Glaucoma is a Disease of Ocular Biomechanics, which can be Modeled and Controlled (possibly)

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Why do some people develop glaucoma and some do not?

Perhaps due to differences in:

- Anatomy / Geometry
- Tissue composition → Mechanical properties

Frail eyes

Robust eyes
Glaucoma is a Multifactorial Disease
Engineering Mechanics - The Basics

- Three Main Concepts in Linear Elasticity:
  - **Stress**, is the amount of force or load per unit area (calculated for each load bearing geometry; NOT MEASUREABLE)
    - e.g. mm Hg, pounds per square inch (psi), or Pascals (N/m²)
  - **Strain**, is the amount of local deformation induced by a load, expressed as a percentage (measured)
  - **Material Properties** express the resistance of the material to a given load, expressed as a Modulus of Elasticity (essentially a stiffness, which is determined by experimental testing)

In simple linear elasticity, these variables are related by Hooke’s Law, which states that:

\[ \text{Stress} = \text{Modulus of Elasticity} \times \text{Strain} \]
Material Properties of biologic tissues are complex: change over time (viscoelasticity), are stiffer in some directions (anisotropy), and are stiffer at higher strains (nonlinear)

So, with the introduction of biology, the relationship between IOP (stress) and ONH deformation (strain), is very complex

Stress → Material Properties ← Strain
Laplace’s Law can be used to estimate stress and strain in perfectly spherical pressure vessels with uniform wall thickness and simple material properties.

\[ \sigma = \frac{pr}{2t} \]

\( \sigma \) = in-wall hoop stress
\( p \) = pressure (IOP)
\( r \) = sphere radius
\( t \) = wall thickness

The eye does not conform to these assumptions.
Biomechanics of the Eye - Stress Concentrations

- Laplace’s Law breaks down in the eye because stress concentrates around the scleral canal.
Biomechanics of the Eye - Stress Concentrations

- In addition, scleral thickness is nonuniform, and the tissue material properties are very complex.
(A) Nonlinearity: Effect of Collagen Fibers

Nonlinear Region
- Physiological IOP

Linear Region
- Highest Fiber Stiffness

Scleral Deformation

IOP

Straight collagen fibers

Uncrimping collagen fibers

Initially Buckled collagen fibers

(B) Anisotropy: Effect of Fiber Orientation

Circumferential

Helicoidal

Longitudinal
Limited Measures of ONH Biomechanics—How can we describe/estimate them?

Factors
- Geometry
- Tissue Stiffness
- IOP

ONH Biomechanics

Models
Finite Element Method (FEM)

- Use finite element modeling to estimate the stress and strain in the posterior scleral shell
  - Computational method that splits complex geometries into smaller, regularly-shaped, geometric elements
  - Assign material properties, and loading and boundary conditions to each individual element
  - Calculate the mechanical response of each element
  - Superpose the results into the aggregate response of the structure

- What does one need to build a finite element model
  - Accurate three-dimensional geometry
  - Accurate material properties
  - Accurate loading and boundary conditions
Generic model
Sigal et al., IOVS, Dec. 2004

Axis of symmetry

Anterior

Posterior
This work identified the five most important determinants of ONH biomechanics (in rank order) as:

1. Stiffness of the sclera
2. Size of the eye
3. IOP
4. Stiffness of the lamina cribrosa
5. Thickness of the sclera
Laminar Microstructure Varies Regionally

Voxel Size: 1.5 x 1.5 x 1.5 μm
Biomechanics at the micro-scale

Parent Continuum FE Model

Parent Continuum Element

Included Laminar Microstructure
Conclusions and Future Directions

- Biomechanics is in its infancy in the eye - there is much left to be done!

- Biomechanical models should help identify those factors that contribute most to individual ONH susceptibility

- The biomechanics of the sclera and ONH may be modulated in the future through clinical techniques that change the material properties (stiffness) of the load bearing tissues
  - Riboflavin with UV-A to crosslink collagen
  - Prostaglandins that break down/alter the ECM
  - Other agents that modify the ECM directly
  - Agents that modify cellular action on the ECM (MMP inhibitors)