doi:10.1038/nature18454

COMPUTATIONAL NEUROSCIENCE

Species-specific motion detectors

A range of neuronal mechanisms can enable animals to detect the direction of visual motion. Computational models now indicate that a factor as simple as eye size might explain some of this diversity.

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Seeing whether and where an object moves is crucial for the survival of any visually oriented animal, whether predator or prey. Consequently, motion and its direction are computed at many levels along the vertebrate visual pathway, starting in the retina. One key element of direction-selective retinal neuronal circuits is the starburst amacrine cell (SAC). In a paper online in *Nature*, Ding *et al.*[1] unpick the mechanisms that mediate SAC direction selectivity in the mouse retina.

Structures called dendrites project radially from the body of the SAC to give the cell its characteristic shape, which resembles an exploding star. The dendrites receive excitatory inputs from the retina's light-sensing photoreceptor cells via bipolar cells, and in turn make inhibitory synaptic connections to neurons called direction-selective ganglion cells (DSGCs) and other SACs. Different types of DSGC are each robustly tuned to movement in a particular (preferred) direction.

The work of numerous labs over past decades has indicated that the inhibitory signals sent by SACs to DSGCs contain information about movement direction. However, an SAC as a whole is not selective for one particular direction; instead, each dendrite is tuned to the direction of movement that is aligned with the direction from the cell body to the dendritic tip[2]. In addition, SAC dendrites tuned to a particular direction make more synaptic connections with DSGCs that prefer the opposite direction than with those of the same preference, providing DSGCs with information that defines their tuning[3].

Although this general layout is broadly accepted, the mechanism that renders SAC synaptic outputs direction-selective is still intensely debated. In mammals, several (not necessarily mutually exclusive) mechanisms have been proposed. Some rely on properties of the dendrites — for instance, the spatial arrangement of channel proteins in the membrane or of a chloride gradient along the dendrite. Others invoke network interactions such as reciprocal inhibition between SACs or a particular spatial arrangement of bipolar-cell inputs that signal to the neuron with different timings (reviewed in refs 4 and 5). But the relative contribution of each mechanism is unclear.

Ding *et al.* investigated the role of network interactions in SAC direction selectivity in mice. They used a large electron-microscopy data set to generate a map of all the synaptic connections to and from SACs. This allowed them to precisely assess the spatial arrangement of both input and output synapses along SAC dendrites. Synapses followed a clear pattern: inputs (both excitatory and inhibitory) were restricted to the proximal section of the dendrites, whereas output synapses were located at the dendritic tips (Fig. 1).

Although this output arrangement comes as no surprise, the proximal restriction of inhibitory inputs is in stark contrast to the situation seen in rabbit SACs, which show much less spatial segregation[6]. This is puzzling. Why should two ground-dwelling mammals that live in similar environments use different solutions to compute motion direction?

To address this question, Ding and colleagues used a computer model to simulate how different synaptic arrangements might affect SAC direction selectivity. They connected a single SAC to bipolar cells and neighbouring SACs. They then varied the arrangement of input synapses along the central SAC's dendrites to mimic the mouse and rabbit 'solutions', and compared the cells' performance. The higher degree of segregation in mice generated more-robust directional tuning, in particular for stimuli that traversed the retinal surface slowly. The authors then went on to confirm these predictions experimentally by recording motion-evoked signals in mouse SAC dendrites.

Why would mice need to compute slower movements than rabbits? After all, the velocities of movement that these animals encounter in the wild are probably similar. The answer is deceptively simple. Mice have smaller eyes than rabbits. A moving object's angular velocity (velocity measured as the angle travelled per unit of time instead of distance per unit of time) translates to a lower absolute velocity across the retinal surface of a smaller eye than that for a larger eye. Therefore, the object's image moves substantially more slowly on the mouse's retinal surface (Fig. 1). Perhaps the less-segregated synaptic arrangement in the rabbit circuit is good enough to encode the relevant range of stimulus velocities, whereas mice needed to

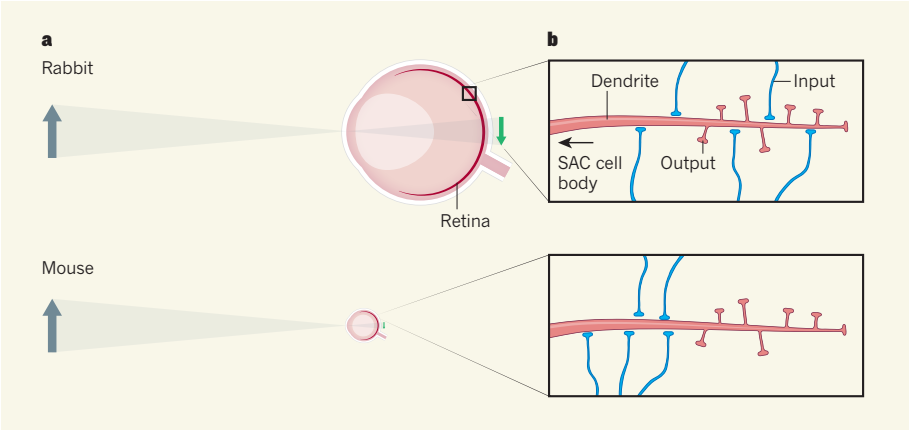

Figure 1 | Direction is in the eye of the beholder. **a**, Rabbits have larger eyes than mice. Therefore, the image of an object travelling a given distance (grey arrows) will traverse different distances across the retina of each species (green arrows). Ding *et al.*[1] hypothesize that neuronal circuits in mice thus need to respond to lower retinal-image velocities to compute information about movement direction. **b**, The authors find that the synaptic connections to direction-selective starburst amacrine cells (SACs) in the retina differ between the two species. As shown in this simplified schematic, inputs (both from other SACs and from bipolar cells) cover the length of the cells' radially projecting dendrites in rabbits, whereas inputs and outputs are well segregated along the dendrites in mice. This difference increases the directional tuning of mouse SAC dendrites at slower retinal velocities.

evolve a solution that also reliably works for slower movements across the retina.

This is a neat study for several reasons. First, it represents a well-balanced synthesis of large-scale, high-resolution circuit anatomy, realistic modelling and synaptic neurophysiology. Second, demonstrating that a simple difference such as eye size can have a direct impact on how circuits and computations are implemented highlights the often-underestimated importance of taking species differences into account. The suggestion that different species may use different adaptations of a general computation for retinal direction selectivity could be the key to reconciling seemingly contradictory findings in the field.

Third, this study takes a crucial step towards the development of a truly integrated model of direction-selective retinal circuitry. A carefully extended version of the model designed by Ding and co-workers (for instance, one that includes more-realistic bipolar inputs) could be instrumental in disentangling different direction-selectivity mechanisms. In addition, this approach will allow researchers to systematically address other mysterious aspects of retinal direction detection, such as the role of the molecule acetylcholine, which is SACs' secondary neurotransmitter and seems to play a part in signalling only under certain stimulus conditions[7,8].

Retinal direction-selective circuits should now be studied in other species, perhaps starting with those that have extreme eye sizes or more-distant evolutionary roots. For instance, the DSGCs of zebrafish larvae have largely similar properties to those of mammalian DSGCs[9], suggesting a similar organization of direction-selective circuits. However, in the tiny larval eye, an object moving at an angular velocity of 1 degree per second crosses the retinal surface at a mere 3 micrometres per second — 10 times more slowly than in mice. Maybe zebrafish have an even more precise synaptic arrangement along SAC dendrites. Or, perhaps more likely, they have another direction-detection mechanism altogether.

Primate and rabbit eyes are not that different in size. However, direction selectivity in the primate retina is a puzzle. SACs are present, but are sparser than in any other mammal studied[10]. Despite long-standing and vigorous attempts, there is no direct evidence so far that primates have DSGCs (discussed in ref. 11). Instead, primates seem to generate direction-selective responses farther along the visual pathway.

What is the take-home message? Maybe, that the goal of neuroscience is not to 'solve' the mouse, rabbit or zebrafish. Instead, neuroscientists should collect different solutions to common computational problems. Which solutions are actually implemented in any particular instance is perhaps secondary. After all, neuroscience is about building an understanding of the general principles by which neurons and networks generate function. ■

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