PROBABILISTIC MODELING OF OCULAR BIOMECHANICS IN VIIP: RISK STRATIFICATION

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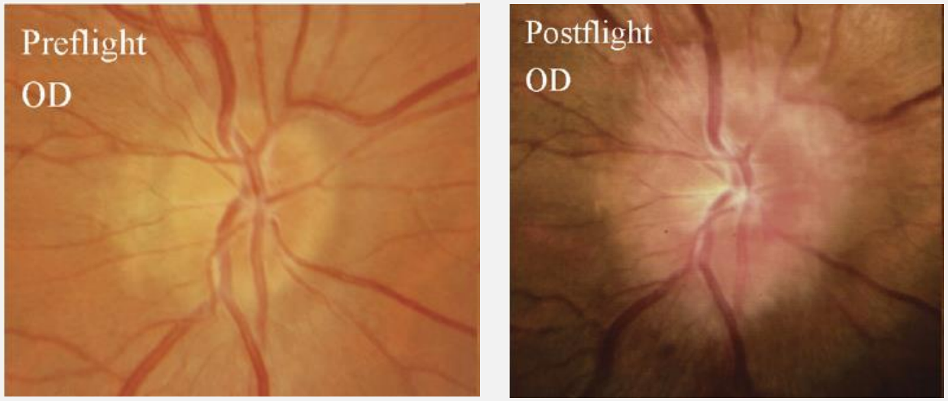
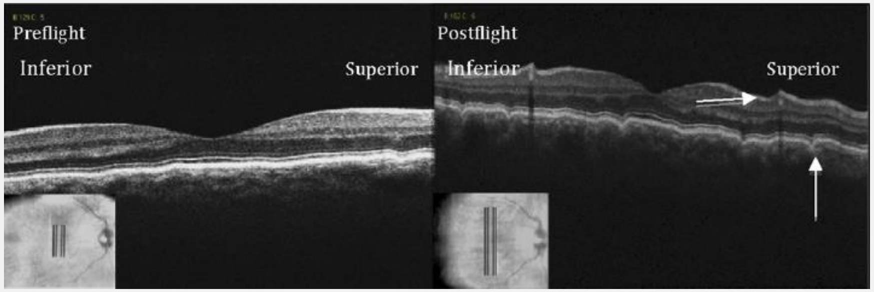
The Eye in Microgravity

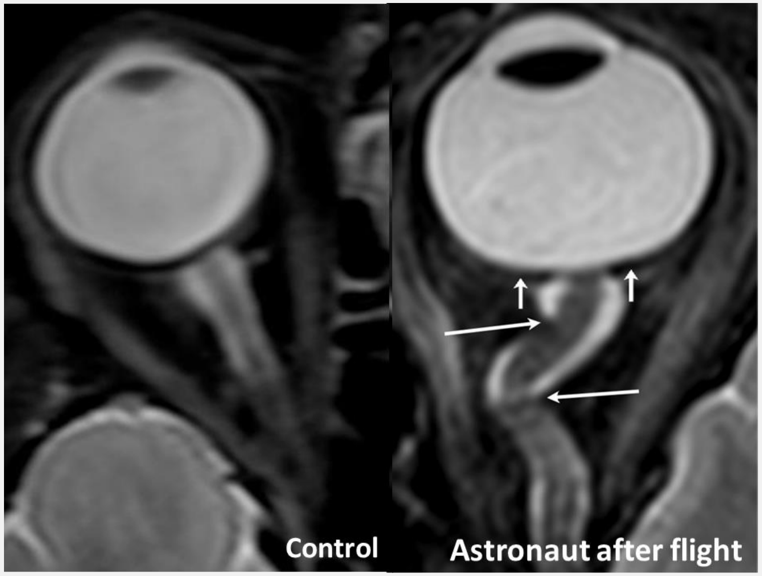
Edema



Choroidal folds



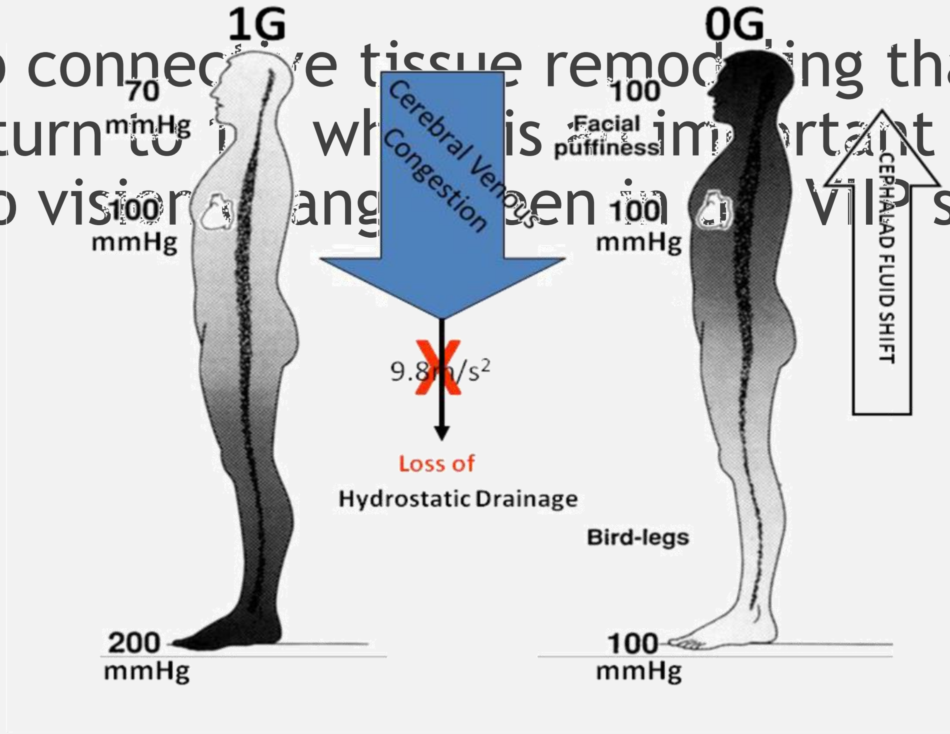
Posterior Globe Flattening
Optic Nerve ‘kinking’



~Mader et al. 2011; Kramer et al. 2012

Hypothesis

- Cephalad fluid shifts in microgravity affect intracranial and intraocular pressures, leading to altered biomechanical loads on the connective tissues of the posterior globe and optic nerve sheath.
  - Leads to connective tissue remodeling that persists upon return to 1G which is an important contributing factor to vision changes seen in the VIIP syndrome.



~humanresearchroadmap.nasa.gov

Goal & Approach

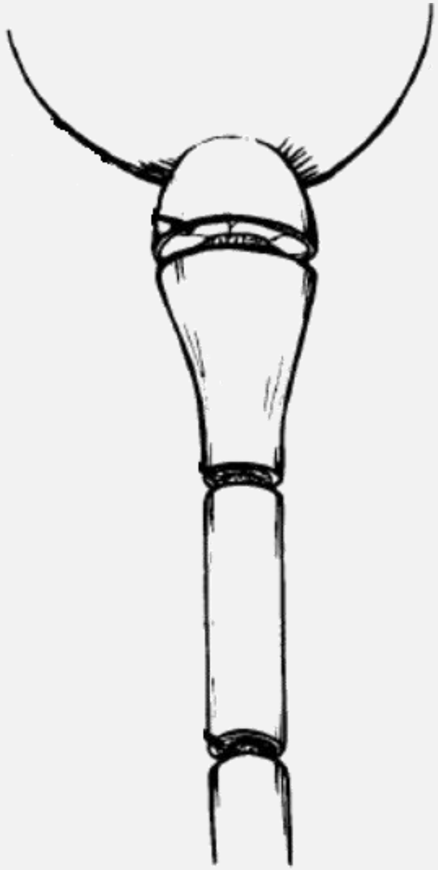
- Goal: To build a computational framework to understand the response at the optic nerve head (ONH) to elevations in intracranial pressure (ICP)
  - Examine how inter-individual variations alter deformations

- Finite Element Analysis (FEA)
  - Simulates effects of loads (pressures) on tissues with complex anatomy/material properties
  - Previously used to understand how intraocular pressure (IOP) alters the strains in the lamina cribrosa

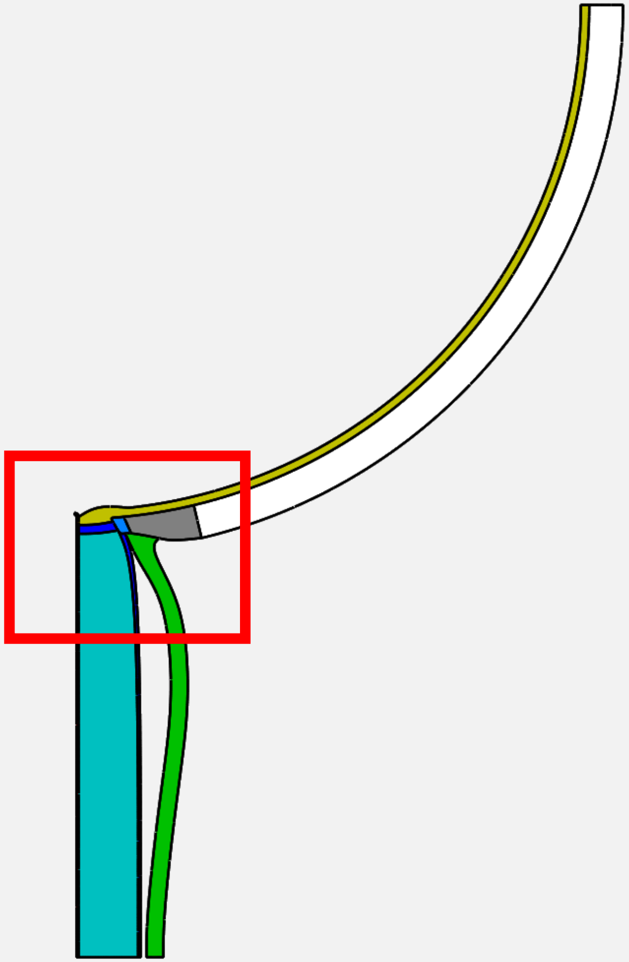
~Sigal et al. 2004; Sigal et al. 2005

Geometric Model

- Overall Geometry

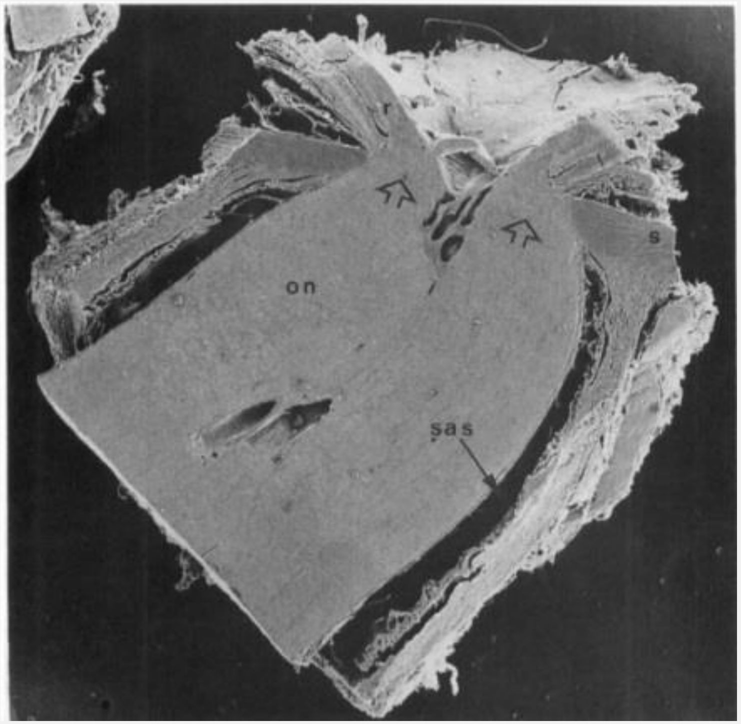


Taken from Liu and Kahn 1993

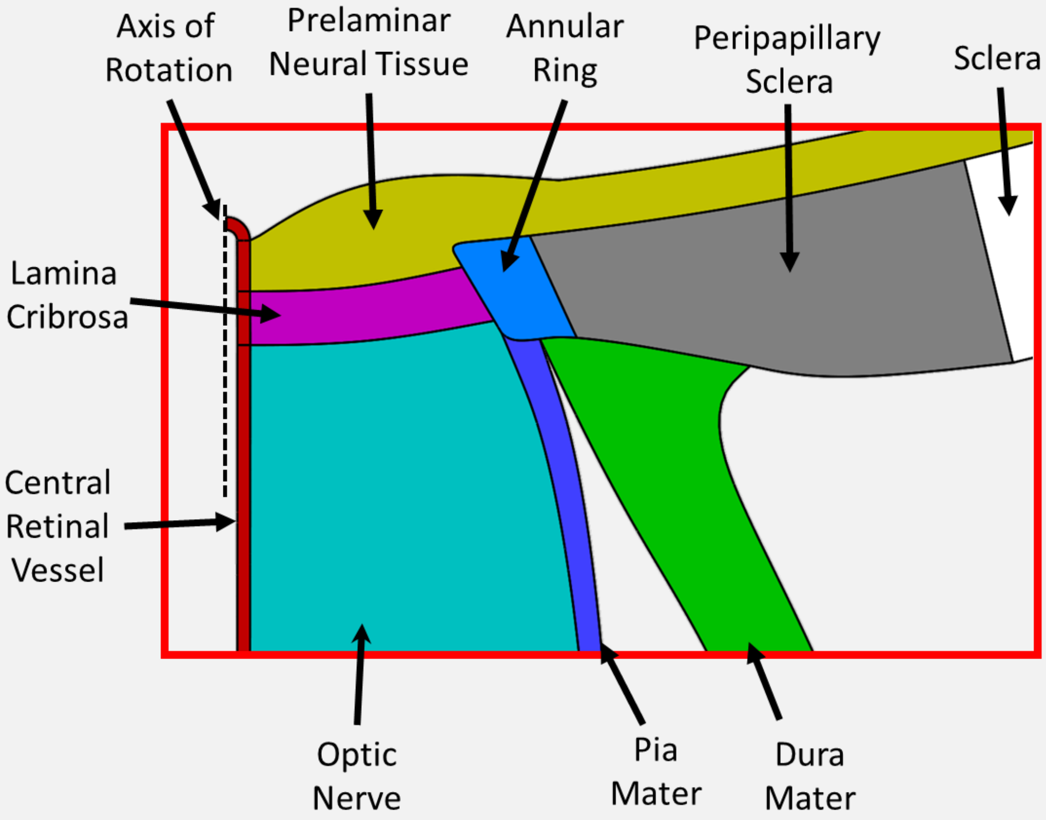


Geometric Model

- Optic Nerve Head



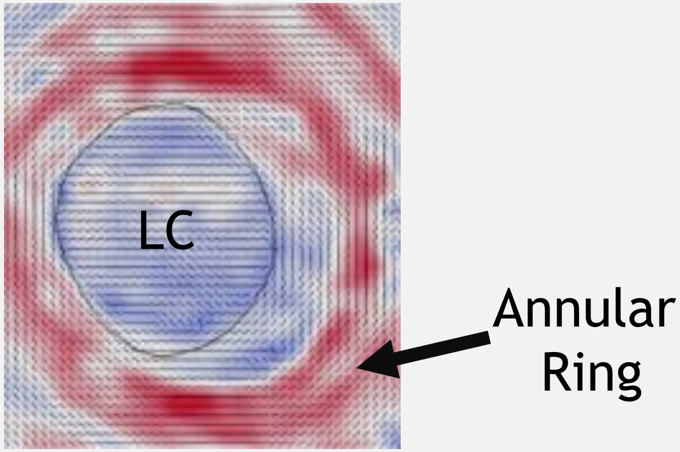
Taken from Elkington et al. 1990



Model Considerations

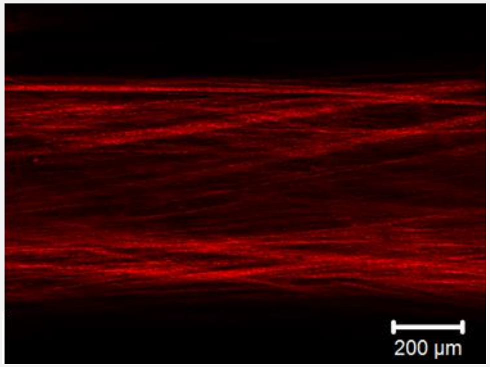
- Incorporate collagen fiber orientation and material properties
  - **Tissues:** sclera, peripapillary sclera, annular ring, pia mater and dura mater
    - Allow for us to incorporate more complex, nonlinear behavior and collagen fiber orientation and stiffness
  - 3 inputs describing tissue mechanical behavior: stiffness of the ground substance (c_1) and of the collagen fibers (c_3 and c_4)

Sclera



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

Dura Mater



~ Raykin et al. 2016; Raspanti et al.; 1992 Noort et al. 1980

Model Considerations

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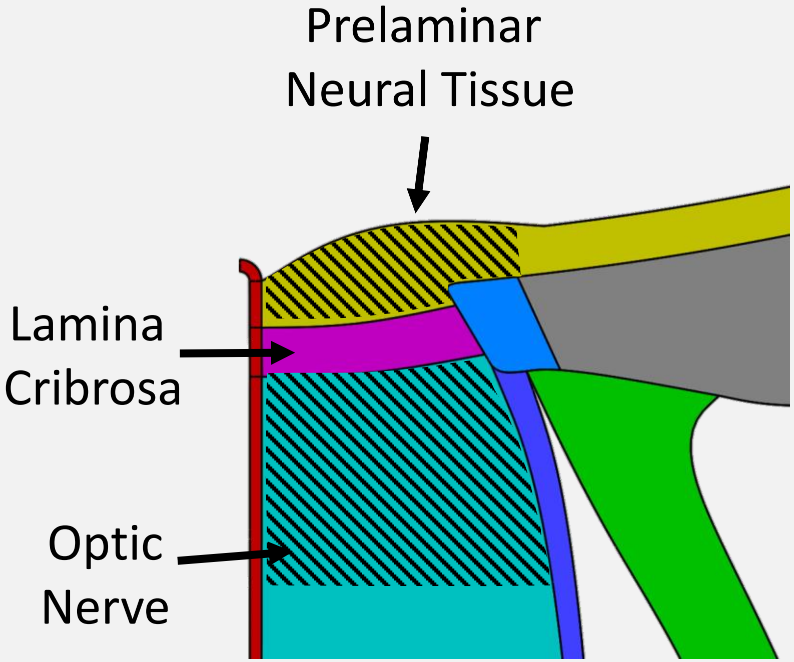
- Linear-elastic, homogenous and isotropic
  - **Tissues:** lamina cribrosa, optic nerve, retina and retinal vessel
    - Simplifications of complex tissue behavior, but chosen due to limited information on the biomechanical properties
  - 2 input parameters: stiffness (E) and tissue compressibility (v)

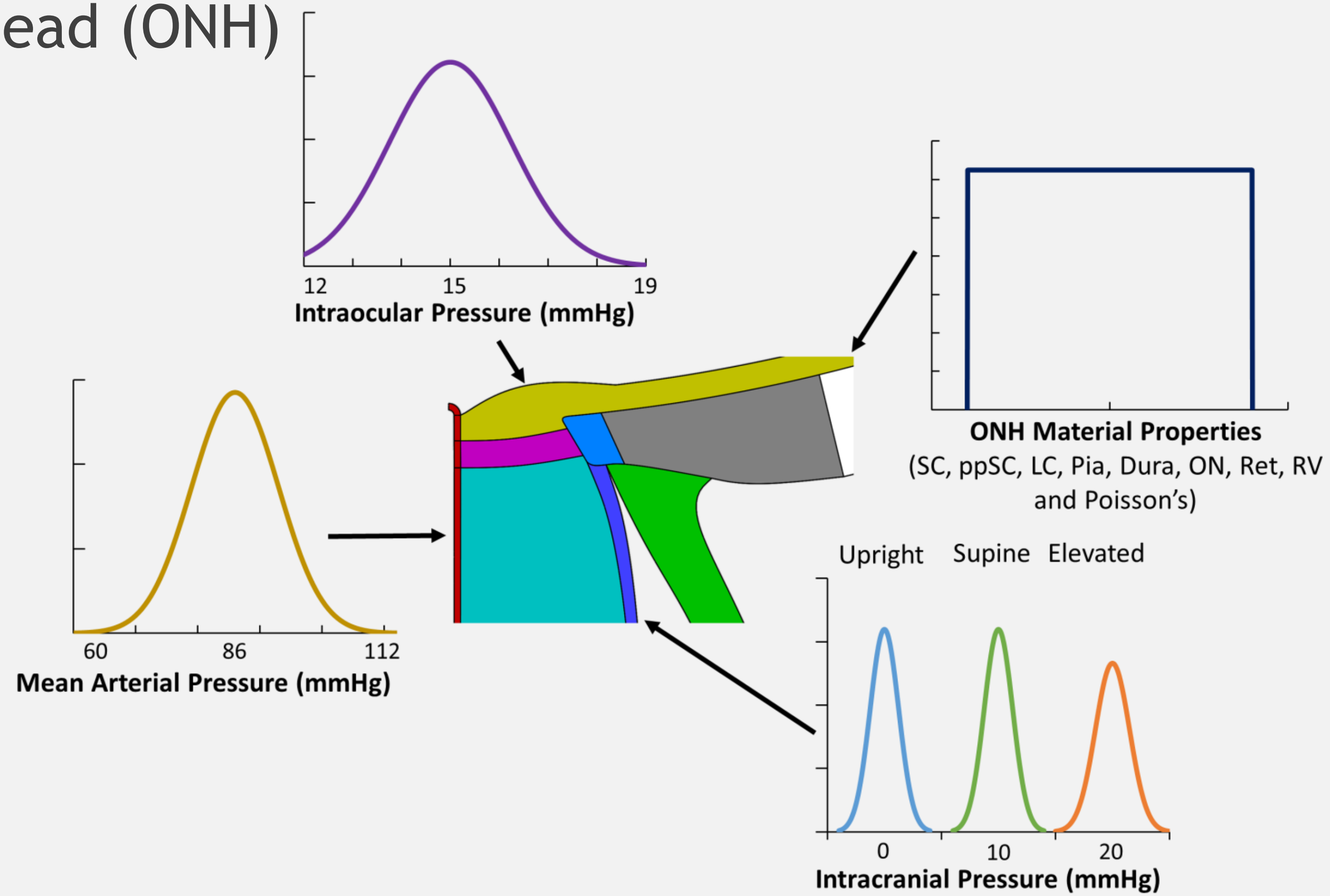
Outcome Measures

- Peak tensile and compressive strains in the prelaminar neural tissue, lamina cribrosa (LC) and optic nerve



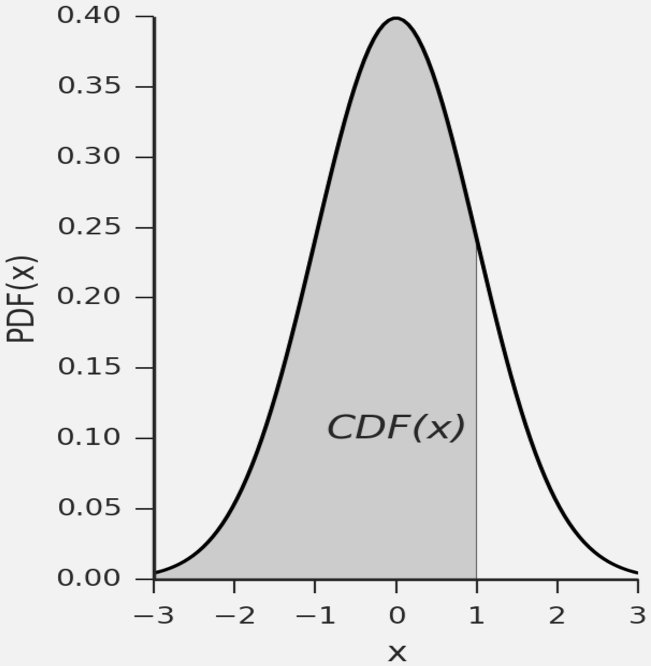
Latin Hypercube Sampling (LHS)

- Examine how variation in the pressures and tissue mechanical properties altered the strains in the optic nerve head (ONH)



Peak Strain Distributions in the ONH

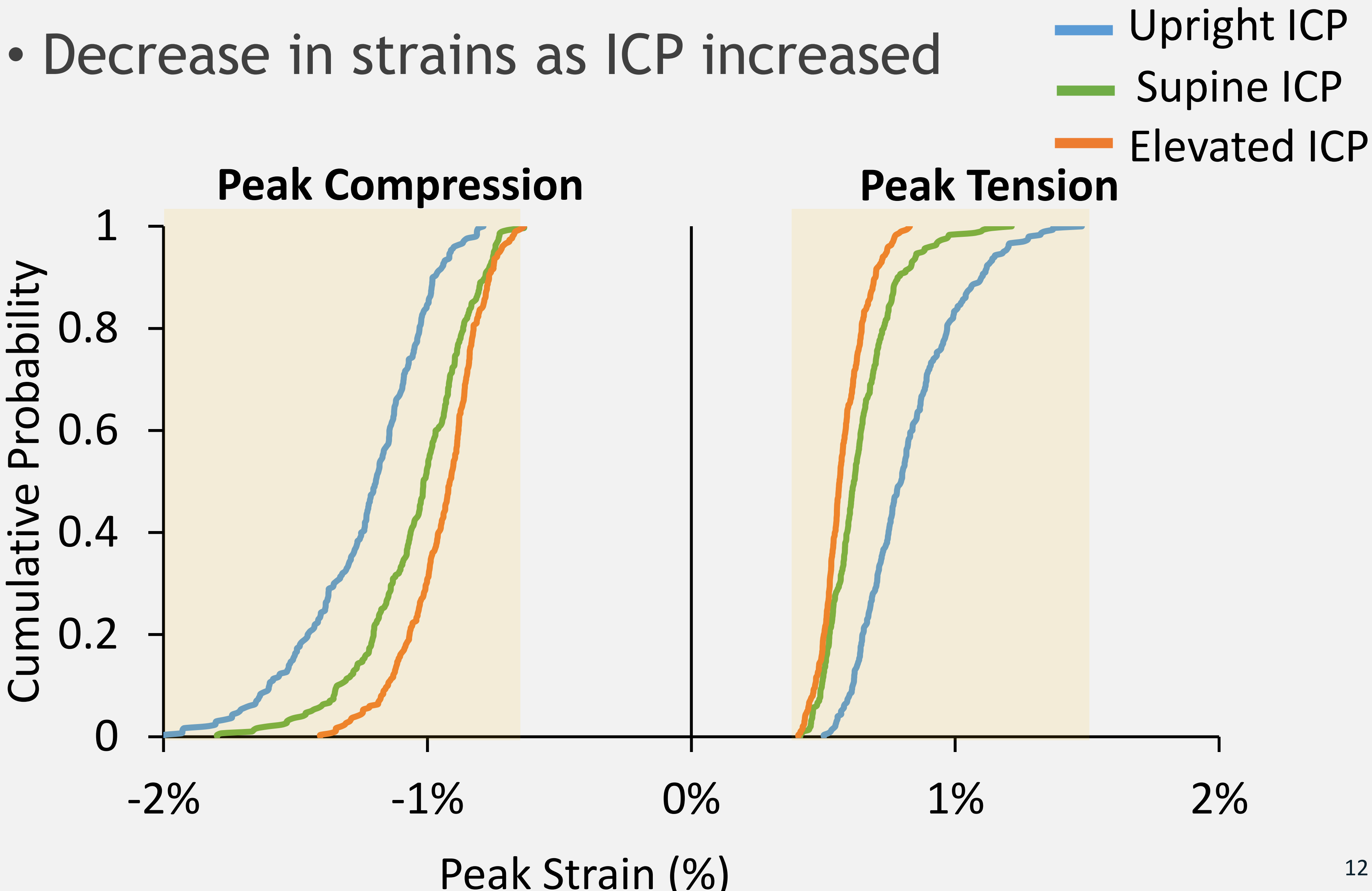
- Examined the histograms and cumulative distribution functions (CDFs) of the peak strains of the lamina cribrosa, optic nerve and retina from each set of input parameters
  - Represents the distribution of peak strains over a population of individuals with our eye geometry



~ Haslwanter 2015

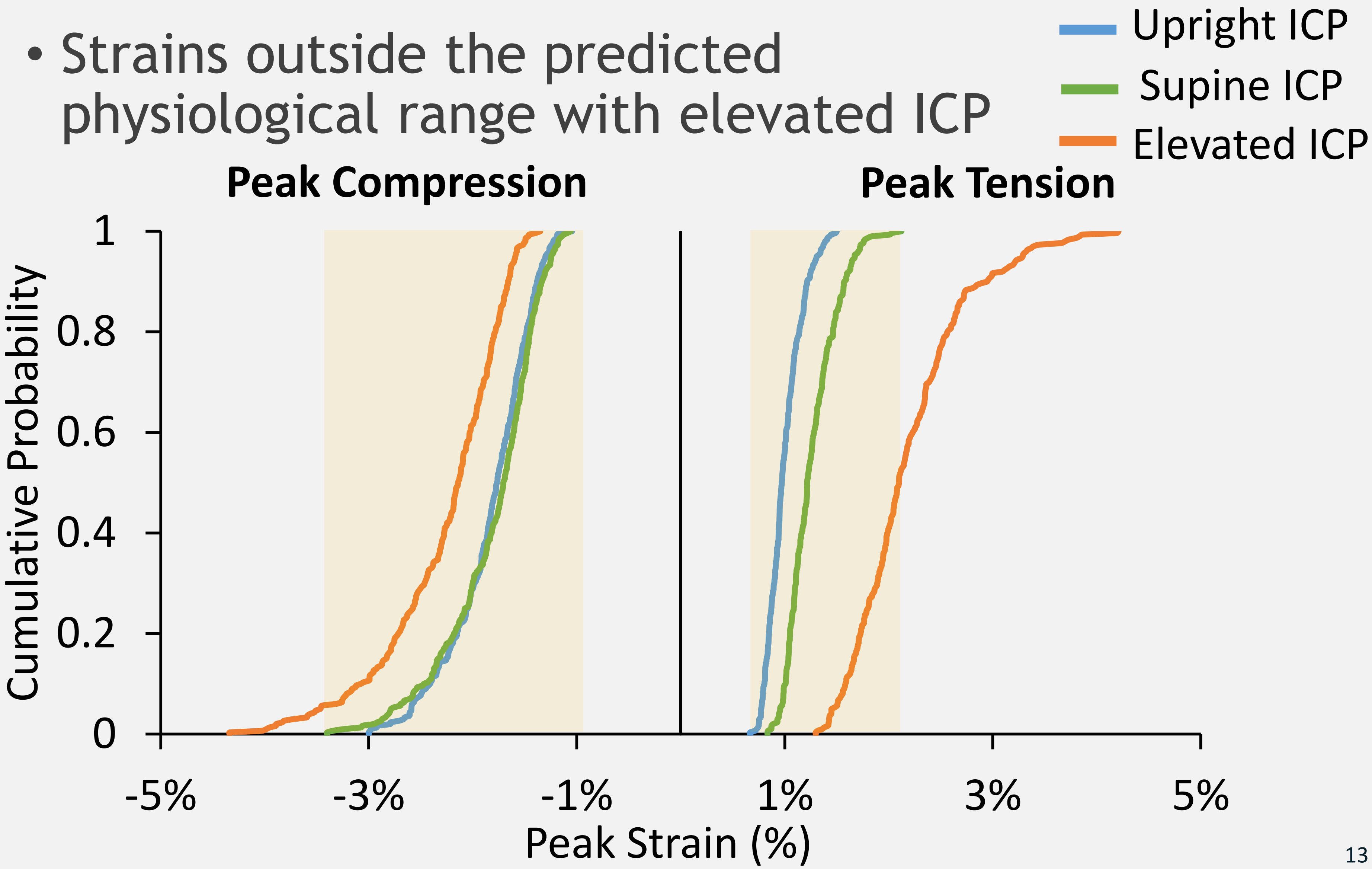
Lamina Cribrosa

- Decrease in strains as ICP increased



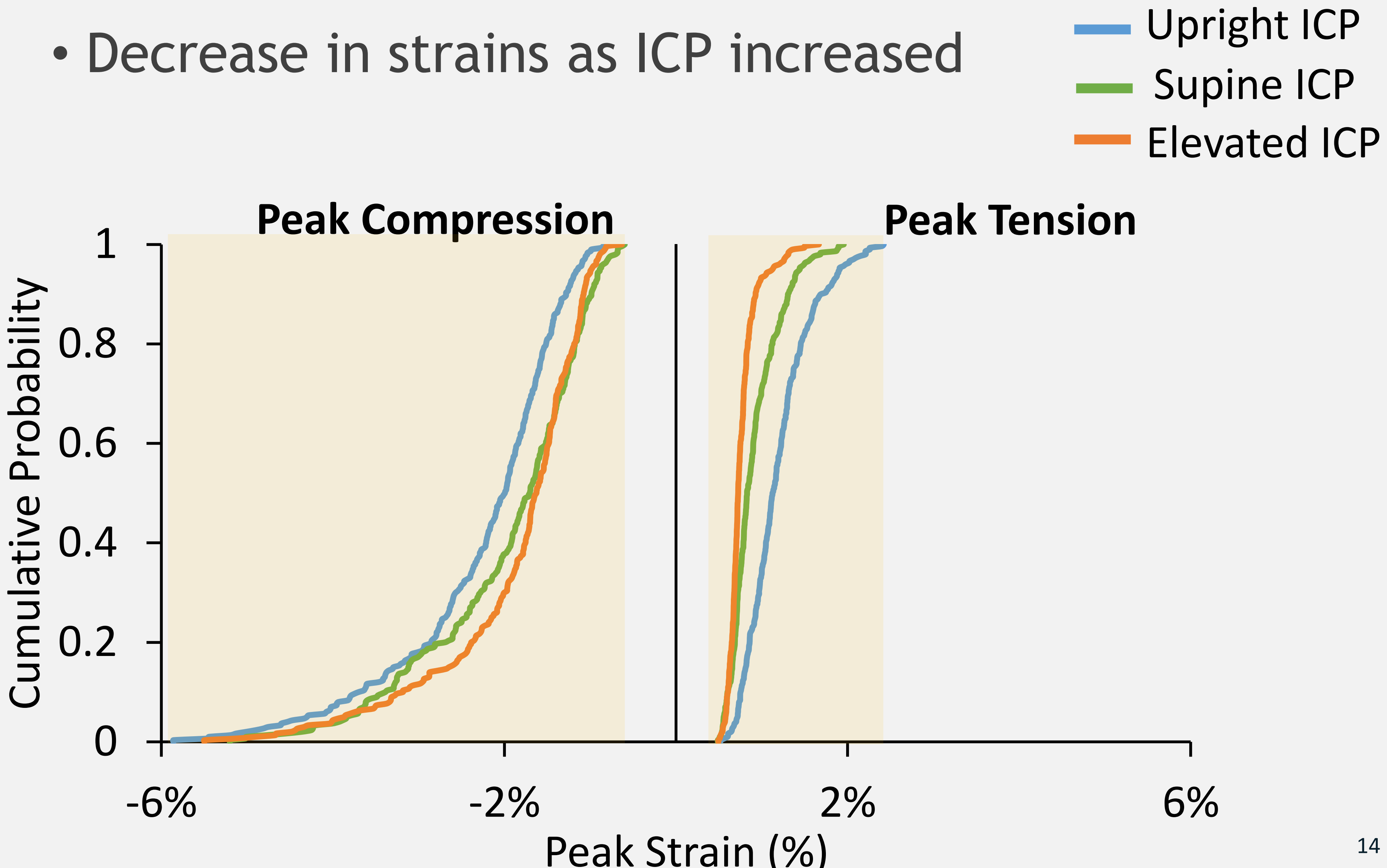
Optic Nerve

- Strains outside the predicted physiological range with elevated ICP



Prelaminar Tissue

- Decrease in strains as ICP increased

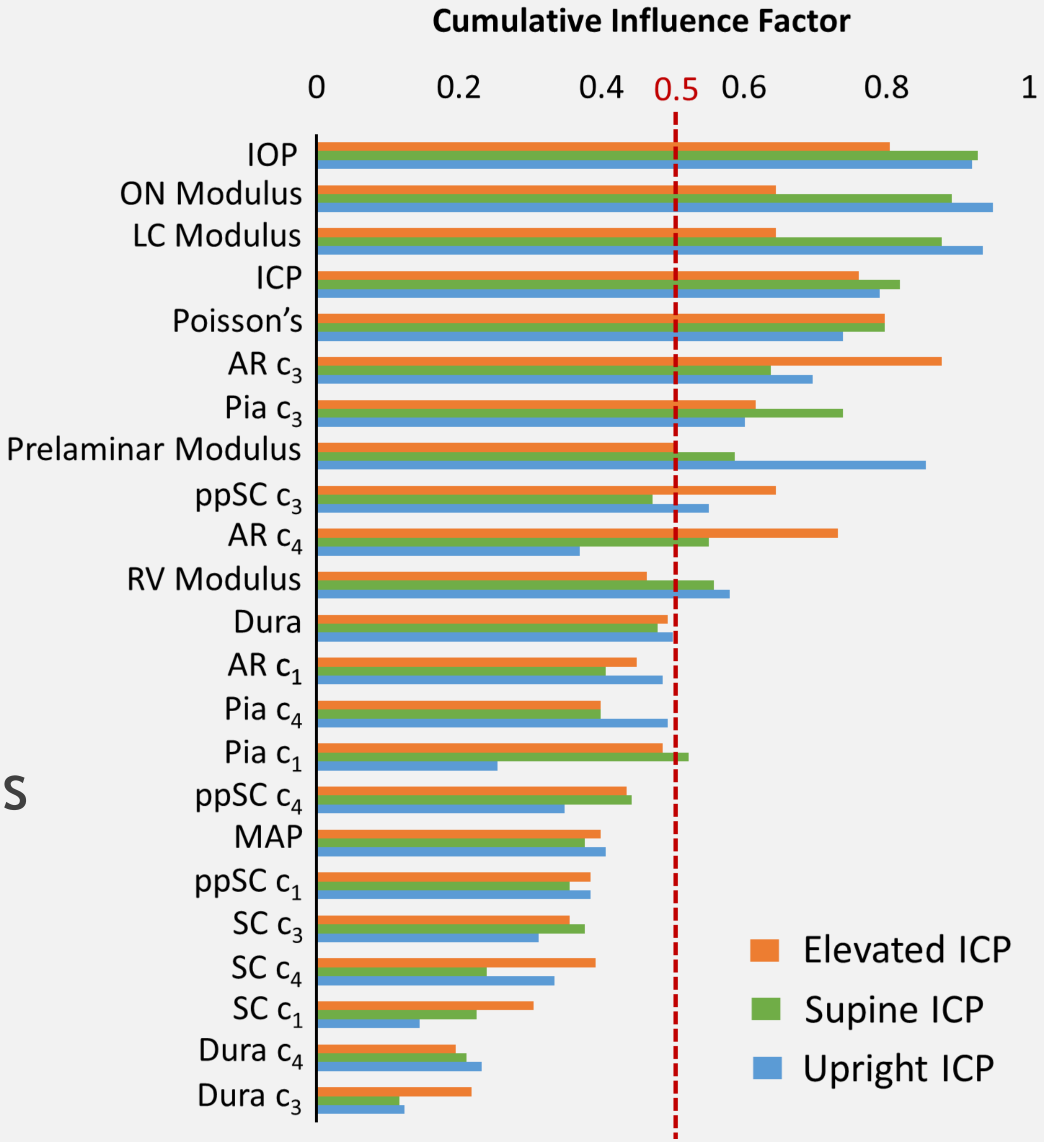


LHS/PRCC

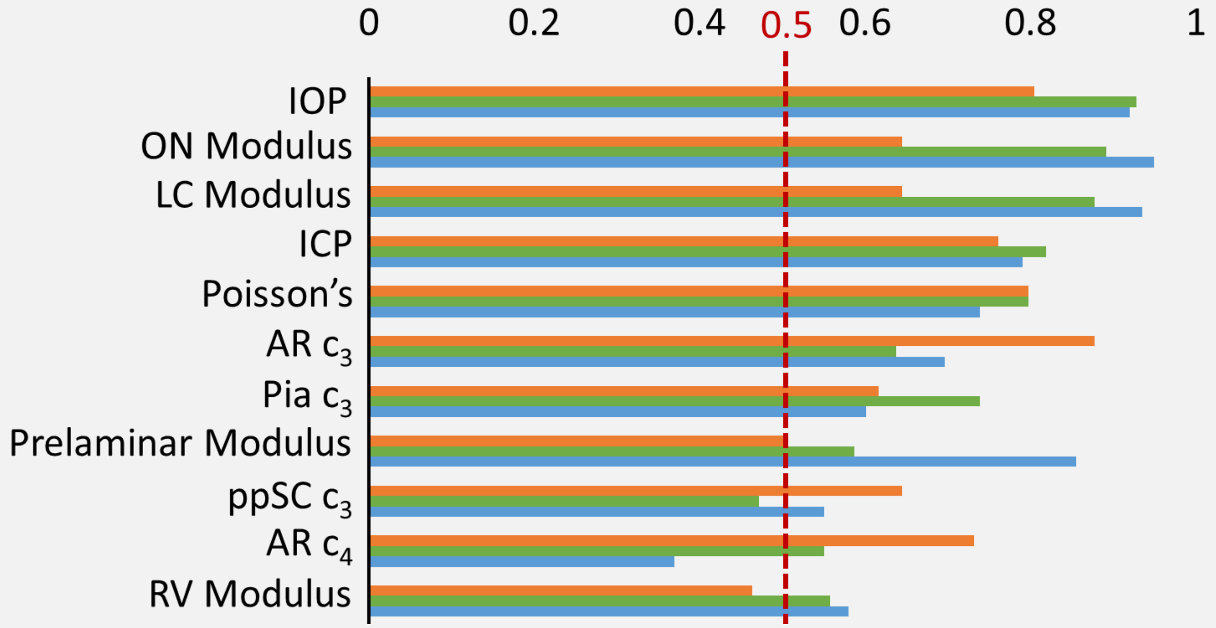
- Determines how the uncertainty in each input parameter influenced the peak tensile and compressive strains
  - Results in a correlation coefficient (±1) for each input parameter to each outcome measure
  - We ranked the magnitude of the correlation coefficient and summed them across each tissue region
  - Normalized this ranking to the highest possible ranking (i.e. 138) to determine the “cumulative influence factor”

Cumulative Influence Factor

- Cumulative influence factor for all 23 model inputs
- Considered input parameters with an average cumulative influence factor for all three ICPs > 0.5 as the most relevant for influencing peak strains in the ONH



Cumulative Influence Factor



- IOP and ICP had a large influence on the peak strains
- Stiffness of the optic nerve (ON), lamina cribrosa (LC), nerve compressibility (Poisson's), and retina (Ret)
- Collagen fiber stiffness of the pia mater (pia c_3), peripapillay sclera (ppSC c_3)and annular ring (AR c_3 & AR c_4) had a large influence on peak strains

Conclusions

- Examined how ICP affects the peak strains in the ONH
- Identified pressures and tissue properties that had the largest influence on the peak strains in the ONH
- From our CDF’s we found that c. 47% of individuals would experience “extreme strains” in the optic nerve
    - These strains may induce connective tissue remodeling
        - Note: This simulated population with extreme strains is coincidently similar to the 41% of astronauts suffering from VIIP syndrome
    - These CDF’s also identified specific factors that are associated with these extreme strains
        - ICP and a weak pia mater stiffness

Future Work

- Examine the influence of geometry on the peak strains in the ONH
- Compare strains in the lamina cribrosa and optic nerve predicted from the computational model to those strains measured from elevated ICP in an experimental model
- Investigate how strains initiate a remodeling response in the optic nerve and optic nerve sheath

Acknowledgements

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