

feature of spatial location is quite distinct from all other features in the authors' formulation, with an imposed anisotropy that then determines the patterns of all the other maps. This would suggest an underlying molecular marker rather than a purely activity-driven mechanism, although it is possible that constraints posed by the overall shape of V1 may lead to similar outcomes. Some recent work suggests that spatial mapping in V1, in particular, is driven by activity rather than molecular markers (Eglen et al., 2003). On the other hand, while a large body of literature suggests that ocular dominance is determined by neural activity, some recent work suggests that a molecular message may also be involved (Crowley and Katz, 2000). It would be very interesting to see whether insights from development could be used to inform models of cortical organization and whether formal, testable models can be developed that specifically discriminate between mechanisms that demand molecular markers, or activity alone, or some particular interaction between the two so as to gain further understanding of this important process.

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Noncommutativity of Eye Rotations and the Half-Angle Rule

In order to produce kinematically efficient behavior

when dealing with the noncommutativity of rotations, the oculomotor system has developed strategies such as the half-angle rule. In this issue of *Neuron*, Ghasia and Angelaki demonstrate that during smooth pursuit eye movements the half-angle rule is implemented by the mechanical properties of the eye plant.

Our eyes can rotate in three dimensions (3D): horizontally, vertically, and torsionally. A major goal in studies of oculomotor control is to determine the mechanisms governing such rotations. However, in order to properly study such mechanisms one must take into account a fundamental principle of rotational geometry; rotations of a rigid body in 3D are noncommutative. This can be easily seen in Figure 1.

Imagine we are holding a globe of the earth positioned to face the African continent (Figure 1A). If we rotate it 90° to the left around a vertical axis, we will face the Americas (Figure 1B), and if we then rotate it 90° up around a horizontal axis, we will face Antarctica (Figure 1C). On the other hand, if from the same initial position, facing Africa, we rotate the globe first 90° up (Figure 1D) and then 90° to the left, we will end up facing a tilted view of the Americas (Figure 1E). This demonstrates that “left and then up” ≠ “up and then left,” i.e., rotations are noncommutative. It is important to note that in both cases the axes were similar, only the order of rotations changed. This principle, applied to the study of eye rotations by Tweed and Vilis (1987), made existing commutative models using simple integrators of angular velocity to position insufficient to predict oculomotor behavior.

An example of how the oculomotor system deals with noncommutativity is the half-angle rule in Listing's law. Listing's law, described more than a century ago by Johannes Benedict Listing (1808–1882), states that when the head is fixed, there is an eye orientation called “primary position” from which all other orientations that the eye assumes can be reached by a single rotation around an axis in a plane (i.e., Listing's plane). Consequently, during eye movements that obey Listing's law (e.g., saccades and smooth pursuit), the eyeball assumes a unique torsion for each possible eye orientation (Crawford et al., 2003). In fact, if we define torsion about the head-fixed axis of rotation orthogonal to Listing's plane, then Listing's law simply states that torsion is held at zero.

A critical aspect concerning Listing's law is the half-angle rule, which states that in order to keep eye position within Listing's plane, the angular velocity axes of eye rotation must tilt out of the Listing's plane by half the angle of the gaze's deviation from primary position. What are the physiological mechanisms underlying the implementation of the half-angle rule? For years there has been a debate between a neural implementation (Tweed and Vilis, 1987) and a mechanical implementation (Schnabolk and Raphan, 1994), leaving modelers in the awkward situation of trying to simulate the 3D oculomotor system both ways. The difference is important since it requires two very different configurations of signals in the brainstem—albeit signals that are very difficult to record using our current experimental technology.

In this issue of *Neuron*, Ghasia and Angelaki report a

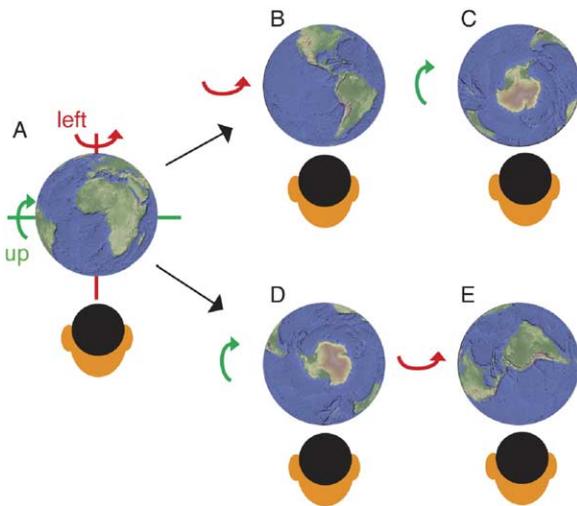


Figure 1. Noncommutativity of Rotations

discovery that may shed some light onto this question (Ghasia and Angelaki, 2005). These authors examined the responses of single neurons that innervate the extraocular muscles of head-restrained macaque monkeys under two different experimental conditions. In the first condition, the animals were trained to pursue a visual target that moved horizontally or vertically at different eccentricities. In the second condition, the animals maintained their gaze on a point fixed in space while their heads and bodies were passively rotated. The latter elicits a vestibulo-ocular reflex (VOR), i.e., a counter-rotation of the eyes of approximately equal amplitude and opposite direction as the head.

In both cases, the authors measured the three velocity components (vertical, horizontal, and torsional) of the eye rotations. They classified the torsional eye velocity generated during smooth pursuit as “noncommutative-driven torsion,” as it represents the torsion needed to implement the half-angle rule. In addition, they defined “sensory-driven torsion” as the torsional velocity generated during the VOR since it is driven by sensory signals coming from the vestibular organs (note that the VOR response does not obey Listing’s law and the half-angle rule).

They elaborated on the following alternatives. If during smooth pursuit motoneurons encode the torsional component of eye velocity through their firing pattern, then the half-angle rule is implemented within the pre-motor neural circuitry that drives the eye muscles. If, on the other hand, motoneurons do not encode the torsional velocity, then the half-angle rule must be implemented by downstream mechanical constraints within the orbit.

An important detail in these experiments is that the oculomotor neurons, whose response was measured, provide the only pathway between neural structures and extraocular muscles. These neurons represent the final result of the neural processing stage (i.e., the commands sent by the brain to the muscles). Therefore, any eye movement parameter that is not specified by the neurons’ firing pattern must be implemented mechanically within the orbit. Figure 2 illustrates this idea.

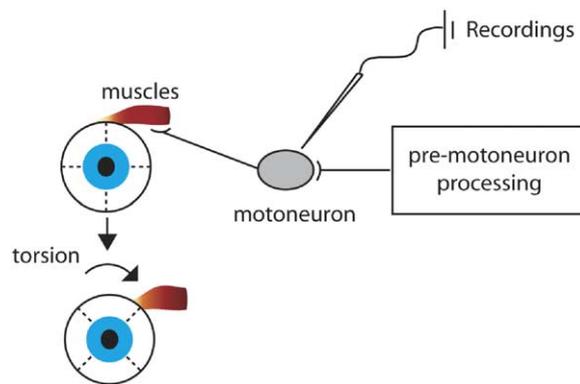


Figure 2. What the Brain Tells the Muscles

The experiments had two main results. During smooth pursuit eye movements, motoneurons innervating the superior and inferior rectus and the oblique muscles, which play a major role in generating eye torsion, did not significantly modulate their firing rate as a function of torsional eye velocity. In contrast, during the VOR, the same units did modulate their response as a function of torsional eye velocity.

From these results, the authors conclude that during smooth pursuit tracking oculomotor neurons do not encode the noncommutative torsion needed to keep the eyes within Listing’s plane (i.e., to implement the half-angle rule). Therefore, this torsion must be implemented by the mechanical properties of the eye plant (eyeball and surrounding tissues). This conclusion has important implications for oculomotor physiology and brings about many new and exciting questions.

For example, which mechanical properties of the eyeball could implement the half-angle rule during smooth pursuit? Demer et al. (1995) have proposed that sheets of connective tissue and smooth muscle attached to the orbit (pulleys) can modify the extraocular muscles axes of rotation as a function of eye orientation. The existence of pulleys has been well documented in anatomical studies (Demer et al., 1995), and model simulations of pulleys’ behavior suggest that they could play a role in eye movements’ kinematics (Quaia and Optican, 2003).

A serious criticism of this hypothesis has been that pulleys must adopt different anatomical arrangements during the VOR (which violates Listing’s law) and during smooth pursuit and saccades. Demer and colleagues have suggested that a possible retraction of the pulleys may account for the violations of Listing’s law during the VOR (Kono et al., 2002). However, Misslisch and Tweed (2001) have demonstrated that the retraction needed to account for such violations is physiologically unrealistic. The latter authors have made an interesting observation: if one takes into account that the VOR is weak in the torsional dimension, then a single mode of pulley action can serve both VOR kinematics and Listing’s law (Misslisch and Tweed, 2001). Currently, it seems to be clear that pulleys play a role in orbital mechanics, but further research must be done in order to fully characterize the extent to which pulleys implement eye torsion.

Other questions arising from the results reported by Angelaki and colleagues are which eye parameters brainstem motoneurons encode and in which coordinate system? Tweed et al. (1999) have proposed that motoneurons encode a combination of eye position and the rate of change of eye position. This idea is compatible with the mechanical implementation of the half-angle rule during pursuit eye movements proposed by Ghasia and Angelaki (2005). Mechanical constraints could alleviate the processing load in the premotor circuitry and provide a default model of the eye plant that at least in some cases—as for movements that obey Listing's law—does not require noncommutative processing at the immediate premotor stage. Regarding the coordinate system, it has been suggested that motoneurons may encode movement parameters in Listing's coordinates (Crawford, 1994). However, further work is needed in order to fully test this idea.

Another question related to the previous one is whether there is noncommutative processing in the neural circuits of the oculomotor system. Using behavioral experiments, Tweed et al. (1999) have provided strong evidence for noncommutative processing in the vestibulo-ocular reflex, and Smith and Crawford (2001) have demonstrated that the process that updates spatial memory across saccades accounts for the noncommutative aspects of eye rotation. These earlier findings are consistent with those of Ghasia and Angelaki, whose experiments deal with the half-angle rule and the variables coded by motoneurons, not the presence or absence of noncommutative processing upstream from the motoneurons. It is important to remember that the half-angle rule is just one aspect of noncommutativity in the oculomotor system.

Together, the data suggest that the eye muscles and pulleys are arranged to simplify the implementation of Listing's law and the half-angle rule, but they still require appropriate neural commands, and when some muscles are paralyzed the brain can adjust its commands to restore Listing's law (Wong, 2004), despite irreversible changes in the oculomotor plant caused by the disease.

An important clinical implication of Ghasia's and Angelaki's findings concerns the surgical treatment of strabismus (a disease resulting in misalignment of the two eyes). Most of the pre- and postsurgery clinical evaluation of this disease has concentrated on determining the degrees of horizontal and vertical misalignment, giving less importance to torsion (Wong, 2004). Since strabismus surgery deals primarily with the eye plant, it is important to determine what a given procedure does to the structures that implement the half-angle rule and control eye torsion and what are the consequences of such manipulations for vision and behavior.

In summary, the experiments of Ghasia and Angelaki are the first to characterize the response properties of motoneurons during dynamic stimuli that require noncommutative oculomotor processing while controlling all three components of eye rotations (horizontal, vertical, and torsional). Their results are relevant not only for the study of the oculomotor system, but also for the study of any system in which noncommutative operations are required—from rotations of the arm about the

shoulder joint to rotations of the foot about the ankle. Such systems seem to be more the rule than the exception in biology.

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