cell Tissue Res 173:287–308.

Buschbeck EK, Strausfeld NJ. 1996. Visual motion detection circuits in flies: small-field retinotopic elements responding to motion are evolutionarily conserved across taxa. J Neurosci 16:4563–4578.

Buschbeck EK, Strausfeld NJ. 1997. The relevance of neural architecture to visual performance: phylogenetic conservation and variation in dipteran visual systems. J Comp Neurol 383:282–304.

Cajal SR, Sánchez D. 1915 Contribución al conocimiento de los centros nerviosos de los insectos. Parte I. Rétina y centros opticos. Trab Lab Invest Biol 13:1–167.

Campos-Ortega JA, Strausfeld NJ. 1972a. The columnar organization of the second synaptic region of the visual system of *Musca domestica* L. I. Receptor terminals in the medulla. Z Zellforsch 124:561–582.

Campos-Ortega JA, Strausfeld NJ. 1972b. Columns and layers in the second synaptic region of the fly's visual system: The case for two superimposed neuronal architectures. In: Wehner R, editor. Information processing in the visual systems of arthropods. New York: Springer Verlag. p 31–36.

Campos-Ortega JA, Strausfeld NJ. 1973. Synaptic connections of intrinsic cells and basket arborisations in the external plexiform layer of the fly's eye. Brain Res. 59:119–136.

Collett T. 1971. Visual neurones for tracking moving targets. Nature 232:127–130.

Collett T. 1972. Visual neurones in the anterior optic tract of the privet hawk moth. J Comp Physiol 78:396–433.

Collett TS, Land MF. 1978. How hoverflies compute interception courses. J Comp Physiol 125:191–204.

Coombe PE, Heisenberg M. 1986. The structural brain mutant *Vacuolar medulla* of *Drosophila melanogaster* with specific behavioral defects and cell degeneration in the adult. J Neurogenet 3:135–158.

Coombe PE, Srinivasan MV, Guy RG. 1989. Are the large monopolar cells of the insect lamina on the optomotor pathway? J Comp Physiol A 166:23–35.

Datum J-H, Weiler R, Zettler F. 1986. Immunocytochemical demonstration of gamma-aminobutyric acid and glutamic acid decarboxyase in R7 photoreceptors and C2 centrifugal fibers in the blowfly visual system. J Comp Physiol 159:241–249.

Douglass JK, Strausfeld NJ. 1995. Visual motion detection circuits in flies: Peripheral motion computation by identified small-field retinotopic neurons. J Neurosci 15:5596–5611.

Douglass JK, Strausfeld NJ. 1996. Visual motion detection circuits in flies: Parallel direction- and non-direction sensitive pathways between the medulla and lobula plate. J Neurosci 16:4551–4562.

Douglass JK, Strausfeld NJ. 1998. Functionally and anatomically segregated visual pathways in the lobula complex of a calliphorid fly. J Comp Neurol 396:84–104.

Douglass JK, Strausfeld NJ. 2000. Optic flow representation in the optic lobes of Diptera: modeling the role of T5 directional tuning properties. J Comp Physiol A 186:783–797.

Douglass JK, Strausfeld NJ. 2003. Retinotopic pathways providing motion-selective information to the lobula from peripheral elementary motion detecting circuits. J Comp Neurol 456:326–344.

Dowling JE, Boycott BB. 1966. Organization of the primate retina: electron microscopy. Proc R Soc Lond B 166:80–111.

Egelhaaf M. 1985. On the neuronal basis of figure-ground discrimination by relative motion in the visual system of the fly. II. Figure-detection cells, a new class of visual interneurones. Biol Cybern 52:195–209.

Egelhaaf M, Borst A. 1993. A look into the cockpit of the fly: visual orientation, algorithms, and identified neurons. J Neureosci 13: 4573–4574.

Fischbach K-F, Dittrich APM. 1989. The optic lobe of *Drosophila melanogaster*. I. A Golgi analysis of wild-type structure. Cell Tissue Res 258:441–475.

Franceschini N. 1975. Sampling of the visual environment by the compound eye of the fly: fundamentals and applications. In: Snyder AW, Menzel R, editors. Photoreceptor optics. Berlin, Heidelberg, New York: Springer. pp 98–125.

Fukushi T. 1990. Colour discrimination from various shades of grey in the trained blowfly *Lucilia cuprina*. J Insect Physiol 36:69–75.

Geesaman BJ, Andersen RA. 1996. The analysis of complex motion patterns by form/cue invariant MSTd neurons. J Neurosci 16:4716–4732.
Gilbert C, Strausfeld NJ. 1991. The functional organization of male-specific visual neurons in flies. J Comp Physiol A 169:395–411.
Gilbert C, Strausfeld NJ. 1992. Small-field neurons associated with oculomotor and optomotor control in muscoid flies: functional organization. J Comp Neurol. 316:72–86.
Gilbert C, Penisten DK, DeVoe RD. 1991. Discrimination of visual motion from flicker by identified neurons in the medulla of the fleshfly *Sarcophaga bullata*. J Comp Physiol A 168:653–673.
Gronenberg W, Strausfeld NJ. 1991. Descending pathways connecting the male-specific visual system of flies to the neck and flight motor. J Comp Physiol A 169:413–426.
Hardie RC. 1979. Electrophysiological analysis of fly retina. I. Comparative properties of R1-R6 and R7 and 8. J Comp Physiol 129: 19–33.
Hardie RC. 1986. The photoreceptor array of the dipteran retina. Trends Neurosci 9:419–423.
Hardie RC, Franceschini N, McIntyre PD. 1979. Electrophysiological analysis of fly retina. II. Spectral and polarisation sensitivity in R7 and R8. J Comp Physiol A 133:23–39.
Hardie RC, Kirschfeld K. 1983. Ultraviolet sensitivity of fly photoreceptors R7 and R8: evidence for a sensitising function. Biophys Struct Mech 9:171–180.
Hassenstein B, Reichardt W. 1956. Systemtheoretische Analyse der Zeit-, Reihenfolgen- unt Vorzeichenauswertung bei der Bewegungsperzeption des Rüsselkäfers *Chlorophanus*. Z Naturforsch 11:513–524.
Hausen K. 1981. Monocular and binocular computation of motion in the lobula plate of the fly. Verh Dtsch Zool Ges 1981:49–70.
Hausen K. 1984. The lobula complex of the fly: Structure, function and significance in visual behavior. In: Ali MA, editor. Photoreception and vision in invertebrates. New York: Plenum Press. p 523–599.
Hausen K, Strausfeld NJ. 1980. Sexually dimorphic interneuron arrangements in the fly visual system. Proc R Soc Lond B 208:57–71.
Harris WA, Stark WS, Walker JA. 1976. Genetic dissection of the photoreceptor system in the compound eye of *Drosophila melanogaster*. J Physiol 256:415–439.
Heisenberg M, Buchner E. 1977. The role of retinula cell types in visual behavior of *Drosophila melanogaster*. J Comp Physiol 117: 127–162.
Heisenberg M, Wolf R. 1984. Vision in *Drosophila*: genetics of microbehavior. Studies of brain function, vol 12. New York: Springer Verlag. 250 p.
Hengstenberg R. 1982. Common visual response properties of giant vertical cells in the lobula plate of the blowfly *Calliphora*. J Comp Physiol 149:179–193.
Hernández de Salomon C, Spatz H-C. 1983. Colour vision in *Drosophila melanogaster:* wavelength discrimination. J Comp Physiol 150: 31–37.
Hertel H. 1980. Chromatic properties of identified interneurons in the optic lobes of the bee. J Comp Physiol A 137:215–232.
Higgins CM, Vaneck T, Joshi PB, Strausfeld NJ. 2001. A model for directional selectivity in an insect based on non-directional motion cells and appropriate to cross phyla comparisons. Soc Neurosci Abstr 27:308.5.
Horridge GA. 1975. The compound eye and vision of insects. Clarendon: Oxford. 595 p.
Horridge GA, Meinertzhagen IA. 1970. The accuracy of the patterns of connections of the first- and second-order neurons of the visual system of *Calliphora*. Proc R Soc Lond B 175:69–82.
Ibbotson MR. 2001. Evidence for velocity-tuned motion-sensitive descending neurons in the honeybee. Proc R Soc Lond B 268:2195–2201.
Järvilehto M, Zettler F. 1971. Localized intracellular potentials from pre- and postsynaptic components in the external plexiform layer of an insect retina. Z Vgl Physiol 75:422–444.
Järvilehto M, Zettler F. 1973. Electrophysiological-histological studies on some functional properties of visual cells and second-order neurons of an insect retina. Z Zellforsch 136:291–306.
Kaiser W. 1975. The relationship between visual movement detection and colour vision in insects. In: Horridge GA, editor. The compound eye and vision of insects. Clarendon: Oxford. pp 358–377.
Keller A. 2002. Genetic intervention in sensory systems of the fly. Ph.D. Thesis. Bayerischen Julius-Maximilians-Universität Würzburg.
Keller A, Sweeney ST, Zars T, O'Kane CJ, Heisenberg M. 2002. Targeted expression of tetanus neurotoxin interferes with behavioral responses to sensory input in *Drosophila*. J Neurobiol 50:221–233.
Kirschfeld K. 1967. Die Projektion der optischen Umwelt auf das Raster der Rhabdomere im Komplexauge von *Musca*. Exp Brain Res 3:248–270.
Koenig J, Merriam JR. 1977. Autosomal ERG mutants. *Drosophila* Inf Serv 52:50–51.
Krapp HG, Hengstenberg R. 1997. A fast stimulus procedure to determine local receptive field properties of motion-sensitive visual interneurons. Vision Res 37:225–234.
Krapp HG, Hengstenberg B, Hengstenberg R. 1998. Dendritic structure and receptive-field organization of optic flow processing interneurons in the fly. J Neurophysiol 79:1902–1917.
Krapp HG, Hengstenberg R, Egelhaaf M. 2001. Binocular contributions to optic flow processing in the fly visual system. J Neurophysiol 85:724–734.
Laughlin SB. 1981. Neural principles in the peripheral visual systems of invertebrates. In: Autrum H, editor. Handbook of sensory physiology VII/6B. Berlin: Springer. p 133–280.
Laughlin SB, Hardie RC. 1978. Common strategies for light adaptation in the peripheral visual systems of fly and dragonfly. J Comp Physiol 128:319–340.
McCann GD, Arnett DW. 1972 Spectral and polarization sensitivity of the dipteran visual system. J Gen Physiol 59:534–558.
McCann GD, Dill JC. 1969. Fundamental properties of intensity, form and motion perception in the visual nervous systems of *Calliphora phaenicia* and *Musca domestica*. J Gen Physiol 53:385–413.
Menne D, Spatz H-Ch. 1977. Colour vision in *Drosophila melanogaster*. J Comp Physiol 144:301–312.
Meinertzhagen IA, O'Neil SD. 1991. Synaptic organization of columnar elements in the lamina of the wild-type in *Drosophila melanogaster*. J Comp Neurol 305:232–263.
Meyer E, Manute C, Streit P, Nässel D. 1986. Insect optic lobe neurons identifieable with monoclonal antibodies to GABA. Histochemistry 84:207–216.
Mimura K. 1970. Integration and analysis of movement information by the visual system of flies. Nature 226:964–966.
Mimura K. 1971. Movement discrimination by the visual system of flies. Z Vgl Physiol 73:105–138.
Moring J. 1978. Spectral sensitivity of monopolar neurons in the eye of *Calliphora*. J Comp Physiol 123:335–338.
Ng M, Roorda RD, Lima SQ, Zemelman BV, Morcillo P, Miesenbock G. 2002. Transmission of olfactory information between three populations of neurons in the antennal lobe of the fly. Neuron. 36:463–474.
Pierantoni R. 1976. A look into the cockpit of the fly: the architecture of the lobular plate. Cell Tissue Res 171:101–122.
Pick B, Buchner E. 1979. Visual movement detection under light- and dark-adaptation in the fly, *Musca domestica*. J Comp Physiol A 134:45–54.
Schuling FH, Mastebroek HAK, Bult R, Lenting BPM. 1989. Properties of elementary movement detectors in the fly *Calliphora erythrocephala*. J Comp Physiol A 165:179–192.
Sinakevitch I, Douglass JK, Scholz G, Loesl R, Strausfeld NJ. 2003. Conserved and divergent organization in the optic lobes of insects and isopods, with reference to other crustarean taxa. J Comp Neurol, in press.
Smakman JG, Stavenga DG.1986. Spectral sensitivity of blowfly photoreceptors: dependence on waveguide effects and pigment concentration. Vision Res 26:1019–1025.
Smola U, Meffert P. 1979. The spectral sensitivity of the visual cells R7 and R8 in the eye of the blowfly *Calliphora erythrocephala*. J Comp Physiol 133:41–52.
Sobel E. 1990. The locust's use of motion parallax to measure distance. J Comp Physiol A 167:579–588.
Srinivasan MV. 1985. Shouldn't directional movement detection necessarily be "colour-blind?" Vision Res 25:997–1000.
Srinivasan MV, Dvorak DR. 1980. Spatial processing of visual information in the movement-detecting pathway of the fly. J Comp Physiol 140:1–23.
Srinivasan MV, Guy RG. 1990. Spectral properties of movement perception in the dronefly *Eristalis*. J Comp Physiol A 166:287–295.
Srinivasan MV, Lehrer M, Kirchner WH, Zhang SW. 1991. Range perception through apparent image speed in freely flying honeybees. Visual Neurosci 6:519–535.
Stavenga DG, Hardie RC, editors. 1989. Facets of vision. Heidelberg: Springer. 454p.
Strausfeld NJ. 1970. Golgi studies on insects. Part II. The optic lobes of Diptera. Philos. Trans Roy Soc Lond B 258:135–223.
Strausfeld NJ. 1976. Atlas of an insect brain. Berlin: Springer. 214 p.
Strausfeld NJ. 1979. The representation of a receptor map within retinotopic neuropil of the fly. Verh Dtsch Zool Ges 1979:167–179.
Strausfeld NJ. 1980. Male and female visual neurons in dipterous insects. Nature 283:381–383.

Strausfeld NJ. 1991. Structural organization of male-specific visual neurons in calliphorid optic lobes. J Comp Physiol A 169:379–393.

Strausfeld NJ 1997. Oculomotor control in insects: From muscles to elementary motion detectors. In: Stein PSG, Grillner S, Selverston AI, Stuart DG, editors. Neurons, networks, and motor behavior. Cambridge Massachusetts, London: MIT Press. pp 277–284.

Strausfeld NJ, Bassemir UK. 1985. Lobula plate and ocellar interneurons converge onto a cluster of descending neurons leading to neck and leg motor neuropil in *Calliphora erythrocephala*. Cell Tissue Res 240:617–640.

Strausfeld NJ, Blest AD. 1970. Golgi studies on insects. Part I. The optic lobes of Lepidoptera. Philos Trans Roy Soc Lond B 258:81–223.

Strausfeld NJ, Braitenberg V. 1970. The compound eye of the fly (*Musca domestica*): connections between the cartridges of the lamina ganglionaris. Z Vergl Physiol 70:95–104.

Strausfeld NJ, Campos-Ortega JA. 1973a. The L4 monopolar neuron: a substrate for lateral interaction in the visual system of the fly *Musca domestica*. Brain Res 59:97–117.

Strausfeld NJ, Campos-Ortega JA. 1973b. L3, the 3rd 2nd-order neuron of the 1st visual ganglion in the "neural superposition" eye of *Musca domestica*. Z Zellforsch Mikrosk Anat 139:397–403.

Strausfeld NJ, Campos-Ortega JA. 1977. Vision in insects. Pathways possibly underlying neural adaptation and lateral inhibition. Science 195:894–897.

Strausfeld NJ, Gilbert C. 1992. Small-field neurons associated with oculomotor and optomotor control in muscoid flies: cellular organization in the lobula plate. J Comp Neurol 316:56–71.

Strausfeld NJ, Gronenberg W. 1990. Descending neurons supplying the neck and flight motor of Diptera: Organization and neuroanatomical relationships with visual pathways. J Comp Neurol 302: 954–972.

Strausfeld NJ, Lee J-K. 1991. Neural basis for parallel visual processing in the fly. Visual Neurosci 7:13–33.

Strausfeld NJ, Nässel DR. 1980. Neuroarchitecture of brain regions that subserve the compound eyes of Crustacea and Insects. In: Autrum H, editor. Handbook of sensory physiology, vol VII/6B. Heidelberg: Springer. pp 1–133.

Strausfeld NJ, Kong A, Milde JJ, Gilbert C, Ramaiah L. 1995. Oculomotor control in calliphorid flies: GABAergic organization in heterolateral inhibitory pathways. J Comp Neurol 361:298–320.

Strauss R, Renner M, Götz K. 2001. Task-specific association of photoreceptor systems and steering parameters in *Drosophila*. J Comp Physiol A 187:617–632.

Tang S, Guo A. 2001. Choice behavior of *Drosophila* facing contradictory visual cues. Science 294:1543–1547.

Young RM. 1990. Mind, brain and adaptation in the nineteenth century: cerebral localization and its biological context from Gall to Ferrier. Clarendon: Oxford University Press. 278 p.

Vigier P. 1909. Mécanisme de la synthèse des impressions lumineuses recueilles par les yeux composés des Diptères. CR Acad Sci 148: 1221–1223.

Wicklein M, Strausfeld NJ. 2000. Organization and significance of neurons that detect change of visual depth in the hawk moth *Manduca sexta*. J Comp Neurol 424:356–376.

Zanker JM, Zeil J, editors. 2001. Motion vision: Computational, neural and ecological constraints. New York: Springer. 400 p.

Zanker JM, Srinivasan MV, Egelhaaf M. 1999. Speed tuning in elementary motion detectors of the correlation type. Biol Cybern 80: 109–116.

Zeil J. 1983. Sexual dimorphism in the visual system of flies: the divided brain of male Bibionidae (Diptera). Cell Tissue Res 229: 591–610.