# Motion Vision: A New Mechanism in the Mammalian Retina

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**In animal eyes, the detection of slow global image motion is crucial to preventing blurry vision. A new study reveals how a mammalian global motion detector achieves this through 'space–time wiring' at its dendrites.**

The last common ancestor of flies, squid, and mice lived over 700 million years ago at a time when vision was mostly confined to circadian tasks and basic light–dark detection. Since then, image-forming vision evolved independently in different lineages, leading to the radically different eyes that are observed in these modern species [1]. Yet despite the many anatomical differences in eye design, their visual systems have converged to support important visual functions. One of these functions is the ability to detect motion. This is useful for tracking predators or prey moving through the animal's environment and, perhaps more importantly, for detecting movement of the whole image 'slipping' across the visual field [2]. This allows the animal, through reflexive control of eye or head muscles, to track the image and keep it fixed on the retina. Sensing global motion slip requires neurons that can detect a specific flavor of motion — large in spatial scale and slow in velocity. A new study by Matsumoto *et al.* [3], reported in this issue of *Current Biology*, has now revealed how a mammalian global motion detector achieves such tuning to slow motion velocities using motion-insensitive neuronal inputs that respond to light at different speeds.

Ever since the discovery of motion-sensing neurons more than 60 years ago [4], scientists have proposed theories of how such detectors could be wired up. During movement, an object or edge changes position over time. Accordingly, a motion detector must have at least two sensors in different spatial locations and a downstream component that can read out whether both of the two sensors were triggered and, crucially, which order they were triggered in. This lets the detector sense motion in one direction.

Two classic ideas for how a neuronal circuit could be wired to achieve this have been proposed. One, the Hassenstein–Reichardt model, was first suggested for the beetle visual system [4]. This model, also called 'preferred direction enhancement' (Figure 1A), uses two excitatory neurons with a time delay that are positioned to detect stimuli at different points in space. When the delayed neuron is activated before the non-delayed one, they trigger a third, downstream neuron at the same time. This causes a larger response than if the non-delayed neuron was activated first. This allows the downstream neuron to be sensitive not only to motion *per se*, but also its direction.

As an alternative, Barlow and Levick [5] suggested a solution for rabbits where two sensors are again spatially offset and feature distinct time-delays, but now in addition provide opposite polarity inputs to a postsynaptic target (Figure 1B). When the inhibitory sensor is activated first, it suppresses its downstream target, canceling out the excitatory input from the other sensor, thus suppressing the response to movement in that direction. In the opposite direction, the excitatory sensor is activated first and there is a brief window during which the downstream neuron is excited. In reference to the cancellation in the non-preferred ('null') direction, this model is called 'null-direction suppression'.

Many groups have worked to determine which, if any, of these models is present in the visual systems of animals, with a recent focus on the fly and mouse [6]. Over the past decade or so, the motion vision field has exploded with the identification of several additional solutions to this same basic problem. Some of these motion detectors are reminiscent of the classical solutions, while others are rather distinct. In the fly, both classical solutions have been observed [6], while in mice a diversity of direction-selective cells appear to utilize different complements of these mechanisms [7]. Here, null-direction suppression is present in all direction-selective ganglion cells (DSGCs) [6], yet in some cases the same DSGCs remain tuned to motion direction when the inhibition is experimentally removed [8,9]. Others have found gap-junction-mediated motion detectors and dendritic integration motion detectors [6]. Rather than 'life finds a way', it seems that 'life finds all of the ways' when it comes to motion detection.

And yet, whether or not mammalian DSGCs use a preferred direction enhancement mechanism has remained unclear. Excitatory currents onto DSGCs are tuned for direction [10,11], but the individual axon terminals of the bipolar cells that provide this excitation are not [11,12]. To reconcile these seemingly disparate results, it has been argued that the directional tuning in the DSGCs' excitatory currents is due to a recording artifact [13].
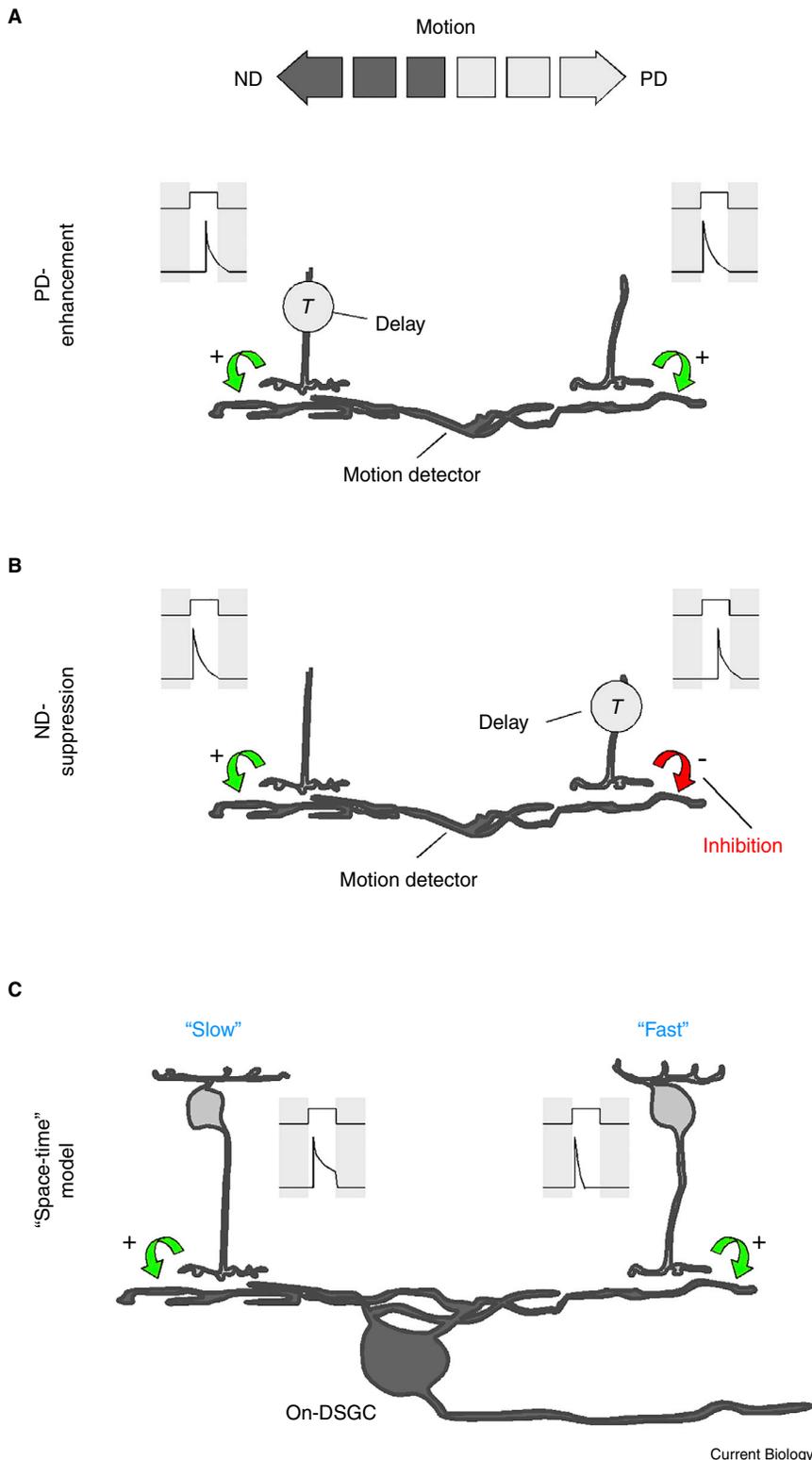
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**Figure 1. An update on the classic motion detector.**
(A) A neuronal circuit that achieves motion detection through preferred direction (PD) enhancement. Two excitatory input neurons synapse (green arrows) onto the downstream motion detector, with the input on the left responding to its stimulus with a time delay (T). Insets show the timing and shape of the inputs' responses to a square light pulse. When a motion stimulus travels in the preferred direction, the left input is activated before the right input, and their activation of the postsynaptic neuron coincides. (B) A

More recently, a 'new' version of the classical preferred-direction enhancement model has been proposed. In this 'space–time wiring' model [14], multiple directionally untuned bipolar cells with different kinetics systematically wire to different locations of the motion detector's dendritic tree: slow inputs to one side and fast inputs to the other (Figure 1C). In this way, the computation of motion direction would occur at the level of the postsynaptic dendrites through coincident summation. Anatomical evidence for such a motion detector was first found on the dendrites of starburst amacrine cells [14] (but see [15]), inhibitory neurons that had long been implicated in vertebrate motion processing [16]. However, evidence that the different bipolar cell types' kinetics could be enough to explain the observed direction selectivity has been mixed [6,17].

Matsumoto *et al.* [3] now report direct functional evidence of a 'space–time wiring' motion detector in a specific mouse retinal DSGC type, the On-DSGC. In the process, the authors have also solved another mystery of the field, which is how some DSGCs achieve the very slow velocity tuning that informs an important gaze stabilization function called the opto-kinetic reflex.

In the mammalian retina, two main groups of DSGCs have been identified. On-Off-DSGCs prefer fast motion velocities; On-DSGC, on the other hand, prefer slow motion velocities and send axons to the accessory optic system in the brain to control the opto-kinetic reflex [18,19]. Both were thought primarily to utilize a null-direction

circuit for null direction (ND) suppression. Now the input on the right is inhibitory to the downstream neuron (red arrow) and delayed in time relative to the excitatory input (left). When motion travels in the null direction, the excitatory input coincides with the inhibitory input and the cell responds less strongly. (C) The 'space–time' model for motion detection: similar to (A), but now the inputs have different release kinetics, slow and sustained vs. fast and transient. For the downstream motion detector (On-DSGC), slow inputs are observed primarily on the one side of the dendritic tree and fast inputs on the other. When motion proceeds in the preferred direction, these inputs co-occur and provide stronger excitation to the DSGC.

suppression mechanism for motion detection supplied by inhibitory amacrine cells. But the difference in their velocity tuning had long suggested that there must be additional differences in the way they compute direction of motion.

Matsumoto et al. [3] found that, indeed, the excitatory currents of On-DSGCs are tuned. Crucially, this tuning is most pronounced at low velocities. In contrast, the tuned inhibition in these On-DSGCs preferred higher velocities, which are less relevant to these cells' functional role in gaze stabilization. Here, glutamate imaging confirmed that the individual excitatory inputs to On-DSGCs are indeed not directionally tuned.

But Matsumoto et al. [3] did a further analysis to examine the response kinetics of these untuned inputs. They found that there was a pronounced distribution of functional input types across the dendritic tree of an On-DSGC. Slow, sustained excitatory inputs synapsed on one end of the tree, while fast, transient inputs synapsed on the other. In their computational model presented alongside, this arrangement could explain the cells' observed velocity and direction tuning. Thus, at least one group of DSGCs in the mouse retina uses preferred direction enhancement.

This result represents one of the strongest examples yet of how the kinetics of a neuron's inputs can shape its functional properties. Recent work has aimed at cataloging the functional properties of retinal interneurons on a mass scale [20], with the goal of using these functionally-defined cell types to elucidate the formation of retinal ganglion cells' output to the brain. This new study [3] provides proof-of-principle that these efforts could result in new mechanistic understanding of retinal function.

Matsumoto et al. [3] also make a valiant attempt to connect their functional input categories to connectomic data on the bipolar cell inputs to On-DSGCs. They find a hint that their functional types correspond to previously-identified anatomical types. However, with only partial branches of On-DSGC dendritic trees available for analysis, these data remain limited for now. Correlating structure and function and finding out how On-DSGCs differ from On-Off-DSGCs with respect to their inputs from bipolar cells are important areas for further research.

Most exciting of all is the idea that with motion detection, the devil appears to be in the details. Even though cephalopods and insects use conceptually similar types of head and eye movements to vertebrates [2], the detailed circuitry of their motion detectors will almost certainly depend on evolutionary and design constraints and which precise stimulus features are needed for survival. Despite this, the basic workings of the detectors (those found so far) still appear to fall into the two general categories of preferred direction enhancement or null direction suppression. There remain only two fundamental types of motion detectors, but many ways to make them.

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