Thank you for inviting me to discuss my work

1. EOM Pulleys & Compartments

My aim will be to distinguish the basic & important EOM Pulley concept from some very dubious ideas that followed.

2. Biomechanical Analysis of Strabismus

- What it can teach us.
- · Limitations of current implementations.

3. Injection Treatment of Strabismus

- What are its various modes?
- How does it compare to incisional surgery?

I have more material than time and will be skipping over some of it, so I've posted the complete lectures at www.eidactics.com.



The Strabismus
Research Foundation





The Strabismus Research Foundation is a 501(c)(3) non-profit operating foundation (EIN 46-1989857) devoted to translational research in ocular motility. Eidactics ("eye-DAK-tics") is a California company (EIN 20-4569747) conducting pure and applied oculomotor research.



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STRABOS 2025 Lectures

- EOM Pulleys and Compartments Sense and Nonsense PDF
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EOM Pulleys & Compartments – Sense & Nonsense

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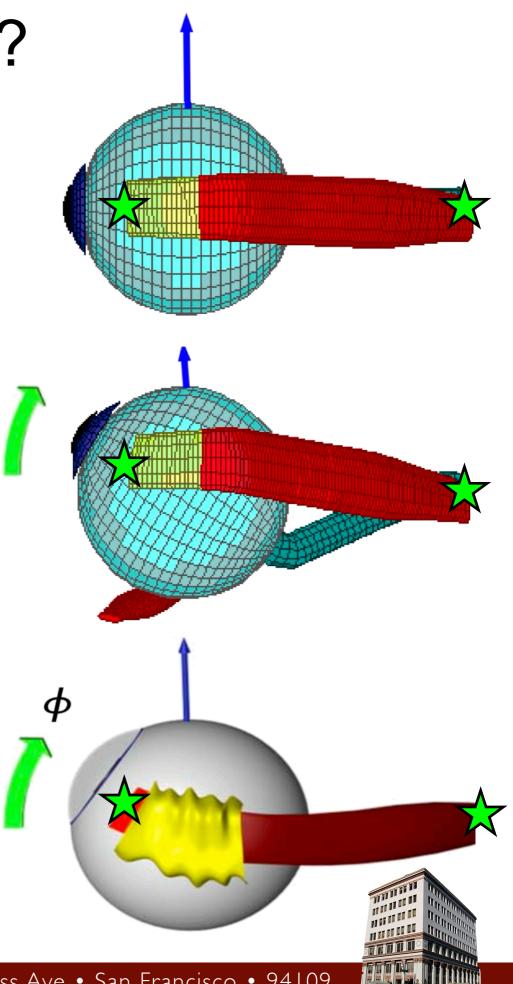
Abstract

- EOM Pulleys are examples of <u>Morphological</u> or <u>Embodied Computation</u> complex behaviors, apparently requiring "intelligence", that are actually done by simple mechanisms.
- The unexpected discovery of EOM pulleys by Miller (1989, 1993) and their elaboration by Demer (2000) resolved a fundamental mystery in oculomotor physiology: Listing's Law requires a particular eye torsion for each gaze angle, but no brain center, no "Listing's Law box" that sent the necessary innervations to the eye, could be found. Now we know why.
- Unfortunately, this surprising refutation of classical ideas of eye movement control created an atmosphere of nihilism in which dubious notions were presented as facts:
 - The <u>Active Pulley Hypothesis</u> (APH) and <u>EOM Compartments</u> notions, which propose to replace 6 EOMs with 17 "mini-muscles", are implausible on their face, and unsupported by evidence.
 - In connection with these notions, various obsolete & invalid methodologies have been promoted, yielding misleading research so complex that it's difficult to evaluate.
- My purpose here is to distinguish the important and basic insight of EOM Pulleys from several dubious notions that followed.



Why Pulleys?

- Classical notions (egs, Boeder, 1962; Krewson, 1951) were that rectus EOMs are constrained only at their ends, and follow a great-circle path from insertion to tangency with the globe, and then a straight path to the origin in the orbital apex.
- Robinson (1975) showed by modeling that this could not be correct because normal eye rotation would cause such muscles to sideslip wildly about the globe, making eye position uncontrollable.
- He proposed simply that sideslip was prevented by connective tissues fixing the anterior muscle to the globe (yellow blob).
- With a plausible model of the eye muscles, attention turned to how they were controlled, which of course meant "controlled by the brain".



Listing's Law

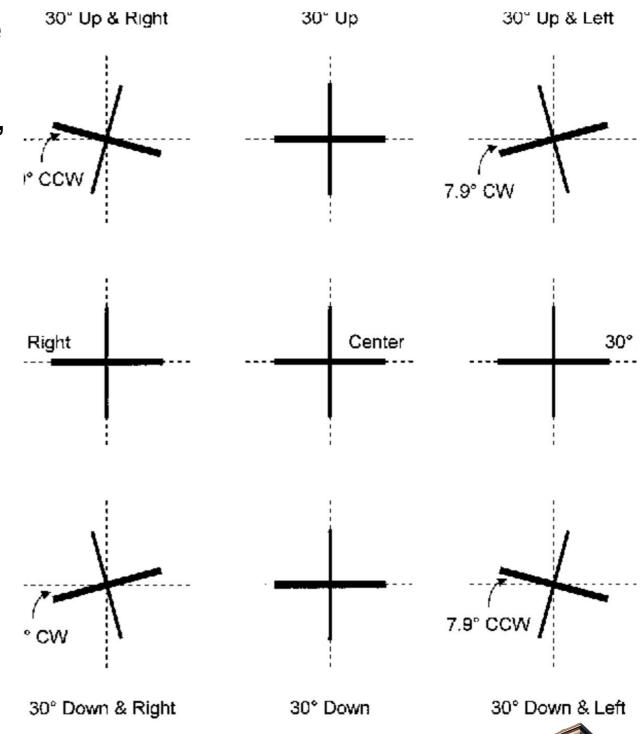
Listing's Law gives the torsional angle (ψ) normally assumed by the eye for each horizontal-vertical gaze angle (ϑ, ϕ) :

$$\psi = \sin^{-1} \frac{\sin \vartheta \cdot \sin \varphi}{1 + \cos \vartheta \cdot \cos \varphi}$$

Horizontal and vertical gaze centers had been identified in the brain stem* and it was natural to assume that ψ was computed by a "Listing's Law box", or center, also in the brain.

Physiologists, however, could find no such center.

* Abducens nucleus & PPRF, and riMLF & interstitial nucleus of Cajal, resp.



Is The Brain is Necessary?

- If the brain implemented Listing's law, cyclovertical motoneurons would have to modulate their firing during eccentric pursuit.
 Ghasia and Angelaki (2005) showed that they do not.
- Klier, Meng, and Angelaki (2005, 2006) stimulated the abducens nerve and nucleus, down-stream of all neural circuits that might contribute to the implementation of Listing's law, and found that eye movements nevertheless had Listing kinematics. <u>This proved</u> that ocular plant mechanics implemented Listing's Law without neural assistance.
- Conclusion: Elastic orbital connective tissues perform mathematically complex functions previously supposed to require the brain!



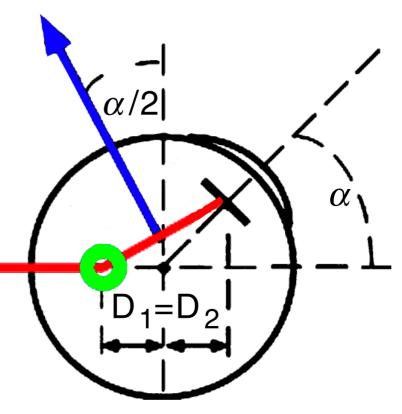
How Could Connective Tissue Calculate Anything?

- We wrongly suppose that our (eg, mathematical) models of natural processes must be performed by those processes themselves.
- Morphological or Embodied Computation ("the body does the math") – is actually quite common, eg:
 - Bat & bird wings adapt instantly to turbulence with only their structure & elasticity.
 - The passive mechanics of human hands adapts to grasp irregular objects.
 - Humans can walk down a slight incline without computing each step, because of the legs' mechanical structure and gravity.
 - Venus flytrap plants snap shut when its hairs are disturbed in a particular sequence.
 Stimuli are integrated by the structure itself, releasing stored mechanical energy.
 - Theo Jansen's Strandbeests.



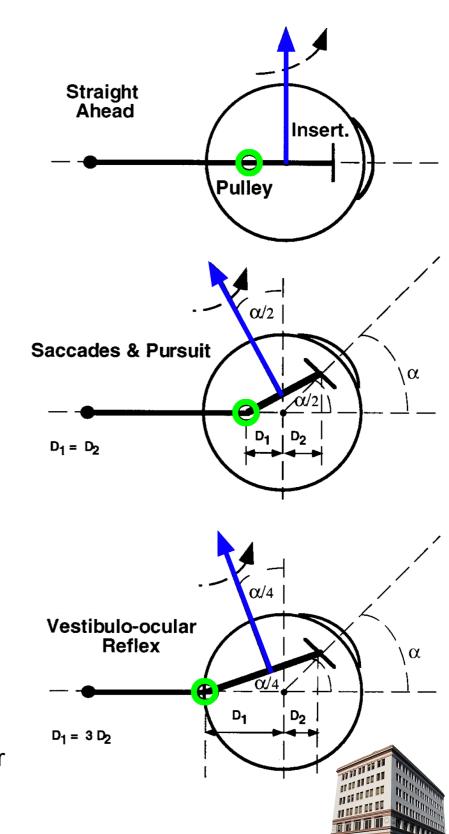
EOM Pulleys Calculate Listing's Law

- EOM Pulleys are condensations of orbital connective tissue that are:
 - Elastically stabilized to the orbital wall (Miller's original concept).
 - Dragged longitudinally by EOM contraction (Demer's contribution), accounting for Listing's Law in eccentric gaze.
- A properly placed pulley would cause a muscle's axis of rotation to tilt backward by half the angle of elevation.
- "Half-angle" behavior is equivalent to Listing's Law.
- MRI studies of muscle paths, particularly before and after muscle transposition surgery, show that orbital connective tissues indeed behave like pulleys, coupled to the orbital wall, at the location required to implement Listing's Law.



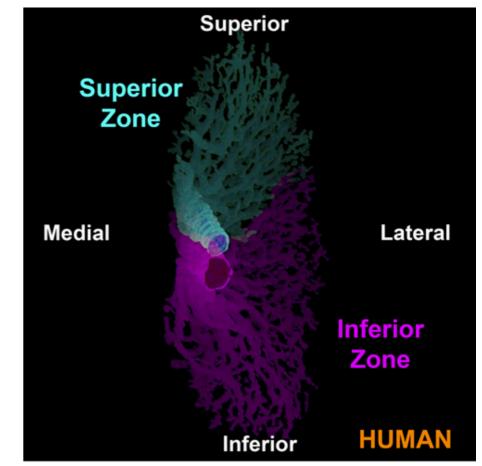
The Active Pulley Hypothesis is Wrong

- Saccades & pursuit obey the <u>half-angle rule of Listing's Law</u>, but the vestibulo-ocular reflex (VOR) follows a different, "quarter-angle rule". Can this be explained by posterior movement of the pulley?
- The APH was born of the well-known micro-anatomic fact that mammalian EOMs generally have a thin layer of small myofibers facing the orbital wall (OL), with different, slower, fiber types than the bulk of the muscle (the GL).
- Demer, Oh & Poukens (2000), hoping to explain "quarter-angle" behavior with pulleys, proposed that whereas GLs rotate the eye, OLs move pulleys independently. This is the APH. Nice try . . .
- But there is no evidence that global and orbital layers move independently, and certainly not by the several millimeters required by the APH.
- X OL and GL are not mechanically independent. Even surgical attempts to separate the layers fail (Scott).
- Shall (et al 1995) & Goldberg (et al 1997) found that many abducens motor neurons innervate both OL and GL. Peng (et al 2010a) and da Silva Costa (et al 2011) found no separation of nerve branches to OL and GL in any muscle. An intermixed nerve supply means that independent control is impossible, clearly disconfirming the APH.
- Misslisch & Tweed (2001) showed mathematically that APH was neither necessary nor sufficient to account for VOR kinematics.



EOM Compartments are Fantasy

- The EOM Compartments notion assumes that the half-widths of most muscles are both <u>innervationally</u> and <u>mechanically</u> independent.
- The evidence cited for EOM Compartments consists of several elegant nerve tracing studies (Peng, et al 2010a; Da Silva Costa, et al 2011; Le, et al 2015) which show that innervation to the LR, MR, IR & SO bifurcates as it enters, and then branches to fill roughly separate regions. This finding was taken to indicate <u>innervational independence</u> of half-width "compartments".
- Such arborization is common in nature. Trees arborize to expose leaves to sunlight, and bronchi to increase contact of air with circulating blood. Motor nerves traverse long distances and then branch repeatedly to synapse throughout target muscles.
- Active processes, such as molecular self-avoidance, support "innervational tiling" (Jan et al 2010), minimizing the inefficient overlap of neighboring domains, which would occur with purely random growth.
- X Branching into non-overlapping neighborhoods is an efficient way to fill space, implying nothing about differential function.
- X Significant <u>mechanical independence</u> of the proposed "minimuscles" is unlikely from micro-anatomy and direct observation.
- Nevertheless, these authors subsequently cite the "newly recognized segregation of intramuscular innervation into distinct compartments", as though differential control was an established fact.

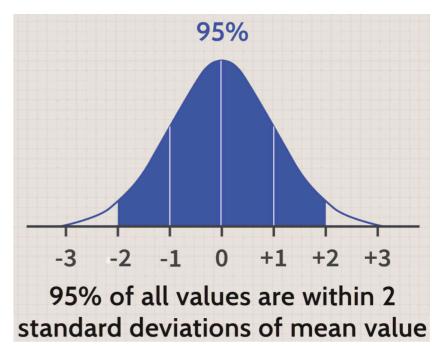




Data Dredging (p-Hacking)

- APH → independent orbital & global layers.
- EOM Compartments → half-widths of most global layers are independent.
- Thus, in place of the familiar 6 EOMs, Demer & colleagues allow themselves 17 mechanically and innervationally independent "mini-muscles" (11 GL Compartments and 6 OLs).
- They pool their eye position data in multiple ways, and use invented measures of contraction on these 17 mini-muscles to generate dozens or hundreds of potential comparisons. These are evaluated with t-tests and correlations to find those yielding the largest (of usually tiny) differences, which are then reported as either confirming and extending previous claims or suggesting new, "revolutionary" EOM capabilities.
- The strategy of performing multiple *ad-ho*c tests referred to as "p-hacking" is problematic because as the number of comparisons increases, so does the probability of finding a "significant difference" by chance, where none actually exists.
 - If we test an hypothesis at the ".05 level", the probability of a wrongly claiming significance is an acceptable 5%.
 - But if we do N independent tests, each at p<.05, the probability of wrongly claiming significance grows quite large:

N	Probability of at least 1 False Positive in N tests = 1 - (.95) ^N
1	0.05
2	0.10
5	0.23
10	0.40
20	0.64
50	0.92

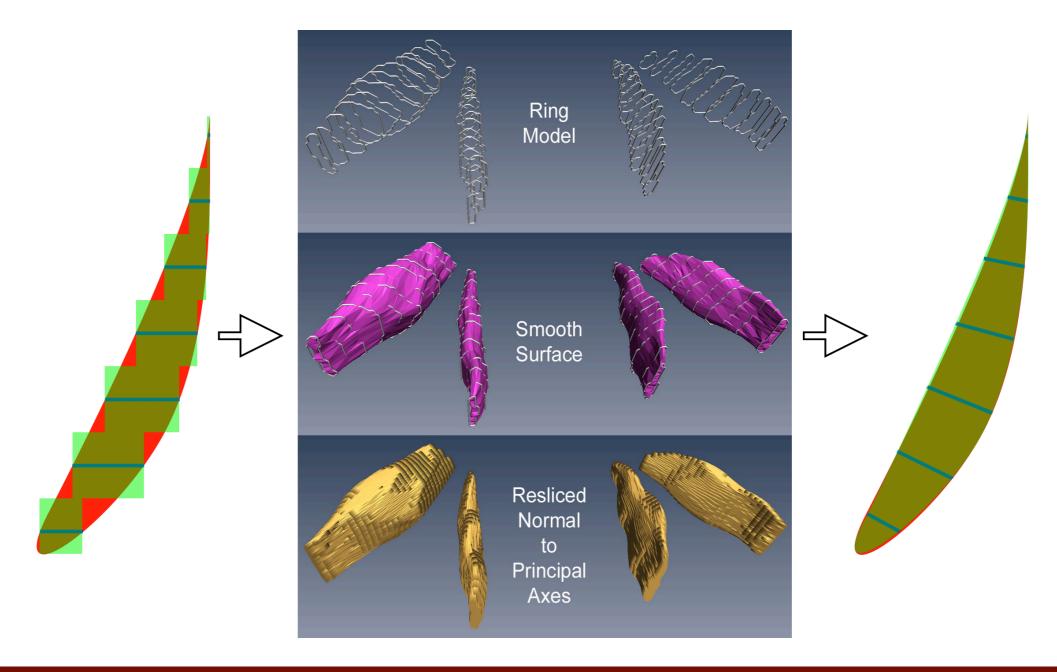


Data Dredging (p-Hacking) Examples

- Clark & Demer (2016b) collected data in central and 6 eccentric gaze positions. Sometimes they pooled all infraductions, other times all supraductions, and still others, changes from maximum infraduction to maximum supraduction. A small 4% compartmental PPV difference pooled across infraductions is reported for LR, although there was no difference across supraductions or across maximal gaze changes (which included infraductions), and nevertheless was taken as support for EOM Compartments and the broad conclusion that all EOMs have complex actions.
- Clark & Demer (2012b, 2016b) wished to show differential compartmental contraction during ocular counterrolling and vertical duction. Although nerve tracing (Peng et al 2010b; Da Silva Costa et al 2011; Le et al 2015) predicts particular compartment boundaries, they created multiple segmentations (12 in the case of the SO!) with the expressed aim of finding the "most likely intercompartmental border", but actually finding segmentations yielding the largest differences, regardless of whether they corresponded to nerve tracing predictions (Clark et al 2016b; page 372). These differences were then tested with paired comparisons.

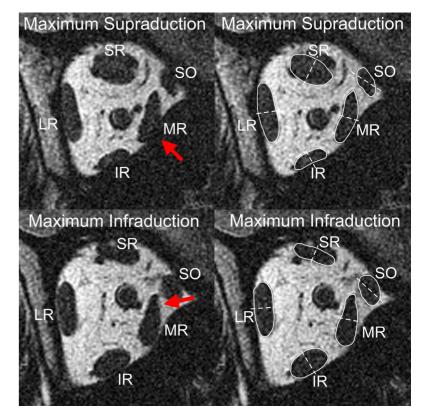
Obsolete Methodologies

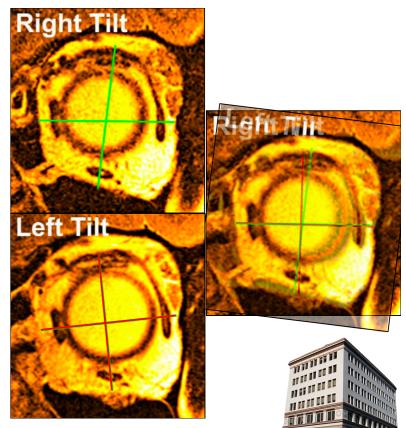
 Calculation of muscle volumes is central to their conclusions about muscle contractions, but unfortunately they use obsolete methods that introduce errors that could easily have been avoided (Miller et al 2013).



Published Images Reveal Bias

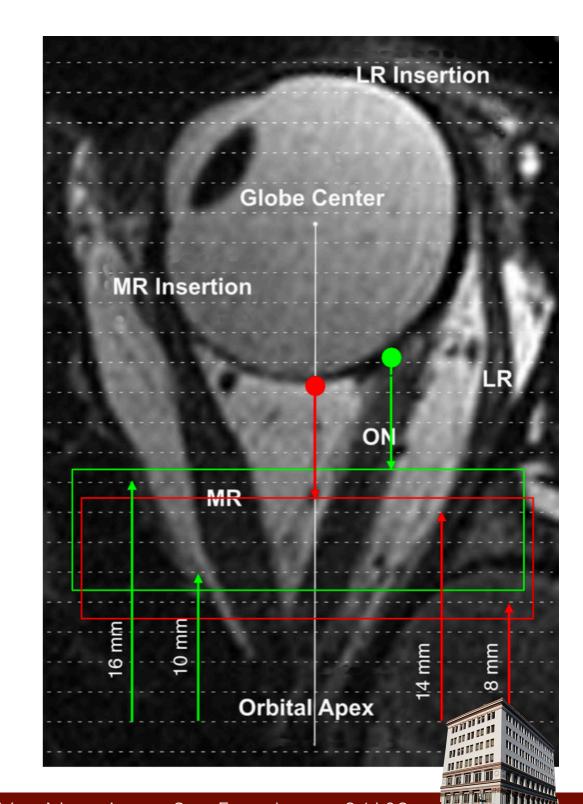
- An image from Clark & Demer's (2016b; fig 3) study of vertical duction claims to show differential contraction of the inferior MR mini-muscle, although it is clear that the apparent increase in the inferior MR crossection is the result of biased segmentation. No explanation is offered for why the inferior LR mini-muscle does not also contract.
- Clark & Demer (2012b) measured ocular counterrolling relative to the interhemispheric sulcus, a soft tissue referent likely to be unstable with head tilt, and which can be seen to have misaligned orbits in the two tilt conditions, creating the appearance of counterrolling where there was actually little or none. Because the head tilt manipulation evidently failed, this experiment provides no support for compartmental contraction during ocular counterrolling.





Posterior Partial Volume (PPV) Does Not Measure Muscle Contraction

- Demer's group measures muscle contraction with an invented measure they call PPV.
- PPV is defined as the volume in an 8 mm thick ROI posterior to the muscle's maximum crossection in central gaze, and moving with the globe-optic nerve junction.
- This ROI is neither fixed in the orbit nor moving with the muscle, but something in between, so as the eye rotates, different parts of a muscle are measured.
- PPV was chosen from many candidate measures for its high correlation with duction (Clark et al 2012a, 2016b), and is therefore a (poor) measure of eye position, and not a measure of muscle contraction at all.
- Eye position, of course, results from contractile and elastic actions of multiple muscles and tissues, and is not interchangeable with the contractile state of any single muscle. Indeed, nontrivial mathematical models are needed to relate the two (Robinson 1975b; Miller et al 1984; Miller et al 1999)



EOM Pulleys & Compartments - Conclusions

- The basic notion of EOM Pulleys describes the mechanism by which Listing's Law is embodied in orbital tissue.
- The APH requires OL-GL relative movements of several mm, which are not possible, are not observed, and in any case, do not account VOR kinematics. Nerve tracing, experimental surgical manipulations, connective tissue studies and mathematical analysis have disproven the APH.
- Although differential layer and compartment <u>movement</u> are not possible, nerve tracing raises the
 possibility of differential <u>tensions</u>, although there is no good evidence that they occur.
- MRI studies from the Demer lab use incorrect measures of muscle contraction that are dominated by artifacts, statistics that do not reasonably account for overall error rates, show evidence of bias, are unconvincing about cause and effect, and lack confirmation from other labs.
- It is unwarranted to state as if proven that eye position is controlled by some 17 extraocular minimuscles, and to urge tests, diagnoses, and treatments on that basis (Clark et al 2014; Demer 2018; Clark 2019).
- The Active Pulley and Compartments papers are so abstruse and difficult to read that almost no one does. Journal reviewers and others likely skim them uncritically, supposing they must be true because of their complexity, their apparent thoroughness, and the authority of the investigators, failing to see that just below the surface they are deeply defective in concept, methodology, analysis and interpretation.