Giordano Ramos-Traslosheros, Miriam Henning and Marion Silies*

Motion detection: cells, circuits and algorithms

https://doi.org/10.1515/nf-2017-A028

Abstract: Many animals use visual motion cues to inform different behaviors. The basis for motion detection is the comparison of light signals over space and time. How a nervous system performs such spatiotemporal correlations has long been considered a paradigmatic neural computation. Here, we will first describe classical models of motion detection and introduce core motion detecting circuits in *Drosophila*. Direct measurements of the response properties of the first direction-selective cells in the *Drosophila* visual system have revealed new insights about the implementation of motion detection algorithms. Recent data suggest a combination of two mechanisms, a nonlinear enhancement of signals moving into the preferred direction, as well as a suppression of signals moving into the opposite direction. These findings as well as a functional analysis of the circuit components have shown that the microcircuits that process elementary motion are more complex than anticipated. Building on this, we have the opportunity to understand detailed properties of elementary, yet intricate microcircuits.

Keywords: Drosophila; motion detection; neurogenetics; neuronal circuits; visual system

Introduction

The environment we live in is ever changing, things are in constant motion. Visual motion originates from moving objects, but also when an entire visual scene moves past our eyes during self-motion. The perception of visual motion is an important sensory function for many animals. Motion could indicate an approaching threat or predator, a wandering pray, or a potential mating partner. In a still surrounding, the motion that emerges as a consequence of self-motion allows animals to safely navigate the environment. These examples also illustrate how motion can be local, when an insect flies past the eye; or global, when the full visual space is moving during navigation. Global and local motion are related in the sense that global motion can be decomposed into the motion of the local features of the visual scene. Thus, visual systems detect local motion in order to perceive both local and global motion. The smallest perceivable motion would be between two points in space at the limit of the resolution of a visual system. The unit that detects these smallest movements is called an elementary motion detector (EMD). At this scale, the visual system has to extract luminance changes over both space and time to produce a direction-selective (DS) signal, which is a hallmark of elementary motion detection. Consequently, each EMD has a direction of motion that it is most sensitive to, its so-called preferred direction (PD).

How are visual systems able to detect movement at such a fine scale? Somewhere in the nervous system, an EMD must be implemented in a way that the output neurons are direction-selective and therefore able to detect local motion. Identifying the biological substrate of the EMDs and the algorithm behind computing the direction of motion has therefore been considered an interesting topic that can shed light onto an important function of nervous systems. Since motion vision is behaviorally salient for many visual animals, it has been studied in species as diverse as monkeys, cats, mice, but also in various fly species including the fruit fly *Drosophila*, which we will mostly focus on in this review.

Classical descriptions of motion detection algorithms

How biological systems extract motion signals has received extensive attention since the 1950s (reviewed in Borst and Euler, 2011). The first popular algorithmic model that could explain direction-selective responses emerged from analyzing behavioral responses to moving stimuli, the so-called optomotor behavior of the *Chlorophanus* beetle (Hassenstein and Reichardt, 1956). This model laid the foundation for subsequent studies of motion detection

*Corresponding author: **Marion Silies,** European Neuroscience Institute Göttingen (ENI), University Medical Center Göttingen, Grisebachstr. 5, 37077 Göttingen, Germany, Mail: m.silies@eni-g.de, Web: www.silieslab.com
Giordano Ramos-Traslosheros, European Neuroscience Institute Göttingen (ENI), University Medical Center Göttingen, Grisebachstr. 5, 37077 Göttingen, Germany; International Max Planck Research School Neuroscience, University of Göttingen, Göttingen, Germany, Mail: l.ramos@eni-g.de
Miriam Henning, European Neuroscience Institute Göttingen (ENI), University Medical Center Göttingen, Grisebachstr. 5, 37077 Göttingen, Germany, Mail: m.henning@eni-g.de

in other species that refined properties of the model and came to be known as the Hassenstein-Reichardt Correlator (HRC). This model proposes the comparison of two signals coming from two locally restricted points in visual space, accounting for the offset in space inherent to motion signals. And, to account for the offset in time, one signal is temporally delayed with respect to the other. Then, the two (delayed and non-delayed) signals are combined, or correlated, in a nonlinear fashion at the output stage of the model (Figure 1A).

For an EMD selective for left-to-right motion, the signal arising from the left point in space will be processed with a delay relative to the signal at the right point (Figure 1A). The delay ensures that, for an object moving in the preferred direction (PD, left-to-right), both signals will temporally overlap at the output stage of the EMD. There, a nonlinear amplification of the overlapping signals generates a strong motion signal. Conversely, when the movement is in the non-preferred or null direction (ND, right-to-left), the delay will cause the signals to arrive at different times to the correlation stage so there is no signal integration, i.e., no motion signaling (Figure 1A). In other words, the HRC model predicts how a direction-selective signal can be generated from two input signals (reviewed in Borst and Euler, 2011; Silies et al., 2014).

The HRC relies on a nonlinear amplification of input signals, using feedforward excitation. Another model explaining direction-selectivity that emerged in the 1960s instead relied on signal suppression, implying inhibitory neuronal processes, in total contrast to the HRC. The Barlow-Levick model (BLM) was developed to explain the responses of direction-selective neurons in the vertebrate retina (Barlow and Levick, 1965). Like the HRC, the BLM also relies on a comparison of signals from two points in space temporally delayed with respect to each other, and nonlinearly combined. However, here they are combined via an AND-NOT operation at the output stage, such that there is only an output signal when there is no signal coming from the delayed input, which would cancel the previous signal (Figure 1A). Taking our previous example of an EMD with a left-to-right motion preference, the corresponding BLM will respond to motion as follows: for movement in the null direction, a signal will emerge first from the delayed component and then temporally overlap with the second signal at the output stage. There, the AND-NOT logical operation will result in a cancellation of the second signal, indicating nulling inhibition. In the EMD's preferred direction, the non-delayed signal will arrive first at the output stage, thus escaping the nulling inhibition from the slow signal, which will arrive later. The outcome of this operation is again a direction-selective signal.

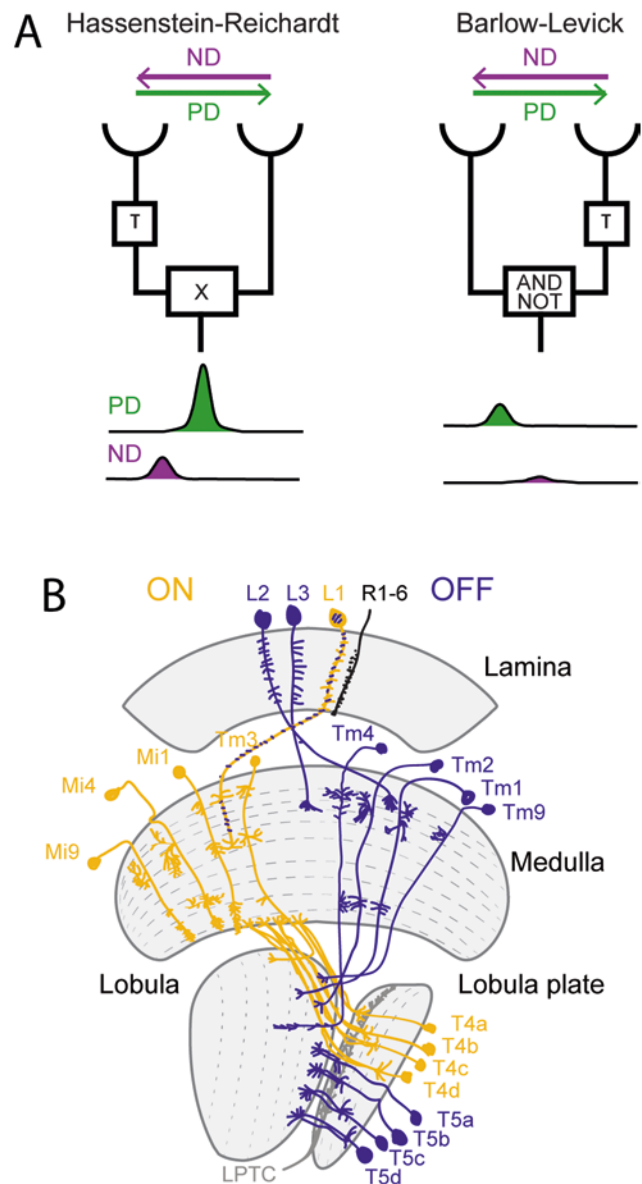

Fig. 1: A. Two models of motion detection. On the left, the Hassenstein Reichardt Correlator (HRC) correlated inputs from two adjacent points in space after one signal has been temporally delayed (τ). The outcome is a direction selective signal, in which signals moving in the preferred direction (PD) are nonlinearly amplified. On the right, the Barlow Levick Model (BLM) compares two signals in space through a logical AND NOT operation, after delaying one signal. The outcome is a direction selective signal, in which signals moving in the null direction (ND) are suppressed. **B.** Schematic of the fly visual system and core motion detecting circuits. Shown are neurons of the ON (yellow) and OFF (blue) pathways for which either behavioral roles have been shown, or a functional requirement for direction-selective responses in T4/T5 neurons. For details, see text.

In insects, the HRC originally gained widespread acceptance by successful predictions of behavioral and neural responses. One example is that the HRC response to a

moving grating is not tuned to the speed of the pattern but to the temporal frequency, which is the rate of contrast change at a particular location. In different fly species, responses were shown to be similar for gratings of different spacing as long as the temporal frequency was maintained (Buchner, 1976; Eckert, 1973; Götz, 1964; Reichardt, 1987). The HRC thus has an optimal speed that depends on the spatial wavelength in a linear way. This hypothesis was further supported by electrophysiological recordings in the lobula plate tangential cells (LPTCs), wide field neurons that integrate inputs from many individual EMDs along their dendritic arbors, in blow flies (Egelhaaf and Reichardt, 1987; Hausen, 1982; Hengstenberg et al., 1982) and the fruit fly (Joesch et al., 2008; Schnell et al., 2010).

The above described features of motion detection (among others) were experimentally confirmed in diverse species including flies, cats, and humans, which led to a wide popularity of the HRC to explain motion responses (Borst and Egelhaaf, 1989). In humans, another model – the motion energy model – is generally favored (Adelson and Bergen, 1985), but this models can be made algorithmically equivalent to the HRC to describe motion perception (van Santen and Sperling, 1985). Extensions of the HRC model to account for visual behaviors of *Anolis* lizards is another recent application in yet another species (Fleishman and Pallus, 2010).

In contrast, the model that has long been favored to describe motion responses in the vertebrate retina was the BLM. Barlow and Levick (1965) originally attributed direction-selective responses of retinal ganglion cells to null direction inhibition. This was strongly supported by the loss of direction-selective responses in retinal ganglion cells upon pharmacological block of GABAergic, inhibitory signaling (Caldwell and Daw, 1978; Wyatt and Day, 1976). Further experiments localized the source of GABAergic inhibition to starburst amacrine cells (Amthor et al., 2002; Yoshida et al., 2001).

A vast amount of literature led to the dominance of the HRC to explain motion detection in insects, and the BLM to explain motion responses in the vertebrate retina. Interestingly, recent work showed that a combination of the two algorithms is in fact used in both systems to establish direction-selectivity (Fisher et al., 2015b; Haag et al., 2016; Leong et al., 2016). In the following, we are first going to describe the identification of motion detection circuits in the fruit fly *Drosophila*. With the knowledge of these circuit elements, we will discuss an experimental handle to directly test the implementation of distinct algorithms at the output stage of the EMD. Finally, the results of such experiments, and their implications for the mechanistic implementation of the EMD will be highlighted in the last chapter of this review.

Mapping motion detecting circuits

Although algorithmic models of motion detection have existed for decades, the circuit implementation of motion computation remained elusive. This changed dramatically with the development of genetic tools to study circuit function in *Drosophila*. These could be applied well in a context where the anatomy of many neurons of the visual system was described with exquisite detail (Fischbach and Dittrich, 1989), and down to individual synapses (Meinertzhagen and O'Neil, 1991; Takemura et al., 2008; 2017).

The visual system of Drosophila melanogaster. The visual system of the fly is organized into the retina and three optic ganglia: the lamina, medulla and lobula complex, the latter being divided into lobula and lobula plate (Figure 1B). The retina is organized in an array of 800 parallel units, the ommatidia. Each ommatidium houses eight photoreceptors out of which the six outer photoreceptors (R1-R6) express the broadband-spectrum rhodopsin Rh1 that is required for motion detection (Heisenberg and Buchner, 1977). All R1-R6 cells that see the same point in space project onto the same targets in the lamina, most notably the L1-L3 neurons. Neighboring points in visual space are encoded by neighboring columns in the lamina, thus creating a retinotopic image of the visual input. This parallel columnar arrangement is maintained in the next ganglion, the medulla, were more than 60 different cell types pass on information to the lobula and the lobula plate.

Genetic strategies to map visual circuits. Major advances in visual circuit analysis came with the possibility to mark or manipulate neurons in the fly brain with great specificity. This included the development of genetic tools to manipulate or measure the activity of neurons on the one hand, and the ability to express these tools very specifically in the brain on the other hand. In *Drosophila*, so-called driver lines exist that control expression in different subsets of neurons. Over the last years, several thousands of these driver lines were developed that can be used to express different genetic tools in any pattern of interest (Gohl et al., 2011; Jenett et al., 2012). The optimal level of specificity would be expression in a single cell type or even in an individual neuron, but expression patterns of individual genes, enhancers, or promotors are often broader than

that. Therefore, intersectional strategies were developed that refine expression patterns to the above-mentioned level of specificity (Gohl et al., 2011; Luan et al., 2006; Pfeiffer et al., 2010). It is now in principle possible to obtain specific genetic access to every single neuron or cell type in the fly brain, including the ~100 cell types of the fly visual system.

The genetic tools that can be expressed with this level of specificity include reporter and effector genes. Reporter genes, such as green fluorescent protein (GFP), are for example commonly used to label all cells within a driver line to describe its expression pattern, or in an individual cell to describe the arborization pattern of a neuron's dendritic tree. Other reporter genes are fluorescent molecules that change their fluorescence with the state of neuronal activity. Such molecules include genetically encoded calcium indicators (e.g. GCaMP6, Chen et al., 2014), synaptopHluorins (Miesenböck et al., 1998), or genetically encoded voltage sensors (e.g. ASAP2, Yang et al., 2016), and allow different measures of neuronal activity, including intracellular calcium signals, vesicle release, or membrane voltage, respectively. In addition to labeling neurons with reporter genes, one can manipulate their activity using effector genes. These are genes that can inactivate or ectopically activate neurons. Among the most popular ones are genetic tools to block neuronal activity by hyperpolarizing a neuron, or by preventing vesicle recycling (Simpson, 2009), or tools to ectopically activate neurons using optogenetics, including Channelrhodopsin or Chrimson (Klapoetke et al., 2014; Mattis et al., 2011). In analogy to molecular genetic studies, this allows performing loss and gain of function experiments at the neuronal or circuit level, and ask which neurons are necessary or sufficient for a specific task.

Elementary motion detecting circuits. With increasingly specific genetic tools at hand, core motion detecting circuits could be identified. In particular, experiments in which behavioral responses to motion cues were measured while the outputs of individual cell types were genetically blocked, led to the identification of neurons that are required for motion detection. It was thus shown that there are two distinct pathways for motion detection, the ON and the OFF pathways, that guide responses to moving dark (OFF) or bright (ON) edges, respectively. These pathways split downstream of R1-R6 photoreceptors, where the first order lamina interneuron L1 is the major input to the ON pathway, whereas its L2 and L3 counterparts provide inputs to the OFF pathway (Clark et al., 2011; Joesch et al., 2010; Silies et al., 2013) (Figure 1B). Blocking the synaptic outputs of either L1 and L2, or L1 and L3 abolished all behavioral responses to motion cues in flies, arguing that these neurons are all required for motion detection (Clark et al., 2011; Rister et al., 2007; Silies et al., 2013). Two synapses further down in the lobula complex, the first direction-selective neurons can be found: T4 neurons respond to moving ON signals, and T5 neurons respond to moving OFF signals (Figure 1B). Both T4 and T5 neurons come in four different subtypes, of which each prefers motion in one of the four cardinal directions: upward, downward, front-to-back and back-to-front (Maisak et al., 2013). Again, genetically blocking the outputs of T4 and T5 neurons abolished behavioral responses to visual motion stimuli, placing these neurons at the output stage of the EMDs of both ON and OFF pathways (Maisak et al., 2013; Strother et al., 2017). Such data argued that a more or less simple one-to-one relationship existed between a visual system cell type and its computational role. If for example L1 neurons provide input to an ON edge detector, and T4 neurons are the direction-selective output neurons of such a detector, all that is in principle needed are two types of interneurons with different temporal filtering properties that connect inputs from two neighboring L1 neurons to the dendrites of the direction-selective T4 cells. This configuration could implement the computation as outlined above in the description of EMD models. Such interneuron candidates were suggested based on reconstructions of electron microscopic data, by identifying the neurons that most strongly connect L1 to T4 neurons as judged by synapse counts (Takemura et al., 2017) (Figure 1B). The two neurons that most strongly connect the L1 inputs to direction-selective T4 outputs were for example the neurons Mi1 and Tm3. Electrophysiological recordings identified differences in their temporal filtering properties, especially in the time to peak of the linear filter, which is shorter in Tm3 (Behnia et al., 2014).

Distributed coding in visual circuits. Both in the ON and the OFF pathways, medulla interneurons that connect lamina inputs to direction-selective T4 and T5 outputs have been described (Figure 1B). While core motion detecting circuits have thus been proposed (Ammer et al., 2015; Behnia et al., 2014; Fisher et al., 2015a; Serbe et al., 2016; Strother et al., 2017), behavioral phenotypes associated with the loss of, e.g., ON pathway interneuron function were surprisingly subtle (Ammer et al., 2015; Strother et al., 2017). Whereas genetic silencing of neural activity in T4 neurons lead to a loss of optomotor responses to ON edge motion, silencing either of the candidate medulla neurons of the ON pathway only reduced behavioral responses (e.g. for both Mi1 and Tm3). Still, blocking the outputs of these

neurons biased the behavioral responses to OFF edges and thus isolated a deficit in ON edge detection, when competing ON and OFF edges were used to probe behavioral function. Isolated behavioral deficits for specific temporal frequencies were found in other ON pathway interneuron candidates. The same story holds for the OFF pathway interneuron counterparts (Fisher et al., 2015a; Serbe et al., 2016). For example, blocking activity in OFF pathway interneuron Tm9 provides a strong preference for ON edges, when the two edge types are competing. At the same time, flies are able to respond to individual OFF edge motion (Fisher et al., 2015a). Phenotypes for other OFF pathway interneurons are even subtler, but can be enhanced by combinatorial silencing of more than one cell type (Serbe et al., 2016).

Together, these data suggest that, at least at this level of peripheral visual processing, a single cell type is not solely required for a specific task. Otherwise, taking out such a cell type would break the system. Instead, coding seems to be more distributed. There are different scenarios that could account for this lack of a phenotype. One possibility is that there are redundant circuit elements, and silencing one cell type alone can be covered up by the presence of other neurons. This would make the behaviorally very relevant motion computation robust to perturbations. Alternatively, we may have not identified all essential neurons so far. In addition to the interneurons that connect lamina neuron inputs (e.g. L1) to direction-selective outputs (e.g. T4) with the most number of synapses, many other neurons also receive inputs from the lamina inputs, or provide output synapses on the T4 or T5 dendrites. Moreover, the function of most of the more than 60 medulla neuron cell types is unknown. While synapse number is considered a strong indicator of functional relevance, there are examples that argue against this: the lamina input L3 receives much fewer synapses from photoreceptors than the L1 and L2 neurons (Rivera-Alba et al. 2011). One synapse further down, L3 synapses onto Tm9, with almost an order of magnitude fewer synapses than have been counted between L1 or L2 and its major downstream neurons (Takemura et al. 2013). Still, silencing Tm9 shows the most striking behavioral phenotype of all OFF pathway neurons tested (Fisher et al., 2015a; Serbe et al., 2016). Finally, interneurons with different temporal filtering properties have been identified in the ON and OFF pathways (Arenz et al., 2017; Behnia et al., 2014; Fisher et al., 2015a; Serbe et al., 2016; Strother et al., 2017; Yang et al., 2016) and might be important for motion vision at different speeds. Likely, a combination of these possibilities will be true.

In summary, core motion detection circuits have been proposed. While the identified cells and their physiological properties are sufficient to predict direction-selective responses in downstream neurons, the definite computational or behavioral roles that they actually implement are still subject to future studies.

Novel insights into motion detection algorithms

At the beginning of this review we described how work in insects led to a preference of the HRC model to describe motion detection, and identifying the underlying neurons was considered the “holy grail” of motion detection (Borst, 2014). In contrast, the BLM was long considered the predominant model to describe motion responses in the vertebrate retina. The identification of neurons of motion detecting circuits in general, and in particular of the T4 and T5 neurons as the first cells that exhibit direction-selectivity, has opened up the opportunity to study the mechanisms of motion detection directly at the output stages of the EMD. Recent work on the T4 and T5 cells has revealed surprising new insights on how motion information might actually be encoded in the fly visual system.

The axon terminals of both T4 and T5 arborize in the lobula plate and provide retinotopic input to the LPTCs. In the lobula plate, the axon terminals are organized in a layered fashion, in which T4 and T5 cells of a given directional preference (e.g. front-to-back motion) project into one layer (Figure 1B). The directional preferences of the four layers together cover the four cardinal directions of motion, making it easy to record from direction-selective cells of one subtype, using *in* vivo two photon calcium imaging (Maisak et al., 2013). At the level of the dendrites, measuring DS responses is not as straightforward. All four T4 subtypes project into the most proximal layer of the medulla, and all T5 subtypes project into the first layer of the lobula (Figure 1B). Nevertheless, elegant genetic experiments allowed to record from individual dendrites, and showed that direction-selectivity already emerges in the dendrites, arguing that this is where core computations are happening (Fisher et al., 2015b). T4 and T5 neurons were also found to be orientation tuned to static objects (Fisher et al., 2015b; Maisak et al., 2013) with an axis that is perpendicular to their preferred motion axis (Fisher et al., 2015b). So what are the algorithms implemented at the dendrites of T4 and T5?

Interestingly, a pharmacological block of GABAergic signaling in the fly visual system caused a loss of direction

as well as orientation selective signals in T4 and T5 cells (Fisher et al., 2015b). This is strikingly similar to results from the vertebrate retina and showed that GABAergic inhibition is crucial for DS responses in T4 and T5 cells of the fly as well.

Subsequent experiments directly mapped the spatiotemporal receptive fields of T4 and T5 cells using spatiotemporal ternary noise stimuli (Leong et al., 2016; Salazar-Gatzimas et al., 2016). These stimuli contained bars of randomly changing contrast that were just wide enough to cover the extent of the receptive field of an input neuron. Thus, they covered one point in space at the fly eye's resolution. The neuron's temporal response to each point in space was obtained using reverse correlation of a cell's change in calcium signal with the change of the contrast of each bar. These receptive fields of T4 and T5 contained an inhibitory and an excitatory subfield, which were tilted along a space-time axis (Figure 2A). The linear receptive field obtained by reverse correlation was qualitatively similar to the receptive field of a full model adding nonlinearities describing neuronal or calcium indicator properties (Leong et al., 2016). The tilt in space and time is consistent with an enhancement of signals moving into the preferred direction of the neuron, as predicted by the HRC. Interestingly, the spatiotemporal offset between the excitatory and inhibitory subfields predicts a suppression of motion in the null-direction by mutually canceling interactions (Figure 2A). Thus, these data suggest a combination of excitatory mechanisms as proposed by the HRC, and inhibitory mechanisms as proposed by the BLM (Leong et al., 2016).

The hypothesis that both HRC and BLM type models together account for motion responses in flies can be directly tested using so-called apparent motion stimuli. These stimuli utilize the fact that the perception of movement can be achieved by showing a temporal sequence of static images that are offset in space (as done in any television) (Figure 2B). If they are presented in fast succession, they are perceived as continuous motion due to the spatiotemporal limitations of visual processing. According to this logic, motion for the fly was mimicked by sequentially activating neighboring points in the visual field (Figure 2B) while recording T4 and T5 responses. To produce a motion response in such an apparent motion stimulus, two stimulation points should ideally hit two neighboring points in visual space in sequence, and with a time delay that matches the temporal delay of the EMD. If the time delay is too long, no motion response will be elicited upon stimulation of two adjacent points. Instead, one can use these isolated responses to build a linear (summed) prediction of the single stimulations to the apparent motion response (Figure 2C). If the two inputs were combined linearly for a fast sequence of stimulation, the predicted sum should fit the actual motion response of the neuron. Conveniently, the HRC or BLM type models make very different predictions about the outcome of the response to these apparent motion stimuli, due to the differences in their output nonlinearities. If an HRC was implemented, one would expect a nonlinear amplification of signals moving into the PD, whereas a BLM would predict a nonlinear suppression of signals moving into the neuron's ND (Figure 2C).

Two separate studies used these apparent motion stimuli to analyze T4 and T5 properties. First of all, (Fisher et al., 2015b) showed apparent motion stimuli mimicking a moving edge by first activating one point in space by displaying a stripe, followed by activation of the same point as well as a neighboring point in space. When calcium signals were measured in T4 and T5 neurons, a significant nonlinear amplification of responses to this apparent motion into the neuron's PD was found, suggesting an HRC like mechanism (Fisher et al., 2015b). The same study had demonstrated that GABAergic mechanisms are important for direction-selective T4 and T5 responses, prompting to look for null direction suppression as suggested by the BLM. However, only weak signs of null direction suppression could be found, that often did not differ from an adaptation control (Fisher et al., 2015b). Subsequently, an apparent moving spot stimulus, that sequentially activated single points adjacent in space, could confirm the results obtained by (Fisher et al., 2015b), and also identified signs of null direction suppression in DS neurons (Haag et al., 2016). A precise stimulation technique might be important to activate the inhibitory subunit of the receptive field and thus the component leading to null direction suppression. This inhibitory subfield would then correspond to the side of the cell's receptive field that the motion stimulus reaches first, if traveling in the null direction of the cell. The results obtained using apparent motion stimuli are thus consistent with the direct measurement of T4 and T5 properties described above. The spatial extent of the receptive fields furthermore suggested that the DS cells get inputs from more than two columns, which was confirmed by visual stimulation of more than two adjacent points in visual space (Haag et al., 2016; Leong et al., 2016; Salazar-Gatzimas et al., 2016). Together, a picture emerges in which a combination of preferred direction amplification as suggested by the HRC, and null direction suppression as proposed by the BLM is used to establish direction-selective responses in early visual processing of the fly.

As previously introduced, the BLM model was strongly favored to describe direction-selectivity in ganglion

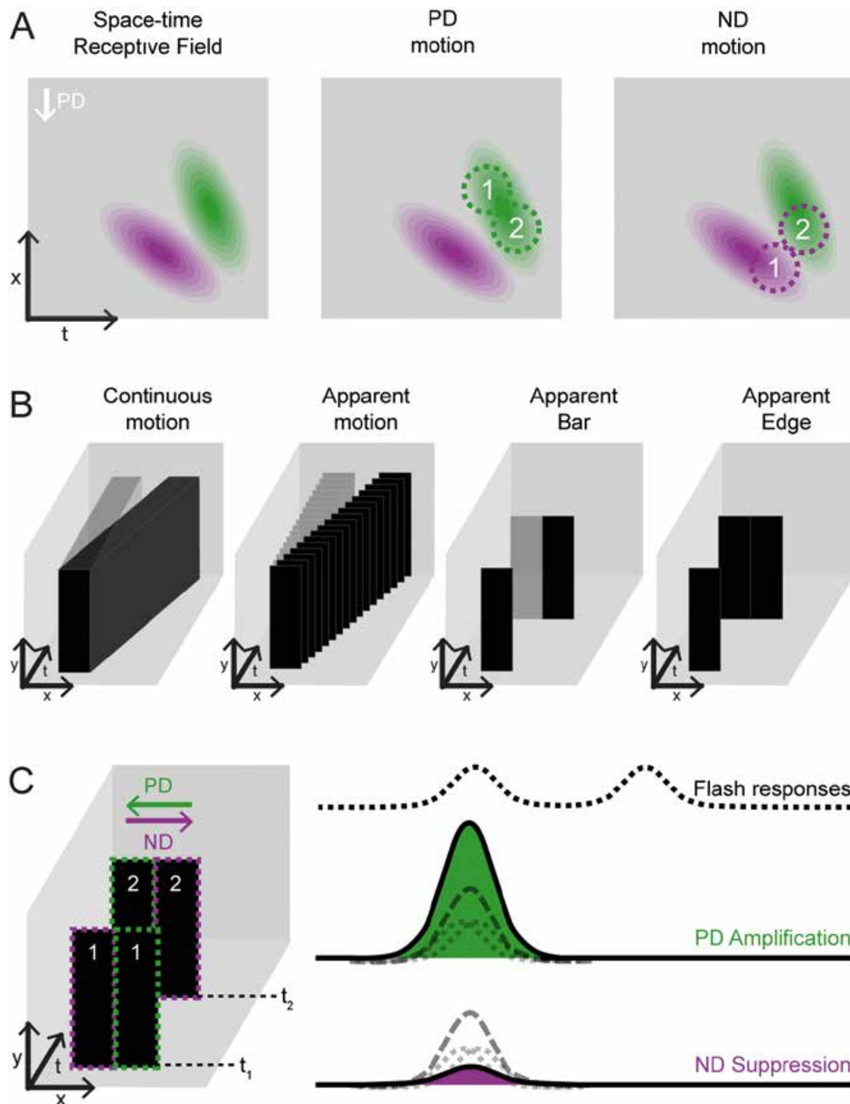

Fig. 2: A. Schematic drawing of a spatiotemporal receptive field of a direction-selective T4 or T5 neuron (after Leong et al. 2016). The receptive field contains excitatory (green) and inhibitory (purple) subfields, which are each tilted along the space-time axis. The preferred direction (PD) of this neuron is indicated. The middle panel shows the same receptive field, illustrating how motion in the preferred direction would sequentially activate the excitatory subfield. The right panels shows how motion in the null direction (ND) would sequentially hit the inhibitory and excitatory subfield, leading to suppression of signals moving in this direction. **B.** X-y-t plots illustrating how continuous motion can be decomposed into apparent motion stimuli. While the black boxes present motion to the right, the grey boxes illustrate a static object. The two rightmost panels illustrate apparent moving bar or edge stimuli that sequentially activate two neighboring points in space. **C.** An apparent moving bar stimulus can be moved in the PD (green) or ND (purple) of a cell. If the two time points are well separated in time, two individual flash responses are recorded (top trace). For short delays, these individual flash responses (dotted lines) can be shifted in time and summed to build a linear prediction (dashed line). If the response to a motion cue moving into the PD is nonlinearly amplified as shown in the middle panel (green, middle trace), this argues for a HRC type model. If the response to a motion cue moving into the ND in suppressed compared to the linear prediction (purple, bottom trace), this argues for the implementation of a BLM.

cells of the vertebrate retina. Presynaptic to these cells are the starburst amacrine cells, which are not only required for DS responses in ganglion cells, but whose dendrites are themselves direction-selective (Briggman et al., 2011; Euler et al., 2002). Interestingly, recent work on direction-selectivity in the dendrites of starburst amacrine cells also suggested that an HRC like mechanism is implemented at the bipolar cell to starburst amacrine cell synapse (Fransen and Borghuis, 2017; Kim et al., 2014) . This shows how the computational mechanisms used in verte-

brates and insects are much more similar than previously thought (see also Borst and Helmstaedter, 2015; Mauss et al., 2017).

Summary and Outlook

The circuits and mechanisms that extract visual motion cues have gotten a lot of attention, because the topic serves as a model to understand how basic computations are implemented in neuronal networks. Notably, the past years have not only seen fast progress in the identification of core motion detecting circuits in *Drosophila*, but have also revisited the algorithmic implementation of motion computation in the fly, and other systems. While the HRC has been a useful theoretical description of many properties of motion detection in insects, recent work showed that the fly visual system uses a combination of two mechanisms: feedforward amplification of preferred direction signals as proposed by the HRC, and null direction inhibition as suggested by the BLM.

To what degree which mechanism is implemented, and if certain algorithms are favored by specific stimulus conditions, is still an open question. One could imagine the existence of distinct circuits that implement either preferred direction amplification or null direction inhibition at different speed regimes. While so far isolated experiments have found evidence for both mechanisms, future studies will have to tell if both models serve together across a wide space of parameters. Especially, direct measurement of synaptic inhibition onto DS cells could probe under which stimulus conditions inhibitory mechanisms play a role.

The identification of neurons upstream of direction-selective cells now leaves the question open, which computational role is fulfilled by each of these cell types. This question can be tackled with the available genetic tools, not only by probing their physiological specialization, but also by defining their requirement for downstream circuit properties. Furthermore, the visual system contains ~100 cell types, many of which have not been studied. While most of the work in the fly visual system was done on motion detection, many other visual properties such as the size of objects could provide salient cues for the animal (Keleş and Frye, 2017; Wu et al., 2016). The circuits extracting these cues could be independent from motion-detection circuits, or share elements with them.

Finally, the molecular and cellular mechanisms implementing either aspect of the computations discussed throughout this review are still elusive. Given recent advances in identifying cell type specific expression profiles (Pankova and Borst, 2016; Tan et al., 2015), it will be interesting to see how many of the individual features of EMD properties are implemented at the biophysical level.

Acknowledgement: Work in the Silies lab is supported by grants of the Deutsche Forschungsgemeinschaft (DFG) through an Emmy Noether grant and the Collaborative Research Center 889 “Cellular Mechanisms of Sensory Processing” (project C08), as well by the European Research Council through ERC Starting Grant “MicroCyFly”.

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Article note: German version available at https://doi.org/10.1515/nf-2017-0028

Bionotes

Dr. Marion Silies
European Neuroscience Institute Göttingen (ENI), University Medical Center Göttingen, Grisebachstr. 5, 37077 Göttingen, Germany
Phone: +49 551 3961331
Mail: **m.silies@eni-g.de**
Web: www.silieslab.com

Marion Silies is a group leader of the "Visual Processing" lab at the European Neuroscience Institute in Göttingen (ENI-G), which is a joined initiative of the University Medical Center Göttingen and the Max Planck Society. Before joining the ENI-G in 2015, she was a Postdoctoral Fellow in the laboratory of Thomas Clandinin at Stanford University (USA). She obtained her PhD in 2009 at the University of Münster in the lab of Christian Klämbt.

Giordano Ramos-Traslosheros
European Neuroscience Institute Göttingen (ENI), University Medical Center Göttingen, Grisebachstr. 5, 37077 Göttingen, Germany; International Max Planck Research School Neuroscience, University of Göttingen, Göttingen, Germany
Mail: **l.ramos@eni-g.de**

(Luis) Giordano Ramos-Traslosheros is a PhD student in the "Visual Processing" lab at the European Neuroscience Institute in Göttingen. He is a member of the International Max Planck Research School (IMPRS) for Neurosciences in Göttingen. He performed his MSc thesis work (2015) in Tim Gollisch's lab at the University Medical Center Göttingen. Before that, Luis studied physics at the Universidad Autónoma de Nuevo León (UANL, Mexico), and at the University of Göttingen (Germany).

Miriam Henning
European Neuroscience Institute Göttingen (ENI), University Medical Center Göttingen, Grisebachstr. 5, 37077 Göttingen, Germany
Mail: **m.henning@eni-g.de**

Miriam Henning is a PhD student in the "Visual Processing" lab at the European Neuroscience Institute in Göttingen. She is a member of the Göttingen Graduate School for Neurosciences, Biophysics and Molecular Biosciences (GGNB), and in particular of the Sensory and Motor Neuroscience (SMN) program. Miriam holds a BSc degree in Biology (2013) and a MSc degree (2016) in Neurobiology, Behaviour and Evolution from the University of Bielefeld, where she performed her thesis work in the lab of Martin Egelhaaf.