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Processing of synaptic signals in fly visual interneurons selectively responsive to small moving objects

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Abstract
In the fly identified visual interneurons are found which respond selectively to small moving objects. Recently, some of the neural elements could be identified which constitute the underlying circuit. We review the available experimental data and compare them with some model circuitries.

1. INTRODUCTION

A moving observer generates on the retina a continuous flow of the images of the environment. The distribution of motion signals on the retina, the so-called optic flow-field, thereby depends both on the trajectory of the observer through the world as well as on the structure of the environment. If the observer passes a nearby object the image of the object moves faster on the retina than the background. Therefore, the flow-field contains discontinuities with a small patch containing larger motion vectors than the rest of the flow-field which indicates the existence of nearby objects. If evaluated appropriately, motion information can, therefore, be used to segregate the environment into salient objects and a more distant background ('figure-ground discrimination').

The importance of relative motion as a visual cue for figure-ground discrimination is illustrated by the fact that many animal species are able to detect objects which differ from their surroundings only by the velocity at which they move (e.g. flies: Egelhaaf et al. 1988; bees: Srinivasan et al. 1990; locusts: Collett and Paterson, 1991; primates: Miles and Kawano, 1987; Regan and Beverley, 1984). Accordingly, neurons that respond best to small objects moving relative to their background are found in various phylogenetically divergent animal groups (e.g. hawkmoths: Collett 1971 1972; dragonflies: Olberg 1981, 1986; hoverflies: Collett and King 1975; blowflies: Egelhaaf 1985b; toads: Tsai 1990; pigeons: Frost and Nakayama 1983, Frost et al. 1988; cats: Grünau and Frost 1983; monkeys: Allman et al. 1985, Tanaka et al. 1986, Davidson and Bender, 1991). Despite the widespread significance of object detection by relative motion, not much is known so far about the underlying cellular mechanisms in most species. As will be shown in this article the situation is different in flies.

To study figure-ground discrimination flies are well suited as experimental animals: (i) They track moving objects in free flight (Land and Collett, 1974; Wehrhahn, 1979; Wagner, 1986). They also detect and fixate objects even when they differ from their background only by motion (Virsik and Reichardt, 1976; Reichardt and Poggio, 1979; Bülthoff, 1981; Reichardt et al. 1983; 1989; Egelhaaf, 1985a). (ii) The major neurons in their main center of motion computation are amenable to electrophysiological analysis and can be identified individually on the basis of their invariant anatomical structure and response characteristics (Hausen, 1981; 1984; Hausen and Egelhaaf, 1989). (iii) Moreover, by comparing behavioral and electrophysiological data obtained under the same stimulus conditions some of these neurons, the so-called figure-detection or FD-cells, have been concluded to play a decisive role in mediating figure-ground discrimination behavior (Egelhaaf, 1985a-c; Egelhaaf, 1987; Egelhaaf et al. 1988; Reichardt et al. 1989).

Here we review recent experiments that led to the elucidation of the neural circuit that tunes a particular interneuron in the fly's visual system to the motion of small objects relative to the background. Knowing the major elements of a circuit, however, is not sufficient to understand how the circuit operates. More information is required on the synaptic relationships, the synaptic transfer characteristics as well as on the passive and active membrane properties of the neurons involved. Since this knowledge is only beginning to be available in the case of the circuit responsible for small-field tuning of the particular fly interneuron discussed here, we try to constrain the possibilities by model simulations of various variants of the basic experimentally established wiring scheme.

2. FIGURE-GROUND DISCRIMINATION BY THE FLY

In a series of experiments (Reichardt et al., 1983, Egelhaaf 1985a, Reichardt et al., 1989), the reaction of a fly flying tethered to a torque compensator has been determined in response to a figure moving relative to a background (Fig.1, left). These experiments undoubtedly demonstrate that flies are able to discriminate between an object and the background solely by means of relative motion between these two: As long as figure and background move in synchrony, the fly's torque follows the motion of the drum. This compensatory optomotor responses would stabilize the visual world on its eyes if it were allowed to turn freely. During this period of synchronous motion no response towards the object is displayed by the fly. Only when figure and background move relative to each other the mean torque of the fly shifts towards the side of the figure and characteristic torque peaks appear in the trace indicating that the animal tries to turn towards the figure (Fig.1, right).

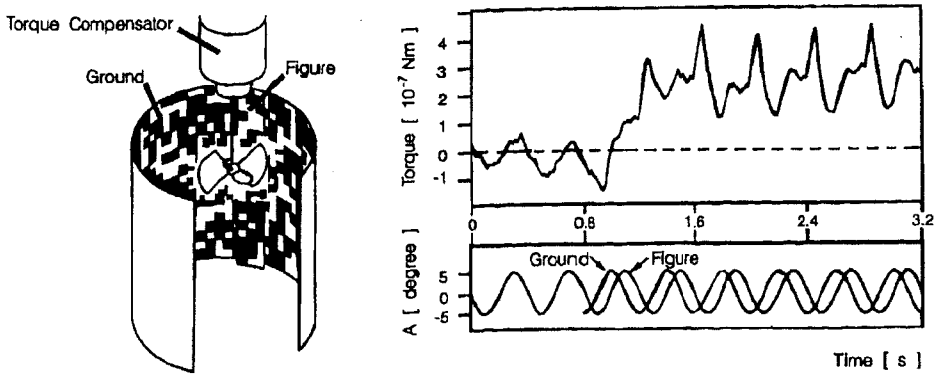

Fig.1 (Left) Experimental set-up of a behavioral figure-ground experiment. A fly is suspended to a torque meter and placed in the middle of a textured drum (background) with a stripe (figure) covered with the same texture placed in front of the fly's right eye. Drum and stripe can be controlled independently. (Right) Torque response profile of the fly *Calliphora erythrocephala*. A textured stripe of 7.2° width was oscillated sinusoidally about an angular position of 30° to the right of the fly (2.5 Hz oscillation frequency, 5° oscillation amplitude). The bottom trace shows the deviation of figure and ground from their mean position. During the first two cycles, figure and ground move in synchrony. At time 0.8s they are set to a phase angle of 90° . The plotted curve represents the average of 50 sweeps of a single fly. (Modified after Egelhaaf, 1985a).

3. RESPONSE PROPERTIES OF FIGURE-DETECTION CELLS

The main center of motion computation of the fly visual system is the posterior part of the third visual neuropil, the lobula plate. There reside about 50 individually identifiable nerve cells with large dendritic trees, the so-called tangential cells (Hausen, 1981; Hausen and Egelhaaf, 1989). They are specifically tuned to various kinds of retinal motion patterns as are encountered by the animal when moving around in its environment. Part of these neurons have been shown to play important roles in visual orientation behavior (Hausen, 1981; Hausen and Egelhaaf, 1989; Hausen and Wehrhahn, 1983; 1990; Egelhaaf et al. 1988; Egelhaaf and Borst, 1993). Most of the tangential cells acquire their characteristic motion selectivity by two basic processing steps. (i) With their extended dendritic trees they spatially pool the output of large numbers of retinotopically organized local motion sensitive elements (Borst and

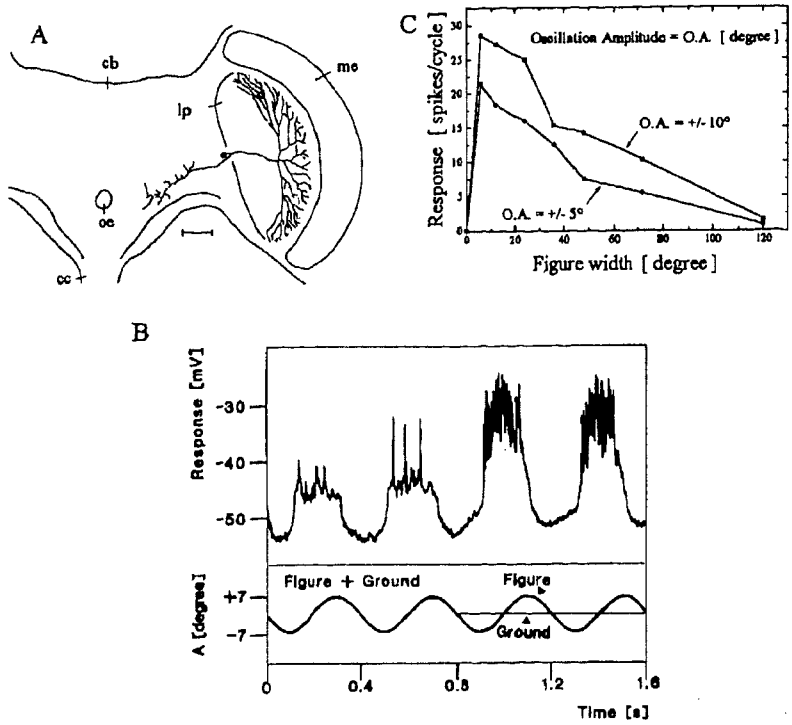

Fig.2 (A) Structure of an FD1-cell as reconstructed from an intracellular LY injection. The cell is drawn into a schematic frontal view of the brain. Abbreviations: cb central brain, cc cervical connective, me medulla, lp lobula plate, oe oesophagus. Scale bar = 100 µm. (B) Intracellular recording of an FD1-cell. After two cycles of synchronous oscillation of a 12°-wide textured figure and a binocular background (from -120° to +120° horizontal extent) the ground stopped moving, while the figure continued oscillating for another two cycles (2.5 Hz oscillations frequency, 7° oscillation amplitude). The figure was positioned in the cells excitatory receptive field at an angular horizontal position of 10°. The FD1-cell is much more excited when the figure oscillates in front of a stationary background than during synchronous motion. (C) Dependence of the FD1-cell response on the angular width of a pattern moving within the ipsilateral visual field. The pattern was oscillating in front of a stationary background at a frequency of 2.5 Hz with two different oscillation amplitudes ('O.A.'). As a distinguishing feature of FD-cells, the cell's response is maximum for small patterns and decreases with increasing pattern size. Note that for the smaller oscillation amplitude the peak response remains at small pattern sizes while only the overall response amplitude is reduced (A,B: Modified after Egelhaaf, 1985b; C: Egelhaaf, unpublished).

Egelhaaf, 1989; Egelhaaf et al., 1989; Borst and Egelhaaf, 1990; Haag et al., 1992). By this retinotopic input, the tangential cells become directionally selective to motion in large parts of the ipsilateral visual field. (ii) The response properties of part of the tangential cells are further shaped by excitatory or inhibitory input from other tangential cells of the ipsi- or contralateral lobula plate.

These network interactions have been unravelled in detail for a particular cell type, the FD1-cell that is most sensitive to the motion of small objects. Fig.2 shows the anatomy of an FD1-cell together with its response characteristics. The cell has an extensive dendritic arborization within the lateral lobula plate and, accordingly, its excitatory receptive field in the fronto-lateral part of the eye. It sends its axon into the central brain (Fig.2A). As is a common property of most invertebrate neurons, the cell body is connected with the axon through a thin cell body fibre. When the cell is stimulated in the same way as in the behavioral experiments (see Fig.1), it displays a pronounced sensitivity for motion when the figure moves relative to the background. The cell responds only weakly when both move in synchrony (Fig.2B). When the response of the FD1-cell is measured as a function of pattern size, its response is maximum for small pattern widths and decreases when the pattern becomes more extended in space ('small-field tuning'). This is true when the pattern is increased within the ipsilateral visual field (Fig.2C). However, the response of the FD1-cell to a small moving object is also reduced when there is large-field motion in front of the contralateral eye (Egelhaaf, 1985b). Consequently, binocular rotatory large-field motion reduces its response to small-field motion most strongly.

4. INPUT CIRCUITRY OF FIGURE-DETECTION CELLS

The specific tuning of the FD1-cell in the right half of the brain to small-field and relative motion has been concluded to be mediated by the inhibitory action of one or several elements that respond best to binocular clockwise large-field motion (Egelhaaf, 1985b,c). There are several lobula plate tangential cells that have the appropriate preferred direction to act as the elements that inhibit the FD1-cell during large-field motion. Two of the HS-cells (HSN-, HSE-cell) as well as the two CH-cells (DCH- and VCH-cell) (Hausen, 1976a,b; 1982a,b; Eckert and Dvorak, 1983) respond maximally to rotatory large-field motion and, hence, under the conditions when the FD1-cell's response is reduced maximally (Egelhaaf, 1985b). From these the CH-cells were the most plausible candidates because they have been suggested to be GABAergic (Meyer et al. 1986) and, thus, most likely inhibitory elements.

From the above mentioned cells only the VCH-cell represents the large-field-inhibitor of the FD1-cell and, thus, mediates its small-field selectivity. This was recently demonstrated by two inactivation techniques: (i) The GABA-antagonist picrotoxinin (Benson, 1988; Rauh et al. 1990) was injected into the haemolymph. As a consequence the sensitivity of the FD1-cell to small moving objects is eliminated (Egelhaaf, 1990;

Warzecha et al., 1993). (ii) Using the photoinactivation technique (Miller and Selverston, 1979; Selverston and Miller, 1980) various candidates of the large field inhibitor were individually ablated and the response of the FD1-cell was recorded before and after ablation. After photoinactivation of the DCH-cell or HSE-cell the response of the FD1-cell did not change significantly. Only when the VCH-cell was ablated the response of the FD1-cell to large-field motion became about three times as large as before, whereas the response to small-field motion did not change considerably. Hence, out of all the candidates, the VCH-cell is the one that appears to be responsible for tuning the FD1-cell to the motion of small objects (Warzecha et al., 1992, 1993).

Knowing the identity of the circuit elements and knowing that one is inhibiting the other is, however, not sufficient to understand how the circuit works at a cellular level. Since the effectiveness of an inhibitory signal depends on the site of inhibition (e.g. Vu and Krasne, 1992), one also needs to have information about the contact sites and the transmission characteristics between these elements. In the present context, it is important to know where the FD1-cell is contacted by the VCH-cell and where the VCH-cell receives its input signals from the contralateral and the ipsilateral eye. The VCH-cell has two arborizations, one in the lobula plate and the other in the ventrolateral brain (Hausen, 1976b; Eckert and Dvorak, 1983). In principle, both arborizations could be input sites either of the ipsi- or contralateral input elements or of both of them. One method which allows to map the synaptically induced spatial activity distribution within single cells is the optical recording technique. In the semi-intact fly where the cells can still be activated and inhibited by their natural synaptic input this technique can be employed because the arborizations of the tangential cells in the lobula plate are more or less two-dimensional lying less than 50 μm below and almost parallel to the surface of the brain. Using the calcium-sensitive dye fura-2 (Grynkiewicz et al., 1985) we could show that, in addition to the presynaptic terminal and the cell body, calcium accumulates also in the dendritic tree. In particular, by motion stimuli restricted to small areas of the visual field, calcium accumulates only in selected parts of the dendrite (Borst and Egelhaaf, 1992).

We applied this technique to the VCH-cell (Egelhaaf et al., 1993). In each of these experiments a single cell was filled with the fluorescent calcium indicator fura-2. Visually induced intracellular calcium accumulation served exclusively as a marker of the sites that are activated by synaptic input. The resulting images represent the relative fluorescence changes of the cell induced by motion stimulation (for details, see Borst and Egelhaaf, 1992). In a first series of experiments a VCH-cell was activated either by front-to-back motion in the ipsilateral visual field or by back-to-front motion presented to the contralateral eye. Ipsilateral motion led to calcium accumulation only in the main arborization in the lobula plate and not in the arborization in the ventrolateral brain. In contrast, contralateral motion induced an increase in calcium concentration simultaneously in both arborizations. Two conclusions can be drawn on the basis of these data: (i) Since the small arborization in the ventrolateral brain is only

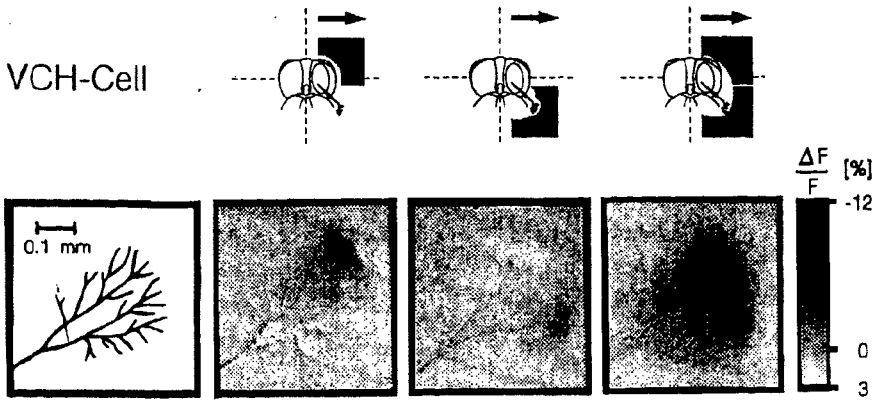

Fig.3 Retinotopic input organization of the VCH-cell. Motion in the preferred direction in the ipsilateral visual field of the VCH-cell leads to an increase in free cytosolic calcium in locally restricted dendritic branches. Two stimulus patterns (diameter about 20°) were placed in the visual field in such a way that each of them, when presented alone, induced membrane potential changes. The stimulus conditions are shown schematically on top of each image with the shaded area indicating the place where the grating was positioned in the visual field of the fly. Left diagram: Reconstruction from the fluorescence intensity image (100x100 pixels; 100 ms exposure time) of a VCH-cell filled with fura-2 taken at 380 nm excitation in the living animal. Other diagrams: Changes in the raw fluorescence (ΔF/F, without background subtraction) of the same cell after 9 s of preferred direction motion in the dorsal, ventral or simultaneously in both parts of the receptive field. Negative ΔF/F coded by darker grey levels correspond to an accumulation of calcium. Motion in the ventral and dorsal part of the receptive field leads to localized calcium accumulation in ventral and dorsal dendritic branches, respectively, revealing the retinotopic input organization of the VCH-cell. Note the overproportional increase in calcium accumulation when the cell is stimulated by motion with both patterns (Modified after Egelhaaf et al., 1993).

labelled during contralateral motion, although the cell is depolarized under both stimulus conditions, it is suggested that it represents a postsynaptic site receiving its input exclusively from the contralateral eye. (ii) The labelling of the main arborization in the lobula plate during motion in front of either eye may indicate that it is postsynaptic to both ipsi- and contralateral input elements.

These conclusions are further substantiated in experiments where the cell injected with fura-2 was stimulated by horizontal motion of a grating pattern in either the dorsal or ventral part of its ipsilateral receptive field, respectively, or in both regions simultaneously (see schematic diagrams above the plots in Fig.3). When the cell is

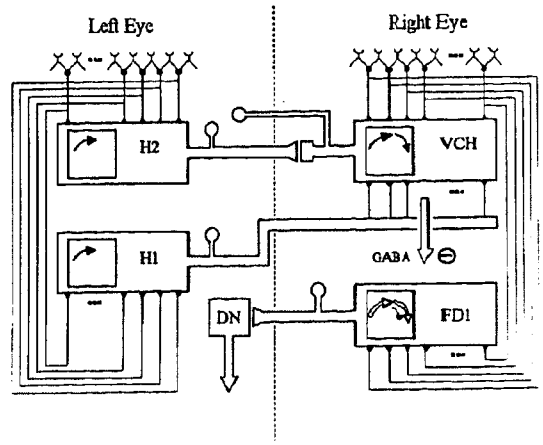

Fig.4 Working hypothesis of the neural circuit responsible for tuning the FD1-cell to small moving objects. The VCH-cell is assumed to receive its ipsilateral input from retinotopically organized local motion sensitive elements and its contralateral input from two tangential cells of the other optic lobe (H1- and H2-cell). The VCH-cell inhibits the FD1-cell that, in turn, is assumed to be involved, via descending neurons (DN), in the detection and fixation of small moving objects. The inhibitory connection between the VCH- and FD1-cell is indicated by an arrow. The arrows in the boxes within the schematic dendrites of the various cells indicate the stimulus conditions that lead to either maximum excitation (filled arrows) or, in the case of the FD1-cell, to maximum inhibition (open arrows); large arrows indicate large-field motion, the small arrow in the schematic FD1-cell indicates small-field motion. The arrows in the left and right halves of the boxes denote motion in the left and the right visual field, respectively. The dashed vertical line indicates the midline of the brain. The thin branches of the axons with their circular endings represent the cell body fibres and the cell bodies, respectively. (Modified after Egelhaaf et al., 1993).

activated by motion stimulation in the upper part of the ipsilateral receptive field, only the dorsal dendrites are labelled. Only the ventral dendritic branches are labelled when the motion stimulus is presented in the lower part of the ipsiilateral visual field. When motion is presented in both regions the entire dendritic tree appears labelled. In conclusion, the activity labelling induced by motion in different parts of the visual field clearly shows that the VCH-cell receives its ipsilateral motion input from retinotopically organized input elements. It should be noted that the labelling induced by motion in both stimulus areas is much larger than the summated activity as induced during motion in each area alone. This feature was observed in most VCH-cells investigated so far and will be further discussed later on.

From these and other experimental data, the following circuit can be derived (Fig.4) which is thought to underly the small-field tuning of the FD1-cell. It consists of at least four identified tangential neurons which are all located in the lobula plate: The H1- and H2-cell, and the VCH- and the FD1-cell. They all receive ipsilateral input from a retinotopic array of local, motion-sensitive elements which they spatially integrate with their large dendrites. By this, the H1- and H2-cell are excited most strongly by back-to-front motion whereas the VCH- and FD1-cell have front-to-back motion as their preferred direction within their ipsilateral receptive field (see arrows indicating preferred directions in Fig.4). The VCH-cell receives additional excitatory input from the contralateral visual field via the H1- and H2-cell at two different locations (Hausen, 1976a,b; Eckert and Dvorak, 1983; Egelhaaf et al., 1993). The VCH-cell, in turn, inhibits the FD1-cell. Interestingly, the lobula plate arborization of the VCH-cell seems to be an input and output-site of the neuron at the same time indicating a dendro-dendritic interaction between VCH- and FD1-cell. The functional consequences of this type of neuronal architecture will be discussed below.

5. MODELING THE CIRCUIT

The knowledge about the identity of the various circuit elements, their contact sites and their response characteristics should, in principle, allow to reconstitute the FD1-cell properties in a model simulation. Closer inspection, however, reveals that all this knowledge is by no means detailed enough to sufficiently constrain the mechanism that may account for the specific selectivity of the FD1-cell for small objects. For instance, it is not clear, so far, how the synaptic input of the various cells is transformed into the corresponding postsynaptic signals. However, as will be shown below, the synaptic transmission characteristics are critical for the performance of the circuit. Since the mechanism underlying small-field tuning of the FD1-cell cannot yet be specified unambiguously, various model alternatives will be compared in the following and related to our experimental findings. Since the optimal object size of the FD1-cell was found to be smaller than the size of its excitatory receptive field, the small-field tuning within the confines of the receptive field is the most challenging aspect of the circuit sketched in Fig.4. Therefore, we restrict our theoretical considerations to this point. All the models we will consider have several properties in common: (i) They consist of two cells which represent the VCH- and the FD1-cell, respectively, one inhibiting the other, and (ii) both cells receive retinotopic synaptic input from an identical array of local motion-sensitive elements. At first glance, these simple assumptions may be expected to lead easily to an element that responds best to small moving objects. However, careful considerations suggest that matters may not be as simple. For instance, as soon as one allows other stimulus parameters to vary in addition to stimulus size and requires the FD1-cell to exhibit small-field tuning not only at a particular stimulus strength but for a wide range of stimulus parameters, the constraints imposed on the mechansim become much more demanding. These problems arise because the VCH-cell, as well as the other lobula plate tangential cells are ambiguous

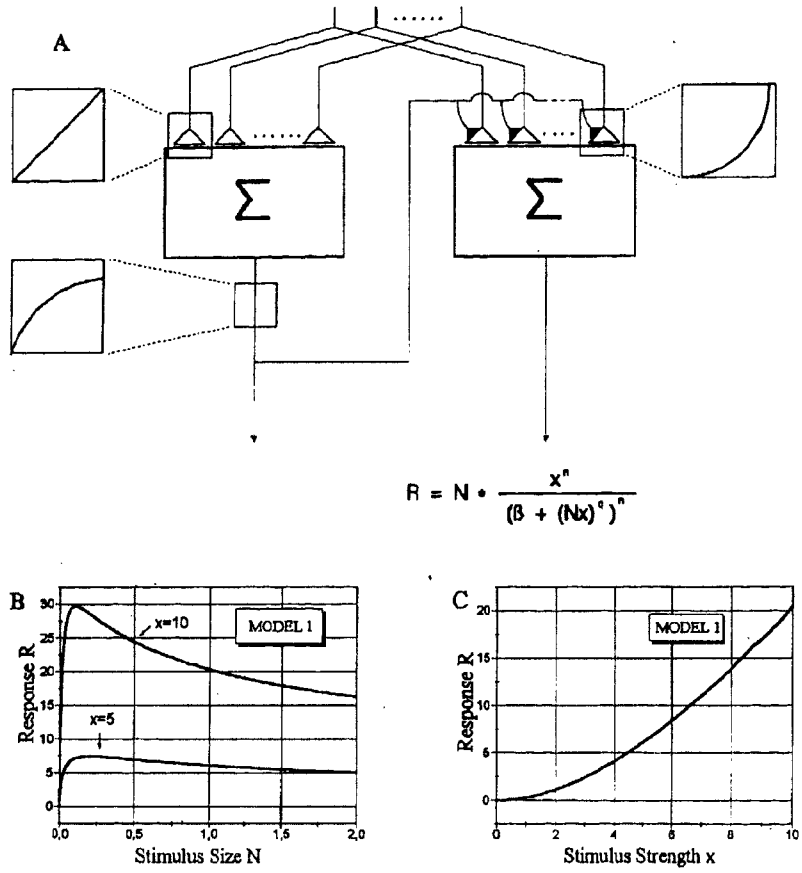

Fig.5 Original model proposed to account for small-field tuning of a nerve cell. (A) Structure of the model: Two cells symbolized by the large rectangles receive input from an array of motion detectors (open synaptic terminals). They are assumed to summate these input signals in a linear way (Σ). The output signal of the left element, the 'pool-cell', inhibits presynaptically (filled synaptic terminals) the input lines to the right element, the FD1-cell. The transmission characteristics of the various synapses shown as input-output functions (input on the x-axis, output on the y-axis) are zoomed in. (B) Output signal of the small-field element as a function of stimulus size for two different stimulus strengths (x=5, x=10). (C) Output signal of the small-field element as a function of stimulus strength at a given stimulus size (N=1). For further explanation see text.

with respect to different stimulus parameters. For instance, they may respond with the same overall amplitude and thus inhibit the FD1-cell in essentially the same way when a small object moves at a high velocity compared with an extended object moving at a smaller velocity. However, the experimental data available so far indicate that the FD1-cell shows small-field tuning at various pattern velocities (see Fig.2C). As will be shown below there are, in principle, two ways to overcome this ambiguity problem at least to some extent. The first model we shall consider was proposed by Reichardt and colleagues to explain the phenomenon of gain-control found in the optomotor behavior and lobula plate tangential cells of flies (Poggio et al., 1981; Reichardt et al., 1983; Fig.5). As it turned out, the property of small-field tuning could also be mimicked by this model by an appropriate choice of parameters (Reichardt et al., 1983; Egelhaaf, 1985c).

Reichardt and colleagues introduced the idea of a pool cell sharing its input with another cell which becomes in turn inhibited by the pool cell. Both neurons are assumed to integrate the output signals of local motion detectors. According to their terminology, the size of the stimulus will be denoted in the following as N and the amplitude of the local motion detector output as x. If everything is linear, the signal of an integrating element is Nx. The different inhibitory effect of stimulus size and local stimulus strength onto the small-field element was modelled by assuming that the two neurons handle their retinotopic input in a different way: Whereas the synapses onto the small-field element posses a pronounced expansive transmission characteristic (modelled by a power function with an exponent of 3), the synapses onto the inhibitory element are assumed to behave linearly. Moreover, the inhibitory neuron is assumed to saturate and its response is approximated by $(Nx)^q$ with $0<q<1$. As a specific type of inhibitory interaction between two neurons the authors assumed a shunting inhibition. In this case, the equilibrium potential of the inhibitory ion is close to the resting potential of the postsynaptic element. To be effective, the conductance change exerted by the inhibitory signal has to be large with respect to the other conductances (leak and excitatory conductance). As follows immediately from the equation for an electrical equivalent circuit for a passive patch of membrane, the excitatory input then becomes essentially divided by the inhibitory input. Thus, given a presynaptic shunting inhibition with β as the shunting coefficient (equivalent to the leak conductance of the cell) the input signals of the small-field element turn into $x/(\beta+(Nx)^q)$, which after expansive transmission (power of n) become $(x/(\beta+(Nx)^q))^n$. Assuming linear spatial integration within the small-field element, the response R becomes

$$R = N*(x/(\beta+(Nx)^q))^n \qquad (1)$$

The model together with its response as a function of stimulus size and amplitude is shown in Fig.5. As one can see, the model displays small-field tuning for various local stimulus strengths (Fig.5B). Furthermore, its response increases monotonically with

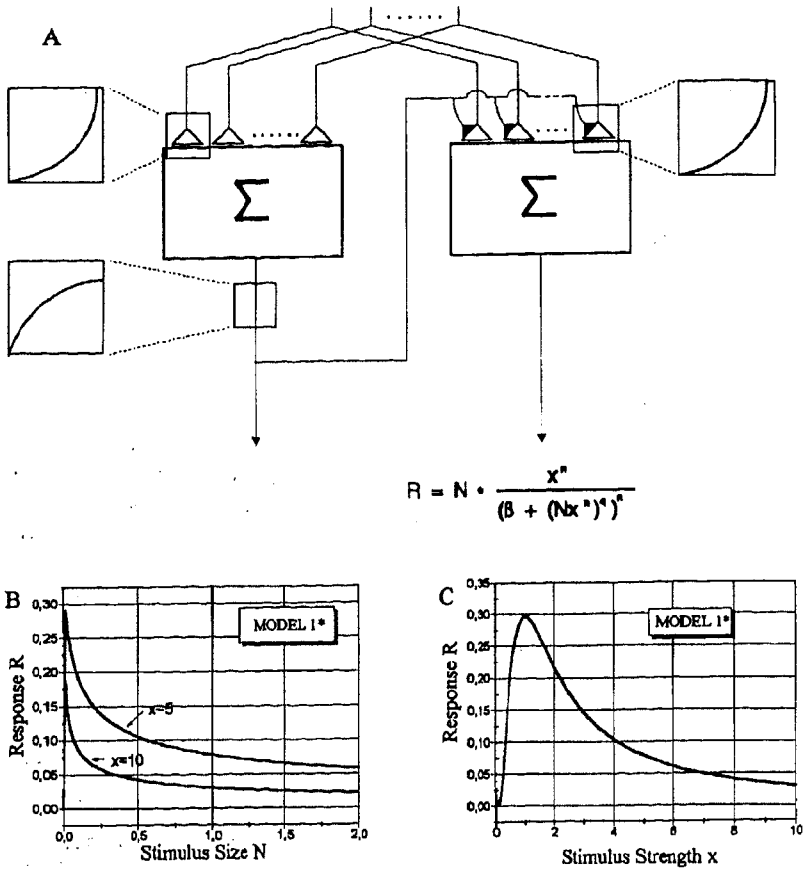

Fig.6 Same model as shown in Fig.5 with the only difference that here the synapses of the motion-sensitive input elements are assumed to have identical expansive transmission characteristics (power of 3) onto both integrating neurons. (A) Structure of the model. (B) Output signal of the small-field element as a function of stimulus size for two different stimulus strengths (x=5, x=10). (C) Output signal of the small-field element as a function of stimulus strength at a given stimulus size (N=1). Note that in contrast to the model shown in Fig.5 the function is no longer monotonically increasing with stimulus strength.

stimulus strength such as velocity (Fig.5C). Hence its behavior quite nicely mimicks the response of the FD1-cell. We can take a second look at the model parameters and ask for which numerical range of the various parameters the model displays these desired properties. To do so, we may simplify equation (1) by setting the shunting coefficient β equal to zero. Then R is proportional to N^{1-nq} and to $x^{n*(1-q)}$. If we ask that R is decreasing with N and increasing with x, n and q have to be chosen such that $1-nq < 0$, and $n(1-q) > 0$. Obviously, this is the case e.g. for $q=0.5$ and $n=3$. These values are chosen in the graphs shown in Fig.5B and C.

The crucial assumption of this model is that both neurons have input synapses with fundamentally different transmission characteristics. To understand the impact of this assumption, the same circuit as is shown in Fig.5 is modelled with the only difference that both neurons treat their retinotopic input in the same manner, i.e. in the example shown in Fig.6 through an expansive nonlinearity (power of 3). The response then becomes

$$R = N*(x/(\beta+(Nx^n)^q))^n \qquad (2)$$

As one can see (Fig.6), this has the following consequences: The neuron still displays small-field tuning for different local stimulus parameters (Fig.6B). However, for a certain range of stimulus parameters the response amplitude becomes the larger the smaller the local stimulus signal is. Hence, if the response is plotted as a function of stimulus strength for a given stimulus size, it shows a peaked dependence with decreasing amplitude for large stimulus amplitudes (Fig.6C). Although such an astonishing response behavior has not been observed in the FD1-cell, so far, the model could still account for the experimental data given that the stimulus parameters are restricted to the operating range of the model where the response is monotonically increasing with local stimulus strength (left part of the graph in Fig.6C). Interestingly, one can demonstrate that the particular features of this model is independent of the specific values of the parameters n and q: If we again ask that R is monotonically decreasing with N and increasing with x, 1-nq has to be smaller than zero, and n(1-nq) has to be larger than zero. Obviously, this can never be the case for any positive values of n and q so ever.

The next model we shall consider takes into account experimentally established facts that were not known when the original model for figure-ground discrimination has been proposed. (i) The dendro-dendritic nature of of the VCH-FD1-cell interaction. Such a construction allows, at least in principle, to have different inhibitory signals for a small pattern moving at a large velocity and a large pattern moving at a small velocity, because both stimuli may lead to a different activity distribution in the VCH-cell dendrite. (ii) The calcium signal observed within the dendrite of the VCH-cell seems to increase overproportionally with stimulus size (see Fig.4). Based on light-microscopical anatomical criteria these arborizations show presynaptic specializations ('blebs') and, therfore, are likely to be also an output region of the cell (Hausen,

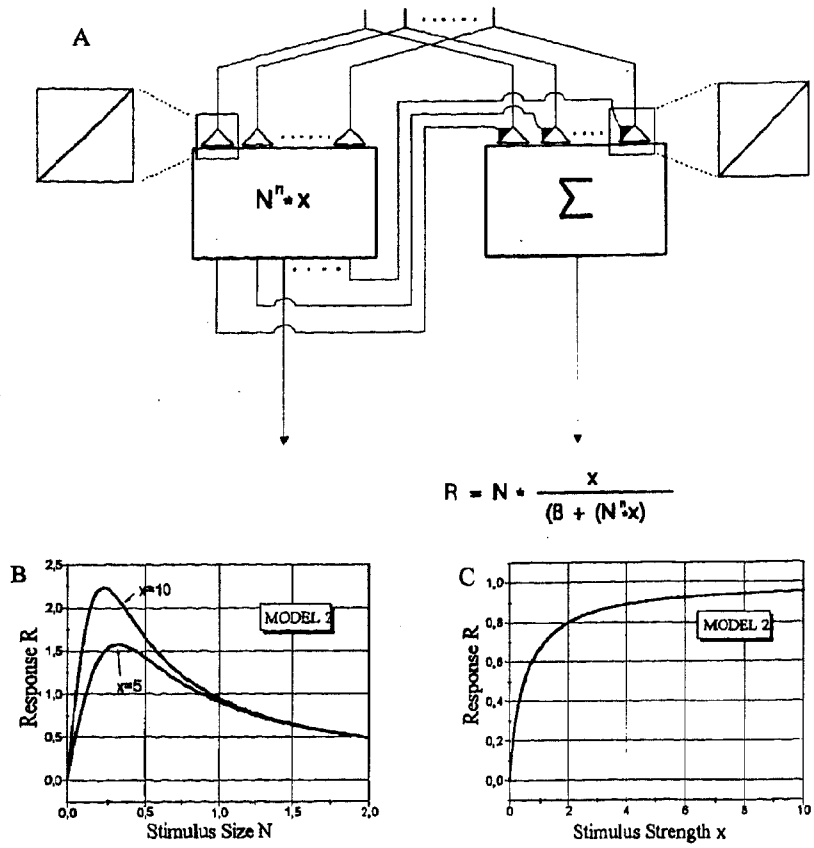

Fig.7 Alternative model to account for small-field tuning of a nerve cell. (A) Structure of the model. In contrast to the model shown in Fig.5 the input synapses to both elements are assumed to possess identical linear transmission characteristics. Here, the crucial assumption is that the inhibitory signals exerted from the left element increases overproportionally with stimulus size but not with stimulus strength. (B) Output signal of the small-field element as a function of stimulus size for two different stimulus strengths (x=5, x=10). (C) Output signal of the small-field element as a function of stimulus strength at a given stimulus size (N=1).

1976a). Since calcium is known to regulate transmitter release, the images shown in Fig.4 are presumed to represent the amplitude and distribution of the inhibitory signal the VCH-cell exerts onto the FD1-cell. Given this, we assume that the inhibitory signal, unlike the electrical response of the VCH-cell, increases overproportionally with stimulus size but not with local stimulus strength. We account for this in formal terms by an expansive nonlinearity which acts only on N but not on x: $N^n x$. Assuming either pre- or postsynaptic inhibition, the response of the small-field neuron becomes

$$R = Nx / (\beta + N^n x) \qquad (3)$$

This circuit together with its resulting behavior is shown in Fig.7. The circuit displays small-field tuning for both local stimulus parameters (Fig.7B). Furthermore, its response is a monotonic function of local stimulus strength. Again, as the model shown in Fig.5, the response is in accordance with the response characteristics of the FD1-cell as recorded from the fly brain. Considering the specific values of the parameter n, one immediately sees that as long as n is larger than 1, the circuit will display small-field tuning, since R is decreasing with N. Independent from that the response is always monotonically increasing with x and shows a saturating behavior.

6. CONCLUSIONS AND PROSPECTS

We have provided experimental evidence for a neural circuit that is responsible for the small-field tuning of a particular nerve cell, the so-called FD1-cell, in the fly visual system. However, the knowledge about the identity and connectivity between different identified neurons is not sufficient to understand at a detailed biophysical level how this circuit provides small-field tuning. Two alternative models are presented. The core of the first one has been proposed by Reichardt and colleagues (Poggio et al., 1981; Reichardt et al., 1983) at a time before the large-field inhibitor of the FD1-cell was identified. This model assumes presynaptic inhibition of the small-field cell through a so-called pool-cell. By the experiments of Warzecha et al. (1992, 1993), this pool-cell has been identified as the VCH-cell.

The anatomical characteristics of the VCH-cell, however, prompted us to propose a slightly different wiring scheme. Since the arborization of this cell in the third visual ganglion is suggested to be postsynaptic to retinotopic motion sensitive elements and, in addition shows presynaptic specializations, it is suggestive to assume that it inhibits the FD1-cell *via* a dendro-dendritic interaction. Furthermore, optical recording experiments revealed an over-proportional increase of calcium concentration in this arborization with increasing pattern size. If calcium is assumed to control transmitter release, this finding would imply that the inhibitory strength increases overproportionally when the stimulus pattern increases.

Both alternative models critically rely on specific assumptions to disentangle the consequences of an increasing pattern size on the one hand and velocity or contrast on the other hand and, thus, to guarantee small-field selectivity of the FD1-cell for a wide range of contrasts and velocities. The original model has to assume different transmission characteristics of the local motion detector output synapses onto the VCH- and FD1-cell. In contrast the new model is less restrictive in this respect, but has to assume that the strength of the inhibitory signal increases overproportionally with increasing pattern size but linearly or less than linearly with variations in contrast or velocity.

Is there experimental evidence to distinguish between these two mechanisms? There are several arguments against assuming different synaptic transmission characteristics between the local motion detectors and the VCH- and FD1-cell, respectively. The most compelling one comes from the recent photoinactivation experiments of Warzecha et al. (1992, 1993). After selectively ablating the VCH-cell, the small-field selectivity of the FD1-cell disappears, obviously because the inhibitor of the FD1-cell has been killed. If the transmission characteristic between the movement detectors and the FD1-cell corresponds to an expansive nonlinearity as proposed by the original model, removal of the inhibitory input should lead to a dramatic increase in the overall response amplitude of the FD1-cell. This, however, is in contrast to the experimental findings where the response amplitude during small-field motion is not much altered after the VCH-cell has been killed (Warzecha et al., 1992, 1993).

The only other way we see at present to achieve small-field tuning irrespective of contrast and velocity is to assume that the inhibitory signal exerted by the VCH-cell depends in a different way on pattern size than on local stimulus strength, such as has been implemented in the model shown in Fig.7. Although this can be easily done formally, it is by no means a trivial problem how real neurons achieve that the inhibitory signal increases overproportionally with pattern size but linearly or according to a compressive nonlinearity with increasing velocity and contrast. The anatomy of the VCH-cell and our recent optical recording results provide a hint how this may be possible. Since the interaction between VCH- and FD1-cell is dendro-dendritic, the activity distribution in the VCH-cell and, thus, the inhibitory signal is likely to differ considerably when it is excited, for instance, by a small pattern moving with a larger velocity or an extended pattern moving with a smaller velocity. The over-proportional increase in calcium concentration with increasing pattern size may well correspond to the required expansive nonlinear increase in inhibitory strength. However, before the model shown in Fig.7 can be accepted to account for the mechanism tuning the FD1-cell to small moving objects, it has to be determined whether the calcium signal increases less than proportionally with increasing pattern velocity or contrast.

Finally one further point should be mentioned that has not yet been taken into account in any model explaining small-field tuning of the FD1-cell. So far the model cells are

fed by detectors that faithfully encode the time course of pattern velocity. However, as is known from many experiments, this assumption is not correct. For instance, the output of each individual local movement detector is not constant even when the pattern moves with a constant velocity but modulated over time with the temporal frequency of the pattern and its second harmonic (Egelhaaf et al., 1989, 1990). Only if also these complexities are taken into account, we will be able to understand the circuit underlying the small-field tuning of the FD1-cell at a really deep level.

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