instance, the loss of dopamine also increases inhibitory synaptic drive from parvalbumin-positive interneurons onto iSPNs, but not dSPNs (Gittis et al., 2011). It will therefore be imperative to determine how the many modifications triggered by dopamine loss combine to influence the spiking properties of dSPNs and iSPNs. Clearly, there is much work to be done to understand the pathology of PD, and this Report by Parker et al. (2016) points to many new and exciting avenues for future investigations.

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Four to Foxtrot: How Visual Motion Is Computed in the Fly Brain

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http://dx.doi.org/10.1016/j.neuron.2016.02.006

In this issue of *Neuron*, Serbe et al. (2016) use cell-type-specific genetic tools to record and manipulate all major inputs to directionally selective neurons in *Drosophila*. Their results localize the site of motion computation and reveal unexpected complexity of temporal tuning in the underlying neural circuit.

An important task for the visual system of many animals, both vertebrate and invertebrate, is the detection of visual motion. Motion detection is essential for a range of visual functions, from maintaining gaze and guiding smooth pursuit eye movements in mammals, to detecting predators and stabilizing flight in flies. It was first hypothesized by Sigmund Exner in the late 1800s that visual motion detection is performed by specialized neural circuits—a prediction that turned out to be true. For more than a century, the challenge has been to delineate these circuits and to unravel their computational mechanisms.

The first algorithmic model for visual motion detection was devised in post-WWII Germany by Bernard Hassenstein and Werner Reichardt (Hassenstein and Reichardt, 1956). Founders of the field of biological cybernetics, Hassenstein and Reichardt applied their expertise in biology and physics to develop algorithmic descriptions of neural functions and behavior. Their studies of the turning behavior of a weevil (*Chlorophanus*), suspended from a post and walking on a Y-maze globe made of straw, led to an elegant and concise model for directional motion selectivity comprising three basic operations: temporal filtering, spatial offset, and multiplication (Figure 1A).

The Hassenstein-Reichardt model for elementary motion detection (HR-EMD) guided the development of systems neuroscience in invertebrates but was also rapidly adopted for studying the visual systems of vertebrates, following the discovery of directionally selective cells in the retina of the rabbit (Barlow and Levick, 1965). Its most significant contribution, however, is that it led to new theories of how neurons implement arithmetic operations like multiplication and subtraction and initiated the search to identify their specific neural substrates.

The search for the physical implementation of the HR-EMD model received a boost when a network of ~60 neurons in the optic lobe of the blowfly was found to respond selectively to distinct patterns of wide-field visual motion (Hausen, 1984). These neurons, the lobula plate

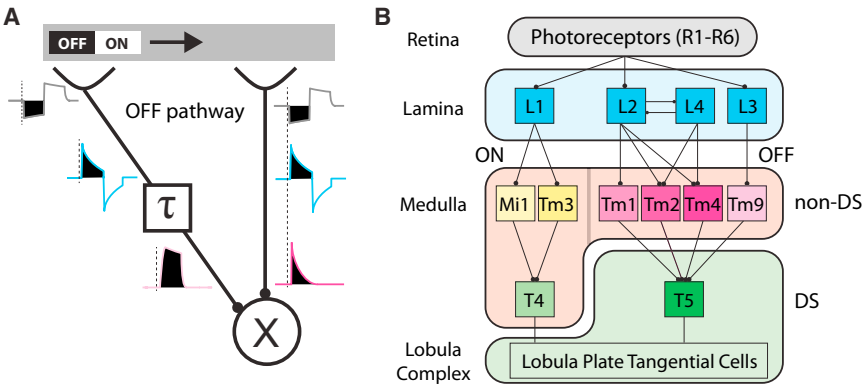

Figure 1. Schematic of a Hassenstein-Reichardt Correlator Subunit and Visual Motion Signaling Pathways in *Drosophila*

(A) Schematic of the Hassenstein-Reichardt model for visual motion detection. Luminance signals pass through a temporal filter (τ) before nonlinear integration (X) with signals from a neighboring optical unit. Waveforms represent responses of individual neurons to moving edges at successive layers within the fly motion circuit: photoreceptors (gray), lamina monopolar cells (cyan), and OFF-pathway transmedulla neurons (Tm; magenta).

(B) Neuronal connectivity of motion circuits in the fly optic lobes. The lamina monopolar cells (L1-L3) invert photoreceptor input; L4 makes reciprocal connections with L2. Lamina signals are transmitted into rectified ON and OFF pathways in the medulla. Medulla neurons exhibit diverse temporal tuning, indicated by color shading. Directional selectivity (DS) first emerges in the T4 and T5 dendrites. Directionally selective ON and OFF signals from T4 and T5 neurons are integrated within the lobula plate tangential cells (LPTCs), which are thought to control visual behavior.

tangential cells (LPTCs), seemed to integrate signals computed by local motion detectors and satisfied many predictions of the HR-EMD model. But details of the presynaptic motion detector circuits remained unclear for several more decades until the introduction of genetic tools to achieve cell-type-specific manipulations in the nervous system of the fruit fly, *Drosophila*, and the application of serial-section electron microscopy (EM) for connectomic reconstruction of visual circuits in the fly brain.

First, the second-order lamina monopolar cells (LMCs) L1 and L2 (Figure 1B) were identified as the primary inputs to the *Drosophila* motion system (Rister et al., 2007). Like the photoreceptors, LMCs respond to both bright and dark stimuli, though the sign of the response is inverted (Clark et al., 2011). L1 and L2 feed into rectified ON and OFF channels, giving rise to parallel light- and dark-selective motion pathways in the medulla (Joesch et al., 2010; Strother et al., 2014; Figure 1B). Simultaneous progress was made on the downstream circuits that provide motion input to the LPTCs. Calcium imaging showed that two neuron types, T4 and T5, exhibit directionally selective responses to moving bright and dark edges, respectively (Fisher et al., 2015a; Maisak et al., 2013), and blocking their output reduces LPTC motion-tuning and impairs optomotor behavior (Maisak et al., 2013). Finally, EM tracing revealed T4 and T5's presynaptic inputs and their spatial organization, establishing the putative circuits for motion computation in both the ON and OFF pathways (Takemura et al., 2013).

In this issue of *Neuron*, Serbe et al. (2016) explore the proposed circuit for the OFF motion pathway. According to previous work (Shinomiya et al., 2014; Takemura et al., 2013) the directionally selective T5 neurons receive the majority of their synaptic input from four excitatory transmedulla neuron types: Tm1, Tm2, Tm4, and Tm9 (Figure 1B). Combining genetic access with two-photon calcium imaging of visually evoked responses, Serbe et al. (2016) found that all four Tm types selectively respond to luminance decreases, confirming their OFF-pathway identity. They also found that the four types exhibit diverse temporal kinetics: Tm2 and Tm4 are transient (fast-adapting); Tm9 is sustained (non-adapting); and Tm1 is intermediate (slow-adapting). None of the four Tm neurons exhibited directional selectivity, and all had narrow-field center-surround receptive fields, although Tm9 showed additional sensitivity to wide-field stimuli. These results are largely consistent with prior physiological studies of Tm1, 2, and 9 (Behnia et al., 2014; Fisher et al., 2015b; Meier et al., 2014; Strother et al., 2014) and provide the first comprehensive physiological survey of the OFF motion pathway.

After characterizing the visual response properties of T5's predominant presynaptic inputs, Serbe et al. (2016) tested what each type contributes to motion detection by measuring the impact of their silencing on downstream motion-evoked responses. For each Tm neuron type, blocking the synaptic output by overexpressing a temperature-sensitive dynamin mutant (shibire^{ts}) decreased LPTC responses to moving OFF edges across a wide velocity range; the LPTC's ON input was unaffected, consistent with the circuit's parallel ON/OFF architecture. Eliminating sustained type Tm9 impacted downstream visual function most (~75% reduction). Subsequent silencing of Tm neuron types in pairwise combinations produced an additive effect, with the overall reduction greater than that of either type alone, supporting these conclusions. Thus, all four Tm neuron types contribute to the detection of moving OFF edges, but based on the dominant effect of silencing Tm9, not all Tm neurons contribute equally.

Next, Serbe et al. (2016) examined the optomotor behavior of walking flies while silencing each of the four Tm neuron types alone or in pairs. Taking advantage of the motion system's parallel ON/OFF architecture to measure OFF pathway function, they presented a visual motion stimulus that contained ON and OFF edges moving in opposite directions. With intact ON and OFF pathways, the opposite motion signals are balanced and fail to evoke turning behavior; loss of function in the OFF pathway would increase the influence of the ON signal, causing the fly to follow the ON edges (Clark et al., 2011). As expected, silencing Tm neurons in the OFF pathway evoked ON-direction turns. For Tm1, Tm4, and Tm9, the effect was restricted to low stimulus speeds, whereas for Tm2 the effect peaked at higher speeds, consistent with Tm2's fast visual response kinetics. Pairwise silencing produced stronger