Engineering and the Eye

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CAMBRIDGE OPHTHALMOLOGICAL SYMPOSIUM

St John's College, Cambridge, UK

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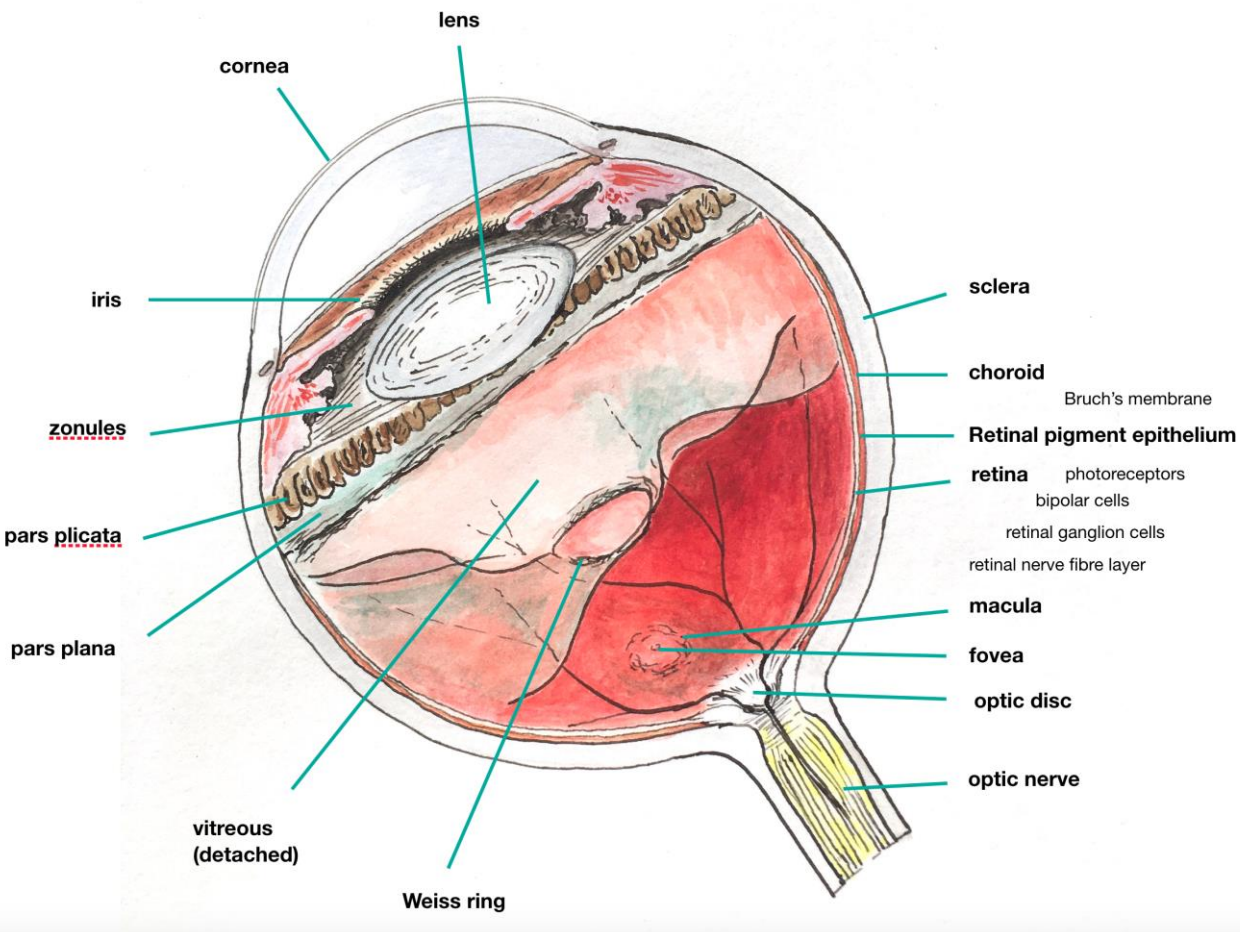
Terms and Concepts

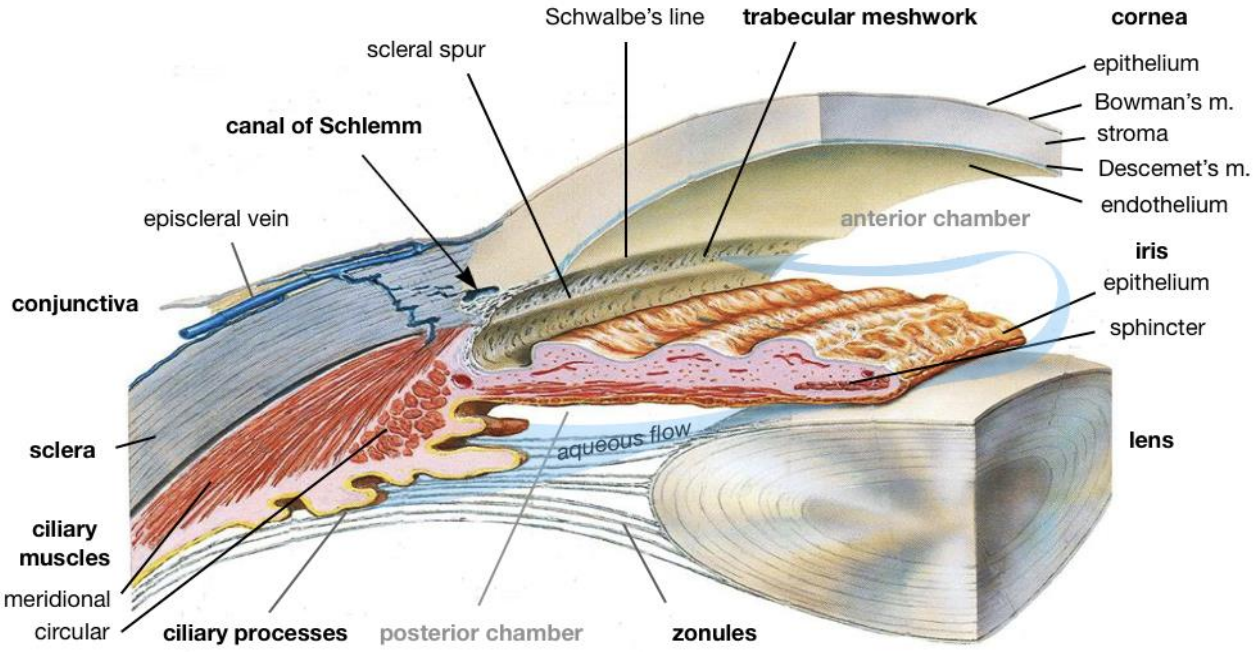
This short document is provided to help engineers follow the ophthalmology presentations and *vice versa*.

Ophthalmic terms and concepts for engineers

Hemi-section of the eye



Anterior segment of the eye



Some generic concepts

Embryology: The eye develops by invagination of embryonic fore-brain tissue to form a cup. The inner layer forms the neuro-retina and posterior iris epithelium; the outer layer becomes retinal pigment epithelium and anterior iris epithelium. Behind the constricting fold of iris epithelium, the cup captures a disc of ectoderm which becomes the lens. Neural crest tissue forms the ciliary muscle and lines the anterior chamber.

Epithelium: name given to the continuous cellular coating of all organs, and of all interfaces between the body and its surroundings. It adheres by the extracellular "basement membrane".

Endothelium: refers to sheets of cells (of neural crest origin) which line spaces within the blood and lymphatic circulations. A sheet of flattened, polygonal endothelial cells lines the inner surface of the cornea and more compact endothelial cells cover the trabecular meshwork.

Collagen: This is the main protein in all connective tissues, including the cornea and sclera. It consists of protein chains, variously coiled to determine their packing and structural characteristics.

Elastin: This is the protein that provides a restoring force in extensible connective tissues.

Fibroblasts**:** Cells that synthesise collagen and other proteins of the extracellular matrix. They are also involved in mediation of the immune response. In the cornea, they are activated keratocytes.

Keratocytes**:** Quiescent corneal cells that change their form if the cornea is stressed.

Stroma: any body of tissue, composed of fibroblasts and the collagen they synthesise.

Inflammation**:** a biochemical cascade, during which cytokines (signalling proteins that are locally secreted and active) increase blood flow and invite cells of the immune system to leave blood vessels, phagocytose foreign material, initiate an immune response, clear pathogens and repair damage.

Phagocytosis: the cell membrane engulfs adjacent material, trapping it in intracellular vesicles, in which it is broken down enzymatically.

Orbit (the bony cavity which cradles the eye globe)

***Extraocular muscles** and **fat pad; eye movements**.*

Within the non-compliant, bony orbit, the eye globe floats over a fat pad. This is contained by the **rectus muscles** ("recti"), which arise from the posterior orbit, insert into anterior sclera and rotate the globe. Medial and lateral recti rotate in the horizontal meridian; superior and inferior recti rotate in the vertical meridian. Contraction of any rectus muscle is matched by relaxation of its antagonist. Superior and inferior oblique muscles stabilise against torsion of the globe. The eye moves rapidly between focus points in motions known as **saccades**.

***Strabismus** (squint)*: movements of the two eyes become dysconjugate.

Pressure relationships in the eye and orbit.

Within the globe, aqueous, secreted behind the iris, extends the sclera (giving rise to the *intraocular pressure*, **IOP**) and mostly flows into episcleral veins on the surface of the globe. These drain into the orbital veins (*orbital pressure*), to the cavernous sinus (*cerebro-spinal fluid pressure*).

The ***optic disc*** forms an interface between the globe (*intraocular pressure*), the optic nerve (*cerebro-spinal fluid pressure*) and the orbit (*orbital venous pressure*).

Tear film, Cornea and Sclera

Tear film

This ensures a perfectly smooth air-tissue interface. The aqueous component of tears is mostly secreted by the lacrimal gland (supero-temporal), is spread by the upper lid and drains into the naso-lacrimal duct (medial). Evaporation is reduced by a superficial lipid layer, secreted by Meibomian glands in the eyelids.

Cornea

This is the transparent and avascular front surface of the collagenous envelope of the eye globe. It forms the first and most powerful refracting surface of the eye. Power of the anterior surface is > 50D.

Its ***epithelium*** is a multi-layered cellular structure. Stem cells divide at the corneal periphery (limbus); their progeny flow centrally and shed into the tear film. Their superficial surfaces have delicate microvilli, which support a mucus layer, secreted by conjunctival goblet cells. When wetted by tears, this gives a perfectly smooth refractive surface.

The ***stroma*** consists of robust bundles of collagen fibres that straddle the cornea from limbus to limbus. They are packed with a separation of less than the wavelength of visible light, hence its transparency.

Corneal ***endothelium*** is a monolayer ("mosaic") of flattened cells, joined by impervious tight junctions. They pump water from the stroma into the anterior chamber, maintaining the tight packing of collagen, hence corneal transparency. Damaged human corneal endothelium does not regenerate: surrounding cells enlarge to cover the gap.

Keratoconus is a non-inflammatory eye condition in which the cornea thins and bulges forward, affecting vision.

Sclera

The near-spherical, collagenous, vascular envelope of the globe. It lacks the compact, uniform structure of the cornea, and is therefore reflective (white) and opaque. Continuous with cornea at the **limbus**.

Anterior segment

Aqueous (= aqueous humour) is a watery liquid containing little protein, secreted behind the iris by a ring of delicate "**ciliary processes**" on the posterior surface of the ciliary body. It usually contains very few cells. It flows forward, between the lens and the iris, into the anterior chamber, and drains through the **trabecular meshwork** (a porous mat, composed of overlapping plates of collagen, proteoglycan and other extracellular proteins, which are coated with phagocytic cells) into a circumferential vessel, the **canal of Schlemm**. From there, it is transported through fine collecting channels into episcleral veins, which traverse the scleral surface, beneath the conjunctiva.

Aqueous frequently forms a clear central column within episcleral venous blood (**aqueous veins**).

Intraocular pressure **(IOP)**: Aqueous extends the collagenous envelope of the eye globe, which returns increasing intra-ocular pressure, until aqueous secretion balances aqueous outflow. The IOP is primarily controlled by drainage through the **trabecular meshwork**.

"*Glaucoma"* is defined as optic nerve damage and loss of visual field in the context of high intraocular pressure.

The ***iris*** is formed from the apex of the embryonic optic cup. It is a diaphragm, composed of radial and circumferential muscles that control pupil diameter (radial - pupil dilation, sympathetic innervation; circumferential - pupil constriction, parasympathetic innervation). The muscles are enclosed by pigmented epithelium.

The ***ciliary body*** is circumferential musculature, located behind the peripheral iris, from which the lens is suspended by radial cords of connective tissue (**zonules**). Relaxation of the ciliary muscles (sympathetic stimulation) flattens the lens, reducing its power. Constriction (parasympathetic stimulation) allows lens sphericity, hence power, to increase.

The ***crystalline lens*** is vascular and transparent. Its resting optical power is approximately 20D. Refocusing (**accommodation**) occurs by alteration of its sphericity, due to adjustment of ciliary muscle tone. Optical power can increase to >30D, but this facility is usually lost between the ages of 40-60 years (**presbyopia**).

A compact central nucleus is surrounded by cortex, all within a complete epithelial envelope. The posterior epithelium is derived from a ring of stem cells at the lens equator. Throughout life, the daughter cells migrate centrally over the posterior surface, then anteriorly, keratinising, dehydrating and thickening the lens from behind.

Posterior segment

Vitreous (vitreous humour) is an avascular gel, formed from short collagen fibres, hydrated with aqueous secreted by the ciliary apparatus. The vitreous is adherent to the retina through early life, but **posterior vitreous detachment (PVD)** - peeling from the retinal surface - commonly takes place with age (accelerated by myopia or inflammation). The process begins at the interface between vitreous and central retina, then spreads peripherally, towards the equator. It is usually uneventful; however, focal persistent adhesions can cause tears in the retina, followed by **retinal detachment**. After PVD, the **post-vitreous space** (**PVS**) fills with aqueous.

Retina:

The retina lines the inner surface of the posterior globe from the **pars plana** (a ring of pale tissue behind the ciliary body), to the **optic disc**. It is separated from sclera by the **retinal pigment epithelium (RPE)**, a carpet of pigmented, phagocytic cells, outside which is the highly-vascular **choroid**.

The retina is transparent and inverted: light traverses the *inner* neuronal layer to reach the *outer* photoreceptors. Structural stability derives from Müller cells, which span its full thickness.

Neural connections:

A dense mosaic of **photoreceptor cells** relay (*inward*) to **bipolar cells**, a network of neurones which, in conjunction with a population of horizontal neurones, are involved in pre-processing of the visual image. They transfer highly modulated signals to the most superficial neurones, the **ganglion cells**. Ganglion cell bodies send transparent, unmyelinated axons (the **nerve fibre layer**) over the innermost surface of the retina to the **optic disc**. Here they acquire a myelin sheath, leave the eye in the **optic nerve** and travel to the brain-stem.

*Photoreceptors***:**

Two types of photoreceptor cells are responsible for image formation**: rods** (sensitive, monochrome) and **cones** (colour derivation).

All have **inner segments** (which relay inwards to the bipolar cells) and **outer segments** (composed of highly-folded plates containing photo-pigment, which are continually replenished). The photoreceptor outer segments traverse the potential cleft between retina and the **retinal pigment epithelium** (**RPE**), and are embedded within pockets in the phagocytic **RPE cells**. Continual outer segment growth is matched by RPE phagocytosis.

Macula

This is a specialised zone of the retina which is rotated to the centre of the visual field by the rectus muscles in order to receive the desired image. It is packed with cones and its central zone, the **fovea**, is avascular, maintained purely by diffusion of nutrients and oxygen from the choroidal circulation.

Retinal pigment epithelium (**RPE**) cells are highly metabolic, continuously pumping fluid out of the **sub-retinal space** (the potential cleft between retina and RPE). They phagocytose photoreceptor outer segments and are heavily pigmented, absorbing stray light. They are joined together by tight junctions to form a monolayer outside the retina, which is impermeable to water. RPE cells pump fluid outwards, through **Bruch's membrane***, into the **choroid** (a highly vascular tissue immediately inside the sclera).

Bruch's membrane is a continuous extracellular membrane, insinuated between the retinal pigment epithelium and the choroidal capillary bed (the **choriocapillaris**). It spreads from the pars plana to the posterior pole.

Retinal detachment occurs when the RPE pump is overwhelmed, due commonly to fluid passing through a retinal break. It may also follow loss of continuity of the retinal pigment epithelium or leakage from choroidal new blood vessels (which, in certain circumstances, may grow inward, through Bruch's membrane and the retinal pigment epithelium). Whatever the cause, the neuroretina floats inwards as **sub-retinal fluid (SRF)** prises photoreceptor outer segments apart from their underlying bed of RPE cells. Most retinal breaks arise anterior to the equator of the globe and can be difficult to localise.

The ***optic disc*** is the intraocular structure in which axons of the nerve fibre layer, which originated from the retinal ganglion cells, acquire their myelin sheaths and enter the optic nerve. It also carries the retinal arteries and veins into the globe; however, its own blood supply arises from the choroidal circulation.

The ***optic nerve*** transfers all visual information to the brain. Axons, now myelinated, are transported from the optic disc to the lateral geniculate nucleus in the brain-stem. There, axons from retinal ganglion cells encounter their first synapses and visual information is passed on to the visual cortex. The optic nerve is surrounded by a cuff of cerebro-spinal fluid (CSF), an extension of the intracranial CSF space.

Blood Circulations

The eye receives most of its blood from the **ophthalmic artery**, which reaches the orbit through an aperture in the skull. This supplies 3 circulations:

- The **central retinal artery** enters the optic nerve, and is admitted into the globe through the optic disc. It divides repeatedly as it ramifies over the surface of the retina, supplying superficial and deep microcirculations.
- "**Anterior ciliary**" branches of the ophthalmic artery follow the rectus muscles to a superficial episcleral arterial circle behind the limbus and penetrate sclera to supply the "major arterial circle" at the root of the iris.
- "**Posterior ciliary**" branches (short posterior ciliary arteries) supply the choroid and optic disc. Medial and lateral long posterior ciliary arteries contribute to the major circle of the iris.

The capillary bed of the choroid, the **choriocapillaris**, lies on its inner surface, adjacent to Bruch's membrane and retinal pigment epithelium.

Stability of anterior ciliary perfusion is ensured by superficial **vascular arcades**. The anterior and long posterior ciliary circulations communicate by trans-scleral arcades, involving the major circle of the iris. However, the retinal circulation remains discrete.

Venous blood drains back to **two orbital veins**, then into the **cavernous sinus** and the cerebral venous circulation; also, forwards into the eyelid circulations.

Some engineering terms

Acronyms and technique terms

CFD Computational fluid dynamics – solving the governing equations numerically.

FLAIR Fluid attenuated inversion recovery – a type of MRI pulse sequence that suppresses the signal from cerebrospinal fluid.

FOV Field of view – the extent of the observable world that can be imaged at a given instant

LSC Liquid scintillation counting

MRA Magnetic resonance angiography – a method to produce images of the vasculature using MRI.

MIP Maximum-intensity-projection. A method of image post-processing that produces pseudo 3D images of the vasculature from MRA acquisitions.

MRI Magnetic resonance imaging

OCT Optical coherence tomography

Refractive index The refractive index determines how much the path of light is bent when encountering a boundary between two materials. The greater the difference in refractive index between the materials, the greater the bending.

STIR Short Tau inversion recovery - a type of MRI pulse sequence that suppresses the signal from fat.

T1w, T2w – Types of MR pulse sequences where the image contrast is weighted towards either T_1 (longitudinal) or T_2 (transverse) relaxation.

TOF Time-of-flight – a type of MRA pulse sequence that is used to visualise blood flow.

Chemical terms

atRA All-trans retinoic acid

Esterification Reaction producing an ester bond between an alcohol and an acid

GBCA Gadolinium-based contrast agent – a chelate of gadolinium that is injected during an MRI examination to increase the MRI signal on T1w images showing where pathology has an increased blood flow.

pεK Poly-ε-lysine – short chain peptide of the amino acid lysine (approx. 25-30 amino acid units)

PVP Polyvinylpyrrolidone –water-soluble linear polymer made from the monomer N-vinylpyrrolidone

PEG Polyethylene glycol – hydrophilic linear polymer

PDMS Polydimethylsiloxane – silicone oil

PDMSMA Methacrylated polydimethylsiloxane

PMMA Polymethylmethacrylate (Perspex® aka acrylic)

OEGMA Methacrylated oligo(ethylene glycol)

Proteoglycan Proteins to which long sugar-like chains are attached

RAFT polymerisation Reversible addition-fragmentation chain polymerisation

SO Silicone oil

Surfactant Molecules (or very small particles) which tend to accumulate at interfaces

Fluid and flow terms

Contact line The line where a liquid/gas or liquid/liquid interface meets a solid surface

Film A thin layer of liquid. A film can be static or moving

Pressure Normal force per unit area

Shear rate The rate at which a packet of fluid moves past its neighbours

Shear stress Sideways acting (as opposed to normal) force per unit area

Viscosity Normally this refers to *shear* viscosity – resistance to a shearing force, as in a pipe flow

Extensional viscosity Resistance to a stretching force, as in saliva between fingers

Dynamic viscosity Ratio of shear stress to shear rate. Units - poise (c-g-s) or Pascal (SI)

Kinematic viscosity Ratio of a fluid's viscosity to its density. Units - Stokes (c-g-s) or m^2s^{-1} (SI)

Inertia The tendency of a fluid to move at the same velocity

Interface The boundary between two phases (gas, liquid, solid

Surface energy The energy required to create 1 m^2 of new interface

Surface tension The force acting in the plane of a surface which will act to shrink it or must be overcome to stretch it. It includes the surface energy **and** any mechanical resistance (such as that imparted by the lipid layer in tear films). Surface tension is often used for liquid/gas interfaces, 'interfacial tension' for liquid-liquid ones.

Tamponade A large bubble of gas or large drop of non-aqueous liquid introduced into the posterior cavity as part of retinal repair surgery.