3307 Biomathematics Notes

Based on the 2015 spring lectures by Prof A Zaikin

Chapter 1

General information and reading list.

1.1 Topics to be covered in lectures

1. Using scaling arguments
2. Oxygen transport and Insect respiration
3. bird flight
4. Simple cell electrophysiology and gene expression
5. Strength of bones
6. Chemotaxis
7. Brain/Memory
8. Blood flood

1.2 Reading list

Warning. This course is not (much) about learning methods and theorems and applying them to standard problems. As such, there is no single book that you can read to cover the course. There are books that you might find helpful, or enjoy reading to supplement the lectures. A list of books that go with the course is the following:

1. **Scaling Laws.**

(a) 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 perfprmance].

(b) 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].

(c) D'arcy Wentworth Thomson. On growth and form. CUP. First published 1961. [Again, no model building, but excellent background and a real classic].

(d) Ludwig von Bertalanffy. General Systems Theory. 1969. george Braziller Inc. New York. [He discusses his growth model in pages 171-184].

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

2. **Diffusion/Insect Respiration.**

(a) Ove Sten-Knudson. Biological Membranes: Theory of transport, potentials and electric impulses. Cambridge University Press, 2002.

(b) G.R. Grimmet and D.R. Stirzaker. Probability and random processes. Clarendon Press, Oxford. 1992.

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

(d) `http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/T/Tracheal_Breathing.html`

3. **Bone.**

(a) I.P. Herman, "Physics of the human body", Springer, ISBN-10: 3540296034, (2007).

4. **Bird flight.**

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

(b) Loghthill, M.J. (1974). Aerodynamics aspects of animal flight. *Bulletin of the Institute of mathematics and its applications*, 10:369 393.

(c) from 1(a) - see above. Chapter 5. Sections 4.1.4.3 may also be useful background reading on fluids.

5. **Electrophysiology.**

(a) see 2(a) above.

(b) J. Keener and J. Sneyd. *Mathematical Physiology*. Interdisciplinary Applied Mathematics 8. Springer-Verlag, New York 1998. [Parts of Chapters 2,3 might be usefull].

6. **Chemotaxis.**

(a) J.D. Murray, *Mathematical biology. I.* Chapter 11, Springer 2001.

(b) J.D. Murray, *Mathematical biology. II.* Chapter 5.

7. **Brain.**

(a) J.D. Murray, *Mathematical biology. I.* Chapter 7, Springer 2001.

8. **Blood.**

(a) S.I. Rubinow, Introduction to Mathematical Biology, A Wiley-Interscience publication, New York. Chapter 4.

Chapter 2

Using scaling arguments

2.1 First steps: Building a simple mathematical model

Warning: In this part of the course we make very simplistic assumptions about the biology. (Nevertheless, our efforts are rewarded with answers that make broad sense.)

2.1.1 Example. Falling flea.

Why would a flea survive a fall from 30-storey building, whereas a human would probably not?

Is it:

1. because the human is much heavier?

2. because the flea has a stronger (exo)skeleton and hence can survive the impact?

3. because the fleas legs can absorb the impact (good shock-absorbers)?

4. some other (sensible) reason?

Galileo (or later Newton) tells us two cannon balls of different sizes reach the ground at the same time - (by experience) this is not what we expect from fleas and humans, so whats missing?

Answer is friction - *the drag on bodies due to air friction* acts to decelerate a falling body. Over long distances, bodies reach terminal velocity, which occurs where the frictional drag force balances weight. So we need to understand how frictional drag depends on the size and shape of a body.

Body weight = Frictional drag

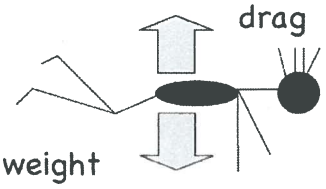
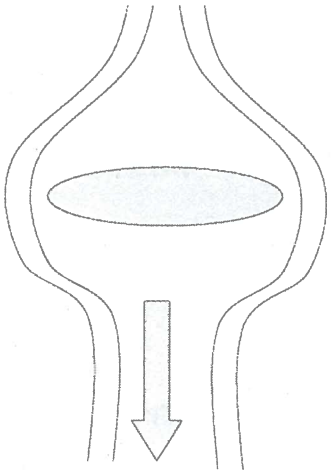


Figure 2.1:



What is Drag?

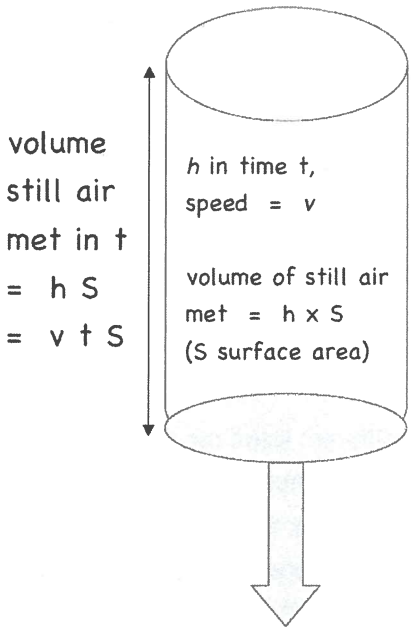
- It is a force due to friction (air/water/soil)

We know:

Force = change momentum / time, $F = dp/dt$

so we can find the drag force from

1. the bodys area in contact with the air
2. how much air is moved from standstill to (terminal) speed v in a given time t (which gives the momentum change in time t)



force × time = change of momentum (of still air)

force × t = air mass × speed

= (density) × volume × v

= ρ × (S × h) × v

= ρ ×(S × v × t) × v

= ρ S v^2 t

hence drag force ∝ S v^2

change of mom. ~ velocity

Assuming terminal velocity is reached by the flea and human:

$$\text{weight} = \text{drag} \quad \text{force} = Mg \propto Sv^2 \Rightarrow v \propto \sqrt{\frac{M}{S}} \tag{2.1}$$

So how does

$$\text{mass/area} = M/S$$

differ for the flea and human?

Approximately:

Flea = 3mm long

Human = 2000mm long

Make the simplest assumption that there is a linear scale L such that

$$M \propto L^3, \qquad S \propto L^2 \tag{2.2}$$

Then for each body

$$M/S \propto L \tag{2.3}$$

Thus the terminal velocity varies with the bodys linear scale L as

$$v \propto \sqrt{L} \tag{2.4}$$

We say that the velocity scales as the square root of the body linear scale

For a flea and human we have (very approximately!)

$$L_{\text{flea}}/L_{\text{human}} \approx 3\text{mm}/2000\text{mm} = 0.0015 \tag{2.5}$$

and the terminal velocity of a human is approx 100mph, so

$$v_{\text{flea}} = v_{\text{human}} \times \sqrt{L_{\text{flea}}/L_{\text{human}}} \approx 4\text{mph} \tag{2.6}$$

This, combined with the strong exoskeleton of the flea, gives it a much better chance of survival!

BTW: $L_{elephant}/L_{human} = 4/2 = 2$, $v_{elephant} = 100\sqrt{2} = 141mph$

2.2 Scaling arguments

The previous example is an example of a scaling argument -by making very simple assumptions we were able to model how terminal velocity scales with linear scale L.

The scaling argument summarizes:

$$\text{weight} = Mg \propto L^3 \tag{2.7}$$

$$\text{drag} \propto \text{projected area} \times v^2 \propto L^2 v^2 \tag{2.8}$$

$$\text{weight} = \text{drag} \Rightarrow L^3 \propto L^2 v^2 \Rightarrow v \propto \sqrt{L} \tag{2.9}$$

Notice that we dropped all boring constants to reach the essential point: v scales as square root of L.

Inherent in our assumptions were that for the linear scale L that distinguishes bodies in the similarity class:

- length $\propto L^1$
- area $\propto L^2$ (so projected area $\propto L^2$)
- volume $\propto L^3$ (so mass $\propto L^3$)

In applying our model, we were also assuming that the model is being applied to two bodies of the same shape (not exactly the case for the flea and human, but this is a first approximation model!).

In the following models, we will assume that we are comparing between families of animals of similar shape, i.e. are isometric, parameterised by linear scale L.

We will be interested in how the size of the animal effects its functions. If L is a length scale, then area scales as L^2 and volume scales as L^3. Since many of life's processes depend on transport of substances across a surface area (e.g. lung surface), and that transport supplies a volume (e.g. blood), it is intriguing to ask how the fact that volume increases faster than area effects (limits) function.

2.2.1 Some basic physics

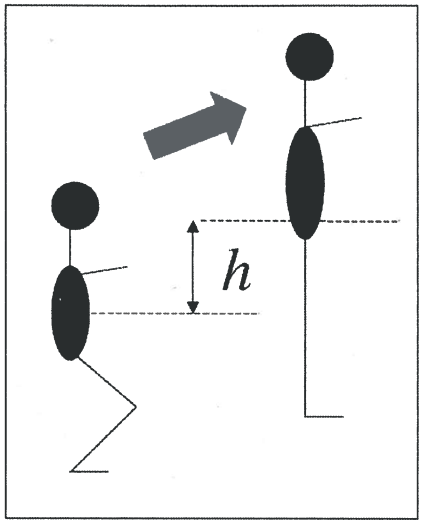
(M=mass, L=length, T=time)

1. force = mass × accn : force = MLT^{-2} $= \frac{M \cdot L}{T^2}$
2. work done = force × distance = ML^2T^{-2}, kinetic energy = $M(LT^{-1})^2$
3. power = work done/time = ML^2T^{-3}
4. flux = amount/area/time
   e.g. mass flux = mass/area/time = $ML^{-2}T^{-1}$
   heat flux = heat energy/area/time = MT^{-3}

5. heat is energy transferred down a temperature gradient

2.2.2 Example 2

How high can an animal jump? Or more precisely: How does the height that an animal from the same similarity class vary with linear scale L?



Assumptions:

1. work done by leg muscles = gain in potential energy
2. muscle force $\propto$ cross-sectional area of muscle $\propto L^2$ (this is not obvious, but there are models that justify this experimentally demonstrated fact).
3. height jumped = height gained h by centre of mass (good approx)

Potential energy gained = $Mgh \propto L^3 \times h$

Work done by muscles =

muscle force $\times$ vertical distance, centre of mass (C.O.M.) displaced

$$\propto (\mathrm{L}^2) \times (\mathrm{L}) = \mathrm{L}^3.$$

$L^2 \cdot L \propto L^3 h$

$h \propto L^0$

Hence, equating PE gained to Wk. Done by muscle

$$\mathrm{hL}^3 \propto \mathrm{L}^3$$

Thus $h \propto L^0$. That is, the simple model predicts that, for animals in the same isometric class, the height they can jump is independent of their size.

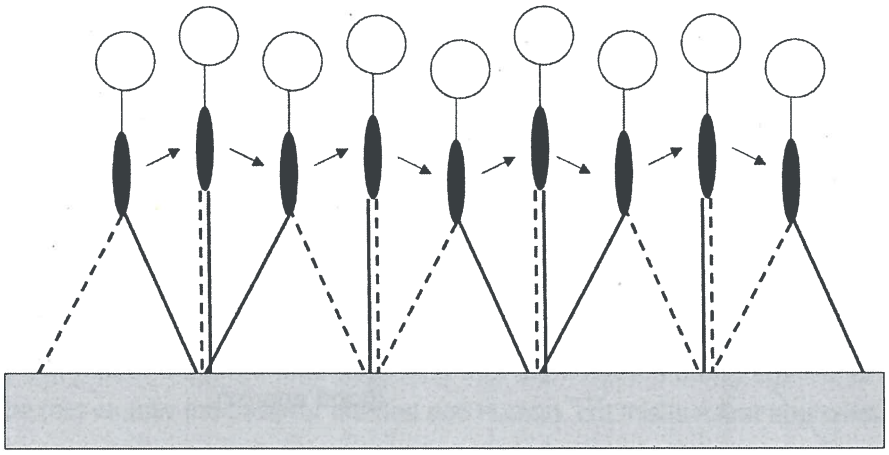
Is this a good model? How high can a flea jump? How high can you jump?

4m 1m

2.2.3 Example: How fast can we walk before breaking into a run?

Consider this (very) simplified picture of the human gait (figure 2.2). The human walks with straight legs, so the the COM moves in a series of circular arcs. The front foot leaves the ground if the

component of weight is not strong enough to provide the centripetal acceleration which increases as v^2. This gives us a limit on the walking speed.



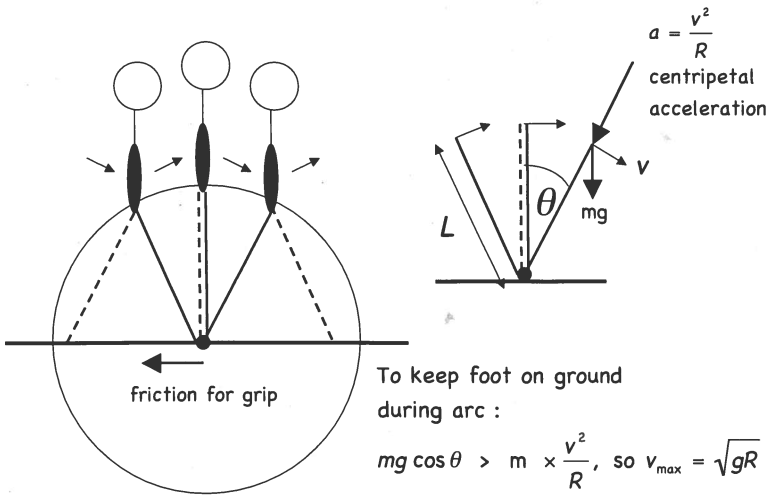
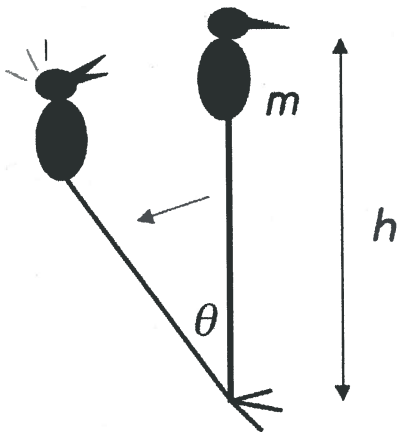


Figure 2.2: Maximal speed: $v < \sqrt{10m/s^2 \times 1m} = 3m/s = 0.003km/0.0003h = 10km/h$

g 10 R

2.2.4 Example

Minimum nerve speed required to make it possible for a animal to balance (e.g. flamingo)



toppling of animal scales like free fall ($md^2x/dt^2 = mg$, $dx/dt = gt + C_1$, $x = gt^2/2 + C_1t + C_2t$): if $t=0$ $x(0)=0 \Rightarrow C_1 = C_2 = 0$, $x \sim \frac{gt^2}{2}$

$$\propto t = \sqrt{\frac{2h}{g}} \propto \sqrt{L}$$

nerve speed required = distance from brain to muscle / time taken

$$\propto L/t$$

Thus
nerve speed scales as $\frac{L}{\sqrt{L}} = \sqrt{L}$

$V_{min} \propto \sqrt{L}$

2.2.5 Models that involve Metabolic Rate

Homeostasis is the property of a system that regulates its internal state to maintain a stable condition of properties, e.g., temperature.

Metabolism is the set of chemical reactions that occur in living organisms in order to maintain life. Animals use Adenosine triphosphate (ATP) to fuel their metabolic demands, e.g. in growth, locomotion, maintenance, immunological defence, etc. The cells power plants" are organelles called mitochondria which generate most of the cell's supply of ATP.

$$\text{food + oxygen} \Rightarrow \text{ATP} \Rightarrow \text{ADP + Phosphate + ENERGY} \Rightarrow \text{muscle force.}$$

The metabolic rate (rate of energy metabolism) of an organism (using aerobic respiration) can be assumed to be equated with the rate of oxygen consumption.

A simple (isometric) scaling argument for variation of metabolic rate (assuming a resting state and after a period of fasting) with size is as follows:

Metabolic rate B = rate of oxygen consumption $\propto$ area of lungs supplying oxygen to mitochondria $\propto L^2$

Body Mass $M \propto L^3$

Thus $B \propto L^2 = (L^3)^{2/3} \propto M^{2/3}$ (Rubners Law). ← Remember!

Another argument, at least for warm-blooded animals, put forward by Rubner, is that a warm-blooded animal maintains a constant body temperature, and so their metabolism runs at a rate such

Metabolic rate = rate of oxygen consumption $\propto$ area of lungs $\approx L^2$

$M \propto L^3$

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

that this temperature is maintained. Since the body loses heat energy at a rate proportional to their body surface area, which scales as L^2, the metabolic rate ought to scale as L^2.

Whatever the argument we (might) accept for the L^2 law, we take the law as fact for now. (However, we will see later that it can be improved upon with the experimentally determined $B \propto M^{3/4}$.)
Thus until stated otherwise, we assume that

$$\boxed{B \propto L^2 \propto M^{2/3}.}$$

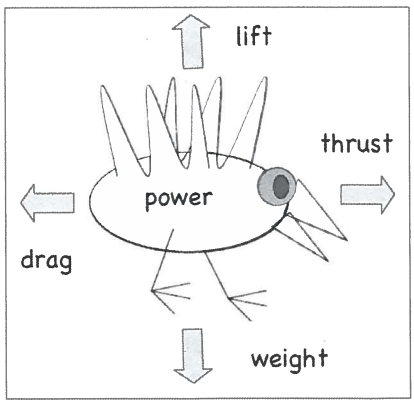
2.2.6 Class Exercise (10mins): How long can a diving mammal stay under water on one breath?

A diving mammal (e.g. whale) stores oxygen in it blood before diving. When that oxygen is exhausted it must surface for more air.

amount of stored oxygen $\propto$ lung volume $\propto$ blood volume $\propto L^3$
Metabolic Rate - rate at which mammal uses stored oxygen is $\propto L^2$
Thus duration of a dive scales as $L^3/L^2 = L$.
Thus the larger you are, the longer you can dive.

NB: We have ignored any specialisation that makes it more efficient for the animal to dive. Thus for example, whales slow their heart beat and blood flow to their muscles is reduced; these factors enable whales to dive for longer. When we build our simple models, we keep them simple by ignoring such specialisations. We are interested in broad statements about how things typically vary with scale.

2.2.7 Example: Why do large birds find it harder to fly?



Facts/assumptions:

1. Drag $\propto L^2v^2$ (see flea/human model)
2. (Not obvious!) Maximum lift during gliding and wing flapping $\propto A_w v^2$ where $A_w = \text{wing area} \propto L^2$
3. Metabolic rate $\propto L^2$ = rate at which energy is available.

2.2.8 How to obtain lift law

Bernoulli's Theorem (Sketch)

For steady flow of inviscid incompressible fluid

$$\frac{\rho v^2}{2} + p + \rho g x = const$$

along streamline. Here p = pressure, z = fluid depth, v = fluid speed, ρ = density.

Proof.

$$m\frac{dv}{dt} = \sum F_i$$

$$\rho A dx \frac{dv}{dt} = -Adp - \rho A dx g$$

$$\frac{dv}{dt} = \frac{dv}{dx}\frac{dx}{dt} = \frac{dv}{dx}v = \frac{d}{dx}\frac{v^2}{2}$$

$$\frac{d}{dx}\left(\rho\frac{v^2}{2} + p + \rho g x\right) = 0, \qquad \rho\frac{v^2}{2} + p + \rho g x = const$$

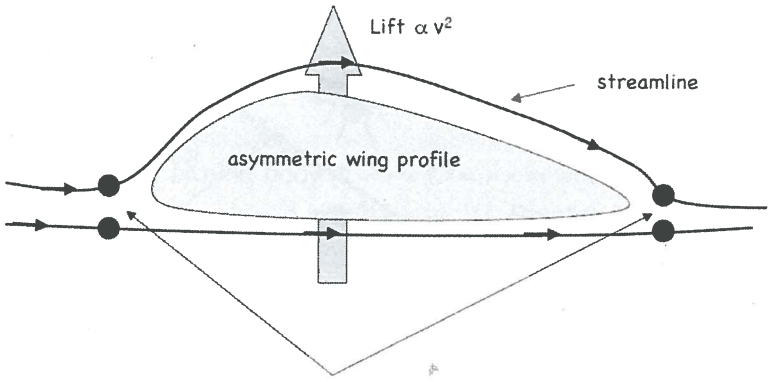


Figure 2.3:

Back to wing lift now. Air particles moving around the wing profile start and end at same time, so top particle must move faster. By Bernoulli, this generates a lift $\propto A_w v^2$, where v is the wind speed, that is the speed of the air relative to the wing.

Max lift must just overcome gravity, so minimum flying speed v is given by

$$A_w v^2 \propto Mg \propto L^3,$$

so that since $A_w \propto L^2$, $v \propto L^{1/2}$.

The required power (for flapping wings to get lift) is Power (work done /time = force x distance /time)

$$\text{Flying power} = \text{drag} \times v \propto L^2 v^3 \propto L^{2+3/2} = L^{7/2}$$

Metabolic power $\propto L^2$, so that required power exceeds supplied power for larger L ($L^{7/2} > L^2$ for L large enough), and hence there is an upper limit on bird size.

2.2.9 Kleibers Law

But experimentally $B \propto M^{2/3}$ is not observed!

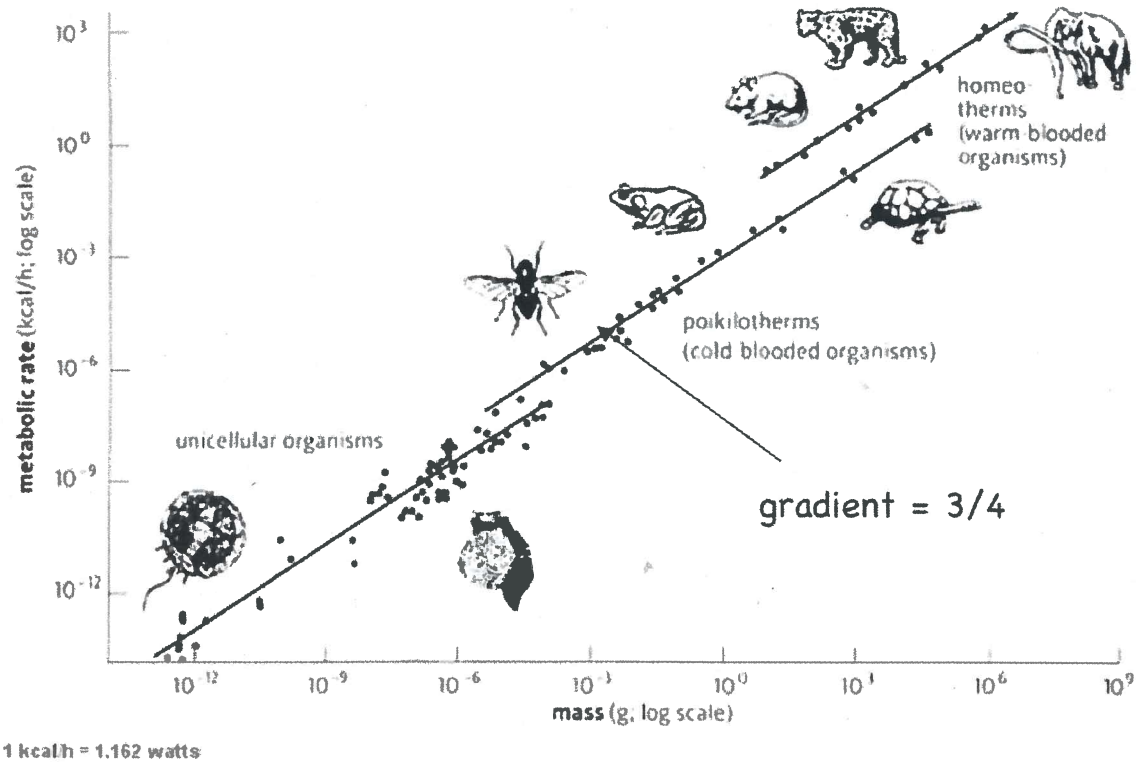


Figure 2.4:

Instead one finds experimentally (by measuring oxygen consumption of animals in a resting state

and after they have fasted for sufficient period) that

$$\text{metabolic rate } B \propto m^{3/4}.$$

Figure 4.12 illustrates the remarkable range of scales over which the $3/4$ law holds.

Aside: An new argument for $3/4$ power law was recently published by West (1997) under the following assumptions:

- mammalian energy distribution networks (circulatory system, lungs) are fractal-like in structure;
- systems have evolved to maximise their metabolic capacity by maintaining networks that occupy a fixed percentage of the volume of the body.

So from now on we will acknowledge experimental data and assume the allometric scaling (as opposed to isometric scaling) law for metabolic rate with mass:

$$B = B_0 m^{3/4}. \quad \text{(Klieber's Law)}.$$

2.2.10 Example. How does heart-rate scale with mass?

Assume that the heart beats fast enough to supply enough oxygen for the organism's metabolism. Facts:

1. Metabolic rate $\propto m^{3/4}$.
2. Blood volume $\propto L^3 \propto m$.

The rate of oxygen is transport around body is $\propto r \times L^3 \propto r \times m$ where r = heart rate (assume pump volume $\propto$ body volume). Thus $r \times m \propto m^{3/4}$ giving $r \propto m^{-1/4}$. Smaller bodies have faster heart rates:

e.g. masked shrew (0.003kg) has r = 600, whereas elephant (4000kg) has r = 30. A human (80kg) has r = 80.

2.2.11 Example: Thickness of fur

Consider a class of similar animals in a cold environment. How does their fur thickness scale with mass?

Recall: Heat is energy transferred down a temperature gradient $\Delta T/\Delta x$. heat flux = heat energy/area/time = $k(\Delta T/\Delta x)$, k = thermal conductivity of material (independent of scale).

To maintain body temperature (in surrounding of constant temperature, so that ΔT is constant) we thus need metabolic rate $\propto$ heat flux $\propto$ surface area $\times$ (temp difference / fur thickness h)

$$m^{3/4} \propto L^2/h \propto m^{2/3}/h,$$

so that fur thickness $h \propto m^{2/3-3/4} = m^{-1/12}$. Hence larger animals tend to have thinner fur.

2.2.12 Class excercise: How long does it take to starve to death?

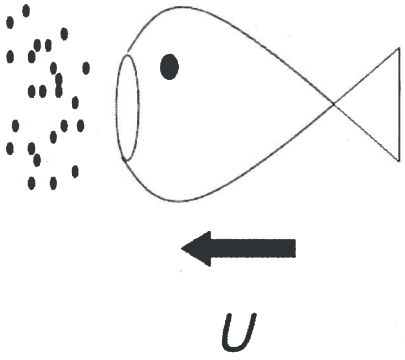
Using Kliebers law, power $\propto m^{3/4}$

And energy reserves $\propto$ mass m, energy used up to starvation $\propto$ power $\times$ time to starve = $m^{3/4} \times t$.

Thus $t \propto m \times m^{-3/4} = m^{1/4}$.

2.2.13 Example: Swimming speed of a filter-feeder

rate of gain of stored energy $\propto$ food energy input rate - metabolism of stores



food input rate $= F_0 U$,

metabolism = basal rate + power to overcome (speed-dependent) drag

$= P_0 +$ drag $\times U$

$= P_0 + (P_1 U^2) \times U = P_0 + P_1 U^3$.

Thus need to look at the function

$G(U) = F_0 U - P_0 - P_1 U^3$.

$G'(U) = F_0 - 3P_1 U^2 = 0$ where $U = \sqrt{F_0/3P_1}$.

Not viable if $G_{max} < 0$, i.e. (after some algebra) $P_0 > \frac{2F_0}{3}\sqrt{\frac{F_0}{3P_1}}$.

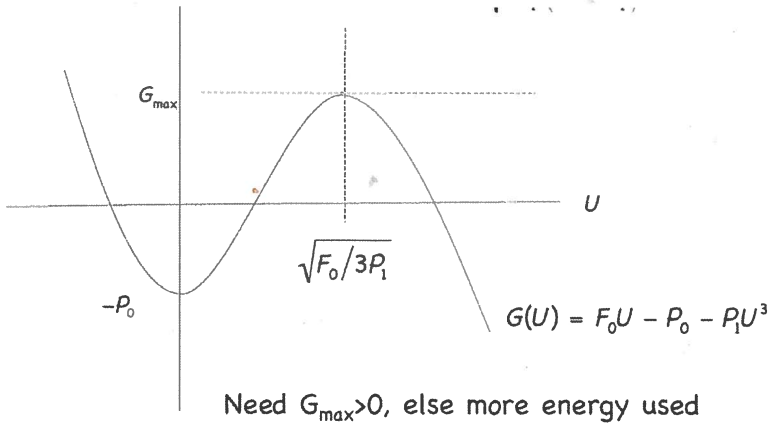


Figure 2.5:

2.3 Example: Ludwig von Bertalanffys Growth Model (1957)

von Bertalanfy was one of the founders of "General Systems Theory" (`http://en.wikipedia.org/wiki/Ludwig_von_Bertalanffy`) Here is a (very) simple model he developed to study growth of an organism.

He assumed that all an organism's available energy is channeled into :

1. Growth of the organism - building new cells, all taking the same energy to generate
2. Maintenance of the existing cells - keeping existing cells alive by supplying resources and removing waste products.

We have:

incoming power (metabolic rate $[B]$) = number of cells in body $N_c(t)\times$ metabolic rate of one cell $[=B_c]$ + energy required to create new cell $[=E_c]\times$ rate of increase in number of cells $N_c(t)$

$$\Rightarrow B = \underbrace{N_c B_c}_{maintenance} + \underbrace{E_c \frac{dN_c}{dt}}_{growth}$$

Now:

body mass $m = N_c m_c$, where m_c =mass of 1 cell (assumed identical for all cells). Take $B = B_0 m^{2/3}$ (isometric scaling, i.e. $\propto L^2$ [see exercise sheet 1 for the $m^{3/4}$ case]). Thus

$$B_0 m^{2/3} = \frac{B_c m}{m_c} + \frac{E_c}{m_c}\frac{dm}{dt} \quad \text{rearrange} \quad \Rightarrow \quad \frac{dm}{dt} = \alpha m^{2/3} - \beta m,$$

where $\alpha = m_c B_0 / E_c$, $\beta = B_c / E_c$.

Solve:

$$\frac{dm}{dt} = \alpha m^{2/3} - \beta m, \quad m(0) = m_0 \quad \text{(small, since organism starts small!)}.$$

Write as

$$\frac{dm}{dt} = m^{2/3}(\alpha - \beta m^{1/3})$$

and substitute $u = m^{1/3}$. Then $3du/dt = m^{-2/3} dm/dt$ which gives

$$\frac{du}{dt} = \frac{1}{3}(\alpha - \beta u), \quad u(0) = m_0^{1/3}.$$

This has general solution $u(t) = \frac{\alpha}{\beta} + A\exp^{-\beta t/3}$. To find A, use initial data:

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

Hence we obtain:

$$u(t) = \frac{\alpha}{\beta}(1 - \exp^{-\beta t/3}) + m_0^{1/3} \exp^{-\beta t/3},$$

and finally in terms of m:

$$m(t) = \left(\frac{\alpha}{\beta}(1 - \exp^{-\beta t/3}) + m_0^{1/3} \exp^{-\beta t/3}\right)^3.$$

(Sketch similar in Q2, sheet 1).

2.3.1 Case Study: Incubating Eggs

- An egg is a self-contained unit. It has all the nutrients it needs for the embryo to develop - except for oxygen. Oxygen is needed from outside. It diffuses through the shell through small pores
- But must also be rid of waste products, such as carbon dioxide and water. The shell is mainly calcium carbonate with pores that allow influx and outflux of nutrients and waste products (gases and water).
- The shell must be strong enough to withstand roosting, but weak enough to allow chick to break out when hatching.

Consider a spherical Egg!
Questions:

1. How does the egg incubation time scale with the mass of the egg?
2. How does the shell thickness vary with egg size?

Assumptions/Notes

1. Loss of water is the limiting effect - must not be too rapid else the embryo dehydrates. Oxygen and CO_2 diffuse across embryo and egg shell faster than water (so can be considered instantaneous on the time scale of water movement).
2. Rate of water production $\propto$ metabolic rate
3. Would expect shell thickness to increase with shell size, since shell has to contain and protect yolk.
4. Total water loss $\propto$ size of egg
5. Water is lost via pores length = shell thickness d and with total area A_{pores} over the shell.

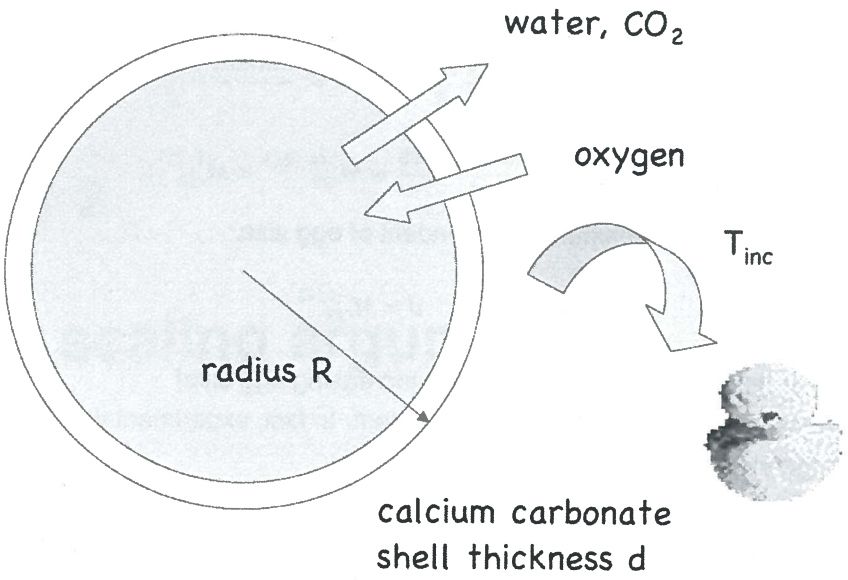


Figure 2.6:

Total water lost in T_{inc} = daily water loss $\times T_{inc}$

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

and daily water loss $\propto$ metabolic rate $\propto M_{egg}^{3/4}$. Hence

$$T_{inc} \propto \frac{M_{egg}}{M_{egg}^{3/4}} = M_{egg}^{1/4},$$

which agrees quite well with the experimentally observed $M^{0.217}$.
But how might the shell thickness d change with egg size?

$$\text{water flux} \propto \text{ pore area } \times \frac{\text{concentration gradient}}{\text{pore length}}$$

(see later lectures on diffusion).

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

Since the area of the shell is proportional to R^2, and ΔC is constant,

$$\Rightarrow M_{egg}^{3/4} \propto \frac{\text{density pores} \times R^2}{d} \propto \frac{\text{density pores} \times M_{egg}^{2/3}}{d}$$

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

Hence if pore density is a constant, independent of egg size,

$$d \propto M_{egg}^{-1/12}$$

which would mean that eggs get thinner with increasing egg size!

So the density of pores must be size dependent. In fact, experimentally it is observed pore density $\propto M^{4/3}$ and the shell thickness scales as $d \propto M_{egg}^{5/4}$.

02/00/14

Homeostasis is a property of a system that requires its internal state to maintain a stable condition of properties e.g. temperature

Metabolism is a set of chemical reactions that occur in living organisms to maintain life

food + oxygen $\Rightarrow$ ATP $\rightarrow$ ADP + Phosphate + Energy $\Rightarrow$ muscle force

Metabolic rate B = rate of oxygen consumption $\approx$ area of lungs $\approx L^2$

Body mass $M \sim L^3$, $B \sim L^2 \sim M^{2/3}$ Rubner's law

since $M = \rho \cdot V$

heat flux $\sim S \sim L^2$
(loss of heat)

Example: How long can a diving animal stay under water on one breath?

Amount of oxygen $\propto$ lungs volume $\approx L^3$

$B \approx L^2$

Duration $\sim L^3/L^2 \sim L$ rough model

Example: Why do large birds find it difficult to fly?

Bernulli's law (exam q.)

$$m\frac{d\vec{v}}{dt} = \sum \vec{F}_i$$

$$\rho A dx \frac{dv}{dt} = -A dp - \underbrace{\rho A dx g}_{\text{weight} = mg}$$

(dp: change in pressure; g: accel. of grav.)

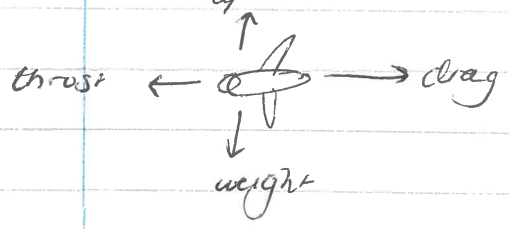
$$\rho \frac{dv}{dt} = -\frac{dp}{dx} - \rho \cdot g$$

$$\frac{dv}{dt}(x,t) = \cancel{\frac{\partial v}{\partial t}} + \frac{\partial v}{\partial x}\frac{\partial x}{\partial t} = \frac{dv}{dx}v = \frac{1}{2}\frac{d(v^2)}{dx}$$

stationary
i.e.
not dep. on time

$$\frac{d}{dx}\left(\frac{\rho}{2}v^2 + p + \rho g x\right) = 0$$

$$\frac{\rho}{2}v^2 + p + \rho g x = \text{const.}$$



$$\text{Drag} \sim L^2 v^2 \quad \text{(flea model)}$$

$$\text{Lift} \sim A_w v^2 \sim L^2 v^2$$

(A_w ← wing area)

$$\mathcal{B} \sim L^2$$

Minimum speed $\quad A_w \cdot v^2 = mg \sim L^3$

$$V = \sqrt{\frac{L^3}{L^2}} = L^{1/2}$$

The required power $\quad \frac{\text{work done}}{\text{time}} = \frac{\text{force} \cdot \text{distance}}{\text{time}} = \text{force} \cdot \text{velocity}$

$$= \text{drag} \cdot v = L^2 v^3$$

$$= L^2 L^{3/2} \sim L^{7/2}$$

To fly $\quad \mathcal{B} >$ power, or $L^2 > L^{7/2}$

for large sizes $\quad$ required > supplied

limit of size

Kleiber's Law $B \sim M^{3/4}$

Ludwig Von Bertalanffy's Growth model (1957)

Assume { All available energy is channelled in to
a) growth of organism (building new cells
b) maintaining existing cells

Metabolic rate = (power to maintain one cell) × (number of cells) + (energy to produce one new cell) × (rate at which cells are produced)

$$B = B_c \cdot N_c(t) + E_c \cdot \frac{dN_c(t)}{dt}$$

($N_c(t)$: number of cells)

If m_c - mass of one cell

$m(t) = m_c \cdot N_c(t)$ ($m(t)$: mass of body)

$$m_c B = B_c m(t) + E_c \frac{dm(t)}{dt} \leftarrow \text{mult. by } m_c$$

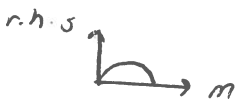
$B = B_0 m^{2/3}$ Rubner's law

isomeric scaling

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

$$\frac{dm}{dt} = \alpha m^{2/3} - \beta m \qquad \alpha = \frac{m_c B_0}{E_c} \qquad \beta = \frac{B_c}{E_c} \Big\} \text{ model}$$

$m(0) = m_0$ - small



To solve

$u = m^{1/3}$

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

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

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

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

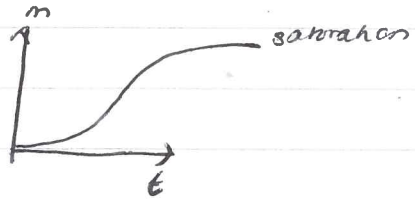
$u(t) = \frac{\alpha}{\beta} + A e^{-\beta t/3}$

$u(0) = m_0^{1/3} = \frac{\alpha}{\beta} + A \implies A = m_0^{1/3} - \alpha/\beta$

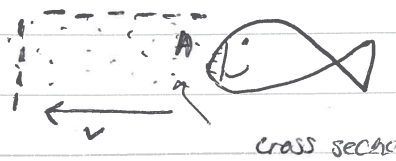
$u(t) = \frac{\alpha}{\beta} + \left(m_0^{1/3} - \alpha/\beta \right) e^{\frac{-\beta t}{3}}$

$m(t) = \left(\text{—} \; " \; \text{—} \right)^3$ ← same as above, but cubed.

= mass of a growing organism



Example: Swimming filter feeder



Energy input rate $\sim F_0 \cdot v$

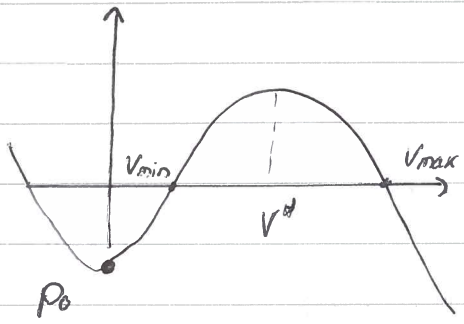
cross sectional area const.

Basal metabolic rate $\sim P_0$

Power $\sim$ force $\times$ velocity $= \underbrace{\rho_1 v^2}_{\text{drag} \sim \rho_1 v^3} \cdot v$

To swim, power balance

$$G(v) = F_0 v - P_0 - \rho_1 v^3 > 0$$



in the range $[v_{min}, v_{max}]$

$$G'(v) = F_0 - 3\rho_1 v^2 = 0$$

$$v^* = \sqrt{\frac{F_0}{3\rho_1}}$$

$$P_0 < F_0 v^* - \rho_1 (v^*)^3 = F_0 \left(\frac{F_0}{3\rho_1}\right)^{1/2} - \rho_1 \left(\frac{F_0}{3\rho_1}\right)^{3/2}$$

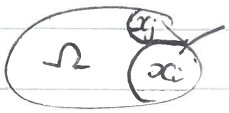
$$= \frac{2}{3} F_0 \sqrt{\frac{F_0}{3\rho_1}}$$

Oxygen Transport (respiration)

How is transport from the lungs (or other medium) to the energy dissipating organs managed by the animal?

Simple diffusion

Probability



mutually exclusive

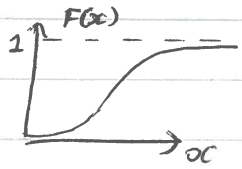
We introduce a probability $P(x_i)$ that has the following properties

1) $P(x_i) \geq 0 \quad \forall i$
2) $P(x_i \cup x_j) = P(x_i) + P(x_j)$
3) $\sum P(x_i) = P(\Omega) = 1$

The cumulative distribution function

$$F(x) = P(X \leq x)$$

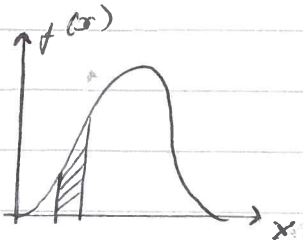
(X: variable)



Probability density function:

$f(x)$: $P[a \leq X \leq b] = \int_a^b f(x)\,dx$

$$f(x) = \frac{dF(x)}{dX}$$



$$\int_{-\infty}^{\infty} f(x) = 1$$

Expected value of X

$$E[X] = \int_{-\infty}^{\infty} x f(x)\,dx$$

Variance

$$Var[X] = E[(X - E[X])^2]$$

(doesn't matter if in one or other dir^n)

$$= E[(X)^2] - E[2XE[X]] + E[(E[X^2])^2]$$
$$- 2(E(X))^2 \qquad (E(X))^2$$
$$= E[X^2] - (E(X))^2$$

Central limit theorem (CLT)

Let $X_1 \dots X_n$ be a sequence of i.i.d random variables (identically & independently distributed) with mean μ and variance σ^2

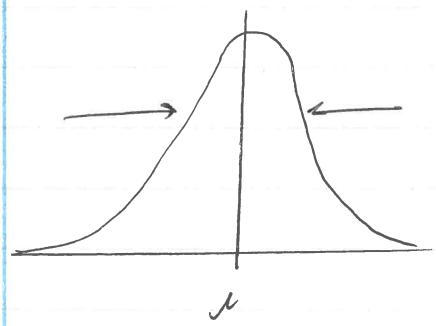
Let $S_n = X_1 + \dots + X_n$

Then $Z_n = \dfrac{S_n - n\mu}{\sigma\sqrt{n}} \xrightarrow{\text{converge}} N(0,1)$

$\sigma\sqrt{n}$ ← square of n variances

standard normal dist. w/ mean = 0, variance = 1

$$N(0,1): \quad f(x) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{(x-\mu)^2}{2\sigma^2}}$$



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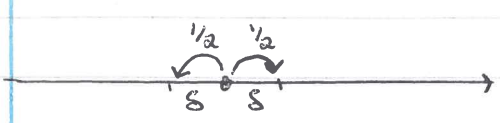
Diffusion (gas transport in animals)



Particles move δ to L or R w/ prob 1/2

Let X_i be $-\delta$ + δ be random var. for i's step. After n steps

$S_n = X_1 + \dots + X_n$, by CLT, $S_n \to N(0, n\delta^2)$
normal dist. w/ mean $\mu = 0$
variance $\sigma^2 = n\delta^2$

$$E[X_i] = P(X_i = -\delta)\cdot(-\delta) + P(X_i = \delta)\cdot\delta = -\frac{1}{2}\delta + \frac{1}{2}\delta = 0$$

So
$$E[S_n] = E\left[\sum_i X_i\right] = \sum_i E[X_i] = 0$$

- If $i \neq j$, $E[X_i X_j] = P(-\delta)P(-\delta)\delta^2 + P(-\delta)P(\delta)(-\delta)(\delta) + P(\delta)P(-\delta)(\delta)(-\delta) + P(\delta)P(\delta)\delta^2$
$$= \frac{1}{4}\delta^2 - \frac{1}{4}\delta^2 - \frac{1}{4}\delta^2 + \frac{1}{4}\delta^2 = 0$$

- If $i = j$ $\quad E[X_i^2] = \frac{1}{2}\delta^2 + \frac{1}{2}(-\delta)^2 = \delta^2$

$$\sum_i E[X_i^2] = n\delta^2$$

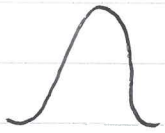
For variance
$$\sigma^2 = E[S_n^2] = E\left[\sum_i X_i^2 + 2\sum_{i<j} X_i X_j\right]$$

$$= E\left[\sum_i X_i^2\right] + 2E\left[\sum_{i<j} X_i X_j\right] = n\delta^2$$

"0"

As $n \to \infty$ the pdf fn is

$$f_n(x) = \frac{1}{\sqrt{2\pi n \delta^2}} \exp\left(\frac{-x^2}{2n\delta^2}\right)$$



If τ - time between collisions

t - time elapsed

$n = t/\tau$, if $D = \delta^2/2\tau$

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

D - coeff. of diffusion

Which eq. does f satisfy?

$$\frac{\partial f}{\partial x} = \left(-\frac{x}{2Dt}\right) f$$

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

$$\frac{\partial f}{\partial t} = \left(-\frac{1}{2t}\right) f + \left(\frac{x^2}{4Dt^2}\right) f$$

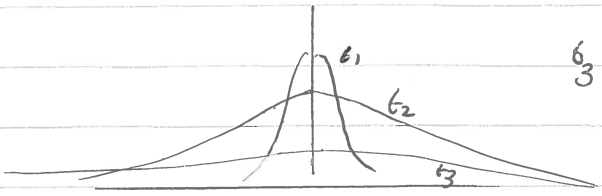
Diffusion equation $\frac{\partial f}{\partial t} = D\frac{\partial^2 f}{\partial x^2}$

Limit $\tau, \sigma \to 0$ but D remains fixed

$$\frac{\partial f}{\partial t} = -\frac{\partial J}{\partial x} \qquad J = -D\frac{\partial f}{\partial x} \quad \text{- flux}$$

The Green Function (fundamental solution)

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



$t_3 > t_2 > t_1$

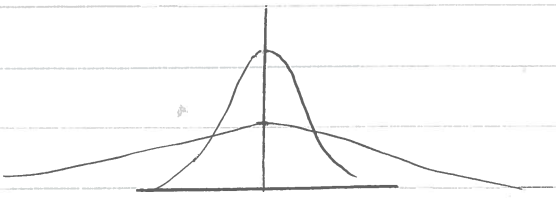
For initial conditions $C(y,0)$

$$C(x,t) = \int_{-\infty}^{\infty} \frac{1}{\sqrt{4\pi t D}} \exp \frac{-(x-y)^2}{4Dt} \; C(y,0)\, dy$$

$$= \int_{-\infty}^{\infty} f(x-y,t)\, C(y,0)\, dy$$

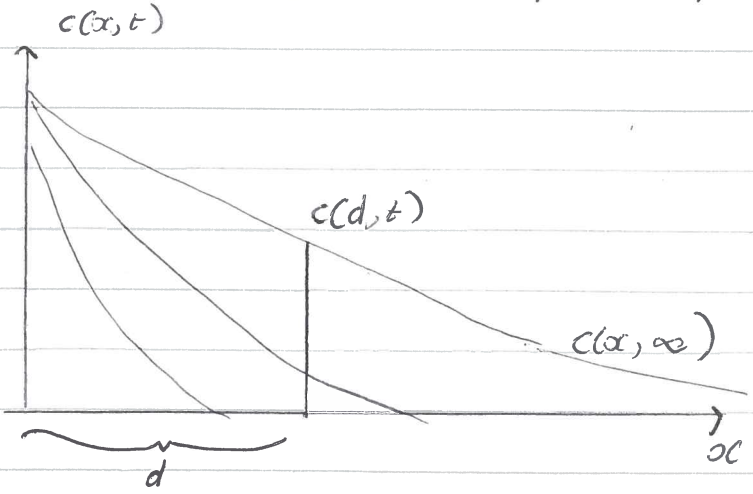
If $C(y,0) = \delta(y)$ the delta function $\int_{-\infty}^{\infty} f(x)\,\delta(x)\,dx = f(0)$

$C(x,t) = f(x,t)$



In 3D $\frac{\partial C}{\partial t} = D \Delta C$ ← Laplace operator

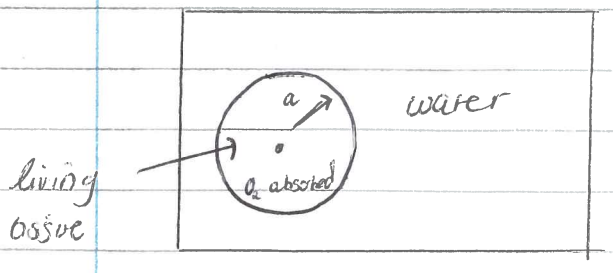
Time taken to reach 99% from a plane



time T when $C(d,T) = 0.99\,C(x,\infty)$

d	T
0.1 μm	0.0005 sec
10 μm	0.05 sec
1 mm	76 min
1 cm	127 hours
10 cm	50 days

Example Diffusion and absorption in a tissue



Tissue in a sphere of radius a

$r = a$ is a surface

Assume that $C(\infty) = \bar{C}$ ← const value

Assume polar coordinates

O_2 diffuses in tissue β in water with same D

Q_R is absorbed in tissue w/ rate μ

Solve for $C(r, \infty)$ – steady concentration i.e. does not depend on time

passive diffusion ↓ absorption ↙

$$\frac{\partial C}{\partial t} = \begin{cases} D\Delta C - \mu C & \text{in tissue } r \le a \\ D\Delta C & \text{in water } r > a \end{cases}$$

$$\frac{\partial C}{\partial t}(r) = \begin{cases} \frac{D}{r}\frac{\partial^2}{\partial r^2}(rC) - \mu C & r \le a \\ \frac{D}{r}\frac{\partial^2}{\partial r^2}(rC) & r > a \end{cases}$$

← written Laplace op in ~~polar~~ spherical coords

↑ spherical symmetry

09/10/14

check it says this last line — not polar

Note that in spherical coordinates

$$\Delta C(r) = \frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial C}{\partial r}\right) = \frac{1}{r^2}\left(2r\frac{\partial C}{\partial r} + r^2\frac{\partial^2 C}{\partial r^2}\right)$$

$$= \frac{1}{r}\left(\frac{\partial C}{\partial r} + \frac{\partial C}{\partial r} + r\frac{\partial^2 C}{\partial r^2}\right)$$

$$= \frac{1}{r}\left(\frac{\partial C}{\partial r} + \frac{\partial}{\partial r}\left(r\frac{\partial C}{\partial r}\right)\right) = \frac{1}{r}\frac{\partial}{\partial r}\left(C + r\frac{\partial C}{\partial r}\right)$$

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

$$\begin{cases} \frac{D}{r}\frac{\partial^2}{\partial r^2}(rC) = \mu C & r \le a \\ - \text{ " } - = 0 & r > a \end{cases}$$

let $r^2 = \frac{a}{D}$

- $r \le a$ $\quad \frac{d^2}{dr^2}(rC) - \nu^2(rC) = 0$

$$rC = Ae^{\nu r} + Be^{-\nu r}$$

$$c(r) = \frac{A'\sinh(\nu r)}{r} + \frac{B'\cosh(\nu r)}{r}$$

For C finite at $r=0$, $B' = 0$

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

- $r > a$ $\quad rC = \alpha + \beta r$

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

For $r \to \infty$ $\quad C = \bar{C}$ some const. $\Rightarrow \beta = \bar{C}$

$$C = \bar{C} + \frac{\alpha}{r}$$

At $r = a$ 1) concentration is continuous

2) flux is continuous

Using 1) $c(a) = \bar{c} + \frac{\alpha}{a} = \frac{A' \sinh(ra)}{a}$ ①

2) flux $= -D\frac{\partial c}{\partial r}$

$$-D\left(\frac{-\alpha}{a^2}\right) = -DA'\left(-\frac{\sinh(ra)}{a^2} + \frac{r\cosh(ra)}{a}\right) \quad ②$$

Sum ① + ② $\bar{c} = A' r \cosh(ra)$

$$A' = \frac{\bar{c}}{r\cosh(ra)}$$

$$\frac{\alpha}{a} = \frac{\bar{c}}{r\cosh(ra)}\frac{\sinh(ra)}{a} - \bar{c}$$

$$\Rightarrow \quad \alpha = \frac{\bar{c}}{r}\tanh(ra) - \bar{c}a$$

$$c(r) = \begin{cases} \frac{\bar{c}}{r\cosh(ra)}\frac{\sinh(rr)}{r} & r < a \\ \bar{c}\left(1 - \frac{a}{r}\right) + \frac{\bar{c}\tanh(ra)}{rr} & r > a \end{cases}$$

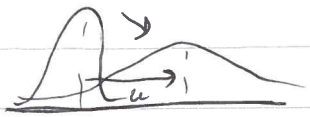
Diffusion with dryt included

In the Brownian motion we add a bias so there is a dryt

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

$$f(x) = \frac{1}{\delta\sqrt{2\pi n}} \exp\left(-\frac{(X - nu\tau)^2}{2n\delta^2}\right)$$

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



Dif. equation?

$X = x - ut$, for $F(X,t)$: $\frac{\partial F}{\partial t} = \frac{\partial^2 F}{\partial X^2}$

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

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

$$\frac{df}{dt} = \frac{dF}{dt} = \frac{\partial f}{\partial t} + \frac{\partial f}{\partial x}\frac{\partial x}{\partial t} \overset{x = X + ut}{=} \frac{\partial f}{\partial t} + u\frac{\partial f}{\partial X}$$

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

drift diffusion

$$f(x,t) = \int_{-\infty}^{\infty} \left(\frac{1}{\sqrt{4\pi D t}} \exp\frac{(x-y-ut)^2}{4Dt}\right) \underbrace{f(y,0)}_{\text{initial conditions}}\, dy$$

For concentration: drift, diffusion, absorption

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

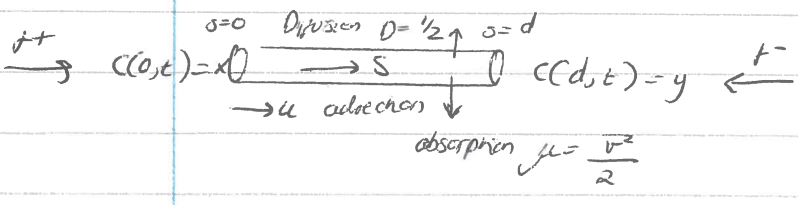
$$\frac{\partial C}{\partial t} = -\frac{\partial}{\partial x}\underbrace{\left(uC - D\frac{\partial C}{\partial x}\right)}_{\text{flux}} - \mu C$$

Strategy: what happens in individual pipes $\overset{\mu+}{\circ}\!\!=\!\!=\!\!\circ\overset{\mu-}{}$, then extend our findings for a network

Assumptions:

1) Normalise equation for Q_2, such that $D = 1/2$: $\mu = \frac{v^2}{2}$
2) Constant cross-section pipes
3) Tube is thin relative to its length
   $\Rightarrow$ concentration C just a function of distance

Assume both ends of a tube are open



Then $\frac{\partial C}{\partial t}(s,t) = -u\frac{\partial C}{\partial s} + \frac{1}{2}\frac{\partial^2 C}{\partial s^2} - \frac{v^2}{2}C$

B.C.s: $C(0,t) = x$

$C(d,t) = y$

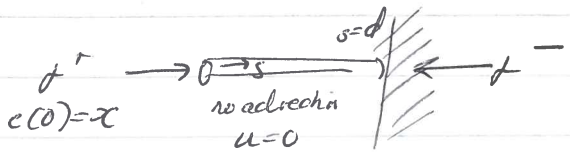
Only interested in steady state $\left(\frac{\partial}{\partial t} = 0\right)$ solution

$$\frac{1}{2}\frac{\partial^2 C}{\partial s^2} = u\frac{\partial C}{\partial s} + \frac{v^2}{2}C \qquad C(0) = x \quad C(d) = y$$

f^+ - flux in to the pipe $\left(uC - \frac{1}{2}\frac{\partial C}{\partial s}\right)_{s=0}$

f^- - flux in to the end of pipe $-\left(uC - \frac{1}{2}\frac{\partial C}{\partial s}\right)_{s=d}$

Simple case: closed end



$$\frac{1}{2}\frac{\partial^2 C}{\partial s^2} - \frac{v^2}{2}C = 0$$

Gen. sol: $C(s) = Ae^{-vs} + Be^{vs}$

$C(0) = x = A + B$ since closed end $f^- = 0$

$$uC = \frac{1}{2}\frac{\partial C}{\partial s} \quad \text{at } s=d$$

$$C'(d) = v\left(Be^{vd} - Ae^{-vd}\right) = 0 \longrightarrow A = Be^{2vd}$$

$$x - B = Be^{2vd} \qquad B = \frac{x}{1+e^{2vd}} = \frac{xe^{-vd}}{2\cosh(vd)}$$

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

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

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

at $s=d$ $\quad C(d) = \frac{x}{\cosh(vd)} = y$

This will be on exam in some form

More generally $\frac{\partial c}{\partial t} = \frac{1}{2}\frac{\partial^2 c}{\partial s^2} - u\frac{\partial c}{\partial s} - \frac{v^2}{2}c$

with open ends at $s=0$, $s=d$

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

For steady solution:

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

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

Flux densities

$f^+ \rightarrow$ [ ] $\leftarrow f^-$

$$f^+ = \left(uc - \frac{1}{2}\frac{\partial c}{\partial s}\right)_{s=0} = \underbrace{\left(\frac{1}{2}u + \frac{\sigma}{2}\coth(\sigma d)\right)}_{a^+}x - \underbrace{\left(\frac{\sigma}{2}e^{-du}\operatorname{cosech}(\sigma d)\right)}_{b^-}y$$

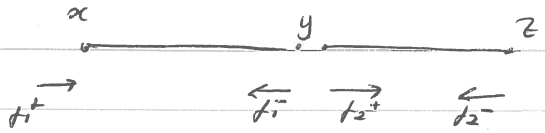
or $f^+ = a^+x - b^-y$

$$f^- = -\left(uc - \frac{1}{2}\frac{\partial c}{\partial s}\right)_{s=d} = \underbrace{\left(\frac{-1}{2}u + \frac{\sigma}{2}\coth(\sigma d)\right)}_{a^-}y - \underbrace{\left(\frac{\sigma}{2}e^{du}\operatorname{cosech}(\sigma d)\right)}_{b^+}x$$

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

Consider a simple 2 tube network

Assume the same cross section for 2 pipes



By dynamics: $f_1^+ = a^+ x - b^- y$

$f_1^- = a^- y - b^+ x$

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

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

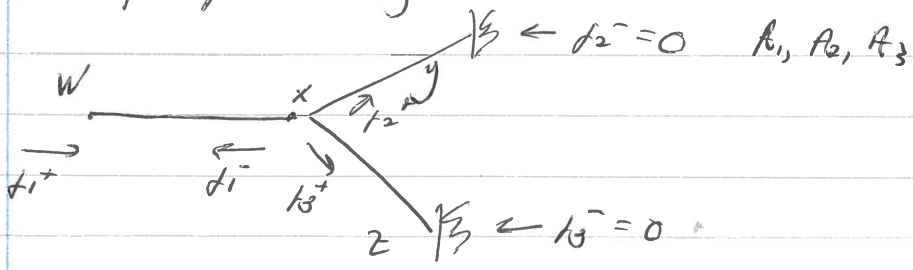
Conservation of flux at join (Kirchoff's current law)

$f_1^- + f_2^+ = 0$

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

$$y = \frac{b_1^+ x + b_2^- z}{a_1^- + a_2^+} \leftarrow \text{concentration at join}$$

Example of branching network



At closed ends: $f_2^- = a_2^- y - b_2^+ x = 0$ $\quad y = \frac{b_2^+ x}{a_2^-}$

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

$$z = \frac{b_3^+ x}{a_3^-}$$

At centre node

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

13/10/14

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

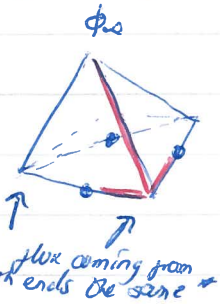
$$A_1 (a_1^- x - b_1^+ w) + A_2 (a_2^+ x - b_2^- y) + A_3 (a_3^+ x - b_3^- z) = 0$$

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

$$(A_1 a_1^- + A_2 a_2^+ + A_3 a_3^+) x - A_2 b_2^- \underbrace{\frac{b_2^+}{a_2^-} x}_{y} - A_3 b_3^- \underbrace{\frac{b_3^+}{a_3^-} x}_{z} = A_1 b_1^+ w$$

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

Using symmetry in branching networks



Identical pipes joined in a tetrahedron

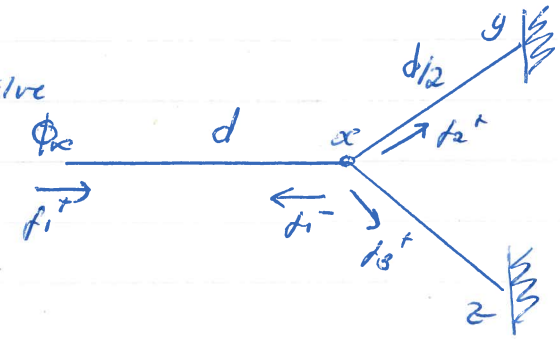
No advection

All corners are closed, but one connected to oxygen source

By symmetry flux at y or z is $= 0$

so we have 0 at • points

— use only this section to solve



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

$$f_2^+ = a_2^+ x - b_2^- y = \left(a_2^+ - \frac{b_2^- b_2^+}{a_2^-}\right) x = A_2 x$$

(i) In A_2 d is replaced by $d/2$

By symmetry $z = y \therefore f_3^+ = f_2^+$

At x: $f_1^- + f_2^+ + f_3^+ = 0 \Rightarrow f_1^- + 2A_2 x = 0$

$$\underbrace{a_1^- x - b_1^+ \phi_\infty}_{f_1^-} + 2A_2 x = 0$$

$$x = \frac{b_1^+ \phi_\infty}{a_1^- + 2A_2}$$

In pipe 2: $b_1^+ = \frac{\nu}{2} \operatorname{cosech}(\nu d) = b_1^-$

$$a_1^+ = \frac{\nu}{2} \coth(\nu d) = a_1^-$$

$$A_2 = a_2^+ - \frac{b_2^- b_2^+}{a_2^-} = \frac{\nu}{2} \coth\left(\frac{\nu d}{2}\right) - \frac{\left(\frac{\nu}{2} \operatorname{cosech}\left(\frac{\nu d}{2}\right)\right)^2}{\frac{\nu}{2} \coth\left(\frac{\nu d}{2}\right)}$$

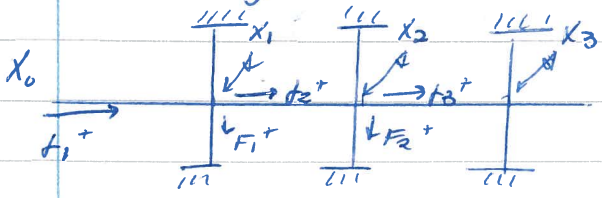
$$= \frac{\nu}{2} \tanh\left(\frac{\nu d}{2}\right)$$

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

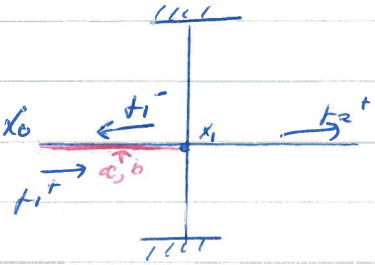
Simple model of the insect tracheal system

- a network of thin tubes
- small insects: diffusion
- large insects: add uniform advection
- include absorption to model metabolism of breathing tissues

Tracheal system as a semi-infinite network of pipes



Left end



easy to find

$F_1^+ = A x_1$

Define $\lambda = \frac{f_1^+}{x_0}$

Then by symmetry

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

$2F_1^+ + f_2^+ + f_1^- = 0$ at first join

$2A_1 x_1 + \lambda x_1 + (a^- x_1 + b^+ x_0) = 0$

$$x_1 = \frac{b^+ x_0}{2A_1 + \lambda + a^-}$$

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

$\lambda x_0 = a^+ x_0 - \frac{b^- b^+ x_0}{2A_1 + \lambda + a^-}$

$\lambda^2 + \underbrace{(2A + a^- + a^+)}_{B}\lambda + b^- b^+ - a^+(2A + a^-) = 0$

$$\lambda_{1,2} = -\frac{B}{2} \pm \frac{1}{2}\sqrt{B^2 \mp 4C}$$

$a^+a^- - b^-b^+ = \frac{\nu^2}{4}$: λ is positive

$$\lambda = -\frac{(2A + a^- - a^+)}{2} + \frac{1}{2}\sqrt{(2A+a^- - a^+)^2 + 8a^+A + \Gamma^2} \quad ; \quad \lambda_1^+ = \lambda_{CC}$$

Chapter 3

Oxygen transport and Insect respiration

Motivation: Gas transport in animals

Oxygen is needed to fuel aerobic metabolism. How is transport from the lungs to the energy dissipating body structures - the organs - managed by the animal?

For very small organisms, the oxygen need only travel small distances, but as the animal size increases the oxygen needs to be transported significant distances.

We start by examining simple diffusion of oxygen. We first look at some toy mathematical problems to get a handle on how distance diffused depends on time.

Diffusion of particle in 1 dimension

Particle moves δ to left or right with (independent) probability 1/2 at each step.
Let $X_i \in \{-\delta, \delta\}$ be the random variable for ith step
and consider
$S_n = X_1 + X_2 + \ldots + X_n$ (= r.v. for position after n steps).

ONE approach for those familar with probability is :
Since the X_i are independently and identically distributed (i.i.d.) mean 0 and variance δ^2, by the central limit theorem (sums of iid rv's) - OR SEE NEXT SLIDE - as $n \to \infty$, $S_n \to N(0, n\delta^2)$
[the normal distribution with mean 0, variance = $n\,\delta^2$]
So
root mean square of distance moved $\propto \sqrt{n}$

Notice that we have

$$E[X_i] = p(x = -\delta)(-\delta) + p(x = \delta)\delta = \frac{1}{2}(-\delta) + \frac{1}{2}\delta = 0,$$

so that $E[S_n] = E[\sum_i X_i] = \sum_i E[X_i] = 0.$

Similarly, if $i \neq j$,

$$E[X_i X_j] = p(x = -\delta)p(x = -\delta)(-\delta)^2 + p(x = -\delta)p(x = \delta)(-\delta)(\delta) +$$
$$p(x = \delta)p(x = -\delta)(\delta)(-\delta) + p(x = \delta)p(x = \delta)(\delta)^2 \; (= E[X_i]E[X_j])$$
$$= 0$$

whereas if $i = j$,

$$E[X_i^2] = \frac{1}{2}\delta^2 + \frac{1}{2}\delta^2 = \delta^2 \Rightarrow \sum_i X_i^2 = n\delta^2.$$

This gives for the variance

$$\sigma^2 = E[(S_n - E[S_n])^2] = E[\sum_i X_i^2 + 2\sum_{i<j} X_i X_j] = \sum_i E[X_i^2] + 2\sum_{i<j} E[X_i X_j] = n\delta^2$$

i.e. as $n \to \infty$, the pdf f_n has

$$f_n(x) \approx \frac{1}{\delta\sqrt{2\pi n}} e^{-x^2/2n\delta^2}$$

If τ is time between collisions, t time elapsed,

then $n\tau = t$.

$$f(x,t) \approx \frac{1}{\sqrt{4\pi Dt}} e^{-x^2/4Dt} \quad \text{with } D = \frac{\delta^2}{2\tau}$$

Now take limit as $\tau, \delta \to 0$ such that D is finite :

$$f(x,t) = \frac{1}{\sqrt{4\pi Dt}} e^{-x^2/4Dt} \quad \text{pdf for particle position}$$

$\Rightarrow$ distance moved $\propto \sqrt{\text{variance}}\ \alpha\ \sqrt{t}$

So good for small distances, e.g. across a cell wall, or the shell of an egg, but too slow for transport between organs.

Time taken to reach 99% diffusion equilibrium as a function of distance from a plane (Jacobs 1935)

Distance from boundary	time
10 cm	53 days
1 cm	12.75 hours
1 mm	7.6 minutes
100 μm	4.56 seconds
10 μm	0.0456 seconds
1 μm	0.000456 seconds
0.1 μm	0.00000456 seconds

Now for $f(x,t) = \frac{1}{\sqrt{4\pi Dt}} e^{-x^2/4Dt}$,

$$\frac{\partial f}{\partial x} = \frac{-2x}{4Dt\sqrt{4\pi Dt}} e^{-x^2/4Dt} = \frac{-x}{2Dt} f$$

$$\frac{\partial^2 f}{\partial x^2} = \frac{-1}{2Dt} f - \frac{x}{2Dt}\frac{\partial f}{\partial x} = \frac{-1}{2Dt} f + \frac{x^2}{4D^2t^2} f$$

Whereas

$$\frac{\partial f}{\partial t} = \frac{1}{\sqrt{4\pi D}}\left(\frac{-1}{2}\right) t^{-3/2} e^{-x^2/4Dt} + \frac{1}{\sqrt{4\pi Dt}}\left(\frac{-x^2}{4D}\right) e^{-x^2/4Dt}$$

$$= \frac{-1}{2t} f + \left(\frac{x^2}{4Dt^2}\right) f.$$

Thus f satisfies the Diffusion equation:

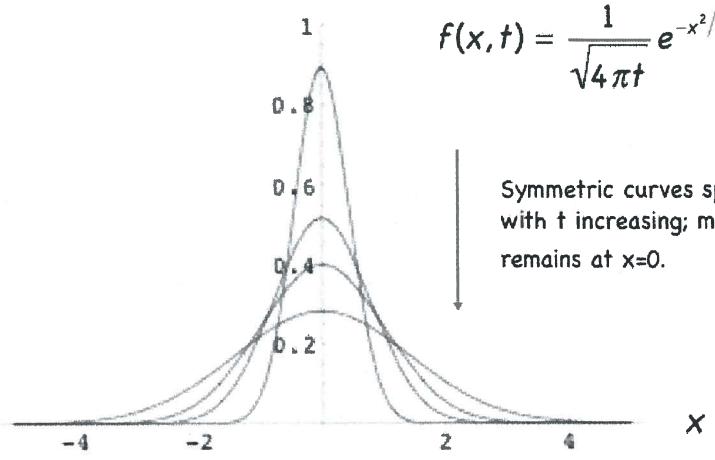
$$\boxed{\frac{\partial f}{\partial t} = D\frac{\partial^2 f}{\partial x^2}} \quad \text{i.e.} \quad \boxed{\frac{\partial f}{\partial t} = -\frac{\partial J}{\partial x},\ J = -D\frac{\partial f}{\partial x} = \text{flux}}$$

From this "fundamental solution" for a single particle, we may construct solutions on $(-\infty, \infty)$ of diffusion equation for initial concentrations $C(x,0)$ by convolution :

$$C(x,t) = \int_{-\infty}^{\infty} \left(\frac{1}{\sqrt{4\pi Dt}} e^{-(x-y)^2/4Dt}\right) C(y,0)\, dy$$

For example if we start with $C(y,0) = \delta(y,0)$, the Kronecker delta function at the origin we get

$$C(x,t) = \frac{1}{\sqrt{4\pi Dt}} e^{-x^2/4Dt}.$$



$$f(x,t) = \frac{1}{\sqrt{4\pi t}} e^{-x^2/4t}$$

More generally in 3D we have

$$\frac{\partial C}{\partial t} = D\nabla^2 C = div(D\nabla C) = -divJ, \quad J = -D\nabla C = flux$$

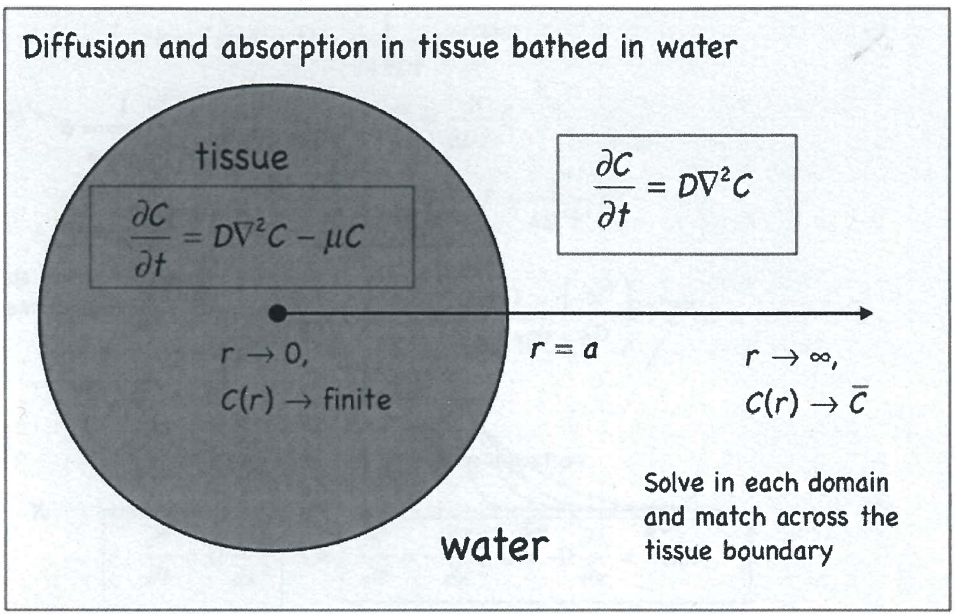
Example : Diffusion and absorption within a tissue

Now consider levels of oxygen concentration in a spherical tissue radius a immersed in water.

Assume :

- oxygen diffuses with same constant D in both tissue and water
- oxygen is absorbed by tissue (for aerobic metabolism) at rate μ

$$\frac{\partial C}{\partial t} = \underset{\text{passive diffusion}}{D\nabla^2 C} - \underset{\text{absorption}}{\mu C}$$



Suppose body is in water and that D for water is same as for tissue and let $\mu = Dv^2$. $\mu = 0$ in the water (since no absorption there)

Spherical symmetry : $C = C(r, t)$ where

$$\frac{\partial C}{\partial t} = \begin{cases} \frac{D}{r}\frac{\partial^2}{\partial r^2}(rC) - \mu C & r \le a \text{ (tissue)} \\ \frac{D}{r}\frac{\partial^2}{\partial r^2}(rC) & r > a \text{ (water).} \end{cases}$$

Let us find the steady state solution $C_\infty(r) = \lim_{t\to\infty} C(r, t)$.

Thus solve :

$$\begin{cases} \frac{D}{r}\frac{d^2}{dr^2}(rC) - \mu C = 0 & r \le a \\ \frac{D}{r}\frac{d^2}{dr^2}(rC) = 0 & r > a \end{cases}$$

subject to $C(0)$ finite, $C(a-) = C(a+)$ [continuity across interface], $-D\,C'(a-) = -D\,C'(a+)$ [continuity of flux] and $C(\infty) = \bar{C}$ fixed.

For r > a, we have rC is linear in r :

$$rC_\infty(r) = Ar + B \Rightarrow C_\infty(r) = A + \frac{B}{r} \quad (A).$$

For $r \le a$,

$$C_\infty(r) = \frac{1}{vr}\left(A'\sinh(vr) + B'\cosh(vr)\right).$$

For finiteness at r = 0 we require B' = 0. For $C_\infty(\infty) = \bar{C}$ $A = \bar{C}$. For continuities at a :

$$\text{conc. :} \quad \frac{1}{va}A'\sinh(va) = \bar{C} + \frac{B}{a} \quad (B)$$

$$\text{flux :} \quad -\frac{1}{va^2}A'\sinh(va) + \frac{A'}{a}\cosh(va) = -\frac{B}{a^2} \quad (C)$$

Add (C) + (1/a) x (B) :

$$\frac{A'}{a}\cosh(va) = \frac{\bar{C}}{a} \Rightarrow A' = \frac{\bar{C}}{\cosh(va)}.$$

So from (B)

$$B = \frac{A'}{v}\sinh(va) - a\bar{C} = \frac{\bar{C}}{v}\tanh(va) - a\bar{C}$$

Hence we obtain :

$$C_\infty(r) = \begin{cases} \dfrac{\bar{C}\sinh(vr)}{vr\cosh(va)} & r \le a \\ \bar{C}\left(1 - \dfrac{a}{r}\right) + \bar{C}\left(\dfrac{\tanh(va)}{vr}\right) & r > a \end{cases}$$

Note that $C_\infty(0) = \bar{C}\,\mathrm{sech}(va)$.

Diffusion with drift included

We also need to be able to model the situation where oxygen is transported around a body using constant speed advection through "pipes" (for larger bodies where diffusion is not rapid enough, the lungs push the oxygen to where it is needed.)

In the Brownian motion model, the particle now moves with a bias u, i.e. the mean speed is not zero, but there is a drift u:

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

So that our asymptotics now read

$$f_n(x) \approx \frac{1}{\delta\sqrt{2\pi n}} e^{-(x-nu\tau)^2/2n\delta^2}$$

$$f(x,t) = \frac{1}{\sqrt{4\pi Dt}} e^{-(x-ut)^2/4Dt}$$

This pdf also satsfies a diffusion - like equation. Let

X = x - ut. Then $F(X,t) = \frac{1}{\sqrt{4\pi Dt}} e^{-X^2/4Dt} = f(x,t)$

satisfies the standard diffusion equation

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

By the chain rule,

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

$$\frac{\partial f}{\partial x} = \frac{\partial F}{\partial X}\frac{\partial X}{\partial x} = \frac{\partial F}{\partial X}\frac{\partial (x-ut)}{\partial x} = \frac{\partial F}{\partial X},$$

and similarly $\frac{\partial^2 f}{\partial x^2} = \frac{\partial^2 F}{\partial X^2}$.

Hence f(x, t) satisfies

$$0 = \frac{\partial F}{\partial t} - D\frac{\partial^2 F}{\partial x^2} = \frac{\partial f}{\partial t} - \frac{\partial f}{\partial x}(-u) - D\frac{\partial^2 f}{\partial x^2},$$

that is

$$\frac{\partial f}{\partial t} = -u\frac{\partial f}{\partial x} + D\frac{\partial^2 f}{\partial x^2}. \quad \text{Diffusion with drift u.}$$

As for standard diffusion, if the initial concentration on $(-\infty, +\infty)$ is C(x, 0) then

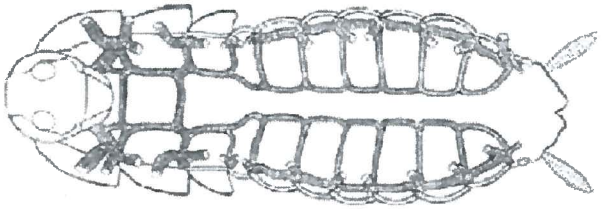
$$C(x,t) = \int_{-\infty}^{\infty} \left(\frac{1}{\sqrt{4\pi D t}} e^{-(x-y-ut)^2/4Dt} \right) C(y,0)\,dy$$

Hence same as standard diffusion, except also moving to the right with speed u as it decays.

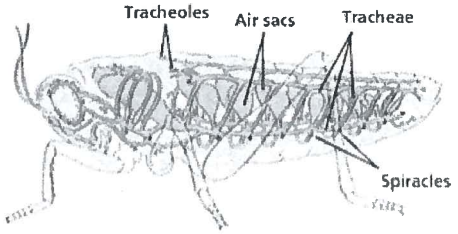
NB : The substitution X = x - ut enables us to move with the oxygen with speed u so that it appears just like normal diffusion.

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 closed to a tracheal branch and they utilize the oxygen for metabolism. So we have passive diffusion with advection in thin pipes, and with absorption.



Inside the tracheal system



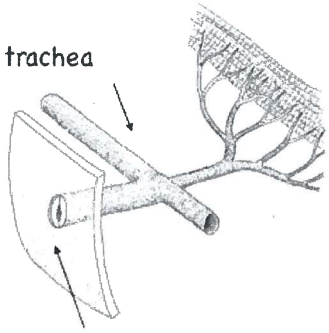
Images of spiracles, muscles and trachea:

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

General information on insect biology:

http://ag.ansp.purdue.edu/~shan/bio/lecture2.ppt

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

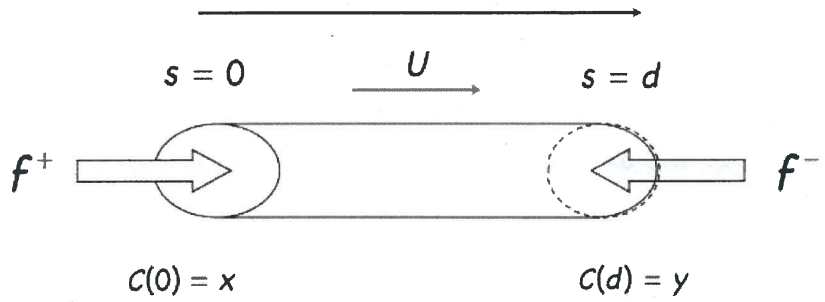


Gated spiracle

Diffusion with advection along a thin tube

Assumptions:

- normalise so that passive diffusion constant D=1/2, and $\mu = v^2/2$
- constant advection speed u along tube
- tube constant cross section
- tube thin relative to length; oxygen concentration is uniform C(s,t) in a cross section at s along the tube (also this allows us to connect tubes together and not worry about effects at the join)
- both tube ends are open (for now).



f^+ = flux density into end s = 0

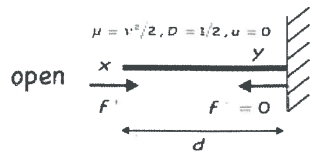
$$= \left(uC - \frac{1}{2}\frac{\partial C}{\partial s} \right)_{s=0}$$

f^- = flux density into end s = d

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

(flux density = rate of molecule transport per unit cross-sectional area)

Simplest case: no advection: u=0.



Steady state $\frac{\partial C}{\partial t} = \frac{1}{2}\frac{\partial^2 C}{\partial s^2} - \frac{\nu^2}{2}C = 0 \Rightarrow \frac{d^2C}{ds^2} = \nu^2 C$

with boundary conditions C(0) = x, C(d) = y, and at d : flux = $-\frac{1}{2}\frac{dC}{ds}(d) = 0$

So

$C(s) = Ae^{\nu s} + Be^{-\nu s}$

gives $x = A + B$, $y = Ae^{\nu d} + Be^{-\nu d}$

and $-Ae^{\nu d} + Be^{-\nu d} = 0$

Hence

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

and hence

$C(s) = Ae^{\nu s} + Be^{-\nu s} = \frac{x}{2\cosh(\nu d)}(e^{\nu s + \nu d} + e^{-\nu s + \nu d}) = \frac{x\cosh(\nu(s-d))}{\cosh(\nu d)}$,

and $y = C(d) = x / \cosh(\nu d)$.

Diffusion with non-zero advection u

The equation for the evolution of the concentration C(s, t) of the oxygen is

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

Diffusion with (mean) drift u and absorption rate $\mu=\nu^2$

The advection speed is u, and s distance along the pipe with s = 0 at the left end. Suppose the concentration is fixed at the ends : $C(0,t) = x$, $C(d,t) = y$ $\forall t \geq 0$.

Then the steady state oxygen concentration is

$$C_\infty(x) = \frac{e^{su}}{\sinh(\sigma d)}\left\{x\sinh(\sigma(d-s)) + ye^{-du}\sinh(s\sigma)\right\} \qquad \sigma = \sqrt{u^2+\nu^2}$$

The flux density into the end s = 0, is given by

$$f^+ = \left(\frac{1}{2}u + \frac{\sigma}{2}\coth(\sigma d)\right)x - \left(\frac{\sigma}{2}e^{-du}\operatorname{cosech}(\sigma d)\right)y$$

and the flux density into the end s = d is

$$f^- = -\left(\frac{\sigma}{2}e^{du}\operatorname{cosech}(\sigma d)\right)x + \left(-\frac{1}{2}u + \frac{\sigma}{2}\coth(\sigma d)\right)y$$

where $\sigma^2 = u^2 + v^2$.

You should memorise these equations.

The flux density into the end s = 0, is given by

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

$$a^+ = \frac{1}{2}u + \frac{\sigma}{2}\coth(\sigma d), \qquad b^- = \frac{\sigma}{2}e^{-du}\operatorname{cosech}(\sigma d)$$

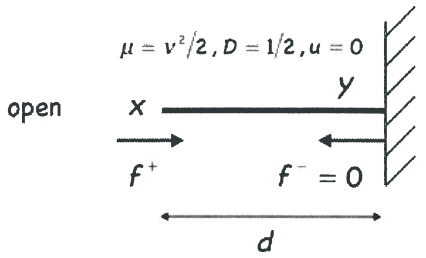
and the flux density into the end s = d is

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

$$a^- = -\frac{1}{2}u + \frac{\sigma}{2}\coth(\sigma d), \qquad b^+ = \frac{\sigma}{2}e^{du}\operatorname{cosech}(\sigma d)$$

These expressions will enable us to study oxygen transport in networks by working out how the fluxes divide at branches. Thus we only need to know the fluxes at the ends of the pipes where they join. There is an electrical circuit analogy with fluxes the currents and concentrations the voltages. Note that here the fluxes (=currents) are not constant along each pipe.

Example: single tube, one end open, other closed



If pipe cross-sectional is A, then flux into pipe is Af^+

Since right end is closed, there is no flux into that end: $f^- = 0$.

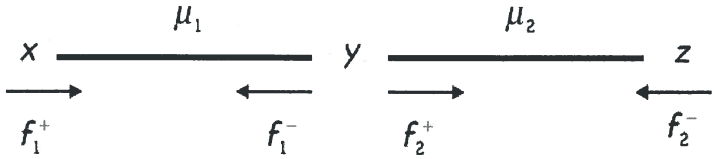
$$f^- = a^- y - b^+ x = 0 \Rightarrow y = b^+ x / a^-$$

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

So total flux density

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

Consider now a simple 2 tube network: (assume both pipes have same constant cross-section here.)



By definition

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

Conservation of flux (≈ Kirchhoff's current law) at join :

$$0 = f_1^- + f_2^+ = a_1^- y - b_1^+ x + a_2^+ y - b_2^- z$$

So the concentration at the join is

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

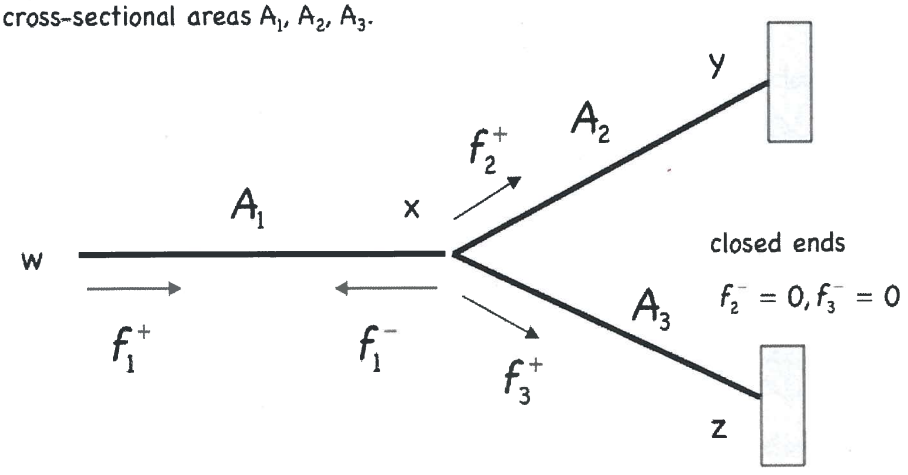
So we can find the effective flux density through the single joined tube in terms of the start and end concentrations x, z:

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

$$f_2^- = a_2^- z - b_2^+ y = \left(a_2^- z - b_2^+ \left[\frac{b_1^+ x + b_2^- z}{a_1^- + a_2^+}\right]\right)$$
$$= \left(a_2^- - \left[\frac{b_2^+ b_2^-}{a_1^- + a_2^-}\right]\right)z - \left(\frac{b_1^+ b_2^+}{a_1^- + a_2^+}\right)x$$

Examples of branching networks

3 pipes all joined at one end. Two ends closed, one open. Different cross-sectional areas A_1, A_2, A_3.



At the closed ends :

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

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

Hence $y = \frac{b_2^+ x}{a_2^-}, z = \frac{b_3^+ x}{a_3^-}$.

At the centre node, sum of all fluxes is zero : $A_1 f_1^- + A_2 f_2^+ + A_3 f_3^+ = 0$

Hence

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

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

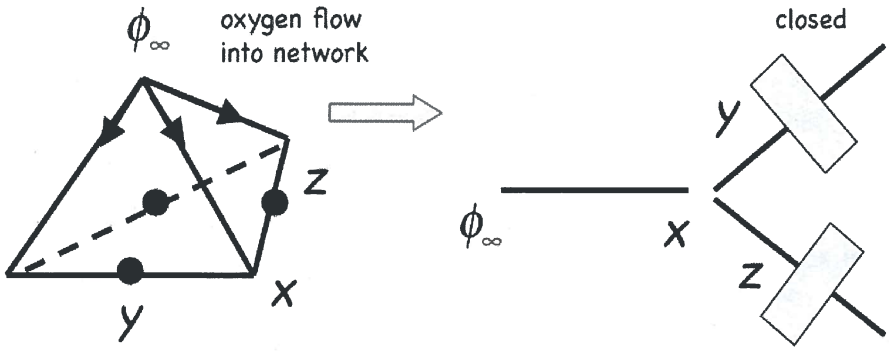
$\Rightarrow (A_1 a_1^- + A_2 a_2^+ + A_3 a_3^+)x - A_1 b_1^- w - A_2 b_2^- y - A_3^+ b_3^- z = 0$

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

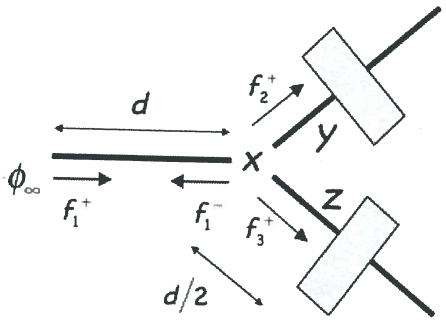
$$\Rightarrow x = \frac{A_1 b_1^+ w}{A_1 a_1^- + A_2 a_2^+ + A_3 a_3^+ - A_2 b_2^- \frac{b_2^+}{a_2^-} - A_3^+ b_3^- \frac{b_3^+}{a_3^-}}$$

Using symmetry in branching networks.

Identical pipes joined into tetrahedron. No advection. All corners but closed, but one connected to oxygen source.



By symmetry zero flux at midpoints of bottom triangle



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

$$f_2^+ = a_2^+ x - b_2^- y = (a_2^+ - b_2^- \frac{b_2^+}{a_2^-})x = A_2 x$$

where $A_2 = (a_2^+ - b_2^- \frac{b_2^+}{a_2^-})$

By symmetry $y = z$, $f_2^+ = f_3^+$

At x, $f_1^- + f_2^+ + f_3^+ = 0 \Rightarrow f_1^- + 2A_2 x = 0$

$$f_1^- + 2A_2 x = (a_1^- x - b_1^+ \phi_\infty) + 2A_2 x$$

Caution: In A_2, d is replaced by d/2

$$0 = (a_1^- x - b_1^+ \phi_\infty) + 2A_2 x$$

$$\Rightarrow x = \frac{b_1^+ \phi_\infty}{a_1^- + 2A_2}$$

Now in pipe 1, length d, $b_1^+ = \frac{v}{2}\operatorname{cosech}(vd) = b_1^-$, $a_1^+ = \frac{v}{2}\coth(vd) = a_1^-$

For pipes 2, 3 the lengths are d/2 :

$$A_2 = a_2^+ - \frac{b_2^- b_2^+}{a_2^-} = \frac{v}{2}\coth(\frac{vd}{2}) - \frac{\left(\frac{v}{2}\operatorname{cosech}(\frac{vd}{2})\right)^2}{\frac{v}{2}\left(\coth(\frac{vd}{2})\right)}$$

$$= \frac{v}{2}\coth(\frac{vd}{2}) - \frac{\left(\frac{v}{2}\operatorname{cosech}(\frac{vd}{2})\right)^2}{\frac{v}{2}\left(\coth(\frac{vd}{2})\right)} = \frac{v}{2}\frac{\left(\coth(\frac{vd}{2})\right)^2 - \left(\operatorname{cosech}(\frac{vd}{2})\right)^2}{\left(\coth(\frac{vd}{2})\right)}$$

$$= \frac{\nu}{2}\frac{\left(\coth(\frac{\nu d}{2})\right)^2 - \left(\operatorname{cosech}(\frac{\nu d}{2})\right)^2}{\left(\coth(\frac{\nu d}{2})\right)} = \frac{\nu}{2}\tanh(\frac{\nu d}{2})$$

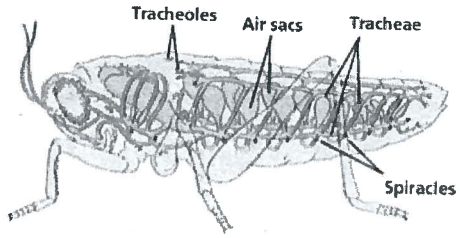
Hence

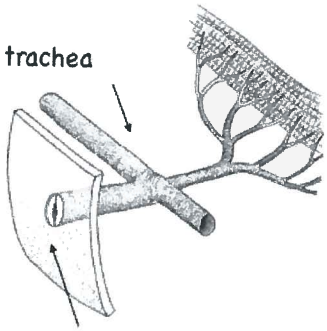
$$x = \frac{b_1^+\phi_\infty}{a_1^- + 2A_2} = \frac{\frac{\nu}{2}\operatorname{cosech}(\nu d)\phi_\infty}{\frac{\nu}{2}\coth(\nu d) + 2\frac{\nu}{2}\tanh(\frac{\nu d}{2})} = \frac{\operatorname{cosech}(\nu d)\phi_\infty}{\coth(\nu d) + 2\tanh(\frac{\nu d}{2})}$$

So, how do insects breathe without lungs?

- exchange oxygen, carbon dioxide, water vapour between their tissues and outside environment by a network of air-filled tubes know as trachae. Each cell is close to a trachae.
- trachae open to the outside via small holes called spiracles
- spiracles are gated via muscle-controlled valves and have hairs that filter out dust
- for small insects, gas transport is passive diffusion (no advection)
- larger insects, such as grasshoppers, forcibly ventilate their trachae by contracting their abdominal muscles and compressing their internal organs
- grasshoppers can control this ventilation to the extent that air flow is unidirectional through their body

Inside the tracheal system





Gated spiracle

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

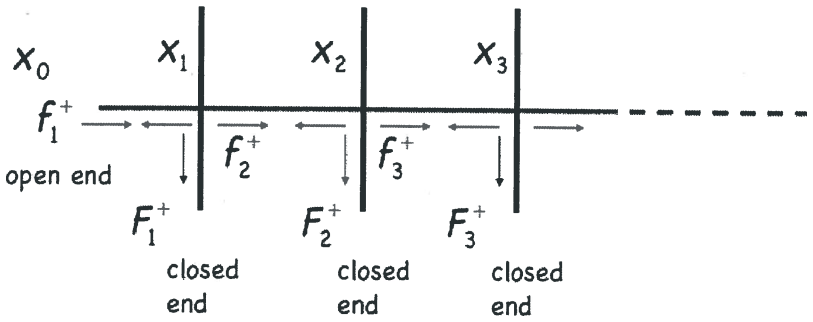
General figures: http://images.google.co.uk/
(and search for insect trachea)

Simple mathematical models of the insect tracheal system

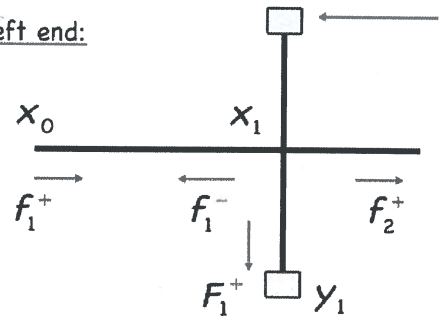
- We will model the insect tracheal system with a network of thin hollow tubes through which oxygen will diffuse and possibly advect.
- When we are considering larger insects, we will add uniform advection of (constant) speed u to model the ventilation
- We will also include absorption of oxygen for metabolism by the surrounding tissue

Tracheal System as a semi-infinite network of pipes

(use capital F for fluxes in the side branches)



Left end:



$F_1^+ = Ax_1$ (simple pipe closed end, A easy to find)

Exact form of A depends on the branch pipe lengths. We also keep the a's and b's for generality here.

Also, define λ by $\lambda = f_1^+ / x_0$. Then by symmetry,

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

So now we have to find the ratio !

Using conservation of flux at first node :

$$2F_1^+ + f_2^+ + f_1^- = 0$$

$$\Rightarrow 2Ax_1 + \lambda x_1 + (a^- x_1 - b^+ x_0) = 0$$

Rearranging,

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

Now,

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

so that we obtain $\lambda x_0 = a^+ x_0 - b^- \dfrac{b^+ x_0}{2A + \lambda + a^-}$

Hence we must solve the quadratic

$$\lambda^2 + (2A + a^- - a^+)\lambda + b^+ b^- - a^+(2A + a^-) = 0.$$

$$\lambda_{\pm} = -\frac{(2A + a^- - a^+)}{2} \pm \frac{1}{2}\sqrt{(2A + a^- - a^+)^2 + 4a^-(2A + a^-) - 4b^- b^+}$$

$$= -\frac{(2A + a^- - a^+)}{2} \pm \frac{1}{2}\sqrt{(2A + a^- - a^+)^2 + 8a^+ A + 4(a^+ a^- - b^- b^+)}.$$

Now,

$$a^+ a^- - b^- b^+ = \frac{v^2}{4},$$

so

$$\lambda_{\pm} = -\frac{(2A + a^- - a^+)}{2} \pm \frac{1}{2}\sqrt{(2A + a^- - a^+)^2 + 8a^+ A + v^2}$$

We expect the ratio λ to be positive, so we must take λ_+.

This gives, for the flux into the left end :

$$f_1^+ = \left(-\frac{(2A + a^- - a^+)}{2} + \frac{1}{2}\sqrt{(2A + a^- - a^+)^2 + 8a^+ A + v^2}\right) x_0$$

A similar model is introduced in Q1 of Coursework Sheet 3

16/10/14

How do fish breathe without lungs?

- whales and dolphins (not fish!) use lungs to store air (see earlier lectures on duration of dive), but fish do not have lungs.
- oxygen conc. in water low compared to air: 210,000 ppm of oxygen in air, but just 5ppm in water
- gills have a large surface area, with high blood flow
- diffusion distance from water to blood is small
- efficiency is increased by a counter current flow (the focus of the model now to be developed) where blood and water flow across the gill lamellae in opposite directions.

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")

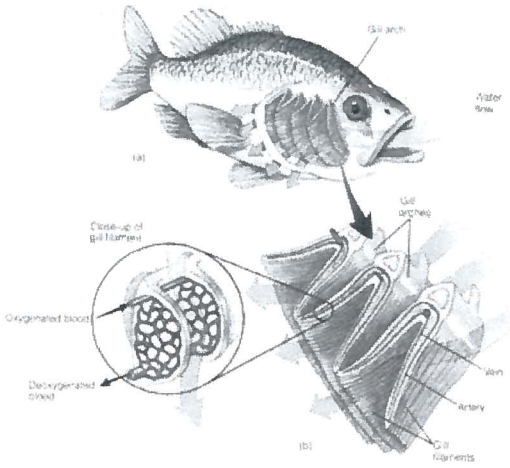
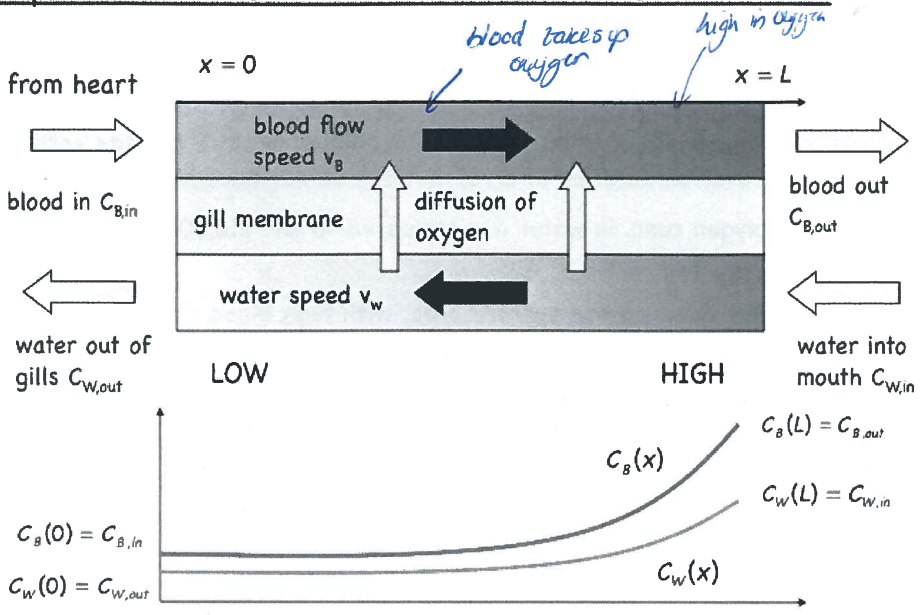


Figure 13.1 The Gills of a Fish

http://thumb11.webshots.net/t/thumb3_0_9d_48_8309848NeDNkVhZX_th.jpg

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

Simple model for countercurrent diffusion across membrane



PDE's for membrane diffusion of oxygen

difference of concentrations

$$\frac{dC_B}{dt} = \frac{\partial C_B}{\partial t} + v_B \frac{\partial C_B}{\partial x} = D(C_W - C_B)$$

is 0 diffusion

$$\frac{dC_W}{dt} = \frac{\partial C_W}{\partial t} - v_W \frac{\partial C_W}{\partial x} = -D(C_W - C_B)$$

sum = 0
so assuming no O_2 lost in membrane

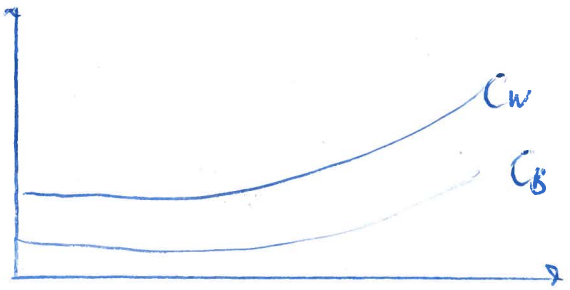
Boundary conditions :

$$C_B(0) = C_{B,in},\ C_B(L) = C_{B,out}$$
$$C_W(0) = C_{W,out},\ C_W(L) = C_{W,in}$$

Here :

C_B = blood oxygen conc., C_W = water oxygen conc.

v_B = blood flow speed > 0, v_W = water flow speed > 0



← correct diagram

Increased in steady state solutions so all $\frac{\partial}{\partial t} = 0$

so now have pde derivatives

At steady state :

$$v_B \frac{dC_B}{dx} = D(C_W - C_B) \quad \Rightarrow \frac{dC_B}{dx} = \frac{D}{v_B}(C_W - C_B)$$

$$-v_W \frac{dC_W}{dx} = -D(C_W - C_B) \Rightarrow \frac{dC_W}{dx} = \frac{D}{v_W}(C_W - C_B)$$

both increase or decrease

Hence C_B, C_W either both increasing or both decreasing

Boundary conditions :

$C_B(0) = C_{B,in}$, $C_B(L) = C_{B,out}$

$C_W(0) = C_{W,out}$, $C_W(L) = C_{W,in}$

$$v_B \frac{dC_B}{dx} - v_W \frac{dC_W}{dx} = 0 \Rightarrow v_B C_B(x) - v_W C_W(x) = \text{constant} = \alpha$$

where $\alpha = v_B C_{B,out} - v_W C_{W,in}$.

$$v_B \frac{dC_B}{dx} = D(C_W - C_B) = D\left(\frac{v_B}{v_W} C_B - \frac{\alpha}{v_W} - C_B\right)$$

Hence

$$\frac{dC_B}{dx} = \theta C_B - \varphi, \quad \theta = D\left(\frac{1}{v_W} - \frac{1}{v_B}\right) \varphi = \frac{\alpha D}{v_B v_W} = \frac{D(v_B C_{B,out} - v_W C_{W,in})}{v_B v_W}$$

So oxygen concentration will vary exponentially along lamellae

$$\Rightarrow C_B(x) = C_B(0)e^{\theta x} + \frac{\varphi}{\theta}(1 - e^{\theta x}) = \frac{\varphi}{\theta} + (C_{B,in} - \frac{\varphi}{\theta})e^{\theta x}$$

$$\Rightarrow C_W(x) = \frac{v_B}{v_W}\left(\frac{\varphi}{\theta} + (C_{B,in} - \frac{\varphi}{\theta})e^{\theta x}\right) - \frac{\alpha}{v_W}.$$

Hence

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

$$\text{i.e. } C_{B,out} = \frac{(v_B C_{B,out} - v_W C_{W,in})}{v_B - v_W} + \left(C_{B,in} - \frac{(v_B C_{B,out} - v_W C_{W,in})}{v_B - v_W}\right)e^{\theta L}$$

$$\boxed{C_{B,out} = C_{W,in} + \frac{(C_{W,in} - C_{B,in})(v_B - v_W)}{v_W e^{DL\left(\frac{1}{v_B} - \frac{1}{v_W}\right)} - v_B}}$$

do this at home could be on exam!

This gives the ratio :

$$\frac{C_{B,out}}{C_{B,in}} = \frac{C_{W,in}}{C_{B,in}} + \frac{(C_{W,in}/C_{B,in} - 1)(v_B - v_W)e^{DL\left(\frac{1}{v_W}\right)}}{v_W e^{DL\left(\frac{1}{v_B}\right)} - v_B e^{DL\left(\frac{1}{v_W}\right)}} \quad \text{(counter - current)}$$

higher ratio — more efficient

to examine efficiency ←

Compare with flow in opposite direction : interchange $C_{B,in}$ and $C_{B,out}$ and change v_B to $-v_B$. Now look at $C_{B,out} = C_B(0)$

invert direction

Takes half page calculations ; do this! could be on exam

$$\frac{C_{B,out}}{C_{B,in}} = \frac{v_B + (C_{W,in}/C_{B,in})v_W + v_W(1 - C_{W,in}/C_{B,in})e^{-\frac{DL}{v_B v_W}(v_B + v_W)}}{v_B + v_W} \quad \text{(same direction)}$$

Take $L \to \infty$ limit and suppose $v_W > v_B$

$$\frac{C_{B,out}}{C_{B,in}} \to \frac{C_{W,in}}{C_{B,in}} \quad \text{(counter - current),}$$

whereas if $v_W < v_B$,

$$\frac{C_{B,out}}{C_{B,in}} \to \frac{C_{W,in}}{C_{B,in}} + \left(1 - \frac{C_{W,in}}{C_{B,in}}\right)\left(1 - \frac{v_W}{v_B}\right) \quad \text{(counter - current)}$$

} counter current two flows

Now compare with flows in same direction

$$\frac{C_{B,out}}{C_{B,in}} = \frac{v_B + (C_{W,in} / C_{B,in})v_W}{v_B + v_W} \quad \text{(same direction)}$$

} same direction only one flow

Let $\delta = C_{W,in} / C_{B,in}$ = fixed const. Then the difference

$$\Delta = \frac{C_{B,out}}{C_{B,in}} \text{ (counter)} - \frac{C_{B,out}}{C_{B,in}} \text{ (same)} = \begin{cases} \dfrac{v_B(\delta - 1)}{v_B + v_W} & \text{if } v_W > v_B \\ \dfrac{v_W^2(\delta - 1)}{v_B(v_B + v_W)} & \text{if } v_W < v_B. \end{cases}$$

831

Hence $\Delta > 0$ if $C_{W,in} > C_{B,in}$, i.e. if O_2 conc. in water exceeds that of blood returning to heart, counter - current is more efficient.

Chapter 4

Bird flight

We have found
Lift ∝ velocity

4.1 Basics of bird flight.

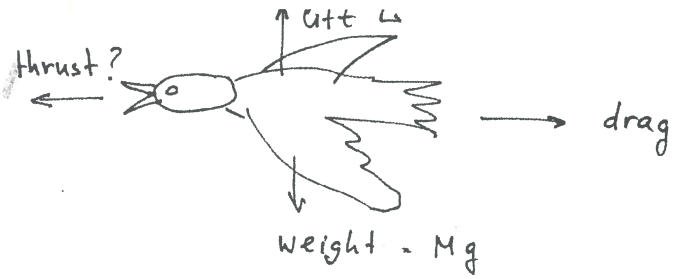


Figure 4.1:

In planes: wings produce lift. Propeller or jet engine produces thrust. In birds: wings must produce both thrust and lift.

Birds have evolved so that they

- have light weight skeleton - have smaller porous bones, hollow bones with strengthening struts, skull $\approx$ 1% body weight
- efficient respiratory system to provide for high metabolic rate required for flight. Anterior air sacs lungs, posterior air sacs.
- eat beries and other high energy foods

4.2 Basics of lift

The lift force is always perpendicular to the forward motion and the drag is along the line of forward motion.

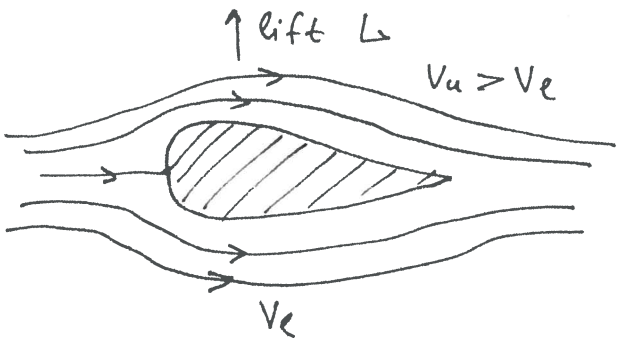


Figure 4.2: $V_u > V_l \Rightarrow$ pressure difference by Bernoulli $\Rightarrow$ lift force.

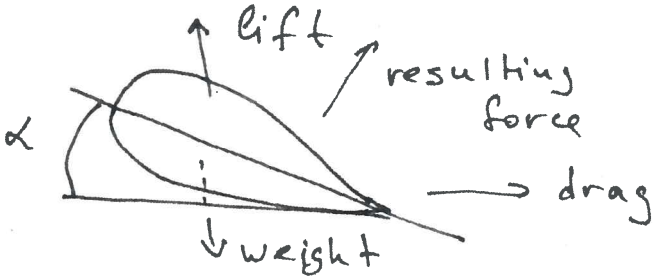


Figure 4.3: Angle of attack.

Why evolve an airfoil shape? Why not just use the angle of attack for lift?
Asymmetry of wing

1. produces lift at zero angle of attack
2. produces more lift than any symmetric wing at any angle of attack
3. produces less (pressure) drag.

Stalling: large angle of attack leads to large drag.

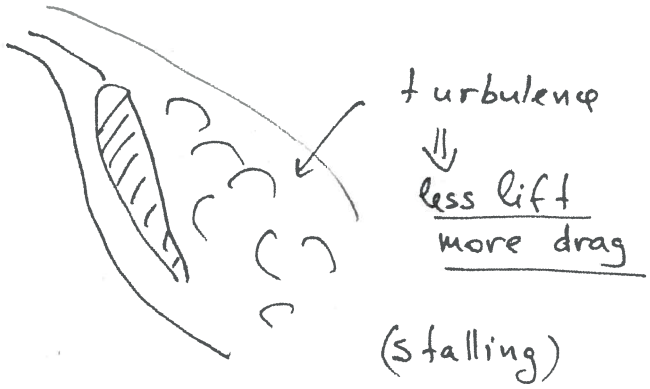


Figure 4.4: Turbulent flow ⇒ less lift, more drag.

The Kutta-Joukowski theorem is a fundamental theorem of aerodynamics. It states that the lift per unit of the wing length is a product of density of the fluid, velocity at some distance, and the circulation around the wing.

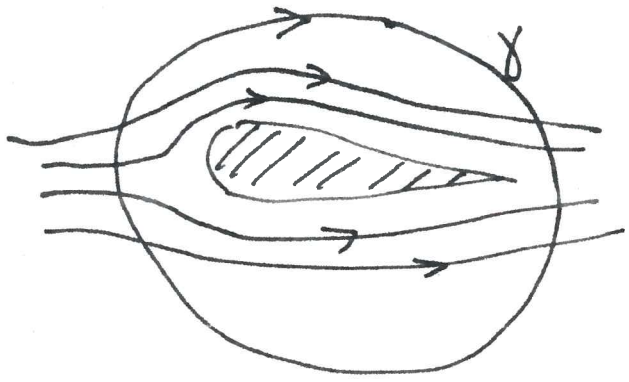


Figure 4.5: Calculation of the velocity circulation.

$$\bar{L} = -\rho \bar{u} \times \Gamma \qquad (4.1)$$

u - speed of flight
ρ - density

where Γ is a velocity circulation, i.e.

$$\Gamma = \oint_{\gamma} V \cos\theta \, d\theta$$

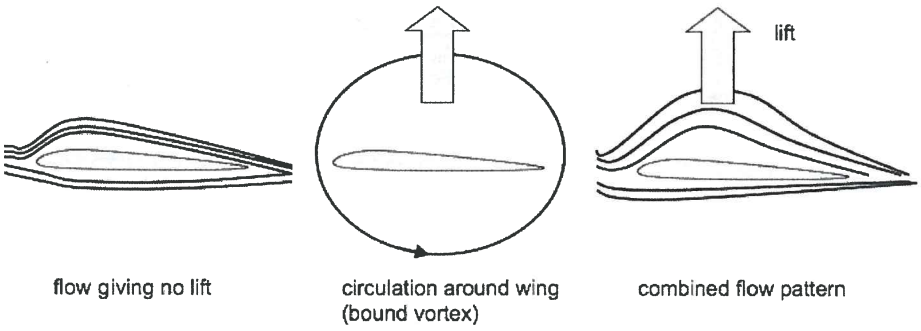


Figure 4.6: Actual flow around wing is the mathematical sum of flow yielding no lift and a flow of pure circulation

As the wing starts from rest in stationary air, a vortex with circulation $-\Gamma$ appears behind the wing and is matched by a circulation Γ around the wing itself (conservation of vorticity). The circulation comes off the tips of the wings and leaves as vortices that trail behind the wings. The circulation around the wings, in the form a bound vortex, gives rise to lift given by equation (4.1). However, the energy used to create the trailing vortices manifests as "induced" drag on the wing. If there is no lift then there is no induced drag.

4.3 Energy is required to counter:

- weight
- parasitic drag = frictional drag (body surface drag) + pressure drag (low pressure "suck" behind wing)
- induced drag $\propto L^2$, where L^2 =lift generated. This is from the energy in the trailing vortices or disturbances in a large region of air in the wake of the wing

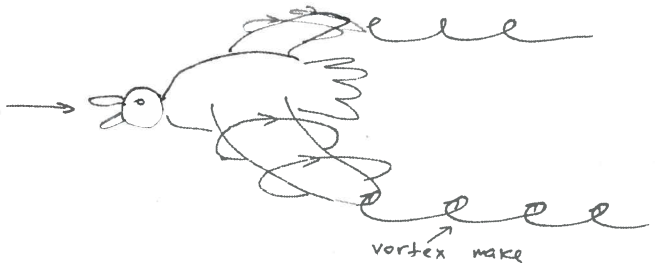


Figure 4.7: Vortex wake leads to a trailling vortex behind the wing. The vortices dissipate eventually, but may persist for some time.

4.3.1 Parasitic drag D_p.

We assume that the pressure drag is small in comparison to the frictional drag . D_p = rate of transfer of momentum from the surface of the bird to the thin mass of air (boundary layer) which is dragged forward with speed u.

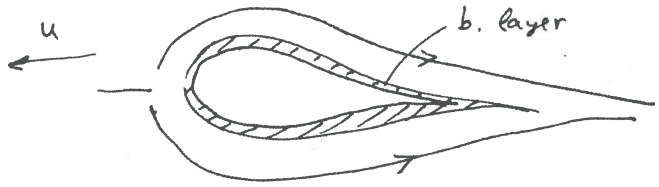


Figure 4.8: Boundary layer. Zero velocity on surface ⇒ air speed in a small distance.

$$\text{frictional drag force} = \frac{d}{dt}(\text{momentum of air displaced by wing}) \propto u^2$$

$F \cdot dt = m \cdot du = \rho S \cdot u\,dt\,du = \frac{1}{2}\rho S\,du^2$ (volume)

$\Rightarrow F \sim \frac{1}{2}\rho S u^2$

Define dimensionless drag coefficient

$$C_d = \frac{D_p}{\frac{1}{2}\rho S u^2},$$

where u = air speed of wing.

$$D_p = \frac{1}{2} C_d \rho S u^2,$$

where ρ is air density and S wing area.

Introducing a coeff. C_d

Drag force $D_p = \frac{1}{2} C_d \rho S u^2$ (wing area; air density)

$D_i \sim$ KE of trailing vortex system / per unit length

4.3.2 Induced drag D_i (because of induced turbulence)

Induced drag = rate of transfer of momentum to the trailing vortices
= Kinetic Energy per unit length in the trailing vortex system.

$$\frac{\text{mass M in vortex region} \times \text{air speed } U}{T} = \frac{MU^2}{TU} = \frac{MU^2}{d}$$

Also we have

Momentum transferred per unit length to vortices = Lift force $L \times (1/U)$

Hence

$$\frac{L}{U} = \frac{\text{momentum of vortices}}{\text{length of vortex system}}$$

mass per unit length of vortex system $\propto \rho \times$ wing area $\propto \rho b^2$,

where b is wing semi-span. So the induced drag

$$\begin{aligned} D_i &= \text{K. E. per unit length} \\ &= \frac{1/2(\text{momentum})^2/\text{mass}}{\text{length } d \text{ of vortex system}} \\ &= 1/2(\text{momentum/length } d)^2/\text{mass/length } d \\ &\propto (L/u)^2/(\rho \times b^2) = \frac{L^2}{\rho b^2 u^2}. \end{aligned}$$

momentum $p = mv$, $KE = \frac{1}{2}mv^2$, $KE = \frac{p^2}{2m}$

$= \frac{1}{2}\frac{p^2}{md}$, $\frac{1}{2}\left(\frac{p}{d}\right)^2 \frac{d}{m}$

d = length of vortex system

Define

$$D_i = \frac{KL^2}{\frac{1}{2}\rho b^2 u^2},$$

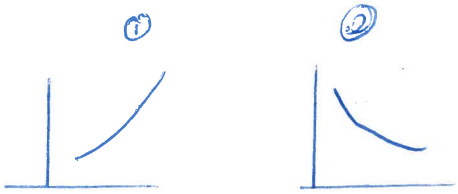
b is semi span of wing

where K is some factor for wing shape, etc. Hence total drag

$$D(u) = \frac{1}{2}C_d \rho S u^2 + \frac{KL^2}{\frac{1}{2}\rho b^2 u^2}$$

① ②

$= D_p + D_i$



4.4 Steady level flight

We have $L = Mg$

$$drag = \frac{KL^2}{\frac{1}{2}\rho b^2 u^2} + \frac{1}{2}\rho S u^2 C_d \qquad (4.2)$$

$L = \text{Lift} \sim \frac{\Delta p}{\Delta t}$: $L\Delta t \sim \Delta p \Rightarrow L\frac{d}{u} \sim p$: $\frac{L}{u} \sim \frac{p}{d}$

Sub $\frac{p}{d}$ $\Rightarrow$ $D_i \sim \frac{1}{2}\left(\frac{L}{u}\right)^2 \frac{d}{m} \sim \frac{1}{2}\left(\frac{L}{u}\right)^2 \frac{d}{\rho b^2 d} = \frac{KL^2}{\frac{1}{2}\rho b^2 u^2}$

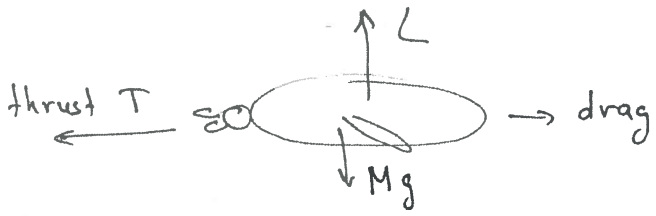


Figure 4.9:

In level flight $L = Mg$ so in equation (4.2)

$$D = \frac{KM^2g^2}{\frac{1}{2}\rho b^2u^2} + \frac{1}{2}\rho S u^2 C_d$$

is the drag under these conditions. The bird must produce a thrust $T = D$ to counteract the drag. The rate at which the bird does work to counter the drag, the power=P = thrust $\times$ velocity = force $\times \frac{\text{distance}}{\text{time}}$, i.e.

$$\text{Power} = P = U \times D(U) = \frac{KM^2g^2}{\frac{1}{2}\rho b^2 u} + \frac{1}{2}\rho S C_d u^3.$$

4.5 Stable gliding

This is where the bird glides in a *downward* straight line without flapping its wings (at least between wing movements that allow it to change direction). Birds with suitable wing characteristics, e.g. buzzards, albatrosses, can travel large distances using this mode of flying. Here the power to counter the drag and provide lift comes from the gravitational pull on the bird, and we are interested in a glide downwards at a constant angle θ to the horizontal.

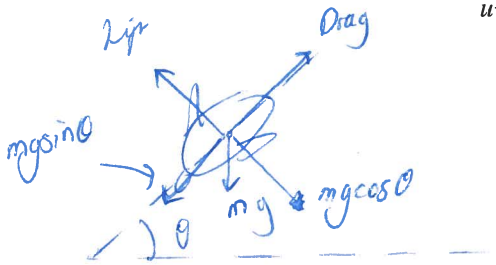
$$D = \frac{1}{2}\rho u^2 S C_d + \frac{KL^2}{\frac{1}{2}\rho u^2 b^2}$$

Write as

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

where $\alpha = \frac{1}{2}\rho S C_d$ and $\beta = \frac{2KL^2}{\rho b^2}$. To find D_{min}, differentiate w.r.t. u and set the gradient of D to zero:

$$2\alpha u - \frac{2\beta}{u^3} = 0 \quad \Rightarrow \quad u^4 = \beta/\alpha, \quad u_{md} = (\beta/\alpha)^{1/4}$$



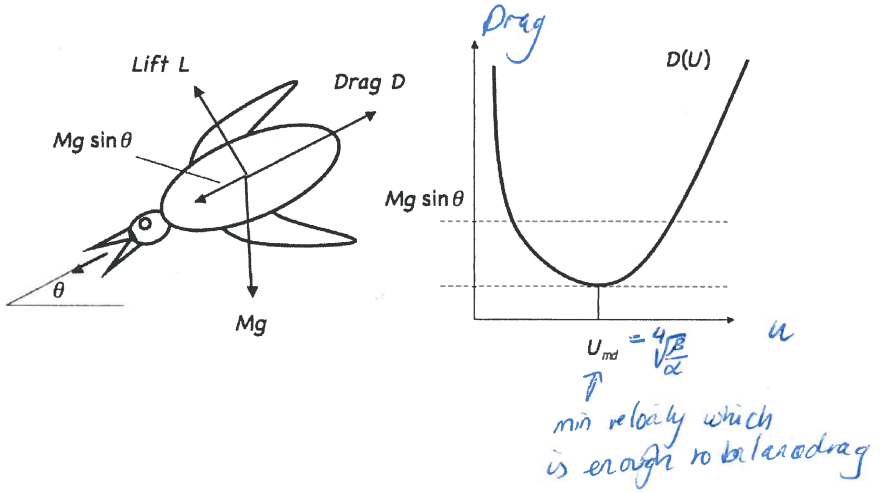


Figure 4.10: Forces by gliding. D as a function of u.

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

So need

$$mg\sin\theta \geq 2\sqrt{\alpha\beta}$$

But at critical angle θ_{min},

$$\frac{1}{2}mg\sin\theta_{min} = \left(\frac{1/2\rho u^2 SC_d KL^2}{1/2\rho u^2 b^2}\right)^{1/2} = \left(\frac{SC_d KL^2}{b^2}\right)^{1/2}$$

$$\frac{1}{2}mg\sin\theta_{min} = (SC_d K)^{1/2}\frac{L}{b} = \frac{(SC_d K)^{1/2}}{b}mg\cos\theta_{min}$$

$$\tan\theta_{min} = \frac{2}{b}(SC_d K)^{1/2}$$

$$\theta_{min} = \tan^{-1}\left(\frac{2}{b}(SC_d K)^{1/2}\right)$$

θ_{min} is the minimum glide angle possible. for stable gliding

What is the air speed u_{md} (md=minimum drag) at this minimum angle?

$$u_{md} = \left(\frac{\beta}{\alpha}\right)^{1/4} = \left(\frac{KL^2}{\frac{1}{2}\rho b^2} / \frac{1}{2}\rho S C_{Df}\right)^{1/4} = \left(\frac{4KL^2}{\rho^2 b^2 S C_{Df}}\right)^{1/4} = \left(\frac{4Km^2 g^2 \cos^2\theta_{min}}{\rho^2 b^2 S C_{Df}}\right)^{1/4}$$

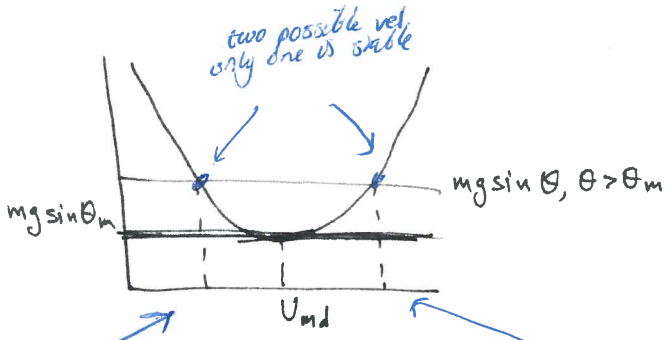


Figure 4.11: But this is not a stable glide.

if velocity is slightly decreased, it will not come back so
unstable
stable

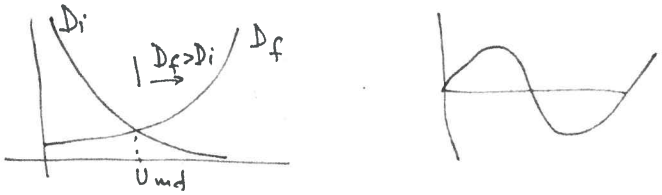


Figure 4.12:

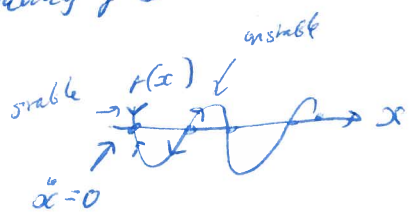
For steeper angles, $\theta > \theta_{min}$, a stable glide is possible. $mg\sin\theta = D(u)$ has more than one root u^* (see figure 4.10) but only one of them is stable, namely $u > u_{md}$. To see why consider how the bird responds to a small perturbation in its speed when at the higher speed u_{high} where D_f dominates. If the speed slightly increases, the drag increases and reduces the speed. If the speed decreases, then the drag is less than the weight component $mg\sin\theta$ and so there is an acceleration and the speed increases back to u_{high}. On the other hand, if the speed is u_{low} where D_i dominates, then a slight increase in speed will decrease the drag, and lead to an acceleration, increased speed and so on, so that the speed would build up to u_{high} where it is stable. If at u_{low} the speed slightly decreased then it would continue to decrease until the lift becomes too small and the bird would stall.

To confirm these ideas we may do the linear stability analysis:

increased in stability g eqn

$\dot{x} = f(x)$

stable unstable



can use similar analysis

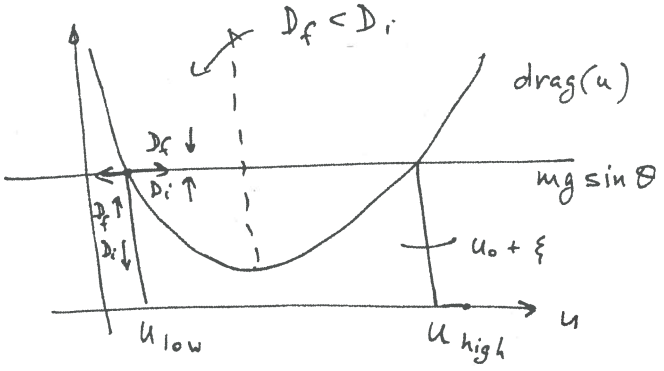


Figure 4.13:

4.5.1 Linear stability analysis of a glide

Consider a small perturbation ξ away from the glide speed u^*: $u = u^* + \xi$.

$$m\dot{u} = mg\sin\theta - D(u^* + \xi)$$

$$m(\dot{\xi}) = mg\sin\theta - [D(u^*) + D'(u^*)\xi + \ldots] = [(mg\sin\theta - D(u^*)) = 0(glide)] - D'(u^*)\xi + \ldots$$

$$m\dot{\xi} = -D'(u^*)\xi, \quad \text{to first order in } \xi.$$

Hence

$$\dot{\xi} = -\frac{D'(u^*)}{m}\xi$$

giving

$$\xi(t) = \xi(0)\exp\left(-\frac{D'(u^*)}{mt}\right)$$

for growth of the perturbation.

Hence the glide is stable only if $D'(u^*) > 0$, i.e. the bird needs the larger velocity u_{high} of the two for a stable glide at a glide angle θ.

Thus for a stable glide with air speed u, we need $D'(u) > 0$, which is equivalent to $D_p = D_f > D_i$, i.e. at speed u,

$$u^2 S C_{Df} > \frac{4KL^2}{\rho^2 u^2 b^2}$$

$$b^2 > \frac{4KL^2}{\rho^2 S C_{Df} u^4}$$

$$b > \left(\frac{KS}{C_{Df}}\right)^{1/2} \frac{L}{\frac{1}{2}\rho u^2 S}$$

Hence at lower speeds, need b larger. That is the bird spreads its wings.

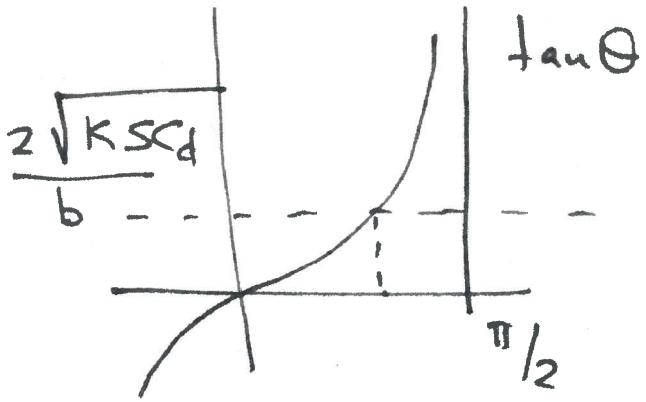


Figure 4.14:

See fig. 4.15

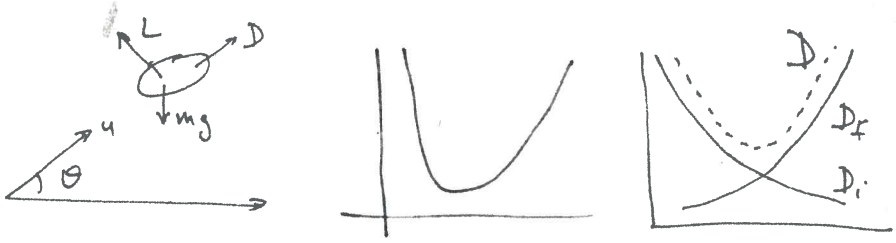


Figure 4.15:

$L = mg\cos\theta$, $D = mg\sin\theta$. Need $D_f > D_i$ so see fig 4.15 (middle and right).

4.5.2 Stable glide speeds and angles

For a stable glide, we have the force balance

$$mg\sin\theta = \frac{KL^2}{\frac{1}{2}\rho b^2 u^2} + \frac{1}{2}SC_d\rho u^2$$

Hence

$$mg\sin\theta = \frac{2Km^2g^2\cos^2\theta}{\rho b^2 u^2} + \frac{1}{2}SC_d\rho u^2$$

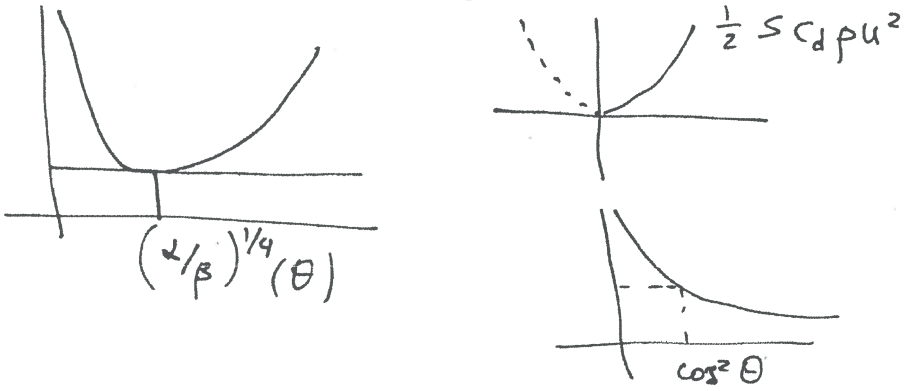


Figure 4.16:

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

$$\frac{\alpha}{\beta} = \frac{4Km^2g^2\cos^2\theta}{\rho^2 b^2 S C_d}$$

We solve for u:

$$\frac{\alpha}{u^2} + \beta u^2 = \gamma (= mg\sin\theta)$$

$$\beta u^4 - \gamma u^2 + \alpha = 0$$

$$u^2 = \frac{\gamma}{2\beta} \pm \frac{1}{2\beta}(\gamma^2 - 4\alpha\beta)^{1/2}$$

For stability we take the larger root:

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

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

Notice that since $\theta > \theta_{min}$,

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

the speed u is real.

4.5.3 Some crude estimates for stable glide speeds.

As we have seen, for stable glide we need $D_f > D_i$. This gives $D = D_f + D_i < 2D_f \Rightarrow D_f > \frac{1}{2}D$ and $D = D_f + D_i \geq D_f > \frac{1}{2}D$. Since $D = mg\sin\theta$, we then have $mg\sin\theta \geq D_f > \frac{1}{2}mg\sin\theta$ which gives

$$mg\sin\theta \geq \frac{1}{2}\rho u^2 S C_f > \frac{1}{2}mg\sin\theta$$

$$\sqrt{\frac{2mg\sin\theta}{\rho S C_f}} \geq u > \sqrt{\frac{mg\sin\theta}{\rho S C_f}} \tag{4.3}$$

which is a crude estimate for the stable glide speed at a glide angle $\theta > \theta_{min}$.

4.6 Soaring flight

This is where the bird glides, but takes advantage of upward air currents to maintain or gain their height, such as from the windward side of cliffs, or from a thermal). All that is required is that vertical rate of descent is less than the upward component U_{air} of the rising air:

$$U_{air}\sin\phi \geq U\sin\theta. \tag{4.4}$$

For a seagull to remain stationary with respect to the cliff, then, it needs to adjust its stable glide speed U and angle θ (see figure 4.17) to satisfy

$$\begin{aligned} U\sin\theta &= U_{air}\sin\phi \\ U\cos\theta &= U_{air}\cos\phi. \end{aligned}$$

Hence the seagull chooses $\theta = \phi$ and $U = U_{air}$ if it is remain stationary. That is, the seagull aligns itself head on into the wind and adjusts its wings so that it remains stationary. The balance between the air speed U, angle θ satisfies equation (4.5), provided that u exceeds the stalling speed of the seagull and the full-span (maximised b) minimum drag speed.

Some birds, such as vultures and buzzards, use rising air currents known as thermals for lift. They soar in circles using the energy in the thermal to provide lift. If the upward air speed is v (so $\phi = \pi/2$ here) then they can fly in a circle at the same altitude and at speed u when $v = u\sin\theta$. From equation (4.5) this gives that u satisfies

$$\sqrt{\frac{2mg(v/u)}{\rho S C_f}} \geq u > \sqrt{\frac{mg(v/u)}{\rho S C_f}} \tag{4.5}$$

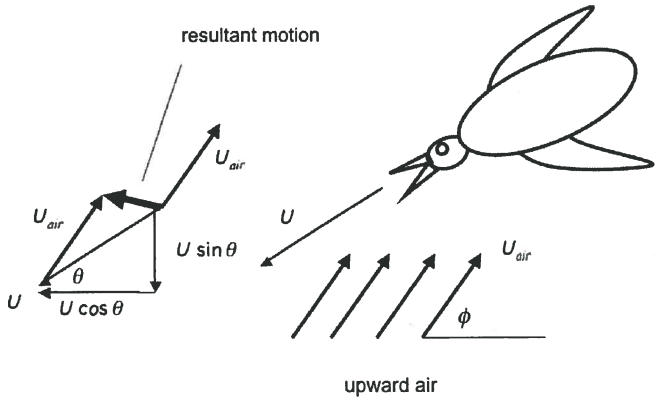


Figure 4.17: Soaring flight. The bird takes advantage of rising air currents to remain aloft for long periods of time.

so that

$$\left(\frac{mgv}{\rho S C_d}\right)^{\frac{1}{3}} < u \leq \left(\frac{2mgv}{\rho S C_d}\right)^{\frac{1}{3}}. \tag{4.6}$$

4.7 Bounding flight

In class: $\left(\frac{mgv}{\rho S C_d}\right)^{1/3} < u \leq \left(\frac{2mgv}{\rho S C_d}\right)^{1/3}$

This is the mode of flying used by many small birds that do not have the wing area or span for gliding. The bounding flight consists of periodic change between essentially parabolic projectile motion, where the wings are folded, and flapping in order to regain height. Here we are concerned with the efficiency of flapping fight over pure glides.

What scope is there for energy saving for birds flying at speeds well in excess of the minimum drag speed u_{md}? At such speeds the induced drag ($\propto 1/U^2$ = energy cost per unit distance to support weight with lift) is relatively small, but the parasitic drag from the loss of momentum to the boundary layer around the outstretched wings and body is large. Some small birds have evolved a mode of flying called "bounding flight" where they reduce the drag cost by fold their wings for part of their flight pattern. Thus bounding flight consists of periods where the bird flaps and glides (so the wings are outstretched) to gain height alternating with periods when their wings are folded (so no lift) and their flight path is parabolic (projectile motion). Since on average, for level flight, the lift has to balance the weight, if the wings are to be folded for some of the time, the lift has to be enhanced when the wings

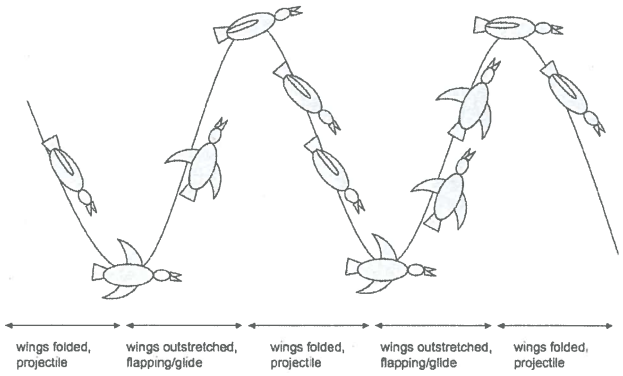


Figure 4.18: Bounding flight. The bird flies with alternating periods of flapping/gliding (wings outstretched) and free fall (wings folded).

are outstretched. Thus (as suggested by Mr S. B. Furber [unpublished]) if the wings are outstretched for a fraction f of the time, then the enhanced lift must be

$$L = \frac{mg}{f}.$$

This increases the induced drag when the wings are outstretched, but they are not outstretched for all of the time. So is there any benefit from bounding flight?

For normal flight ($f = 1$) let D_i be the induced drag and $D_f = D_b + D_w$ be the frictional drag split into body drag D_b (which is always present) and D_w the drag from the outstretched wing. The average drag is

$$\bar{D} = D_b + f\left(D_w + \frac{K(mg/f)^2}{\frac{1}{2}\rho b^2 u^2}\right) = D_b + fD_w + \frac{D_i}{f}.$$

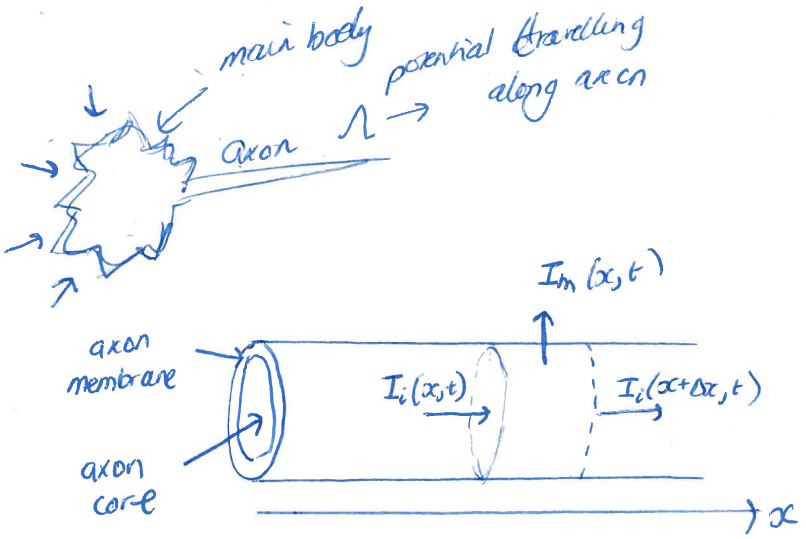
How does this drag vary with f?

$$\frac{d\bar{D}}{df} = D_w - \frac{D_i}{f^2},$$

so that $\bar{D}$ is extremal at $f = \sqrt{\frac{D_i}{D_w}}$ which is a minimum. So bounded flight is less costly when the bird flies at speeds such that $D_i/D_w < 1$. Indeed, at the minimum $\bar{D} = D_b + 2\sqrt{DwD_i}$ and comparing with the drag for normal flight $f = 1$ we obtain

$$D_b + D_w + D_i - (D_b + 2\sqrt{DwD_i}) = D_w + D_i - 2\sqrt{DwD_i} > 0,$$

by the arithmetic-geometric mean inequality.



Chapter 5

Electrophysiology

5.1 Electrodiffusion

charged small particles

Electrodiffusion occurs when ions diffusing through a medium are subject to an external force due to the interaction of the ionic charge with an electric field.

We recall that the diffusive flux J for a substance with concentration $C(x,t)$ in a medium of diffusive constant D is given by

$$J = -D\nabla C.$$

The presence of an electric field causes the ions to have an additional migrational flux

$$J_{mig} = \mu qCE,$$

where q is the charge of the ion, E the electric field strength, and μ the mobility of the ion. Hence the total flux is

$$J = -D\nabla C + \mu qCE.$$

Introducing the electric potential (i.e. the voltage) ϕ we have $E = -\nabla\phi$ so that

$$J = -\left(D\nabla C + \mu qC\nabla\phi\right).$$

Finally we use Einstein's relation $D = k_B T\mu$ (k_B Boltzmann's constant, T temperature in Kelvin) to give

$$J = -\mu\left(k_B T\nabla C + qC\nabla\phi\right). \tag{5.1}$$

Using $k_bT/q_e = RT/F$ (R= gas constant, q_e charge on electron) gives the alternative form:

$$J = -D\left(\nabla C + \frac{Fz}{RT}C\nabla\phi\right). \tag{5.2}$$

where z is valency of the ion ($q = q_e z$). Hence, with suitable boundary conditions on a domain Ω we have

$$\frac{\partial C}{\partial t} = -\text{div}J = \mu\,\text{div}\,(k_BT\nabla C + qC\nabla\phi).$$

This equation is highly nonlinear and presents a major challenge! We make two simplifying assumptions: (i) our domain is an interval of the real line, (ii) we are only interested in the steady state concentration (i.e. $\frac{\partial C}{\partial t} = 0$). In this case the steady state condition reads

$$\frac{\partial C}{\partial t} = -\frac{\partial J}{\partial x} = 0,$$

so that the flux is independent of x.

5.2 Excitable cells - basics

Many cells, such as for example, nerve axons, heart pacemaker cells, muscle cells are capable of generating action potentials - sudden depolarizations of the membrane (from a negative potential of around -70 millivolts to a positive potential of around +55 millivolts). Surprisingly such depolarizations are brought about by the transfer of relatively small numbers of ions. The potential changes occur due to changes in the permeability of the cell membrane to the ions K^+ and Na^+.

Let us suppose that (in the resting state) the membrane in the simple cell model above is permeable to potassium ions only (the membrane in this state is relatively impermeable, but the small permeability is due to potassium channels). For a typical cell, there are strong chemical gradients of Na and K across the cell membrane. Extracellular K (20mmol/litre) is much lower than intracellular K (400 mmol/litre). (We will ignore the role of chloride ions in what follows.) On the other hand extracellular sodium (440mmol/litre) is much higher than intracellular sodium (50mmol/litre).

Then the *Nernst equilibrium potential* for potassium E_K is given by setting $P_{Na} = P_{Cl} = 0$ in equation (**??**). We obtain, for a typical cell, $\frac{RT}{F} = 58$ and

$$E_K = 58\log(20/400) \approx -75mV.$$

Simiilarly

$$E_{Na} = 58\log(440/50) \approx 55mV.$$

The sudden changes in membrane potential are brought about by the changes in membrane permeability to sodium and potassium. Prior to a stimulus, when the excitable cell is in its resting state, the membrane potential is at the so-called *resting potential*, which is about -72mV. Thus the membrane is initially relatively impermeable, but substantially more permeable to potassium than sodium. When subject to a sufficiently strong (suprathreshold) stimulus (see figure 5.2), however, a depolarization causes voltage-dependent sodium channels in the membrane to open and sodium ions surge in under the combined electric and chemical gradients. These sodium channels are sensitive to changes in membrane potential, in that they can open as the cell membrane potential increases. Since the entry of sodium cations into the cell depolarizes the membrane (increases the membrane potential), more sodium channels open. This leads to further depolarization and further opening of sodium channels. This positive feedback results in a rapid depolarization of the membrane to a value close to the sodium equilibrium potential of around 55mV (since now the permeability of the membrane is dominated by sodium). As the peak is approached the sodium channels tend to close under the positive potential and potassium channels begin to open and potassium ions surge out of the cell and the membrane repolarizes back to the cell resting potential. After a brief *refactory period* the cell is ready to respond to new stimuli. The spike in the voltage lasts around one millisecond. If the stimulus is not strong enough, the feedback mechanism that leads to rapid opening of the sodium channels is not triggered and the cell returns to the resting state. Such a stimulus is *subthreshold*. There is a threshold, usually around 15millivolts above resting potential, beyond which the *suptratheshold* stimulus triggers an action potential.

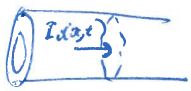
Later in the course, the *Fitzhugh-Nagumo model* for excitable cells will be introduced. Here we are concerned with the propagation of the action potential from a nerve cell down a long thin nerve axon. The propagation ensues because local action potentials trigger action potentials in neighbouring sections of the axon. We will now develop a simple model for action potential propagation down an axon modelled as a conducting cylinder covered by a excitable membrane whose voltage-current characteristic $I_{ion}(V)$ is designed to model the complex membrane conductance changes outlined above.

The above description is a substantial simplification of the whole action potential generation process, leaving out actions of sodium pumps that pump out the sodium ions that enter the cell on depolarization, or other ions and ion channels involved. Nevertheless, it suffices for our simple model of action potential propagation.

5.3 The Cable Equation

We now consider the transmission of an action potential along a nerve axon (see figure 5.3). The distance down the centreline of the axon is x, and the currents and voltages are all assumed to

$I_i(x,t)$ - longitudinal current in x direction



r_i resistance

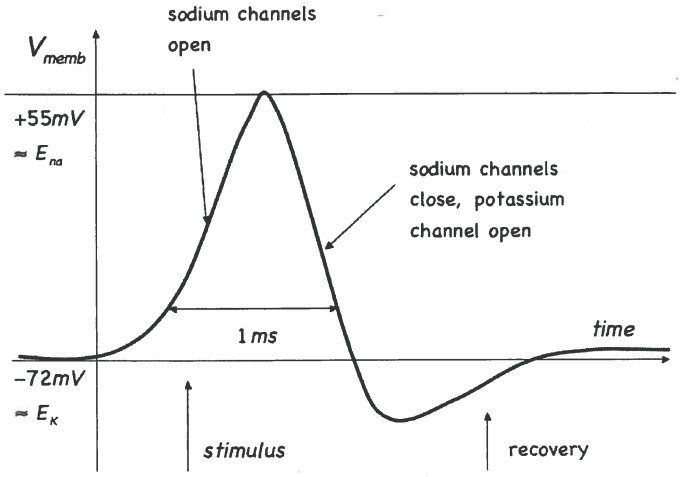


Figure 5.1: Membrane voltage changes during generation of an action potential

be radially independent. We let $I_i(x,t)$ be the longitudinal current at x,t along the axon. The voltage inside the axon is $V_i(x,t)$ and the extracellular voltage is assumed constant set at zero. The membrane potential is thus $V_m(x,t) = V_i(x,t) - V_e(x,t) = V_i(x,t)$. We let r_i denote the resistance of the axon core measured in Ohm/cm. Then by Ohm's law,

per unit length

$V_m(x,t) = V_i - V_e$

$$V_m(x+\Delta x,t) - V_m(x,t) = -I_i(x,t) r_i \Delta x,$$

to first order in Δx. Hence

$$I_i = -\frac{1}{r_i}\frac{\partial V_m}{\partial x}. \tag{5.3}$$

Now let $I_m(x,t)$ be the total membrane current per unit length of the axon. By KCL,

↑ Kirchhoff's circuit laws

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

(again to first order) so that

$$I_m(x,t) = -\frac{\partial I_i}{\partial x}. \tag{5.4}$$

Combining equations (5.3) and (5.4) we obtain

$$I_m = \frac{1}{r_i}\frac{\partial^2 V_m}{\partial x^2}. \tag{5.5}$$

Ohm's law: the current through a conductor between two points is directly proportional to the potential difference across the two points

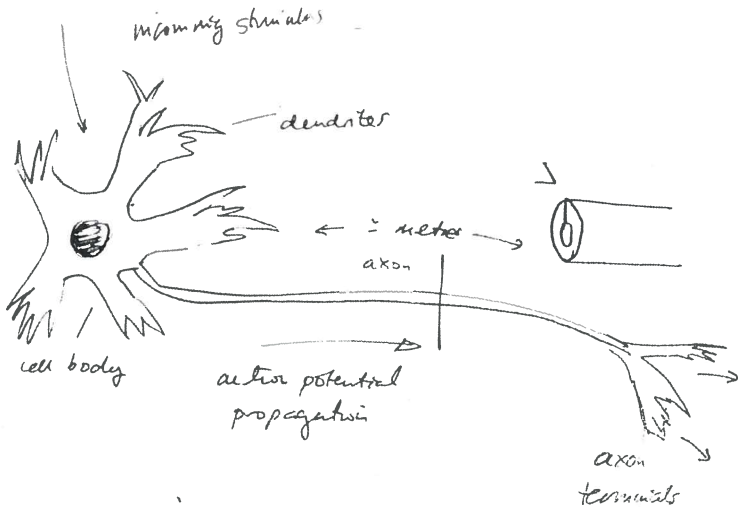


Figure 5.2: Propagation of an action potential from a nerve cell down a nerve axon.

Now using KCL again, the total membrane current is the sum of the capacitative current and the membrane ionic current I_{ion} per unit length of the membrane:

$$I_m = \left(c_m \frac{\partial V_m}{\partial t} + I_{ion} \right). \tag{5.6}$$

Here c_m is capacitance per unit length of the membrane. Hence putting (5.5) with (5.6) we obtain the *cable equation*:

$$c_m \frac{\partial V_m}{\partial t} = -I_{ion}(V_m) + \frac{1}{r_i} \frac{\partial^2 V_m}{\partial x^2}. \tag{5.7}$$

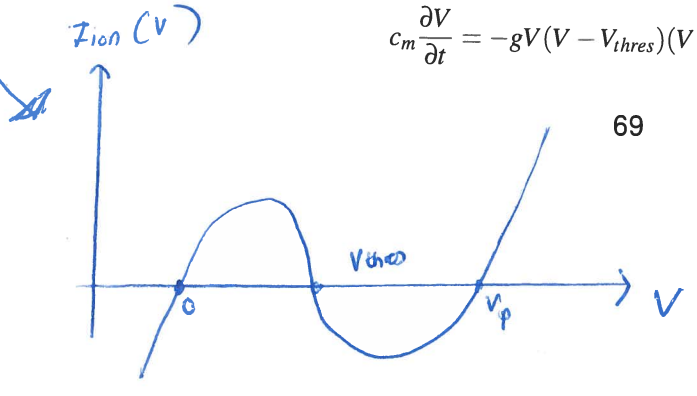
5.3.1 A simple model for action potential propagation

Let us model the ionic current as

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

where $0 < V_{thres} < V_p$, and $g > 0$ (see figure 5.4). Then the cable equation reads

$$c_m \frac{\partial V}{\partial t} = -gV(V - V_{thres})(V - V_p) + \frac{1}{r_i} \frac{\partial^2 V}{\partial x^2}.$$



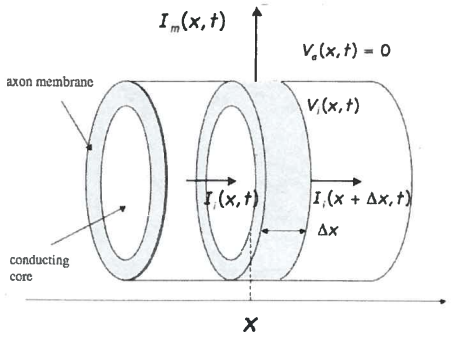


Figure 5.3: Small section of nerve axon, thickness Δx

Rescaling:

Now introduce $\alpha = \frac{V_{thres}}{V_p}$, $U = \frac{V}{V_p}$, $\tau = \frac{gV_p}{c_m V_{thres}}$, so that we obtain

$$\frac{\partial u}{\partial \tau} = f(u) + D\frac{\partial^2 u}{\partial x^2}, \qquad \text{cable eq}^{n} \tag{5.8}$$

where $f(u) = u(\alpha - u)(u - 1)$ and $D = gr_i V_p^2$. We will now seek travelling front solutions of (5.8). The

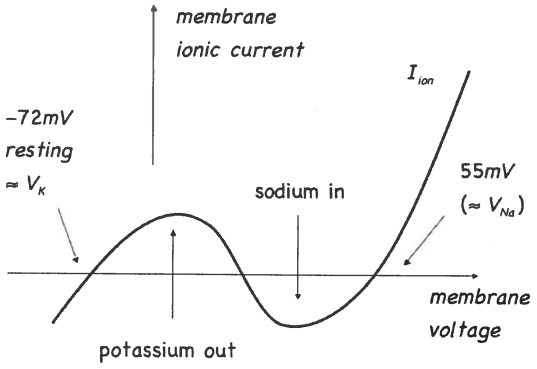


Figure 5.4: Voltage-current characteristic for membrane in cable equation model. Note how the current changes correspond to the movement of various ions following membrane permeability changes.

travelling front of speed $c > 0$ is a wave that has constant profile to an observer moving at speed c. Thus we seek a profile U such that $u(x,\tau) = U(x - c\tau)$. If such a wave exists then it is a solution of

Class. Rescaling: $\alpha = \frac{V_{thres}}{V_p}$ $u = \frac{V}{V_p}$ $\tau = \frac{gV_p}{C_m}t$

Try both to work out which is right $D = 1/(gV_p r_i)$ but still end up with (5.8)

(5.8). Now we have, setting $\xi = x - c\tau$,

$$\frac{\partial u}{\partial \tau} = U'(\xi)\frac{\partial \xi}{\partial \tau} = -cU'(\xi),$$

and

$$\frac{\partial u}{\partial x} = U'(\xi)\frac{\partial \xi}{\partial x} = U'(\xi), \quad \frac{\partial^2 u}{\partial x^2} = U''(\xi).$$

Hence (5.8) transforms into the following second order ordinary differential equation:

$$DU''(\xi) + cU'(\xi) + f(U(\xi)) = 0.$$

What about boundary conditions? We want our wavefront to propagate from left to right ($c > 0$) exciting the cells from resting state $u = 0\,(V = 0)$ to $u = 1\,(V = V_p)$ as it progresses. Hence for our profile $U : (-\infty, \infty) \to (-\infty, \infty)$ we would expect $u(\xi) \to 1, u'(\xi) \to 0$ as $\xi \to -\infty$ (see figure 5.6). On the other hand $u(\xi) \to 0, u'(\xi) \to 0$ as $\xi \to \infty$. We may represent such a curve in (U, U') space (see figure 5.5), where the curve is given by the points $(U(\xi), U'(\xi))$ as ξ ranges form $-\infty$ to $+\infty$. Let $X = U'$.

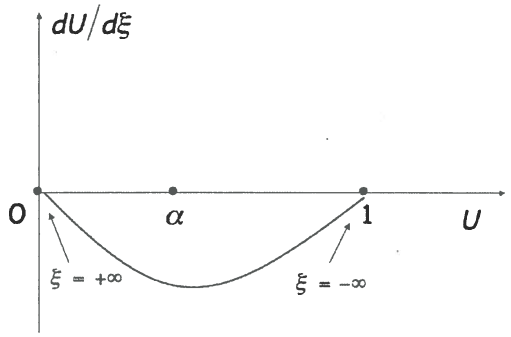


Figure 5.5:

Then we are solving $X' = -\frac{1}{D}(cX + f(U))$, so that

$$\frac{dX}{dU} = \frac{-cX - f(U)}{DX}.$$

We look for a quadratic solution $X(U)$. This must satisfy $X(0) = 0$ and $X(1) = 0$, and so $X(U) = \theta U(U-1)$ for some θ which we must find.

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

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

Powers of U and U^0

$2D\theta^2 = 1$

$-D\theta^2 = -c\theta - \alpha$

Equating coefficients leads to

$$c = \sqrt{\frac{D}{2}}(1-2\alpha), \quad \theta = \frac{1}{\sqrt{2D}}.$$

This shows that the profile U satisfies

$$\frac{dU}{d\xi} = \theta U(U-1).$$

This last equation may be solved (using partial fractions) to obtain

$$U(\xi) = \frac{e^{-\theta\xi}}{K + e^{-\theta\xi}},$$

where K is an arbitrary constant of integration. Notice that this U satisfies all the boundary conditions that we have stated. A sketch of the profile can be seen in figure 5.6.

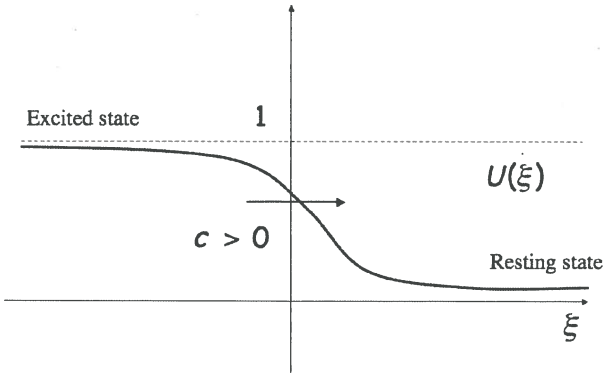


Figure 5.6: Profile of travelling wavefront for action potential model ($\alpha < 1/2$)

Later we will come back to a model of neuron

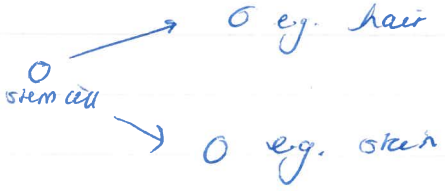
27/10/14 and 31/10/14

Modelling gene expression

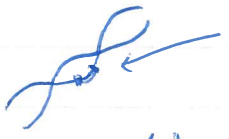
Genetics is a not-cited

- Most cellular functions are performed by proteins
- Proteins are produced from genome (DNA) which is inherited & together with genes organise gene-regulatory networks (GRNs)
- GRNs control the function of every cell e.g.

1) circadian oscillations - ability of a cell to count time
2) cell differentiation



DNA has a form of double stranded spiral & during cell proliferation each strand is coupled with a new one



Some parts of DNA organise a gene)

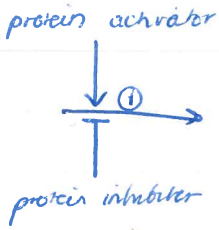
Newton's laws per biology:

Gene $\xrightarrow{①}$ mRNA $\xrightarrow{②}$ protein

① Transcription (from nucleotides of 4 elements → 4)

② Translation (from 4 → 20)

some 3 nucleotides organise 1 amino acid (genomic code)



Regulation of gene expression

Let P - monomer concentration
P_2 - dimer (two proteins) concentration
} if we assume that only dimers can regulate transcription

Let O_u (unbounded) be concentration of unbounded DNA
O_b of bounded

Then for constant concentration of DNA: $O_u + O_b = N$

$$P + P \underset{k_{-d}}{\overset{k_d}{\rightleftharpoons}} P_2 \quad \text{rate of reaction}$$

$$O_u + P_2 \underset{k_{-b}}{\overset{k_b}{\rightleftharpoons}} O_b$$

In steady state: $k_d \cdot P^2 = k_{-d} P_2$ plus $O_u + O_b = N$
$k_b O_u P_2 = k_{-b} O_b$

Extra note

Soaring flight

$$\sqrt{\frac{2mg\,(v/u)}{\rho S C_f}} \geq u > \sqrt{\frac{mg\,(v/u)}{\rho S C_f}}$$

$$\sqrt{\frac{\alpha}{u}} \geq u > \sqrt{\frac{\beta}{u}}$$

$$\sqrt{\alpha} \geq u\sqrt{u} \geq \sqrt{\beta}$$

$u^{3/2}$

$$\alpha \geq u^3 > \beta$$

Note: chemical balance

$$A + B + A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} C$$

$$k_1 B A^2 = k_2 C$$

Then

$$O_u = \frac{k_{-b} O_b}{k_b P_2} = \frac{k_{-b}(N - O_u)}{k_b P_2}$$

$$O_u + \frac{k_{-b} O_u}{k_b P_2} = \frac{k_{-b} N}{k_b P_2}$$

$$O_u = \frac{\frac{k_{-b} N}{k_b P_2}}{1 + \frac{k_{-b}}{k_b P_2}} = \frac{k_{-b} N}{k_b P_2 + k_{-b}}$$

$$= \frac{N}{1 + \frac{k_b}{k_{-b}} P_2} = \frac{N}{1 + \frac{k_b}{k_{-b}} \frac{k_d}{k_{-d}} P^2} \quad \text{since} \quad P_2 = \frac{k_d}{k_{-d}} P^2$$

$$= \frac{N}{1 + \left(\frac{P}{K}\right)^2} \quad \text{where} \quad K = \sqrt{\frac{k_{-b} k_{-d}}{k_b k_d}}$$

In the same way we can calculate O_b

$$O_b = \frac{N \left(\frac{P}{K}\right)^2}{1 + \left(\frac{P}{K}\right)^2}$$

$$O_u = \frac{N}{1 + \left(\frac{P}{K}\right)^2}$$

These are Hill's equations where 2 is the Hill constant β can take any value from 1 to 6

If expression works with coefficient

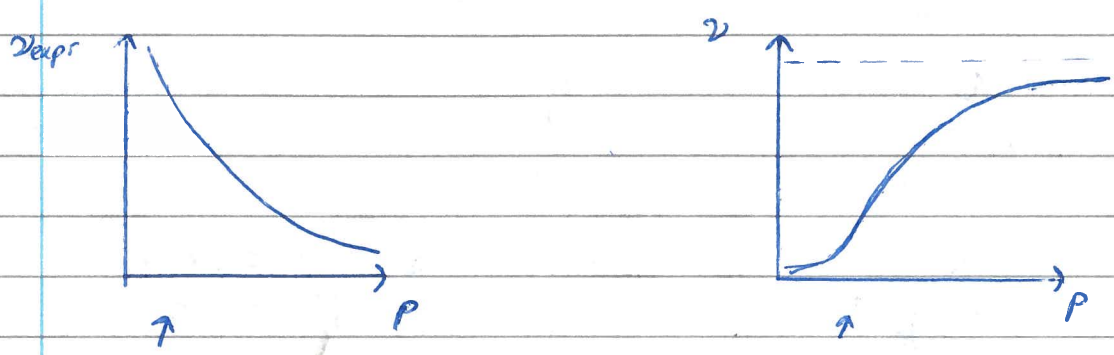
α_u when unbounded

α_b when bounded

the total rate of expression is

$$v_{expr}(P) = \alpha_u \theta_u + \alpha_b \theta_b$$

$$= \alpha_u \frac{N}{1+\left(\frac{P}{k}\right)^2} + \alpha_b \frac{N\left(P/k\right)^2}{1+\left(P/k\right)^2}$$



Taking account of degradation, for protein concentration we get

PROTEIN SYNTHESIS

$$\dot{X} = \alpha_u \frac{N}{1+\left(\frac{P}{k}\right)^2} + \alpha_b \frac{N\left(P/k\right)^2}{1+\left(P/k\right)^2} - r_{deg}(x)$$

e.g. $r_{deg}(x) = \beta x$ - exponential degradation

Taking account of mRNA synthesis

$$\dot{m} = \frac{\alpha_u N}{1+\left(\frac{P}{k}\right)^2} + \frac{\alpha_b N \left(P/k\right)^2}{1+\left(P/k\right)^2} - r_{deg}(m)$$

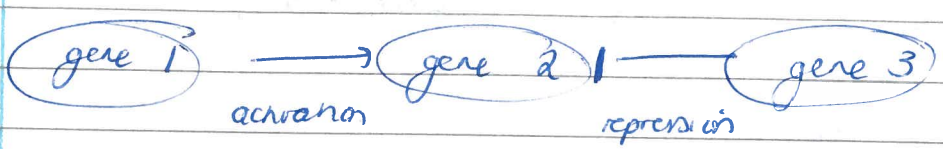
← what does this say

$$\dot{x} = r_{te}\, m - r_{\alpha}(x)$$

r_{te} = coeff of translation

Controlled synthesis of mRNA & proteins

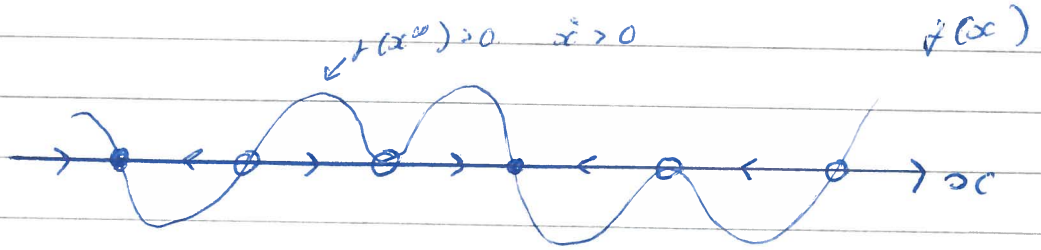
P can be any protein, also x



1D dynamical system $\dot{x} = f(x)$

don't think $\dot{x}$ is derivative

Conditions: { equilibrium x^* $f(x^*) = 0$; stability $f'(x^*) < 0$



- stable
- unstable

No oscillations are possible as system cannot cross equilibrium point

2D dynamical system $\dot{x}_1 = f_1(x_1, x_2)$

$\dot{x}_2 = f_2(x_1, x_2)$

Conditions of equilibrium $f_1(x_1^*, x_2^*) = 0$

x_1^*, x_2^* $f_2(x_1^*, x_2^*) = 0$

Conditions of stability

$$\text{Det}\begin{pmatrix} \partial_{x_1} f_1 - \lambda & \partial_{x_2} f_1 \\ \partial_{x_1} f_2 & \partial_{x_2} f_2 - \lambda \end{pmatrix} = 0$$

Characteristical equation

$\lambda^2 + \tau\lambda + D = 0$

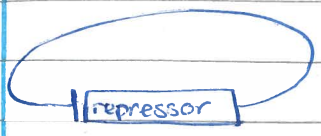
Two roots λ_1, λ_2 : stability if $\text{Re}\,\lambda_1, \lambda_2 < 0$

Changing parameters, we change stability

→ bifurcations. See handout

Example : autorepressor

Dynamics: $\dot{x} = \frac{\alpha}{1+x^n} - x$

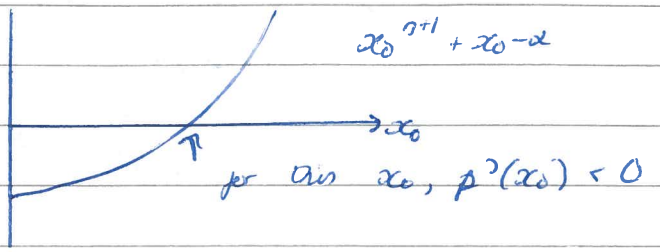


some const. excluded by rescaling

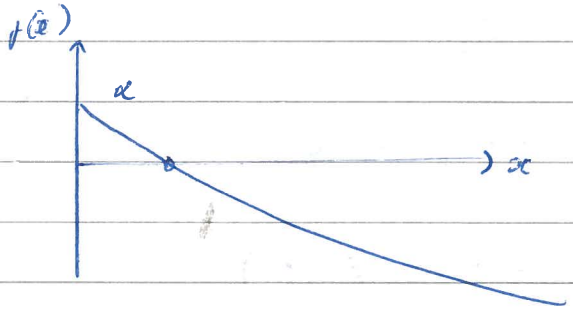
For equilibrium x_0

$x_0^{n+1} + x_0 - \alpha = 0 \qquad f(x_0) = 0$

$x_0 > 0$



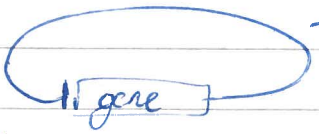
for this x_0, $f'(x_0) < 0$



1 stable equilibrium

No oscillations because in 1D

Example of generic oscillations: autorepressor with delay



τ-delay

Dynamics: $\dot{x} = \frac{\alpha}{1+x^n(t-\tau)} - x$

Let us linearise this system around equilibrium

$x_0^{n+1} + x_0 - \alpha = 0$ (*)

$x = x_0 + \xi$

$\dot{\xi} = \frac{\alpha}{1+(x_0+\xi(t-\tau))^n} - x_0 - \xi(t)$

$x \approx 0$

$\frac{1}{1+x} \approx 1 - x$ (**)

$$\dot{\xi} = \frac{\alpha}{1 + x_0^n + n x_0^{n-1} \xi_\tau + \dots} - x_0 - \xi_t$$

$$\dot{\xi} = \frac{\alpha}{(1+x_0^n)\left(1 + \frac{n x_0^{n-1} \xi_\tau}{1+x_0^n}\right)} - x_0 - \xi_t$$

by ##

$$= \underbrace{\frac{\alpha}{1+x_0^n}} - \frac{\alpha n x_0^{n-1}}{(1+x_0^n)^2} \xi_\tau - x_0 - \xi_t$$

$$\underbrace{\qquad}_{=0}$$

since $\frac{\alpha}{1+x_0^n} = x_0$

$$= -\frac{1}{\alpha} n x_0^{n-1} \xi_\tau - \xi_t$$

since $x_0^n = \frac{\alpha}{x_0} - 1$

$$= -\frac{x_0}{\alpha} n \left(\frac{\alpha}{x_0} - 1\right) \xi_\tau - \xi_t$$

$$= n\left(\frac{x_0}{\alpha} - 1\right) \xi(t-\tau) - \xi(t)$$

Assuming $\xi(t) \sim e^{\lambda t}$

$$\lambda = n\left(\frac{x_0}{\alpha} - 1\right) e^{-\tau\lambda} - 1$$

In A-H bifurcation (condition of oscillations) $\lambda = \pm i\omega$

$$\lambda = n\left(\frac{x_0}{\alpha} - 1\right) e^{\mp i\omega\tau} - 1$$

$$\mathrm{Re}(\lambda) = 0 = n\left(\frac{x_0}{\alpha} - 1\right)\cos\omega\tau - 1 \Rightarrow \cos\omega\tau = -\frac{1}{n\left(1 - \frac{x_0}{\alpha}\right)}$$

$$\mathrm{Im}(\lambda) = \omega = -n\left(\frac{x_0}{\alpha} - 1\right)\sin\omega\tau$$

$$n\left(\frac{x_0}{\alpha} - 1\right)\cos\omega\tau = 1, \qquad n\left(\frac{x_0}{\alpha} - 1\right)\sin\omega\tau = -\omega$$

Squaring & taking sum

$$n^2\left(\frac{x_0}{\alpha} - 1\right)^2 = \omega^2 + 1$$

$$\begin{cases} \omega^2 = n^2\left(1 - \frac{x_0}{\alpha}\right)^2 - 1 \qquad (***) \\ \omega^2 > 0 \\ \cos\omega\tau = -\frac{1}{n\left(1 - \frac{x_0}{\alpha}\right)} \end{cases}$$

Taking account that $x_0 < \alpha$ because $x_0^{n+1} = \alpha - x_0 > 0$
We get the necessary conditions of osallations

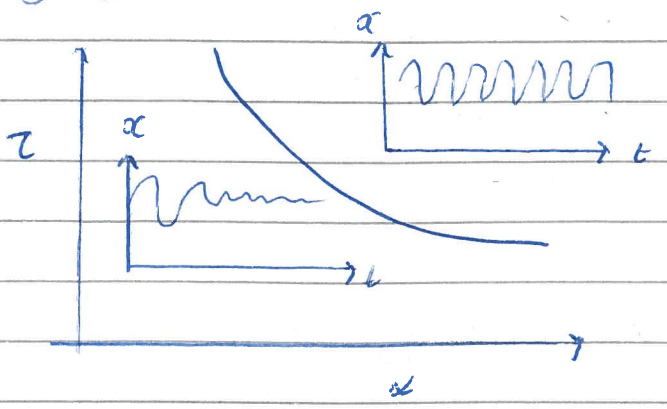
$$n^2\left(1 - \frac{x_0}{\alpha}\right)^2 - 1 > 0 \qquad \text{i.e.} \qquad n > 2$$

$$\cos\omega\tau = -\frac{1}{\sqrt{1+\omega^2}}$$

Hence for $\omega \gg 1$ $\cos\omega\tau \approx 0$
$\omega\tau \approx \frac{\pi}{2}$ and period
$T = \frac{2\pi}{\omega} \sim 4\tau$ - much larger than the delay τ

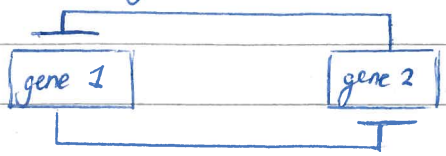
See handout for other networks w/ negative feedback

Solving (***) and * we get bifurcation curve, or boundary of oscillations



03/11/14

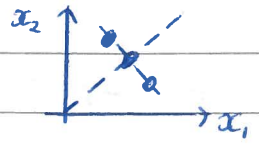
Bistable genetic switch



Dynamics: $\dot{x}_1 = \frac{k}{1+x_2^n} - x_1$

$\dot{x}_2 = \frac{k}{1+x_1^n} - x_2$

Because of symmetry, equilibrium states are either on $x_1 = x_2$ or symmetrical (x_1, x_2) (x_2, x_1)



If $x_1 = x_2 = x_0$ then

$x_0^{n+1} + x_0 - k = 0 \Rightarrow$ we have one real positive root

Linearizing around it, we have $x = x_0 + \xi$

$$\begin{cases} \dot{\xi}_1 = \frac{k}{1+(x_0+\xi_2)^n} - \xi_1 - x_0 \\ \dot{\xi}_2 = \frac{k}{1+(x_0+\xi_1)^n} - \xi_2 - x_0 \end{cases}$$

As before

$$\begin{cases} \dot{\xi}_1 = \frac{n}{k} x_0^{n+1} \xi_2 - \xi_1 = f_1 \\ \dot{\xi}_2 = \frac{n}{k} x_0^{n+1} \xi_1 - \xi_2 = f_2 \end{cases}$$

$$\begin{vmatrix} \frac{\partial f_1}{\partial \xi_1} - \lambda & \frac{\partial f_1}{\partial \xi_2} \\ \frac{\partial f_2}{\partial \xi_1} & \frac{\partial f_2}{\partial \xi_2} - \lambda \end{vmatrix} = \begin{vmatrix} -1-\lambda & \frac{n x_0^{n+1}}{k} \\ \frac{n x_0^{n+1}}{k} & -1-\lambda \end{vmatrix}$$

$$= (-1-\lambda)^2 - \frac{n^2 (x_0^{n+1})^2}{k^2} = \lambda^2 + 2\lambda + 1 - \frac{n^2}{k^2} x^{2(n+1)}$$

$$\lambda_{1,2} = -1 \pm \frac{n}{k} x^{n+1}$$

λ crosses 0 when equilibrium changes from stable node to unstable saddle. This happens when

$$-1 + \frac{n}{k} x^{n+1} = 0 \qquad x^{n+1} = \frac{k}{n} \qquad \underline{\underline{x = \sqrt[n+1]{\frac{k}{n}}}}$$

Now substitute in to $x^{n+1} + x - k$

$$\frac{k}{n} + \sqrt[n+1]{\frac{k}{n}} - k = 0$$

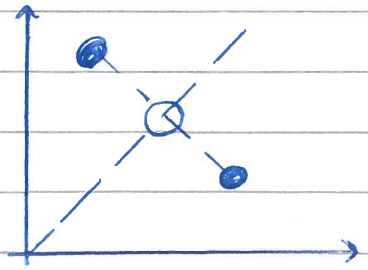
$$k\left(1 - \frac{1}{n}\right) = \sqrt[n+1]{\frac{k}{n}} \Rightarrow k^n \left(\frac{n-1}{n}\right)^{n+1} = \frac{1}{n}$$

$$k_{crit} = \frac{n}{n-1 \sqrt[n]{n-1}}$$

$k < k_{crit}$ stability

$k \geq k_{crit}$ instability

ϕ pair of soln's



○ unstable

● stable

Note that $n > 1$ to have instability

For $n=2$, $k_{crit} = 2$ we can find all points of equilibrium using $x^3 + x - k = 0$ for one point

We have

$$x_1 = \frac{k}{1 + x_2^2}$$

$$x_2 = \frac{k}{1 + x_1^2}$$

$(k - x_2)(1 + x_2^2)^2 - k^2 x_2 = 0$ per both x_1 & x_2 - change to x

$$(k - x)(1 + 2x^2 + x^4) - k^2 x = 0$$

$$-x^5 + kx^4 - 2x^3 + 2kx^2 - (1 + k^2)x + k = 0$$

Divide by $x^3 + x - k$

$$(-x^5 + kx^4 - 2x^3 + 2kx^2 - (1+k^2)x + k)$$

$$= (x^3 + x - k)(-x^2 + kx - 1)$$

So $x^2 - kx + 1 = 0$ per asymmetrical states of equilibrium

$$x_{1,2} = \frac{k \pm \sqrt{k^2 - 4}}{2} \quad \text{per} \quad k > k_{crit} = 2$$

Modelling gene expression

Most of cellular functions are performed by complex molecules - proteins. Proteins are produced from genome (DNA) which is inherited and together with genes organise gene-regulatory networks GRN. GRN are controlling the life of cells and responsible, e.g. for

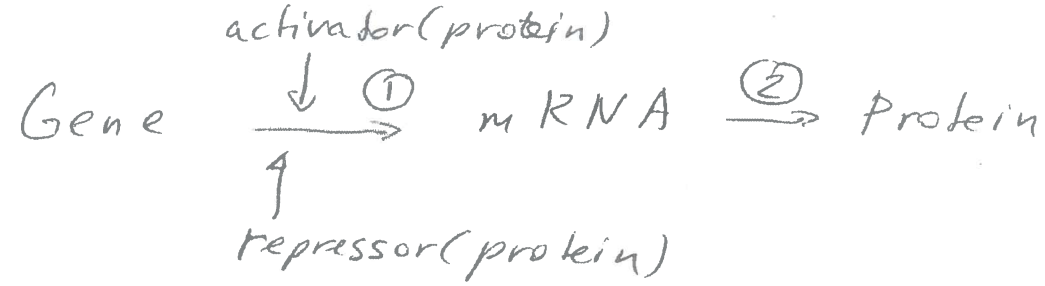
1.) circadian oscillations, i.e. ability of cells to count the time
2) cell differentiation (in embryonal development, or from stem cells),

How?

DNA has a form of (double-stranded) spiral, and during cell proliferation, each strand is coupled with a new one.

Some parts of DNA organise a gene. ← gene.

"Newton's" law for living systems



① transcription (from molecules of 4 elements → 4 elements)

② translation (from 4 elements → 20 elements amino acid)

Genome code: ~~each~~ 3 nucleotides → to 1 aminoacid.

Transcriptional regulation of ~~protein synthesis~~ gene expression (see handout)

Let P - monomer concentration, P_2 - dimer concentration, only dimer can bound as transcriptional factor (TF). O_u - concentration of unbounded DNA, O_b - of bounded. Then for const. concentration of DNA we have:

$$P + P \underset{k_{-d}}{\overset{k_d}{\rightleftarrows}} P_2$$

- rate of reaction

$$O_u + P_2 \underset{k_{-b}}{\overset{k_b}{\rightleftarrows}} O_b$$

In steady state $\quad k_d P^2 = k_{-d} P_2 \quad (*)$

$$k_b O_u P_2 = k_{-b} O_b$$

plus $\quad O_u + O_b = N$ - total DNA concentration (fixed nr. of DNA molecules)

Then

$$O_u = \frac{k_{-b} O_b}{k_b P_2} = \frac{k_{-b}(N - O_u)}{k_b P_2}, \qquad P_2 = k_d P^2 / k_{-d}$$

$$O_u + \frac{k_{-b} O_u}{k_b P_2} = \frac{k_{-b} N}{k_b P_2}, \quad O_u = \frac{\frac{k_{-b} N}{k_b P_2}}{1 + \frac{k_{-b}}{k_b P_2}}$$

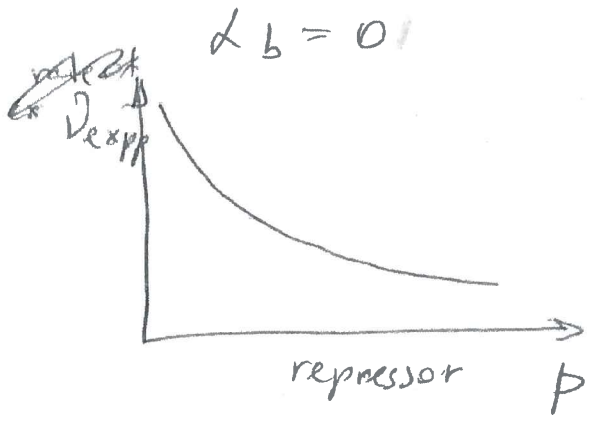
$$O_u = \frac{N}{1 + \frac{k_b}{k_{-b}} P_2} = (*) = \frac{N}{1 + \left(\frac{P}{K}\right)^2}, \text{ where } K = \sqrt{\frac{k_{-b} k_{-d}}{k_b k_d}}$$

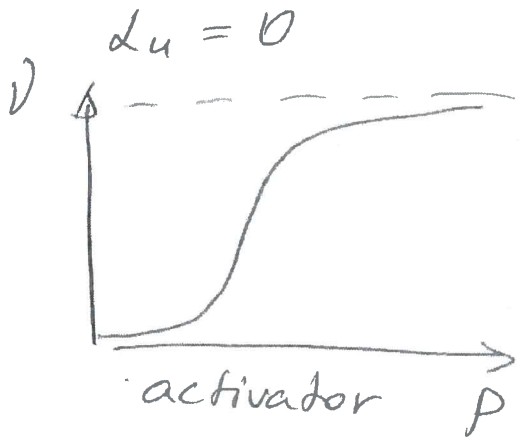
In the same way $O_b = \dfrac{N\left(\frac{P}{K}\right)^2}{1+\left(\frac{P}{K}\right)^2}$

These are Hill equations. 2 is the Hill constant, can take any value from 1 to 6.

Now, if expression works with coeff. α_u, when unbounded, and with α_b, when bounded, for total rate of expression we get

$$V_{expr.}(P) = \alpha_u O_u + \alpha_b O_b = \alpha_u \frac{N}{1+\left(\frac{P}{K}\right)^2} + \alpha_b \frac{N(P/K)^2}{1+(P/K)^2}$$





Taking account of degradation, for protein concentration we get

$$\dot{X} = \alpha_u \frac{N}{1+(P/K)^2} + \alpha_b \frac{N(P/K)^2}{1+(P/K)^2} - r_{deg}(x)$$

For example, $r_{deg}(x) = \gamma X$ – exponential degradation

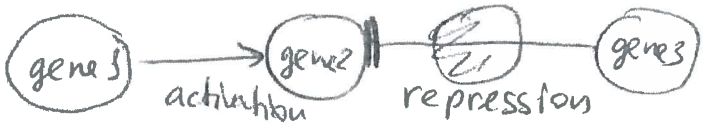
This equation for protein synthesis.

Taking account of mRNA synthesis

$$\begin{cases} \dot{m} = \dfrac{\alpha_u N}{1+\left(\frac{P}{K}\right)^2} + \dfrac{\alpha_b N (P/K)^2}{1+(P/K)^2} - r_{deg}(m) \\ \dot{*} = r_{te}\, m - r_x(x) \end{cases}$$

Controlled Synthesis of mRNA and proteins.

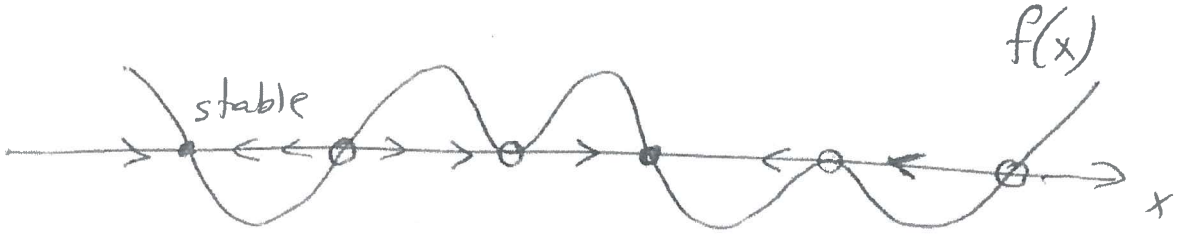
P can be & any protein, also x. We denote



Equilibrium in 1D

1D dynamical system $\dot{x} = f(x)$

condition of { equilibrium x^* $f(x^*) = 0$; stability $f'(x^*) < 0$



● stable

○ unstable

No oscillations are possible, as system cannot cross point of equilibrium.

2D dynamical system $\dot{x}_1 = f_1(x_1, x_2)$

$\dot{x}_2 = f_2(x_1, x_2)$

conditions of equilibrium x_1^*, x_2^* $f_1(x_1^*, x_2^*) = 0$

$f_2(x_1^*, x_2^*) = 0$

Conditions of stability

$$\mathrm{Det}\begin{pmatrix} \partial_{x_1} f_1 - \lambda & \partial_{x_2} f_1 \\ \partial_{x_1} f_2 & \partial_{x_2} f_2 - \lambda \end{pmatrix} = 0$$

Characteristical equation

$\lambda^2 + \tau\lambda + \Delta = 0$, two roots λ_1, λ_2

stability if $\mathrm{Re}\,\lambda_{1,2} < 0$

Changing parameters, we change stability $\longrightarrow$ bifurcations. See handout,

Example: autorepressor

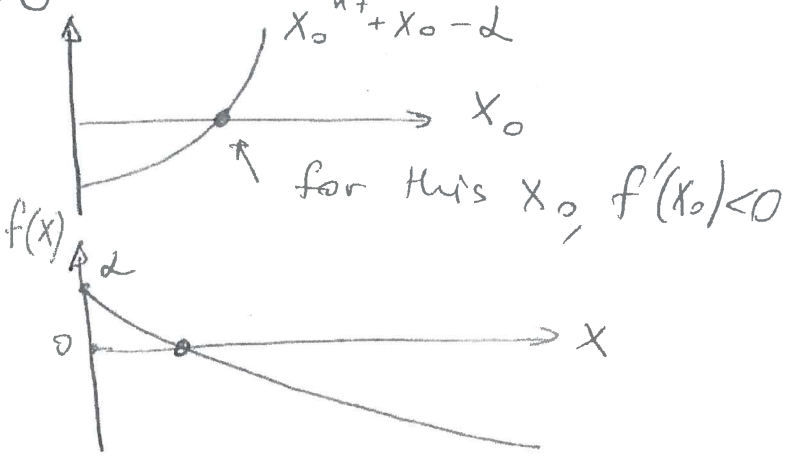
Dynamics $\dot{x} = \dfrac{\alpha}{1 + (x)^n} - x$

(where some constants are excluded by rescaling.)

For equilibrium x_0

$$x_0^{n+1} + x_0 - \alpha = 0$$

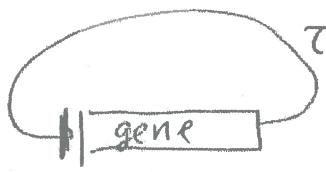
$$x_0 > 0$$



1 stable equilibrium

No oscillations, because in 1D

Example of genetic oscillations: autorepressor with delay



Dynamics: $\dot{X} = \frac{\alpha}{1 + X^n(t-\tau)} - X$

Let us linearise this system around equilibrium $X_0^{n+1} + X_0 - \alpha = 0$ (*)

$$X = X_0 + \xi$$

$$\dot{\xi} = \frac{\alpha}{1 + (X_0 + \xi(t-\tau))^n} - X_0 - \xi(t)$$

for $x \approx 0$ $\quad \frac{1}{1+x} \simeq 1 - x$ (**)

$$\dot{\xi} = \frac{\alpha}{1 + X_0^n + n X_0^{n-1} \xi_\tau + \dots} - X_0 - \xi_t$$

$$\dot{\xi} = \frac{\alpha}{(1+X_0^n)\left(1 + \frac{n X_0^{n-1} \xi_\tau}{1+X_0^n}\right)} - X_0 - \xi_t$$

Using (**)

$$\dot{\xi} = \underbrace{\frac{\alpha}{1+X_0^n}}_{= X_0 \text{ as } (*)} - \frac{\alpha n X_0^{n-1}}{(1+X_0^n)^2} \xi_\tau - X_0 - \xi_t$$

$$\dot{\xi} = -\frac{1}{\alpha} n X_0^{n+1} \xi_\tau - \xi_t \qquad \text{as } \frac{\alpha}{1+X_0^n} = X_0 \text{ from (*)}$$

or $\quad X_0^n = \frac{\alpha}{X_0} - 1$

$$\dot{\xi} = -\frac{X_0}{\alpha} n \left(\frac{\alpha}{X_0} - 1\right) \xi_\tau - \xi_\tau$$

$$\dot{\xi} = n\left(\frac{X_0}{\alpha} - 1\right) \xi(t-\tau) - \xi(t)$$

Assuming $\xi(t) \sim e^{\lambda t}$, we get

$$\lambda = n\left(\frac{x_0}{\alpha} - 1\right) e^{-\tau\lambda} - 1$$

In A-H bifurcation (condition of oscillations) $\lambda = \pm i\omega$

$$\lambda = n\left(\frac{x_0}{\alpha} - 1\right) e^{\mp i\omega\tau} - 1$$

$$Re(\lambda) = 0 = n\left(\frac{x_0}{\alpha} - 1\right)\cos\omega\tau - 1 \Rightarrow \cos\omega\tau = -\frac{1}{n\left(1 - \frac{x_0}{\alpha}\right)}$$

$$Im(\lambda) = \omega = -n\left(\frac{x_0}{\alpha} - 1\right)\sin\omega\tau$$

or

$$n\left(\frac{x_0}{\alpha} - 1\right)\cos\omega\tau = 1$$

$$n\left(\frac{x_0}{\alpha} - 1\right)\sin\omega\tau = -\omega$$

Squaring and taking sum

$$n^2\left(\frac{x_0}{\alpha} - 1\right)^2 = \omega^2 + 1$$

$$\begin{cases} \omega^2 = n^2\left(1 - \frac{x_0}{\alpha}\right)^2 - 1 \\ \cos\omega\tau = -\dfrac{1}{n\left(1 - \frac{x_0}{\alpha}\right)} \end{cases} \quad (***)$$

ω^2 should be positive

Taking account that $x_0 \leq \alpha$, because $x_0^{n+1} = \alpha - x_0 \geq 0$

we get the necessary condition of oscillations

$$n^2\left(1 - \frac{x_0}{\alpha}\right)^2 - 1 > 0 \quad \text{i.e, only if} \quad n \geq 2$$

Also $\cos\omega\tau = -\dfrac{1}{\sqrt{1+\omega^2}}$, hence for $\omega \gg 1$

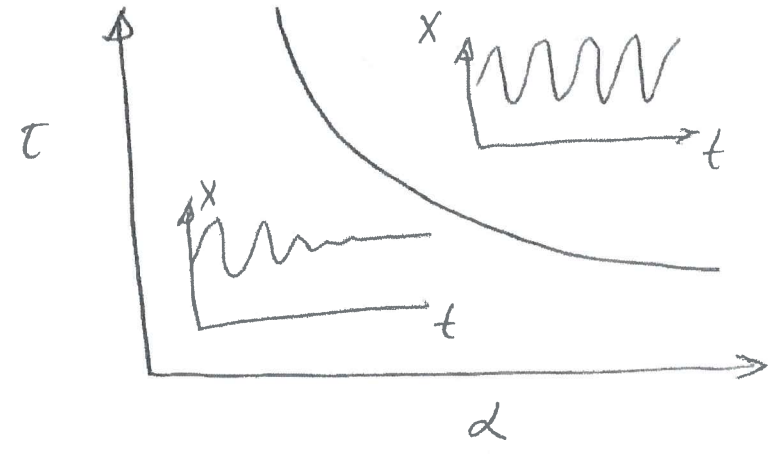
$\cos\omega\tau \simeq 0$; $\omega\tau \simeq \frac{\pi}{2}$ and period $T = \frac{2\pi}{\omega} \sim 4\tau$

much larger than the delay τ.

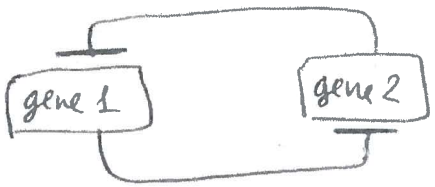
See also handout other networks with negative feedback.

~~Bistable genetic~~

Solving (***) and (*) we can get bifurcation curve, or boundary of oscillations



Bistable genetic switch



Dynamics

$$\dot{X}_1 = \frac{K_*}{1 + X_2^{\,n}} - X_1$$

$$\dot{X}_2 = \frac{K}{1 + X_1^{\,n}} - X_2$$

Because of symmetry, equilibrium states are either on $X_1 = X_2$

or symmetrical (X_1, X_2) (X_2, X_1)

If $X_1 = X_2 = X_0$ then

$$X_0^{n+1} + X_0 - K = 0 \rightarrow \text{we have}$$

one real positive root.

Linearizing around it, we have $X = X_0 + \xi$

$$\begin{cases} \dot{\xi}_1 = \dfrac{K}{1+(x_0+\xi_2)^n} - \xi_1 - x_0 \\ \dot{\xi}_2 = \dfrac{K}{1+(x_0+\xi_1)^n} - \xi_2 - x_0 \end{cases}$$

As before

$$\begin{cases} \dot{\xi}_1 = \dfrac{n}{K} x_0^{n+1} \xi_2 - \xi_1 = f_1 \\ \dot{\xi}_2 = \dfrac{n}{K} x_0^{n+1} \xi_1 - \xi_2 = f_2 \end{cases}$$

$$\begin{vmatrix} \dfrac{\partial f_1}{\partial \xi_1} - \lambda & \dfrac{\partial f_1}{\partial \xi_2} \\ \dfrac{\partial f_2}{\partial \xi_1} & \dfrac{\partial f_2}{\partial \xi_2} - \lambda \end{vmatrix} = \begin{vmatrix} -1-\lambda & \dfrac{n x_0^{n+1}}{K} \\ \dfrac{n x_0^{n+1}}{K} & -1-\lambda \end{vmatrix} =$$

$$= (-1-\lambda)^2 - \frac{n^2 (x_0^{n+1})^2}{K^2} = \lambda^2 + 2\lambda + 1 - \frac{n^2}{K^2} x^{2(n+1)} = 0$$

$$\lambda_{1,2} = \frac{-2 \pm \sqrt{4 - 4\left(1 - \frac{n^2}{K^2} x^{2(n+1)}\right)}}{2} = -1 \pm \frac{n}{K} x^{n+1}$$

λ crosses 0, when the equilibrium changes from stable node to unstable saddle. This happens when

$$-1 + \frac{n}{K} x^{n+1} = 0 \;;\; x^{n+1} = \frac{K}{n} \;;\; x = \sqrt[n+1]{\frac{K}{n}}$$

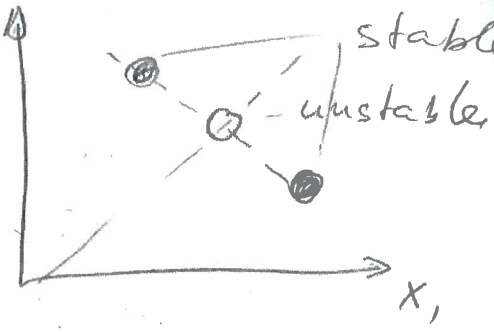
substitute in $x^{n+1} + x - K = 0$

$$\frac{K}{n} + \sqrt[n+1]{\frac{K}{n}} - K = 0 \;;\; K\left(1 - \frac{1}{n}\right) = \sqrt[n+1]{\frac{K}{n}}$$

$$K^n \left(\frac{n-1}{n}\right)^{n+1} = \frac{1}{n} \;;\; K_{crit} = \frac{n}{n-1 \sqrt[n]{n-1}}$$

$K < K_{crit}$ stability, $K \geq K_{crit}$ unstability

and pair of solutions



Note that $n > 1$ to have unstability

For $n = 2$ ($k_{crit} = 2$) we can find all points of equilibrium, using $X^3 + X - k = 0$ for one point

We have $X_1 = \frac{k}{1+X_2^2}$; $X_2 = \frac{k}{1+X_1^2}$

$(k - X_2)(1 + X_2^2)^2 - k^2 X_2 = 0$, for X_2, but the same for X_1. We change it by X.

$(k - x)(1 + 2x^2 + x^4) - k^2 x = 0$

$-x^5 + kx^4 - 2x^3 + 2kx^2 - (1+k^2)x + k = 0$

dividing by $x^3 + x - k$

$-x^5 \quad - x^3 + kx^2$

$kx^4 - x^3 + kx^2 - (1+k^2)x + k$

$kx^4 \quad + kx^2 - k^2 x$

$-x^3 - (k)x^2 - (1+k^2)x + k$

$-x^3 \quad - x + k$

$-(k)x^2 - kx$

0

$-x + k^2 x$

$-x^2 + kx - 1$

So

$(-x^5 + kx^4 - 2x^3 + 2kx^2 - (1+k^2)x + k) = (x^3 + x - k)(-x^2 + kx - 1)$

So $x^2 - Kx + 1 = 0$

for asymmetrical states of equilibrium

so

$$x_{1,2} = \frac{K \pm \sqrt{K^2 - 4}}{2} \quad \text{for } K > K_{crit} = 2$$

two asymmetrical eq. states for $K_{crit} > 2$

Taking into account mRNA synthesis

DNA $\rightarrow$ mRNA $\rightarrow$ protein eg. regulation by dimer

$$\dot{m} = \frac{\alpha_a N}{1 + \left(\frac{P_1}{K}\right)^2} + \frac{\alpha_b N \left(\frac{P_2}{K}\right)^2}{1 + \left(\frac{P_2}{K}\right)^2} - \gamma_m$$

($\dot{m}$: conc^n of mRNA)

$$\dot{x} = r_{transl.} \, m - \gamma x$$

($\dot{x}$: conc^n of protein)

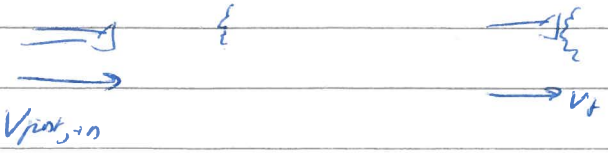
13/11/14

~~Synthetic = risk neutral~~

VI Bone dynamics

Review of linear momentum

Boxing w/ gloves = inelastic collision



$$\frac{m_{arm} V_{post,in}}{2} = \frac{m_{arm} V_{post,f}}{2} + m_{head} V_f \quad \text{(cons. of mom.)}$$

$V_{post,f} = V_f$

divide by 2 as COM is at elbow which moves half distance of post

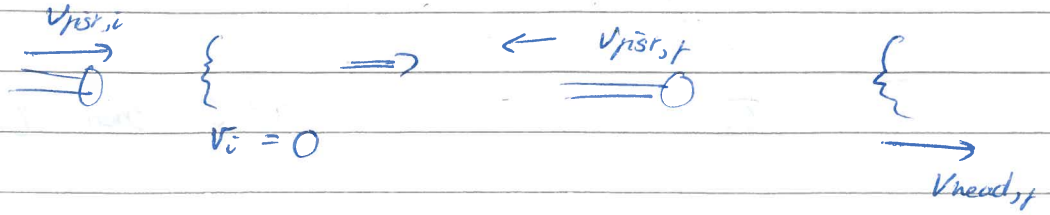
$$V_f = \frac{\frac{m_{arm} V_{post,in}}{2}}{\frac{m_{arm}}{2} + m_{head}} = \frac{V_{post,in}}{1 + 2\frac{m_{head}}{m_{arm}}} = 0.236\, V_{post,in}$$

$m_{arm} = 0.05\, m_{body}$

$m_{head} = 0.031\, m_{body}$

With gloves, $v_f = 0.236\, v_{pist,i}$ 13/11/14

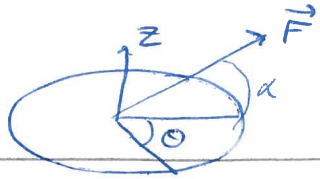
Boxing w/o gloves - elastic collision



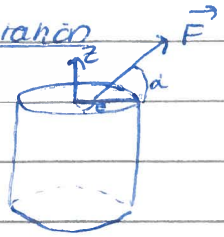
$$\frac{m_{arm}\, v_{pist,i}}{2} = \frac{m_{arm}\, v_{pist,f}}{2} + m_{head}\, v_{head,f}$$

$$\frac{m_{arm}}{2}\left(\frac{v_{pist,i}}{2}\right)^2 = \frac{m_{arm}}{2}\left(\frac{v_{pist,f}}{2}\right)^2 + \frac{m_{head}}{2}\left(v_{head,f}\right)^2$$

Solving $v_{head,f} = \dfrac{v_{pist,i}}{1 + \frac{m_{head}}{m_{arm}}} = \dfrac{v_{pist,i}}{1 + \frac{0.081 m_{body}}{0.05 m_{body}}} = 0.382\, v_{pist,i}$



Rotation



The torque $\vec{\tau}$ about some axis z is defined as $\vec{\tau} = \vec{r} \times \vec{F}$

$\tau_z = r \cdot F \cdot \sin\alpha$ if $\alpha = 0$ then $\tau_z = 0$

This torque leads to change in the angle Θ & angular frequency $\Omega = \frac{d\Theta}{dt}$ giving

$\tau = I \frac{d\Omega}{dt} = I \frac{d^2\Theta}{dt^2}$ where I is the moment of inertia

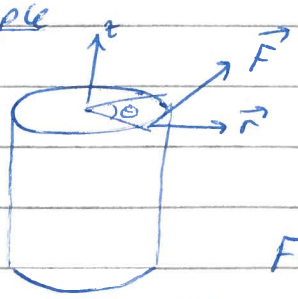
(Note analogy between linear & rotational motion
$F = m \frac{d^2x}{dt^2}$)

A Moment of inertia around some axis (doesn't exist like mass on a body - only defined around some axis) is

$$I = \sum_i m_i R_i^2 = \int \rho(\vec{r}) R^2 dV$$

R_i: distance from axis; ρ: density; dV: volume; $m = \rho V$

Example

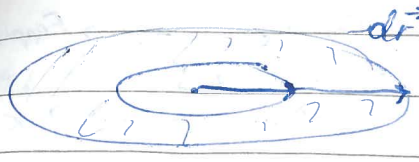


A force $\vec{F}$ is applied to the surface of cylinder $\alpha = 90°$

Find equation of motion (w/o friction)

Moment of inertia $I = \int r^2 \rho \, dV$

Consider integration with respect to r from 0 to R where R - radius of cylinder



height of cylinder

$$I = \int_0^R \rho r^2 \pi \left((r+dr)^2 - r^2\right) \cdot h$$

$\to 0$ faster

$$= \rho \pi h \int_0^R r^2 \left(r^2 + 2r\,dr + (dr)^2 - r^2\right)$$

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

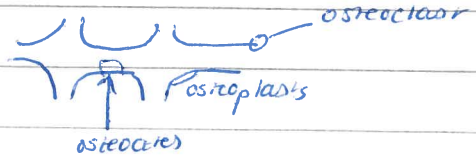
$$= 2\rho\pi h \frac{R^4}{4} = \frac{mR^2}{2}$$ where m - cylinder mass

So

$$F \cdot R = \frac{mR^2}{2} \frac{d^2\theta}{dt^2} \Rightarrow \frac{d^2\theta}{dt^2} = \frac{2F \cdot R}{mR^2} = \frac{2F}{mR}$$

Bone functions: - a structural framework to attach organs & muscles
- provide physical protection
- store minerals
- produce cells for immune system

Bone - complex, porous composite material
Very dynamical, always under bone remodelling



Basic stress-strain relations

spring constant, deformation

$F_{response} = -k(x - x_0)$

$= -k(L - L_0)$ L length L_0 relaxed length

$= -F_{applied}$ $L > L_0$ tension

$L < L_0$ compression

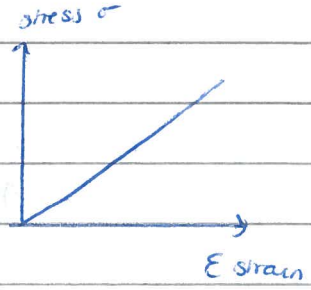
If the object has a cross sectional area A and length L, we can rewrite it

$$\frac{F_{applied}}{A} = \frac{K L_0}{A} \frac{L - L_0}{L_0}$$

stress; elastic or Young's modulus; strain (relative deformation)

σ Y ε

So $\boxed{\sigma = Y\varepsilon}$ Hooke's Law



σ depends linearly on strain

How much do our bones shorten under compression?

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

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

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

$L = 0.5m$

$Y = 17 \cdot 9 \cdot 10^2 \ N/mm^2$

$F = 70kg \cdot 10 m/s^2 = 700N$

$A = 370 mm^2$

$\sigma = \frac{700N}{370mm^2} = 2 \cdot 1 \frac{N}{mm^2}$

$$\Delta L = \frac{\sigma L_0}{Y} = \frac{2 \cdot 1\ N/mm^2 \cdot 0.5\ m}{179 \cdot 10^2\ N/mm^2} = 0.06\ mm$$

$$\varepsilon = \frac{\Delta L}{L_0} = 0.01\%$$

Until ultimate compression stress (UCS) occurs?

$$UCS = 170\ MPa = 170\ \frac{N}{mm^2}$$

so fractional shortening is $\Delta L = \frac{UCS}{Y} \cdot L_0 = \frac{170\ N/mm^2}{179\ N/mm^2} \cdot 500\ mm$

$= 0.5\ cm$

compression which leads to fracture

Energy storage in elastic media

Potential energy (PE): $PE = -\int_0^x F \cdot dx' = \int_0^x kx'\,dx'$

$= \frac{1}{2} kx^2$

or $PE = \frac{1}{2} k(L - L_0)^2$ using $Y = \frac{kL_0}{A}$ $k = \frac{YA}{L_0}$

and $L - L_0 = \varepsilon L_0$

$PE = \frac{1}{2} \frac{YA}{L_0} (\varepsilon L_0)^2 = \frac{1}{2} (Y\varepsilon^2) AL_0$

$= \frac{1}{2} \frac{\sigma^2}{Y} AL_0$

AL_0 ~ V-volume

How can we design the best elastic storage medium for the body, to maximize PE

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

$$= \frac{1}{2} \frac{F_{applied}^2}{YA} L_0$$

to max PE: max L_0, min Y, min A } tendons

How much energy is stored in bones during one step?

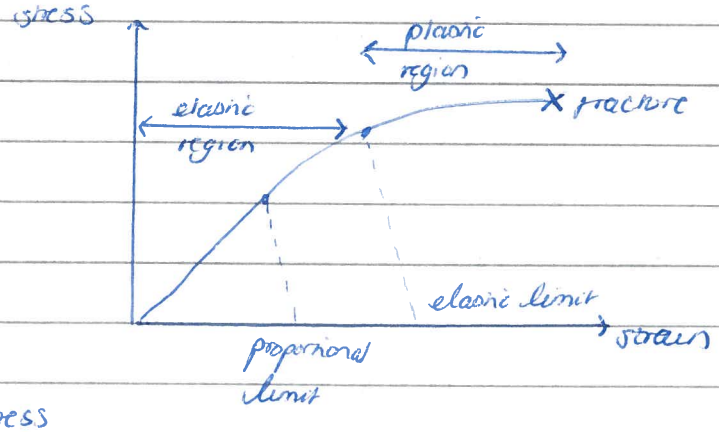
$L_0 = 500mm$

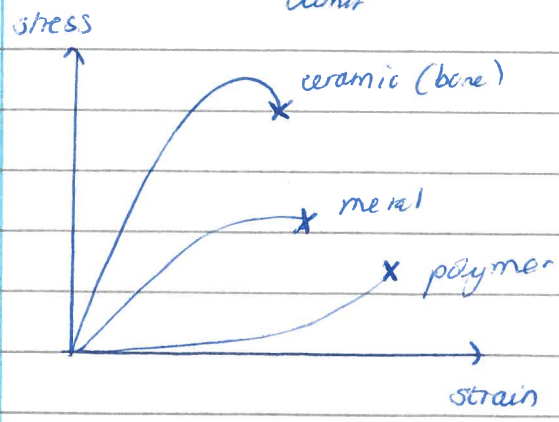
$A = 330\,mm^2$ $\quad Y = 17900\ N/mm^2$

$V = 165 \cdot 10^3\,mm^3$ $\quad F = 6400\ N/mm^2$

$$PE = \frac{1}{2} \frac{(F/A)^2}{Y} V = 1.73N \cdot m \approx 2\% \text{ from usual KE}$$

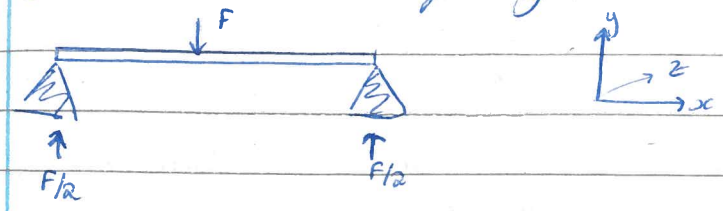
General stress-strain relation:





Why long bones are hollow? (bending of bones)

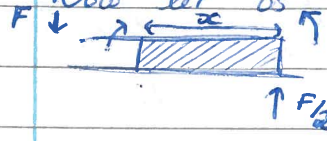
Consider the beam of length L under load F



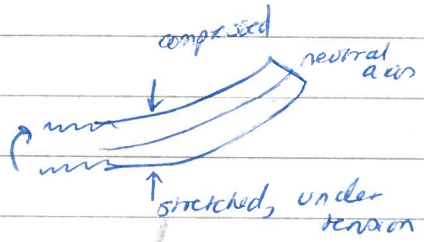
$$\sum F_y = 0$$

$$\sum \tau_z = 0 \quad \text{if the beam is static}$$

Now let us consider the RHS of the beam

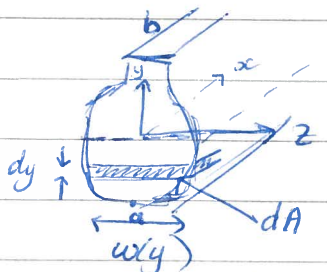


How does internal torque arise



$$\text{So} \quad \tau_z = \tau_{internal} + \frac{1}{2} F \cdot x = 0$$

What is $\tau_{internal}$?



(notice it changes)

$dA = w(y)\,dy$ (area, width)

There is a force acting on dy

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

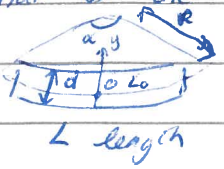
so a torque per dy:

$$|d\tau_{internal}| = |y \cdot \sigma(y) \cdot dA(y)|$$

So the total torque

$$|\tau_{internal}| = \int_{y=a}^{y=b} y \cdot \sigma(y) \cdot dA(y) = \left|\frac{1}{2} F \cdot x\right|$$

What is the disturbance y of?



If $y = 0$ then $L_0 = R \cdot \alpha$

so $\alpha = \frac{L_0}{R}$

If a thickness in the y direction is d then on the top of the beam $L(y) = (R - d/2) \cdot \alpha$

bottom $L(y) = (R + d/2) \cdot \alpha$

In general $L(y) = (R - y) \cdot \alpha = (R-y)\frac{L_0}{R} = \left(1 - \frac{y}{R}\right) L_0$

so elongation $L(y) - L_0 = \left(1 - \frac{y}{R}\right) L_0 - L_0 = \frac{-y}{R} L_0$

so the strain $\varepsilon = -y/R$

since $\sigma(y) = Y \cdot \varepsilon = -\frac{y}{R} \cdot Y$

so the internal torque

$$|T_{internal}| = \left| \int_{y=a}^{y=b} y \cdot \frac{y}{R} Y \, dA(y) \right| = \frac{Y}{R} \int_a^b y^2 \, dA(y)$$

$$= \frac{1}{2} F \cdot \alpha$$

17/11/14

$$|T_{internal}| = \left| \frac{y}{R} \int_a^b y^2 \, dA(y) \right| = \left| \frac{1}{2} F \cdot x \right|$$

The area moment of inertia:

$$I_A = \int_a^b y^2 \, dA(y)$$

since the bending moment $M_B = \frac{1}{2} F \cdot x$

we have $|M_B| = \frac{y}{|R|} \cdot I_A$ (*)

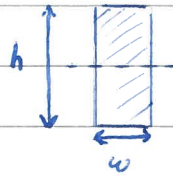
& the magnitude of the curvature $\frac{1}{|R|} = \frac{|M_B|}{y \cdot I_A}$ (**)

→ large I_A, small bending

Equations * and ** interrelate

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

Example Consider a rectangle of height h & width w



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

$$= \frac{1}{12} w h^3$$

$w = 2cm \quad h = 6cm \quad I_A = 36 cm^4$

$w = 6cm \quad h = 2cm \quad I_A = 4 cm^4$

Why? We are asking: how much material is located at a large distance from the neutral axis

I_A describes shape & describes how much material is far away from neutral axis

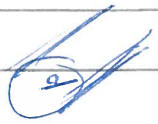
If I_A is large  the 'best' shape

This is used in construction, rails

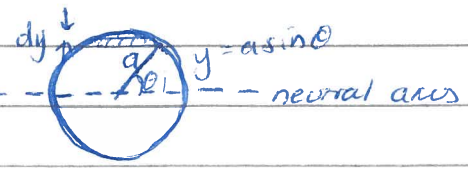
Cross sectional area is small - so not heavy

This is given an exam question

Consider a cylinder of radius a



I_a - ?



$y = a\sin\theta$

$dy = a\cos\theta\, d\theta$

width

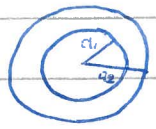
$dA(y) = 2a\cos\theta \cdot \underbrace{a\cos\theta\, d\theta}_{dy} = 2a^2\cos^2\theta\, d\theta$

$$I_A = \int_{-\pi/2}^{\pi/2} \underbrace{a^2\sin^2\theta}_{y^2} \cdot 2a^2\cos^2\theta = 2a^4 \int_{-\pi/2}^{\pi/2} \sin^2\theta\cos^2\theta\, d\theta$$

$\sin^2\theta(1-\sin^2\theta)$

$$= \frac{1}{4}\pi a^4$$

For hollow cylinder



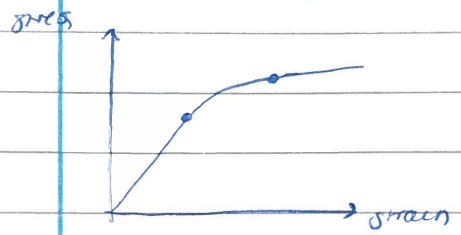
$$I_{A,\text{hollow}} = \frac{\pi}{4}\left(a_2^4 - a_1^4\right)$$

$$m_{\text{hollow}} = \rho\pi\left(a_2^2 - a_1^2\right)\cdot L$$

$\pi \cdot \text{radius}^2 \cdot \text{length} \times \text{density}$

$\frac{a_1}{a_2}$	$I_{A,\text{hollow}} / I_{A,\text{solid}}$	$m_{\text{hollow}} / m_{\text{solid}}$
solid ◎ 0	1	1
◎ 0.5	0.987	0.75
	6% decrease in I_A	25% decrease of mass

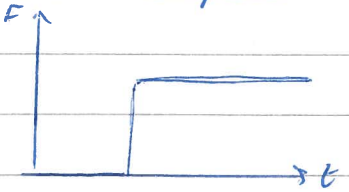
That's why long bones are hollow.
but limited by risk of fracture

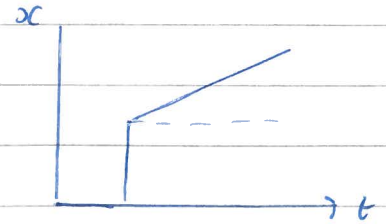


Viscoelasticity Suppose that force is applied fast or slow relative to an internal time scale
The response of the material depends on these temporal characteristics
This type of behaviour is called viscoelasticity

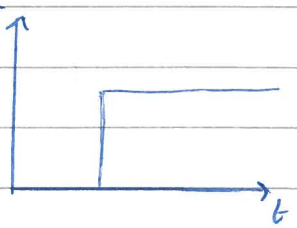
Three main manifestations

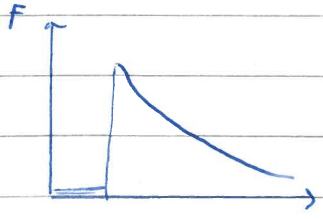
1) Creep



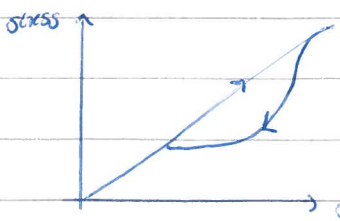


2) Relaxation



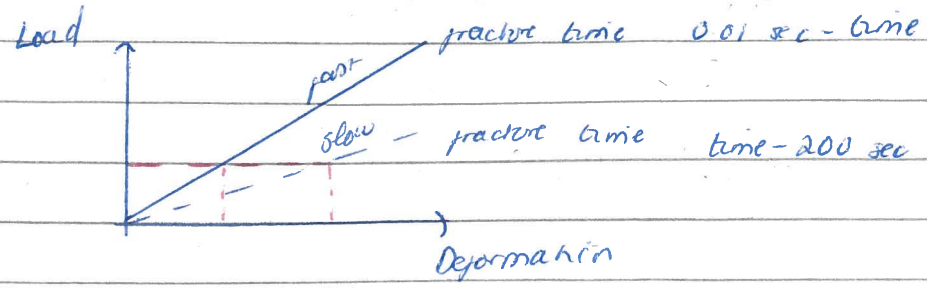


3 Hysteresis



The stress strain cycles are not reversible

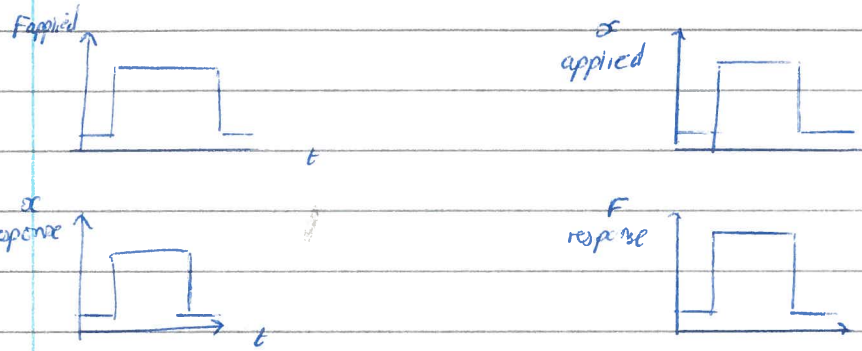
Experimental results for fast & slow force (Fig *)



For slow force, for the same load, deformation is almost doubled!

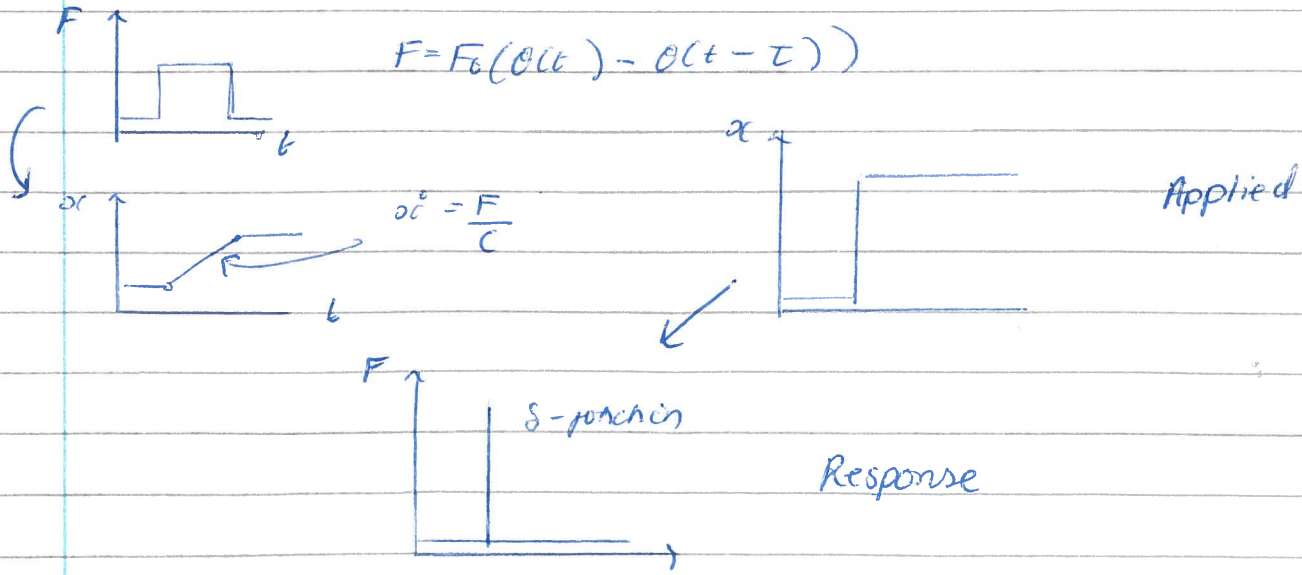
Elements of modelling

1) Perfect spring $F = kx$



2) perfect dashpot $F_{applied} = c \frac{dx}{dt}$

c / dashpot constant



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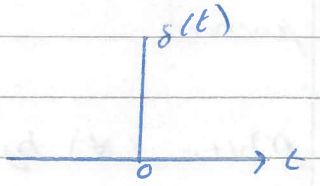
Review δ-function (generalized function)

Solve $\dot{x} + x = \delta(t)$ (*)



0 everywhere except 0

integral under curve = 1

generalized function maps whole function to one number

$$\delta(t) = \int_{-\infty}^{\infty} \varphi(t)\,\delta(t)\,dt = \varphi(0)$$

which is why it is called a functional

For $t<0$ $\quad x = c_1 e^{-t}$

$t>0$ $\quad x = c_2 e^{-t}$ } (**)

So we have soln for $t<0$, $t>0$

Need to treat as functionals

The equation includes generalized functions

Let us take $\varphi(t)$, any function, such that

$\varphi(t) \to 0$ if $t \to \pm\infty$

$\varphi(t) f(t) \xrightarrow{t \to \pm\infty} 0 \quad \forall\ f(t)$

Then $\delta : \varphi(t) \longrightarrow \varphi(0)$ as

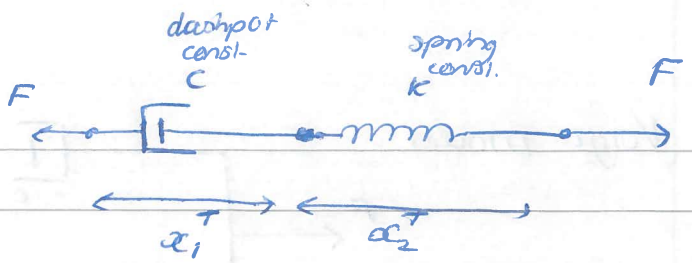
$$\int_{-\infty}^{\infty} \varphi(t)\,\delta(t) = \varphi(0)$$

$$x : \varphi(t) \longrightarrow \int_{-\infty}^{\infty} \varphi(t)\,x(t)\,dt$$

$$\dot{x} : \varphi(t) \longrightarrow \int_{-\infty}^{+\infty} \varphi(t)\,\dot{x}(t)\,dt$$

$$= -\int_{-\infty}^{\infty} x(t)\,\dot{\varphi}(t)\,dt$$

Maxwell model



$x_i^T = x_i^E + x_i \qquad i = 1, 2$

x_i^T: total; x_i^E: eq. length; x_i: deformation

For dashpot $F = c\frac{dx_1}{dt}$

spring $F = k x_2$

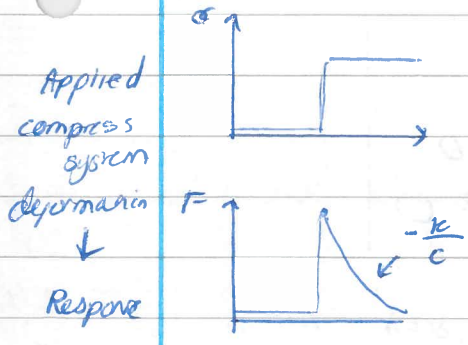
$\dot{x}^T = x_1^T + x_2^T \Rightarrow \frac{dx}{dt} = \frac{dx_1}{dt} + \frac{dx_2}{dt}$

$\frac{dx}{dt} = \frac{F}{c} + \frac{1}{k}\frac{dF}{dt}$ because F the same in 1 and 2

Dashpot can't be compressed immediately - will be compressed until spring returns to eq. point

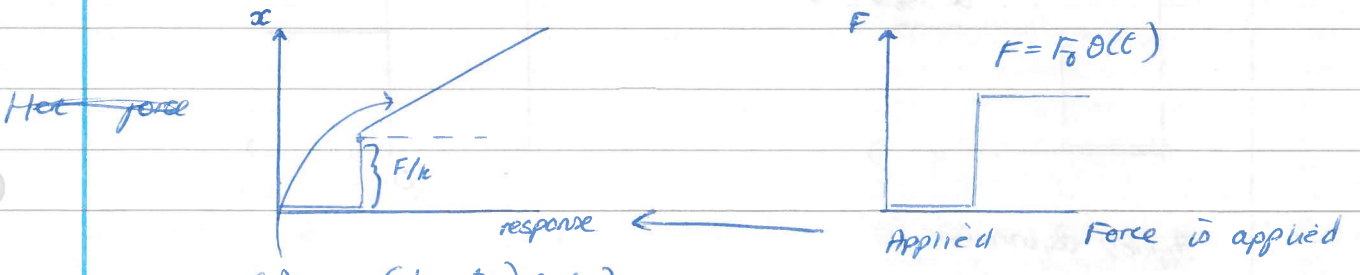
For spring: force immediately appears & then decays

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



derivative here = δ function since 0 everywhere apart from 1 point where = ∞

$F = k x_0 \exp\left(-\frac{k}{c}t\right)\cdot\theta(t)$



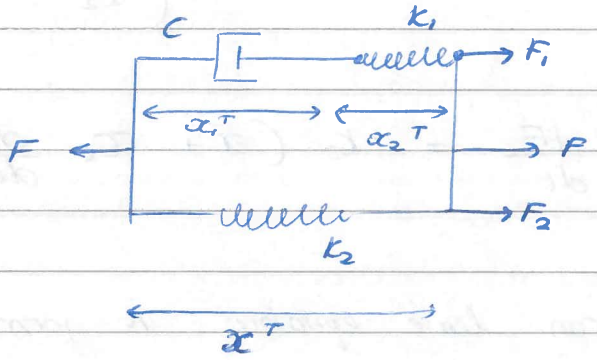
$x(t) = F_0\left(\frac{1}{k} + \frac{t}{c}\right)\theta(t)$

Do not have to memorise these eq^ns: can get them from solving eq^ns

$$F = c x_0 \delta(t) + k x_0 \theta(t)$$

Will consider one more model

Kelvin model



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

$$F_1 = c\frac{dx_1}{dt} = k_1 x_2 \quad \text{as in Maxwell model}$$

$$F_2 = k_2 x$$

$$F = F_1 + F_2 \quad \text{as in Voigt model}$$

hope to avoid non physical behaviour

$$\frac{dx_1}{dt} = \frac{F_1}{C} \qquad x_2 = \frac{F_1}{k_1} \Rightarrow \frac{dx_2}{dt} = \frac{1}{k_1}\frac{dF_1}{dt}$$

$$\frac{dx}{dt} = \frac{dx_1}{dt} + \frac{dx_2}{dt} = \frac{F_1}{C} + \frac{1}{k_1}\frac{dF_1}{dt} \quad \text{we need } F$$

$$F_1 = F - F_2 = F - k_2 x; \quad \frac{dF_1}{dt} = \frac{dF}{dt} - k_2\frac{dx}{dt}$$

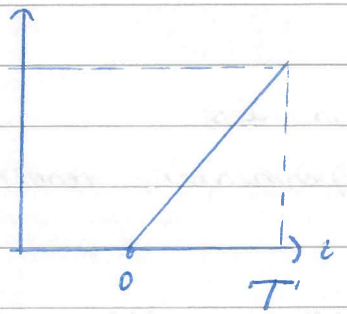
Substituting F_1 and $\frac{dF_1}{dt}$

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

$$F + \frac{c}{k_1}\frac{dF}{dt} = k_2 X + c\left(1 + \frac{k_2}{k_1}\right)\frac{dx}{dt} \qquad (1)$$

Let us use Kelvin model to describe fast or slow application of the force

Apply



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

changing T, we change the speed of F

$$\frac{dF}{dt} = \frac{F_0}{T} \quad \text{so (Kelvin)} \quad K_2\left(x + \tau_0 \frac{dx}{dt}\right) = F + \tau_E \frac{dF}{dt}$$

$$= F_0 \frac{t}{T} + \frac{F_0}{T} \tau_0$$

$$\text{or} \quad x + \tau_0 \frac{dx}{dt} = \frac{F_0}{K_2 T} t + \frac{F_0}{K_2} \frac{\tau_E}{T}$$

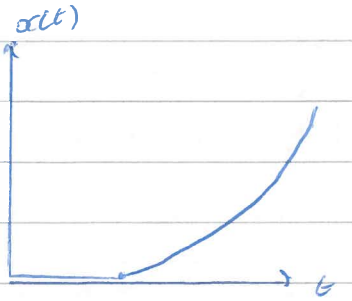
Using: $x + a\frac{dx}{dt} = bt + e$

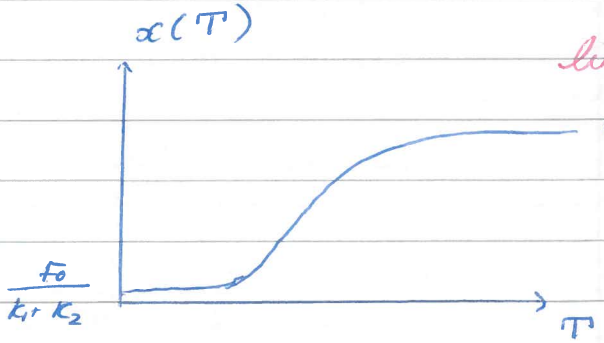
$$\Rightarrow x(t) = bt + (e - ab)\left(1 - \exp\left(-\frac{t}{a}\right)\right)$$

$$\text{So} \quad x(t) = \frac{F_0}{K_2 T} t - \frac{cF_0}{K_2^2 T}\left(1 - \exp\left(\frac{-t}{\tau_0}\right)\right) \qquad 0 < t < T$$

at $t = T$

$$x(T) = \frac{F_0}{K_2} - \frac{cF_0}{K_2^2 T}\left(1 - \exp\left(-\frac{T}{\tau_0}\right)\right)$$

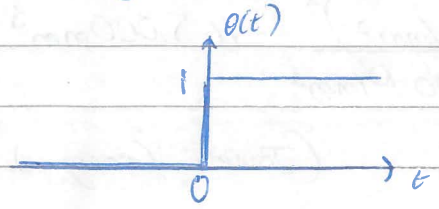




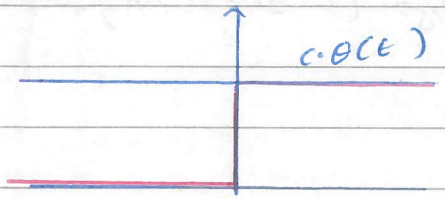
limit of slow force

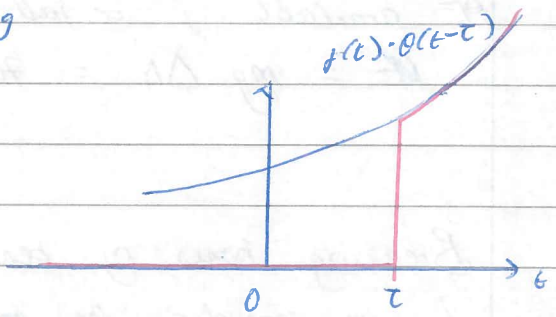
24/11/14

Modelling with $\theta(t)$ ~ heavy side punches

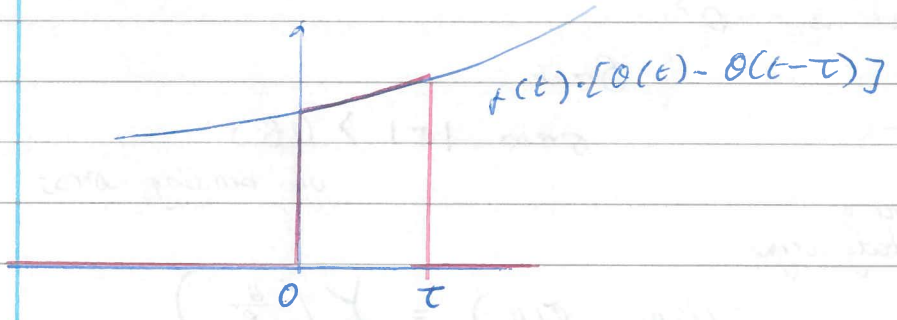


Why is it convenient for modelling





If 'we' hit the punches



Bone fractures - ~~Bones absorb~~

Stiff bones absorb little energy

The femoral bone is about 2/3 as stiff in children as in adults (children fall a lot - but their bones absorb a lot of energy & this is why they don't break as easily?

Energy of fracture

energy UCS = 170 N/mm^2

ultimate compression stress

stress = $\frac{\text{force}}{\text{area}}$

UCS is when force = $170\ N/mm^2 \cdot 370\ mm^2$

= 56000 N ~ 6 tons ~ 80 body weights !

area moment of inertia

$$D \gg \frac{2UBS \cdot I_a}{d|W_{body} - W_{leg}|} = \frac{\pi a^4}{2 \cdot 2a} \cdot \frac{UBS}{|W_{body} - W_{leg}|}$$

a - radius of bone

Pascal

$$= \frac{\pi (1cm)^3}{4} \cdot \frac{2.13 \times 10^2 \, MPa}{|750 - 110| N}$$

$$\approx 25 cm$$

i.e. if displacement of center of mass is $\gg 25cm$

Have considered
linear compression
compression formation per bending (i.e. compression & stretching of springs in bones
viscoelasticity (i.e. force applied fast or slow)

Applying the divergence theorem

divergence (not grad since $\cdot$)

$$\int_V (\nabla \cdot \bar{J})\, dV = \int_S \bar{J} \cdot d\bar{S}$$

$$\int_V \left[\frac{\partial c}{\partial t} + \nabla \cdot \bar{J} - f(c, \bar{x}, t) \right] dV = 0$$

Since V is arbitrary

$$\frac{\partial c}{\partial t} + \nabla \cdot \bar{J} = f$$

or for classical diffusion $\bar{J} = -D \nabla c$

$$\frac{\partial c}{\partial t} = f + \nabla \cdot (D \nabla c)$$

Reaction diffusion equation

reaction / diffusion = change in material of some volume

Example In ecological context, f could represent the birth - death process & c - population density with logistic growth

$$f = r \cdot c \left(1 - \frac{c}{K}\right)$$

r: reproduction rate; K: carrying capacity

function grows & dies at rates

Then

$$\frac{\partial c}{\partial t} = r \cdot c \left(1 - \frac{c}{K}\right) + D \nabla^2 c$$

27/11/14

$\frac{\partial n}{\partial t} = rn\left(1 - \frac{n}{K}\right) + D^* \nabla^2 n$ Fisher Kolmogorov eq^n

Chemotaxis (a kind of taxis) is a phenomenon in which cells, bacteria or other organisms direct their movement according to certain chemicals (pheromones) in the environment

Examples: for bacteria, swimming toward the highest concentration of certain molecules

- movement of leucocytes towards inflammation eg. in healing
- flee from poison
- movement of sperm towards egg

Let us suppose that the presence of a gradient of an attractant $a(\vec{x}, t)$ gives rise to a movement something

Hence the chemotactic flux: $J_{chem} = n\chi(a)\cdot\nabla a$ (χ: function of chem. conc. attractant)

Using general conservation eq^n

$\frac{\partial n}{\partial t} + \nabla\cdot\vec{J} = f(n)$

$J = J_{chem} + J_{diff}$ $\quad J_{diff} = -D\nabla n$ $\quad J_{chem} = n\chi(a)\nabla a$

So $\frac{\partial n}{\partial t} = f(n) - \nabla n\chi(a)\nabla a + \nabla D\nabla n$

a basic reaction chemotaxis diffusion

Model (experiment of Budrene & Berg, 1991)

The bacteria diffuse, more chemotactically, proliferate & die

Chemoattractant diffuses, is produced & consumed by bacteria

The stimulant (food) diffuses & is consumed by bacteria

Rate of change of cell density, n	=	diffusion n	+	chemotaxis of n to c

$$\pm \boxed{\text{proliferation or death of } n}$$

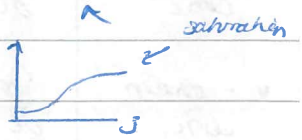
Rate of change conc of chemoattr, c	=	diffusion c	+	production of c by n	−	uptake of c by n

Rate of stimulant concentration s	=	diffusion of s	−	uptake of S by n

$$\frac{\partial n}{\partial t} = D_n \Delta n - \nabla\left[\frac{k_1 n}{(k_2 + c)^2} \nabla c\right] + k_3 n\left(\frac{k_4 s^2}{k_5 + s^2} - n\right)$$

diffusion (Woodward) chemotaxis

Won't be expected to remember this



$$\frac{\partial c}{\partial t} = D_c \Delta c + k_6 \frac{s\, n^2}{k_6 + n^2} - k_7 n c$$

diffusion for chemoattr. conc.

$$\frac{\partial s}{\partial t} = D_s \nabla^2 s - k_8 n \frac{s^2}{k_9 + s^2}$$

where k_i – constant

We look for the solution in the form

$$u(x,t) = 1 + \varepsilon \sum_{k=1}^{\infty} f_k(t)\, e^{ikx}$$

$$v(x,t) = \frac{t}{\mu+1} + \varepsilon \sum_{k=1}^{\infty} g_k(t)\, e^{ikx}$$

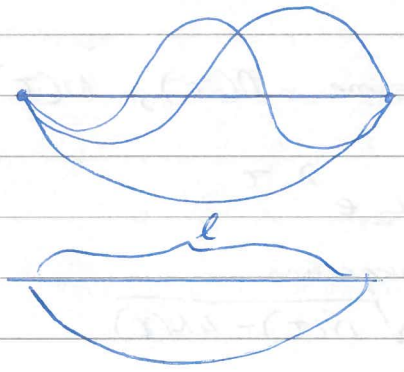
k - wave number $\quad k = \frac{m\pi}{\ell}$ where ℓ - system size

ε - small parameter $\quad 0 < \varepsilon << 1$

$$kx = \frac{2\pi x}{T_{period}} = \frac{2\pi x m}{2\ell} = \frac{\pi m x}{\ell} = \omega x$$

(ω: spatial frequency)

$k, m = 1, 2, \ldots$



$m, k = 1 \quad \frac{T}{2} = \ell \quad T = 2\ell$

Substituting solutions in the system of equations & linearizing them w.r.t. ε, then for each k

$$\frac{dF(t)}{d\tau} = -\alpha k^2 F(t) + \alpha(\mu+1)^2 \frac{k^2}{\tau^2} G(t)$$

$$\frac{dG(\tau)}{d\tau} = -k^2 G(\tau) + \frac{2a}{(\mu+1)^2} F(\tau)$$

where $\quad \tau = \mu + 1 + t \qquad F(\tau) = f_k(t)$

$$G(\tau) = g_k(t)$$

Not explained in detail since it is HW.

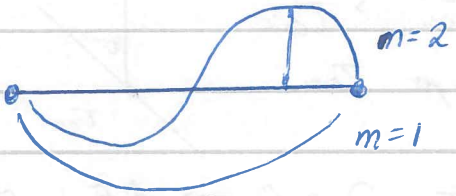
Recalculate everything we have done for exam!
Exam based mostly on derivations

01/12/14

$$\frac{\partial^2 F}{\partial \tau^2} + \underbrace{\left[\kappa^2 (d+1) + \frac{2}{\tau} \right]}_{D(\tau)} \frac{dF}{d\tau} + \underbrace{\kappa^2 \left(d\kappa^2 + \frac{2d}{\tau} - \frac{2\alpha\mu}{\tau^2} \right)}_{N(\tau)} F = 0$$

$$\tilde{F}(\tau) = L_1 e^{\lambda_+ \tau} + L_2 e^{\lambda_- \tau}$$

$$\lambda_\pm = \frac{1}{2} \left[-D(\tau) \pm \sqrt{D(\tau)^2 - 4N(\tau)} \right]$$



λ_- always -ve
λ_+ can be +ve
in which case have exponential growth

D coef. of diffusion
α strength of chemotactic flux
N depends on α

this should be τ small - not -ve ↓

If α is sufficiently large, then $N(\tau) < 0$ for $\tau < 0$
As τ increases $N(\tau)$ will increase through zero & become positive > 0

So there is τ_{crit}: $\tau < \tau_{crit}$ one component of $\tilde{F}(\tau)$ will grow, $\tau > \tau_{crit}$ all components of $\tilde{F}(\tau)$ will decay

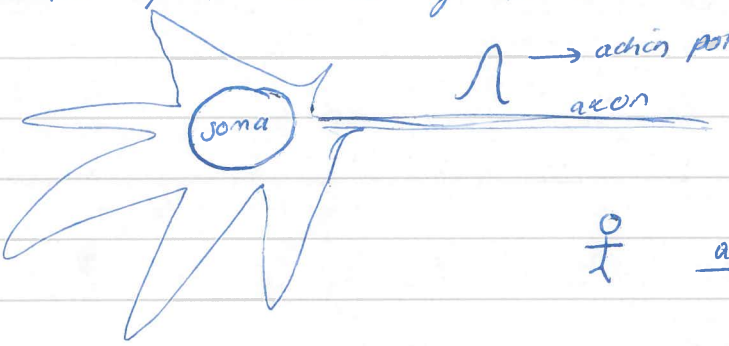
Indeed α (chemotaxis) plays destabilising role
At $\tau \approx \tau_{crit}$ $F(\tau)$ should have maximum

The location $\tau_{crit} \approx \tilde{\tau}_{crit}$ can be obtained from $N(\tilde{\tau}_{crit}) = 0$ (approximation of τ_{crit})

Neurons

The human brain contains 100 000 000 000 neurons, each linked with up to 10,000 synaptic connections

Consumes up to 20% of all our calories



We don't yet understand how the system of neurons work - to find out more Ⓖ google Theory of Integrated Information

Some neurons emit action potential constantly (regularly or irregularly) whereas other neurons are in excitable regime

Hodgkin & Huxley (1952) 04/12/14

Model of neuron firing (Nobel Prize 1963)

The electric pulse arises because the axon membrane is preferentially permeable to various chemical ions

potassium (K^+), sodium (Na^+)

The current $I(t)$ — current of individual ions: I_{Na}, I_K, I_L – leakage – all other ions parcelled

— the contribution from the time variation in the transmembrane potential

$C \frac{dV}{dt}$ — voltage

capacity

So $I(t) = C\frac{dV}{dt} + \sum_i I_i$

I_a

From observations

$\sum I_i = g_{Na} n_1^3 n_3 (V - V_m) + g_K n_1^4 (V - V_K) + g_L (V - V_L)$

$I_{Na} + I_K + I_L$

conductance, equilibrium potential

contribution because of Na

should be n_2?

K

L

where $n_i(t)$ & $i = 1, 2, 5$

HH model

$$\frac{dn_i}{dt} = \alpha_i(V)(1 - n_i) - \beta_m(V) n_i$$

If external current is applied I_a

$$C\frac{dV}{dt} = -g_{Na} n_1^3 n_3 (V - V_m) - g_K n_2^4 (V - V_K) - g_L (V - V_L) + I_a$$

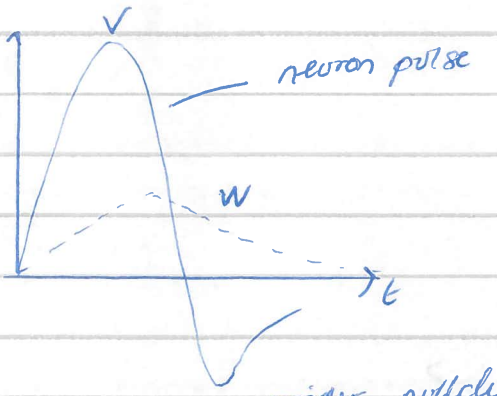
← external current applied additionally

If $I_a = 0$ – excitable region — small perturbation, nothing happens

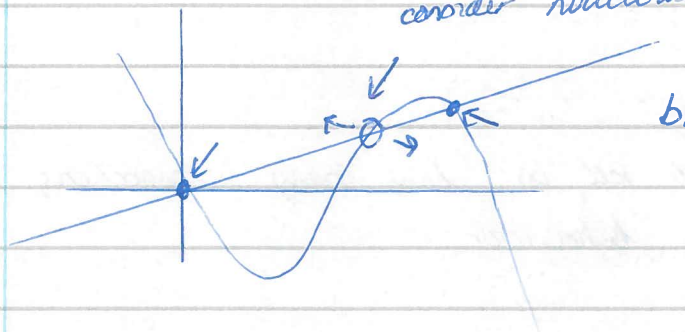
large perturbation → large excursion

This is not included in the exam.

1



consider nullclines - see this is unstable point



bistable region

So for $I_a = 0$ we observe either excitable or bistable regime

form of the excursion does not depend on perturbation

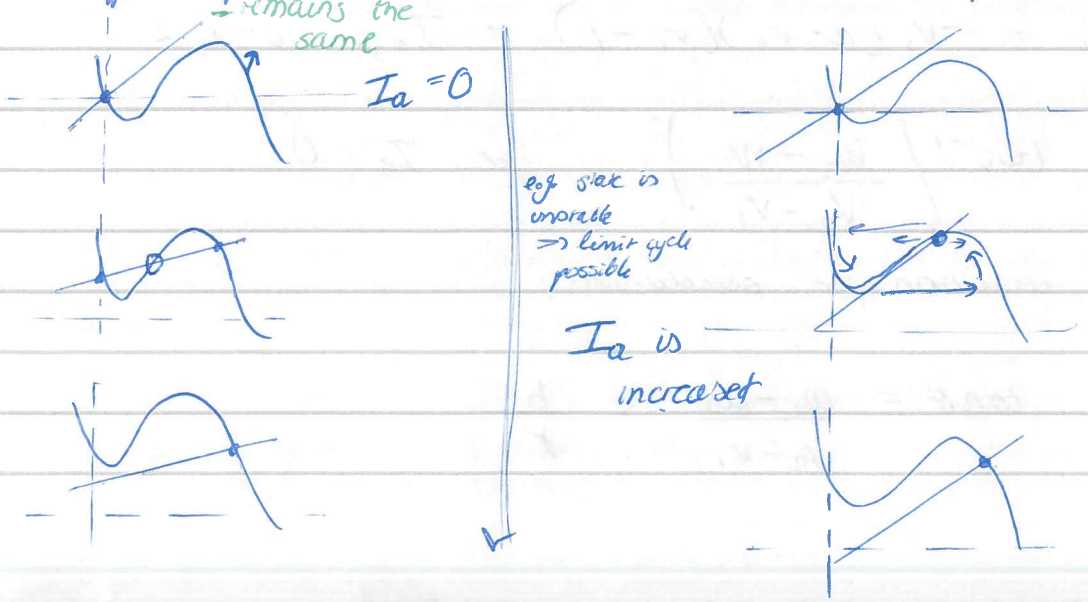
We have seen:

No current - model can demonstrate ~~example~~ excitable region

Case $I_a > 0$

Because $\frac{dV}{dt} = f(V) - w + I_a \Rightarrow w = f(V) + I_a$

the effect of nullcline is to move nullcline upwards



and $I_1 < I_a < I_2$

FHN model:

$I_a = 0 \Rightarrow$ excitability

$I_a > 0 \Rightarrow$ neuron pulses (periodicity)

The total change of mass

$$\frac{\partial \rho}{\partial t}\Delta x \Delta y \Delta z = \rho u \Delta y \Delta z - \left[\rho u + \frac{\partial}{\partial x}(\rho u)\Delta x\right]\Delta y \Delta z$$

in — out

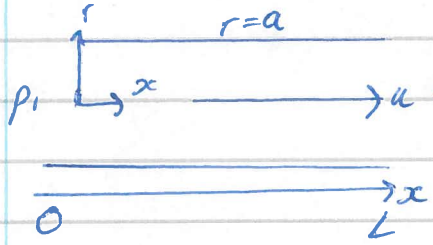
$$\frac{\partial \rho}{\partial t} + \frac{\partial}{\partial x}(\rho u) = 0$$

equation of continuity

BC $v_n = 0$ on solid bdy

if viscous $v_t = 0$ on solid bdy

The Poiseuille's flow



Consider the motion of a fluid through a long cylindrical tube of length L, radius a & two pressures $p_1 > p_2$

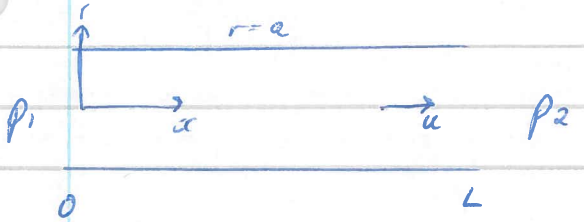
Assume steady flow $\partial/\partial t = 0$

ρ = const.

$\Rightarrow$ from continuity equation $\frac{\partial \rho}{\partial t} + \frac{\partial}{\partial x}(\rho u) = 0$

$$\Rightarrow \frac{\partial}{\partial x} u = 0$$

Poiseuille's Law 8/12/14



cylindrical coords, steady flow

$$0 = -\frac{\partial p}{\partial x} + \mu \Delta u$$

symmetrical in θ

In cylindrical coordinates

$$\mu \frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial u}{\partial r}\right) = \frac{\partial p}{\partial x}$$

because of the mass conservation $u = u(r)$ give $\frac{\partial}{\partial x}$

$$\frac{d^2 p}{dx^2} = 0 \Longrightarrow \frac{dp}{dx} = \text{const}$$

$$p = k \cdot x + k'$$

(const.)

Using boundary conditions p_1 at $x = 0$

p_2 at $x = L$

$$p = p_1 + \frac{(p_2 - p_1)}{L}x \Longrightarrow \frac{dp}{dx} = -\frac{(p_1 - p_2)}{L}$$

$$\frac{d}{dr}\left(r\frac{\partial u}{\partial r}\right) = \frac{r}{\mu}\frac{dp}{dx} \quad (\text{const}) \qquad r\frac{\partial u}{\partial r} = \frac{r^2}{2\mu}\frac{dp}{dx} + A \quad (\text{const})$$

$$u = \frac{r^2}{4\mu}\frac{dp}{dx} + A\log r + B \qquad u = u(r)$$

(B: const)

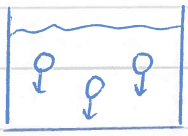
$A = 0$ o/w $u \to \infty$ as $r \to 0$

$u(a) = 0$ because of viscosity

$r = a$

The density of red cells (erythrocytes)

$\rho_c = 1.06$ & of plasma $\rho_p = 1.03$



← rate = the erythrocyte sedimentation rate

ESR

red cells sink
- can measure diff. in density & estimate how many rd cells there are & velocity they travelled

Mathematics (Stokes law 1851)
for slow motion

Reynolds number $R = \frac{\rho v a}{\mu}$ — density / velocity/speed / radius or some size / viscosity

This is dimensionless

For $R >> 1$ turbulent fast motion

$R << 1$ slow motion, laminar flow

For $R << 1$, a drag force F_D for slowly moving sphere

$F_D = 6\pi\mu a v$ - Stoke's law

$$\underbrace{v \cdot \rho_e \cdot \frac{dv}{dt}}_{\text{mass of one cell}} = \underbrace{V\rho_c \cdot g}_{\text{gravity}} - \underbrace{V\rho_p \cdot g}_{\text{the buoyant force}} - 6\pi\mu a v$$

volume of sphere

$V = \frac{4}{3}\pi a^3$

For a steady rate of fall

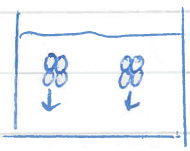
Have put LHS = 0 since steady

$$ESR = v\Big|_{\text{steady motion}} = \frac{4}{3}\pi a^3 \cdot \frac{1}{6\pi\mu a}(\rho_e - \rho_p)g$$

$$= \frac{2}{9\mu} a^2 (\rho_e - \rho_p) g$$

ESR can be measured. In illness, ESR increases dramatically. Why?

a is increased, drag force increased

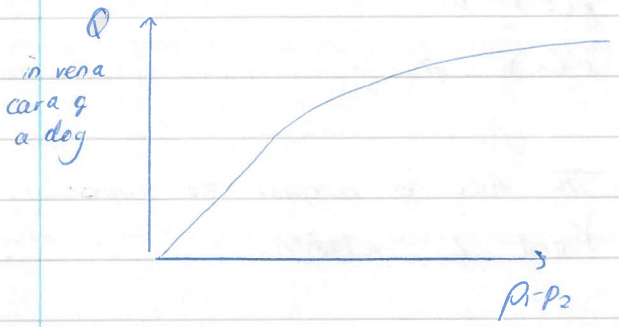


↑ cells bound together

ie. red cells form aggregates

11/12/14 ①

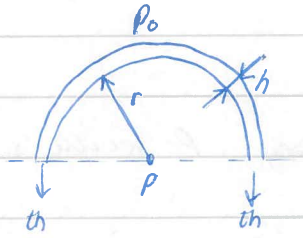
The steady flow q blood through a vessel



Why?

Because a vein is not a rigid tube but elastic

Consider cross section



p - the interior fluid pressure

p_0 - the exterior pressure

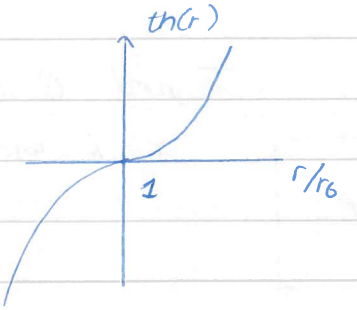
The downward force per unit length is $2th$

t - tension per unit length per unit thickness

The upward force is $(p-p_0)\cdot 2r$ per unit length

So $th = (p-p_0)r$ Young & Laplace relation

In experiment the tension - radius curve



determining experimentally Δp needed to change r_0 to r

Using Hooke's law for elastic regions

$$t = Y\left(\frac{r-r_0}{r_0}\right)$$

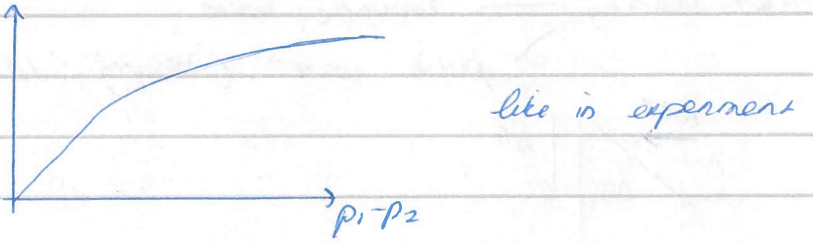
Y: Young's modulus

So if $(p_1 - p_0)$ remains fixed and $p_2 - p_0 \to -\infty$
Q attains a constant value

$$Q \sim \frac{\pi}{8\mu L} \int_{-\infty}^{p_1 - p_0} r^4(p')\, dp' \qquad \text{doesn't depend on } p_2$$

Or if $p_2 \to 0$ then $p_2 - p_0 \to -p_0$, again Q indep. of p_2
In physiology called 'vascular waterfall'

Using $h(r)$ diagrams & $p - p_0 = \frac{t \cdot h}{r}$ relation we get



Hence the equation of motion

$$\rho A\left[\frac{\partial u}{\partial t} + u\frac{\partial u}{\partial x}\right] = -\frac{\partial}{\partial x}\left[(p-p_0)A\right] \qquad (1)$$

Equation of continuity

$$\frac{\partial A}{\partial t} + \frac{\partial}{\partial x}(Au) = 0 \qquad (2)$$

because $\frac{\partial}{\partial t} A \cdot \delta x = u \cdot A - \left[uA + \frac{\partial}{\partial x}(uA)\,\delta x\right]$ should this be on outside

Plus a consequence of Young-Laplace relation

$$p - p_0 = \frac{Y \cdot h}{r_0}\left[1 - \left(\frac{A_0}{A}\right)^{1/2}\right] \qquad (3)$$

h = constant

$A = \pi r^2 \quad A_0 = \pi r_0$

We will now linearise (1), (2), (3) assuming that u, $p-p_0$, $A-A_0$ and their derivatives are small

Neglecting all terms of second order or higher

From (1) $\rho A \frac{\partial u}{\partial t} = -\frac{\partial}{\partial x}\left[(p-p_0)A\right]$

$$= -\frac{\partial}{\partial x}(pA) + \frac{\partial A}{\partial x}p_0 = -A\frac{\partial p}{\partial x} - p\frac{\partial A}{\partial x} + \frac{\partial A}{\partial x}p_0$$

(small, small)

$$= -A\frac{\partial}{\partial x}(p-p_0) - (p-p_0)\frac{\partial A}{\partial x}$$

second order so skip

$$= -A\frac{\partial p}{\partial x} \Rightarrow \rho\frac{\partial u}{\partial t} = -\frac{\partial p}{\partial x} \qquad (1)$$

From (2) $\frac{\partial A}{\partial t} + A_0\frac{\partial u}{\partial x} = 0$ (because $A = A_0 + \frac{\partial A}{\partial x}\delta x$)

11/12/14 ②

From ③ expanding RHS in Taylor series

$$1-\left(\frac{A_0}{A}\right)^{1/2} = 1-\left(\frac{A_0}{A_0}\right)^{1/2} + \frac{1}{2}\frac{A_0^{1/2}}{A_0^{3/2}}(A-A_0)$$

$$\Rightarrow p-p_0 = \frac{Y\cdot h\cdot 1}{2r_0 A_0}(A-A_0)$$

Differentiate ① and ② to get:

$$\rho\frac{\partial^2 u}{\partial t\,\partial x} = -\frac{\partial^2 p}{\partial x^2} \quad ; \quad \frac{\partial^2 A}{\partial t^2} + A_0\frac{\partial^2 u}{\partial x\,\partial t} = 0$$

Eliminating u: $\frac{\partial^2 A}{\partial t^2} = \frac{A_0}{\rho}\frac{\partial^2 p}{\partial x^2}$

From ③ $\frac{\partial^2 p}{\partial t^2} = \frac{Y\cdot h}{2r_0}\frac{1}{A_0}\frac{\partial^2 A}{\partial t^2}$

Eliminating A: $\boxed{\frac{1}{c^2}\frac{\partial^2 p}{\partial t^2} = \frac{\partial^2 p}{\partial x^2}}$ pulse the wave eqn

speed of ~~project~~ propagation $c = \sqrt{\frac{Y\cdot h}{2\rho r_0}}$

The solution $p = f(x-ct) + g(x+ct)$

The same equation for u or A

$c \approx 4.6$ m/sec

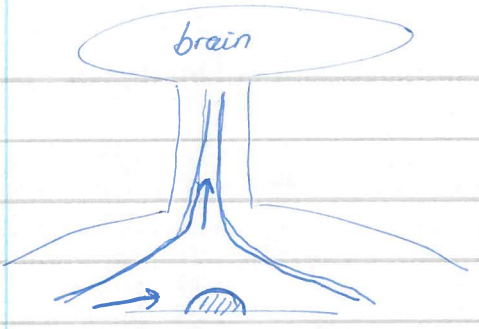
velocity of blood in aorta $\approx$ 24cm/sec

capillaries $\approx$ 25mm/sec

speed of acoustic wave $\approx$ 1000m/sec

Made a mistake $t\cdot h = (p-p_0)r$ ← there should not be a zero here

$$t = Y\left(\frac{r-r_0}{r_0}\right)$$



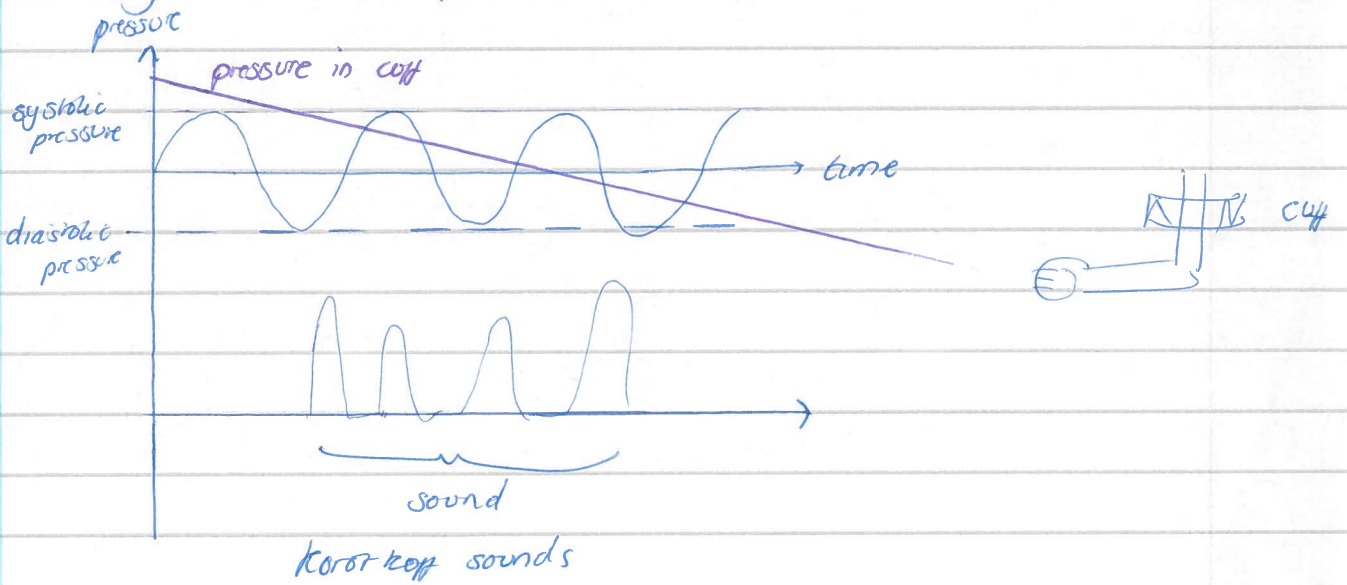
A is smaller

ρ is smaller

less blood for brains

⟹ transient ischemich attack

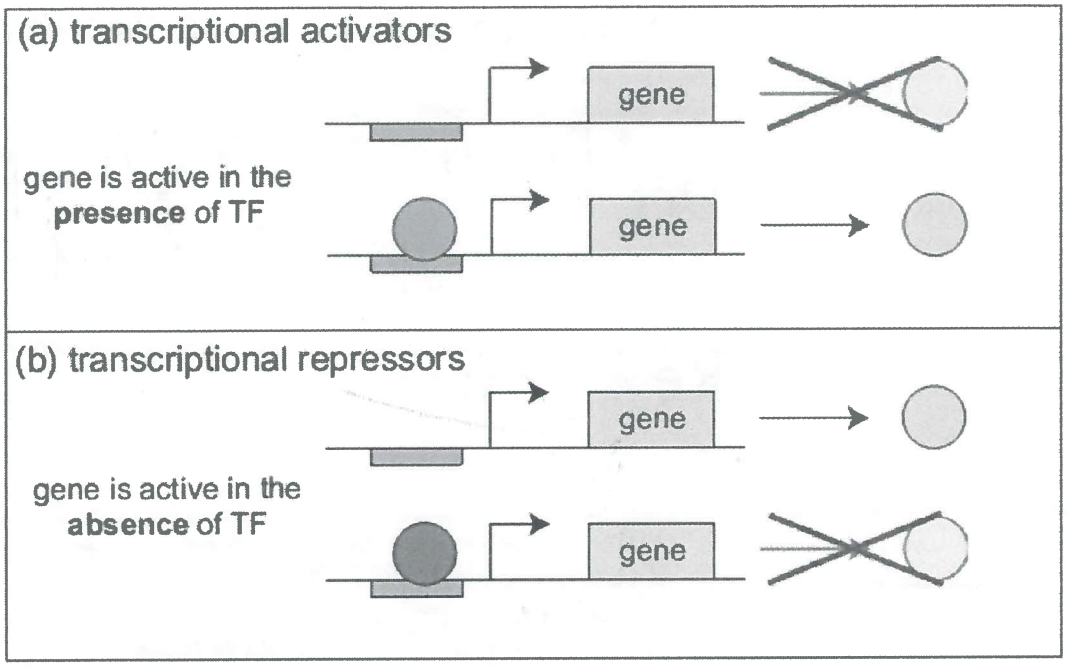
Measuring the blood pressure:



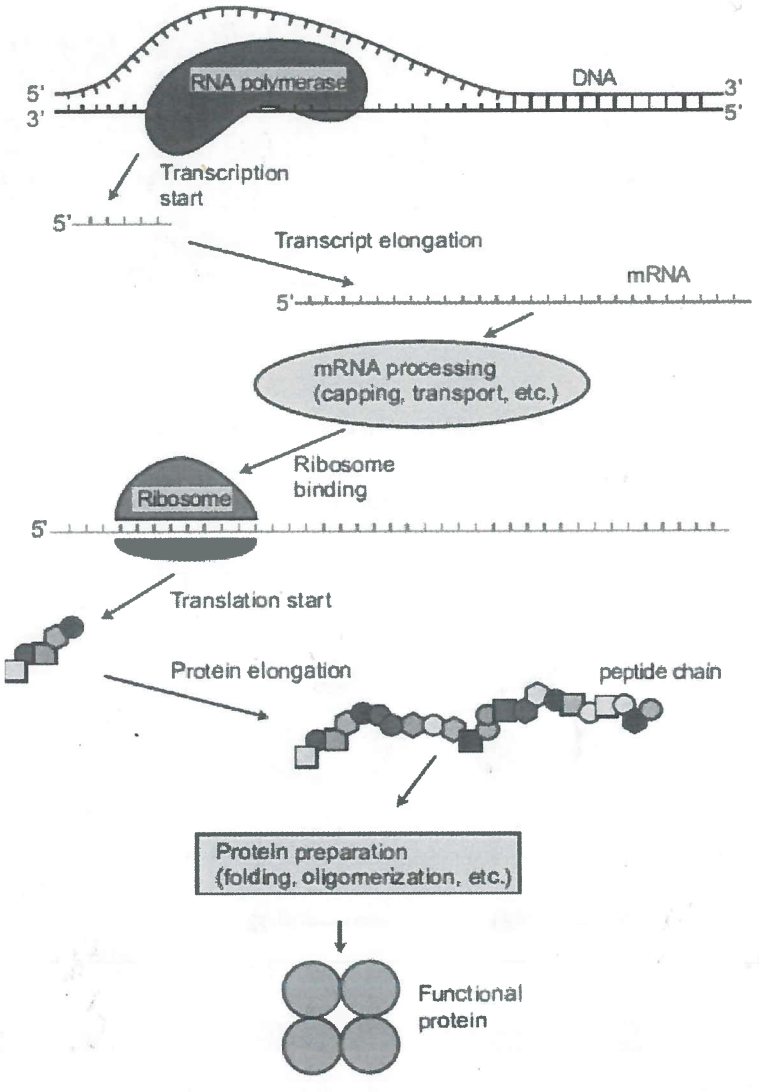
Korotkoff sounds

turbulent flow of blood ⟹ generates acoustic sounds

Transcriptional regulation of gene expression :



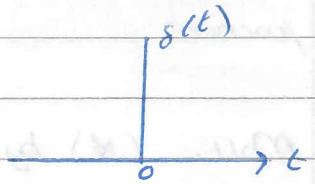
Protein synthesis



20/11/14

Review δ-function (generalized function)

Solve $\dot{x} + x = \delta(t)$ (*)



0 everywhere except 0

integral under curve = 1

generalized function maps whole function to one number

$$\delta(t) = \int_{-\infty}^{\infty} \varphi(t)\,\delta(t)\,dt = \varphi(0)$$

which is why it is called a functional

For $t<0$ $\quad x = c_1 e^{-t}$

$t>0$ $\quad x = c_2 e^{-t}$ } (**)

So we have soln for $t<0$, $t>0$

Need to treat as functionals

The equation includes generalized functions

Let us take $\varphi(t)$, any function, such that

$\varphi(t) \to 0$ if $t \to \pm\infty$

$\varphi(t) f(t) \xrightarrow{t \to \pm\infty} 0$ $\forall$ $f(t)$

Then $\delta : \varphi(t) \longrightarrow \varphi(0)$ as

$$\int_{-\infty}^{\infty} \varphi(t)\,\delta(t) = \varphi(0)$$

$$x : \varphi(t) \longrightarrow \int_{-\infty}^{\infty} \varphi(t)\,x(t)\,dt$$

$$\dot{x} : \varphi(t) \longrightarrow \int_{-\infty}^{+\infty} \varphi(t)\,\dot{x}(t)\,dt$$

$$= -\int_{-\infty}^{\infty} x(t)\,\dot{\varphi}(t)\,dt$$

Will mult. by $\varphi(t)$ & integrate to get generalized functions

Mult. (*) by $\varphi(t)$ and $\int_{-\infty}^{\infty}$ we get

$$-\int_{-\infty}^{+\infty} x(t)\,\dot{\varphi}(t)\,dt + \int_{-\infty}^{+\infty} x(t)\,\varphi(t)\,dt = \varphi(0)$$

Using (**)

$$\int_{-\infty}^{0} c_1 e^{-t}\varphi\,dt - \int_{-\infty}^{0} c_1 e^{-t}\dot{\varphi}\,dt + \int_{0}^{\infty} c_2 e^{-t}\varphi\,dt$$

$$-\int_{0}^{\infty} c_2 e^{-t}\dot{\varphi}\,dt = \varphi(0)$$

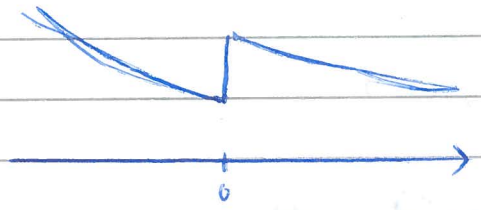
Integrating $\int$ with $\dot{\varphi}(t)$ by parts we get

$-c_1 + c_2 = 1$ $\qquad c_2 = c_1 + 1$ ← do this at home to check.

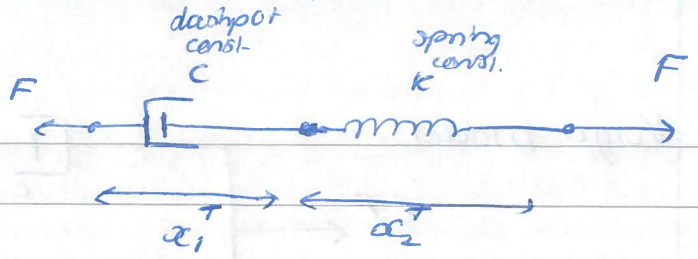
the solution is

$x = c_1 e^{-t} \quad t < 0$

$x = (c_1 + 1)e^{-t} \quad t > 0$



Maxwell model



$x_i^T = x_i^E + x_i \qquad i = 1, 2$

x_i^T — total; x_i^E — eq. length; x_i — deformation

For dashpot $F = c\frac{dx_1}{dt}$

spring $F = k x_2$

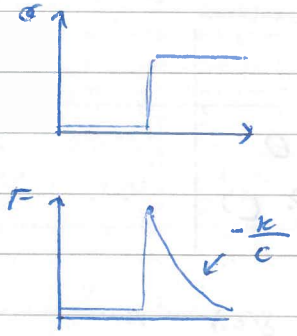
$\dot{x}^T = x_1^T + x_2^T \Rightarrow \frac{dx}{dt} = \frac{dx_1}{dt} + \frac{dx_2}{dt}$

$\frac{dx}{dt} = \frac{F}{c} + \frac{1}{k}\frac{dF}{dt}$ because F the same in 1 and 2

Dashpot can't be compressed immediately - will be compressed until spring returns to eq. point
For spring: force immediately appears & then decays

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

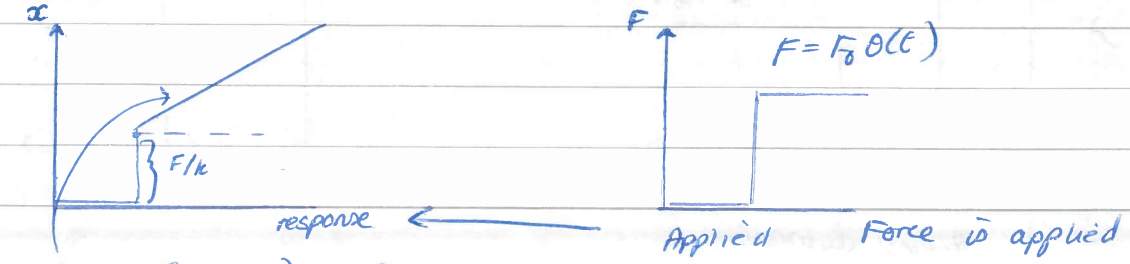
Applied compress system deformation ↓ Response



derivative here = δ function since 0 everywhere apart from 1 point where = ∞

$F = kx_0 \exp\left(-\frac{k}{c}t\right)\cdot\theta(t)$

Heat ~~force~~

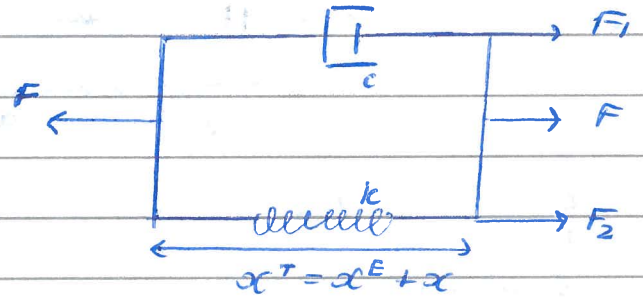


$x(t) = F_0\left(\frac{1}{k} + \frac{t}{c}\right)\theta(t)$

Do not have to memorise these eq's: can get them from solving eq's

$\theta(t)$

Voigt model



Immediately compress - get δ function in dashpot

Force & response just constant

Total force $F = F_1 + F_2$

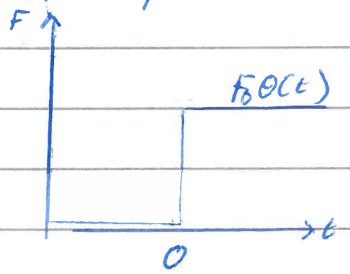
no x_1, just x

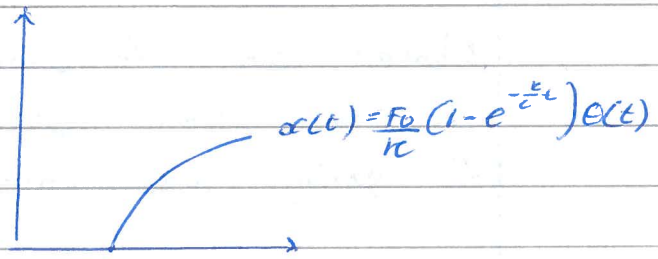
$x_1 = x_2 = x$, $F_1 = c\frac{dx_1}{dt}$, $F_2 = kx$

$$F = c\frac{dx}{dt} + kx$$

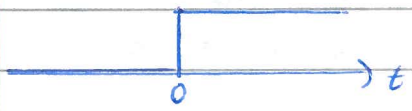
I.C. $x(t=0) = 0$

Applied force



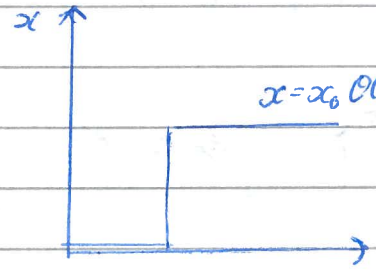


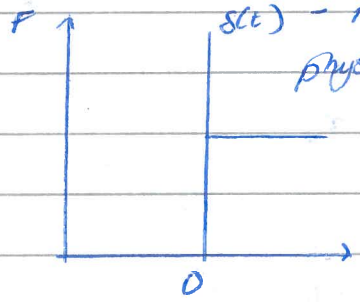
$\theta(t)$ - Heavyside function



$\theta(t) = 0$ $t < 0$

$\theta(t) = 1$ $t \gg 0$



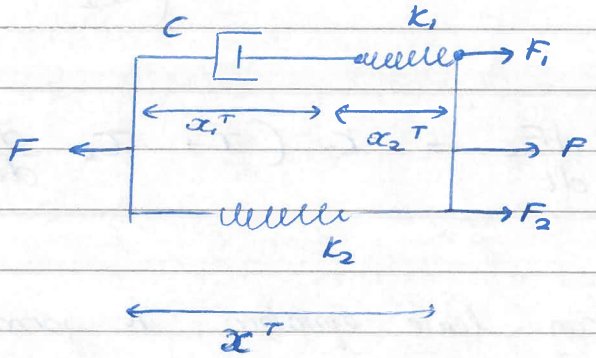


Applied deformation

$F = C x_0 \delta(t) + k x_0 \theta(t)$

Will consider one more model

Kelvin model



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

$F_1 = C\frac{dx_1}{dt} = k_1 x_2$ as in Maxwell model

$F_2 = k_2 x$

$F = F_1 + F_2$ as in Voigt model

hope to avoid non physical behaviors

$\frac{dx_1}{dt} = \frac{F_1}{C}$ $\quad x_2 = \frac{F_1}{k_1} \Rightarrow \frac{dx_2}{dt} = \frac{1}{k_1}\frac{dF_1}{dt}$

$\frac{dx}{dt} = \frac{dx_1}{dt} + \frac{dx_2}{dt} = \frac{F_1}{C} + \frac{1}{k_1}\frac{dF_1}{dt}$ we need F

$F_1 = F - F_2 = F - k_2 x$; $\frac{dF_1}{dt} = \frac{dF}{dt} - k_2\frac{dx}{dt}$

Substituting F_1 and $\frac{dF_1}{dt}$

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

$$F + \frac{C}{k_1}\frac{dF}{dt} = k_2 X + C\left(1 + \frac{k_2}{k_1}\right)\frac{dx}{dt} \quad (1)$$

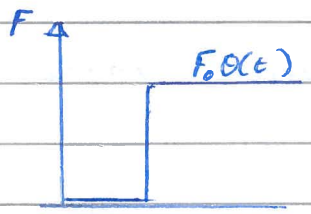
Introducing

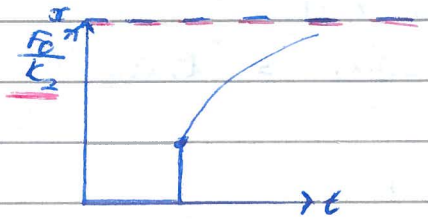
$$\tau_\varepsilon = \frac{c}{k_1} \qquad \tau_\sigma = \frac{c}{k_2}\left(1 + \frac{k_2}{k_1}\right)$$

$$= c\left(\frac{1}{k_2} + \frac{1}{k_1}\right)$$

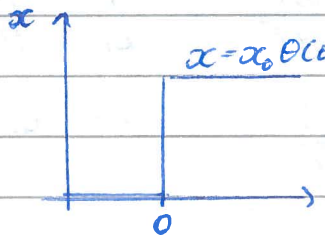
$$\boxed{F + \tau_\varepsilon \frac{dF}{dt} = k_2\left(x + \tau_\sigma \frac{dx}{dt}\right)} \quad \text{Kelvin model}$$

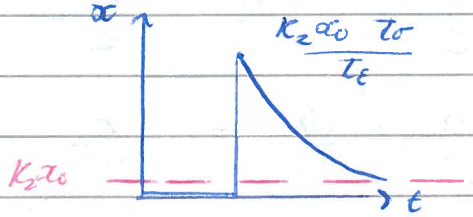
In exam can leave equation in form (1)





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





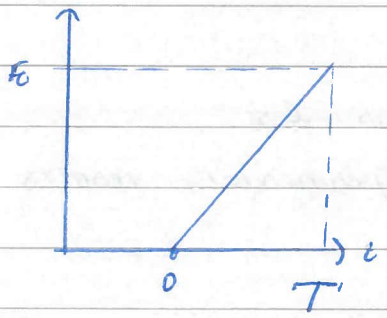
$$F(t) = k_2 x_0\left[1 - \left(1 - \frac{\tau_\sigma}{\tau_\varepsilon}\right)\exp\left(\frac{-t}{\tau_\varepsilon}\right)\right]\Theta(t)$$

Can obtain these expressions easily – will do so in the HW

This model incorporates features of both Maxwell & Voigt models but doesn't have any unrealistic behaviour.

Let us use Kelvin model to describe fast or slow application of the force

Apply



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

changing T, we change the speed of F

$$\frac{dF}{dt} = \frac{F_0}{T} \quad \text{so (Kelvin)} \quad K_2\left(x + \tau_0 \frac{dx}{dt}\right) = F + \tau_\varepsilon \frac{dF}{dt}$$

$$= F_0 \frac{t}{T} + \frac{F_0}{T} \tau_\varepsilon$$

$$\text{or} \quad x + \tau_0 \frac{dx}{dt} = \frac{F_0}{K_2 T} t + \frac{F_0}{K_2} \frac{\tau_\varepsilon}{T}$$

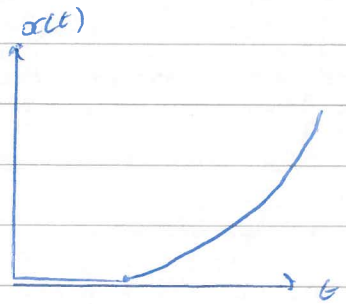
Using: $x + a\frac{dx}{dt} = bt + e$

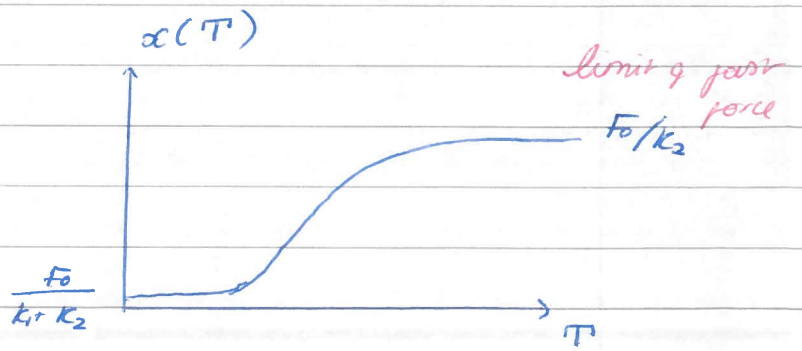
$$\Rightarrow x(t) = bt + (e - ab)\left(1 - \exp\left(-\frac{t}{a}\right)\right)$$

$$\text{So} \quad x(t) = \frac{F_0}{K_2 T} t - \frac{cF_0}{K_2^2 T}\left(1 - \exp\left(\frac{-t}{\tau_0}\right)\right) \qquad 0 < t < T$$

at $t = T$

$$x(T) = \frac{F_0}{K_2} - \frac{cF_0}{K_2^2 T}\left(1 - \exp\left(-\frac{T}{\tau_0}\right)\right)$$



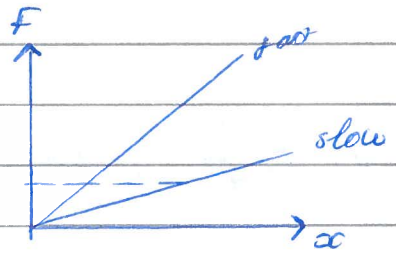


limit of slow force

For fast force $\tau \gg \tau_0$: $x(\tau) \longrightarrow \frac{F_0}{k_2}$

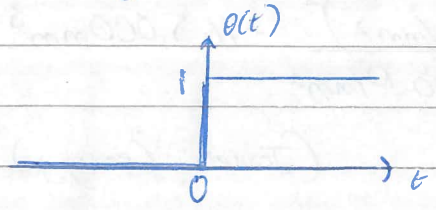
slow $\tau \ll \tau_0$: $x(\tau) \rightarrow \frac{F_0}{k_1 + k_2}$

With faster force deformation is less
This agrees well with experimental results

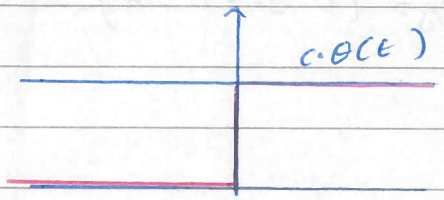


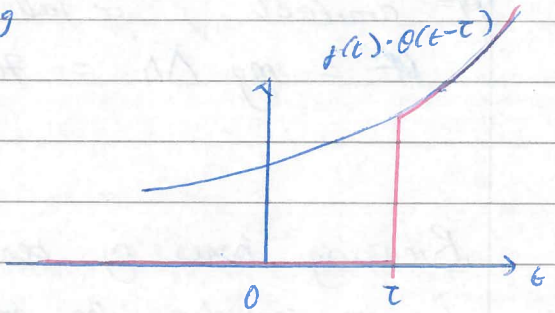
24/11/14

Modelling with $\theta(t)$ - heavy side function

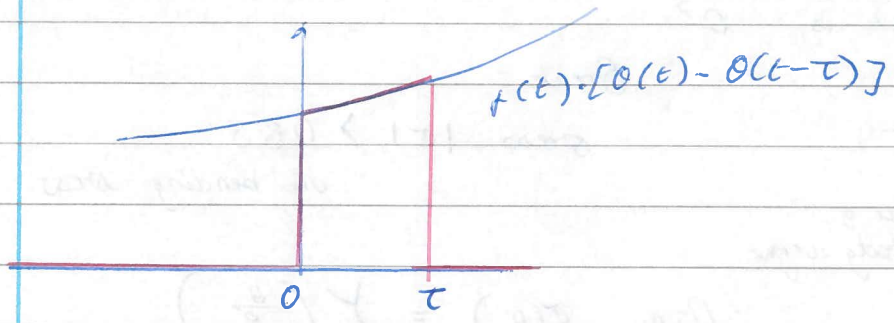


Why is it convenient for modelling





If 'we' use the function



Bone fractures - ~~bones rubber~~

Stiff bones absorb little energy

The femoral bone is about 2/3 as stiff in children as in adults (children fall a lot - but their bones absorb a lot of energy ∴ this is why they don't run as fast?

Energy of fracture

energy UCS = 170 N/mm^2

ultimate compression stress

stress = force / area

UCS is when force = $170\ N/mm^2 \cdot 370\ mm^2$

= 56000 N ~ 6 tons ~ 80 body weights !

Bot energy is needed

$$PE = \frac{UCS}{2Y} \cdot A \cdot L = \frac{(170\ N/mm^2)^2}{2 \cdot 17900\ N/mm^2} \cdot 165000\ mm^3$$

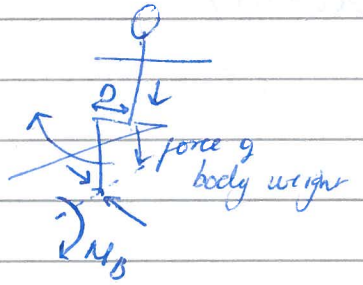
$$= 133\ J \quad \text{(Joules (energy))}$$

PE available if we fall

$$PE = mg\,\Delta h = 70kg \cdot 10\,m/s^2\,(0.5m - 0.1m) = 550\,J$$

Breaking bones by bending

Let us consider the example of one foot fixed at the ankle (e.g. rigid ski boot) while the other is slipping - what is θ?



Break:

stress $|\sigma| > UBS$

ult. bending stress

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

with $y = \frac{d}{2}$ where d - diameter of leg bone

$$\sigma_{max} = \frac{Y \cdot d}{2R} = \frac{Yd}{2} \cdot \frac{1}{R}$$

radius of curvature

$$= \frac{Y \cdot d}{2} \quad \frac{M_B}{YI_n} = \frac{dM_B}{2I_n}$$

fracture: $\frac{dM_B}{2I_n} > UBS \Rightarrow$

$$\frac{d \cdot D\,|W_{body} - W_{leg}|}{2I_n} > UBS$$

area moment of inertia

$$D \gg \frac{2UBS \cdot I_a}{d|W_{body} - W_{leg}|} = \frac{\pi a^4}{2 \cdot 2a} \cdot \frac{UBS}{|W_{body} - W_{leg}|}$$

a - radius of bone

$$= \frac{\pi (1cm)^3}{4} \cdot \frac{2.13 \times 10^2 \, MPa}{|750 - 110| N}$$

(Pascal)

$$\approx 25 cm$$

i.e. if displacement of centre of mass if $\gg$ 25 cm

Have considered
linear compression
compression formalism for bending (i.e. compression & stretching of springs in bones
viscoelasticity (i.e. force applied fast or slow)

CHEMOTAXIS

Bacteria can 'talk' to eachother - by one generating molecules for others & sensing change & gradient

Diffusion the flux J is proportional to the ∇ (gradient) of concentration

In 1D $J = -D\frac{\partial c}{\partial x}$ where $c(x,t)$ - concentration ← diffusion coefficient

Conservation equation

$$\frac{\partial}{\partial t}\int_{x_0}^{x_0+\Delta x} c(x,t)\,dx = J(x_0,t) - J(x_0+\Delta x, t)$$

& using $J = -D\frac{\partial c}{\partial x}$

$\Delta x \to 0$ $\quad \frac{\partial c}{\partial t} = -\frac{\partial J}{\partial x} = D\frac{\partial^2 c}{\partial x^2}$

diffusion equation

because $\left.\frac{\partial J}{\partial x}\right|_{x_0} = \lim_{\Delta x \to 0} \frac{J(x_0+\Delta x, t) - J(x_0,t)}{\Delta x}$

Reaction - diffusion equation

Consider diffusion in 3D

Let S be an arbitrary surface enclosing volume V

Conservation law: change in V = flow across S + material created in V

$$\frac{\partial}{\partial t}\int_V c(\bar{x},t)\,dV = -\int_S \bar{J}\,d\bar{s} + \int_V f(\bar{x}, c, \bar{c}, t)\,dV$$

flux created will depend on conc. inside volume

We have scalars everywhere so integral should be scalar.

Applying the divergence theorem

divergence (not grad since .)

$$\int_V (\nabla \cdot \bar{J})\, dV = \int_S \bar{J} \cdot d\bar{S}$$

$$\int_V \left[\frac{\partial C}{\partial t} + \nabla \cdot \bar{J} - f(C, \bar{x}, t) \right] dV = 0$$

Since V is arbitrary

$$\frac{\partial C}{\partial t} + \nabla \cdot \bar{J} = f$$

or for classical diffusion $\bar{J} = -D \nabla C$

$$\frac{\partial C}{\partial t} = f + \nabla \cdot (D \nabla C)$$

Reaction diffusion equation

reaction | diffusion = change in material in some volume

Example In ecological context, f could represent the birth - death process & C - population density with logistic growth

$$f = r \cdot C \left(1 - \frac{C}{K}\right)$$

reproduction rate | carrying capacity

function grows & then saturates

Then

$$\frac{\partial C}{\partial t} = r \cdot C \left(1 - \frac{C}{K}\right) + D \nabla^2 C$$

Flux - a vector

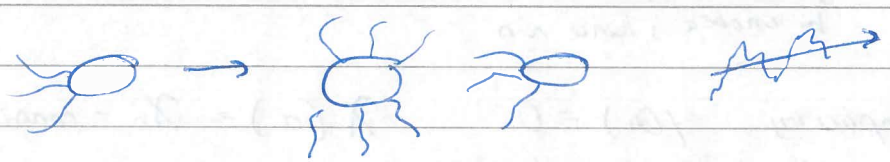
- amount that flows through a unit area per unit time

27/11/14

$\frac{\partial n}{\partial t} = rn\left(1 - \frac{n}{K}\right) + D^* \nabla^2 n$ Fisher Kolmogorov eq^n

Chemotaxis (a kind of taxis) is a phenomenon in which cells, bacteria or other organisms direct their movement according to certain chemicals (pheromones) in the environment

Examples: for bacteria, swimming toward the highest concentration of certain molecules



- movement of leucocytes towards inflammation eg. in healing
- flee from poison
- movment of sperm towards egg

Let us suppose that the presence of a gradient of an attractant $a(\vec{x}, t)$ gives rise to a movement something

Hence the chemotactic flux: $J_{chem} = n \chi(a) \cdot \nabla a$ (χ: function of chem. conc. attractant)

Using general conservation eq^n $\frac{\partial n}{\partial t} + \nabla \cdot \vec{J} = f(n)$

$J = J_{chem} + J_{diff}$ $J_{diff} = -D \nabla n$ $J_{chem} = n \chi(a) \nabla a$

So $\frac{\partial n}{\partial t} = f(n) - \nabla n \chi(a) \nabla a + \nabla D \nabla n$

a basic reaction chemotaxis diffusion

If classical diffusion then $D\nabla\nabla n = D\Delta n$

Since $a(x,t)$ is a chemical it will also diffuse

$$\frac{\partial a}{\partial t} = \underbrace{g(a,n)}_{\text{source term}} + \underbrace{\nabla D_a \nabla a}_{\text{diffusion of } a}$$

Normally $D_a \gg D$

Example Keller & Segel model for slime mould

$g(a,n) = h \cdot n \xleftarrow{\text{const.}} - \xrightarrow{} k a$ — decay of attractant

production of a by amoeba, hence $\sim n$

for simplicity $f(n) = 0$ $\chi(a) = \chi_0$ - const.

i.e. amoeba production rate is negligible

Then in 1D

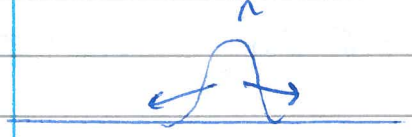
KS model

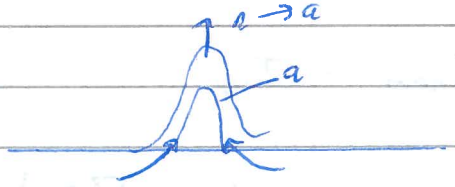
$$\begin{cases} \frac{\partial n}{\partial t} = D\frac{\partial^2 n}{\partial x^2} - \chi_0 \frac{\partial}{\partial x}\left(n \frac{\partial a}{\partial x}\right) \\ \frac{\partial a}{\partial t} = hn - ka + D_a \frac{\partial^2 a}{\partial x^2} \end{cases}$$

n - amoeba conc. e.g. bacterial population

a - chem. a. conc. e.g. food it consumes

Key idea: diffusion is a stabilizing force, whereas chemotaxis can destabilise





any small fluctuation in time can grow to give a large peak

Model (experiment of Budrene & Berg, 1991)

The bacteria diffuse, more chemotactically, proliferate & die

Chemoattractant diffuses, is produced & consumed by bacteria

The stimulant (food) diffuses & is consumed by bacteria

Rate of change of cell density, n	=	diffusion n	+	chemotaxis of n to c

$$\pm \quad \text{proliferation or death of } n$$

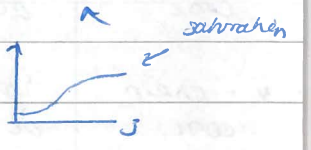
Rate of change conc of chemoattr, c	=	diffusion c	+	production of c by n	−	uptake of c by n

Rate of stimulant concentration s	=	diffusion of s	−	uptake of s by n

$$\frac{\partial n}{\partial t} = \underbrace{D_n \Delta n}_{\text{diffusion}} - \nabla\left[\frac{K_1 n}{(K_2 + c)^2} \nabla c\right] + K_3 n\left(\frac{K_4 s^2}{K_5 + s^2} - n\right)$$

(Woodward) chemotaxis

Won't be expected to remember this



$$\frac{\partial c}{\partial t} = \underbrace{D_c \Delta c}_{\substack{\text{diffusion} \\ \text{for chemoattr.} \\ \text{conc.}}} + K_6 \frac{s\, n^2}{K_6 + n^2} - K_7 n c$$

$$\frac{\partial s}{\partial t} = D_s \nabla^2 s - K_8 n \frac{s^2}{K_9 + s^2}$$

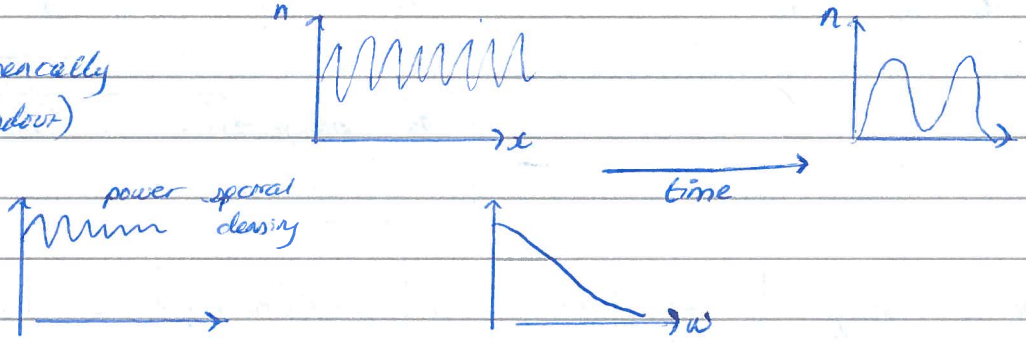
where K_i – constant

In liquid medium, eliminate cell growth / ~~decay~~ death because of poor pattern formation
Also skip chem degradation & consumption of stimulant

Then $\frac{\partial n}{\partial t} = D_n \Delta n - \nabla\left[\frac{k_m}{(k_2+c)^2} \nabla c\right]$

$$\frac{\partial c}{\partial t} = D_c \Delta c + k_5 s \frac{n^2}{k_6 + n^2}$$

Numerically (Chardour)



Bacterial pattern formation (analytical treatment)
Consider 1D
Assume zero flux boundary conditions & uniform distribution of stimulant $\Delta s = 0$
If we non dimensionalise the equations

diffusion coeff. / coeff. per chemotaxis

u - bact. conc. $\quad \frac{\partial u}{\partial t} = d \frac{\partial^2 u}{\partial x^2} - \alpha \frac{\partial}{\partial x}\left[\frac{u}{(1+v)^2} \frac{\partial v}{\partial x}\right]$

v - chem conc. $\quad \frac{\partial v}{\partial t} = \frac{\partial^2 v}{\partial x^2} + \frac{u^2}{\mu + u^2}$ $\quad d, \alpha, \mu$ = const.

The normal $u \neq 0$ spatially independent solution with
$u(x,0) = 1 \quad v(x,0) = 0$ is
$u(x,t) = 1 \quad v(x,t) = \frac{1}{\mu+1} t$

We look for the solution in the form

$$u(x,t) = 1 + \varepsilon \sum_{k=1}^{\infty} f_k(t)\, e^{ikx}$$

$$v(x,t) = \frac{t}{\mu+1} + \varepsilon \sum_{k=1}^{\infty} g_k(t)\, e^{ikx}$$

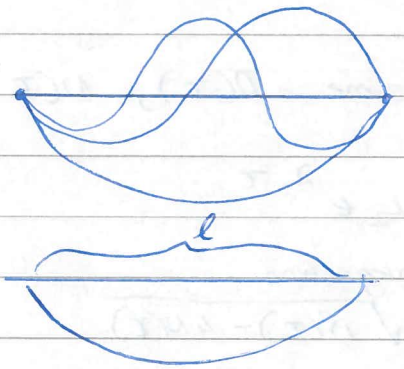
k - wave number $\quad k = \frac{m\pi}{\ell}$ where ℓ - system size

ε - small parameter $\quad 0 < \varepsilon << 1$

$$kx = \frac{2\pi x}{T_{\text{period}}} = \frac{2\pi x m}{2\ell} = \frac{\pi m x}{\ell} = \omega x$$

spatial frequency

$k, m = 1, 2, \ldots$



$m, k = 1 \quad \frac{T}{2} = \ell \quad T = 2\ell$

Substituting solutions in the system of equations & linearizing them w.r.t. ε, then for each k

$$\frac{dF(t)}{d\tau} = -dk^2 F(t) + \alpha(\mu+1)^2 \frac{k^2}{\tau^2} G(t)$$

$$\frac{dG(\tau)}{d\tau} = -k^2 G(\tau) + \frac{2a}{(\mu+1)^2} F(\tau)$$

where $\quad \tau = \mu + 1 + t \qquad F(\tau) = f_k(t)$

$$G(\tau) = g_k(t)$$

Not explained in detail since it is HW.

We solve first equation to find $G(\tau)$, then diff. & find $\frac{dG(\tau)}{d\tau}$ & sub in second eq^n:

$$\frac{d^2F}{d\tau^2} + \underbrace{\left[k^2(d+1) + \frac{2}{\tau}\right]}_{D(\tau)}\frac{dF}{d\tau} + \underbrace{k^2\left(dk^2 + \frac{2d}{\tau} - \frac{2\times\mu}{\tau^2}\right)}_{N(\tau)}F = 0$$

$$\frac{d^2F}{d\tau} + D(\tau)\frac{dF}{d\tau} + N(\tau)F = 0$$

Note $D(\tau)$ is always >0, $N(\tau)$ can be <0, $=0$, >0
for large τ $N(\tau) > 0$

For some small interval of τ, assume $D(\tau)$, $N(\tau) \approx$ const.

Solving: $\tilde{F}(\tau) = L_1 e^{\lambda_+ \tau} + L_2 e^{\lambda_- \tau}$

const. of integration

$$\lambda_\pm = \frac{1}{2}\left[-D(\tau) \pm \sqrt{D^2(\tau) - 4N(\tau)}\right]$$

$D(\tau) > 0 \rightarrow Re(\lambda_-) < 0$ - decay, sign of $Re(\lambda_+)$
depends on $N(\tau)$

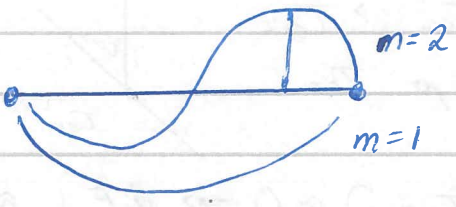
Recalculate everything we have done for exam!
Exam based mostly on derivations

01/12/14

$$\frac{\partial^2 F}{\partial \tau^2} + \underbrace{\left[k^2(d+1) + \frac{2}{\tau} \right]}_{D(\tau)} \frac{dF}{d\tau} + \underbrace{k^2\left(dk^2 + \frac{2d}{\tau} - \frac{2\alpha\mu}{\tau^2} \right)}_{N(\tau)} F = 0$$

$$\tilde{F}(\tau) = A_1 e^{\lambda_+ \tau} + A_2 e^{\lambda_- \tau}$$

$$\lambda_\pm = \frac{1}{2}\left[-D(\tau) \pm \sqrt{D(\tau)^2 - 4N(\tau)} \right]$$



λ_- always -ve
λ_+ can be +ve
in which case have exponential growth

D coeff of diffusion
α strength of chemotactic flux
N depends on α

this should be τ small - not -ve

If a is sufficiently large, then $N(\tau) < 0$ for $\tau < 0$
As τ increases $N(\tau)$ will increase through zero & become positive > 0

So there is τ_{crit}: $\tau < \tau_{crit}$ one component of $\tilde{F}(\tau)$ will grow, $\tau > \tau_{crit}$ all components of $\tilde{F}(\tau)$ will decay

Indeed α (chemotaxis) plays destabilising role
At $\tau \approx \tau_{crit}$ $F(\tau)$ should have maximum

The location $\tau_{crit} \approx \tilde{\tau}_{crit}$ can be obtained from $N(\tilde{\tau}_{crit}) = 0$ (approximation of τ_{crit})

$$\tilde{\tau}_{crit} = \frac{1}{k^2}\left[-1 + \sqrt{1 + \frac{2a_{ij}k^2}{0}}\right]$$

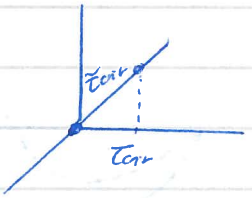
at τ_{crit}

$\left.\frac{dF}{d\tau}\right|_{\tau=\tau_{crit}} = 0$ (because maximum) so skip it from equation per $F(\tau)$

$\left.\frac{\partial^2 F}{\partial \tau^2}\right|_{\tau=\tau_{crit}} = -N(\tau_{crit})F < 0$ because max

So $N(\tau_{crit}) > 0 \Rightarrow \tau_{crit} > \tilde{\tau}_{crit}$

and $\tilde{\tau}_{crit}$ gives minimum estimate for τ_{crit}



But $\tilde{\tau}_{crit} \approx \tau_{crit}$ hence $N(\tau_{crit}) \approx 0 \Rightarrow \left.\frac{d^2F}{d\tau^2}\right|_{\tau_{crit}} \approx 0$

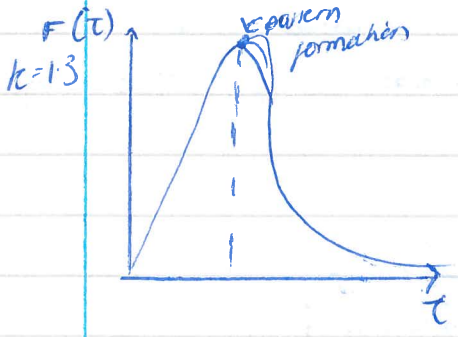
We can skip $\frac{d^2F}{d\tau^2}$ from equation per $F(\tau)$

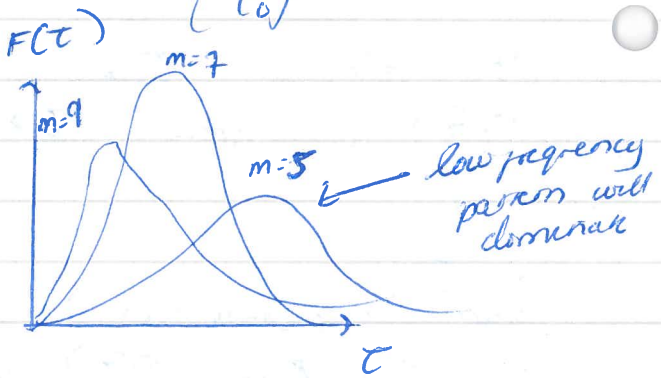
$$D(\tau)\frac{dF}{d\tau} + N(\tau)F = 0$$

$\tau = \mu_1 t + \epsilon$

$\tau_0 = \mu_1 \quad (t=0)$

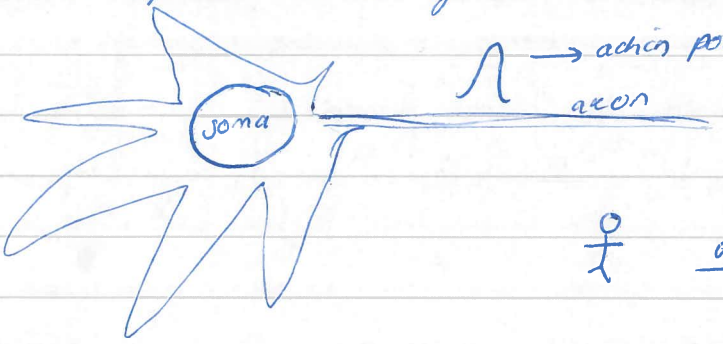
$$F(\tau) = \left[\frac{(d+1)k^2\tau_0 + 2}{(d+1)k^2\tau + 2}\right]^{\alpha_{ij}\mu_i k^2 - \frac{2d(d-1)}{(d+1)^2}} \left[\frac{\tau}{\tau_0}\right]^{\alpha_{ij}\mu_i k^2} e^{\left[\frac{d}{d+1}\right]k^2(\tau_0 - \tau)}$$

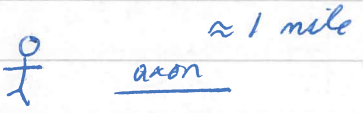




Neurons

The human brain contains 100 000 000 000 neurons, each linked with up to 10,000 synaptic connections
Consumes up to 20% of all our calories





dendrites

We don't yet understand how the system of neurons work - to find out more Q google Theory of Integrated Information

Some neurons emit action potential constantly ∿∿∿ (regularly or irregularly) whereas other neurons are in excitable regime

Hodgkin & Huxley (1952) 04/12/14

Model of neuron firing (Nobel Prize 1963)

The electric pulse arises because the axon membrane is preferentially permeable to various chemical ions

potassium (K^+), sodium (Na^+)

The current $I(t)$ — current of individual ions
- I_{Na}
- I_K
- I_L - leakage - all other ions particles

the contribution from the time variation in the transmembrane potential

$C\frac{dV}{dt}$ — voltage

capacity

So $I(t) = C\frac{dV}{dt} + \sum_i I_i$

I_a

From observations

$\sum I_i = g_{Na} n_1^3 n_3 (V - V_m) + g_K n_1^4 (V - V_K) + g_L (V - V_L)$

$I_{Na} + I_K + I_L$

equilibrium potential; conductance

contribution because of Na

should be n_2?

K

L

where $n_i(t)$ & $i = 1, 2, 3$

HH model

$$\frac{dn_i}{dt} = \alpha_i(V)(1 - n_i) - \beta_m(V) n_i$$

If external current is applied I_a

$$C\frac{dV}{dt} = -g_{Na} n_1^3 n_3 (V - V_m) - g_K n_2^4 (V - V_K) - g_L (V - V_L) + I_a$$

external current applied additionally

If $I_a = 0$ - excitable region — small perturbation, nothing happens

large perturbation → large excursion

This is not included in the exam.

1

If $I_a > 0$ – periodic behaviour

Here v is like membrane potential V

The Fitz Hugh – Nagumo Model

The system can be approximated by V ($\Leftarrow v$) and W ($\Leftarrow n_i$) — voltage

$$\begin{cases} \frac{dv}{dt} = f(v) - w + I_a \\ \frac{dw}{dt} = bv - \gamma w \end{cases}$$

– responsible for voltage, sum of currents & external current

where $f(v) = v(a-v)(v-1)$

a – const. $\quad 0 < a < 1$

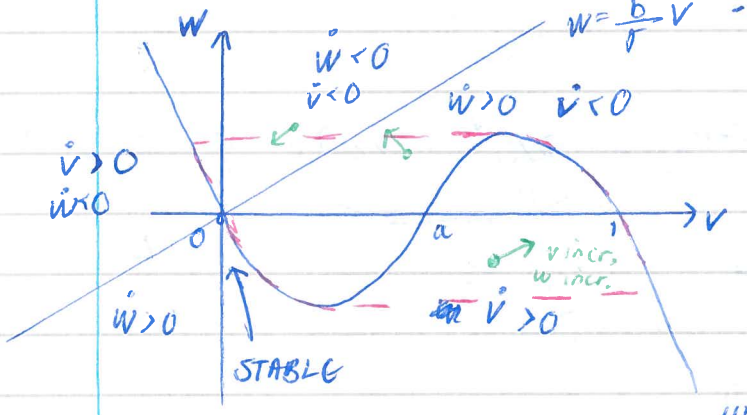
$b, \gamma > 0$ constants

β opening channel

γ closing channel

that depends on b, γ.

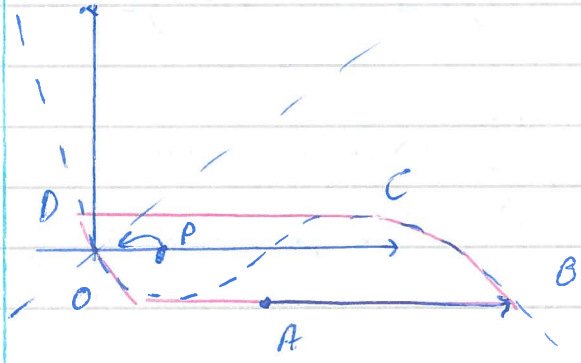
Analysis: Phase plane for $I_a = 0$

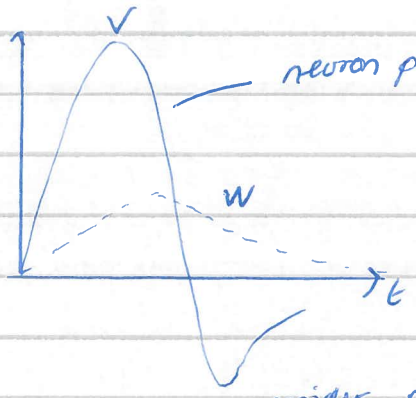


$w = \frac{b}{\gamma} v$ – nullclines $\left(\frac{dw}{dt} = 0\right)$

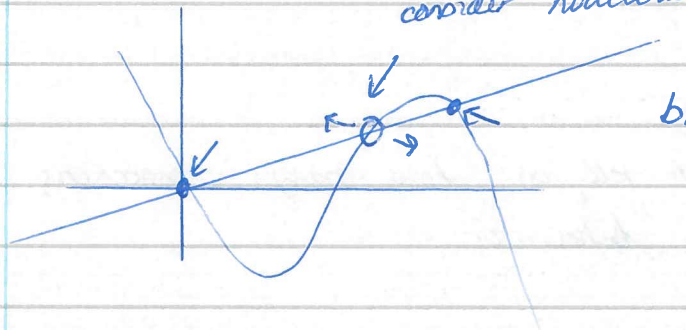
$w = f(v) = v(a-v)(v-1) \left(\frac{dv}{dt} = 0\right)$

In excitable region





consider nullclines - see this is unstable point



So for $I_a = 0$ we observe either excitable or bistable regime

form of the excursion does not depend on perturbation

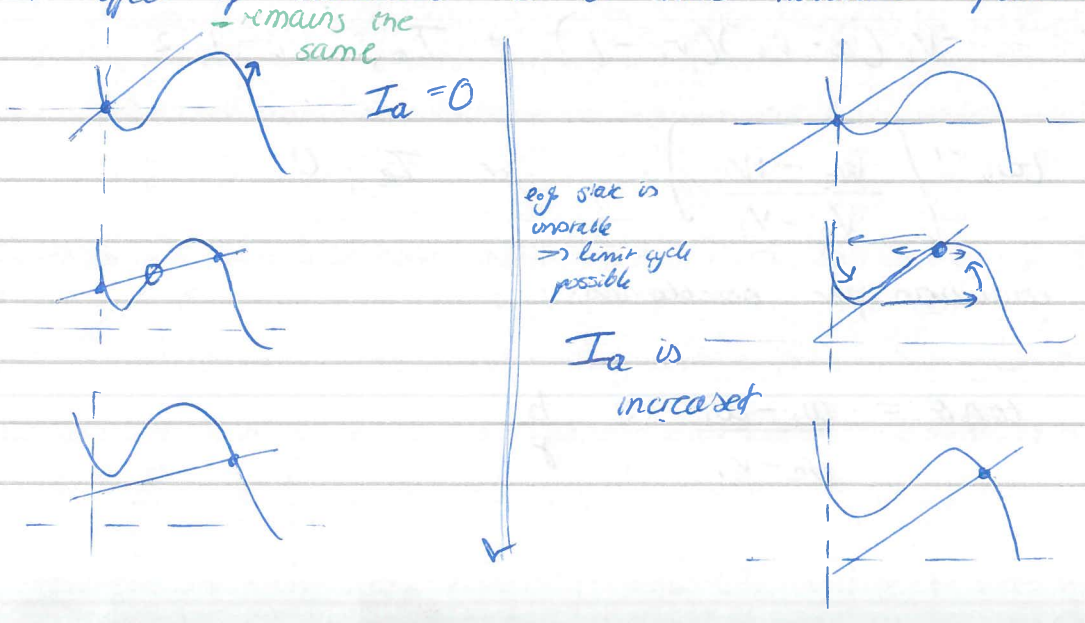
We have seen:

No current - model can demonstrate ~~simple~~ excitable region

Case $I_a > 0$

Because $\frac{dV}{dt} = f(v) - w + I_a \Rightarrow w = f(v) + I_a$

the effect of nullcline is to move nullcline upwards



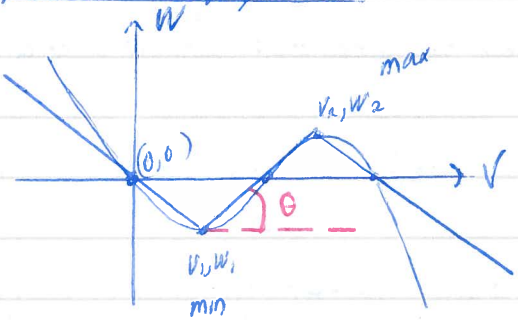
So for some $I_1 < I_a < I_2$

$\Rightarrow$ periodic behaviour

What is the condition for it?

Gradient of nullclines will tell us how many intersections & whether we observe periodic behaviour

Further simplification



We approximate V null cline by piecewise linear function

The positions of min & max can be obtained

$$(V(a-v)(v-1)) = 0$$

$$V_2, V_1 = \frac{1}{3}\left[a+1 \pm \sqrt{(a+1)^2 - 3a} \right]$$

$$W_i = -V_i(a-v_i)(v_i-1) + I_a, \quad i = 1, 2$$

$$\theta = \tan^{-1}\left[\frac{W_2 - W_1}{V_2 - V_1} \right] \quad \text{for } I_a = 0$$

The condition for osallations:

and $\tan\theta = \frac{w_2 - w_1}{v_2 - v_1} < \frac{b}{\gamma}$

and $I_1 < I_a < I_2$

FHN model:

$I_a = 0 \Rightarrow$ excitability

$I_a > 0 \Rightarrow$ neuron pulses (periodicity)

vessels twice round world

Blood dynamics

Macroscopic: any small volume V contains a very large number of molecules

Continuous medium

At any point (x,y,z): pressure $p(x,y,z,t)$
density $\rho(-,"-)$
velocity $v(-"-)$

ρ = const $\Rightarrow$ incompressible fluid, otherwise compressible

Fluids are sticky $\Rightarrow$ viscosity

Newtonian fluids: stress ~ strain (Hooke's law)

Basic equations

1) The equation of motion (Navier Stokes equation)

velocity $\underline{v}(u,v,w)$ only $u \neq 0$

$$\rho\left[\frac{\partial u}{\partial t} + u\frac{\partial u}{\partial x}\right] = -\frac{\partial p}{\partial x} + \mu\left(\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2} + \frac{\partial^2 u}{\partial z^2}\right) + f$$

ρ: density

$\frac{du}{dt} = \frac{\partial u}{\partial t} + \frac{\partial u}{\partial x}\frac{dx}{dt}$, u"

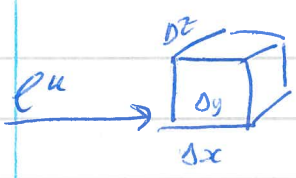
$-\frac{\partial p}{\partial x}$: gradient of pressure

$\mu\left(\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2} + \frac{\partial^2 u}{\partial z^2}\right) = \mu \Delta u$ because of viscosity

f: external force eg. gravity

2) Continuity equation

Consider the mass flux in & out of some volume



per unit time

The total change of mass

$$\frac{\partial \rho}{\partial t}\Delta x \Delta y \Delta z = \rho u \Delta y \Delta z - \left[\rho u + \frac{\partial}{\partial x}(\rho u)\Delta x\right]\Delta y \Delta z$$

(in) (out)

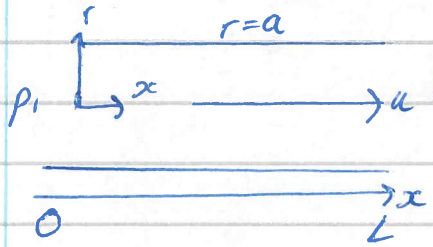
$$\frac{\partial \rho}{\partial t} + \frac{\partial}{\partial x}(\rho u) = 0$$

equation of continuity

BC $v_n = 0$ on solid bdy

if viscous $v_t = 0$ on solid bdy

The Poiseuille's flow



Consider the motion of a fluid through a long cylindrical tube of length L, radius a & two pressures $p_1 > p_2$

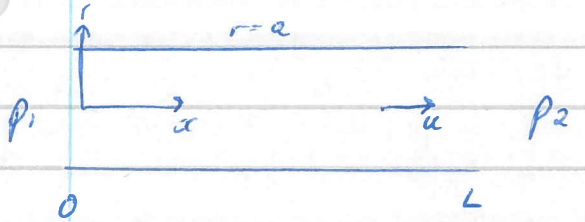
Assume steady flow $\partial/\partial t = 0$

ρ = const.

$\Rightarrow$ from continuity equation $\frac{\partial \rho}{\partial t} + \frac{\partial}{\partial x}(\rho u) = 0$

$$\Rightarrow \frac{\partial}{\partial x} u = 0$$

Poiseuille's Law 8/12/14



cylindrical coords, steady flow

$$0 = -\frac{\partial p}{\partial x} + \mu \Delta u$$

symmetrical in θ

In cylindrical coordinates

$$\mu \frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial u}{\partial r}\right) = \frac{\partial p}{\partial x}$$

because of the mass conservation $u = u(r)$ give $\frac{\partial}{\partial x}$

$$\frac{d^2 p}{dx^2} = 0 \Longrightarrow \frac{dp}{dx} = \text{const}$$

$$p = k \cdot x + k'$$

(const.)

Using boundary conditions p_1 at $x = 0$

p_2 at $x = L$

$$p = p_1 + \frac{(p_2 - p_1)}{L}x \Longrightarrow \frac{dp}{dx} = -\frac{(p_1 - p_2)}{L}$$

(const)

$$\frac{d}{dr}\left(r\frac{\partial u}{\partial r}\right) = \frac{r}{\mu}\frac{dp}{dx} \qquad r\frac{\partial u}{\partial r} = \frac{r^2}{2\mu}\frac{dp}{dx} + A$$

(const)

$$u = \frac{r^2}{4\mu}\frac{dp}{dx} + A\log r + B \qquad u = u(r)$$

(B: const)

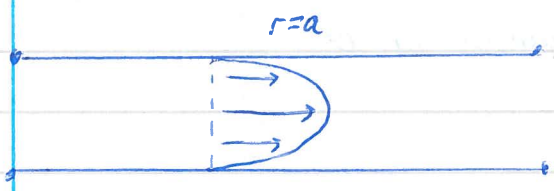
$A = 0$ o/w $u \to \infty$ as $r \to 0$

$u(a) = 0$ because of viscosity

$r = a$

$$\beta = -\frac{a^2}{4\mu}\frac{dp}{dx}$$

$$u = +\frac{1}{4\mu}\frac{p_1 - p_2}{L}(a^2 - r^2)$$

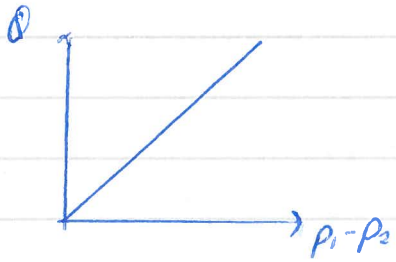


Volume flux Q (in unit time)

$$Q = \int_0^a u \cdot 2\pi r\, dr = \int_0^a \frac{1}{4\mu}\frac{(p_1 - p_2)}{L}(a^2 - r^2)\, 2\pi r\, dr$$

recall $(\pi(r+dr)^2 - \pi r^2)$

$$= \frac{\pi}{8}\frac{(p_1 - p_2)}{\mu L} a^4$$



Properties of blood Poiseuille's law is well established experimentally β used to measure viscosity of blood

$\mu_{blood} \sim 5\mu_{water}$ at 37°C

but in capillaries $\mu_{blood} \sim 1.5\mu_{water}$

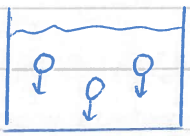
Blood is not Newtonian fluid (has complicated structure)

Blood < plasma / blood cells (red & white) - a suspension with plasma being a suspending medium

$N_{red} \approx 600 N_{white}$

The density of red cells (erythrocytes)

$\rho_c = 1.06$ & of plasma $\rho_p = 1.03$



← rate = the erythrocyte sedimentation rate

ESR

red cells sink

- can measure diff. in density & estimate how many red cells there are & velocity they travelled

Mathematics (Stokes law 1851) for slow motion

Reynolds number $R = \frac{\rho v a}{\mu}$ — density / velocity/speed — radius or some size — viscosity

This is dimensionless

For $R >> 1$ turbulent fast motion

$R << 1$ slow motion, laminar flow

For $R << 1$, a drag force F_D for slowly moving sphere

$F_D = 6\pi\mu a v$ - Stoke's law

$$\underbrace{v \cdot \rho_e \cdot \frac{dv}{dt}}_{\text{mass of one cell}} = \underbrace{V\rho_e \cdot g}_{\text{gravity}} - \underbrace{V\rho_p \cdot g}_{\text{the buoyant force}} - 6\pi\mu a v$$

volume of sphere ← $V = \frac{4}{3}\pi a^3$

For a steady rate of fall

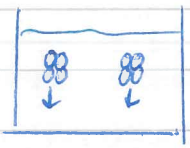
Have put LHS = 0 since steady

$$ESR = v\Big|_{\text{steady motion}} = \frac{4}{3}\pi a^3 \cdot \frac{1}{6\pi\mu a}(\rho_e - \rho_p)g$$

$$= \frac{2}{9\mu} a^2 (\rho_e - \rho_p) g$$

ESR can be measured. In illness, ESR increases dramatically. Why?

a is increased, drag force increased

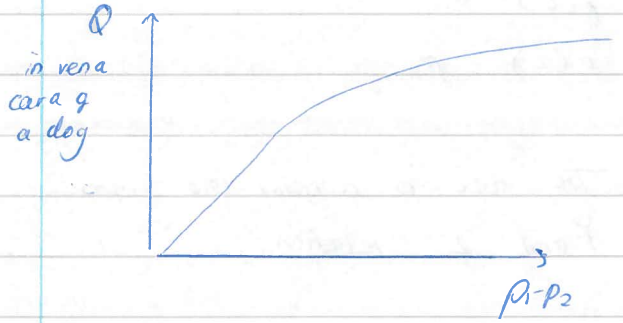


↑ cells bound together

i.e. red cells form aggregates

11/12/14 ①

The steady flow g blood through a vessel

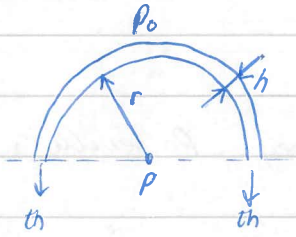


p_1 was const.
p_2 was varied

Why?

Because a vein is not a rigid tube but elastic

Consider cross section



p - the interior fluid pressure

p_0 - the exterior pressure

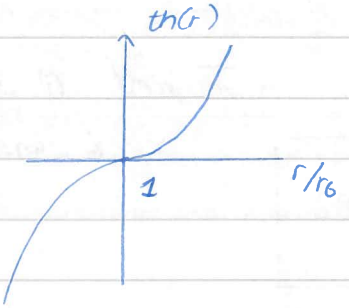
The downward force per unit length is $2th$

t - tension per unit length per unit thickness

The upward force is $(p-p_0)\cdot 2r$ per unit length

So $th = (p-p_0)r$ Young & Laplace relation

In experiment the tension - radius curve



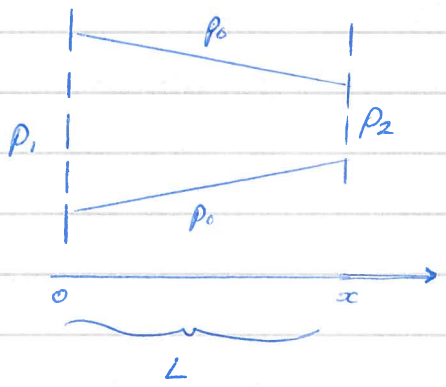
determining experimentally Δp needed to change r_0 to r

Using Hooke's law for elastic regions

$$t = Y\left(\frac{r-r_0}{r_0}\right)$$

Y: Young's modulus

Now consider long tube, & the pressure is a function of x alone, $p(x)$



$p(0) = p_1$

$p(L) = p_2$

The tube is circular so from Y and L relation

$$p(x) - p_0 = \frac{t \cdot h}{r} \quad \text{or} \quad p - p_0 = Y\left(\frac{r - r_0}{r_0}\right)\frac{h}{r} = \frac{Yh}{r_0}\left(1 - \frac{r_0}{r}\right) \qquad (**)$$

r_0 - equilibrium radius for which $t = 0$

The flow through the tube is assumed to obey Poiseuille's law locally i.e.

$$Q = \frac{-\pi}{8\mu}\frac{dp}{dx} r^4 ; \text{ integrating}$$

$$Qx = \frac{\pi}{8\mu}\int_{p}^{p_1} r^4 (p - p_0)\, dp$$

↑ - comes in here

r is a function of $(p - p_0)$ as in $(**)$

Changing variable $p' = p - p_0$

$$Qx = \frac{\pi}{8\mu}\int_{p-p_0}^{p_1 - p_0} r^4(p')\, dp'\, dp'$$

To find Q set $x = L$ and $p = p_2$

So
$$\boxed{Q = \frac{\pi}{8\mu L}\int_{p_2 - p_0}^{p_1 - p_0} r^4(p')\, dp'}$$

When $p_1 - p_2$ is small, and $r^4(p_1 - p_0)$ is not too rapidly varying

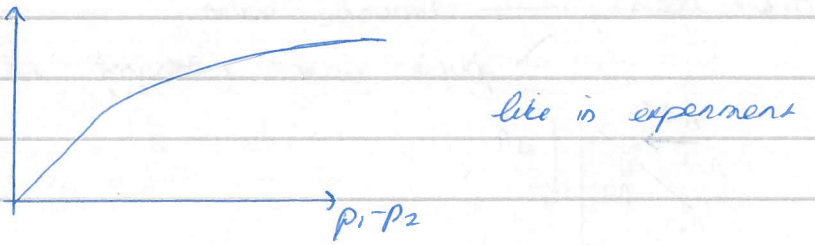
$$Q \sim \frac{\pi}{8\mu L} r^4(p_1 - p_0)(p_1 - p_2)$$

So if $(p_1 - p_0)$ remains fixed and $p_2 - p_0 \to -\infty$
Q attains a constant value

$$Q \sim \frac{\pi}{8\eta L} \int_{-\infty}^{p_1 - p_0} r^4(p')\, dp' \qquad \text{doesn't depend on } p_2$$

Or if $p_2 \to 0$ then $p_2 - p_0 \to -p_0$, again Q indep. of p_2
In physiology called 'vascular waterfall'

Using $\eta(r)$ diagrams & $p - p_0 = \frac{t \cdot h}{r}$ relation we get

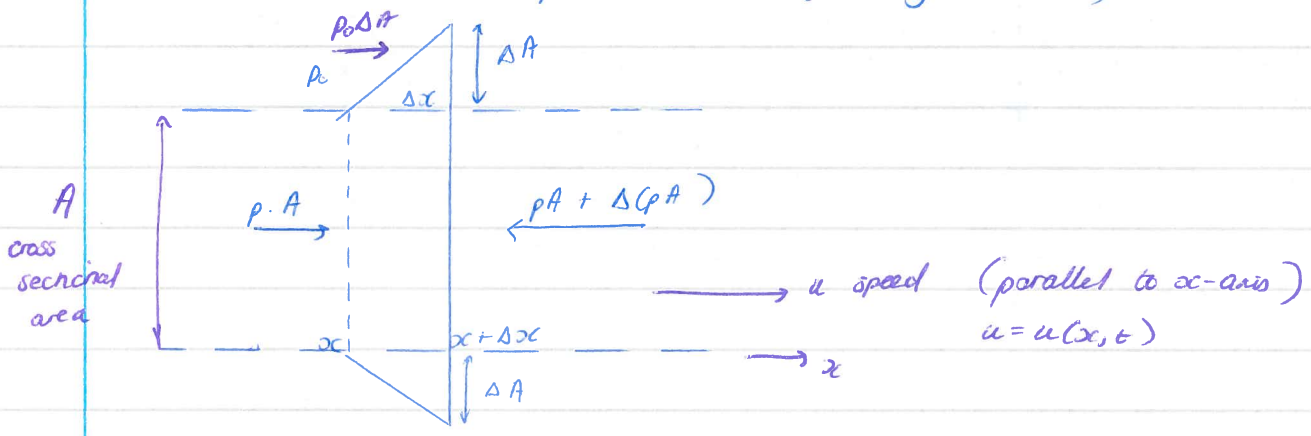


The pulse wave

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. It is not the same as the acoustic wave

Such acoustic waves are from compressibility whereas the pulse wave exists even for incompressible fluid due to elasticity of vessels

Heart beating → blood flow
Heart beating → acoustic wave
Heart beating → pulse wave (Young 1808)



ρ = constant, p_0 - exterior pressure, $p(x,t)$ - interior pressure
$u(x,t)$ parallel to x axis

The force in the positive x-axis direction on the volume element is

$$pA + p_0 \Delta A - [pA + \Delta(pA)] = pA + p_0 \frac{\partial A}{\partial x} \Delta x - \left[pA + \frac{\partial}{\partial x}(pA) \Delta x\right]$$

$$= -\frac{\partial}{\partial x}\left[(p - p_0)A\right] \Delta x$$

From Navier Stokes equation the mass $\rho A \Delta x$ times accelerates

$$\rho A \Delta x \left[\frac{\partial u}{\partial t} + u \frac{\partial u}{\partial x}\right]$$

Hence the equation of motion

$$\rho A\left[\frac{\partial u}{\partial t} + u\frac{\partial u}{\partial x}\right] = -\frac{\partial}{\partial x}\left[(p-p_0)A\right] \qquad (1)$$

Equation of continuity

$$\frac{\partial A}{\partial t} + \frac{\partial}{\partial x}(Au) = 0 \qquad (2)$$

because $\frac{\partial}{\partial t} A \cdot \delta x = u \cdot A = \left[uA + \frac{\partial}{\partial x}(uA)\delta x\right]$ ← should this be on outside

Plus a consequence of Young-Laplace relation

$$p - p_0 = \frac{Y \cdot h}{r_0}\left[1 - \left(\frac{A_0}{A}\right)^{1/2}\right] \qquad (3)$$

h = constant

$A = \pi r^2 \quad A_0 = \pi r_0$

We will now linearise (1), (2), (3) assuming that u, $p-p_0$, $A-A_0$ and their derivatives are small

Neglecting all terms of second order or higher

From (1) $\rho A \frac{\partial u}{\partial t} = -\frac{\partial}{\partial x}\left[(p-p_0)A\right]$

$$= -\frac{\partial}{\partial x}(pA) + \frac{\partial A}{\partial x}p_0 = -A\frac{\partial p}{\partial x} - p\frac{\partial A}{\partial x} + \frac{\partial A}{\partial x}p_0$$

(small, small)

$$= -A\frac{\partial}{\partial x}(p-p_0) - (p-p_0)\frac{\partial A}{\partial x}$$

second order so skip

$$= -A\frac{\partial p}{\partial x} \Rightarrow \rho\frac{\partial u}{\partial t} = -\frac{\partial p}{\partial x} \qquad (1)$$

From (2) $\frac{\partial A}{\partial t} + A_0\frac{\partial u}{\partial x} = 0$ (because $A = A_0 + \frac{\partial A}{\partial x}\delta x$)

11/12/14 ②

From ③ expanding RHS in Taylor series

$$1-\left(\frac{A_0}{A}\right)^{1/2} = 1-\left(\frac{A_0}{A_0}\right)^{1/2} + \frac{1}{2}\frac{A_0^{1/2}}{A_0^{3/2}}(A-A_0)$$

$$\Rightarrow p-p_0 = \frac{Y\cdot h\cdot 1}{2r_0 A_0}(A-A_0)$$

Differentiate ① and ② to get:

$$\rho\frac{\partial^2 u}{\partial t\,\partial x} = -\frac{\partial^2 p}{\partial x^2} \quad ; \quad \frac{\partial^2 A}{\partial t^2} + A_0\frac{\partial^2 u}{\partial x\,\partial t} = 0$$

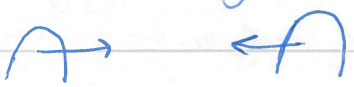
Eliminating u: $\frac{\partial^2 A}{\partial t^2} = \frac{A_0}{\rho}\frac{\partial^2 p}{\partial x^2}$

From ③ $\frac{\partial^2 p}{\partial t^2} = \frac{Y\cdot h}{2r_0}\frac{1}{A_0}\frac{\partial^2 A}{\partial t^2}$

Eliminating A: $\boxed{\frac{1}{c^2}\frac{\partial^2 p}{\partial t^2} = \frac{\partial^2 p}{\partial x^2}}$ pulse the wave eqn

speed of propagation $c = \sqrt{\frac{Y\cdot h}{2\rho r_0}}$

The solution $p = f(x-ct) + g(x+ct)$



The same equation for u or A

$c \approx 4.6$ m/sec

velocity of blood in aorta $\approx$ 24cm/sec

capillaries $\approx$ 25mm/sec

speed of acoustic wave $\approx$ 1000m/sec

Made a mistake $t\cdot h = (p-p_0)r$ ← there should not be a zero here

$$t = Y\left(\frac{r-r_0}{r_0}\right)$$

$$\gamma \cdot h \left(\frac{r - r_0}{r_0} \right) = (p - p_0) r$$

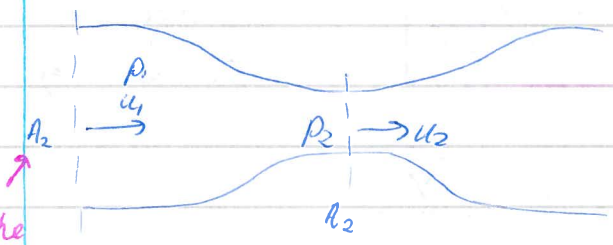
$$\frac{\gamma \cdot h}{r_0} \left(1 - \frac{r_0}{r} \right) = (p - p_0)$$

$$A = \pi r^2$$

$$A_0 = \pi r_0^2$$

$$\frac{\gamma \cdot h}{r_0} \left(1 - \left(\frac{A_0}{A} \right)^{1/2} \right) = p - p_0$$

What happened to Arturo Toscanini in 1952
Suffered a memory lapse (a transient ischemic attack)



does he mean A_1?

Bernoulli's law: $p_1 + \frac{1}{2} \rho u_1^2 = p_2 + \frac{1}{2} \rho u_2^2$ conserved for steady flow

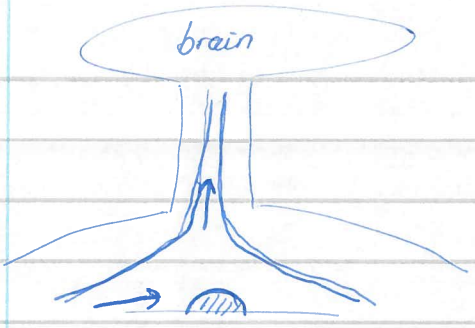
+ continuity

$$A_1 u_1 = A_2 u_2$$

$$p_1 + \frac{1}{2} \rho u_1^2 = p_2 + \frac{1}{2} \rho \left(\frac{A_1}{A_2} u_1 \right)^2$$

$$p_2 - p_1 = \frac{1}{2} \rho u_1^2 \left(1 - \left(\frac{A_1}{A_2} \right)^2 \right)$$

with $A_2 < A_1$: $u_2 > u_1$ but $p_2 < p_1$ pressure is lower for smaller A



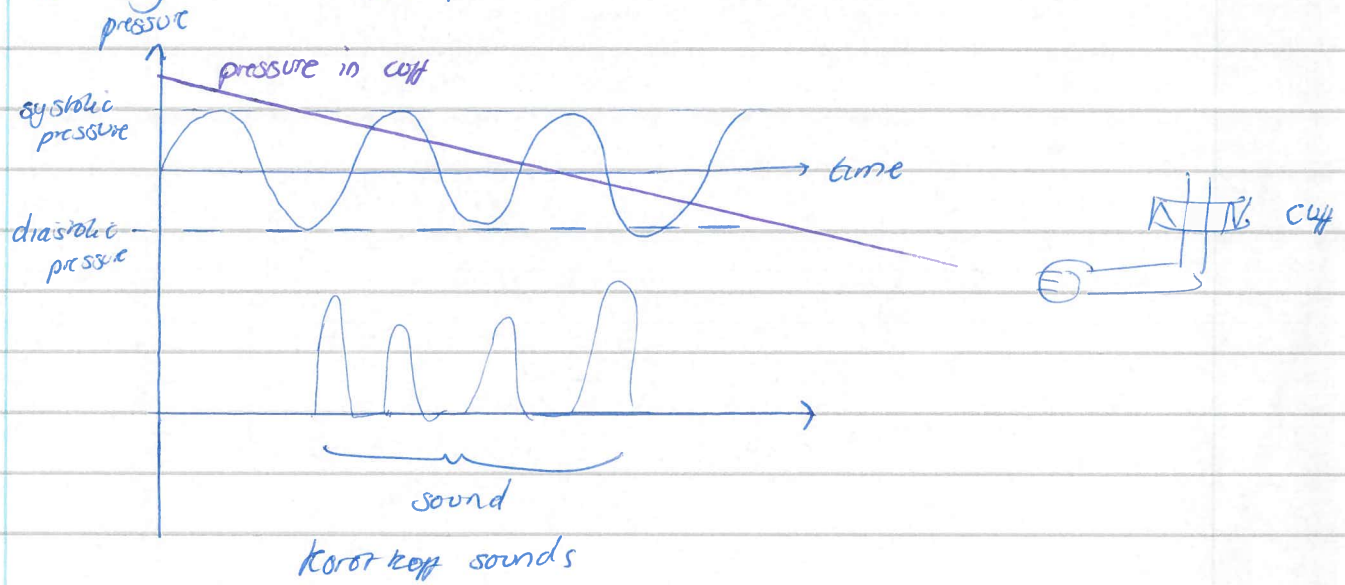
A is smaller

ρ is smaller

less blood for brains

⟹ transient ischemich attack

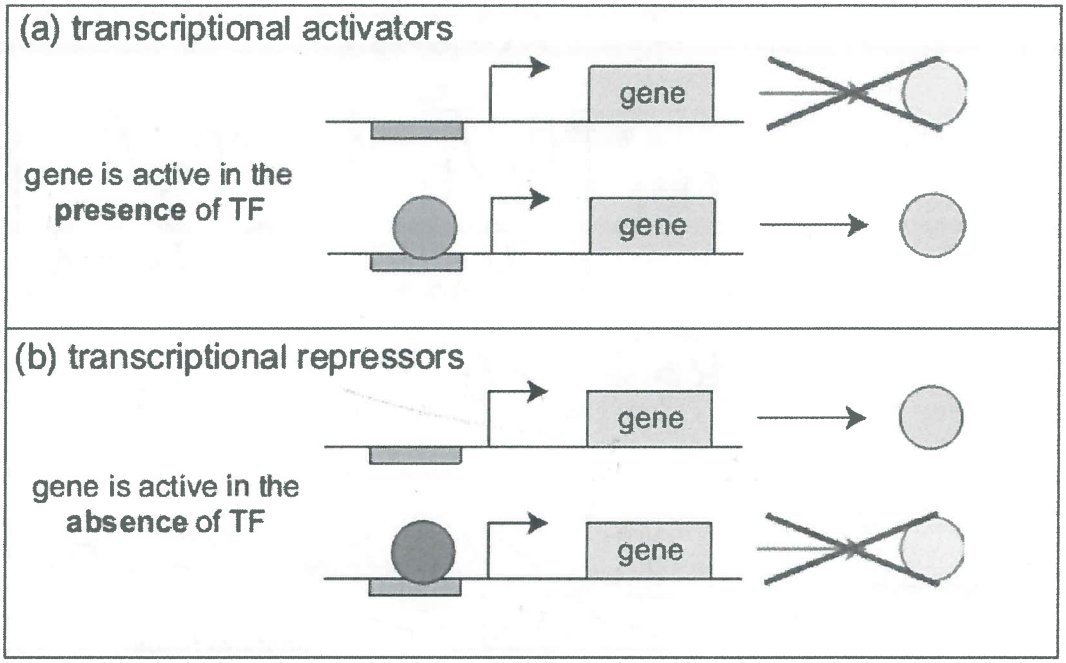
Measuring the blood pressure:



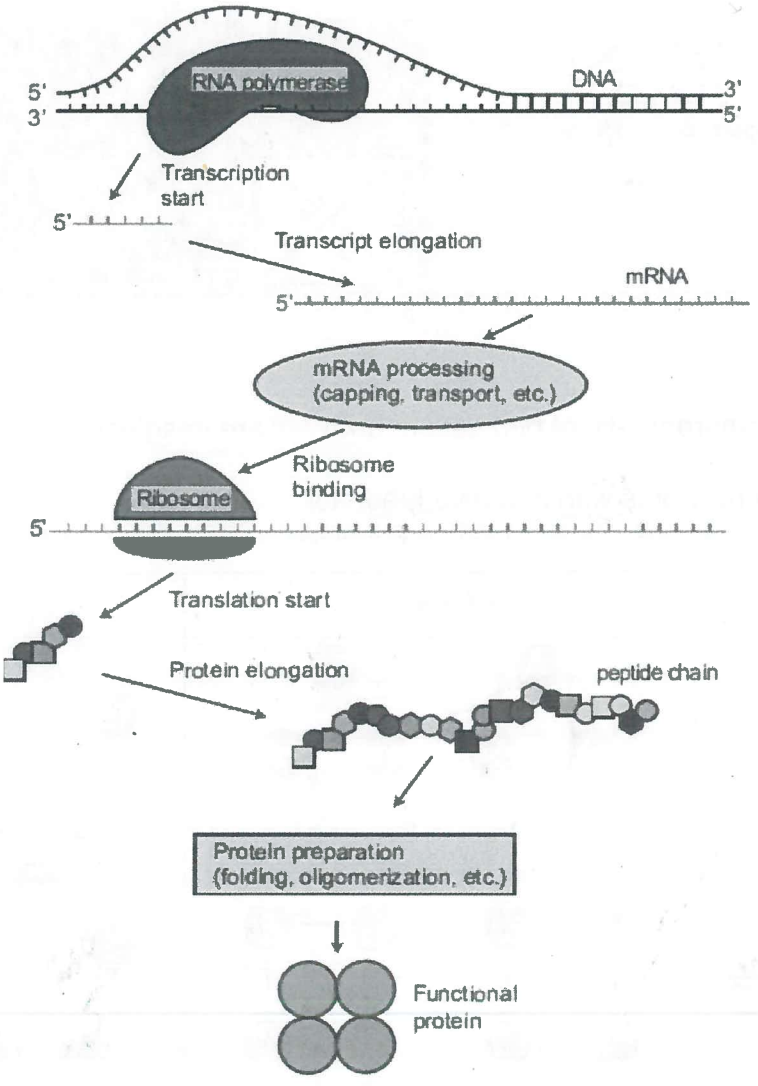
Korotkoff sounds

turbulent flow of blood ⟹ generates acoustic sounds

Transcriptional regulation of gene expression :



Protein synthesis

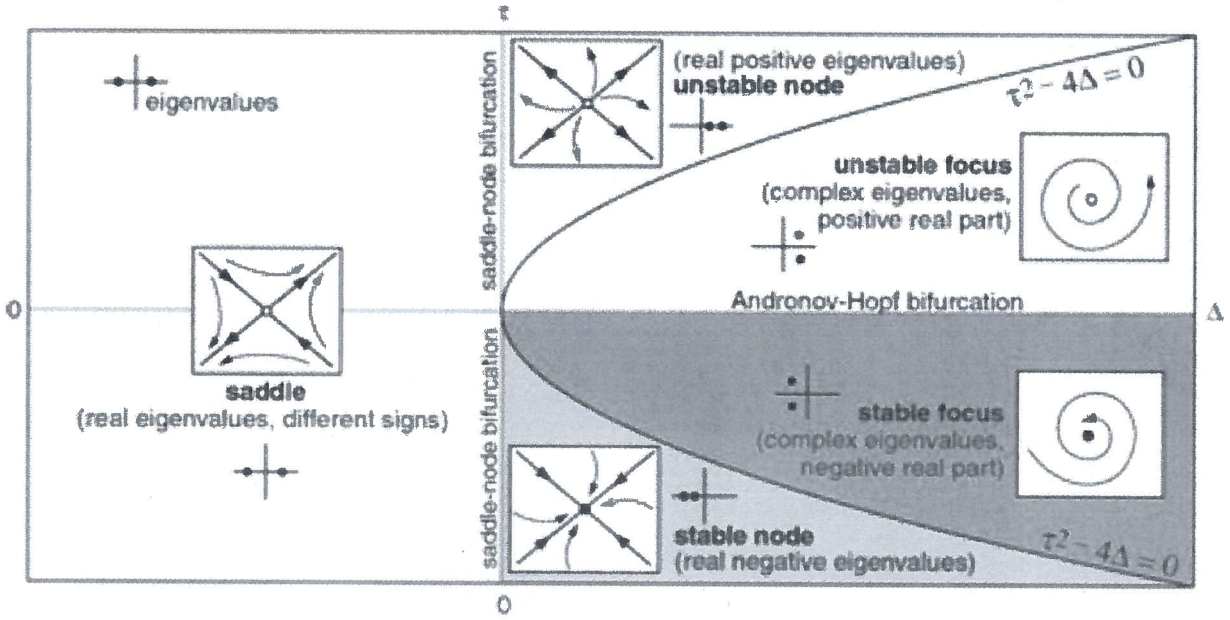


Bifurcations in 2D system

$$\dot{x}_1 = f(x_1, x_2)$$
$$\dot{x}_2 = f(x_1, x_2)$$

$$\mathrm{Det}\begin{pmatrix} \partial_{x_1} f_1 - \lambda & \partial_{x_2} f_1 \\ \partial_{x_1} f_2 & \partial_{x_2} f_2 - \lambda \end{pmatrix} = 0$$

$$\mathrm{Re}\,\lambda_{1,2} < 0$$



Note that in Andronov-Hopf bifurcation, both λ-s are imaginary.

Examples of networks with negative feedback: