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Neural encoding of behaviourally relevant visual-motion information in the fly

Martin Egelhaaf, Roland Kern, Holger G. Krapp, Jutta Kretzberg, Rafael Kurtz and Anne-Kathrin Warzecha

Information processing in visual systems is constrained by the spatial and temporal characteristics of the sensory input and by the biophysical properties of the neuronal circuits. Hence, to understand how visual systems encode behaviourally relevant information, we need to know about both the computational capabilities of the nervous system and the natural conditions under which animals normally operate. By combining behavioural, neurophysiological and computational approaches, it is now possible in the fly to assess adaptations that process visual-motion information under the constraints of its natural input. It is concluded that neuronal operating ranges and coding strategies appear to be closely matched to the inputs the animal encounters under behaviourally relevant conditions.

Martin Egelhaaf*
Roland Kern
Jutta Kretzberg
Rafael Kurtz
Anne-Kathrin Warzecha
Lehrstuhl für Neurobiologie, Fakultät für Biologie, Universität Bielefeld, Postfach 10 01 31, D-33501 Bielefeld, Germany.
*e-mail: martin.egelhaaf@biologie.uni-bielefeld.de

Holger G. Krapp
Dept of Zoology, University of Cambridge, Downing Street, Cambridge, UK CB2 3EJ.

The goal of neuroethology is to explain behaviour in terms of the activity of nerve cells and their interactions. This can only be achieved if the experimental animal can be analysed at different levels ranging from behaviour to individual neurons. Cellular mechanisms underlying processing of neuronal information are frequently analysed using *in vitro* preparations where artificial stimulation replaces the natural sensory input. Although such studies provide fascinating insights into the complex computational abilities of neurons [1], the results may not be extrapolated easily to *in vivo* conditions, where the range of response amplitudes of neurons and their temporal activity patterns may differ considerably from artificially induced activity. In systems such as the retina of the horseshoe crab *Limulus* [2], and various brain areas of pigeons [3], cats [4] and monkeys [5,6], it is now feasible to analyse the neuronal representation of visual input as it is experienced during behaviour (reviewed in Refs [7,8]). Until now, however, in most systems the underlying neuronal mechanisms have been difficult to unravel.

In the fly it is possible to employ both quantitative behavioural approaches as well as *in vivo* electrophysiological and imaging methods to analyse how behaviourally relevant visual input is processed [9–20]. Although the latter techniques are mainly employed in the blowfly, which is relatively big, they are complemented by studies of the smaller fruitfly, *Drosophila*, where a broad range of genetic approaches can be applied to dissect the visual system in an increasingly specific way [21,22].

We review recent progress on the encoding of optic-flow information in the blowfly. Optic flow is an important source of information about self-motion and the three-dimensional layout of the environment, not only for flies but for most moving animals including humans (Box 1, [4,23–25]). Flies exploit optic flow to guide their locomotion [13] and to control compensatory head movements [26], and understanding the computational principles underlying optic-flow processing in flies could provide insights into visual-motion analysis in general.

Box 1. Processing of optic flow in the fly visual system

During locomotion the entire retinal image is continually displaced. This optic flow depends on the particular type of self-motion and on the three-dimensional layout of the environment (Fig. Ia) [a,b]. Optic flow is characterized by global rather than local features. This imposes constraints on the neuronal mechanisms that evaluate optic flow as measurements of local motion from large areas of the visual field need to be combined. Accordingly, in animal taxa from insects to primates, neurons sensitive to optic flow were found to have large receptive fields (reviewed in Ref. [c]).

In the fly, the combination of local-motion measurements takes place in a strictly retinotopic way on the extended dendritic trees of a set of so-called tangential cells (TCs) (Fig. Ib). About 50 TCs of different individual morphology and functional properties have been identified in each half of the brain and found to respond to different aspects of optic flow [d–g]. Spatial pooling of local motion information is highly nonlinear. This computational feature is the consequence of both the input organization of TCs and their biophysical properties [f,h–l].

Spatial pooling of local-motion information from one eye is not usually sufficient to analyse the various types of optic flow with a high specificity. For instance, during forward translation the optic flow across both eyes is directed backwards (Fig. Ia). In contrast, during a pure rotation about the vertical axis, optic flow is directed backwards across one eye, but forwards across the other eye. Hence, translational and rotational self-motion can be distinguished by taking into account motion information from both eyes, a computational strategy used by many animals with lateral eyes, such as pigeons, rabbits and many insect species [m–p]. In the fly, specificity for certain types of optic flow is achieved by synaptic interactions between TCs in the ipsi- and/or contralateral half of the visual system (Fig. Ib) [d,e,q–t]. As a consequence, some TCs respond best to the optic flow induced when an animal turns about one of its body axes. Other TCs are tuned to relative motion between an object and its background [e,f].

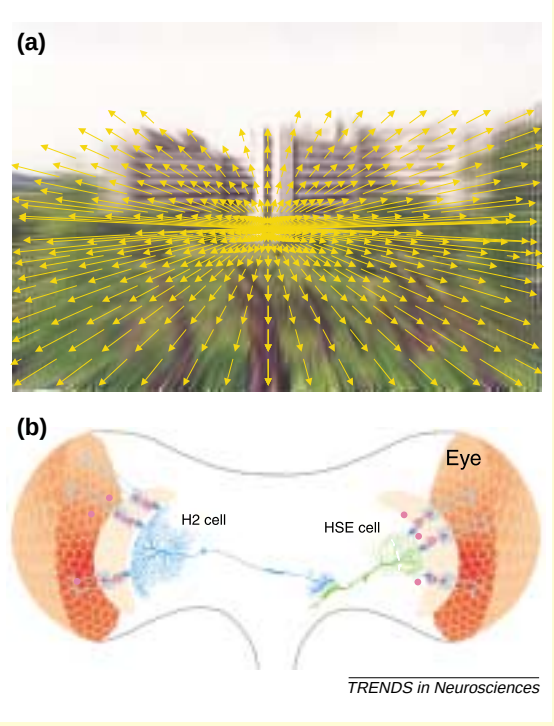

Fig. I. (a) Optic-flow field elicited when approaching an object on a straight course (forward translation). The arrows indicate schematically the velocity vectors of image points on the retina. During forward translation, velocity vectors point backwards from a focus of expansion in the middle of the visual field. (b) Schematic of the visual motion pathway of the fly (caudal view). The compound eyes are indicated in orange. The visual system is organized in a retinotopic way by columnar elements. Synaptic interactions within, as well as between, columns lead to motion-sensitive responses (for details see Refs [11,28]). The outputs of such small-field motion-sensitive elements are pooled spatially by the large dendrites of tangential cells (TCs). Two types of TC (the HSE cell and H2 cell) are shown. The HSE cell receives additional input from the H2 cell and from the H1 cell (not shown), and thus integrates visual-motion information from both eyes. Reconstructions of HSE- and H2 cells courtesy of K. Hausen.

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To understand the significance of the mechanisms involved in optic-flow processing, we should consider the behavioural context in which optic flow is generated. In the following, we summarize: (1) the sophisticated organization of retinotopic input in neurons processing optic flow; (2) the combination of optic-flow information from both eyes; (3) the accuracy with which motion information can be evaluated; and

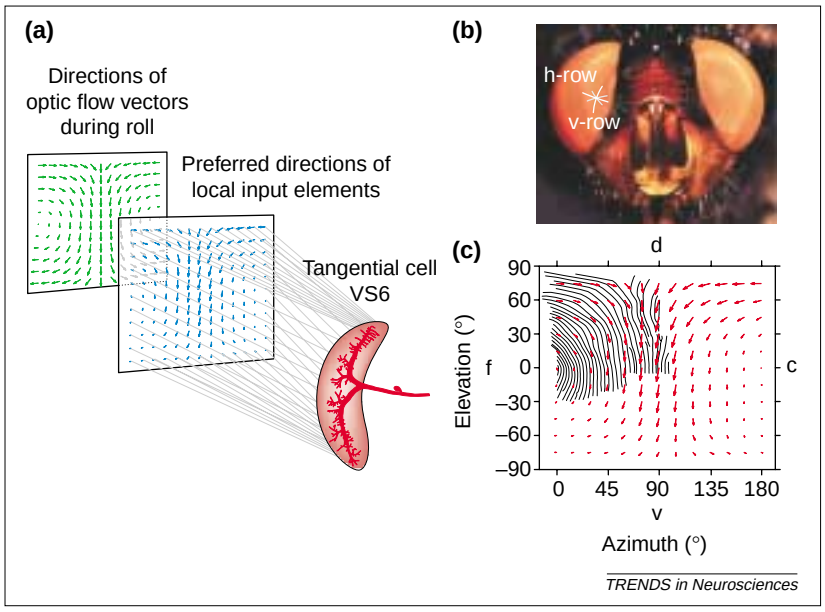

Fig. 1. Retinotopic input organization of tangential cells (TCs). (a) Self-motion generates panoramic optic flow over the eyes. The green arrows represent the local motion vectors on the eye when the animal rolls around its longitudinal body axis. The local response properties of a TC, the VS6 cell, are adapted to detect this particular self-rotation. It is assumed that with its large dendrite the cell integrates signals from local input elements whose preferred directions (blue arrows) correspond to the direction of local motion vectors in roll-induced optic flow. (b) Head of a female blowfly (*Calliphora vicina*). White lines over the right eye indicate the course of ommatidial rows in the hexagonal eye lattice. (Photograph courtesy of R. Hengstenberg.) (c) Organization of the receptive field of a VS6 cell. Orientation and length of arrows at different angular positions indicate the neuron's local preferred direction and motion sensitivity in the right visual hemisphere. 0° azimuth and 0° elevation corresponds to the point directly in front of the animal. f, c, d, and v refer to the frontal, caudal, dorsal and ventral aspects of the visual field. Black lines in the upper-left quadrant indicate the course of ommatidial rows, which are orientated vertically in the equatorial region of the eye (v-row). The direction of visual motion is thought to be analysed mainly by interactions between ommatidia along the rows in the hexagonal eye lattice (c.f. orientation of rows and arrows). In the dorso–frontal eye region the course of the v-rows strongly shifts towards a horizontal orientation. This change in orientation is reflected by the change in local preferred directions of VS6 cells in corresponding regions of its receptive field. Experimental data from Refs [29,32].

(4) the neuronal performance under stimulus conditions that occur during active locomotion.

Exploiting global features of optic flow by spatial pooling of retinotopic inputs

The motion vectors describing the local image displacements on the retina are not constant across the visual field, but change in a characteristic way depending on self-motion (see Box 1). Flies can exploit the global features of optic flow to gain neuronal representations of self-motion [12,27]. This is accomplished by the organization of the spatial input of the tangential cells (TCs, see Box 1). The large dendritic trees of TCs pool the outputs of many retinotopically organized small-field elements, which are thought to estimate the direction of local retinal-image shifts [11,28]. The preferred directions of the small-field elements that synapse onto a given TC appear to coincide with the directions of the velocity vectors characterizing the optic flow induced during particular types of self-motion (Fig. 1a) [27,29,30]. The sophisticated global patterns of preferred directions do not depend on visual experience and thus represent phylogenetic rather than developmental adaptations to optic-flow analysis [31].

The computation of self-motion based on optic flow is facilitated by the geometry of the compound eye lattice (Fig. 1b). The orientations of ommatidial rows along which directional motion is thought to be computed coincide with the local preferred directions of particular TCs, and thus with the direction of local velocity vectors that occur during locomotion, for instance, during forward translation or rotation around the animal's longitudinal body axis (Fig. 1c) [12,32,33]. Matching the geometrical properties of the compound eye to the global structure of frequently encountered optic flow allows the sophisticated input organization of some TCs to be established by interactions along the anatomical rows of the compound eye in what is a rather simple wiring scheme. Hence the geometry of the fly compound eye appears to be a phylogenetic adaptation to parsimonious processing of optic flow. Similarly, the design of crab eyes is adapted to life in different habitats [34] and the sensitivity distribution of photoreceptors of bees and ants depends on the celestial pattern of polarized light [35]. Moreover, locomotion in primates is likely to be a phyologenetic determinant of the topography of the visual system [36]. These examples indicate that visual systems make use of predictable sensory input to find low-level computational solutions to seemingly high-level tasks.

Combining information on optic flow from both eyes

Integration of motion signals from one eye is often not sufficient to yield a high specificity of TCs with respect to particular types of self-motion, such as rotation or translation. By combining motion information from both eyes (Box 1) specificity may be greatly enhanced. This is accomplished by TCs that convey motion information gathered within the visual field of one eye to the contralateral side of the brain where they interact with other TCs [12,13,30,37–39]. Unless the intervening synapse is carefully adjusted to the presynaptic activity levels that occur during sensory stimulation, synaptic transmission may distort the information being transmitted. This hazard is particularly daunting because signal transfer across synapses is inherently noisy and, in many systems, is nonlinear (reviewed in Refs [40,41]).

Combined electrophysiological and optical-imaging experiments (Figs 2a,b) reveal that, despite these potential nonlinearities, the entire range of depolarization levels that can be elicited by motion in the 'preferred direction' in the presynaptic terminal of a TC is transformed approximately linearly into the spike rate of the postsynaptic TC. The relationships between presynaptic potential and presynaptic Ca^{2+} concentration (the latter representing a second messenger involved in transmitter release) and between presynaptic Ca^{2+} concentration and postsynaptic spike rate are also linear (Fig. 2c). Motion in the antipreferred direction hyperpolarizes the

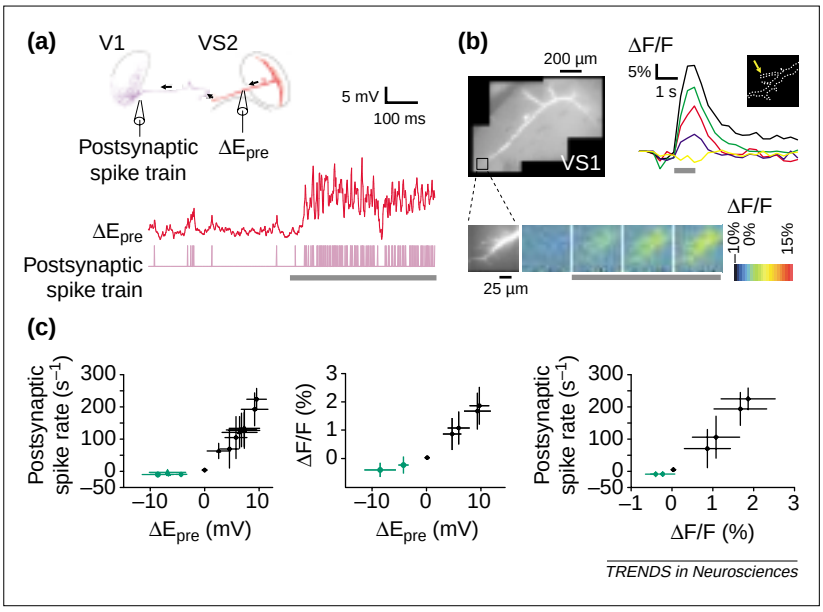

Fig. 2. Transmission of optic flow information between a pair of tangential cells (TCs). (a) The V1 TC receives input from VS (vertical system) TCs and transmits this motion information to the contralateral visual system, where it forms an extended output arborization. Presynaptic membrane potential changes (ΔE_{pre}) and postsynaptic spike trains (occurrence of a spike indicated by a vertical line) are recorded simultaneously *in vivo*. Visual motion in the preferred direction (grey horizontal bar) leads to depolarization of the presynaptic cell and to an increase in postsynaptic spike rate. (b) Presynaptic Ca^{2+} accumulation in a VS cell filled with a Ca^{2+}-sensitive fluorescent dye (raw fluorescence images of the entire cell and of the presynaptic region, left diagrams) during presentation of preferred direction motion (grey horizontal bar). Warm colours in the colour-coded images correspond to increases in Ca^{2+} concentration (measured as relative change in fluorescence: ΔF/F). The time course of the change in presynaptic Ca^{2+} concentration is plotted for variable stimulus strengths (coloured lines, upper right diagram). The inset in the upper right diagram shows the outline of the terminal region (dotted line) as seen on the raw fluorescence image and the region of the presynaptic terminal over which the fluorescence change was spatially integrated (white area indicated by yellow arrow). (c) Linearity of the transfer of preferred direction motion. Left: Postsynaptic spike rate (relative to resting activity) is plotted versus the presynaptic membrane potential change (ΔE_{pre}) for visual stimuli of variable strengths, moving either in the preferred direction (black symbols) or in the null direction (green symbols). The gain of signal transfer is approximately constant for the entire range of visually induced excitations, resulting in a linear relationship between presynaptic potential and postsynaptic spike rate upon motion in the preferred direction. A rectification is prominent for motion in the null direction. Linear dependencies for preferred direction motion are also present in the relationship between changes in presynaptic Ca^{2+} and in presynaptic membrane potential (middle) and in that between postsynaptic spike rate and changes in presynaptic Ca^{2+} (right). Electrophysiological and optical recording data reproduced from Ref. [42], cell reconstructions shown in (a) reproduced from Refs [13,29].

presynaptic neuron, whereas both the presynaptic Ca^{2+} concentration and the postsynaptic spike rate decrease only slightly below their resting levels. Thus, apart from this rectification, motion information is transmitted largely undistorted to the contralateral visual system [42] with a functional consequence that the synaptic transfer does not affect the dependence of the motion signals on the stimulus parameters, such as the velocity of motion.

Accuracy of encoding of optic flow information

There are constraints to coding of stimuli imposed by noise- and spike generation in any system. Noise leads to variable neuronal responses to repeated presentation of the same stimulus (Fig. 3a). Although the variance in spike count across trials of fly TCs is small compared to motion-sensitive neurons in the primate cortex [43,45], variability in the neuronal response constrains the precision with which stimulus events can be encoded by the timing of spikes and, thus, the accuracy with which time-varying optic-flow characteristics of behavioural situations can be conveyed.

Analysis of spike trains shows that the precision of spike timing depends on stimulus dynamics. Spike generation *per se* does not limit the accuracy of representing motion information, because spikes time-lock to rapid fluctuations in membrane potential with a millisecond precision [46–48]. As a consequence, spikes are time-locked precisely to a stimulus only if the stimulus-induced changes in membrane potential are sufficiently fast and large, relative to membrane-potential noise. In contrast, slow stimulus-induced fluctuations in membrane potential mainly affect the spike rate and normally do not cause precise time-locking of spikes; the exact timing of spikes is then determined by the high-frequency components of the membrane potential noise (Fig. 3b) [49]. Because computations that underlie direction selectivity inevitably require time constants of some tens of milliseconds [50], they attenuate the neural responses to high-frequency velocity fluctuations (Fig. 3c) [51,52]. Hence, TC depolarizations are sufficiently pronounced to elicit spikes with a millisecond precision only when the velocity changes are very rapid and large [17,18,53]. Otherwise, the exact timing of spikes is determined mostly by membrane-potential noise and visual motion is represented by the spike rate.

Key evidence for these conclusions is the finding that spikes in pairs of TCs with largely overlapping retinotopic input tend to be synchronized with a millisecond precision. This implies that both TCs share high-frequency signals originating from their common input. As, on average, these TCs are time-locked to velocity fluctuations with much less accuracy, it is suggested that the synchronization is attributable to high-frequency noise in their common input and not to the stimulus (Fig. 3d) [49,52]. Although to what extent rapid- and slow velocity changes, and thus the exact timing of spikes, are functionally significant is still debated [17,18], it is generally agreed that this issue can only be resolved by taking into account the dynamics of retinal-image displacements in different behavioural contexts.

Evaluation of behaviourally generated optic flow

The dynamics of optic flow are largely determined by the dynamics of the animal's self-motion. The direction of self-motion may change rapidly, such as during saccadic turns during flight [54,55] or an order of magnitude more slowly, such as during walking [19]. Because it is not possible currently to record from neurons in freely moving flies, indirect approaches have been used to determine the responses of TCs to behaviourally generated optic flow. Recordings can be made from the brains of flies that are oscillated with dynamics that mimic the rotational self-motion component experienced in free flight [20]. In another approach, the optic flow

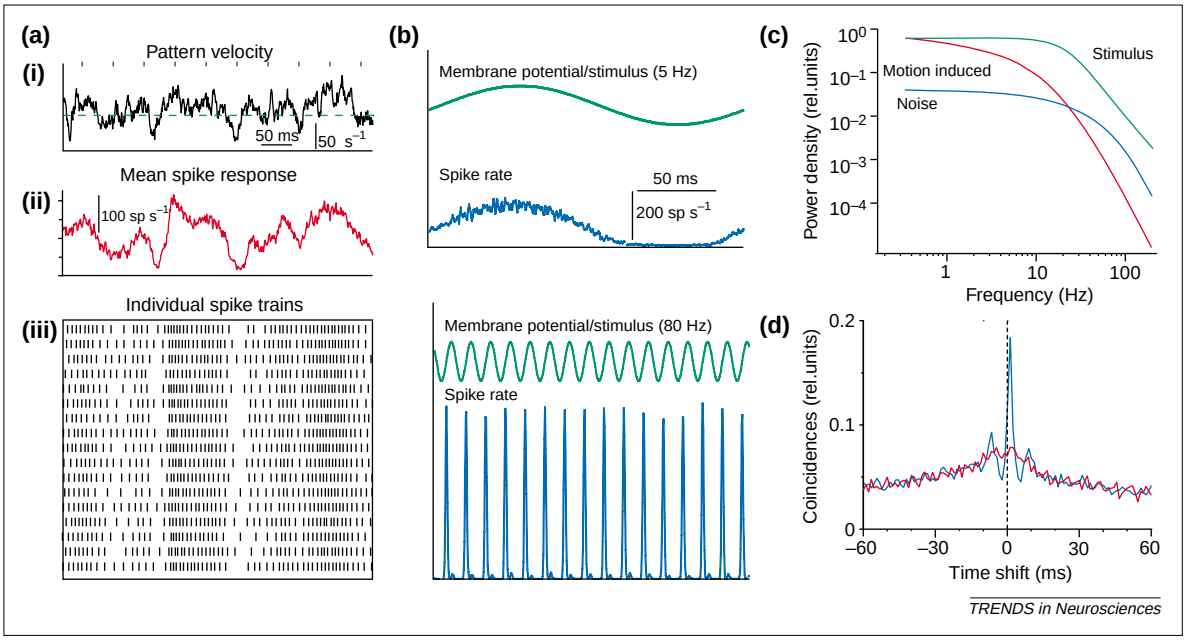

Fig. 3. Variability of neural responses and the accuracy with which optic-flow information is signalled. (a) Variability of spike activity of a tangential cell (TC), the H1 cell. Velocity profile of the motion stimulus. (i) Velocities above the dashed line denote motion in the preferred direction of the cell, velocities below the dashed line signal motion in the antipreferred direction. (ii) Spike rate of the H1 cell as a function of time. The response follows the overall time course of pattern velocity. (iii) Individual responses to repeated presentation of the same motion trace. Vertical lines denote spike occurrence. Although the overall pattern of neuronal activity is similar from trial to trial, there is variability in the temporal fine structure across trials (for details see Refs [44,52]). (b) Time-locking of spikes to sinusoidal stimulus-induced fluctuations in membrane potential (5 Hz or 80 Hz, green traces) in a model cell. The model is adjusted to fit the responses of a fly TC to motion stimuli. Noise is added to the stimulus-induced component of the membrane potential. The noise differs from presentation to presentation. Spike frequency histograms (blue traces) illustrate that fast stimulus-induced membrane potential fluctuations are needed to trigger spikes with a high temporal precision. Slow stimulus-induced fluctuations lead to spike activity with a rate approximately proportional to the membrane potential (for details see Ref. [49]). (c) Dynamic properties of membrane potential fluctuations in a fly TC (the HSE cell) elicited by band-limited white-noise velocity fluctuations; power spectra of the motion stimulus (green), the motion-induced response component (red) and the stochastic membrane potential fluctuations (blue). The motion-induced-response component was determined by averaging many individual response traces, thereby attenuating stochastic membrane-potential fluctuations. It contains most power below 20 Hz, although the stimulus contained higher frequencies. In the low-frequency range, the motion-induced-response component is larger than the stochastic-response component. At higher frequencies this relationship reverses (for details see Ref. [52]). (d) Cross-correlogram of the responses of two TCs (H1 and H2) with common synaptic input to fluctuations in the velocity of band-limited white noise. Either synchronously recorded responses were used (blue trace) or responses that were not recorded synchronously but obtained from repetitive presentation with the same motion stimulus (red trace). Although TCs can generate spikes very precisely (blue trace), most spikes time-lock to dynamic-motion stimulation on a much coarser timescale (red trace) (for details see Ref. [52]).

experienced by moving flies was reconstructed and replayed to a fixed animal during nerve-cell recordings. This approach has been employed for various behavioural situations during tethered flight in a flight simulator [56,57] and during unrestrained walking in a three-dimensional environment [19,58]. The results indicate that information obtained from optic flow about the layout of the environment [57] or the animal's self-motion [19] is much less ambiguous than concluded from earlier studies using conventional stimuli, such as moving gratings.

This conclusion is exemplified in Fig. 4 by the performance of a TC (the HSE cell) whose input connections suggest a role in signalling turns of the animal around its vertical axis [12,38,39]. Despite this input organization the HSE cell also responds to translation and to changes in the texture of conventional stimuli [12,13,19]. Analyses using conventional stimuli indicate that the cell's response is ambiguous. However, when challenged with optic flow generated during walking, most of these ambiguities disappear and the cell provides information about the animal's turning direction largely independent of the translational optic-flow component and the layout of the environment (Fig. 4b) [19]. Model simulations indicate that the computations underlying optic-flow processing are well matched to optic flow experienced in behavioural situations [59]. This is because: (1) natural stimuli are characterized by a wide range of spatial frequencies, in contrast to conventional grating patterns (see also Ref. [60]); (2) the local-movement inputs of the TCs operate in a range where velocity is no longer represented linearly; and (3) the nonlinear spatial-integration characteristics of TCs (see Box 1) make their responses largely independent of texture density.

The characteristics of motion computation may differ in insect species that have different visually guided orientation behaviours and thus may be matched to the spatio–temporal properties of their different retinal inputs [61,62]. Moreover, the properties of fly TCs change as a result of stimulus history [63–69]. Although the functional significance of these adaptational processes is debated, they may

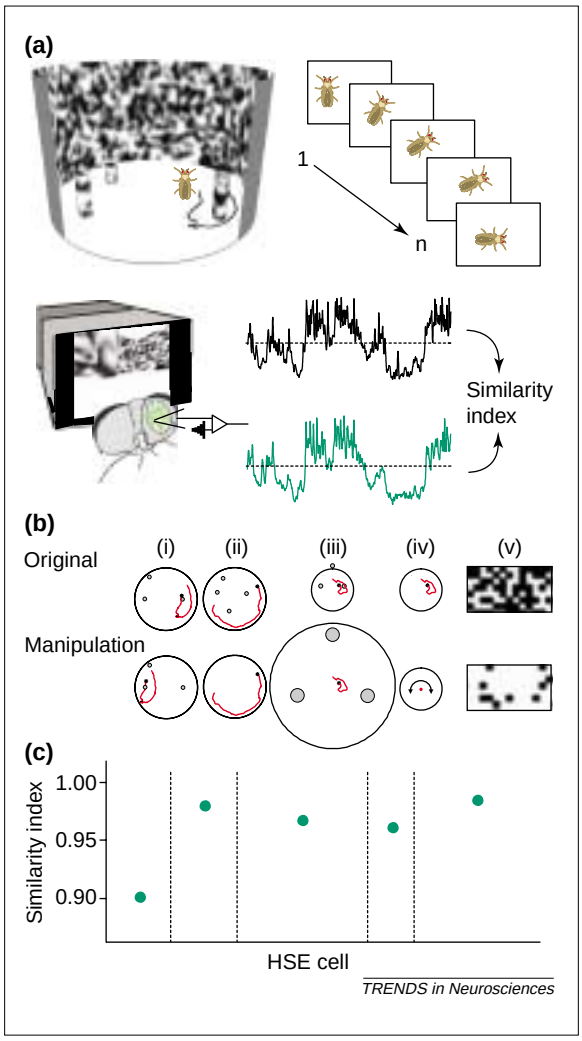

Fig. 4. Responses of a tangential cell (TC) to naturalistic optic flow. (a) The experimental approach. Flies walking freely in an arena are video-recorded and the position and orientation of the fly are determined in each digitized frame. The trajectory data are used to control the path of a simulated camera in a virtual 3D-environment that mimics the arena. The size of the field-of-view of the camera is adjusted to approximate the receptive field of the TC recorded in subsequent electrophysiological experiments. During an electrophysiological recording, the TC is visually stimulated by the sequence of reconstructed images. Recording traces are shown in response to simulated optic-flow sequences seen by the walking fly (black) and as seen on the same track in a manipulated virtual environment (green) (see below). (b) Original behavioural situation (upper diagrams) and manipulations (lower diagrams). The original walking trajectories are shown in red. The circles illustrate the arena as seen from above, with the position and the diameter of objects indicated by dots: (i) the original track was displaced to the opposite side of the textured arena; (ii) objects that were present during the original walk were removed in the playback; (iii) the textured arena was enlarged by a factor of 3.0, thereby reducing the translational optic-flow component; (iv) the translational component of the original walking track was eliminated in the playback so that the stimulus corresponded to a rotation around the arena centre; (v) the original 50% black and white arena texture was replaced with a texture having 12% black elements in the playback. (c) Similarity of responses of the HSE cell to the original and manipulated optic flow stimuli as indicated in (b). A similarity index of one indicates that the time courses of responses to two different stimuli are as similar as the time courses of responses to the same stimulus. All tested manipulations of the environment (and thus of the visual input to a fly walking spontaneously in its environment) have little effect on the time course of the HSE-cell response (for details see Refs [19,59]).

well play a role in adjusting the operating range of the mechanisms underlying optic-flow processing to different behavioural contexts.

Conclusions and perspectives

Neurophysiological investigations applying visual stimuli specifically designed for systems analysis are essential to unravel the computations that underlie the processing of visual information. However, on their own, these approaches are not sufficient to assess how neuronal circuits represent complex natural input. Thus, systems analysis should be complemented by studying neuronal performance under behaviourally relevant conditions. To date, most studies employing stimuli generated by the moving fly have been performed indoors. However, recently, responses of a fly TC were concluded to cover a larger dynamic range and to be more reliable in bright sunlight than under dimmer laboratory conditions [20]. Although these conclusions are not accepted unanimously, and to what extent brightness affects neuronal performance is still debated [70], it is becoming increasingly clear that the visual system of the fly is exquisitely adapted to process the complex optic flow elicited in behavioural situations. Adaptations to natural operating conditions reveal themselves in the structural properties of the compound eye, the specific features of the mechanisms underlying motion computation, the spatial input organization of the TCs and the signal transfer between them. Evolution has shaped the fly nervous system to solve efficiently and parsimoniously those computational tasks that are relevant to the survival of the species. In this way animals with even tiny brains are often capable of performing extraordinarily well in specific behavioural contexts.

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