RCoA
Royal College of Anaesthetists

e-LA
e-Learning Anaesthesia

e-LA Revision Guide: Physics

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These revision notes have been compiled from sessions in the Physiology module of e-Learning Anaesthesia to support your preparation for the Primary Exam.

The notes are presented as an interactive pdf document which can be downloaded to your smart phone, tablet or desktop computer for offline access

The Table of Contents contains active hyperlinks which allow you to jump straight to a section or topic.

Each topic also contains links to the relevant e-Learning sessions which you can access by clicking on the session id below the title of the topic e.g 07d_03_01. This will take you to the session information page on the e-LfH Hub from which you can log in and access the session

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Contents

ATOMS AND MOLECULES IN MOTION 4

SI Units 5

Kinetic Theory of Gases 6

Newtonian Mechanics 9

Pressure 11

Gas Laws 14

Gases in Solution 17

Density and Viscosity 19

Gas Storage 22

Gases and Vapours 25

Humidity 30

Solvents and Solutes 34

Osmosis 39

Heat Transfer and Temperature 42

Hydrostatics 48

PHYSIOLOGICAL MODELS 53

Fick Principle & Input-Output Principle (IOP) 54

Alveolar Gas Equation 59

Apnoeic Oxygenation and Differential Equations 62

Pre-Oxygenation and e 64

SUBATOMIC PROCESSES 66

Atomic Structure 67

Chemical Bonds and Reactions 69

Molecular Structure and Isomerism 72

Reaction Rates and Thermodynamics 76

Acids and Bases 78

Electromagnetic Spectrum 82

Light 85

LASERs 90

ELECTRICITY AND MAGNETISM 93

Definitions and Simple Circuits 94

Electronic Circuits 99

Amplifiers and Interference 104

Excitable Tissues and Biological Potentials 106

Magnetism and Current 109
Nuclear Magnetism and MRI... 115
Energy and Value Index.. 122

ATOMS AND MOLECULES IN MOTION

SI Units

(07d_01_01)

The Système International d'Unités (**International System of Units**, **SI**) is a metric system of measurement comprising **seven base units**, **derived units**, and **prefixes**. These can be used to produce fractions or multiples of units by a factor of 10.

Seven Base Units

Unit (symbol)	Quantity of	Description
Second (s)	Time	The duration of a certain number of oscillations of a caesium-133 atom
Mole (mol)	Amount of substance	The amount of substance that contains the same number of particles as there are atoms in 0.012 kg (12 g) of carbon-12
Metre (m)	Length or distance	Length travelled by light in a vacuum in 1/300 000 000 of a second
Ampere (A)	Electric current	The current in two parallel conductors of infinite length, placed 1 metre apart in a vacuum that would produce force of 2×10^{-7} N/m
Candela (cd)	Intensity of illumination	Luminous intensity of monochromatic light
Kelvin (K)	Thermodynamic temperature	1/273.16 of the thermodynamic triple point of water
Kilogram (kg)	Mass	The mass of the prototype kilogram held in Sèvres, France. Note that the only physical quantity within the base units is the kilogram. However, there is debate about whether to change this as the prototype is slowly degrading.

Remembered by the mnemonic **SMMACKK**

Prefixes

Any SI unit can have a prefix to give it a **fraction or multiple of 10** – still considered an SI unit:

Pico - p	10^{-12}	0.000 000 000 001
Nano - n	10^{-9}	0.000 000 001
Micro - μ	10^{-6}	0.000 001
Milli - m	10^{-3}	0.001
Centi - c	10^{-2}	0.01
Deci - d	10^{-1}	0.1
	10^{0}	0
Deca - da	10^{1}	10
Hecto - h	10^{2}	100
Kilo - k	10^{3}	1 000
Mega - M	10^{6}	1 000 000
Giga - G	10^{9}	1 000 000 000
Tera - T	10^{12}	1 000 000 000 000
Googol	10^{100}	1 000 000 000 000 000 000 000 000 000 000 000…

Kilogram is confusing…

Derived Units

Derived measurement	Derived unit	Symbol
Area	Square metre	m^2
Volume	Cubic metre	m^3
Speed	Metres per second	$m.s^{-1}$
Velocity	Metres per second, with direction	$m.s^{-1}$
Acceleration	Metres per second squared	$m.s^{-2}$
Current density	Ampere per square metre	$A.m^{-2}$

These are the simple derived units that we are expected to know.

Complex Derived Units

Name	Symbol	Quantity of	Equivalents	SI base unit
Hertz	**Hz**	Frequency		s^{-1}
Newton	**N**	Force		$kg \cdot m \cdot s^{-2}$
Pascal	**Pa**	Pressure, stress	N/m^2	$kg \cdot m^{-1} \cdot s^{-2}$
Joule	**J**	Energy, work, heat	N·m, C·V, W·s	$kg \cdot m^2 \cdot s^{-2}$
Watt	**W**	Power	J/s, V·A	$kg \cdot m^2 \cdot s^{-3}$
Coulomb	**C**	Electrical charge or quantity		s·A
Volt	**V**	Voltage, electrical potential	W/A, J/C	$kg \cdot m^2 \cdot s^{-3} \cdot A^{-1}$
Farad	**F**	Capacitance	C/V, s/Ω	$kg^{-1} \cdot m^{-2} \cdot s^4 \cdot A^2$
Ohm	**Ω**	Resistance, impedance	V/A	$kg \cdot m^2 \cdot s^{-3} \cdot A^{-2}$
Henry	**H**	Inductance	V·s/A	$kg \cdot m^2 \cdot s^{-2} \cdot A^{-2}$
Weber	**Wb**	Magnetic flux	$T \cdot m^2$	$kg \cdot m^2 \cdot s^{-2} \cdot A^{-1}$
Tesla	**T**	Magnetic flux density	Wb/m^2	$kg \cdot s^{-2} \cdot A^{-1}$

These units are derived from the scientist who discovered it.

The name i.e. **pascal** can be expressed as base units ($kg/m^{-1}/s^{-2}$) or a combination of base and derived units (N/m^2):

Force = Newton = $kg.m.s^{-2}$

Pressure = Force/Area

Pressure = $kg.m^{-1}.s^{-2}$

Many **non-SI units** are used in anaesthesia as it is easier. For example,

- 1 day instead of 86 400s
- Litre instead of $1000cm^3$.
- **Degrees Celsius** can be converted to **Kelvin** by adding 273.15.
- **Pressure** is also measured in mmHg and cmH_2O:

Pressure

To make maths easier, assume:

1 atm = 1 bar = 101.3kPa = 101 325 Pa = 760mmHg = 1033cmH_2O = 14.5PSI

mmHg → kPa = **Divide by 7.6** i.e. 760mmHg = 101kPa

cmH_2O → mmHg = **multiply by 0.76**

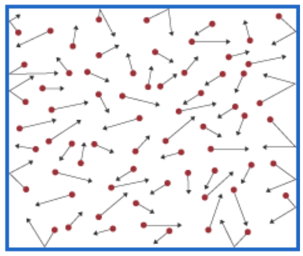
<u>Kinetic Theory of Gases</u>

(07d_01_02)

The **kinetic theory** describes **behaviour of gases** at a **molecular level**. This will help explain the macroscopic properties such as temperature and pressure.

<u>Postulates</u>

1. **Gases consist of a large number of particles** (atoms or molecules): the space between them is larger than the particle itself and therefore the volume of the particles is negligible compared to the volume of the gas itself.
2. **Particles move in random directions at different speeds**
3. **Collisions between particles and with the walls are elastic so do not change total kinetic energy of the gas**.
4. **No attractive** or **repulsive forces between particles** as this would breach postulate 3 and cause a change in phase.

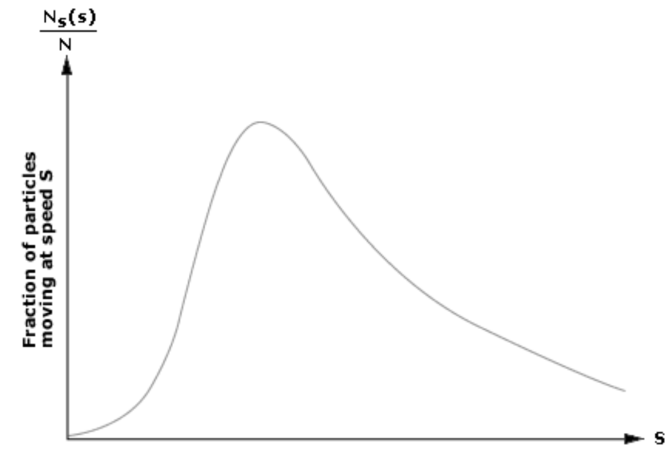


NB real gases behave differently from the ideal gas as the particles occupy a small but absolute volume (1) *and they do have attractive/repulsive forces between them* (4).

BROWNIAN MOTION: Describes the observed constant chaotic movements of fluids observed initially by Robert Brown who observed this with pollen in water. Einstein had explained this through the collision of pollen with invisible water molecules – similar to dancing dust in a sunbeam.

<u>Macroscopic Behaviour of Gases</u>

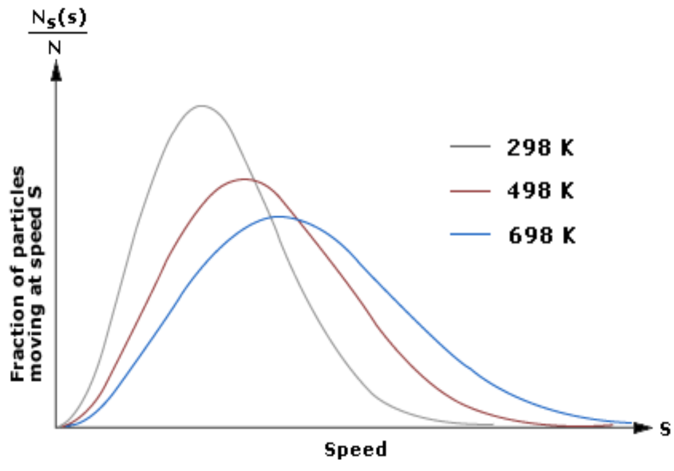
At a given time, the **particles of a gas are moving at random speeds**. The **Maxwell-Boltzmann distribution** shown right illustrates the distribution of the probability that any random particle will have a given speed.



<u>Temperature</u>

When **heat energy is added** the **kinetic energy** of the gas particles **increases** and therefore the average speed of gas molecules increases. In summary:

Temperature is a reflection of the average kinetic energy of the particles of a gas.



Molecular Weight

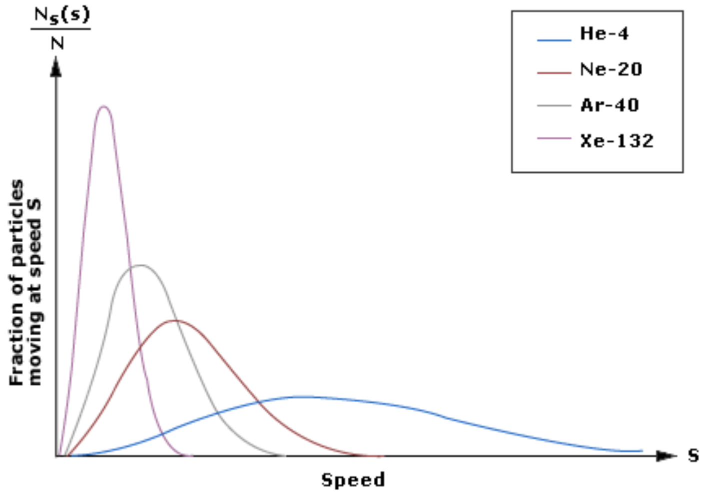
At a **given temperature** the **average kinetic energy of particles across all gases is the same**.

$$\text{Kinetic energy} = \frac{1}{2} mv^2$$

m = mass

v = velocity

Therefore, gases with **higher molecular weight** will have a **lower average speed** at a given temperature to compensate to achieve the given kinetic energy:



Pressure

The **force exerted by particles impacting on the walls of their container**. This can be explained through illustration of a particle colliding with a wall in a right angle and with perfect elasticity. If velocity is $+2m/s^2$, this will change to $-2m/s^2$.

Acceleration is the rate of change of velocity, therefore this particle will experience acceleration as it bounces off the wall and will **exert a force when it bounces off the wall**.

FORCE = MASS x ACCELERATION

Pressure is defined as the cumulative force generated, divided by the total area over which that force is applied.

Thus, pressure can be increased through:

1. Increasing the frequency of collisions of gas particles with the container walls, or
2. By reducing the area over which the collisions occur

Gas Laws

You can now relate the kinetic theory of gases to the following gas laws:

BOYLE'S LAW: As the volume of a gas is decreased at a **constant temperature**, its pressure will increase.

CHARLES' LAW: At a **constant pressure**, the volume of a gas varies with its absolute temperature

GUY-LUSSAC'S LAW: At a **constant volume**, the absolute pressure of a given mass of gas varies directly with the absolute temperature

Newtonian Mechanics

(07d_01_03)

Sir Isaac Newton in 1642 had solved the problems surrounding the laws of motion, the laws of planetary orbits and the concept of calculus. The foundation of the theory of motion is based on **force and mass**. The **relevance to the anaesthetist** of Newtonian mechanics applies best to the behaviour of gases.

Force: **defined as that which changes or tends to change the state of rest, or motion, of an object.** This definition takes into account objects with an exerted force without motion – i.e. a book on a table exerts weight but does not move so is a force that *tries* to make it move downwards.

$$\text{NEWTON} = \text{FORCE} = \text{KG.M.S}^{-2}$$

Newton's first law of motion

In the absence of external forces, an object at rest remains at rest and an object in motion continues in motion with a constant velocity

In other words, if a surface without friction is present, an object will remain stationary with no exerted forces or will continue to move at constant velocity AFTER application of a force.

Inertia: The **tendency to resist change in velocity**. For example; Think of a small boat that breaks free from its moorings. The water supports the boat's weight and offers very little resistance to its movement; the boat starts moving very gradually, but once it is moving, it is very difficult to stop. The greater the mass the greater the inertia i.e. bowling ball vs football.

Momentum**:** As with velocity, it has magnitude and direction and is therefore a **vector quantity**. Momentum will remain constant unless an external force is applied – implied by Newton's first law. **Momentum** (P) is overall a **product of its mass** (m) **and velocity** (v):

$$P = mv$$

Therefore, any object that is moving has momentum. A stationary object has inertia but no momentum.

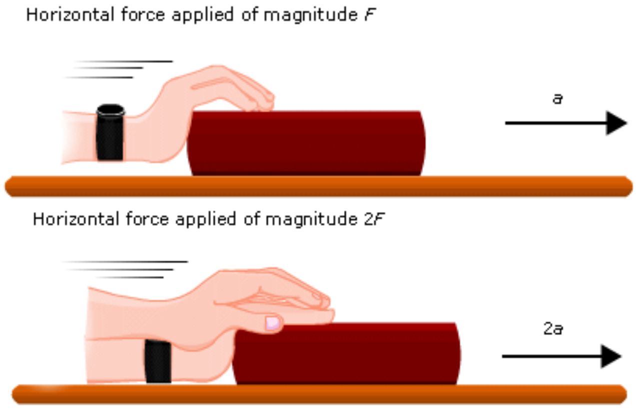
Mass: **the property of an object that specifies how much inertia that object has**. The greater the mass of an object, the less that object accelerates under the action of a given applied force. Also, the greater the mass of a moving object, the less it decelerates when it meets a given opposing force

Newton's second law of motion

Acceleration (a) of an object with a given mass is **directly proportional to the force** (F) **applied** and **inversely proportional to its mass** (m):

$$F = ma$$

See image. Conversely, if 2 books with magnitude F was applied – a/2 would occur.

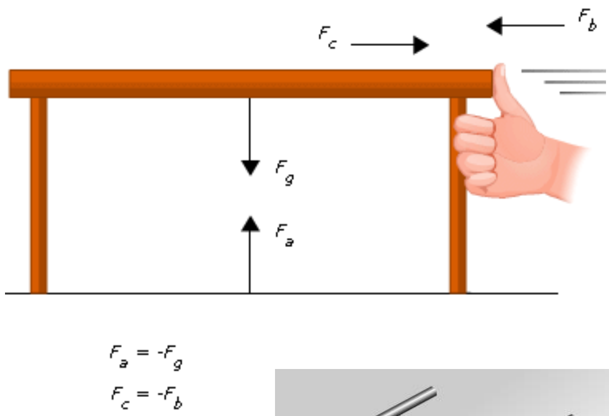


Weight: Is a measure of the **heaviness of an object** and is the **force with which an object is pulled towards earth by gravity** and therefore measured by Newtons. **Gravity** = **9.81m/s²**

Weight (N) = mass (kg) x 9.81 (m/s²)

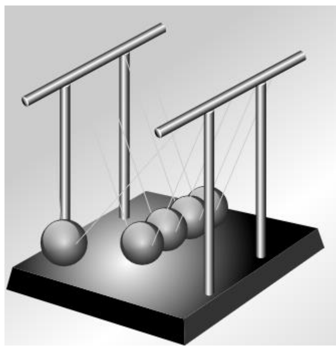
Newton's third law of motion

For every action there is an equal and opposite reaction. For example, placing your thumb against a desk and applying an increasing force may not move the desk but increase the opposing force against your thumb. These are known as **action and reaction forces:**



Conservation of Momentum

Providing no other external forces are at play, the **total momentum before a collision equals the momentum of all objects after the collision.** This is well explained by **Newton's cradle**.



Another example would be in a car crash: if a van traveling at momentum **70,000 kg.m.s⁻¹** hit a stationary car, the van would lose momentum and the car would gain but no momentum would have been lost in the crash:

Van	
Mass (kg)	3500
Vel. (m/s)	20.0
mom. (kg.m/s)	70,000

Car	
Mass (kg)	1500
Vel. (m/s)	0.0
mom. (kg.m/s)	0

Would lead to…

Van	
Mass (kg)	3500
Vel. (m/s)	14.0
mom. (kg.m/s)	49,000

Car	
Mass (kg)	1500
Vel. (m/s)	14.0
mom. (kg.m/s)	21,000

Pressure

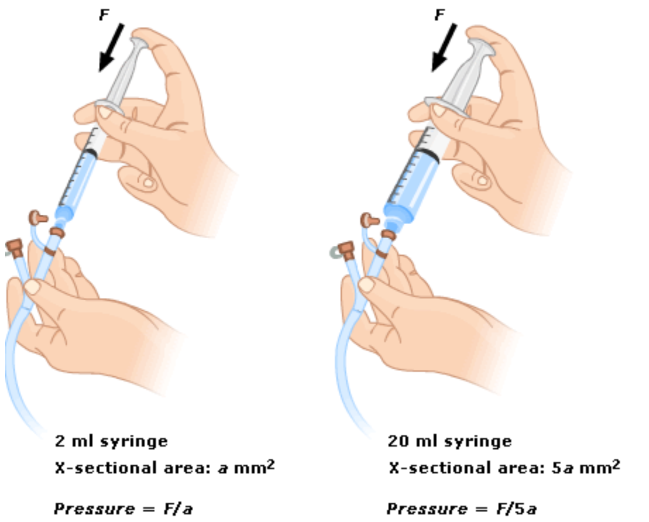
(07d_01_04)

Pressure = Force/Area

Pressure (Kg.m^{-1}.s^{-2}) is a force per unit area and is measured frequently in anaesthesia with patients and equipment. It may be described in **pascals/kilopascals/bar/atm/mmHg/cmH$_2$O**.

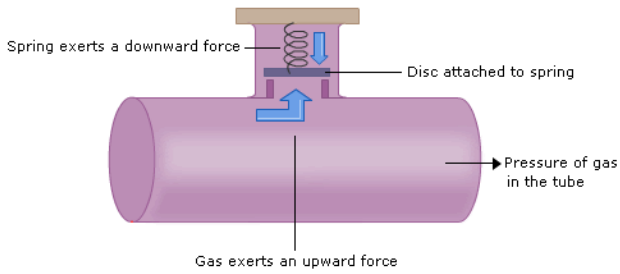
There is a large **difference between force and pressure**. Examples include carrying a backpack with thick padded straps vs thin wire straps → same force but the latter exerts increased pressure as is spread over a much reduced area.

In anaesthetics, if asked to unblock the lumen of a nasogastric feeding tube, which had become obstructed with feed, a **2ml syringe** will **exert greater pressure** with a given force than a **20ml syringe** which applies the force to a plunger with a **cross sectional area 5x larger**.



Pressure Relief Valve

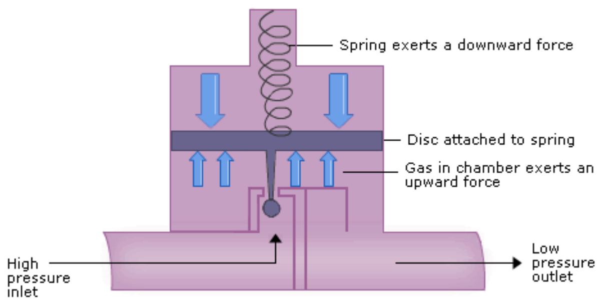
Used on the back bar of the anaesthetic machine to prevent damage to the components of the machine. The gas exerts a force against the valve and when the gas exerts a pressure higher than that exerted by the spring of the valve on the disc, gas will release to lower the pressure in the pipe.



Pressure Reducing Valve

AKA **Pressure regulators** to reduce gas pressure to a constant lower pressure. In gas cylinders, the constant pressure amounts to around 400kPa.

- **High pressure gas enters via inlet**
- Passes into a **chamber via valve**
- **Gas pressure exerts upward force** and the occluding ball moves upward to **close the valve**
- **As pressure in chamber falls, the valve opens.**



Gauge and Absolute Pressures

The 2 must be distinguished as when all the oxygen is taken out of the cylinder, the gauge reads 0 bar which is incorrect as 1atm of pressure still remains:

- **Gauge pressure:** The pressure on the cylinder gauge
- **Absolute pressure:** Total pressure in cylinder **= Atmospheric pressure + gauge pressure**

Therefore, in a full oxygen cylinder, the absolute pressure is 137 bar (gauge pressure) + 1 bar.

Similarly **blood pressure is expressed relative to atmospheric pressure** and therefore are **gauge pressures**. Clinical measurements are expressed as gauge pressures relative to atmospheric pressure

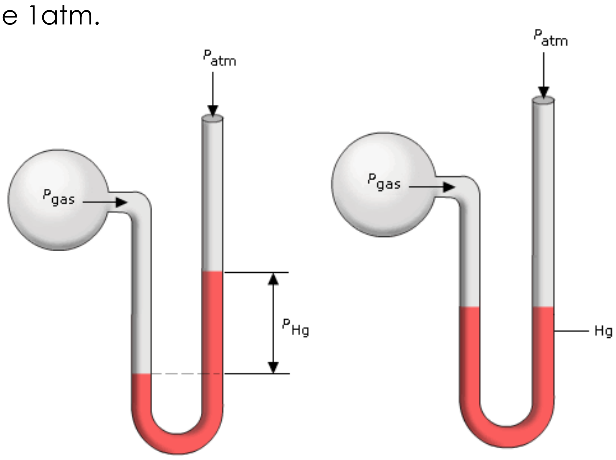
Measuring Pressures

There are 2 main types, **manometers** (displacement of a column of liquid) and **mechanical gauges** to measure pressures significantly higher than atmospheric pressure.

Open-ended Manometers

The open-ended manometer consists of a vertical column of liquid within a tube. Mercury is frequently used, but other fluids such as water may be used. One end is closed to the gas in question and the other end is open to atmospheric air and hence 1atm.

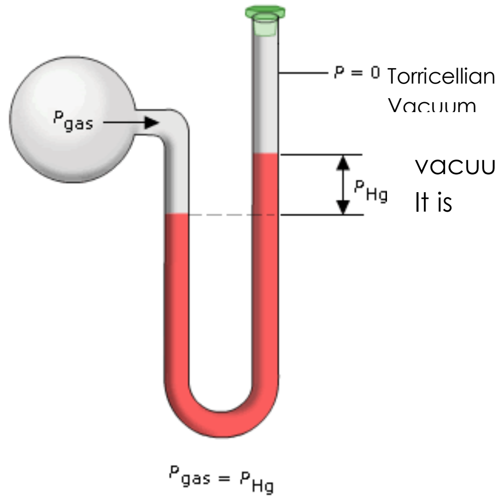
- If the **Pgas = Patm** – then the fluid level on each arm will be equal
- If the **Pgas > Patm –** then the fluid will be displaced to the open end and the difference in height of the 2 arms will be the Pgas value (**gauge pressure**).
- The opposite will occur if the Pgas<Patm.



If mercury is the liquid used, the value will be mmHg. **Sphygmomanometers** are an example when measuring BP.

Closed-ended Manometers

In a closed-ended manometer the arm furthest from the gas sample is sealed. The space above the mercury is a vacuum so that no atmospheric pressure exists above the mercury. It is useful in **Pgas <Patm** and is a direct measure of **absolute pressure**.



The **mercury barometer** is an example which measures atmospheric pressure.

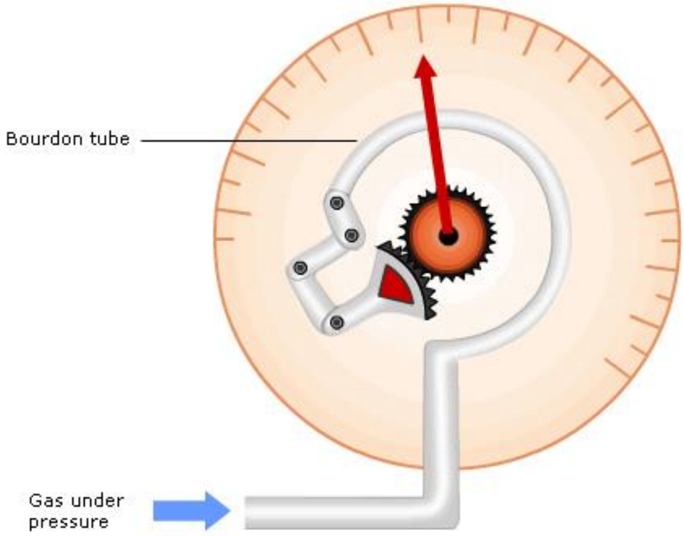
Water manometers are non-toxic, readily available but are **less dense than mercury** and therefore, less useful in measuring higher pressures. A pressure which supports a 7.5 mm column of mercury will support a 102 mm column of water. Therefore, to measure 100kPa (750mmHg and 10.2m H_2O), the column heights for this measurement to take place in water and mercury will be as follows:

- **Water:** 10.2m
- **Mercury**: 7.5cm

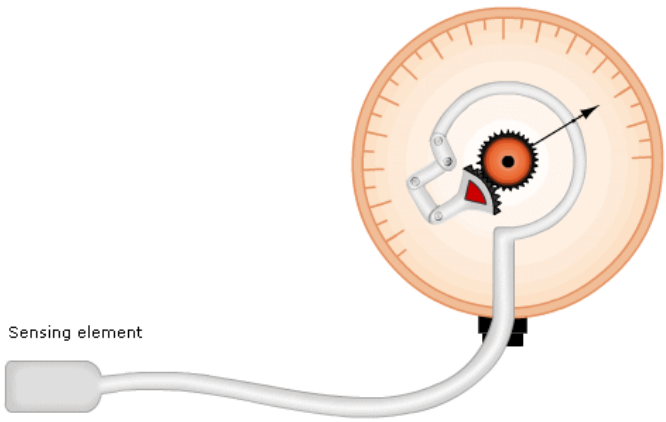
<u>Bourdon Gauge</u>

May be used to measure **high pressures** greater than 100 kPa. A gas at high pressure enters a coiled tube (the Bourdon tube), causing it to uncoil; as the tube uncoils, the motion is transferred through a linkage to a gear train connected to a pointer, which moves over a scale on a dial.

Also known as an **aneroid gauge** which by definition, contains no liquid



This can also be used to **measure temperature** as a sensing element may be attached containing a gas. According to the **third ideal gas law**, a constant volume the absolute pressure of a given mass varies **directly** with the absolute temperature. The scale must be calibrated in units of temperature.



Gas Laws

(07d_01_05)

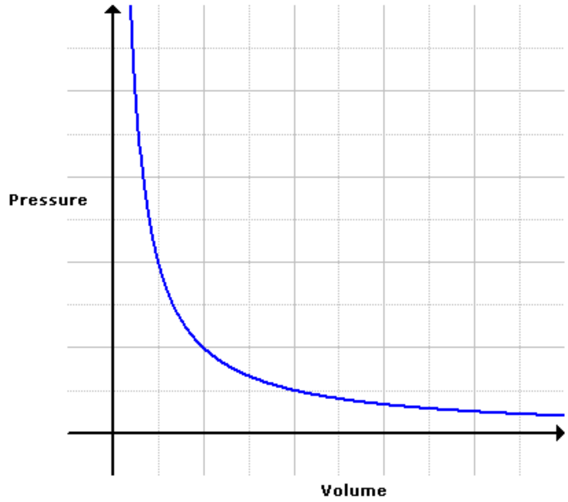
Describe the relationship between the **thermodynamic temperature**, **pressure** and **volume** of gases. They refer to the **ideal gas** (which does not exist).

Boyle's Law

At a constant temperature the volume of a given mass of gas varies inversely with the absolute pressure. Think of pushing a syringe plunger down against a closed end…

If you halved the volume in the syringe, the pressure measured would double, if the temperature was kept constant. Therefore:

$V \propto 1/P$ and $P_1 \times V_1 = P_2 \times V_2$



Clinical Application

From this, one may work out **how much gas i.e. oxygen is left in a cylinder prior to transfer**. If the gauge on a **10L cylinder** reads **137 bar**, then:

Absolute pressure = 13 700 kPa + 100 kPa = 13 800 kPa

If $P_1 \times V_1 = P_2 \times V_2$ then…

→ **P1 is 13 800 kPa, V1 is 10 litres, and P2 is 100 kPa** (released into atmospheric pressure)

$V_2 = P_1 \times V_1 / P_2$

⇒ **V_2 = 13 800 x 10/ 100 = 1380 Litres.**

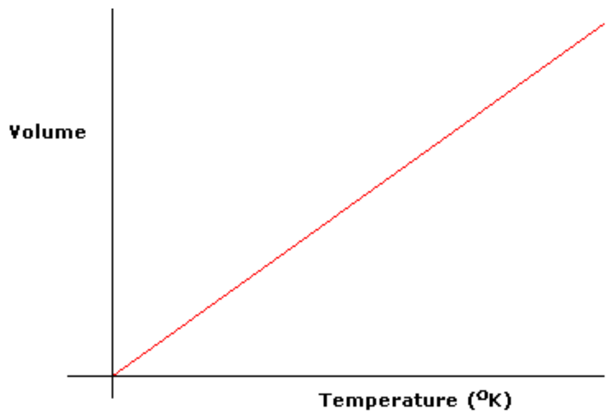
Remember that 10 litres will remain in the oxygen cylinder, therefore only 1370 litres can actually be used on your transfer.

Charles' Law

At a constant pressure the volume of a given mass varies directly with the absolute temperature. Imagine that the syringe was allowed to freely move at a normal temperature, as you increase the temperature, the volume will rise proportionally.

$V \propto T$

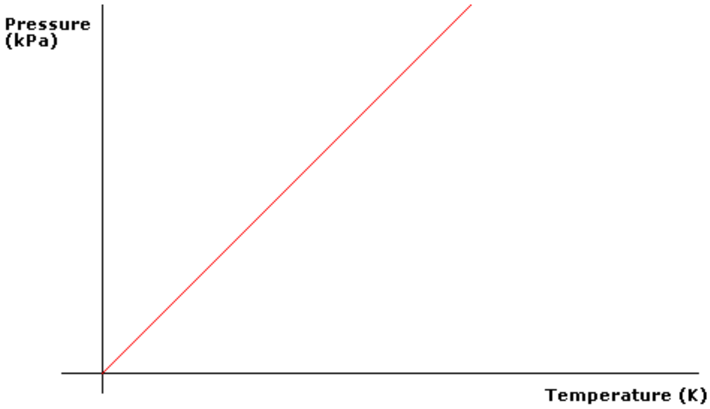
This is used to explain the expansion of a **hot air balloon**.



Third Gas Law (Gay-Lussac's Law)

At a constant volume the absolute pressure of a given mass varies directly with the absolute temperature. Imagine now, that the syringe plunger was prevented from moving and the other end was attached to a pressure gauge, when heated, the pressure would rise.

$P \propto T$



This is why aerosol cans or other closed containers should not be thrown into a fire – pressure rises and then can explode if the container is not strong enough to hold the pressure.

Combined Gas Law

If you combine all 3 laws:

- Boyle's Law states that at a constant temperature: PV = constant
- Charles's Law states that at a constant pressure: V/T = constant
- The third gas law states that at a constant volume: P/T = constant

Therefore, if combined, **PV/T = constant**. These conditions change according to the gas in question:

Avogadro's Principle: equal volumes of all gases, at the same temperature and pressure, have the same number of molecules.

As different gases have different molecular weights, thus rather than express quantity in terms of mass, it is easier to express it in terms of molecules – **MOLE.**

A mole is the **quantity of substance containing the same number of particles as there are atoms in 12 g of carbon 12**. This is equal to **6.022×10^{23}**.

One mole of **any gas** at standard temperature and pressure (1 atm and 273.15 K) **occupies 22.4 litres.** THEREFORE:

Ideal Gas Law

PV/T = constant. The value of the constant is **number of moles of gas present (n).** This is multiplied by the **universal gas constant (R)** which represents the behaviour of a single mole of gas and has the value of 8.31 J K^{-1} mol^{-1}. OVERALL:

$$PV = nRT$$

In practice…

A full cylinder of nitrous oxide contains 3.4 kg of nitrous oxide, but how much gas are you able to get out of the cylinder?

Nitrous oxide molecular weight = 44.

- ➔ Therefore, 1 mole N_2O = **44g** and occupies **22.4L**.
- ➔ **3400g/44 = 77.2**. There are 77.2 moles in the cannister
- ➔ **77.2 x 22.4 = 1730L** *Don't forget the residual volume which will be left!*

Dalton's Law of Partial Pressures

In a mixture of gases, **the pressure exerted by each gas is the <u>same</u>** as that which it would exert **if it alone occupied the container**.

$$PV = (n_1 + n_2 \ldots) \times RT$$

In a cylinder of air at **100kPa**, there is 20.9% oxygen and 79% nitrogen. The total pressure would be **100kPa** but the 2 gases will exert **20.9kPa** and **79kPa** respectively.

When are gases not ideal

When the **state changes to liquid/solid** due to a change in pressure/temperature:

- **Critical Temperature:** the temperature above which a substance cannot be liquefied however much pressure is applied
    - The critical temperature of nitrous oxide is 36.5°C, whilst that of oxygen is -119°C
- **Critical Pressure:** the pressure required to liquify a substance at its critical temperature (or *minutely* just below)

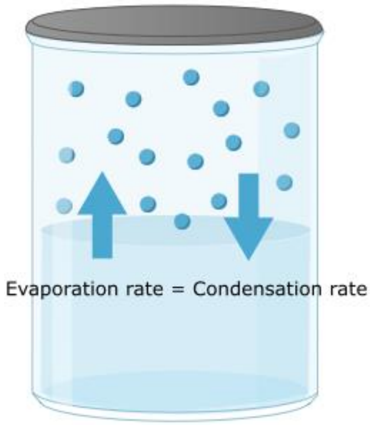
Gases in Solution

(07d_01_06)

Solubility

A liquid in **equilibrium** exists in **2 phases** in a closed container: **liquid** phase at the bottom and **vapour of the liquid** at the top (as well as a gas depending on the ambient temperature).

A liquid in equilibrium is the point at which the evaporation rate equals the condensation rate so there is no net change in the 2 different phases.



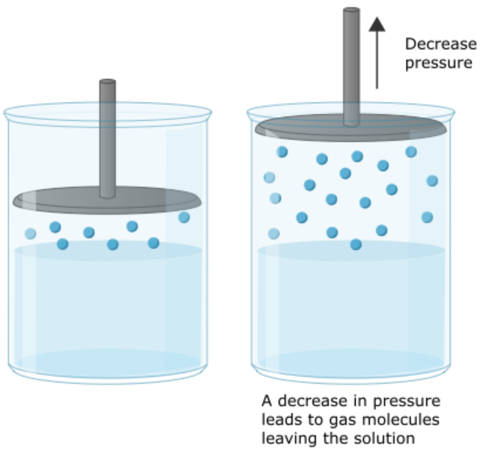
Saturated Vapour pressure: The partial pressure exerted by the vapour at equilibrium **at constant temperature**.

Henry's Law

At a fixed temperature the **amount of gas dissolved is directly proportional to increasing partial pressure of the gas** when in equilibrium.

This is applicable in diving as rapid decompression → **nitrogen comes out of solution** in joints → formation of the bends.

This law applies to a given liquid and a given gas as different gases and liquids have different solubilities i.e. N_2O is more soluble than N_2.



Temperature: As temperature increases, the solubility of a gas decreases – i.e. gas bubbles form in a hot can of coke.

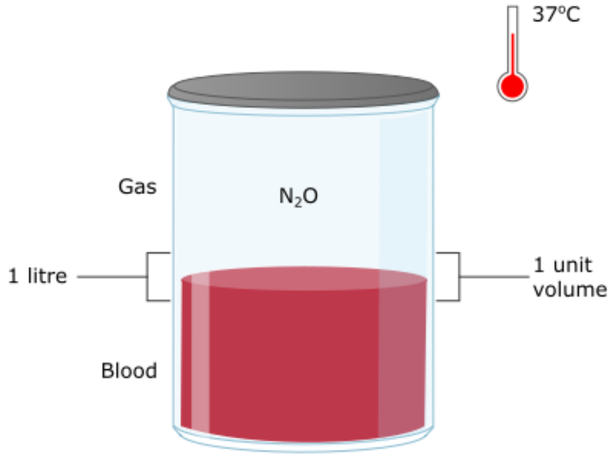
Gas Tension is another way of describing partial pressure. The tension of a gas **in solution** is the partial pressure of the gas in equilibrium with it

Describing Solubility

Solutions of gases are described as volumes of gas dissolved in a volume of liquid. There are ***solubility coefficients*** used to describe this:

1. **Bunsen**: volume of gas ***corrected to standard temperature and pressure*** (***STP***) dissolved in a unit volume of a liquid where the partial pressure of the gas above the liquid is 1 atm at an ambient temperature of 0°C.
2. **Ostwald:** the volume of gas dissolved in a unit volume of liquid at the temperature concerned. More preferred by anaesthetist as not corrected to standard temperature but measured at a specified pressure.

Partition Coefficient



Describes the distribution of a substance in 2 phases and expressed as a ratio when both phases are of **equal volume** and **at equilibrium** at standard temperature and pressure). It is described at specific temperatures and phases (as with Ostwald). However, unlike Ostwald's coefficient, the **order of phases** must be specified.

For example, the **blood-gas partition coefficient** of **N_2O is 0.47.**

The lower the number, the less soluble it is.

Agent	Blood gas coefficient
Desflurane	0.45
Nitrous oxide	0.46
Sevoflurane	0.68
Isoflurane	1.4
Enflurane	1.91
Halothane	2.4
Ether	12
Xenon	0.12

Therefore, Sevoflurane will anaesthetise faster than ether as will achieve equilibrium faster in the alveoli.

Density and Viscosity

(07d_01_07)

Density

Density (ρ) is a **mass (m)** (kg) per **unit volume (v)** (m^3)

$$\rho = m / V$$

Density applies to all states and has an impact on gas flow and its measurement, which in turn has important implications for anaesthesia.

Gas Density

Increases with **decreasing temperature** and with **increasing pressure** as they both increase the number of particles in a given volume.

Specific gravity of gas is the density of the gas divided by that of **air** (1.2 kg/m^3). >1 = more dense than air.

Solids and liquids are given a **specific gravity** compared to **water.**

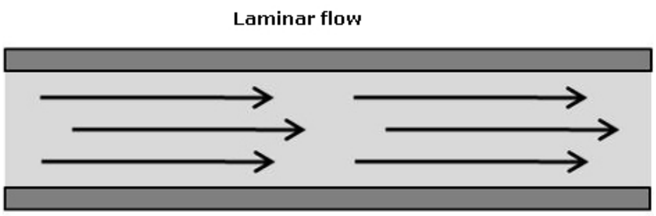
Viscosity

Viscosity (η) is the **tendency of a fluid to resist flow** or, to put it another way, ***'fluid friction'***. It is measured in poise (P). For example, blood runs slower than crystalloids through a giving set as blood has greater viscosity.

Newtonian fluid: is one where the **viscosity of the fluid** is **unaffected** by the **shear or tangential stresses** inflicted upon it. **Viscosity** is **dependent solely on temperature** and **pressure.** Water is an example. Maple syrup is not. Viscosity increases with increasing pressure and decreasing temperature.

Flow

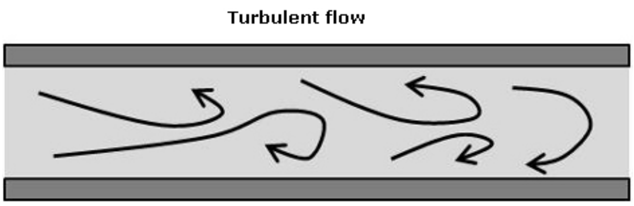
Movement of a volume of fluid from one place to another per unit time. Measured in **m^3/s**.



Streamlined flow in smooth layers or laminae. **Viscosity** is therefore important. At a **critical velocity**, flow will change from laminar to turbulent

$$\text{Laminar flow} = \Delta P r^4 \pi / 8 l \eta$$

- **ΔP** = pressure difference from the start of the flow to the end;
- **r** = radius of the tube
- **l** = length of the tube
- **η** = fluid viscosity



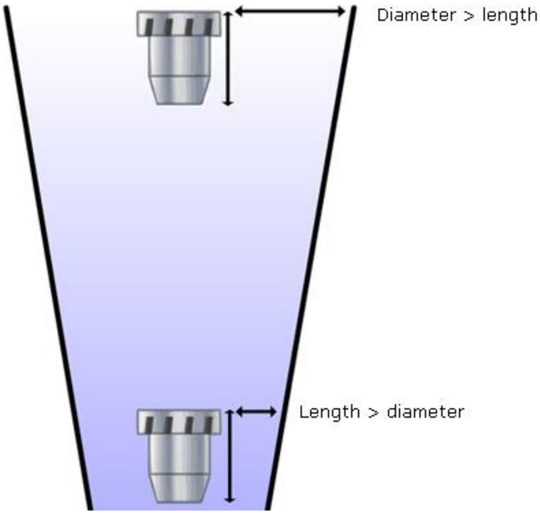
Interrupted by swirls and eddies. **Density** is more important in affecting the rate of flow. Viscosity becomes less important.

Turbulent flow ∝ r^2 and $\sqrt{\Delta P}$ and 1/length and density of the fluid

Measuring Flow

Calculated simply by passing a known volume of fluid past a point in a measured time. Gas flows used in anaesthesia require constant measurement, and this can be achieved with **indirect measurement** by looking at the **change in pressure across a fixed orifice**.

- A **TUBE** will produce **laminar flow** when able.
- **An ORIFICE is a tube in which the diameter exceeds the length** and will produce **turbulent flow**.



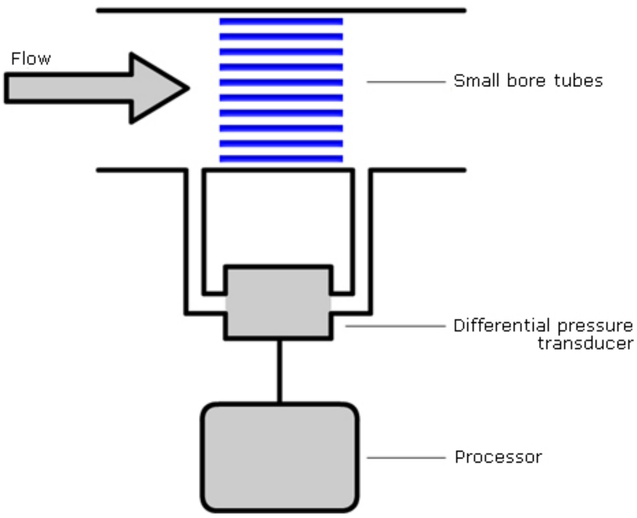
In a **tube of variable diameter**, there will be a point reached where the relationship to an internal bobbin becomes that of an orifice rather than a tube (see diagram):

- At the base, flow is lower – **laminar flow** prevails
- At the top, there is an orifice effect around the bobbin with higher flows – **turbulent flow** is predominant

Types of Flowmeter

1. **CONSTANT ORIFICE, VARIABLE PRESSURE**

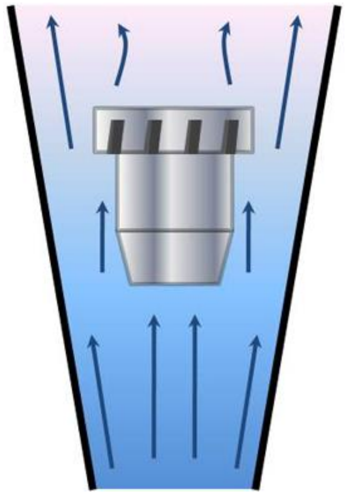
Where measurement of flow is determined by the pressure difference. A **pneumotachograph** creates **laminar flow** through multiple small diameter tubes or mesh and uses the **linear relationship between flow and pressure difference** as per the Hagen-Poiseuille equation. The small resistance offered by the tubes causes a pressure drop proportional to the flow which is then transduced.



Constant calibration of the pressure difference is necessary through the use of a **known flow rate**. This must be repeated with different gases and with a change in viscosity and density.

A simple **pressure gauge** can be used to calculate flow if upstream pressure is constant. An example is the pressure gauge of an oxygen cylinder, using a pressure gauge at the outlet of the oxygen cylinder.

2. CONSTANT PRESSURE, VARIABLE ORIFICE



A **rotameter** uses a bobbin of fixed size, which moves up and down in a tapered column of flowing gas, which is introduced via a needle valve. **Pressure from gas flow** pushes the bobbin up till it is counteracted by gravity. This is what is described in the tube of variable diameter above. Flow measurement should be read from the top of a flat-topped bobbin and from the middle of a spherical bobbin.

Gases have varying densities and viscosities, so the rotameter must be calibrated for each gas.

Peak expiratory flow meters (PEFM) are an example where a piston is moved to a point dependent on the peak flow rate. If helium was exhaled – as it is less dense – the flow would increase.

Different Gases

Oxygen storage as a gas is impractical as no vessel would be large enough for the amount used in a hospital. It is therefore stored in liquid form as bulk and small quantities in cylinders.

Nitrous oxide is 40x more soluble than N_2 so can diffuse into air cavities faster than N_2 out and may expand air filled spaces if used i.e. raised IOP, pneumothorax. Manufactured by heating ammonium nitrate to 240^{0}C and extracting the nitrous oxide from the impurities. Above this temperature may cause detonation…

Entonox is the trade name for **50% Oxygen, 50% N_2O**. Formed by bubbling oxygen through liquid nitrous oxide known as the **Poynting effect**.

Carbon Dioxide very rarely used in anaesthesia now – more for fire extinguishers!

Helium has lower density, but higher viscosity than N_2 (helium specific gravity at 0^{0}C = 0.138). Therefore, **increases flow when turbulent** so in a mixture with oxygen (Heliox), has been used to treat upper airway obstruction.

Key features of common gases

	Boiling point (^{0}C)	Melting point (^{0}C)	Critical Temp.(^{0}C)	Critical Pressure (Bar)	SVP at 20^{0}C(Bar)
Oxygen	-183	-219	**-118**	50	1.4
Nitrous Oxide	-88	-91	**36.5**	**72**	50.8
Carbon Dioxide	-79	-57	**30**	**73**	57
Helium	-269	-272	-268	2.3	n/a

A Wright's Respirometer is used to measure volume; only with the addition of a timing device can it measure flow

Gas Storage

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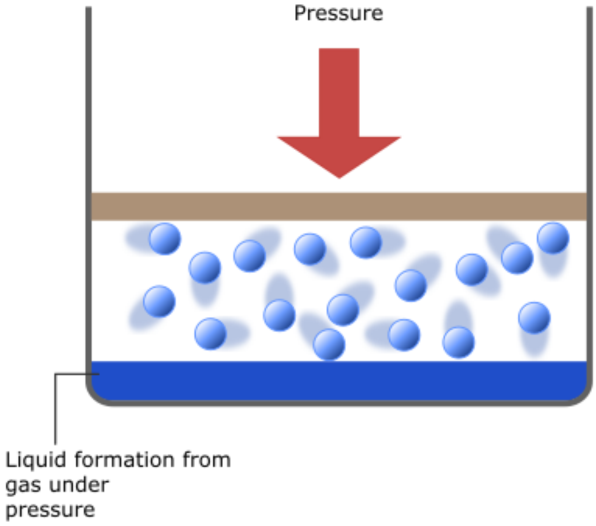
Kinetic Theory

As mentioned previously, gases can be converted to liquid under increased pressure below the critical temperature. The substance is considered a **vapour** rather than a gas when **below the critical temperature**.



Critical Temperature and Pressure

The critical temperature of a substance is the temperature above which it cannot be liquefied, however much pressure is applied.

GAS: When **above the critical temperature**, a reduction in volume will increase gas pressure. The substance is referred to as a **gas.**

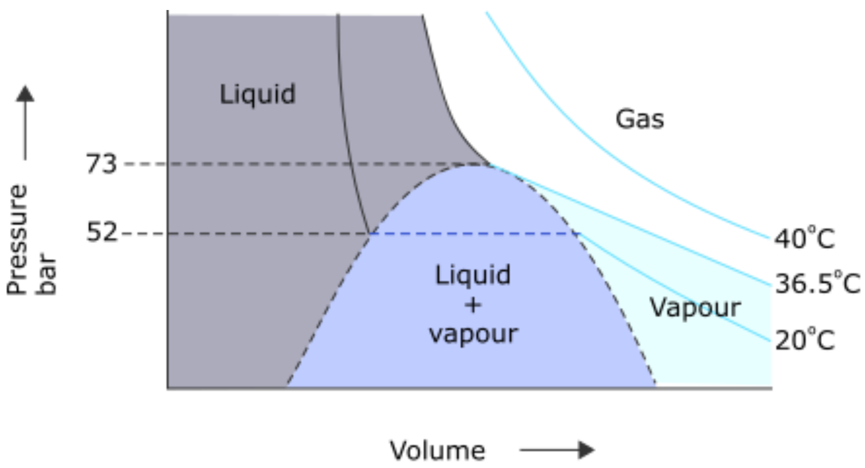
VAPOUR: When **below the critical temperature**, a reduction in volume will cause substance liquidation.

Critical pressure refers to the vapour pressure of a substance at its critical temperature and is thus the pressure required to liquefy the gaseous component at that temperature.

Isotherms

A **series of lines** that describe the way in which **temperature and pressure determine the physical state of a substance** above and below the critical temperature.

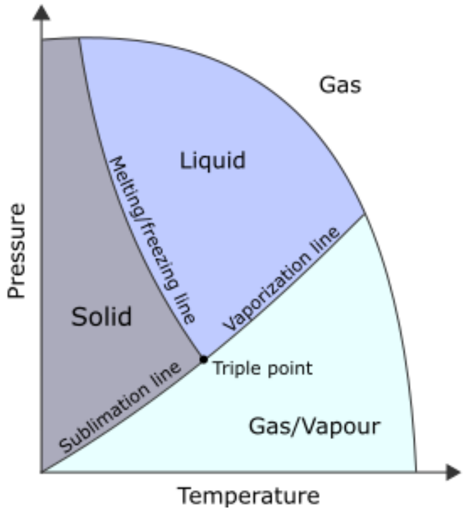
This diagram shows the effect of **Nitrous oxide** compression at 3 different temperatures.



- **40°C:** Above critical temperature – exists as a gas and follows **Boyle's law**
- **36.5°C:** At its critical temperature – liquifies at the critical pressure of 73 bar. Liquids are relatively incompressible which is why the pressure rises steeply with reducing volume
- **20°C:** Below critical temperature – at 52 bar, there is partial compression to a liquid. Further reduction in volume causes more vapour condensation with no change in pressure. This is characteristic of N_2O cylinders at room temperature.

The Triple Point

A phase diagram showing the effects of pressure and temperature on the state of a substance. The **triple point** is where the **temperature and pressure at which the solid, liquid and gaseous phases of a substance can exist in equilibrium**.



The Kelvin is defined according to the triple point of water (0.01°C). At this temperature, the SVP is referred to as the **sublimation pressure**. At the freezing point of water, the SVP is not zero, but 4.6 mmHg. Note that (uniquely) for water the freezing/melting point decreases with increased ambient pressure.

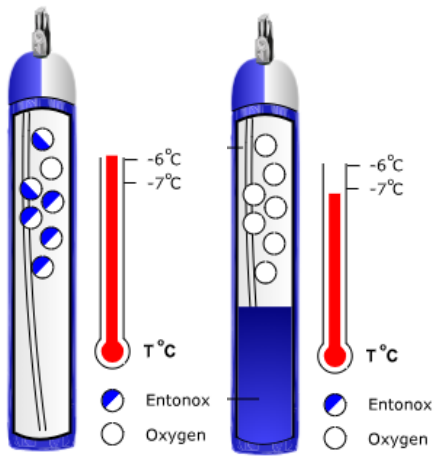
Gas Storage

Entonox

Entonox® is produced by **bubbling oxygen through an N_2O liquid** in a 50:50 ratio.

LIQUEFACTION: This is when the mixture of Entonox is cooled to below -7°C (the pseudocritical temperature of Entonox) and N_2O subsequently liquifies. This solution has about 20% oxygen (hypoxic mixture). Also known as ***separation*** or ***lamination***.

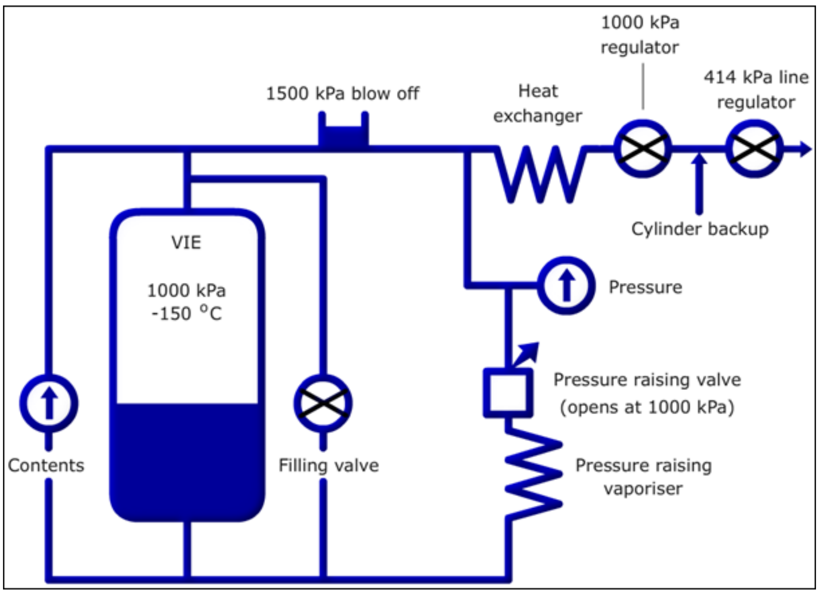
One must be aware that this may have occurred if stored outside previously. A **dip tube** reaches to the base of the cylinder to siphon off the liquid N_2O first (see image) and hence delivers the hypoxic mixture first. The remaining mixture will lack N_2O but not be hypoxic. It also needs to be stored **horizontally** in a **maintained temperature**.



Oxygen

Due to high demand, safe storage can only realistically be achieved in its **liquid form**. This type of storage is known as a **vacuum insulated evaporator** (**VIE**):

It requires a cooling system, held under vacuum. The temperature is maintained between -170°C and -150°C using a vacuum insulator and **oxygen usage** (as it is used, **latent heat is expended** cooling the liquid). If **none is used**, **temperature rises → increased pressure** via third gas law and oxygen blows off through the **safety valve** (1500kPa) which also reduces temperature through **latent heat of vaporisation**.



O_2 vapour passes from the top of the tank to a **heat exchanger** and a series of pressure regulators before being passed into the pipeline.

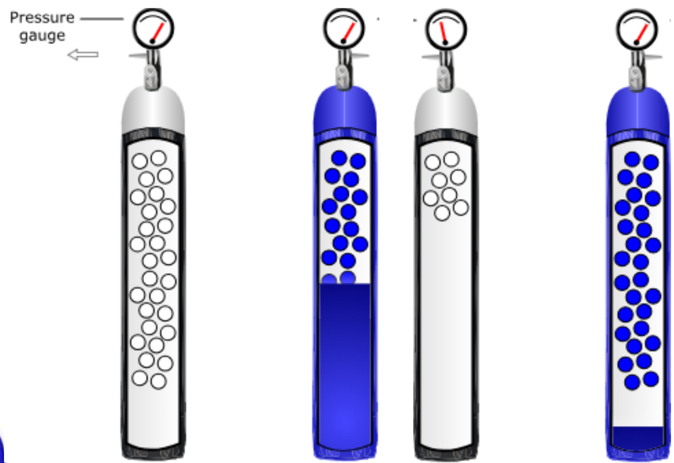
With **heavy usage** and fast flow rates, the pressure will drop in the VIE so the liquid O_2 passes through the **pressure raising vaporiser** and returns to the VIE in gaseous form to restore the pressure within.

Nitrous Oxide Cylinders

Stored as a **liquid** where the vapour pressure is **44 bar**. Liquid is less compressible than vapour so cylinders have a **filling ratio** of 0.75 as to allow expansion and prevent explosion. In warmer climates this is 0.67. The filling ratio describes the weight of fluid within a nitrous cylinder compared with the weight of the cylinder when filled completely with water. Stored vertically. **Tare weight** is the weight of the empty cylinder.

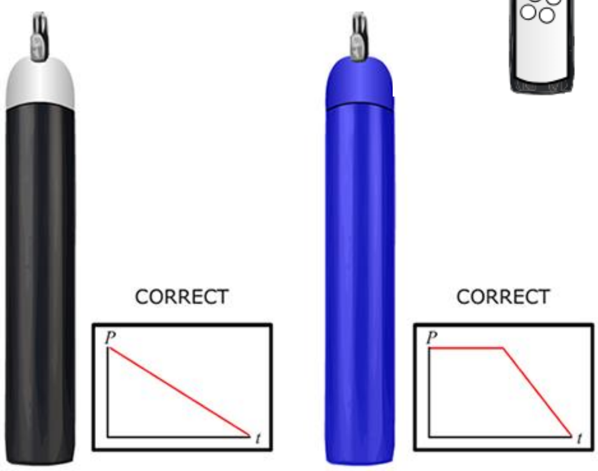
Oxygen and Air Storage Cylinders

Stored as **gases** at **137 bar** when the cylinders are full. Unable to store as a liquid as the critical temperatures are too low. Unlike N_2O then, the **amount of gas** is **directly related to the pressure within** so a pressure gauge can give an indication of how much is left. They also have a **pressure reducing valve** for safe delivery to the anaesthetic back bar.



Cylinder Emptying Patterns

N_2O is stored as liquid and vapour held above in equilibrium. It is the vapour that exerts a pressure. When used, more liquid becomes vapour to replace that which is used. This continues until all liquid is used. Therefore, the contents cannot be determined by pressure until all liquid has been vaporised. This is in contrast to oxygen and air cylinders.



Gases and Vapours

(07d_01_09)

Vapour is a gaseous substance below its critical temperature which can be liquefied by pressure alone. Heat increases the rate of evaporation.

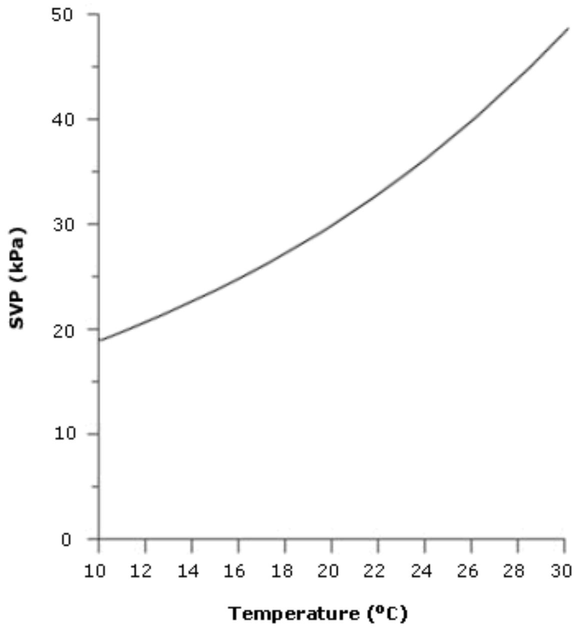
Saturated Vapour Pressure

…is the **pressure exerted by molecules in the vapour component at the point of equilibrium** at a **specific temperature**. This occurs with storage of a liquid in an enclosed space which evaporates and exists in its 2 phases at equilibrium.

The **higher the SVP** the **more volatile** a substance is (its tendency to vaporise). With volatile anaesthetic agents, the use of the wrong vaporiser may result in delivery of a dangerously low or high concentration of agent.

Factors affecting SVP

Raising temperature will result in increased kinetic energy and a greater number of vapour molecules. Once equilibrium is achieved, the SVP will be raised. This is a **non-linear relationship**.



If the SVP becomes atmospheric pressure (100kPa) the liquid boils and 100% becomes vapour.

Ambient pressure: The pressure of the surrounding medium. SVP is unchanged with ambient pressure changes, however, the proportion of total pressure occupied by the given vapour changes with changes in ambient pressure…

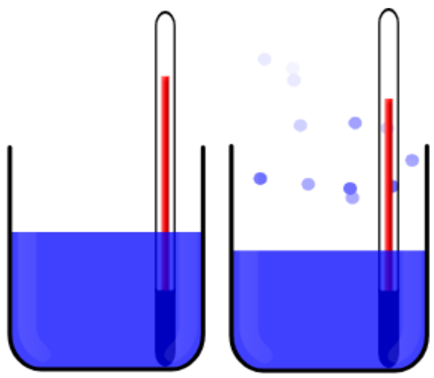
For example: **Boiling point decreases** with **decreased ambient pressure** (in altitude). Therefore, to make a *good* cup of tea is harder in altitude as the temperature may not be high enough to allow it to brew in altitude before it is released as vapour.

Here is a table of the common volatiles showing the relationship between the BP and SVP as well as the MAC of each agent:

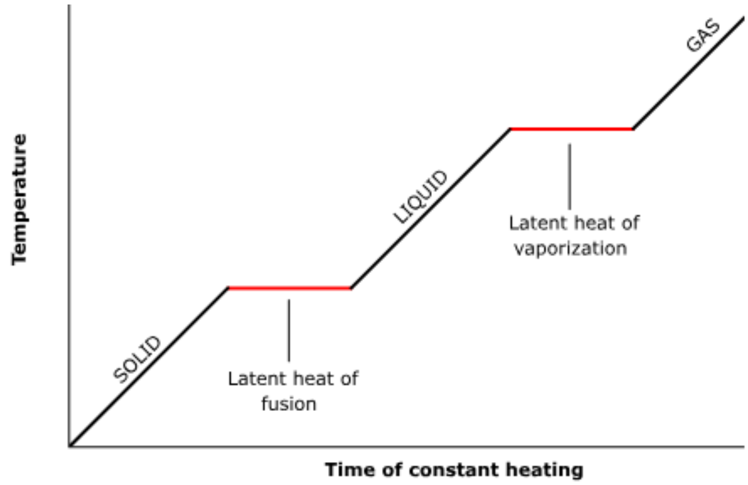
Characteristics	Desflurane	Sevoflurane	Isoflurane	Enflurane	Halothane
Boiling Point *(°C @ ATM)*	23	59	48	56.5	50.2
SVP (@20°C)	88.5	21.3	32	23	32.5
MAC	6.0	2.0	1.15	1.68	0.75

Latent Heat

Not all molecules in a liquid have the same energy. The more vigorous molecules have a greater tendency to escape to the gaseous phase. This means the average energy of those left behind is lower. To enter the gaseous phase, the molecules extract energy as heat from the liquid → reduction in temperature of the liquid.



- ***Latent heat of vaporisation:*** heat energy required to convert a given mass of liquid into vapour whilst maintaining the same temperature
- ***Latent heat of fusion:*** heat energy required to convert a given mass of solid into liquid at the same temperature.

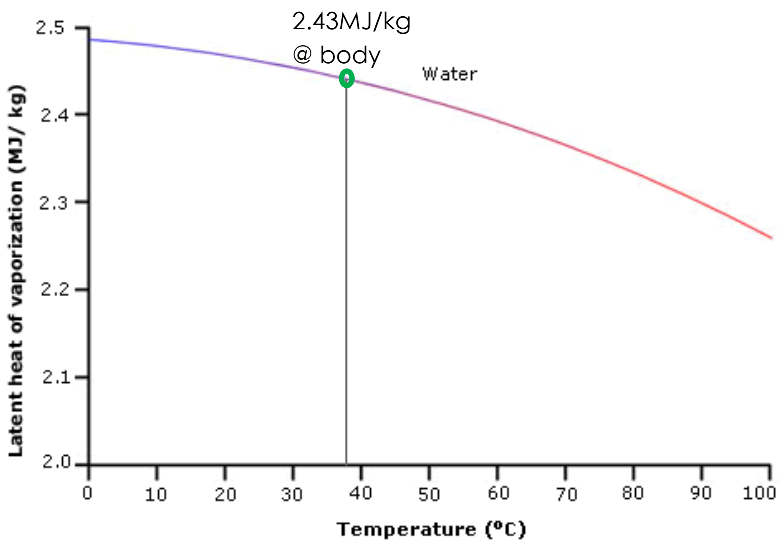


Heat is a form of energy whilst temperature is the measure of the hotness/coldness of a substance. The temperature does not change at the change of phases as heat energy is used to convert the molecules into their specific phases.

Latent Heat of Vaporisation

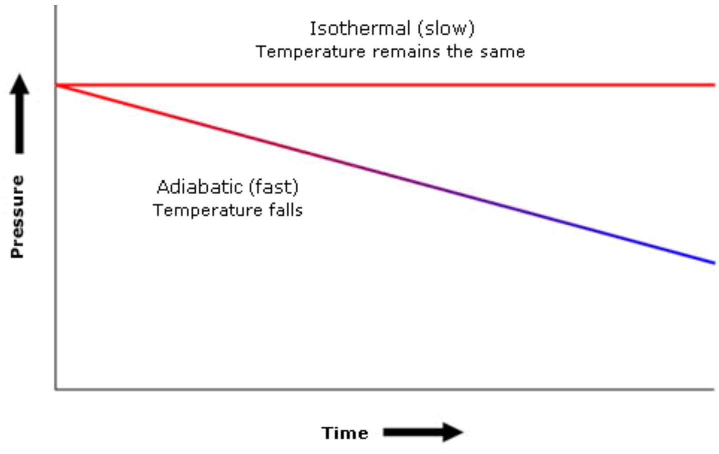
Varies with the temperature of the liquid. Water closer to boiling point will require less latent heat to achieve complete vaporization than water at room temperature.

Specific latent heat: The heat required to convert one kilogram of a substance from one phase to another; units are **J/kg**. This must be quoted with reference to temperature:



Adiabatic and Isothermal Change

Adiabatic Change: The state of a gas is altered without a change in heat energy to or from the gas into the surroundings. The energy causes a **change in gas temperature**.



- **Decompression:** Gases expand and energy required to overcome Van der Waal's forces. As this is adiabatic, the source of energy derives from the molecule's own kinetic energy and not the surroundings – the gas cools.
- **Compression:** Temperature rises with rapid gaseous compression (Joule-Kelvin principle). May be seen if a cylinder connected to an anaesthetic machine is turned on too quickly with a rapid rise in temperature…may cause an explosion or fire in presence of combustibles

Isothermal Change: If the compression or expansion occurs sufficiently slowly, heat can be conducted through the walls of the container, leading to **no change in the temperature of the gas**.

Vaporisers

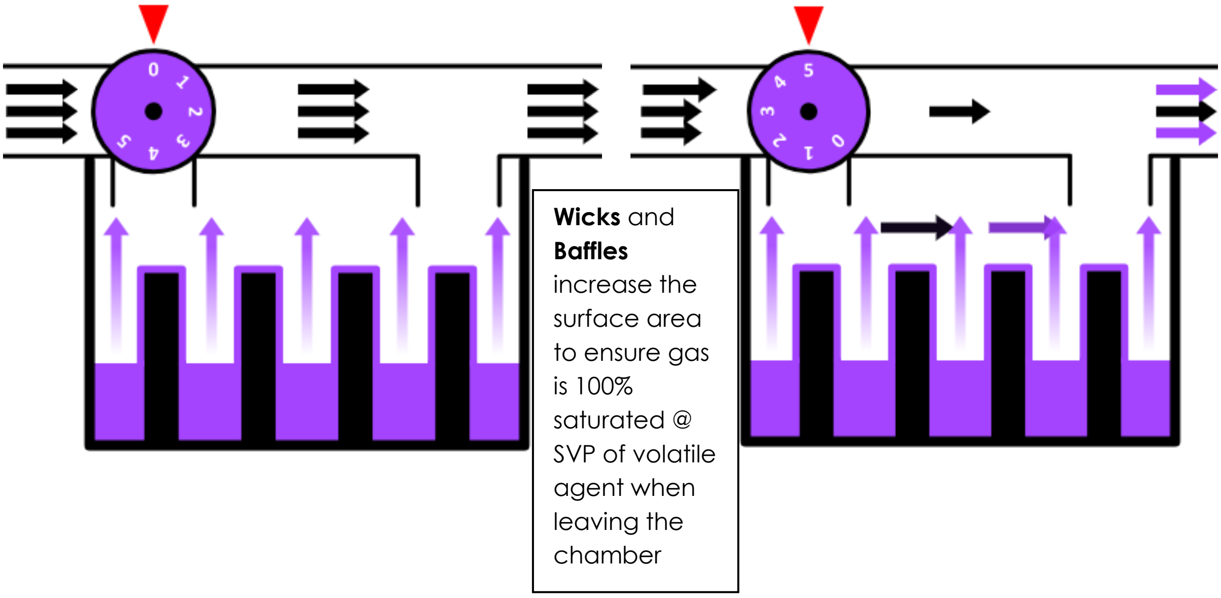
Used to **deliver a controlled** and **predictable partial pressure** of **anaesthetic agent in a carrier gas** at the common gas outlet.

As the SVP of volatile agents are much higher than that required for anaesthesia at room temperatures, the vaporiser acts as an SVP divider and allows for splitting of gas flow, mixing and provision of an appropriate dose to the patient. A dial controls the **splitting ratio** (ratio of gas passing through each route).

Types of Vaporiser

1. **Plenum Vaporisers** use positive pressure upstream to force gas through the vaporiser and is the standard used in the UK. *Because of high internal resistance, only appropriate to use as **vaporiser out of circle** (**VOC**)).*
2. **Draw-over Vaporisers** use negative pressure downstream through bellows or via respiratory effort and are more common in field or developing world medicine. *May be incorporated as a **vaporiser in circle** (**VIC**) **or VOC**)*

The standard in the UK is known as the **Tec (temperature compensated) vaporiser chamber**. A network of internal channels and wicks create a high surface area for vaporisation so SVP can be achieved without change in vaporiser temperature. A dial alters the carrier gas **splitting ratio** of bypass and vaporisation chamber flow so the final partial pressure and concentration of anaesthetic in the gas leaving the vaporizer is known.



Safety precautions with Volatility

With a **higher SVP**, the **volatility is increased** and the concentration will be higher of the agent. They therefore require a lower proportion of gas flow (**lower splitting ratio**) to give the required concentration. If a gas with higher SVP was placed in a vaporiser designed for gases with a lower SVP, there would be a grave risk of overdosing.

Effect of Temperature and Flow on Vaporiser Function

Latent heat of vaporisation causes **cooling** of the liquid agent → **lower SVP** and **reduced concentration delivery**. Modern vaporisers have temperature compensation mechanisms in place (see below).

Increased flow rate also **cools** the liquid agent and again reduces the concentration able to be delivered. It also causes difficulty in achieving equilibrium in the vaporization chamber, which alters the efficiency of vaporization.

Changing flow rates also affects the change in proportion of the carrier gas entering the vaporiser chamber. This has greatest significance at lower flows due to relative resistances of flow between the two gas paths.

Temperature compensation mechanism

Simple mechanisms such as reducing flow rates may be utilised. Other mechanisms may either provide heat energy to the vaporiser or creating a mechanical change within the vaporizer to alter the splitting ratio with changing temperature:

Bimetallic strip	Bonded strips consist of two metals with different coefficients of thermal expansion, which cause the composite strip to bend and open or partially close an orifice. Popular on **Tec vaporisers** which are named TEC 1→5 according to where the strip is placed
Bellows	Bellows are small, flexible and expand or contract to open or shut valve, e.g. Ohio
Metal rod orifice that expands and contracts	Thermal expansion of a metal rod simply adjusts an orifice to modify flows
Metal heat sink	Large metal heat sinks have great heat capacities and buffer latent heat loss instead of the liquid (Copper is used)
Water bath to control temperature fluctuations	Water baths are more rarely used these days even though water has a great specific heat capacity

Humidity

(07d_01_10)

Humidity is the **amount of water contained within a defined volume of gas**. The more water present within a gas, the more likely it is to precipitate on surrounding objects, whether condensing on a cool object or providing moisture to the respiratory tract.

This is useful in the respiratory tract. Too much humidity however can inhibit evaporation of sweat and may cause one to overheat.

ABSOLUTE HUMIDITY: mass of water vapour present in a given volume of gas at a given temperature and pressure. It is expressed as **g/m³** or **mg/L.**

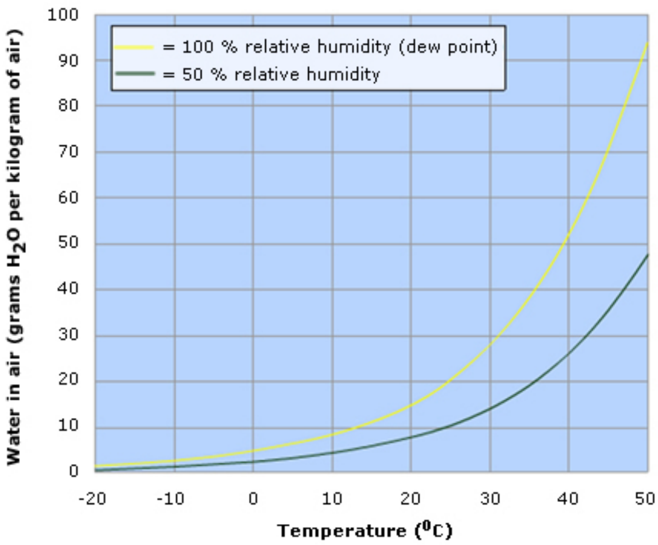
$$\frac{\textbf{Mass of water vapour}}{\textbf{Volume to saturate}}$$

RELATIVE HUMIDITY: ratio of actual mass of water vapour in a gas compared to the maximum amount of water vapour that the gas could contain. This can be expressed in terms of vapour pressure or as a percentage.

$$\frac{\textbf{Actual vapour pressure}}{\textbf{Saturated vapour pressure}}$$

Effect of Temperature on Humidity

Increasing temp **does not affect absolute humidity** as the mass of water vapour is the same. However, increasing temperature **increases SVP** (the max amount of water vapour a gas may contain) and hence **reduces relative humidity**.



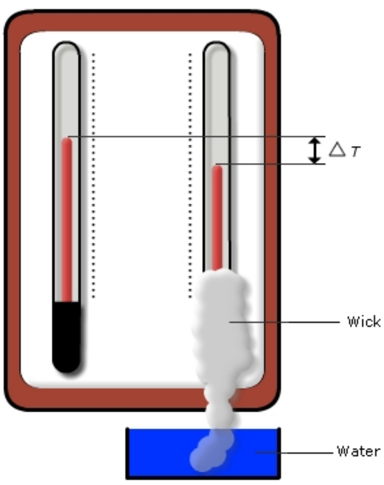
At sea level, 20°C, SVP = 17g/m³

At sea level, 37°C, SVP = 44g/m³

If 2 m³ air, fully saturated with water vapour at 20°C and at sea level, is then heated to 37°C:

- Absolute humidity: 17g/m³
- Relative humidity: 17/44 = 39%

Effect of humidity on temperature: A change in humidity will also cause a change in temperature through **latent heat of vaporisation**. This can be used in the measurement of humidity using a **wet and dry bulb thermometer** (measures relative humidity). By principle, the greater the humidity of the atmosphere, the less likely the water to evaporate and cause a drop in the temperature reading. At 100% SVP, there will be no drop.



Effect of Pressure on Humidity

The SVP is unaffected by changes in pressure. The ideal gas law applies for gas which is not yet vapour and therefore, a compression in volume of air results in **increased water vapour pressure** according to Dalton's law and **relative humidity will increase**.

Dew Point

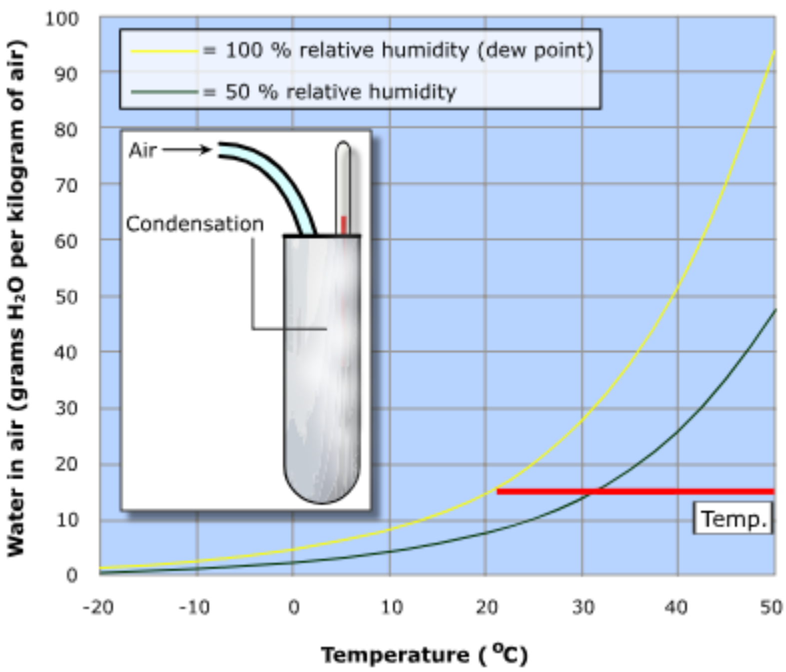
The temperature to which a **given volume of gas must be cooled** in order for **water vapour to condense** out into water – **this is the point at which 100% relative humidity is achieved**. If this point falls **below freezing**, it is called the **frost point**.

The **higher the relative humidity**, the **less temperature drop** is required to reach dew point and vice versa. On a typical British summer day, with a temperature of 18°C, the dew point is about 8°C. In the early evening, when it is 12°C outside, the dew point is still 8°C. If the temperature reaches about 7°C overnight then the water vapour condenses out and forms dew on the ground.

Measuring Humidity

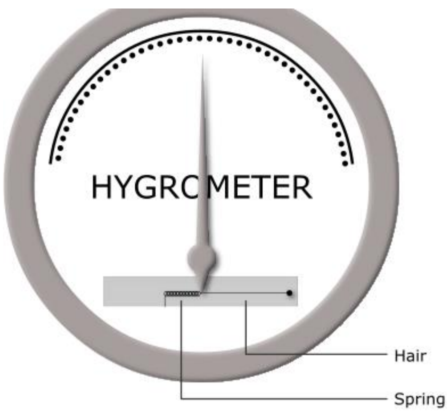
The relationship between humidity and dew point can be used to calculate relative humidity when the dew point and saturated vapour pressure is known.

Regnault's Hygrometer: has a silver tube containing ether through which air is bubbled reducing its temperature. The point at which condensation forms on the outside of the tube is the **dew point** (100% relative humidity).



There are other ways of measuring humidity using physical principles that are altered by varying levels of moisture and effect of moisture on substances and may include:

- Mass measurement
- Temp changes from latent heat of vaporisation
- Effect of moisture on electrical circuits
- Formation of dew point
- Physical change in a porous material i.e. **hair hygrometer** which also measures relative humidity.



Humidity in the Respiratory Tract

Effective humidification allows prevention of respiratory epithelial damage and its products and function i.e. moist secretions, prevention of mucus plugs, ciliary activity, improved gas exchange etc.

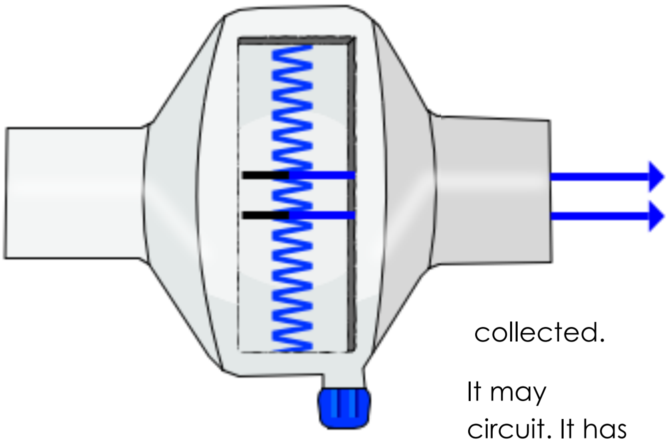
Normally, air entering the upper trachea has 34 g/m^3 (compared to 17g/m^3 at room temperature). This is unlikely in an intubated patient where the mucous membranes are bypassed and anaesthetic gases are supplied dry and minimally humidified. The following section describes methods of humidification:

Methods of Humidification

Droplet size is important when providing humidification:

- **1 micron –** deposited in the alveoli and exhaled.
- **5 microns –** deposited in trachea (does not humidify the distal airways)
- **20 microns –** condensation on equipment

Heat and Moisture Exchanger

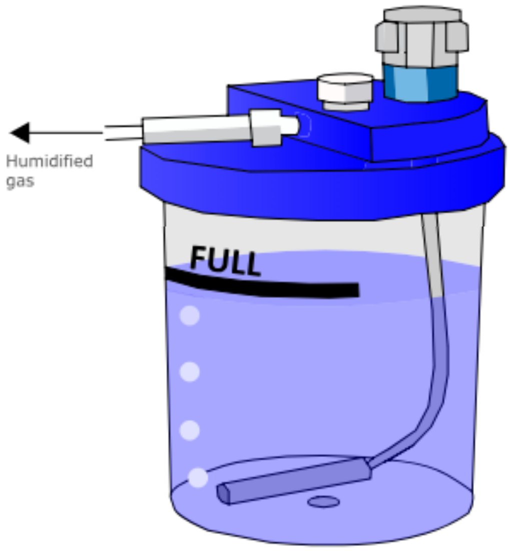


Most commonly used for invasively ventilated patients. It has an internal paper/sponge/foam impregnated with a **hygroscopic substance**. When water vapour passes through, it condenses and provides latent heat to the HME so that the next inhale will warm the cooler inspired air and absorb the moisture collected.

It is cheap and can have a bacterial/viral filter. It may however increase resistance in the breathing circuit. It has 70% efficiency.

Max: 35g/m^3

Cold Water Bath/Bubble Humidifier



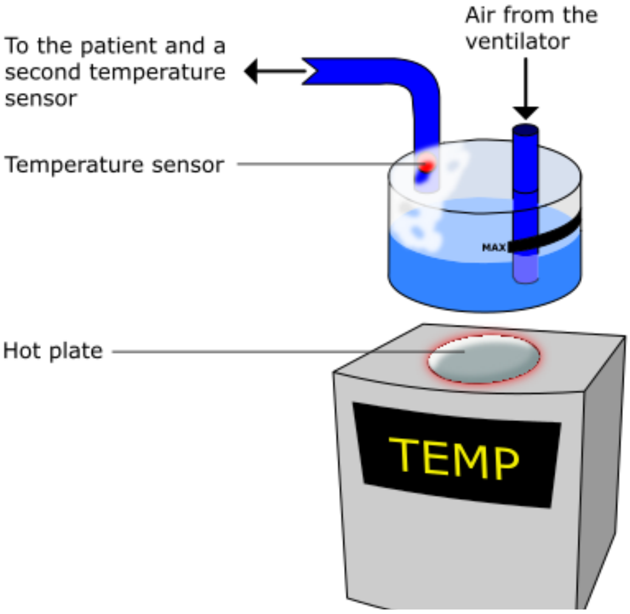
Most commonly used in the ward setting. Dry gas is bubbled through water at room temperature. Cheap and easy to run with no power source required. There is a loss of heat through latent heat of vaporisation so relative humidity is reduced. It is 30% efficient due to this and the formation of large bubbles.

Max: 10g/m^3

Hot Water Bath

As with the cold-water bath but with a heated element as to prevent heat lost through latent heat of vaporisation increasing the efficiency to 90%. There is a possibility of scalding and hyperthermia in young children. There is therefore a controlled temperature at the humidifier site and patient end. Temp is usually 40-45°C.

Max: 40g/m³

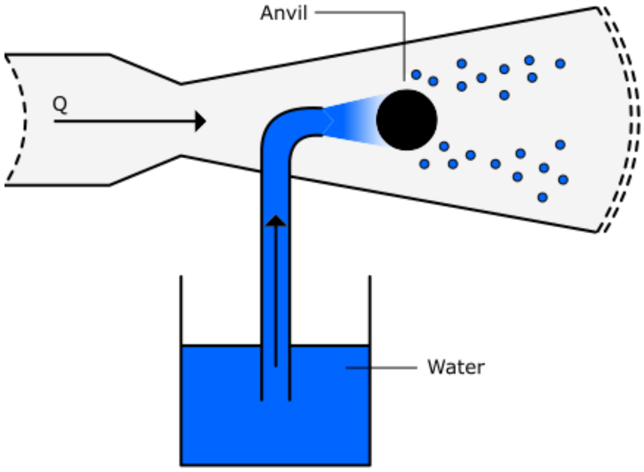


Nebulizer

These may be gas driven or ultrasonic.

- **Gas driven:** high flow gas is ejected close to the exit of a tube filled with water. This causes a drop in pressure (**Bernoulli effect**) and brings up water. The steam then hits an anvil to divide the droplets: *50-60g/m³*

- **Ultrasonic:** Water is dropped onto a vibrating plate at ultrasonic frequency where tiny droplets are formed (most effective). *80-90g/m³*



This has optimal effectiveness at 100% efficiency. This may even be too effective and may cause water overload – especially in children.

Heated Element Humidifier

Not common due to the risk of burns and alteration of chemical properties of anaesthetic agents. Water is vaporised by dropping onto a 100°C heated element

Cascade Humidifier

This is a refined heated water bath. Gas is bubbled through a perforated screen at the base of a tube within the heated water bath. There is a large surface area allowing full humidification whilst avoiding risk of burns to the patient. Equipment is bulky however.

Solvents and Solutes

(07d_01_11)

Solution: a homogenous mixture of two or more substances.

The simplest example of a solution involving 2 substances is when a **solute** (substance) is dissolved in a **solvent** (another substance). The result will usually be of the same liquid state as the original solvent. The solute may be:

- **Solid**: i.e. salts
- **Liquid** i.e. ethanol
- **Gas** i.e. O_2 in water (fish extract this) and CO_2 in carbonated drinks. Depressurising the drink will release gas from solution and is known as **effervescence**.

Note:

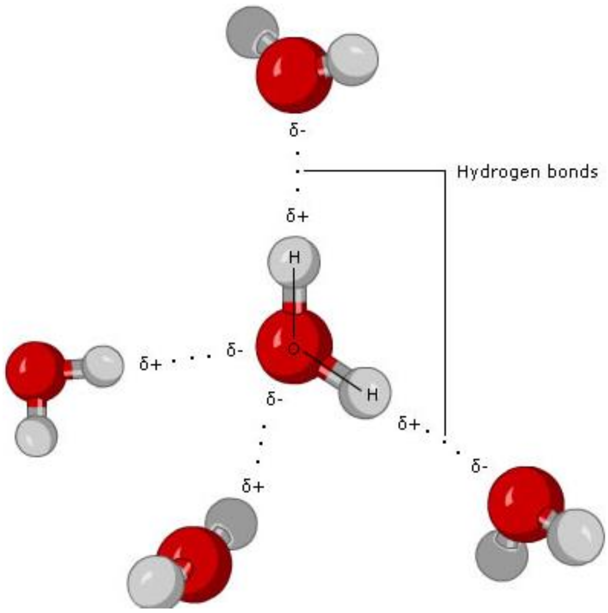
- Some solid metals can dissolve in other metals to form a special type of solution known as an **alloy**
- A mixture of gases, e.g. air, would usually be called just that - a **mixture**
- Solutions should be differentiated from non-homogenous mixtures such as suspensions and colloids

Water

It is one of the best solvents on Earth due to its **polar nature**. Furthermore, despite its relatively low molecular size, it has a much higher melting/boiling point, heat of vaporisation and surface tension that would be predicted due to its **hydrogen bonds** unique to water.

Covalent O-H bonds form through shared pairs of electrons → **non-linear** arrangement making it **polar** to allow **negative O** and **positive H** prominences.

Water can form 4 H-bonds per molecule which is the reason for its properties mentioned above:

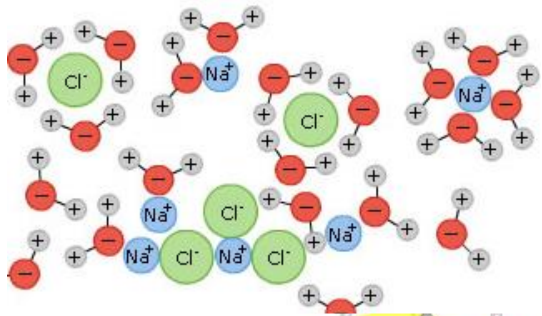


ICE

Hydrogen bonds form a space filling 3D structure and actually **expands on freezing**. It is the only non-metallic substance to expand when solidifying. It is **less dense than liquid water** (most dense at +4°C). This is why marine life can exist below the surface of ice.

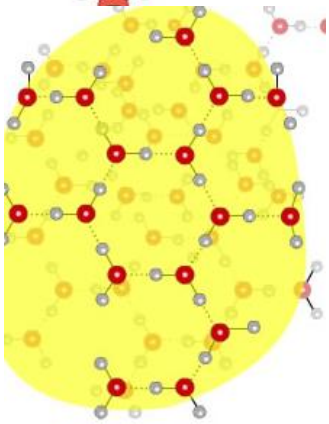
Water as a Solvent

Solutes that dissolve in water are known as **hydrophilic.** These include ionic salts, non-ionic but polar substances i.e. DNA and other molecules such as ketones. Non-polar molecules are **hydrophobic** such as benzene.



Water forms **hydration shells** surrounding the components of a salt i.e. Cl^- and Na^+ (right)

Larger more complex hydration shells may form around larger, non-polar solutes in a cage-like structure known as **clathrate formation** (right):



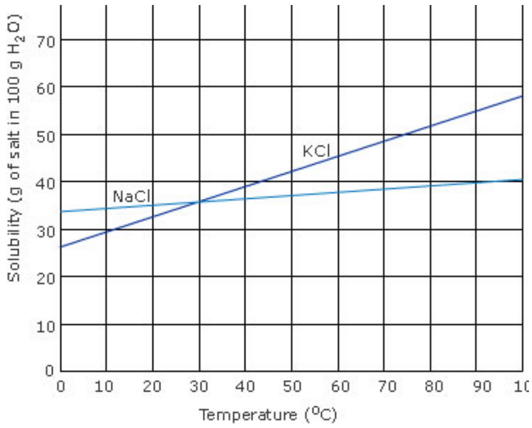
Solubility

Describes the **ability of a substance** to **dissolve in a solvent**. This is determined by the balance of intermolecular forces between solvent and solute which subsequently is affected by:

- Pressure
- Temperature
- The nature of the solvent
- The nature of the solute

Pressure: This **influences gases** as solutes more than solids in liquids through **Henry's law**. The CO_2 is put under pressure in the manufacture of carbonated drinks. They come out of solution when pressure reduces through **effervescent bubbles**.

Temperature: For *most* **solid** solutes, **increasing temperature increases solubility** to varying degrees (see chart).



For **gaseous** solutes, **increasing temperature reduces solubility**. To be aware when warming IVI. In hot conditions, carbonated drinks fizz less as less CO_2 is dissolved.

Polarity: **Polar molecules** are hydrophilic and have **greater solubility** in **polar solvents**, for example NaCl in water.

Non-polar lipophilic solutes are relatively insoluble in polar solvents, for example oil in water. They do, however, dissolve well in non-polar solvents such as benzene.

Quantifying Solubility

Solubility therefore, is a **measure of the maximum amount of solute that can dissolve per amount of solvent** under specified conditions of temperature and pressure.

The volume and hence proportion of solute to solvent will vary by temperature; therefore, the **concentration** is better expressed in **mass in mass** i.e. mg of solute in mg of solvent. Lidocaine 1% means 1g in 100g of water or 1g in 100ml.

Mixtures, Suspensions and Colloids

Mixture describes any 2 or more substances dispersed through each other but retaining their original identity i.e. flour and water. Unlike solutions then, they do not combine chemically to make a new homogenous substance – rather are **non-homogenous**.

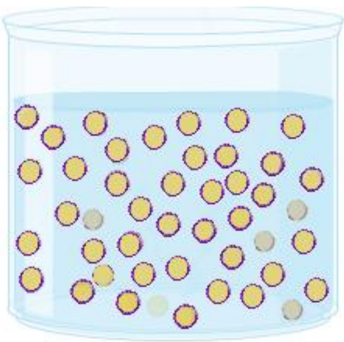
Suspensions are mixtures that eventually separate out over a varying amount of time i.e. mud and clay in water, cinnamon and water and the heavier settling out first.

Colloids: a type of mixture where a substance is dispersed evenly through another and consists of:

- *Internal phase:* the dispersed substance of small 1-1000nm diameter particles
- *External phase:* In which the internal phase is dispersed.

They do not settle under the influence of gravity. Liquid in liquid systems are known as **emulsions**. Another example is smoke in air and whipped cream (air internal phase within a liquid external phase).

Emulsions



Defined as a **mixture of ≥2 immiscible liquids** which evenly disperse after input of energy but these tend to revert back to their normal phase (i.e. become separated like oil and water) and are no longer emulsions. To prevent reversion, **emulsifiers** can help stabilise the emulsions including **surfactants** such as egg yolk and soya lecithin (*purple in image*). This binds **electrostatically** to the **internal phase** (*yellow balls*) to help maintain its position in relation to the molecules in the other substance (*liquid seen*) through electrostatic forces.

Propofol is an example which is lipid soluble held in a watery base through the help of egg and soya lecithin emulsifiers.

Colloid Suspensions

- **Gelatin colloids:** molecular weight of 30 000 Da formed from hydrolysed collagens in animal tissue and will remain within the circulation for about 2-4 hours until the protein is broken down into peptides. Risk of anaphylaxis.
- **Dextran colloids:** Dextran 70 has a molecular weight of 70 000 Da and additionally helps reduce viscosity of plasma. They are made from polymerisation of glucose and can vary in molecular weights.
- **Starch colloids:** (for example HES, hydroxyethyl starch) large range of molecular weights (up to 200 000 Da) and will remain within the circulation for up to 24 hours. Formed from amylopectins linked to hydroxyethyl groups – expensive. Reduced risk of anaphylaxis but there is a risk of coagulopathy and persisting pruritus.

Colligative Properties

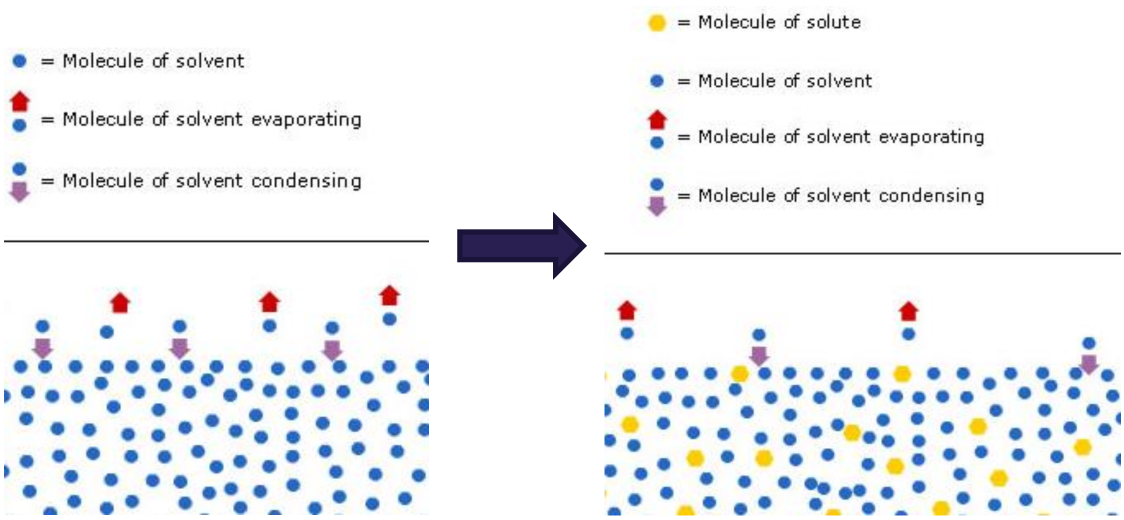
Physical properties of a solution that vary by the number of dissolved particles rather than by the identity of the solute. For example, addition of salt to water will change the following properties according to the *number of particles dissolved*:

- Fall in vapour pressure
- Elevation of boiling point
- Depression of freezing point
- Changes in osmotic pressure

Fall in Vapour Pressure

Raoult's Law: The overall vapour pressure of a solution depends on the vapour pressure of each component in solution.

The solvent will have a specific saturated vapour pressure… With continual addition of a solute, the mole fraction of the solute increases and therefore, the total vapour pressure of the solvent decreases to keep the SVP constant.

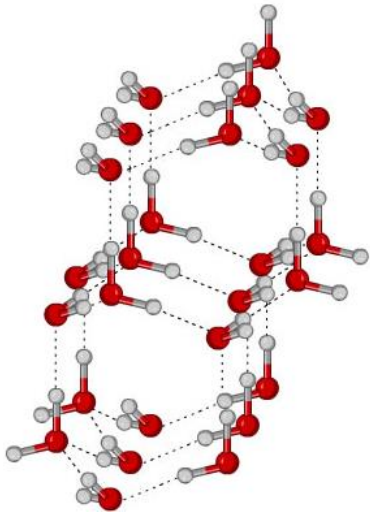


Elevation of Boiling Point

Solvent boils when its vapour pressure matches the atmospheric pressure. With the addition of a solute, **the vapour pressure falls** and therefore, a **higher temperature** is required to make the solution boil.

1 mole of solute dissolved in 1kg of water elevates boiling point by 0.51°C which is why potatoes cook quicker in boiling water with salt added!

Depression of Freezing Point



When liquids solidify, they form **regular, ordered matrix-like** molecular structures (ice shown in image). **Solutes** disrupt the formation of the solid structure and freezing point is depressed.

1 mole of solute dissolved in 1kg of water reduces freezing point by 1.86°C. This is the reason why salt is spread on icy roads!

Changes in Osmotic Pressure

A form of hydrostatic pressure produced due to a difference in concentration of solutions separated by a semi-permeable membrane. Solutes increase the molarity which will increase the osmotic pressure by the **van 't Hoff formula** (dealt with in the osmosis lecture).

Colligative property	Change/mole of solute /kg of solvent
Boiling point elevation	0.52°C
Freezing point depression	1.86°C
Vapour pressure depression	0.04 kPa
Osmotic pressure elevation	2261 kPa

Osmosis

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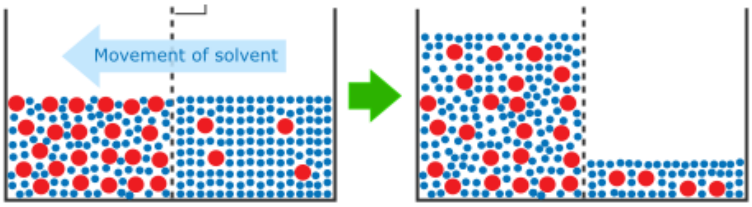
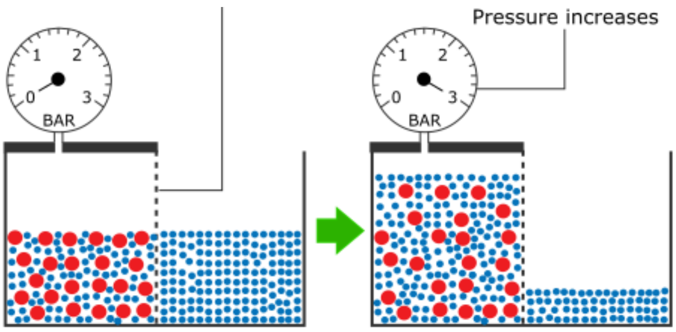


Osmosis is a physical process in which solvent moves across a **semi-permeable membrane**, from a solution of **low concentration** (hypotonic) to a solution of **high concentration** (hypertonic). The semi-permeable membrane is permeable to the solvent but not the solute.

This process occurs with slugs and in erythrocytes.

Osmotic pressure



This is defined as the **hydrostatic pressure** exerted within a **container of solution** separated by a semi-permeable membrane.

Although the solution in the container may still be relatively hypertonic, once it reaches the osmotic pressure of the solution, osmosis will cease.

This is a **colligative property** of a solution which means it is dependent on the number of solute molecules (molar concentration) rather than the nature of the solute. I.e. the same moles of glucose will exert the same oncotic pressure as the same number of moles of NaCl solute.

Measuring osmotic pressure

Osmometers use colligative properties such as the reduction in vapour pressure or freezing point depression to indirectly determine the number of osmotically active particles in a solution.

Urine or plasma samples are put into a tube within a refrigerated bath, and the temperature at which the specimen freezes gives an indirect measurement of its osmolality.

Van 't Hoff Equation

Osmotic pressure (π) is determined by the following equation:

$$\pi = iMRT$$

i = the van 't Hoff factor
M = the molarity
R = the Universal Gas Constant, 8.31 joules/Kelvin/mole
T = absolute temperature in Kelvin

The molarity shows that osmotic pressure is a colligative property.

The ideal gas analogy: In a 22.4L _solution_ containing 1 mole of solute at 0°C (273.15 K).

Oncotic pressure = (1x8.31x273.15)/22.4 = 101.325 kPa (or 1bar).

Note that this is analogous to Avogadro's hypothesis and the principle that 1 mole of a _gas_ will exert 1atm pressure in 22.4L volume.

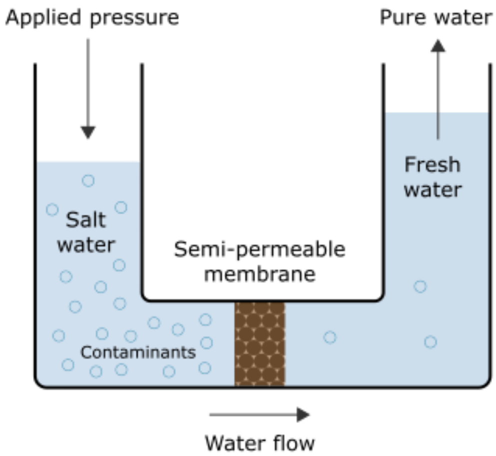
Note: A 1 molar solution is not the same as a solution containing 1 mole of solute. 22.4 litres of a 1 molar solution would exert 22.4 atmospheres of osmotic pressure.

In humans, the osmotic gradient never equals as this will result in death and is due to ionic pumps maintaining concentrations of ions across cell membranes.

Reverse Osmosis

This is when an **increased pressure is applied** to the area of **high solute concentration** to allow **movement** of solute **up the concentration gradient to** the area of low solute concentration.

This technique is used to desalinate seawater to produce fresh drinking water at a pressure of **50 bar.** The **osmotic pressure of seawater is around 24 bar**.



Osmolality

Osmole is the number of moles of a compound contributing to the total osmotic pressure. 1 mole of NaCl gives 2 osmoles whilst 1 mole of glucose gives 1 osmole in solution.

Osmolality is the preferred term over osmolarity because osmolality is not affected by a change in temperature as osmolarity is:

- **OsmolaLity**: Number of osmoles per ***kg of solvent***
- **OsmolaRity**: Number of osmoles per ***litre of solvent***

Tonicity is the osmotic property of a solution **in relation to the specific semi-permeable membrane**. Therefore, this term is not used interchangeably with osmolality. In medicine, tonicity is compared to the cell membrane.

Plasma Osmolality

Normal is 280-303 mosmol/kg. Intracellular osmolality will be affected accordingly. This property is employed by cancer surgeons in the hope of flooding a tumour field following excision with hypotonic solution to cause cell lysis.

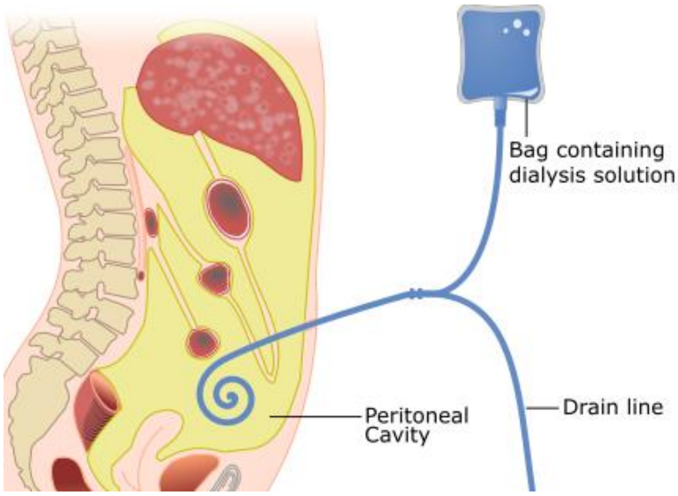
IV fluid manufacturing requires referencing to the plasma (or extracellular) osmolality:

Electrolyte	Plasma	Hartmann's (Ringer's lactate)	Normal saline	5% Glucose (50 g in 1000 ml)
Na^+	143	131	154	-
K^+	5	5	-	-
Ca^{2+}	1.3	2	-	-
Lactate/ HCO_3^-	24	29	-	-
Cl^-	103	111	154	-
Urea	5	-	-	-
Glucose	5	-	-	278
Proteins	1.1	-	-	-
Osmolality	**287.4**	**278**	**308**	**278**

In Practice

DIALYSIS:

Peritoneal Dialysis: A sterile solution of glucose and salts is run into the peritoneal cavity via a special catheter called a Tenckhoff catheter. Water and toxins move via osmosis and diffusion out from the circulating plasma across the semi-permeable membrane of the peritoneum. They are then removed from the body when the dialysis fluid is run out again via the catheter.



Haemodialysis: A countercurrent system, where the blood and dialysate are pumped in opposite directions, improves the efficiency and efficacy of the haemodialysis.

Continuous veno-venous haemofiltration (CVVH): is a further form of renal replacement therapy, often employed in ICU. Haemofiltration uses hydrostatic pressure, rather than osmotic pressure, to drive fluid and small solutes across a semi-permeable membrane and out from the circulating blood

Mannitol: Is freely filtered at the glomerulus and not reabsorbed so increases osmolality of filtrate and increases loss of free water from the body. This therefore, **increases plasma osmolality** and may help in reduction of ICP in head injury patients.

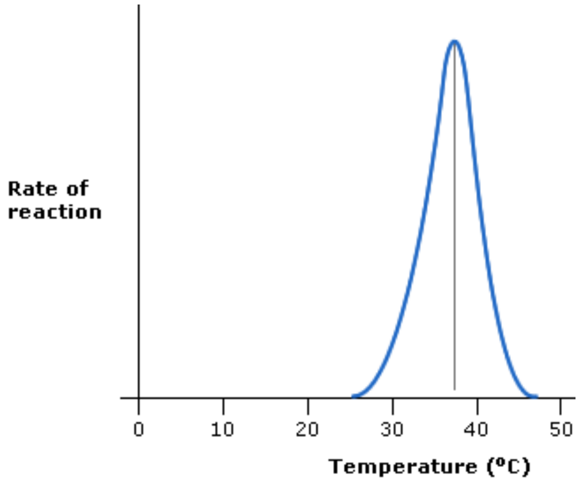
Heat Transfer and Temperature

(07d_01_13 **AND** 07d_01_14)

Temperature dependent enzymatic reactions

This is the core of all physiology, biochemistry and pharmacology. As the **temperature increases**, the **kinetic energy** of molecules **increases** with increasing likelihood of substrate-enzyme collision → **increased rate of reaction**.

After a point, the enzyme structure **denatures/breaks down** due to molecular binding disruption. The temperature at which enzyme activity is maximal is known as **optimal temperature**. This is around 37°C in the human body. This is much less in the testes.



Definitions

ENERGY: the ability to **do work** and can be mechanical, chemical, electrical or thermal (heat) energy

HEAT (energy): measurement of the **total energy of molecular motion** in a substance (which cannot be measured directly) and is dependent on the:

- *Kinetic energy* of the molecules in the substance
- *Physical state* of the substance
- *Mass* of the substance

TEMPERATURE: measure of the **average kinetic energy** of the atoms which make up a substance. When measured in Kelvin, it is directly proportional to the average kinetic energy of the molecules of that substance.

Comparison between temperature and heat: When comparing a pan of boiling water to an iceberg: The **iceberg** has much **more total heat energy** due to its **greater mass**. However on contact, **heat energy** is transferred from **boiling water to the iceberg** so **temperature** is defined by the **likelihood for one substance to transfer heat energy to another**.

Likewise, an operating theatre has greater heat energy than a human body but the body has higher temperature so will transfer heat energy to the operating theatre.

Heat Capacity

Specific heat capacity is the amount of heat energy required to raise the temperature of a mass of 1kg by 1 Kelvin.

$$c = \Delta Q / m\Delta T$$

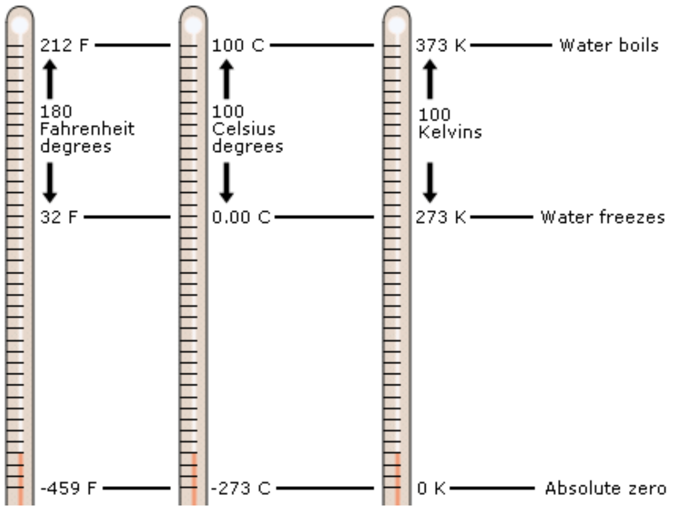
where…

- ***c*** = the specific heat capacity of the substance
- Δ***Q*** = the amount of heat energy required in kilojoules (kJ)
- ***m*** = the mass of the substance being heated in kilograms (kg)
- Δ***T*** = the change in temperature in Kelvin (K)

As an example, specific heat capacity of **water** is **4.18kJ/kg/K**

1 kcal = 4.18 kJ, therefore = **1 kcal/kg/K**.

As 1 Kelvin is 1°C, it can also be: **1 kcal/kg/°C**



Heat Capacity is the amount of heat energy required to raise the temperature of a given object by 1 Kelvin. For example… 5L of water is 5kg in mass (density = 1g/cm³), therefore, is: 4.18 kJ/kg/K × 5 kg = **20.9 kJ/K**

Heat Capacity = Specific Heat Capacity X Weight

Worked example…

Transfusion of 1L 4°C blood with a specific heat capacity of 3.6 kJ/kg/°C to a 70kg patient at 37°C with specific heat capacity of 3.5 kJ/kg/°C. What is the final temperature of the patient? Density of blood is approximately 1.125kg/L.

The amount of heat lost by the patient must be equal to the amount of heat energy gained by the blood. Therefore, from rearrangement of the equation above:

The amount of heat transferred = mass × change in temperature × specific heat capacity

OR

$$\Delta Q = c.m.\Delta T$$

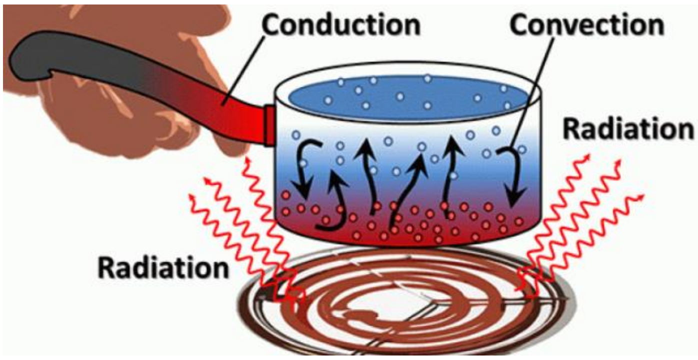
1.125 kg × (*T* – 4°C) × 3.6 kJ/kg/°C = 70 kg × (37°C - *T*) × 3.5 kJ/kg/°C

T = 36.5 °C

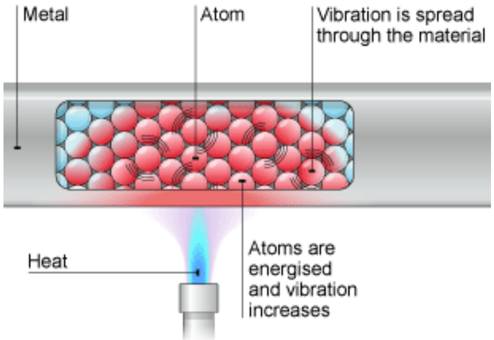
Heat Transfer

The passage of energy from a warmer body to a cooler body. There are 3 main methods of heat transfer (evaporation being a combination of the following):

1. Conduction
2. Convection
3. Radiation



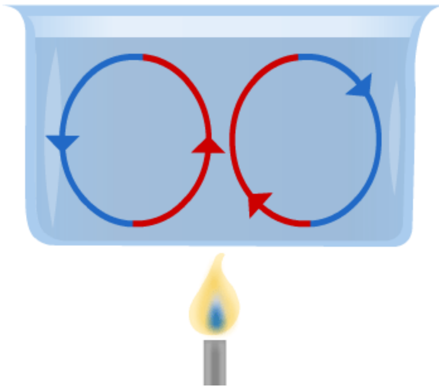
1. CONDUCTION



Heat transfer due to **collision of molecules** of two substances with differing temperatures. **Molecules** of the substance with **higher temperature have a higher kinetic energy** and collide **with molecules of lower temperature with lower kinetic energy**.

In the OT, air is a poor conductor of heat, the table is well insulated and the area of contact between the table and patient is relatively small. Therefore, conduction is not an important method of heat loss in theatre.

2. CONVECTION



Heat transfer by **circulation through a gas or liquid**. In theatre, the surrounding air around the patient is warmed → made less dense → rises → new cooler air current is closer to the patient to be warmed and a **convection current** is created. This is continuous until an equilibrium of surrounding temperature is reached and accounts for 30% of heat loss in theatre.

3. RADIATION

Differs as **does not require matter for heat transfer** (the method the sun heats the earth). All objects >0 Kelvin emit radiation as **electromagnetic waves**. The overall amount of radiation emitted and absorbed by an object is a function of the temperature of the object. Accounts for 40% of the body's heat loss in theatre.

Electromagnetic waves falling in the **infrared spectrum** are felt as heat. The **Stefan-Boltzmann law** relates the total amount of radiation emitted as a function of its temperature:

$$E = sT^4$$

- E = the total amount of radiation emitted per m^2 of an object
- **s** = a constant
- T = the temperature in Kelvin of the object

Evaporation: This loses heat through the process of latent heat of vaporisation (see prev lecture). Evaporative heat loss may occur when sweat or antiseptic solution evaporates from the skin or fluid evaporates from exposed moist internal body cavities. Heat may be transferred to fluid on the exposed surface through conduction and taken away by convection. Accounts for **20%** of heat loss.

Overall

Radiation	40%
Convection	30%
Evaporation	20%

The remaining 10% of heat loss is accounted for by losses through the respiratory tract due to **humidification (8%)** and **warming (2%)** of the inspired gases. This occurs through the combination of the above 3 processes.

Factors Affecting Heat Loss

Theatre Environment

Radiation: The temperature in theatre needs to be kept lower than the ward environment for staff comfort, therefore, increased radiation of heat occurs from the patient

Convection: Theatres have **laminar flow** systems to replenish air in theatre to minimise risk of bacterial contamination. Therefore, this increases heat loss via convection

Evaporation: This is dependent on the relative humidity of the environment which decreases with increasing temperature. Theatre relative humidity is usually kept at around 50%.

Anaesthesia

Results in increased heat loss and decreased heat production whilst obtunding the normal physiological response to hypothermia.

Increased Heat Loss: Most anaesthetic agents cause **vasodilation** resulting in radiative and conductive heat loss. Convection occurs to bring the blood from the core to the periphery causing rapid reduction in central temperature. **Latent heat of vaporisation** causes the loss of heat in the respiratory tract and therefore, humidification and warming of inhaled gases is required.

Reduced Heat Production:

Basal metabolic rate	General anaesthesia results in a fall in basal metabolic rate and, therefore, reduces heat generation by metabolically active tissues such as the liver.
Spontaneous respiration	NMBs and high dose opioids obtund spontaneous respiration in the patient and this reduces heat generation by respiratory muscle contraction.
Resting muscle tone	All resting muscle tone is reduced which also reduces heat production.
Physiological response to hypothermia	Anaesthetic agents blunt the normal physiological response to hypothermia. An anaesthetised patient is unable to generate heat by moving or shivering and has impaired vasoconstriction and piloerection in response to hypothermia.
Behavioural responses	The normal behavioural responses, such as finding a warmer environment and dressing appropriately, are removed.

The problem is further compounded by administration of cold fluids (room temp) and blood products (4°C).

Surgical

Moist body cavities exposed during operations cause increased evaporative heat losses. Sometimes, **cold irrigation fluids** are used. Long cases have greater potential for total heat loss. Surgery that promote 3rd space losses mean more IVI below body temperature is administered…

The Patient

Worsened heat loss at **extremes of age**:

- **Paediatric patients: increased body surface area to weight ratio** and therefore lose heat more quickly. Disproportionate losses may occur through the head, as it is much larger in relation to the rest of the body in this age group
- **Elderly population:** reduction in basal metabolic rate and lower muscle mass, resulting in reduced heat production. They also have a reduced shivering response and commonly have a reduced layer of insulating adipose tissue

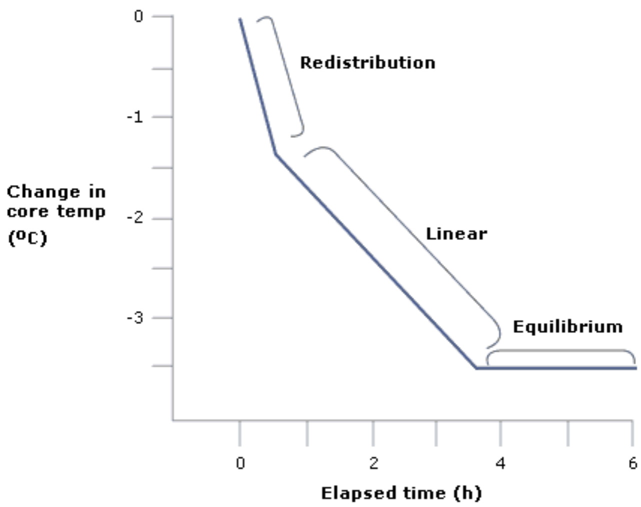
Other pathological conditions may result in a reduced BMR i.e. hypothyroidism

Temperature Loss Patterns in Anaesthesia

There is an **initial sharp decline** on induction of anaesthesia due to **vasodilation** and **redistribution** of core blood to periphery.

There is subsequent **gradual linear loss** of heat until a temperature it reached which is the **new set point** for thermoregulation.

At this point **equilibrium is reached** where loss to environment equals that generated by the patient.



Management of Intraoperative Heat Loss

There are 2 main methods to combat heat loss in theatre:

1. Minimizing the increased heat losses, as incurred through environmental, anaesthetic, surgical and patient factors
2. Actively warming the patient

Minimising Heat Losses

- **Avoid unnecessary exposure** of the patient – pre- & intraoperatively
- Use **head wraps** to combat losses through the head
- Use **reflective space blankets** – reduce heat loss via radiation but are an electrical hazard so mainly used post-operatively.
- Consider **avoiding the use of muscle relaxants**
- Consider the use of **spontaneous breathing techniques**
- Minimize the exposure of moist body cavities – i.e. plastic covering over exposed bowel.
- The theatre environment should be kept warm
- Inhaled gases should be warmed and humidified
- Warm irrigative fluids to body temperature before use

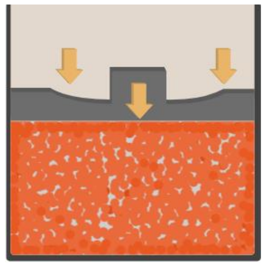
Warming Methods

- **Hot air blankets** aka bear huggers
- Warmer ambient temperatures with use of **overhead radiant heaters** and **warm mattresses** – more common in paediatric theatre.
- **Warming of IV fluids**

Hydrostatics

(07d_01_15)

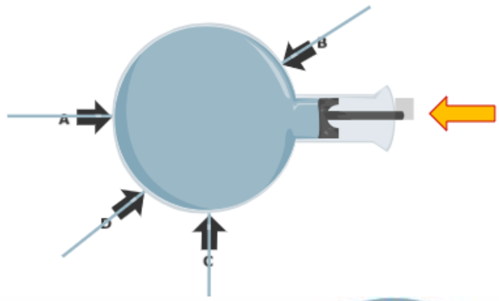
Describes the behaviour of fluids at rest. A fluid is a substance that **cannot exert any permanent forces tangential to a boundary**. It **cannot resist a shearing stress**, so that **pressures are perpendicular to confining surfaces**.



Pressure

Liquids are considered **incompressible to pressure** and therefore do not change density. Pascal's observations (how forces interact with fluids) relate to fluids that are compressed to their maximum and can be compressed no further.

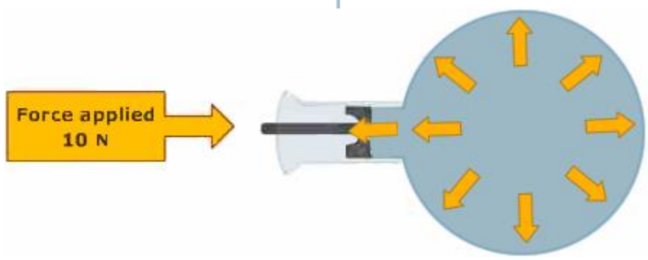
Remember **pressure (Pa) = Force (N) / Area (m^2)**



Pascal's Principle:

The angle at which fluid escapes from a container bears no relation to the direction in which the pressure is applied but leaves perpendicular to where the opening is i.e. punctures at point A, B, C and D.

From this, Pascal concluded that if a uniform pressure was exerted at any point in a liquid, the pressure gives rise to **forces perpendicular to the walls of the container** and forces are not diminished at any point throughout the liquid i.e. 10N represents all arrows.



Jets of Liquid

The pressure at which liquid escapes a hole in a container. This is dependent on the:

1. Force applied
2. Area of the hole in the container

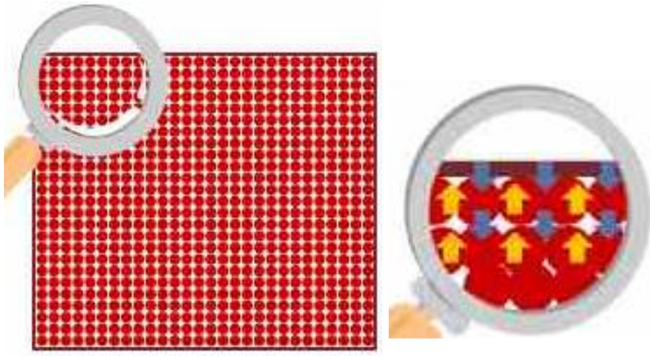
Using the equation above, in the image shown, a 10N force is applied and let's say the area was $0.05m^2$. Therefore, the initial pressure as liquid leaves the container would be:

10/0.05 = 200Pa

In multiple perforations, the total leak area would increase but the 10N force remains the same so the pressure in each jet would be proportionately less.

Liquid in a Container

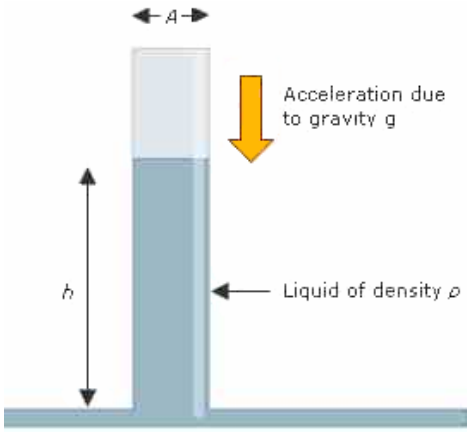
The uppermost/top molecular layer of a fluid will be exerting an upward force against the container wall due to constant collisions. This is balanced if in equilibrium by an inward pressure exerted by the vessel wall resulting in a state of compression. This force is equal according to Newton's third law. The same amount of pressure (according to Pascal) will be exerted upwards by the 2nd layer and throughout the liquid.



Static Fluid Pressure

Forces in a Column

Stevin's Law: Describes the pressure of liquid due to gravity. His law shows that the **pressure exerted by liquid** at the base of a column is *not due to the diameter* of the column but rather **due to the height**.



The force of the liquid is shown by the following formula:

$$F = \rho g h A.$$

Where…

- ρ: The density of the liquid:
- g: The acceleration due to gravity
- h: The height of the liquid in the column
- A: The area of the column (a cross-section will show this)

NB this formula can be derived from F = ma; Volume = Ah; Density = mass/volume

Therefore…

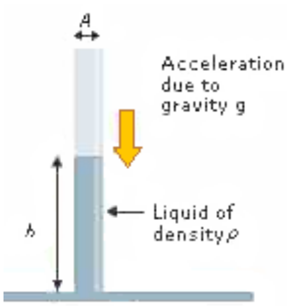
Pressure = Force/Area *or* **F/A** *from the above equation:*

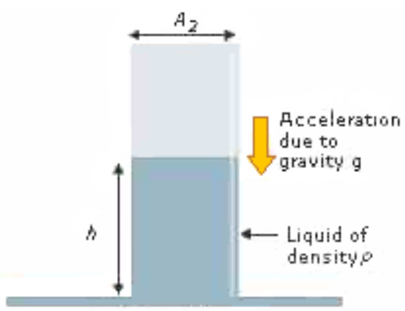
F/A = ρghA/A = *Pressure*

$$\text{Pressure} = \rho g h$$ *that is Pressure = density x acceleration x height*

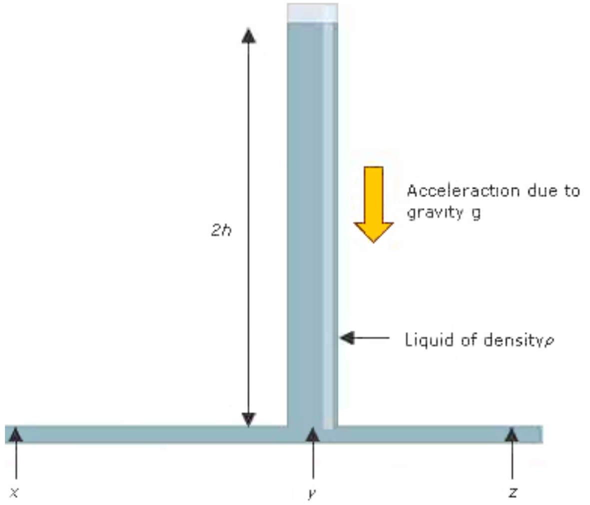
This shows that pressure is not related to the cross-sectional area of the liquid but through height. The pressure exerted by the 2 columns in the images are exactly the same.

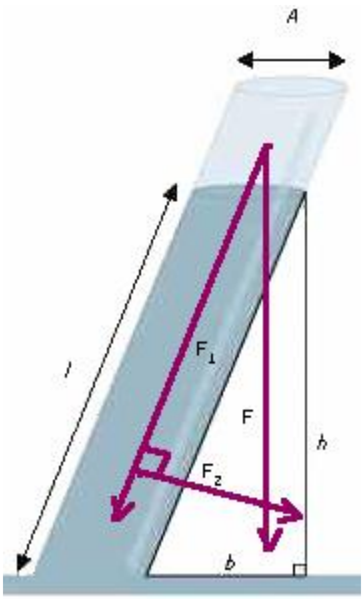
Pressure increases linearly with height of the column of fluid.





Combining Pascal's and Stevin's laws, the pressure exerted by a static column of fluid will be the same across all areas of the liquid (at point x, y and z).



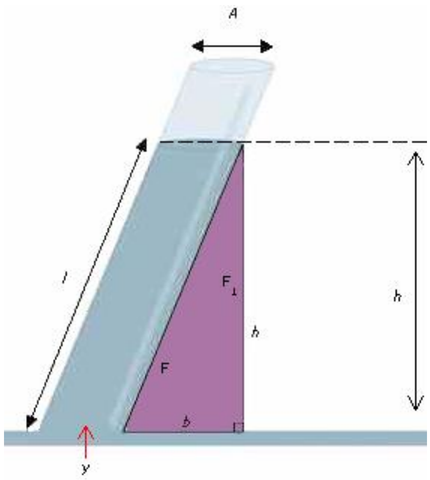


<u>*Angled Column Pressure*</u>

Stevin also described the changes that occur in an angled column. There are different possible directions at which a force may act in this diagram:

If you flip the triangle created by the forces (*F*, F_1, F_2) and rotate it so that the right angles overlie each other you will see that:

- F_1 corresponds to *h*
- F_2 corresponds to *b*
- F corresponds to *l*



This *h* is now used in the **Pressure = ρgh** equation. If the column were vertical, the height would be represented by *l* and therefore, everything remains the same apart from the vertical height, which reduces. Therefore, the **pressure reduces** with the same volume of liquid in an angled column compared to a vertical column.

Additional effect of atmospheric pressure: Stevin only describes the effect of gravity on the pressure of a column of liquid. However, if exposed to atmospheric pressure, the total pressure would be:

$Pa = P_{atm} + \rho gh$

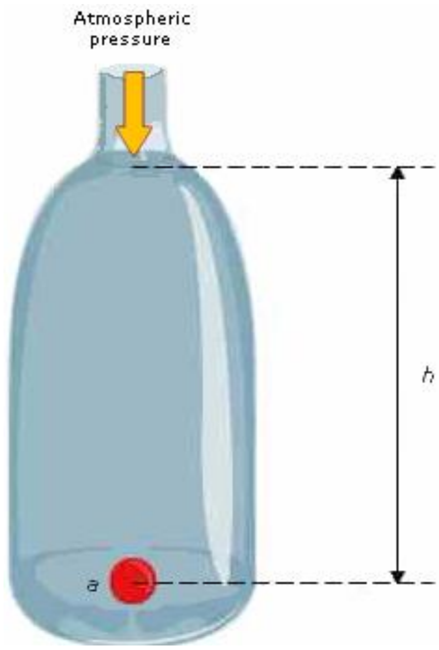
Therefore, the general formula will be:

$$Pa = Pb + \rho gh$$

Where Pb may be any other pressure exerted onto the liquid in the container.

Liquid in a shallow container is affected much more by atmospheric pressure, as the component of height (*h*) is so small. The opposite example can be taken with a submarine where the water pressure makes Patm negligible.

The equation that describes the change of pressure of the atmosphere with height is an exponential one cf. P = ρgh.



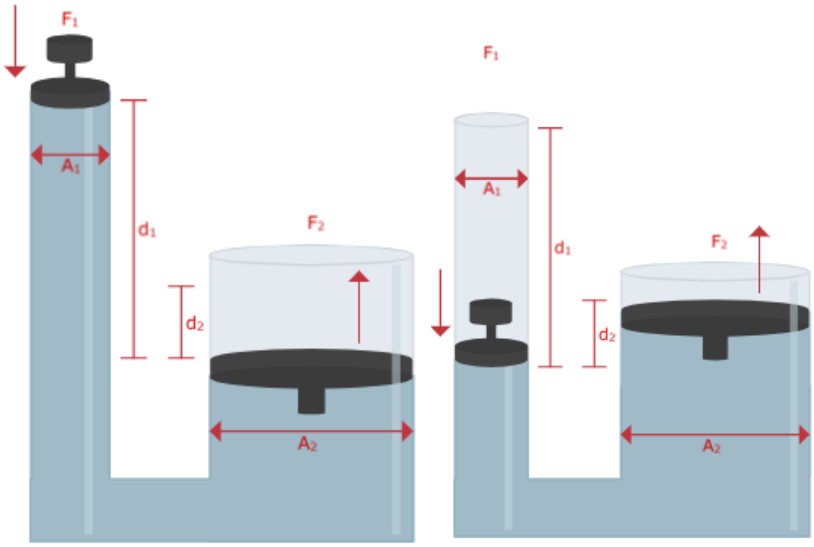
Practical Implications

Hydraulic Press

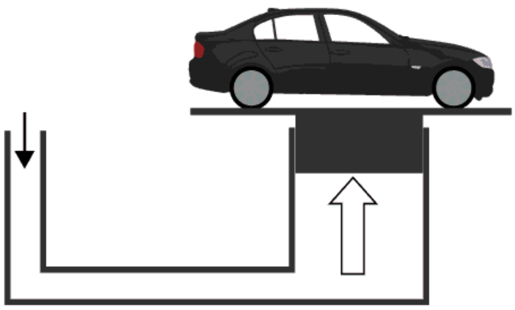
Work = Force x Distance

A heavy load (or force), travelling distance d_2 will be equal to a smaller force travelling a further distance d_1.

Pascal's principle that force transmits equally in a body of liquid due to incompressibility is exploited in this example. Now a heavy mass can move a shorter distance using a smaller force over a longer distance…



For example, this can be used in a **car lift.**



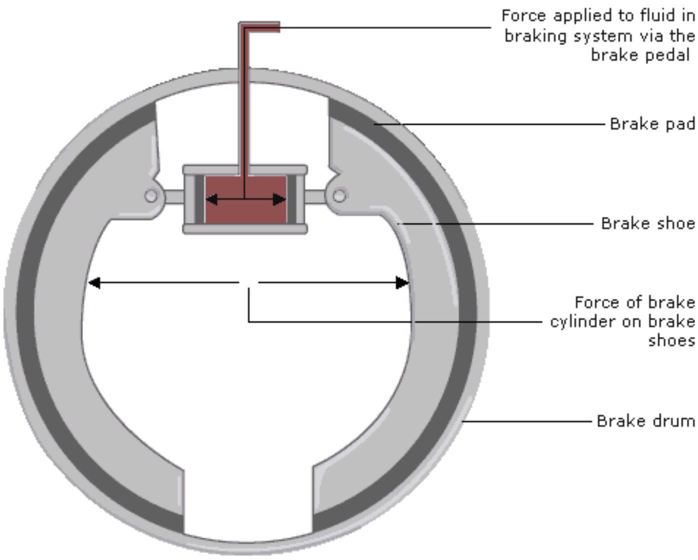
If the lift cylinder was 25cm in diameter and the small cylinder were 1.25cm in diameter, the ratio of the areas would be 1:400. Therefore, **Fn** in the small cylinder would exert **F(nx400)** on the large cylinder. However, to lift the car of **D**, you would have to move the fluid in the small cylinder **Dx400**.

Now try and work out examples of F=6000N to travel *d=10cm*.

Hydraulic brakes use the same principle:

Fluid is transmitted from the pedal to the following mechanism:

The brake cylinder acts as a hydraulic press squeezing the brake pads against the metal drum – friction is generated to stop the car.



Air bags: The air is compressed to its maximum within its casing so Pascal's law applies in this scenario. With a short stopping distance, the seatbelt stretches extending the stopping distance of the driver. The airbag deploys on impact and spreads equally across the larger are of the driver's body in contrast to the seatbelt which would exert large force over a smaller area of the body (increased pressure).

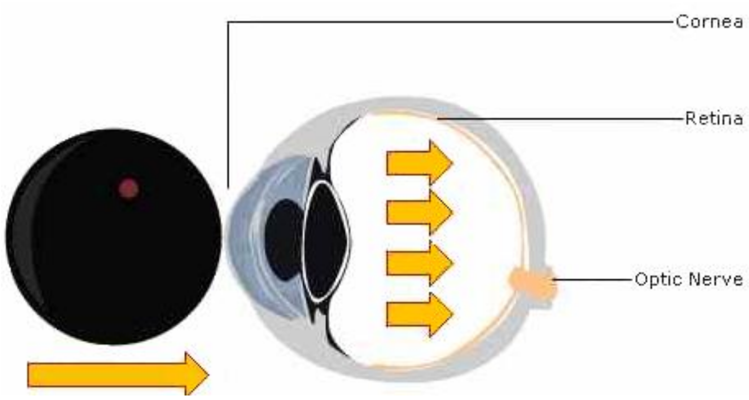
Medical Implications

An air mattress takes advantage of the fact that pressure equals force/area to protect sleepers from bumpy ground, rocks and twigs.

Once the air is compressed to a point it is not compressible any further, Pascal's principle occurs to spread the force over an even distribution. The same principle applies to water beds and clinical beds, which reduce the incidence of ulcers in patients confined to bed for lengthy periods.

Eye impact injury: A blow to the eye by a squash ball can cause more damage than expected due to transmission of pressure to the back of the eye.

By Pascal's principle (although still relatively compressible) states that the force exerted will distribute evenly across all areas of the retina.



PHYSIOLOGICAL MODELS

Fick Principle & Input-Output Principle (IOP)

(07d_02_01)

Fick's principle states that during any time interval, the quantity of a substance entering a compartment in the inflowing blood must equal the sum of the accumulation in the compartment and the quantity leaving in the efferent blood.

Amount IN = Amount taken up by organ + Amount OUT

This fits into the ***umbrella term*** **Input-output principles** but in relation to blood flows, it can be used to measure cardiac output and specific organ flows such as renal blood flow and creatinine clearance.

Calculating Cardiac Output

Using Oxygen

Assumption 1: If we give 100% inspired oxygen from a Bell-Spirometer, we can measure average **oxygen uptake** over time **(VO_2)** and assuming this is **constant** over a **specific time frame** i.e. few minutes, then we can derive a value for VO_2 per minute (depicted with a dot above the V of VO_2 (**$\dot{V}O_2$**)).

Assumption 2: The lungs take up this oxygen and pass it on to arterial blood.

Using an arterial line and a Pulmonary Artery Catheter (PAC), samples of blood may be drawn either side of the lungs to measure oxygen content. Difference in oxygen content should match oxygen uptake when (the unknown) pulmonary blood flow is factored in.

Measurements required to derive flow:

- **VO_2 (oxygen uptake)** can be measured using a Bell spirometer.
- **C_vO_2 (mixed venous** blood oxygen content) can be measured from a pulmonary artery sample.
- **C_aO_2 (arterial blood** oxygen content) can be measured from a peripheral ABG sample.

NOW, the only unknown is Pulmonary Blood Flow **(Q)** (or right ventricular ouput = CO) which can now be determined.

The Equation:

In time (t) of 1 minute; the VO_2 is equal to:

$$VO_2 = Q \times (C_aO_2 - C_vO_2)$$

OR *rearranged into:*

$$Q = VO_2 / (C_aO_2 - C_vO_2)$$

This method presumes the following:

- C_aO_2 and C_vO_2 is constant
  - This is false in developing hypoxia
- **Q** is constant
  - This is false in unstable cardiac output

Therefore, in a sick patient, these are not safe assumptions.

Using Carbon Dioxide

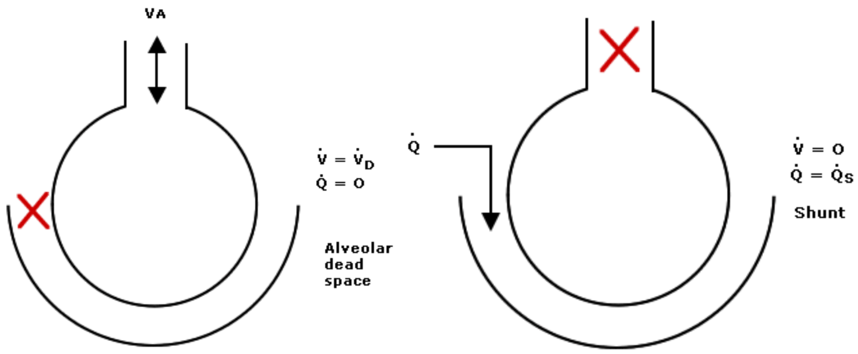
The same equation above can be substituted to account for CO_2 production and removal. This is much less reliable than using oxygen as CO_2 is very easily changeable according to alveolar ventilation.

In contrast, VO_2 is determined by the metabolic rate and elevation of FiO_2 will make little difference to its uptake.

Alveolar Considerations

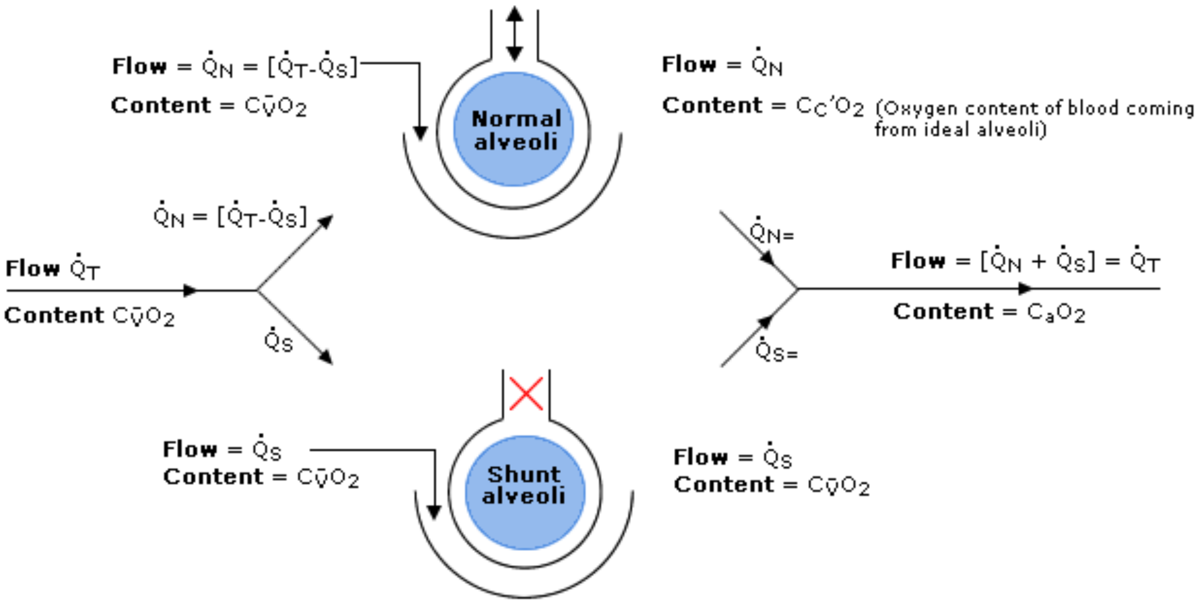
This model works well when considering the lungs act as one giant alveolus. However there are times of **ventilation perfusion mismatching** with the following scenarios:

1. Optimal ventilation and perfusion: *V/Q=1*
2. Ventilated but under-perfused: **Alveolar dead space:** *V/Q >1*
3. Perfused but not ventilated: **Shunt:** *V/Q <1*



Shunt Equation

Using Fick's principle, we can derive the **shunt equation** using normal alveoli and shunted alveoli. This shunt equation will quantify what we expect in arterial oxygen concentration of varying degrees of venous admixture. Whilst it is great to be able to regurgitate this in the exam, it is the ***principles*** of how and why measurements fit into the equation that are more important:



- **QT** = **Total cardiac output flow**
- **QN = Flow through normal alveoli**
- **QS = Flow through unventilated alveoli (SHUNT)**

Think about blood flow (Q) and oxygen content at each point in the pulmonary circulation:

At the Pulmonary Artery: **QT (=QN+QS)** and $\mathbf{CvO_2}$

Afferent → Normal Alveoli: **QN** and $\mathbf{CvO_2}$

Afferent and Efferent to shunted alveoli: **QS** and $\mathbf{CvO_2}$ (REMAINS UNCHANGED)

Normal Alveoli → Efferent: **QN** and $\mathbf{CcO_2}$

Total Efferent CO: **QT** and $\mathbf{CaO_2}$

NOW… for the **shunt equation** which estimates the proportion of blood flow that is not being oxygenated in unventilated alveoli…

(Shunt flow x shunt content) + (Normal flow x content) = (Total flow x O_2 content)

$$(Q_S.C_VO_2) + (Q_N.C_CO_2) = Q_T.C_aO_2 \qquad \text{then, as } Q_N = Q_T - Q_S$$

$$Q_S.C_VO_2 + Q_T.C_CO_2 - Q_SC_CO_2 = Q_T.C_aO_2$$

$$Q_T(C_CO_2 - C_aO_2) = Q_S(C_CO_2 - C_VO_2)$$

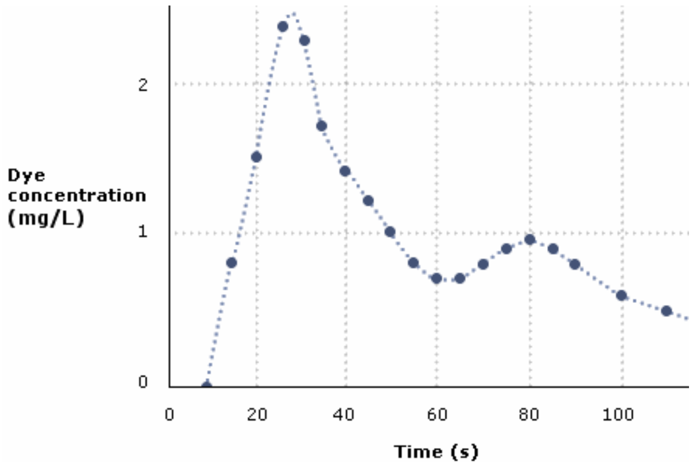
$$Q_S / Q_T = (C_CO_2 - C_aO_2) / (C_CO_2 - C_VO_2)$$

C_CO_2 must be estimated from the alveolar gas equation and haemoglobin-O_2 dissociation curve.

Measuring Cardiac Output

Dye Dilution

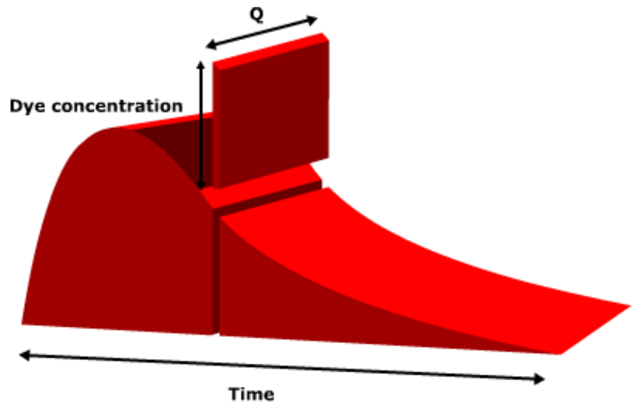
Instead of having to measure oxygen uptake, a known mass of dye (indocyanine) can be injected IV. Dye concentration downstream = mass /volume. Volume over time represents flow or cardiac output. Serial measurements of arterial dye concentration made in the following minutes look like this:



2 peaks arise according to the circulation and recirculation of the dye. Despite the non-steady dye concentration pattern, it is important to realize that this is a steady-state method – depends upon there being a constant cardiac output during the measurement interval

The curve can be imagined 3D with a **flat top** (unlike the image) representing a certain mass of dye as wafers and the sum of these subtracting the recirculation peak must be the injected mass of dye (m):

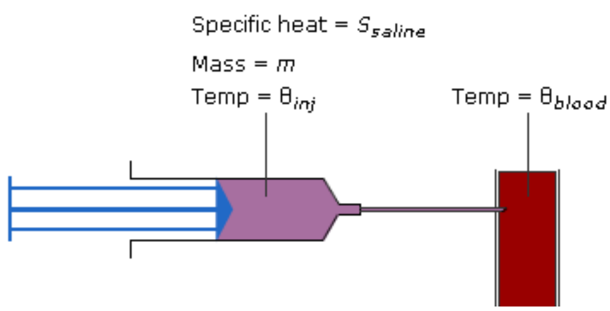
Q = m (mass of dye) **/ AUC** (area under curve)



Thermodilution

Energy content is **measured by temperature** instead of a concentration/mass of dye. In practice this is done by injecting cold saline via the central venous port of a PAC. The saline is thoroughly mixed with blood in the right atrium and ventricle and resulting blood temperature is measured continuously by a thermistor located near the tip of the PAC in the pulmonary artery. The greater the flow (CO) the less the measured change in blood temperature. This results in a much smoother measurements curve without a recirculation peak, is quick to determine and can be repeated frequently.

Methodology…



- **A volume of saline is injected (m) of certain temperature (cold) (θ_{inj})**
- This is **warmed towards body temperature (θ_{blood})** by heat energy from the blood

The total energy required to do this is calculated as

volume x specific heat x change in temperature

OR

$$m \times s_{saline} \times (\theta_{blood} - \theta_{inj})$$

The measured change is no longer an indicator concentration but is a temperature difference so is a measure of the **energy concentration** and is related to the *energy* content of unit mass of substance by the specific heat, *s*.

Now the energy content difference of the saline can be equated with the total volume and therefore flow in the system:

$$m \times s_{saline} \times (\theta_{blood} - \theta_{inj}) = AUC \times s_{blood} \times Q$$

If specific heat of blood and saline have the same value…

$$Q = m(\theta_{blood} - \theta_{inj}) / AUC$$

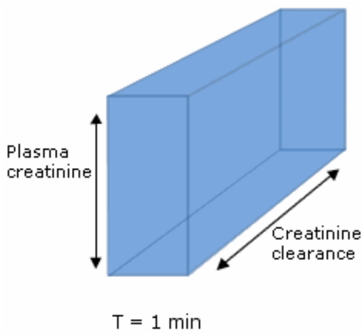
Renal Blood Flow and Creatinine Clearance

The difference between the creatinine content of the renal artery (RA) and renal vein (RV) equals the mass lost to urinary excretion. This measurement would be too invasive for everyday clinical use.

$$M = (C_{RA} - C_{RV})\ Q_{renal}$$

Creatinine Clearance is the volume of blood cleared of creatinine in 1 minute. This is determined through measuring the mass of urinary excretion of creatinine (M) over a timed period and is non-invasive

M = (Urinary Conc X Volume) / Time



As changes in plasma concentration will be reflected in urine concentration if creatinine is totally cleared from renal blood without being reabsorbed:

Therefore: **M = Creatinine clearance X 1 X Plasma Creatinine**

Creatinine clearance = M / Plasma creatinine

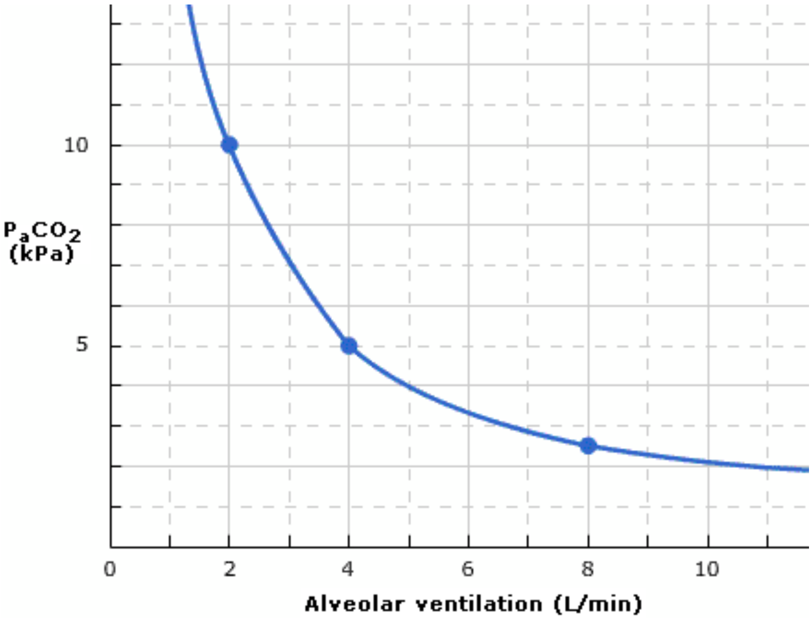
OR

= **Urinary concentration x volume / plasma creatinine concentration**

Alveolar Gas Equation

(07d_02_02)

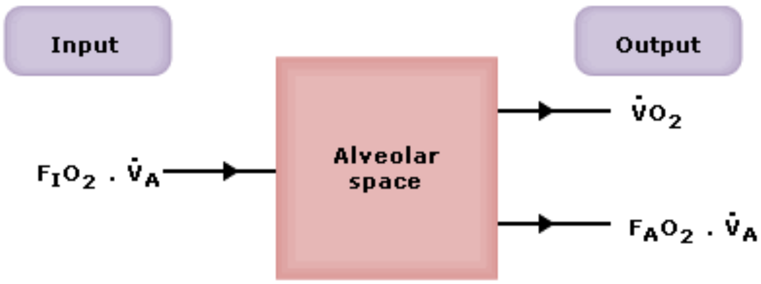
This is modelled again as an input-output model. The input is VCO_2 (production of CO_2) and output is the product of alveolar ventilation and the alveolar fraction of CO_2 (F_ACO_2):



This relationship shows the following graph derived from the following equation:

$$P_aCO_2 = \frac{\dot{V}CO_2 \cdot P_I}{\dot{V}_A}$$

With O_2, the relations are a little more complicated but the inputs and outputs are as follows:



There is a **single input** as a product of flow, concentration.

2 outputs cf 1 for CO_2 with O_2 uptake and O_2 in the expired gas.

THERE IS NO NEED TO REMEMBER THE DERIVATION OF THE ALVEOLAR GAS EQUATION (AGE):

Overall for CO_2 and O_2 the input and output derivations are:

$$\dot{V}O_2 = \dot{V}_A \cdot (F_IO_2 - F_AO_2)$$
$$\dot{V}CO_2 = \dot{V}_A \cdot F_ACO_2$$

The relationship between VCO_2 and VO_2 is the following:

$$R = \frac{\dot{V}CO_2}{\dot{V}O_2}$$

THEREFORE: $\frac{\dot{V}CO_2}{\dot{V}O_2} = R = \frac{\dot{V}_A \, . \, F_ACO_2}{\dot{V}_A \, . \, (F_IO_2 - F_AO_2)}$ → $R = \frac{F_ACO_2}{F_IO_2 - F_AO_2}$

$$F_IO_2 - F_AO_2 = \frac{F_ACO_2}{R}$$

$$F_AO_2 = F_IO_2 - \frac{F_ACO_2}{R}$$

Then convert to Partial Pressure (multiply through by P_I) and put $P_ACO_2 = PaCO_2$

AGE: $P_AO_2 = P_IO_2 - \frac{P_aCO_2}{R}$

So the following variables alter the Alveolar Gas Equation:

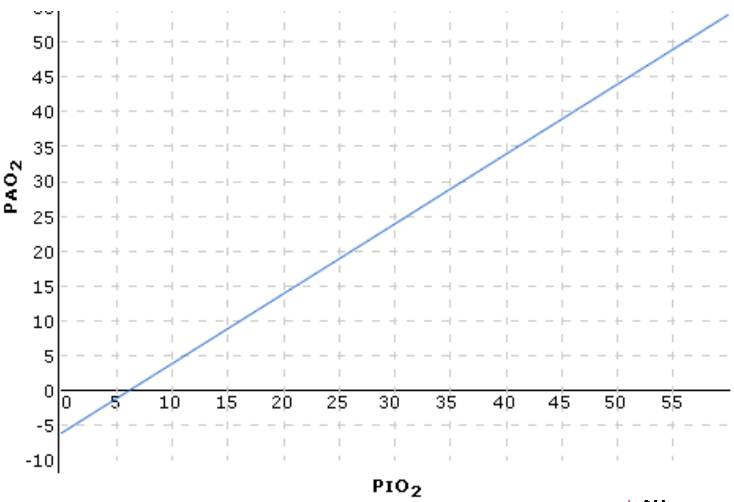
- **PiO_2** (= Barometric pressure x **FiO_2**)
- **$PaCO_2$** easily adjusted with ventilation
- **R** is the respiratory quotient and is the ratio of CO_2 production to O_2 consumption. It is a non-adjustable quantity and variations make such a small difference so it doesn't really change much if changed anyway! A typical value for R is 0.8 i.e. VO_2 = 250ml/min, VCO_2 = 200ml.

If the values were 5, 5, 0.8 respectively, (a very hypoxic mixture), there will be a -'ve value. This does not make sense as it depends on **steady state conditions** which is impossible with an FiO_2 of 5kPa. It will give us a good prediction of P_AO_2 in steady state conditions.

Fixed Constants and Variables

P_IO_2 variable:

If the AGE was substituted for y = mx + c; if c is constant, then the y = mx + c curve if c is -6.25kPa, then the graph would be as follows:

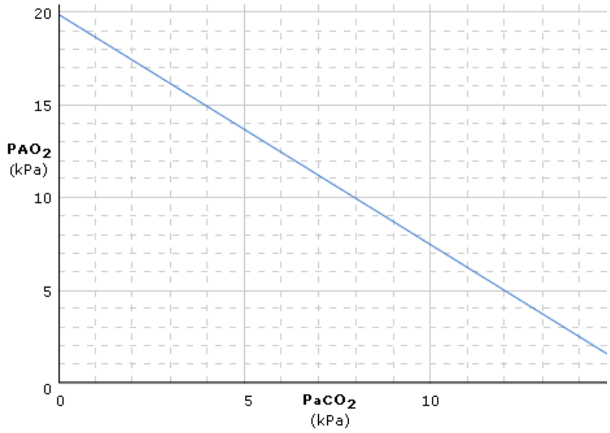


Therefore, the **P_AO_2 will equal whatever the P_iO_2 is – 6.25kPa**. However, as mentioned before, there is a violation of the steady state condition somewhere when P_IO_2 is <8kPa.

P_aCO_2 variable

Let's say P_IO_2 is 20kPa and R is 0.8 and x is P_aCO_2. m will be -1/R. The y=mx + c graph is follows:

If we now look at what happens to PAO_2 when $PaCO_2$ is varied, the graph is linear with gradient of -1.25. This shows that severe hypoventilation when breathing air will lead hypoxia – a consideration for post-op recovery.



as a -ve to

Altering Alveolar Ventilation:

Consider R as 1 for now…

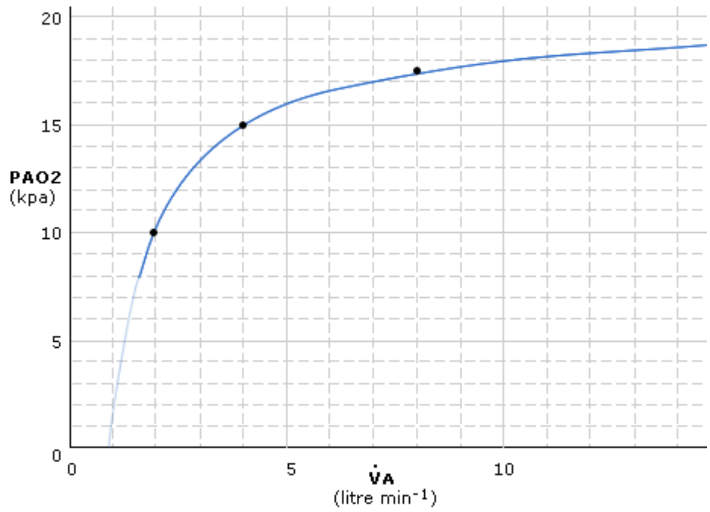
AGE becomes:

$P_AO_2 = P_IO_2 – P_aO_2$

If $P_aCO_2 = \frac{\dot{V}CO_2 \cdot P_I}{\dot{V}_A}$ as mentioned above, $P_AO_2 = P_IO_2 - \frac{(\dot{V}CO_2 \cdot P_I)}{\dot{V}_A}$ then

Now we have a version of AGE that is expressed in terms of alveolar ventilation instead of P_aCO_2. Therefore, the equation takes the form:

Y = c – k/x which is seen as the following graph:



Note that this is upside down compared to the P_aCO_2 and V_A graph. This shows that:

1. Increasing V_A may provide little difference in the P_AO_2 which is feeble compared to that seen by giving more FiO_2
2. Hypoventilation gives a rapid decline in P_AO_2 emphasising the importance of O_2 in the recovery room post anaesthesia.

If changing back the R to 0.8, the shape of the graph is unchanged but reduces the P_AO_2 further. Try to work this out from the above equation.

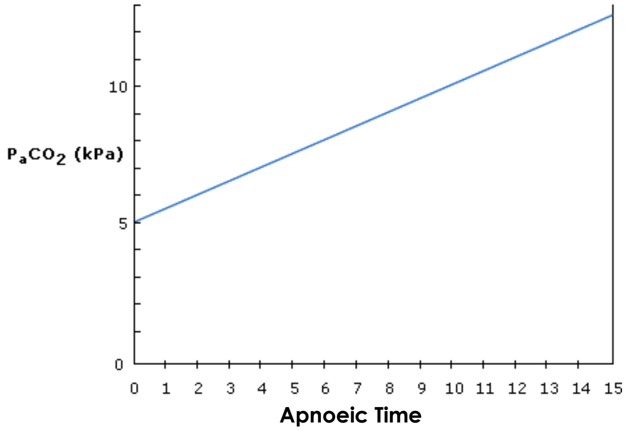
Apnoeic Oxygenation and Differential Equations

(07d_02_03)

Apnoea and CO_2 production v O_2 uptake

The rate of rise of P_aCO_2 in apnoea is linear and steady at gradient 0.5 i.e. 0.5kPa/min as shown in the graph.

Let's assume that during apnoea, the FRC remains an unchanging 2L…



The models so far have not taken into account that as well as the R of 0.8 (extract more O_2 than return to it as CO_2), **the FRC inflow is not accounted for…** This influx causes an increase in P_AO_2 and is accounted for by the following equation:

$$P_AO_2 = P_IO_2 - \frac{P_aCO_2}{R} + \left[F_IO_2 \times P_ACO_2 \times \left(\frac{1-R}{R}\right)\right]$$

This is of little clinical significance normally.

However, if the airway is kept open during a period of apnoea, as the chest wall remains static and fixed and FRC does not change, then a potential volume discrepancy between VO_2 and VCO_2 will by sub-atmospheric pressure draw gas down the airway.

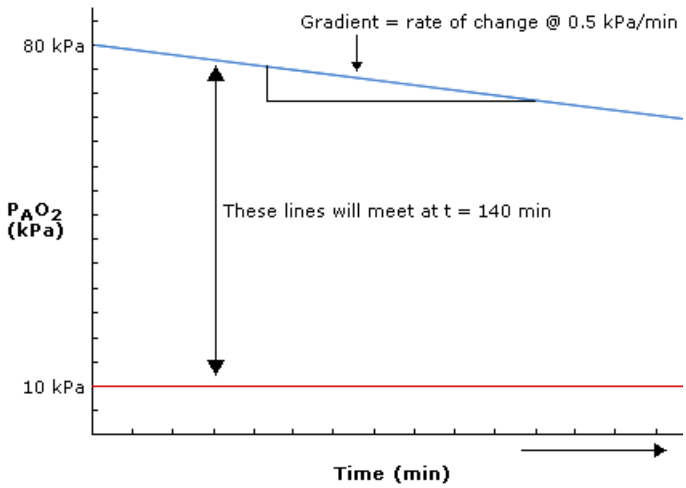
This is a **passive ventilation process** and can be explained by the PV = nRT gas law.

R, T and V are constant; therefore, pressure falls below atmospheric due to less n and mass transfer occurs down the concentration pressure gradient. This is known as **apnoeic mass transfer oxygenation (AMTO).**

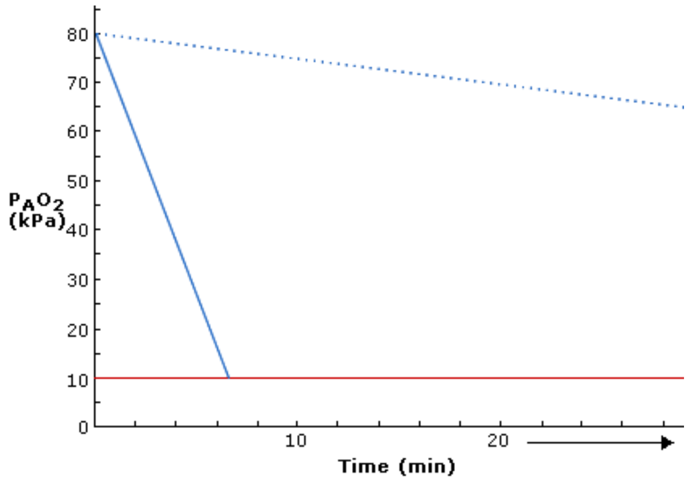
Duration of Apnoea Tolerated

If the starting P_AO_2 is 80kPa and the rate of reduction is 0.5kPa/min due to CO_2 rise, then it will take **140mins** for the P_AO_2 to fall below 10kPa. Therefore, before this can happen **P_aCO_2 will rise to toxic levels and is therefore, preoxygenation is limited by hypercapnia.**

This presumes, open airway, fresh gas flow of 100% O_2 and adequate preoxygenation.



Differential Equations



These are the type required to work out the **rate of change of a quantity**. This is easy if the rate of change is constant i.e. P_ACO_2 or P_AO_2 over time (t).

If 50% O_2 of fresh gas flow is used in the airway during apnoea, then the volume discrepancy is still there but less of this will be O_2.

In the **absence of preoxygenation**:

The maximum P_AO_2 is 15kPa at the start of apnoea. This means 15% of FRC (300ml) is O_2. Rate of gain of O_2 from AMTO is much reduced. Overall loss of O_2 then will be 12kPa/min. To reach the threshold of P_AO_2 of 10kPa (200ml O_2) would be 0.62mins

Overall Factors determining hypoxic threshold

Preoxygenation	This affects the starting point and determines for any particular FRC the store of O_2 we can call upon to make up for the discrepancy caused by the excess of uptake over delivery
FRC size	This determines the store of O_2 for any given F_AO_2
F_IO_2	This determines the proportion of the indrawn gas that is O_2 and hence delivery into the alveolar space by AMTO
VO_2	The uptake decides the demand upon the stores in the alveolar space and hence the rate of fall of P_AO_2
VCO_2	This determines the rate of rise of P_aCO_2 which in turn determines the rate of transfer of CO_2 across the alveolar membrane

Pre-Oxygenation and e

(07d_02_04)

This session looks at the mathematics behind **proportional change**, a process that is examined in relation to many time-dependent anaesthetic topics: volatile agent wash-in and wash-out; establishment of steady state infusions; viral spread; and in the context of this example, preoxygenation.

Consider the desired effect of alveolar ventilation (FIXED) at 4L/min on N_2 washout and oxygenation. Let's assume pre-oxygenation is perfect with no leaks, no rebreathing and then see what happens with a number of breaths. Each breath replaces a **proportion** of FRC containing F_AN_2 and F_AO_2 with FiO_2 of 100% and FiN_2 of zero. The size of each breath determines the magnitude of each step change, but each breath builds on the change produced by the previous breath.

Number of breaths	Initial F_AN_2	F_AN_2 after 30 s	Initial F_AO_2	F_AO_2 after 30 s	Proportional change	Ratio
1	0.8	0.4	0.15	0.55	0.5	$(1/2)^1$
2	0.8	0.36	0.15	0.59	0.444	$(2/3)^2$
4	0.8	0.33	0.15	0.62	0.41	$(4/5)^4$
8	0.8	0.31	0.15	0.64	0.3897	$(8/9)^8$
16	0.8	0.30	0.15	0.65	0.38	$(16/17)^{16}$

The Formula

Now the formula for the graph describing the change in nitrogen is:

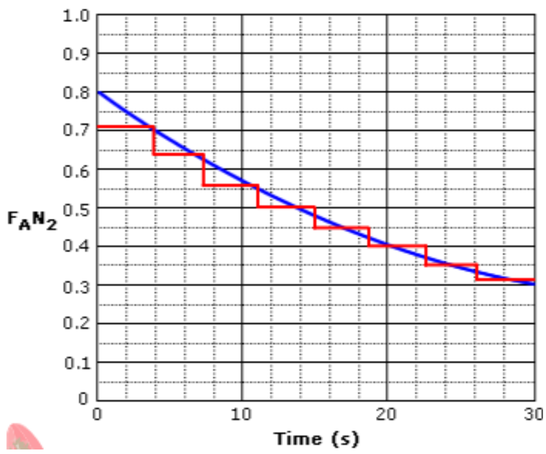
(Number of breaths/Number of breaths +1)$^{\text{N breaths}}$ OR

$$(n/(n+1))^n$$

The greater the number of breaths (n), the closer the fractional steps tend towards a smooth curve and the closer the fractional change tends towards a constant **known as e**.

e= 0.3678.

The formula above is 1/e or e^{-1}.



Applying this to other anaesthetic processes

To modify the above washout function to fit any particular scale and to consider the starting value, the function would be:

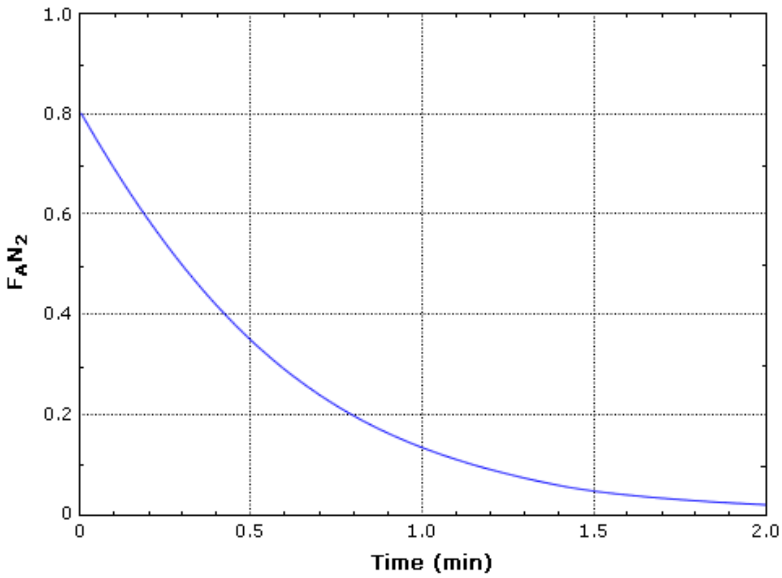
$$y = Ae^{-kt}$$

Where…

A is the starting value and

k is a rate constant (number of volumes taken to fill a container over a time frame). Or Q/V – the ratio of flow to container volume. This is large if the flow is large in relation to the container size.

t is the time constant, the time to hit the baseline if the initial rate of fall at A had continued. Because this rate of fall is not maintained in a proportional exponential process: at 1t, 37% of A remains (**e= 0.3678**); at 2t 15.5% remains; at 3t 5%. The process is considered 'complete' after 5t.



In the preoxygenation example, this would be:

- A = F_AN_2 (= 0.80)
- k = 2 per minute
- t = 0.5 mins

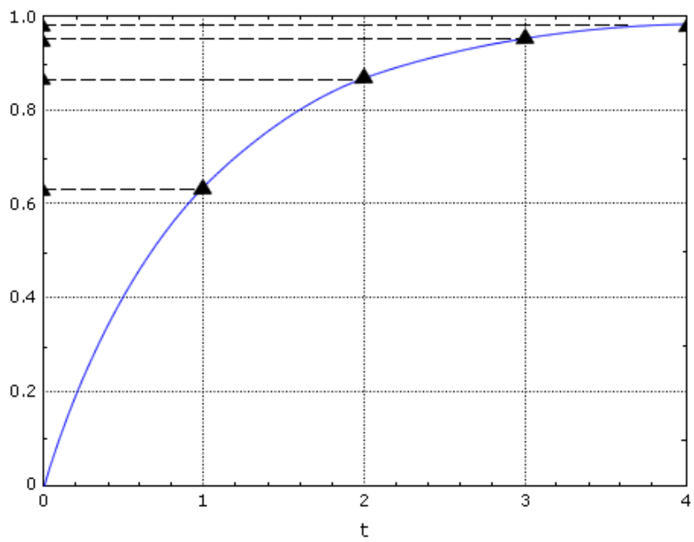
Therefore, the function is:

$$y = 0.8 \times e^{(2 \times 0.5)}$$

Wash-in function: this is represented by:

$$y = A(1-e^{-kt})$$

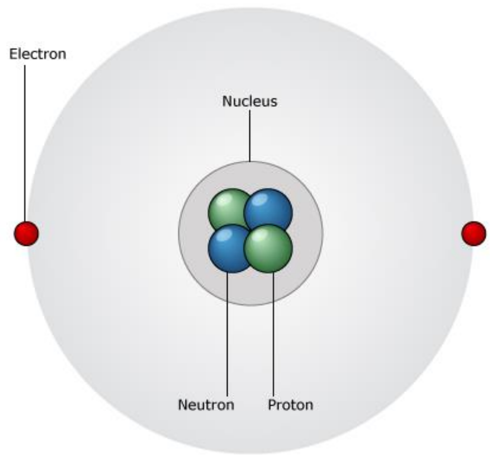
as shown in the graph with y values (for example for F_AO_2 in preoxygenation) that are the inverse of those quoted above for washout.



SUBATOMIC PROCESSES

Atomic Structure

(07d_03_01)



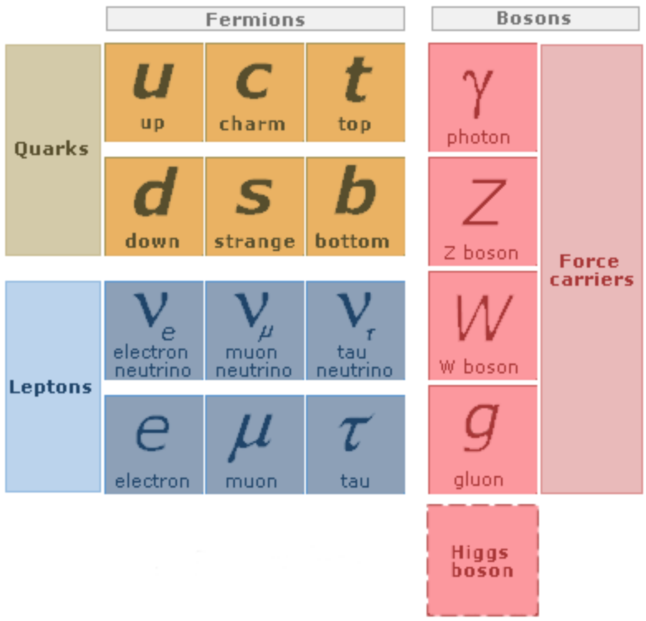
The word comes from the Greek word *ατομοσ* meaning; that which cannot be cut or divided. However, whilst it is the smallest known particle, it can be divided – 'splitting the atom'.

Structure: Centrally is the **nucleus** and surrounding it is a **region of space** known as **orbitals** in which **electrons** are likely to be found. We *do not know* how an electron moves within the orbital.

Subatomic particles

Neutrons and protons are made up of subatomic particles called quarks; and quarks are just one type of subatomic particle that form the Standard Model:

The Standard Model states that all matter is ultimately made up from only twelve elementary particles, known collectively as **fermions** (quarks and leptons), which interact through force-carrying particles known as **bosons** (photons, Z & W & Higgs bosons, Gluons).



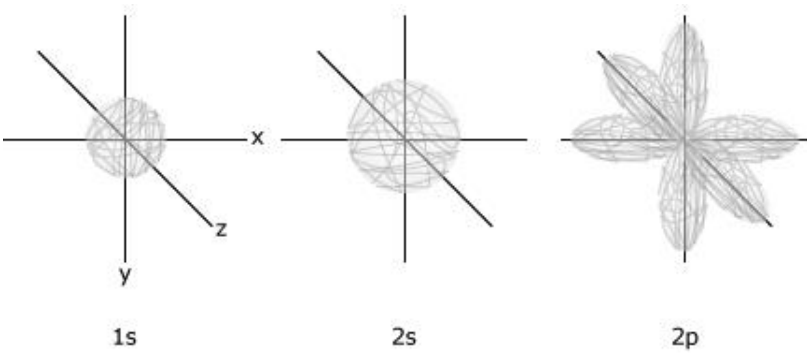
Nucleus and Electrons

The atom has a **tiny nucleus**… if the atom was the size of a football stadium, the nucleus is the size of the pea in the referee's whistle but it carries **99.9% of the atom's mass**.

There is also 99.9% empty space in the atom…

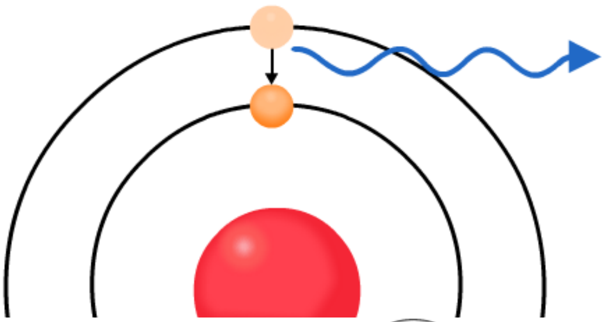
The nucleus is surrounded by electrons which have negligible mass and are negatively charged. They exist anywhere within the **orbitals of different energy levels:**

- **Number:** refers to the energy level of electrons where 1 is the lowest.
- **Letter:** The shape of the orbital:
  - **S orbital:** spherical shaped
  - **P orbital:** 2 balloons on end shape

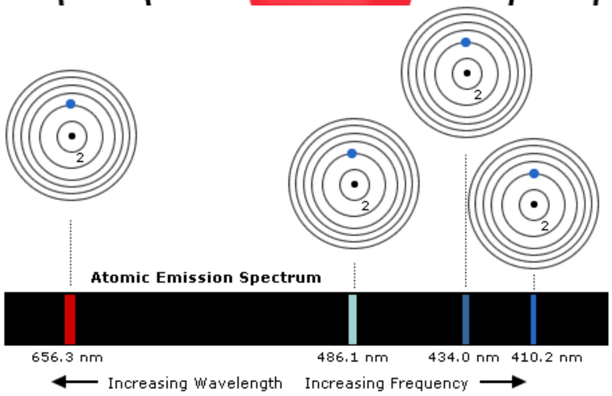


Each energy level of orbital has a specific number of electrons it can carry.

Quantum Mechanics: We won't get into too much detail about this! One key feature is that **matter acts as both a wave and a particle** i.e. photons and electrons. It describes why electrons can only exist on one energy level and why **photons are taken in or emitted** when electrons change orbitals. This allows **spectroscopic analysis** of the photons.



When electrons are excited, they can move to higher energy orbitals; when they lose energy, they make a transition back to the lower energy orbital and photons are emitted with differing amounts of energy:



Atoms are different through their number of protons in the nucleus. Each number of protons are matched to the electrons. Some orbitals remain ready to fill with other electrons and ready to give up electrons to make the outer energy level complete which determines the way the atom will react with other atoms. i.e. H^+ ion following loss of an electron.

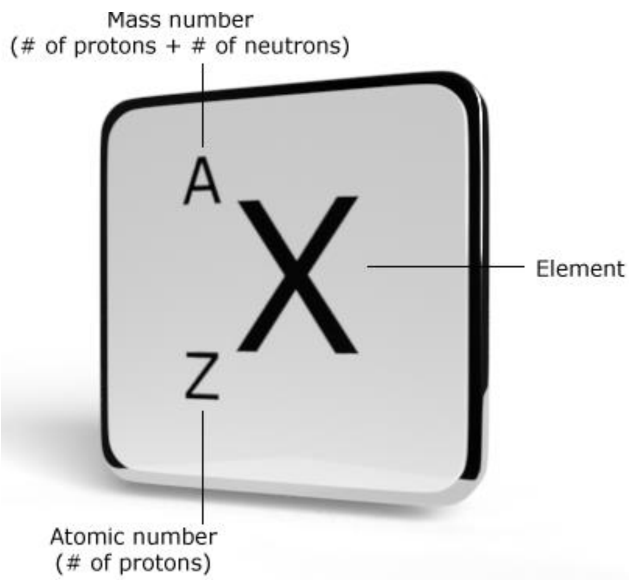
Isotopes

This is when a nucleus **acquires a neutron** which will increase the atomic weight. i.e. with hydrogen – will become deuterium with an atomic weight of 2. This is not common so the average atomic weight of hydrogen is 1.00794.

In the 19th century, a scientist called Mendeleev arranged atoms, or elements, in order of atomic weight from left to right, in a table with columns and rows – the beginnings of the **periodic table**.

The differing numbers of neutrons together with protons give rise to the difference in the atomic number and mass number.

Element	Atomic Weight	Atomic Number
Hydrogen (H)	1.00794	1
Carbon (C)	12.0107	6
Nitrogen (N)	14.00674	7
Oxygen (O)	15.9994	8
Fluorine (F)	18.998	9
Chlorine (Cl)	35.453	17
Bromine (Br)	79.9	35
Gold (Au)	196.966	79



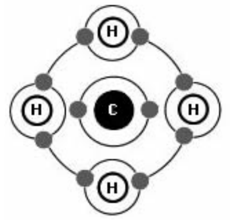
The atomic weight varies according to the average number including the isotopes of the atom with the specific atomic number.

Chemical Bonds and Reactions

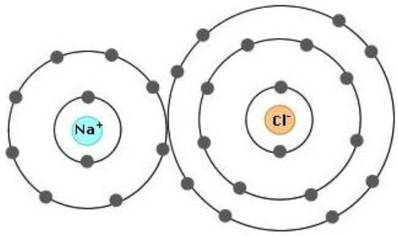
(07d_03_02)

Atomic Bonds

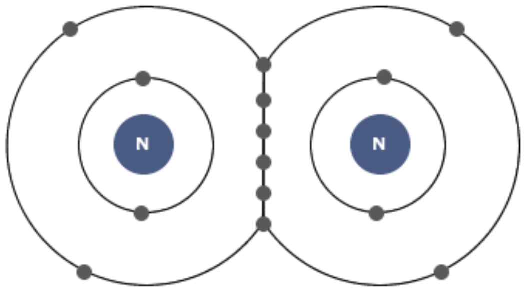
Atoms tend towards their lowest energy level (most stable) by giving, receiving or sharing electrons to fill these orbitals.



COVALENT BONDING: Sharing Electrons: These substances tend to be organic (carbon found in living things) and specific. For example covalent bonding with 1 carbon atom (4 electrons in outer shall (max = 8)) and 4 hydrogen atoms (1 electron (max = 2)):



IONIC BONDING: Transferring Electrons: These are often found with acids and bases which form electrostatic forces that hold the atoms together i.e. NaCl:



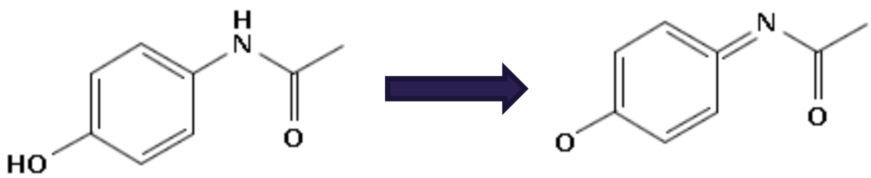
Covalent bonds are stronger and **less reversible** than ionic bonds. Water soluble salts where ionic bonds take place can dissociate into ions.

If covalent bonding involved the sharing of > 1 pair of electrons, then it would be much stronger and more rigid. Free rotation becomes impossible and isomerism results. O_2 shares 2 pairs of electrons (double bonded) and N_2 shares 3 pairs of electrons (triple bonded) and is the strongest bond in nature.

The atoms in molecules join together in a number of different ways depending on the conditions when they are joined. The lecture gives examples of nitrogen and oxygen… N_2O, NO, NO_2, N_2O_3 etc.

Covalent bonding and drugs

Covalent bonds are so strong and stable they are not involved with many drug interactions. However, when they are metabolised by enzymes, they break covalent bonds and form reactive intermediates that allow formation of new bonds at body temperature. e.g. paracetamol → NAPQI:



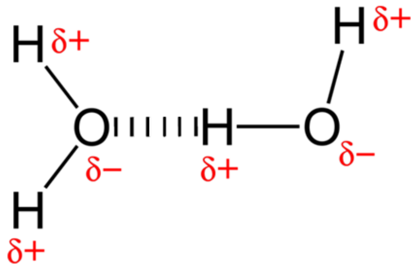
Another example is the covalent binding of organophosphate compounds (pesticides or nerve gases) with cholinesterase preventing the breakdown of Ach → cholinergic crisis.

Attractive and Repulsive Molecular Forces

This describes the key attractive forces that hold **groups of molecules** together in specific shapes in given directions which result in their unique physical characteristics:

Hydrogen Bonding

This is when a **hydrogen atom** (**+ve**) **covalently binds** to a **more electronegatively charged atom** to create the initial strong **dipolar attractive force** to initiate the hydrogen bond between water molecules:



This is also found in DNA.

Hydrophobic Bonding

Interaction between **non-polar molecules** to exclude water molecules between them. This occurs to allow molecules to achieve a lower energy state. Found in phospholipid tails and the inside of the large protein molecules.

Van der Waals Forces

These are attractions that occur between the electron clouds of neighbouring atoms that **aren't very strong**. However, they occur in large numbers and hence influence the shape of molecules.

Repulsive Forces

Electrostatic and dipole repulsion both influence the shape of molecules, in that they will determine locations into which molecules simply will not fit. RBCs cannot aggregate as their charge keeps them apart.

Certain parts of the molecule will also be of **differing size** or a **rigid shape** which prevents certain parts of molecules from combining through a molecule's structure. This is known as **steric hindrance.**

Electrostatic Binding/Ionic Binding **not to be confused with ionic bonding**

Results from binding of oppositely charged molecules. The pH of the environment affects the acidity/alkalinity of a molecule (proton donor/acceptor respectively) and allows **drug binding to proteins** that exist. The remaining **active free drug concentration** may be low. Warfarin is a good example of such a drug.

If the patient were to take aspirin also – it is more electrostatically attractive than the warfarin so proteins will preferably bind the aspirin and release more free drug concentration of warfarin.

Organic Chemistry

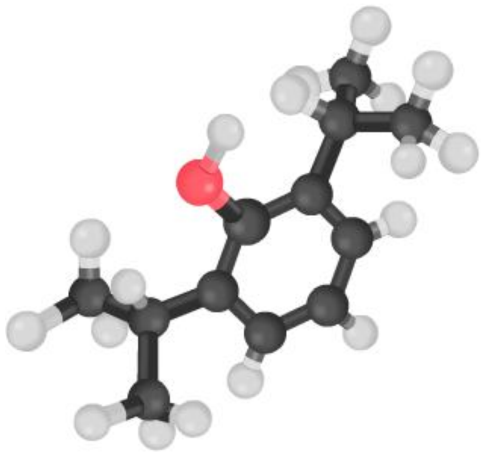
The study of carbon molecules. They can form a large variety of different molecules through different combinations, arrangement and bonding of simple atoms. Diamond, coal, gas etc.

Long chain hydrocarbons occur after butyl (C_4) known as **paraffins** and if a double bond arises between carbon atoms in the chain, then **olefins** (alkenes, as opposed to alkanes) are created.

As soon as a group substitution or double C=C bond arises, there is the possibility of **different isomers to form**. Groups can include:

- OH (hydroxyl)
- NH_2 (amino)
- COOH (carboxyl)
- OCH_3 (methyl ether)

When 6 carbon atoms join to form a ring, this is the basis of **aromatic compounds** typified by benzene. For example, **propofol** has a **benzene ring** with a **hydroxyl group** → making a **phenol.** This has 2 carbon chains attached:



Molecular Structure and Isomerism

(07d_03_03)

Isomerism is the existence of two or more substances, usually molecules, composed of the same atoms in the same proportions, but with **variations in the arrangement of the atoms**. These generally fall into 2 broad groups:

1. Constitutional aka Structural (including tautomers)
2. Stereoisomers (including optical, geometric, cis-trans, and racemic mixtures)

This is clinically important as many anaesthetic drugs display isomerism which can lead to a significant variation in effect. Some examples include:

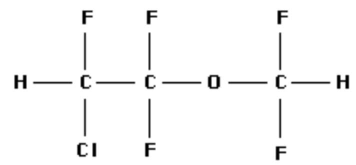
- Enflurane and isoflurane
- Bupivacaine and levobupivacaine
- Ketamine and (S) ketamine
- Atracurium and cisatracurium
- Midazolam (open-ring and closed-ring forms)
- Verapamil
- Atropine

Constitutional (Structural) Isomers

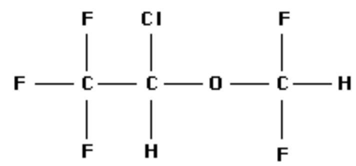
They have identical chemical formulae but the **order of atomic bonds varies**. Enflurane and Isoflurane are good examples:

They differ in potency, physical characteristics and side effects. Isoflurane has less CV effects than its isomer.

Enflurane

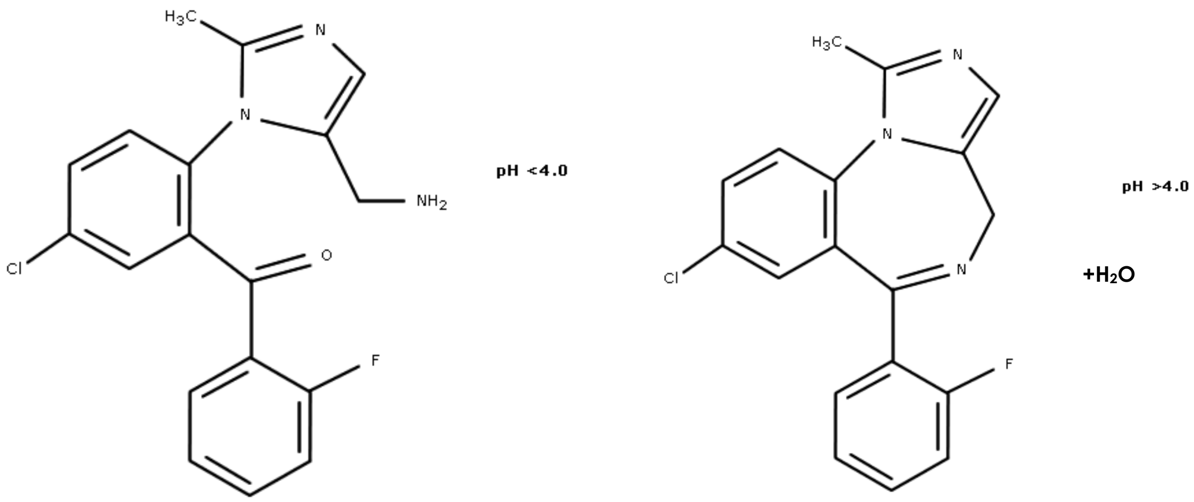


Isoflurane



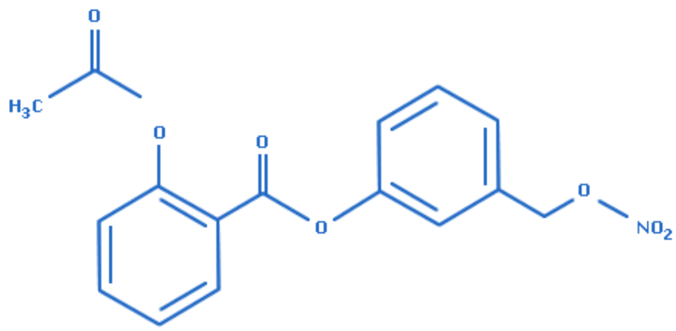
Tautomers: Are organic compounds that are interconvertible by a chemical reaction called **tautomerization** involving the migration of a hydrogen atom accompanied by the switch of a single bond and adjacent double bond:

Midazolam spontaneously converts to a water-soluble form at acidic pH due to a reversible ring-opening reaction and possibly due to ionization of the imidazole nitrogen (standard preparation). Once in physiological pH (right), it is more lipid soluble and able to penetrate the CNS.



Aromatic Isomers: Chemical group is bonded to different positions on a benzene ring. Nitric oxide-modified aspirin (NO-ASA) is an example.

The molecule in the picture shows the **aspirin molecule** to the left of the C-O-C bond; the **benzene ring spacer** and the **nitric oxide releasing group** to the right. The NO releasing group can change position to 3 different places on the benzene ring (above and below the carbon pictured) and causes different biological behaviour. They are known as the:



- **Ortho** (lowest/1st),
- **Meta** (middle/2nd – pictured) and
- **Para** (above/opposite) NO-ASA isomers.

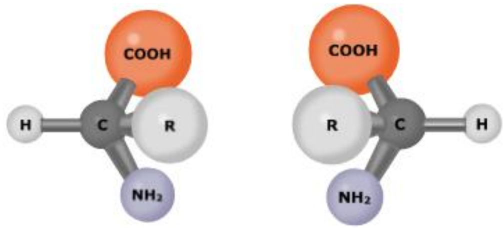
Stereoisomers

The same atoms connected in the **same order** but have **different 3D arrangements** of the atoms. A carbon atom with 4 **different** groups attached to it satisfies this condition. There are two basic types of stereoisomer:

a) **Optical**
b) **Geometric**

Optical isomers

They are related to each other as non-superimposable mirror images and they come in pairs or **enantiomers**. They are known to be **chiral.** The word comes from the Greek 'cheir' which means hands and are an example (think of open palms side by side). 60% of anaesthetic drugs are chiral. A **carbon atom** that is bonded to **4 different chemical species** will always have **2 enantiomers** and the carbon atom is referred to as the **chiral centre**.



Enantiomers had been known just as optical isomers in the past as they were defined as the direction that light deflected off them. Now, they are known based on the distribution of groups around the chiral centre:

- Left-handed (**S**) configuration
- Right-handed (**R**) configuration

If the mixture of the enantiomers is equal, it is known as a **racemic mixture** i.e. adrenaline.

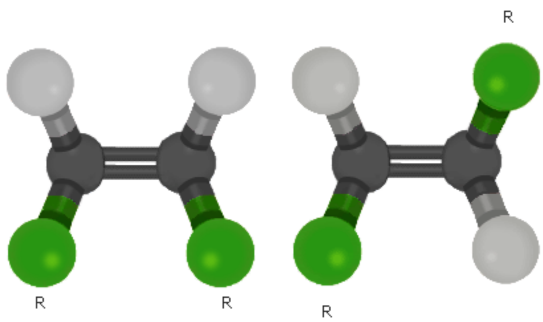
Enantiomers can also be synthesised in a single enantiomer form i.e. **(S) bupivacaine** (levobupivacaine – less cardiotoxic) and **(S) ketamine** (less psychotic s/e).

Geometric isomers

If they are **not simple mirror images of each other**. Diastereomers exist when a molecule has **>1 chiral centre** and the spatial configuration is different only around a subset of the chiral centres. This might be two adjacent but double-bonded carbon atoms or a ring structure in an organic molecule.

1. Cis-trans

Cis-trans isomers occur in relation to a **C=C bond.** The presence of the second carbon bond prevents other groups attached to the carbon atoms from rotating so that two potential fixed versions of the molecule exist **cis** (both groups on the **same** side, as shown left) or **trans** (groups exist further apart, as shown right).

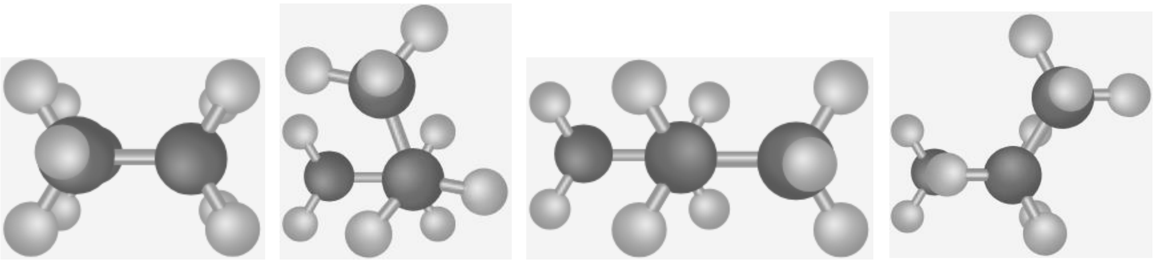


Atracurium and Cisatracurium are examples with the latter having more CV stability with less histamine release.

2. Conformers

Rotation about ≥ 1 single bond(s). Single conformers cannot be isolated. Butane is an example (see below from L → R: Syn (CH_3/CH_3 eclipsed), gauche, anti and CH_3/H eclipsed).

Atropisomers however, are a group of stereoisomers which result from hindered rotation around the single bonds. The barrier to rotation is enough to allow the isolation of different conformers. Vancomycin is an example.



When trying to classify isomers for the exam, consider different examples in anaesthesia and how they affect function, desired effect and side effect profiles. This is more important than attempting to apply difficult to remember terms such as diastereomer, atropisomer etc.

Reaction Rates and Thermodynamics

(07d_03_04)

Mechanical Equivalent of Heat

The theory goes that **mechanical work may be transformed into heat**, and conversely **heat into work**, the magnitude of the one being always **proportional to that of the other**.

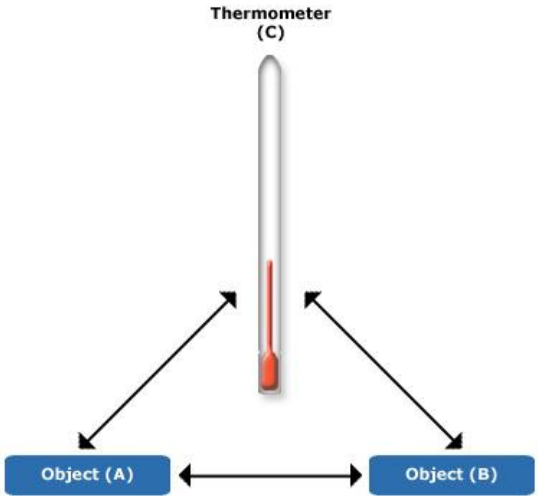
If 2 ice cubes are rubbed together, the mechanical work generates heat through friction which melts the ice. Contraction of muscles generates heat.

Laws of Thermodynamics

Thermodynamics is a branch of physics that governs the effects of **heat, work and energy** on systems at a macroscopic level. This was used to design the steam engine. The following laws existed

The Zeroth Law

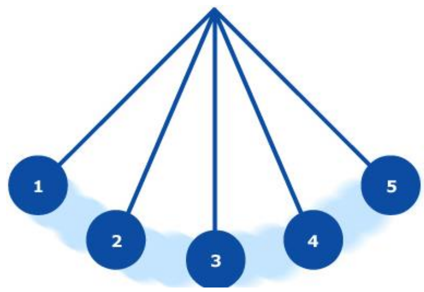
The latest law and most fundamental. **If two thermodynamic systems are separately in equilibrium with a third system, then they must also be in equilibrium with each other**. This occurs to a system when properties such as temperature and pressure do not change with time.

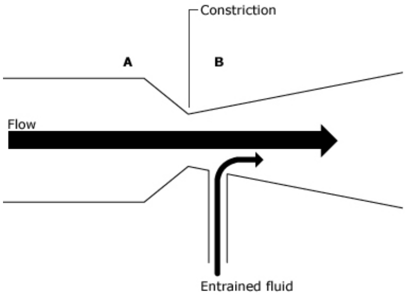


This law allows us to make thermometers by placing them in thermal contact to a second system as a reference point until thermal equilibrium is reached i.e. boiling water and freezing water. Now if it were to be placed against a 3rd system i.e. human body, the temperature can be determined by observation of the change in the thermal property of the thermometer.

The First Law

Energy can neither be created nor destroyed. The total energy within a system remains constant. This law can explain why a pendulum will keep moving with gravitational potential energy being converted to kinetic energy and vice versa. Kinetic energy is maximal at 3 but at points 1 and 5; kinetic energy is nil but all has been converted into gravitational potential energy.





Another example is the **Venturi principle**. When fluid moves through a tube with a constriction, the kinetic energy increases but at expense of a drop in pressure and potential energy past the constriction. This is used to entrain a second fluid/gas.

This method is similar to the use of the nebuliser.

Adiabatic Processes: (example of the 1st law). In such a process, a **change in the system occurs without any exchange of heat energy from the surroundings**.

For example, if a compressed gas is allowed to expand adiabatically, the gas will cool. This is because the energy required to break down the van der Waals forces between molecules can only come from the kinetic energy of the molecules themselves. This is used in a **cryoprobe** for freezing of skin lesions.

Similarly, if a gas is rapidly compressed, the temperature rises and may occur when a cylinder is attached to the anaesthetic machine and turned on too quickly.

Second Law

Known as the law of **increased entropy**. Entropy tends to increase over time and is a measure of chaos or disorganization – may be thought of as a measure of unavailable energy.

Example: cup falls and breaks, the pieces will not spontaneously form into a cup and the entropy has increased. Although some of the energy went into sound and heat, the total energy is unchanged but is no longer available for usage.

Third Law

As a **system approaches the absolute zero of temperature** (Kelvin)**, all processes cease and the entropy of the system approaches a minimum value.** All molecular motion comes to a halt.

However, due to the 2nd law, absolute zero cannot be reached as it has to draw heat energy from the surrounding systems, and therefore equilibrium at a zero state could never be achieved with the container.

The Combined Law

Is simply a mathematically derived summation of the first and second laws subsumed into a single concise mathematical statement that relates distribution of kinetic or thermal energy and entropy, showing how little this will change overall energy in the system:

$$\Delta U = T\Delta S + p\Delta V \leq 0$$

Where…

- **U** = Internal Energy of the system
- **T** = temperature
- **S =** Entropy
- **P =** pressure
- **V =** Volume

Acids and Bases

(07d_03_05)

Change in H^+ ion concentration causes ionisation and affects ionic bonding in molecules within metabolic pathways. With the exception of gastric proteases, physiological enzymes only work optimally within the very narrow body pH range of 7-7.4.

Definitions

ACID: Literally means 'sour'. Has been described as a substance which:

- Dissociates in water to form H^+ ions
- **Proton donor**
- Potential electron pair acceptor

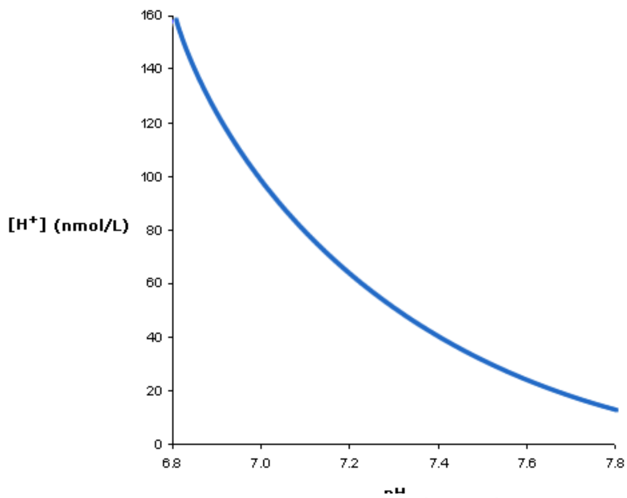
CO_2 (no H^+ ions) behaves as an acid by increasing the dissociation of H^+ ions of water.

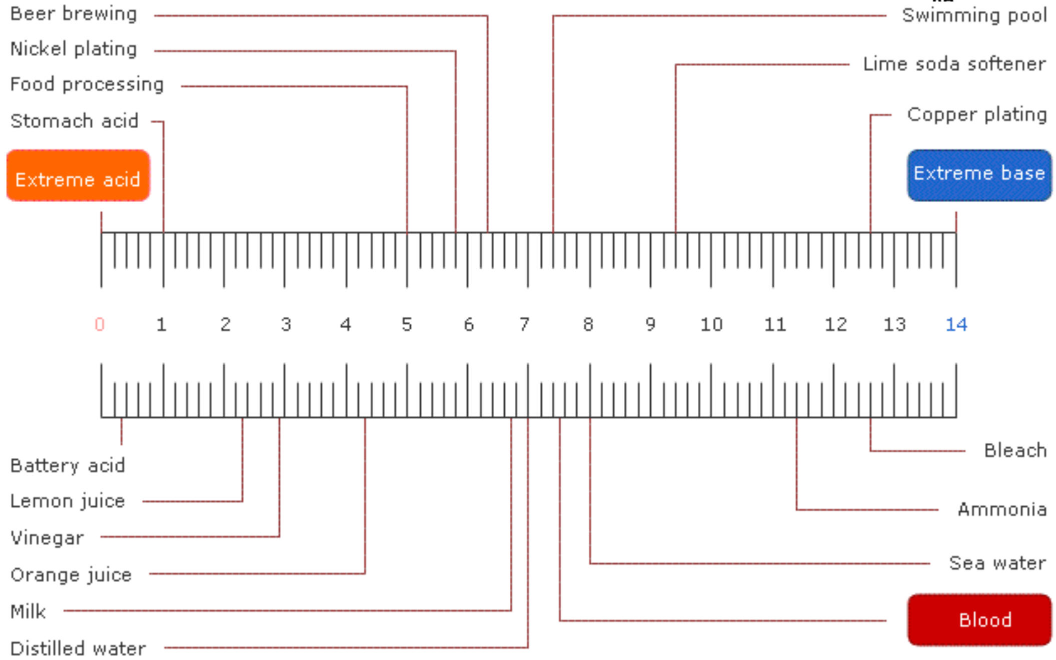
BASE: Reasonable definitions include:

- **Proton Acceptor**
- Substance which dissociates in water to form OH^- ions.

pH: Is the **negative logarithm to the base of 10** of the **H^+ concentration:**

$$pH = -\log_{10} [H^+]$$



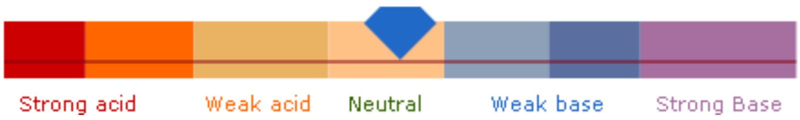


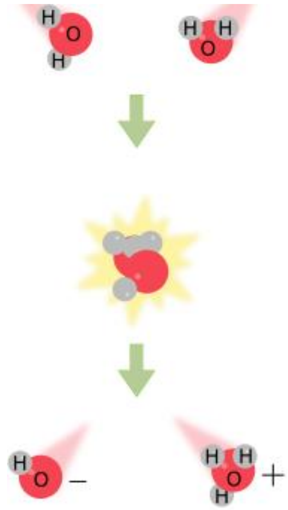
Because of the peculiarity of a negative logarithmic scale, blood:

- pH of 7.4 equates to a hydrogen ion concentration of 40 nmol/L
- pH of 7 equates to 100 nmol/L
- pH of 8 to 10 nmol/L

pH indicators use chemicals with special properties that change their spectral properties in the presence of H^+ concentration. This includes **litmus, phenolphthalein, methyl orange, methyl red**. With litmus, bases turn it blue and acids turn it red.

Universal indicator paper has a mixture of dyes which allow a semi-quantitative measure of pH.





pH has been criticised as it may not give the overall picture of an acid-base solution. **For example,** As H_2O is polar and O is electronegative, it accepts H^+ (base) to make hydronium (H_3O^+) ions. H_2O **dissociates into H^+ and OH^- ions in equal proportions at all temperatures**.

The extent of this dissociation however varies with temperature with **increasing degrees of dissociation with increased temperature**. Therefore, at increased temperatures, there is more H^+ ion dissociated into solution and by definition, pH falls.

Dissociation

Complete dissociation is characteristic in compounds with **ionic bonds**.
These substances produce **strong ions** and examples include Na^+, K^+, Ca^{++}, Mg^{++}, sulphate and lactate.

Compounds that undergo **partial dissociation** are known as **weak ions**. An example is carbonic acid. This requires a **dissociation constant (k)** which determines the **proportions of molecular and ionic compound** respectively. i.e. Henderson's:

$$K = \frac{[H^+] \times [HCO_3^-]}{[H_2CO_3]}$$

Strong and Weak Acids

Strong Acid is one that undergoes **complete dissociation** to H^+ and X^- i.e. HCl and Lactic acid (physiologically

Weak Acid undergoes **incomplete dissociation** where the acid and ions are in equilibrium such that a weak acid dissociation constant may be formed.

$$K_a = \frac{[H^+] \times [A^-]}{[HA]}$$

This can be rearranged as:

$$[H^+] \times [A^-] = K_a \times [HA]$$

Strong and Weak Bases

Same as above but with OH^- ions from dissociation in aqueous solution: **$B + H_2O \leftrightarrow BH^+ + OH^-$**

The weak base dissociation constant:

$$K_b = \frac{[BH^+] \times [OH^-]}{[B]}$$

Examples include **ammonia** and **local anaesthetics**:

$$\mathbf{NH_3 + H_2O \leftrightarrow NH_4^+ + OH^-}$$

pKa and pKb

The pK of a substance is the pH at which a weak acid or weak base exists in its ionized and un-ionized forms to an equal degree. The table shows some of these values:

Weak acid	Acid anion	pK_a
CH_3COOH (acetic)	CH_3COO^- (acetate)	4.76
$CH_3CH(OH)COOH$ (lactic)	$CH_3CH(OH)COO^-$ (lactate)	3.86
H_3PO_4 (phosphoric)	$H_2PO_4^-$ (dihydrogen phosphate)	2.14
$H_2PO_4^-$ (dihydrogen phosphate)	HPO_4^{2-} (monohydrogen phosphate)	6.86
H_2CO_3 (carbonic)	HCO_3^- (bicarbonate)	6.37
HCO_3^- (bicarbonate)	CO_3^{2-} (carbonate)	10.25
C_6H_5OH (phenol)	$C_6H_5O^-$ (phenolate)	9.89

Henderson-Hasselbalch equation relates the concentration of bicarbonate to that of carbon dioxide in the blood as the pH of the blood changes.

$$pH = pK_a + \log_{10}\left(\frac{[HCO_3^-]}{[CO_2]}\right)$$

See previous physiology lectures for its derivation.

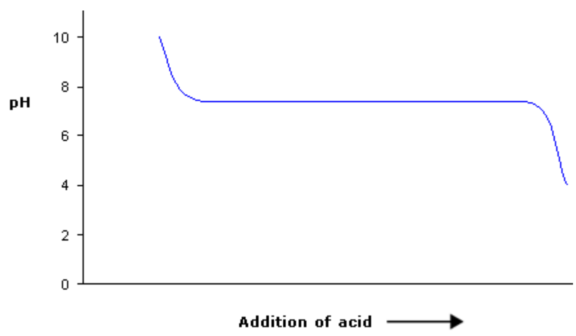
Buffers

Solutions that resist changes in H^+ and OH^- concentrations. They are usually solutions of weak acids and less commonly weak bases.

$$HA \leftrightarrow H^+ + A^-$$

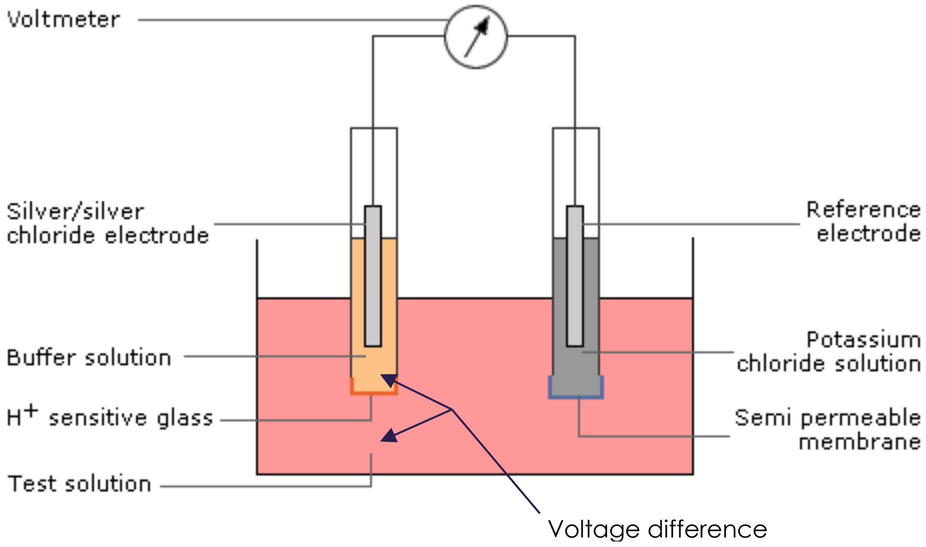
Addition of acid to these solutions will shift the equilibrium to the undissociated form effectively 'mopping up' the extra H^+ ions and therefore, **changes in H^+ concentrations are reduced or 'buffered'**. Addition of OH^- will react with H^+ to form H_2O pushing the equation to the right.

The graph shows the effect of adding acid to a buffer solution:



Measurement of pH – The pH Glass Electrode

Relies on the presence of **H^+ sensitive glass**. With a concentration gradient of H^+ ions either side of the glass, a **potential difference** develops. If one side is kept constant using a buffer with no net movement of H^+ ions across the glass occurring, the change in potential difference can be used to determine the pH using an **electrical circuit.**



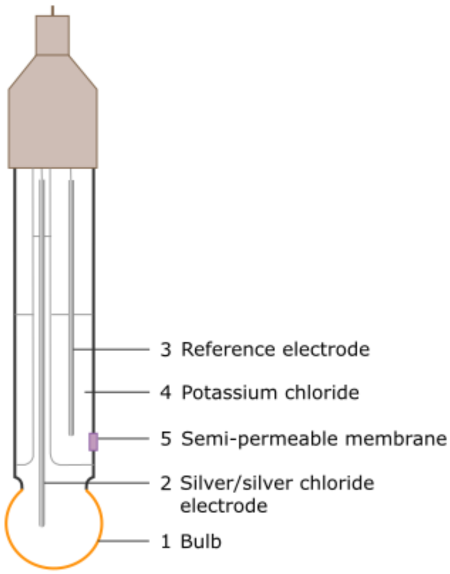
(**Mercury/Mercury Chloride**)

Combination pH Electrode

In practice, both electrodes are contained within the same housing and the pH sensitive glass is located on the bulb at the tip which is placed into the test solution. Similar to above, the silver/silver chloride electrode is bathed in the buffer solution and the semipermeable membrane located on the casing which must be in contact with the test solution.

The pH electrode must be calibrated before next use using reference solutions.

This MUST be performed at a **constant temperature** to ensure accurate measurements as dissociation increases as temperature increases and also less proportion of CO_2 is dissolved in solution at higher temperatures.

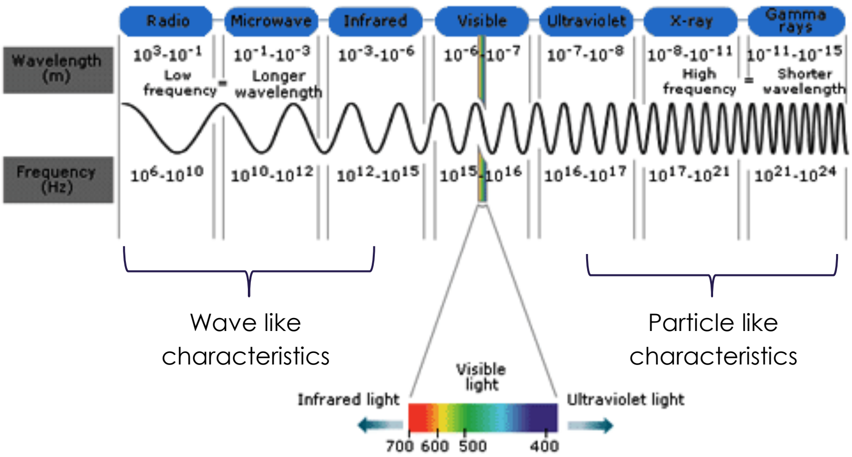


Electromagnetic Spectrum

(07d_03_07)

Electromagnetic (EM) Radiation is a form of energy and means of energy transfer with the most obvious being light. Some forms are invisible to the human eye. The **wavelength** determines position and wave frequency on the **electromagnetic spectrum**.

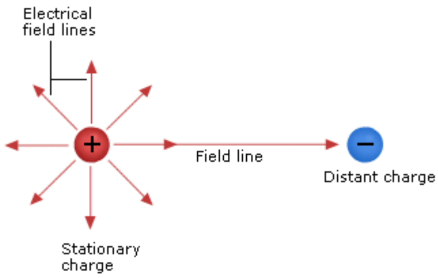
The use of EM radiation is widespread in the hospital.



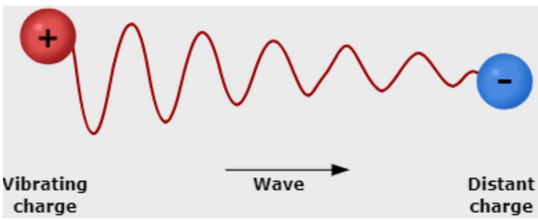
Nature of EM Radiation

EM radiation exists as 2 different conceptual forms simultaneously: **particles and waves**. This is known as **wave/particle duality**. **Longer wavelengths** such as radio waves will exhibit more **wave properties** whilst **shorter wavelengths** i.e. gamma rays will exhibit more **particle** characteristics and this huge amount of energy may be harmful to biological tissue.

For example, light exhibits properties of **particles** known as **photons/quanta**. It also behaves as a **wave** where light will diffract and reflect.



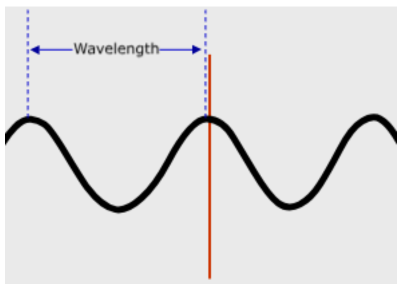
EM radiation is formed by the **oscillation of charged particles** namely protons and/or electrons. These charged particles **exert electrical field lines** which opposite charged particles are attracted to and these oscillate also along with the particles resulting in an **electrical force** in the **form of a wave**:



In a vacuum, the EM radiation will propagate at the speed of light and is constant. Demonstrated 1st by James Maxwell that electrical and magnetic fields (components of EM radiation) can travel through a medium at a constant speed.

Waveform Characteristics

Sine Wave



The **frequency** of the wave is defined as the number of wavelengths passing a fixed point in one second, or the number of cycles per second given in **Hertz** (Hz). Therefore, the wavelength (λ) and frequency (v) is related by the speed of travel which is a constant and is the speed of light (c).

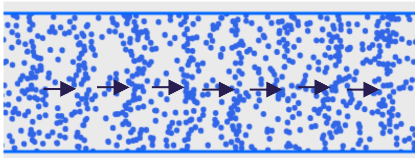
$$\lambda \times v = c$$

Longer wavelength = lower frequency **Shorter wavelength = higher frequency**

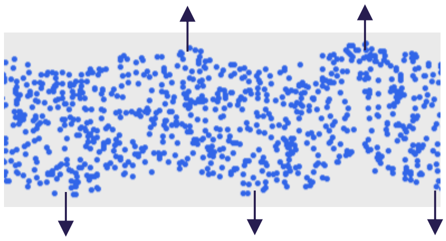
Wave Transmission

There are 2 kinds of oscillating sine waves:

1. **Longitudinal wave:** Direction of oscillation is parallel to the direction of travel of the waveform. Sound is a good example propagating through compression and refraction of air molecules.

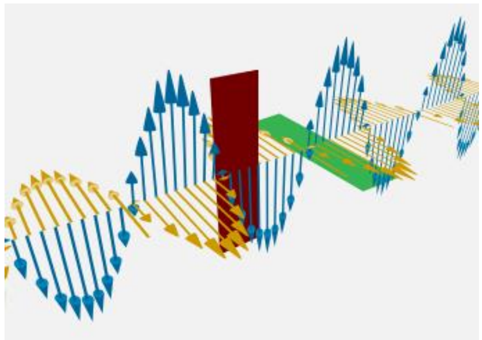


2. **Transverse wave:** Direction of oscillation is at **right angles** to the direction of travel of the waveform. For example, in sea waves, they travel towards the shore but the swell is caused by up and down movements of water molecules.



EM radiation is an example of a transverse wave. In fact, it consists of 2 distinct oscillations perpendicular to the direction of travel of the wave:

One is an **electrical field** and the other is a **magnetic field** which also oscillate at right angles to each other and to direction of travel.



Energy in EM Waves

EM radiation carries energy in discrete packets known as **quanta** and is given by the following relationship:

$$E = h \times v$$

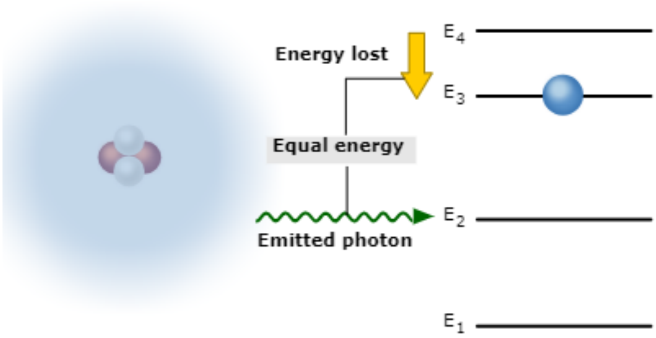
Where…

E = energy h = **Planck's constant** v = frequency

Planck's constant therefore relates the energy in one quantum with that of the frequency. Gamma radiation (shorter wavelength, higher frequency) has much more energy than radio waves.

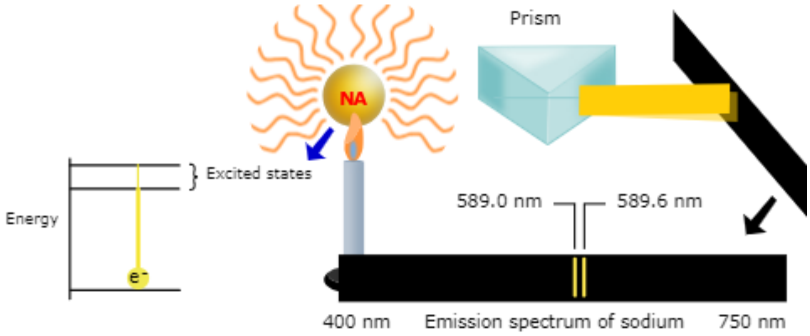
Particle Characteristics of EM Radiation

In an atom, each electron possesses an amount of energy **specific to its orbital level**. The **specific amount of energy** required to move the **electron to a higher energy level orbital** is known as a **quantum**. This is measured through emission of the quantum energy when the electron moves back to its ground state through EM radiation in the form of **photons.** This is the principle behind Raman Scatter.



From the above equation, as specific amounts of quanta of energy are released, there will be emission of EM radiation of a **specific wavelength** governed by Planck's constant and will be specific and characteristic to each atom (all have differing energy levels).

This is demonstrated when heating specific elements on a Bunsen burner flame. Heating **Barium** on a flame produced **green light** and **sodium** – **yellow light** as these emit light on the visible spectrum. If placed through a prism, this will only contain 2 types of yellow light rather than the full spectrum seen with ordinary light



Practical uses

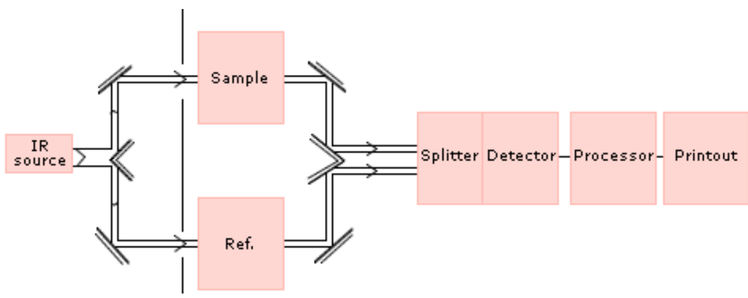
Sodium energisation is used in street lamps.

LASER: acronym for **light amplification** by **stimulated emission** of **radiation.** A lasing medium i.e. CO_2 or Argon is stimulated by a high energy source i.e. xenon flash lamp pushing electrons to a higher energy orbital and when they fall back to their original orbitals, they emit EM radiation of a specific wavelength. The specific nature of the lasing medium will determine its specific application.

Absorption Spectroscopy: If a gas contains **two or more different atoms in its molecules**, specific amounts of energy will be **absorbed** from an energy source by a change in the conformation of the energy state of the chemical bond between the different atoms. This is analysed by a sensor which will see missing spectral lines. With known wavelengths of gases, this gas can be analysed.

NB, this is why O_2 cannot be measured in this way.

Infrared Gas Analyzer: This makes use of **absorption spectroscopy** on the **infrared region of the EM spectrum**. The amount of infrared energy absorbed at each specific wavelength (according to *type of* gas present) depends on the amount of each gas present.



Therefore, it is able to detect the **type** and **concentration** of gases present by comparing with a **reference chamber** of **known gases** and their **concentration.**

Light

(07d_03_08)

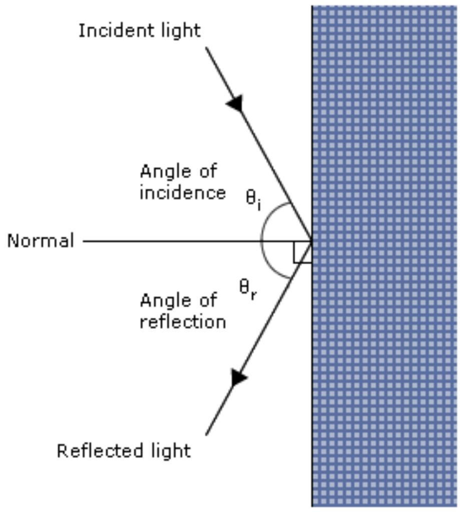
Light is used commonly in anaesthesia with the fibreoptic laryngoscope which relies on the **total internal reflection** property of light.

Capnograph and pulse oximeters rely on the **absorption of light** to transduce electrical readings.

Principles of Light

Luminous Intensity

Measured by the SI base unit **Candela (cd)**. It is defined as something I will never understand… and probably don't ever need to…



Reflection

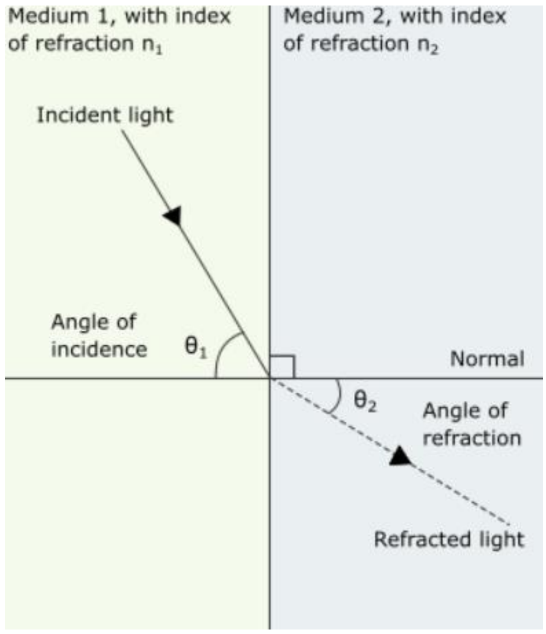
Light normally travels in a straight line but bounces off any shiny surfaces i.e. a mirror – **reflection.** The angle at which light hits the surface is the **angle of incidence** which reflects at an **angle of reflection** from a line perpendicular to the surface.

Angle of incidence (θ_i) = Angle of reflection (θ_r)

Refraction

When light bends at the **junction between 2 mediums**. For example, in water a straw will appear to bend. This is affected by 2 factors:

1. **The angle of incidence**
2. **The nature of the medium**



Light travels at different speeds in different substances. By comparing the speed of light in a particular medium when comparing it to the speed of light in a vacuum, you obtain the **index of refraction (n)**.

Speed of light (**c**) = 299,792,458 m/s
Index of refraction: Air 1.0, Water 1.3, Glass 1.6

Snell's Law describes the amount of refraction that will occur:

$$n_1 \sin\theta_1 = n_2 \sin\theta_2$$

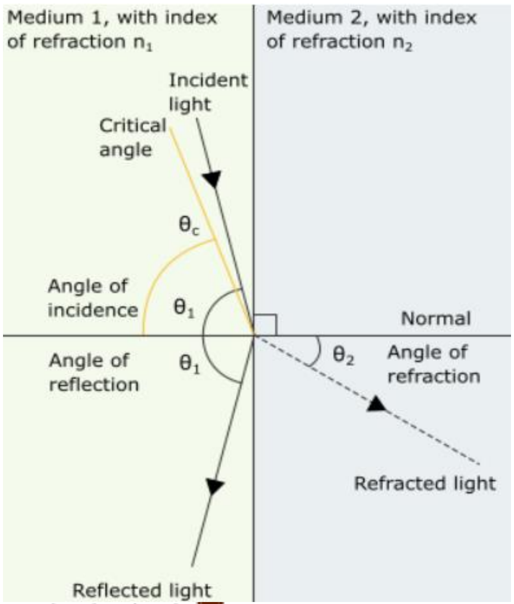
As the refractive indices (n) are constant, the angle has to change…

Total Internal Reflection

If the **angle of incidence is greater than the critical angle** when approaching the medium, **the light will reflect** rather than pass through the 2nd medium. The **critical angle** is determined by the refractive indices of the 2 substances through the equation:

$$\theta_c = \arcsin(n_2/n_1)$$

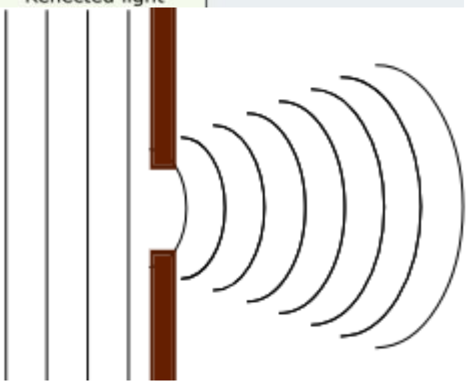
Where n_2 is less dense than n_1. This is the principle used by fibreoptic laryngoscopes.



Diffraction

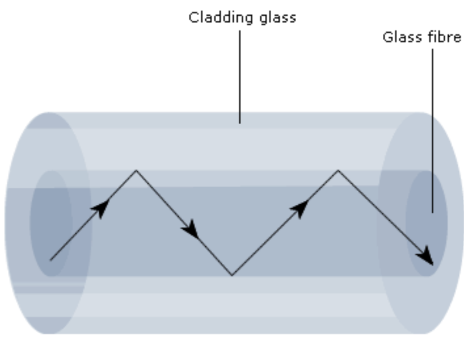
This is the **spreading of waves** as it **travels through a gap**. The extent of diffraction depends on the **wavelength of the wave** and the **width of the gap**. The narrower the gap, the wider the diffraction.

Oil on water has a complex series of gaps which is why white light that passes through it appears as a multicolour pattern.



Fibreoptic Laryngoscope

Constructed with 36,000-85,000 bundles of fine glass fibres 8-10 µm in diameter, which are each coated by a 1 µm thick layer of cladding glass. This outer layer has a **lower index of refraction** to ensure **total internal reflection** without light leaking to other fibres.



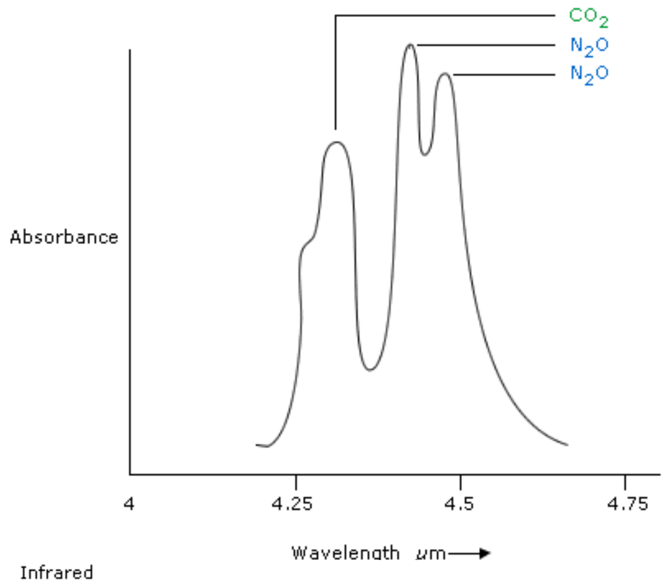
Gas Analysis

The anaesthetic gas analyser uses a **spectrophotometric** technique. This involves shining light (EM radiation) through a sample and analysing the quantity that is absorbed. 2 laws describe how radiation is absorbed as it passes through a substance (**Beer's** and **Bouguer's (Lambert's) law**):

- **Bouguer's** and **Lambert's law:** Each layer of equal thickness absorbs an equal fraction of radiation that passes through it. *I.e. increased absorption with increased distance travelled*
- **Beer's law:** The absorption of radiation by a given thickness of solution of a given concentration is the same as that of double the thickness of half the concentration. *I.e. increased absorption with increased concentration of medium.*

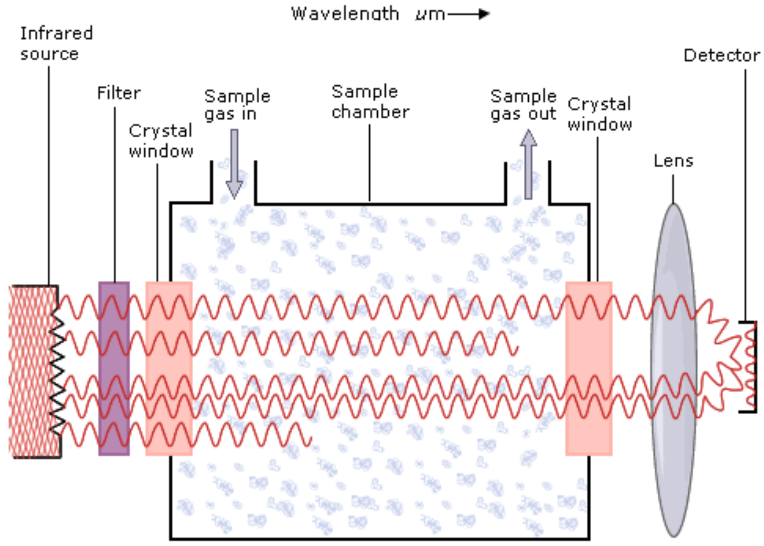
Absorption occurs if the gas has more than 1 atom of different elements in a molecule. CO_2 and N_2O will absorb infrared radiation, whereas O_2 will not. Volatile anaesthetics have a wide variety of elements and therefore absorb infrared light.

CO_2 maximally absorbs at a wavelength of **4.26 µm.**



Mechanism

Infrared is emitted from a source. Passes through a filter to allow only the specific wavelength desired through, then a crystal (sapphire) window which does not absorb infrared light, into the sample chamber where the sampling gas is present where some light will be absorbed. The remaining light travels via another crystal window and lens to focus on a detector.



The analyser has a **known length of path** and a **known wavelength of light**. Therefore, any change in the expected amount detected will be due to a **change in the concentration of the absorbing gas**.

This is compared to a **known reference gas** to allow measurement.

Optical Density: This is a **unitless measure of the absorbance of a substance**. It combines the 3 factors of length of path, wavelength of light and substance concentration as mentioned above.

Imagine in a heavy fog, the further away an object is, the fading of this object occurs at an exponential rate – at doubling the distance, it is 10x more difficult to see.

THEREFORE…

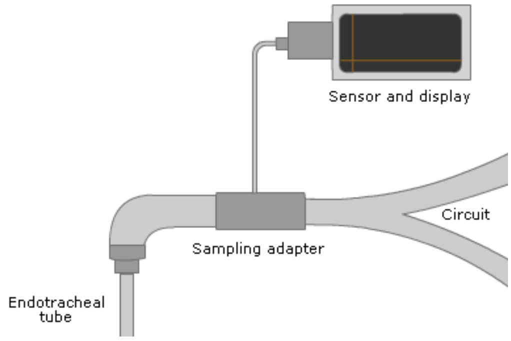
Assertion: Optical density is used to determine the concentration of a substance with infrared gas analysis

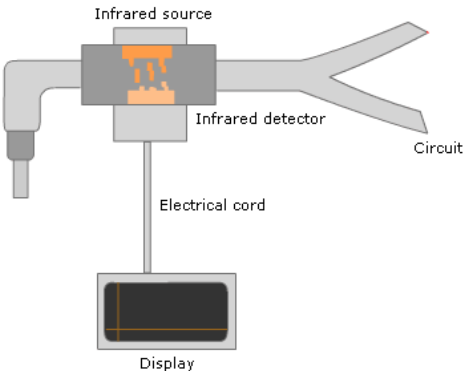
because

Reason: As the wavelength of light and length of path are known, only the concentration of substance can be variable

Types of Infrared Gas Analysers

Side-stream analyser: Sample is drawn from breathing circuit and analysed after water is removed through an analyser at the far end. This has a **lag time** but is lightweight.





Main-stream analyser: The analyser sits on the breathing circuit across a sapphire window. There is no lag time but the in-line sensor chambers are bulky and easily damaged.

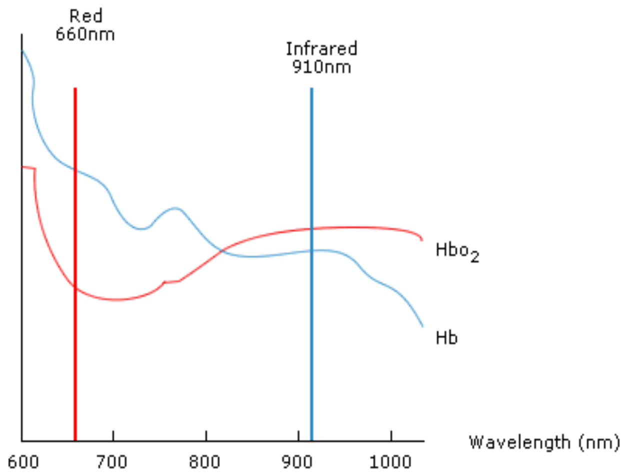
These tend to only measure CO_2.

Problems with IR analysers: Interference between absorption peaks of different gas molecules containing dissimilar atoms (especially if they have similar IR absorption wavelengths such as N_2O and CO_2) causes **broadening** that will give falsely high readings if the presence of the second agent is not carefully compensated for by the monitor. The effect is most marked in the presence of nitrous oxide. O_2 can also to a lesser extent broaden the CO_2 absorption spectra and hence cause interference but this is by **collision** with CO_2 molecules rather than IR absorption by oxygen. Water vapour leads to falsely high CO_2 readings by absorbing light as well. Reduced through use of Teflon tubing travelling to the spectrometer and a water trap.

Pulse Oximeter

This also uses a **spectrophotometric technique** to measure oxygenated haemoglobin in patient's blood. The pulse oximeter emits **pulses of red (660nm) and infrared (910nm) light** from **2 light emitting diodes** every 5-10 microseconds.

- **Red light** – the absorbance of oxyhaemoglobin < deoxyhaemoglobin. This is why oxyhaemoglobin appears red
- **Infrared light** – absorbance of deoxyhaemoglobin < oxyhaemoglobin.



The pulsatile (arterial blood) component is measured at each of the 2 wavelengths and the constant component is subtracted. The O_2 saturation can now be measured by comparison with previous experimental values.

The **isobestic point** is the point at which the absorption of the 2 types of haemoglobin is identical (590nm and 805nm for oxy and deoxyhaemoglobin). This point is **only dependent on the haemoglobin concentration** so was useful in the old oximeters to compensate for low haemoglobin levels.

Problems with the Pulse Oximeter

Errors calculating the pulsatile component of light absorption:

Problem	Examples
Hypoperfusion – more difficult for the oximeter to define the points of maximum and minimum absorbance	Low pulse pressure Profound vasoconstriction Venous pulsation, e.g. torrential tricuspid regurgitation
Abnormal haemoglobins and **intravenous compounds** may interfere with light absorption	***Carboxyhaemoglobin*** - Will lead to a misleadingly high reading for oxygen saturation ***Methaemoglobin*** (MetHb) – Will give a misleadingly false reading (MetHb gives saturation reading of 85%) ***Methylene blue and indocyanine green*** also interferes with measurement
Arrythmias make it harder for the oximeter to predict/define the points of minimum and maximum absorbance	Atrial fibrillation

Machine Dysfunction when there is **electrical interference** i.e. with diathermy.

Increased ratio of non-pulsatile component of light absorption: An increase in non-pulsatile absorption i.e. nail varnish/dirty fingernails will reduce the measurable pulsatile component. There may also be **optical interference** with non-constant background flickering room lights and newer LED surgical operating lights which will superimpose a more rapid ‘pulsatile’ waveform.

LASERs

(07d_03_09)

This is an acronym for the principle of **Light Amplification of Stimulated Emission of Radiation**. It is an **intense monochromatic, non-divergent, narrow beam** of light which produces a **very large amount of energy distributed over a small area of tissue**.

Physics of Laser

As described previously, when electrons move from one energy shell to another, quantum energy is either taken up or released as **photons**.

Spontaneous Emission

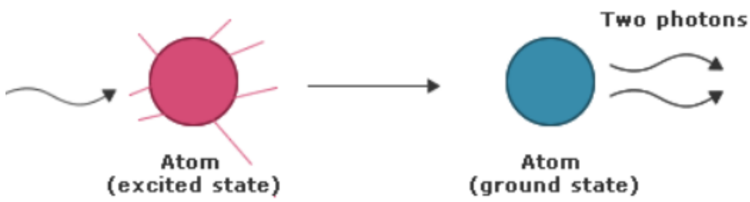
If a **photon is applied** above a certain threshold to an atom, **electrons move to higher energy orbits** and the atom becomes **excited** to a **higher energy level.** This level of excitement depends on the amount of energy applied.

In an **excited state**, the tendency is for an electron to **move back to the ground state** and in the process, **releases light energy as a photon.** This is known as **spontaneous emission**.

NB the light emitted from a material of the same atoms may not be of the same wavelength and may not be in phase. This type of spontaneous emission is known as ***fluorescence***.

Stimulated Emission

Energised electrons act as energy sources for neighbouring atoms to achieve the same energised state. When a photon of energy from a stimulated atom interacts with an identically stimulated atom, it will move to an even higher energy state, known as **stimulated emission**. *When it relaxes, it will release* ***2 identical photons of light*** *that are* ***in phase with each other***.

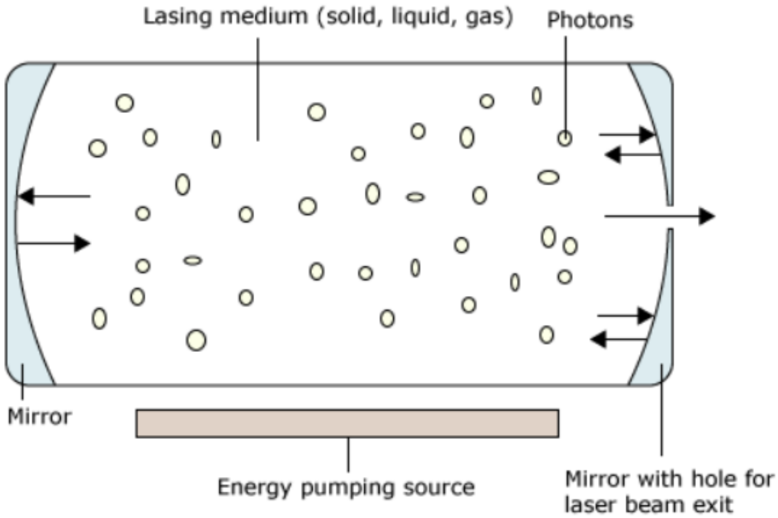


Population inversion describes when a sufficient number of atoms are energised and there is a **majority of atoms with electrons in the higher energy state**. LASER light is created from stimulated emission and has the **following 3 properties:**

1. **Monochromatic:** One specific wavelength
2. **Coherent:** All waves are in phase with each other
3. **Collimated:** Highly directional

LASER Device

A LASER is a **device that amplifies the way energised atoms release photons.** With any LASER, there is a **lasing medium** (all of the same atom). The lasing medium may be either solid, gas or dyes (liquid solutions). This is pumped with **energy** usually in the form of light or electricity in order to create **stimulated emission**.



It is housed with **mirrors each end of the medium** which allows photons to travel back and forth to increase further release of photons and **achieve population inversion**. There will be a small opening to allow light energy, once intense, to leak through and provide its desired physical property.

Clinical Applications

The range of physical interactions includes **optical**, **thermodynamic** and **photochemical** effects. This depends on the medium used and the tissue in question. Generally speaking, light from the ultraviolet and far infrared end of the spectrum has poor penetration being absorbed near the tissue surface, whereas light from the red end of the spectrum penetrates tissues well:

- **Infrared (IR):** induces molecular vibration leading to **heating effects** of the tissue.
    - CO_2 LASER: **10,600nm** is far IR: absorbed by tissue water within 1mm of the tissue surface allowing **bloodless cutting** and **vaporisation**. *Surgical applications*
    - Nd:YAG LASER: **1064nm** is near IR: increased penetration to 3-5mm depth absorbed by **Hb, melanin** and **water**. *Dermatological applications*
    -
- **Visible light:** Photochemical effects
    - Argon LASER: **488-515nm blue-green:** Penetrates to 2mm and absorbed by tissues of complimentary colour i.e. Hb. Therefore, can be used for **blood coagulation** whilst **avoiding transparent tissues** i.e. retinal photocoagulation.

- **Ultraviolet light:** molecular bond dissociation and skin burns.

Energy Levels

Low output devices can thermally stimulate tissues and may be useful for example in physiotherapy. **Medium output** i.e. 40 J/cm will sensitise agents within cells. 10x this energy will cause tissue temp to rise to 60°C and protein denaturation and photocoagulation.

Higher output even to above will result in cellular fluid vaporisation and destruction. Therefore, LASERS are **pulsed** to allow **heat dissipation** and reduce destruction to neighbouring tissues – this is known as a **Q-switching** technique.

Health and Safety

Classified into **four groups of energy output**, in terms of their hazard potential. It is a potential hazard to everyone in theatre and because it is non-divergent in nature (unlike XR beams) – distance does not add any measure of safety.

Most medical LASERs are class 4. They need **appropriate training**, **safety goggles** that are specific to the wavelength of light being used and **environmental factors** i.e. locked and screened doors and windows with signs.

Class 1	Cannot emit radiation at any known hazard levels (for the eye); this means very low power output.
Class 2	Low-power visible lasers, at a radiant power **<1 mW**
Class 3	Intermediate and moderate power lasers, and are **hazardous only if the beam itself is directly viewed**; • **Class 3a** devices can have a power output **up to 5 mW** through a sufficiently divergent beam and the eye may be protected by the blink reflex; • **Class 3b** devices have power output **up to 500 mW**, when direct viewing maybe hazardous to the eye
Class 4	High power lasers **(>500 mW, continuous beam)**, which are very hazardous to view and are a hazard to skin as well.

Other Risks

Flammability: This is an issue with airway surgery with high FiO_2 or use of N_2O. This can also be an issue if directed to the drapes. Modern volatile agents are non-flammable. Reduced O_2 concentration in the vicinity of the beam will reduce this risk – maximum suggested at FiO_2 0.25.

For **airway surgery** specific **LASER tracheal tubes** should be used and plastic tubes avoided. The cuffs of ETT are usually doubled and both ETT and LMA cuffs are filled with saline rather than air.

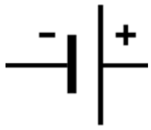
Reflected light: Almost as powerful as the incident beam so non-reflective i.e. matt black instruments should be used. Neighbouring tissues should be protected with wet swabs.

ELECTRICITY AND MAGNETISM

Definitions and Simple Circuits

(07d_04_01)

Glossary of Terms

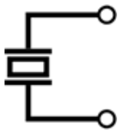


CELL: A power source that supplies electricity as a direct current (DC)

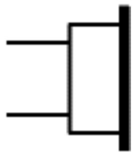
RESISTOR: A device that opposes electrical current by producing a voltage drop in proportion to the current flow (Ohm's Law: V=IR):

TRANSDUCER: A device for conversion of 1 form of energy into another. This includes:

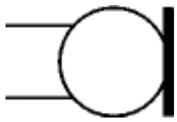
1. **Piezoelectric sensor**: Converts pressure → electrical energy



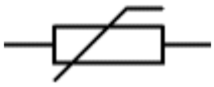
2. **Earphone:** Converts electrical energy → sound



3. **Microphone:** Converts sound → electrical energy



4. **Thermistor:** Converts temperature → resistance

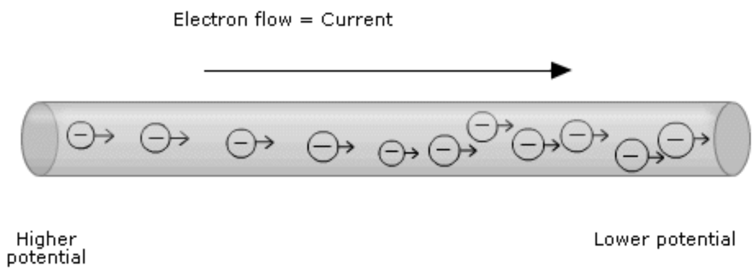


Electrical Charge

CHARGE: (Q) is the **presence** (negative) **or absence** (positive) of a **quantity of electrons** on a conducting or insulating surface. Unit is **coulomb (C).** *1 Coulomb = 6.24 x10^{18} electrons.*

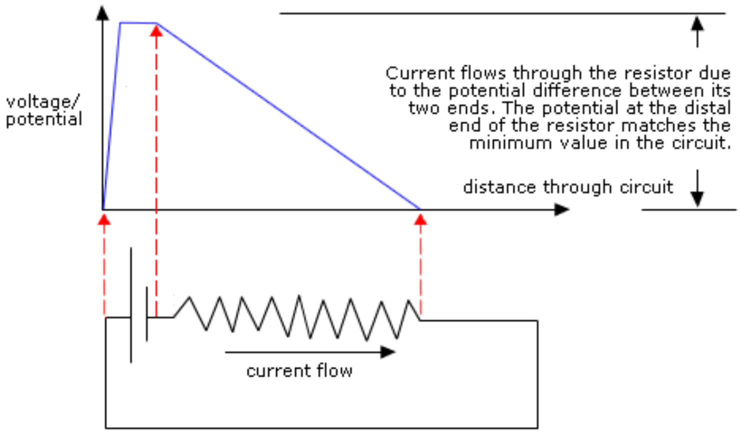
Batteries drive electrons onto conducting plates and if remain on it – generates a negative Q.

CURRENT: (I) is the **flow of electrons** through a conductor or around a circuit. It may be considered as the **rate of change of a charge**. It flows from high→low potential. **Amps**



1 amp = 6.24 x10^{18} electrons/s

Voltage and Potential



VOLTAGE: (V) Also known as potential and is the **driving force for the current.** The potential of any point (V) is the voltage above zero (referenced to **earth**). Unit is **volt**

A drop in voltage occurs as current flows through the circuit and is according to the potential difference or voltage difference between 2 points.

ELECTROMOTIVE FORCE (EMF): (E) Simply the **voltage delivered by a battery or mains supply** also shown in the above diagram.

ENERGY = Joules (J) = Voltage (V) x Charge (Q)

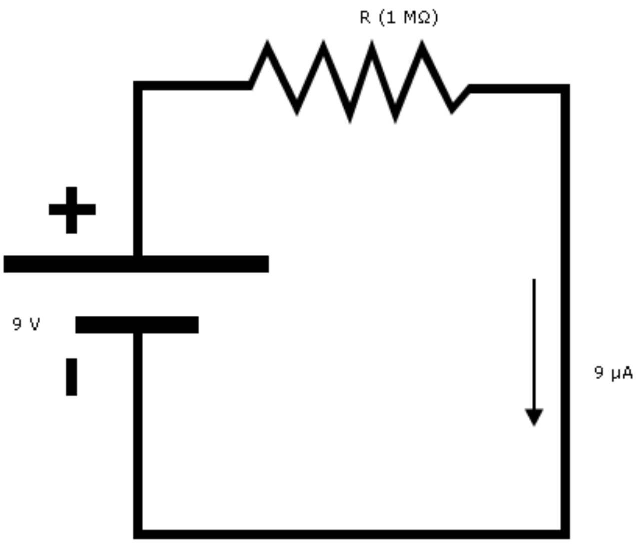
POWER = Watts (W) = Voltage (V) x Current (I) = I^2R *(see below). Energy dissipated per unit time*.

Resistance and Ohm's Law

A circuit with **resistance (R) (ohm, Ω)** will **impede current (I)** causing a **voltage drop (V)** across it. This is known as Ohm's law and can apply to individual elements or the circuit as a whole:

V = IR OR **I = V/R**

Simple Series Circuit



REMEMBER, flow is from –ve to +ve but in diagrams, is depicted as flowing from +ve to -ve.

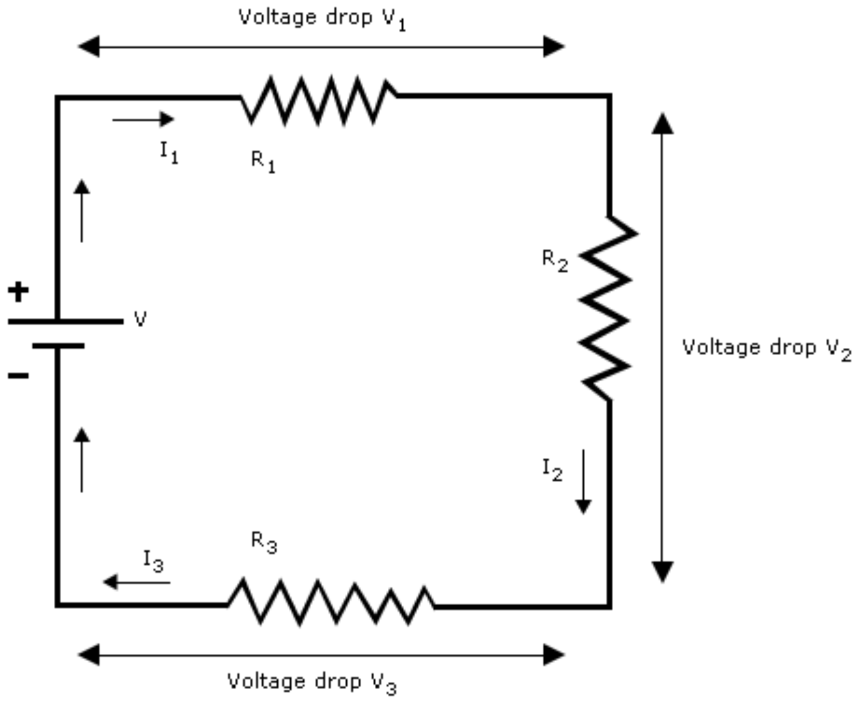
1 mega-ohm (MΩ) resistance = 1×10^6 Ω.

I = V/R

I = $9/1\times10^6$ **=** 9×10^{-6} **amps**

= 9 microamps (μA)

Series Circuit



Now we have 3 resistors in a circuit. The same current goes through all points of the circuit i.e. $\mathbf{I_1 = I_2 = I_3 = I}$

Individually, the voltage drop across each component is:

- $\mathbf{V_1 = I_1 \times R_1}$
- $\mathbf{V_2 = I_2 \times R_2}$
- $\mathbf{V_3 = I_3 \times R_3}$

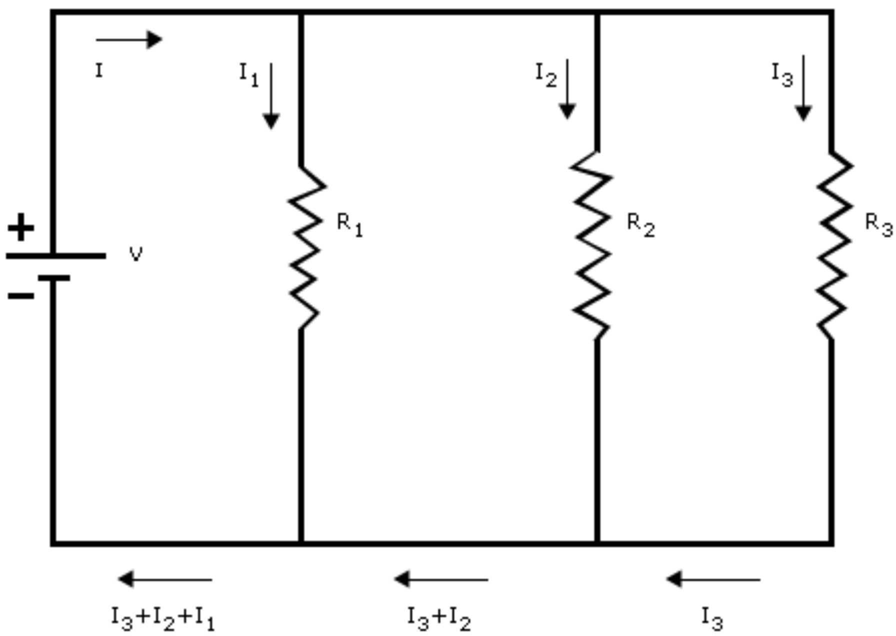
The total voltage drop (EMF) is matched through all 3 voltage drops:

- $\mathbf{V = V_1 + V_2 + V_3}$
- $\mathbf{V = I \times (R_1 + R_2 + R_3)}$

Total circuit resistance is $\mathbf{R_1 + R_2 + R_3}$

Parallel Circuit

Consists of a number of elements arranged in a parallel way:



The **current is divided** between the elements:

$\mathbf{I = I_1 + I_2 + I_3}$

The **voltage drop** is separate in each element i.e.

$\mathbf{V = I_1 \times R_1}$

Therefore…

$\mathbf{I = V_1/R_1 + V_2/R_2}$ **…etc**
$\mathbf{I = V \times (1/R_1 + 1/R_2 + 1/R_3)}$

As $\mathbf{1/R = 1/R_1 + 1/R_2 + 1/R_3}$

$\mathbf{I = V/R}$

Total resistance in parallel is NOT the sum of all resistance. $\mathbf{1/R_x = 1/R_1 + 1/R_2 + 1/R_3 + 1/R_4}$ …etc.

Voltage Dividers

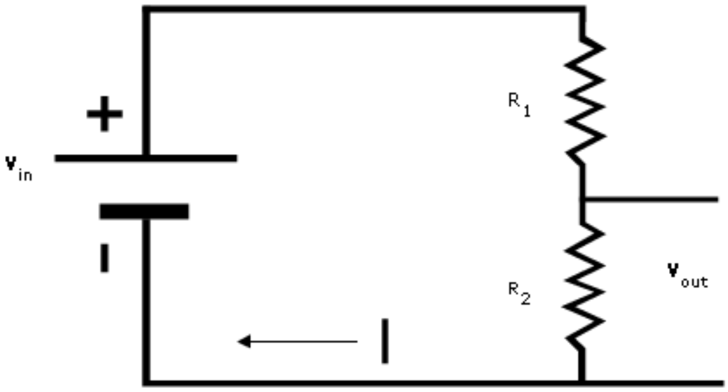
A device for producing an output voltage that is a proportion of the input voltage.

A wire is placed between the 2 resistors in series so that:

$$V_{in} = I \times (R_1 + R_2)$$
$$V_{out} = I \times R_2$$

Therefore:

$$V_{IN}/V_{OUT} = (R_1 + R_2) / R_2$$



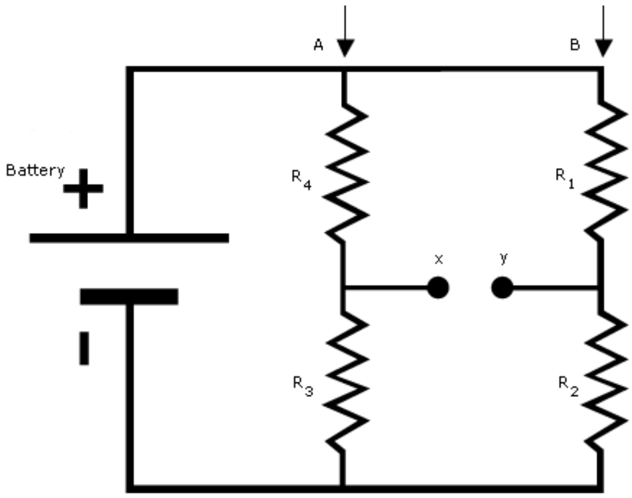
NB. Think of the direction of current and *think of V_{out} as a separate circuit with same current*.

2 Voltage Dividers: A **Bridge circuit**

Now 2 voltage dividers are connected back to back in parallel.

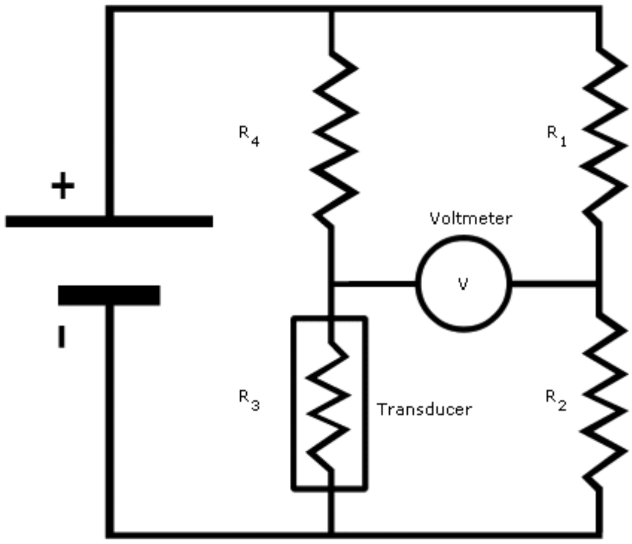
There is a potential state of the resistors when no voltage difference exists between x and y and if they were connected, no current would flow between them. Therefore, the resistor values can be arranged to make the V equal at x and y.

The bridge is now balanced and is useful in circuit quality control to compare circuits with both R_1 and R_2 vs circuits with R_3 and R_4 and is the basis for the **Wheatstone bridge**.



Wheatstone Bridge

The pair of voltage dividers is used to equally divide any **unwanted high voltage signals** common to a whole circuit to cancel each other out i.e. mains, diathermy and then to **allow a possibly much smaller signal** (such as an arterial waveform from a strain gauge transducer) to be detectable at a meter applied between the two arms of the bridge



The transducer in an arterial line is a wire that increases its resistance when stretched. This signal is placed across 1 bridge to produce a measurable voltage on the voltmeter. Now R_1, R_2 and R_4 are constant, and R_3 varies with mechanical strain.

$$R4/R3 = R1/R2$$

There is **increased sensitivity** if another transducer was placed on R_1 as there an enhancement of the difference in signal between the 2 arms of the bridge.

<u>Electronic Circuits</u>

(07d_04_02)

<u>Circuit Elements</u>

CAPACITANCE (C): Is the **ability of an object to store electrical charge**. It is equal to the **charge per unit voltage**. It is measured in **farads (F)** but as this is large, mostly in **microfarads (μF)**.

$$C = Q/V$$

Capacitor comprises of a **pair of conducting plates** divided by a space filled with an insulator:

An equal and opposite charge is induced on the opposite plate

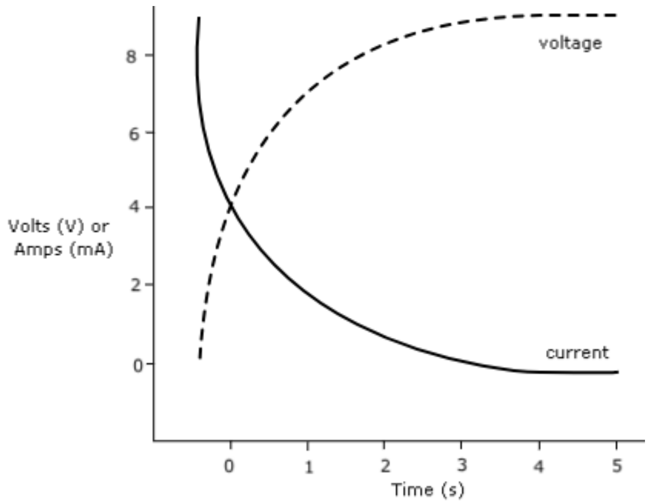
Charge is stored on the proximal plate

Capacitance (C) is equal to the permittivity (E) of the insulating material (capacity of the material to allow an electric field to exist between the plates) multiplied by the surface area of the plate (A), over the distance between the conducting plates (d):

$$C = EA/d$$

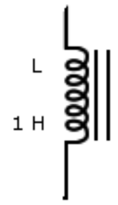
With DC i.e. from a battery/cell, the potential on the proximal plate rises to a maximum (becomes saturated) when the circuit is closed and the opposite charge is induced on the distal/opposite plate to ensure current flow.

If the proximal plate becomes increasingly charged, the **rate of rise of its potential** or voltage decreases. Therefore, the current also decreases. Once the voltage reaches a maximum (9V on diagram), the rate of change stops and no further current flows.



It can be seen that current is proportional to rate of change of voltage. In a capacitor, the rate of change of current or voltage in a capacitor occurs in an exponential fashion in response to a step (**DC**) change of input voltage or current, with an associated time constant, τ. (For a circuit containing R and C elements, τ = R.C).
Therefore, **discharge does not occur instantaneously.**

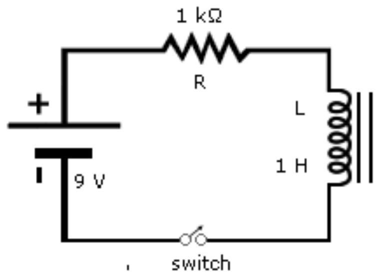
INDUCTANCE (L): is the tendency of a conductor (carrying an AC current) to induce an electromotive force (EMF) that opposes the voltage drop due to the circuit resistance. This is measured by **henry (H)**.



Part of a circuit diagram showing how inductance (L) of 1 H is represented

Any wire carrying a current has an associated magnetic field around it that induces voltage (EMF) and current in nearby (but unconnected) conductors. **Coiling of the wire** results in an **EMF** to **oppose the main voltage drop**.

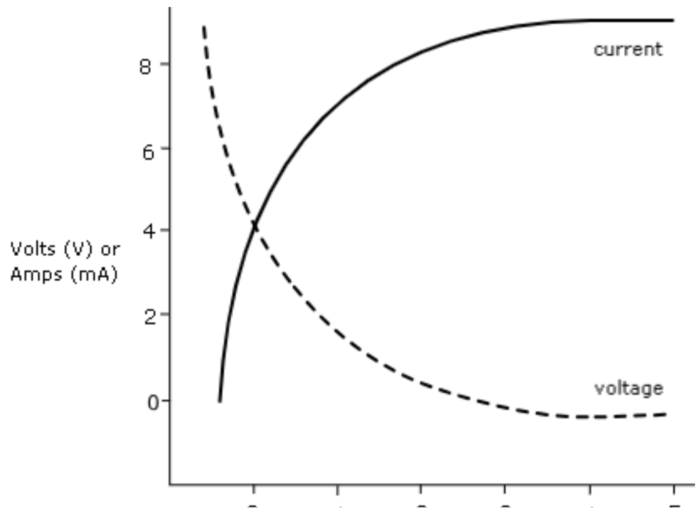
An initial high voltage drop across the inductor induces a magnetic field in the coil. This produces an opposing EMF that in turn reduces the voltage across it and limits the rate of change of the current flow.



Circuit diagram showing a 1 H inductor (L); a 1 kilo-ohm (1 kΩ) resistor (R) and a 9 volt battery

This is essentially the opposite of a capacitor.

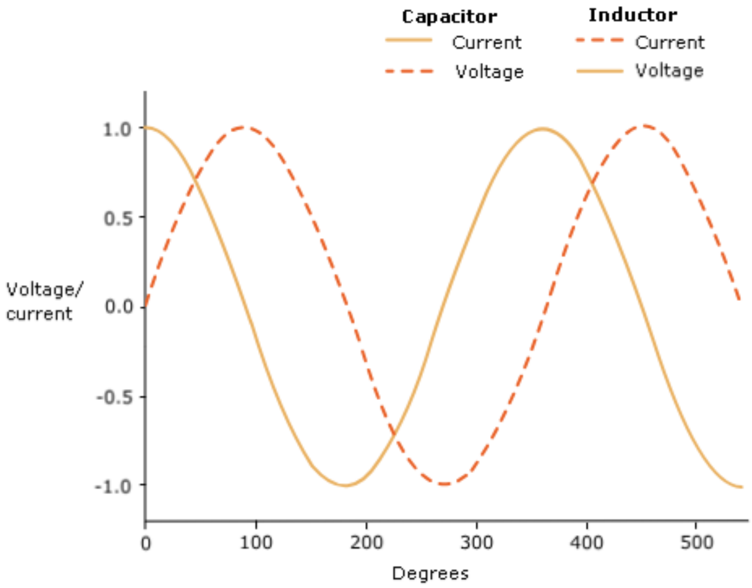
The **rate of change** of current or voltage in an inductor (L) occurs in an exponential fashion in response to a step (DC) change of input voltage or current, with an associated time constant (τ). (For a circuit containing R and L elements, τ = L/R.)



AC Current

The behaviours of above have now only been described in a DC circuit. This changes in the AC current in the following fashion:

- **CAPACITOR:** There is changing charge on the plates so the **current** is induced to flow round the circuit beyond the capacitor **proportional to the rate of change** of **voltage**. The current waveform leads the voltage waveform:
- **INDUCTOR:** The EMF on the inductor is constantly changed and the current is induced to flow through and beyond the inductor. The **voltage is proportional to the rate of change** of **current** and leads the current waveform.



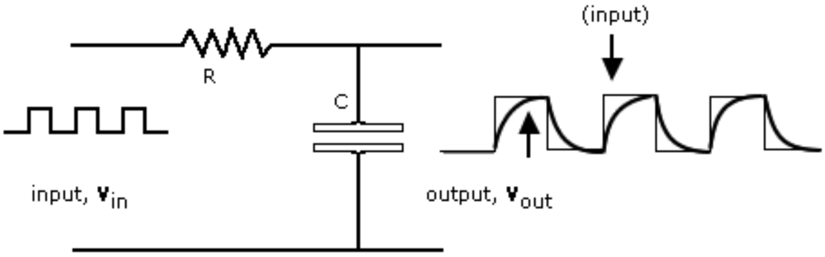
Circuits

RC Circuit

Looks like a voltage divider circuit to produce an output waveform.

f is the **waveform frequency.**

If *f* is high, then the V_{OUT}/V_{IN} is small:



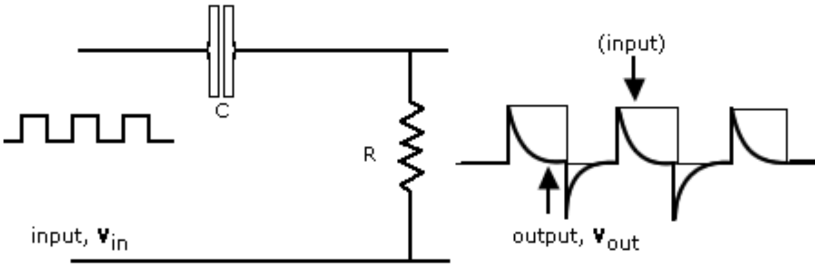
$$\frac{V_{out}}{V_{in}} = \frac{1}{2\pi RfC + 1}$$

The circuit therefore tends to block high frequency signals and allows low frequency signals to pass. It acts as a **low-pass electronic filter** and a mathematical integrator.

CR Circuit

The R and C are in reversed positions.

If *f* is low, then, V_{OUT}/V_{IN} is small.

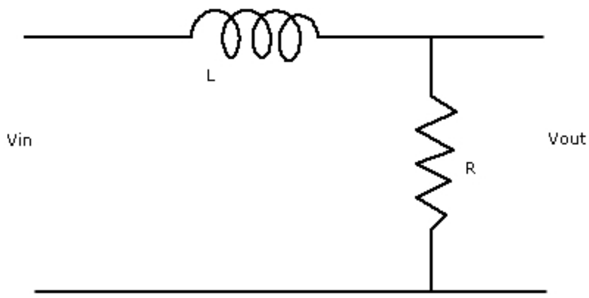


$$\frac{V_{out}}{V_{in}} = \frac{2\pi fRC}{2\pi RfC + 1}$$

The circuit tends to block low frequency signals and allows high frequency signals to pass. It acts as a **high-pass electronic filter** and can be used to **clean up a noisy signal**. Acts as a mathematical differentiator.

LR Circuit

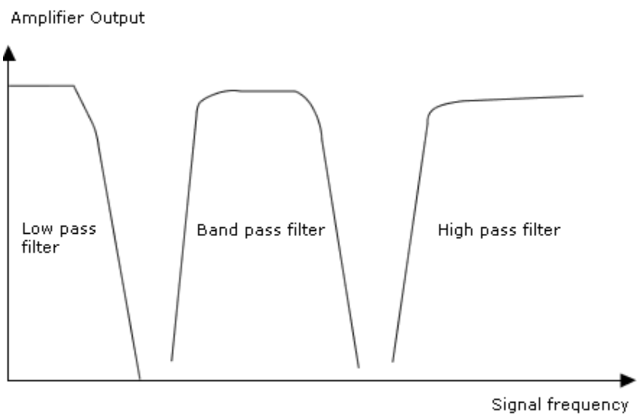
$$\frac{V_{out}}{V_{in}} = \frac{R}{R + 2\pi fL}$$



This is another **low-pass filter**.

Electronic Filters

As seen above, signal outputs from different filter circuits vary with frequency:

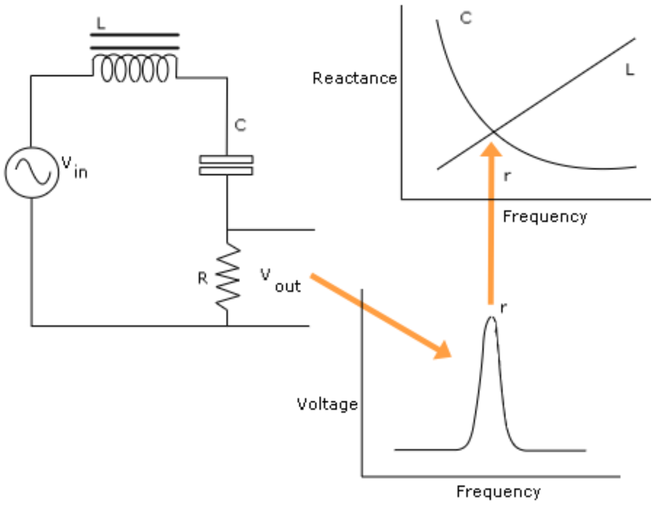


- A **low-pass filter** allows through signals of low frequency
- A **high-pass filter** allows through signals of high frequency
- A **band-pass filter** allows through signals within a specified bandwidth, blocking high and low frequency components

LRC Circuit

Note:

- L element's R is directly proportional to *f*
- C element's R is inversely proportional to *f*



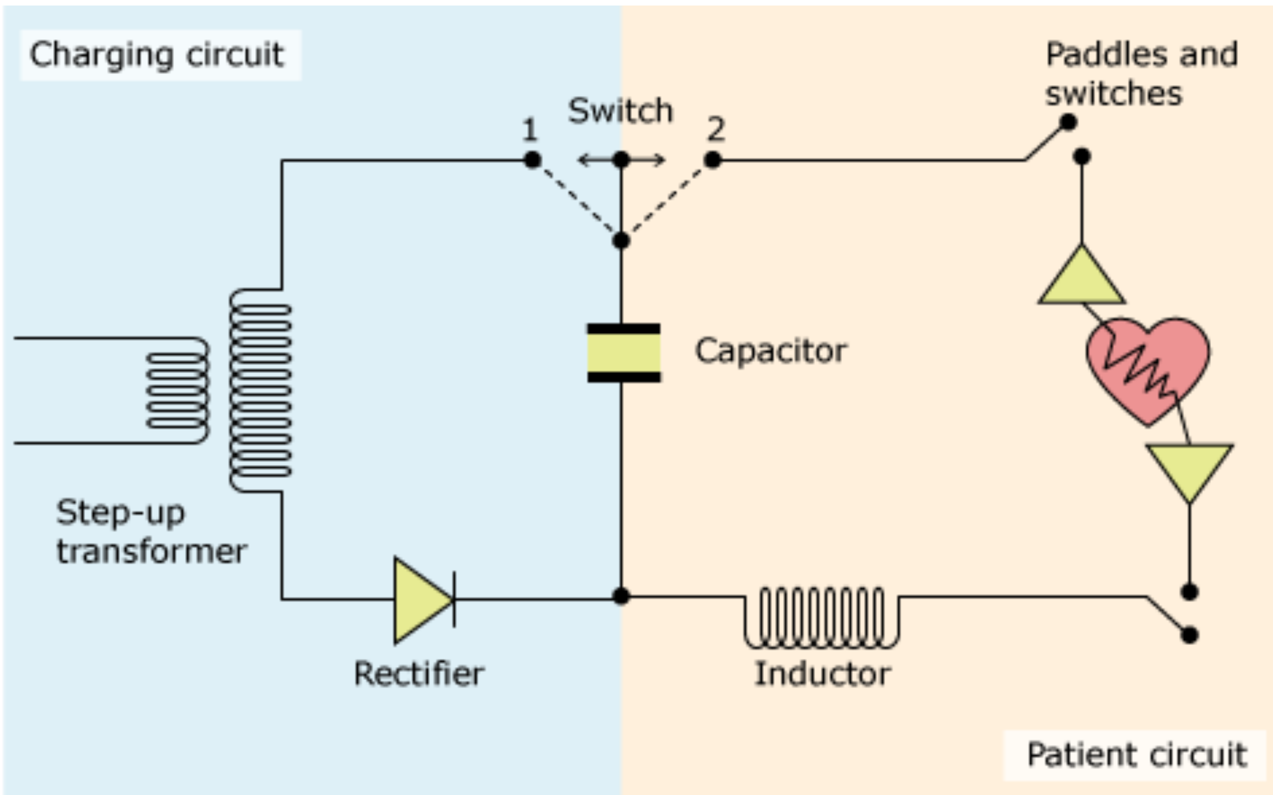
Frequency-dependent resistance is called **'reactance'**, and a circuit element which has components of R, L, and C has a **combination of reactance and resistance** called **'impedance'**

At the 'resonant' frequency (r) for this circuit, the circuit reactance is at a minimum, and V_{out}/V_{in} is at a maximum as shown in the lower curve.

IMPEDANCE: (Z) Is the measure of a circuit's resistance to flow of current taking into account the effects of inductance and capacitance. Therefore, unlike resistance, it takes into account the current frequency.

Defibrillation

Understanding the mechanism and the principles behind defibrillation is an important principle to learn.

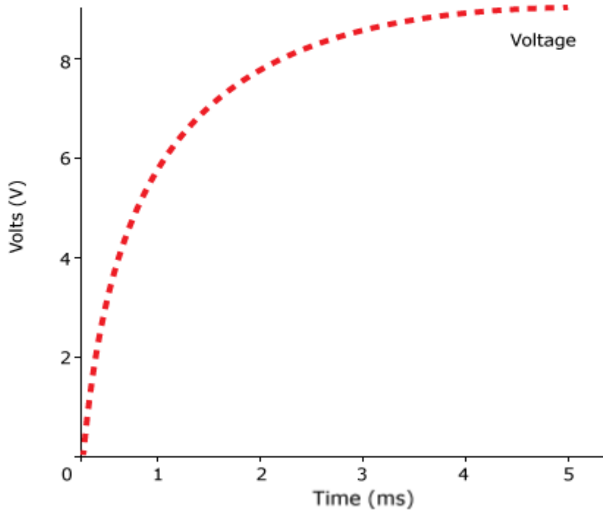


The defibrillator can be divided into 2 components:

Charging circuit: This is designed to store a large amount of electrical energy in readiness to be discharged to the patient. Voltage is applied to the circuit via a **step-up transformer** and current delivered in a **DC** fashion via a **rectifier**. The current is **delivered onto a capacitor** and stored as charge (Q) creating a **potential difference (V)** across the capacitor plates. The larger the voltage applied by the transformer, the greater the charge that is stored by the capacitor **(C = Q/V)** – remember capacitance is specific to the device (usually 32μF in the defib circuit).

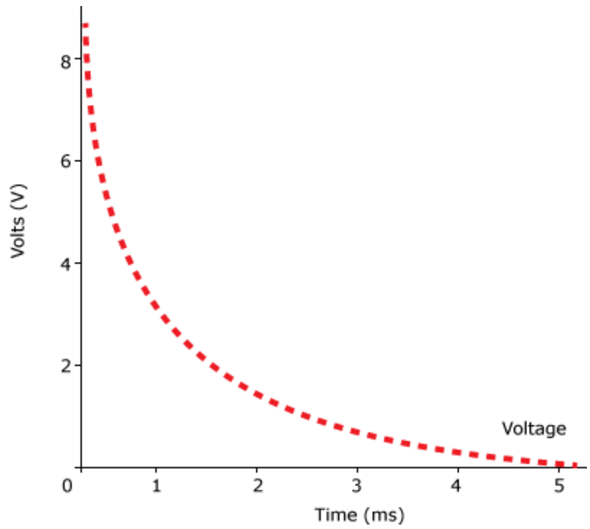
Work (W) to move charge (Q) through a potential difference (V) is governed by the equation: **W=VQ**

As V increases across the plates, W must increase to store Q on the capacitor and hence, the increase in voltage across the capacitor will slow down in an exponential manner as it reaches a maximum (proportional to the applied voltage):



At this point, the **switch** is closed to the charging circuit and open to the patient circuit (position 1) preventing discharge to the patient.

Patient circuit: Once the switch is closed to the patient circuit (patient completing the circuit via conductive pads) and open to the charging circuit (position 2), the **charged capacitor is discharged** and energy applied to the patient until the voltage across the capacitor falls back to 0. This is also an exponential process:



An **inductor** is placed on the patient circuit in order to **prolong the time over which energy is discharged** to the patient and is shown to increase the likelihood of successful defibrillation. Remember, inductors oppose the flow of current due to electromagnetic induction. It shifts the curve seen on the graph to the right.

Energy delivered is calculated from the following equation:

E = ½ QV where half of the energy is dissipated through circuit resistance and radiation.

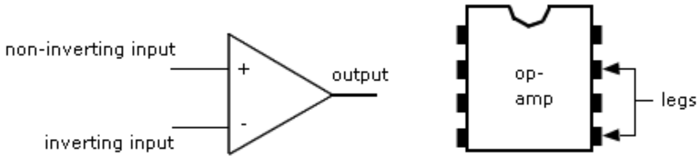
Not all energy delivered is applied to the myocardium as some is lost through impedance of the skin, thoracic wall and other intrathoracic structures.

Amplifiers and Interference
(07d_04_03)

Operational Amplifiers were a major step forward in electronic circuits in the 1940s. it is desirable to know something of the ideal properties of 'op-amps' in order to recognize whether an electromedical signal is a faithful representation of a patient's physiological recording.

Design

Designed to **amplify** i.e. increase or gain an electrical signal by a factor of 10^6 or more in a **linear fashion** without distortion. They have a very **high input resistance** (impedance) more than 1MΩ in order not to draw current from the upstream circuit.



The inputs consist of one which maintains the sign of the input signal and one which switches the sign (inverts) the input signal:

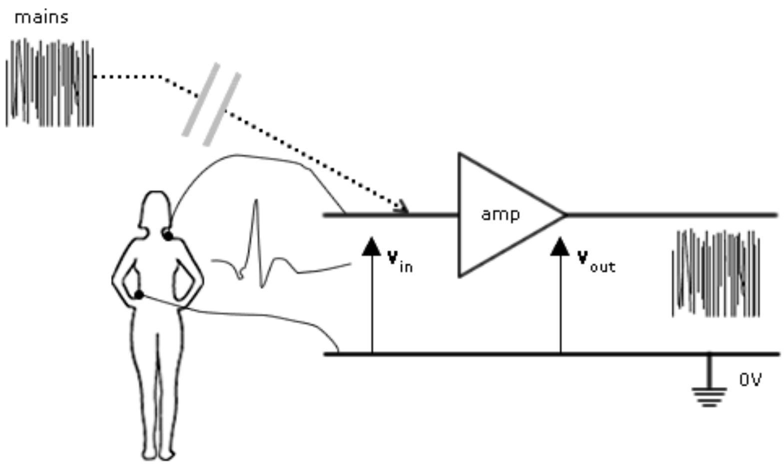
Common mode rejection ratio (CMRR): These amplifiers have inverting and non-inverting differential inputs in order to **neutralize upstream circuit noise**, i.e. signals common to both inputs, and only amplify input voltage difference (signal which is not common to both inputs). This is called a **high common mode rejection ratio**.

A CMRR of 10^4 means a common mode signal of 10 000 mV is needed before 1 mV enters the op-amp for amplification

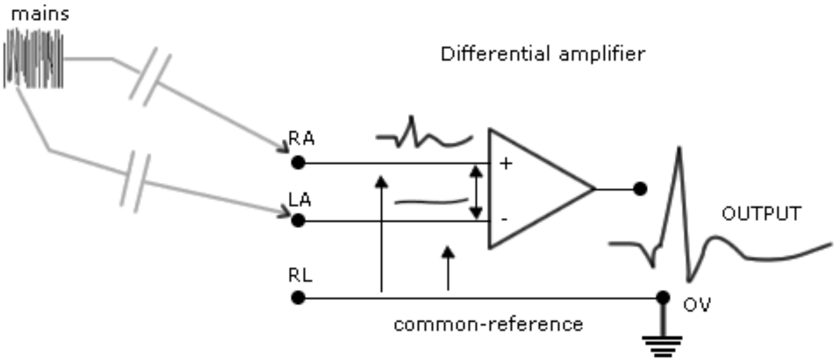
Single Vs Differential Inputs

Example with **ECG**:

Single input: into the amplifier. It may cause **capacitance coupling** (transfer of energy via capacitance) will amplify mains hum in which an ECG signal may become swamped and unreadable:



Differential input op-amp will cancel out noise common to both inputs. The smaller differential signal will amplify and appear as the amplifier output. A good quality op-amp will have a high common mode rejection ratio.

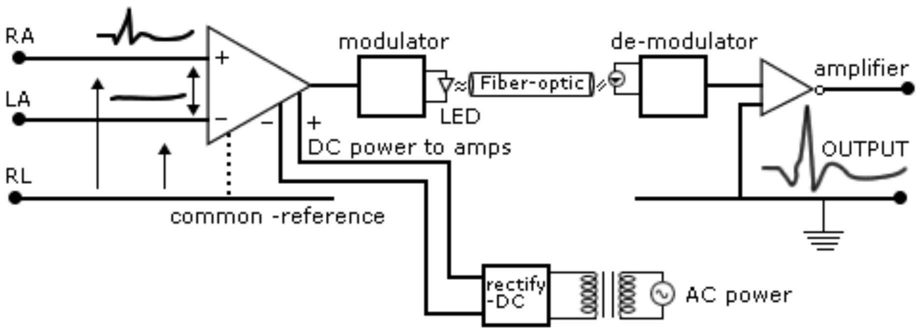


Gain is the ratio of amplifier output to signal output and is measured in Decibels.

ECG

Additional safety features are seen on the circuit:

- No patient connection earthed. The patient circuit is 'floating'
- DC, non-earthed power source to op amp
- An opto-isolating circuit connected to a further (earthed) op amp circuit designed to produce a signal output waveform, which is completely isolated from the patient



Signal Processing

Other signals apart from those that are amplified by a differential amplifier i.e. ECG, may be amplified via a **single input amplifier** i.e. via a **transducer from a Wheatstone bridge**.

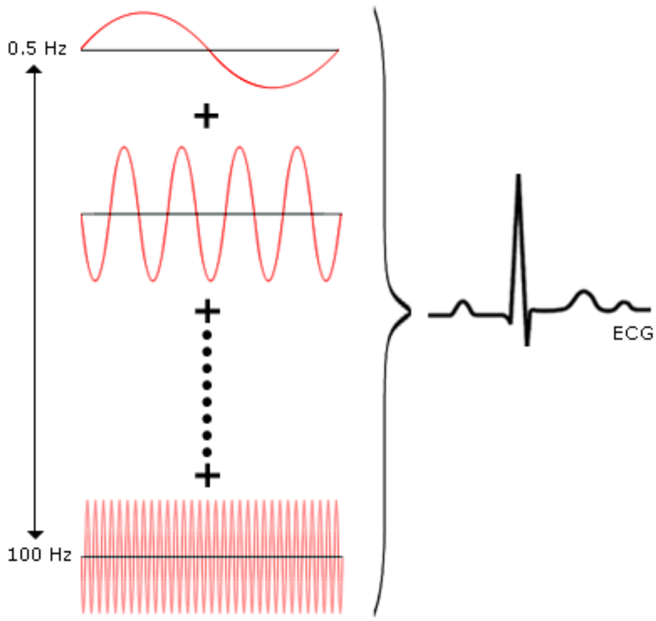
Electronic band pass filters may then amplify the signal specific across a range of frequencies i.e. with an ECG signal of 0-100Hz.

Further processing of the signal may occur using other components i.e. differentiate or integrate signals. See previous lectures.

Excitable Tissues and Biological Potentials

(07d_04_04)

Biological potentials are composed of sine waves with different frequencies and phases. A complex waveform i.e. ECG can be analysed using **Fourier analysis** which breaks down a composite wave into its simpler components:



Electrocardiogram (ECG)

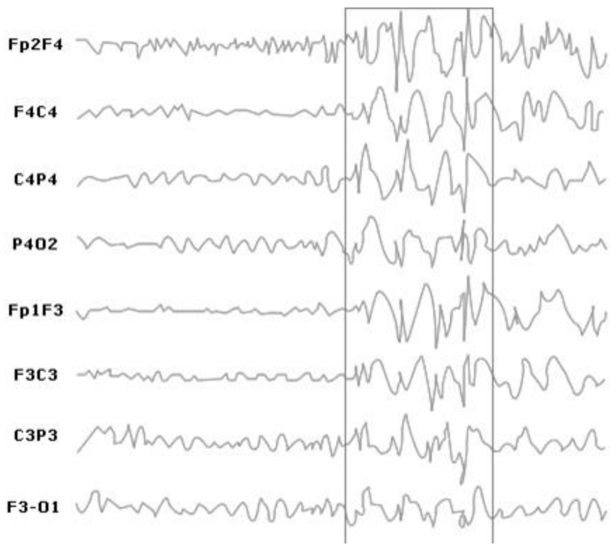
Measure of the electrical activity of the **heart**. The size of the measured potential depends on the:

1. **Mass of excitable tissue** and the
2. **Extent of mass separating the heart from the recording electrode.**

This is why the measured ECG is **1-2 mV** and not 90 mV. Between 3-100Hz.

Electroencephalogram (EEG)

Measure of the electrical activity of the **brain.** Similar to the ECG, the scalp electrode recording is reduced from meninges, CSF, and skull, so measured potentials are in the region of **50 μV**.



Depending on the region and the activity observed, there is a predominant frequency. The order of waves seen in reducing conscious levels are as follows:

1. **Beta:** awake and concentrating (12-25Hz)
2. **Alpha**
3. **Theta**
4. **Delta:** Slow wave sleep (3Hz).

The measured EEG frequencies are variable and between **3 Hz to 100 Hz.**

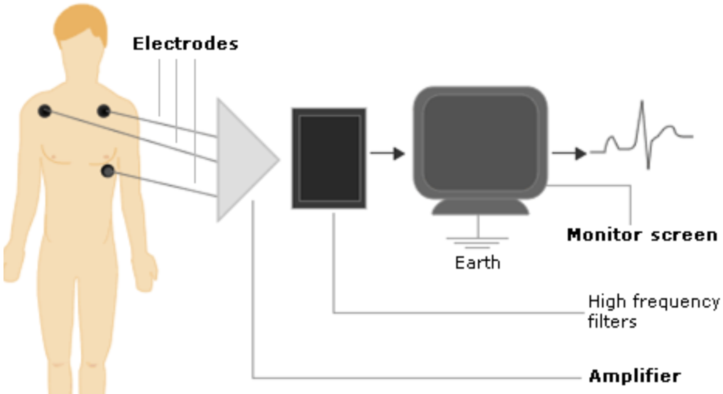
The EEG above shows development of epileptiform activity.

Electromyogram (EMG)

Measures electrical activity in **skeletal muscle.** Activity is dependent on the number of motor units stimulated and is between **50 μV up to 30 mV**. The **short repolarisation** leads to a frequency between **5Hz to 100Hz** which is greater than that in cardiac muscle.

Recording Systems

This has been covered in previous lectures but simply, requires recording through **electrodes,** an **amplifier** (could be an op-amp) and an Analogue to Digital Converter (ADC) to a **display unit**.

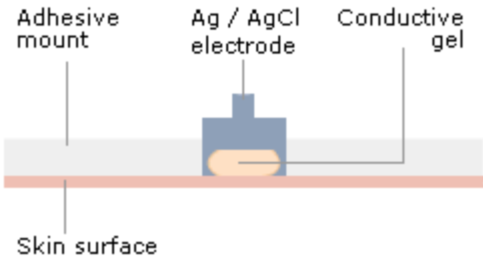


The electrodes are usually non-invasive – this may lead to problems including:

1. **Poor contact** which will lose the signal display.
2. **Chemical changes** in the recording electrode from the biological signal. This is called polarization and leads to altered performance of the sensor.
3. **Moisture trapping** – battery effect where the recording system itself generates a potential.

This has been solved by the construction of modern electrodes with silver (Ag) electrodes in contact with silver chloride (AgCl) and a conductive gel rich in Cl^- ions.

An adhesive disc surrounds it to provide best contact with the skin.



Amplifiers increase the biological signal amplitude through **gain** and is measured in **decibels**. The **bandwidth** describes the range of frequencies this device will function satisfactorily. As mentioned before, the interference is removed by differential amplifiers that use the property of **common-mode rejection ratio** (**CMRR**).

Clinical Applications

Defibrillators

It is a **capacitor** that collects and **discharges electrical charge**. The energy discharged is described as **joules** which is **directly proportional to the voltage applied** and the **charged stored across the plates**.

An **inductor** modulates the shape of the current delivered to the patient and is picked up by the myocardium. A gel pad **minimises the impedance** when applying paddles to the patient.

Electroconvulsive Therapy

Is analogous to defibrillation but applied to the brain, of smaller current and delivered in pulses.

Peripheral Nerve Stimulators

Used in anaesthesia to assess degree of NMB. Gel electrodes stimulate the peripheral nerve via the skin at a current of 50-80mA. A common example is stimulation of the ulnar nerve at the wrist and contraction of the adductor pollicis muscle.

Needle Nerve Stimulators

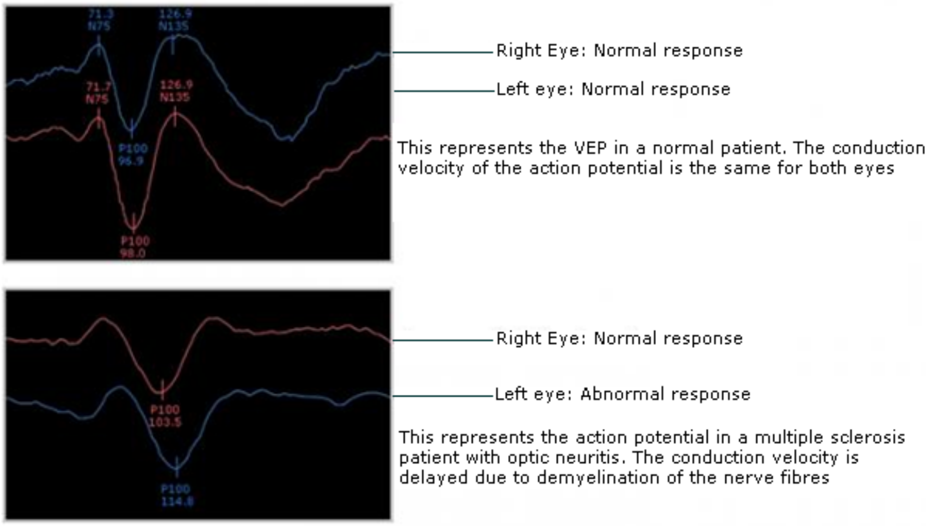
Used during regional anaesthesia or plexus blockade. The current is directly applied to the tip of the needle (cathode) to **locate** the nerve/plexus and induce contraction of the innervated muscle. This uses a **much lower current** of <2mA as is much closer to the nerve.

If stimulation to cause contraction occurs at a very low current i.e. <0.3mA, the tip may be within the nerve. A good test to prevent intraneural injections.

Evoked Potentials

Stimulation of neural tissue causes electrical changes that may occur at distal sites in the pathway. For example, with **visual evoked potential**, visual stimuli are induced and the potential is measured in the neural circuit. Any abnormalities may indicate damage to the conducting pathway.

This can also involve motor pathways.

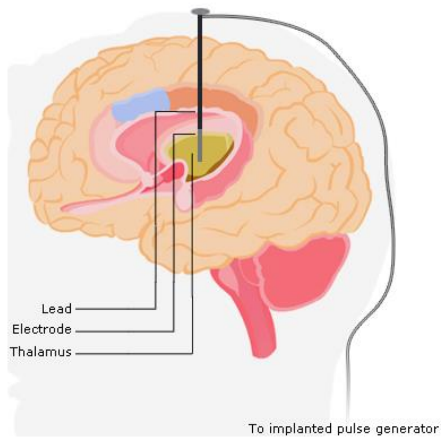


Cardiac Pacemakers

Simple transcutaneous pacemakers may cause myocardial stimulation. More complex cardiac pacemakers include a sensing electrode (endocardial), pacemaker box (inframammary) and a pacing lead (endocardial). One can choose which chamber to sense and pace.

Deep Brain Stimulators

Used to treat **movement disorder**. Placed in close proximity to the centres that regulate movement, such as the thalamus. This electrode is then connected to an implantable pulse generator which delivers a set current to stimulate the relevant part of the brain. Provided it is correctly placed, this does not result in activation of other areas of the cortex.



Magnetism and Current

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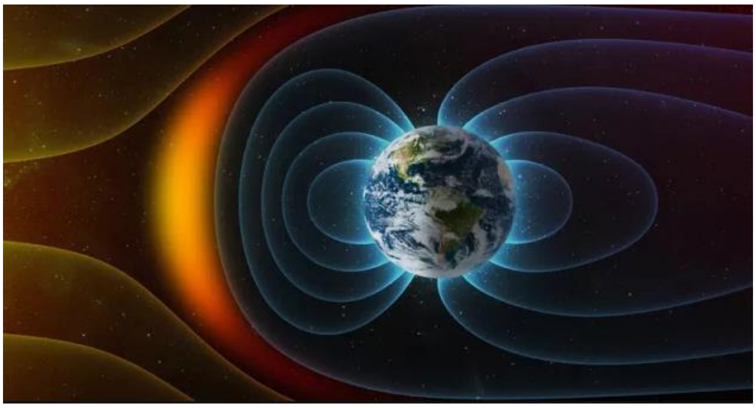
Magnetism

Macroscopically



The Earth's magnetic field protects us from harmful radiation. Not all planets have a magnetic field.

A **magnetic field** is **created or induced around a conductor carrying moving electrical charge** (current). Thus, magnetic fields can be created using electrical power, and can be used to provide mechanical force, as in an electric motor or a galvanometer.

Conversely, a **current may be induced** in a **conductor moved through a magnetic field** proportional to its speed of movement. Therefore, **mechanical force can create electric current, as in a dynamo**.

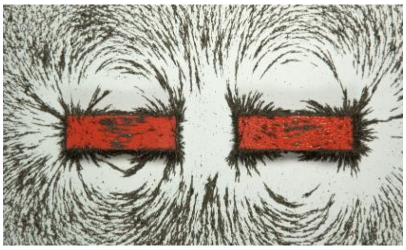
Microscopically

The **spin of an electron** in its orbital is in essence an **electrical charge in motion** at a localised level. In most materials, neighbouring atoms spin also and cancel each other out. The effect of an applied magnetic field of high intensity on these electron spins in human tissues forms the basis of MRI.

Materials with unbalanced electron spinning are known as **ferromagnetic materials** i.e. iron. These atoms align themselves in randomly oriented microscopic domains, so that within each domain there is an intense localized magnetic field. Macroscopically the domain orientations cancel each other out and the material exhibits no magnetic field externally.

If an external magnetic field is applied to the ferromagnetic material, the electrons polarise (align themselves with the magnetic field) i.e. a compass needle in the earths magnetic field.

Magnetic Field, Flux and Flux Density



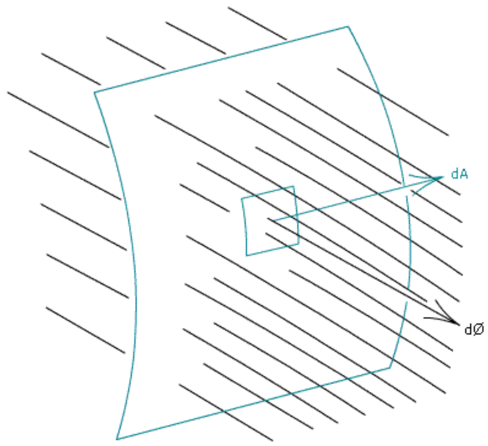
Magnetic flux are the lines that are drawn to represent the magnetic field around a magnet. Where the **lines of flux are closer together**, the **flux density is high** and the current produced with high flux density is high.

A **magnetic flux density** B (tesla) is said to exist when an **electric charge** Q (coulomb), **moving perpendicular** to the field **at a velocity** U ($m.sec^{-1}$), **experiences a force F** (newtons), where:

$$F = QUB$$

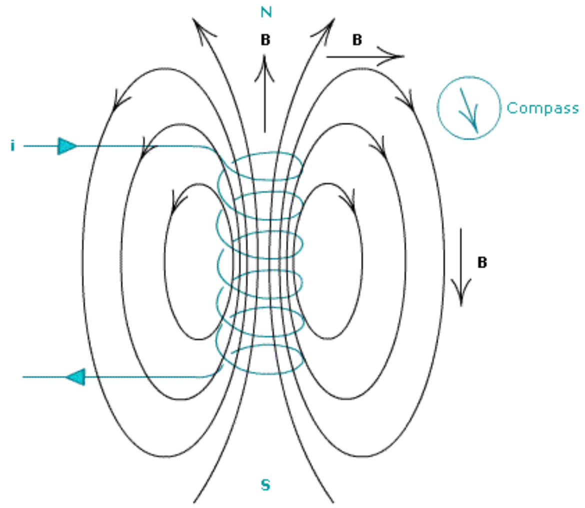
This equation therefore links, electrical, mechanical and magnetic phenomena and is very simple. It follows that **flux density**, B, can be **summed over an area** to give **total flux**, Φ (Weber).

This figure represents a magnetic field and shows the lines of flux of specific density over a specific area where:



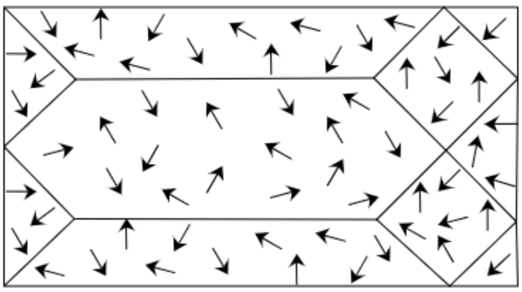
$$\delta\Phi = \delta B \times \delta A$$

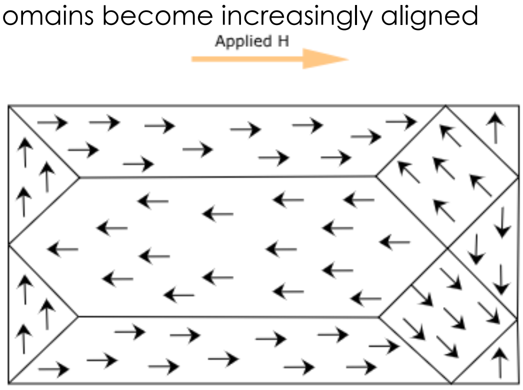
These lines of flux arealso shown when a current (I) is passed through a coiled wire:



Ferromagnetic Materials

If an increasing **magnetic field strength** (**H**) (amp.m^{-2}) is applied to a ferromagnetic material, an **increased flux density** (**B**) (tesla) develops as the magnetic domains become increasingly aligned with the applied field through spin of unpaired electrons.

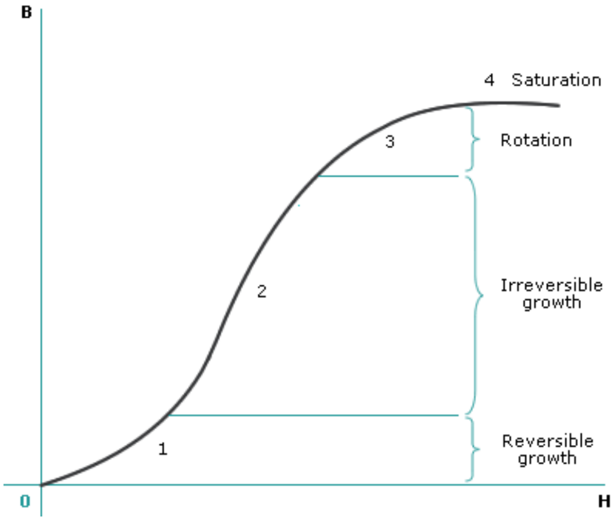




A curve can be produced to describe the behaviour of ferromagnetic materials.

- **Region 1:** Reversible pathway of magnetic domains
- **Region 2:** Onset of irreversibility
- **Region 3:** Domains are irreversibly aligned aka **saturated** and the metal is a magnet. In Iron, this occurs at 1-2 tesla.

This curve shows that as magnetic field strength (H) increases, the flux density (B) increases in ferromagnetic materials.

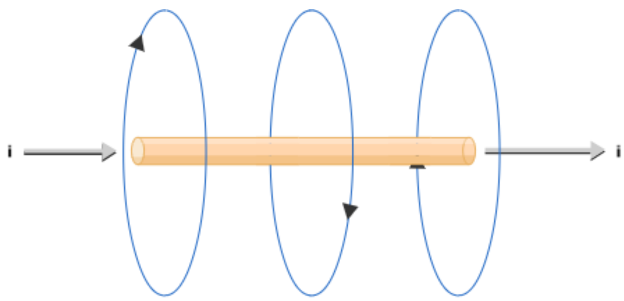


$$\mathbf{B = \mu \times H}$$

μ is the permeability of the material where the more permeable it is, the higher degree the material will respond to an applied magnetic field – high for ferromagnetic materials and low for air.

Electrical Current

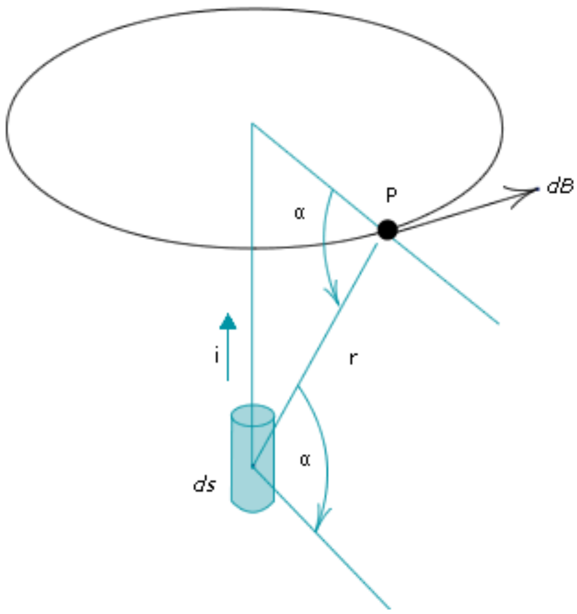
As mentioned previously, a wire carrying an electrical current induces a magnetic field around it in a **clockwise manner** when looking in the **direction of current flow**.



Ampere (1820) discovered that the contribution of **current** (**i**) in an element of **wire of length** (**δs**) to the **magnetic flux density** (**δB**) at a **point P** is **proportional to the current and to the cosine of angle a, and inversely proportional to the square of the distance** (**r**):

$$\delta B = \mu . i . \ \delta s . \cos a/(4\pi r^2)$$

If this is integrated for the whole wire, B = (μi)/(2πr)

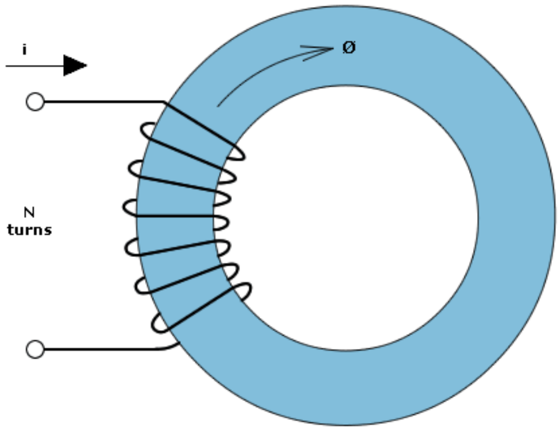


If the wire is **coiled** the flux density is magnified from the close proximity of the coils. The **flux induced is proportional to the number of coil turns**.

Henry discovered that a **voltage induced is directly proportional to the rate of change of the magnetic field** in the coil and Lenz said that the **induced voltage opposes the change of magnetic flux which produced it** (reduce current change flowing in the coil).

Therefore, the voltage is proportional to the number of coil turns and the rate of change of magnetic flux (dΦ/dt)

$$V = N (d\Phi/dt)$$

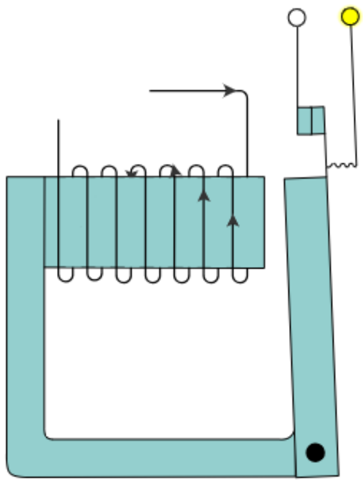


Round an Iron Core

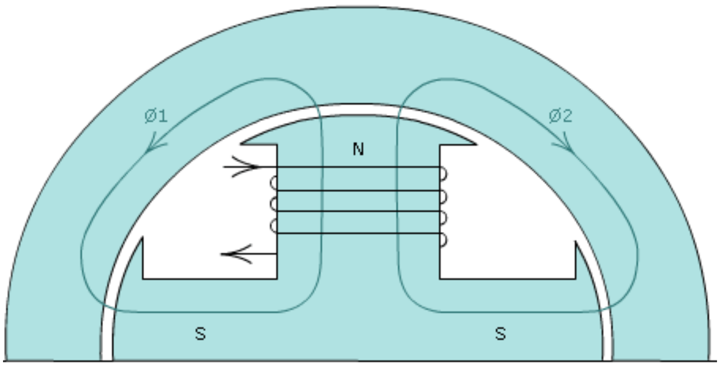
If the wire was coiled around a **toroidal shaped** (donut) iron core, the **flux density increases** for a given magnetic field strength due to the **high permeability of iron.** Remember that B=μH.

Uniform Flux Density

Some magnetic circuits use geometry to ensure uniform flux density. This may be used in a relay switch (right):

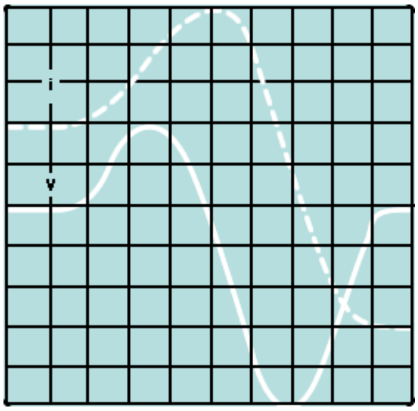


It may also be used in a generator. A 4-pole generator uses 4 stationary magnets surrounding a rotating central coil (outside rim). The force driving the generator turns the central section. As the coil crosses the magnetic field electrical current is generated in the wire



Inductance

If an **AC generator** was used to drive a current across a coil of wire; there will be an **alternating flux density** which will induce a **voltage proportional to the rate of change of flux density** dB/dt. The **magnetic flux opposes the change in current** which had produced it. Therefore, the **voltage required to drive the current is proportional to the rate of change of the current.** Represented by the graph and following equation:



$$V = L \times di/dt$$

Where…

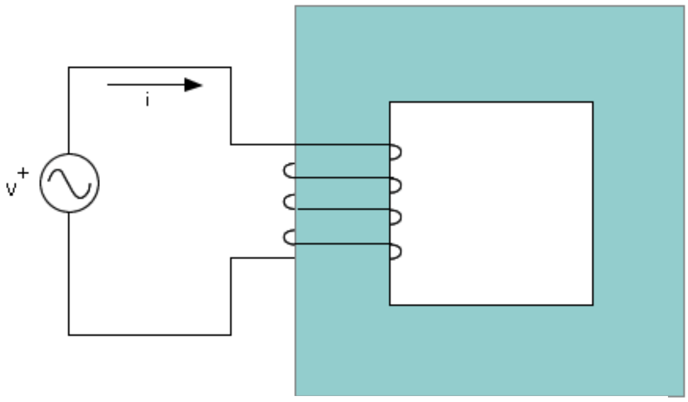
L = inductance (Henry) of the coil of wire

The concept of inductance can therefore only occur in an AC but not in a DC.

Magnetic Circuits

In the pictured circuit, when a **DC voltage** is applied, the **current is determined** by the **resistance** of the wire.

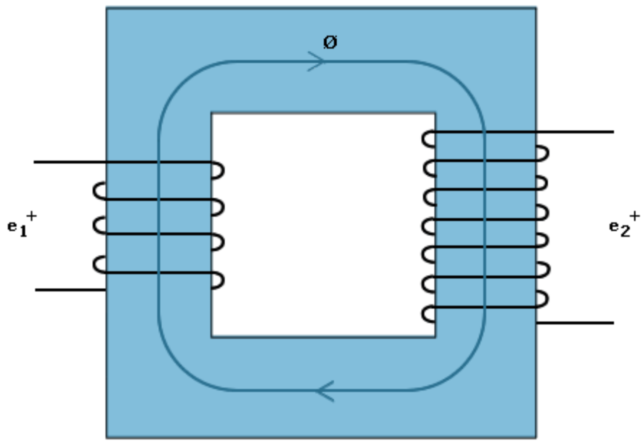
When an **AC voltage** is applied (pictured), the current which flows is governed partly by resistance but mainly by **inductance of the coil**.



Mutual Inductance and Transformers

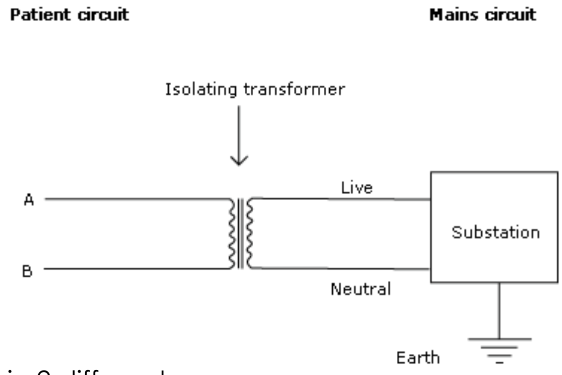
Transformers transfer electrical energy from one circuit to another by means of a magnetic field linking both circuits.

As voltage is induced from the rate of change of a current which also causes a change in magnetic flux, the transformer can **only work in an AC current.**



Isolating Transformer

Consists of 2 coils electrically insulated from one another. One circuit is attached to the mains with AC to the **primary coil** which induces an EM field around it and hence a current in the **secondary** (aka patient) **coil** which is on a '*floating*' circuit that is **not earthed** (unlike the primary coil's circuit).

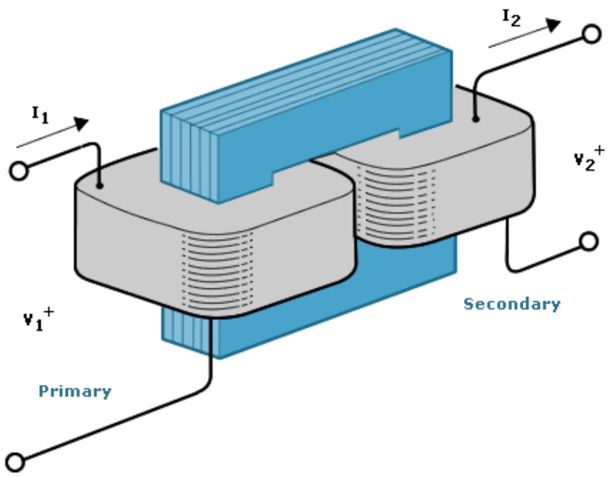


If someone touched the mains circuit whilst touching the earth, they will be electrocuted (full circuit achieved). In the isolating circuit, the wires A and B are not connected so current cannot flow. They can be used in 2 different ways:

1. **Isolate an entire operating theatre** but if one piece of equipment were to faulter, the power will be lost to the entire theatre)
2. **Isolate individual instruments** used in UK.

Transformer Operation

Step-up or **step-down transformers** are used to adjust appropriately the voltage difference between the input and output. This is done through adjustment of the **number of coils** (**N**) which are made out of copper to reduce losses with a steel core (high permeability) to minimise hysteresis losses.



Eddy currents are opposing flows of current that can develop due to variations in the magnetic field or relative movement of the conductor. This will in turn create their **own magnetic field** and this opposition will result in resistive losses.

The components are therefore **laminated** in high electrical resistant materials to minimise the eddy flows in the boundary of these components.

$$V_2/V_1 = N_2/N_1 \quad \text{and} \quad N_1 \times I_1 = N_2 \times I_2$$

$$V_2 \times I_2 = V_1 \times I_1$$

Nuclear Magnetism and MRI

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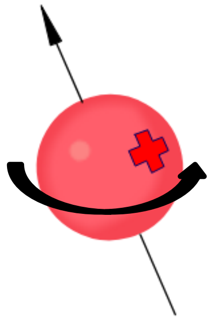


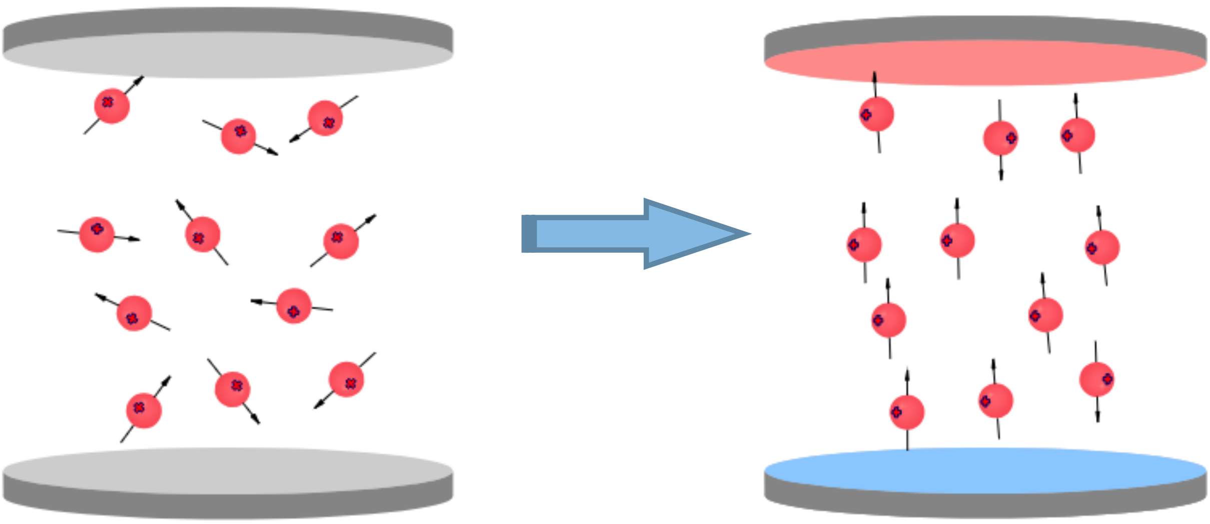
Nuclear Magnetism: The imbalance of the number of protons and neutrons in an atom's nucleus gives the property spin. A +ve electrical charge + spin = magnetism.

Hydrogen is the main isotope with the imbalance that is imaged in MRI as it is in abundance throughout the body. Hydrogen with a single proton (1H) produces the strongest MR signal when compared to other nuclear magnetic isotopes.

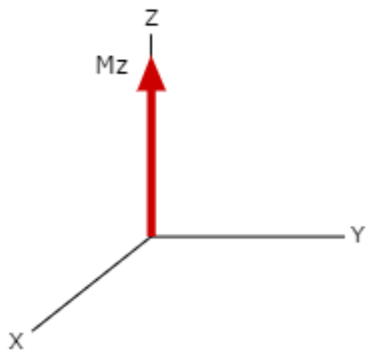
Magnetic Resonance

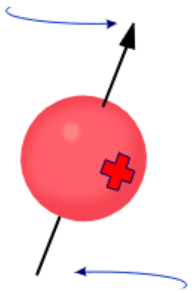
With all these isotopes present in the body, similarly to ferromagnetic materials, they cancel each other's magnetic field out as are orientated randomly.

When placing a **strong magnetic field** externally, the **majority orientate with the field.** There are always some that are aligned against the magnetic field. This is due to **inherent energy** within these protons allowing them to oppose the magnetic field.



Net Magnetisation is the sum of all the magnetisation of tissues depending on the number of hydrogen protons that align in the magnetic field. This is also known as **Mz** and can be represented in this graph:





Precession

Spins with a motion in which the axis of rotation describes a cone: Rather than complete alignment with the magnetic field, they are at a slight angle to the main field. Combined with the property of spin within the hydrogen nucleus produces **precession**.

Larmor frequency (Hz) describes the **rate of procession** and is determined by the following equation:

$$\dot{\omega} = \gamma \times B_0$$

$\dot{\omega}$ = Precessional frequency

γ = Constant of isotope (gyromagnetic ratio)

B_0 = Magnetic field

Magnetic field strength is **directly proportional to precessional frequency**.

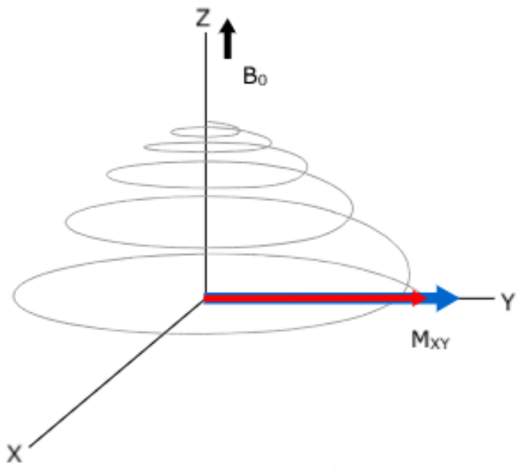
Equilibrium

Resonance

Involves the **absorption of energy** by precessing systems. For **resonance to occur** the **energy must be delivered at the same rate of oscillation/precession** referred to by the **Larmor frequency** in MRI.

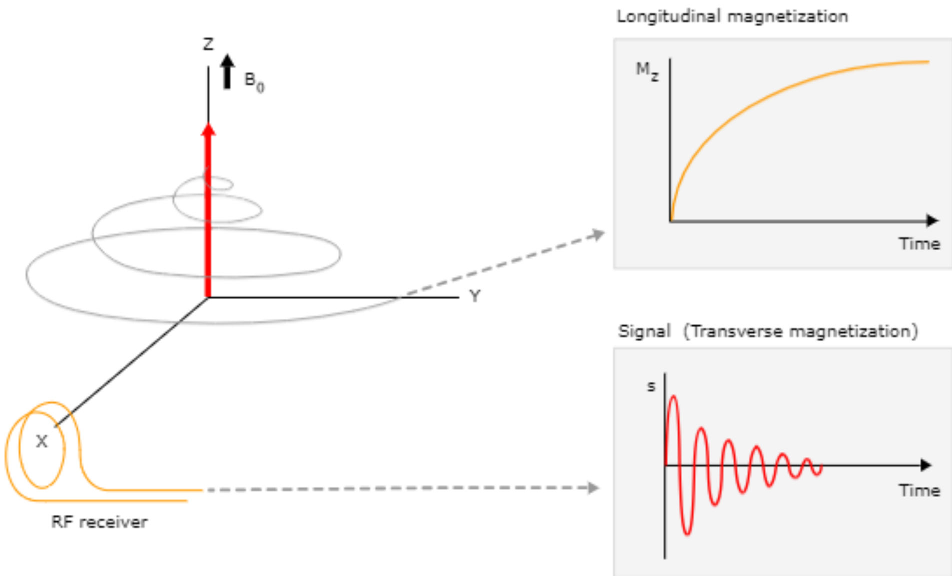
If a strong magnetic field initially lined up the protons; another energy at the Larmor frequency will cause the protons to oppose the magnetic field (usually in the form of a **radiofrequency pulse**). This will affect the rotation and **net magnetisation** towards **Mxy** which is 90º to the main magnetic field.

A 90º radio-frequency (RF) pulse therefore, produces the maximum tissue signal.



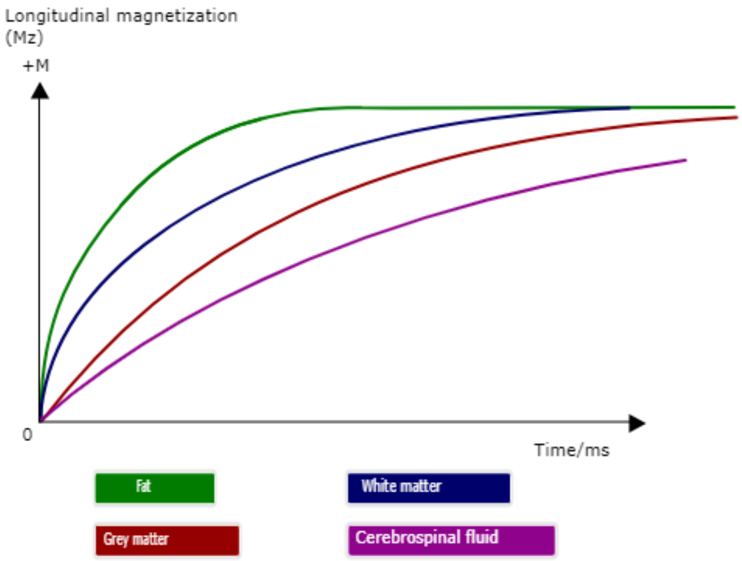
Relaxation

Refers to the processes after **RF is switched off** and the **net magnetisation returns to equilibrium**. There are two main components to the relaxation process. These occur at the same time, although they are separate phenomena:



1. **T1 relaxation aka 'spin lattice relaxation' – Longitudinal magnetisation**

This is the time taken for the rotated net magnetization to realign with the main magnetic field. Energy transfer takes place when the **nuclei of neighbouring tissues interact with one another**.



As you can see, the realignment of the main magnetic field occurs in an exponential manner in all tissues. However, the time it takes varies:

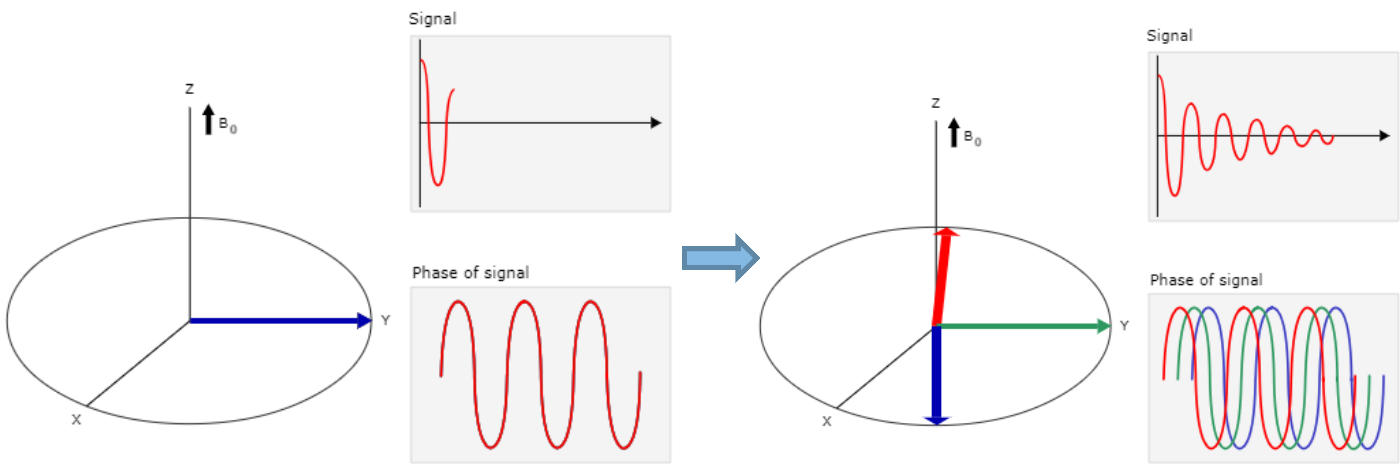
One T1 time equates to the point at which **63% of the tissue has returned to equilibrium**. This is unique to the type of tissue due to its chemical makeup and also changes for different magnetic field strengths (flux density) (tesla). See the following table (**time in ms**):

	1.5 Tesla	0.5 Tesla
Skeletal muscle	870	600
Liver	490	323
Kidney	650	449
Spleen	780	554
Fat	260	215
Grey matter	920	656
White matter	790	539
Cerebrospinal fluid (CSF)	>4000	>4000

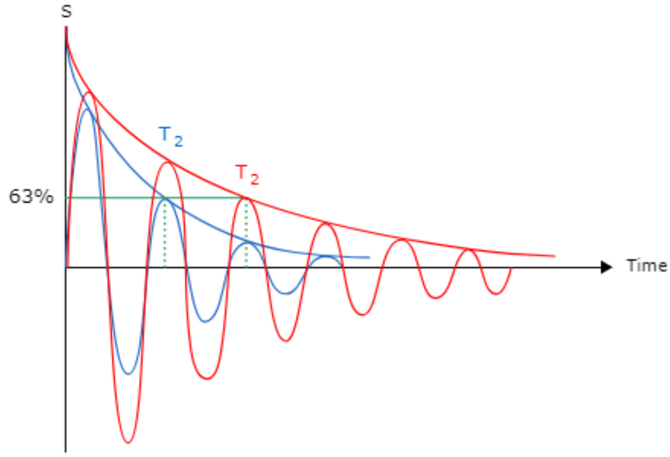
2. **T2 relaxation aka 'spin-spin relaxation' – Transverse magnetisation**

Time taken for the loss of phase **coherence of the net magnetization,** following the **rotation of the net magnetization.** Each individual proton is exposed to a slightly **different microscopic magnetic environment** and this will affect the individual magnetic movements and hence, the overall net magnetisation and processional frequencies. Remember the Larmor frequency equation.

Loss of phase: With an RF pulse, the protons spin in phase with each other. As time progresses, as mentioned above, the T2 interactions occur where some protons gain/lose frequencies relative to each other. **When loss of phase occurs, the detected MR signal decreases**.



The loss of signal due to T2 relaxation is known as **free induction delay (FID)** and like T1 relaxation, occurs in an exponential fashion.



T2 time is the time taken for 63% of signal to be lost. The following table shows this time in **ms** for different tissues.

Skeletal muscle	47
Liver	43
Kidney	58
Spleen	62
Fat	84
Grey matter	101
White matter	92
CSF	>2000

Overall

T1 and **T2 relaxation** occurs **at the same time**. However, they are not routinely performed in conventional MRI scanners as most disease processes have a good overlap between T1 and T2 relaxation times. Rather, it is the relative difference in relaxation times that is used to produce contrast on MR images and it is this that allows diagnostic information to be obtained.

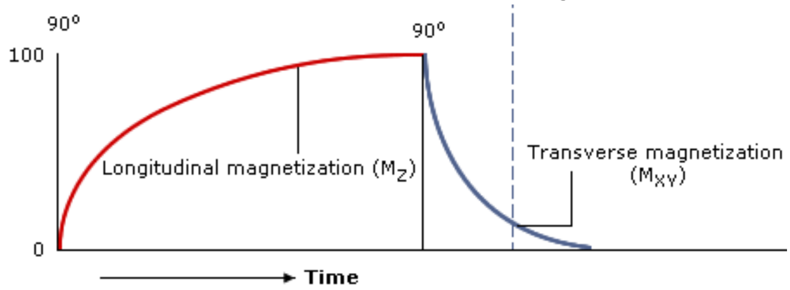
Production of Images

The process of exciting tissues with specifically timed and measured RF pulses are known as **pulse sequences**. Multiple have been developed in the hope to further improve the MRI diagnostic quality.

Images obtained from the pulse sequences require 100s of 1000s of measurements to allow the data acquired to be converted into recognisable MR images. This is why it takes ages! The same section of anatomical tissue is repeatedly exposed to the RF pulses.

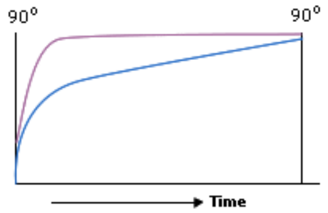
The main factors that determine the T1 and T2 influence on the contrast of the images are:

- **Repetition Time (TR):** The time between each of the RF pulse sequences (**red**)
- **Echo Time (TE):** The time between the tissue being excited until a signal is detected (**blue**)

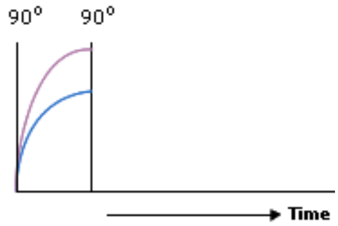


T1-Weighted Image Contrast

TR is a reflexion on the T1 relaxation time:



If TR is long i.e. >2000ms, then there is a strong likelihood that a large proportion of most tissues will have returned to equilibrium (right)

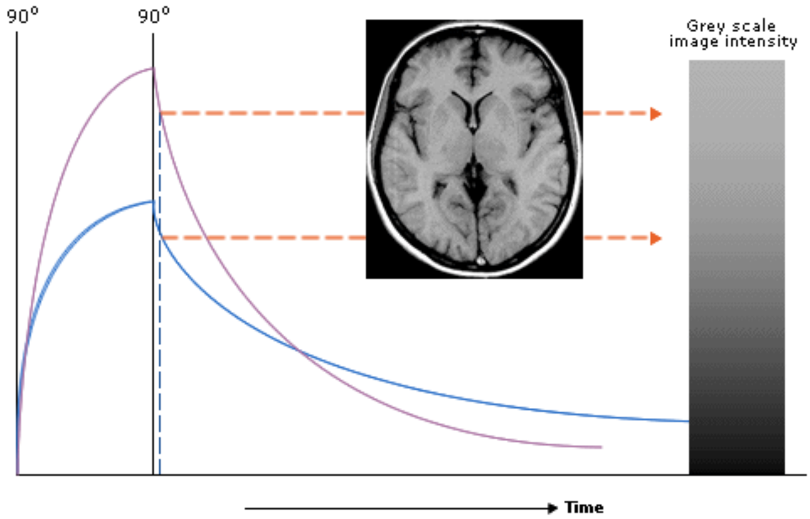


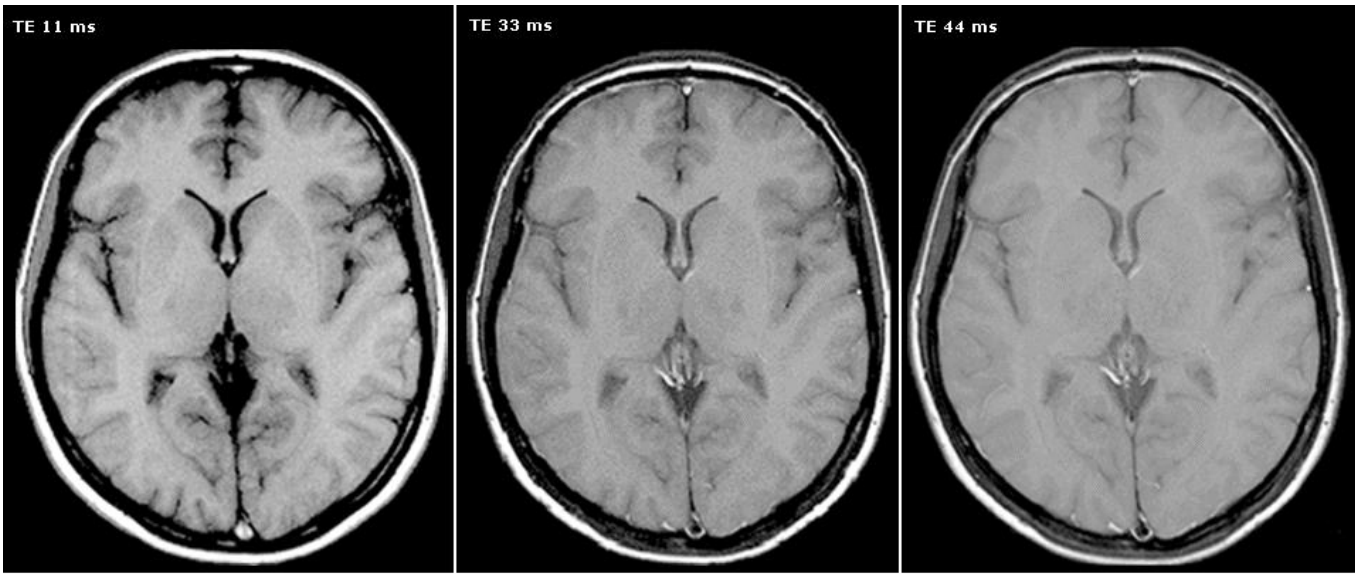
If TR is short i.e. 500ms, then there is a strong likelihood that 2 tissues with different T1 relaxation times will be differentiated as may not have returned to equilibrium (left)

Contrast Generation

In addition, now we know a short TR is likely to differentiate T1 relaxation times, a **TE** must be selected to **minimise any other effects on the MR signal** through T2 relaxation time.

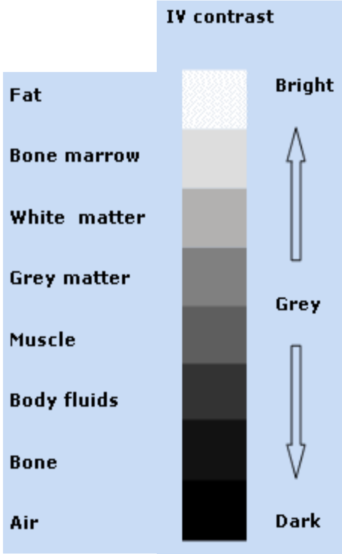
Manipulation of parameters allow differing images as shown below. Conversion into images from MR signals is known as **Fourier transformation**: Image on R shows short TE:





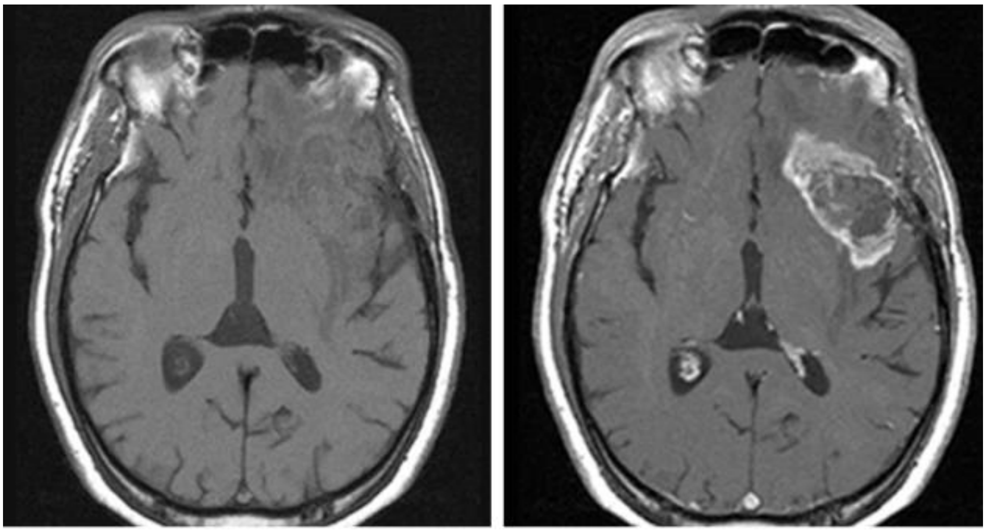
It is important to realize that these images bring out the **differences in T1 relaxation** of different tissues and are not a direct measure of T1 relaxation times. They are, therefore, **designed to differentiate differences in T1 relaxation of tissues** and are known as **T1-weighted images**. The shorter the TR, the more heavily T1-weighted the image. The **shorter the TE** the **less the T2 influences** there are.

The typical appearance of tissue on T1 weighted scans are shown:



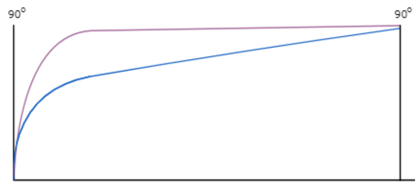
Contrast Media

Intravenous paramagnetic contrast media are often used in conjunction with T1 weighted MR imaging for lesion characterization. They can **shorten the T1 relaxation times** to increase the signal on T1 weighted images. The increased vascularity of tumours also allows them to take up more contrast media to make them clearly demonstrated (left = pre-contrast; right = post-contrast).

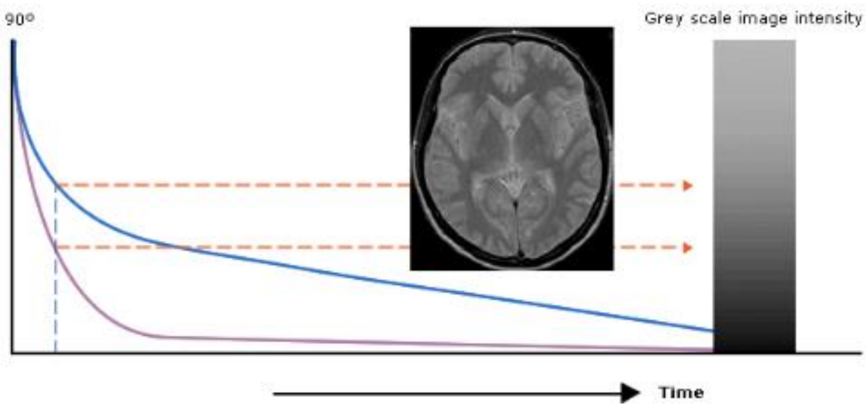


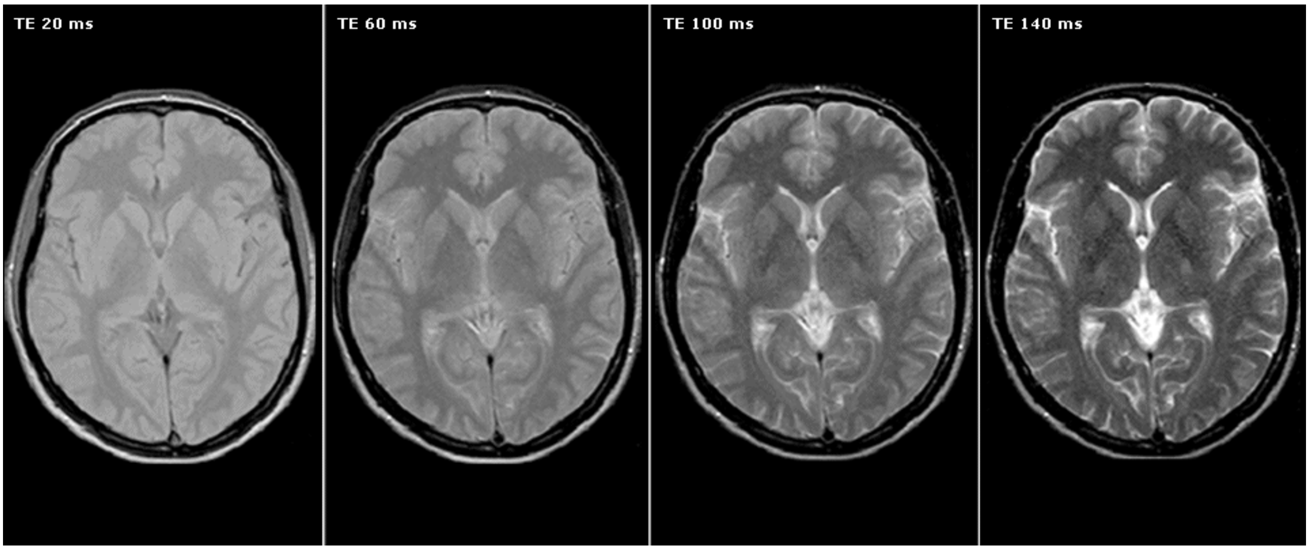
T2-Weighted Image Contrast

By lengthening the TR, the differences in T1 relaxation are minimised.



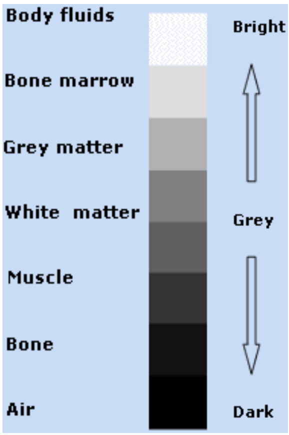
T2 differences can be maximised through lengthening of the TE. The images show variations in TE. Image on the right processed over a short TE.





Once again, these images bring out the differences in T2 relaxation of different tissues and are not a direct measure of T2 relaxation times. These images are, therefore, designed to differentiate differences in T2 relaxation of tissues and are known as **T2-weighted images**.

The typical appearance of tissue on T2 weighted scans are shown. Notably, the body fluids in contrast to T1 images light up whilst soft tissues remain dark.



Essentially, it is important to realize that each scanning sequence used, in conjunction with each scanning plane imaged, provides useful additional information contributing towards lesion identification and characterization.

Energy and Value Index

Energy Equations

Kinetic energy = 0.5 x mass x velocity^2

Metabolic energy = Energy content of substance x mass

Amount of heat transferred = Specific heat capacity x mass x change in temperature

Potential energy = gravity x mass x height

Electrical power (Watts) = voltage x current

Electrical energy (Joules) = Voltage x charge

Work = Force x Distance

Values

Specific heat capacity of water = 4.18kJ/kg/K

Celsius → Kelvin = +273.15

1 atm = 1 bar = 101.3kPa = 101 325 Pa = 760mmHg = 760 Torr = 1033cmH_2O = 14.5PSI

Ambient pressure is halved 5500m above sea level (0.5atm)

Desflurane vaporiser kept in constant conditions of 2atm @39°C

SVP of water at 20°C = 17g/m^3

SVP of water at 37°C = 44g/m^3

	Boiling point (°C)	Melting point (°C)	Critical Temp (°C)	Critical Pressure (Bar)	SVP at 200°C (Bar)
Oxygen	-183	-219	-118	50	1.4
Nitrous Oxide	-88	-91	36.5	72	50.8
Carbon Dioxide	-79	-57	30	73	57
Helium	-269	-272	-268	2.3	n/a

Particles in 1 mole = 6.22 x 10^{23}

1 mole of a gas will exert 1 atm pressure in a closed container of 22.4L volume

1 Coulomb = charge of 6.24x10^{18} electrons

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