The fluid mechanics of the optic nerve

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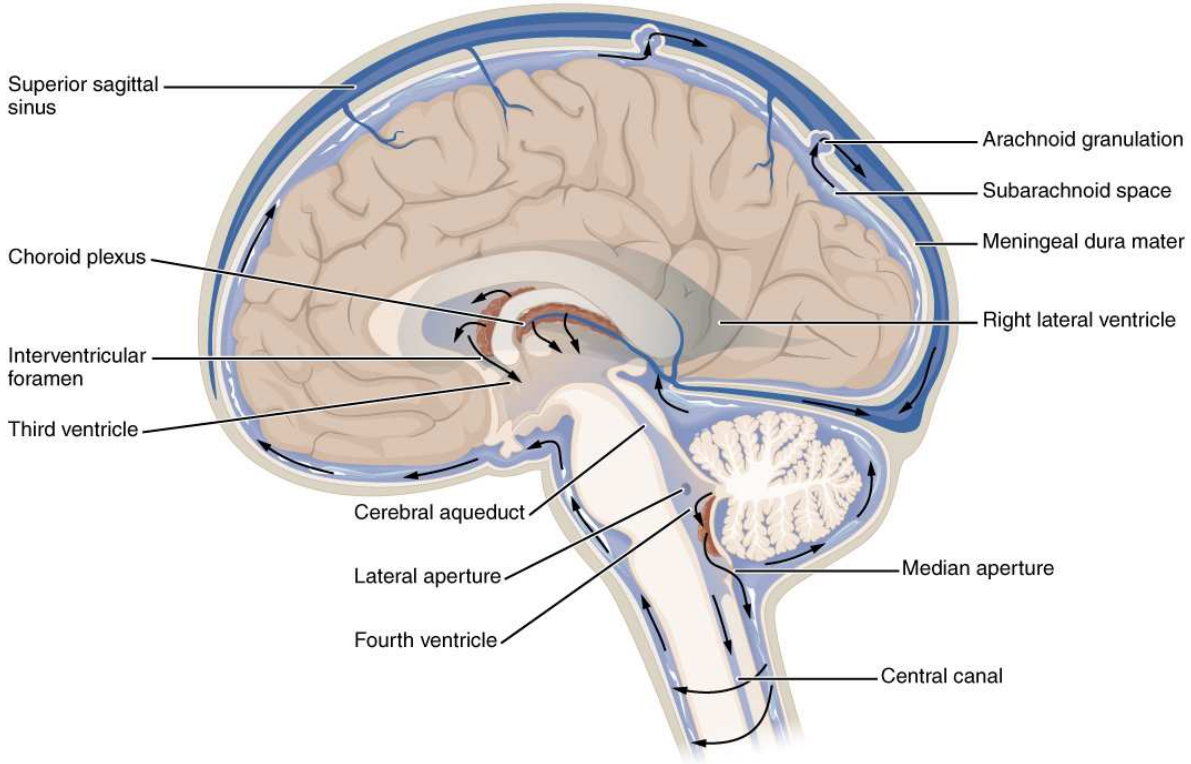
Predicting the condition of the brain

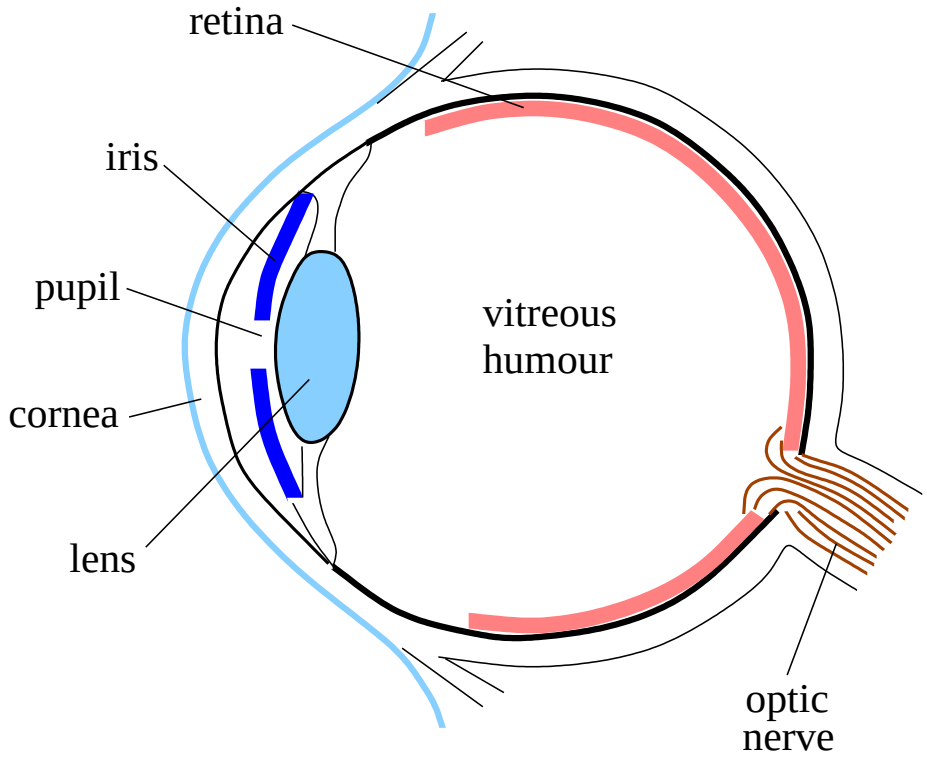


In normal adults the intracranial pressure is approximately 8-12 mmHg
Accurately measuring ICP is extremely difficult without an intracranial probe
TWO QUESTIONS FOR THIS TALK:

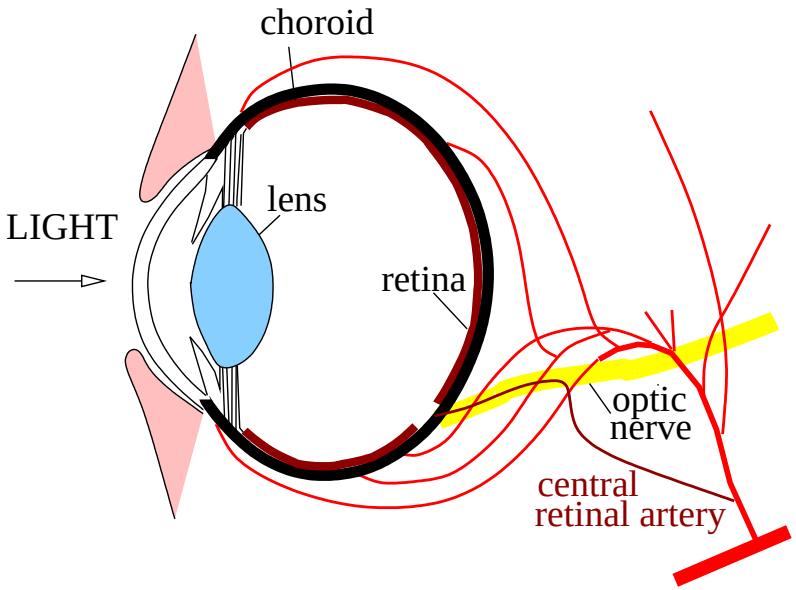
1. Predicting ICP non-invasively using the retinal venous pulse
2. Optic nerve bleeding following traumatic head injury

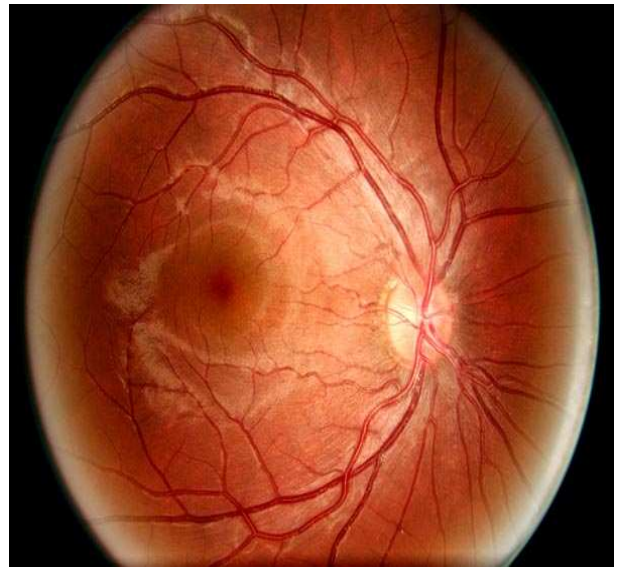
Simple anatomy of the eye

- The eye sits within a portion of the skull known as the orbit cushioned by a region of fat
- The eye is bounded by a layer of (relatively) stiff tissue known as the sclera (white portion)
- Light is interpreted by photoreceptor cells in the retina which lie on the inner surface of the sclera



The retinal blood supply



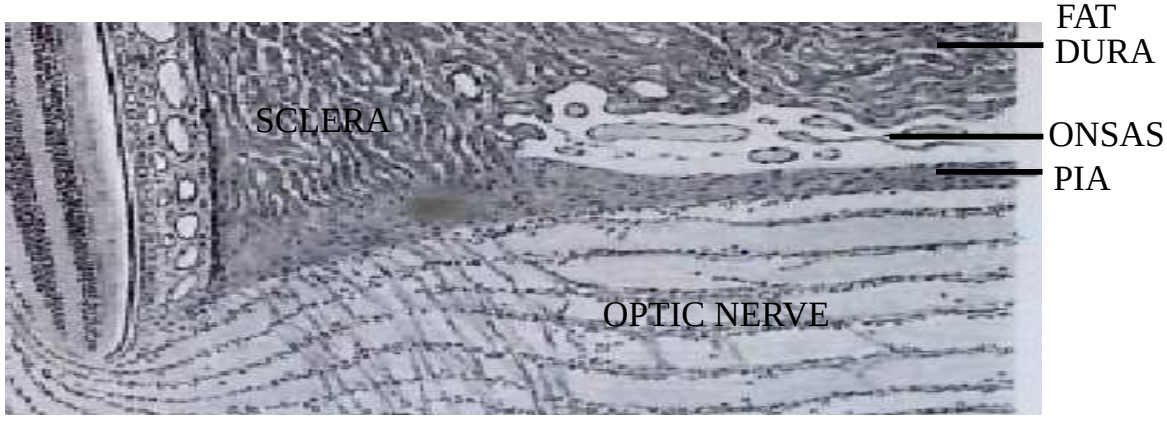


Histology between humans and higher primates is distinct to other mammalian species because the retina is supplied with blood by two mechanisms. Animal models are not always very useful.

- Retinal circulation The inner surface of the retina (closest to the vitreous) is supplied by the retinal circulation fed by the central retinal artery and central retinal vein which are branches of the ophthalmic artery and vein
- Choroidal circulation The outer surface of the retina (against the sclera) is supplied by the choroid which is fed by a number of arteries and veins which penetrate from outside the surface of the globe

The optic nerve

The optic nerve forms the bridge between the eye and the brain connecting the photoreceptors in the retina to the thalamus in the brain
Careful measurements of ON geometry by S.S. Hayreh in 1960s
Histological image of the optic nerve as it enters the eye:



Optic nerve subarachnoid space (ONSAS) contains CSF and is directly connected to the CSF compartments of the brain

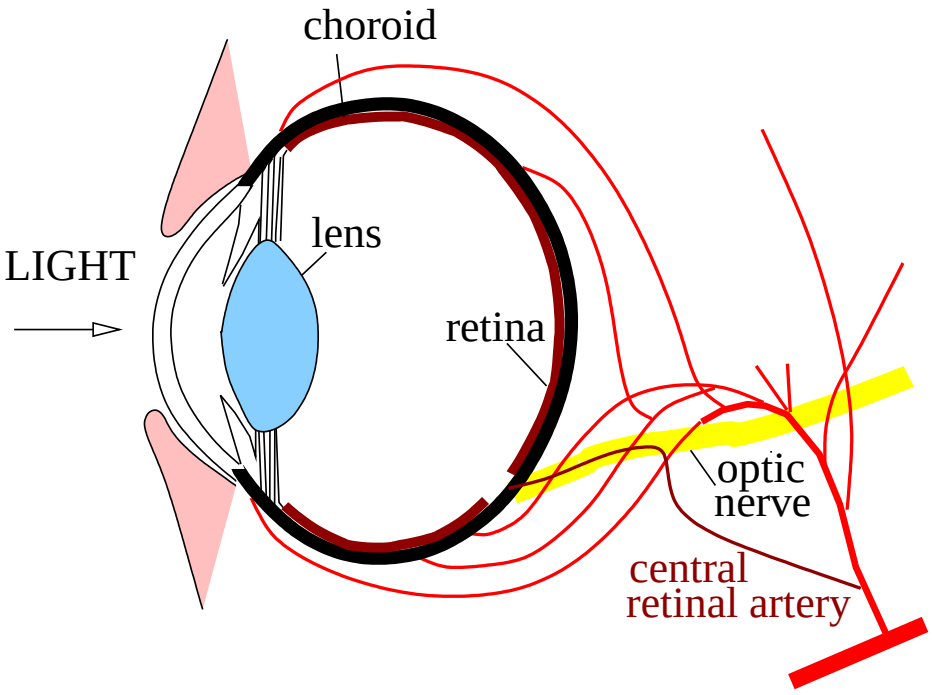
The ventricular CSF pressure (ICP) is well correlated to the CSF pressure in the ONSAS (pressure gradients are not sufficient to induce significant differences)

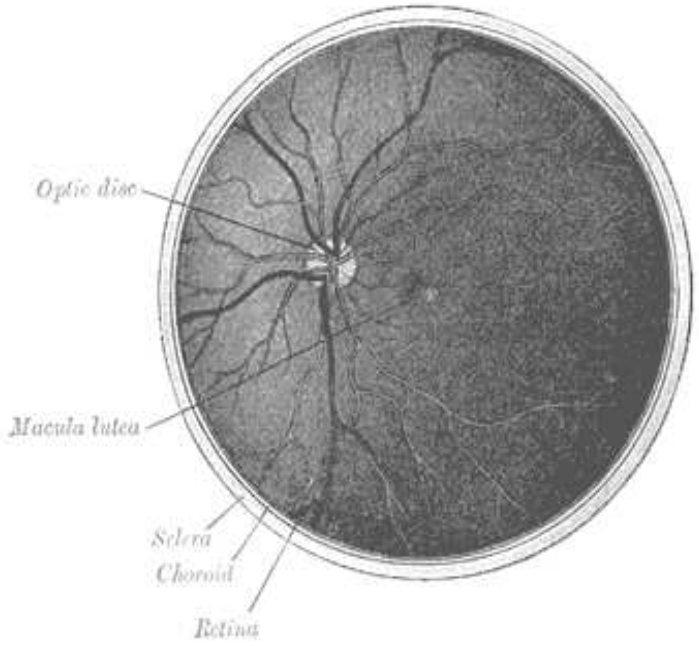
Part 1: Predicting intracranial pressure

with OE Jensen and AJE Foss

The retinal venous pulse

The retinal circulation is supplied by the central retinal artery and vein:





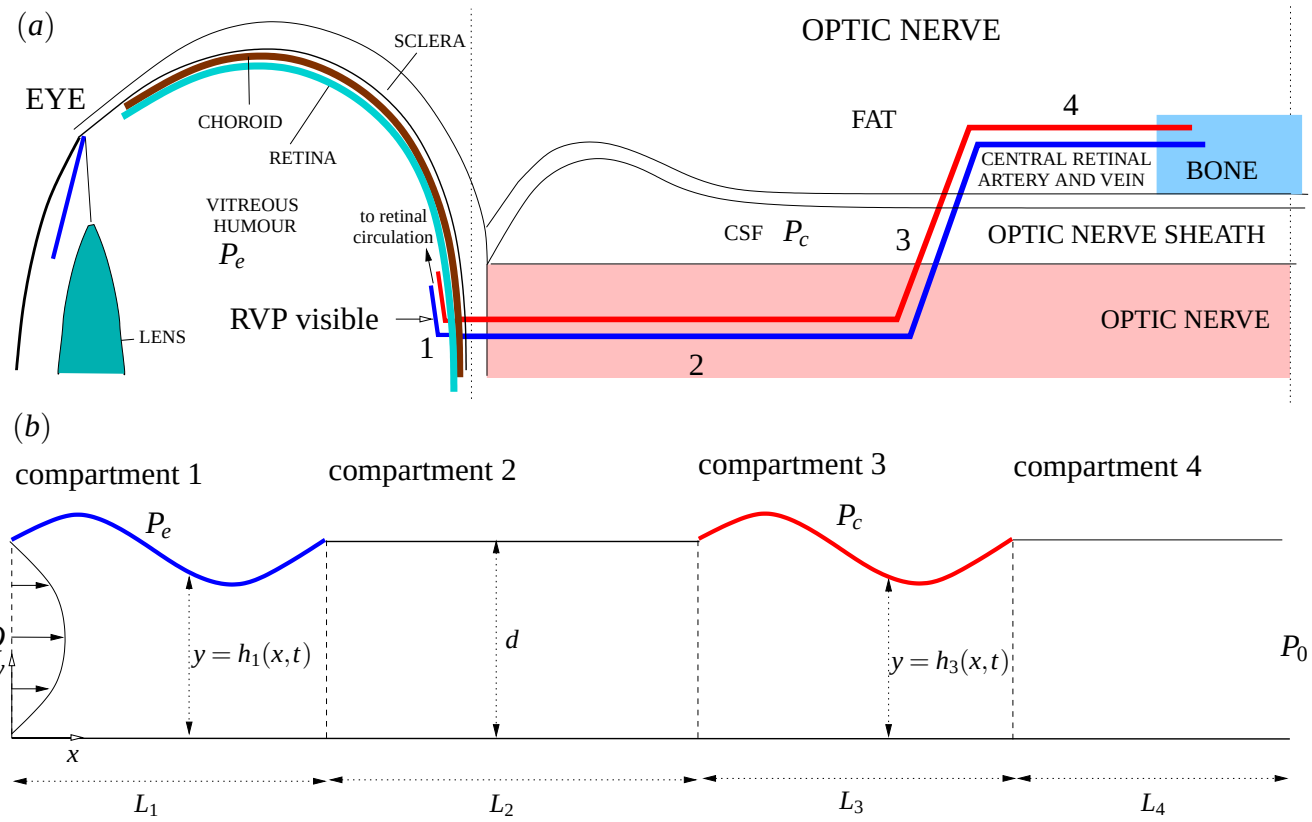
Retinal venous pulse

The retinal vein pulsates violently at the rear of the eye close to the optic disc

On increasing the intraocular pressure (IOP), clinicians observe spontaneous transition to large amplitude high-frequency pulsations in the vein known as the Retinal Venous Pulse (RVP)

- presence can be an early clinical indicator of glaucoma (normal ICP)
- absence of RVP can be an indication of increased ICP (normal IOP)

Path of the vein through the orbit



Split the course of the vein into 4 regions:

- 1: Exits eye at optic disk
- 2: Intra-neural portion
- 3: Crosses ONSAS
- 4: Extra-neural portion

The model

Construct a model for blood flow along the retinal vein:

- blood is homogeneous and Newtonian with constant density and viscosity (vessel diameter $> 100\mu$m)
- blood vessel wall is formed by a tensioned membrane with a large axial pre-stress
- flow is planar (two-dimensional)
- flow is driven by a fixed upstream flux into the vein
- downstream boundary condition of prescribed pressure into the ophthalmic vein

Flow satisfies the (2D) dimensionless Navier–Stokes equations:

$$\nabla \cdot \mathbf{u} = 0, \qquad \frac{\partial \mathbf{u}}{\partial t} + \mathbf{u} \cdot \nabla \mathbf{u} = -\nabla p + R^{-1} \nabla^2 \mathbf{u},$$

where R is the Reynolds number.

Normal stress balance on each compliant wall $(j = 1, 3)$

$$p = p_{ext} - T_j \frac{h_{j,xx}}{(1 + h_{j,x}^2)^{3/2}},$$

where T_j $(j = 1, 3)$ is a dimensionless membrane tension parameter.

Could solve directly (even 3D), but this has a high computational cost

Model Reduction

Make a series of assumptions: PSS, Waters & Jensen, *Eur J Mech B* (2009)

- long-wavelength disturbances (closure problem *cf.* boundary layer eqns)
- flow-profile assumption (flow is everywhere parabolic)

Conservation of mass and momentum in the compliant compartments ($j = 1, 3$)

$$h_{j,t} + q_x = 0,$$

$$q_t + \frac{6}{5}\left(\frac{q^2}{h_j}\right)_x = T_j h_j h_{j,xxx} - \frac{12}{R}\frac{q}{h_j^2}.$$

In the rigid compartments, conservation of mass requires $h = 1$, $q = q(t)$, while conservation of momentum takes the form

$$q_t = -p_x - \frac{12}{R}q.$$

Coupling between the compartments

Boundary conditions at ends of the compartments:
Vein wall is pinned at the ends of the compliant segments

$$h_1(0,t) = h_1(L_1,t) = 1, \qquad h_3(L_1+L_2,t) = h_3(L_1+L_2+L_3,t) = 1.$$

Fixed upstream flux and prescribed downstream pressure:

$$q = 1 \qquad (x = 0),$$

$$T_3 h_{3,xx} = \mathrm{ICP} - L_4\left[q_t + \frac{12}{R}q\right], \qquad (x = L_1+L_2+L_3).$$

Imposing continuity of liquid flux and continuity of liquid pressure across the junctions between regions 1 and 2 and regions 2 and 3 leads to the following additional constraints,

$$T_1 h_{1,xx}(L_1,t) - T_3 h_{3,xx}(L_1+L_2,t) = \mathrm{IOP} - \mathrm{ICP} - L_2\left[q_t(L_1,t) + \frac{12}{R}q(L_1,t)\right],$$

$$q(L_1,t) = q(L_1+L_2,t).$$

Typical parameters

- constant flow rate into the vein $Q \approx 7.5\mu l/\text{min}$
- vessel radius $150 - 225\mu\text{m}$
- typical compartment length $L_1 \approx L_3 \approx 1mm$, $L_2 \approx L_4 \approx 10mm$
- typical beat frequency of the heart $\Omega \approx 80\text{bpm}$
- downstream pressure at vein outlet $p_0 \approx 0\text{mmHg}$

INTRACRANIAL PRESSURE ICP is typically -5-15 mmHg in healthy individuals

$$\text{ICP} = P_c + A_3 \sin(2\pi\Omega t).$$

INTRAOCULAR PRESSURE IOP is typically 15-35 mmHg in healthy individuals

$$\text{IOP} = P_e + A_1 \sin(2\pi\Omega t - \tau),$$

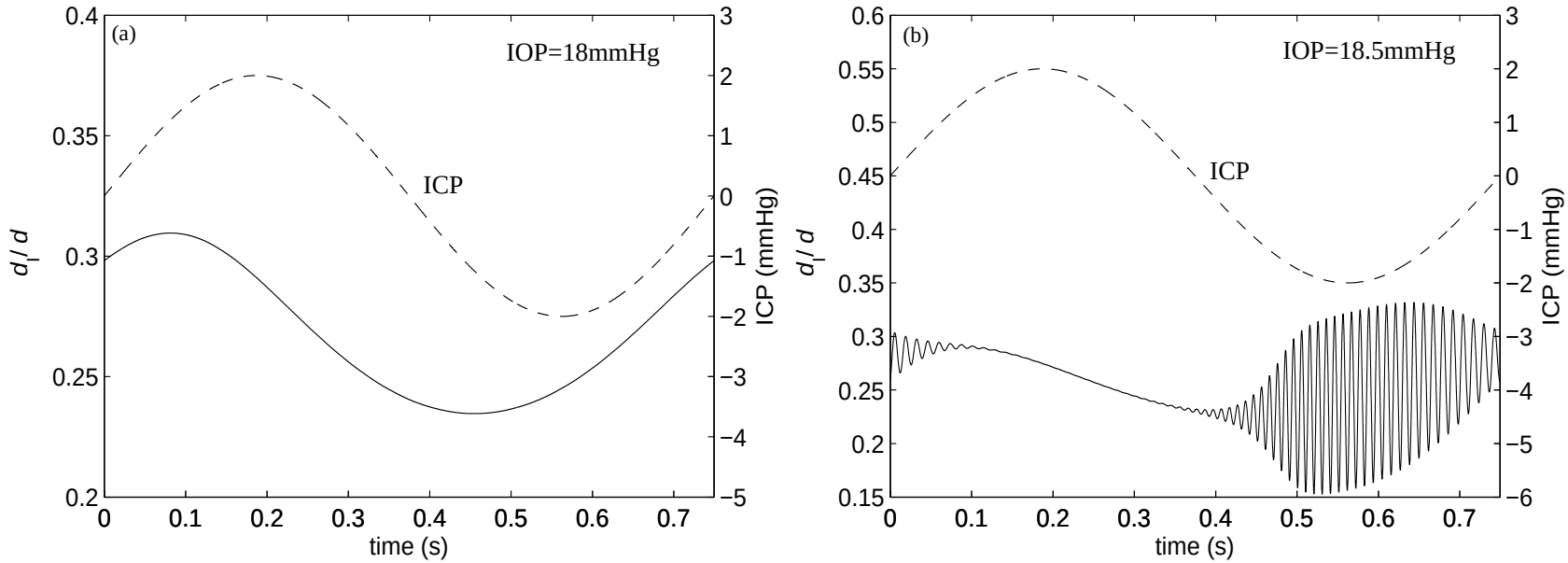
where τ is phase shift (unknown).

Low IOP

Large IOP

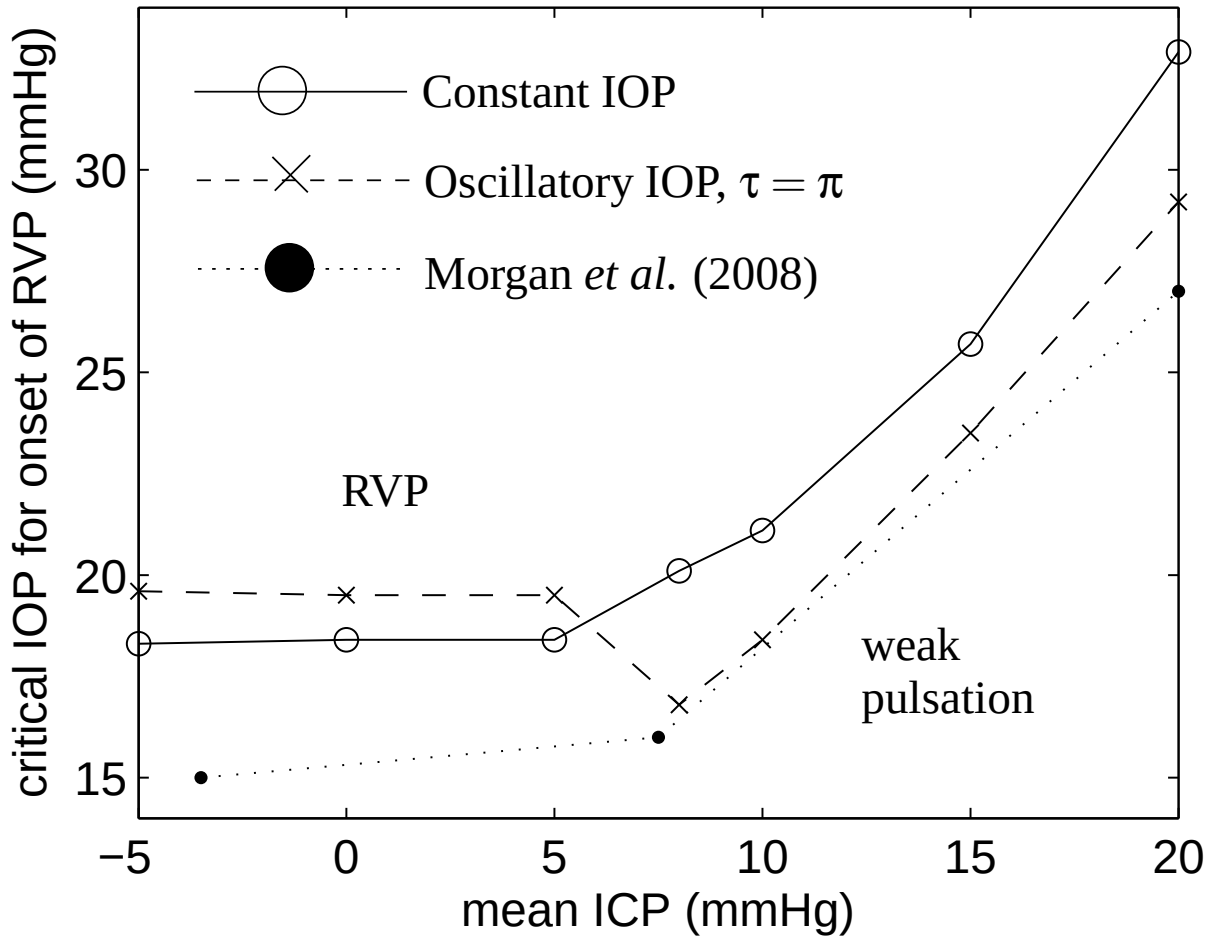
Typical results

Simulations with constant IOP for oscillatory ICP



Minimal channel width for (a) IOP = 18.0mmHg; (b) IOP = 18.5mmHg.

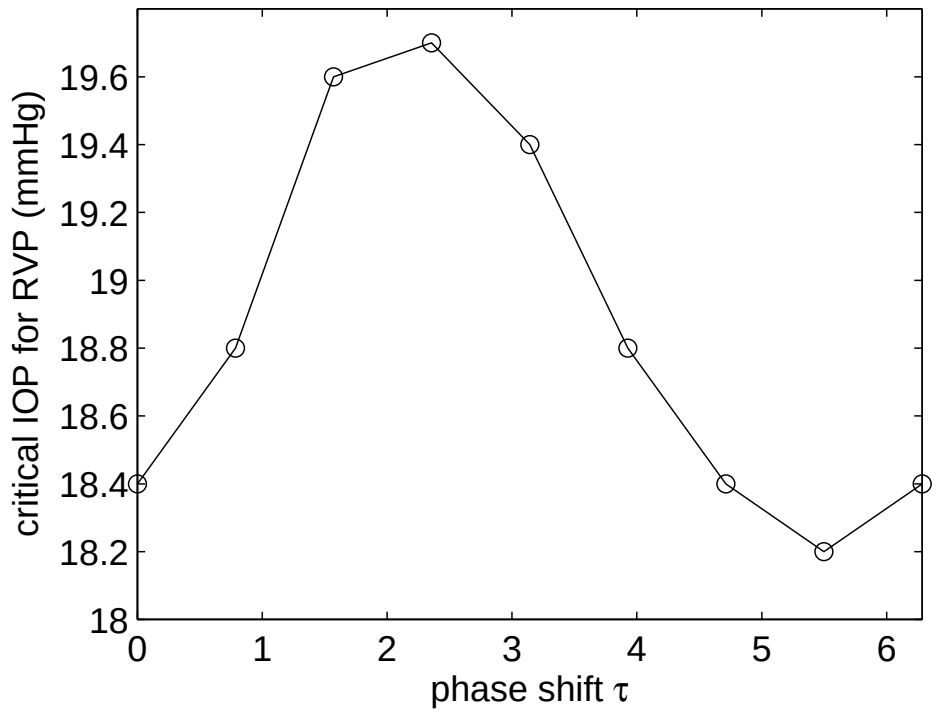
Onset curve for constant IOP



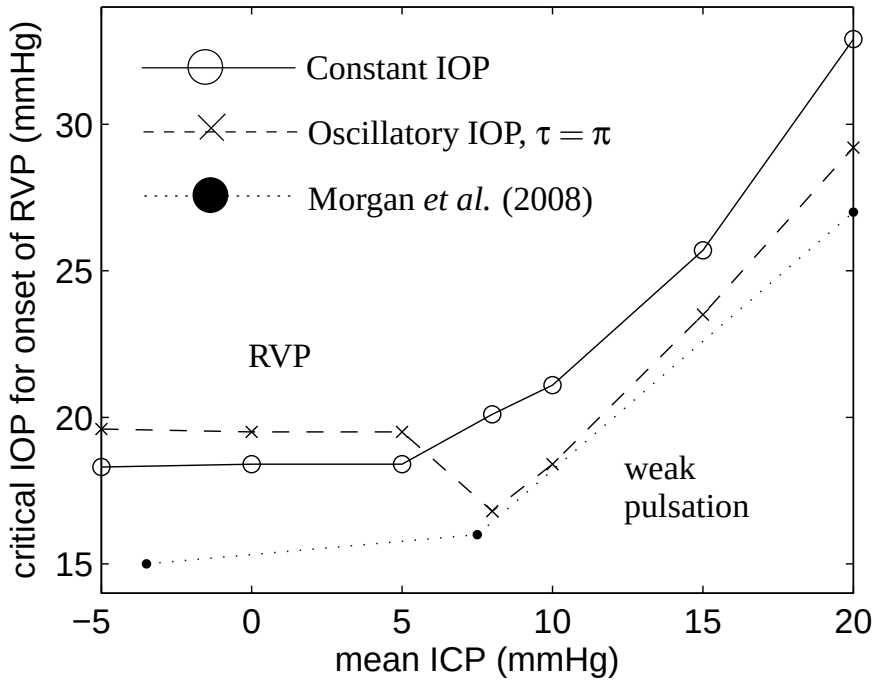
Excellent qualitative agreement with canine data of Morgan *et al.* J. Glaucoma (2008)

The influence of phase shift

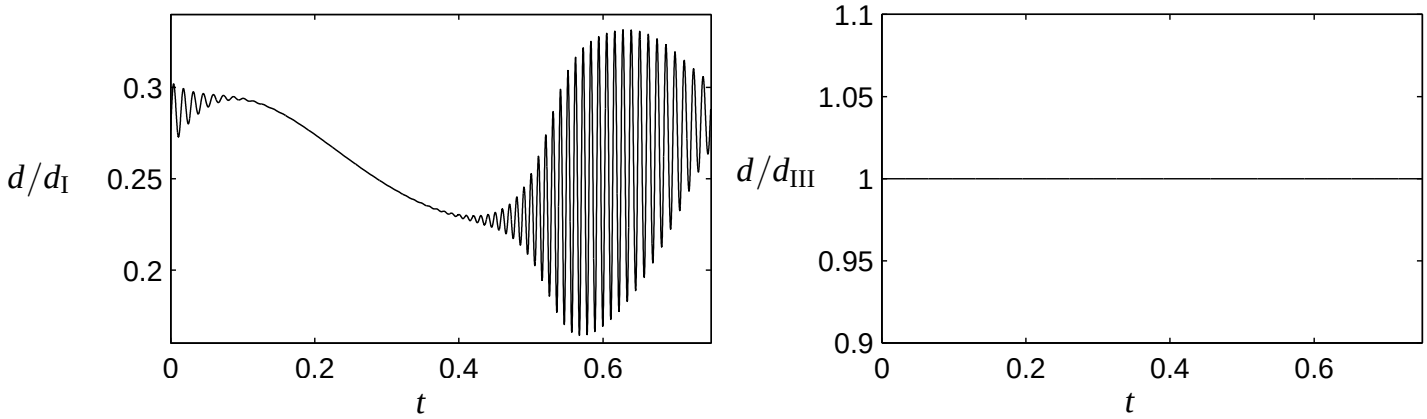
The critical intraocular pressure (IOP) for the onset of RVP is approximately independent of the phase shift



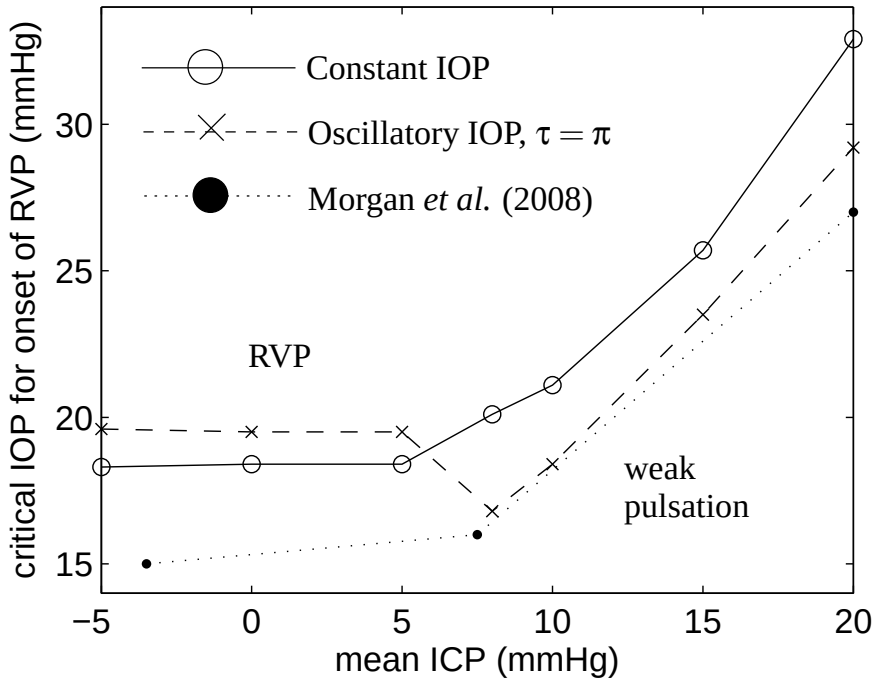
Observation of the oscillation profile



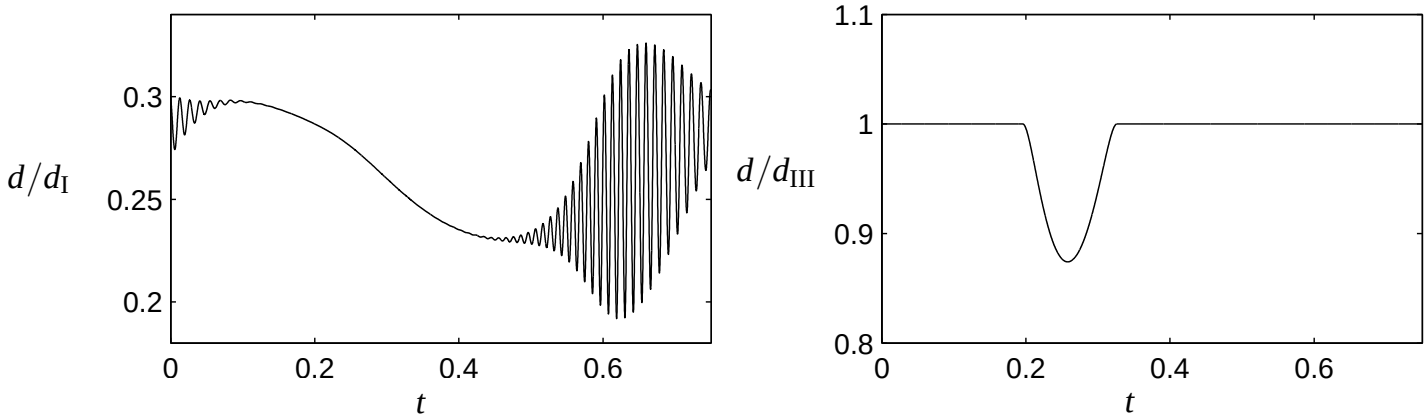
ICP=0mmHg, IOP=18.4mmHg



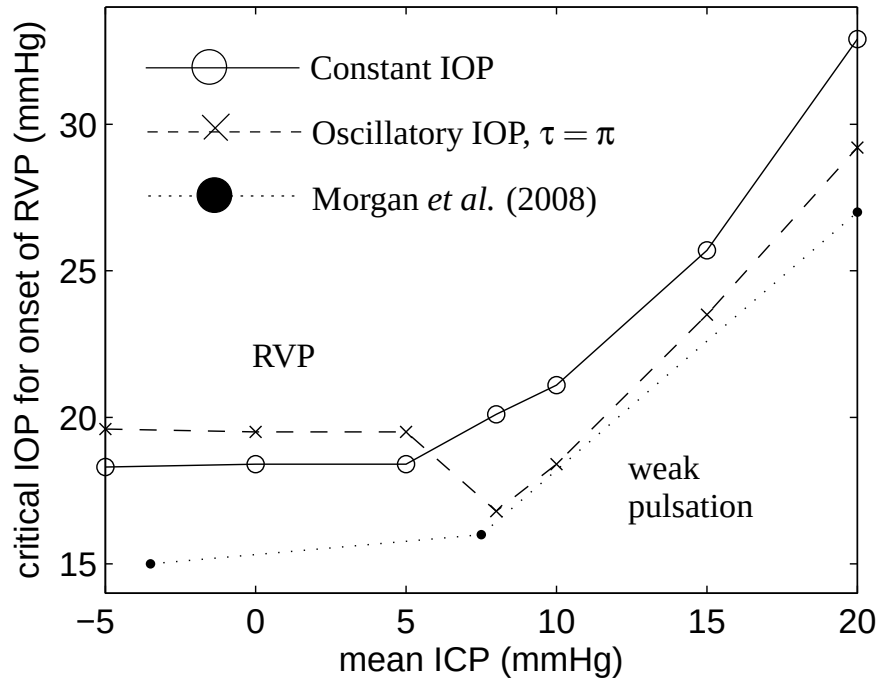
Observation of the oscillation profile



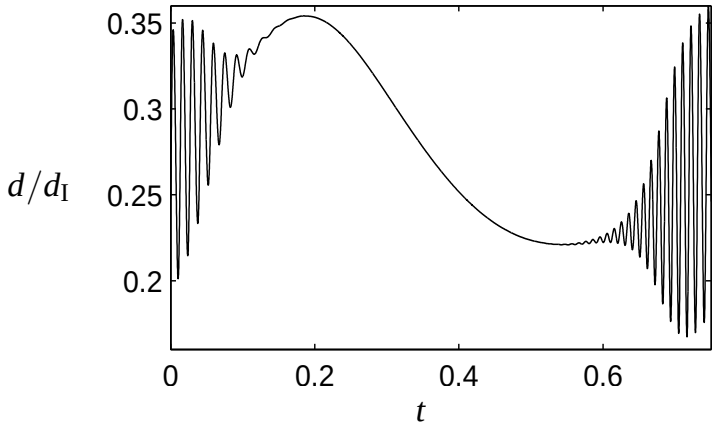
ICP=5mmHg, IOP=18.4mmHg

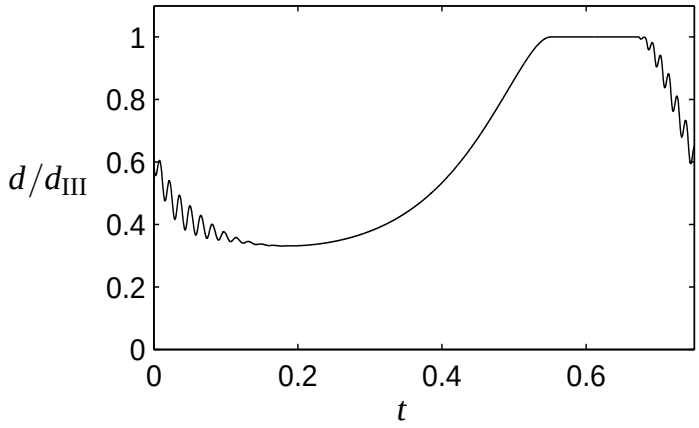


Observation of the oscillation profile

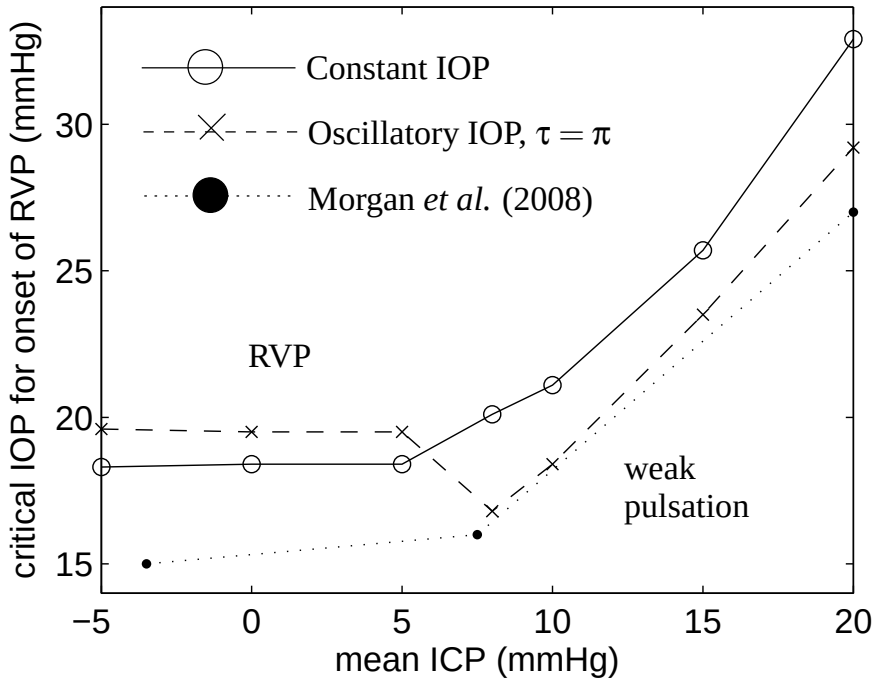


ICP=8mmHg, IOP=20.2mmHg

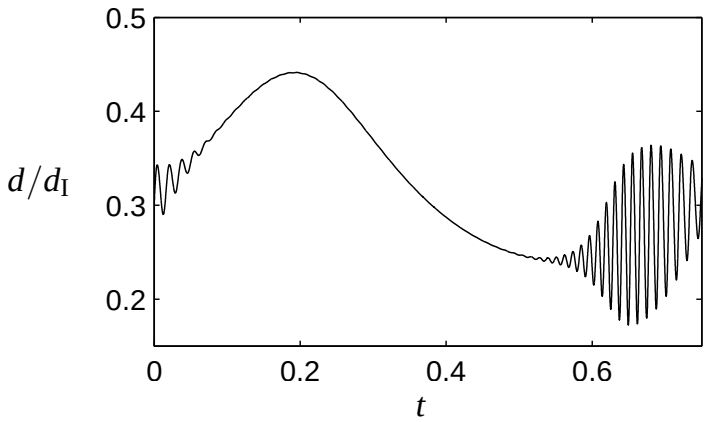


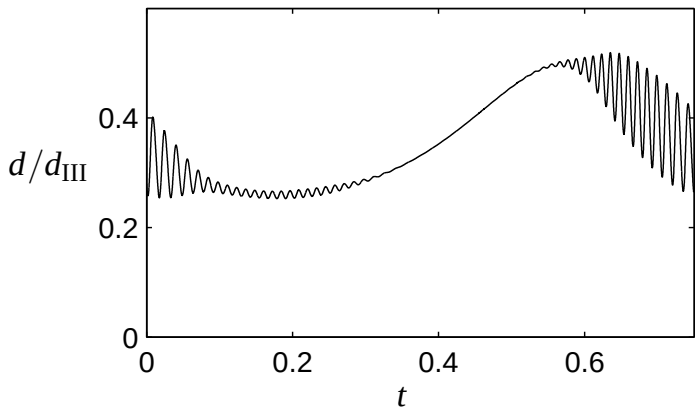


Observation of the oscillation profile



ICP=10mmHg, IOP=21.2mmHg





Predicting ICP: summary

Predicting Intracranial pressure by observation of the Retinal Venous Pulse

- Retinal vein at the rear of the eye can be observed to pulsate
- Mathematical modelling indicates a clean transition between a small amplitude oscillation and large amplitude (high-frequency) pulsation
- The onset trend agrees well with data from canine experiments (Morgan *et al.*, Glaucoma, 2008)
- Phase lag between oscillations in ICP and IOP makes only a small difference to the onset pressure
- Provides a theoretical basis for a new method for non-invasive measurement of ICP based on measurement of IOP

Further details can be found in:

- PSS, Jensen & Foss, Invest. Ophthalmol. Vis. Sci. 55 (2014)
- PSS & Foss, under review

Part 2: Optic nerve bleeding following a traumatic head injury

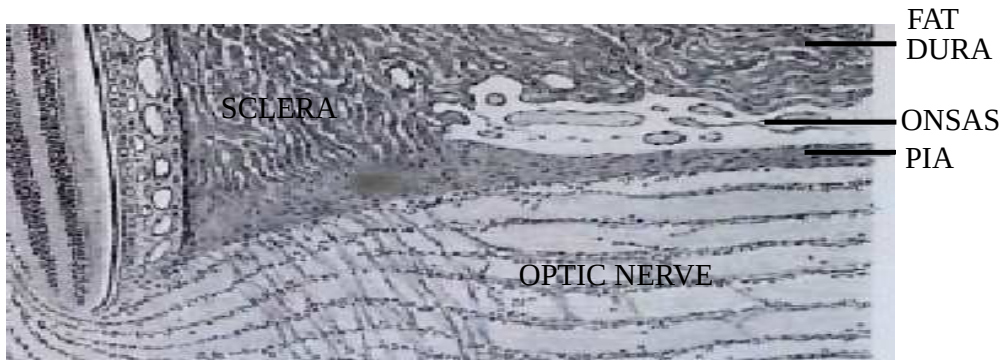
with OE Jensen and RE Bonshek

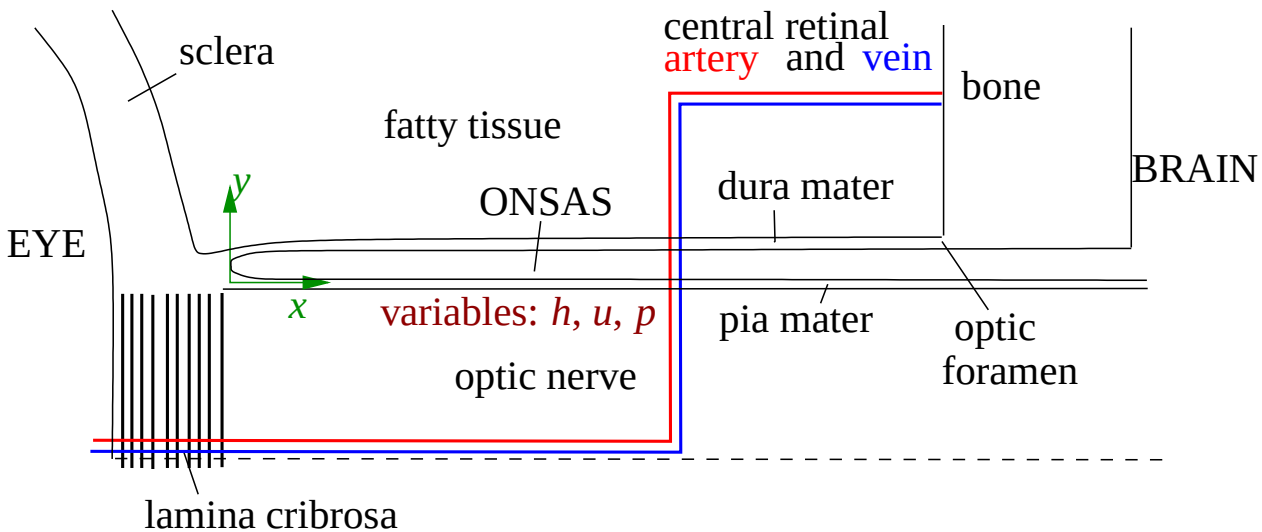
Traumatic brain injuries

Traumatic brain injuries are associated with a large increase in intracranial pressure

Traumatic brain injuries

The rise in CSF pressure is spatially non-uniform across the brain
This rise in CSF pressure is communicated to the optic nerve along the ONSAS





Predicting CSF flow along the optic nerve

Construct a model for the rapid CSF flow along the optic nerve subarachnoid space (ONSAS):

- CSF is homogeneous and Newtonian with constant density ρ
- elastic wall of the ONSAS (dura mater) is formed by an elastic sheet of stiffness K
- the ON surface (pia mater) is rigid and impermeable
- flow is planar (two-dimensional) (ignoring circumferential flow)

The resulting CSF flow is rapid, and so it can be approximated as inviscid, satisfying the 2D Euler equations:

$$\nabla \cdot \mathbf{u} = 0,$$

$$\mathbf{u}_t + \mathbf{u} \cdot \nabla \mathbf{u} = -\frac{1}{\rho} \nabla p,$$

subject to boundary conditions on $y = h(x, t)$

$$v = 0, \qquad (y = 0),$$

$$v = h_t + u h_x, \qquad (y = h(x, t)),$$

along with the normal stress condition on the vessel wall

Shallow water approximation

In normal adults the ONSAS is between 0.7-1mm thick and about 27mm long

Take a shallow water approximation (integrating across the ONSAS width) Simplified equations for conservation of mass and momentum which incorporate the flow boundary conditions:

$$h_t + (uh)_x = 0,$$

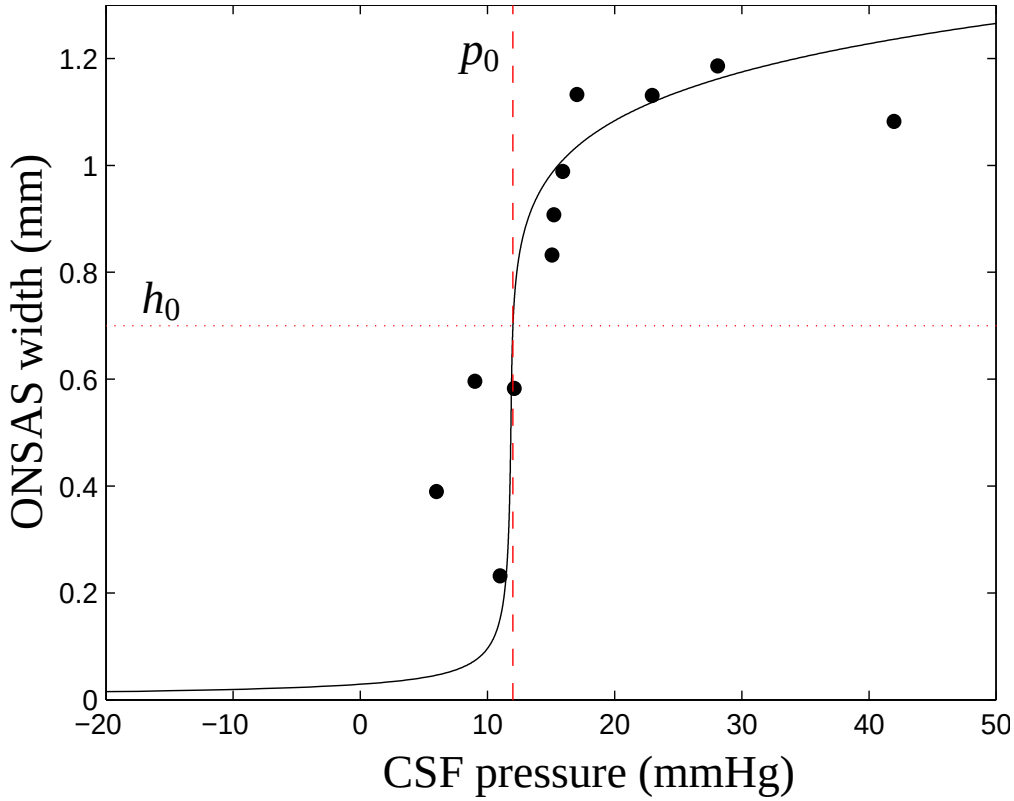
$$u_t + uu_x = -\frac{1}{\rho} p_x.$$

This system is not closed, requiring a final condition for the fluid pressure.

Model for the elasticity of the dura

Need a constitutive relationship for the elasticity of the dura mater

Agrawal & Brierley *Eur. J. Trauma Emerg. Surg.* (2012) measured the diameter of the optic nerve sheath as a function of the CSF pressure during infusion tests



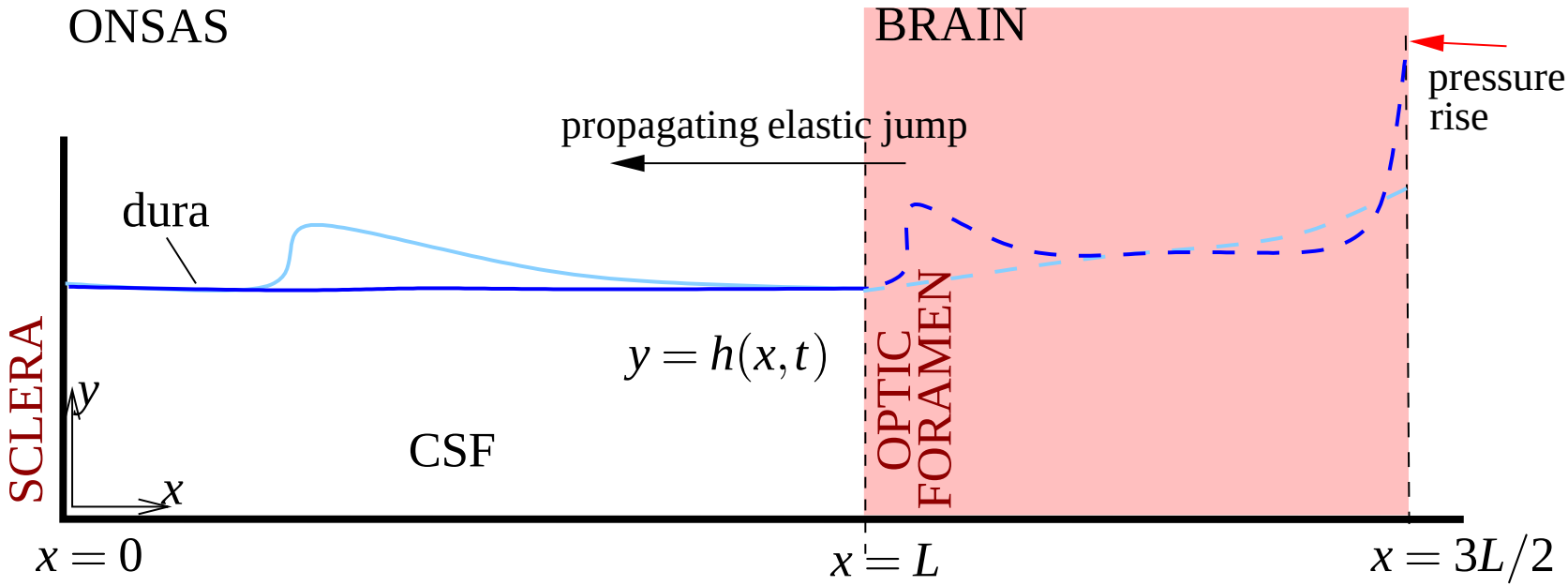
Fitted relationship (commonly used for modelling arteries and veins)

$$p - p_0 = \mathcal{P}(h/h_0) = K\left((h/h_0)^{10} - (h/h_0)^{-3/2}\right),$$

Disturbance setup

Consider the ONSAS as a domain $0 \leq x \leq L$ between the sclera $(x = 0)$ and the optic foramen $(x = L)$

Disturb the system a distance $L/2$ upstream (mimicking an injury) and allow the disturbance to propagate into the ONSAS



Use a sinusoidal pressure disturbance at the upstream end of the domain $(x = 3L/2)$

$$p(3L/2, t) = p_0 + (\Delta P)\sin^2(\pi t/T), \qquad (0 < t \leq T),$$
$$p(3L/2, t) = p_0, \qquad (t > \tau).$$

Solving the nonlinear equations

The hyperbolic system of governing equations can be written in conservative form

$$\left(\frac{\partial}{\partial t} + (u \pm c)\frac{\partial}{\partial x}\right)\left[u \pm \int_{h_0}^{h} \frac{c}{h^*}\, dh^*\right] = 0$$

with nonlinear wavespeed

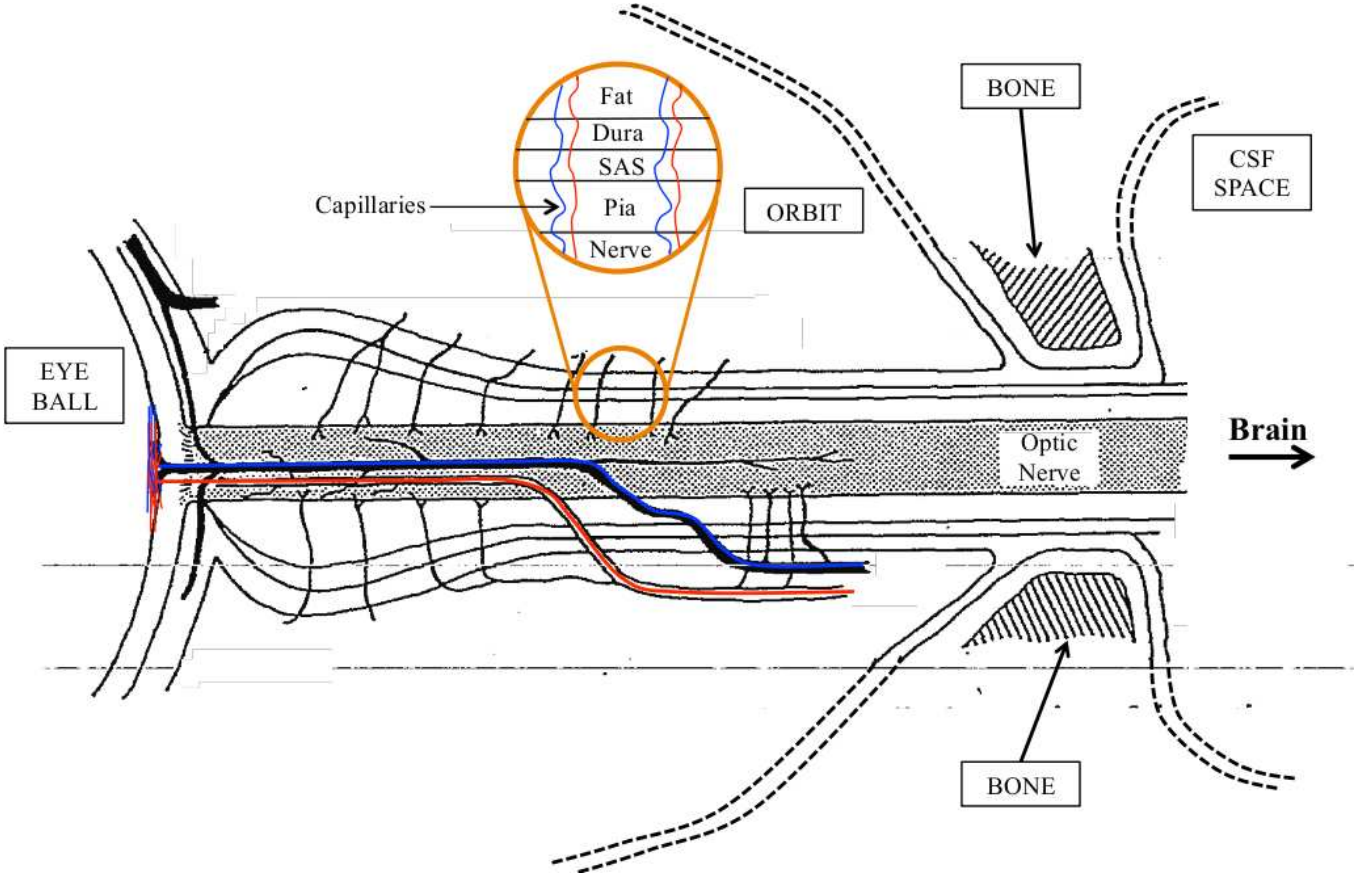
$$c = \left(\frac{h}{\rho}\frac{\mathrm{d}\mathcal{P}}{\mathrm{d}h}\right)^{1/2}.$$

In the absence of tensile forces in the vessel wall the model admits discontinuities in the width of the ONSAS (elastic jumps) which can propagate in either direction

Adopt the numerical method developed by Brook, Falle & Pedley *J. Fluid Mech.* (1999) to study propagating elastic jumps in the giraffe jugular vein using an explicit (upwind) Gudunov scheme with shock capture

A typical example

ONSAS bleeding



NEW MECHANISM FOR ON BLEEDING: Large CSF pressures at the distal end of the ONSAS and associated rapid ONSAS widening can induce rupture of blood vessels bridging across the ONSAS and lead to localised bleeding

Clinical implications

This prediction is especially important in suspected cases of Non-accidental head injury in infants

Shaken Baby Syndrome The medical symptoms in such cases are hard to ignore, typically involving:

- subdural haemorrhage (bleeding in the region between the skull and the brain)
- retinal haemorrhage (bleeding of the retinal circulation at the back of the eye)
- brain swelling

Optic nerve bleeding: is one form of subdural haemorrhage (especially at the scleral end); this observation is often used as a clinical indicator of non-accidental injury in post-mortem

Discussion

- Predicting Intracranial pressure by observation of the Retinal Venous Pulse
  - Retinal vein at the rear of the eye can be observed to pulsate
  - Mathematical modelling indicates a clean transition between a small amplitude oscillation and large amplitude (high-frequency) pulsation
  - Observed trend agrees well with data from canine experiments (Morgan *et al.* J Glaucoma 2008)
- Optic nerve bleeding following traumatic brain injury
  - Traumatic brain injury can lead to a large increase in CSF pressure
  - This rise in pressure is transmitted to the optic nerve subarachnoid space
  - This large CSF pressure is significantly amplified as the elastic jump reflects at the sclera
  - The model predicts an optimal timescale for maximising the scleral pressure

Acknowledgements

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