1B P8: Bioengineering

Ocular Biomechanics and Biomaterials

Lecturer: Prof Yan Yan Shery Huang (yysh2)

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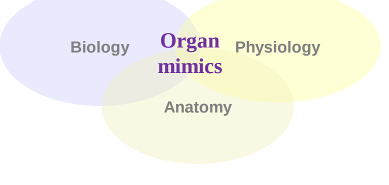
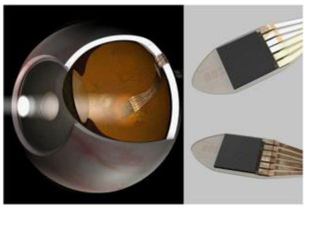
Learning Objectives

Based on the case study of Ocular Biomechanics and Biomaterials, appreciate the following for general applications of bioengineering:

- **When** to apply Engineering concepts? When biological functions can be 'substituted' by engineering devices?
- **How** to reduce system complexity for problem solving and to gain mechanistic insights?
- Define the problem/ research question/ system → **Why**?
- **What** is the broader impact?





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Biomechanics course outlines

1. Tissues in the Eye
   – Normal eye anatomy
   – Composition and structure of tissues
   – Biomaterial mechanical properties

2. Structural and Fluid Mechanics
   – The eye as a shell
   – Flow of blood and aqueous humour
   – Modelling glaucoma

3. Disorder, Disease and Repair
   – Disorder in focal function
   – Contact and intraocular lenses
   – Cataracts, corneal opacity
   – Tissue engineering for eye repair

Define the problem

↓

When to apply Engineering & **How** to solve

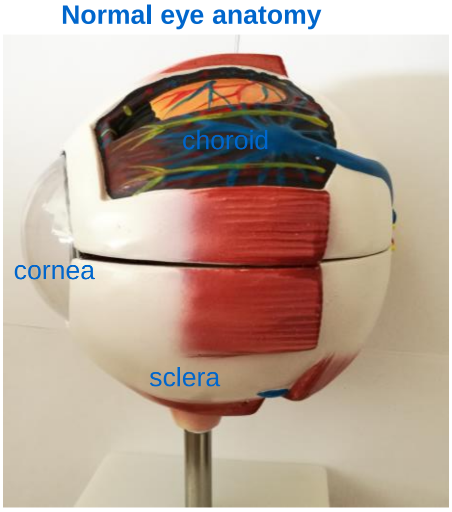
↓

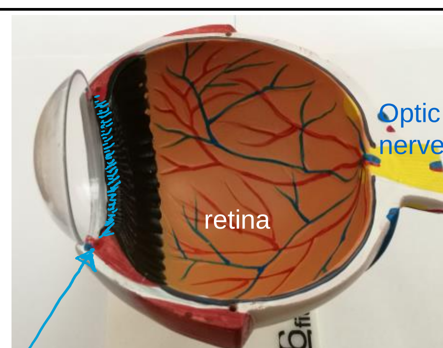
What is the broader impact

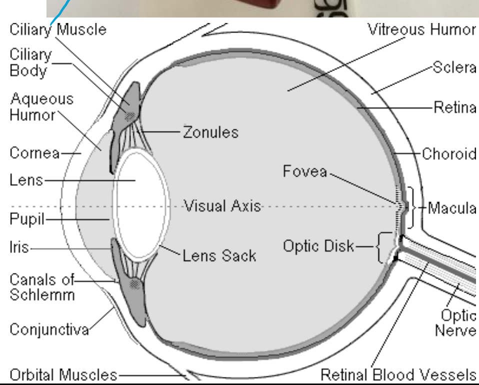
3

Lecture 1. Tissues in the eye

Normal eye anatomy



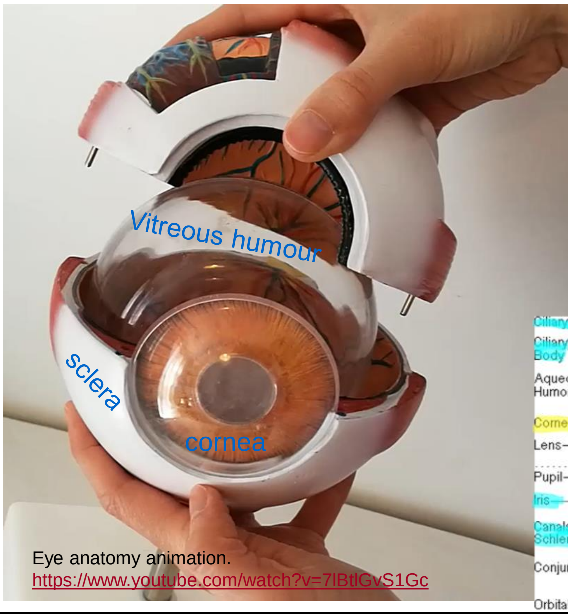




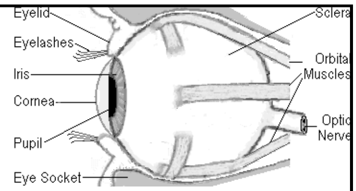
Exterior
Mid
Innermost

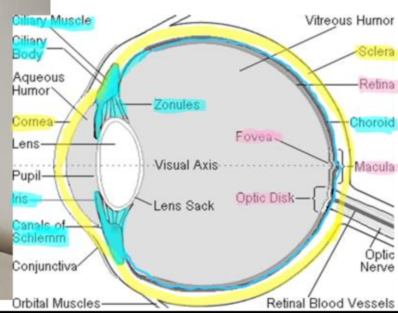
4

Normal eye anatomy:
Fibrous layer and the vitreous humour as load bearing components



Eye anatomy animation.
https://www.youtube.com/watch?v=7lBtlGvS1Gc



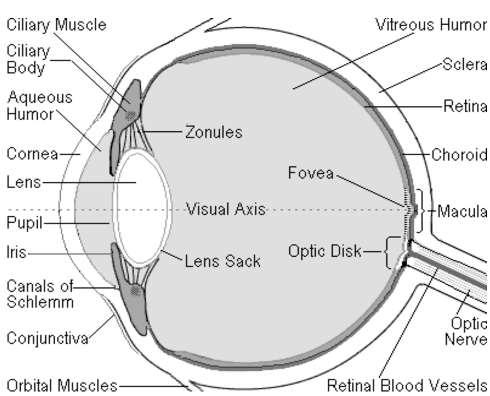


Normal Eye Anatomy: Material/Structure to Function (Focusing)

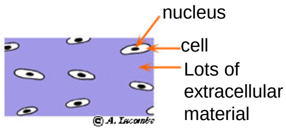
The cornea contributes the majority (2/3) of the eye's focusing power but is fixed focus.

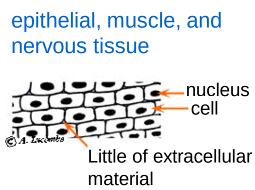
The (crystalline) lens sits behind the iris and contributes the remainder (1/3) of the eye's focusing power.

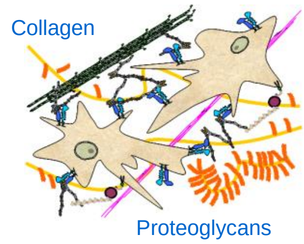
The focal distance of the eye is altered by changing the shape of the lens via the action of the ciliary muscles.



- Tissues: functional building block of an organ
- Tissues consist of Cells & ECM (structured living materials)







- In biology, extracellular matrix (ECM) is any material part of a tissue that is not part of any cells
- Extracellular matrix dominance is the defining feature of connective tissue.
- Most connective tissues are:
  - Involved in structure and support.
  - Physical properties characterized largely by the non-living constituent.
  - Examples: bone, cartilage, ligaments and tendons; cornea and sclera.

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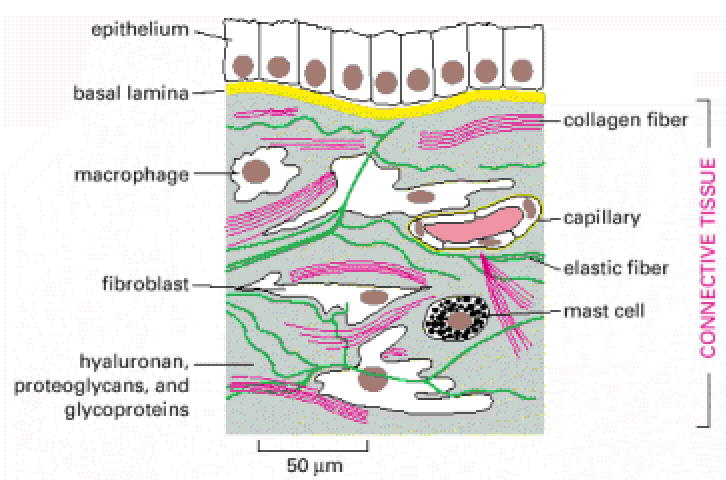
Connective Tissue

Cells, proteins, sugars



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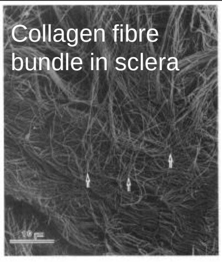
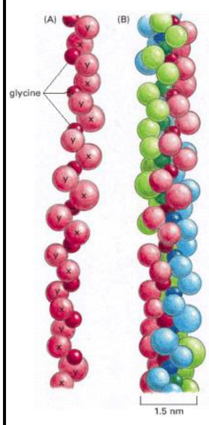
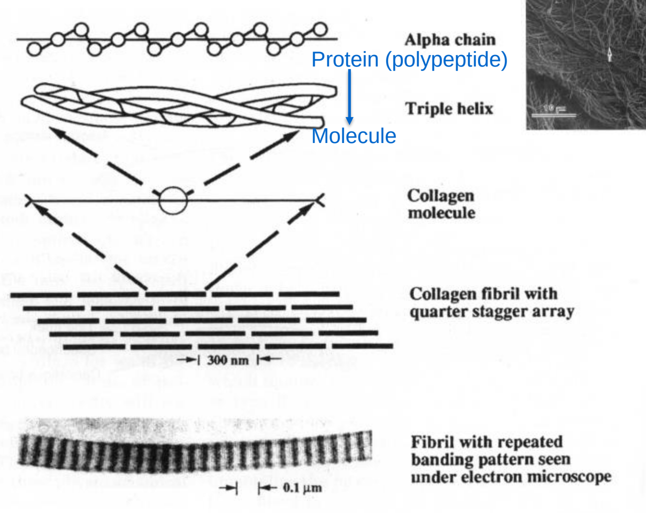
Collagen







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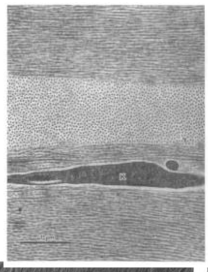
Collagen fibrils

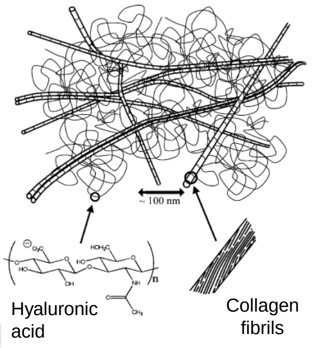
In section

Cornea

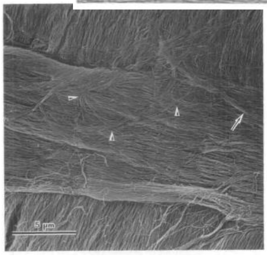


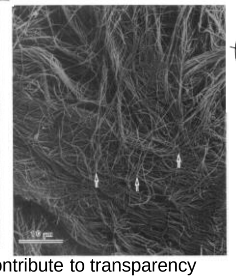
Sclera

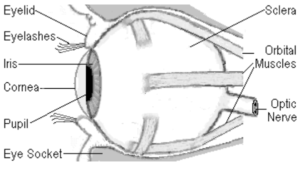
Schematic of the vitreous space



SEM







- Parallel bundles of similar size in cornea contribute to transparency
- Sclera characterized by more random web.
- Low levels of interweaving between layers.
- Low solid density random gel network gives structural properties and transparency of vitreous
- Similarity with synthetic textiles.

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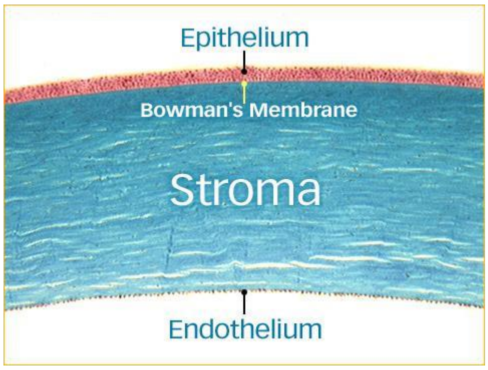
Tissues in The Eye: Cornea



Cells

Collagen and some sugars

Cells

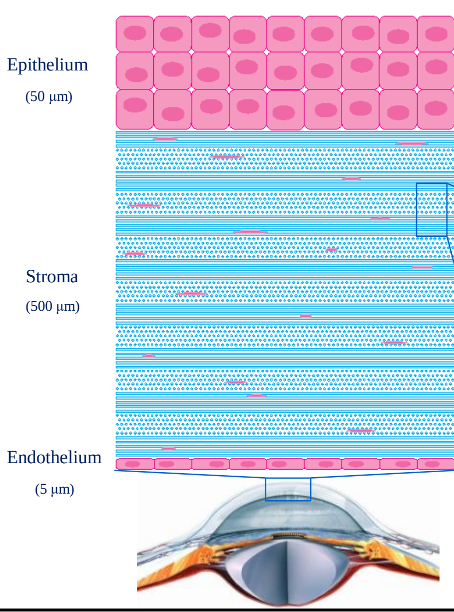
In humans, the cornea has a diameter of about 11.5 mm and a thickness of 0.5–0.6 mm in the centre and 0.6–0.8 mm at the periphery.

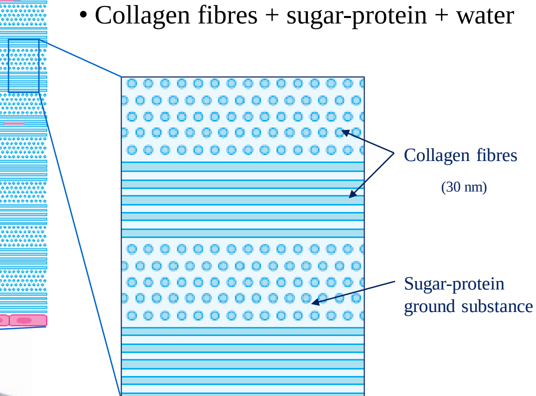
There is no blood supply to the cornea.

Anatomy of cornea

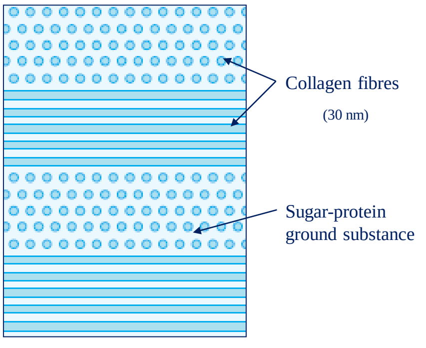
A cornea has 3 main parts.

- Stroma has 90% of total thickness and contributes to its toughness & transparency
- Collagen fibres + sugar-protein + water





Corneal collagen



refraction index of n = 1.376

Corneal collagen is crystalline

- The collagen fibril diameter is nearly constant
- The collagen fibril spacing is regular (and nearly perfect)
- Collagen packing → function

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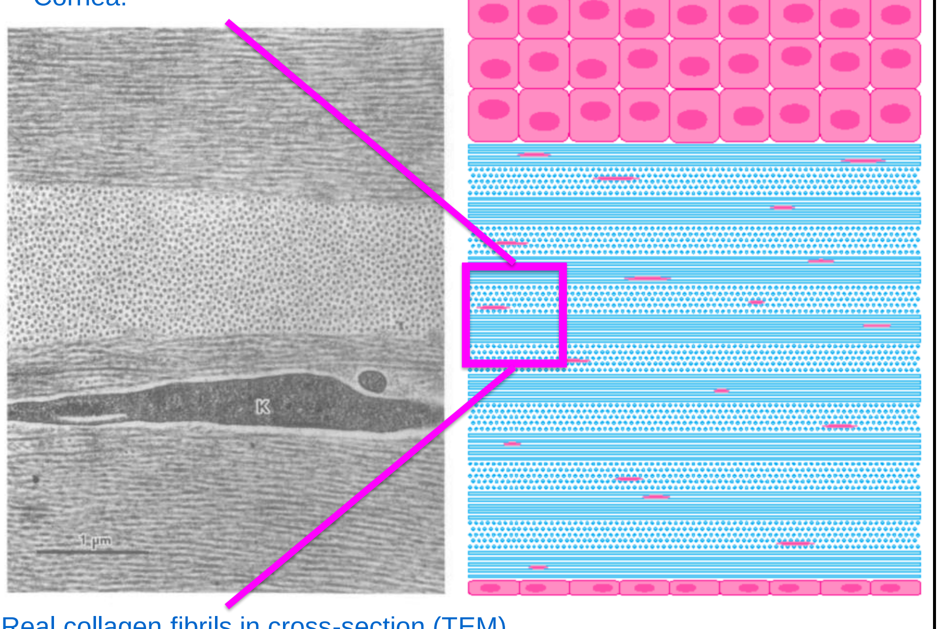
Cornea:



Real collagen fibrils in cross-section (TEM)
K: corneal keratocyte (fibroblast)

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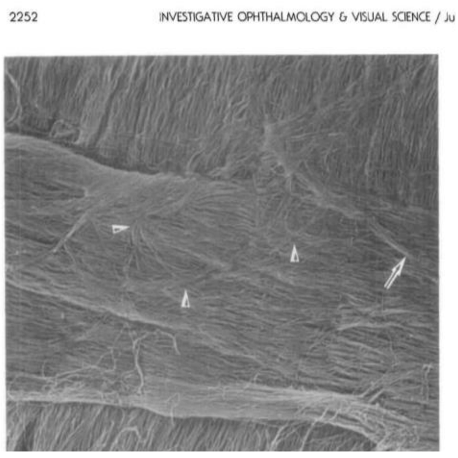
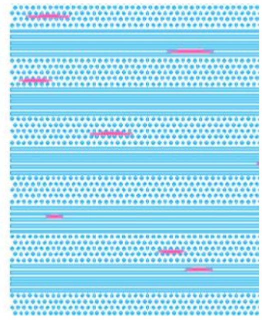
Cornea:
Collagen fiber → composite design of load bearing but light-weight

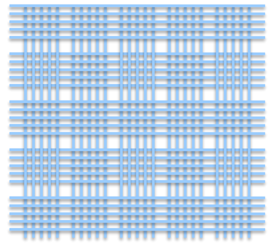


Collagen fibrils in SEM (Top view).

Side view



= Top view (basket weave)



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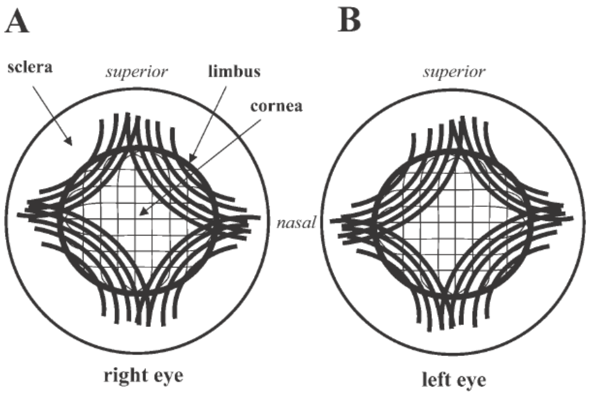
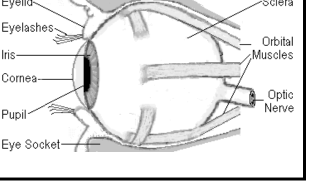
Alignment of Corneal Collagen Fibrils

- The fibril orientation in the left and right eyes are mirror images
- Pattern of fibrils provides support to the cornea
- Basket weave structure in the central region of the cornea
- Fibrils are directed towards extra-ocular muscles at the edges





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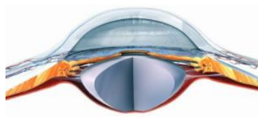
Tissues in The Eye: Crystalline Lens

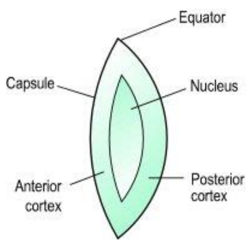
The cornea and sclera are typical soft connective tissues in the body.

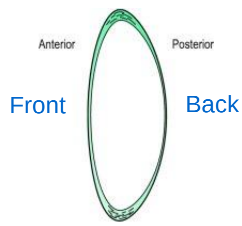
The lens **capsule** is also a typical connective tissue with collagens and sugars. It varies in thickness.

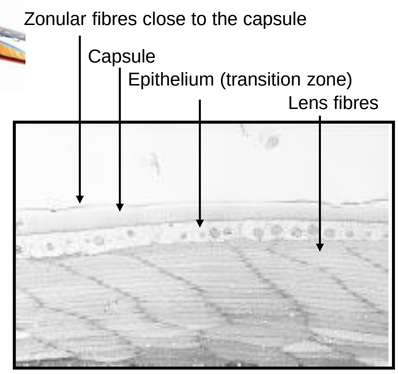
Directly beneath the capsule is a layer of epithelial cells. These cells are a source for the **cortex** and **nucleus** of new lens fibres which have a specialized structure.

The lens is about 10mm in diameter and 3.5-5mm thick at its centre.





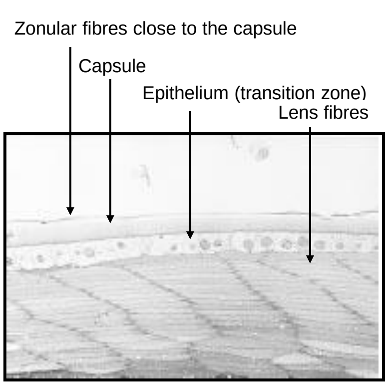


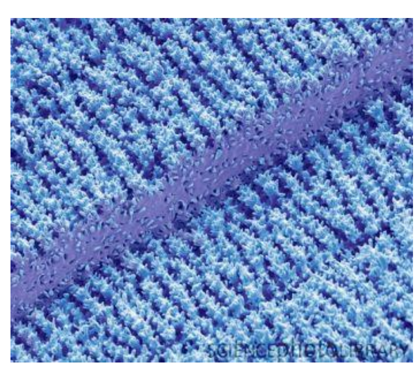


Crystalline Lens

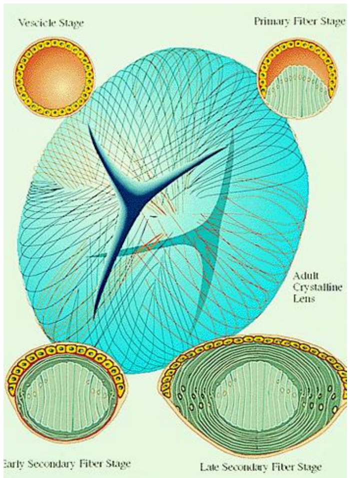
The bulk of the lens, the cortex (newer fibres) and the nucleus (older fibres), is cellular. These specialized cells are the “lens fibres” and they are vastly elongated lens epithelial cells that have lost most of the normal cell contents (nucleus and organelles).

The lens is 30% protein by mass and the proteins are the very unusual “crystallins”.





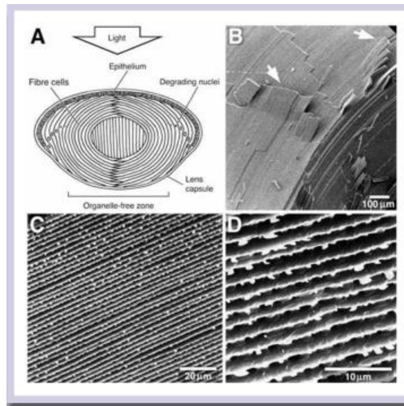
Lens Structure



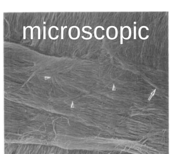
As with the cornea, a large degree of organization is found in the lens and this gives rise to its optical transparency (in a manner that is actually not understood very well).

The overall layered structure of the lens fibres is often compared to the layers of an onion.

In common with the cornea there are no blood vessels in the lens.

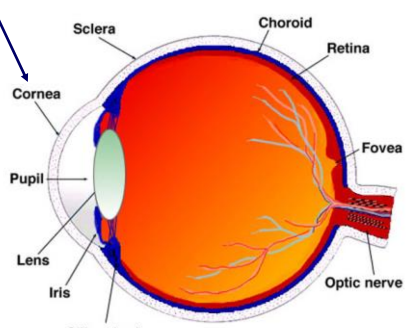


Physical function of the lens: focusing



Measuring material properties of the eye

Macroscopic



Difficult to measure biological material properties for a variety of reasons

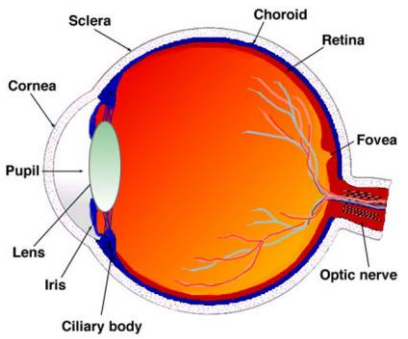
- small features/inhomogeneity
- inconvenient shape
- anisotropy
- complex loading
- time-dependence
- specimen/person variability
- species variability
- in vitro behaviour not representative of in vivo
- ethical/practical procurement problems

Sometimes approximate values are adequate

Measuring material properties of the eye

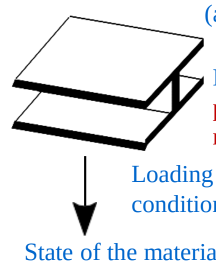
- **When** to apply Engineering concepts?
- **How** to reduce system complexity for problem solving and to gain mechanistic insights?

Macroscopic



At what length scale the material can be treated as continuum?

Structure (anatomy)

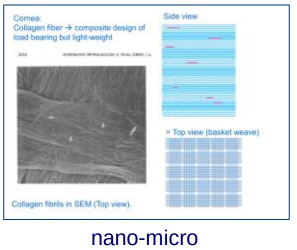


Material (living; passive vs. reactive)

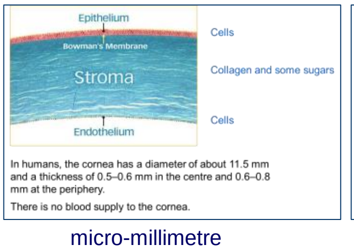
Loading conditions

State of the material: functions, deformation, failure

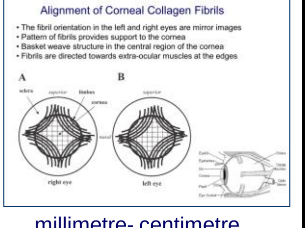
Material Property of Cornea



nano-micro



micro-millimetre



millimetre- centimetre

'Prioritisation'; Reduced system

Structure (anatomy)
- small features/inhomogeneity
- inconvenient shape

Material
- inhomogeneity
- anisotropy
- passive vs. reactive
- time-dependence

Loading conditions
- complex loading

Testing mechanical properties of corneal tissue

millimetre- centimetre

Strip extensometry test

- Dissect strip of corneal tissue
- Inherent challenges:
  - Strip is from spherical surface – centreline is longer than along sides
  - Flattening of curved specimen
    - Initial compressive and tensile strains
    - Compressive stresses cause reduced tensile stresses under external tensile loading
  - Corneal thickness increases with distance from centre

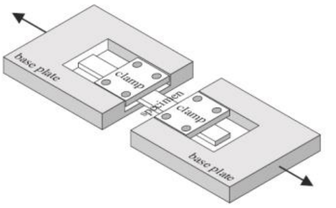


Figure 9. Strip extensometry test rig.

Corneal inflation test

- More complicated to perform and analyse

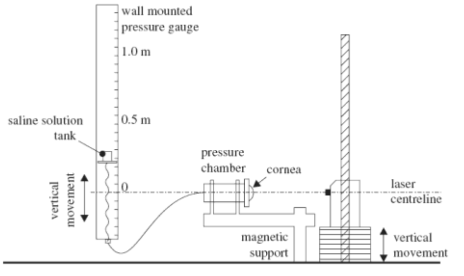


Figure 8. Trephinate inflation test rig.

Testing mechanical properties of corneal tissue

millimetre- centimetre

Strip extension

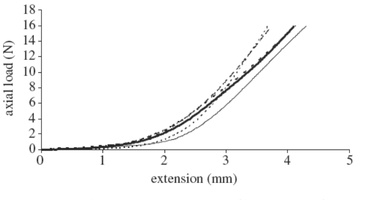


Figure 12. Load–elongation behaviour of a selection of strip tests.

Inflation

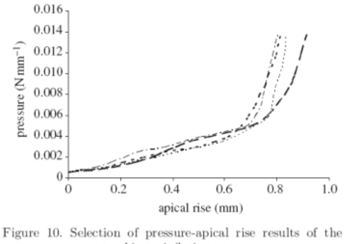


Figure 10. Selection of pressure-apical rise results of the trephinate inflation tests.

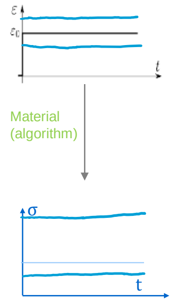
J. R. Soc. Interface (2005) **2**, 177–185

- Nonlinear material response.
- Rupture occurs under an axial load between 23 and 26 N.
- Behaviour beyond 16 N (not shown) remains linear until rupture in extension test.
- Gradual stiffening in inflation test.
- In this case the strip extension tests overestimate the stiffness by about 32%.

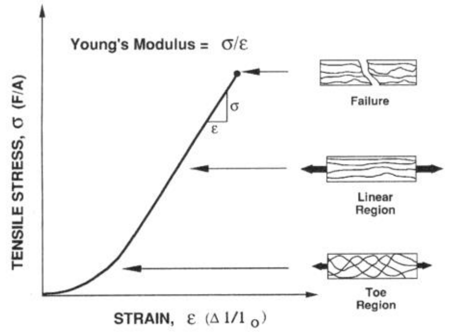
Tissue Biomechanics - Nonlinear Elasticity

nano-micro

$\varepsilon(t) = \varepsilon_0 H(t)$



Rate-independent

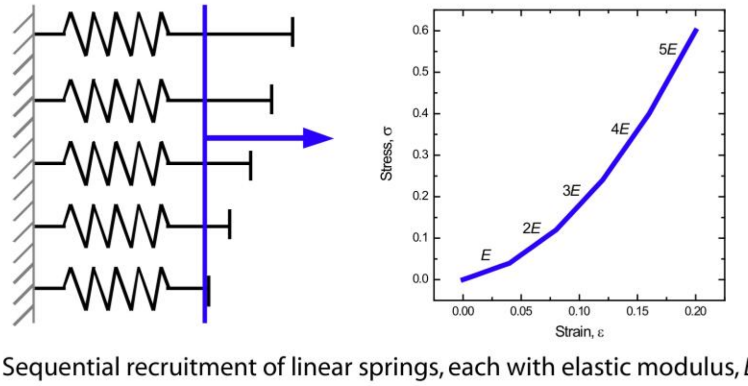


- This shape results from the reorientation and sequential “recruitment” of collagen fibrils.
- As the fibres reorient, they can then support force
- We assume each collagen fibril acts as an elastic spring

Constitutive Model for Nonlinear Elasticity: Elastic Recruitment

nano-micro

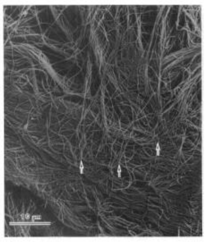
ELASTIC RECRUITMENT:

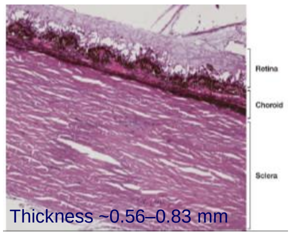


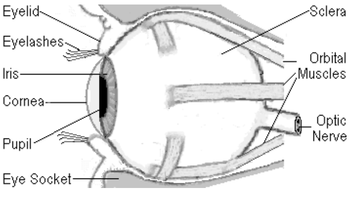
Sequential recruitment of linear springs, each with elastic modulus, *E*. Figure after [7]

Springs in parallel act with increasing stiffness

Material Property of Sclera







nano-micro | micro-millimetre | millimetre- centimetre

'Prioritisation'; Reduced system

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- inconvenient shape

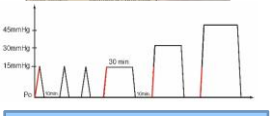
Material
- inhomogeneity
- anisotropy
- passive vs. reactive
- time-dependence

Loading conditions
- complex loading

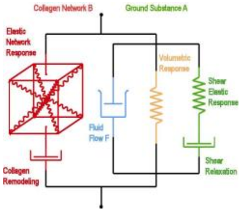
DOI:10.1186/s13244-021-01000-x

Material properties of the sclera

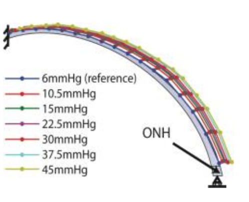
1. Mechanical Testing



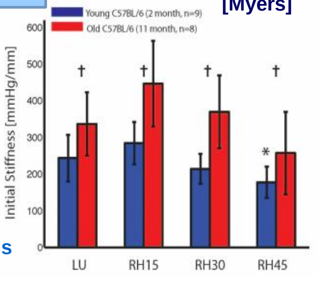
2. Constitutive Modelling



3. Inverse Finite Element Material Parameter Optimization



[Myers]



RH15=ramp-hold 15 mins

- Direct inflation – mimicking in vivo loading
- Deflection measured by video
- Need statistical analysis

Summary

Define the context

- Macro-anatomy of the eye
- Composition and structure of tissues, with a particular focus on the fibrous layer and lens of the eye

When to apply Engineering & **How** to solve

- Biomaterial mechanical properties of the cornea and sclera
- Physical measurement enabled by system simplification

What is the broader impact

- Macroscopic tissue behaviour explainable by microstructures
- Prediction: when could the eye component(s) be damaged by mechanical loadings?
- Diagnostic marker