Insect Neurobiology: An Eye to Forward Motion

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For many animals, visual motion provides essential information for navigating through the environment. A new study in flies reveals novel neurons capable of multiplexing information of a visual scene and encoding relative depth perception from motion disparity.

Deciding to go off trail when you walk through the woods can take your hike to a new level of ducking around branches and searching for stable footholds. You suddenly need a good sense of the three-dimensional world just to avoid knocking yourself out. Most animals, from humans to ants, need to carefully control their paths as they move through the environment. They determine which routes will be passable and safe, and will get them to their destinations rather than taking them in circles. This is complicated because even static landscapes can take on nearly infinite appearances. But when visual animals move, they get useful information from the patterns of apparent motion (or flow-fields) of objects, surfaces and edges in the world. In fact, when an animal walks, swims or flies along a straight path, the local motion in otherwise ambiguous scenes can reveal the three-dimensional layout [1]. A paper in this issue of *Current Biology* [2] describes a new type of neuron in the blowfly that is sensitive to translational optic flow and tuned to cluttered images moving at multiple depths: in other words, a type of neuron that can extract distance information from real, natural scenes during flight.

The potential for self-motion to help analyze a scene is somewhat undermined by the dizzying number of ways we can move. The optic flow generated for an Olympic platform diver, twisting towards the water, would only seem to complicate the task of evaluating images. But even the most convoluted movements still cleanly divide into rotational and translational components [3], the basis of rigid-body motion. Over wide angles you can tease this information out of flow fields. Rotating is in some ways the simpler of the two: the visual flow depends only on angular speed and the angle to the rotating axis (Figure 1A). When you turn your head, nearby branches, distant mountains, and the moon in the sky all seem to move in your visual field — slowly if they are above, quickly if they are near your 'equator' at eye level. Translation, on the other hand, generates a clearly different configuration of motion on the retina: images in the heading direction are still, while those outside move in centrifugal directions (Figure 1B). The flow now depends on your speed of motion and the angle to the forward heading point (the 'focus of expansion'), but additionally on the inverse of actual object distance. This relationship to distance is the reason that, when you walk, nearby branches slide past you, but mountains and the moon seem to hover in place. This more intricate flow-field is a computational challenge, but rich with hints about object distance (Figure. 1B), a visual cue called motion parallax [4]. It is a way to infer the three-dimensional structure of the world from the two-dimensional image on the retina.

Behavioral responses to optic flow have been studied in many animals [5–10], but few models allow the investigation of their neuronal underpinnings. Studying individual neurons responding to flow requires accessing them with electrophysiological methods in visually functional animals. As has often been the case in neurobiology, an invertebrate model offers exceptional advantages. The blowfly, *Calliphora vicina*, has neurons dedicated to processing optic flow in an accessible brain area called the lobula plate (see below for the anatomical context of this area). This region performs visual analysis of self-motion [11,12], and *Calliphora* has provided remarkable advances towards the physiological mechanisms and computational principles implemented in neurons and circuits extracting optic flow information [11–14]. However, studies to date have often concentrated on rotational optic flow, both because of the simplicity of generating such flow in cylinders, and because the lobula plate has yielded a beautiful set of neurons responsive to such flow.

But flying insects must translate through the world or they would never get anywhere. In their new study, Longden *et al.* [2] identified novel neuronal types from the blowfly lobula plate that process translational optic flow, including one capable of multiplexing information using single spikes and spike burst coding, to convey different aspects of the visual scene. This includes coding of multiple depth planes, implicating it in motion parallax and depth perception during navigation.

In arthropods, light signals captured by the photoreceptors are processed by columnar neurons through three optic neuropils: the lamina, the medulla, and finally the lobula complex, which in many animals is divided into the lobula and lobula plate [15]. The medulla contains about 40 different types of columnar elements [16], betraying some of the complexity of arthropod visual processing. But these columnar neurons are small, making them hardly accessible for electrophysiological recording, and hence for investigating their function (but see, for example, [17]).

Columnar neurons from large regions of the visual space feed into wide tangential

neurons in the lobula. Happily, these neurons are large and suitable for electrophysiology. About 60 such neurons have been identified in the lobula plate of the blowfly, specialized for processing optic flow [8]. These neurons, generically called lobula plate tangential cells (LPTCs), play a central role in course control during flight [9,11,12]. Different sets of LPTCs have been identified and characterized, most notably the horizontal system (HS) and the vertical system neurons (VS) [12,13], which are sensitive to flow fields generated by yaw and roll rotations, respectively. Studies of these neurons have provided tremendous insight into the processing of rotatory optic flow. But navigating flies do more than simply adjust their rotational movements. While piloting through cluttered environments, flies also need information on the straight component of their travel, yet neurons for translational optic flow have remained elusive. But Longden *et al.* [2] have now described three neuronal types sensitive to translatory optic flow, which they term VT1–3 cells. The authors focused on characterizing the response properties of the VT1 cell, which encodes self-motion in the forward-sideslip direction. This cell fires both single action potentials, and short barrages of action potentials, known as spike bursts.

With a clever series of visual stimuli, including motion in the center or in patches surrounding the focus of expansion, Longden *et al.* [2] progressively obtained evidence indicating that VT1 might compute relative distance by image motion disparity, in other words, might encode motion parallax. To test this assumption, they recorded VT1 cells responding to flow simulating forward-sideslip movement through a panorama of different heights. Their results show that VT1 is sensitive to height differences, and can convey this information with spike burst coding. Interestingly, the single spike activity was unaffected by motion parallax stimulation. Thus, the VT1 cell seems capable of encoding parallel streams of information, resembling a property already observed in cortical visual neurons of mammals [18]. In addition to VT1, the authors further describe two other novel cells specialized for translational optic flow: these VT2 and VT3 cells are sensitive to flow matched to motion in the vertical, lift direction. As with VT1, these cells present greater motion sensitivity in the ventral visual field, in agreement with their function of detecting translational self-motion.

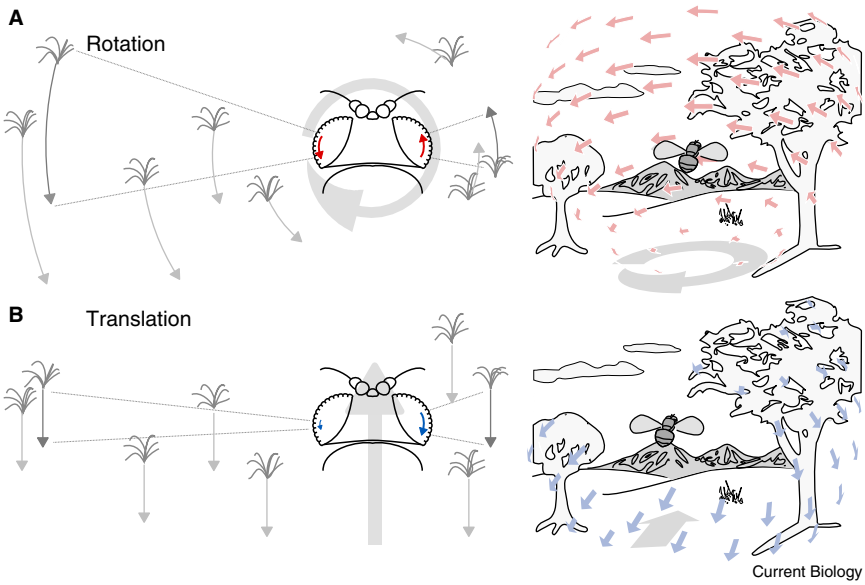

Figure 1. Rotation and translation generate distinct patterns of optic flow.
(A) A rotating viewer sees images slip over the retina with a speed proportional to the angular speed. This creates a flow-field where all objects, except those along the axis of rotation, seem to move. (B) A translating viewer sees images moving with a speed proportional to the viewer's motion, but inversely proportional to object distance. The flow-field is more complex, but quickly moving images are exposed as likely to be nearby objects, and still images are likely far away.

Watching flies buzz around, you will surely notice their remarkable ability for avoiding obstacles, chasing one another, and stabilizing flight at breathtaking speeds. Such ability largely exceeds that attained by human-designed flying machines [9], implying there is still much to learn from nature-designed machines, such as *Calliphora* [19]. Remarkably, the computations required for keeping the fly aloft reside in a small area of a tiny brain. The performance of this network, operating from the cockpit of the fly, is becoming progressively better understood, but remains full of difficult problems. The discovery of VT1–3 cells by Longden *et al.* [2] helps to fill in crucially incomplete information about translational optic flow and parallax processing, an important step towards cracking this puzzle.

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Mechanosensation: A Catch Bond That Only Hooks One Way

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Single-molecule force spectroscopy and modeling have revealed that the adhesion molecule vinculin and F-actin form a catch bond that is dependent on the direction of forces along the actin filament. This may underlie the mechanisms by which cells sense directional physical cues.

In the past decade, advances in mass spectrometry, structural biology, force spectroscopy and imaging tools have contributed to great progress in understanding how cells feel and respond to strain, shear stress, and extracellular matrix stiffness in a process termed cellular mechano-transduction. However, it is well established that cells sense not only the magnitude, but also the direction of physical cues, by mechanisms that remain mysterious: flow-mediated shear stress on endothelia induces inflammatory or atheroprotective signaling depending on the flow direction [1]; left–right asymmetry of vertebrates is established by directional fluid flow in the ventral node of developing embryos [2]; several cell and tissue types re-orient their cytoskeletons and polarize relative to the direction of applied strain or shear stress [3]; and cell migration up extracellular matrix stiffness gradients is thought to mediate development and cancer metastasis [4]. In a recent study, Dunn and colleagues [5] provide important new insight into the molecular-scale basis of the cellular response to directional physical cues by showing differential bond dynamics and strength between two critical mechanotransduction proteins, actin and vinculin, depending on the direction of applied force.

Many cellular responses to physical cues are mediated by interactions between transmembrane integrins and their extracellular ligands [6]. Integrins transmit mechanical information across the cell membrane via a series of protein–protein interactions between the extracellular ligand and the actin cytoskeleton. Transmission of mechanical cues by integrins is transduced into cytoskeletal and adhesion remodeling, tuning cellular adhesion strength to counter mechanical perturbations and coordinate intracellular signaling pathways.

The molecular basis of force-induced adhesion strengthening via integrins has been attributed to either force-dependent recruitment of additional adhesion proteins (i.e. increased avidity) or force-mediated increase in bond strength and lifetime between individual proteins (i.e. increased affinity) [7]. Although mechanical regulation of avidity and affinity is most often considered in the context of integrin clustering and activation, similar principles also apply to other adhesion proteins.

A well-studied example of force-induced avidity changes is the strengthening of the integrin–actin connection via force-mediated increase in the number of talin–vinculin–actin interactions. Talin mediates a relatively weak link between integrin and actin by binding both proteins simultaneously [8]. When force is applied across this link, talin unfolds, revealing several binding sites for the actin-binding protein vinculin [9]. The integrin–actin linkage is thus thought to be strengthened by increasing the number of talin–actin connections through the recruitment of