J Comp Physiol A (2002) 188: 419–437
DOI 10.1007/s00359-002-0316-8

REVIEW

A. Borst · J. Haag

Neural networks in the cockpit of the fly

Accepted: 13 April 2002 / Published online: 7 June 2002

Abstract Flies have been buzzing around on earth for over 300 million years. During this time they have radiated into more than 125,000 different species (Yeates and Wiegmann 1999), so that, by now, roughly every tenth described species is a fly. They thus represent one of the most successful animal groups on our planet. This evolutionary success might, at least in part, be a result of their acrobatic maneuverability, which enables them, for example, to chase mates at turning velocities of more than 3000° s^{-1} with delay times of less than 30 ms (Land and Collett 1974; Wagner 1986). It is this fantastic behavior, which has initiated much research during the last decades, both on its sensory control and the biophysical and aerodynamic principles of the flight output (Dickinson et al. 1999, 2000). Here, we review the current state of knowledge about the neural processing of visual motion, which represents one sensory component intimately involved in flight control. Other reviews on this topic have been published with a similar (Hausen 1981, 1984; Hausen and Egelhaaf 1989; Borst 1996) or different emphasis (Frye and Dickinson 2001; Borst and Dickinson 2002). Because of space limitations, we do not review the extensive work that has been done on fly motion-sensitive neurons to advance our understanding of neural coding (Bialek et al. 1991; Rieke et al. 1997; de Ruyter et al. 1997, 2000; Haag and Borst 1997, 1998; Borst and Haag 2001). Unless stated otherwise, all data presented in the following were obtained on the blowfly *Calliphora vicina* which we will often casually refer to as 'the fly'.

Keywords Calcium-imaging · Compartmental modeling · Motion vision · Dendritic processing

A. Borst (✉) · J. Haag
Max-Planck-Institute of Neurobiology,
Department of Systems and Computational Neurobiology,
Am Klopferspitz 18a, 82152 Martinsried, Germany
E-mail: borst@neuro.mpg.de
Tel.: +49-89-85783250
Fax: +49-89-85783252

Abbreviations *CH-cells* centrifugal horizontal cells · *H1-4 cells* cells responding to horizontal image motion · *HS-cells* horizontal system cells · *LPTC* lobula plate tangential cell · *ND* null direction · *PD* preferred direction · *R1-6* photoreceptor cells · *V-cells* cells sensitive to vertical image motion · *VS-cells* vertical system cells

The fly visual system

The processing of visual motion starts in the eye. In flies, like in most invertebrates, this structure is built from many single elements called facets or ommatidia. Each ommatidium possesses its own lens and its own set of photoreceptors. The latter send axons into a part of the brain exclusively devoted to image processing called the 'visual ganglia'. In flies, the visual ganglia consist of three successive layers of neuropile where the columnar composition reflects the relative position of facets within the eye. Thus, visual images perceived by the eye are retinotopically projected onto sheets of neuropile such that neighborhood relationships between image points are conserved within the nervous system.

As can be seen in Fig. 1, these layers are called lamina, medulla and lobula complex. The latter is split into the lobula and the lobula plate and receives input from medulla elements in parallel. Each column of these layers is formed by a stereotyped set of neurons that are repeated throughout the layer. Using the Golgi-staining method these columnar elements have all been characterized and anatomically described in two species, i.e., *Calliphora vicina* (Strausfeld 1984) and *Drosophila melanogaster* (Fischbach and Dittrich 1989). The somata of columnar neurons are located in the periphery while their main processes typically ramify in specific sublayers. Based on the anatomical overlap between the various columnar elements, the retinal images are thought to be processed by at least three different retinotopic pathways in parallel (Bausenwein et al. 1992). Except for the lamina neurons (Laughlin and Osorio

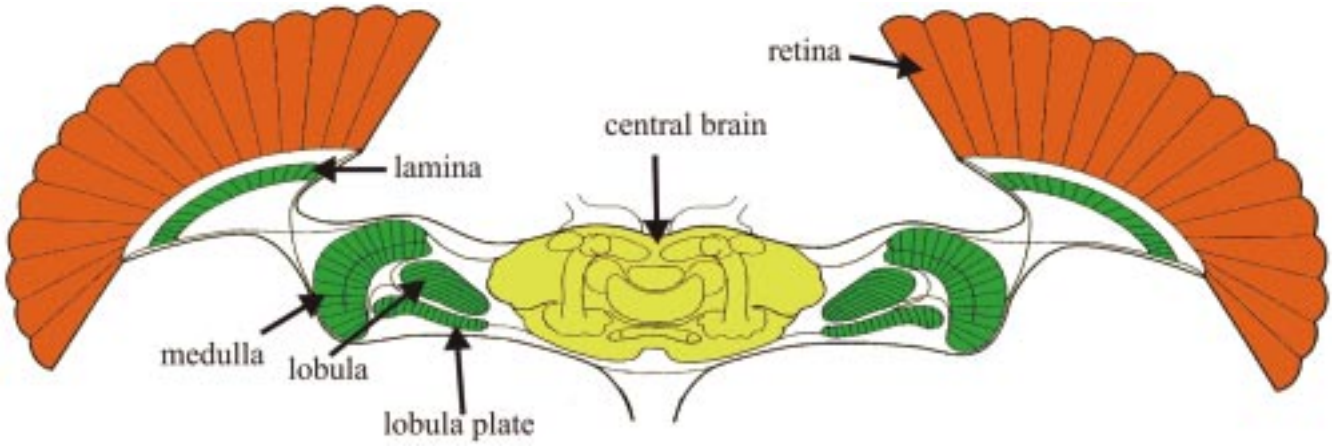


Fig. 1. Schematic horizontal cross-section through the fly head

1989), most columnar elements have escaped electrophysiological recordings due to their small size (but see Gilbert et al. 1991 in the fleshfly *Sarcophaga*; Douglass and Strausfeld 1995, 1996 in the blowfly *Phormia*). Hence their response characteristics are largely unknown.

The lobula plate forms the posterior part of the lobula complex. It is here that a prominent group of visual interneurons, called lobula plate tangential cells (LPTCs) are found (Fig. 2). Because of the large diameter of their processes (up to 10 μm), these cells were amongst the first visual interneurons of the fly to be recorded from intracellularly. On each hemisphere, there exist about 60 different LPTCs each of which is individually identifiable based on its characteristic anatomy and response properties. In general, LPTCs are sensitive to visual motion in a directionally selective way. They are excited by motion in one direction (called their preferred direction, PD), and inhibited by motion along the opposite direction (their anti-preferred or null direction, ND). Based on ablation experiments, as well as the similarities between the LPTC response properties and different types of motion-driven behaviors of flies (Geiger and Nässel 1981, 1982; Hausen and Wehrhahn 1983, 1990; Heisenberg et al. 1978 using the fruitfly *Drosophila*; Borst and Bahde 1988 using the housefly *Musca*; Borst 1991), it is concluded that LPTCs are involved in the fly's visual course control.

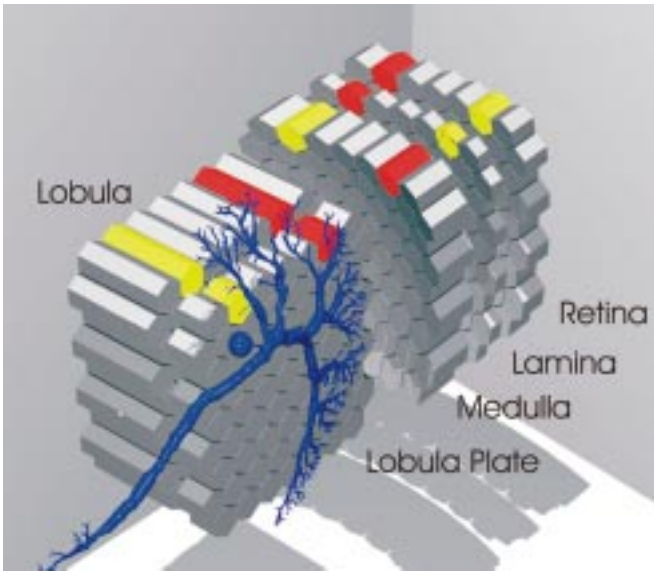


Fig. 2. 3-D schematics of the retina and the optic lobes together with a tangential cell. The *columns* in each layer can be seen to represent the facets of the retina in a one-to-one fashion leading to a retinotopic projection of the visual surround onto the dendrites of the lobula plate tangential cells (LPTCs). Not shown are two chiasms, one between the lamina and the medulla, and one between the medulla and the lobula-complex. Note that, in reality, the columns of the lobula complex are organized in a coarser mosaic than the ones of the medulla and lamina (Strausfeld 1989)

Lobula plate tangential cell types

LPTCs can be grouped into different subclasses according to their different response characteristics: (1) according to their preferred orientation (Fig. 3), i.e., whether they respond primarily to horizontal or vertical image motion; (2) according to their prevalent electrical response mode (Fig. 4), i.e., whether they respond to image motion along their preferred direction by a graded shift of membrane potential, by an increase of action potential frequency or a mixture of both modes; (3) according to their projection area, i.e., whether the neurons send their axon to the contralateral brain hemisphere (heterolateral LPTCs) or whether the axon terminates on the ipsilateral side (ipsilateral LPTCs); and finally (4) according to their spatial integration properties, i.e., whether their response increases as the visual pattern grows, or whether they respond better to small moving patterns (see Fig. 10).

When grouped according to their preferred orientation, LPTCs fall in two classes: horizontally and vertically sensitive cells. Within the first class, we find three cells of the horizontal system, the HS-cells (Hausen 1982a, 1982b). HS-cells share many response features except for their dendrites that cover different, but

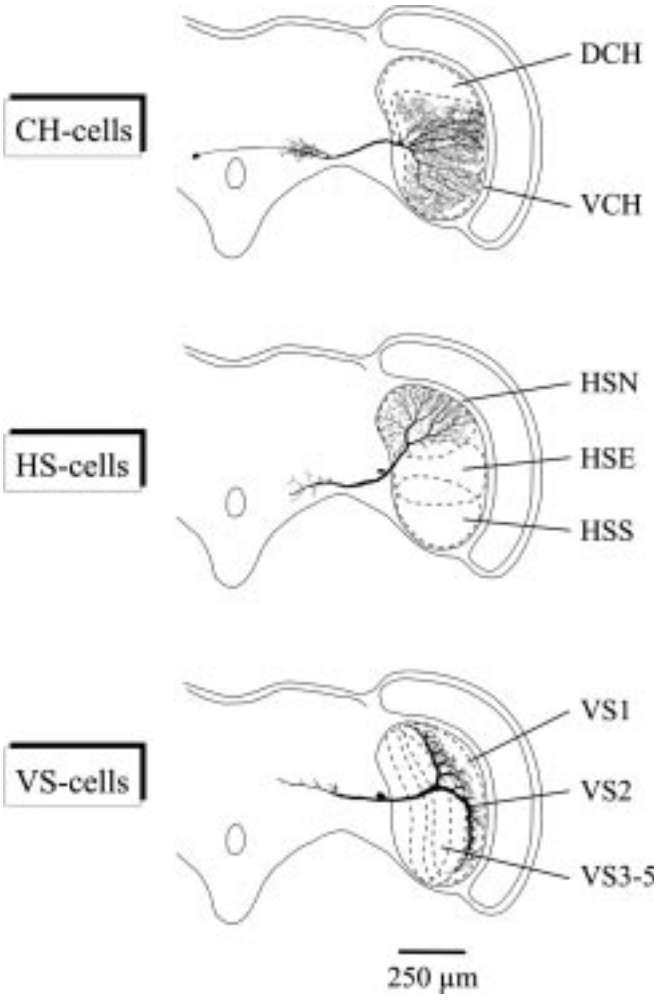


Fig. 3. Lobula plate tangential cells as seen from a posterior view of frontal brain sections. The neuropile to the right is the medulla, while the lamina and the retina are not shown at all. From each of three cell families, only one member is represented. The hatched lines in the lobula plate indicate those areas covered by the dendrites of the other family members (modified from Borst and Haag 1996)

overlapping, areas of the lobula plate: the northern HSN-cell extends its dendrite in the dorsal part of the lobula plate, the equatorial HSE-cell in the medial part and the southern HSS-cell in the most ventral part. Concomitantly, HS-cells have different but overlapping receptive fields reaching from the dorsal (HSN) to the ventral (HSS) part of visual space (Fig. 3). Also in this class are the two centrifugal horizontal cells, called CH-cells (Eckert and Dvorak 1983). In this family, there exist only two cells per brain hemisphere, a dorsal dCH- and a ventral vCH-cell (Fig. 3).

HS- as well as CH-cells respond to image motion with a graded shift of membrane potential that, in the case of HS-cells, is superimposed by action potentials of irregular amplitude. Other neurons responding to horizontal image motion are the H1, H2, H3 and H4 cells (Hausen 1984). In contrast to HS- and CH-cells, these neurons all project to the contralateral brain hemisphere. As a further difference to the former groups, H1–4 cells all produce full-blown action potentials and respond to image motion primarily by modulating the frequency of these (Bialek et al. 1991). Another heterogeneous class of horizontally sensitive neurons are the FD- (Egelhaaf 1985) and CI-neurons (Gauck and Borst 1999). These neurons produce regular action potentials but are distinct from all other cells listed so far in that they respond preferentially to small moving objects: when the pattern exceeds a certain size, their response becomes small again. Most of these cells are in addition inhibited by heterolateral neurons.

The other group of LPTCs comprises those cells that respond preferentially to vertical image motion. There are 11 neurons of the vertical system, the VS-cells (Hengstenberg et al. 1982; Hengstenberg 1982; Krapp and Hengstenberg 1996). VS-cells orient their dendrites along the dorso-ventral axis in the lobula plate, which gives them, together with their horizontally running axon, a particular T-shaped appearance making them recognizable and distinct from HS- and CH-cells (Fig. 3). VS-cells are numbered sequentially according to the location of their dendrite from most lateral to proximal. With respect to their mixed response mode, VS-cells are similar to HS-cells. In response to downward motion, VS-cells depolarize, and this depolarization again is superimposed on irregular amplitude action potentials. In response to null direction motion, i.e., upward, VS-cells hyperpolarize and any spiking activity is suppressed. As amongst the neurons sensitive to horizontal image motion, there also exist neurons sensitive to vertical image motion which produce regular action potentials like the V1-cell. Again, as in the horizontal system, these spiking neurons project heterolaterally, i.e., extend their axon across the midline of the brain to contact other neurons.

The synaptic distribution on LPTCs has been addressed by only a few studies (Hausen et al. 1980; Strausfeld and Lee 1991; Gauck et al. 1997). In general, the results indicate that HS- and VS-cells are postsynaptic in the lobula plate and pre- and postsynaptic in the protocerebrum where their axon ends. Thus, it seems as if these different branches are correctly named dendrite and axon. However, the situation is much different for CH-cells. As the name already suggests (centrifugal horizontal cells) these neurons have always been suspected of being presynaptic in the lobula plate and postsynaptic in the protocerebrum. This assumption is based on the observation that certain varicosities (blobs), which have often been found to be presynaptic specializations in invertebrates, are seen in the lobula plate branches of CH-cells, at the light microscope level. This presumption was indeed confirmed by subsequent ultrastructural investigations (Gauck et al. 1997). The protocerebral branches were found to house exclusively postsynaptic densities and presynaptic sites were clearly visible in the lobula plate branches of CH-cells. However, as a further complication, the lobula plate arborizations of CH-cells were also found to house

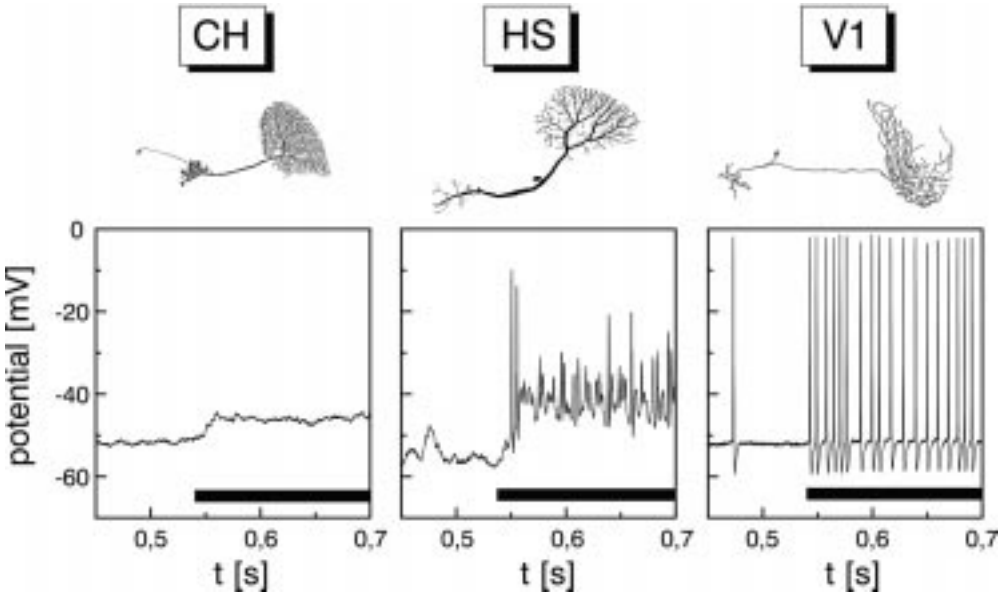


Fig. 4. LPTCs respond to preferred direction motion in various ways, from purely graded (centrifugal horizontal cells, *CH-cells*), over mixed (horizontal system cells, *HS-cells*) to purely spiking (cells sensitive to vertical image motion, *V1-cells*). The neurons shown on top of the response traces were taken from Borst and Haag 1996 (CH- and HS-cells) and from Hausen 1984 (V1-cell)

presynaptic sites that makes the lobula plate arbor of CH-cells a dendrite and an axon terminal at the same time. No such data exist about the spiking heterolateral neurons H1–4 or V1.

Mechanisms of direction selectivity

The most significant response characteristic of LPTCs is their directionally selective response to visual motion. In the sample intracellular recording of an HS-cell (Fig. 5), it can be seen that the response of LPTCs discriminate strictly between two opposite directions of image motion. Thus, the direction of image motion is explicitly represented at the level of LPTCs. An interesting fact here is that the direction of image motion is not explicitly represented in the output signal of a single photoreceptor. In response to a moving grating, the photoreceptor signal is just modulated according to the number of stripes passing by per second, no matter in what direction the pattern is moving. Only when at least two photoreceptor signals, displaced along the

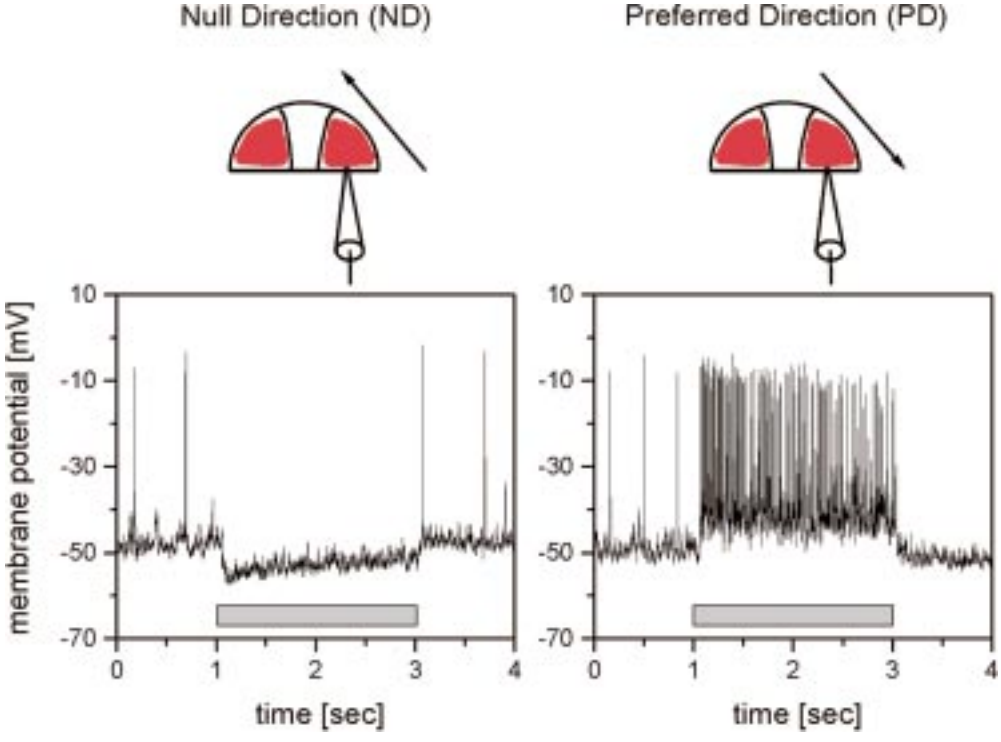


Fig. 5. Intracellular recording from an equatorial horizontal system cell (HSE-cell). The neurons hyperpolarizes in response to motion from the back to the front of the animal (null direction, *ND*). In response to motion along the opposite direction of motion, i.e., from the front to the back, the neuron depolarizes and fires trains of action potentials (preferred direction, *PD*). The stimulus situation is schematically shown on top of the recording traces

orientation of image motion, are considered can the direction of motion be derived by an external observer based on the shift of the signals relative to each other.

A basic mechanism of how such a comparison between the signals of neighboring photoreceptors might be realized was proposed by Reichardt and Hassenstein (Reichardt 1961, 1987; for review see: Borst and Egelhaaf 1989, 1993). Their model, called the 'correlation-type of motion detector', is shown in Fig. 6. It incorporates two essential operations: asymmetrical temporal filtering and a nonlinear interaction stage where the low-pass filtered signal from one image location is multiplied with the high-pass filtered signal from the neighboring image location. At each image location there exists at least four such units with four different orientations: one for rightward, one for leftward, one for downward, one for upward motion. There is good evidence that each LPTC receives input from two fields of such units with opposite preferred directions, one field providing excitatory, the other one inhibitory input to the dendrites.

Such a processing scheme can account for many response properties of both motion sensitive neurons (LPTCs) and visually guided behavior (optomotor response; reviewed in Borst and Egelhaaf 1989). First of all, the spatially integrated response of such arrays of motion detectors exhibit, unlike a speedometer, a velocity optimum beyond which the response declines. Interestingly, the detector model responses also depend on the structure of the moving pattern: low contrast patterns elicit smaller responses than high contrast ones, although they move at exactly the same velocity. Furthermore, the velocity optimum depends on the spatial pattern wavelength in such a way that the ratio of velocity optimum and spatial wavelength remains constant, resulting in an invariant temporal frequency optimum. Such particular detector properties also come to light when motion in two-dimensional space is considered (Borst et al. 1993): here, partly occluded patterns moving along a strictly horizontal or vertical orientation lead to predictable cross talk between the horizontal and the vertical system, respectively, which can be seen at the level of LPTCs as well as in the optomotor response of flies. A distinct fingerprint of a correlation-scheme of motion detection was derived when local signals were analyzed instead of the spatially integrated detector output (Egelhaaf et al. 1989; Single and Borst 1998). According to the correlation model, such local output signals should consist of two components, one that is directionally selective and one reflecting the change of local luminance. Therefore, movement of a periodic grating should result in a local depolarization of the dendrite, which is superimposed by modulations reflecting the temporal frequency of the moving pattern. Such local signals could indeed be observed when a moving grating was presented through a small aperture while recording the axonal membrane potential of the neuron (Egelhaaf et al. 1989). Local modulations were also seen during full-field visual motion, when local signals were recorded in small dendritic regions using

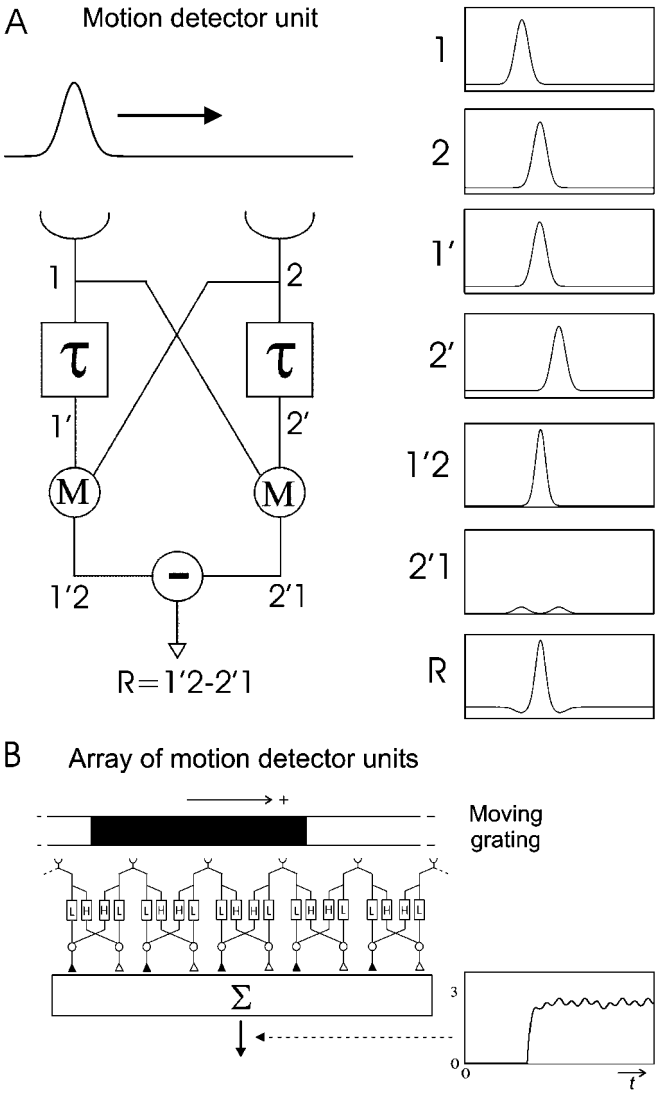


Fig. 6A, B. A Basic scheme of a correlation-type motion detector together with the signals in the various processing lines. **A** Gaussian luminance distribution is shown moving to the right. The input lines *1* and *2* reflect this luminance change as the stimulus passes by (note the delay between the signals in line 1 and 2). The delay line shifts these signals to the right (*1'* and *2'*). Thus, the signals coincide at the left multiplication stage but are displaced at the right multiplication stage. This leads to strong output signals for the left detector subunit (*1'2*) but to only small signals in the right one (*2'1*). After subtraction of these signals, the final output shows a strong direction selectivity. **B** An array of detectors is used to simulate the neural layers between the photoreceptors and tangential cells. The amplitude of the summed responses of all synapses reflects the pattern velocity. Note that in contrast to the principal mechanism outlined in **A**, first-order low-pass filters (*L*) and high-pass filters (*H*) were used in this simulation

in vivo calcium measurement (Single and Borst 1998). Since local modulations are phase shifted only along the direction of motion, they only cancel when spatially integrated along this axis and not orthogonal to it. This might be one explanation of the fact that neurons sensitive to vertical image motion extend their dendrite along the vertical axis in the lobula plate, while horizontal cells do so along the horizontal axis.

Evidence for the correlation-type of motion detector was also derived from apparent motion experiments where, instead of actually moving a grating pattern, local luminance was changed in a stepwise manner in adjacent areas within the receptive field of H1. Using sophisticated optics, single ommatidia (Schuling et al. 1989) or even single photoreceptors within one ommatidium (Riehle and Franceschini 1984; Franceschini et al. 1989) could be sequentially stimulated. These studies revealed that sequential stimulation of photoreceptor R1 and R6 within one ommatidium is sufficient to elicit directionally selective responses in H1 (Riehle and Franceschini 1984; Franceschini et al. 1989). Furthermore, during daylight conditions, interactions between ommatidia separated by up to eight times the interommatidial angle were shown to contribute to the total response of the neuron (Schuling et al. 1989). Comparing sequentially occurring luminance changes of different sign (on-on, off-off, on-off, off-on), the sign rule of the correlation-type motion detector was proven to hold for fly motion-sensitive cells: presenting the luminance changes along the preferred direction of H1, sequences of the same sign (on-on, off-off) produced positive motion responses, while mixed sign sequences (on-off, off-on) resulted in negative motion responses, just as predicted by the model (Egelhaaf and Borst 1992).

Pathways for local motion detection

Having accumulated experimental evidence that the correlation-type of motion detector provides input to the LPTCs and, thus, is responsible for their direction selectivity (see above), the question about its actual implementation arises. What neurons in the fly optic lobes constitute this detector and what biophysical mechanisms underlie such formal operations as temporal filtering or multiplication? Here, unfortunately, experimental evidence is rare leaving room for many speculations. At present, it is not even clear what columnar neurons provide synaptic input to the LPTCs. Most evidence speaks in favor of the bushy T-cells, T4 and T5, as potential input candidates to LPTCs. So far, a single study has shown unequivocally a chemical synapse between an HS-cell dendrite and a columnar T4-cell (Strausfeld and Lee 1991). Additional circumstantial evidence in favor of T4- and T5-cells comes from the observation that both of these cell types exist in four different sub-types per column, each of which ramify in a different stratum of the lobula plate. Anatomical investigations have revealed that horizontally and vertically sensitive LPTCs extend their dendrites to four different strata of the lobula plate, according to their preferred direction. Horizontally sensitive cells extend dendrites to the anterior two strata, while vertically sensitive cells to the two posterior strata. These four layers have also been labeled in the Drosophila brain, by use of the 2-deoxy-glucose (2-DG) method (Buchner et al. 1984; Bausenwein et al. 1992; Bausenwein and Fischbach 1992), simultaneously with the most proximal layer of the medulla exactly where T4-cells ramify and the posterior layer of the lobula where T5-cells extend their branches. The direction of motion that activates a specific stratum, as labeled using the 2-DG method, matches the preferred direction of those LPTCs extending their dendrite in this stratum. Further hints about the connectivity between T4- and T5-cells, as well as other columnar neurons, are based on co-ramifications of the cells in identical strata of the medulla and lobula, and activity labeling using the 2-DG method. Using this type of reasoning, first Strausfeld (1984) and later, with minor modifications, Bausenwein et al. (1992) proposed two different pathways leading from the photoreceptors through the optic lobes to the LPTC dendrites (Fig. 7).

One pathway uses the photoreceptors R1–6, which synapse onto the lamina neuron L1. L1 in turn activates the intrinsic medulla neuron Mi1 synapsing onto T4-cells, and from there, connects to the LPTC dendrites. Another pathway, which also originates in R1–6, uses the lamina neuron L2. L2 connects to the trans-medulla neuron Tm1, which connects to the most posterior stratum of the lobula. There, it contacts T5 cells, which bring the information onto LPTC dendrites. As attractive as this scheme may be as a working hypothesis, it needs to be emphasized that to date neither physiological nor ultrastructural data exist to solidify these presumptions. This situation might change in the future. Promise comes from recently developed genetic techniques in Drosophila: here, combining cell-specific expression lines (enhancer trap or Gal4-lines; Brand and Perrimone 1993) with genetically encoded indicators of neural activity (Miyawaki et al. 1997) or blockers of synaptic transmission (van der Bliek and Meyerowitz 1991) might help to unequivocally identify those columnar elements involved in motion processing.

Despite all these reservations regarding the physiological nature of the correlation-type of motion detector summarized above, it nevertheless should be appreciated that operations as specified in this model are indeed taking place in the visual ganglia of the fly and that such processes endow the LPTCs with direction selectivity in the first place. How such direction selective signals are further processed by the tangential cells intrinsic membrane properties, and become modified by the intra- and inter lobula plate circuitry, between different tangential cells, to finally result in the complex visual response properties of LPTCs is the topic of the forthcoming sections.

Intrinsic membrane properties of lobula plate tangential cells

In principle neural signals are shaped by their input signals along with their intrinsic membrane properties which can be grouped into passive, i.e., voltage insensitive, and active, i.e., voltage-sensitive ionic currents. In

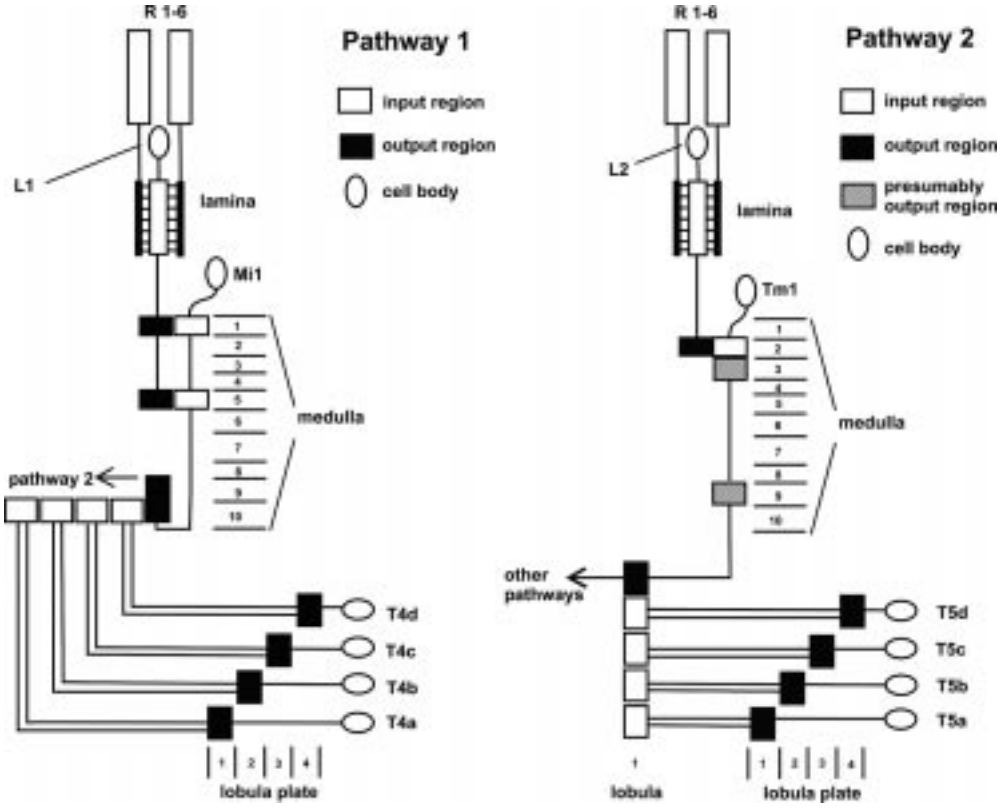


Fig. 7. Different proposed pathways leading from photoreceptors R1–6 to the lobula plate tangential cells (modified from Bausenwein et al. 1992)

case of the analysis of direction selectivity, knowledge about the intrinsic membrane properties of the lobula plate tangential cells is important because it allows, through combined experimental/modeling studies, to dissect out the input signals in an indirect way and to assess the potential contribution of network interactions to various phenomena such as gain control (see below).

As is quite obvious from the various types of electrical responses that different LPTCs produce when stimulated by visual motion along their preferred direction, i.e., graded, spiking and mixed (Fig. 4), pronounced differences must exist between the intrinsic membrane properties of the neurons. Whereas, an LPTC responding in a purely graded way might not be endowed with voltage-gated ion channels at all, and thus is regarded as totally passive, LPTC producing full-blown action potentials have to possess voltage-gated ionic currents in their axons. In addition, LPTCs responding in a mixed mode must also have voltage-activated membrane currents: when released from a long lasting hyperpolarizing current injection, they produced large-amplitude rebound action potentials (Hengstenberg 1977; Haag and Borst 1996). However, going beyond such qualitative statements requires a thorough investigation of all ionic currents using various protocols of current injection into the cells without visual stimulation. In addition, the electrical response to synaptic input is shaped by the particular anatomy of cell. Therefore, our experiments on the intrinsic membrane properties of the tangential cells were accompanied by compartmental modeling taking into account a detailed 3-dimensional description of each LPTC (Fig. 8).

As a first step of our analysis (Borst and Haag 1996), we built a digital base of the cells by 3D-reconstructing individual tangential cells from cobalt-stained material including both CH-cells (vCH- and dCH-cell), all three HS-cells (HSN-, HSE- and HSS-cell) and most members of the VS-cell family. In a first series of experiments, hyperpolarizing and depolarizing currents were injected to determine steady–state I-V curves. It appeared that at potentials more negative than resting, a linear relationship holds, whereas at potentials more positive than resting, an outward rectification was observed. Therefore, in all subsequent experiments, when a sinusoidal current of variable frequency was injected, a negative DC current was superimposed to keep the neurons in a hyperpolarized state. The resulting amplitude and phase spectra revealed an average steady–state input resistance of 4–5 MΩ and a cut-off frequency between 40 Hz and 80 Hz. To determine the passive membrane parameters R_m (specific membrane resistance), R_i (specific internal resistivity) and C_m (specific membrane capacitance), the experiments were repeated in computer simulations on compartmental models of the cells. Assuming a spatially homogeneous distribution of these parameters, the 3-D parameter space was screened through. In comparing the model response with the experimental data set a single optima for each neuron was found (see Table 1).

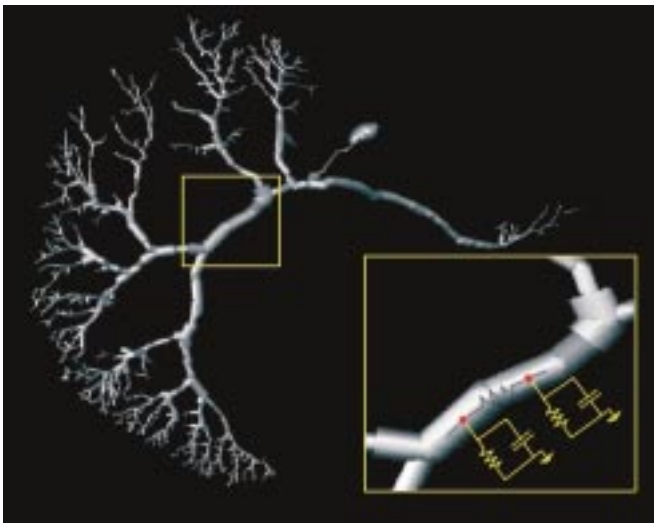


Fig. 8. Compartmental model of a VS1-cell. The inset shows a simplified version of an electrical equivalent circuit representing each compartment in the simulation. The cell is not shown plane parallel, but rotated by 20–30° around the dorso-ventral axis with the dendrites towards the viewer

No characteristic differences between different members of the same cell class were found. We also applied an error analysis of the fitting procedure to see how much the different membrane parameters could be varied away from the point of best fit and still lead to acceptable behavior of the model as compared to the experimental data set given the statistical fluctuations inherent in the experiments.

In the next step, voltage-activated membrane currents were studied using the switched electrode voltage clamp technique (Haag et al. 1997). In CH-cells, two currents were identified: a slow calcium inward current, and a delayed rectifying, non-inactivating potassium outward current. HS- and VS-cells appeared to possess similar currents as did CH-cells but, in addition, exhibited a fast activating sodium inward current and a sodium-activated potassium outward current. While the delayed rectifying potassium current in all three cell classes was responsible for the observed outward rectification described previously (Borst and Haag 1996), the sodium inward current produced the fast and irregular spike-like depolarizations found in HS- and VS-cells but not in CH-cells. It was found that when blocking the sodium current by either TTX or intracellular QX314, action potentials could not be elicited in HS-cells under current-clamp conditions. Again, as in the analysis of passive membrane properties, voltage-activated currents were incorporated with the appropriate characteristics into compartmental models of the cells. After fitting the current parameters to the voltage-clamp data the resulting behavior of the model cells qualitatively mimicked the fly tangential cells under current clamp conditions in response to current injection (Fig. 9).

Table 1. Summary of passive membrane parameters and voltage-activated ionic currents in lobula plate tangential cells. Data from Borst and Haag 1996 and Haag et al. 1997 (*CH-cells* centrifugal horizontal cells, *HS-cells* horizontal system cells, *VS-cells* vertical system cells, *LVA* low-voltage activated, R_m specific membrane resistance, R_i specific internal resistivity, C_m specific membrane capacitance)

	CH-cells	HS-cells	VS-cells
R_m	2.5 kΩcm^2	2.0 kΩcm^2	2.0 kΩcm^2
R_i	60 Ωcm	40 Ωcm	40 Ωcm
C_m	1.5 μF cm^{-2}	0.9 μF cm^{-2}	0.8 μF cm^{-2}
Delayed rectifying K current	+	+	+
Fast Na-dependent K current	–	+	+
Fast Na-current	–	+	+
Non-inactivating LVA Ca-current	Fast	Slow	Slow

Calcium currents were further analyzed combining the switched-electrode voltage clamp technique with optical recording using calcium sensitive dyes (Haag and Borst 2000). This allowed the study of calcium currents, which were too small to be detectable in voltage-clamp experiments and revealed in addition, their spatial distribution. For all three cell types considered, CH-, HS- and VS-cells, the activation curve turned out to be rather flat covering a voltage range from –60 mV to –20 mV in dendritic as well as presynaptic areas of the cells. The calcium increase was fastest for CH-cells with a time constant of about 70 ms. In HS- and VS-cells the time constant amounted to 400–700 ms. The calcium dynamics as determined in different regions of the cells were similar, except for a small segment between the axon and the dendrite in HS- and VS-cells, where the calcium increase was significantly faster. In summary, these results show the existence of a low-voltage-activated (LVA) calcium current in dendritic as well as presynaptic regions of fly LPTCs with little or no inactivation.

Beside ionic currents another crucial property of neurons is the repertoire of transmitter receptors on their dendrites. Transmitter-gated currents were studied in HS- and VS-cells using an in vitro preparation of the fly brain (Brotz and Borst 1996). In such an acute explant, LPTCs were stimulated by iontophoresis of various potential receptor agonists. To isolate the LPTCs synaptically from their network partners, all experiments were conducted in zero-Ca^{2+}/high-Mg^{2+} saline to block synaptic transmission. From all chemicals tested, only agonists of nicotinic acetylcholine receptors like acetylcholine, nicotine and carbachole turned out to effectively depolarize the neurons. These depolarizing responses were antagonized by α-bungarotoxin, mecamylamine, d-tubocurarine and bicuculline, but not by decamethonium and scopolamine, confirming the nicotinic pharmacology of such receptors. Switching to a high-Ca^{2+}/low-Mg^{2+} saline to allow for synaptic transmission, depolarizing responses, again sensitive to mecamylamine and *d*-tubocurarine, could be elicited by electrical stimulation of the medulla. These data suggest

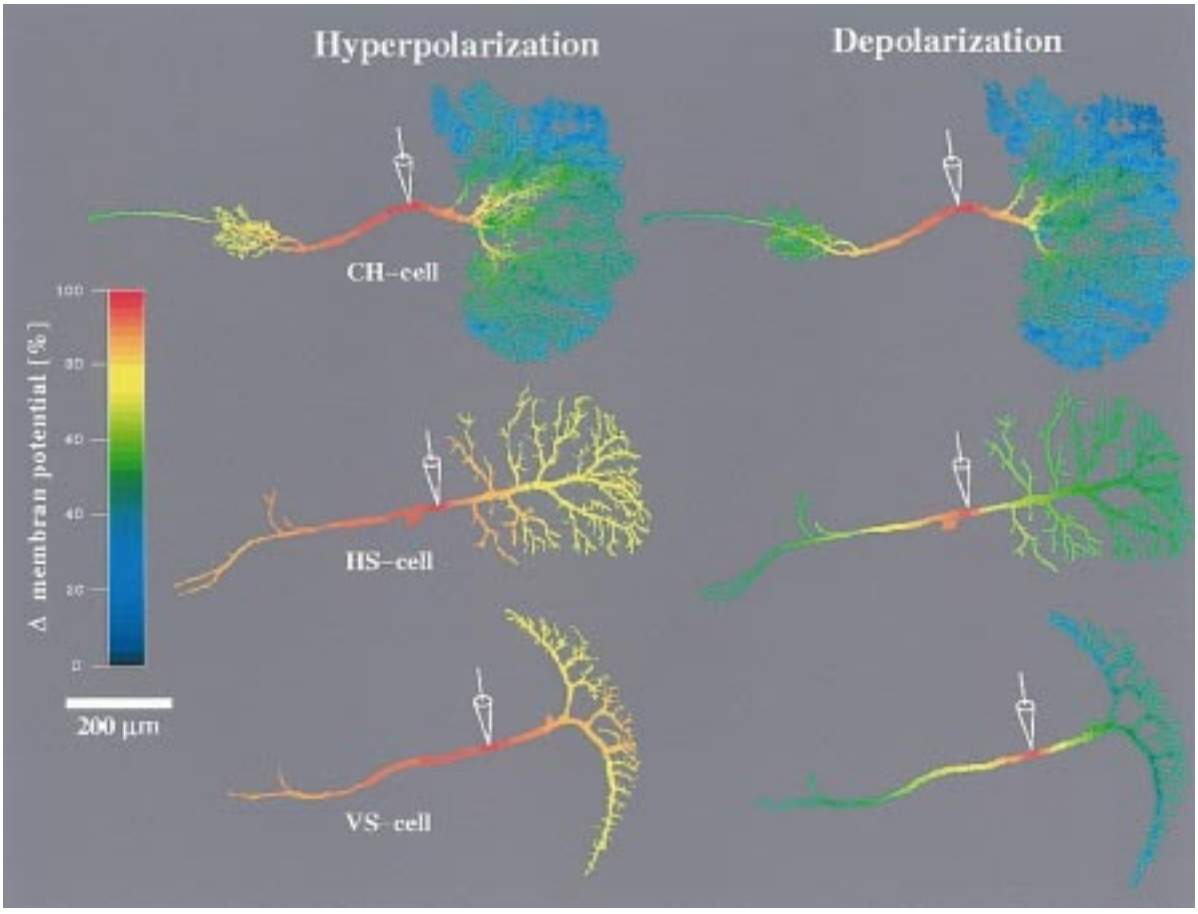


Fig. 9. Steady-state voltage distribution in compartmental models of fly LPTCs after simulated current injection into the axon. False-color code represents the local voltage in percentage of voltage at injection site

that columnar elements in the medulla are in fact exciting LPTCs via nicotinic acetylcholine receptors, either directly or indirectly. Using antibodies raised against a structural subunit of the *Drosophila* nicotinic acetylcholine receptor (ARD) revealed, amongst other areas in the optic lobes, a distinct staining in the lobula plate of the blowfly brain, supporting the existence of nicotinic receptors on LPTC dendrites (Brotz et al. 2001).

Interestingly, neural nicotinic receptors in insects were recently found to also be permeable to calcium, in addition to Na and K-ions (Goldberg et al. 1999; Oertner et al. 1999, 2001). Together with the voltage-activated calcium current described above, nicotinic receptors, constitute a second gate for calcium entry in these neurons. This fact has important consequences for the interpretation of in vivo calcium imaging experiments when the neurons were synaptically stimulated by visual motion.

Beside this excitatory input, muscimol, a GABA-receptor agonist, was found to strongly hyperpolarize the LPTCs (Brotz and Borst 1996). As previously found in other insect neurons, the muscimol response was antagonized by picrotoxinin but not by bicuculline, a $GABA_A$ receptor antagonist in vertebrates. In summary, the experiments provided an insect-typical pharmacological profile of $GABA_A$ receptors in blowfly LPTCs. Varying the external chloride concentration had a strong effect on the reversal potential of the current activated by muscimol, indicating that the GABA receptor controlled a chloride conductance. For the inhibitory input, however, it could not be established whether it was brought in by columnar elements since electrical stimulation of the medulla did not result in any distinct hyperpolarizing responses of LPTCs. Using an antibody raised against a subunit of the *Drosophila* GABA receptor (ARD) revealed strong staining in the blowfly brain. In particular, the lobula plate showed clear activity, substantiating the existence of GABA receptors on LPTC dendrites (Brotz et al. 2001).

It should be noted at this point that, despite the many studies summarized above, our knowledge about the various components of background, voltage- and transmitter-gated currents in LPTCs is still limited. First of all, no such data exist for the spiking, heterolaterally projecting neurons like H1–4 or V1, since in general their processes are rather small for stable intracellular recording. Almost all recordings on these neurons were done extracellularly using tungsten electrodes. Furthermore, immunohistochemical labeling summarized above has not yielded single cell resolution. Thus, the staining cannot be attributed to specific LPTC dendrites and it

might be that the diversity with respect to transmitter receptors is larger than anticipated. So far, most data in all these respects exist for CH-, HS- and VS-cells, and our further analysis will therefore concentrate on these three LPTC families.

Primary motion response properties

Having summarized what is known so far about the properties of the input columnar circuitry and the intrinsic membrane properties of LPTCs, we now ask whether this knowledge is sufficient to account for the response characteristics of LPTCs when stimulated by visual motion on their ipsilateral side, i.e., when motion stimuli are displayed on the side of the animal where LPTCs extend their primary dendrite. This type of visual response will be referred to in the following as their primary motion response. Their flow-field selectivity where the additional input from other lobula plate neurons is taken into account will be discussed further below.

Our approach to answer the question about the sufficiency of our knowledge again is through modeling. As in the section where the intrinsic membrane properties were dealt with, we took the compartmental models of the various cell types, equipped them with the ionic currents revealed by current and voltage-clamp experiments and connected their dendrite to an array of correlation-type of motion detectors as specified in Fig. 3. As additional parameters, excitatory and inhibitory conductances as well as the reversal potentials of both types of synapses had to be fixed. Total synaptic conductances were determined by adjusting the input resistance of the compartmental models during motion stimulation to the respective data set determined by injecting current into the neurons while displaying motion stimuli to them (Borst et al. 1995; Haag et al. 1999). Reversal potentials were estimated to be –70 mV for the inhibitory chloride conductance and –10 mV for the nicotinic excitatory input (for further details of the model parameters see Haag et al. 1999). These circuit models were then stimulated, as in the experiments, by a moving grating and the resulting model responses were finally compared with the experimental data.

In general, the electrical responses of the compartmental models of CH, HS- and VS-cells to an optimal stimulus, i.e., full contrast pattern motion along the preferred direction, looked similar to the experimental data: the cells depolarized in a graded way by a few millivolts. However, without the addition of noise, model responses of HS- and VS-cells did not produce any spike-like depolarizations so that their response was almost indistinguishable from CH-cell model responses. This changed dramatically when, instead of ongoing motion, dynamic stimuli were used. When the pattern velocity was sinusoidally modulated at various frequencies, HS-cell models started to produce small amplitude action potentials at about 10 Hz modulation frequency, just as what has been seen before in experiments (Haag and Borst 1996). Another striking parallel to real HS-cells was that these action potentials gradually built up during the presentation of the first few cycles presented. This type of high-frequency amplification was not produced by CH-cell models nor real CH-cells. For the facultative spiking behavior of HS- and VS-cells the following explanation arose from these modeling studies: (1) these cells possess the voltage-gated ionic conductances needed for action potential generation; (2) however, current density is rather small compared to background membrane conductance; and (3) sodium currents are mostly inactivated at the cells' resting potential of about –50 mV. For all these reasons such neurons do not produce action potentials when depolarized by preferred direction motion unless they are (1) permanently artificially hyperpolarized by current injection, or (2) dynamically stimulated such that a null direction motion stimulus hyperpolarizes them just before they become depolarized by preferred direction motion.

Another feature of LPTCs studied intensively in the past (Hausen 1982b; Haag et al. 1992; Borst et al. 1995; Single et al. 1997) concerns their spatial integration characteristics: when enlarging the area in which the motion stimulus is displayed the response saturates significantly (Fig. 10). The interesting fact is the observation that such a saturation occurs not only for motion along the preferred, but also along the null direction of the cell. Furthermore, for patterns moving at different velocities, different saturation plateaus are assumed (Fig. 11A). This latter phenomenon has also been called 'gain control'. In general, our modeling studies, along with measurements of motion induced changes of input conductances, revealed that the circuit model of a single tangential cell and its presynaptic array of motion detectors is fully sufficient to produce the observed saturation of membrane response. For understanding the phenomenon of gain control, one needs to realize that the presynaptic elements are only weakly tuned to null directions of motion: they not only respond to motion along their preferred direction but also, to a lesser extent, to motion along the opposite direction (see panel 2'1 in Fig. 6). Therefore, motion along one direction leads to a joint, though differently weighed activation of excitatory and inhibitory input, resulting in a mixed reversal potential at which the postsynaptic response settles for large field stimuli. As can be calculated from such correlation-type input elements, the activation ratio of these opponent inputs is a function of pattern velocity. Consequently, motion in one direction jointly activates excitatory and inhibitory inputs with a ratio that depends on velocity. This explains how the postsynaptic membrane potential saturates with increasing pattern size at different levels for different pattern velocities. In summary, thus, gain control is produced without the need of any further network interactions. These assumptions were experimentally verified by blocking the inhibitory input with picrotoxinin (Single et al. 1997)

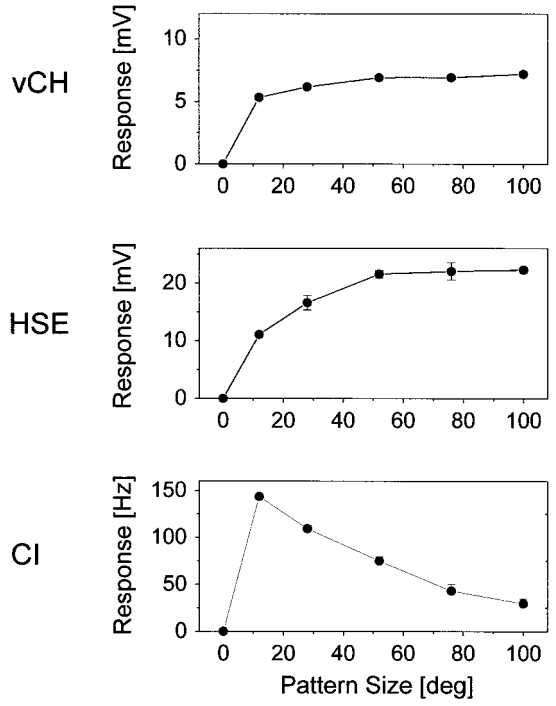


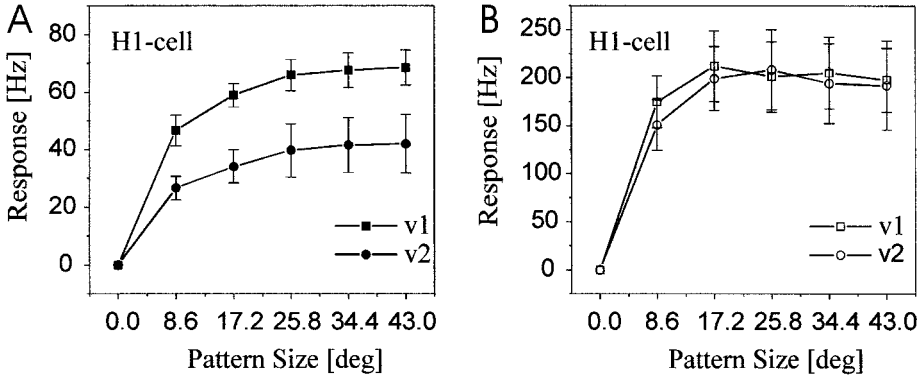
Fig. 10. Responses of different types of LPTCs to drifting gratings as a function of the pattern size. Data from Gauck and Borst 1999, Figs. 3 and 4, modified

resulting in three observations: (1) the preferred direction response grew larger and the null direction response changed its sign from a hyper- to a depolarization, (2) the change of input resistance induced by preferred direction motion decreased showing that, before, inhibitory currents were activated as well; and (3) as a final proof of the above explanation, gain control was abolished (Fig. 11B).

Models of HS- and VS-cells produced a spatial saturation curve indistinguishable from their natural counter parts. Real CH-cells, however, saturated much more strongly leading to a discrepancy between experimental and model data. Originally, this finding led to the assumption that CH-cells might have spatially inhomogeneous membrane parameters with very high values of trans membrane resistance in their dendrite (Haag et al. 1999). A detailed modeling study following up on this revealed, however, that even when allowing for such complex model no satisfying fit between all available data sets and the respective model behavior can be achieved (Cuntz 2000). A possible explanation might come from the observation that in contrast to the model outline, real CH-cells do not seem to receive direct input from retinotopically arranged arrays of motion-sensitive elements but rather are connected indirectly to the visual surround via HS-cells (Haag and Borst 2002). Whether this finding can resolve all existing discrepancies is currently being investigated.

Besides the electrical responses of LPTCs to moving stimuli, calcium imaging has been used as a tool to study the activity distribution in a spatially resolved way. This technique has led to the following key findings: (1) when stimulated by a spatially restricted motion stimulus, such as either a grating moving behind an aperture (Borst and Egelhaaf 1992) or a moving bar (Borst and Single 2000), calcium accumulates locally within the dendritic branches receiving retinotopic input (Fig. 12). (2) In contrast to the electrical response, dendritic calcium increases for both, preferred as well as null direction motion (Borst and Single 2000; Single and Borst 2002). Using compartmental modeling, an explanation for both these phenomena could be obtained. The first finding was that despite the fact that VS-cells are considered as electrically compact for steady-state current injection into the axon, they are not so for a local current injected into a small dendritic branch. Thus, the membrane potential distribution in response to local motion stimuli reveals a steep drop from the point of stimulation. Accordingly, even when the model neuron was only equipped with voltage-activated calcium currents, calcium distribution was found to be local. Adding a transmitter-gated calcium influx enhanced this local calcium accumulation, but was not found to be necessary for the phenomenon described (Fig. 13B). In order to reproduce the calcium accumulating in response

Fig. 11A, B. Gain control in lobula plate tangential cells. **A** The response of H1-cells is measured as a function of the pattern size. In normal fly saline, it increases as pattern size increases but saturates at different plateaus for different pattern velocities ($v1 = 72°\ s^{-1}$, $v2 = 360°\ s^{-1}$). **B** After application of picrotoxinin, the response still increases with increasing pattern size, but now saturates at the same level for both velocities (modified after Single et al. 1997)



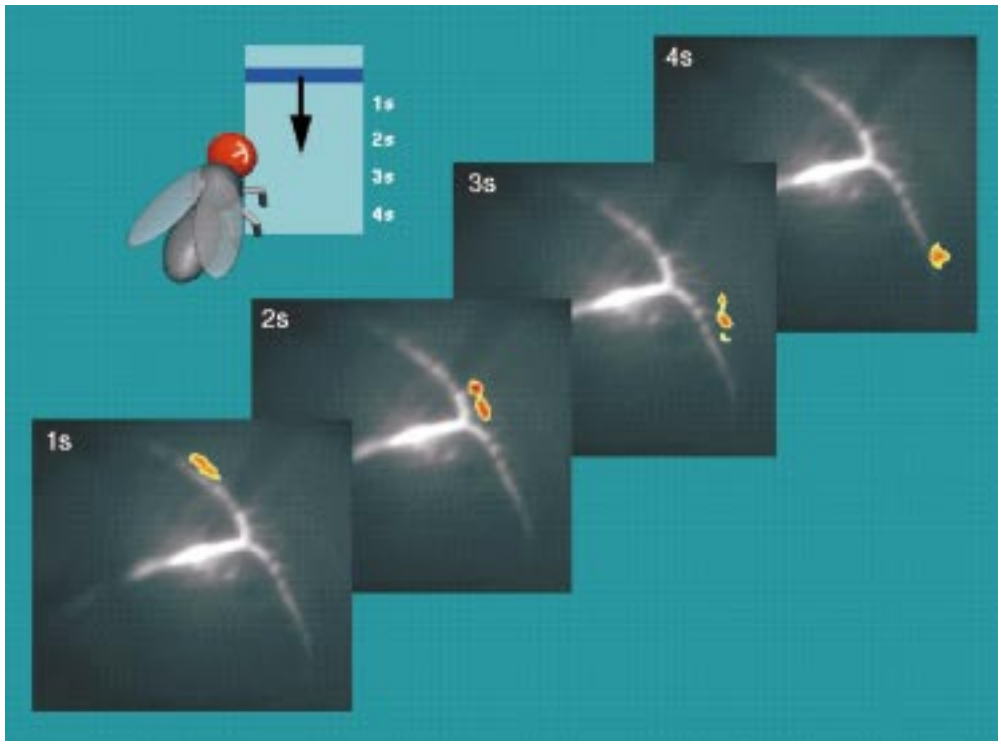


Fig. 12. Dendritic calcium accumulation in a VS2-cell in response to a moving bar. Shown is the temporal derivative of the relative change of fluorescence corresponding to the additional calcium arriving at each point in time, false color coded (with warmer colors indicating stronger increases) and overlaid on the raw fluorescence image of the cell

to null direction motion, however, the transmitter-gated calcium influx through nicotinic acetylcholine receptors was a 'conditio sine qua non': With voltage-activated calcium currents alone, a slight decrease of calcium was observed in the model following the dendritic membrane potential (Fig. 13C, D). Whereas the picrotoxinin experiments summarized above showed an activation of the inhibitory input during preferred direction motion, the null direction calcium accumulation revealed an activation of the excitatory input during null direction motion. Together with previous experiments (Borst and Egelhaaf 1990), these data provide a strong argument in favor of the weak direction selectivity of the input elements in general: only at the level of postsynaptic tangential cells is full direction selectivity achieved through the opponent action of inputs with opposite preferred directions.

Adaptive properties of motion response

As in many other animals, the visual system of flies reveals adaptive properties at all levels studied so far, from the periphery to more central neurons. The motion response of the lobula plate tangential cells does not make an exception in this respect. There are two features of the LPTC motion response that were found to change with stimulus history: the dynamics of the response and the amplitude of the response as measured in the graded membrane potential or the spike frequency, depending on the neuron under study. The initial observation, made by Maddess and Laughlin (1985) on the H1-cell of the fly *Lucilia cuprina*, was that in response to gratings moving at a constant velocity for several seconds the response declined substantially. However, when the grating, while continuing to move, was switched to a different location within the receptive field of H1, the response returned to its initial strength (Fig. 14A). This velocity adaptation was, thus, concluded to be a local phenomenon, possibly not taking place at the level of the integrating H1-cell but rather in some of its presynaptic, columnar elements. Taking an information theoretic approach to study the phenomenon of velocity adaptation, Brenner and colleagues (Brenner et al. 2000) used a random velocity profile with a Gaussian, zero-symmetrical distribution to stimulate H1 of the blowfly (Fig. 14B). When the variance of this distribution, i.e., the range of velocities over which the stimulus was varied, was changed from one value to the other, the sensitivity of H1 as measured in its input-output function changed along with it. For narrow distributions, i.e., a small range of velocity variations, the sensitivity of H1 was high: plotted as function of velocity, the response had steep increase at a velocity of 0° s^{-1} reaching a saturation already at low-velocity values. For wide distributions, i.e., a large range over which the velocity varied, the sensitivity of H1 was low: now the response had a flat slope at 0° s^{-1} velocity saturating only at high velocities. The time-course at which this change of sensitivity occurs revealed several regimes reaching from tens of milliseconds up to minutes (Fairhall et al. 2001). These observations are in line with the notion that adaptation insures that H1 covers the prevailing stimulus with an optimal sensitivity such as to provide a maximum amount of information about the stimulus given a

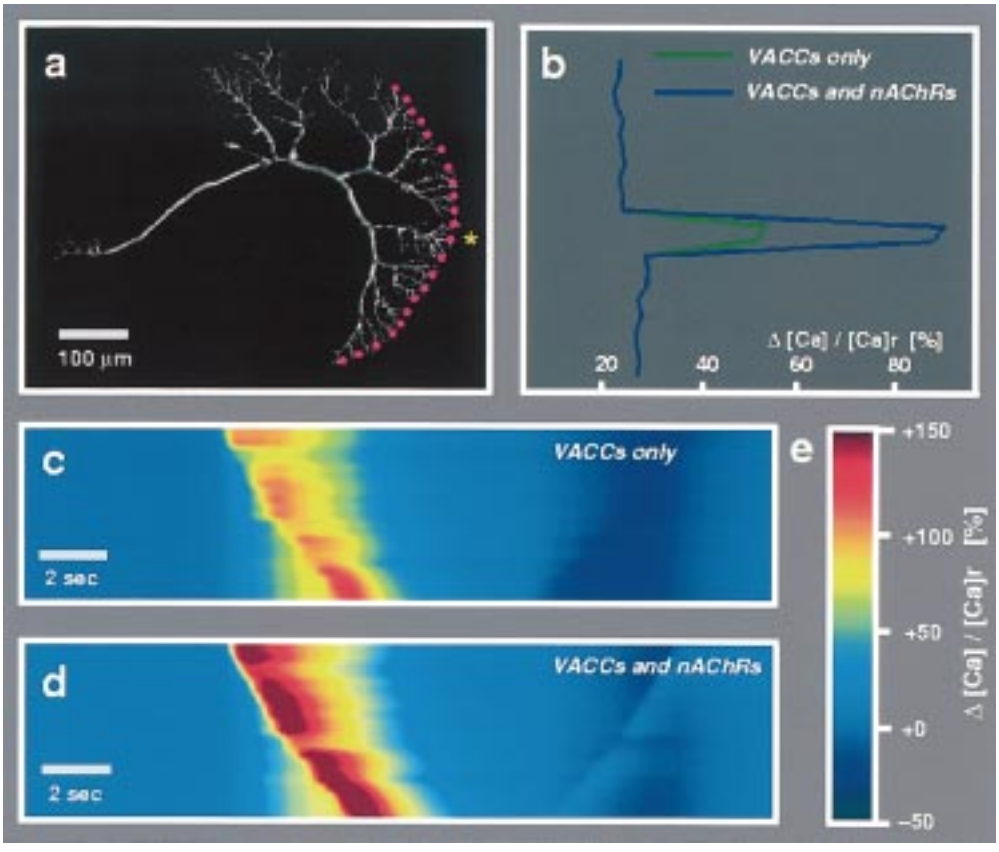


Fig. 13A–E. Simulations of an active compartmental model of a VS1-cell stimulated with different types of local motion. **A** Locations at which calcium concentrations were measured in **B**, **C** and **D**, are indicated by *purple circles*. **B** Local stimulation (*yellow asterisk* in **A**) by PD motion of a periodic grating. The spatial distribution of relative change of calcium concentration averaged over time is plotted for two models: In one case, calcium enters only through voltage-activated calcium channels (VACCs), in the other model, calcium enters in addition through nicotinic acetylcholine receptors (nAChRs). **C**, **D** Space-time plots of relative changes of calcium concentration during single bar motion. Space is along the *y*-axis, time along the *x*-axis. **E** False-color code bar used in **C** and **D**

certain stimulus statistic. But the response of lobula plate tangential cells not only adapts with respect to its velocity sensitivity: changes in their sensitivity for stimulus contrast are found as well. This has been documented by Harris et al. (2000) who used a traditional adapt-and-probe paradigm in HS-cells of the dronefly *Eristalis tenax* to measure the 'contrast gain', i.e., the response as a function of stimulus contrast, before and after exposure to an adapting motion stimulus of several seconds duration (Fig. 14C). As the most significant effect of adaptation, these authors found a pronounced rightward shift of the contrast-gain function indicating that driving a motion-sensitive cell to its half-maximum response requires at least twice as high pattern contrast when the cell is adapted as compared to its unadapted state.

While all the above adaptive phenomena affect the response strength, another class of adaptation was described in lobula plate tangential cells which affects the response dynamics. When stimulated by a sudden displacement of a grating or, expressed in terms of the stimulus velocity, a velocity pulse, H1 and other tangential cells respond with a steep increase of spike frequency or membrane potential followed by an exponential decrease back to resting level. When the grating was immobile for many tens of seconds, the time-constant of the exponential decay back to resting amounts to several hundreds of milliseconds. However, when the velocity pulse is delivered shortly after a pattern motion, the time constant can be as short as 30 ms (Fig. 14D). Thus, depending on the stimulus history, the time constant of the exponential decay can adapt over one order of magnitude (de Ruyter van Steveninck et al. 1986). As the adaptation of response strength, this time-constant adaptation was found to be a local process (de Ruyter van Steveninck et al. 1986): when the stimulus screen was divided in two parts, time-constant adaptation only occurred when both the adapting and the test stimulus were delivered within the same area. Interestingly, only the dynamics of the light level at a given location seems to drive this kind of adaptation: preferred direction motion as well as null direction stimuli as well as temporal modulation of the mean luminance level of a uniform field ('field flicker') all lead to adaptation of the time-constant to a similar degree (Borst and Egelhaaf 1987).

Since the neurons presynaptic to the lobula plate tangentials have, in general, escaped electrophysiological analysis, the mechanisms underlying their adaptive properties are to date completely in the dark, too. The only hint, thus, comes from possible contributions of lobula plate tangentials themselves to the adaptive properties of their motion response. These contributions do not necessarily express themselves in global changes of responsiveness, i.e., throughout the receptive field of the neuron, since, for example, changes of cytosolic calcium level can well be spatially restricted to a certain area of the LPTC dendrite (Borst and Egelhaaf 1992;

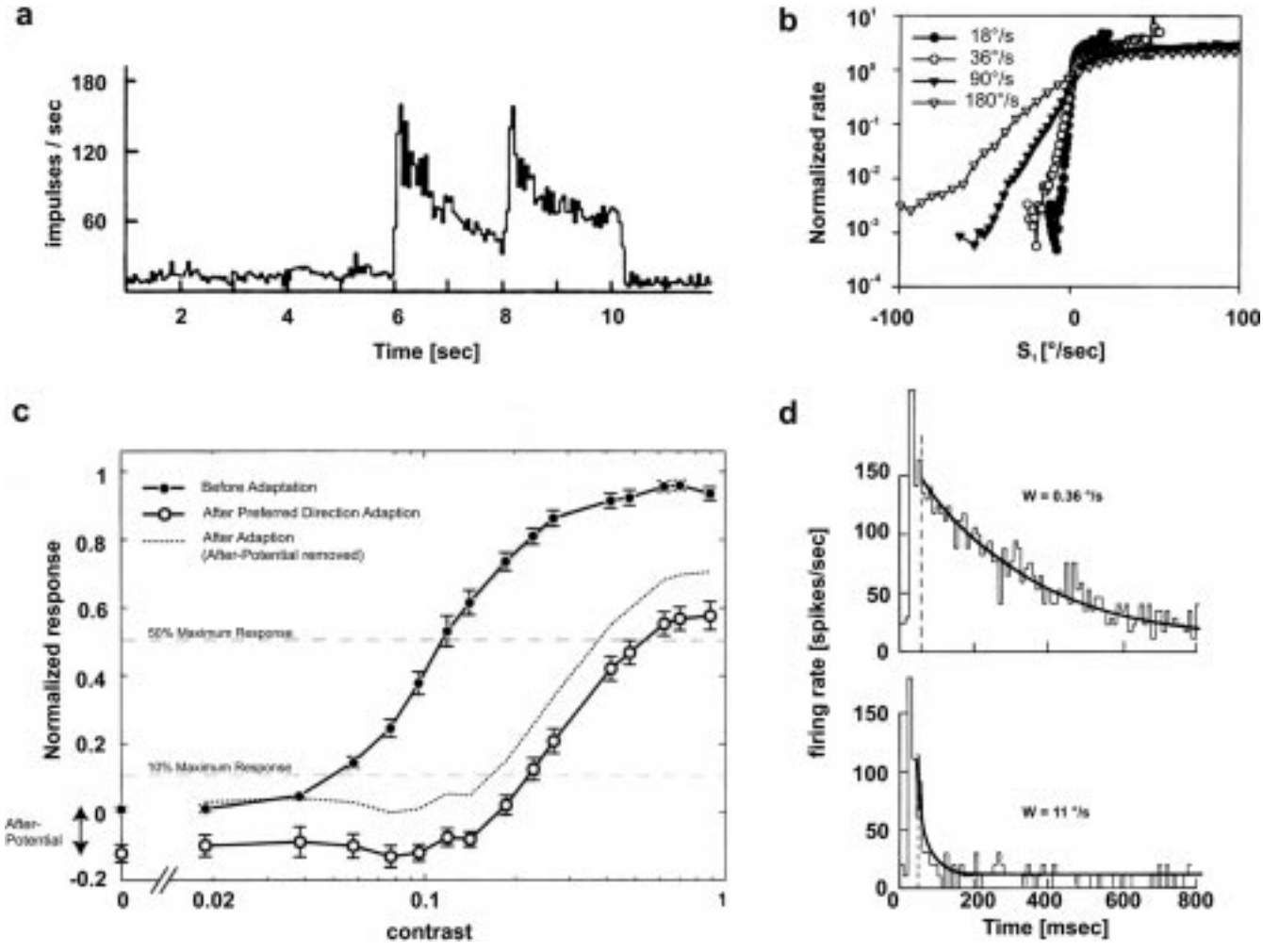


Fig. 14A–D. Adaptive properties of motion responses in fly lobula plate tangential cells. **A** Using an apparent motion paradigm (two bars sinusoidally modulated over time with 90° out of phase), H1 was stimulated for 2 s before the bars shifted to a new location in the receptive field. The response drops during the first 2 s but reaches its initial level after being shifted (modified after Maddess and Laughlin 1985). **B** Input-output relationship of H1 during random velocity stimulation with different variances. Note the different slopes for the different stimulus velocities (modified after Brenner et al. 2000). **C** The response was probed before and after an adapting stimulus as a function of stimulus contrast: the significant rightward shift indicates a strong loss in sensitivity (modified after Harris et al. 2000). **D** In response to a brief velocity pulse, the response of H1 decays exponentially to zero. The time-constant of this decay strongly depends on the stimulus history (modified after de Ruyter van Steveninck et al. 1986)

Borst and Single 2000). Indeed, it was recently observed that local calcium levels correlate well with a certain after-hyperpolarization occurring at the end of preferred direction motion stimulus (Kurtz et al. 2000). Assuming that local calcium increases would open calcium-dependent potassium conductances could lead to a diminished responsiveness of the integrating neuron and, thus, to a local decrease in its sensitivity as was shown to be the case e.g. in the cricket omega neuron (Sobel and Tank 1994).

Lobula plate circuitry and flow-field selectivity

Many of the LPTCs have been found to be sensitive to image motion in front of the contralateral eye, in addition to motion in front of their ipsilateral eye. In the case of LPTCs of the graded or mixed response type, i.e., HS and CH-cells, this was found to be true for HSN, HSE, dCH and vCH, but not for HSS-cells. All these cells are excited on their ipsilateral side by motion from the front to the back and receive additional excitatory input by contralateral back-to-front motion (Hausen 1977, 1981, 1984; Eckert and Dvorak 1983; Haag 1994; Haag et al. 1999; Horstmann et al. 2000). Hence, they are tuned to a rotatory flow-field. Fig. 15 shows an example of recording from a dCH-cell: clearly the neuron prefers rotatory over translatory motion.

Using dual recording techniques, one extracellular recording from the spiking neuron and one intracellular recording from the CH-cell, two heterolateral neurons were identified as providing the excitatory input to HS- as well as CH-cells: the H1- and the H2-cell (Hausen 1977). As is indicated in Fig. 15, these cells have the appropriate preferred direction to tune the CH-cells to rotatory motion. In addition, an hitherto unidentified

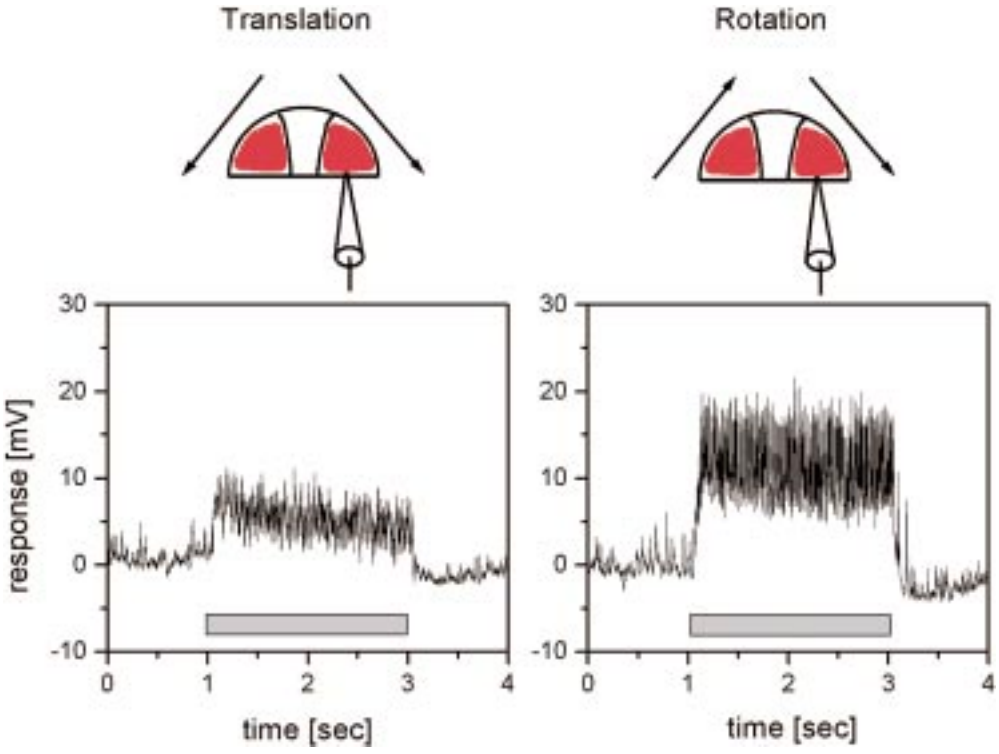


Fig. 15. Intracellular recording from a dCH-cell. This neuron responds not only to motion in front of its ipsilateral eye, but also to motion in front of the contralateral eye. The contralateral input has such a sign that it leads to a particular sensitivity of the cell for rotational stimuli: translatory stimuli lead to a much smaller response

neuron with an opposite preferred direction is inhibiting the contralateral CH-cells. While these findings provide a sufficient explanation for the selectivity of CH-cells for rotational cues, additional connections between LPTCs within one lobula plate were recently discovered (Haag and Borst 2001). Again using dual recording techniques, CH- and HS-cells were found to excite those cells which have identical preferred directions like Hu, and CH-cell were found to inhibit those neurons with opposite preferred direction, like H1 and H2 (see Fig. 16). Through this kind of ipsilateral connections onto heterolateral neurons, HS- and CH-cells could be demonstrated to inhibit their contralateral counterparts; excitation e.g., in the left dCH-cell should inhibit the right dCH-cell, and vice versa, while inhibition in the left CH-cell should facilitate excitation in the right one.

Moreover, close inspection of the circuit diagram reveals the existence of feedback loops bringing back the signals onto the cell where they started from. Several of these predictions could indeed be experimentally verified (Haag and Borst 2001). The conclusion from these experiments is that the intrinsic connectivity between the different tangential cells within one lobula plate and between the lobula plates in both hemispheres favors an asymmetrical distribution of excitation. Such an asymmetry will be imposed on the network from the sensory input when rotational flow-fields stimulate the eyes, but not when translational stimuli occur. The flow-field selectivity of LPTCs therefore seems not only determined by their feed-forward connectivity, but also by the intrinsic wiring within the network formed by LPTCs in both hemispheres.

These ideas received recent support from electrophysiological recordings where HS-cells were stimulated by visual flow-fields, which were identical to those ones, experienced before by a freely moving fly (Kern et al. 2001). Surprisingly, HS-cells were primarily flipping between two states back and forth, one hyperpolarized, one depolarized. Furthermore, this response was only dependent on the rotational component in the flow-field and largely invariant against the translational one. While it is not clear at the moment in what respect the results will change when reconstructed flow-field are taken from flying instead of walking flies, the data of Kern et al. (2001) could well be the result of the intrinsic network interaction between the LPTCs, summarized above. To gain a further understanding in the functional consequences of such network interactions, more modeling work is needed taking into account the closed-loop situation of behaving animals as well as the sometimes critical signal-to-noise ratios in natural scenes.

In contrast to the specificity for rotational flow-fields in horizontal cells described above, the FD1-cell and the CI-neurons are inhibited when contralateral back-to-front motion is additionally displayed to an excitatory ipsilateral front-to-back stimulus (Fig. 17). There is evidence that the vCH-cell is responsible for conveying this type of inhibitory input since the FD1-cell was shown to loose its inhibitory input after photo-inactivation of the vCH-cell (Warzecha et al. 1993). To what extend the CI-cells are also inhibited by the vCH-cell and whether the inhibition of the FD1- and/or CI-neurons by the vCH-cell is also responsible for their ipsilateral small-field

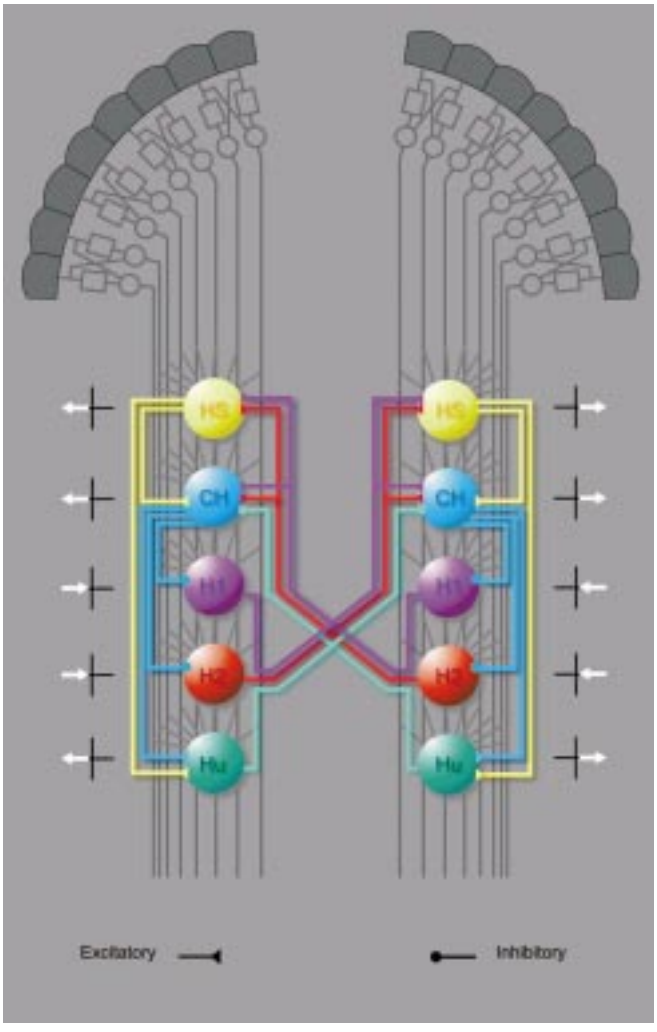


Fig. 16. Circuit diagram of the lobula plates on both sides of the brain showing the connectivity between several tangential cells sensitive to horizontal image motion. Excitatory and inhibitory connections are displayed as open triangles and filled circles, respectively. Black arrows indicate preferred directions of each cell group on its ipsilateral side

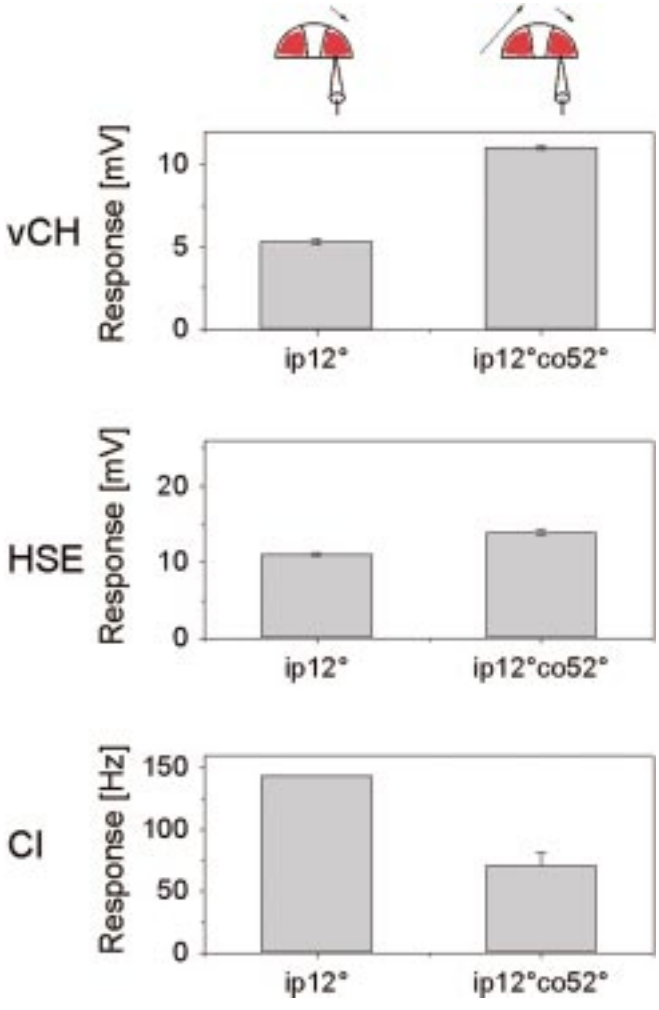


Fig. 17. Influence of contralateral back-to-front motion in CH-, HS-, and CI-neurons. Data are from Gauck and Borst 1999, Figs. 3 and 4, modified. Neurons are identical to the ones shown in Fig. 10

tuning, i.e., their preference for small objects moving, is not clear at the moment.

Another point of present speculation is the question what neurons of the lobula plate are responsible for the fly's translational control system. Here, two neurons seem feasible candidates: The HSS-cell, which is the only HS-cell that does not receive contralateral input and therefore is not specifically predestined for rotational flow-fields, and one of the CI-neurons that receives strong contralateral inhibitory input but does not display ipsilateral small-field tuning (Fig. 3e in Gauck and Borst 1999). However, there exist no data at present to lift this point above the level of plausibility.

In contrast to many neurons of the horizontal system, VS-cells (VS1–4) do not receive significant input from the contralateral eye (Hausen 1977). Although a detailed analysis of the possible connectivity between the different VS-cells within one brain hemisphere and VS- and HS-cells has not been done so far, at least one heterolateral neuron, the V1-cell, has been shown to be postsynaptic to the VS1-cell by dual recordings (Kurtz et al. 2001). Despite the general lack of significant contralateral input, VS-cells seem to be roughly tuned to rotational flow-fields occurring when the animal rotates around its longitudinal body axis: Bilaterally presented rotational stimuli (ipsilateral downward, contralateral upward) led to a response that was slightly stronger than the response to an ipsilateral downward stimulus alone (Hengstenberg 1984). Further evidence for a tuning to VS-cells to rotational flow-fields comes from studies where the local preferred direction was probed using a rotating point within a small segment of the ipsilateral hemisphere of the receptive field only (Krapp and Hengstenberg 1996; Krapp et al. 1998). The receptive fields determined this way furthermore revealed a rather complex structure showing that VS-cells are not just sensitive to vertical image motion but respond also, though to a lesser degree, to horizontal or oblique

directions of motion in particular parts of their receptive fields. Whether the receptive field of these neurons represents a matched filter optimized to sense certain self-induced optic flows or not cannot be answered in general: while model calculations agree with the distribution of local preferred directions of VS4–6, they fail to explain the receptive field structure of VS1–3 and VS7–10 cells (Franz and Krapp 2000).

Beyond the lobula plate

From all the LPTCs discussed above, HS and VS-cells are known to be output elements making contact to so-called descending neurons that connect the brain with the thoracic ganglion (Strausfeld and Bassemir 1985; Gronenberg and Strausfeld 1990; Gronenberg et al. 1995). However, compared to the tangential cells of the lobula plate, our knowledge about the descending neurons is limited. In those studies which have explicitly addressed their flow-field specificity, some of them were found to be highly non-linear (Borst 1991): one type responded strongly to bilateral front-to-back motion, another strongly to binocular rotatory motion, but both types remained completely silent during presentation of the monocular stimulus components. Since the detailed connectivity between these or other descendings and the HS- and VS-cells is not known at present, it is unclear how such non-linear receptive field properties arise.

Descending neurons are thought to be presynaptic to neck and flight muscle motor neurons and, thus, represent an intermediate processing level of visual motion information. While for descending neurons supplying neck motor neurons, an analog conversion of the signals for the control of head movements is completely feasible, the situation for flight control requires both the recruitment of appropriate steering motor neurons and the adjustment of their firing phase. Here, the visual input must in some way incorporate mechanosensory feedback, since on the one hand the effect of many flight steering muscles is critically sensitive on the phase of their action relative to the wing beat cycle, yet, on the other hand, the visual system does not encode wing motion and thus cannot tune muscles to fire at mechanically appropriate phases of the stroke cycle. Sensory systems carrying the relevant mechanosensory information are the halteres, little club-shaped organs in dipteran flies that are evolutionarily derived from hind wings (Fraenkel and Pringle 1938). The halteres beat in antiphase to the wings and act as gyroscopes to detect angular rotations of the body during flight (Nalbach 1993). An elegant hypothesis of how such a multimodal convergence is achieved is that descending visual interneurons alter firing phase and recruitment of steering motor neurons indirectly through their influence on efferent pathways that affect the firing of mechanosensory afferents. Like the wing, the haltere is equipped with a set of tiny control muscles that insert upon sclerites at its base (Bonhag 1948). Motor neurons of at least two of these muscles receive input from motion-selective descending visual interneurons (Chan et al. 1998). The haltere muscle B2 responds to moving gratings with a directional sensitivity that is reminiscent of VS-cells within the lobula plate, while the tuning of the haltere I1 muscle is reminiscent of cells within the HS-cells. These steering muscles might influence the recruitment or firing phase of halteres campaniform neurons that in turn could relay these temporal changes to wing muscles via their strong connections with steering motor neurons (Fayyazuddin and Dickinson 1996). In summary, thus, visual course control in flies seems to require quite a sophisticated series of data processing steps, not only to extract visual motion information from the changing retinal images but also to represent this information in a meaningful way for flight control. We have only begun to understand how this is achieved in this milligram of a nervous system.

Acknowledgements We would like to thank all members of our group, past and present, for contributing to the work presented above. In particular, we are grateful to K. Farrow for carefully reading the manuscript and to H.Cuntz for help with the artwork in Fig. 2.

References

Bausenwein B, Fischbach KF (1992) Activity labeling patterns in the medulla of *Drosophila melanogaster* caused by motion stimuli. Cell Tissue Res 270:25–35

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

Bialek W, Rieke F, Ruyter van Steveninck R de , Warland D (1991) Reading a neural code. Science 252:1854–1857

Bliek AM van der, Meyerowitz EM (1991) Dynamin-like protein encoded by the *Drosophila* shibire gene associated with vesicular traffic. Nature 351:411–414

Bonhag PF (1948) The thoracic mechanism of the adult horsefly (Diptera: Tabanidae). Mem Cornell Univ Agric Exp Stat 285:3–39

Borst A (1991) Fly visual interneurons responsive to image expansion. Zool Jb Physiol 95:305–313

Borst A (1996) Dendritic processing of synaptic signals in motion-sensitive interneurons of the fly. Verh Dtsch Zool Ges 89.2:109–122

Borst A, Bahde S (1988) Visual information processing in the fly's landing system. J Comp Physiol A 163:167–173

Borst A, Dickinson M (2002) Visual course control in flies. In: Arbib M (ed) The handbook of brain theory and neural networks, 2nd edn. Bradford Books/MIT Press

Borst A, Egelhaaf M (1987) Temporal modulation of luminance adapts time constant of fly movement detectors. Biol Cybern 56:209–215

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

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

Borst A, Egelhaaf M (1992) In vivo imaging of calcium accumulation in fly interneurons as elicited by visual motion stimulation. Proc Natl Acad Sci USA 89:4139–4143

Borst A, Egelhaaf M (1993) Detecting visual motion: theory and models. In: Miles FA, Wallman J (eds) Visual motion and its role in the stabilization of gaze. Elsevier, pp 3–27

Borst A, Haag J (1996) The intrinsic electrophysiological characteristics of fly lobula plate tangential cells. I. Passive membrane properties. J Computat Neurosci 3:313–336
Borst A, Haag J (2001) Effect of mean firing on neural information rate. J Comput Neurosci 10:213–221
Borst A, Single S (2000) Local current spread in electrically compact neurons of the fly. Neurosci Lett 285:123–126
Borst A, Seung S, Egelhaaf M (1993) Two-dimensional motion perception in flies. Neural Comput 5:856–868
Borst A, Egelhaaf M, Haag J (1995) Mechanisms of dendritic integration underlying gain control in fly motion-sensitive interneurons. J Comput Neurosci 2:5–18
Brand AH, Perrimone JH (1993) Targeted gene expression as a means of altering cell fates and generating dominant phenotypes. Development 118:401–415
Brenner N, Bialek W, Steveninck R de R von (2000) Adaptive rescaling maximizes information transmission. Neuron 26: 695–702
Brotz T, Borst A (1996) Cholinergic and GABAergic receptors on fly tangential cells and their role in visual motion detection. J Neurophysiol 76:1786–1799
Brotz T, Gundelfinger E, Borst A (2001) Cholinergic and GABAergic pathways in fly motion vision. Biomed Central Neurosci 2:1
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
Chan WP, Prete F, Dickinson MH (1998) Visual input to the efferent control system of a fly' s 'gyroscope'. Science 280: 289–292
Cuntz H (2000) Räumliche Verteilung von Membranparametern in Fliegenneuronen: eine Simulationsstudie. Diploma Thesis, Tuebingen
Dickinson MH, Lehmann FO, Sane SP (1999) Wing rotation and the aerodynamic basis of insect flight. Science 284:1954–1960
Dickinson MH, Farley CT, Full RJ, Koehl MAR, Kram R, Lehman S (2000) How animals move: an integrative view. Science 288:100–106
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
Eckert H, Dvorak DR (1983) The centrifugal horizontal cells in the lobula plate of the blowfly *Phaenicia sericata*. J Insect Physiol 29:547–560
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 interneurons. Biol Cybern 52:195–209
Egelhaaf M, Borst A (1992) Are there separate ON and OFF channels in fly motion vision? Vis Neurosci 8:151–164
Egelhaaf M, Borst A, Reichardt W (1989) Computational structure of a biological motion detection system as revealed by local detector analysis in the fly's nervous system. J Opt Soc Am A 6:1070–1087
Fairhall AL, Lewen GD, Bialek W, Ruyter van Steveninck R de (2001) Efficiency and ambiguity in an adaptive neural code. Nature 412:787–792
Fayyazuddin A, Dickinson MH (1996) Haltere afferents provide direct, electrotonic input to a steering motor neuron of the blowfly, *Calliphora*. J Neurosci 16:5225–5232
Fischbach KF, Dittrich APM (1989) The optic lobe of *Drosophila melanogaster*. I. A Golgi analysis of wild-type structure. Cell Tissue Res 258:441–475
Fraenkel G, Pringle JWS (1938) Halteres of flies as gyroscopic organs of equilibrium. Nature 141, 919–920
Franceschini N, Riehle A, Le Nestour A (1989) Directionally selective motion detection by insect neurons. In: Stavenga DG, Hardie RC (eds) Facets of vision. Springer, Berlin Heidelberg New York, pp 360–390
Franz MO, Krapp HG (2000) Wide-field, motion-sensitive neurons and matched filters for optic flow fields. Biol Cybern 83:185–197
Frye MA, Dickinson MH (2001) Fly flight: a model for the neural control of complex behavior. Neuron 32:385–388
Gauck V, Borst A (1999) Spatial response properties of contralateral inhibited lobula plate tangential cells in the fly visual system. J Comp Neurol 406:51–71
Gauck V, Egelhaaf M, Borst A (1997) Synapse distribution on VCH, an inhibitory, motion-sensitive interneuron in the fly visual system. J Comp Neurol 381:489–499
Geiger G, Nässel DR (1981) Visual orientation behaviour of flies after selective laser beam ablation of interneurons. Nature 293:398–399
Geiger G, Nässel DR (1982) Visual processing of moving single objects and wide-field patterns in flies: behavioural analysis after laser-surgical removal of interneurons. Biol Cybern 44:141–149
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
Goldberg F, Grünewald B, Rosenboom H, Menzel R (1999) Nicotinic acetylcholine currents of cultured Kenyon cells from the mushroom bodies of the honey bee *Apis mellifera*. J Physiol (Lond) 514:759–768
Gronenberg W, Strausfeld NJ (1990) Descending neurons supplying the neck and flight motor of Diptera: physiological and anatomical characteristics. J Comp Neurol 302:973–991
Gronenberg W, Milde JJ, Strausfeld NJ (1995) Oculomotor control in calliphorid flies: organization of descending neurons to neck motor neurons responding to visual stimuli. J Comp Neurol 361:267–284
Haag J (1994) Aktive und passive Membraneigenschaften bewegungsempfindlicher Interneurone der Schmeissfliege *Calliphora erythrocephala*. Doctoral Thesis, Tuebingen
Haag J, Borst A (1996) Amplification of high-frequency synaptic inputs by active dendritic membrane processes. Nature 379:639–641
Haag J, Borst A (1997) Encoding of visual motion information and reliability in spiking and graded potential neurons. J Neurosci 17:4809–4819
Haag J, Borst A (1998) Active membrane characteristics and signal encoding in graded potential neurons. J Neurosci 18:7972–7986
Haag J, Borst A (2000) Spatial distribution and characteristics of voltage-gated calcium currents within visual interneurons. J Neurophysiol 83:1039–1051
Haag J, Borst A (2001) Recurrent network interactions underlying flow-field selectivity of visual interneurons. J Neurosci 21:5685–5692
Haag J, Borst A (2002) Dendro-dendritic interactions between motion-sensitive large-field neurons in the fly. J Neurosci (in press)
Haag J, Egelhaaf M, Borst A (1992) Dendritic integration of motion information in visual interneurons of the blowfly. Neurosci Lett 140:173–176
Haag J, Theunissen F, Borst A (1997) The intrinsic electrophysiological characteristics of fly lobula plate tangential cells. II. Active membrane properties. J Comput Neurosci 4:349–369
Haag J, Vermeulen A, Borst A (1999) The intrinsic electrophysiological characteristics of fly lobula plate tangential cells. III. Visual response properties. J Comput Neurosci 7:213–234
Harris RA, O'Carroll DC, Laughlin SB (2000) Contrast gain reduction in fly motion adaptation. Neuron 28:595–606
Hausen K (1977) Struktur, Funktion und Konnektivität bewegungsempfindlicher Interneurone im dritten optischen Neuropil der Schmeißfliege *Calliphora erythrocephala*. Doctoral Thesis, Tuebingen
Hausen K (1981) Monocular and binocular computation of motion in the lobula plate of the fly. Verh Dtsch Zool Ges 74:49–70
Hausen K (1982a) Motion sensitive interneurons in the optomotor system of the fly. I. The horizontal cells: structure and signals. Biol Cybern 45:143–156

Hausen K (1982b) Motion sensitive interneurons in the optomotor system of the fly. II. The horizontal cells: receptive field organization and response characteristics. Biol Cybern 46:67–79
Hausen K (1984) The lobula-complex of the fly: structure, function and significance in visual behaviour. In: Ali MA (ed) Photoreception and vision in invertebrates. Plenum Press, New York, pp 523–559
Hausen K, Egelhaaf M (1989) Neural mechanisms of visual course control in insects. In: Stavenga DG, Hardie RC (eds) Facets of vision. Springer, Berlin Heidelberg New York, pp 391–424
Hausen K, Wehrhahn C (1983) Microsurgical lesion of horizontal cells changes optomotor yaw response in the blowfly *Calliphora erythocephala*. Proc R Soc Lond Ser B 219:211–216
Hausen K, Wehrhahn C (1990) Neural circuits mediating visual flight control in flies. II. Separation of two control systems by microsurgical brain lesions. J Neurosci 10:351–360
Hausen K, Wolburg-Buchholz K, Ribi WA (1980) The synaptic organization of visual interneurons in the lobula complex of flies. Cell Tissue Res 208:371–387
Heisenberg M, Wonneberger R, Wolf R (1978) Optomotor-blind (H31): A *Drosophila* mutant of the lobula plate giant neurons. J Comp Physiol 124:287–296
Hengstenberg R (1977) Spike response of "non-spiking" visual interneurone. Nature 270:338–340
Hengstenberg R (1982) Common visual response properties of giant vertical cells in the lobula plate of the blowfly *Calliphora*. J Comp Physiol A 149:179–193
Hengstenberg R (1984) Roll-stabilization during flight of the blowfly's head and body mechanical and visual cues. In: Varjú D, Schnitzler H-U (eds) Localization and orientation in biology and engineering. Springer, Berlin Heidelberg New York, pp 121–134
Hengstenberg R, Hausen K, Hengstenberg B (1982) The number and structure of giant vertical cells (VS) in the lobula plate of the blowfly *Calliphora erytrocephala*. J Comp Physiol A 149:163–177
Horstmann W, Egelhaaf M, Warzecha AK (2000) Synaptic interactions increase optic flow specificity. Eur J Neurosci 12:2157–2165
Kern R, Petereit C, Egelhaaf M (2001) Neural processing of naturalistic optic flow. J Neurosci 21:RC139
Krapp HG, Hengstenberg R (1996) Estimation of self-motion by optic flow processing in single visual interneurons. Nature 384:463–466
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
Kurtz R, Dürr V, Egelhaaf M (2000) Dendritic calcium accumulation associated with direction-selective adaptation in visual motion-sensitive neurons in vivo. J Neurophysiol 84:1914–1923
Kurtz R, Warzecha AK, Egelhaaf M (2001) Transfer of visual motion information via graded synapses operates linearly in the natural activity range. J Neurosci 21:6957–6966
Land MF, Collett TS (1974) Chasing behavior of houseflies (*Fannia canicularis*). J Comp Physiol 89:331–357
Laughlin SB, Osorio D (1989) Mechanism for neural signal enhancement in the blowfly compound eye. J Exp Biol 144: 113–146
Miyawaki A, Llopis J, Heim R, McCaffery JM, Adams JA, Ikura M, Tsien RY (1997) Fluorescent indicators for Ca^{2+} based on green fluorescent proteins and calmodulin. Nature 388:882–887
Maddess T, Laughlin SB (1985) Adaptation of the motion-sensitive neuron H1 is generated locally and governed by contrast frequency. Proc R Soc Lond B 225:251–275
Nalbach G (1993) The halteres of the blowfly *Calliphora*. I. Kinematics and dynamics. J Comp Physiol A 173:293–300
Oertner TG, Single S, Borst A (1999) Separation of voltage- and ligand-gated calcium influx in locust neurons by optical imaging. Neurosci Lett 274:95–98
Oertner TG, Brotz T, Borst A (2001) Mechanisms of dendritic calcium signaling in fly neurons. J Neurophysiol 85:439–447
Reichardt W (1961) Autocorrelation, a principle for the evaluation of sensory information by the central nervous system. In: Rosenblith WA (ed) Sensory communication. MIT Press/Wiley, New York, pp 377–390
Reichardt W (1987) Evaluation of optical motion information by movement detectors. J Comp Physiol A 161:533–547
Riehle A, Franceschini N (1984) Motion detection in flies: parametric control over ON-OFF pathways. Exp Brain Res 54:390–394
Rieke F, Warland D, Ruyter van Steveninck R de, Bialek W (1997) Spikes. Exploring the neural code. MIT Press, Cambridge
Ruyter van Steveninck R de, Zaagman WH, Mastebroek HAK (1986) Adaptation of transient responses of a movement-sensitive neuron in the visual system of the blowfly *Calliphora erytrocephala*. Biol Cybern 53:451–463
Ruyter van Steveninck R de, Lewen GD, Strong SP, Koberle R, Bialek W (1997) Reproducibility and variability in neural spike trains. Science 275:1805–1808
Ruyter van Steveninck R de, Borst A, Bialek W (2000) Real-time encoding of motion: answerable questions and questionable answers in the flýs visual system. In: Zeil J, Zanker JM (eds) Motion vision – computational, neural, and ecological constraints. Springer, Berlin Heidelberg New York, pp 279–306
Schuling FH, Masterbroek HAK, Bult R, Lenting BPM (1989) Properties of elementary movement detectors in the fly *Calliphora erythrocephala*. J Comp Physiol A 165:179–192
Single S, Borst A (1998) Dendritic integration and its role in computing image velocity. Science 281:1848–1850
Single S, Borst A (2002) Different mechanisms of calcium entry within different dendritic compartments. J Neurophysiol 87:1616–1624
Single S, Haag J, Borst A (1997) Dendritic computation of direction selectivity and gain control in visual interneurons. J Neurosci 17:6023–6030
Sobel EC, Tank DW (1994) In vivo Ca^{2+}dynamics in a cricket auditory neuron: an example of chemical computation. Science 263:823–826
Strausfeld NJ (1984) Functional neuroanatomy of the blowfly's visual system. In: Ali MA (ed) Photoreception and vision in invertebrates. Plenum Press, pp 483–522
Strausfeld NJ (1989) Beneath the compound eye: neuroanatomical analysis and physiological correlates in the study of insect vision. In: Stavenga DG, Hardie RC (eds) Facets of vision. Springer, Berlin Heidelberg New York, pp 317–359
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, Lee JK (1991) Neuronal basis for parallel visual processing in the fly. Vis Neurosci 7:13–33
Wagner H (1986) Flight performance and visual control of flight of the free-flying housefly (*Musca domestica*). II. Pursuit of targets. Philos Trans R Soc Lond B 312:553–579
Warzecha AK, Egelhaaf M, Borst A (1993) Neural circuit tuning fly visual interneurons to motion of small objects. I. Dissection of the circuit by pharmacological and photo-inactivation techniques. J Neurophysiol 69:329–339
Yeates DK, Wiegmann BM (1999) Congruence and controversy: toward a higher-level phylogeny of diptera. Annu Rev Entomol 44:397–428