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Non-commutative, Nonlinear, and Non-analytic Aspects of the Ocular Motor Plant

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Abstract

The ocular motor plant, consisting of the globe, extraocular muscles (EOMs), and connective tissue suspension, constitutes an intricate and non-linear actuator of eye movements. The pulley system of the rectus EOMs constitutes a non-linear inner gimbal actuated by the orbital layers of these EOMs that renders the sequence of ocular rotations effectively commutative to the central controller, and can be rotated by the outer gimbal driven by the oblique EOMs. Optic nerve (ON) length is insufficient to permit large angle adduction without tethering by the by the ON and sheath, creating at and beyond this threshold a large additional load on the medial rectus muscle. Finite element modeling suggests that adduction may eventually cause repetitive strain injury to the ON and glaucomatous optic nerve damage.

Keywords

commutativity; finite element analysis; glaucoma; optic nerve; pulley

Introduction

Lance M. Optican, like his mentor David A. Robinson before him, has been a great exponent of computational models to understand and explain phenomena by simplification of mechanisms sufficiently to permit quantitative analysis. This approach has yielded an enormous body of insights, sometimes motivating the feeling that we understand the entire complexity of the ocular motor system simply because we can model some aspects of it so accurately and elegantly. Both Optican and Robinson have also understood the limitations on simple linear models. This chapter illustrates ocular motor examples where more elaborate modeling approaches have been helpful.

Non-Commutativity and How to Circumvent It

As emphasized by Quaia and Optican, eye rotations in all three directions of freedom are not commutative in the sense that the final outcome of a sequence of rotations depends upon the order of rotations (Quaia and Optican, 1998). While the 90° sequence of rotations illustrated in Figure 1 is an extreme example Figure 2 of the difference in ultimate eye positions

resulting from reversal of the ordering of a pair of horizontal and vertical rotations, the principle applies to all rotational angles. In one dimension, such as for a purely horizontal eye movement, the saccadic velocity command encoded neurally as a pulse can simply be integrated to obtain the required neural position command. In more than one dimension, such as for simultaneous horizontal and vertical eye rotations, the ocular motor system cannot simply integrate the horizontal and vertical pulses to obtain the innervational steps required to minimize post-saccadic drift (Quaia and Optican, 1998). The solution offered by Tweed and Vilis was the quaternion model employing non-commutative per-motor operators in the brain to generate the required saccadic pulse and step (Tweed and Vilis, 1987). It has since emerged that the mechanical behavior of the ocular motor plant provides a solution to non-commutativity without non-commutative neural operators. Quaia and Optican showed that if the pulling direction of each eye muscle changes by half the change in eye orientation, then the ocular motor plant itself corrects for pulse-step mismatches that would have arisen from a commutative neural controller. Under this assumption, the ocular motor plant thus appears commutative to the controller, because the errors arising from this approximation are physiologically negligible (Quaia and Optican, 1998). At the time this model was proposed, however, it was not understood if or how the ocular motor plant might exhibit the favorable behavior.

Subsequent magnetic resonance imaging (MRI) of the paths of the extraocular muscles in humans has demonstrated that muscle pulling directions do indeed change by half the change in eye orientation (Demer, 2004). The array of the four rectus muscles are arranged as an “inner gimbal” for the eye. Each of these muscles contains an oculorotary global layer in continuity with the tendinous insertion on the sclera, as well as an orbital layer that inserts on a connective tissue sleeve surrounding the muscle called its “pulley (Demer et al., 2000).” The pulley, which is part of the inner gimbal system, is suspended by elastic tissues from the orbital bones, from which it is retracted by orbital layer tension so as to lie as far posterior to the globe center as the respective muscle insertion is anterior to globe center. The pulley is transversely supported by connective tissues and constitutes the functional mechanical origin of the muscle, because the anterior portion of the muscle pulls the scleral insertion towards the pulley. As far as the globe is concerned, only anterior to the pulley is the muscle path relevant to the direction of muscle force. Under the small angle geometric assumption, maintenance of the pulley in this position with respect to the rotating globe causes the anterior muscle path to change by half the change in eye orientation. Thus, were the eye initially oriented upwards at 20° , horizontal saccades from this position would be activated by horizontal rectus muscles whose anterior paths are angled upwards at about 10° , thus changing their pulling directions by 10° . When a rectus muscle contracts, its orbital layer retracts its pulley so that the distance between the pulley and scleral insertion is maintained constant at about 16 mm (Kono et al., 2002). This enables anterior muscle paths to change by half of eye orientation even among tertiary gaze positions that incorporate combinations of horizontal and vertical rotation. Moreover, the foregoing “half angle behavior” is a sufficient condition to enforce Listing’s Law of torsion, which states that, with the head upright and stationary, any eye position can be attained from a starting “primary position” by a rotation about a single axis, and that all such axes lie in a plane (Tweed and Vilis, 1990).

The orbital layers of the oblique muscles insert on the rectus pulley system. The superior oblique orbital layer inserts on its sheath, which in turn traverses the trochlea to insert on the nasal aspect of the superior rectus pulley (Kono et al., 2005). The inferior oblique orbital layer inserts on the inferior rectus and lateral rectus pulleys (Demer et al., 2003b). Coordinated activity of the oblique muscles thus acts as an “outer gimbal” to torsionally rotate the rectus pulley “inner gimbal” to torsionally offset Listing’s plane. Listing’s law is enforced within the inner gimbal, but the gimbal itself is subject to rotation to add or subtract torsion from Listing’s plane. Such torsional offsets of the rectus pulley array and Listing’s plane are observed during ocular counter-rolling induced by head tilt (Demer and Clark, 2005), and rectus pulley extorsion also occurs during convergence to a near target (Demer et al., 2003a).

There is neurophysiological evidence that the brain does indeed avoid the task of non-commutatively encoding half angle ocular kinematics. Klier *et al.* electrically stimulated the monkey abducens nerve from a range of starting vertical eye positions, but the evoked horizontal eye movements had half angle kinematics conforming to Listing’s Law (Klier et al., 2005). Ghasia *et al.* recorded motor innervation to the vertical rectus and oblique muscles in monkeys during eye pursuit movement having half angle kinematics, but found no neural commands for Listing’s torsion in their cyclovertical muscle innervation (Ghasia and Angelaki, 2005). However, while the neurons driving the cyclovertical muscles did not encode half angle behavior, they also failed to command the violations of half angle kinematics that were notable during the vestibulo-ocular reflex (VOR) (Ghasia and Angelaki, 2005). This combination of observations created a paradoxical question: since the pulley gimbal mechanically enforces Listing’s Law of torsion via half angle kinematics, how can the VOR violate these kinematics in the absence of activity by the torsionally acting muscles? The answer is that the horizontal rectus can create the necessary torsion. Horizontal rectus muscles each consist of two transverse oculorotary compartments that have vertically displaced effective insertion positions on the sclera due to the roughly 10 mm breadth of their tendons (Demer, 2014). Thus, differential activation of the compartments of a single horizontal rectus muscle imparts a shear effect at the insertion that can produce cyclovertical actions, as evident from MRI for the lateral rectus during the static VOR known as ocular counter-rolling (Clark and Demer, 2012), and for several rectus muscles during upward gaze (Clark and Demer, 2016). Presumably differential compartmental activity in rectus muscles could contribute to violations of half angle kinematics during the angular rotational VOR as well.

Nonlinearity

Linear systems enjoy the benefits of mathematical simplicity and the application of transfer functions. While few if any properties of the ocular motor plant are strictly linear over their full ranges of input and output, most processes are close to linear over a small range of variations, and are discussed elsewhere in this volume. Other processes are subject to hard nonlinearities that cannot be avoided. One example is inhibitory cutoff in the firing of neurons; neuronal firing rates cannot exceed maximum values, and certainly cannot become less than zero. A newly-recognized hard nonlinearity in the ocular motor plant arises from the finite length of the optic nerve and its sheath. With progressive adduction, the

previously-redundant an slack optic nerve becomes taut, and begins to act as a load opposing further adduction by the medial rectus muscle (Demer, 2016). This nonlinear load change phenomenon has a threshold of about 26° adduction, where optical coherence tomography (OCT) demonstrates abrupt onset of progressive deformation in and around the optic nerve head with further adduction (Suh et al., 2017). Three-dimensional optic nerve path is significantly straighter in adduction than in central gaze and abduction, consistent with tethering only in adduction (Demer et al., 2017). Modeling of this phenomenon necessarily requires a non-linear shift from the tethered to non-tethered optic nerve state.

Non-analytic Modeling

Of course when complex phenomena involve highly nonlinear relationships, closed form mathematical expressions are impossible. Numerical approximations must suffice. An excellent example of the utility of this approach is Joel M. Miller's elaboration with David A. Robinson (Miller and Robinson, 1984) of the pioneering modeling work of Robinson (Robinson, 1975). Together they developed a binocular simulation the Miller subsequently elaborated and refined as the *Orbit 1.8* computational simulation of binocular alignment that has remained for nearly two decades the premier numerical model for understanding of ocular motility and strabismus (Miller et al., 1999). Another form of numerical modeling is finite element analysis (FEA), a computational approach parsing large mechanical structures into numerous discrete elements whose mechanical behavior is characterized by individual constitutive equations, and whose overall geometry is structurally constrained (Sigal et al., 2004). For the oculomotor system, such structural constraint can be defined by MRI. Tensile loading can characterize viscoelastic constitutive properties needed for realistic FEA; these parameters may be anisotropic, requiring measurement in multiple directions. Analysis of surface deformation by a hard sphere using the Hertzian mathematical formulation has emerged as a technique to characterize viscoelastic properties of small, geometrically irregular biomaterial samples (Cheng et al., 2005, Reed et al., 2009). The Hertz method yields elastic moduli (Cheng et al., 2005) and can scale to the subcellular level (Reed et al., 2009). This novel approach is suitable for non-EOM orbital tissues such as optic nerve, optic nerve sheath, and sclera. The Poisson ratio between transverse and longitudinal strain is usually assumed ~ 0.5 for biomaterials, but can now be directly measured by imaging (Jurvelin et al., 1997), such as OCT during tensile loading. Conventional tensile testing by stretching of tissue samples can provide valuable data on elasticity (deformation-dependent) and viscosity (rate dependent).

We have in bovine and human ocular specimens measured the constitutive properties required to simulate the effects on the eye of optic nerve tethering in adduction. However, it was necessary to avoid the nonlinearity at the onset of tethering itself, since the transition from a slack to taut optic nerve is a major computational problem for FEA, fundamentally changing the geometric structure of the model. This nonlinearity is avoided by beginning the simulation at the adduction angle where the optic nerve has just become taut, so that it remains in a straight configuration during a further 6° adduction. Only the posterior half of the ocular globe was represented, with the anterior hemispherical boundary rotated as the forcing function to achieve adduction. Resulting simulations demonstrated marked tensile strain on the temporal side of the optic nerve head, and the temporal and posterior sclera

(Shin et al., 2017). However, the modeling has revealed some complexities that deserve consideration and further study. In addition to local tissue properties, the local stresses and strains in and around the optic nerve head predicted by FEA during adduction tethering depend strongly upon some important assumptions. These include the rotational center of the globe, which in general is not the same as the geometric globe center, and the way that rotational force is applied to the globe. While it is computationally convenient to assume that the globe rotates about a particular point that may be considered a boundary condition, in actuality there is no structure in the internal eye that serves the function of a pivot. Instead, the location of the ocular rotational center is the consequence of all the extraocular forces on the globe, including both the muscle forces tending to translate the globe posteriorly, and the connective tissue gimbal providing counterforce to the muscles.

The assumed distribution of muscle forces at the scleral insertions also has major effects on stresses and strains in and around the optic nerve head predicted to arise from optic nerve tethering in adduction. There are very different predicted effects of a 6° adduction past the point of tethering, depending upon this factor alone. Figure 3 shows for a human eye the predicted strains when all the adducting force is applied at the medial rectus insertion, with a different pattern from Fig. 4, when the entire anterior sclera is assumed to rotate *en bloc*. Both Figs. 3 and 4 assume the same worst-case combination of constitutive properties of the optic nerve, nerve sheath, and various local regions of the sclera, based upon actual measurements from fresh human specimens obtained from eye banks. Other combinations of local tissue properties result in lesser and different combinations of local stresses and strains.

Different assumptions about the forcing functions and boundary conditions on the globe and optic nerve result in different predicted stresses and strains in and around the optic nerve head during ocular rotations. Another example is the FEA of Wang et al. who assumed an initially sinuous course of the optic nerve through impeding orbital fat and connective tissue, and computed strains in the optic nerve during both ab- and adduction (Wang et al., 2016, Wang et al., 2017). These investigators computed large strains as the optic nerve moved through a locally homogeneous connective tissue material in the central orbit, even when not straightened in adduction tethering. These results highlight several key issues in FEA of the ocular motor system: distinguishing flexibility of tissues designed to move from loading strains occurring at the limits of this flexibility, local tissue properties and the possible effects of their fine structure, and assumptions about boundary conditions and forcing functions. The value of computational mechanical models of the ocular motor system will likely be found in carefully-defined and limited situations where the assumptions are clear, and where simulations are interpreted in context of those assumptions.

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Fig. 1. Non-commutativity of ocular rotations. In the upper row, 90° rotation upward followed by leftward leaves the eye looking to the left. In the lower row, 90° leftward rotation followed by upward leaves the eye looking up.

Fig. 2.
The orbital pulley system.

Fig. 3. Finite element model of strain in the globe and optic nerve during 6° adduction past the point of optic nerve straightening, assuming that the anterior sclera and cornea are rotated en bloc about the globe's geometric center. Illustration courtesy of Joseph Park.

Fig. 4. Finite element model of strain in the globe and optic nerve during 6° adduction past the point of optic nerve straightening, assuming all adducting force is exerted by the medial rectus on its scleral insertion at lower left, and that the eye rotates about its geometric center. Illustration courtesy of Joseph Park.