Microgravity-driven Optic Nerve/Sheath Biomechanics Simulations

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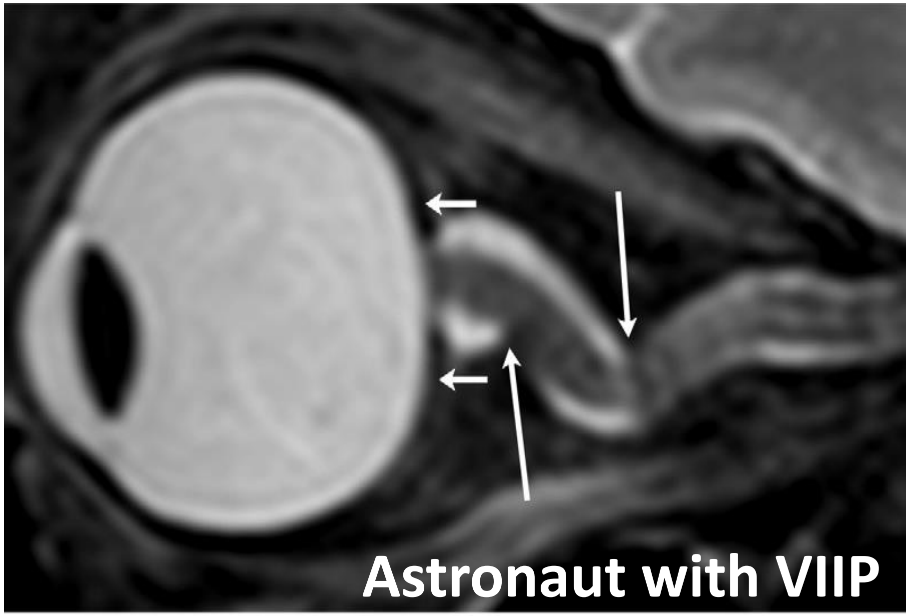
Structural Changes in the Posterior Eye



Kramer et al. Radiology, 2012.

Hypothesis

Increased CSF pressure, transmitted to the RB-SAS, drives remodeling of connective tissues in the posterior eye and optic nerve sheath

Eventually leads to the vision disturbances characteristic of VIIP

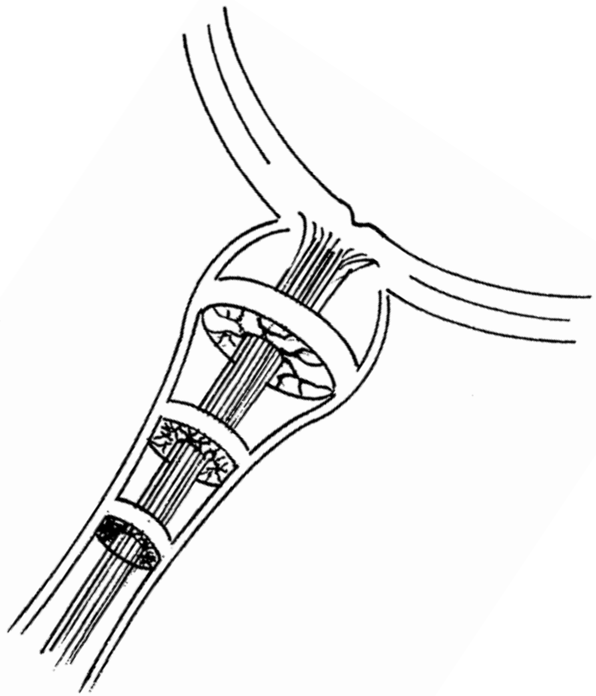
Goal

Study the biomechanical response of the optic nerve sheath and posterior eye to elevated CSF pressures

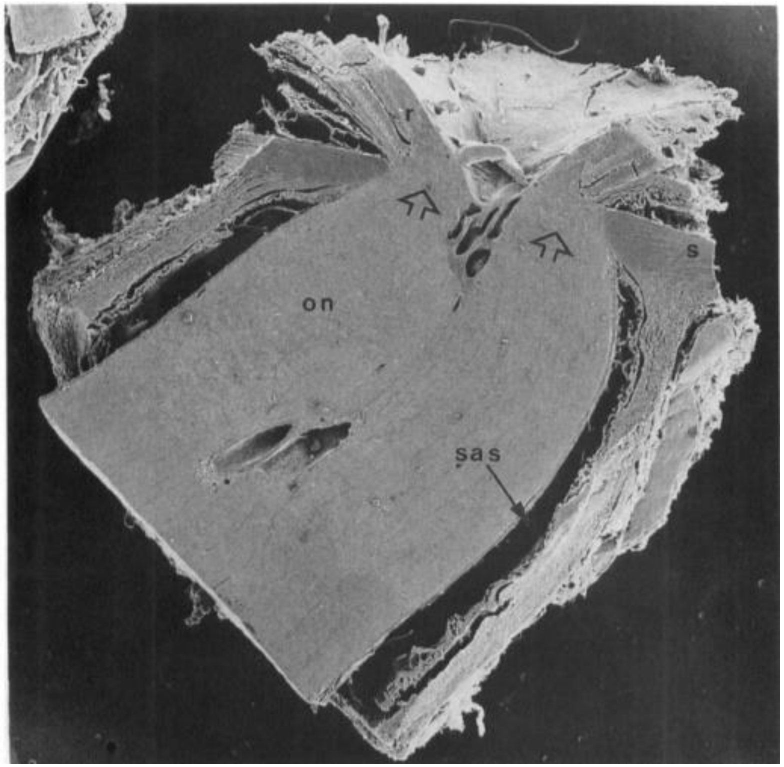
Key tool: Finite element modeling

Methods

Basic Modeled Geometry

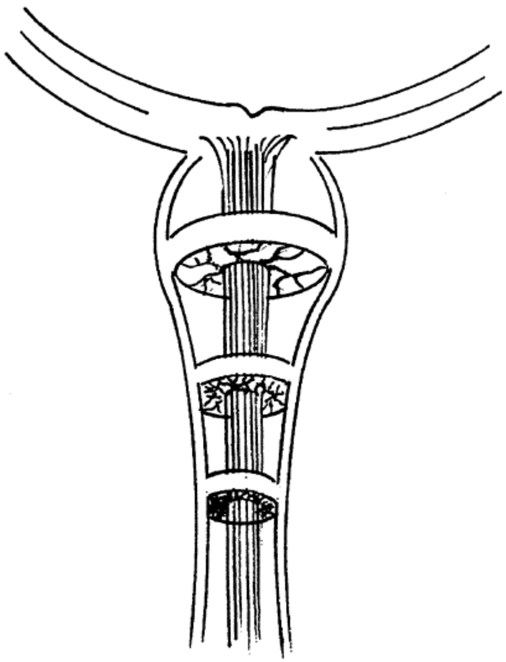


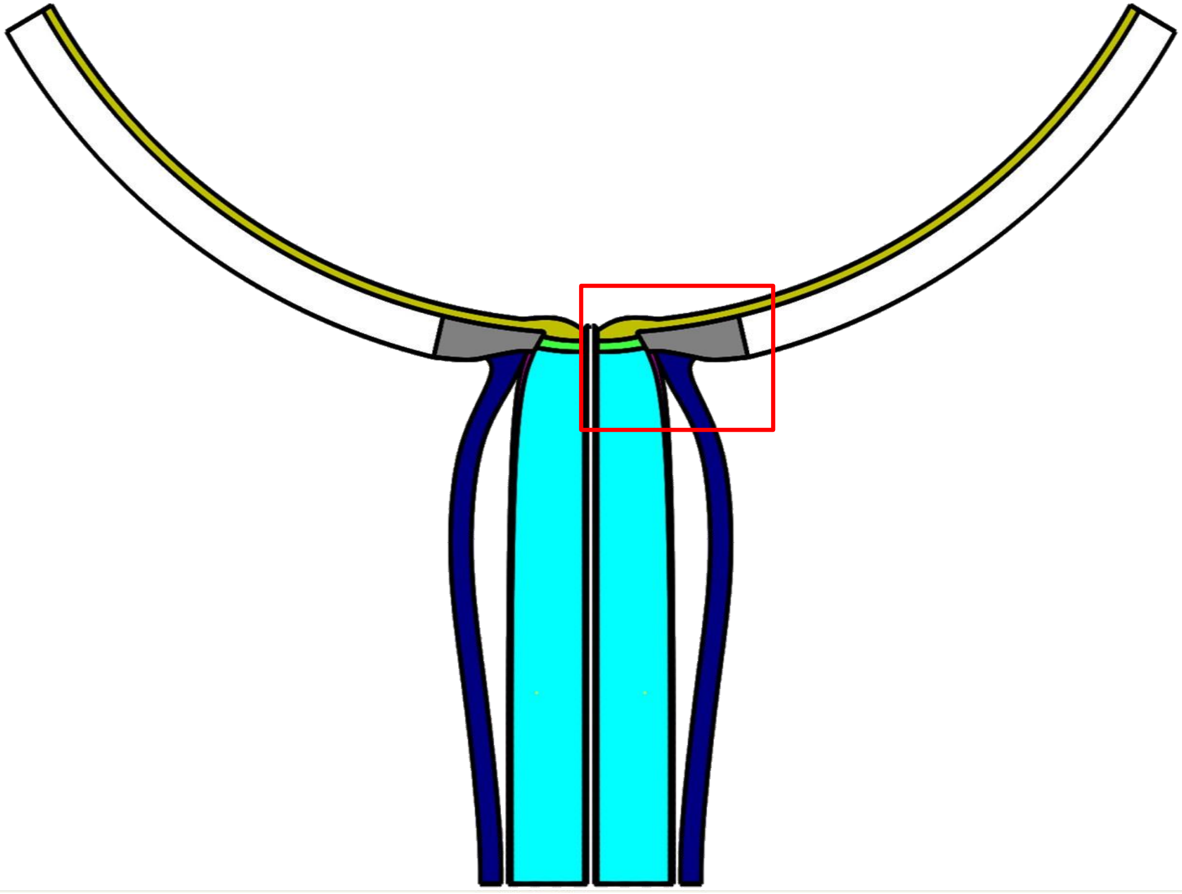
Hansen et al. Acta Ophthalmologica, 2011.



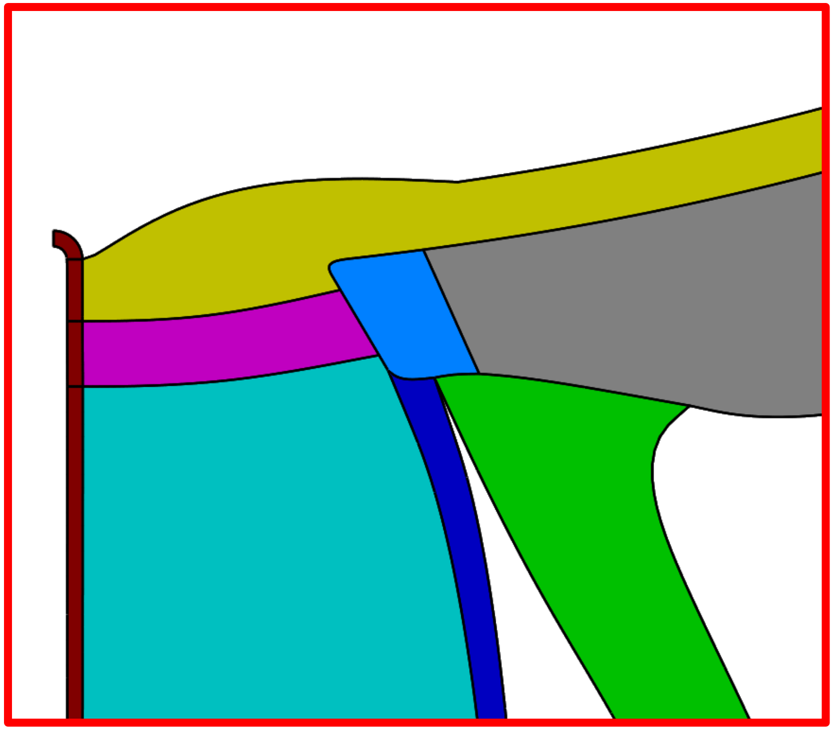
Adopted from Ekington et al. 1990

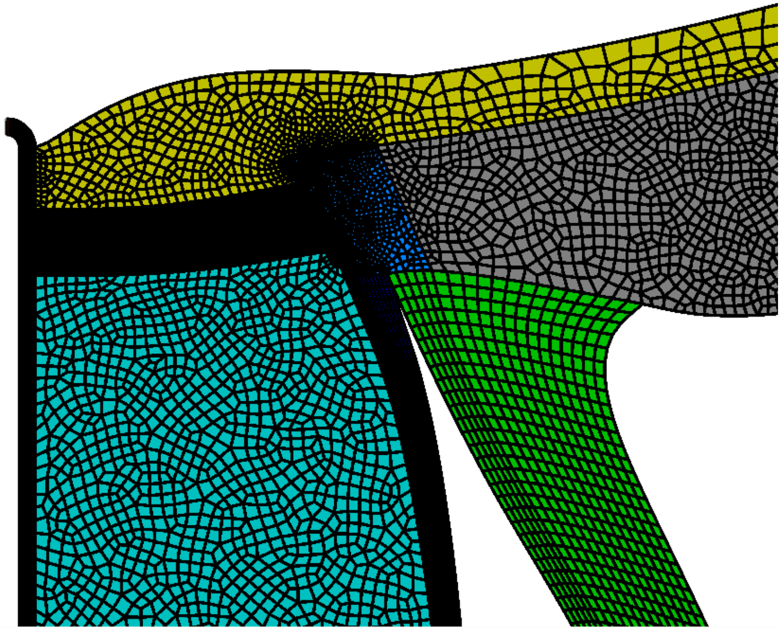
Model Overview





Finite element model





Tissue Constitutive Models

- Mooney-Rivlin plus von Mises Distributed Fibers
  - Proposed by Girard and Ethier for the the sclera
  - Implemented into FEBio V2 by Gouget and Girard for thin tissues

$$\Psi = F_1\left(\tilde{I}_1, \tilde{I}_2\right) + \int_{\theta_p-\frac{\pi}{2}}^{\theta_p+\frac{\pi}{2}} P(\theta)\, F_2\left(\tilde{\lambda}[\theta]\right) d\theta + \frac{K}{2}[\ln(J)]^2$$

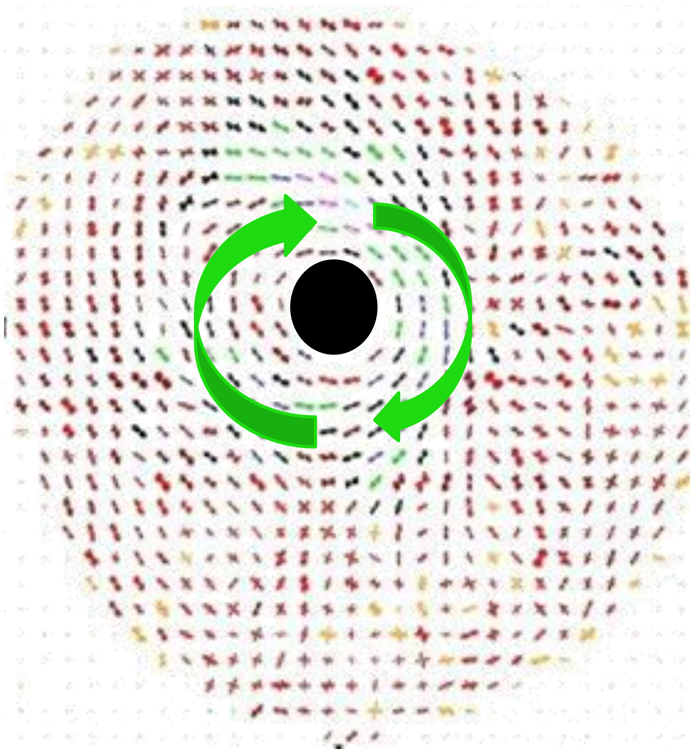
- F_1 represents ground substance (neo-Hookean): $F_1 = C_1\left(\tilde{I}_1 - 3\right)$
- F2 represents collagen fibers
  - Collagen fibers are loaded within their non-linear region

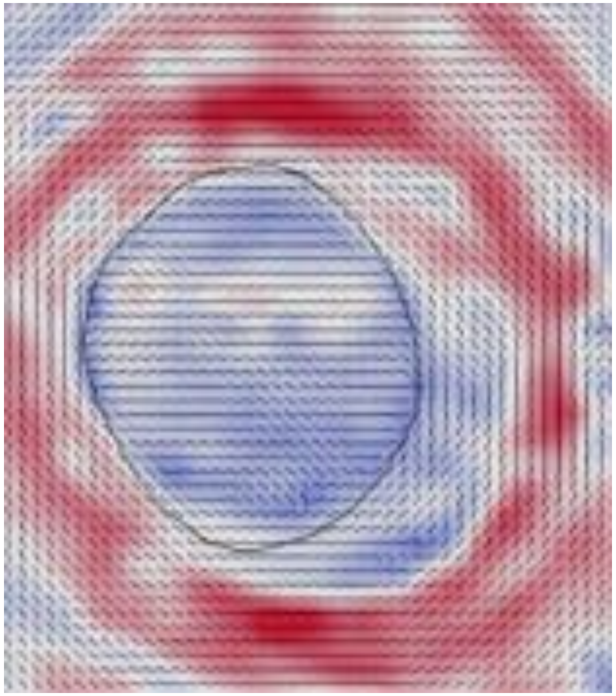
$$\check{\lambda}\frac{\partial F_2}{\partial \check{\lambda}} = 0, \check{\lambda} \leq 1$$

$$\check{\lambda}\frac{\partial F_2}{\partial \check{\lambda}} = C_3\left(e^{C_4(\lambda-1)} - 1\right), 1 < \check{\lambda} \leq \lambda_m$$

Collagen Orientation in the Sclera

- Sclera: collagen fibers treated as transversely isotropic
- Peripapillary sclera: moderately aligned collagen fibers
- Annular ring: highly aligned collagen fibers





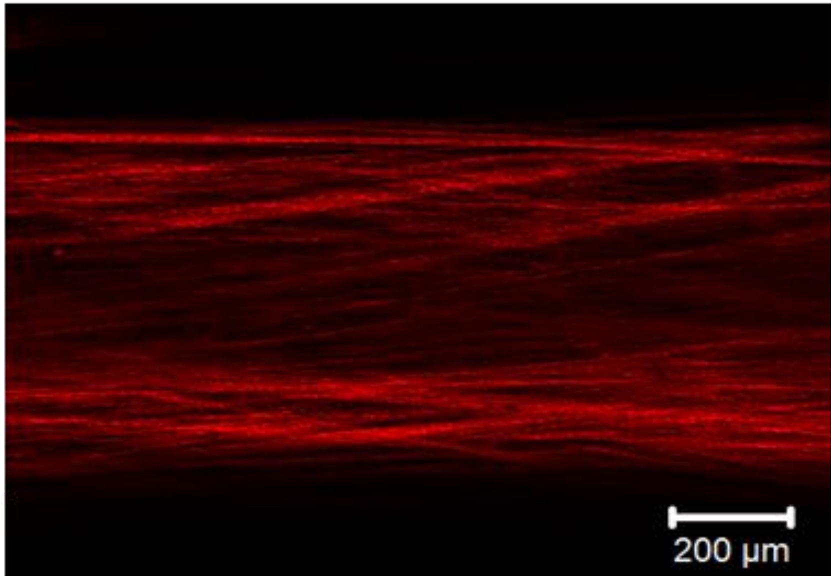
~ Pijanka et al. 2012 & Zhang et al. 2015

Collagen Orientation in the ONS

Pia mater and dura mater: fibers were modeled as transversely isotropic

~Raspanti et al. 1992 Noort et al. 1980 & Raykin et al. 2015

Dura Mater

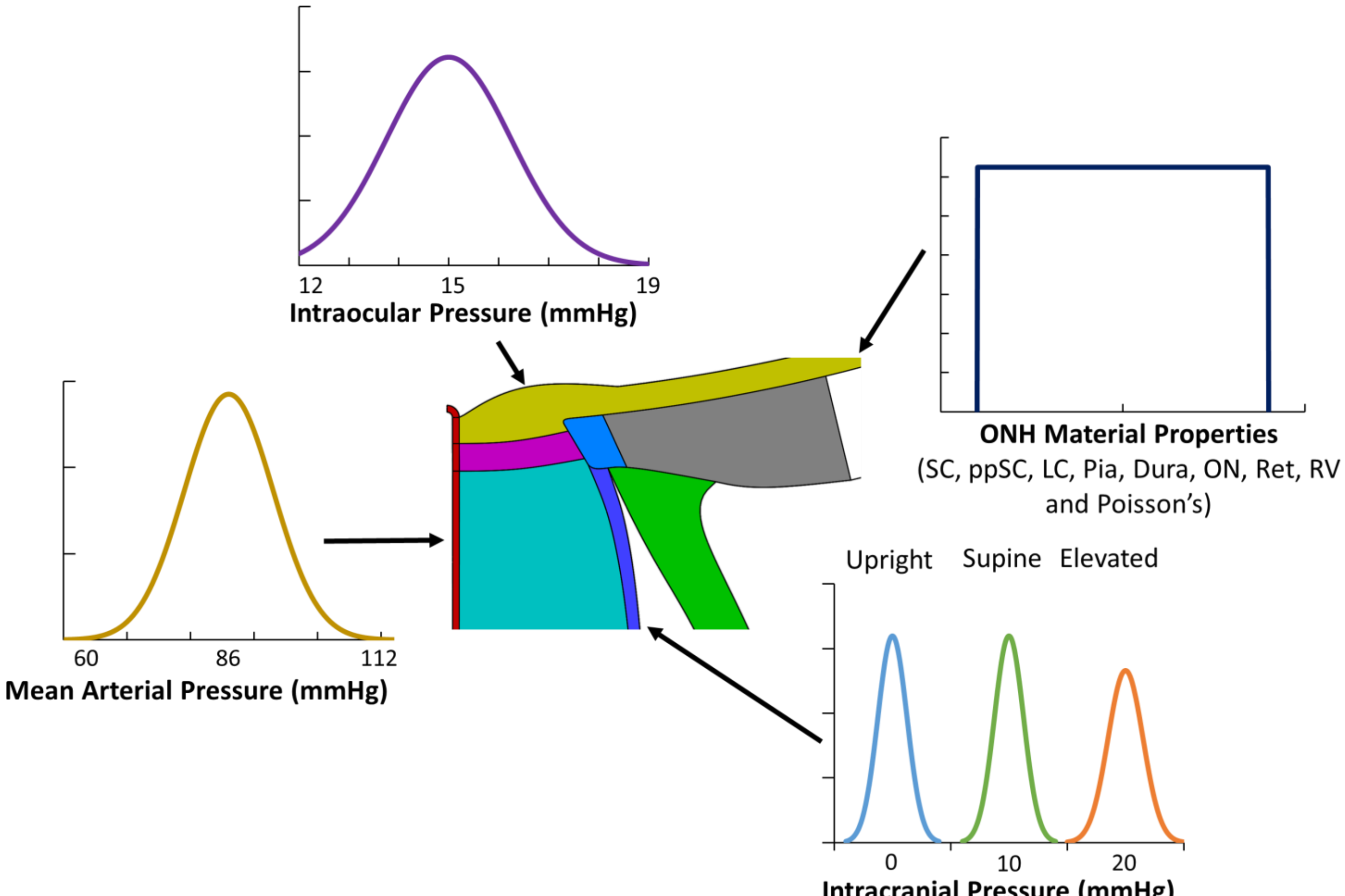


Outcome measures

- Strain (fractional tissue elongation) in all tissue regions
  - Strain is a tensor and can be decomposed into 3 primary components
    - First principal strain (stretch)
    - Second principal strain
    - Third principal strain (compression)
- Why do we care about strain?
  - Cells are mechanosensitive and alter their phenotype in response to mechanical strain

Latin Hypercube Sampling (LHS)

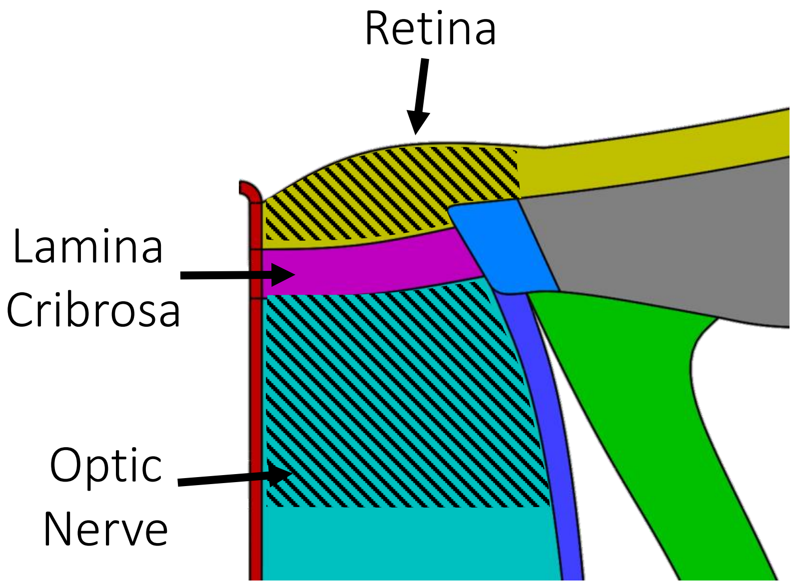
How do variations in pressures and tissue mechanical properties affect tissue strains?



Latin Hypercube Sampling (LHS)

Primary outcome measures: peak tensile and compressive strains in the retina, lamina cribrosa and retrolaminar optic nerve

<u>Regions of Interest:</u>

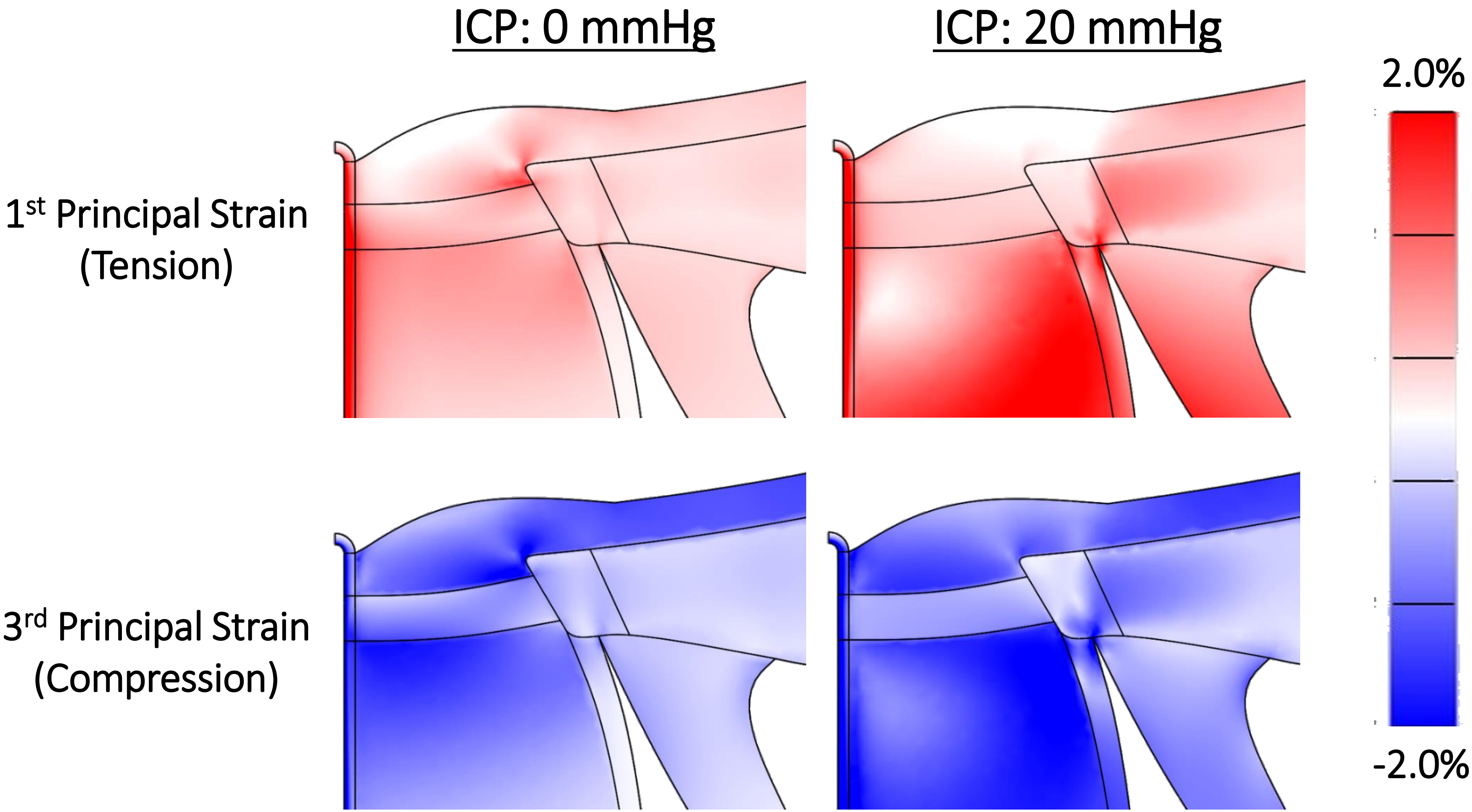


Tissue Material Properties

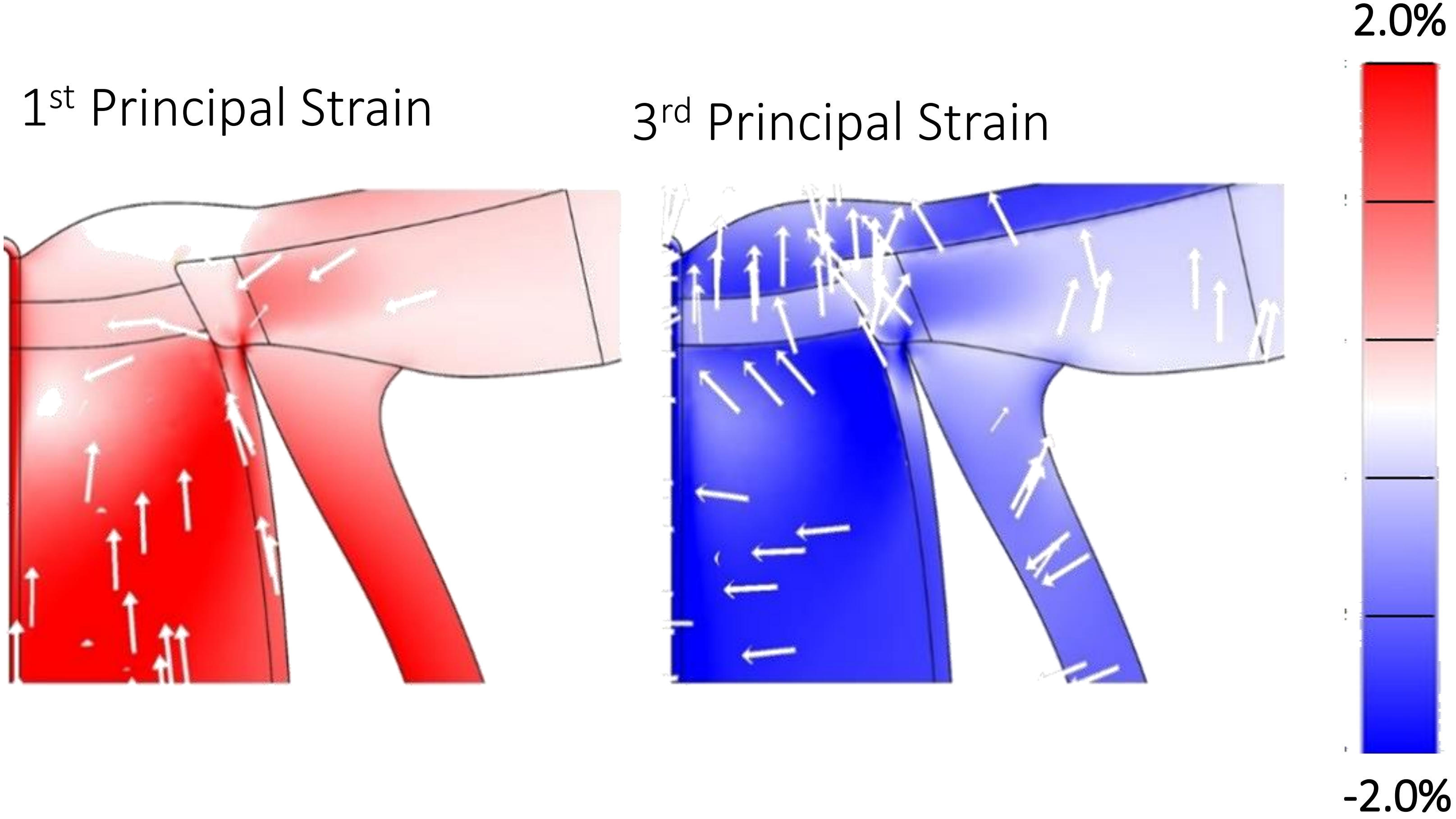
1. Linear-elastic, homogenous and isotropic
   - **Tissues:** lamina cribrosa, optic nerve, retina and retinal vessel
     - Simplification chosen due to limited information & low impact
   - 2 input parameters: stiffness (E) and tissue compressibility (ν)
2. Mooney-Rivlin solid with embedded collagen fibers
   - **Tissues:** sclera, peripapillary sclera, annular ring, pia mater and dura mater
     - Allows more complex, nonlinear behavior and collagen fiber orientation and stiffness

Results

Principal Strain Magnitudes



Principal Strain Directions

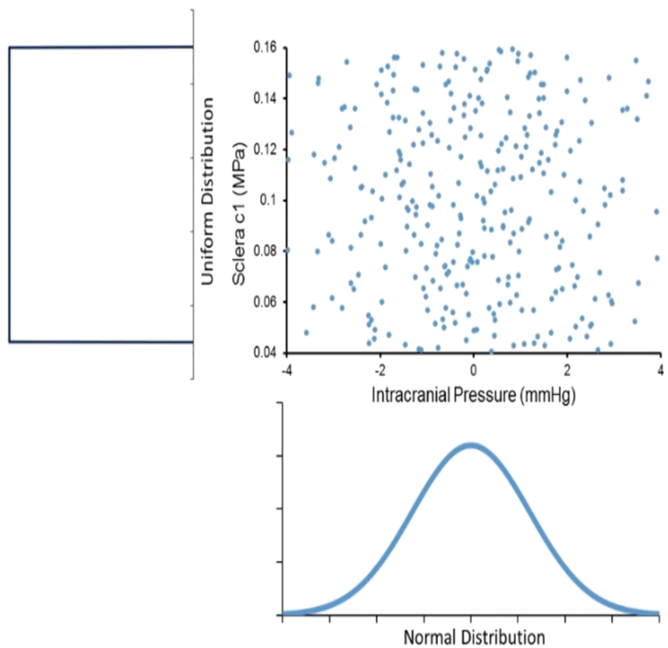


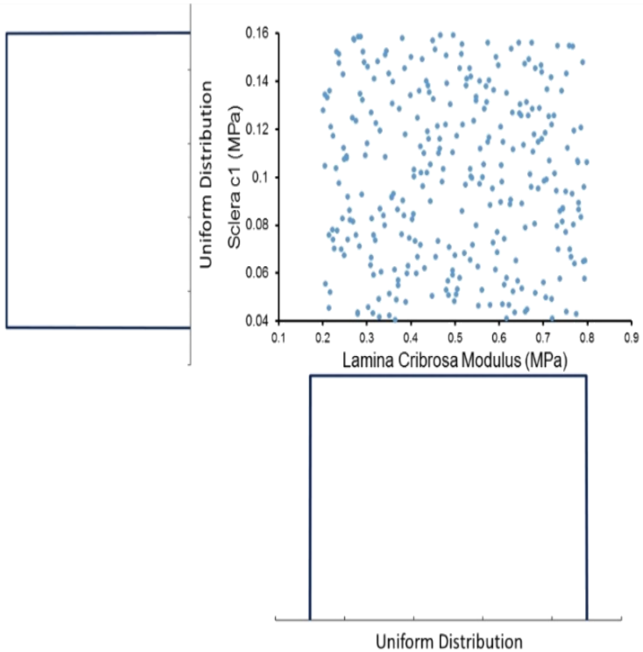
Is LHS Sampling Unbiased?

Use sign test to identify possible sampling bias

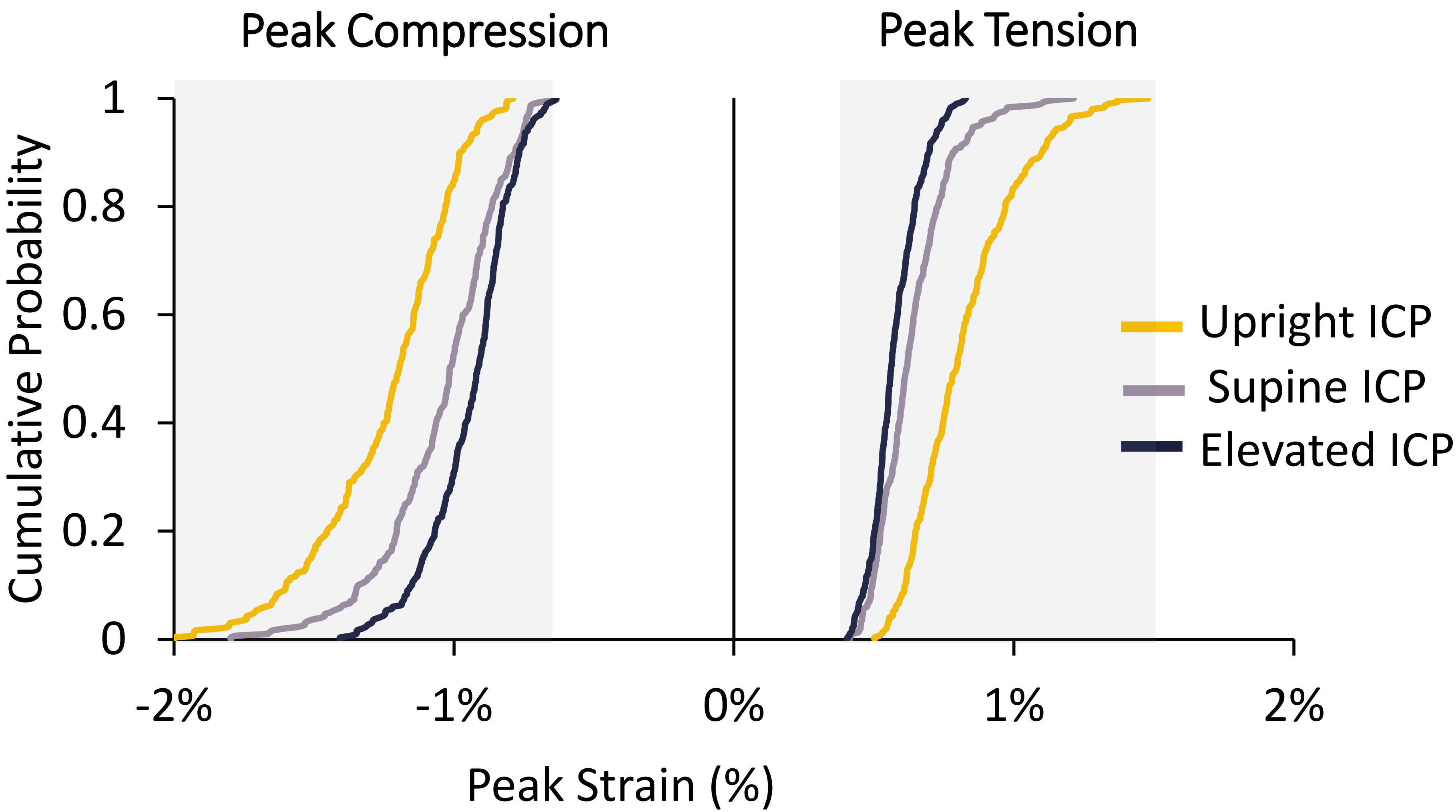
- Do input parameters generated by LHS have a median value significantly different than our baseline value?
- Answer: no ($p>0.48$ for all input parameters)

Confirmed by scatter plots

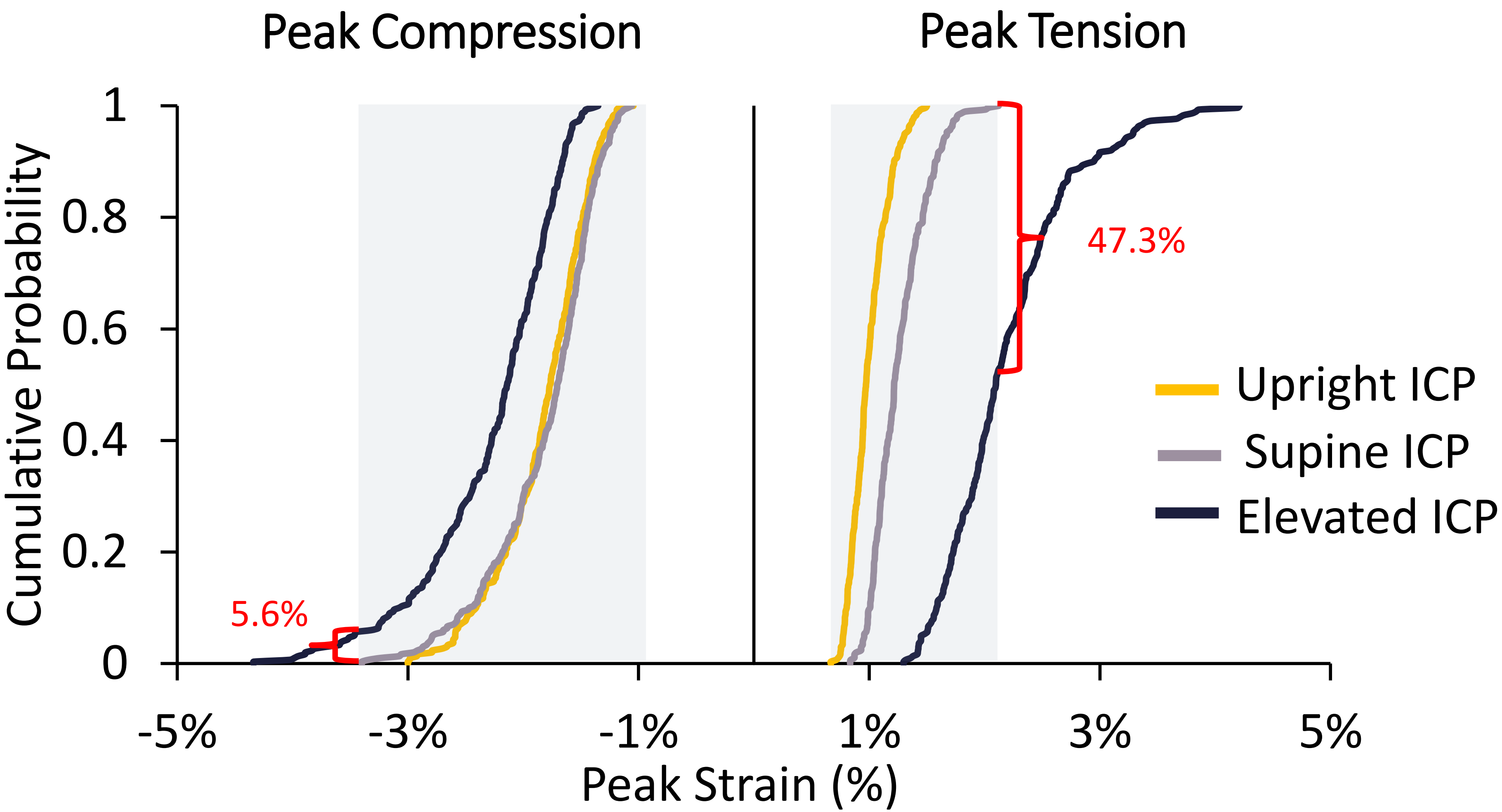




Lamina Cribrosa

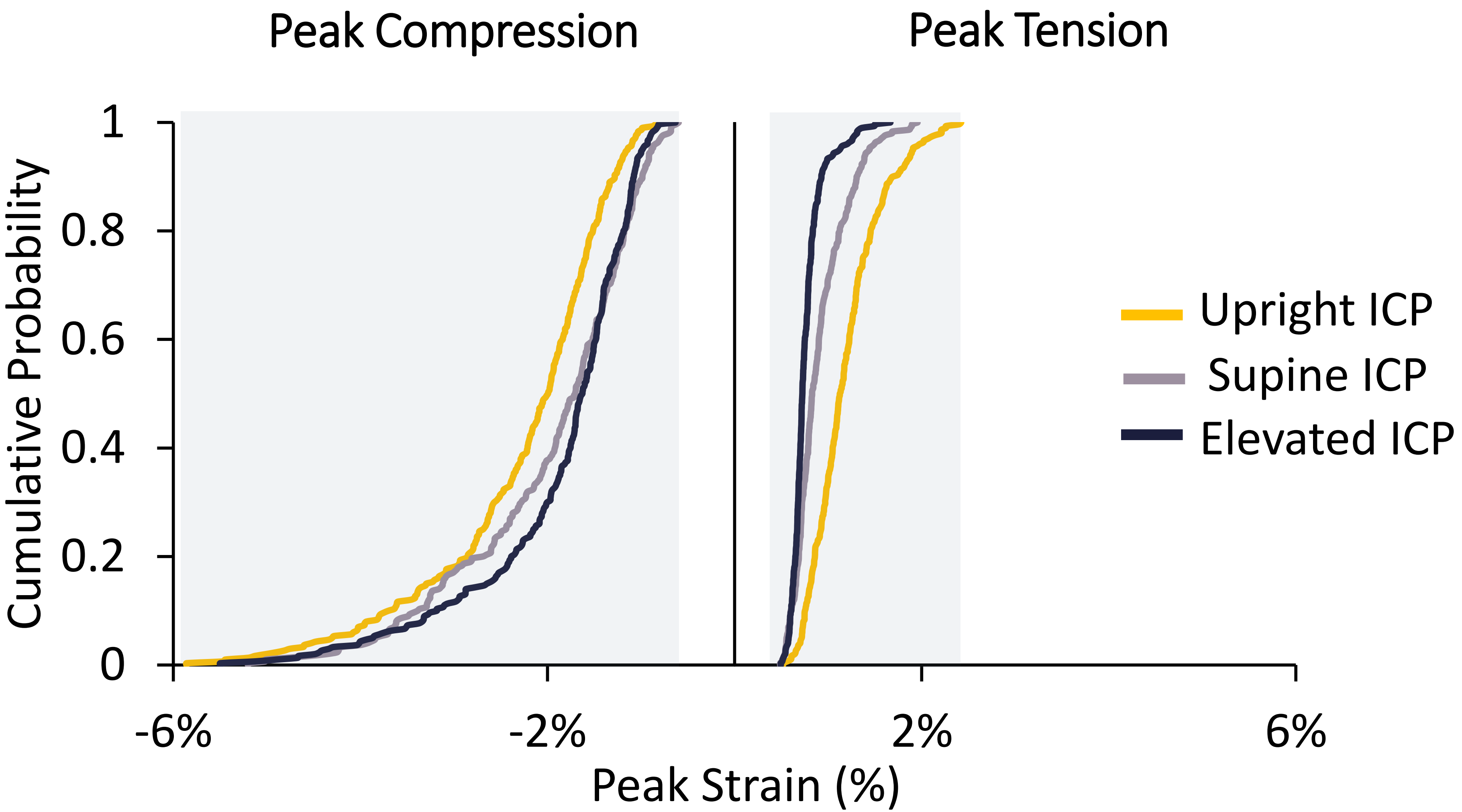


Optic Nerve



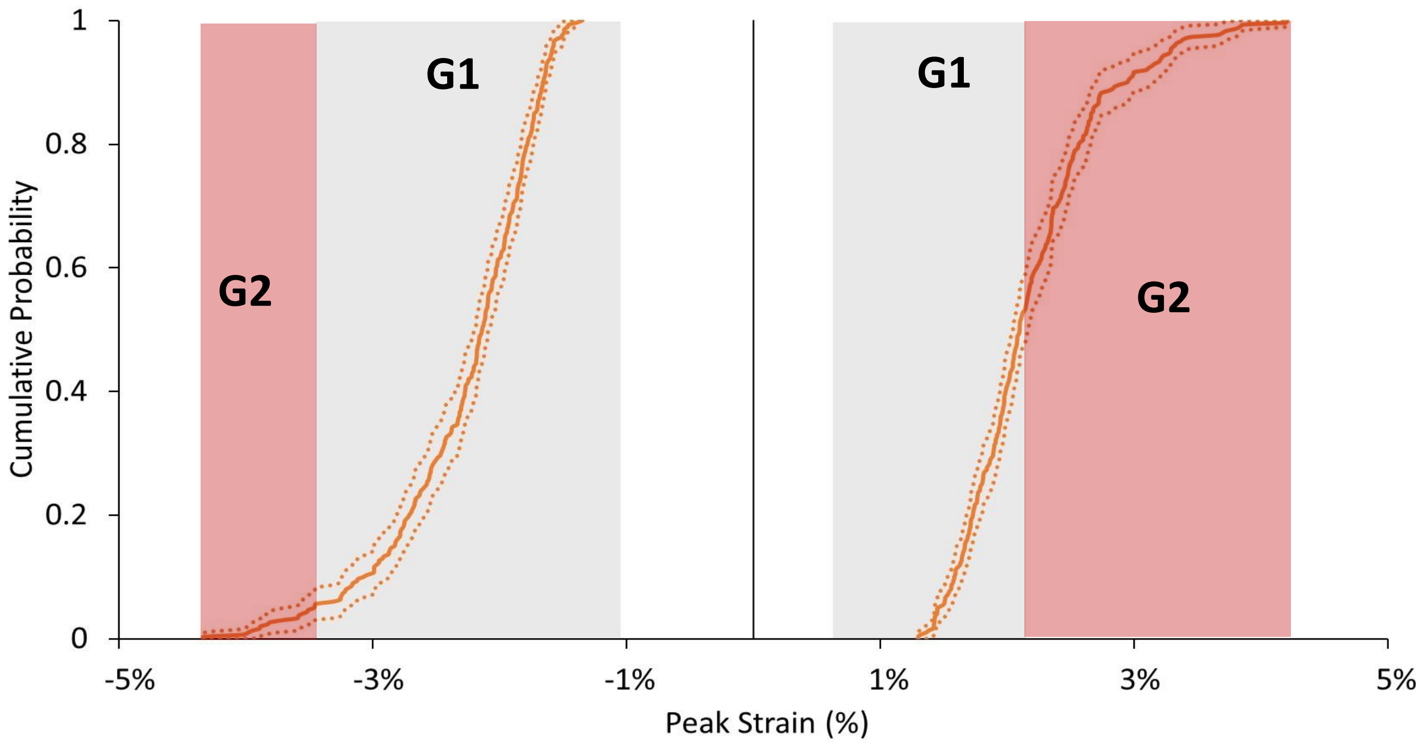
Peak Compression
Peak Tension
Cumulative Probability
1
0.8
0.6
0.4
0.2
0
5.6%
47.3%
Upright ICP
Supine ICP
Elevated ICP
-5%
-3%
-1%
1%
3%
5%
Peak Strain (%)

Prelaminar Tissue



What creates “extreme strains”?

- ICP significantly higher in G2
- Lower pia mater ground substance and fiber stiffness in G2
- Lower MAP and higher optic nerve compressibility in G2



Summary

- 47% of individuals experience “extreme strains” in the optic nerve (c.f. 41% of astronauts suffering from VIIP syndrome)
- Identified specific factors that are associated with these extreme strains
  - Elevated ICP, weak pia mater
- Future experimental work should examine how strains initiate a remodeling response in the optic nerve and optic nerve sheath

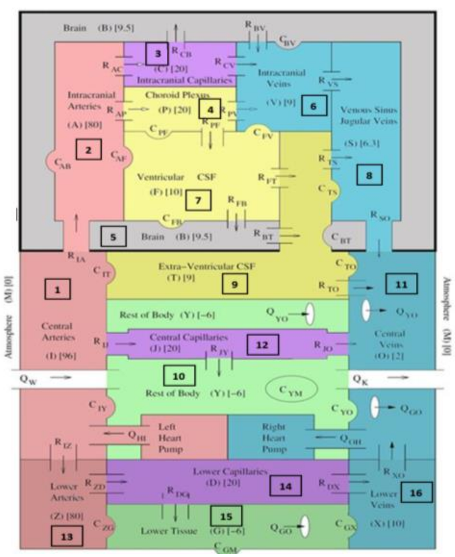
Ongoing Work

Integration

LHS Inputs

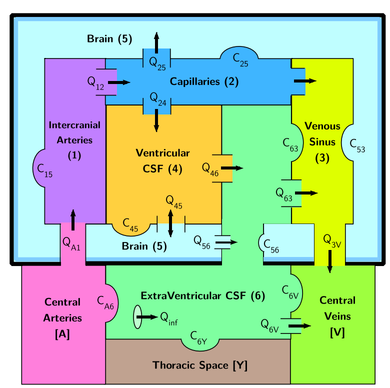
	Cardiovascular	Central Nervous	Eye FE
Run 1	$x_1 \ldots x_{42}$	$y_1 \ldots y_{17}$	$z_1 \ldots z_{20}$
Run 2	$x_1 \ldots x_{42}$	$y_1 \ldots y_{17}$	$z_1 \ldots z_{20}$
Run N	$x_1 \ldots x_{42}$	$y_1 \ldots y_{17}$	$z_1 \ldots z_{20}$

16 Compartment Cardiovascular System

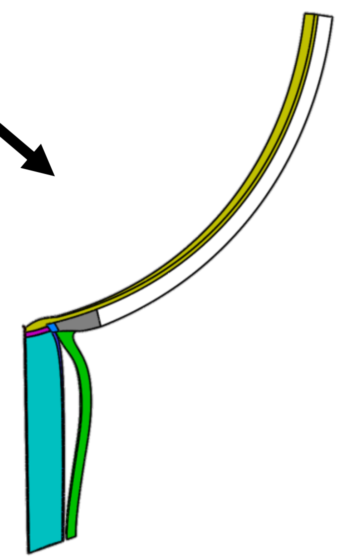


Blood Pressure

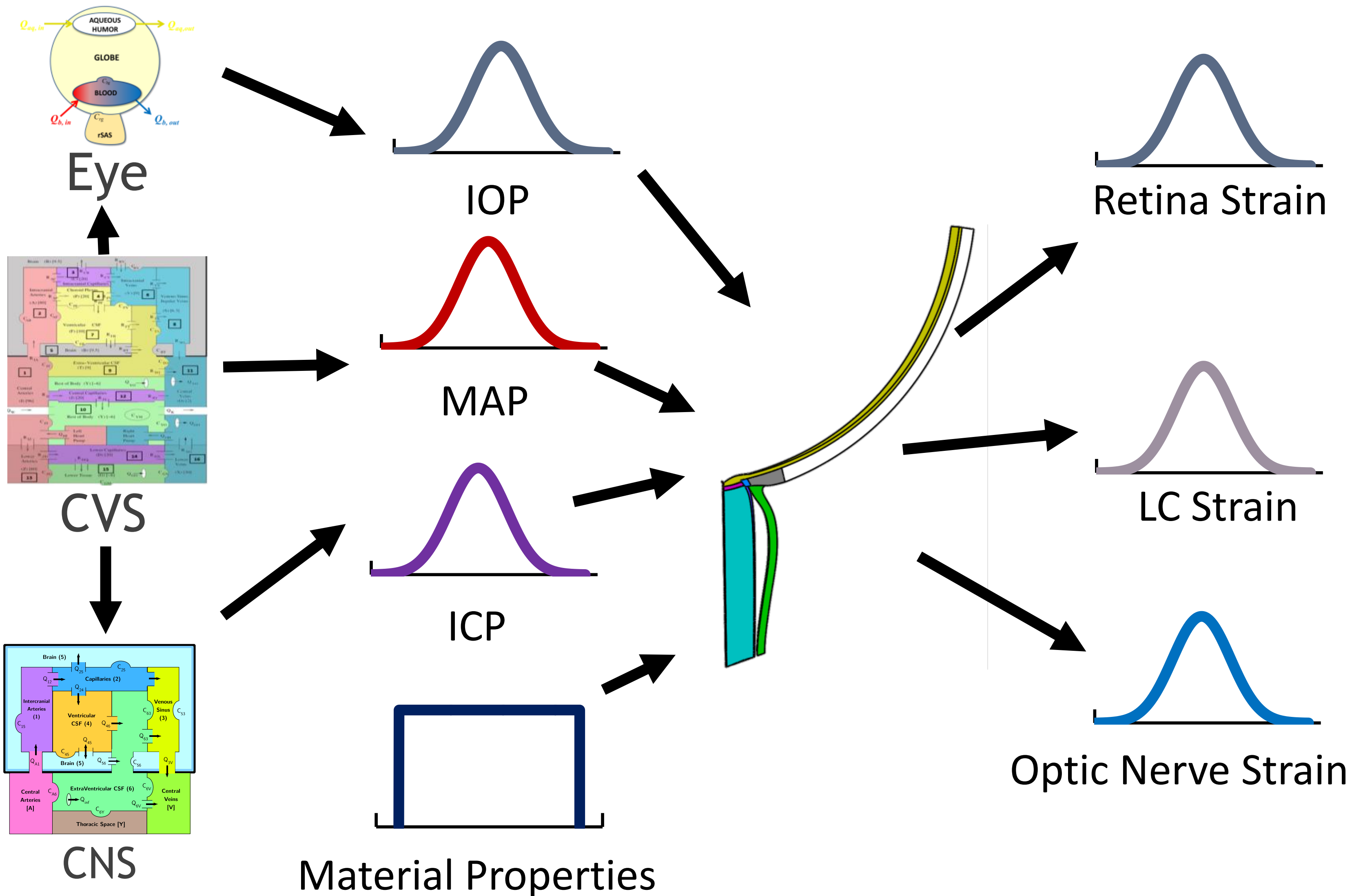
6 Compartment Central Nervous System



Intracranial Pressure (ICP)



Model Integration



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