3307 Biomathematics Notes

Based on the 2010 autumn lectures by Dr S A Baigent and Dr A Zaikin

The Author has made every effort to copy down all the content on the board during lectures. The Author accepts no responsibility what so ever for mistakes on the notes or changes to the syllabus for the current year. The Author highly recommends that reader attends all lectures, making his/her own notes and to use this document as a reference only.

BIOMATHEMATICS
PART I

MATH3307 Biomathematics Weeks 1-5: Some references

Scaling Laws

A1 Andrew A Biewener. *Animal Locomotion.* Oxford Animal Biology Series. CUP, 2003. [Good general reading, but particularly pages 10-14. Chapter 7 has an interesting section on jump performance.]

A2 Knut Schmidt-Nielsen. *Scaling: Why is animal size so important?* CUP, 1984. [Does not build models, but is good background information on scaling in biology]

A3 D'arcy Wentworth Thompson. *On growth and form.* CUP. First published 1961. [Again, no model building, but excellent background and a real classic]

A4 Ludwig von Bertalanffy. *General Systems Theory.* 1969. George Braziller Inc. New York. [He discusses his growth model in pages 171-184].

A5 `http://online.itp.ucsb.edu/online/pattern_i03/west/`
For general interest, and also von Bertalanffy's model]

Diffusion/Insect Respiration

B1 Ove Sten-Knudson. *Biological Membranes: Theory of Transport, Potentials and Electric Impulses*, Cambridge University Press, 2002. [Can be previewed, e.g. page 62+, at (http://books.google.co.uk/books?id=xfJyHiIKBiMC)]. [You might find pages 138+ useful for the particle model of diffusion.]

B2 G. R. Grimmett & D. R. Stirzaker. Probability and Random Processes. Clarendon Press, Oxford. 1992. [For expectation and variance, and also Chapter 13 Diffusion Processes.]

B3 `http://www.livescience.com/animals/061011_giant_insects.html`
[Readable article on oxygen and insect size limitations.]

B4 `http://users.rcn.com/jkimball.ma.ultranet/BiologyPages`
`/T/Tracheal_Breathing.html`

Bird flight

C1 Rayner, J. M. V. (2001): Mathematical modelling of the avian flight power curve, *Math. Meth. App. Sci.*, **24**: 1485–1514.

C2 Lighthill, M. J. (1974): Aerodynamic aspects of animal flight. *Bulletin of the Institute of Mathematics and its Applications*, 10:369 393. [Also published 5th Fluid Science Lecture, BHRA; reprinted in Swimming and Flying in Nature, vol. 2, WuTY-T, Brokaw CJ, Brennen C (eds). Plenum Press: New York, 1975, 423 491].

A1 (see above). Chapter 5. Sections 4.1-4.3 may also be useful background reading on fluids.

Electrophysiology

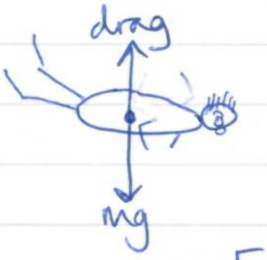
B1 (as above)

D1 J. Keener & J. Sneyd. *Mathematical Physiology.* Interdisciplinary Applied Mathematics 8. Springer-Verlag, New York 1998. [Parts of Chapters 2,3 might be useful]

1. SCALING LAWS

Example I A flea stands atop a 30-storey building and jumps off. It survives the jump. Now Dr Baigent tries it and <u>dies</u>. What is the difference?

Possibilities:
(1) Human is heavier → DISCOUNTED BY GALILEO
(2) Exoskeleton of flea protects it → YEAH BUT TINY
(3) Flea's legs are better designed to absorb impact → YEAH BUT TINY
(4) Air friction → MAIN REASON *.
(5) Some other sensible reason



Terminal velocity V
Tall building ⇒ V is reached.

$$F = ma$$
$$= mg - \text{drag}$$
$$= 0 \text{ at terminal velocity.}$$

How to model drag? Assume it is proportional to surface area S of the body.

How does drag vary with speed?

Measure so:

In time t, slab moves $h = vt$.
⇒ mass displaced in time t $\propto$ volume $= hS = vtS$.

$$
\begin{aligned}
\text{Force} \times \text{time} &= \text{change in momentum} \\
Ft &= mv \\
&= (\text{density} \times \text{volume}) \cdot v \\
&= \rho (S \times h) v \\
&= \rho (S \times vt) v \\
F\cancel{t} &= \rho S v^2 \cancel{t}
\end{aligned}
$$

$$\Rightarrow \boxed{\text{drag} \propto v^2 S}$$

So, drag $\propto Sv^2$

At terminal velocity, weight = drag

$$mg \propto SV^2$$

$$\Rightarrow V \propto \sqrt{\frac{mg}{S}} \propto \sqrt{\frac{m}{S}}$$

Let's compare this for flea and Dr Baigent.

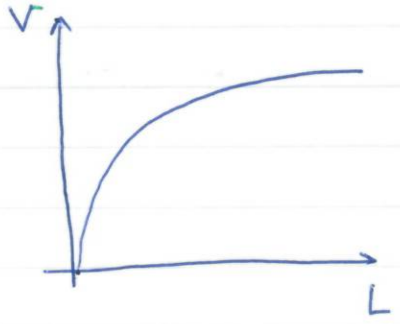
Flea: $\approx$ 3mm long

Dr B: $\approx$ 2000m long (yeah, right)

For simplicity, suppose that mass $\propto$ a linear length scale L^3

SA $\propto L^2$

$$\Rightarrow \frac{m}{S} \propto \overset{L^3/L^2}{L} \Rightarrow \underset{\sim\sim\sim}{V \propto \sqrt{L}}$$



For flea/Dr B,

$$\frac{L_{\text{flea}}}{L_{\text{DrB}}} = \frac{3}{2000} \approx 0.0015$$

$$\frac{V_{\text{flea}}}{V_{\text{DrB}}} = \sqrt{\frac{3}{2000}} \approx 0.04$$

For Dr B, $V_{DrB} \approx 100\text{mph}$
$\Rightarrow V_{flea} \approx 4\text{mph}$

Coupling this with the exoskeleton and the shock absorbers in the legs, flea will survive!!

We will be considering organisms in the same isometric class (i.e. they are of similar shape), and we'll use a linear scale L to distinguish those amongst the class.

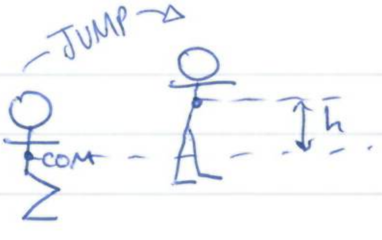
Typically, height $\propto L$
volume (mass) $\propto L^3$
area (of lungs, e.g.) $\propto L^2$

Let M be mass
ℓ length
T time.

Basic physics: 1. $F = MA$, dimensions $M \ell T^{-2}$
2. WORK DONE $= F \times d$ $\quad M \ell^2 T^{-2}$
3. POWER $= {}^{W.D.}/_{T}$ $\quad M \ell^2 T^{-3}$
4. FLUX $=$ amount/area time $\quad M \ell^{-2} T^{-1}$ (mass flux)

Example 2

Considering any isometric class, e.g. humans.
How does height affect how high we can jump from rest?



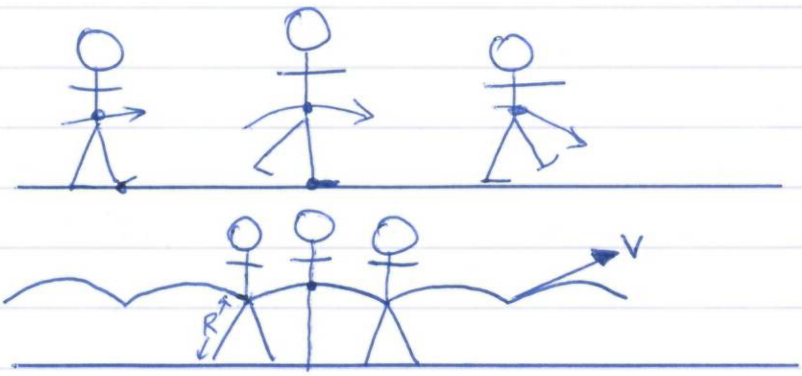
PE gained = Mgh
= Work done by muscles
= Force × distance
$\propto \underset{\uparrow \text{ explained later}}{L^2} \times L$
$= L^3$

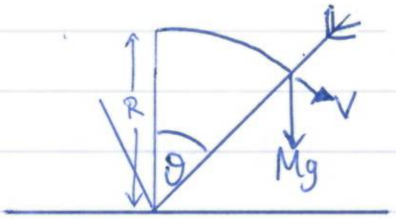
$\Rightarrow Mgh \propto L^3$
But $M \propto L^3$ $\Rightarrow$ $h \propto \frac{L^3}{L^3} = L^0 = 1$

i.e. max height someone can jump is independent of their size.

Example 3

How fast can we walk before breaking into a run?





$a = \frac{V^2}{R}$

If foot leaves the ground,
$\frac{MV^2}{R} = Mg\cos\theta$
$V^2 = Rg\cos\theta$

Must have $V^2 < Rg\cos\theta \quad \forall\theta$

$\Rightarrow$ need $V^2 < Rg$

$\Rightarrow \underset{\sim\sim\sim}{V \propto \sqrt{L}}$

Models which involve metabolic rate

Metabolism is the set of chemical reactions in the organism which provide the energy for life. These reactions occur in the mitochondria and are limited by the rate at which O_2 can be supplied.

A simple isometric scaling argument tells us how metabolic rate varies with length scale.

B = Metabolic rate $\propto$ SA of lungs $\propto L^2$

Mass $\propto L^3$

$\Rightarrow B \propto M^{2/3}$

Example 4

How long can a diving animal dive on one lung of air?

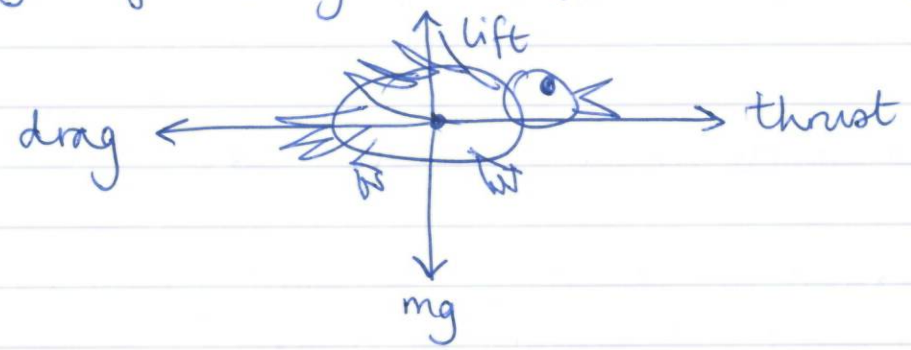
Volume of air in lung $\propto L^3$

Metabolic rate $\propto L^2$

$\Rightarrow T_{dive}$ scales as $\frac{L^3}{L^2} = L \Rightarrow \underset{\sim\sim\sim}{T_{dive} \propto L}$

Example 5

Why might larger birds find it harder to fly

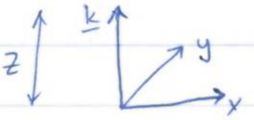


1. Metabolic rate B = rate at which energy is available
2. Drag $\propto L^2 V^2$ (surface area × speed^2)
3. Max lift during gliding and flapping (not obvious) $\propto V^2 A_w$ (wing area) $\propto L^2 V^2$

Rough argument for lift $\propto V^2$:

Bernoulli's law : $P + \frac{1}{2}\rho v^2 + g\rho \overset{\text{fluid height}}{z} = \text{const}.$

We have F = MA



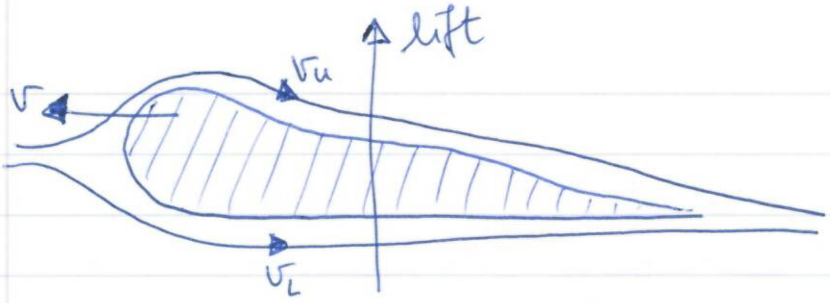
$$\rho \frac{D\underline{v}}{Dt} = -\rho g \underline{\hat{k}} - DP$$

$$\underline{v} \cdot \rho \frac{D\underline{v}}{Dt} = -\rho g \underline{v} \cdot \underline{\hat{k}} - \underline{v} \cdot \nabla P$$

$$\frac{1}{2} \rho \frac{D}{Dt} |\underline{v}|^2 = -\rho g \frac{Dz}{Dt} - \frac{DP}{Dt}$$

$$\Rightarrow \frac{D}{Dt}\left[\frac{\rho}{2} |\underline{v}|^2 + g\rho z + P \right] = 0$$

$$\Rightarrow \frac{1}{2} \rho |\underline{v}|^2 + g\rho z + P = \text{const. along streamline}$$



$v_u > v_L$

lift on a wing generated by a pressure difference across wing surfaces: by Bernoulli, this is $\propto V^2$.

Required power for flight

$$= \frac{\text{work done}}{\text{time}} = \frac{\text{force} \times \text{distance}}{\text{time}} = \text{drag} \times V$$

$$\propto L^2 V^2 \times V = L^2 V^3$$

Metabolic power $\propto L^2$

But max lift must overcome gravity

$$A_w V^2 \propto Mg \propto L^3$$

$$\Rightarrow V^2 \propto L \Rightarrow V \propto \sqrt{L}$$

So required power $\propto L^2 L^{9/2} = L^{7/2}$

Rate of available energy $\propto L^2$

$\Rightarrow$ for large enough L, power required for flight > power available

But $B = M^{2/3}$ is not observed in nature!!

In fact $B \propto M^{3/4}$ over a huge range of scales!

Example 6

How does heart beat scale with mass?

Metabolic rate $B \propto M^{3/4}$
Blood volume pumped by heart in a beat $\propto M$
Rate pumped $\propto RM$ (R = heartbeat rate)

$$\rightarrow RM \propto M^{3/4} \Rightarrow R \propto M^{-1/4}$$

Masked Shrew : 0.003 kg has $R \approx 600$
Elephant : 4000 kg has $R \approx 30$

Example 7

Fur thickness: How does thickness of fur of an animal in a cold climate vary with size?

Assume warm-blooded animal ⇒ keeps body temp. constant. Heat generated by metabolism is lost through animal's surface to the cold environment, through a temperature gradient which is proportional to $1/d$, d fur thickness.

Heat flux = heat energy/area/time.
$$= \frac{k\,\Delta T}{d} \quad (k = \text{thermal conductivity of fur})$$

metabolic rate $\propto$ heat flux × body surface area

$$M^{3/4} \propto \frac{1}{d} \times L^2 = \frac{1}{d}\, M^{2/3}$$

$$\Rightarrow \quad d \propto \frac{M^{2/3}}{M^{3/4}} = M^{-1/12}$$

$\Rightarrow$ fur thickness scales as $M^{-1/12}$.

Example 8

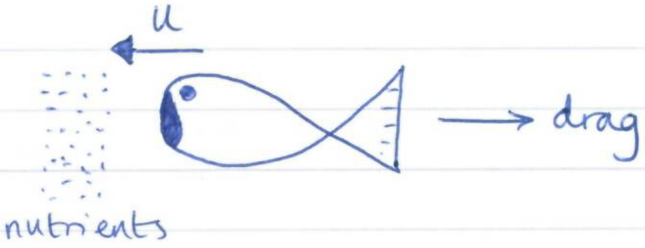
Say we were now all locked in room 707. Assuming that we don't cannabalise Annoying Question Guy, how long will we last?

Energy reserves $\propto M$
Rate at which used $\propto M^{3/4}$

$\Rightarrow$ Time taken to exhaust reserves $\propto \frac{M}{M^{3/4}} = M^{1/4}$.

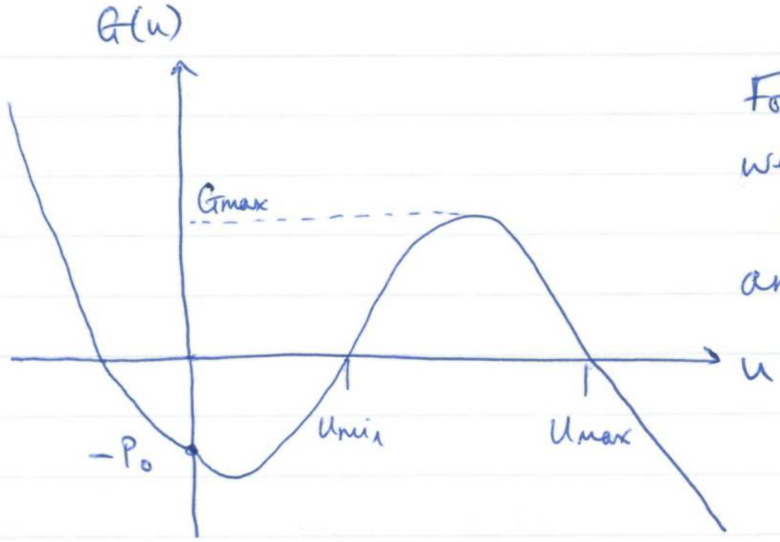
Example 9

Filler feeder:



Energy (nutrients) input rate $= F_0 u$ $\quad (F_0 \sim \text{const})$
Basal metabolic rate $= P_0$
Power = rate of doing work against drag $= \underbrace{P_1 u^2}_{\text{drag force}} \times u = P_1 u^3$

Look at power balance.
Consider $G(u) = F_0 u - P_0 - P_1 u^3$



For viable filter feeder, we need $G_{max} > 0$ (so net energy input) and swims in the range $U_{min} \leq U \leq U_{max}$.

$$G(u) = F_0 u - P_0 - P_1 u^3$$
$$G'(u) = F_0 - 3P_1 u^2 \quad \Rightarrow \quad G'(u) = 0 \text{ when } u = u^* = \sqrt{\frac{F_0}{3P_1}}$$

Need $G(u^*) \geqslant 0$

$$\Rightarrow \quad F_0\sqrt{\frac{F_0}{3P_1}} - P_0 - P_1\left(\frac{F_0}{3P_1}\right)^{3/2} \geqslant 0$$

$$\Rightarrow \quad P_0 \geqslant F_0\left(\frac{F_0}{3P_1}\right)^{1/2}\left(1 - \frac{1}{3P_1}\right)$$

Ludwig Von Bertalangfy's Growth Model (1957)

Ludwig developed a very simple model for the growth of an organism.

He assumed: All available energy is channelled into:
1. growth of organism
2. maintaining existing cells, removing waste products etc.

We have: incoming power
= power for maintaining existing cells
+ power required to generate new cells.

$$\Rightarrow \text{metabolic rate} = \begin{pmatrix}\text{power to maintain}\\ \text{one cell}\end{pmatrix} \times \begin{pmatrix}\text{n}^{\circ}\text{ of}\\ \text{cells}\end{pmatrix}$$

$$+ \begin{pmatrix}\text{energy req}^{d}\text{ to}\\ \text{generate 1 new cell}\end{pmatrix} \times \begin{pmatrix}\text{rate at which}\\ \text{cells are generated}\end{pmatrix}$$

$$\boxed{B = \underset{\substack{\uparrow \\ \text{power to maintain} \\ \text{one cell}}}{B_c} N_c(t) + E_c \frac{d}{dt} N_c(t)}$$

assuming B_c, E_c, same $\forall$ cells.

Let m_c = mass of one cell $\Rightarrow$ $m(t)$ = mass of all cells at time t
= mass of organism
= $m_c N_c(t)$.

$$\Rightarrow m_c B = B_c m(t) + E_c \frac{dm(t)}{dt} \qquad (\times m_c)$$

Take $B = B_0 m^{2/3}$

$$m_c B_0 m(t)^{2/3} = B_c m(t) + E_c \frac{dm(t)}{dt}$$

Say $\frac{dm}{dt} = \alpha m^{2/3} - \beta m$ $m(0) = m_0$ (small)

$\alpha = m_c B_0 / E_c$

$\beta = B_c / E_c$

$\downarrow$

Solve this by substitution.

Sub $u = m^{1/3} \Rightarrow \frac{du}{dt} = \frac{1}{3} m^{-2/3} \frac{dm}{dt}$

$$\Rightarrow \frac{du}{dt} = \frac{1}{3} m^{-2/3} \left(\alpha m^{2/3} - \beta m \right)$$

$$= \frac{1}{3} \left(\alpha - \beta m^{1/3} \right)$$

$$= \frac{1}{3} \left(\alpha - \beta u \right)$$

$u(t) = \frac{\alpha}{\beta} + A e^{-\beta t/3}$ $A \sim$ const.

Know $u(0) = m(0)^{1/3} = m_0^{1/3}$

$$m_0^{1/3} = \frac{\alpha}{\beta} + A \Rightarrow A = m_0^{1/3} - \frac{\alpha}{\beta}$$

$$\Rightarrow u(t) = \frac{\alpha}{\beta} + \left(m_0^{1/3} - \frac{\alpha}{\beta} \right) e^{-\beta t/3}$$

$$\Rightarrow m(t) = \left[\frac{\alpha}{\beta} + \left(m_0^{1/3} - \frac{\alpha}{\beta} \right) e^{-\beta t/3} \right]^3$$

Egg shells

Case study: incubating eggs

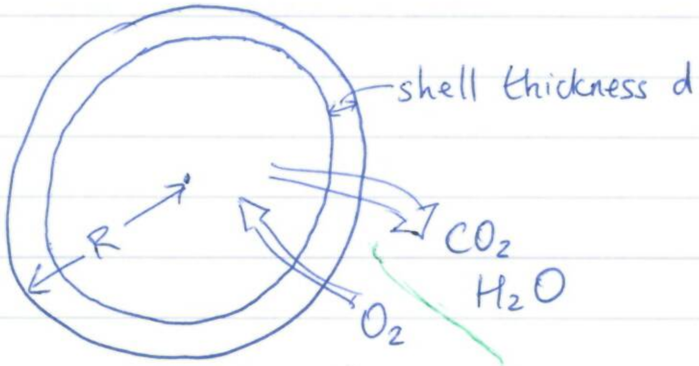
Facts:
- An egg is a self-contained unit. The embryo has all nutrients inside shell, but O_2 is needed from outside. It diffuses through the shell through small pores.
- Waste products, e.g. water, CO_2, diffuses out of egg into outside environment.

Egg shell
- Egg shell must be strong enough to support roosting bird and to protect from outside disturbances.

- Shell is mainly calcium carbonate, with small pores for diffusion in/out of gases, water.

- Shell must be weak enough for chick to hatch out.

Consider a spherical egg:



Questions:
1. How long does the egg incubate?
2. How does the shell thickness vary?

} scale with egg mass

Assumptions:
1. Assume that water loss (and subsequent dehydration) is the limiting effect, water loss is slow compared to O_2, CO_2 flux.

2. Rate of production of water is proportional to metabolic rate.

3. Would expect shell thickness to increase with mass.

4. Total water loss $\propto$ egg mass.

5. Water is lost via pores in the shell.
Length of pores $= d =$ shell thickness.
Assume total area of pores is A_{pores}.

Let $T_{inc} =$ incubation period. (in days)

$$\text{Total water loss over } T_{inc} = \text{daily water loss} \times T_{inc}$$

$$\Rightarrow T_{inc} = \frac{\text{total water loss}}{\text{daily water loss}} \propto \frac{M_{egg}}{\text{daily water loss}}$$

$$\text{Daily water loss} \propto \text{metabolic rate} \propto (M_{egg})^{3/4}$$

$$\Rightarrow T_{inc} \propto (M_{egg})^{1/4}$$

Now for shell thickness d,

$$\text{water flux} = (\text{pore area}) \times \frac{\overbrace{\text{concentration gradient}}^{\text{we prove this later.}}}{\text{pore length}}$$

$$\propto \frac{\text{density of pores} \times \text{area}}{\text{shell thickness}} \times \Delta C$$

$$\text{Total water flux} \propto M_{egg}^{3/4}$$

$$\propto \frac{\text{density of pores} \times R^2}{d}$$

$$= \frac{\text{density of pores} \times M_{egg}^{2/3}}{d}$$

$$\Rightarrow \frac{\text{density of pores}}{d} \propto M_{egg}^{3/4-2/3} = M_{egg}^{1/12}$$

So if pore density is a constant (indpt of R, mass)

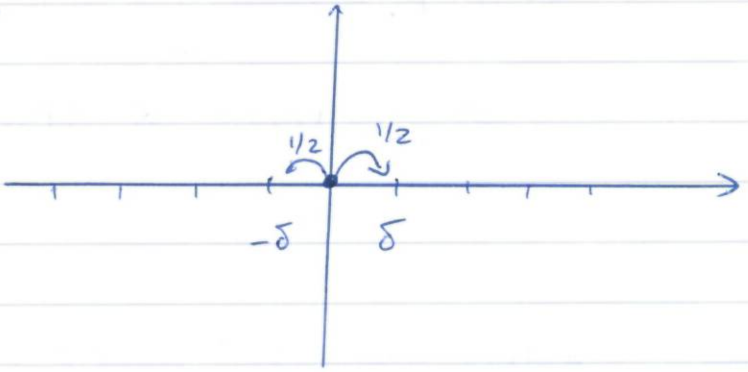
$\Rightarrow$ thickness $\propto (M_{egg})^{-1/12}$ $\leftarrow$ <u>NOT REASONABLE</u>.
thickness decreases
as mass increases ?!?!

Hence we might expect pore density is egg mass dependent.
Experimentally found, pore density scales as $M_{egg}^{4/3}$
and $d \propto M_{egg}^{1/2}$

2. OXYGEN TRANSPORT

Diffusion in one dimension

Consider a particle on $\mathbb{R}$ that at each time step goes δ left or δ right with equal probability $\frac{1}{2}$.



Random variable x_i = distance moved at i^{th} step.
$x_i \in \{-\delta, \delta\}$.

Let $S_n = \sum_{i=1}^{n} x_i$ = random variable for distance moved in n steps.

Let $P(x=\delta) = \frac{1}{2}$ = prob. δ to right
$P(x=-\delta) = \frac{1}{2}$ = prob. δ to left.

$$E(x_i) = P(x=\delta)\cdot(\delta) + P(x=-\delta)\cdot(-\delta)$$
$$= \tfrac{1}{2}\delta + (-\tfrac{1}{2})\delta$$
$$= 0$$

↑ expectation

$$E(S_n) = \sum_{i=1}^{n} E(x_i) = \sum_{i=1}^{n} 0 = 0.$$

- Variance $= E\big[(S_n - \underbrace{E(S_n)}_{=0})^2\big] = E(S_n^2)$

$$= E\Big[\big(\sum_{i=1}^{n} x_i\big)^2\Big]$$
$$= E\Big[\sum_{i=1}^{n} x_i^2 + 2\underbrace{\sum_{i<j} x_i x_j}_{\text{gonna show this} = 0}\Big]$$

$i \neq j$:
$$E(x_i x_j) = P(x=-\delta)P(x=-\delta)\cdot(-\delta)^2 + P(x=-\delta)P(x=\delta)(-\delta)(\delta) + P(x=\delta)P(x=-\delta)(\delta)(-\delta) + P(x=\delta)P(x=\delta)(\delta)^2 = 0$$

$$E(x_i^2) = \frac{1}{2}\delta^2 + \frac{1}{2}\delta^2 = \underbrace{\delta^2}_{\downarrow}$$

$$\Rightarrow \text{variance} = E\left[\sum_{i=1}^{n} x_i^2\right] = n\delta^2$$

For large n, $$\underset{\substack{\uparrow \\ \text{prob. density f}^{\text{n}}}}{f_n(x)} \approx \frac{1}{\delta\sqrt{2\pi n}} \cdot e^{\frac{-x^2}{2n\delta^2}}$$

Let τ = time between steps.
Then t = time elapsed = $n\tau$.

Let $D = \frac{\delta^2}{2\tau}$. Take limit as $\delta \to 0$, $\tau \to 0$
such that D remains constant.

$$\Rightarrow f(x,t) = \boxed{\frac{1}{\sqrt{4\pi Dt}} \exp\left(\frac{-x^2}{4Dt}\right)}$$

= Probability density f^n for particle position after time t.

Now we'll find the PDE that $f(x,t)$ satisfies.

$$\frac{\partial f}{\partial t} = \underset{\text{(product rule)}}{\frac{1}{\sqrt{4\pi D}}\left(-\frac{1}{2}\right)t^{-3/2} \cdot \exp\left(\frac{-x^2}{4Dt}\right) + \frac{1}{\sqrt{4\pi Dt}}\exp\left(\frac{-x^2}{4Dt}\right)\left(\frac{x^2}{4Dt^2}\right)}$$

$$= \underline{-\frac{1}{2t}f(x,t) + f(x,t)\frac{x^2}{4Dt^2}} \quad \text{(simplifying)}$$

$$\frac{\partial f}{\partial x} = \frac{1}{\sqrt{4\pi Dt}}\exp\left(\frac{-x^2}{4Dt}\right) \cdot \left(\frac{-x}{2Dt}\right) = \underline{f(x,t)\left(\frac{-x}{2Dt}\right)}$$

$$\frac{\partial^2 f}{\partial x^2} = -\frac{1}{2Dt} \cdot f(x,t) - \frac{x}{2Dt} \cdot \frac{\partial f}{\partial x} \quad \text{(product rule)}$$

$$= \underline{-\frac{1}{2Dt}f(x,t) + \left(\frac{x}{2Dt}\right)^2 f(x,t)}$$

$$\Rightarrow \frac{\partial f}{\partial t} - D\frac{\partial^2 f}{\partial x^2} = f(x,t)\left[-\cancel{\frac{1}{2t}} + \frac{x^2}{4Dt^2} + \cancel{\frac{1}{2t}} - D\left(\frac{x}{2Dt}\right)^2\right]$$

$$= 0.$$

Hence, $f(x,t)$ satisfies the diffusion equation

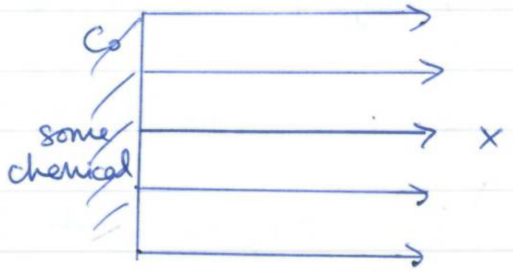
$$\frac{\partial f}{\partial t} = D\frac{\partial^2 f}{\partial x^2}$$

or

$$\underbrace{\frac{\partial f}{\partial t} = -\frac{\partial J}{\partial x}}$$

where $J = -D\frac{\partial f}{\partial x}$ = flux.

Time taken to reach 99% ___ equilibrium as a f^n of distance from a plane (Jacobs 1935)



Want t s.t.
$C(t,d) = 0.99 \times C_\infty(d)$.

distance from boundary	time taken
10 cm	50 days
1 cm	12.7 hours
1 mm	7.6 minutes
100 μm	4.50 seconds
10 μm	0.05 sec
1 μm	0.0005 sec
0.1 μm	0.000005 sec

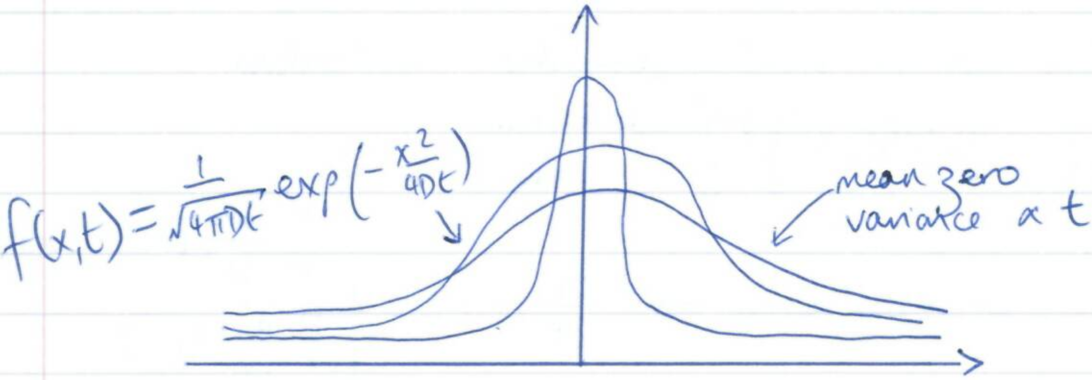
$$C(x,t) = \frac{1}{\sqrt{4\pi Dt}} \exp\left(\frac{-x^2}{4Dt}\right) \qquad \text{concentration at } (x,t)$$

Let us suppose at $t=0$, the concentration of $\overbrace{(-\infty,\infty)}^{\text{the real line}}$ is $C(x,0)$, then at time t,

$$C(x,t) = \int_{-\infty}^{\infty} C(y,0) \cdot \frac{1}{\sqrt{4\pi Dt}} \exp\left[\frac{-(x-y)^2}{4Dt}\right] dy \qquad \text{by convolution}$$

For example, if $C(y,0) = \delta_{y0}$ (Kronecker delta)

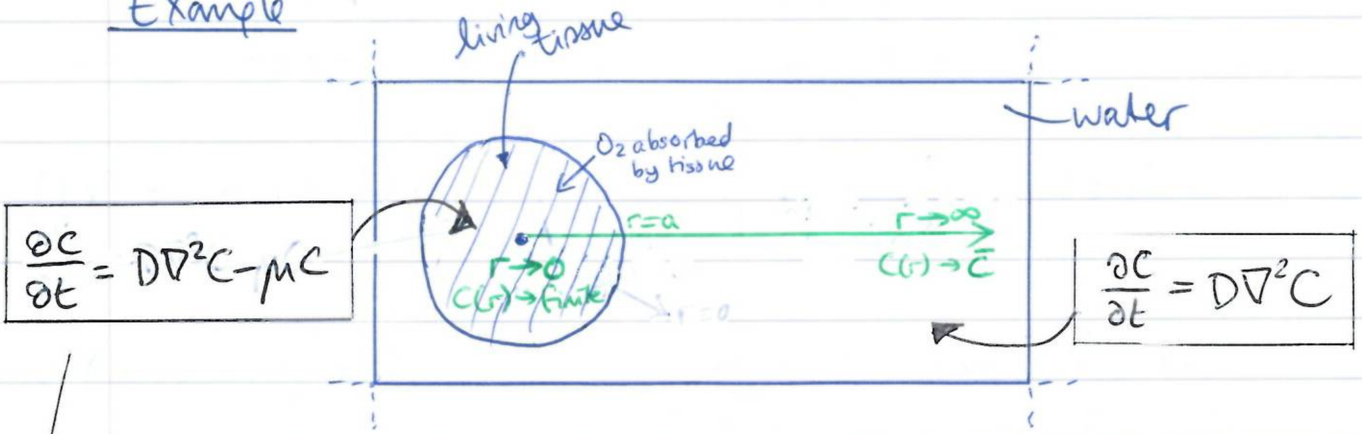
$$C(x,t) = \frac{1}{\sqrt{4\pi Dt}} \exp\left(\frac{-x^2}{4Dt}\right)$$



In higher dimensions, $C(\underline{x},t)$ $\underline{x} \in \mathbb{R}^3$, say

$$\frac{\partial C(\underline{x},t)}{\partial t} = D\nabla^2 C(\underline{x},t)$$
$$= -\operatorname{div}(J) \quad \text{where } J = -D\nabla C$$

Example



Tissue is a sphere of radius a. Let centre of the tissue be $r=0$, and $r=a$ is the surface of the sphere, and the rest of the system is water.
Assume $C(\infty) = \bar{C}$ fixed concentration of O_2 at $r=\infty$.

O_2 diffuses in tissue and water with same diffusion constant (for simplicity), and in tissue O_2 is absorbed at a rate μ.

FIND C.

Solve for $C(r,\infty)$ = steady concentration.

$$\frac{\partial C}{\partial t} = D\nabla^2 C - \begin{cases} \mu C & \text{TISSUE} \\ 0 & \text{WATER} \end{cases}$$

Spherical symmetry $\Rightarrow$ $$\frac{\partial C}{\partial t}(r,t) = \begin{cases} \frac{D}{r}\frac{\partial^2}{\partial r^2}(rC) - \mu C & \text{TISSUE} \\ \frac{D}{r}\frac{\partial^2}{\partial r^2}(rC) & \text{WATER} \end{cases}$$

$$\Rightarrow \nabla^2 C = \frac{1}{r}\frac{\partial^2}{\partial r^2}(rC)$$

At equilibrium, $\frac{\partial C}{\partial t} = 0 \Rightarrow \frac{D}{r}\frac{d^2}{dr^2}(rC) = \mu C$ TISSUE

$\frac{D}{r}\frac{d^2}{dr^2}(rC) = 0$ WATER

In TISSUE, $\frac{d^2(rC)}{dr^2} = \frac{\mu}{D}(rC)$ (rearranged)

Let $\nu^2 = \frac{\mu}{D} \Rightarrow \frac{d^2}{dr^2}(rC) = \nu^2(rC)$

$\Rightarrow rC = Ae^{\nu r} + Be^{-\nu r}$ (A-level)

$\Rightarrow C(r) = \frac{A' \sinh(\nu r)}{r} + \frac{B' \cosh(\nu r)}{r}$ TISSUE (alternative representation with new constants)

For C finite at $r=0$ we must have $B' = 0$

$$\Rightarrow \underline{C(r) = \frac{A' \sinh(\nu r)}{r}}$$ TISSUE

In WATER $\Rightarrow rC = \alpha + \beta r$

$\Rightarrow C = \beta + \frac{\alpha}{r}$ WATER

As $r \to \infty$, $C \to \bar{C} \Rightarrow \beta = \bar{C}$

$$\Rightarrow \underline{C(r) = \bar{C} + \frac{\alpha}{r}}$$ WATER

Now, see what happens at the BOUNDARY

1. Concentration is continuous at $r=a$
2. flux is continuous across $r=a$.

Using continuity of C at $r=a$,

$$C(a) = \underbrace{\bar{C} + \frac{\alpha}{a}}_{\text{water}} = \underbrace{\frac{A' \sinh(\nu a)}{a}}_{\text{tissue}} \quad \ldots\ldots (1)$$

Using continuity of flux at r=a :   flux $= -D\frac{\partial c}{\partial r}$

$$\cancel{+}\cancel{D}\left(-\frac{\alpha}{a^2}\right) = \cancel{+}\cancel{D}A'\left(-\frac{\sinh(\nu a)}{a^2} + \frac{\nu\cosh\nu a}{\cancel{a}}\right) \cdots (2a)$$

$$\left(-\frac{\alpha}{a}\right) = A'\left(-\frac{\sinh(\nu a)}{a} + \nu\cosh\nu a\right) \cdots\cdots (2b)$$

Add (1) + (2b)

$$\bar{c} + \frac{\alpha}{a} + \left(-\frac{\alpha}{a}\right) = A'\frac{\sinh\nu a}{a} + \left(-\frac{A'\sinh\nu a}{a} + A'\nu\cosh\nu a\right)$$

$$\Rightarrow A' = \frac{\bar{c}}{\nu\cosh\nu a}$$

$$\Rightarrow \frac{\alpha}{a} = \frac{1}{a}\sinh(\nu a)\frac{\bar{c}}{\nu\cosh\nu a} - \bar{c}$$

$$\alpha = \bar{c}\left(\frac{1}{\nu}\tanh(\nu a) - a\right)$$

$$c(r) = \begin{cases} \dfrac{\bar{c}}{\nu\cosh(\nu a)}\left(\dfrac{\sinh\nu r}{r}\right) & r \leq a \\ \bar{c}\left(1-\dfrac{a}{r}\right) + \dfrac{\bar{c}\tanh(\nu a)}{\nu r} & r > a \end{cases}$$

note $\Rightarrow$ $c(0) = \bar{c}\,\frac{\nu\cosh(\nu 0)}{\nu\cosh(\nu a)} = \frac{\bar{c}}{\cosh(\nu a)}$ (as an aside.)

a mean drift

Diffusion with drift

In the Brownian motion model we add a bias, so there's a drift u:

$$X_i \in \{-\delta + u\tau,\ \delta + u\tau\}$$

using same notation as before

$$f_n(x) \approx \frac{1}{\delta\sqrt{2\pi n}} \exp\left[\frac{-(x-nu\tau)^2}{2n\delta^2}\right]$$

$$\Rightarrow f(x,t) = \frac{1}{\sqrt{4\pi Dt}} \exp\left[\frac{-(x-ut)^2}{4Dt}\right]$$

Derive PDE for $f(x,t)$? Let $X = x - ut$ (change of vars) so that

$$f(x,t) = F(X,t) = \frac{1}{\sqrt{4\pi Dt}} \exp\left(\frac{-X^2}{4Dt}\right)$$

$$\Rightarrow \frac{\partial F}{\partial t} = D \cdot \frac{\partial^2 F}{\partial X^2} \Rightarrow$$

so now work out how $\frac{\partial F}{\partial X}$ relates to $\frac{\partial f}{\partial x}$ etc...

$$X = x - ut$$

$$\frac{\partial f}{\partial t} = \frac{\partial F}{\partial t} + \frac{\partial F}{\partial X}\frac{\partial X}{\partial t} = \frac{\partial F}{\partial t} + \frac{\partial F}{\partial X}(-u)$$

$$\frac{\partial f}{\partial x} = \frac{\partial F}{\partial X} \cdot \frac{\partial X}{\partial x} = \frac{\partial F}{\partial X}$$

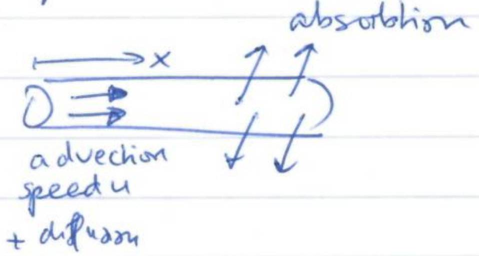
$$\Rightarrow \frac{\partial^2 f}{\partial x^2} = \frac{\partial^2 F}{\partial X^2}$$

$$\Rightarrow \frac{\partial f}{\partial t} = \underbrace{-u\frac{\partial f}{\partial x}}_{\text{ADVECTION}} + \underbrace{D\frac{\partial^2 f}{\partial x^2}}_{\text{PASSIVE DIFFUSION}}$$

advection speed u
+ diffusion

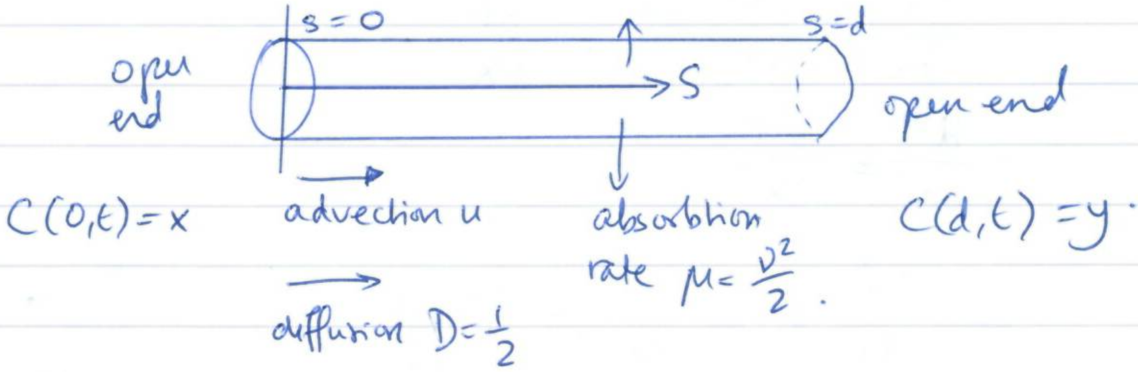
Add an extra term for absorbtion and change f to C:

$$\frac{\partial C}{\partial t} + u\frac{\partial C}{\partial x} = D\frac{\partial^2 C}{\partial x^2} - \mu C$$



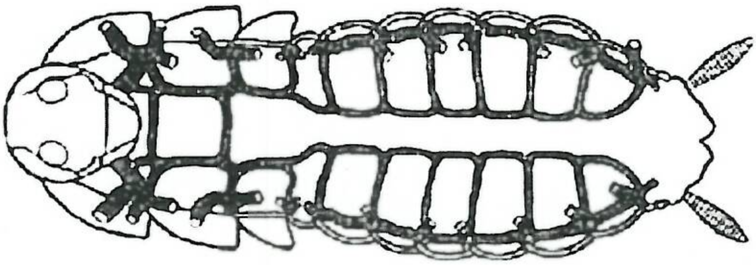
Diffusion and advection along a thin tube

Assumptions :
- Normalise eqⁿ for flow of O_2 s.t. $D = \frac{1}{2}$, $\mu = \frac{\nu^2}{2}$.
- Constant cross-section of tube
- Constant speed of advection u along tube
- Assume tube is thin relative to its length ⇒ can assume that concentration is just a fⁿ of distance S down the tube.
- Assume both ends of tube are open.

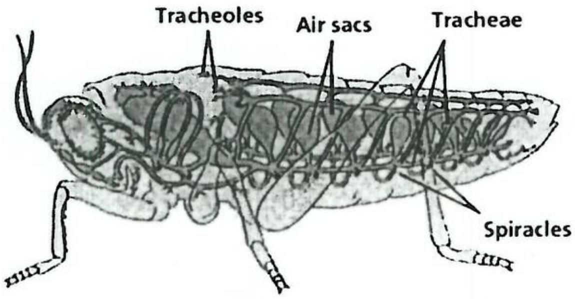


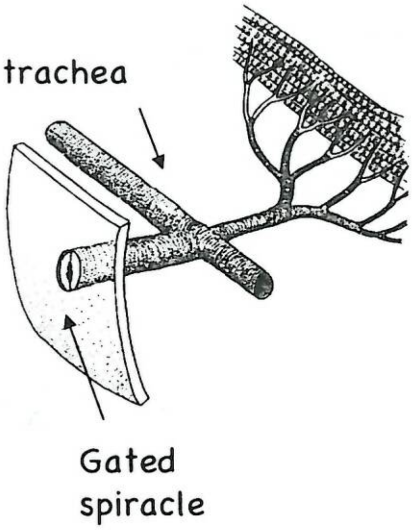
Problem: Insects have no lungs, so how do they breathe?

They have a complex network of air-filled tubes that carry oxygen around the body. Oxygen diffuses round network, sometimes assisted by advection. All cells are close to a tracheal branch and they utilise the oxygen for metabolism. So we have passive diffusion with advection in thin pipes, and with absorption.



Inside the tracheal system





Images of spiracles, muscles and trachea:

http://www.biology-resources.com/images/spiracle-big.jpg

General information on insect biology:

http://aesop.rutgers.edu/~hamilton/lecture2.htm

General figures: http://images.google.co.uk/
(and search for insect trachea)

Then $$\frac{\partial C}{\partial t} = -u\frac{\partial C}{\partial s} + \frac{1}{2}\frac{\partial^2 C}{\partial s^2} - \frac{\nu^2}{2}C$$

advection diffusion absorbtion.

b.c. $C(0,t) = x, \quad C(d,t) = y.$

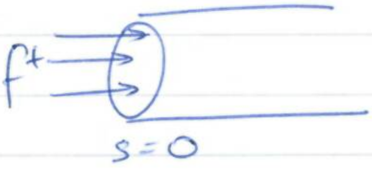
Only interested in the steady state concentration.

$$\frac{1}{2}\frac{d^2C}{ds^2} = u\frac{dC}{ds} + \frac{\nu^2}{2}C \qquad \begin{array}{l} C(0) = x \\ C(d) = y \end{array}$$

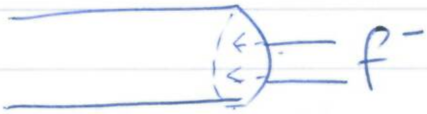
Flux at the ends $s=0$, $s=d$.

Interested in the flux densities at the ends $s=0$, $s=d$.

f^+ = flux density into pipe at $s=0$
= moles of O_2 per unit area per unit time



$$= \left(uC - \frac{1}{2}\frac{dC}{ds}\right)_{s=0}$$

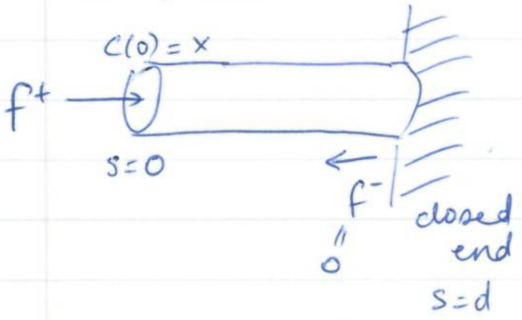


f^- = flux density into $s=d$.

$$= -\left(uC - \frac{1}{2}\frac{dC}{ds}\right)_{s=d}$$

Simple case:

$\mu = \frac{\nu^2}{2}$ $D = \frac{1}{2}$ $u = 0$ (no advection)



Closed end at $s=d$

Open end at $s=0$ where $C(0)=x$.

Solving: $\frac{1}{2}\frac{d^2C}{ds^2} - \mu C = 0$

$$\Rightarrow \frac{1}{2}\frac{d^2C}{ds^2} - \frac{\nu^2}{2}C = 0$$

$$\Rightarrow \frac{d^2C}{ds^2} = \nu^2 C$$

$$\Rightarrow C(s) = Ae^{\nu s} + Be^{-\nu s} \quad \text{(gen. sol}^{\text{n}}\text{)}$$

To find constants, $C(0) = x \Rightarrow A + B = x$.

And since $s=d$ is closed, $f^- = 0$

$\Rightarrow \frac{1}{2}\frac{dC}{ds} = 0$ at $s=d$.

Hence $C'(d) = \nu\left(Ae^{\nu d} - Be^{-\nu d}\right) = 0$

$$\Rightarrow Ae^{\nu d} = Be^{-\nu d}$$

$$\Rightarrow A = Be^{-2\nu d}$$

$\Downarrow$

And $A+B=x \Rightarrow$ $x - B = Be^{-2\nu d}$

$$\Rightarrow B = \frac{x}{1+e^{-2\nu d}} = \frac{xe^{\nu d}}{2\cosh(\nu d)}$$

$$\Rightarrow \quad A = \frac{x e^{-vd}}{2\cosh(vd)}$$

$$\Rightarrow \quad C(s) = \frac{x}{2\cosh(vd)}\left(e^{v(s-d)} + e^{v(d-s)}\right)$$

$$= \frac{x}{2\cosh(vd)}\, 2\cosh v(s-d)$$

$$= \underbrace{\frac{x \cosh v(s-d)}{\cosh(vd)}}$$

At $s=d$, $\quad C(d) = \dfrac{x}{\cosh(vd)}$

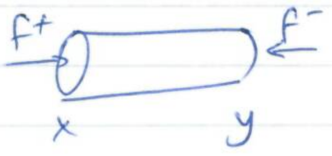
More generally, $\dfrac{\partial C}{\partial t} = \dfrac{1}{2}\dfrac{\partial^2 C}{\partial s^2} - u\dfrac{\partial C}{\partial s} - \dfrac{v^2}{2}C$

with open ends $\quad s=0 \quad C(0,t) = x$
$\quad s=d \quad C(d,t) = y.$

For steady solution, (to work out in h/w)

$$C(s) = \frac{e^{su}}{\sinh(\sigma d)}\left[x\sinh(\sigma(d-s)) + y e^{-du}\sinh(\sigma s)\right]$$

where $\sigma = \sqrt{u^2+v^2}$



$$f^+ = \left(uC - \frac{1}{2}\frac{dC}{ds}\right)_{s=0}$$

$$= \left(\tfrac{1}{2}u + \tfrac{\sigma}{2}\coth(\sigma d)\right)x - \left(\tfrac{\sigma}{2}e^{-du}\,\mathrm{cosech}(\sigma d)\right)y$$

$$= a^+ x - b^- y$$

where $\boxed{\begin{aligned} a^+ &= \frac{1}{2}u + \frac{\sigma}{2}\coth(\sigma d) \\ b^- &= \frac{\sigma}{2}e^{-du}\operatorname{cosech}(\sigma d) \end{aligned}}$

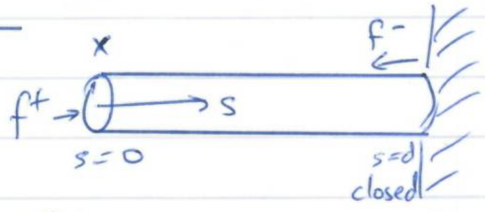
$$f^- = -\left(uC - \frac{1}{2}\frac{dC}{ds}\right)_{s=d}$$

$$= -\left(\frac{\sigma}{2}e^{du}\operatorname{cosech}(\sigma d)\right)x + \left(-\frac{u}{2} + \frac{\sigma}{2}\coth(\sigma d)\right)y$$

$$= a^- y - b^+ x$$

where $\boxed{\begin{aligned} a^- &= -\frac{1}{2}u + \frac{\sigma}{2}\coth(\sigma d) \\ b^+ &= \frac{\sigma}{2}e^{du}\operatorname{cosech}(\sigma d) \end{aligned}}$

Example



$\mu = \frac{U^2}{2}$ $u=0$ $D=\frac{1}{2}$

$C(0)=x$ $C(d)=y$

$$f^+ = a^+x - b^-y$$

$$f^- = a^-y - b^+x = 0 \text{ at closed end}$$

$$\Downarrow$$

$$\Rightarrow \quad y = \frac{b^+x}{a^-}$$

$$\Rightarrow \quad f^+ = a^+x - \frac{b^+b^-x}{a^-}$$

$$= \frac{x}{a^-}\left(a^+a^- - b^+b^-\right)$$

But since $u=0$, by def^n of a^+, $a^+ = \frac{\sigma}{2}\coth(\sigma d)$

$$\sigma^2 = u^2 + v^2 = v^2 \Rightarrow \sigma = v$$

$$= \frac{v}{2}\coth(vd)$$

Similarly, $a^- = a^+$

$$b^+ = \frac{\sigma}{2}\operatorname{cosech}(\sigma d) = \frac{v}{2}\operatorname{cosech}(vd)$$

$$b^- = b^+$$

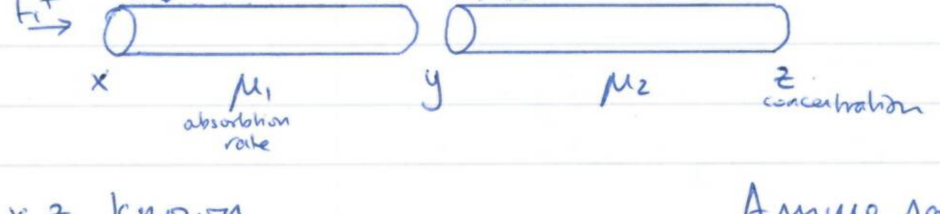
$\Rightarrow f^+ = \frac{x}{a^-}(a^+a^- - b^+b^-)$ becomes

$$f^+ = \frac{x}{\frac{v}{2}\coth(vd)}\left[\frac{v^2}{4}\coth^2(vd) - \frac{v^2}{4}\operatorname{cosech}^2(vd)\right]$$

$$= \frac{xv^2}{4}\,\frac{1}{\frac{v}{2}\coth(vd)}$$

$$= \frac{xv}{2}\tanh(vd)$$

Example: two pipes together



x, z known
y, f_1^+ etc unknown.

Assume same X-section.

$$f_1^+ = a_1^+ x - b_1^- y \qquad f_2^+ = a_2^+ y - b_2^- z$$
$$f_1^- = a_1^- y - b_1^+ x \qquad f_2^- = a_2^- z - b_2^+ y$$

Conservation of mass at join where concentration is y:

$$f_1^- + f_2^+ = 0.$$

i.e. $a_1^- y - b_1^+ x + a_2^+ y - b_2^- z = 0$

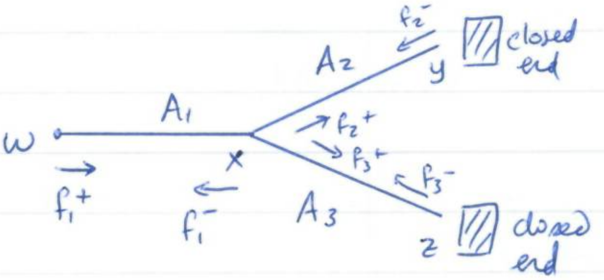
$$\Rightarrow \quad y = \frac{b_1^+ x + b_2^- z}{a_1^- + a_2^+}$$

and now $f_1^+ = a_1^+ x - b_1^- y = a_1^+ x - b_1^- \left(\frac{b_1^+ x + b_2^- z}{a_1^- + a_2^+}\right)$

$$= \left(a_1^+ - \frac{b_1^- b_1^+}{a_1^- + a_2^+}\right) x - \left(\frac{b_1^- b_2^-}{a_1^+ + a_2^+}\right) z$$

and similarly for f_2^- . . .

<u>Example</u>



A_i = X-sect. area of pipe

$$f_1^+ = a_1^+ w - b_1^- x$$
$$f_1^- = a_1^- x - b_1^+ w$$

$$f_2^+ = a_2^+ x - b_2^- y$$
$$f_2^- = a_2^- y - b_2^+ x = 0$$

$$f_3^+ = a_3^+ x - b_3^- z$$
$$f_3^- = a_3^- z - b_3^+ x = 0$$

Closed ends $\Rightarrow$ $y = \dfrac{b_2^+ x}{a_2^-}$ $\qquad z = \dfrac{b_3^+ x}{a_3^-}$.

At the join, (use A_i's since the f's are flux densities)

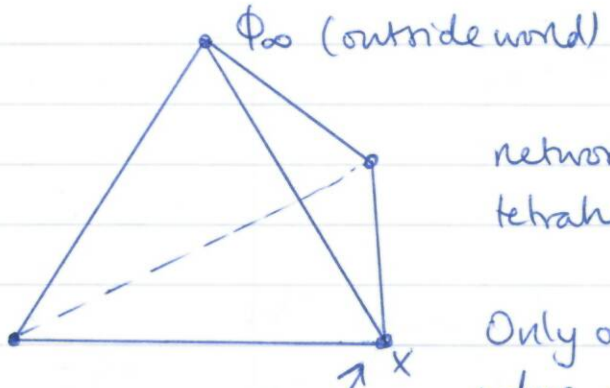
$$A_1 f_1^- + A_2 f_2^+ + A_3 f_3^+ = 0$$

i.e. $A_1(a_1^- x - b_1^+ w) + A_2(a_2^+ x - b_2^- y) + A_3(a_3^+ x - b_3^- z) = 0$

i.e. $x(A_1 a_1^- + A_2 a_2^+ + A_3 a_3^-) = A_1 b_1^+ w + A_2 b_2^- y + A_3 b_3^- z$

$$\Rightarrow x = \frac{A_1 b_1^+ w + A_2 b_2^- y + A_3 b_3^- z}{A_1 a_1^- + A_2 a_2^+ + A_3 a_3^-}.$$

Example



network of pipes making tetrahedron.

Only one pipe open at a corner where concentration is ϕ_∞.

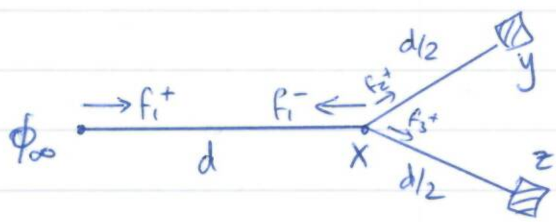
find concentration here.

Identical pipes

$u=0$ i.e. no invection

Let pipes have length d. Since no flux at midpts:

this is clever insight !!



$$f_1^+ = a_1^+ \phi_\infty - b_1^- x$$
$$f_1^- = a_1^- x - b_1^+ \phi_\infty$$

Since pipe 2 is closed,

$f_2^- = 0 \Rightarrow y = \frac{b_2^+}{a_2^-} x = z$ by symmetry.

At the join: $f_1^- + 2f_2^+ = 0$ $\quad$ $f_2^+ = f_3^+$ by symmetry.

$$f_2^+ = a_2^+ x - b_2^- y$$

$$\Rightarrow a_1^- x - b_1^+ \phi_\infty + 2(a_2^+ x - b_2^- y) = 0$$
$$a_1^- x - b_1^+ \phi_\infty + 2\left(a_2^+ x - \frac{b_2^- b_2^+ x}{a_2^-}\right) = 0$$

$$\Rightarrow x = \frac{b^+ \phi_\infty}{a_1^- + 2\left[a_2^+ - \frac{b_2^+ b_2^-}{a_2^-}\right]}$$

Using values for $a_i^\pm, b_i^\pm$, we obtain

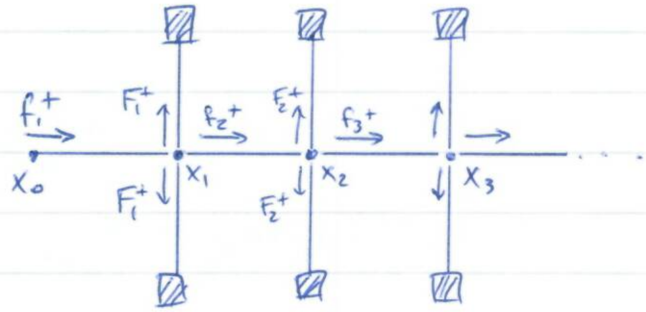
$$x = \frac{\operatorname{cosech}(\nu d)\phi_\infty}{\coth(\nu d) + 2\tanh\left(\frac{\nu d}{2}\right)}$$

This preliminary maths leads us to...

Insect respiration

- Trachae are open to the outside oxygen-rich environment, and are open or closed through action of gates called SPIRACLES.

- Small insects, no ventilation is necessary – passive diffusion suffices ($u=0$). For larger insects (e.g. grasshopper), intricate muscle contraction achieves a constant $u \neq 0$ around the tracheal network.



Semi-infinite system of pipes all closed to the outside environment, except the first node at concentration x_0.

Find f_1^+.

Since side branches are closed, then

$$F_i^+ = A x_i$$

Define $\lambda = \frac{f_1^+}{x_0}$. Then by symmetry,

$$\lambda = \frac{f_1^+}{x_0} = \frac{f_2^+}{x_1} = \frac{f_3^+}{x_2} = \dots$$

Find λ.

Conservation of flux at first node

$$2F_1^+ + f_1^- + f_2^+ = 0$$
$$2Ax_1 + (a^- x_1 - b^+ x_0) + \lambda x_1 = 0 .$$

Hence $x_1(2A + a^- + \lambda) = b^+ x_0$

$$\Rightarrow x_1 = \frac{b^+ x_0}{2A + a^- + \lambda}$$

$$f_1^+ = \lambda x_0 = a^+ x_0 - b^- x_1$$

$$\Rightarrow \lambda x_0 = a^+ x_0 - \frac{b^- b^+ x_0}{2A + a^- + \lambda}$$

$$\Rightarrow \lambda \cancel{x_0} (2A + a^- + \lambda) = a^+ \cancel{x_0} (2A + a^- + \lambda) - b^- b^+ \cancel{x_0}$$

$$\Rightarrow \underbrace{\lambda^2 + (2A + a^- - a^+)\lambda + (b^+ b^- - a^+ a^- - 2A a^+) = 0.}_{} \quad \ldots \circledast$$

$$a^+ a^- - b^+ b^- = \left(\frac{u}{2} + \frac{\sigma}{2}\coth(\sigma d)\right)\left(-\frac{u}{2} + \frac{\sigma}{2}\coth \sigma d\right) - \left(\frac{\sigma^2}{4}\right)\left(e^{du} e^{-du}\right) \operatorname{cosech}^2(\sigma d)$$

$$= -\frac{u^2}{4} + \frac{\sigma^2}{4}\coth^2(\sigma d) - \frac{\sigma^2}{4}\operatorname{cosech}^2(\sigma d)$$

$$= \frac{\sigma^2}{4}\left(\coth^2(\sigma d) - \operatorname{cosech}^2(\sigma d)\right) - \frac{u^2}{4}$$

$$= \frac{\sigma^2}{4} - \frac{u^2}{4}$$

$$= \frac{\nu^2}{4}$$

$\circledast$ becomes $\lambda^2 + (2A + a^- - a^+)\lambda - \left(\frac{\nu^2}{4} + 2a^+ A\right) = 0. \quad \ldots \text{Ⓐ}$

If Ⓐ has roots λ_1, λ_2, $(\lambda-\lambda_1)(\lambda-\lambda_2) = 0$

$$\lambda^2 - (\lambda_1 + \lambda_2)\lambda + \lambda_1\lambda_2 = 0$$

$\Rightarrow$ since $-\left(\frac{u^2}{4} + 2a^+A\right) < 0$,

then λ_1, λ_2 opposite sign.

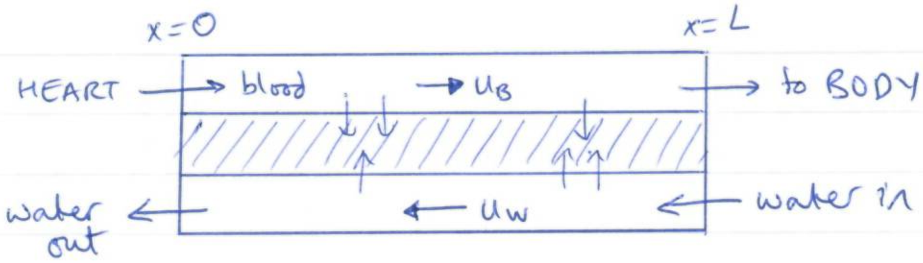
Since we need $\lambda > 0$, we choose

$$\lambda = \frac{2A + a^- - a^+}{2} + \frac{1}{2}\sqrt{(2A + a^- - a^+)^2 + u^2 + 8a^+A}$$

How do fish obtain their oxygen?

Facts:

- Whales, dolphins etc, use lungs to store O_2 but fish don't.
- Oxygen in water $\ll$ concentration of O_2 in air
  5ppm $\ll$ 210,000 ppm
- Gills are intricate system of membranes ~~separated~~ separating oxygenated water from blood; O_2 diffuses from water across membrane to blood and then transported to the cells.
- Gills have a very large surface area.
- Counter-current flow (essentially blood and oxygen pass in opposite direction on each side of gill membrane). which makes O_2 extraction more efficient.



<u>Equation</u>: $C_B(x,t)$ = concentration of O_2 in blood
$C_W(x,t)$ = ... water

$$\frac{\partial C_B}{\partial t}(x,t) + u_B \frac{\partial C_B(x,t)}{d\cancel{x}} = -D\left[C_B(x,t) - C_W(x,t)\right]$$

$$\frac{\partial C_W}{\partial t}(x,t) - u_W \frac{\partial C_W}{\partial \cancel{x}}(x,t) = D\left[C_B(x,t) - C_W(x,t)\right]$$

In steady state:
$$\left.\begin{aligned} u_B \frac{dC_B}{dx} &= -D\left(C_B - C_W\right) \\ -u_W \frac{dC_W}{dx} &= D\left(C_B - C_W\right) \end{aligned}\right\}$$

<u>Boundary conditions</u>: 1. Water-in has constant $C_W(L) = C_{W,in}$
and assume
2. Blood from heart has constant concentration
$C_B(0) = C_{B,in}$

$$u_B \frac{dC_B}{dx} - u_W \frac{dC_W}{dx} = 0$$

$$\Rightarrow \quad \Rightarrow u_B C_B(x) - u_W C_W(x) = \text{const} := \alpha.$$

Hence
$$\begin{aligned} u_B \frac{dC_B}{dx} &= -D\left(C_B - C_W\right) \\ &= -D\left[C_B - \frac{(u_B C_B - \alpha)}{u_W}\right] \\ &= \frac{-D}{u_W}\left[C_B(u_W - u_B)\right] - \frac{D\alpha}{u_W} \end{aligned}$$

Some fish actively pump water through their gills (so-called "gill irrigation")

Others (e.g. sharks) use swimming to push the water through (so-called "ram ventilation")

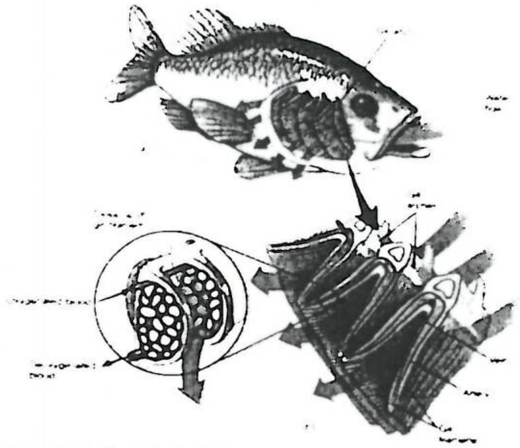
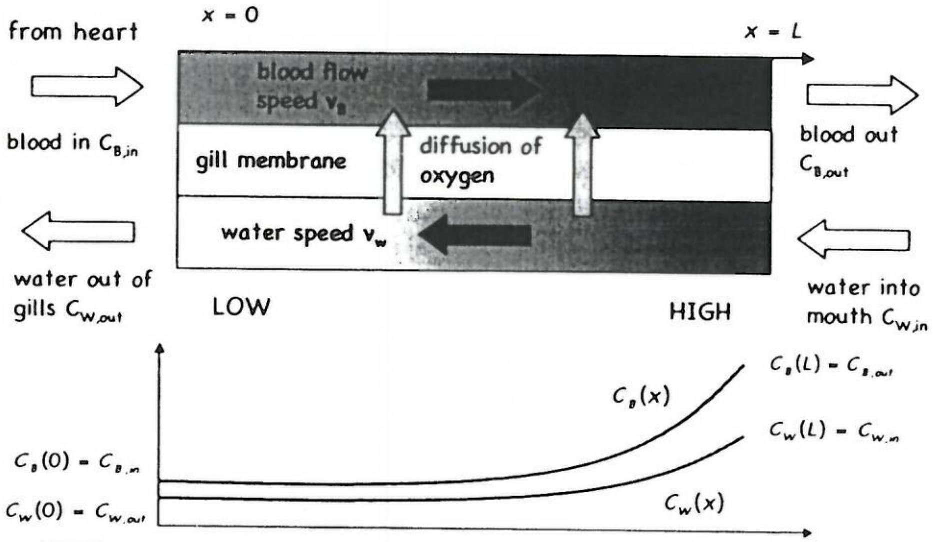


Figure 13.1 The Gills of a Fish

http://thumb11.webshots.net/s/thumb3/0/98/45/3309848NhDN_xVhZX_th.jpg

Or go to
http://images.google.co.uk/
and search for fish gills

Simple model for countercurrent diffusion across membrane



$$\frac{dC_B}{dx} = -D\left(\frac{1}{u_B} - \frac{1}{u_w}\right) C_B - \frac{D\alpha}{u_w u_B}$$

$$\theta := D\left(\frac{1}{u_w} - \frac{1}{u_B}\right), \quad \varphi := \frac{D\alpha}{u_w u_B}$$

$$\Rightarrow C_B' = \theta C_B - \varphi$$

$$\Rightarrow C_B(x) = \frac{\varphi}{\theta} + \left(C_{B\,in} - \frac{\varphi}{\theta}\right) e^{\theta x}$$

and $$C_w(x) = \frac{u_B}{u_w}\left(\frac{\varphi}{\theta} + \left(C_{B\,in} - \frac{\varphi}{\theta}\right) e^{\theta x}\right) - \frac{\alpha}{u_w}$$

We have $C_B(L) = C_{B\,out}$ = oxygen concentration fed to body

$$C_B(L) = \frac{\varphi}{\theta} + \left(C_{B\,in} - \frac{\varphi}{\theta}\right) e^{\theta L}$$

$$= \frac{u_B C_{B\,out} - u_w C_{w\,in}}{u_B - u_w} + \left[C_{B\,in} - \left(\frac{u_B C_{B\,out} - u_w C_{w\,in}}{u_B - u_w}\right)\right] e^{\theta L}$$

$$C_{B\,out} = C_{W\,in} + \frac{(C_{w\,in} - C_{B\,in})(u_B - u_w)}{u_w e^{DL\left(\frac{1}{u_B} - \frac{1}{u_w}\right)} - u_B}$$

Hence, $$\frac{C_{B\,out}}{C_{B\,in}} = \frac{C_{w\,in}}{C_{B\,in}} + \frac{\left(\frac{C_{w\,in}}{C_{B\,in}} - 1\right)(u_B - u_w)}{u_w e^{DL\left(\frac{1}{u_B} - \frac{1}{u_w}\right)} - u_B}$$

Compare with the case where blood and water flow in same direction: replace u_B by $-u_B$
and interchange $C_{B\,in}$ and $C_{B\,out}$

For this arrangement,

$$\frac{C_{B\,out}}{C_{B\,in}} = \frac{u_B + \left(\frac{C_{w\,in}}{C_{B\,in}}\right) u_w + u_w\left(1 - \frac{C_{w\,in}}{C_{B\,in}}\right) e^{-DL\left(\frac{1}{u_w} - \frac{1}{u_B}\right)}}{u_w + u_B}$$

Take $L \to \infty$ to simplify:

1. If $u_w > u_B$ $\quad \frac{C_{B\,out}}{C_{B\,in}} \to \frac{C_{w\,in}}{C_{w\,out}}$ [counter current].

2. If $u_w < u_B$ $\quad \frac{C_{B\,out}}{C_{B\,in}} \to \frac{C_{w\,in}}{C_{B\,in}} + \left(1 - \frac{C_{w\,in}}{C_{B\,in}}\right)\left(1 - \frac{u_w}{u_B}\right)$

[same direction]

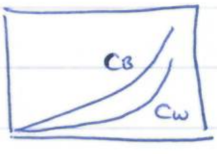
For the 2nd arrangement where blood, water flow in same direction,

$$\frac{C_{B\,out}}{C_{B\,in}} = \frac{u_B + \left(\frac{C_{w\,in}}{C_{B\,in}}\right) u_w}{u_B + u_w}$$

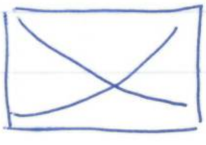
$\Rightarrow$ Let $\Delta = \frac{C_{B\,out}}{C_{B\,in}}$ (counter current) $-$ $\frac{C_{B\,out}}{C_{B\,in}}$ (same dir^n)

$$\Delta = \begin{cases} \dfrac{u_B(\delta - 1)}{u_B + u_w} \\ \quad\shortparallel \\ \dfrac{u_B^2(\delta - 1)}{u_B(u_B + u_w)} \end{cases} > 0 \text{ if } \delta > 1$$

where $\delta = \frac{C_{w\,in}}{C_{B\,in}}$

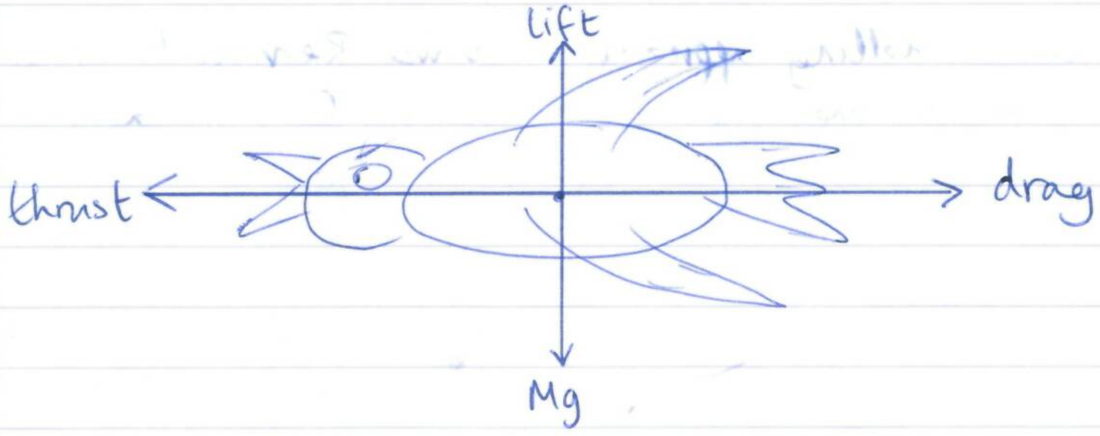


$C(x)$ countercurrent



$C(x)$ same dir^n,

3. BIOMECHANICS OF BIRD FLIGHT



Bird flight is achieved by the provision of power to overcome the bird's mass and drag (of various forms)

We'll consider three types of flight:

(1) gliding = constant speed at constant angle to horizontal

(2) soaring = bird uses energy in air movement for gaining lift

(3) bounding flight = period of gliding alternating with flapping of wings to regain height.

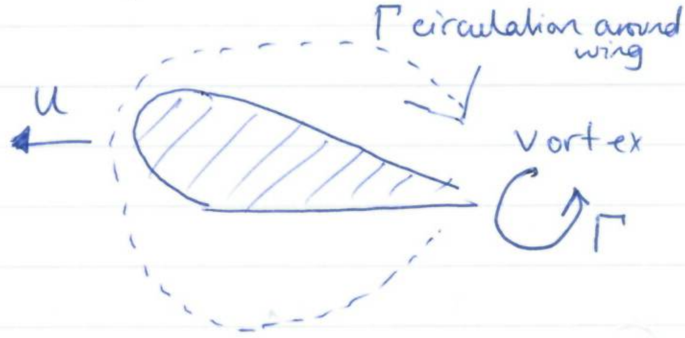
Birds have:
- light skeleton - hollow bones, porous structure
- light skull - ~1% of body weight
- highly developed respiratory system to provide power needed for flight.
- fuel is high-energy foods; berries etc. high energy yield per mass.

Aerodynamics of flight

Wing profile:

One modelling approach is to use Bernoulli's theorem to relate pressures and velocities for a steady inviscid flow. This gives lift $\propto$ (air speed u)^2

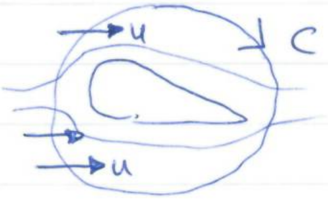
Or

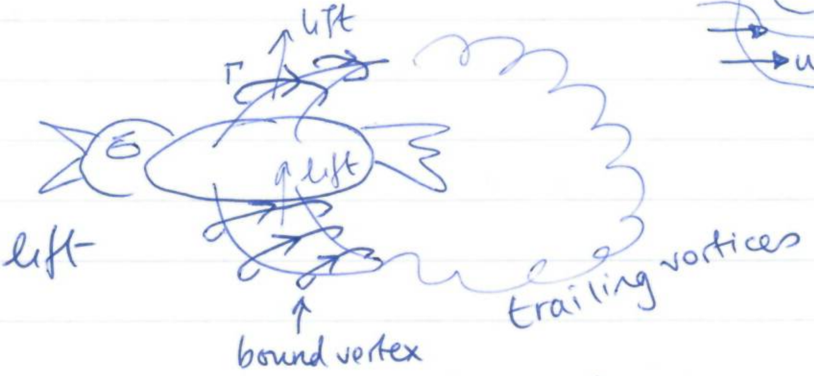


The lift on the wing is proportional to the circulation Γ

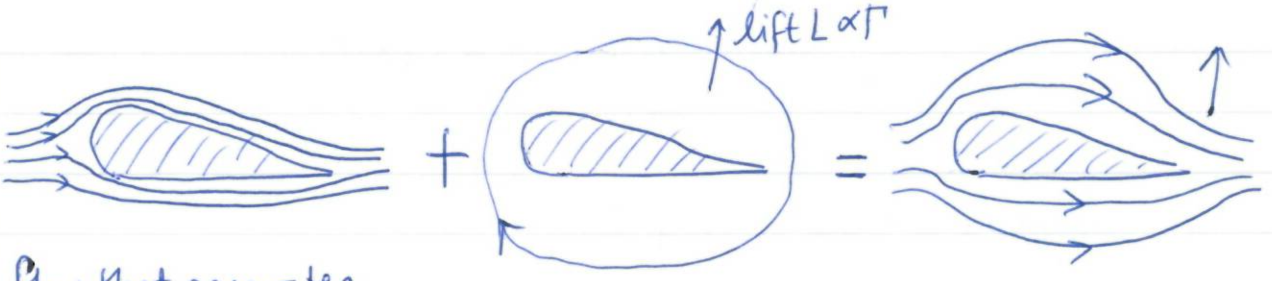
$$\text{lift } L = -\rho u \times \Gamma$$ (quoted result)

where $\Gamma = \oint_c u \cos\theta \, d\theta$





$\Gamma \propto$ lift



flow that generates no lift

bound vortex strength Γ

Actual flow is mathematically equivalent to a flow that generates no lift (but does generate drag) + flow equivalent to a vortex of strength Γ that yields lift $L \propto \Gamma$.

Let Drag $= D =$ parasitic drag + induced drag

$= D_p + D_i$

D_p = <u>Parasitic drag</u> = drag due to friction of wing surface with air + pressure drag (caused by low pressure in the wake of the wing)

Here we only consider frictional drag.

<u>Frictional drag</u> = $D_f = \frac{1}{2}\rho S C_d u^2$,

ρ = density of air

S = SA of wing

C_d = drag coeff.

so frictional drag goes up quadratically with air speed u.

<u>Induced drag</u> = lift-induced drag

$= 0$ for no lift.

Sketch of how D_i varies with u.

Find that $D_i \propto \frac{1}{u^2}$.

Induced drag = rate of transfer of momentum to trailing vortex system.

= kinetic energy per unit length in the vortex system.

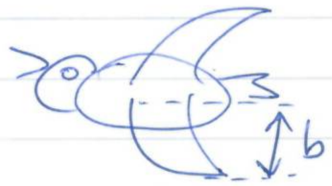
$$\left(= \text{mass } M \text{ in vortex system} \times \frac{\text{air speed } u}{T} = \frac{Mu^2}{Tu} = \frac{Mu^2}{d} \right)$$

d length of vortex system generated in T.

$$\text{Momentum transferred} \times \text{per unit length} = \text{lift force} \cdot \frac{1}{u} = \frac{L}{u}$$

Also, mass per unit length in vortex system $\propto \rho b^2$

where b = semi-span of wing.



$$\Rightarrow D_i = \text{KE per unit length}$$

$$= \frac{1}{2} \frac{(\text{momentum})^2 / \text{mass}}{\text{length}^d \text{ of vortex system}} = \frac{1}{2} \left(\frac{\text{momentum}}{\text{length}^d}\right)^2 / (\text{mass} / \text{length})$$

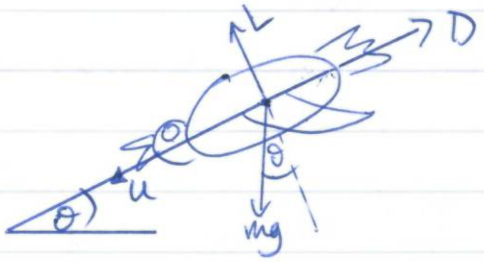
$$\Rightarrow D_i \propto \left(\frac{L}{u}\right)^2 \cdot \frac{1}{\rho b^2} = \frac{L^2}{\rho b^2 u^2} \propto \frac{1}{u^2} \quad \left(\begin{array}{l}\text{and } = 0 \\ \text{when } L = 0\end{array}\right)$$

Set $D_i = \dfrac{KL^2}{\frac{1}{2}\rho b^2 u^2}$ K constant.

$$\Rightarrow \text{total drag} = \underbrace{\frac{1}{2}\rho S C_d u^2}_{\text{frictional}} + \underbrace{\frac{KL^2}{\frac{1}{2}\rho b^2 u^2}}_{\text{induced}}$$

NB// induced drag ↓ with increasing b e.g. albatross.

Type of flight 1: Gliding flight



Resolving

$mg\sin\theta = D$

$mg\cos\theta = L$

for steady glide

$$= D$$

$$= D_p \quad + \quad D_i$$

$$\Rightarrow \quad mg\sin\theta = \underbrace{\tfrac{1}{2}\rho S C_d}_{} u^2 + \underbrace{\frac{Km^2g^2\cos^2\theta}{\tfrac{1}{2}\rho b^2 u^2}}_{}$$

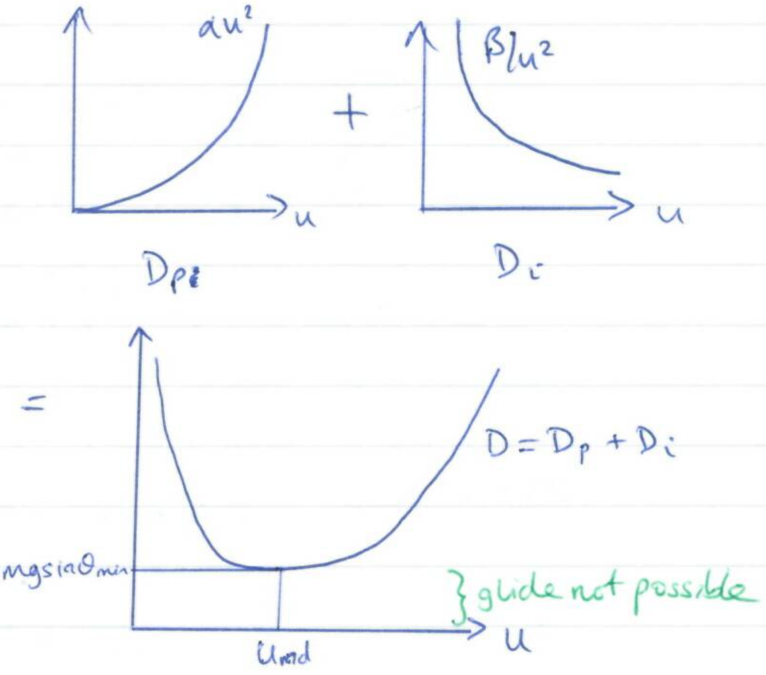
$$= \alpha u^2 + \frac{\beta}{u^2}$$

where $\alpha = \tfrac{1}{2}\rho S C_d$, $\quad \beta = \dfrac{KL^2}{\tfrac{1}{2}\rho b^2} = \dfrac{Km^2g^2\cos^2\theta}{\tfrac{1}{2}\rho b^2}$

Here, $D = D_p + D_i$, $\quad D_p = \alpha u^2$, $\quad D_i = \beta/u^2$

D_p increases with airspeed u.
D_i decreases with airspeed u.

$D = \alpha u^2 + \beta/u^2$



There is a unique speed u_{md} (md=minimum drag) where the drag on the bird is minimised. So for steady glider of angle θ, $mg\sin\theta = D(u)$.

So for $\theta < \theta_{min}$ where $mg\sin\theta_{min} = D(u_{md})$ a glide is not possible. To find u_{md}, θ_{min}:

$$D'(u) = 2\alpha u - \frac{2\beta}{u^3}$$
$$= 0 \text{ at } u_{md} = \left(\beta/\alpha\right)^{1/4}$$

obviously a minimum from graph of $D(u)$.

$$D_{min} = \alpha\sqrt{\frac{\beta}{\alpha}} + \beta/\sqrt{\beta/\alpha} = 2\sqrt{a\beta}.$$

$$\Rightarrow u_{md} = \left(\frac{KL^2}{\frac{1}{2}\rho b^2}\cdot\frac{1}{\frac{1}{2}\rho S C_d}\right)^{1/4} = \left(\frac{4KL^2}{\rho^2 b^2 S C_d}\right)^{1/4}.$$

$$D_{min} = 2\left(\tfrac{1}{2}\rho S C_d \frac{KL^2}{\frac{1}{2}\rho b^2}\right)^{1/2} = 2\left(\frac{SKC_dL^2}{b^2}\right)^{1/2}$$

$$= 2\frac{L}{b}\sqrt{SKC_d}$$

At the critical angle θ_{min},

$$mg\sin\theta_{min} = D_{min} = \frac{2mg\cos\theta}{b}\sqrt{SC_dK}$$

$$\Rightarrow \tan\theta_{min} = \frac{2}{b}\sqrt{SC_dK}$$

$$\Rightarrow \theta_{min} = \tan^{-1}\left(\frac{2}{b}\sqrt{SC_dK}\right)$$

below θ_{min} glide is not possible.

Above θ_{min}:

There are two possible solutions, $u_{high} > u_{low}$.

$$\Rightarrow mg\sin\theta = \alpha u^2 + \beta/u^2$$

Let $z = u^2$. $mg\sin\theta = \gamma$ (say) $= \alpha z + \beta/z$

$$\Rightarrow \gamma z = \alpha z^2 + \beta$$

$$\Rightarrow \alpha z^2 - \gamma z + \beta = 0$$

$$\Rightarrow \quad z = \frac{\gamma}{2\alpha} \pm \frac{1}{2\alpha}\left[\gamma^2 - 4\alpha\beta\right] = \frac{\gamma}{2\alpha}\left[1 + \left(1 - \frac{4\alpha\beta}{\gamma^2}\right)^{1/2}\right]$$

Want $z > 0$ roots. If $1 > \frac{4\alpha\beta}{\gamma^2}$ then both roots for z are real and > 0.

$$\gamma^2 - 4\alpha\beta > 0$$

$$\gamma^2 > D_{min}^2 = 4\tfrac{1}{2}\rho S C_d \frac{K m^2 g^2 \cos^2\theta}{\tfrac{1}{2}\rho b^2}$$

$$m^2 g^2 \sin^2\theta > 4K\frac{m^2 g^2}{b^2}\cos^2\theta \, S C_d$$

$$\tan^2\theta > \frac{4KSC_d}{b^2}$$

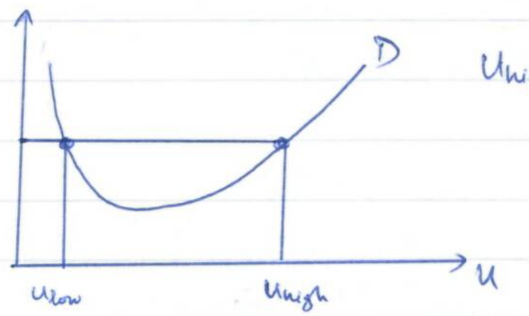
$$\tan\theta > \frac{2}{b}\sqrt{KSC_d} = \tan\theta_{min} \quad \checkmark$$

Hence

$$u = +\left[\frac{\gamma}{2\alpha}\left(1 \pm \left(1 - \frac{4\alpha\beta}{\gamma^2}\right)^{1/2}\right)\right]^{1/2}$$

$$= \left[\frac{mg\sin\theta}{\rho S C_d}\left(1 \pm \left(1 - \frac{4\cot^2\theta \, KSC_d}{b^2}\right)^{1/2}\right)\right]^{1/2}$$

But which to choose? We have u_{high} and u_{low}. Which does bird choose?

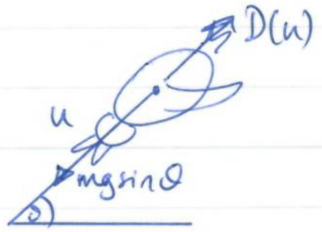


u_{high}: if u increases, Drag increases $\Rightarrow u$ decreases $\Rightarrow$ **STABLE**

u_{low}: if u decreases, Drag increases $\Rightarrow$ stalls. $\Rightarrow$ **UNSTABLE**.

Analytically, let speed be u^* ($u^* = u_{high}$ or u_{low})
Consider perturbation $u = u^* + \varepsilon$, ε small.

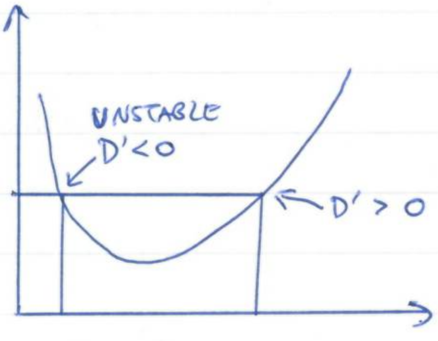
F=ma after perturbation:



$$m\dot{u} = mg\sin\theta - D(u)$$
$$m\dot{\varepsilon} = mg\sin\theta - D(u^* + \varepsilon)$$
$$m\dot{\varepsilon} = mg\sin\theta - \left[D(u^*) + \varepsilon D'(u^*) + O(\varepsilon^2)\right]$$
$$= \left[mg\sin\theta - D(u^*)\right] - \varepsilon D'(u^*) + O(\varepsilon^2).$$
$$= 0 - \varepsilon D'(u^*) \quad \text{to first order in perturbation } \varepsilon.$$

$$\Rightarrow \dot{\varepsilon} = \frac{-D'(u^*)}{m}\varepsilon \Rightarrow \varepsilon(t) = e^{-\frac{D'(u^*)}{m}t} \cdot \varepsilon(0).$$

If $D'(u^*) > 0$, $\varepsilon(t)$ decays, i.e. u^* is stable
If $D'(u^*) < 0$, $\varepsilon(t)$ grows, i.e. u^* is unstable.



Stable glides For $\theta > \theta_{min}$ stable glides at $u^* > u_{md}$,
$D_p > D_i$ at stable glide
$D > D(u_{md})$

$$D_p - D_i = \alpha u^2 - \beta/u^2$$
$$= \alpha u^2 (1 - \beta/\alpha u^4)$$
$$= \alpha u^2 (1 - u_{md}^4/u^4) > 0 \text{ if } u > u_{md}.$$

Since $u_{high} > u_{md}$, $D_p > D_i$ for a stable glide.

To find a crude estimate for u_{high} at a given $\theta > \theta_{min}$.

$mg\sin\theta = D = D_i + D_p$ and for u_{high}, $D_p > D_i$

$\Rightarrow D < 2D_p$ and $D = D_p + D_i > D_p > \frac{1}{2}D$

$\Rightarrow D/2 < D_p < D$

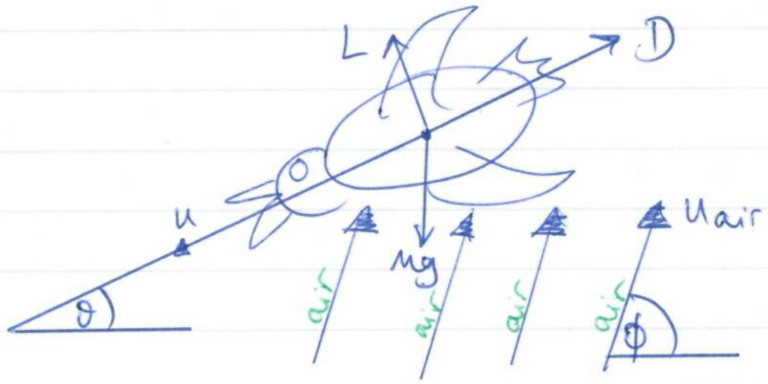
$\Rightarrow \frac{mg\sin\theta}{2} < \frac{1}{2}\rho S C_d u^2 < mg\sin\theta$

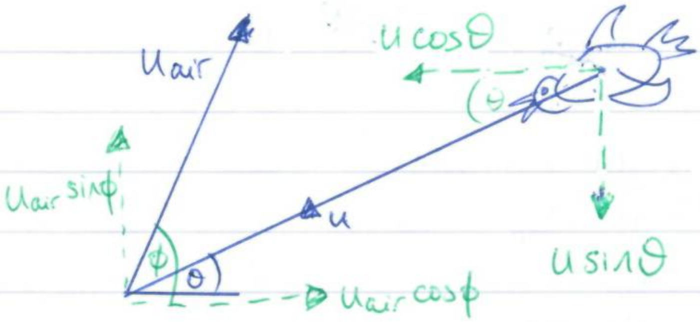
$$\Rightarrow \left(\frac{mg\sin\theta}{\rho S C_d}\right)^{1/2} \leq u < \left(\frac{2mg\sin\theta}{\rho S C_d}\right)^{1/2}$$

↑ crude estimate for stable glide speed at angle θ

Type of flight 2: Soaring flight

Up to now, air is considered to be still. Now consider the possibility of air currents that lift the bird. Soaring flight is where the bird glides, but takes advantage of the upward air currents to obtain light.

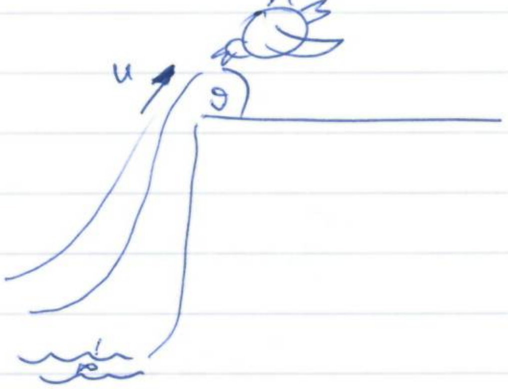




If the bird wishes to remain stationary in the upward draft then.

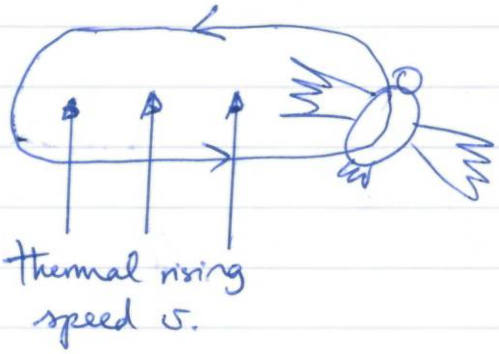
resolving $u\sin\theta = u_{air}\sin\phi$
$u\cos\theta = u_{air}\cos\phi$ $\Rightarrow$ $\theta=\phi$
$\underline{u=u_{air}}$

bird can remain stationary ⟶
and survey surroundings for prey, etc.



Upward wind speed u at angle θ ≡ downward glide angle.
Speed u in still air.

For a thermal (rising air at speed v), $\phi = \pi/2$,



e.g. vulture/buzzard

For bird riding a thermal at constant height, taking a wide circular path, need

$$u\sin\theta = v \implies \sin\theta = \frac{v}{u}$$

So the estimate for u becomes

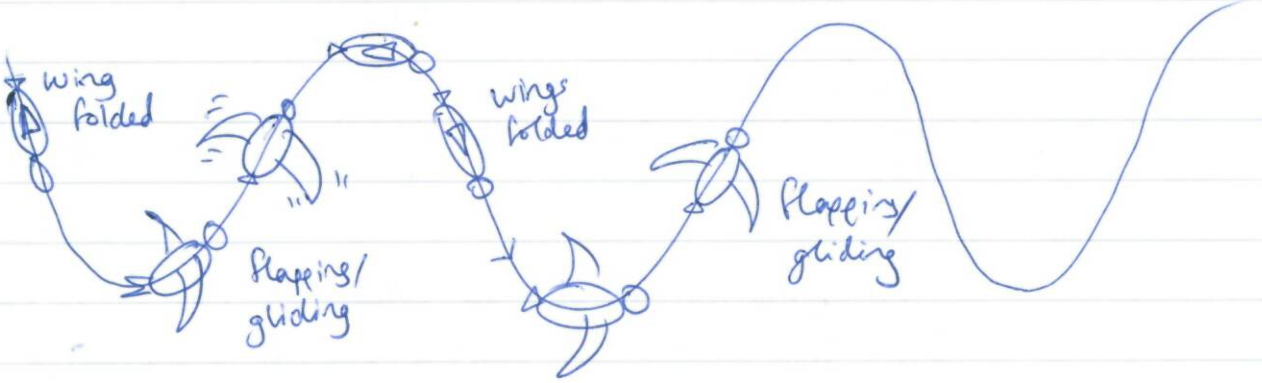
$$\sqrt{\frac{mg\sin\theta}{\rho C_d S}} < u \leq \sqrt{\frac{2mg\sin\theta}{\rho C_d S}}$$ from 2 pages ago

$$\frac{mg(v/u)}{\rho C_d S} < u^2 \leq \frac{2mg\, v/u}{\rho C_d S}$$

$$\sqrt[3]{\frac{mgv}{\rho C_d S}} < u \leq \sqrt[3]{\frac{2mgv}{\rho C_d S}}$$

Type of flight 3: Bounding flight

Now including flapping of wings to provide lift.



Bounding flight is used by small birds that do not have the semispan b to generate sufficient lift for gliding. Flight is alternating flapping/gliding on upward path, followed by folded wings and essentially parabolic projectile motion

In order to maintain height, the lift during flapping must be enhanced over normal flight (since $L=0$ when wings are folded).

$$L = \frac{mg}{f}, \quad f \in [0,1] = \text{fraction of time wings are open.}$$

Look at the mean drag. We have

$$D = \hat{D}_p + \hat{D}_i = (\underset{\text{body}}{\hat{D}_b} + \underset{\text{wing}}{\hat{D}_w}) + \hat{D}_i$$

$$\hat{D}_i = \frac{(mg)^2 K}{\frac{1}{2}\rho b^2}$$

$\uparrow$ i.e. if $f=1$.

When wings are closed, $D_w = D_i = 0$, so the mean drag

$$\tilde{D} = \hat{D}_b + f(\hat{D}_w + D_i(f)) = \hat{D}_b + f\left(\hat{D}_w + \frac{K\left(\frac{mg}{f}\right)^2}{\frac{1}{2}\rho b^2 u^2}\right)$$

$$\Rightarrow \tilde{D} = \hat{D}_b + f\hat{D}_w + \frac{1}{f}\hat{D}_i$$

So $$\frac{d\tilde{D}}{df} = \hat{D}_w - \frac{1}{f^2}\hat{D}_i = 0 \quad \text{when} \quad f = \sqrt{\frac{\hat{D}_i}{\hat{D}_w}}$$

So for bounding flight we need $f \in (0,1)$ so can occur when $\hat{D}_i < \hat{D}_w$, so for higher speeds of flight.

Drag for normal flight, $f=1$, $D = \hat{D}_i + \hat{D}_b + \hat{D}_w$

$$D - \tilde{D} = (\hat{D}_b + \hat{D}_i + \hat{D}_w) - (\hat{D}_b + f\hat{D}_w + \frac{1}{f}\hat{D}_i)$$

$$= \hat{D}_i\left(1 - \frac{1}{f}\right) + \hat{D}_w(1-f)$$

$$= \frac{1}{f}\left[\hat{D}_i(f-1) + f(1-f)\hat{D}_w\right]$$

$$= \frac{1}{f}(f-1)\left[\hat{D}_i - f\hat{D}_w\right]$$

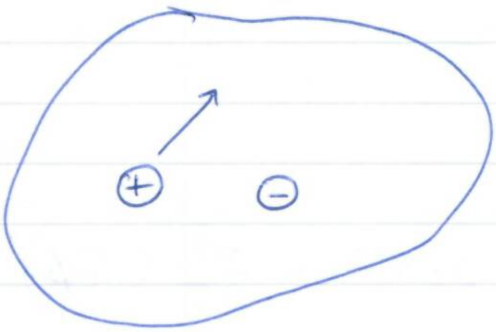
$f = \sqrt{\hat{D}_i / \hat{D}_w}$ and $\hat{D}_i < \hat{D}_w$ $\qquad \hat{D}_i = f^2\hat{D}_w$

$$= \frac{1}{f}(f-1)\left[\hat{D}_i - \sqrt{\frac{\hat{D}_i}{\hat{D}_w}}\,\hat{D}_w\right]$$

$$= \frac{1}{f}(f-1)\sqrt{\frac{\hat{D}_i}{\hat{D}_w}}\left(\sqrt{\hat{D}_i} - \sqrt{\hat{D}_w}\right) \qquad > 0.$$

4. ELECTROPHYSIOLOGY

Electrodiffusion



electric field, strength $\underline{E}$.

diffuse passively
flux $J_{diff} = -D\nabla C$
where D = diffusion const.

Migrational flux due to force on ions from interaction of ionic charge with electric field $\underline{E}$.

$$J_{total} = J_{diff} + J_{mig}$$
$$= -D\nabla C + \mu q \underline{E}.C$$

μ = mobility of ion
q = charge on ion
$= zq_e$ where z = valency of ion, and q_e = charge on electron.

For electric field $\underline{E}$, $\exists$ a potential ϕ s.t.

$$\underline{E} = -\nabla\phi$$
$$\Rightarrow \quad J = -D\nabla C - \mu q C\nabla\phi$$
$$= -D\nabla C - \mu q_e z C\nabla\phi$$

Use Einstein's Relation: $D = \mu k_B T$
(relates mobility of ion to diffusion constant D.

$$\Rightarrow \quad J = -D\nabla C - \frac{Dq_e z}{k_B T} C\nabla\phi$$

$$\Rightarrow \qquad J = -D\left(\nabla C + \frac{q_e z}{k_B T} C \nabla \phi\right)$$

Finally use $\frac{k_B T}{q_e} = \frac{RT}{F}$ where R = gas const.
T = temp in Kelvin
F = Faraday's const.

$$\Rightarrow \qquad \boxed{J = -D\left(\nabla C + \frac{zF}{RT} C \nabla \phi\right)}$$

For concentration, we typically are faced with the PDE

$$\frac{\partial C}{\partial t} = -\mathrm{div}(J) = \mathrm{div}\left[D\left(\nabla C + \frac{zFC\nabla\phi}{RT}\right)\right]$$

$$= D\left[\nabla^2 C + \frac{zF}{RT}\mathrm{div}(C\nabla\phi)\right]$$

$$\frac{\partial C}{\partial t} = D\left[\nabla^2 C + \frac{zF}{RT}\left(\nabla C . \nabla\phi + C\nabla^2\phi\right)\right]$$

in $\underline{x} \in \Omega$

This is highly non-linear and difficult to solve, moreover need second eqn for ϕ from knowing the charge distributed.

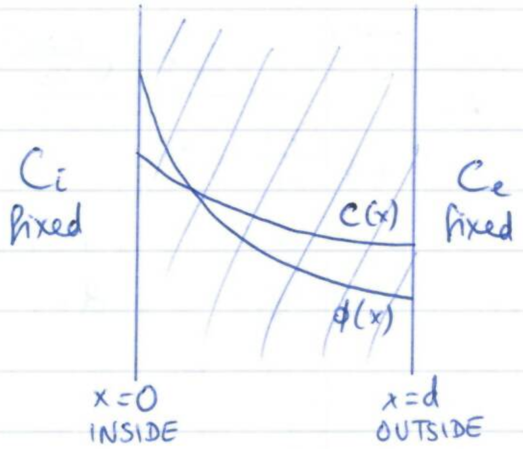
Consider one-dimensional domain, say an interval $I \subseteq \mathbb{R}$.
Then
$$\frac{\partial C}{\partial t} = -D\left[\frac{\partial^2 C}{\partial x^2} + \frac{zF}{RT}\frac{\partial}{\partial x}\left(C\frac{\partial\phi}{\partial x}\right)\right] = -\mathrm{div} J$$
from above

and
$$J = -D\left(\frac{\partial C}{\partial x} + \frac{Fz}{RT} C\frac{\partial\phi}{\partial x}\right)$$
from above, boxed.

Consider the steady state problem $\frac{\partial C}{\partial t} = 0$.

i.e. $0 = -\frac{\partial}{\partial x}(J)$.

$\Rightarrow$ flux J is independent of x. This makes progress beyond the full time-dependent problem much easier.



C = concentration of ion
i = inside
e = outside (extracellular)

$C_{i,e}$ are fixed, there's a voltage
$V = \phi(0) - \phi(d)$
= membrane voltage

from bottom of opposite page $$J = -D\left(\frac{dC}{dx} + \frac{zF}{RT}C\frac{d\phi}{dx}\right) \qquad x \in (0,d)$$

where J is a constant wrt x (steady $\Rightarrow$ J indpt of x).

Let $V_0 = \frac{RT}{F}$, then $\Rightarrow$ $J = -D\left(\frac{dC}{dx} + \frac{z}{V_0}C\frac{d\phi}{dx}\right)$

Solve: Integrating factor for RHS = $\exp\left[\frac{z\phi(x)}{V_0}\right]$.

$$\Rightarrow \quad J\exp\left[\frac{z\phi(x)}{V_0}\right] = -D\left(\frac{d}{dx}\left(C\exp\left[\frac{z\phi(x)}{V_0}\right]\right)\right)$$

(**Check**: $\frac{d}{dx}C\exp\left(\frac{z\phi}{V_0}\right) = \frac{dC}{dx}\exp\left(\frac{z\phi}{V_0}\right) + \frac{z}{V_0}\frac{d\phi}{dx}C\exp\left(\frac{z\phi}{V_0}\right)$
$= \exp\left(\frac{z\phi}{V_0}\right)\left(\frac{dC}{dx} + \frac{z}{V_0}C\frac{d\phi}{dx}\right)$)

Integrate from 0 to d:

$$-\frac{J}{D}\int_0^d \exp\left[\frac{z\phi(x)}{V_0}\right]dx = \left[C\exp\left(\frac{z\phi(x)}{V_0}\right)\right]_0^d$$

$$= C(d)\exp\left(\frac{z\phi(d)}{V_0}\right) - C(0)\exp\left(\frac{z\phi(0)}{V_0}\right)$$

$$\Rightarrow J = -D\left(\frac{C_e\exp\left(\frac{z\phi(d)}{V_0}\right) - C_i\exp\left(\frac{z\phi(0)}{V_0}\right)}{\int_0^d \exp\left(\frac{z\phi(x)}{V_0}\right)dx}\right)$$

Choose ϕ s.t. $\phi(d) = 0$, $V = \phi(0) - \phi(d) = \phi(0)$.

$$\Rightarrow \underline{J = D\left(\frac{C_i e^{zV/V_0} - C_e}{\int_0^d \exp\left(\frac{z\phi(x)}{V_0}\right)dx}\right)}$$

steady state problem sol^n.

However, we don't know $\phi(x)$ ... yet. But even so this does predict for which voltage the flux vanishes.

$$\text{i.e. } J=0 \Rightarrow C_i e^{zV/V_0} = C_e$$

$$\Rightarrow V = -\frac{V_0}{z}\log\left(\frac{C_i}{C_e}\right)$$

Constant field approximation

In some circumstances it is a reasonable approximation that the electric field is constant, so $\phi(x)$ is linear.

$$\phi(x) = \left(1 - \frac{x}{d}\right)V$$

So now we can calculate the denominator: of the steady state problem sol^n:

$$\int_0^d \exp\left[\frac{zV}{V_0}\left(1-\frac{x}{d}\right)\right]dx = e^{zV/V_0}\int_0^d e^{-zVx/dV_0}\,dx$$

$$= e^{zV/V_0}\frac{dV_0}{zV}\left[e^{-zVx/dV_0}\right]_d^0$$

$$= e^{zV/V_0}\frac{dV_0}{zV}\left(1-e^{-zV/V_0}\right)$$

Hence $$J = \frac{D\left[C_i e^{zV/V_0} - C_e\right]}{\frac{dV_0}{zV}\left(e^{zV/V_0}-1\right)}$$

$$= \frac{Dz}{d}\frac{V}{V_0}\left(\frac{C_i e^{zV/V_0} - C_e}{e^{zV/V_0}-1}\right)$$

STEADY STATE + CONST. FIELD

$$\boxed{J = zP\frac{V}{V_0}\left(\frac{C_i e^{zV/V_0} - C_e}{e^{zV/V_0}-1}\right)}$$

$P = \frac{D}{d}$ = permeability of membrane to that ion

Example In cells, the main ions are Na, K and Cl. Consider a membrane permeable to Na^+, K^+, Cl^-, with fixed concentration on each side of the membrane, e.g. Na_i = internal sodium concentration
Na_e = external " "

$$J_K = (+1)P_K\frac{V}{V_0}\left(\frac{K_i e^{V/V_0} - K_e}{e^{V/V_0}-1}\right)$$

$$J_{Na} = (+1)P_{Na}\frac{V}{V_0}\left(\frac{Na_i e^{V/V_0} - Na_e}{e^{V/V_0}-1}\right)$$

$$J_{Cl} = (-1)P_{Cl}\frac{V}{V_0}\left(\frac{Cl_i e^{-V/V_0} - Cl_e}{e^{-V/V_0}-1}\right)$$

Current carried by flux J_K is

$$I_K = zFJ_K = FJ_K$$

$$I_{Na} = FJ_{Na}$$

$$I_{Cl} = -FJ_{Cl}$$

Net current through membrane is

$$I = I_{Na} + I_K + I_{Cl}$$

$$= F(J_{Na} + J_K - J_{Cl})$$

$$= \frac{V}{V_0}\left(\frac{P_K K_e + P_{Na} Na_e + P_{Cl} Cl_i - (P_K K_i + P_{Na} Na_i + P_{Cl} Cl_e) e^{V/}}{1 - e^{V/V_0}}\right.$$

Hence the voltage for which there is no net current is

$$V = V_0 \log\left(\frac{P_K K_e + P_{Na} Na_e + P_{Cl} Cl_e}{P_K K_i + P_{Na} Na_i + P_{Cl} Cl_e}\right)$$

Poisson-Nernst-Planck Equations (PNP)

We have looked at the flux through a membrane

$$J = -D\left(\frac{dc}{dx} + \frac{zF}{RT} c \frac{d\phi}{dx}\right)$$

$$J = D\left(\frac{C_{in} \exp\left(\frac{zV}{V_0}\right) - C_{out}}{\int_0^d \exp\left(\frac{z\phi(x)}{V_0}\right) dx}\right)$$

So far ϕ is unknown.

We need a relation that gives the potential $\phi(x)$ as a f^n of the charge density at x, which is determined by the ion concentrations.

$$\nabla^2 \phi(x) = \frac{-\rho(x)}{k\varepsilon_0}$$

where $\rho(x)$ = charge density
k = relative dielectric constant
$\varepsilon_0 = 8.85 \times 10^{-12}$ Farad/metre.

$$\rho(x) = F\Big(\sum_{\substack{k \\ \text{cations}}} C_k(x) z_k - \sum_{\substack{k \\ \text{anions}}} |z_k| C_k(x)\Big)$$

recall anions are negatively charged ions
" cations " positively " " .

$$\Rightarrow \quad \nabla^2 \phi(x) = -\frac{F}{k\varepsilon_0}\Big(\sum_{\substack{k \\ \text{cations}}} z_k C_k(x) - \sum_{\substack{k \\ \text{anions}}} |z_k| C_k(x)\Big) \quad \text{- - - (A)}$$

The PNP eq^{n}s are (A) together with the eq^{n}s

$$J_s = -D_s\left(\nabla C_s + \frac{z_s F}{RT} C_s \nabla \phi\right)$$

from 5 pages back.

where s varies over the anions and cations.

Example Hydrochloric acid dissociates into H^+ and Cl^-, so for Poisson's eq^n for ϕ we get (in 1 dimension)

$$(A) \Rightarrow \quad \frac{d^2\phi}{dx^2} = -\frac{F}{\varepsilon_0 k}\left(C_H - C_{Cl}\right)$$

write as

$$\varepsilon \frac{d^2\phi}{dx^2} = -\left(C_H - C_{Cl}\right), \quad \text{- - - } (*) \qquad \varepsilon = \frac{\varepsilon_0 k}{F} \ll 1.$$

Now suppose there are no large electric field gradients in a region of interest.

$$\Rightarrow \frac{d^2\phi}{dx^2} \text{ is not large.}$$

$$\phi(x) = \phi_0(x) + \varepsilon\phi_1(x) + \varepsilon^2\phi_2(x) + \dots$$

Let $\sigma = C_H - C_{Cl}$

$$\sigma(x) = \sigma_0(x) + \varepsilon\sigma_1(x) + \varepsilon^2\sigma_2(x) + \dots$$

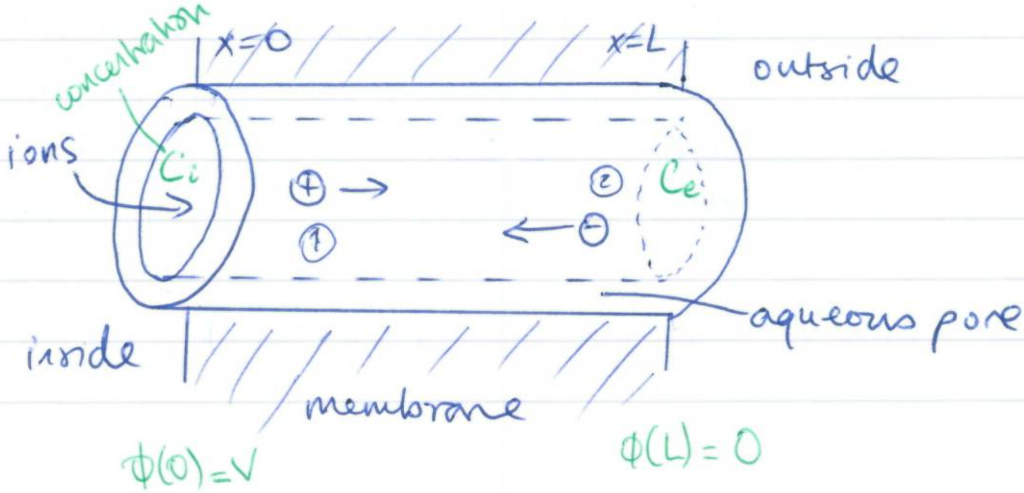
Substitute in (*)

$$\varepsilon(\phi_0'' + \varepsilon\phi_1'' + \varepsilon^2\phi_2'' + \dots) = -(\sigma_0 + \varepsilon\sigma_1 + \varepsilon^2\sigma_2 + \dots)$$

$$\Rightarrow \sigma_0 = 0$$
$$\phi_0'' = -\sigma_1 \quad \dots \text{ etc}$$

But then $\sigma = \sigma_0 = 0$ to first order in $\varepsilon \Rightarrow C_H \approx C_{Cl}$.
i.e. electroneutrality.
or the ~~sys~~ solution in this region is electrically neutral.

Example Ion channel model



There are two types of ion with concentrations
$C_1(x)$, $C_2(x)$.

At $x=0$, there's a concentration
$C_1(0) = C_i = C_2(0)$

At $x=L$, $C_1(L) = C_e = C_2(L)$

C_e, C_i fixed concentrations. Suppose ion 1 is a cation and ion 2 is an anion. There is a potential $\phi(x)$ in $x \in [0, L]$.

At the channel ends, $\phi(0) = V$, $\phi(L) = 0$.

<u>PNP:</u>

$$\varepsilon \frac{d^2\phi}{dx^2} = -\left(C_1(x) - C_2(x)\right)$$

$$J_1 = -D_1\left(\frac{dC_1}{dx} + \frac{FC_1}{RT}\frac{d\phi}{dx}\right)$$

$$J_2 = -D_2\left(\frac{dC_2}{dx} - \frac{FC_2}{RT}\frac{d\phi}{dx}\right)$$

These three equations are very tricky to solve without some form of approximation.

<u>Rescale equations:</u> $\bar{x} = \frac{x}{L}$, $\bar{C}_1 = \frac{C_1}{\mathcal{C}}$, $\bar{C}_2 = \frac{C_2}{\mathcal{C}}$

$\mathcal{C} = C_e + C_i$, $\psi = \frac{F\phi}{RT}$

$$\frac{d^2\psi}{d\bar{x}^2} = -\frac{L^2 C}{RT\varepsilon}\left(\bar{C}_1 - \bar{C}_2\right)$$

$$-\frac{J_1 L}{D_1 C} = \frac{d\bar{C}_1}{d\bar{x}} + \bar{C}_1 \frac{d\psi}{d\bar{x}}$$

$$-\frac{J_2 L}{D_2 C} = \frac{d\bar{C}_2}{d\bar{x}} - \bar{C}_1 \frac{d\psi}{d\bar{x}}$$

B.C.s: $\bar{c}_1(0) = \bar{c}_2(0) = \dfrac{c_i}{\varepsilon}$

$\bar{c}_1(1) = \bar{c}_2(1) = \dfrac{c_e}{\varepsilon}$

$\psi(1) = 0, \quad \psi(0) = V$

Assume large channel $\Rightarrow$ L large, let $\eta = \dfrac{RT\varepsilon}{L^2 C} \ll 1$.

Let $\bar{J}_k = \dfrac{J_k L}{D_k C}$ $\quad k = 1, 2, \ldots$

Now drop all the bars for ease of notation

$$\left.\begin{aligned} \eta \frac{d^2\psi}{dx^2} &= -(c_1 - c_2) \\ -\bar{J}_1 &= \frac{dc_1}{dx} + c_1 \frac{d\psi}{dx} \\ -\bar{J}_2 &= \frac{dc_2}{dx} - c_2 \frac{d\psi}{dx} \end{aligned}\right\} \quad \eta \ll 1 \qquad \begin{aligned} &(B1) \\ &(B2) \\ &(B3) \end{aligned}$$

Since $c_1 = c_2$ at the ends, we can find an expansion in ε that is uniform throughout $x \in [0, 1]$.

To first order in ε, $c_1 = c_2$ in $x \in [0, 1]$

(B2)+(B3) $\Rightarrow$ $-(\bar{J}_1 + \bar{J}_2) = 2\dfrac{dc}{dx}$ $\qquad c = c_1 = c_2 =$ 1st order conc. term

$\Rightarrow c(x)$ is linear, $c(x) = \dfrac{c_i}{\varepsilon} + (c_e - c_i)\dfrac{x}{\varepsilon}$

Now for ψ: subtract (B2)−(B3):

$$\bar{J}_2 - \bar{J}_1 = 2c\frac{d\psi}{dx}$$

$$\frac{d\psi}{dx} = \frac{\frac{1}{2}(\bar{J}_2 - \bar{J}_1)\epsilon}{c_i + (c_e - c_i)x}$$

$$\psi(x) = \frac{\frac{1}{2}(\bar{J}_2 - \bar{J}_1)\epsilon}{c_e - c_i}\log(c_i + (c_e - c_i)x) + \underset{\substack{\uparrow \\ \text{const.}}}{B}$$

$$\psi(0) = V. \qquad \psi(x) = \frac{\frac{1}{2}(\bar{J}_2 - \bar{J}_1)\epsilon}{c_e - c_i}\log\left(\frac{c_i}{c_e} + \frac{(c_e - c_i)}{c_e}x\right)$$

$$\psi(x) = \frac{V}{\log(c_i/c_e)}\log\left[\frac{c_i}{c_e} + \left(1 - \frac{c_i}{c_e}\right)x\right]$$

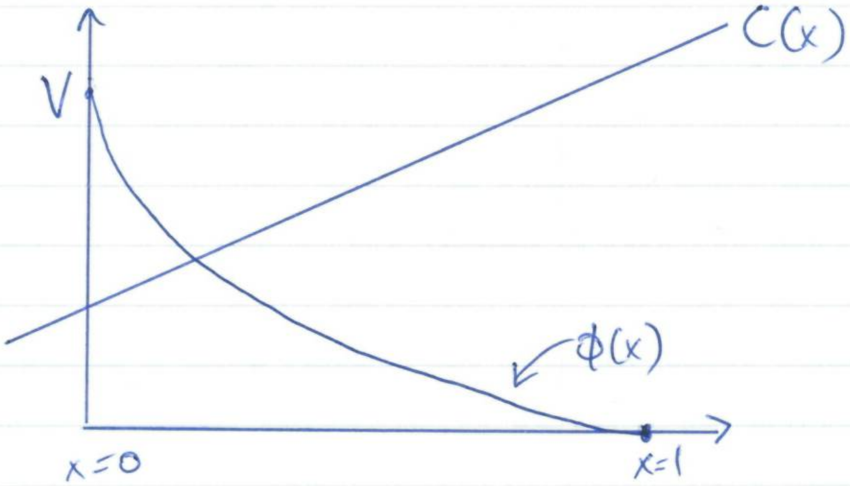
Let $V_1 = -\log(c_i/c_e)$

$$\psi(x) = -\frac{V}{V_1}\log\left(\frac{c_i}{c_e} + \left(1 - \frac{c_i}{c_e}\right)x\right)$$

Flux: $\bar{J}_1 = \frac{dc_1}{dx} + c_1\frac{d\psi}{dx}$

$$= \left(\frac{c_e - c_i}{\epsilon}\right) + \left(\frac{c_i}{\epsilon} + \left(\frac{c_e - c_i}{\epsilon}\right)x\right)\left(-\frac{V}{V_1}\frac{c_e - c_i}{c_i + (c_e - c_i)x}\right)$$

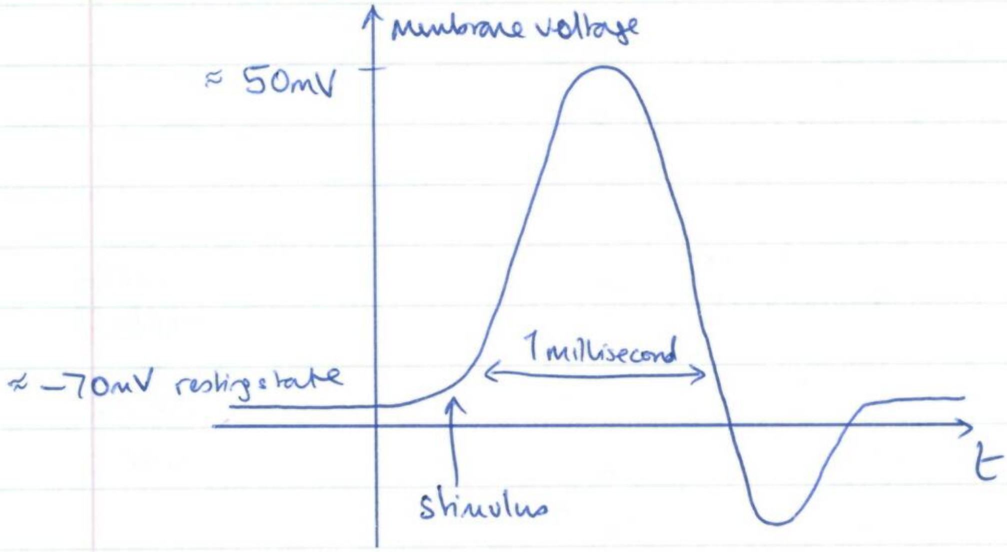
$$= \frac{(c_e - c_i)(V - V_1)}{\epsilon V_1}$$



$C_i < C_e$

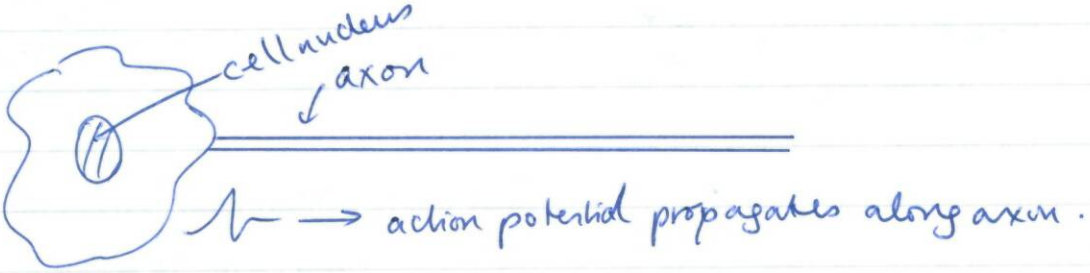
Can now translate back into original coordinates:
But we're not going to do that.

Action Potential Propagation



For excitable cells a sufficiently strong stimulus will produce a spike in the voltage that lasts approximately 1ms.

Nerve cells use these action potentials to transmit a signal to neighbouring cells.



Action potential creation

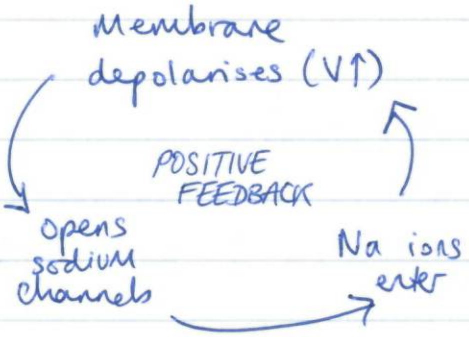
Initially in resting state, cell is at the cell resting potential ≈ -70 mV ≈ Nernst Eq^{m} Potential for Potassium.

$$K_i/K_e \approx \frac{400\text{ mmol}}{20\text{ mmol}} \Rightarrow E_K \approx -70\text{mV}$$

$$\left(E_K = -\frac{F}{RT} \log\left(\frac{P_k K_i}{P_k K_e}\right)\right)$$

If the permeability is dominated by sodium

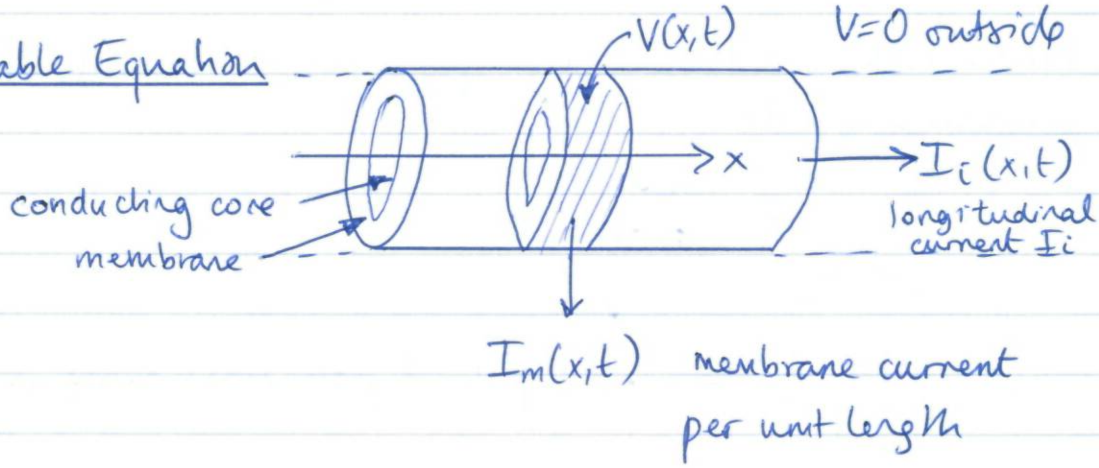
$$V = E_{Na} \approx 50\,\mathrm{mV}$$



more detail in online notes

Want to model the propagation of such an action potential down a nerve axon.

Cable Equation



membrane voltage

$$V_m(x+dx) - V_m(x) = -I_i(x,t)\, r_i\, \Delta x \quad \text{(to first order)}$$

where r_i = resistance of core in Ω/m. ($V=IR$)

$$\Rightarrow \frac{\partial V_m(x,t)}{\partial x} = -r_i I_i(x,t) \quad \cdots\cdots (1)$$

$$-I_i(x+dx,t) + I_i(x,t) = I_m(x,t).\,\Delta x$$

$$\Rightarrow \frac{\partial I_i(x,t)}{\partial x} = -I_m(x,t) \quad \cdots\cdots (2)$$

$$(1)+(2) \Rightarrow \frac{\partial^2 V_m}{\partial x^2}(x,t) = r_i I_m(x,t)$$

$$I_m(x,t) = \text{ionic} + \text{capacitance current}$$

$$= I_{ionic}(V_m) + C_m \frac{\partial V_m}{\partial t}$$

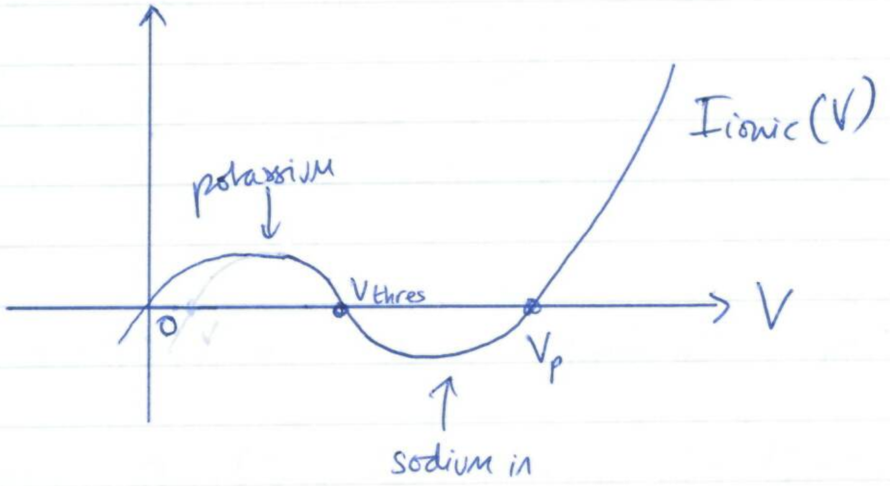
C_m = capacitance in F/m.

$$\Rightarrow \frac{\partial^2 V_m}{\partial x^2} = r_i\left(I_{ionic}(V_m) + C_m \frac{\partial V_m}{\partial t}\right)$$

$$C_m \frac{\partial V_m}{\partial t} = -I_{ionic}(V_m) + \frac{1}{r_i}\frac{\partial^2 V_m}{\partial x^2}$$

CABLE EQ^{N}

$\underline{I_{ionic}}$



$$I_{ionic}(V) = gV(V - V_{thres})(V - V_p)$$

Set $\alpha = \frac{V_{thres}}{V_p}$ $\quad D = g r_i V_p^2$ $\quad u = \frac{V_m}{V_p}$ $\quad \tau = \frac{g V_p}{C_m V_{thres}} t$

Cable eq^{n} $\Rightarrow \frac{\partial u}{\partial \tau} = f(u) + D\frac{\partial^2 u}{\partial x^2}$ where $f(u) = u(\alpha - u)(u-1)$

Seek travelling front solutions from left to right $(c > 0)$

$\xi = x - ct$ $\qquad$ c = vel. of wave

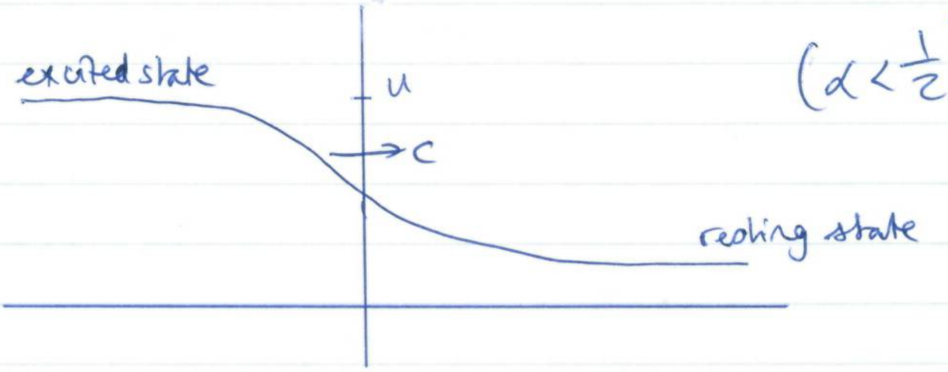
$$u(x,t) = u(\xi) = u(x-ct)$$

$$\frac{\partial u}{\partial t} = u'(\xi)\cdot\frac{\partial \xi}{\partial t} = -cu'$$

$$\frac{\partial u}{\partial x} = u'\cdot\frac{\partial \xi}{\partial x} = u' \qquad \Rightarrow \frac{\partial^2 u}{\partial x^2} = u''$$

$$\Rightarrow \; -cu' = f(u) + Du'' \qquad \text{(ODE)}$$

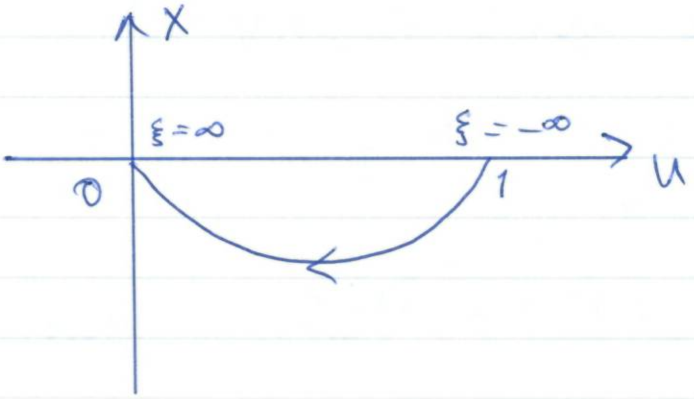
Let $X = u' \Rightarrow X' = \frac{1}{D}(-cX - f(u))$



$(\alpha < \frac{1}{2})$

This is the front we seek; so $u'(\xi) \to 0$, $\xi \to \pm\infty$.

$u(\xi) \to 1$, $\xi \to -\infty$ as $u(\xi) \to 0$ $\xi \to +\infty$



We have $u' = X$

$$X' = -\frac{1}{D}\left(f(u) + cX\right)$$

$$\frac{dX}{du} = -\frac{1}{DX}\left(f(u) + cX\right)$$

Try solution $X(u) = \theta u(u-1)$

$$D\theta u(u-1)\theta(2u-1) = -u(\alpha-u)(u-1) - \theta c u(u-1)$$

$$\Rightarrow \quad D\theta^2(2u-1) = -c\theta + u - \alpha$$

$\Rightarrow$ comparing coeffs of u $\quad 2D\theta^2 = 1, \quad -D\theta^2 = -c\theta - \alpha.$

$$\theta = \frac{1}{\sqrt{2D}}, \qquad c = \frac{D\theta^2 - \alpha}{\theta} = \frac{\frac{1}{2} - \alpha}{1/\sqrt{2D}} = \sqrt{\frac{D}{2}}(1-2\alpha)$$

$$\Rightarrow \quad X(u) = \frac{1}{\sqrt{2D}} u(u-1)$$

$$\frac{du}{d\xi} = \theta u(u-1)$$

$$\Rightarrow \quad u(\xi) = \frac{e^{-\theta\xi}}{K + e^{-\theta\xi}}$$

$K \sim$ const of int.

$$u(x,t) = \frac{e^{-\theta(x-ct)}}{K + e^{-\theta(x-ct)}}$$

BIOMATHEMATICS
PART II

Chapter
5. Bones (design, viscoelasticity)
6. Chemotaxis (pattern formation)
7. Brain (neuronal activity)
8. Blood (ESR, pressure, pulse waves)

Prof. Alexey Zaikin
Office hour: Monday 10-11
www.ucl.ac.uk/~rmjbale/3307.html

5. BONES

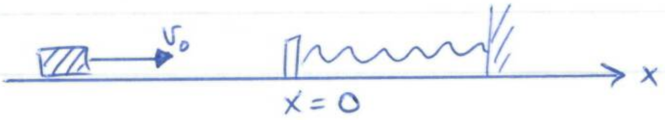
Revision of mechanics

If a location is described by $\underline{x}(t)$,

$\frac{dx}{dt}$ is a velocity

$m\frac{d^2x}{dt^2} = \sum \underline{F}$ is the motion equation.

Example A mass m hitting a spring



$$m\frac{d^2x}{dt^2} = -kx(t) - \underbrace{\delta\frac{dx}{dt}}_{\text{friction}}$$

with initial conditions $x(0) = 0$

$$\left.\frac{dx}{dt}\right|_0 = v_0$$

Conservation laws

Conservation of momentum: NII: $\frac{d\underline{p}}{dt} = \underline{F}$. If $\underline{F} = 0 \Rightarrow \frac{d\underline{p}}{dt} = 0$

$\Rightarrow \underline{p}$ const, $\underline{p} = m\underline{v}$

Conservation of kinetic energy: Let A be mechanical work, i.e. amount of energy transferred by a force acting over a distance:

$$A = \sum \underline{F}\, d\underline{r} = \sum \underline{F}\,\underline{v}\, dt = m\underline{v}\, d\underline{v}$$

Change of KE

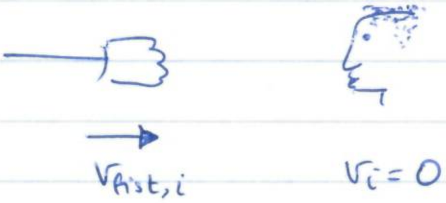
$$dW = A = m\underline{v}\,d\underline{v} = \underline{v}\,d\underline{p}$$

Without force, $d\underline{p} = 0$

$$W = \text{const} = m\int \underline{v}\,d\underline{v} = \frac{1}{2}mv^2$$

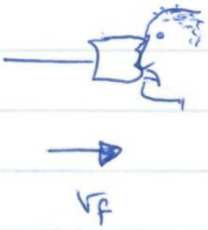
Example: Boxing with gloves

Inelastic collision



$\frac{1}{2}$ because we consider movement of arm (think how far elbow moves rel. to fist)

$$\frac{M_{arm}v_{fist,i}}{2} = \frac{M_{arm}v_f}{2} + M_{head}v_f$$

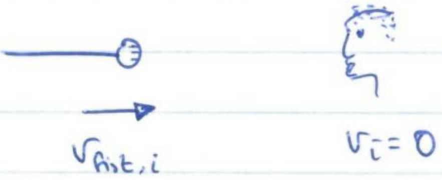


$$\Rightarrow v_f = \frac{v_{fist,i}}{1+\frac{2M_{head}}{M_{arm}}} = 0.236\,v_{fist}$$

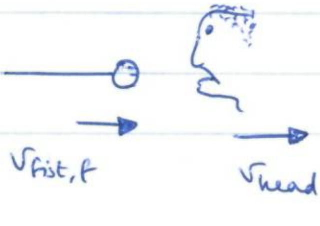
if we assume $m_{arm} = 0.05\,M_{body}$
$m_{head} = 0.081\,M_{body}$

Example: Boxing without gloves

Elastic collision:



$$\frac{M_{arm}v_{fist,i}}{2} = \frac{M_{arm}v_{fist,f}}{2} + M_{head}v_h$$



$$\frac{M_{arm}}{2}\left(\frac{v_{fist,i}}{2}\right)^2 = \frac{M_{arm}}{2}\left(\frac{v_{fist,f}}{2}\right)^2 + \frac{M_{head}}{2}v_{head}^2 \qquad \left(\begin{matrix}\text{KE}\\ \text{eq}^{\text{n}}\end{matrix}\right)$$

$$v_{head,f} = \frac{v_{fist,i}}{1+\frac{m_{head}}{M_{arm}}} = \underset{\substack{\uparrow \\ \text{1.6 times larger} \\ \text{than with gloves.}}}{0.38\, v_{fist,i}}$$

$\Downarrow$

fractures,
or DEATH

Rotation

The torque $\underline{\tau}$ about some axis is defined as

$$\underline{\tau} = \underline{r} \times \underline{F}.$$

and $\tau_z = rF\sin\theta$, if τ is in z-dirⁿ.

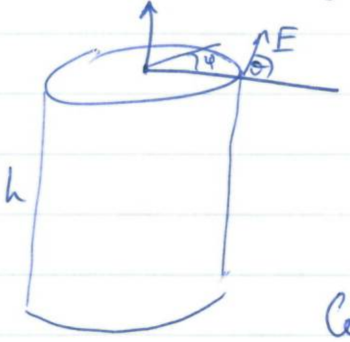
A torque leads to change of the angle φ and angular frequency $\Omega = \frac{d\varphi}{dt}$, giving

$$I \cdot \frac{d\Omega}{dt} = \underline{\tau}$$

where I is the moment of inertia.

The MoI about some axis is $I = \sum_i m_i R_i^2 = \int \overset{\text{density}}{\rho(\underline{r})} R^2 \overset{\text{volume}}{dv}$

Example A force $\underline{F}$ is applied to the surface of a cylinder with height h, radius R and density ρ.



$\theta = 90°$. Eq^{n} of motion?

$$\varphi(t=0) = 0$$
$$\varphi(t) = ?$$

Compute MoI:

$$I = \int \rho r^2 dV = \int_0^R \rho r^2 \left[\pi(r+dr)^2 - \pi r^2\right] h$$

$$= \int_0^R \rho h r^2 \pi \left(r^2 + 2r\,dr + \overset{\text{too small order}}{\cancel{dr^2}} - r^2\right)$$

$$= \int_0^R 2\rho h \pi r^3 dr$$

$$= \int_0^R 2\rho\pi h \frac{R^4}{4} = \frac{MR^2}{2}$$

Hence $F \cdot R = \frac{MR^2}{2}\frac{d^2\varphi}{dt^2}$

$$\frac{d^2\varphi}{dt^2} = \frac{2F}{MR} \Rightarrow \frac{d\varphi}{dt} = \frac{2F}{MR}t + C$$

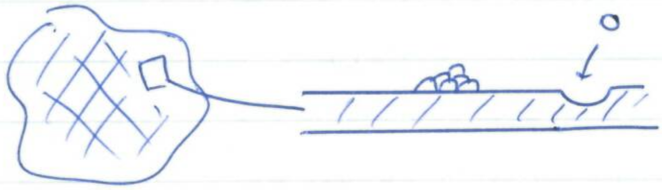
$$\varphi = \frac{F}{MR}t^2 + Ct + D$$

Bone functions

- A structural framework to attach organs and muscles
- enable movement
- physical protection
- storage for minerals
- produce cells for immune system

Bone is a complex composite material. It usually has a hallow design and porous structure.

Bone is a dynamical structure, destroyed by osteoclasts and formed by osteoblasts

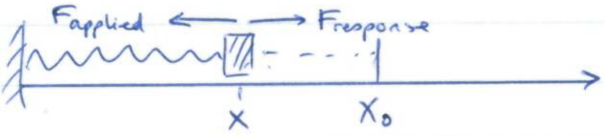


If there's little gravity, bones will lose mass, e.g. Mars trip 3yrs, 50% bone mass lost

This disease is called osteoporosis (norm. after 60 yo)

Basic stress-strain relationships

Elastic materials are modelled as perfect strings obeying Hooke's law:



$$F_{response} = -\underset{\text{spring const.}}{k}\,\underset{\text{deformation}}{(x-x_0)}$$

Alternatively $F_{response} = -k(x-x_0) = -k(L-L_0)$
where L length of the material
L_0 its relaxed length.

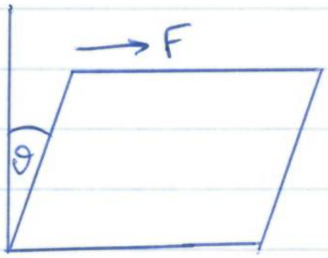
Obvious that $L > L_0$, material is under tension
$L < L_0$, material is under compression

If the object has a cross-sectional area A and length L, we can rewrite the Hooke's law as following:

$$\underbrace{\frac{F_{\text{applied}}}{A}}_{\substack{\text{stress}\\ \sigma}} = \underbrace{\frac{kL_0}{A}}_{\substack{\text{Young's}\\ \text{(elastic)}\\ \text{modulus}}} \underbrace{\left(\frac{L-L_0}{L_0}\right)}_{\substack{\text{strain}\\ \varepsilon}}$$

ie. $\underset{\sim\sim\sim}{\sigma = Y\varepsilon}$ ← Hooke's law.

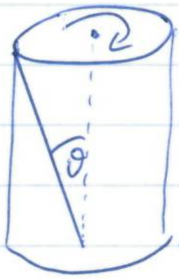
Other stress-strain relations



Shear stress $\tau = \dfrac{F}{A}$

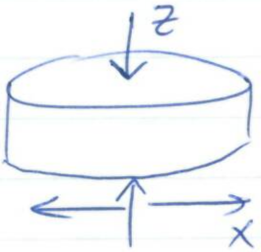
Shear strain $\gamma \approx \tan\theta \approx \theta$

$\Rightarrow$ $\underset{\sim\sim\sim}{\tau = G\gamma}$ ↑ shear modulus



Torsion deformation

Consider deformation of a cylinder



A relationship between longitudinal and latitudi strains is provided by

Poisson relation $\nu = -\frac{\varepsilon_x}{\varepsilon_z}$

For isotropic materials, $\underbrace{Y = 2G(1+\nu)}$

↑ i.e. contents of material is same everywhere

Bone shortening

How much do our bones shorten under compression?

$$\sigma = Y\frac{L-L_0}{L_0} \Rightarrow \Delta L = L - L_0 = \frac{\sigma L_0}{Y}$$

and fractionally $\varepsilon = \frac{\Delta L}{L_0} = \frac{\sigma}{Y}$

How much does the femur shorten when you stand on one foot?

$Y = 179 \times 10^2\ \mathrm{N/mm^2}$.
$L = 500\ \mathrm{mm}$
$F = 70\ \mathrm{kg} \times 10\ \mathrm{m/s^2} = 700\ \mathrm{N}$
$A = 370\ \mathrm{mm^2}$

So $\sigma = \frac{700\ \mathrm{N}}{370\ \mathrm{mm^2}} = 2.1\ \frac{\mathrm{N}}{\mathrm{mm^2}}$

$$\Delta L = \frac{\sigma L_0}{Y} = \frac{2.1\ \frac{\mathrm{N}}{\mathrm{mm^2}} \times 500\ \mathrm{mm}}{17900\ \mathrm{N/mm^2}} = 0.06\ \mathrm{mm}$$

$$\frac{\Delta L}{L} = \frac{\sigma}{Y} = 0.01\,\%$$

How much can you compress bones until they break?
i.e. until $\underbrace{\text{ultimate compression stress}}_{=}$ (fraction)

$$UCS = 170 \text{ MPa}.$$

Fractional shortening is:

$$\Delta L = \frac{UCS}{Y} \cdot L = \frac{170 \text{ N/mm}^2}{17900 \text{ N/mm}^2} \cdot 500\text{mm}$$

$$= \underset{\sim}{0.5 \text{ cm}}$$

Energy storage in elastic media

Potential energy (PE)

$$PE = -\int_0^x F\,dx' = \int_0^x kx'\,dx' = \frac{1}{2}kx^2$$

Or $PE = \frac{1}{2}k(L-L_0)^2$

Because $Y = \frac{kL_0}{A} \Rightarrow k = \frac{YA}{L_0}$

$$\varepsilon = \frac{L-L_0}{L_0} \Rightarrow L-L_0 = \varepsilon \cdot L_0$$

So $PE = \frac{1}{2}\frac{YA}{L_0} \cdot (\varepsilon L_0)^2 = \frac{1}{2}(Y\varepsilon^2)(\overbrace{AL_0}^{\text{Volume } V})$

$$= \frac{1}{2}Y\varepsilon^2 V$$

$$= \frac{1}{2}\sigma\varepsilon V$$

$$= \frac{1}{2}\frac{\sigma^2}{Y}V$$

How can we design the best elastic storage medium for the body?

$$PE = \frac{1}{2}\frac{\sigma^2}{Y}V = \frac{(F_{applied}/A)^2}{2Y}AL_0 = \frac{F_{applied}^2 L_0}{2YA}$$

Maximise L_0, minimise Y and A $\Rightarrow$ tendons.

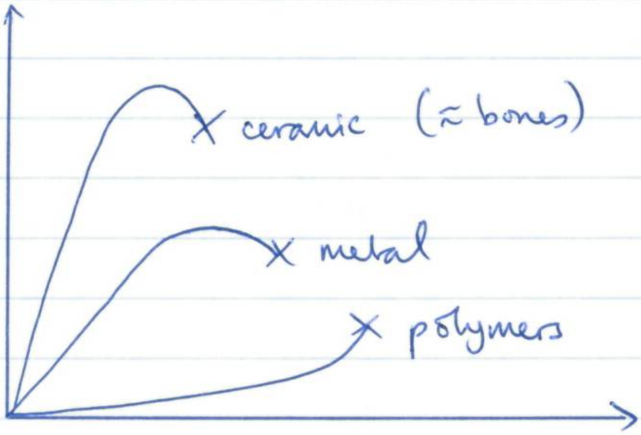
How much energy is stored in bones during one step?

Consider the femur: $L_0 = 500\,mm$
$A = 330\,mm^2$
$Y = 17900\,N/mm^2$
$V = L_0 A = 165 \times 10^3\,mm^3$

Upward force in 1 step $F = 6400\,N$

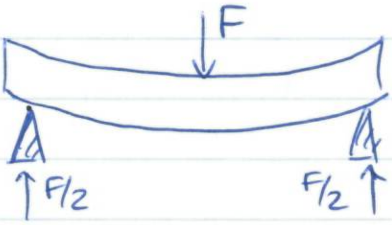
$$\Rightarrow PE = \frac{1}{2}\frac{\sigma^2}{Y}V = \frac{1}{2}\frac{(F/A)^2}{Y}\cdot V = 1.73\,Nm$$
$$\approx 2J$$
$\approx$ 2% from loss of KE.

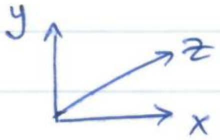
General stress-strain relationship:



Bending of bones or why long bones are hollow?

Consider the beam of length L under load F

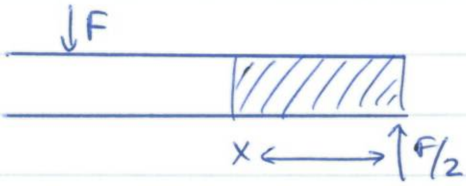




$\sum F_y = 0$ (∵ static beam)

and $\sum \tau_z = 0$.

Consider now the right side of the beam till x.

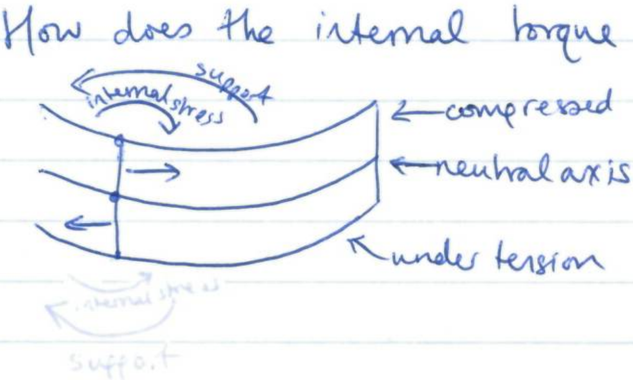


Forces in y dir?

$$\sum F_y = \frac{1}{2} F$$

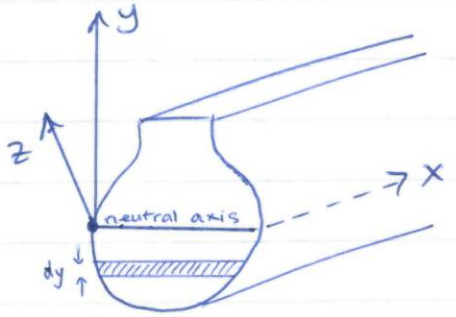
$$\sum \tau_z = \frac{1}{2} x \cdot F$$

How does the internal torque arise?



So $\sum \tau_z = \tau_{internal} + \frac{1}{2}Fx = 0$

What is the total internal torque?



$$dA(y) = \overset{\text{width}}{w(y)} \cdot dy$$

There is a force acting on dy

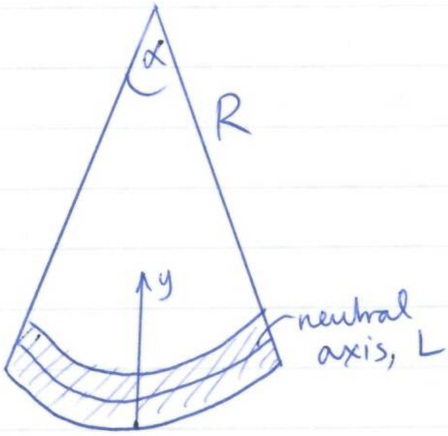
$$dF(y) = \sigma(y)\, dA(y)$$

So a torque : $-y\,dF = -y\,\sigma(y)\, dA(y)$ [recall $\tau = r \times F$]

So the total internal torque

$$\tau_{internal} = -\int_{y=-L}^{y=L'} y\,\sigma(y)\, dA(y) = -\frac{1}{2}Fx$$

What is the distribution of σ?



If $y=0$
$L = R \cdot \alpha$

So $\alpha = \frac{L}{R}$

If a thickness in the y-dir^n is d, then for the top of the beam, $L = (R - \frac{d}{2})\alpha$

and for bottom, $L = (R + \frac{d}{2})\alpha$

In general, $L(y) = (R-y)\alpha$

$$= (R-y)\frac{L}{R}$$

$$= L\left(1-\frac{y}{r}\right)$$

So the elongation is

$$L(y) - L = -y\frac{L}{R} \quad \text{and strain} \quad \varepsilon(y) = -\frac{y}{R}$$

Since $\sigma = Y\varepsilon$, $\quad \sigma(y) = -\frac{y}{R}Y$

So the internal torque $T_{\text{internal}} =$

$$T_{\text{internal}} = \int_{y_{\text{bottom}}}^{y_{\text{top}}} \left(\frac{y}{R}Y\right) y \, dA(y)$$

$$= \frac{Y}{R}\int_{y=-d/2}^{y=d/2} y^2 \, dA(y)$$

$$= \frac{1}{2}Fx$$

Now let us define the <u>area moment of inertia</u>

$$I_A = \int_{y_{\text{bottom}}}^{y_{\text{top}}} y^2 \, dA(y)$$

Since the bending moment $M_B = \frac{Fx}{2}$

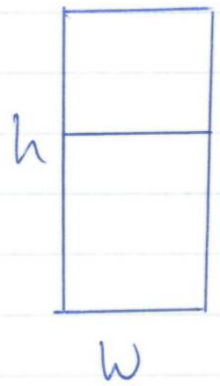
We have $M_B = \frac{Y}{R} I_A$

and the magnitude of the curvature $\frac{1}{R} = \frac{|M_B|}{Y I_A}$

This eq^n interrelates:

1) the applied force, through bending moment M_B
2) the material properties, through Y
3) the physical deformation, through R
4) the shape of the object through I_A.

<u>Example:</u> Consider a rectangle of height h and width w



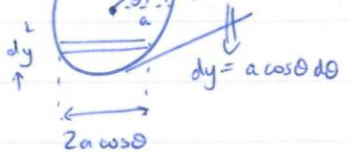
$$I_A = \int_{-h/2}^{h/2} y^2 w \cdot dy = \frac{1}{12} w h^3$$

e.g. $W = 2\text{cm}$, $h = 6\text{m}$,  $\rightarrow I_A = 36\text{cm}^4$

$w = 6\text{cm}$, $h = 2\text{cm}$  $\rightarrow I_A = 4\text{cm}^4$

$$\left(\text{Recall } \frac{1}{R} = \frac{M_B}{Y I_A}\right)$$

<u>Example:</u> Consider a solid cylinder



$$I_{A,\text{solid}} = \int_{-a}^{a} y^2 \, dA(y)$$

$$dA = dy \cdot 2a\cos\theta$$
$$= 2a^2\cos^2\theta \, d\theta$$

$$\Rightarrow \quad I_{A,\text{solid}} = \int_{-\pi/2}^{\pi/2} \underbrace{a^2\sin^2\theta}_{y^2} \, 2a^2\cos^2\theta$$

int. between these: we are looking at whole $2a\cos\theta$

Then, using $\sin^2\theta\cos^2\theta = \sin^2\theta(1-\sin^2\theta)$
$= \sin^2\theta - \sin^4\theta$

$$I_{A,\text{solid}} = \frac{\pi a^4}{4}$$

So $I_{A,\text{hollow}} = \dfrac{\pi(a_2^4 - a_1^4)}{4}$ $\qquad$ a_2 - external radius
a_1 - internal radius

~~A~~ $\Rightarrow$ $m_{\text{hollow}} = \rho\pi(a_2^2 - a_1^2)\cdot L$

a_1/a_2	$I_{A,\text{hollow}}/I_{A,\text{solid}}$	$m_{\text{hollow}}/m_{\text{solid}}$
0	1	1
0.5	0.937	0.75
	↑ decrease by 6%	↑ decrease by 25%

(limited by risk of fracture)

How to solve $\dot{X} + X = \delta(t) = \begin{cases} \int_{-\infty}^{\infty} \delta(t)\,dt = 1 \\ 0 \quad t \neq 0 \end{cases}$ $\qquad (*)$

$$\left.\begin{array}{ll} \text{For } t<0, & X = C_1 e^{-t} \\ t>0, & X = C_2 e^{-t} \end{array}\right\} \quad (**)$$

The eq^n includes generalised function.
Consider $\varphi(t)$, any f^n s.t. $\varphi(t) \to 0$ if $t \to \pm\infty$

$$\delta: \quad \varphi(t) \longmapsto \varphi(0) \quad \text{as} \quad \int_{-\infty}^{\infty} \varphi(t)\,\delta(t)\,dt = \varphi(0)$$

$$X: \quad \varphi \longmapsto \int_{-\infty}^{\infty} X\varphi(t)\,dt$$

$$\dot{X}: \quad \varphi \longmapsto \int_{-\infty}^{\infty} \dot{X}\varphi(t)\,dt = -\int_{-\infty}^{\infty} X\varphi'(t)\,dt \quad \text{(by parts)}$$

Multiplying $(*)$ by $\varphi(t)$ and integrating, using generalised f^{n}s:

$$-\int_{-\infty}^{\infty} X\varphi'(t)\,dt + \int_{-\infty}^{\infty} X\varphi\,dt = \varphi(0)$$

Using $(**)$, $\overbrace{\int_{-\infty}^{0} C_1 e^{-t} \varphi \, dt}^{\text{from 1st term}} - \int_{-\infty}^{0} C_1 e^{-t} \varphi' dt$

$$+ \int_0^\infty C_2 e^{-t} dt - \underbrace{\int_0^\infty C_2 e^{-t} \varphi' dt}_{\text{from 1st term}} = \varphi(0)$$

Integrating terms with φ' by parts, we get $-C_1 + C_2 = 1$

$$\Rightarrow C_2 = C_1 + 1$$

Viscoelasticity

Suppose the force is applied fast or slow relative to an internal time scale. The response of most materials inside the body depend on these temporal dependencies (history). This type of mechanical behaviour is called viscoelasticity.

Experimental results for load vs deformation for dog tibiae for fast and slow force

for slow force deformation is always doubled!

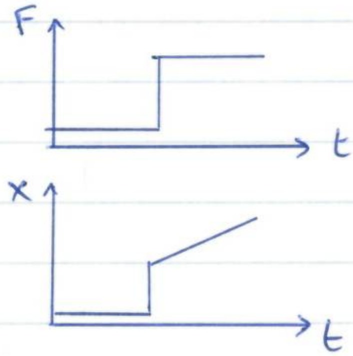
Elements of modelling

Perfect spring , perfect elastic

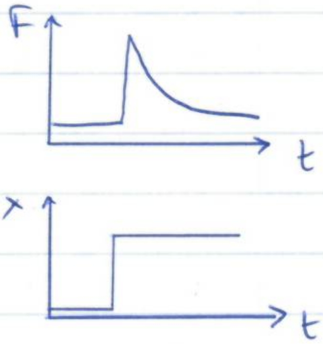
$F_{applied} = kx, \quad x = \frac{F}{k}$

Note three manifestations of viscoelasticity

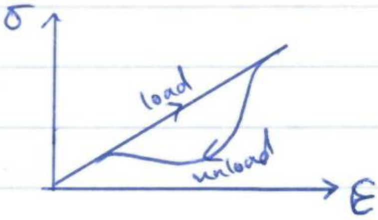
1) Creep



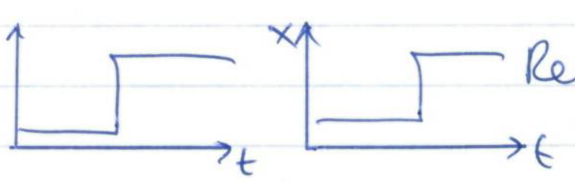
2) Relaxation



3) Hysteresis:

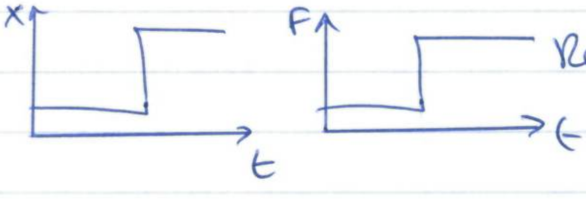


Back to spring: Applied F force



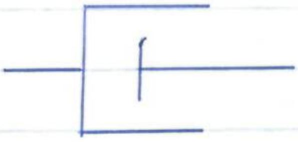
Response def.

Applied deformation



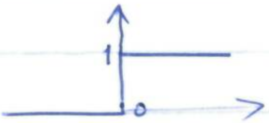
Response force

Perfect dashpot

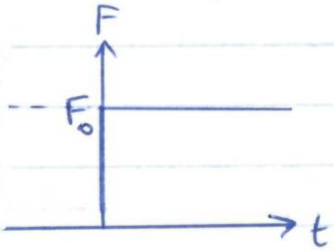


$$F_{applied} = \underset{\uparrow \text{dashpot constant}}{c}\,\frac{dx}{dt}$$

A: $F = F_0 \underbrace{\Theta(t)}_{\text{Heaviside step } f^n}$



A:



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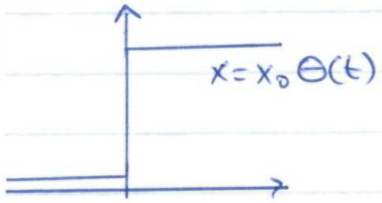
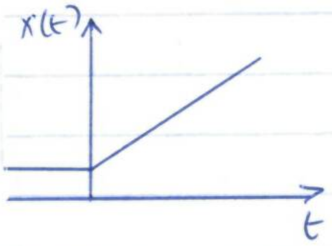
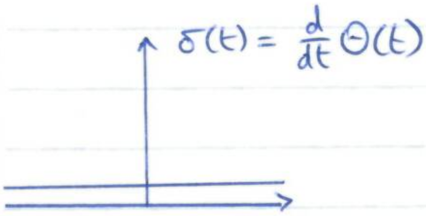


R:

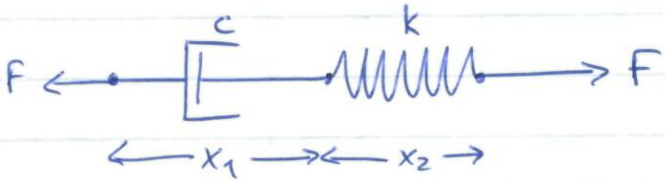


R:



Let us consider simple viscoelastic models

Maxwell's model



$$\underset{\uparrow \text{Total deformation}}{x_i^{Total}} = \underset{\uparrow \text{eq}^{\underline{m}} \text{ length}}{x_i^{Eq^{\underline{m}}}} + \underset{\uparrow \text{deformation}}{x_i}$$

For dashpot, $F = c\dfrac{dx_1}{dt} = c\dfrac{dx_1^T}{dt}$

For spring, $F = k\left(x_2^T - x_2^E\right) = kx_2$

$x^T = x_1^T + x_2^T \Rightarrow \underline{\dot{x} = \dot{x}_1 + \dot{x}_2}$

Hence $\frac{dF}{dt} = k\frac{dx_2}{dt}$

and $\frac{dx_2}{dt} + \frac{F}{c} = \frac{dx}{dt}$ ...... $(*)$

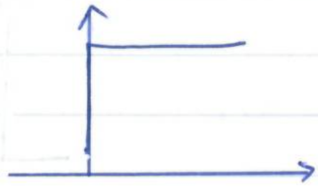
$$\Rightarrow \boxed{\frac{dx}{dt} = \frac{F}{c} + \frac{dF/dt}{k}}$$

because the force F is the same.

This eq^n ↑ interrelates force F(t) and deformation x(t).

Creep:

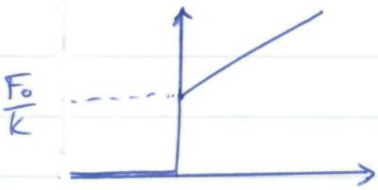
A :



$F = F_0\,\Theta(t)$

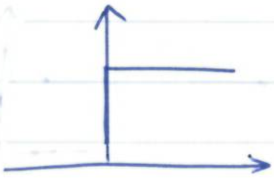
from $(*)$: $\frac{dx}{dt} = \frac{F_0}{c}\Theta(t) + \frac{1}{k}F_0\,\delta(t)$

R :



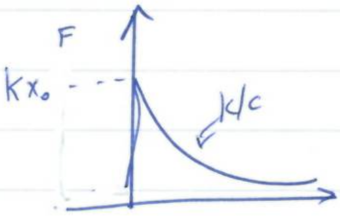
$x(t) = F_0\left(\frac{1}{k} + \frac{t}{c}\right)\Theta(t)$

A :



$x = x_0\,\Theta(t)$

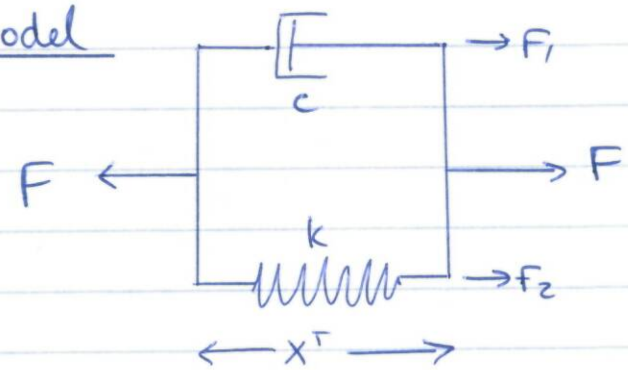
R



$F(t) = kx_0 \exp\left[-\left(\frac{k}{c}\right)t\right]\Theta(t)$

from $\frac{dF}{dt} = kx_0\,\delta(t) - \frac{Fk}{c}$

Voigt model



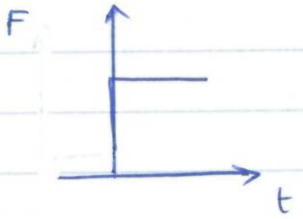
$x_1^T = x_2^T = x^E + x,$ total force $= F = F_1 + F_2$
and $x = x_1 = x_2$

Since $F_1 = c\dfrac{dx}{dt}$ and $F_2 = kx,$

we get $\boxed{F = kx + c\dfrac{dx}{dt}}$

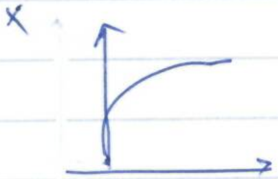
initial condition:
$x(t=0) = 0$ for any applied force because
dashpot prevents any immediate deformation.

A:



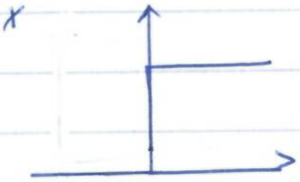
$F = F_0\,\Theta(t)$

R:



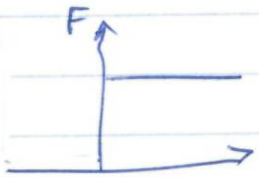
$x(t) = \dfrac{F_0}{k}\left(1 - e^{-\frac{k}{c}t}\right)\Theta(t)$

A:



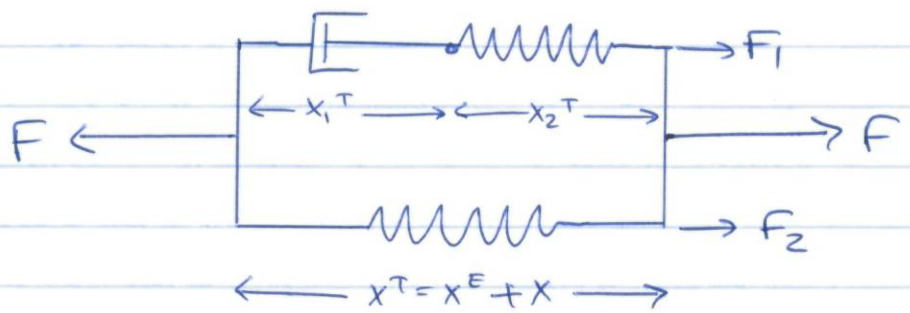
$x = x_0\,\Theta(t)$

R



$F = cx_0\,\delta(t) + kx_0\,\Theta(t)$

Kelvin model



$$x^T = x_1^T + x_2^T$$

$$F_1 = c\frac{dx_1}{dt} = k_1 x_2 \qquad \text{(as in the Maxwell model)}$$

$$F_2 = k_2 x$$

$$F = F_1 + F_2 \qquad \text{(as in the Voigt model)}$$

So $$\frac{dx}{dt} = \frac{dx_1}{dt} + \frac{dx_2}{dt} = \frac{F_1}{c} + \frac{dF_1/dt}{k_1}$$

But $$F_1 = F - F_2 = F - k_2 x$$

$$\Rightarrow \frac{dF_1}{dt} = \frac{dF}{dt} - k_2\frac{dx}{dt}$$

$$\Rightarrow \frac{dx}{dt} = \frac{F - k_2 x}{c} + \frac{1}{k_1}\left(\frac{dF}{dt} - k_2\frac{dx}{dt}\right)$$

$$F + \left(\frac{c}{k_1}\frac{dF}{dt}\right) = k_2\left[x + \frac{c}{k_2}\left(1 + \frac{k_2}{k_1}\right)\frac{dx}{dt}\right]$$

Introducing $\tau_\varepsilon = \frac{c}{k_1}$ and $\tau_\sigma = \frac{c}{k_2}\left(1 + \frac{k_2}{k_1}\right) = c\left(\frac{1}{k_1} + \frac{1}{k_2}\right)$

very likely to be on exam

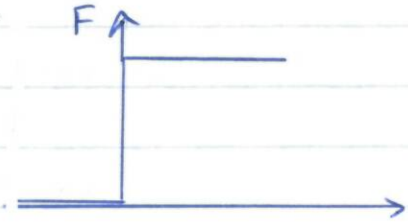
we get

$$\boxed{F + \tau_\varepsilon \frac{dF}{dt} = k_2\left(x + \tau_\sigma \frac{dx}{dt}\right)}$$

force relaxes with τ_ε

x relaxes with τ_σ.

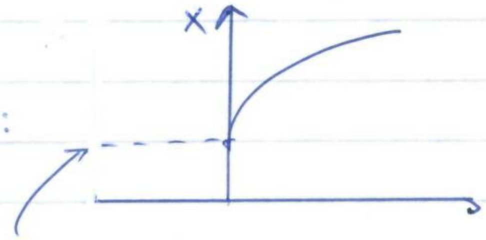
A:



$F = F_0 \Theta(t)$

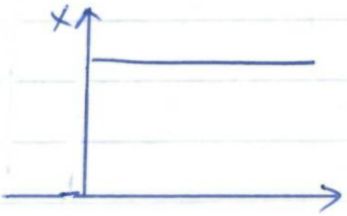
$x(t) = \frac{F_0}{k_2}\left[1 - \left(1 - \frac{\tau_\varepsilon}{\tau_\sigma}\right)\exp\left(-\frac{t}{\tau_\sigma}\right)\right]\Theta(t)$

R:



$\frac{\tau_\varepsilon F_0}{k_2 \tau_\sigma}$

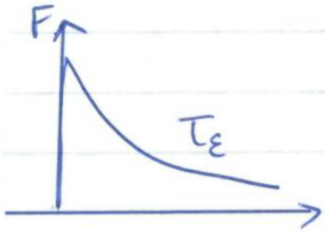
A:



$x = x_0 \Theta(t)$

$F = k_2 x_2\left[1 - \left(1 - \frac{\tau_\sigma}{\tau_\varepsilon}\right)\exp\left(-\frac{t}{\tau_\varepsilon}\right)\right]\Theta(t)$

R:



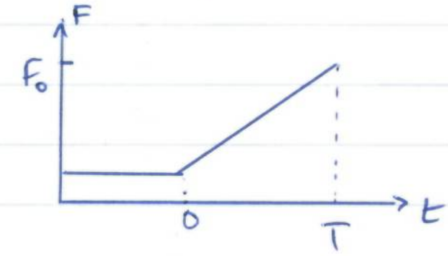
This response incorporates both properties of the Voigt and Maxwell models. Additionally, there is no unphysical behaviour like δ-f^n in stress response (as in Voigt model)

Viscoelasticity in bone

The stress does not depend only on the current value of the strain, but also on whether the strain was applied quickly or slowly.

Let us examine it quantitatively using the Kelvin model.

Apply



$$F = F_0 \frac{t}{T}$$

$\frac{dF}{dt} = \frac{F_0}{T}$, so using the eqⁿ for Kelvin model, we get

$$k_2\left(x + \tau_\sigma \frac{dx}{dt}\right) = F + \tau_\varepsilon \frac{dF}{dt} = F_0 \frac{t}{T} + \frac{\tau_\varepsilon F_0}{T}$$

or $$x + \tau_\sigma \frac{dx}{dt} = \frac{Ft}{k_2 T} + \frac{\tau_\varepsilon F_0}{k_2 T}$$ with $x(t=0) = 0$.

and if we have an eqⁿ of the form

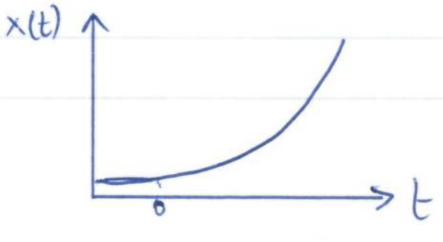
$$x + a\frac{dx}{dt} = bt + e,$$

the solⁿ is

$$x = bt + (e - ab)\left(1 - \exp\left(-\frac{t}{a}\right)\right)$$

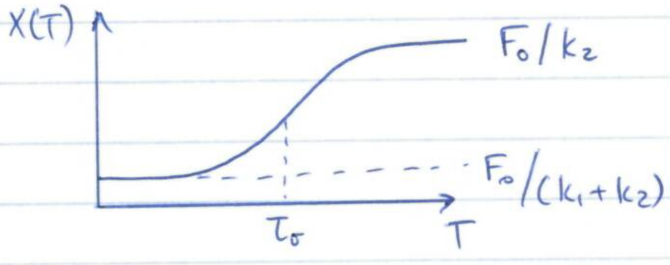
So our solⁿ is

$$x = \frac{F_0 t}{k_2 T} - \frac{cF_0}{k_2^2 T}\left(1 - \exp\left(-\frac{t}{\tau_\sigma}\right)\right) \quad 0<t<T$$



at the end of T,

$$x(t=T) = \frac{F_0}{k_2} - \frac{cF_0}{k_2^2 T}\left(1-\exp\left(-\frac{T}{\tau_\sigma}\right)\right)$$

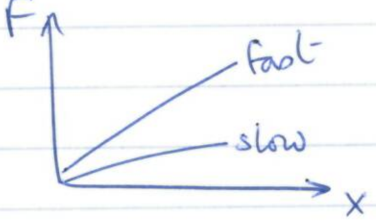


Applying force quickly or slowly means

$$T \gg \tau_\sigma \quad \text{or} \quad T \ll \tau_\sigma$$

In these limits, $x(T) \rightarrow \frac{F_0}{k_2}$ or $x(T) \rightarrow \frac{F_0}{k_1+k_2}$

The deformation is less if force applied quickly!
This is in agreement with the experimental result!



Bone fractures: if bones are stiff, they absorb little energy before the fracture. Compromise is needed. The femoral bone is about 2/3 as stiff in children as in adults and requires 50% more energy for movement. For children, efficiency is less important than fractures.

Energy of fractures

femur: ultimate compressive stress (UCS) = 170 MPa

UCS is reached when there is a force of

$$\frac{170\,\text{MPa}}{370\,\text{mm}^2} = 56{,}000\,\text{N} \approx 6\ \text{tons} \approx 80\ \text{body weight}$$

fortunately we are quite good designed!

<u>But</u> energy needed?

$$PE = \frac{(UCS)^2}{2Y}\cdot \overset{\swarrow\text{volume}}{V} = \frac{(UCS)^2}{2Y} A\cdot L = 133\,\text{J}$$

If we fall, potential energy available "if I sit on the table then fall"

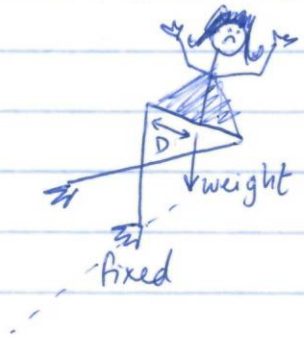
$$PE = mg\Delta h = 70\,\text{kg}\cdot 10\,\text{ms}^{-2}\cdot \overbrace{(0.9\text{m} - 0.1\text{m})} = 550\,\text{J}.$$

If all of this energy will be transferred to the bone
$\Rightarrow$ #FRACTURE.

Learn aikido · (make muscles absorb)

Breaking of bones by bending

Let us consider the example of one foot pinned at the ankle while the other foot is slipping.



$$\sigma(y) = Y\left(\frac{y}{R}\right)$$

$$\text{stress}\quad \sigma = Y\frac{\overset{\leftarrow\text{diameter of the bone}}{d}}{\underset{\uparrow\text{radius of curvature}}{2R}} > UBS \leftarrow \text{ultimate bending stress.}$$

$$\text{Using}\quad \frac{1}{R} = \frac{M_B}{YI_A} \Rightarrow M_B = \frac{YI_A}{R} = \frac{2\sigma I_A}{d}$$

see diagram earlier

So $|M_B| = D\left(W_{body} - W_{leg}\right) \geqslant \frac{2\,UBS\,I_A}{d}$

for the bone of radius $a = \frac{d}{2}$,

$$I_A = \frac{\pi a^4}{4}$$

$$D \geqslant \frac{\pi a^3}{4} \frac{UBS}{(W_B - W_L)} \approx 25\,\text{cm}$$

6 CHEMOTAXIS

Diffusion:

The flux J is proportional to the gradient of the concentration.

In one dimension, $J = -D\frac{\partial C}{\partial x}$ where C = concentration
D = diffusion const.

Transport occurs from high to low concentration.

Conservation eq^n: $\frac{\partial}{\partial t}\int_{x_0}^{x_0+\Delta x} C(x,t)\,dx = J(x_0,t) - J(x_0+\Delta x, t)$

$\Delta x \to 0$ and use $J = -D\frac{\partial C}{\partial x}$ to give

$$\frac{\partial C}{\partial t} = -\frac{\partial J}{\partial x} = \frac{\partial}{\partial x} D\frac{\partial C}{\partial x}$$

$$\text{or } \underbrace{\frac{\partial C}{\partial t} = D\frac{\partial^2 C}{\partial x^2}} \quad \text{if } D \text{ constant}$$

(also heat eq^n!)

Reaction diffusion

Consider now diffusion in 3D. Let S be an arbitrary surface enclosing volume V.

Conservation law: rate of change in V = flow across S
+ material created in V.

$$\frac{\partial}{\partial t}\underbrace{\int_V \underbrace{C(\underline{x},t)}_{\text{concentration}}\,dv}_{\text{mass}} = -\int_S \underline{J}\,d\underline{s} + \int_V f(\underline{x},t)\,dv$$

Applying the divergence thm $\left(\int_V \operatorname{div} \underline{J} \, dv = \int_S \underline{J} \, ds \right)$
to give

$$\int_V \left[\frac{\partial C}{\partial t} + \nabla \cdot \underline{J} - f(\underline{x}, t) \right] dv = 0$$

Since V is arbitrary $\frac{\partial c}{\partial t} + \nabla \cdot \underline{J} = f$

For classical diffusion $\underline{J} = -D \nabla C$

$$\rightarrow \boxed{\frac{\partial C}{\partial t} = f + \nabla(D \nabla C)}$$ general reaction diffusion eq^n.

<u>Example</u> In an ecological contest, f could represent the birth-death process and c could be the population density, $c = n$.
With logistic growth, $f = \underset{\text{reproduction rate}}{r} n \left(1 - \frac{n}{\underset{\text{carrying capacity of the environment}}{k}}\right)$

$$\frac{\partial n}{\partial t} = rn\left(1 - \frac{n}{k}\right) + \underset{\text{const. diffusion coeff.}}{D} \nabla^2 n$$

Chemotaxis

Chemotaxis is a type of transport (taxis) which is the phenomenon in which cells, bacteria, and other single cell or multicellular organisms direct their movement according to a certain chemical (pheromone) in the environment.

Examples:
- for bacteria, swimming towards food
- or fleeing from poison
- movement of sperm towards the egg.
- students moving towards nice perfume

Chemotaxis plays an important role in

- wound healing
- cancer growth
- leucocytes movement

Let us suppose that the presence of a gradient of an attractant $a(\underline{x}, t)$ gives rise to a movement. The flux of cells will increase with $n(\underline{x}, t)$. Hence, the chemotactic flux $J = n\chi(a)\nabla a$

$\chi(a)$: f^n of attraction concentration.

Using conservation eq^n:

$$\frac{\partial n}{\partial t} + \nabla \cdot \underline{J} = f(n)$$

and $\underline{J} = \underline{J}_{diff} + \underline{J}_{chem} = -\nabla(D\nabla n) + n\chi(a)\nabla a$

We get: $$\boxed{\frac{\partial n}{\partial t} = f(n) - \nabla n\chi(a)\nabla a + \nabla(D\nabla n)}$$ a general reaction diffusion chemotaxis eq^n.

Since $a(\underline{x}, t)$ is a chemical, it can also diffuse and be produced:

$$\frac{\partial a}{\partial t} = \underbrace{g(a,n)}_{\text{Source term}} + \nabla D_a \nabla a$$

Normally $D_a \gg D$

Keller and Segel model for slime mould (1971)

$$g(a,n) = hn - ka$$

hn: production of attractant, proportional to n

ka: decay of attractant activity

for simplicity, set $f(n)$, so mould production rate was negligable.

$\chi(a) = \chi_0$ - constant.

Then in 1D,

$$\frac{\partial n}{\partial t} = D\frac{\partial^2 n}{\partial x^2} - \chi_0 \frac{\partial}{\partial x}\left[n \frac{\partial a}{\partial x}\right]$$

$$\frac{\partial a}{\partial t} = hn - ka + D_a \frac{\partial^2 a}{\partial x^2}$$

where a = food concentration

Note: whereas a diffusion is generally stabilising, chemotaxis can be destabilising and lead to pattern formation.

Model building in 2D (Experiments of Budrene & Berg 1991)

1) The bacteria diffuse and move chemotactically. They proliferate and become dead. The chemoattractant diffuses, produced by bacteria, and can be uptaken by bacteria.
The stimulant (food) diffuses and can be consumed by bacteria

2) $$\begin{pmatrix}\text{rate of change}\\ \text{of cell density}\\ n\end{pmatrix} = \begin{pmatrix}\text{diffusion}\\ \text{of } n\end{pmatrix} + \begin{pmatrix}\text{chemotaxis}\\ \text{of } n \text{ to } c\end{pmatrix} + \begin{pmatrix}\text{proliferation}\\ \text{or death}\\ \text{of } n\end{pmatrix}$$

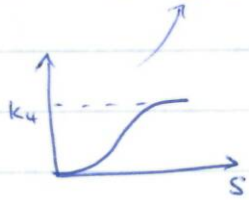
$$\begin{pmatrix}\text{rate of change}\\ \text{of chemoattractant}\\ \text{density, } c\end{pmatrix} = \begin{pmatrix}\text{diffusion}\\ \text{of } c\end{pmatrix} + \begin{pmatrix}\text{production}\\ \text{by } n\end{pmatrix} - \begin{pmatrix}\text{uptake}\\ \text{by } C\end{pmatrix}$$

$$\begin{pmatrix}\text{rate of change}\\ \text{of stimulant}\\ S\end{pmatrix} = \begin{pmatrix}\text{diffusion}\\ \text{of } S\end{pmatrix} - \begin{pmatrix}\text{uptake of}\\ S \text{ by } n\end{pmatrix}$$

Chemotaxis $\nabla \cdot \underline{J}_{chemo} = -\nabla\left[\chi(n,c)\nabla c\right]$

1995 Woodward suggested: $\chi(n,c) = \dfrac{k_1 n}{(k_2+c)^2}$ k_i constants $i = 1, \dots, 9$

Proliferation Cell growth or death $= k_3 n \left(\underbrace{k_4 \dfrac{S^2}{k_9 + S^2}} - n \right)$



Stimulant consumption $= k_8 n \dfrac{S^2}{k_9 + S^2}$

Chemoattractant production and consumption $= k_5 S \dfrac{n^2}{k_6 + n^2} - k_7 n c$

Mathematical model for bacterial pattern formation:

$$\frac{\partial n}{\partial t} = D_n \nabla^2 n - \nabla\left[\frac{k_1 n}{(k_2+c)^2}\nabla c\right] + k_3 n\left[k_4 \frac{S^2}{k_9+S^2} - n\right]$$

$$\frac{\partial c}{\partial t} = D_c \nabla^2 n + k_5 S \frac{n^2}{k_6 + n^2} - k_7 n c$$

$$\frac{\partial S}{\partial t} = D_S \nabla^2 S - k_8 n \frac{S^2}{k_9 + S^2}$$

Bacterial pattern formation (analytical treatment)

Assume zero flux boundary conditions and uniform distribution of stimulant. Consider one-dimensional case:

$$\frac{\partial u}{\partial t} = d\frac{\partial^2 u}{\partial x^2} - \alpha \frac{\partial}{\partial x}\left[\frac{u}{(1+v)^2}\frac{\partial v}{\partial x}\right] \quad \left\{ \begin{array}{l}\text{bacterial} \\ \text{concentration}\end{array}\right.$$

$$\frac{\partial v}{\partial t} = \frac{\partial^2 v}{\partial x^2} + \frac{u^2}{\mu + u^2} \qquad (*) \quad \left\{ \begin{array}{l}\text{chemoattr.} \\ \text{concentration}\end{array}\right.$$

(dimensionless form)

The nontrivial $u_0 \neq 0$ spatial independent solution with $u(x,0) = 1$, $v(x,0) = 0$ is

$$u(x,t) = 1 \quad \text{and} \quad v = \frac{t}{\mu+1}$$

We look for solutions of the form

$$\left.\begin{array}{l} u(x,t) = 1 + \varepsilon f(t) \sum_k e^{ikx} \\ v(x,t) = \frac{t}{\mu+1} + \varepsilon g(t) \sum_k e^{ikx} \end{array}\right\} \quad 0 < \varepsilon \ll 1. \quad (**)$$

Set $f(0) = 0$, $g(0) = 0$.

Substitute $(**)$ in $(*)$, linearise in ε, then for each k we obtain:

$$\frac{dF}{d\tau} = -dk^2 F(\tau) + \alpha(\mu+1)^2 \frac{k^2}{\tau^2} G(\tau)$$

$$\frac{dG}{d\tau} = -k^2 G(\tau) + \frac{2\mu}{(\mu+1)^2} F(\tau)$$

where $\tau = \mu + 1 + t$, $F(\tau) = f(t)$, $G(\tau) = g(t)$

[Tip for h/w: $(1+\varepsilon)^2 \approx 1+2\varepsilon$

$$\frac{1}{1+\varepsilon} \approx 1-\varepsilon$$

equate coeffs for k in all exponents]

We solve first eq$^{\underline{n}}$ for $G(\tau)$. We find $\frac{dG}{d\tau}$.
Then sub G and $dG/d\tau$ into the second eq$^{\underline{n}}$

$$\frac{d^2F}{d\tau^2} + \underbrace{\left[k^2(d+1) + \frac{2}{\tau}\right]}_{D(\tau)} \frac{dF}{d\tau} + \underbrace{k^2\left(dk^2 + \frac{2d}{\tau} - \frac{2\alpha\mu}{\tau^2}\right)}_{N(\tau)} F = 0$$

We have $G\left(F(t), \frac{dF}{d\tau}\right)$, $\frac{dG}{dt}\left(F(\tau), \frac{dF}{d\tau}, \frac{d^2F}{d\tau^2}\right)$.

$$\Rightarrow \frac{d^2F}{d\tau^2} + D(\tau)\frac{dF}{d\tau} + N(\tau)F = 0$$

Note: $D(\tau)$ is always > 0, $N(\tau)$ can be $\begin{cases} >0 \\ =0 \\ <0 \end{cases}$.
With large τ, $N(\tau) > 0$.

Over some small interval in time, we assume $D(\tau)$ and $N(\tau) \approx$ const.

Solving:

$$F(\tau) = L_1 e^{\lambda_+ \tau} + L_2 e^{\lambda_- \tau} \quad \left(\lambda_\pm = \frac{1}{2}\left[-D(\tau) \pm \sqrt{D^2 - 4N(\tau)}\right]\right)$$

$Re(\lambda_-) < 0$ decaying
$Re(\lambda_+)$ depends on sign of $N(\tau)$.

If α is sufficiently large, then for small τ, $N(\tau) < 0$.

$N(\tau) < 0 \Rightarrow \lambda_+ > 0 \Rightarrow$ increasing $F(\tau)$.

As τ increases, $N(\tau)$ will also increase through 0 and become > 0.

So there is $\tau_{critical}$, s.t. for $\tau < \tau_{critical}$, one component of F is increasing, and for $\tau > \tau_{critical}$, all components of F are decaying.

At $\tau = \tau_{critical}$, $F(\tau)$ should have maximum.
The $\tau_{critical} \approx \tilde{\tau}_{critical}$, where $N(\tilde{\tau}_{critical}) = 0$

$$\tilde{\tau}_{critical} = \frac{1}{k^2}\left[-1 + \sqrt{\frac{1+2\alpha\mu k^2}{D}}\right]$$

At $\tau_{critical}$, $\frac{dF}{d\tau} = 0$ $\quad (\because \max)$

so eq^n^ for F is $\left.\frac{d^2F}{d\tau^2}\right|_{\tau=\tau_{critical}} = -N(\tau_{critical})F$.

at $\tau = \tau_{critical}$, $\frac{d^2F}{d\tau^2} < 0 \Rightarrow N(\tau_{critical}) > 0$

$\Rightarrow \tau_{critical} > \tilde{\tau}_{critical} \Rightarrow \tilde{\tau}_{critical}$ is the minimum estimation of $\tau_{critical}$.

But $\tau_{critical} \approx \tilde{\tau}_{critical}$, $N(\tau_{critical}) \approx 0$

$\frac{d^2F}{d\tau^2}$ is small.

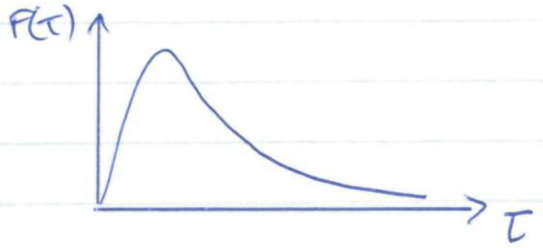
We solve eq^n^ for F using $\frac{d^2F}{d\tau^2} = 0$

$$\Rightarrow D(\tau)\frac{dF}{d\tau} + N(\tau)F = 0.$$

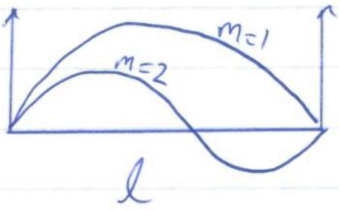
Solving:
$$F(\tau) = \left[\frac{(d+1)k^2\tau_0 + 2}{(d+1)k^2\tau + 2}\right]^{\alpha\mu k^2 - \frac{2d(d-1)}{(d+1)^2}} \cdot \left[\frac{\tau}{\tau_0}\right]^{\alpha\mu k^2} e^{\left[\frac{d}{d+1}\right]k^2(\tau_0-\tau)}$$

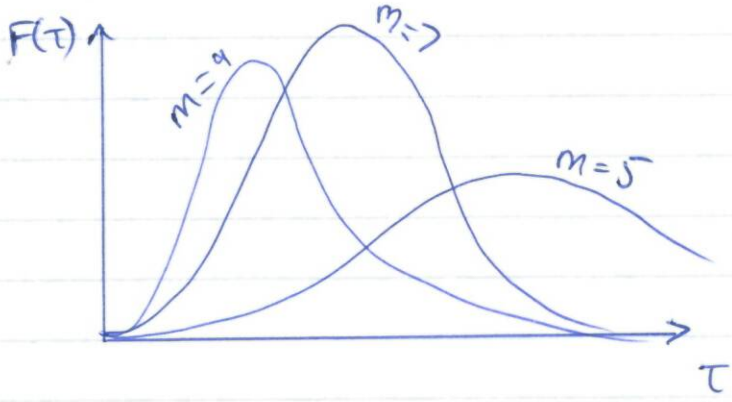
where $F(\tau_0) = 1$, τ_0 const.

For $k=1.3$, this looks like



$k^2 = \frac{m^2\pi^2}{l}$ (k is the frequency)



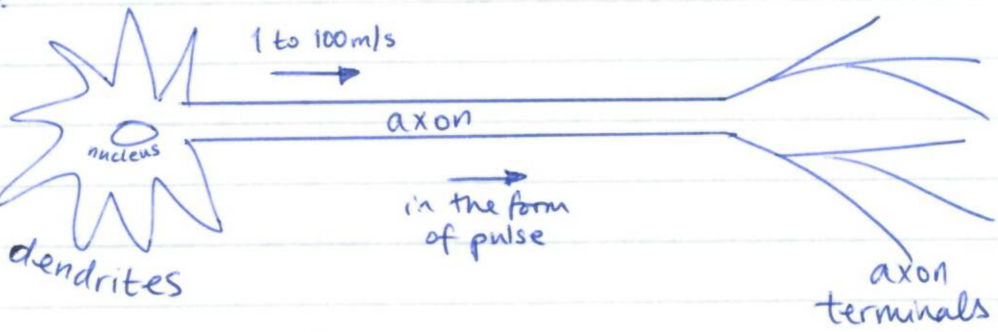


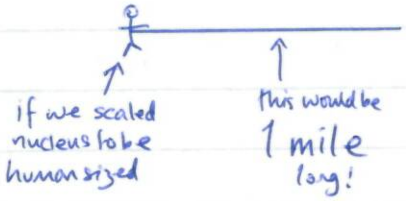
appearance of low frequency pattern.

7 THE BRAIN

The human brain contains ≈ 100bn neurons, linked with up to 10,000 synaptic connections each.

Neuron:



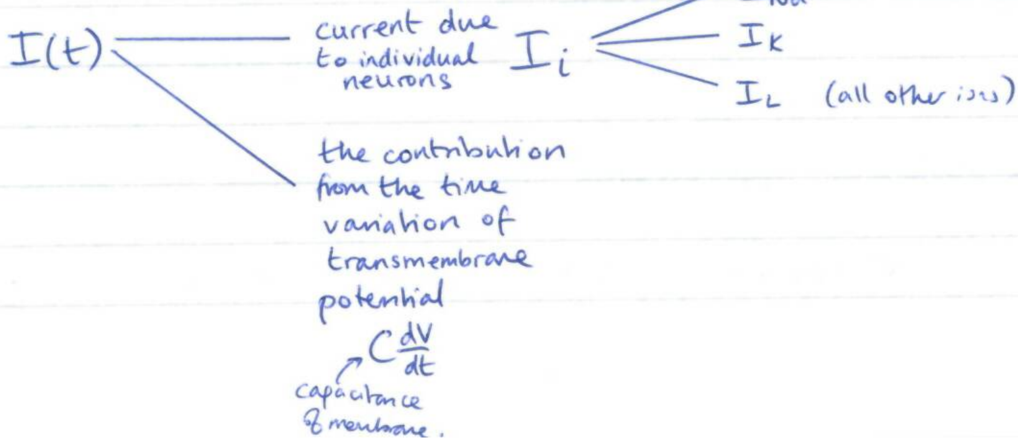


Some neurons emit action potentials constantly (100 pulses / sec), periodically, or irregularly. Other neurons are silent most of the time but then emit burst of action potentials.

Hodgkin and Huxley (1952) made a model of neuron firing (Nobel Prize):

ions: potassium K^+, sodium Na^+

Let us take the positive direction for the membrane current I outward from the axon.



$$\Rightarrow I(t) = C\frac{dV}{dt} + I_i$$

where, based on experimental data,

$$C\frac{dV}{dt} = -\underset{\substack{\uparrow \\ \text{conductance}}}{g_{Na}} m^3 h(V - V_{Na}) - g_K n^4 (V - V_K) - g_L (V - V_L) + I_a$$

equilibrium potentials

where m, n, h are variables between 0 and 1.

$$\frac{dm}{dt} = \alpha_m(V)(1-m) - \beta_m(V)m$$

with same n, h , and I_a externally applied current

If $I_a = 0 \Rightarrow$ excitable — small pertubations $\Rightarrow$ nothings

pertubations larger than some threshold $\Rightarrow$ large excursion independent of the initial perturbation.

If $I_a \neq 0 \Rightarrow$ limit cycle — periodic generation of impulses like in the experiment.

FitzHugh-Nagumo model

(the model of H.H. model)

The system is approximated by 2 variables

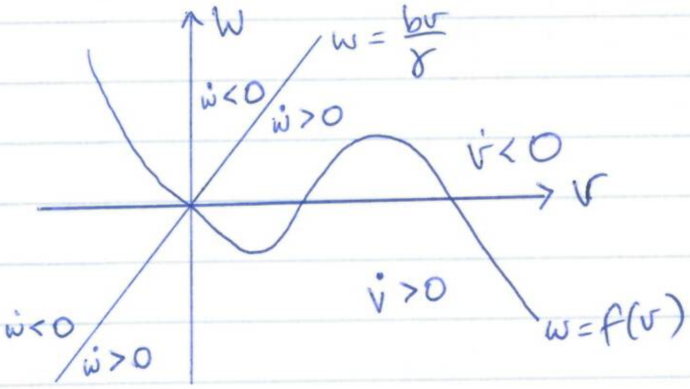
v (old V) and w (old m, n, h)

to give $$\begin{cases} \dfrac{dv}{dt} = f(v) - w + I_a \\ \dfrac{dw}{dt} = bv - \gamma w \end{cases}$$

where $f(v) = v(a-v)(v-1)$

and v plays the role of the membrane potential.

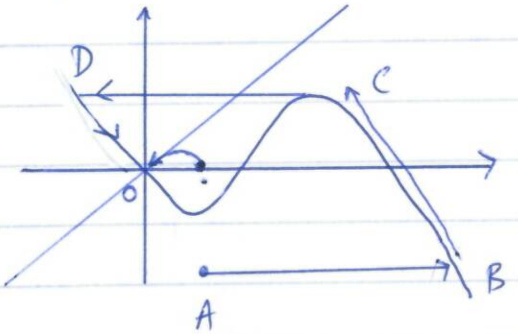
Analysis **$I_a = 0$**

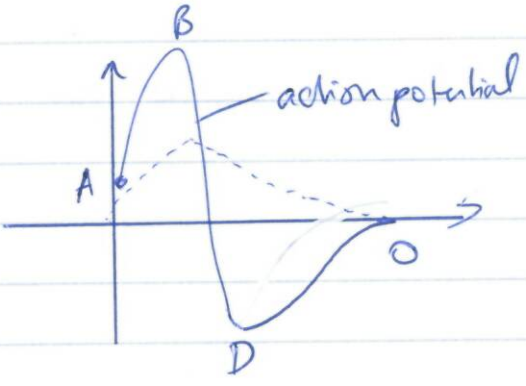


Two regimes are possible:
- excitable
- bistable.

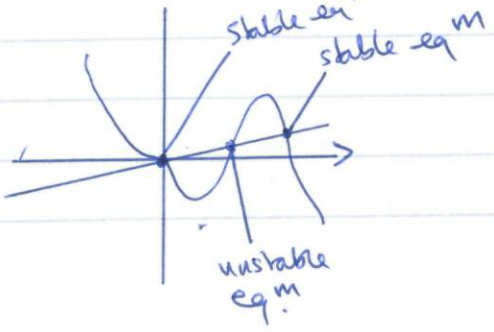
depending on a.

Excitable:





Bistable:

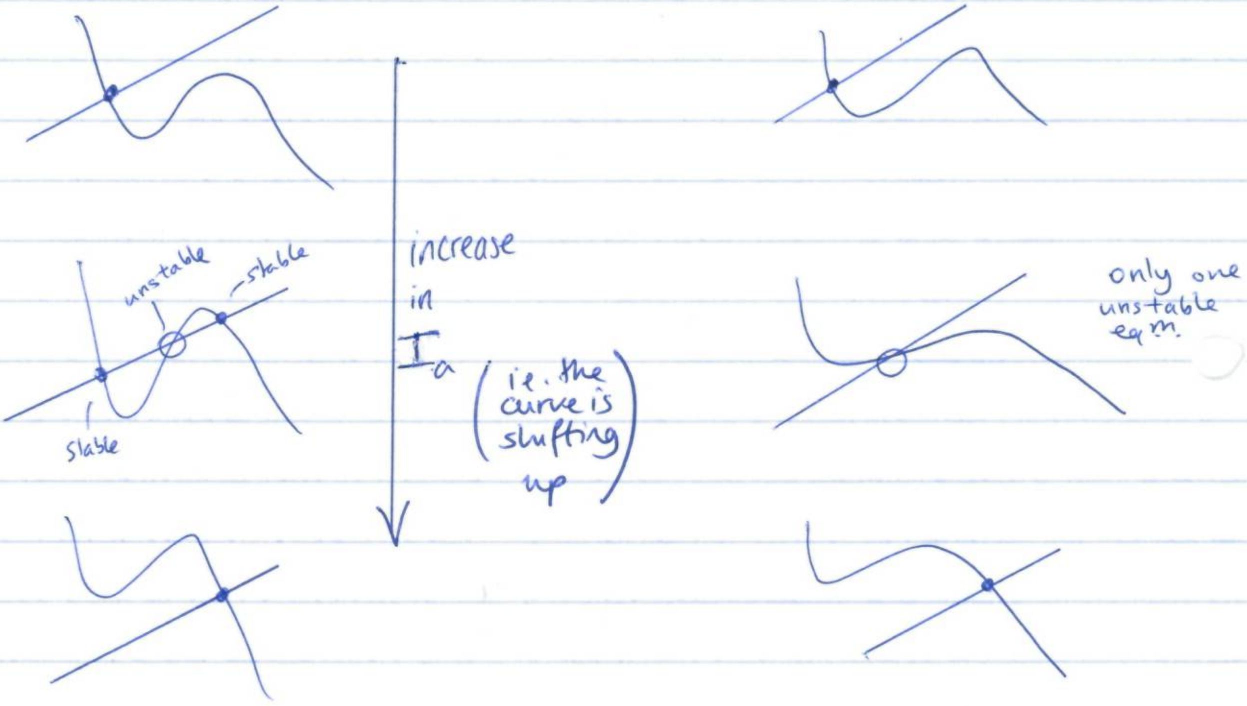


$I_a > 0$

Recall $w = f(v) + I_a$.

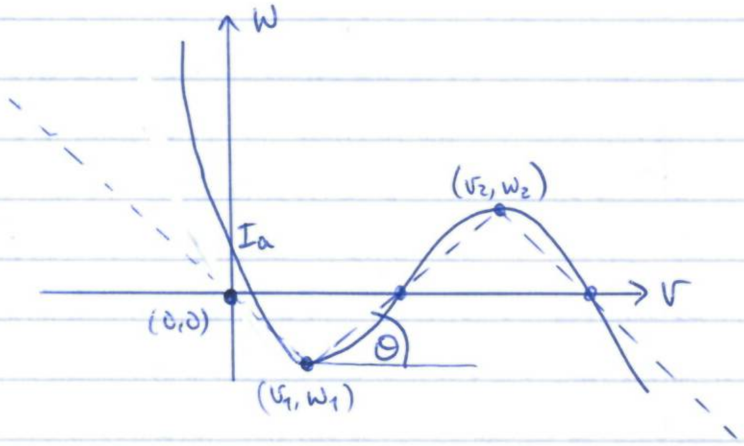
Scenario I

Scenario II



Further simplification

We approximate the v-nullcline by a piecewise linear f^n



The pos^n s of the min. and max. are obtained as

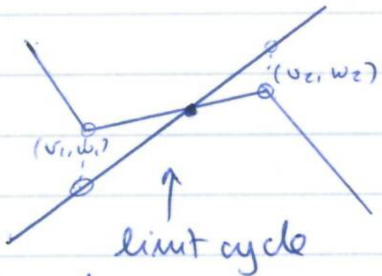
$$v_2, v_1 = \frac{1}{3}\left[a + 1 \pm \sqrt{(a+1)^2 - 3a}\right]$$

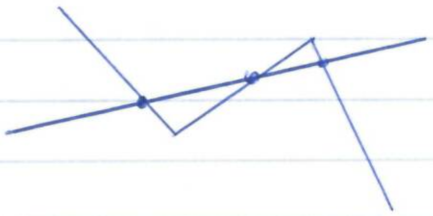
$$w_i = -v_i\,(a-v_i)(1-v_i) + I_a \qquad i=1,2$$

If we define an angle θ as in the graph,

$$\theta = \tan^{-1}\left(\frac{w_2-w_1}{v_2-v_1}\right)$$

we can have two possible situations





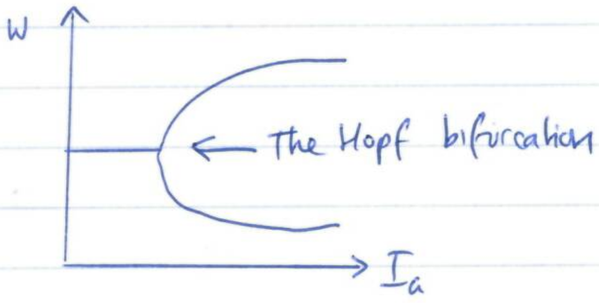
limit cycle

The gradient of v-nullcline should be less than gradient $\frac{b}{\gamma}$:

$$\tan\theta = \frac{w_2-w_1}{v_2-v_1} < \frac{b}{\gamma} \qquad \cdots (*)$$

So the property of this model is that it generates periodic pulses if I_a is in a req^{d} range $I_1 < I_a < I_2$ and $(*)$ holds.

Then if I_a is increased, the model undergoes a bifurcation.



The Hopf bifurcation theorem:

More generally, consider $\dfrac{du}{dt} = f(\underline{u}) \qquad \cdots (*)$

with a bifurcation parameter λ. If λ passes through λ_c, there is a bifurcation.

Let us suppose that $\underline{u}=0$ is a steady state of $(*)$, and that a linearisation about it gives a conjugate pair of eigenvalues,

$$\alpha(\lambda) = Re(\alpha) \pm i\, Im(\alpha),$$

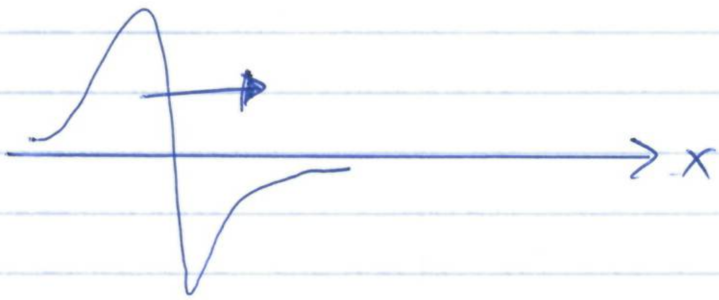
Now suppose that the largest real part of all eigenvalues exists and is such that in the neighbourhood of λ_c:

(1) $Re(\alpha) < 0$ if $\lambda < \lambda_c$
(2) $Re(\alpha) = 0$ and $Im(\alpha) \neq 0$ if $\lambda = \lambda_c$
(3) $Re(\alpha) > 0$ if $\lambda > \lambda_c$

Then, in a small neighbourhood of λ_c, $\lambda > \lambda_c$, the steady state is unstable and at least a.
The small amplitude limit cycle sol.ⁿ exists about $\underline{u}=0$.
Furthermore, the period of this limit cycle $T = 2\pi/\omega_0$, where $\omega_0 = Im(\alpha(\lambda_c))$.

Travelling waveforms:

$$\frac{\partial v}{\partial t} = f(v) - w + \frac{\partial^2 v}{\partial x^2}$$



In the diffusion eq^{n}, no travel waveforms are possible:

$$u(x-ct) \quad ; \quad \frac{\partial u}{\partial t} = -c\frac{\partial u}{\partial z} \quad ; \quad \frac{\partial u}{\partial x} = \frac{\partial u}{\partial z}$$

$$z = x-ct$$

$$\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial x^2} \implies -c\frac{\partial u}{\partial z} = D\frac{\partial^2 u}{\partial z^2}$$ because $u=u(z)$.

$$\rightarrow \quad u(z) = A + Be^{-cz/D}$$ A, B consts.

Since u should be bounded, $B=0$, and $u(z)=A$ is <u>not</u> a wave solution.

8 BLOOD

Blood dynamics

This is a macroscopic approach, i.e. any small volume contains a large n^{o} of particles.

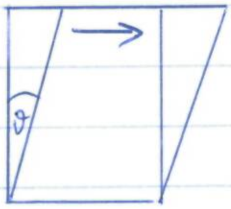
In a continuous medium, at any point (x, y, z), we have

pressure	$p(x,y,z)$
density	$\rho(x,y,z)$
velocity	$\underline{v}(x,y,z)$

ρ constant $\Rightarrow$ uncompressible, else compressible.

Fluids are 'sticky', this is a property of viscosity.
A shearing stress in Newtonian fluids is

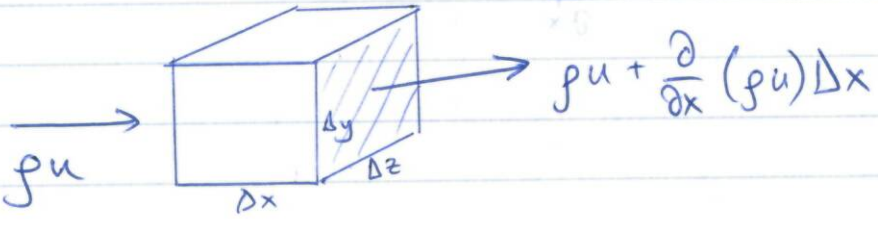
$$\sigma = \underset{\uparrow \text{viscosity}}{\mu}\, \varepsilon$$



The eq^{n} of motion (Navier-Stokes eq^{n}) is
$\underline{v} = (u, v, w)$ Only $u \neq 0$:

$$\underset{\substack{\text{for volume}\\ \text{unit}}}{\rho} \underbrace{\left[\frac{\partial u}{\partial t} + u\frac{\partial u}{\partial x}\right]}_{\substack{\text{mass}\\ \text{acceleration}}} = \underset{\substack{\text{force due}\\ \text{to pressure}}}{-\frac{\partial p}{\partial x}} + \mu \underbrace{\left(\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2} + \frac{\partial^2 u}{\partial z^2}\right)}_{\substack{\text{force due to}\\ \text{shearing stress}}} + \underset{\substack{\text{body}\\ \text{force, e.g.}\\ \text{gravity}}}{f_x}$$

Consider the mass flux into and out of some volume



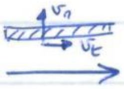
Conservation of the mass:

$$\frac{\partial \rho}{\partial t}\Delta x \Delta y \Delta z = \rho u \overbrace{\Delta y \Delta z}^{\text{square area}} - \left[\rho u + \frac{\partial}{\partial x}(\rho u)\Delta x\right]\overbrace{\Delta y \Delta z}^{\text{square area}}$$

$$\Rightarrow \quad \underbrace{\frac{\partial \rho}{\partial t} + \frac{\partial}{\partial x}(\rho u) = 0}_{} \quad \text{eq}^{n} \text{ of continuity}$$

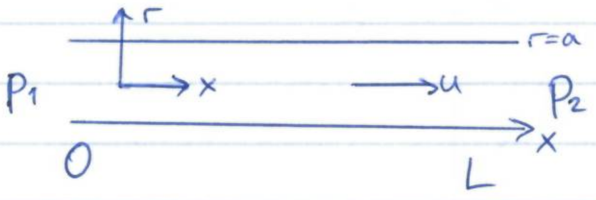
In 3D, $\frac{\partial \rho}{\partial t} = -\operatorname{div}(\rho \underline{v})$

b.c.s: on solid boundary, $\underset{\text{normal vel.}}{v_n} = 0$ and $\underset{\text{tgt vel.}}{v_t} = 0$ if $\mu \neq 0$



Poiseulle's law

Consider the motion of a fluid through a long cylindrical tube of length L, radius a, and two pressures at the ends $p_1 > p_2$



Assume steady flow $\frac{\partial}{\partial t} = 0$.

Assume $\rho =$ const, then $\frac{\partial u}{\partial x} = 0$ because $\frac{\partial \rho}{\partial t} = -\frac{\partial}{\partial x}(\rho u)$

The motion eq^n: $0 = -\frac{\partial p}{\partial x} + \mu \nabla^2 u$.

Let us consider cylindrical coordinates (x, r, θ), everything is symmetrical wrt θ.

In cylindrical coords,

$$\mu \nabla^2 u = \mu \frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial u}{\partial r}\right) = \frac{\partial p}{\partial x} = \frac{dp}{dx} \quad \left(\because u \text{ only in } x \text{ dir}^{\text{n}}\right)$$

$u = u(r)$.

Differentiating wrt x, $\frac{d^2p}{dx^2} = 0 \Rightarrow \frac{dp}{dx} = \text{const}$

$$\Rightarrow p = \text{const}\cdot x + \text{const}'.$$

Using $\left.\begin{array}{l} p = p_1 \text{ at } x=0 \\ p = p_2 \text{ at } x = L \end{array}\right\}$ $p = p_1 + \frac{(p_2 - p_1)}{L}x$

So $\frac{dp}{dx} = -\frac{p_1 - p_2}{L}$

$$\mu \frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial u}{\partial r}\right) = \frac{dp}{dx} = -\frac{p_1 - p_2}{L} = \text{const}.$$

$$\frac{d}{dr}\left(r\frac{\partial u}{\partial r}\right) = \frac{r}{\mu}\frac{dp}{dx}$$

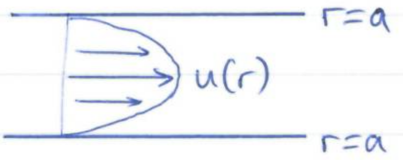
$$r\frac{\partial u}{\partial r} = \frac{r^2}{2\mu}\frac{dp}{dx} + A^{\text{const}}$$

$$u = \frac{r^2}{4\mu}\frac{dp}{dx} + A\ln r + B$$

$A = 0$ because u is regular at $r=0$.

$u = 0$ at $r = a \Rightarrow B = -\frac{a^2}{4\mu}\frac{dp}{dx}$

$$\Rightarrow u = -\frac{1}{4\mu}\frac{dp}{dx}(a^2 - r^2) = \underbrace{\frac{1}{4\mu}\frac{p_1 - p_2}{L}(a^2 - r^2)}$$



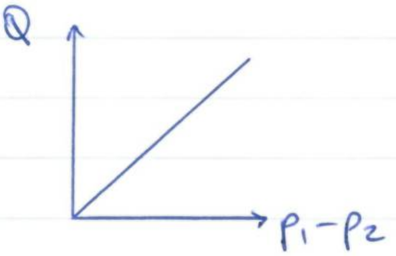
parabolic profile of velocity

Discharge of volume flux Q

In unit time per annular element $2\pi r dr$

$$Q = \int_0^a u 2\pi r dr = \int_0^a \frac{1}{4\mu}\frac{p_1-p_2}{L}(a^2-r^2)2\pi r dr$$

$$= \frac{\pi}{8}\frac{p_1-p_2}{\mu L}a^4$$



Properties of blood

Poiselle's law is so well established that it can be used for measurement of viscosity:

$$\mu_{blood} \approx 5\mu_{water} \quad \text{at } 37°C$$

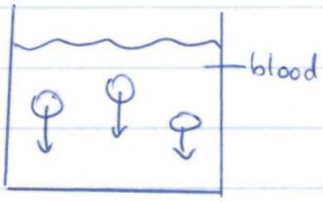
but in capillaries,

$$\mu_{blood} \approx \frac{3}{2}\mu_{water}$$

$$\text{Blood} \begin{cases} \text{plasma} \\ \text{blood cells} \begin{cases} \text{red} \\ \text{white} \end{cases} \end{cases}$$

Blood is a suspension with plasma as the suspending medium.
The density of red cells (erythrocytes) $\rho_e = 1.06$
〃 〃 〃 plasma $\rho_p = 1.03$

Consequently, if blood is allowed to stand in a container, the red cells will settle out of suspension towards the bottom at a certain rate = the erythrocyte sedimentation rate (ESR).



The maths behind this was by Stokes in 1851, and it's simple for <u>slow</u> motion (lamina~~te~~r flow)

The Reynolds number determines it:
$$R = \frac{\overset{\text{density}}{\rho}\,\overset{\text{velocity}}{v}\,\overset{\text{size}}{a}}{\underset{\text{viscosity}}{\mu}}$$

$R \ll 1$ slow motion - laminar flow
$R \gg 1$ fast motion - turbulent flow

For $R \ll 1$, a drag force F_D for slowly moving sphere is
$$F_D = 6\pi\mu \underset{\text{radius}}{a} v.$$

So for motion of red blood cells, by Newton's Second Law we get:
$$\overbrace{V\rho_e}^{m}\frac{dv}{dt} = \underset{\text{gravity}}{V\overset{\rho\,\text{red blood cells}}{\rho_e}g} - \underset{\text{buoyancy}}{V\overset{\rho\,\text{plasma}}{\rho_p}g} - \underset{\text{drag}}{6\pi\mu a v}$$

and $V = \frac{4}{3}\pi a^3$

For a steady rate of fall, $\frac{dv}{dt} = 0$.

$$\Rightarrow \text{ESR} = v_s = \frac{1}{6\pi\mu a}\frac{4}{3}\pi a^3(\rho_e - \rho_p)g$$

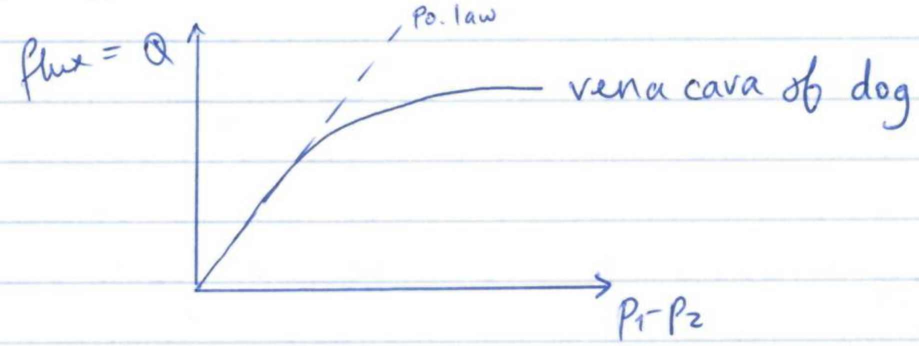
$$= \frac{2}{9\mu} a^2 (\rho_e - \rho_p) g$$

So ESR can be measured and in illness, ESR rises dramatically.

Why?

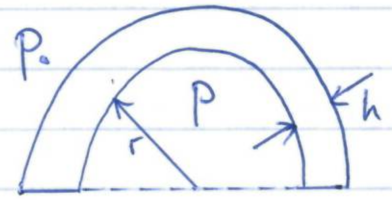
Because a is increased since red blood cells form aggregates

The steady flow of blood through a vessel:



This is because the vein is not a rigid tube but elastic (consider sucking Coke through a straw till it collapses)

Consider a cross-section of a blood vessel.



p - interior pressure
p_0 - exterior pressure

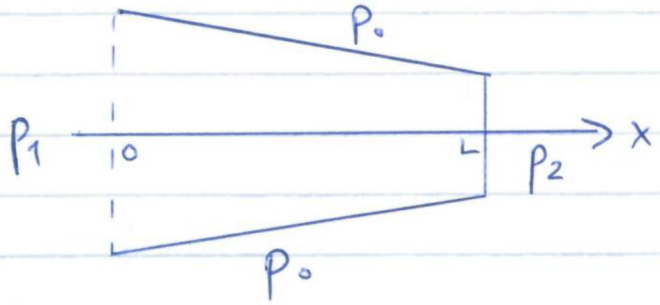
The downward force per unit length is $2th$, where t = tension per unit length per unit thickness.

The upward force is $(p-p_0)2r$. So $\underbrace{th = (p-p_0)r}_{\text{Young \& Laplacian relation}}$

Using the Hooke's Law for region of elasticity

$$t = Y\left(\frac{r-r_0}{r_0}\right)$$ r_0 = radius of relaxed vessel.

Now consider a long tube of non-constant radius



and the pressure is a f^n of x alone.

$p(x)$,
$p(0) = p_1$
$p(L) = p_2$

The tube is circular, so the Y-L relation tells us

$$p(x) - p_0 = \frac{t\,h}{r}$$

or $$p - p_0 = Y\left(\frac{r-r_0}{r_0}\right)\frac{h}{r} = \frac{Yh}{r_0}\left(1 - \frac{r_0}{r}\right) \qquad (**)$$

where r_0 is the eq^{m} radius.

The flow through the tube is assumed to obey Poisseille's law locally:

$$\text{flux} = Q = -\frac{\pi}{8\mu}\frac{dp}{dx}r^4$$

integrating: $$Q\underset{\int dx}{x} = \frac{\pi}{8\mu}\int_{p}^{P_1} \underbrace{r^4(p-p_0)}_{\substack{r \text{ as a } f^n \\ \text{of } p-p_0 \\ \because \text{ of } (**)}}\,dp$$ (minus disappears ∵ of flipped limits)

Changing $p' = p - p_0$

$$Qx = \frac{\pi}{8\mu} \int_{p-p_0}^{p_1-p_0} r^4(p')\, dp'$$

To find Q, we set $x = L$, $p = p_2$

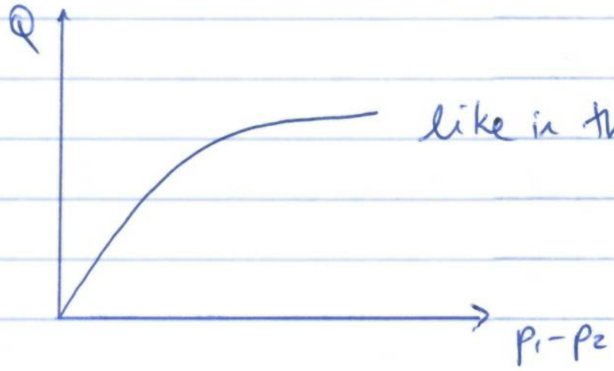
So $$Q = \frac{\pi}{8\mu L} \int_{p_2-p_0}^{p_1-p_0} r^4(p')\, dp'$$

When $p_1 - p_2$ is small and r^4 is not rapidly changing:

$$Q \sim \frac{\pi}{8\mu L} \underbrace{r^4(p_1-p_0)}_{f^n \text{ of } p_1-p_0}(p_1-p_2)$$

If (p_1-p_0) remains fixed, and $p_2 - p_0 \rightarrow -\infty$,

$$Q \rightarrow Q' = \frac{\pi}{8\mu L} \int_{-\infty}^{p_1-p_0} r^4(p')\, dp' \quad = \text{const.}$$



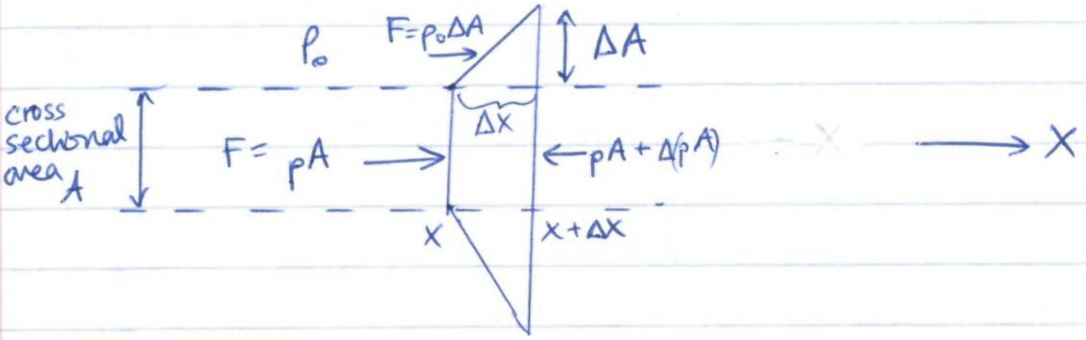
like in the experiment

Exam question!

The pulse wave

The flow of blood is pulsatile as a consequence of the heart beating. The heart produces a pressure wave, and this wave is the pulse felt in the wrist. This wave is not the same as the acoustic wave that one can hear. Such acoustic waves are from compressibility, whereas the pulse wave exists even for incompressible fluid due to the elasticity of blood vessels (Young 1808).

Consider an elastic tube



ρ is constant $\qquad p(x,t),\ u(x,t)$ – parallel to the tube axis.

The net force in the positive x dir^n on the volume element $(X, X+\Delta X)$ is:

$$pA + p_0 \Delta A - \left(pA + \Delta(pA)\right)$$

$$= pA + p_0 \frac{\partial A}{\partial x} \Delta X - \left[pA + \frac{\partial}{\partial x}(pA)\Delta X\right]$$

$$= -\frac{\partial}{\partial x}\left[(p - p_0)A\right] \Delta X$$

From the NS eq^n: $\rho A \Delta X \left[\frac{\partial u}{\partial t} + u \frac{\partial u}{\partial x}\right]$ is the inertia force

Hence, the eq^n of motion:

$$\rho A\left[\frac{\partial u}{\partial t} + u\frac{\partial u}{\partial x}\right] = -\frac{\partial}{\partial x}\left[(p-p_0)A\right] \quad \cdots\cdots (1)$$

Plus the eq^n of continuity:

$$\frac{\partial A}{\partial t} + \frac{\partial}{\partial x}(Au) = 0 \quad \cdots\cdots (2)$$

because $\frac{\partial}{\partial t}(A\,\Delta x) = uA - \left[uA + \frac{\partial}{\partial x}(uA)\,\Delta x\right]$

Plus a consequence of the Y-L relation

$$p - p_0 = \frac{Yh}{r_0}\left[1 - \frac{r_0}{r}\right] = \frac{Yh}{r_0}\left[1 - \left(\frac{A_0}{A}\right)^{1/2}\right] \quad \cdots\cdots (3)$$

when $A = \pi r^2$, $A_0 = \pi r_0^2$ (eq^m area of tube)

We linearise (1), (2) and (3) assuming that u, $p-p_0$, $A-A_0$ and their derivatives are small.

from (1) $$\rho A\frac{\partial u}{\partial t} = -\frac{\partial p}{\partial x}A - \cancel{(p-p_0)}\frac{\partial A}{\partial x} \quad \cdots\cdots (1')$$

So $$\rho\frac{\partial u}{\partial t} = -\frac{\partial p}{\partial x}$$

from (2) $$\frac{\partial A}{\partial t} + \overbrace{A_0\frac{\partial u}{\partial x}}^{A-A_0+A_0} = 0 \quad \cdots\cdots (2')$$

from (3) expanding RHS in Taylor series about $A = A_0$:

$$p - p_0 = \frac{Yh}{2r_0}\frac{1}{A_0}(A - A_0) \quad \cdots\cdots (3')$$

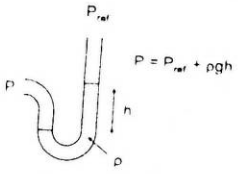


Fig. 7.1. Manometer

7.1.2 Measuring Pressure

One way of directly measuring pressure is with a manometer (Fig. 7.1). The measured pressure is that corresponding to the height of the fluid column plus the reference pressure, so

$$P = P_{ref} + \rho g h \tag{7.1}$$

The most common way to measure blood pressure is with a *sphygmomanometer* (sfig-muh-ma-nah'-mee-ter), which consists of a cuff, a squeeze bulb, and a meter that measures the pressure in the cuff (Fig. 7.2). The cuff is the balloon-like jacket placed about the upper arm above the elbow; this encircles the brachial artery. The cup of a stethoscope is placed on the lower arm, just below the elbow, to listen for the flow of blood. With no pressure in the cuff, there is normal blood flow and sounds are heard through the stethoscope. Gurgling sounds are heard after the cuff is pressurized with the squeeze bulb and then depressurized by releasing this pressure with a release valve in this bulb.

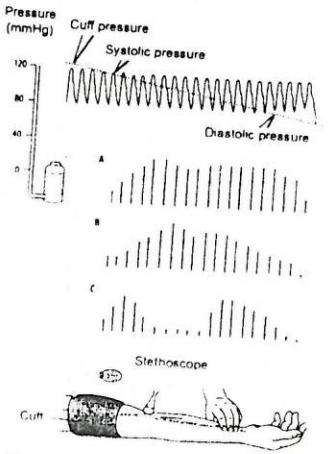


Fig. 7.2. Measuring blood pressure with a sphygmomanometer, listening to Korotkoff sounds (of varying levels during the turbulent flow shown in A–C). (Listening to sounds is called *auscultation*). (From [364])

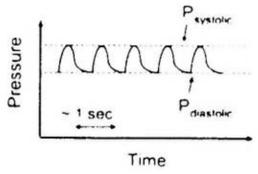


Fig. 7.3. Variation of blood pressure with time, for blood leaving the left heart for the systemic system, with the systolic and diastolic pressures shown

To understand when these sounds occur and their significance, we need to understand how the pressure in the main arteries varies with time. (This will be detailed in Chap. 8.) In every heart beat cycle (roughly 1/s), the blood pressure in the major arteries, such as the brachial artery, varies between the systolic pressure (~120 mmHg) and the diastolic pressure (~80 mmHg), as is depicted in Fig. 7.3. (The units of these cited gauge pressures are in mmHg – see (7.1) and Chap. 2.) When the pressure in the cuff exceeds the systolic pressure, there is no blood flow to the lower arm and consequently there are no sounds. When the pressure in the cuff is lowered with the release bulb to just below the systolic pressure, there is intermittent flow. During the part of the cycle when the arterial blood pressure is lower than the cuff pressure there is no flow, when it is greater, there is flow. This intermittent flow is turbulent and produces gurgling sounds. These sounds, the *Korotkoff* or K *sounds*, are heard by the stethoscope. As the cuff pressure is lowered further, the K sounds get louder and then lower, and are heard until the cuff pressure decreases to the diastolic pressure. Blood flow is not interrupted when the cuff pressure is less than the diastolic pressure and the K sounds cease because the blood flow is no longer turbulent. Therefore, the onset and end of the K sounds, respectively, denote the systolic and diastolic blood pressures. (This auscultatory method of Korotkoff was introduced by Russian army physician Korotkoff [362] who discovered a century ago that sound can be heard distally from a partially occluded limb [349].)

7.2 Basic Physics of Pressure and Flow of Fluids

In this section we overview the basics of fluids. Some of this will be a review for most. Some of the more advanced results are derived, while others are merely presented. These basics will be used in subsequent chapters.

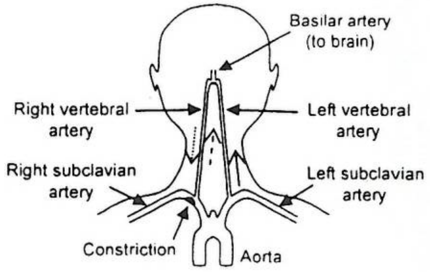


Fig. 8.38. Anterior view of the blood flow to the brain with the subclavian steal syndrome, resulting in a transient ischemic attack. Blood flow in the left vertebral artery is shown by the *unbroken line arrow*. Without the constriction, the blood flow in the right vertebral artery is normal, as shown by the *dashed arrow*, so there is normal blood flow to the basilar artery. With the constriction, there can be blood flow from the left vertebral artery to the right vertebral artery (*dotted arrow*), and there is no blood flow into the basilar artery. (Based on [387])

also supply blood to the arms. The internal carotid and vertebral systems join with each other at the base of the brain, forming the circle of Willis (Fig. 8.39, also see Fig. 8.43). Posteriorly, the flow in the left and right vertebral arteries merge to form a single basilar artery to the brain.

Say there is a constriction in the right subclavian artery near where the vertebral artery branches off (Fig. 8.38). The pressure before the constriction

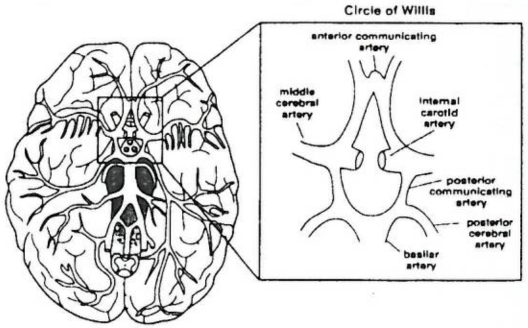


Fig. 8.39. Circle of Willis in the brain. (From [391])

Differentiating (1′) wrt x and (2′) wrt t,

$$\rho \frac{\partial^2 u}{\partial t \partial x} = -\frac{\partial^2 p}{\partial x^2}$$

$$\frac{\partial^2 A}{\partial t^2} + A_0 \frac{\partial^2 u}{\partial x \partial t} = 0$$

Eliminating u: $\frac{\partial^2 A}{\partial t^2} = \frac{A_0}{\rho}\frac{\partial^2 p}{\partial x^2}$

from (3′): $\frac{\partial^2 p}{\partial t^2} = \frac{Yh}{2r_0}\frac{1}{A_0}\frac{\partial^2 A}{\partial t^2}$

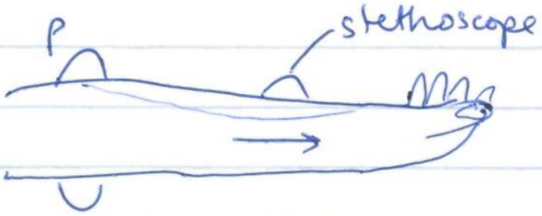
$$\boxed{\frac{1}{c^2}\frac{\partial^2 p}{\partial t^2} = \frac{\partial^2 p}{\partial x^2}}$$ THE WAVE EQUATION

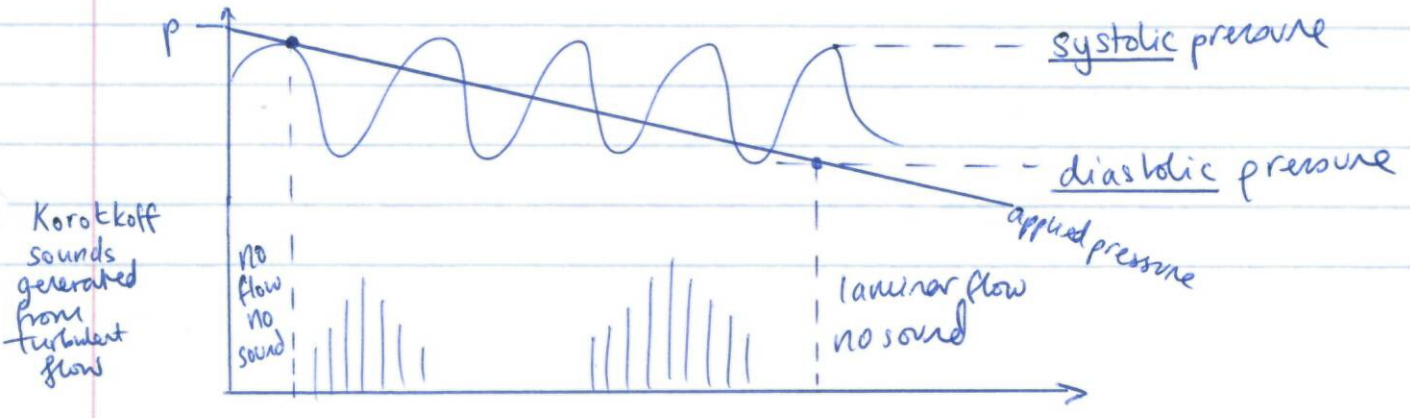
$$c = \sqrt{\frac{Yh}{2\rho r_0}}$$

The same wave eqn for A or u,
and c – the velocity of the pulse wave
Solution: $\underrightarrow{p(x-ct)} + \underleftarrow{p_2(x+ct)}$

Velocity of acoustic wave ≈ 1000 ms⁻¹
Velocity of the pulse wave ≈ 4.6 ms⁻¹
Velocity of the blood flow ≈ 0.24 ms⁻¹ in aorta
0.024 ms⁻¹ in capillaries

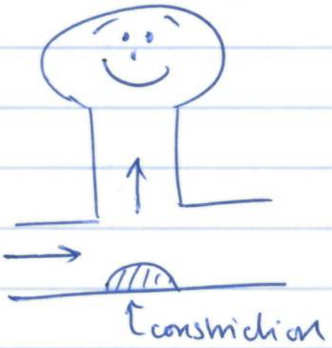
Measuring blood pressure and Korotkoff Sounds

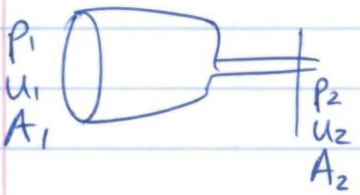




The nature of transient ishemic attack, or what happened to Athuro Toskanini in 1954

During his concert, Toscanini suffered a memory lapse caused by a transient ishemic attack (not enough blood pressure or flow in the brain).





Cross-sectional area $A_2 < A_1$

From Bernoulli's law,

$$p_1 + \frac{1}{2}\rho u_1^2 = p_2 + \frac{1}{2}\rho u_2^2$$

Due to conservation of volume, $A_1 u_1 = A_2 u_2 \rightarrow u_2 = \frac{A_1 u_1}{A_2}$

$$\Rightarrow p_1 + \frac{1}{2}\rho u_1^2 = p_2 + \frac{1}{2}\rho\left(\frac{A_1}{A_2}u_1\right)^2$$

Or $p_2 - p_1 = \frac{1}{2}\rho u_1^2\left[1 - \left(\frac{A_1}{A_2}\right)^2\right]$

If $A_2 < A_1$ and $u_2 > u_1$ $\Rightarrow$ $\underline{\underline{p_2 < p_1}}$!!

So lower pressure in the constricted area
(same reason 2 ships can't sail side-by-side)
so not enough pressure to transport blood into the brain.

The End