A Genetic Push to Understand Motion Detection

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Two articles in this issue of *Neuron* (Eichner et al. and Clark et al.) attack the problem of explaining how neuronal hardware in *Drosophila* implements the Reichardt motion detector, one of the most famous computational models in neuroscience, which has proven intractable up to now.

Motion detection is a critical aspect of vision. It allows animals to locomote, avoid collisions, detect predators and prey, as well as reconstruct a model of the three dimensional world. The neural mechanisms of motion detection were first described in insects by a simple model put forth half a century ago. It consists of two channels sampling changes in the brightness of light at two distinct locations, whose outputs are multiplied after delaying one of them. Subtracting two such mirror symmetric ''half-correlators'' yields a signal that is positive for motion in one direction and negative for the opposite direction, resulting in a fully directional motion detector. Graphically, the Reichardt or Hassenstein-Reichardt correlator is illustrated by the diagram of Figure 1A. The multiplication operation central to this algorithm was originally proposed, in part, because when light of positive (ON) or negative (OFF) polarity was delivered to the two input channels in all four sequence combinations, the resulting optomotor responses (turning left or right), followed the sign rule of a multiplication (Figure 1B). The Reichardt model is universal: variants of it are thought to accurately describe motion detection from insects to higher vertebrates, including primates. Although much has been learned about motion detection since the model was put forth, its biophysical implementation has been very difficult to pinpoint. Explaining how such an algorithm is mapped onto neuronal hardware would shed light on how multiplication is implemented by neurons and neural networks, an important step toward understanding how the brain computes based on sensory inputs (Koch, 1999).

To address this question, an impressive collective effort has been undertaken in the past 10 years, toward applying the genetic tools developed over the past century in the fruit fly *Drosophila* to the visual system (Bellen et al., 2010). This push is mirrored by a similar focus in vertebrate systems neuroscience to study vision in the mouse, where genetic tools are also available. But whereas the architecture of the mouse visual system likely differs in important ways from those of carnivores or primates, the circuitry underlying motion detection is broadly conserved across insects, including *Drosophila* (Buschbeck and Strausfeld, 1996). As a result of this effort, transgenic fly lines now allow the targeting of specific cells in the visual system for inactivation or imaging using genetically encoded calcium indicators (Rister et al., 2007; Gao et al., 2008; Mank et al., 2008). Behavioral assays have been developed that are amenable to simultaneous neuronal monitoring and a complete anatomical wiring diagram of the visual system appears within reach (Seelig et al., 2010; Maimon et al., 2010; Chklovskii et al., 2010). Taking advantage of these tools, two groups describe their first results concerning the mapping of the Reichardt model onto neuronal hardware. The minimal circuitry that is thought to be involved in motion detection consists of photoreceptors in the retina, which synapse onto two types of large monopolar cells called L1 and L2 in the next neuropil, the lamina. These cells project in turn onto neurons in the medulla called Mi1 and Tm1 that contact T4 and T5 cells before reaching large tangential cells in the lobula plate that are well characterized and known to represent the output of the Reichardt model (Figure 1C).

The starting point of the first article, by Eichner and colleagues (2011) (this issue of *Neuron*), is the recognition that multiplication over the entire range of negative and positive brightness fluctuations, as required by the Reichardt model, is unlikely to be achieved by single neurons. This led to the proposal that brightness changes be initially half-wave rectified and then multiplied, which should be much easier to implement in single neurons. That is, multiplication would be carried out on signals that are clipped at zero, $s_{ON}(t) = \max(0, s(t))$ and $s_{OFF}(t) = \max(-s(t),0)$, resulting in four distinct subbranches of the Reichardt model: ON-ON, ON-OFF, OFF-ON, and OFF-OFF, respectively (Figure 1B of Eichner et al., 2011). Indeed, since this formulation is equivalent to the original model, a wealth of experimental data supports it (e.g., Figure 2 of Eichner et al., 2011). Yet, the tangential cell recordings reported by Eichner and colleagues suggest that half-wave rectification of fast brightness fluctuations is not the only signal driving the Reichardt detector: quite remarkably, brightness changes occurring up to 10 s earlier in the first stimulated channel still impact changes in the second one (their Figure 3). Clark et al. (2011) (discussed below) essentially confirms this result at the behavioral level (their Figure 6D). This leads Eichner and colleagues (2011) to formulate a model that includes these much slower changes, or ''DC'' components (terminology borrowed from electrical engineering; their Figure 4A). As a byproduct, two of the four subbranches of the original implementation, the ON-OFF and the OFF-ON, can be entirely disposed of, while still reproducing a wide range of experimental data. The two remaining subbranches, ON-ON and OFF-OFF, are naturally identified with L1 and L2 since their earlier

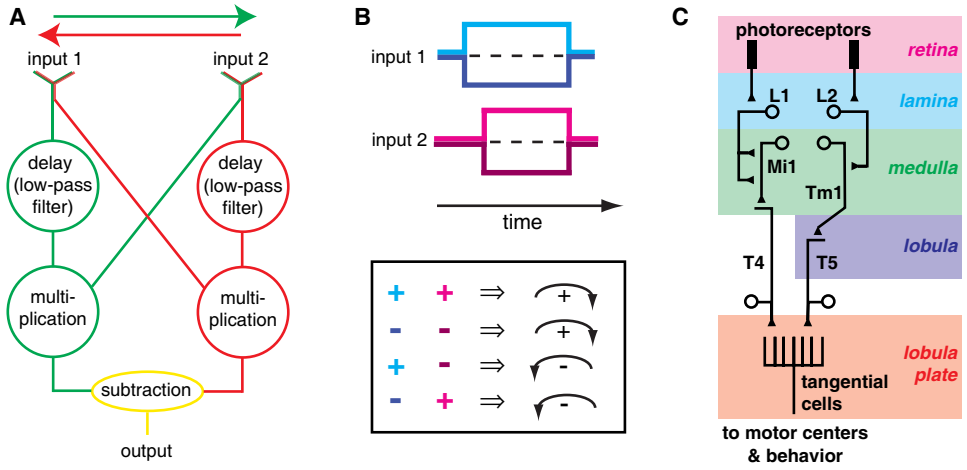

Figure 1. Reichardt Correlator, Multiplication Sign Rule, and Associated Circuitry

(A) Schematics of the Reichardt correlation model. For simplicity, an initial stage emphasizing transient brightness changes (high-pass filter) has been omitted. Green and red half-correlators are most sensitive to motion in the direction of the corresponding arrows.

(B) Top: the main stimuli used by Eichner et al. (2011) and Clark et al. (2011) are brightness step increases and decreases relative to a background level (dashed black line), offset in time and of varying duration. Bottom: these stimuli lead either to turns from left to right (+) or vice-versa, following the multiplication sign rule.

(C) Schematics of minimal circuitry candidate to implement the Reichardt model. For reasons explained by Takemura et al. (2008), this circuit anatomy is not yet definitively confirmed.

characterization is compatible with half-wave rectification (Reiff et al., 2010; Joesch et al., 2010), leading to an economical model that matches well the known anatomy of the motion detection pathway. A final experiment eliminates DC components by presenting brief brightness changes in the two input channels and concludes that the new model accounts for this data while the original Reichardt model does not. Thus, when compared to the two subbranch model, the four subbranch one appears convincingly ruled out.

The second article, by Clark and colleagues (2011) (this issue of *Neuron*), presents an extensive new set of experimental and modeling results that substantially remodels the landscape sketched above. In one of these experiments, the calcium signals generated in response to ON and OFF brightness changes, as well as moving edges, are directly compared in the axonal terminals of L1 and L2 for the first time (Figure 4 of Clark et al., 2011). Since L2 was known to code mainly for OFF brightness changes (Reiff et al., 2010), a separation in two half-wave rectified channels would predict that L1 codes mainly for ON brightness changes. Rather unexpectedly, this is not the case: the calcium signals recorded from L1 are very similar to those obtained from L2. In the next figure, Clark and colleagues (2011) further test the hypothesis of half-wave rectification at the level of L1 and L2 by looking at the encoding of dynamic random brightness changes. The encoding is found to be largely linear, again arguing against half-wave rectification within L1 and L2. The earlier evidence for half-wave rectification was obtained by recording from tangential cells in response to light (ON) and dark (OFF) translating edges (Joesch et al., 2010). In these experiments, selective inactivation of L1 led to a loss of responses to ON edges and L2 inactivation to OFF edges. Clark and colleagues (2011) confirm this finding at the behavioral level (their Figure 3). Thus, taken together these results suggest that half-wave rectification has to occur downstream of L1 and L2. However, the experiment discussed next yields another surprise: Clark and colleagues (2011) measure the turning behavior of flies in response to all four combinations of ON and OFF light pulses, essentially repeating the original 1956 experiment of Hassenstein and Reichardt with an important improvement. Now, they can study the impact of L1 and L2 by selectively inactivating them. The strongest behavioral changes from inactivation are observed in response to OFF-ON and ON-OFF stimuli, with L1 coding for the first and L2 for the second ones. Based on this insight, Clark and colleagues (2011) point out that a dark edge moving from left to right will not only stimulate the half-correlator sensitive to that direction of motion (the green one in Figure 1A of this preview), due to successive OFF-OFF brightness changes as the edge passes by, but also the half-correlator of opposite directional sensitivity (the red one), since it will experience a concurrent ON-OFF sequence of brightness changes. Thus, according to this view, dark edge selectivity does not arise from a half-wave rectified pathway for OFF edges, but rather through the summed output of mirror symmetric OFF-OFF and ON-OFF half-correlators. The resulting model can indeed reproduce the edge selectivity observed behaviorally (their Figure 8).

Given these results and the different conclusions about the internal structure of the Reichardt correlator reached by the two groups, one experiment that would rank high on our wish list would be to record from HS tangential cells in response to all four combinations of ON and OFF pulses during selective inactivation of L1 or L2. The prediction drawn from behavioral experiments is that inactivation of L1 will abolish responses to ON-OFF stimuli and vice

versa for L2. Such an outcome would confirm the behavioral results of Clark et al. (2011) at the neuronal level and help clarify the relative role played by half-wave rectified (ON-ON, OFF-OFF) versus mixed luminance (ON-OFF, OFF-ON) channels along the L1/L2 pathways. Alternatively, it may be that HS cells are not the main determinants of the observed behavioral output, although earlier experiments generally suggested this to be the case (Pflugfelder and Heisenberg, 1995). Even though the models proposed by Eichner et al. (2011) and by Clark et al. (2011) are quite different, both of them reproduce a wide range of experimental data. This results from the inclusion of substantial nonlinear components and the emphasis on different contributions of L1 and L2 in motion processing. We are optimistic that in the near future, as these contributions are considered simultaneously, as additional experimental data become available and additional cells in the circuit become genetically targetable, they will converge toward a unified picture of how *Drosophila* neural circuits implement the Reichardt correlation model. These are indeed exciting times for *Drosophila* and, more generally, insect vision.

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Searching for the Neural Mechanisms of Feature-Based Attention in the Primate Brain

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In this issue, two studies, one by Zhou and Desimone and another by Cohen and Maunsell, provide new insights into the mechanisms of feature-based attention (FBA). The former demonstrates a new role of the frontal eye fields in the origins of FBA and the latter shows that FBA is coordinated across both hemispheres.

The primate brain sensory systems have a limited processing capacity. For example, the visual system, comprising nearly 50% of the neocortex, can only effectively process a small percentage of the information entering the retinas at a given time (Van Essen et al., 1992). An effective solution to this problem has been to develop an attentional filtering mechanism that separates relevant from irrelevant incoming sensory signals in order to concentrate processing resources in the former. Two types of attentional filtering have been identified—one driven by bottom-up (stimulus saliency) and the other by top-down (internal goals) cues. Decades of experimental work have also led to the identification of key structures and mechanisms that play specific roles in both types of attention. For the case of top-down attention, we have learned that the responses of neurons to visual stimuli in feature-selective and retinotopically organized visual areas of the macaque brain are strongly modulated when animals attend to a stimulus feature or location. This has led researchers to classify the top-down attentional modulation of visual neurons response into feature-based (Treue and Martínez Trujillo, 1999), spatial (McAdams and Maunsell, 1999), and a third type called object-based attention (Roelfsema et al., 1998). One controversial topic in attentional research has been whether the two former types of attention share similar neural mechanisms. In this issue of *Neuron*, two different electrophysiological studies using advanced