An integrated biomechanical model for microgravity-induced visual impairment

Emily Nelson[1], Lauren Best [1], Jerry G. Myers[1], and Lealem Mulugeta[2]

1. NASA – Glenn Research Center, Cleveland, OH
2. USRA - Division of Space Life Sciences, Houston, TX

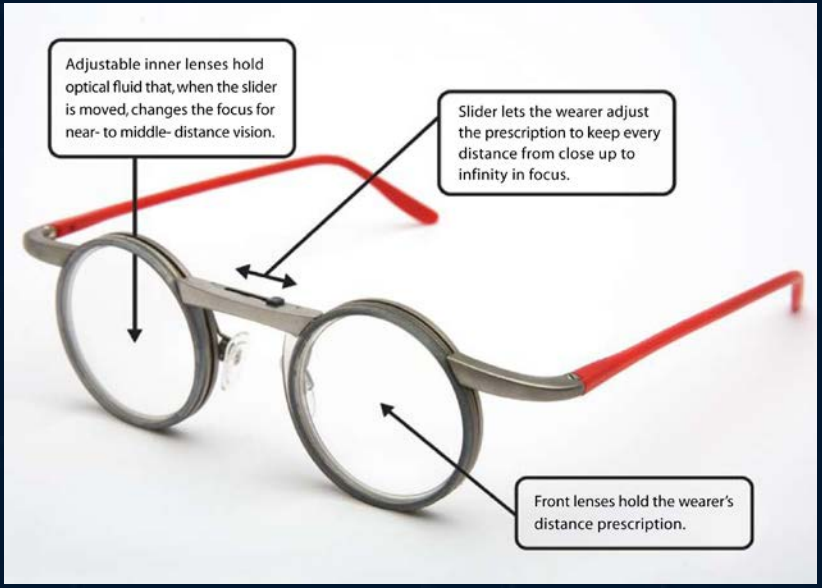
XXII[nd] International Workshop on Computational Mechanics of Materials
Sept 26, 2012

Background

Astronauts in both short- and long-duration spaceflight have reported Visual Impairment (VI) in microgravity (29%[†] / 42.7%[‡])

But relatively recently, severe cases of post-flight ocular pathology have emerged

- There is no definitive explanation as to why VI occurs – yet
- The Digital Astronaut Project is seeking answers through an integrated modeling approach

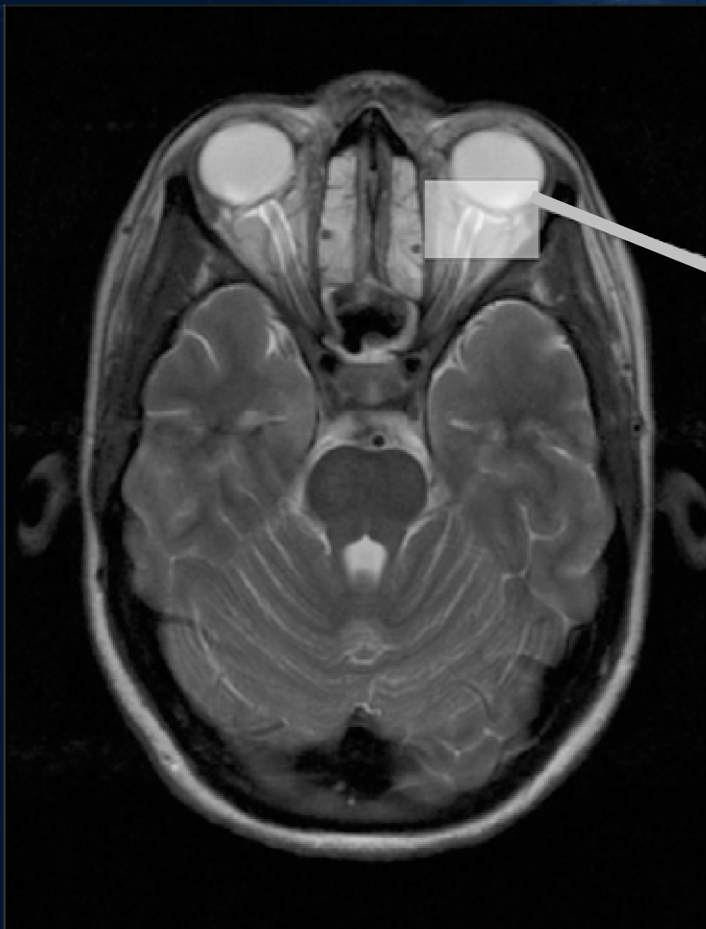


Superfocus glasses
http://www.superfocus.com

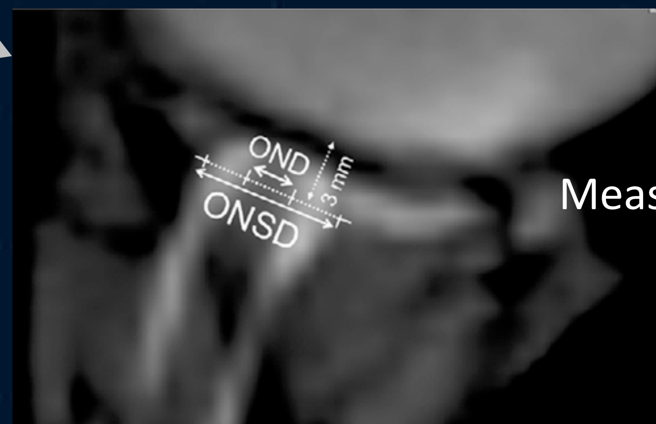
[†]Mader et al. (2011) [‡]Tarver and Otto (2012). Examinations are still in process

The optic nerve and its sheath

In clinical applications on earth, ONSD has become a surrogate for Intracranial Pressure (ICP) in the diagnosis of Idiopathic Intracranial Hypertension (IIH)



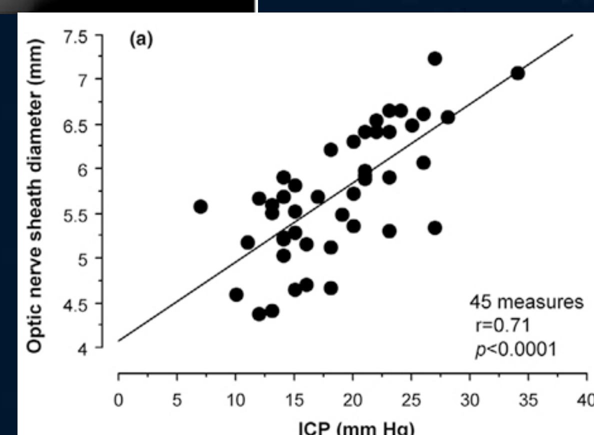
- Geeraerts *et al*. (2008)



Zoomed to 300X

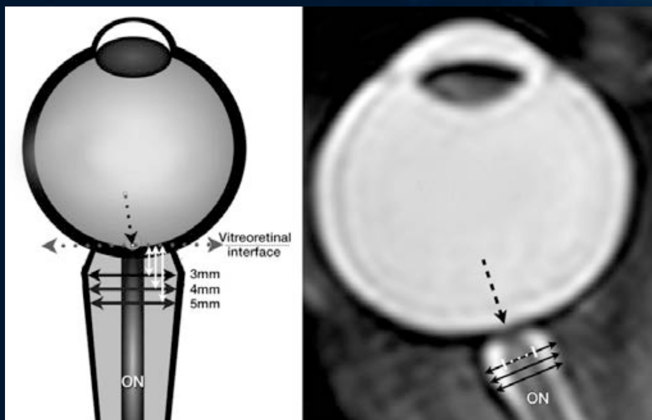
Measurements are made 3mm behind globe

OND = Optic Nerve Diameter
ONSD = Optic Nerve Sheath Diameter



Ophthalmic pathophysiology after µg exposure

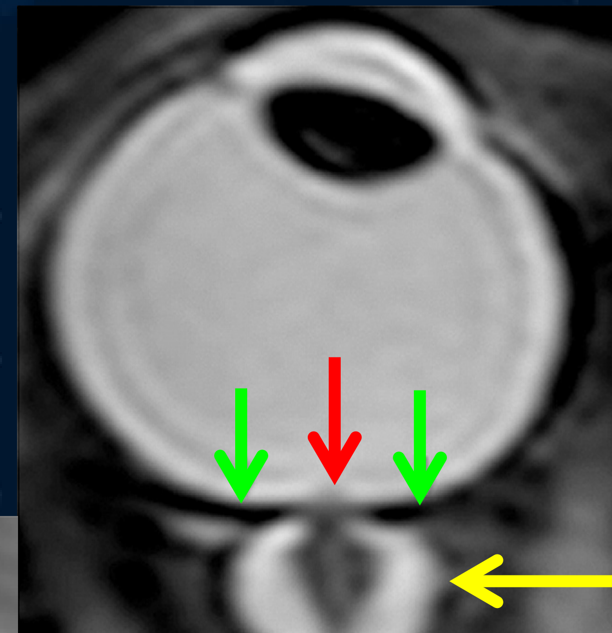
REFERENCE IMAGES



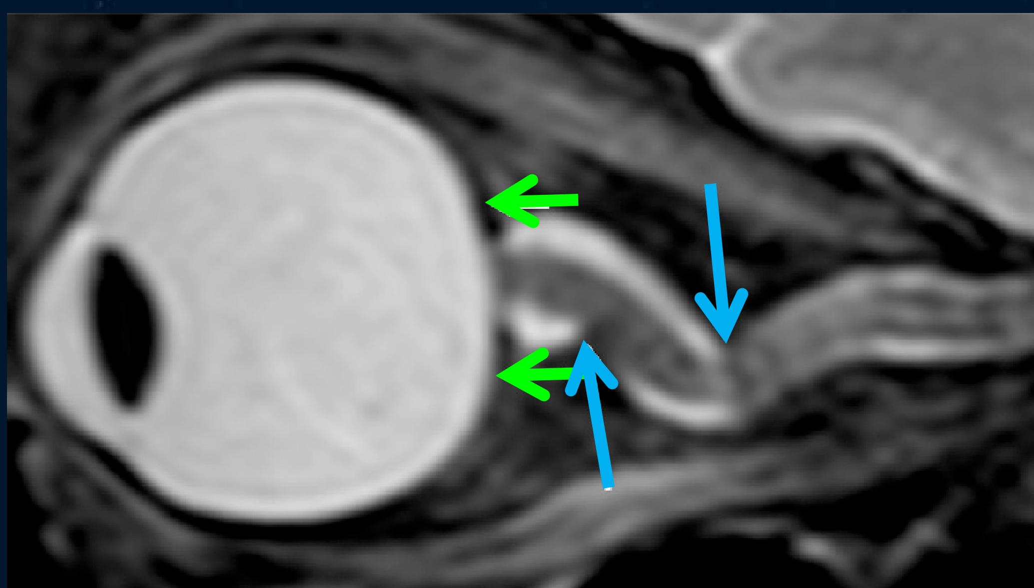
- Kramer et al. (2012)

The VI pathophysiology somewhat resembles IIH seen on earth, which is characterized by high ICP

POST-FLIGHT IMAGE
- Mader et al. (2011)



POST-FLIGHT IMAGE

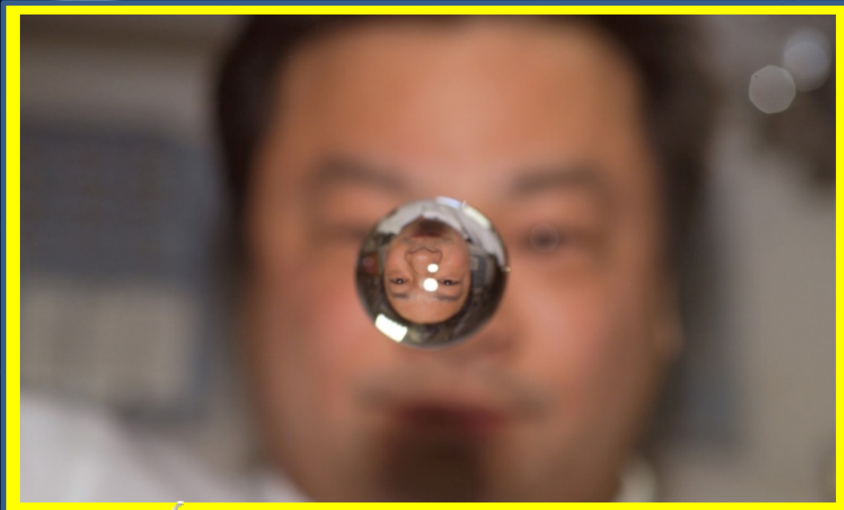


- Kramer et al. (2012)

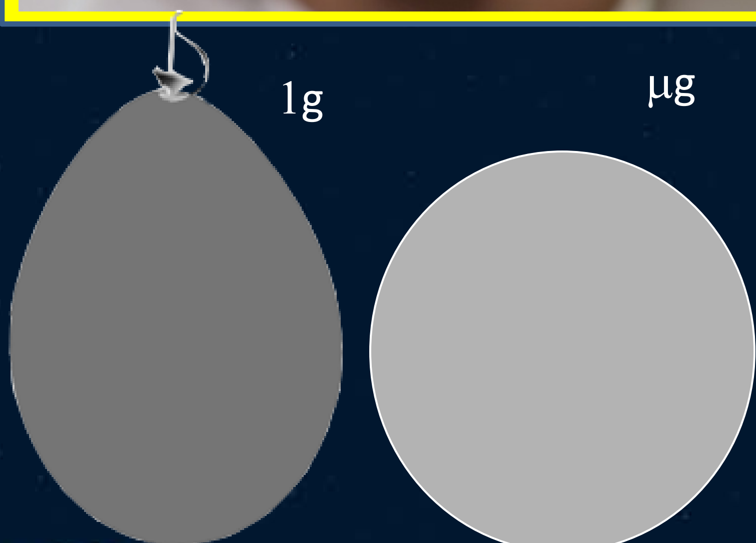
Astronauts exhibit:

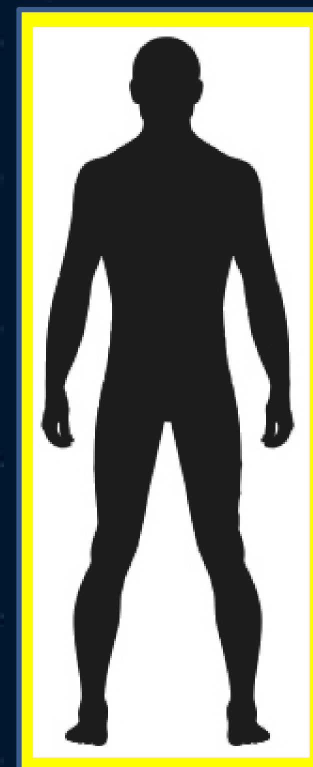
- Optic disk edema
- ONS distension
- Globe flattening
- Choroidal folds
- Increased CSF pressure
- Wool spots
- Decreased IOP post-flight
- ON kinking

Cephalad fluid shift



- The equilibrium shape for a blob of water in μg is spherical (surface tension dominates in reduced gravity)
- When contained in a uniformly elastic sac, like a balloon, it is also spherical





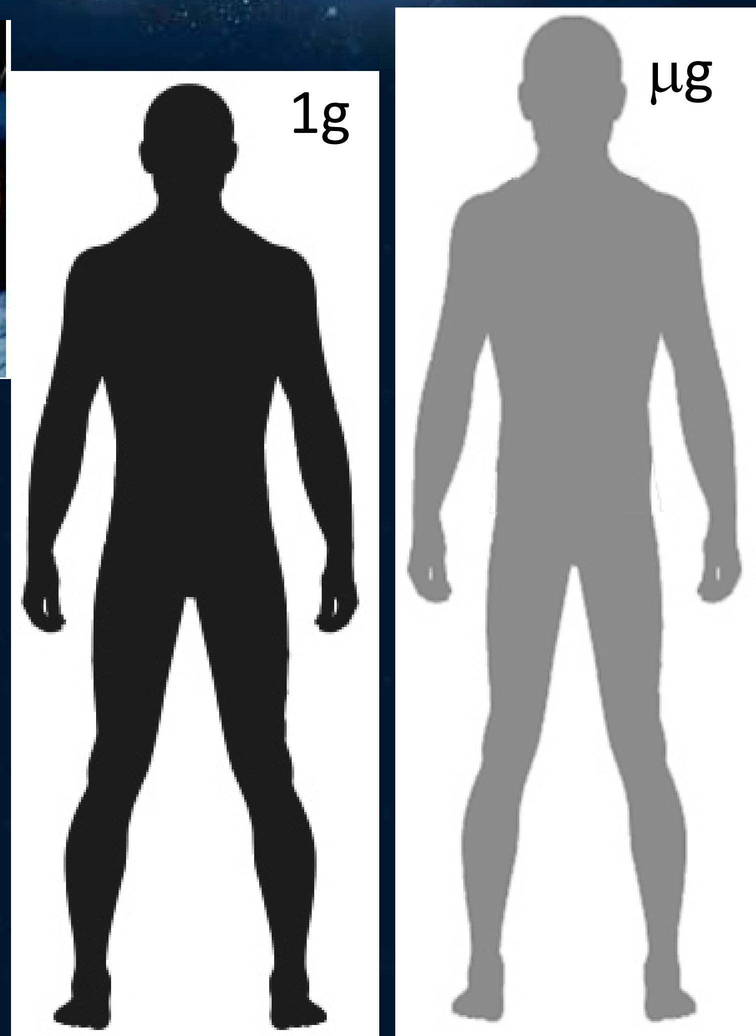
Now consider a human being…

Cephalad fluid shift (cont'd)

Microgravity causes bodily fluids to rush headwards (~2L out of a total 5L)

⇨ **pumpkin head, chicken legs**

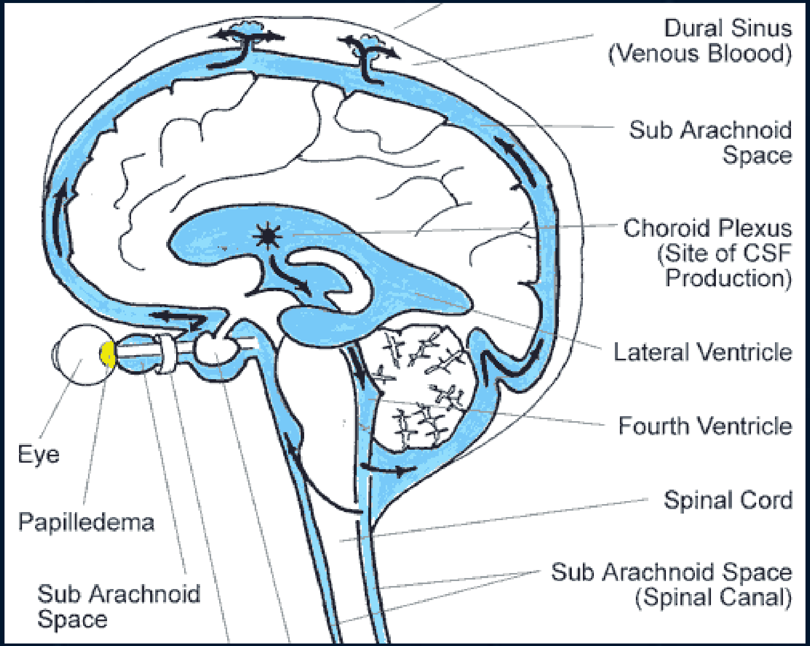
After a period of adjustment, the legs are still scrawny, the spine is elongated, and there is still increased fluid content near the head



Potential culprits

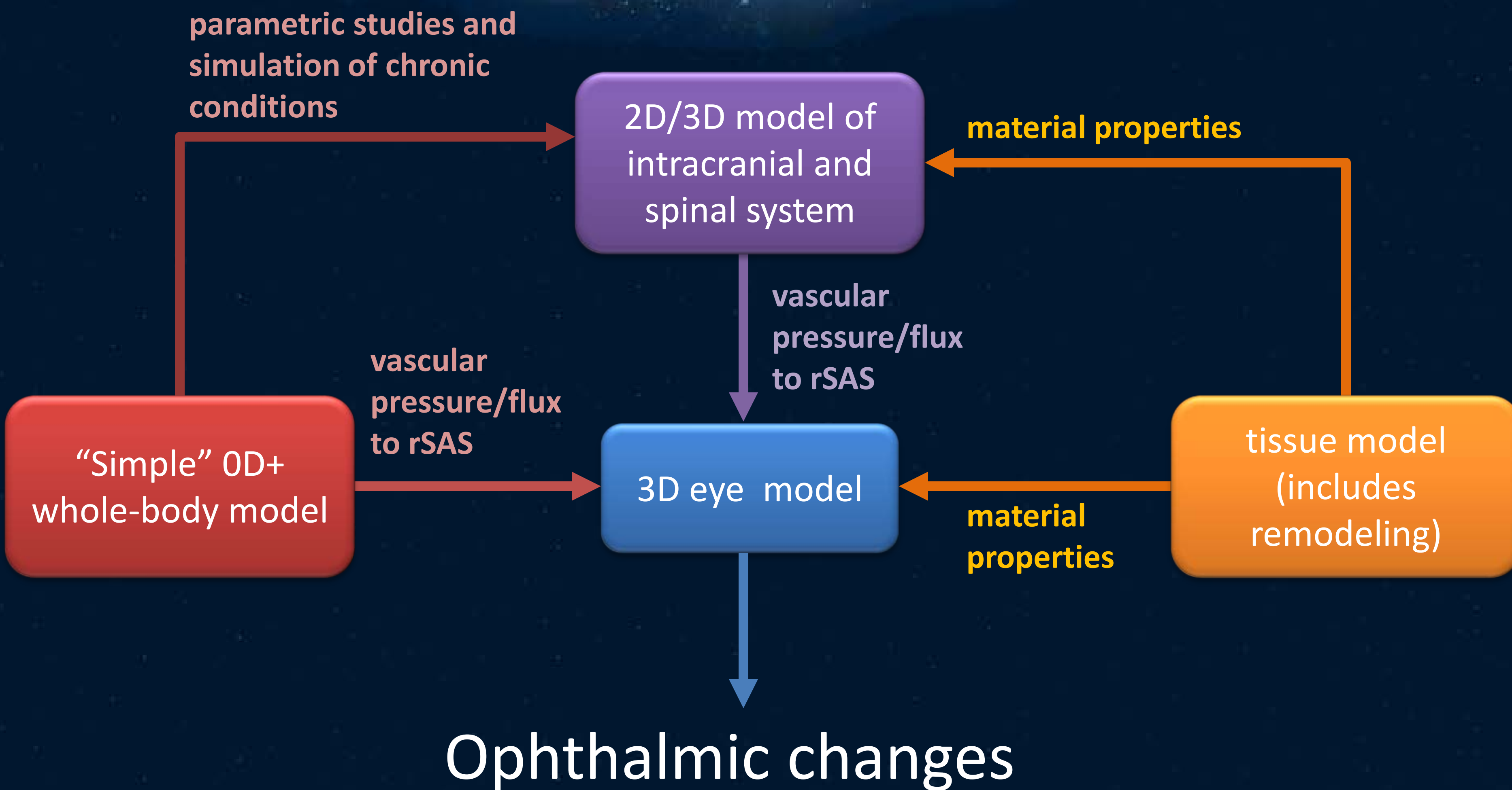
The causal chain linking microgravity and the VIIP syndrome is at present unknown, but key factors are:

- Cephalad fluid shift;
- Disruption of mass transport: blood, cerebrospinal fluid (CSF), and lymph;
- Biomechanical responses of the corneoscleral shell, the optic nerve head (ONH), the choroid, the retrobulbar space (rSAS); and
- Tissue properties and remodeling



Blue region represents subarachnoid space (SAS)

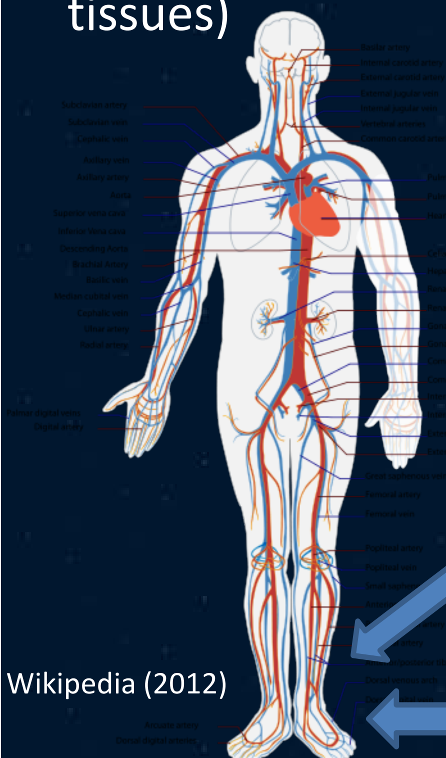
Integrated Systems Analysis



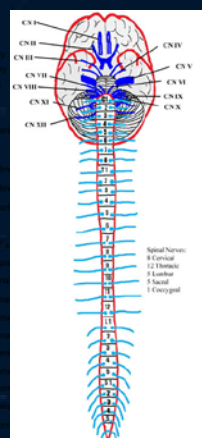
Whole-body lumped-parameter model

Purpose: Provide initial/boundary conditions to a detailed CFD model of the eye

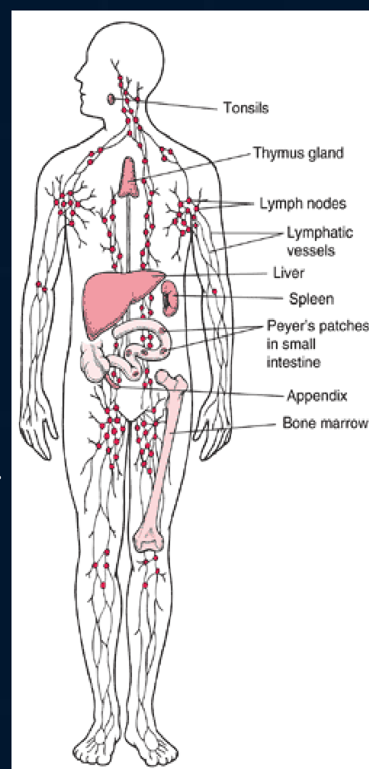
Challenges: Must include cardiovascular (CVS), central nervous (CNS) and lymphatic (LS) systems, which are all linked through mass transport (both direct and through tissues)



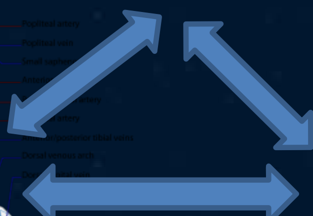
Wikipedia (2012)

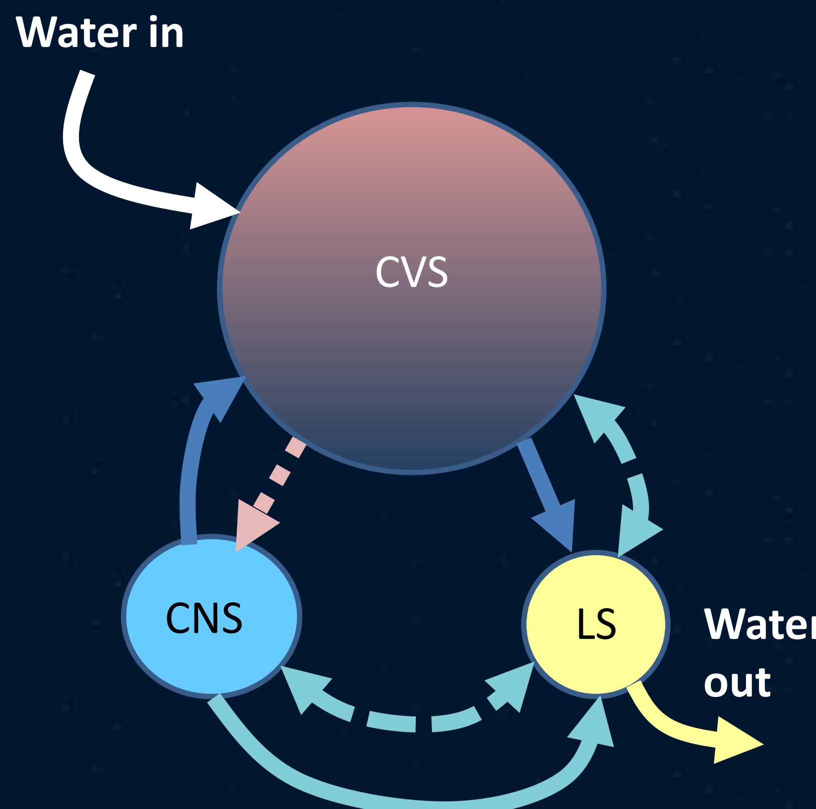


http://www.med.umich.edu



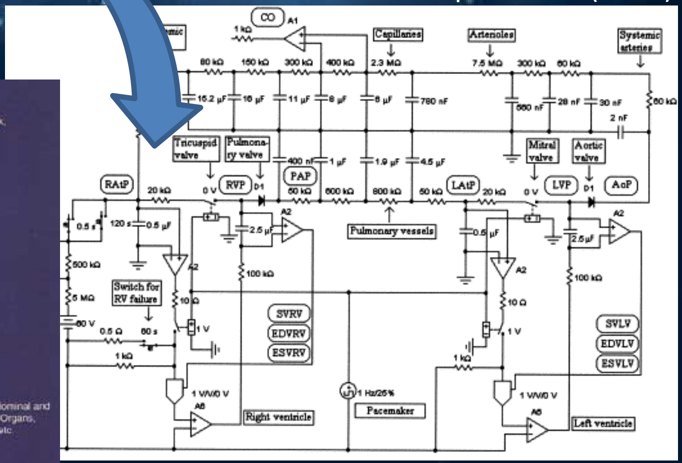
http://www.lgdalliance.org

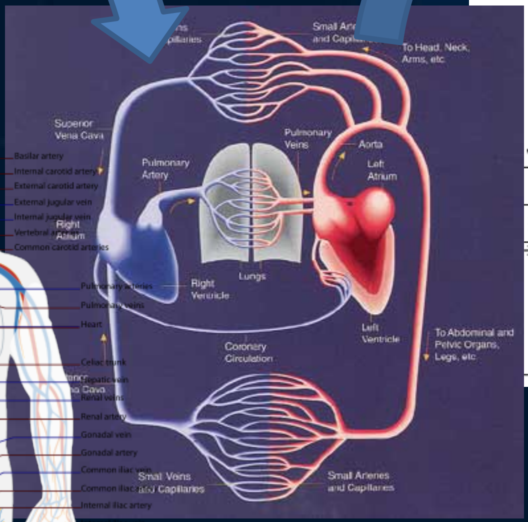




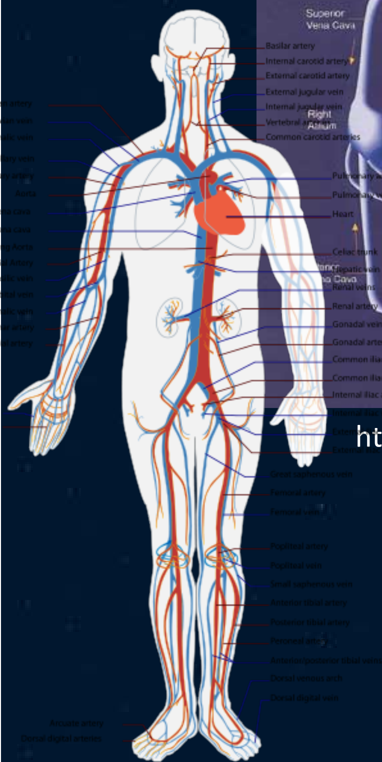
Lumped (0D+) model of the CVS

- Rupnik et al. (2002)





http://www.cilmionline.com/



- Wikipedia (2012)

Successive levels of abstraction allow us to model the CVS as a complex electrical circuit

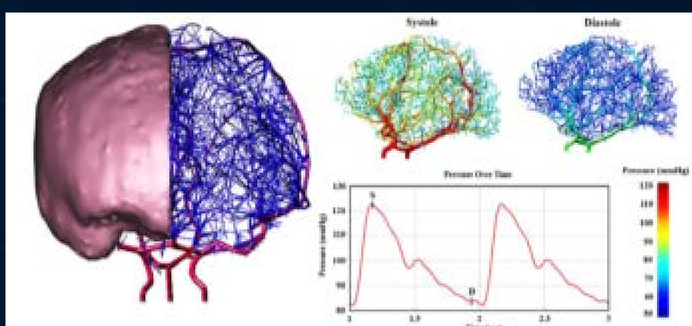
- fluid flow ~ current flow;
- pressure ~ voltage;
- capacitance ~ compliance;
- resistance to (current flow ~ fluid flow);

Spatial resolution is obtained by increasing the number of compartments

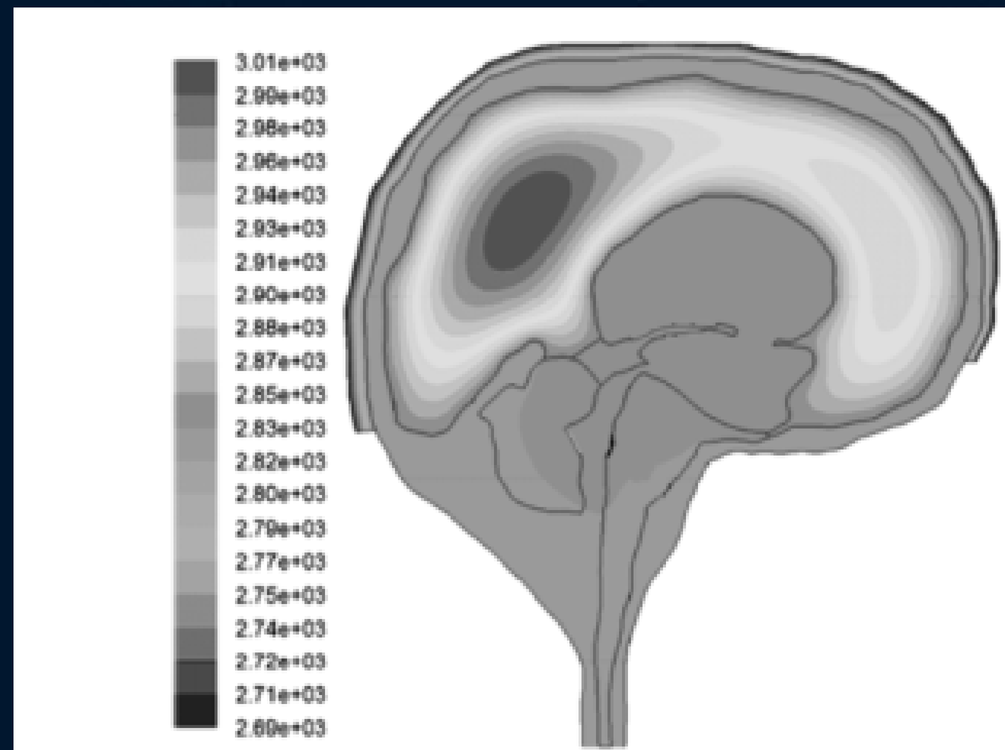
Although there are currently no fully integrated models of the CVS/CNS/LS, there are individual models (0D/1D/2D/3D) of each system/component that are at varying degrees of maturity

CFD modeling of the spinal and intracranial compartments

- 2D/3D CFD for high fidelity prediction of the CSF flow within the spinal and intracranial SAS



- Vaičaitis *et al.* (2011)



- Linninger *et al.* (2007)

Low fidelity model of the lymphatic system

Our understanding of the LS is still evolving

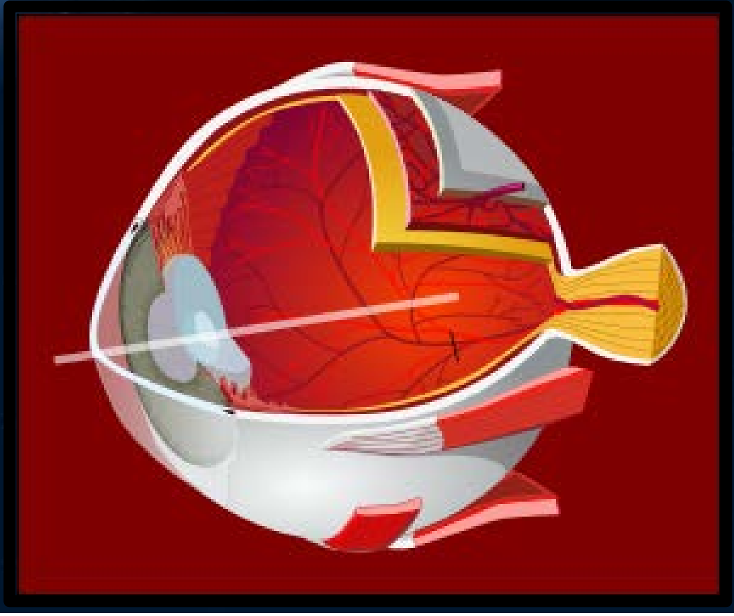
- Returns fluid from CNS to circulation in CVS
- Key player in immune function
- (Very) new discoveries of lymphatic (lymph-like?) systems in the brain and in the vicinity of the ON

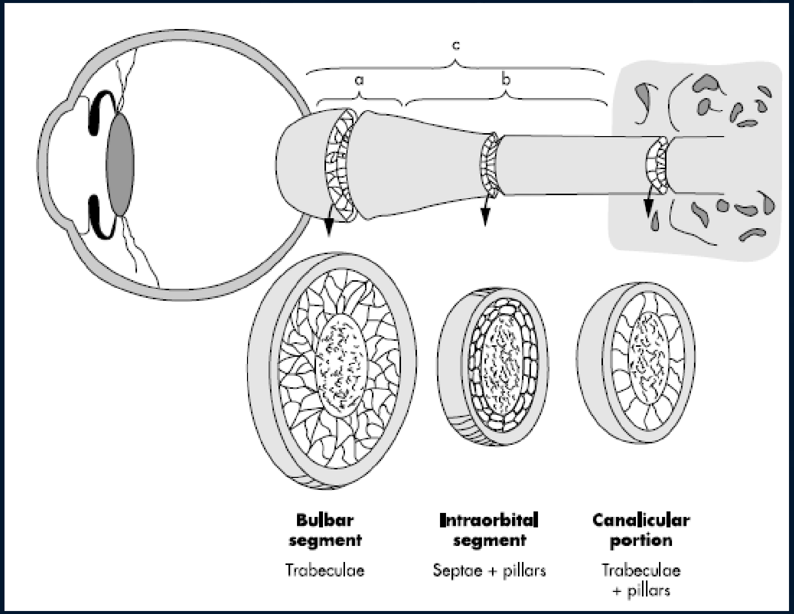
→ Modeling of the LS is still in its infancy

At minimum, we will include a 1-compartment placeholder for the LS which returns fluid from CNS-> CVS, interacts with extracellular matrix, and sends fluid to kidneys for excretion, thus permitting an open-circuit model

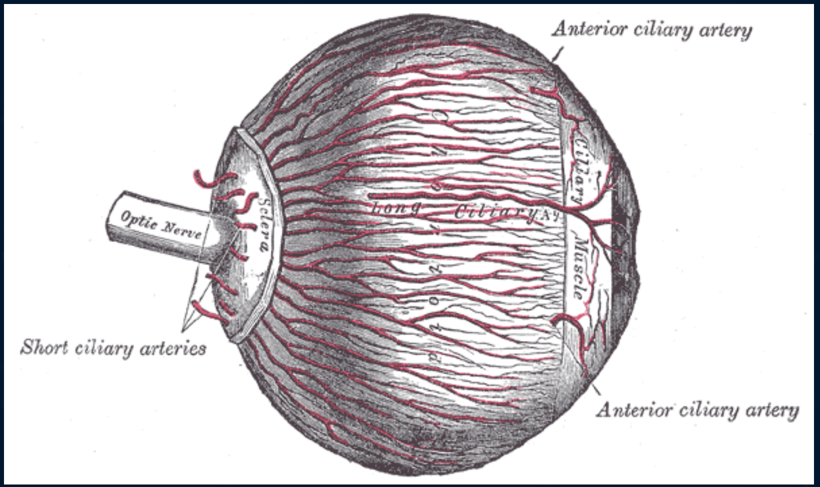
Detailed model of the eye and rSAS

- Idealized geometry includes corneoscleral shell, choroid layer, retina, ONH, rSAS
- Coupled with whole-body model through pressure/fluid flux of CVS, CNS behind the eye



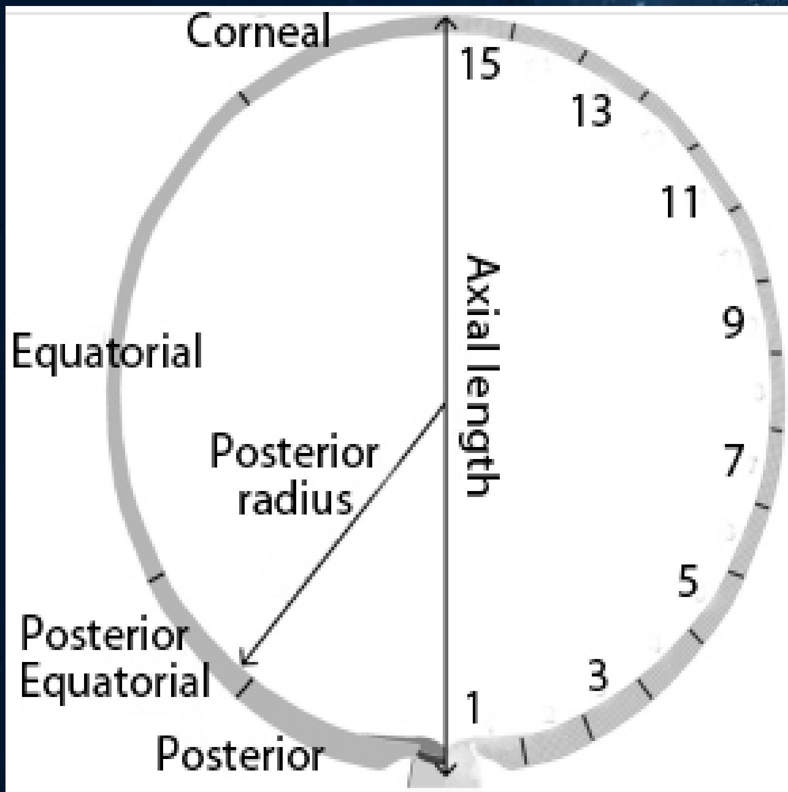


- Killer *et al.* (2003)

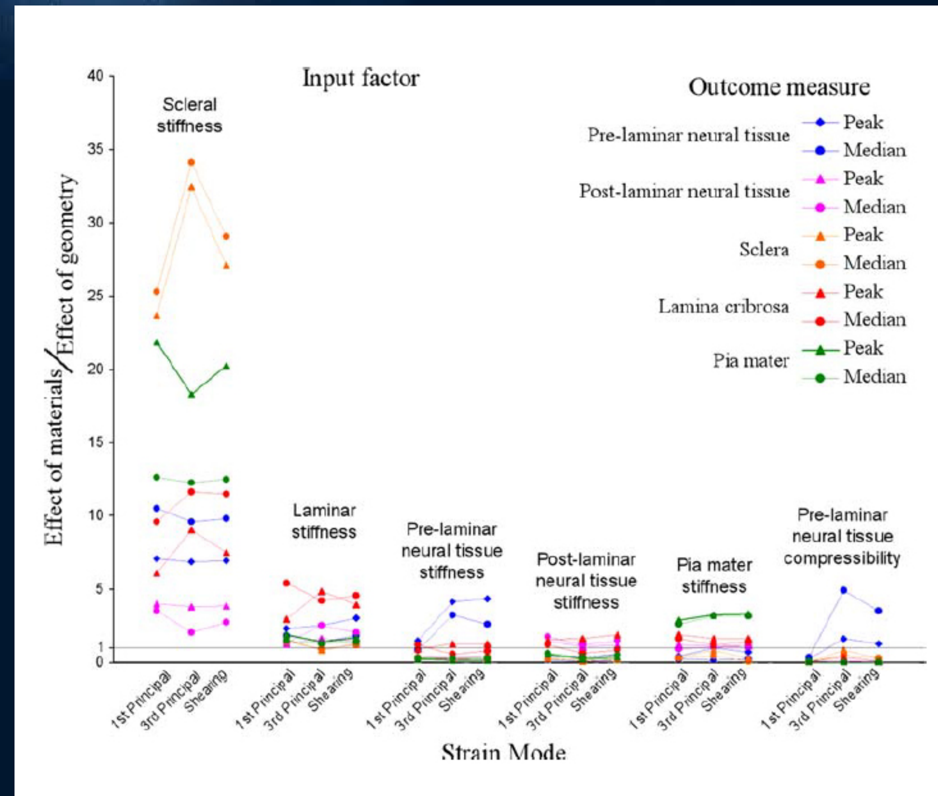


- Standring *et al.* (2005)

Eye modeling (cont'd)



- Norman *et al.* (2011)



- Sigal *et al.* (2009)

- Prior work has shown that the biomechanical response of the ONH is highly sensitive to posterior scleral stiffness and geometry

High Fidelity Tissue Modeling

- Eye tissue stiffness increases at high strain rates, e.g. during valsalva maneuver (Elsheikh et al., 2007)
- Tissue stiffness increases with age (Albon et al., 2000; Elsheikh et al., 2007)
  - The affected crew's mean age of 50.2 ± 4.2 years (Mader et al., 2011)
- Hypothesized remodeling of the ocular and vascular structures due to chronic elevated pressure in the cranial space (Mader et al., 2011; Wu et al., 2005)
- High-fidelity tissue model, such as Grytz and Meschke (2008 &2009), will be necessary to accurately capture the modeling and remodeling process of ocular and intracranial tissues

Conclusions

- Numerical modeling of μg-induced visual impairment requires well-coordinated integration of many submodels:
  - Lumped parameter model of CVS, LS
  - 2D/3D model of CNS intracranial/spinal space
  - Well-resolved model of globe, choroid and rSAS
  - Tissue models that can adapt to chronic modification of biomechanical stress state
- Models will be applied to a problem that is well outside of normal physiological response
  - Verification and validation of each submodel and integrated model will be crucial