

# Pivotal Role of Orbital Connective Tissues in Binocular Alignment and Strabismus

## The Friedenwald Lecture

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The stereotypic structure and location of the orbital connective tissues have long been recognized.<sup>1-3</sup> The notion that these tissues might control extraocular muscle (EOM) paths was proposed in the late 19th century, when Sappey applied the French term "poulie" to their function of bowing EOM paths.<sup>4</sup> The concept was promptly forgotten, displaced by the idea that EOM actions were completely determined by the geometry of their origins and insertions. In the 1970s, the pioneering biomedical engineer David A. Robinson recognized that digital computers might calculate predicted results of strabismus surgery based on known geometry of the globe and EOM insertions.<sup>5</sup> This apparently reasonable enterprise failed, and Robinson quickly realized that the mathematical analysis of ocular motility is impossible without constraints on the EOM pathways. Robinson proceeded with a tentative monocular model based on a seemingly reasonable guess about rectus EOM path constraints,<sup>5</sup> a model later extended into binocular form in collaboration with Joel M. Miller.<sup>6</sup> The Miller model provided satisfactory solutions for simple horizontal strabismus, such as eso- and exotropia and their surgical corrections, but failed in such situations as surgical transposition of cyclovertical muscles.<sup>7</sup> Miller suspected that the major defect of these quantitative models was incorrect specification of EOM paths. He proposed that radiography<sup>8,9</sup> and magnetic resonance imaging (MRI)<sup>7</sup> of the orbits might directly demonstrate EOM paths. In a seminal paper in 1989, Miller repeated MRI scans in normal humans in the full range of secondary and tertiary gaze positions. He found that MRI could be used to assess EOM paths, cross sections, and contractile changes with gaze.<sup>7</sup> Based on the surprising but consistent finding that posterior EOM paths remain stable even during the largest gaze shifts, Miller made the first proposal of the modern notion of pulleys—muscle sheaths at and posterior to the globe equator and coupled to the orbital wall so that they constrain rectus EOM paths.<sup>7</sup> The further demonstration by Miller et al.<sup>10</sup> that posterior EOM paths remain stable even after surgical transposition of the scleral insertions provided compelling, albeit indirect, evidence for the existence of pulleys.<sup>10-12</sup> Pulleys have subsequently proven fundamental to every aspect of ocular motility.

### Structure of Pulleys

One may suppose that rectus pulleys escaped historical recognition as such because of a lack of appreciation of their mechanical necessity and because of technical problems in the study of orbital anatomy. Removal of soft tissues from the orbit, particularly piecemeal, severely distorts connective tissue relationships normally maintained by a mutual distribution of elastic and muscular tension ultimately against dense adhesions to the thick bones of the orbital rim. Pulley structures are easily missed at dissection and microscopy, unless the entire orbit is maintained intact in continuity with the surrounding bones until hardened by fixation, or unless noninvasive imaging is used.<sup>13</sup> Motivated by the compelling MRI evidence of the existence of pulleys supplied by Joel Miller,<sup>7</sup> and Miller et al.,<sup>10</sup> we undertook the labor-intensive process of serially sectioning intact human and animal orbits for histologic processing<sup>13-21</sup> and ultimate digital reconstruction at microscopic resolution.<sup>22</sup> This effort, cumulatively involving some 4000 to 5000 serial sections of 10- $\mu$ m thickness in each of 10 human, 18 monkey, and 3 nonprimate mammalian orbits, has demonstrated consistent anatomy of the pulleys and orbital connective tissues across species as diverse as rat,<sup>23</sup> rabbit, dog, horse, monkey, and human.<sup>15,20</sup>

The following general properties of pulleys have emerged. Each rectus pulley consists of an encircling sleeve and ring of collagen located near the globe equator in Tenon's fascia,<sup>14</sup> coupled to the orbital wall, adjacent EOMs, and equatorial Tenon's fascia by slinglike bands containing collagen, elastin, and richly innervated smooth muscle.<sup>15</sup> Ultrastructure of the arrangement of pulley collagen reveals specialization for high internal rigidity.<sup>24</sup> Pulleys deflect rectus and inferior oblique (IO) EOM paths in a manner qualitatively similar to the inflection of the superior oblique (SO) tendon path by the trochlea, although the rectus pulleys are less rigid. As might have been expected from the classically understood uniformity of orbital connective tissue structure,<sup>1</sup> the coronal plane location of each rectus pulley as determined by MRI is highly uniform in normal subjects.<sup>25</sup> Pulleys are arrayed in the coronal plane roughly as the ends of the arms of a cross. It was classically noticed, but perhaps not broadly recognized, that the EOMs insert not only on the globe via their tendons, but also attach to the enveloping connective tissues of Tenon's capsule.<sup>1,4</sup> Later histologic examinations revealed that it is the fibers of the orbital layer (OL) of each rectus EOM that terminate on the connective tissue.<sup>26,27</sup> The global layer (GL) of each rectus EOM, containing about half of the EOM fibers,<sup>20</sup> passes through the pulley and becomes contiguous with tendon to insert on the globe; the OL, containing the remaining roughly half of the EOM fibers, inserts on the pulley.<sup>16,20</sup> At least to a first approximation, GL fibers rotate the globe, whereas OL fibers translate their respective pulleys to control the direction of globe rotation.

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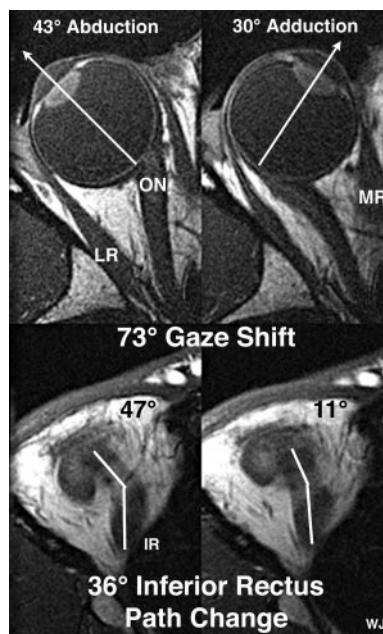
## Kinematics of Pulleys

In 1989 Joel M. Miller first suggested that orbitally fixed pulleys would make the eye's rotational axis dependent on eye position.<sup>7</sup> This insight that pulleys constrain ocular torsion has proved pivotal.<sup>28</sup> Rectus pulleys are fundamental to ocular kinematics, the rotational properties of the eye. Successive rotations of any solid object are not mathematically commutative, in that final eye orientation depends on the order of rotations.<sup>29</sup> Furthermore, angular velocity differs from the rate of change of orientation, being a function of both the time derivative of and instantaneous value of orientation.<sup>30,31</sup> Each combination of horizontal and vertical orientations of an arbitrary sphere could be associated with infinitely many torsional positions.<sup>32</sup> The eye, however, is constrained (with the head upright and immobile) by a relationship known as Donders' Law,<sup>33</sup> stating that there is unique torsion for each combination of horizontal and vertical eye positions.<sup>30</sup> Listing's Law, a specific case of Donders' Law, states that the torsion of the eye in any orientation is that which it would have if it had reached that orientation from primary position by a single rotation about an axis lying in a plane, Listing's plane.<sup>34</sup> Tweed and Vilis<sup>31</sup> showed that Listing's Law is always satisfied if the ocular rotational axis shifts by exactly half of the shift in ocular orientation. For example, if the eye rotates up by 20°, then the vertical axis about which it rotates for subsequent horizontal movement should tip back by 10°. This is called the "half-angle rule." It can be shown mathematically that conformity to the half-angle rule renders successive ocular rotations effectively commutative to motor control centers in the brain.<sup>35</sup> We have come to regard this property of commutativity as the critical feature of the pulley system for neural control of ocular movement, prominent in every aspect yet studied. For brevity, the classic form of Listing's Law is abbreviated L1.

A direct test of the role of rectus pulleys in half-angle kinematics has been provided by MRI of EOM paths during gaze shifts. Figure 1 shows axial views of a right eye before and after rotating horizontally from adduction and abduction. In each case, the image plane that includes the lens and optic nerve shows the direction of gaze (arrow), and the simultaneously acquired more inferior image plane that contains the inferior rectus (IR) muscle shows two linear components of its path. The IR clearly does not rotate the globe toward the anatomic origin at the orbital apex. The posterior IR path is uninfluenced by gaze direction, although anterior to a sharp inflection behind the globe equator, a second straight segment makes a 36° directional change with the 73° gaze shift. The IR's pulling direction, defined by the direction of the segment anterior to the inflection at its pulley, changes by almost precisely half the amount of the gaze change. The rotational axis, which is perpendicular to the path of the terminal segment, also changes by half the gaze change. Simple small-angle trigonometry (Fig. 2) shows that to accomplish this the IR pulley must be located as far posterior to globe center as the IR insertion is anterior to globe center. This arrangement compels the IR to exhibit half-angle kinematics consistent with L1. All four rectus EOMs behave identically.<sup>36</sup> Because the rotational axis of each muscular force acting on the globe observes half-angle kinematics, ocular rotation conforms to L1.

The inflections in rectus EOM paths due to pulleys are not dependent on presence of the globe at all. In fact, after surgical enucleation of the globe for intraocular cancer, the MR path inflection at its pulley continues to shift anteroposteriorly with horizontal gaze, but the angle of inflection sharpens to as much as 90° at the pulley!<sup>37</sup>

The MRI example in Figure 1 illustrates how appropriate pulley location can implement half-angle kinematics during shifts between primary and secondary gaze positions that are

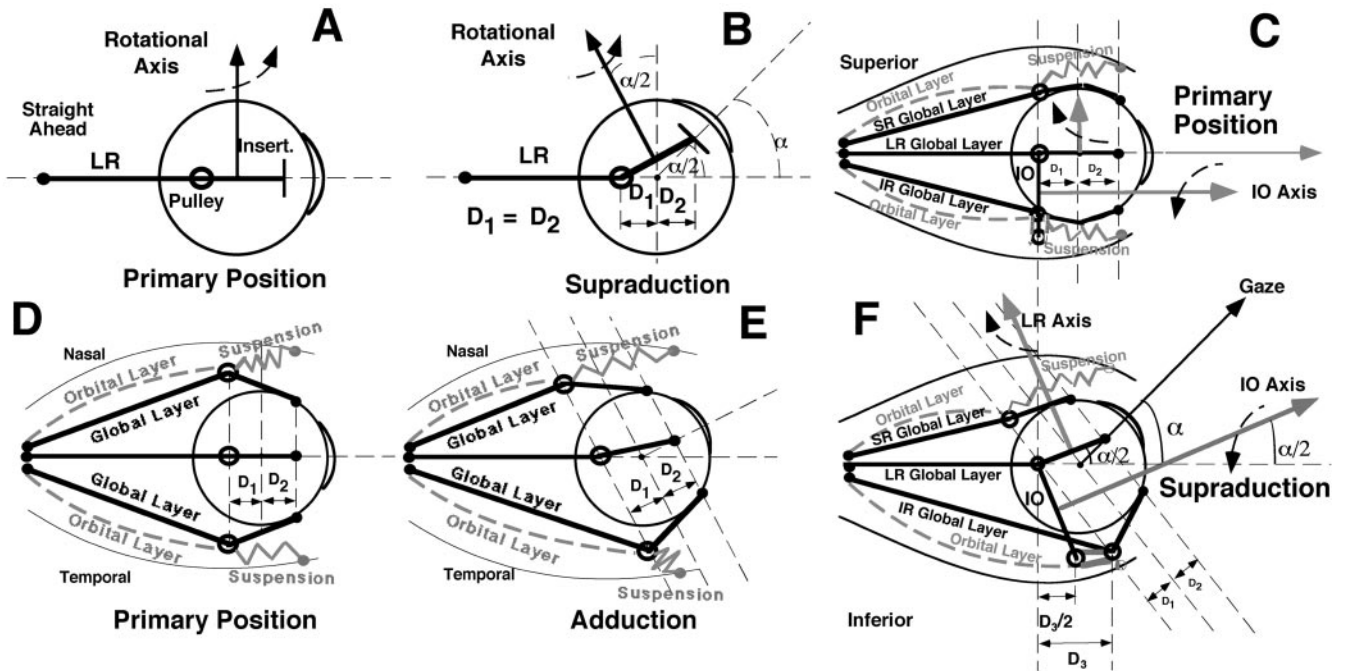


**FIGURE 1.** Axial MRI scans (2 mm thickness, T<sub>1</sub> weighted) of a human right orbit taken at the level of the pupil center and optic nerve (*top row*), and simultaneously along the path of the inferior rectus (IR) muscle (*bottom row*), in abduction (*left column*) and adduction (*right column*). Note the bisegmental IR path. For this 73° horizontal gaze shift, there was a corresponding 36° shift in the path of the IR muscle anterior to the inflection at its pulley. This is a direct demonstration of the half-angle shift of the IR pulling direction with the gaze shift required by L1. Although the pulley tissues are not directly visualized with this technique, pulley location based on the IR path inflection may be inferred to be between the equator and the posterior pole of the globe.

trigonometrically small angles typical of the oculomotor range. (This small-angle assumption is made throughout.) The distance  $D_1$  from pulley to globe center need only be equal to distance  $D_2$  from globe center to scleral insertion for each rectus EOM. If primary and secondary gaze positions were the only ones ever required, the rectus pulleys could be rigidly fixed to the orbit in the proper position. However, tertiary gaze positions such as adducted supraduction require the rectus pulleys to shift anteroposteriorly in the orbit along the EOM's length, so that the relationship  $D_1 = D_2$  is maintained in an oculocentric reference (Fig. 2E).

## Active Pulley Hypothesis

Evidence of posterior shifts of pulley tissues during rectus EOM contraction obtained in humans by MRI motivated proposal of the active pulley hypothesis (APH) that these shifts are generated by the contractile activity of the OLs of each EOM acting against the elasticity of the pulley suspensions.<sup>16-18,36</sup> Specific action of the IR OL to shift the IO pulley can readily be demonstrated in living humans by using MRI in a quasisagittal plane parallel to the IR's path (Fig. 3). Figure 3 shows that the OL and GL are demarcated by a bright fatty septum. The GL is in continuity with the scleral insertion, exhibiting modest contractile thickening in infraduction. The OL terminates in the region of the coupled IR and IO pulleys, exhibiting marked contractile thickening in infraduction associated with straightening of associated connective tissue bands as the IO muscle shifts posteriorly. The coordinated control postulate of the APH is a conjecture for kinematics conforming to L1. Under coordinated control, the rectus pulleys shift anteroposteriorly in the orbit by the same distance as the scleral insertion, while



**FIGURE 2.** Diagram of rectus and IO pulley behavior for half-angle kinematics conforming to Listing's Law L1. (A) Lateral view. For each rectus EOM, the rotational axis is perpendicular to the segment from pulley to scleral insertion. The axis for the LR is vertical in primary position. (B) Lateral view. In supraduction to angle  $\alpha$ , the LR rotational axis tilts posteriorly by angle  $\alpha/2$  if distance  $D_1$  from pulley to globe center is equal to distance  $D_2$  from globe center to insertion. (C) Lateral view. In primary position, the terminal segment of the IO muscle lies in the plane of the LR and IR pulleys into which the IO's OL inserts. The IO rotational axis is parallel to the primary gaze direction. (D) Superior view of rectus muscles and pulleys in primary position, corresponding to (A). (E) Superior view. To maintain  $D_1 = D_2$  in an oculocentric reference in adduction, the MR pulley must shift in the orbit posteriorly and the LR pulley anteriorly. This is implemented by contractile changes in the OLs of these EOMs, working against elastic pulley suspensions. (F) Lateral view similar to (C). In supraduction to angle  $\alpha$ , the IR pulley shifts anteriorly by distance  $D_3$ , as required by the relationship shown in (E). The IO pulley shifts anteriorly by  $D_3/2$ , shifting the IO rotational axis superiorly by angle  $\alpha/2$ .

remaining stable in the transverse direction. Direct, quantitative confirmation of this behavior has been obtained for each of the four rectus EOMs in living humans, by using MRI to locate the path inflections corresponding to the pulleys.<sup>36</sup>

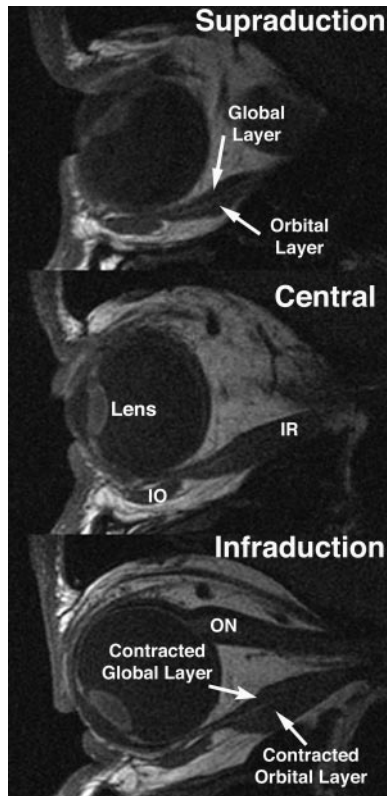
Of course, coordinated control could not be the trivial consequence of simple attachment of rectus pulleys to the underlying sclera. Not only does abundant anatomic evidence from our vast collection of serially sectioned orbits disprove such attachment, but the sclera moves freely relative to pulleys in a direction transverse to the longitudinal EOM axes. Further, anteroposterior rectus pulley movements persist even after removal of the eyeball.<sup>37</sup>

Even during coordinated movements, however, ocular rotation by the GL and pulley translation by the OL require fundamentally different EOM actions and neural commands. The mechanical load on the GL is predominantly the viscosity of the relaxing antagonist EOM, a load proportional to the speed of eye rotation, and thus slight during sustained eccentric gaze.<sup>38</sup> The mechanical load on the OL, however, is due to the elasticity of the pulley suspension. This elastic load is independent of rotational speed, but constantly proportional to the angle of eccentric gaze. Selective electromyography (EMG) in humans correspondingly shows high, phasic activity in the GL during rapid saccadic eye movements, with only a small sustained change in activity in sustained eccentric gaze.<sup>38</sup> In the OL, EMG shows sustained, high activity in eccentric gaze, but no phasic activity during the flight of saccades.

### Muscle Compartmentalization

Differing mechanical loads on the OL and GL are associated with corresponding structural, vascular, genomic, and meta-

abolic specializations. Within individual humans, GLs of each of the four rectus EOMs contain a similar number of fibers, in the range of 8,000 to 16,000. This similarity is appropriate, because all rectus OLs act to rotate the same essentially symmetrical load, the globe. Within individuals, the number of OL fibers varies more widely in the range of 7,000 to 14,000, in rough proportion to the amount of connective tissue suspending each pulley.<sup>20</sup> Most fibers in the OL are fast, twitch-generating, singly innervated fibers (SIFs), whereas the rest are multiply innervated fibers (MIFs) that either do not conduct action potentials or do so only in their central portions.<sup>26</sup> Orbital SIFs are specialized for intense oxidative metabolism and fatigue resistance.<sup>26</sup> Vascular supply in the OL is so much higher than in the GL that intravenous MRI contrast can be seen to perfuse the OL first.<sup>21</sup> The high metabolism, fatigue resistance, and luxurious blood supply of the numerous OL SIFs are tailored to their continuous elastic loading by the pulley suspensions. Expression of unique myosin isoforms in OL SIFs may also be related to the requirements of fast-twitch capability against continuous loading, because alterations in EOM activity patterns can change EOM-specific myosin heavy chain gene expression.<sup>39</sup> Approximately 90% of GL fibers are fast, twitch-generating SIFs, whereas 10% are slow, non-twitch MIFs having a broad range of fatigue resistance.<sup>26</sup> The motor nerve arborization for the OL is distinct from that of the GL for all four human rectus EOMs.<sup>40</sup> Motor unit size is exceedingly fine in the GL, averaging about one axon per muscle fiber for each human rectus EOM.<sup>40</sup> This probably reflects the precision required of ocular rotation. Motor unit size is coarser in the OL, averaging 5 fibers per axon in horizontal rectus and 2.5 in vertical rectus EOMs.<sup>40</sup> Coarser OL motor unit size probably reflects less



**FIGURE 3.** MRI scan (2 mm thickness, T<sub>1</sub> weighted) of human orbit in quasisagittal plane parallel to path of IR muscle in three gaze positions. Note demarcation of the OL and GL layers of the IR muscle by a thin, bright, fatty septum. The GL, in continuity with the scleral insertion, exhibits modest contractile thickening in infraduction. The OL, terminating in the IR pulley (not directly seen using this technique), exhibits marked contractile thickening in infraduction. The IO muscle shifts posteriorly with infraduction, but only half as far as the lens and other ocular structures. ON, optic nerve.

required precision for pulley control, but is still quite precise by skeletal muscle standards.

### Oblique Muscles

The rectus EOMs by themselves seem capable of implementing this rich spectrum of ocular kinematics, leading even to the supposition that the oblique EOMs might be unnecessary to L1 behavior.<sup>41</sup> The differential control postulate of the APH was proposed to account for ocular motor kinematics such as observed during the vestibulo-ocular reflex (VOR)<sup>42</sup> and during convergence<sup>43-45</sup> not conforming to L1. The differential control postulate supposed that pulleys might shift anteroposteriorly along the EOM axes by amounts differing from the shifts of the scleral insertions.<sup>16</sup> Violation of the  $D_1 = D_2$  relationship in Figure 2 would impart non-L1 torsional action to any rectus EOM. The original concept of differential control supposed larger anteroposterior shifts of pulleys during the VOR than during visually guided eye movements.<sup>16</sup> The originally proposed large pulley shifts have been shown to be unable to account for behavior of the VOR during low-frequency sinusoidal head rotation.<sup>46</sup> Although not ruled out by any data, no evidence has yet been obtained for the originally proposed differential control of rectus pulley positions. Instead, MRI has demonstrated unanticipated transverse shifts of pulleys in situations violating L1.

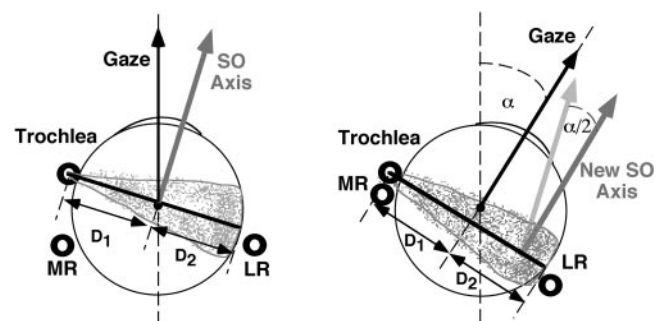
The IO muscle also observes half-angle kinematics, as illustrated in Figures 2C and 2F. Histologic examination of human

and monkey orbits indicates that the IO OL inserts on the conjoined IO-IR pulleys, as well as the LR pulley.<sup>19</sup> In primary position, these two OL insertions constrain the distal segment of the IO to lie in the plane of the IR and LR pulleys, so that IO rotational axis is perpendicular to the primary gaze line, and perpendicular to the rotational axes of the rectus EOMs. In the Listing's coordinate system of the pulleys, the IO then has a purely torsional action, capable of nothing other than violating L1. (In other coordinate systems such as used for clinical examination, the IO would also have supraducting and abducting actions.) As suggested by Figure 3, quantitative analysis of MRI images indicates that with oblique gaze shift from supraducted adduction to infraducted abduction, the IO pulley moves anteroposteriorly by about half the amount of the equal movements of the IR pulley and scleral insertion.<sup>19</sup> Figure 2F illustrates that the half coupling of IO pulley to IR pulley motion in turn causes half-angle shift of the IO rotational axis. Not diagrammed in Figure 2, but following similar reasoning, during horizontal gaze shift, this anteroposterior IO pulley shift is also half the amount of the equal movements of the LR pulley and scleral insertion. Anteroposterior shift of the IO pulley during vertical and horizontal ductions fulfills the kinematic requirements of commutativity, albeit without direct contribution to L1.

The SO, with its immobile pulley at the trochlea, is actually a special case. The remote location of the SO insertion from the trochlea implies that this pulley cannot, as done by the other five soft pulleys, stabilize SO tendon path by preventing sideslip over the globe. Instead, the uniquely broad SO insertion on the sclera resists sideslip by virtue of its fan-like shape as it courses from the narrow trochlea. The SO nevertheless approximates half-angle kinematics, as illustrated in Figure 4 for horizontal eye rotation. Because the distance  $D_1$  from trochlea to globe center is approximately equal to distance  $D_2$  from globe center to insertion, the SO rotational axis shifts by half the gaze angle during horizontal duction. An analogous geometry provides a similar effect for vertical duction.

### Kinematics of Convergence

In addition to horizontal convergence, stereopsis requires adjustments in the torsional positions of the eyes to maintain alignment of corresponding retinal meridians.<sup>47</sup> This amounts to rotation around the line of sight. Excyclotorsion in convergence violates L1, but has been repeatedly confirmed in humans<sup>44,48-52</sup> and monkeys.<sup>53</sup> During asymmetrical convergence to a target aligned to one eye, this temporal rotation occurs in both the aligned and converging eyes, independent of eye position.<sup>45</sup> A concise description of this behavior is that Listing's plane for each eye tilts temporally with conver-



**FIGURE 4.** Axial diagram of SO kinematics. **Bold line:** SO tendon; **small circles:** pulleys. Distance  $D_1$  from trochlea to globe center is equal to distance  $D_2$  from globe center to SO insertion. During abduction by angle  $\alpha$ , SO rotational axis shifts temporally by angle  $\alpha/2$ .

gence,<sup>45,49,50,54,55</sup> formalized as L2, the binocular extension of Listing's Law L1.<sup>43</sup> It has been further proposed that a form of Herring's Law of equal innervation exists for the vergence system, such that both eyes receive symmetric version commands for remote targets, and mirror symmetric vergence commands for near targets.<sup>43</sup>

Convergence to a target aligned to one eye has been performed during MRI in eight humans, by using a mirror arrangement.<sup>56</sup> The experiment confirmed and extended to humans the finding of Miller et al.<sup>57</sup> in monkey that the horizontal rectus EOMs do not co-contract in convergence. In the orbit aligned to the target, analysis of IR, MR, and SR muscle paths demonstrated a 0.3- to 0.4-mm extorsional shift of the their pulleys in the coronal plane during 22° convergence.<sup>56</sup> Although the lacrimal gland prevented determination of LR pulley location, it is likely that all four rectus pulleys shifted extorsionally approximately 1.9°. This amount is similar to estimates of globe extorsion under these conditions.<sup>48</sup> These findings suggest that during convergence, the rectus pulley array rotates in the coronal plane in coordination with ocular torsion, as diagrammed in Figures 5A and 5B. As illustrated in Figure 5B, one consequence of this binocular extorsion of the pulley array is vertical misalignment of the horizontal pulling directions of the horizontal rectus EOM pairs. Unless the brain adjusts cyclovertical EOM innervation to compensate for this misalignment, this finding predicts that other eye movements superimposed on convergence would become misaligned.<sup>56</sup> This prediction has been confirmed for the horizontal angular VOR, evoked by transient, whole-body yaw rotation in darkness.<sup>58</sup> Although the vertical positions of the two eyes remain matched during the VOR for distant viewing, during 22° convergence in central gaze, the adducting eye elevates slightly above the abducting eye. The amount of this vertical skewing of the horizontal VOR varies among individuals, perhaps due to variations in the location of vertical primary position.

### A Prediction Confirmed for Convergence

Simple, fixed pulley shifts during convergence do not account for the temporal tilting of each eye's Listing's plane specified in L2.<sup>56</sup> Temporal tilting during convergence seems most consistent with variable torsional reconfiguration of the rectus pulley array with vertical gaze: extorsion in downward gaze and intorsion in upward gaze that should concomitantly further misalign the pulling directions of the rectus EOM pairs. This prediction has also been confirmed for the horizontal angular VOR, evoked by transient, whole-body yaw rotation in darkness.<sup>58</sup> Vertical skewing of the horizontal angular VOR during convergence increases significantly when the target is moved downward 20° from the center, but reverses significantly when the target is moved upward 20°.

Examination of the orbital microanatomy suggests the mechanism for rectus pulley shift in convergence. The OL of the IO muscle inserts on the IR pulley and, at least in younger specimens, also on the LR pulley. Contraction of the IO OL would directly produce an extorsional shift of the LR and IR pulleys, and corresponding IO contraction has been directly demonstrated during convergence.<sup>56</sup> Inferior LR pulley shift could be coupled to lateral SR pulley shift via the dense connective tissue band between them.<sup>13</sup> The OL of the SO muscle inserts on the SO sheath posterior to the trochlea, with both the tendon and sheath reflected at that rigid pulley. Anterior to the trochlea, the SO sheath inserts on the SR pulley's nasal border. Although not directly demonstrated by MRI, relaxation of the SO OL during convergence is consistent with single-unit recordings in the monkey trochlear nucleus,<sup>59</sup> and could contribute to extorsional shift of the pulley array. The inframedial peribulbar smooth muscle may also contribute to rectus pulley extorsion in convergence.<sup>22</sup>

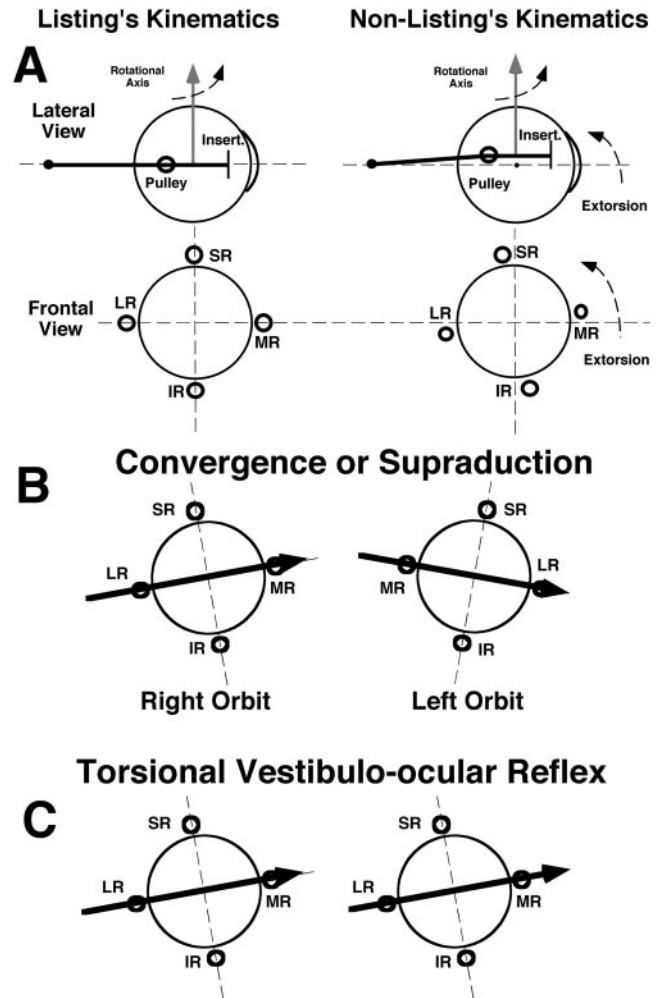
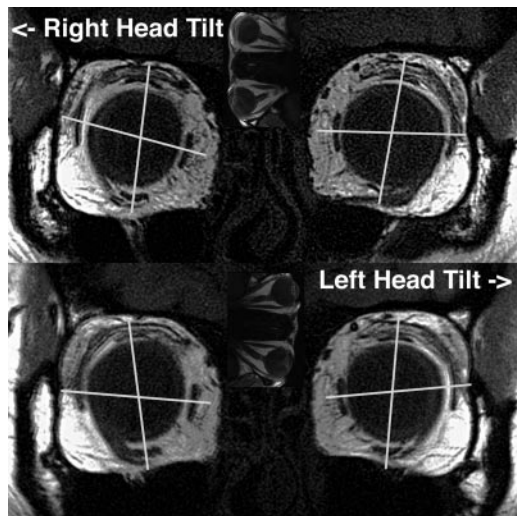


FIGURE 5. Diagram of rectus pulley shifts not conforming to classic Listing's Law L1. (A) Coordinated torsional repositioning of rectus pulleys maintains geometrical relationships responsible for half angle behavior (see Figs. 2A, 2B, 2D, 2E), but introduces a torsional offset. (B) Binocular frontal view. In convergence straight ahead, or in supraduction to a distant target, extorsional repositioning of rectus pulleys is in opposite directions in the two orbits. Note that the vertical actions of the horizontal rectus pairs (**bold arrows**) are vertically misaligned, predicting vertical binocular misalignment. (C) Binocular frontal view. During head tilt to the left, torsional repositioning of rectus pulley array is in same direction in both orbits.

### A Prediction Confirmed for Vertical Gaze

Histologic evidence for mechanical intercouplings among rectus pulleys<sup>13</sup> is supported by MRI in living humans showing small but stereotypic shifts in the coronal plane positions of some rectus pulleys, even during nonconverged, visually guided eye movements.<sup>60</sup> The IR pulley shifts nasally in supraduction and temporally in infraduction, consistent with mechanical coupling to the IO.<sup>25</sup> Also consistent with action of the IO, the LR pulley shifts inferiorly in supraduction and superiorly in infraduction.<sup>25</sup> These shifts do not serve any recognizable physiological function, yet afford an opportunity for experimental testing of the role of pulleys in binocular alignment. The pattern of vertical LR pulley shift in supraducted gaze to a distant target produces extorsion of the pulley arrays of the two orbits qualitatively identical with the effects of convergence in central gaze (Fig. 5B), leading so a similar prediction concerning vertical skewing of the horizontal angular VOR. When looking up during the VOR, the adducting eye



**FIGURE 6.** Coronal MRI scans (2 mm thickness) in lateral decubitus position of human with right (*top row*) and left (*bottom row*) side down, illustrated as upright for ease of comparison. Small axial *insets* in an absolute gravitational reference frame confirm actual head positions. Lines connect centers of rectus EOMs at level of the pulleys. Note the counterrotation of the rectus pulley array during this static torsional vestibulo-ocular reflex.

is predicted to elevate significantly above the adducting eye, with the reverse true when looking down. This is the opposite of the effect of vertical gaze shift on the pattern of skewing of the horizontal angular VOR during convergence. Magnetic search coil oculography in humans undergoing transient, whole body yaw rotation in darkness confirms this prediction of significant vertical skewing of the horizontal angular VOR during distance viewing, and that the pattern is opposite the pattern observed during convergence.<sup>58</sup> The evidence supports the notion that neural control of the VOR does not compensate for deviations of rectus pulleys from the L1 kinematic positions.

### Kinematics of the Vestibulo-ocular Reflex

Although transient vestibular stimulation requires dynamic head motion that is impossible in a MRI scanner, simply altering head orientation relative to gravity can evoke the static torsional VOR. Gravitational stimulation of the otoliths induces counterrolling of the eyes around the visual axis of  $3^\circ$  to  $7^\circ$  in response to sustained  $90^\circ$  head tilt.<sup>61</sup> Scanning in right and left lateral decubitus positions reveals a mean  $3.4^\circ$  difference in conjugate torsional position of the rectus pulley array consistent in direction with the ocular counterrolling evoked by the static torsional VOR (Fig. 6) (Demer JL, et al. *IOVS* 2002;43: ARVO E-Abstract 2736). This reconfiguration is associated with appropriate contractile changes in the cross sections of the IO and SO muscles. Recordings of the preferred ocular directions of burst neurons in monkeys are compatible with torsional shift of rectus pulleys during ocular counterroll induced by static head tilt.<sup>62</sup> In monkeys the displacement plane for three-dimensional (3-D) eye positions during pursuit and saccades also shifts opposite to changes in head orientation relative to gravity.<sup>63</sup> Taken together, these observations strongly suggest that brain stem motor and premotor neurons that control rectus EOMs generally do not compensate for the changes in pulling directions produced by pulley shifts. Neural commands to the rectus EOMs are effective only in the context of instantaneous pulley geometry, and so pulley position probably modulates the neural control of all types of eye movements.

Listing's Law L1 theoretically could be achieved without a contribution from the oblique EOMs.<sup>41</sup> In patients with chronic SO paralysis, for example, L1 is observed, albeit with a temporal tilting of Listing's plane.<sup>64</sup> It has been pointed out that, even if the oblique EOMs did not actively participate in generation of visually guided eye movements conforming to L1, the passive elastic tensions arising from stretching and relaxation of the obliques would lead to violations of L1 unless oblique innervations were adjusted to compensate.<sup>65</sup> Consequently, single-unit neural recordings of changes in oblique EOM innervations during eye movements conforming to L1 (such as pursuit tracking<sup>66</sup>) would not negate the contribution of pulleys, nor would observed dynamic violations of L1 during saccades in SO<sup>64</sup> or IO palsy. Additional mechanical contributions from the oblique EOMs are essential to the VOR, which ideally produces compensatory ocular rotations along axes identical with those of externally imposed head rotations, independent of eye orientation. An ideal VOR should therefore violate the half-angle requirement of L1 by following a zero-angle rule. Depending on the species, the VOR is observed to follow something between a zero- and quarter-angle rule, closely correlated with the strength of the torsional VOR.<sup>46</sup> Whereas the horizontal and vertical angular VORs are nearly perfectly compensatory for head rotations, the torsional VOR has a much lower gain.<sup>46</sup> It is plausible that lower torsional VOR performance is due to the greater difficulty in accomplishing coordinated torsional repositioning of the rectus pulleys, in comparison to the horizontal and vertical VORs that use larger anteroposterior pulley movements shared by L1 kinematics.

### Kinematics and Neural Control in Broad Strokes

Teleology is inherently hazardous in describing physiology. Recognizing this peril, the following, general concepts might be heuristically useful, even if oversimplified. All six EOMs have pulleys implementing half-angle behavior to achieve commutative kinematics. For visually guided eye movements with the head upright and stationary, this results in L1. In special situations non-L1 ocular torsion is advantageous: In convergence, torsion facilitates stereopsis, and for the VOR, torsion facilitates retinal image stability during head motion. Rectus pulley reconfiguration coordinated with ocular torsion maintains commutative ocular kinematics, even during deviations from L1. The binocular misalignments resulting from disconjugate pulley array torsion are usually small enough to be compensated by fusional vergence during normal vision.

The retina, and consequently much lower level central visual processing, provides a two dimensional (2-D, horizontal and vertical) representation of the world. The ability to perform central ocular motor control in 2-D rather than 3-D is highly simplifying but consistent with single-unit neural recordings. In the superior colliculus, saccade targets are encoded in 2-D, implying that any computation of a third dimension, such as torsion, is accomplished downstream.<sup>35,67,68</sup> Even in the oculomotor nucleus and rostral interstitial nucleus of the medial longitudinal fasciculus, saccadic burst commands are better correlated with rate-of-change of 3-D eye position than with angular eye velocity.<sup>67,69</sup> The foregoing analysis indicates that during visually guided eye movements, the pulley system renders horizontal and vertical eye position commands essentially commutative,<sup>35</sup> at the same time achieving ocular torsion conforming to L1. The angular VOR consists of relatively simple brain stem circuits receiving input from 3-D sensory organs in the inner ear. The observed noncommutativity of the angular VOR<sup>70</sup> is appropriate to the noncommutativity of the physiological stimulus, head rotation. During self-rotation, rectus pulley reconfiguration, coordinated with ocular torsion, violates L1 as necessary to stabilize images on

the retina. Rectus pulley reconfiguration may also occur during ocular torsion associated with voluntary gaze shifts involving both eye and head movements, also achieving stability of images on the retina at the end of the gaze shift,<sup>68</sup> and in a more complex way during simultaneous activation of the angular and linear VORs.<sup>71</sup>

Rectus pulley reconfiguration during convergence appears to be a binocularly symmetrical function of both the convergence and vertical gaze angles,<sup>56</sup> and indirect evidence suggests it also depends on visual features.<sup>55</sup> Central processing of vergence commands must include explicit specification of torsion, and therefore the ocular motor commands during vergence must include all three degrees of freedom. Perhaps the greater complexity of 3-D vergence processing compared with 2-D processing of monocular visually guided eye movements underlies the susceptibility of the binocular system to misalignment.

### Pulley Diseases

The foregoing evidence suggests that the orbital connective tissues play a pivotal role in control of ocular kinematics, a role not replaceable or capable of compensation by neural circuits. Even physiological pulley shifts during convergence and extreme vertical gaze are associated with significant vertical binocular misalignments during as ubiquitous a behavior as the VOR. It should then come as no surprise that disease of the pulleys and their associated connective tissues would be associated with predictable and much larger patterns of binocular misalignments—strabismus. Three distinct forms of pulley disease are now recognized as likely causes of strabismus.

**Pulley Heterotopy.** MRI has demonstrated the coronal plane locations of rectus EOM pulleys to be stereotypic in normal persons<sup>25,72</sup> and in most persons with strabismus.<sup>25</sup> The 95% confidence intervals of coronal plane pulley coordinates are less than  $\pm 1$  mm.<sup>25</sup> A computational model of binocular alignment based on the static force balance approach of Robinson<sup>5,6</sup> incorporates elastic pulleys and is now available as the Macintosh application, Orbit.<sup>73</sup> The expected effect of coronal plane heterotopy (malpositioning) of pulleys can be computed using Orbit.<sup>74</sup> Many cases of incomitant cyclovertical strabismus are associated with heterotopy of one or more rectus EOM pulleys more than 2 SD from normal. Patterns of incomitance in individual patients consistently match those predicted by Orbit simulation based on measured pulley locations, suggesting that pulley heterotopy causes the strabismus.<sup>75-77</sup> In most of these cases the strabismus had an “A” or “V” pattern. In an A pattern, for example, there is relatively more esotropia in upward than downward gaze, and one or both LR pulleys are typically located superior to the MR pulleys (Fig. 7). The converse is true in the V pattern, and the SR may be significantly temporal to the IR, as well (Fig. 7). These clinical findings mimic features of what has been heretofore regarded as oblique EOM dysfunction,<sup>75</sup> and suggest that clinical nosology be significantly revised to avoid implications of oblique EOM over- or undercontraction.<sup>78</sup> For example, MRI demonstrates no correlation between IO size or contractility and variations in elevation in adduction in SO palsy.<sup>79</sup> Multiple lines of evidence suggest that ocular torsional component of strabismus does not cause the pulley heterotopy: (1) Typically only one or two pulleys are heterotopic; (2) the amount of ocular torsion is insufficient to account for the amount of pulley heterotopy; and (3) patients with similar ocular torsion due to SO palsy lack this sort of pulley heterotopy.<sup>76</sup> Extreme pulley heterotopy is associated with esotropia and hypotropia in axial high myopia.<sup>72,80,81</sup>

Although the preceding cases of pulley heterotopy were presumably congenital, acquired heterotopy may be the com-

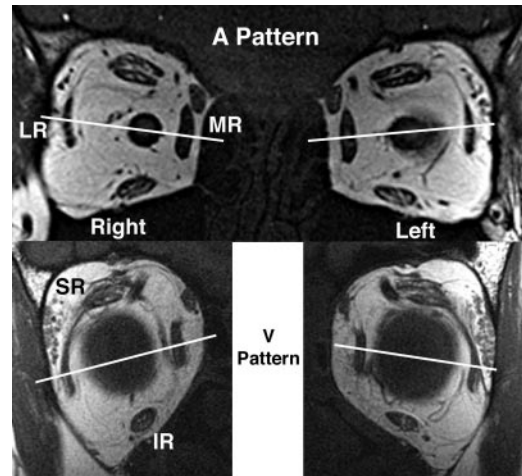


FIGURE 7. Quasicoronal MRI scans of left and right orbits of two patients with strabismus obtained in central gaze. White lines connect centers of horizontal rectus EOMs just posterior to their pulleys. (A) LR pulleys are superior to the MR pulleys in an A-pattern strabismus. (B) LR pulleys are inferior to MR pulleys in V pattern.

mon consequence of simple aging. The horizontal rectus pulleys of normal older people sag inferiorly in a symmetric manner<sup>82</sup> probably related to reduction in the range of supra-duction.<sup>83</sup> Asymmetric rectus pulley sag would be expected to produce incomitant vertical strabismus. Histologic examination shows marked age-related degeneration of attachments of the IO OL to connective tissues.<sup>13</sup> The OL appears in the oldest specimens to lose its insertion to the temporal IO sleeve and to the LR pulley. These connective tissue changes might be expected to compromise EOM kinematics, perhaps leading to violations of L1 in older humans.

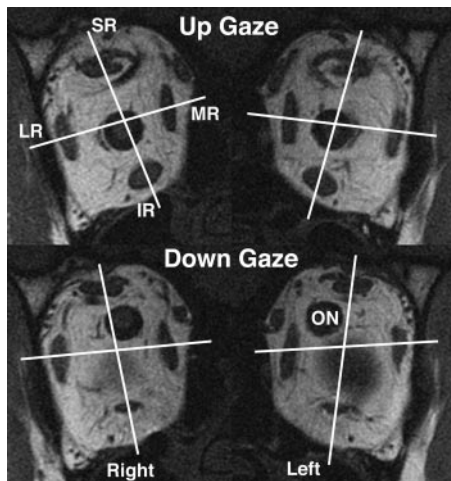
**Pulley Instability.** Although normal pulleys shift only a little with gaze changes, one or several pulleys may become unstable and shift markedly with gaze to alter EOM action. This shift may occur in one gaze position only. Inferior LR pulley shift in adduction may be acquired and can mimic the restrictive hypotropia in adduction traditionally attributed to SO tendon sheath disease (Brown syndrome), or X-pattern exotropia.<sup>84</sup> This pathologic condition has been termed gaze-related pulley shift (GROPS).<sup>85</sup> An exaggeration of the physiologic excyclorotation of the rectus pulley array in convergence may produce a marked Y-pattern exotropia, one present only in elevated gaze (Fig. 8). Pulley instability can be diagnosed only by orbital imaging in multiple gaze positions.

### Pulley Hindrance.

Abnormally anterior pulley location or failure of a pulley to move posteriorly during EOM contraction results in pulley collision with the scleral insertion and consequent hindrance to ocular duction. As is also the case after fadenoperation,<sup>86</sup> there is restriction to passive forced duction of the eye. Hindrance to posterior IR pulley shift due to scarring from inferior orbital<sup>87</sup> or lid<sup>88</sup> surgery creates incomitant, restrictive hypertropia. Release of the adhesions hindering IR pulley motion is effective in treating this form of strabismus.

### Pulley Surgery

Central to the initial recognition of pulleys is the stability of rectus EOM paths after large surgical transpositions of the scleral insertions. Only slight shifts of pulleys are observed by MRIs after insertional transposition.<sup>11,12</sup> Posterior suturing of the transposed EOMs<sup>89</sup> increases the desirable pulley shift,



**FIGURE 8.** Quasicoronal MRI images of a patient with Y-pattern exotropia due to pulley instability. *White lines* connect the centers of the rectus EOMs just posterior to their pulleys. Note extorsion of the pulley array in up gaze, with normal pulley positions in down gaze. ON, optic nerve.

markedly increasing the effectiveness of transposition in treatment of paralytic strabismus.<sup>12</sup>

Before recognition of pulleys, posterior fixation of rectus tendons to the underlying sclera (“fadenoperation,” in German) very far posteriorly was performed to reduce ocular rotation, specifically in the field of a particular EOM’s contraction.<sup>90</sup> This was believed to be effective because of a reduction in the EOM’s scleral arc of contact and lever arm in rotating the globe.<sup>91</sup> It is now known from MRI performed after posterior fixation surgery that these concepts are erroneous.<sup>86</sup> Instead, posterior fixation produces hindrance to normal posterior pulley shift during EOM contraction, restricting ocular rotation in that direction only. Based on this physiological clarification, the operation can be modified to avoid risky and counterproductive dissection of pulley tissues, placing the suture in a much more convenient anterior location.<sup>86</sup> In fact, the sutures need not be placed into the sclera at all. Posterior fixation of the MR for esotropia with excessive accommodative convergence is at least as effective if the sutures simply join the pulley to a more posterior site on the MR muscle belly,<sup>92</sup> increasing the tension of the pulley suspension.

Pulley heterotopy can be treated surgically by large transpositions of the scleral insertions, augmented by posterior fixation to the sclera. Although this conventional sort of strabismus surgery can correct horizontal and vertical incomitancies, insertional transposition always has an adverse effect on torsional alignment. An optimal strategy would be to operate to correct the pulley malpositioning directly. Pulley instability can be treated in conventional fashion by posterior fixation of the tendon to the underlying sclera, but might optimally be treated by surgical reinforcement of the pulley suspensions. However theoretically optimal, direct pulley surgery is currently in the earliest stages of clinical development and will probably require orbital and even craniofacial approaches in some cases.

### Philosophical Conclusion

This lecture has sought to provide a broadly unifying paradigm for conceptualizing the role of the orbital connective tissues in ocular motility. Some of the material presented, such as the structure of the connective tissues and EOMs, represents a set of readily verifiable observations that can be incorporated into any favorite way of thinking about eye movements. The functional anatomic descriptions of EOM paths and their changes

with gaze area are also verifiable observations whose kinematic consequences seem unavoidable as long as classic mechanics are accepted. Beyond these issues lie matters of interpretation and speculation. This is particularly true of teleological arguments, which by nature can only be subjective. This risky business has been undertaken to encourage a novel paradigm for studying ocular motility. Novel paradigms are not accepted because they are more “correct” or because older paradigms are in “error.”<sup>93</sup> Among the reasons for acceptance of novel paradigms is a kind of “intellectual neatness” that leads to the feeling that loose ends have been tied up better than with older paradigms. The broad theoretical presentation has been aimed at tying up many loose ends. More concrete, if no less compelling, reasons to adopt a novel paradigm include the ability to explain previously mysterious phenomena, the ability to predict correctly entirely new observations, and the accurate ability to practical outcomes from measurements.<sup>93</sup> Examples of these sorts have been included in this presentation.

The task of understanding ocular motility is far from complete, however. Even within the general paradigm of ocular motility stated herein, there remain numerous unanswered questions and related topics that are not addressed. Vastly more must be learned about the organization of the brain stem motor nuclei involved in eye movement. For example, what are the roles of oculomotor subnuclei, and how, for example, might they be involved in proprioception?<sup>94</sup> How are the precise properties and locations of the EOMs and pulleys specified by genes, regulated during development, and repaired during a lifetime of accumulated wear and tear? What are the relative contributions of mechanical, muscular, and neural factors to the development of strabismus? In the process of answering such important questions through specifically designed experiments it may well emerge that some of the “loose ends” tied up in this broad scheme have been tied up incorrectly. The important thing is that progress will nonetheless have occurred.

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