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Image Processing: How the Retina Detects the Direction of Image Motion

In the retina, the beautifully symmetrical 'starburst' amacrine cells interact with each other in a way that creates asymmetrical responses to moving images at their dendritic tips. This computation, occurring in a retinal interneuron, is a foundation of the directional signals transmitted by the retina to the brain.

Shelley I. Fried and Richard H. Masland

A classic problem of both computational and experimental neurobiology is the mechanism by which the retina can derive the direction of motion of stimuli crossing its surface. The direction of motion is signaled to the brain by a specialized type of retinal ganglion cell called the directionally selective ganglion cell (ganglion cells are the output neurons of the retina; their long axons form the optic nerve). Directly impinging on directionally selective ganglion cells are a type of interneuron, the starburst amacrine cells, which receive signals about light from earlier retinal neurons. Starburst cells have long been suspected of playing an important role in the directional response [1–3]. But a surge of studies over the last few years has shown that the starburst cells not only supply the critical inhibitory signal to make directionally selective cells directional, but are themselves able to discriminate movements [4–6]. This makes starburst cells the earliest neuron in the retina to have directional properties. While we had to wait nearly 40 years to learn the mechanism by which directionally selective ganglion cells became directional, it has taken less than four for starburst cells. A new study by Lee and Zhou [7] reveals an elegantly simple synaptic mechanism underlying the computation.

The directional properties of starburst cells differ radically from the conventional synaptic calculation performed by directionally selective ganglion cells. Whereas directionally selective ganglion cells can distinguish between left and right or up and down motion crossing the whole cell [8], the starburst cells each contain six to ten semi-autonomous dendritic regions [9,10], each responsive to a different direction of motion [5]. These regions — actually pie-shaped dendritic sectors — are arranged radially around the cell body, and each distinguishes between centripetal (inward) and centrifugal (outward) motion, generating a larger response to centrifugal stimuli (Figure 1).

How is this accomplished? Lee and Zhou [7] performed technically demanding double patch-clamp experiments between neighboring starburst cells, exploring the effect of depolarization of one of the starburst cells on the other. Reversing the clamp levels allowed them to determine whether connections were reciprocal. They found that, as long as the processes of two neighboring starburst cells overlap, they were likely to have a reciprocal inhibitory connection (Figure 2). A series of further experiments revealed how these connections shape the directionally selective light response. First, as expected, the area of the retina from which an individual starburst cell could be inhibited by light — its 'inhibitory'

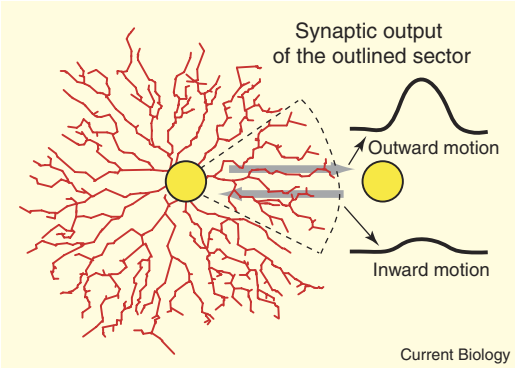

Figure 1. Starburst amacrine cells discriminate directions of motion.

Previous work had shown that pie-shaped sectors (dotted lines) of the starburst amacrine cells have responses that discriminate the direction of movement of stimuli across the retinal surface. Each sector generates a large response to outward movement of a stimulus (yellow spot) and a small response to inward movement of the same stimulus. The sectors are electrotonically semi-autonomous, so that each can have a different preferred direction. Lee and Zhou [7] have now elucidated the synaptic mechanism underlying these differences.

receptive field — was widened by the starburst–starburst connections (Figure 2, shaded blue circle). The magnitude of the extension was approximately 150 μm, as would be predicted from the approximate length of a starburst process. The excitatory receptive field, which does not receive input from these starburst connections, was confined to the extent of the individual starburst cell's dendritic field (Figure 2).

Then, to demonstrate how the spatial offset between receptive fields leads to asymmetrical responses, Lee and Zhou [7] measured the input currents to starburst cells in response to inward and outward motion (Figure 2, bottom). An inward moving stimulus crosses first into the surrounding inhibitory receptive field — the field that 'belongs' to a neighboring, synaptically connected starburst cell — before coming into the excitatory receptive field. As a consequence, for inward motion inhibitory input arrives before excitatory input (Figure 2, bottom right). The hyperpolarizing effect of the early inhibitory input lasts a relatively long time; it reduces the depolarizing effect of the subsequent excitatory input, reducing the cell's overall response. On the other hand, for outward motion the main excitatory input arrives before inhibitory; in this case the depolarizing effect from excitation is not reduced and the starburst cell has a maximal response (Figure 2, bottom left). For the stimulated sectors of the starburst cell's dendritic arbor (see below) this generates a maximal output to its postsynaptic partners.

An elegant twist on this mechanism is that the reciprocal connections create a positive feedback loop, further enhancing the difference between inward and outward responses (Figure 3). Consider a light stimulus moving from left to right in Figure 3. Prior to the arrival of the stimulus, processes from the two reciprocally connected starburst cells release a baseline level of inhibitory transmitter (Figure 3A). As the stimulus begins to move across the dendritic arbor of the left starburst cell, the processes become depolarized and increase their release of inhibitory transmitter (Figure 3B). This results in an increased inhibitory input to the starburst processes on the right, causing hyperpolarization with a corresponding reduction in (inhibitory) transmitter release (Figure 3C). The resulting reduction in inhibitory transmitter from the right starburst process has a depolarizing effect on the left process, leading to further hyperpolarization of the right process (Figure 3D,E). This positive feedback loop enhances the difference in response between the two cells, further increasing the inhibitory output of one and decreasing it for the other.

Lee and Zhou [7] uncovered several additional mechanisms underlying the response. They found that inward motion not only delivers a larger, earlier inhibitory signal, it also reduces the excitatory input (presumably by

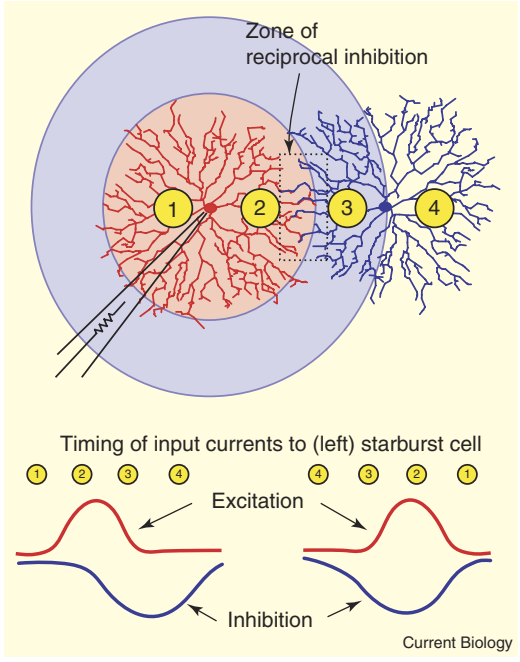

Figure 2. An offset of excitatory and inhibitory zones shapes the asymmetric response in starburst cells.

Starburst cells receive excitatory input over the extent of their dendritic field (excitatory receptive field); for the cell on the left (red) this is depicted by the small circular region (red). Neighboring starburst cells that have overlapping processes (red, blue) supply direct reciprocal inhibitory input to each other. These connections extend the region over which each receives inhibitory input (inhibitory receptive field); this is depicted by the large circular shaded region (blue) for the cell on the left. For the left starburst cell, movement of an inward stimulus (position 4 → position 1) activates the inhibitory receptive field (position 3) prior to activating the excitatory receptive field (position 2); this translates into an earlier onset of inhibition relative to excitation, illustrated schematically below. For the same cell, outward movement (position 1 → position 4) activates the excitatory receptive field (position 2) prior to activating the inhibitory receptive field (position 4); this translates into an earlier arrival of excitation vs. inhibition (bottom, left).

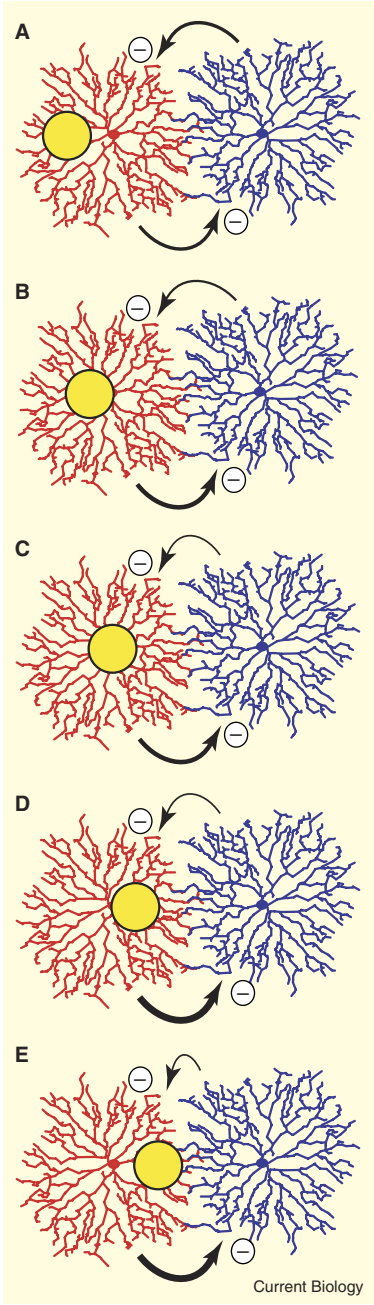

Figure 3. Reciprocal connections enhance the asymmetry of the starburst response to motion.

(A) At rest, reciprocal starburst connections each release a baseline level of transmitter. (B) An outward moving stimulus enters into the receptive field of the left starburst cell activating the cell and increasing its release of inhibitory transmitter. (C) Increased release of inhibitory transmitter from the left starburst cell hyperpolarizes the right starburst cell, in turn reducing its release of neurotransmitter. (D,E) Positive feedback loop continues to increase release from the left starburst and simultaneously decrease release from the right starburst processes.

reducing stimulation to the starburst cell from its presynaptic drivers). This reduction in excitatory input could be activated by stimuli up to 870 μm away, well outside the spatial extent of a starburst cell, suggesting that this mechanism is mediated by a different laterally conducting neuron, most likely a wide field amacrine cell [11]. Finally, they used Ca^{2+} imaging, which allows a direct look at the synaptic output of the starburst cell, to show that, in addition to all of the inhibitory mechanisms at work in the inward direction, there is at least one facilitory mechanism (as yet unknown) operating in the outward direction.

How do we get from asymmetrically responding sectors of a starburst cell to directionally selective responses of the retinal ganglion cell? Starburst cells make specific direction-dependent connections with directionally selective cells, releasing inhibitory transmitter to 'null' the response to movement in one direction. The critical element in all of this — and still the most magical part of the story — is the selective wiring of starburst sectors to individual ganglion cells. Starburst sectors that 'point' — have their preferred axis of movement — in one direction must synapse upon ganglion cells that report upon a specific direction of motion [6], and must avoid synapsing upon ganglion cells that report different directions. Other sectors of the same starburst cell, which 'point' in different directions, synapse upon these other ganglion cells. Note that this mechanism requires that the starburst sectors are functionally (electrophysiologically) independent of each other, as is in fact observed [5]: if the whole starburst cell were activated at once — as would happen for most other neurons — then different sectors could not simultaneously signal different directions of motion.

The asymmetric response of individual starburst sectors appears to lie at the heart of the retina's computation of direction selectivity, but there is much more to learn. Although the selective connectivity of starburst sectors, first hypothesized 15 years ago by Vaney [12] is now fairly well established, the challenge it poses for developmental wiring mechanisms is great and they remain to be even faintly understood. In addition, the role of the excitatory neurotransmitter acetylcholine remains elusive, despite the fact that it co-localizes with the inhibitory transmitter (GABA) in starburst cells. Finally, these ganglion cells perform reliably across ~2.5 orders of magnitude of velocities — a range that challenges the timing capabilities of imaginable neural microcircuits. Other laboratories have shown additional layers of motion-discriminating mechanisms [4,6,13–18]; perhaps these act in concert with those described here to expand the range over which the directionally selective ganglion cells can reliably describe image movement to the brain.

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Mating Behaviour: Promiscuous Mothers Have Healthier Young

A small marsupial has thrown new light on the question of why females typically mate with several males: promiscuous female antechinuses have many more surviving offspring because males that are successful in sperm competition also sire healthy offspring.

Martin Edvardsson, Fleur E. Champion de Crespigny and Tom Tregenza

The myth of the coy and chaste female is all but shattered. We now know that in most animals females are surprisingly promiscuous. Surprising, because it has often been difficult to see the benefits of female promiscuity. While males typically have the potential to fertilise the eggs of a large number of females, female reproduction is usually limited by material resources rather than by access to sperm or willing males. Males of some species do provide benefits such as food or access to a territory in exchange for sex, but in most cases females seem to get little more than sperm from their mates. That many females nonetheless mate with several males is puzzling because sexual encounters inevitably carry costs — they take time and energy and involve risks of disease or even harm by males [1].

The key to understanding female promiscuity may be that by mating around, females acquire sperm from several mates. This would be to their advantage if, for some reason, sperm from more suitable sires were more likely to fertilise the eggs. The simplest way this could occur is if males carrying better genes win out in sperm competition with inferior rivals, either because they are able to produce ejaculates with larger numbers of sperm or because the individual sperm they produce are better [2,3]. Alternatively, rather than simple ejaculate competition, promiscuous females might be able to store and use sperm from males with good genes and reject sperm from others based on signals they receive during mating or from the ejaculates themselves [4]. A new study from Australia [5] has provided the clearest evidence yet that promiscuous females can indeed exploit differences in male fertilisation success to improve the genetic quality of their young.

The antechinus is a small carnivorous marsupial similar to a shrew with some dramatic reproductive tactics. During their winter breeding season, males show a dedication to mating that includes copulations lasting between five and 14 hours and that ends with the entire male population dying from their exertions [6]. In an elegant new study, Fisher *et al.* [5] mated wild-caught female brown antechinuses (*Antechinus stuartii*, Figure 1) either three times to the same male or to three different males. They found that, when mated females were released back into the wild with their pouch young, the proportion of offspring that survived to weaning was three times higher for polyandrous (mating with several males) females than for monandrous (mating with one male only) females.

A similar effect was seen when females were kept under less stressful conditions in the laboratory. Offspring from the two groups showed no differences in survival until a few weeks before weaning when many of the monandrous females' offspring died despite milk still being available. The size of the difference in survival between the two groups reveals a truly staggering benefit of taking multiple mates; just the magnitude of this effect is informative because it is impossible to conceive of any costs of mating that could outweigh such a large advantage. Promiscuity definitely pays for these females.

So, are these huge benefits of taking multiple mates really genetic effects? A key piece of evidence revealed by this study is that males that are good at winning in competition for fertilisations have offspring that are much more likely to survive. Fisher *et al.* [5] showed this by genetically determining the paternity of offspring of females that had mated to three males. They then mated other females to only one of the males each and found that offspring of males with more competitive ejaculates had a much better chance of survival than offspring of males that were poor sperm competitors. This is, of course, just what you would expect if polyandrous females