

## SECTION 15 - GENETICS

### 15.1 What is Genetics?

Genetics is the branch of biology concerned with the principles and

mechanisms of heredity – the means by which traits are passed from parent to offspring

- We know that chromosomes contain all the genes that produce all the proteins a cell may need to survive – we refer to the positions of these genes as loci (singular: locus)
- Humans have 46 chromosomes – 23 maternal, and 23 paternal → every chromosome has an identical copy from each parent – these pairs are called homologous chromosomes (note that the sex chromosomes, XX or XY, are unique as the XY pair is not the same but are paired together regardless)
- Since paired homologous chromosomes would also have paired genes – we call these matching genes alleles (one maternal, and one paternal)
  - If both alleles are identical → the individual is homozygous at that locus
  - If both alleles are different → the individual is heterozygous at that locus

The set of genetic alleles that an individual has is referred to as its genotype, the physical or detectable expression of these alleles is called the phenotype

- For example, considering the gene locus responsible for eye colour: the allele that encodes for brown eyes is dominant (A) over the allele that would produce blue eyes, which is recessive (a)
- Dominant alleles are symbolised with capital letters (A), recessive alleles are symbolised with lower case letters (a) → this gives us three allelic combinations:
  - Homozygous Dominant (AA)
  - Heterozygous (Aa or aA)
  - Homozygous Recessive (aa)

#### Alleles of the eye color gene:

**B** Allele for brown eyes (dominant over the b allele)

**b** Allele for blue eyes (recessive to the B allele)

Possible genotypes:

Phenotypes:

**BB** Homozygous = brown eyes



**Bb** Heterozygous = brown eyes



**bb** Homozygous = blue eyes



These three would be the genotypes of a locus, however, if the dominant allele is present, it will suppress the phenotype of the recessive allele

- This only gives us two phenotypes: AA and Aa would produce brown eyes, and aa would produce blue eyes – we can see the effect of the dominant allele
  - This is known as Mendel's Law of Dominance

There are exceptions to this: incomplete dominance, and codominance

- Incomplete dominance occurs when the phenotype of the heterozygote is a hybrid of the phenotypes of the two homozygous parents → a red and white flower, when crossed will produce a pink flower

## 15.2 ABO Blood Types – Codominance

Codominance occurs when multiple alleles exist for a particular gene, and more than one of these alleles is dominant – this means that if two codominant alleles are present at a locus, both genes are equally present and expressed in the phenotype

The four blood types: A, B, AB, and O, are examples of phenotypes produced by the codominant combinations of the following three alleles →  $I^A, I^B$ , and  $i^o$

- Both A and B are the codominant alleles, and o is recessive → this gives six genotypes, with four potential phenotypes

Blood Groups				
Phenotype (Blood Type)	Genotype	Antigen on Red Blood Cell	Safe Transfusions	
			To	From
A	$I^A I^A$ or $I^A i$	A	A, AB	A, O
B	$I^B I^B$ or $I^B i$	B	B, AB	B, O
AB	$I^A I^B$	A and B	AB	A, B, AB, O
O	$ii$	none	A, B, AB, O	O

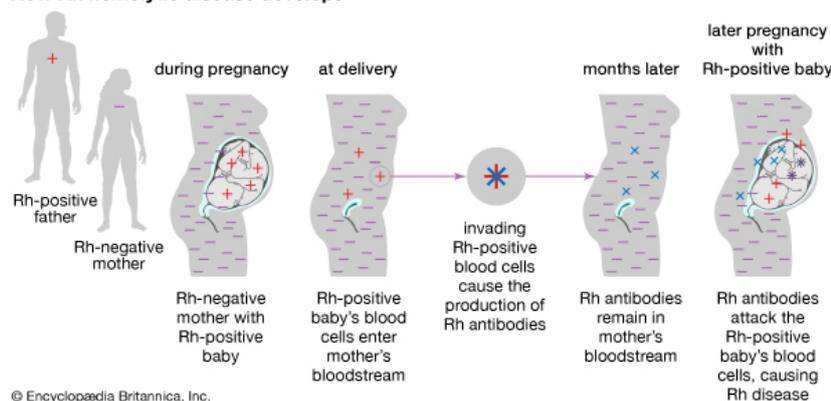
The  $I^A$  and  $I^B$  alleles causes antigens (called agglutinogens) A and B to be expressed on the plasma membranes of red blood cells – the  $i^o$  allele results in no antigen production

- People with blood type A have anti-B antibodies in their blood
- People with blood type B have anti-A antibodies in their blood
- People with type AB have neither, while people with type O have both
  - If you were to donate type B blood into a person of blood type A → the anti-A antibodies from the type B blood would lead to fatal agglutination and clotting of blood
- This means that O cannot receive any blood other than from people of the same type – conversely this means AB can receive blood from all four types

You may have heard of blood as being Rh+ or Rh- → another allele on a separate locus can generate Rh Factors (antigens) which are either there (positive) or not (negative)

- Mixture of Rh+ and Rh- blood is not usually fatal, unless exposure occurs during pregnancy (a Rh+ baby in a Rh- mother)

How Rh hemolytic disease develops

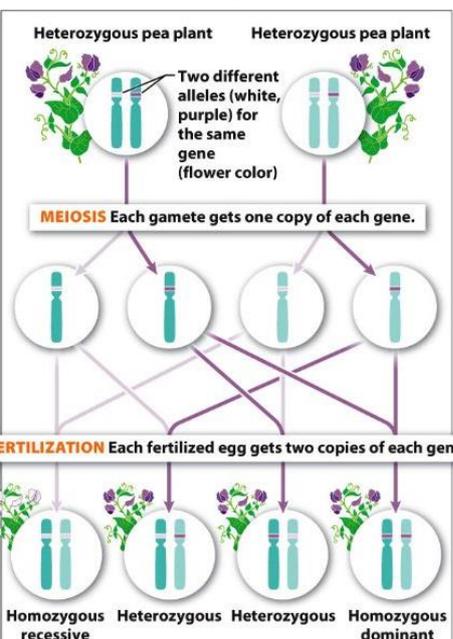


### 15.3.1 Mendelian Genetics

In consideration of how maternal and

paternal alleles are passed on, the segregation during the first meiotic division separates homologous chromosomes: This is Mendel's First Law of Segregation

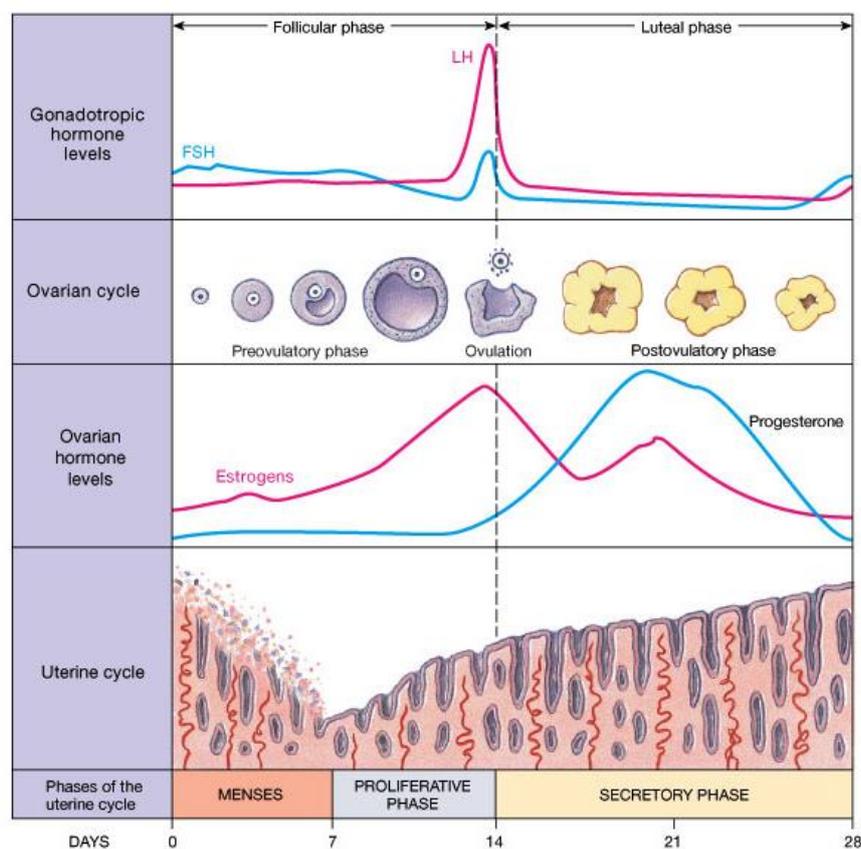
Mendel's Second Law of Segregation states that different chromosomes separate independently from one another → this means that during Meiosis I, although we get 23 chromosomes in each secondary spermatocyte – not all 23 are solely paternal/maternal, but a mix of both (this is how we can have phenotypic traits from both parents



### 14.3 The Menstrual Cycle

The Uterine or Menstrual cycle is an approximate 28 day cycle divided into four key phases:

1. Menses: days 1-4 of the cycle begin with the shedding of the uterine lining that occurs due to a dramatic drop in estrogen and progesterone levels following failure to fertilise the ovum → the uterus experiences strong vasoconstriction the uterine lining (endometrium) comes away and essentially falls off (often quite painfully)
  2. Follicular/Proliferative Phase: days 5-14 of the cycle involves FSH stimulating follicles to mature, with one of them becoming the Graafian follicle (the remainder will break down) → the Graafian follicle will begin producing massive amounts of estrogen which will cause the uterine lining to progressively thicken (proliferate)
  3. Ovulation: (can occur between days 12-16) → a high enough estrogen concentration will cause a very dramatic surge in LH and also FSH which stimulates ovulation
  4. Luteal/Secretory Phase: days 15-28 of the menstrual cycle involve the follicular cell degenerating into the yellow corpus luteum → this will secrete progesterone which stimulates further growth of the uterine wall alongside estrogen, which inhibits LH and FSH secretion (negative feedback)
- If the ovum is fertilised → the embryo will implant itself into the uterine wall and release human chorionic gonadotropin (hCG) which is a key indicator of pregnancy → hCG would allow the corpus luteum to continue its secretions
  - If the ovum is not fertilised → the corpus luteum degenerates, causing a drop in estrogen/progesterone → the cycle repeats



Bile is a yellow-green fluid made up of water, cholesterol, and pigments from the destruction of RBCs, as well as bile salts → the bile salts have a digestive function → emulsification of fat by dissolving and surrounding fat molecules into droplets called micelles → this allows absorption of fat through the lumen of the GI tract (which is a phospholipid bilayer)

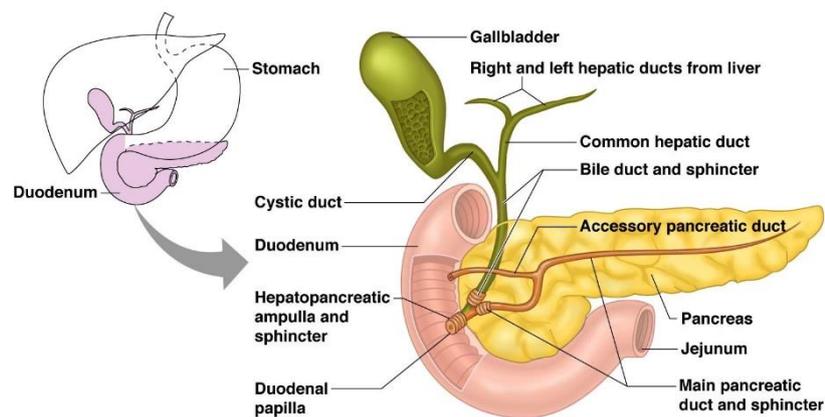
- The bile salts orient the hydrophilic heads outward, and their hydrophobic tails onto the fats in order to encapsulate them
- This facilitates absorption of fat soluble vitamins: A, D, E, K
- Bile and bile salts is stored and concentrated in a sac called the gall bladder → overconcentration of bile salts is how gallstones (kidney stones) form

#### 9.4.2 The Pancreas

- The pancreas sits adjacent and to the left of the duodenum, and has both endocrine and exocrine functions (endocrine functions involve glucagon/insulin secretion)
- Its exocrine function is secretion of pancreatic juice → which contains alkaline fluid and digestive enzymes → it secretes them through the pancreatic duct which joins onto the common bile duct → both pass out to the major duodenal papilla

The hormones secretin and CCK are released by the duodenum in response to chyme – secretin acts on pancreatic ductal cells to stimulate the release of acid neutralising  $\text{HCO}_3^-$  – CCK stimulates release of multiple pancreatic digestive enzymes and proenzymes (zymogens) including:

- Pancreatic amylase (which breaks down carbs into monosaccharides), pancreatic lipase (which breaks down fats into monoglycerides), and pancreatic nuclease (which breaks down nucleic acids)
- Proteases such as trypsin, chymotrypsin, and carboxypeptidase, which can break down polypeptides into amino acids, or di- / tri-peptides



#### 9.5.1 The Small Intestine

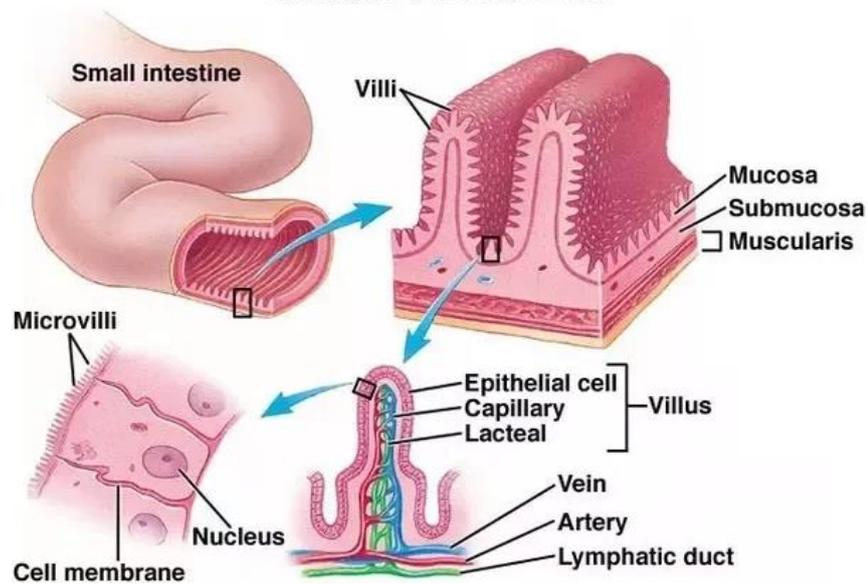
- The small intestine starts at the duodenum, which leads into the jejunum, which then leads down to the ileum → this part of the GI tract is where the majority of nutrient absorption occurs
- Food is propelled through the tract via peristalsis, this contraction permits ideal absorption of food by exposing all chyme to digestive surfaces along the small intestine → this process is parasympathetically stimulated
- This absorption is aided by increasing surface area using small, cell-lined hairs called villi and microvilli → these evaginations provide over 20 times the surface area than if the intestinal surface were flat

# Small Intestine

Carbohydrates can only be absorbed if they are broken down into glucose, fructose, or galactose

Proteins can be absorbed via transporters as long as they are small enough (amino acid, dipeptide, tripeptide)

Lipids can be absorbed into the lymphatic system via the lacteals in the form of fatty acids, monoglycerides, and cholesterol – the remaining nutrients will go into the bloodstream for processing at the liver via the hepatic portal vein

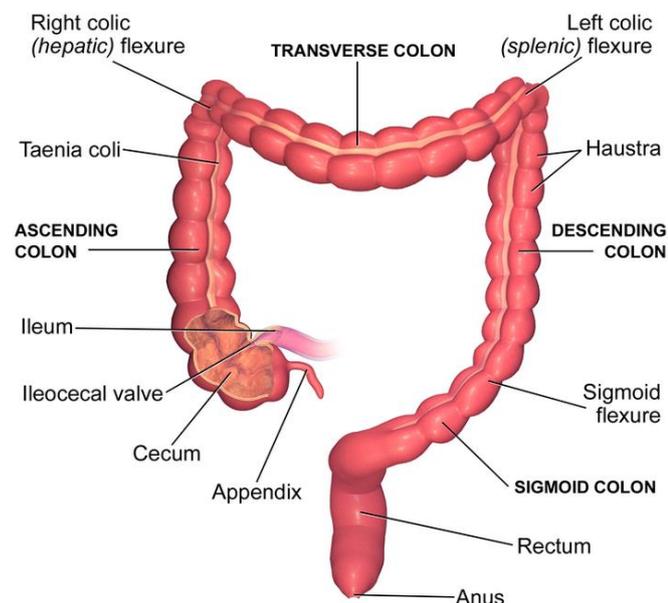


## 9.5.2 The Large Intestine

The large intestine starts at the caecum which receives chyme from the ileum – projecting away from the path of food travel is a vestigial appendix (the appendix has no role in human digestion)

Overall, very little nutrient absorption occurs along the large intestine – the colon – which forms the majority of this section, and is divided into the ascending, transverse, descending, and sigmoid colon

By the time the chyme has reached the rectum in the form of faeces, it has been drained of much of its water and electrolyte content by the colon

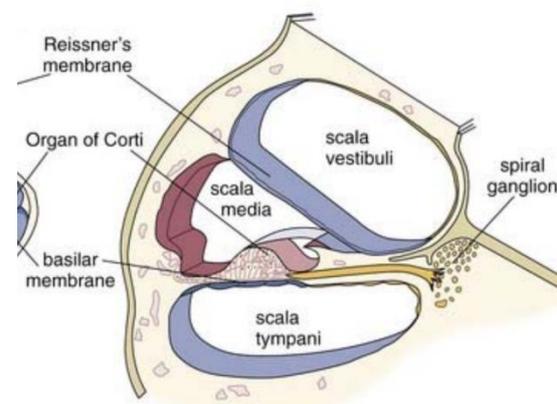


What remains is still mostly composed of water, but also consists of undigested material (fibre, and plant cellulose is indigestible), mucous, bile pigments, and gut flora (bacteria) → this gut bacteria lives in a symbiotic and mutualistic relationship with its host (i.e. humans) by assisting in digestion, training the immune system, preventing harmful bacteria from growing, and even vitamin K production, and fermentation of digestive products

The inner ear consists of the bony labyrinth containing a membranous labyrinth

- The bony labyrinth houses the semicircular canals, the cochlea, and the vestibule
  - The semicircular canals contain the semicircular ducts of the membranous labyrinth → these detect angular acceleration
  - The vestibule detects linear acceleration using the hair lined saccule and utricle
    - Together, the canals and vestibule form the vestibular system and are responsible for detection of all acceleration (movement) of the head
- The cochlea is divided into three spaces: the scala tympani, scala media (cochlea duct), and the scala vestibuli
  - The cochlear duct contains the spiral organ of Corti → it is involved in sound reception of varying frequencies
- The eustachian (auditory) tube connects the middle ear down to the pharynx, and facilitates equal pressures on both sides of the head, and on the outside/inside of the ear → yawning can open the tube to allow pressure equalisation

Sound is caused by compression of waves that are funnelled by the external ear to strike the tympanic membrane → this triggers movement of the ossicles, whereby the stapes moving on the oval window disturbs lymph fluid in the cochlea → this moves hairs on the basilar membrane of the Organ of Corti → this causes depolarisation of the membrane and triggering of the auditory nerve → the impulse is carried to the auditory area of the temporal lobe for processing



### 6.2.5 Vision: Eye Structure and Function

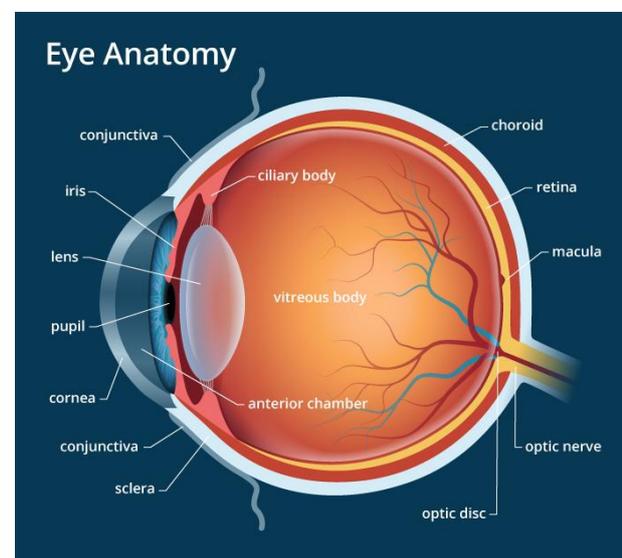
The eyeball consists of three layers:

- The outer fibrous tunic consisting of the sclera and cornea
- A vascular coat (uvea) or choroid, the ciliary body, and the iris
- The retina (formed of pigment and sensory layers)

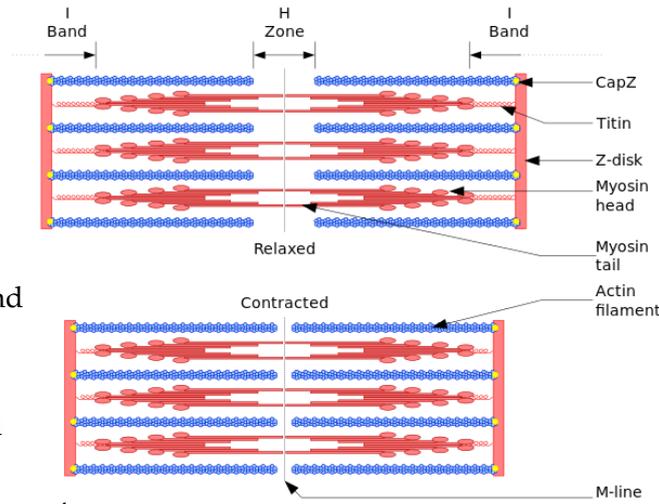
The anterior chamber of the eyes lies between the cornea and the iris (which lies in front of the pupil); the posterior chamber lies between the iris and the lens

The cornea consists of the front (anterior) one-sixth of the eye, and is the receiver of light from the environment → the sclera forms the back (posterior) five-sixths of the fibrous tunic

- The lens can focus like onto the retina by contracting/relaxing the muscles of the ciliary body → contraction makes the lens more convex (to focus on nearby objects), relaxation makes the lens less convex (to focus on afar objects)

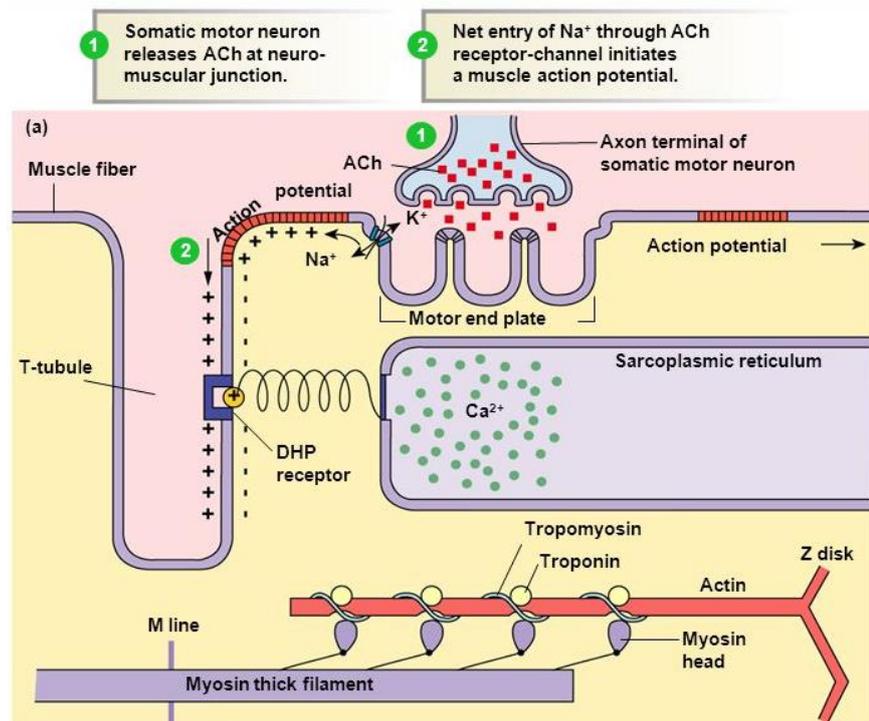


- A sarcomere consists of the material between the Z-lines which are the centres of the I-bands, the M-line is the centre of the A-band
- The region where M-line resides is called the H-zone and only contains thick filaments
  - The arrangement patterns of the thick and thin filaments interdigitating form a hexagonal pattern of one thick myosin filament being surrounded by six thin actin filaments
- When a muscle contracts, the thick and thin filaments do not shorten but overlap, causing the H-zone to shrink in width as the Z-lines are brought closer together



The plasma membrane of muscle fibres is called the sarcolemma, which has special invaginations deep into the muscle called T-tubules → the t-tubules connect to the A-I band junction and the sarcoplasmic reticulum (ER of muscle fibres) → thousands of triads facilitate uniform contraction of muscle fibres

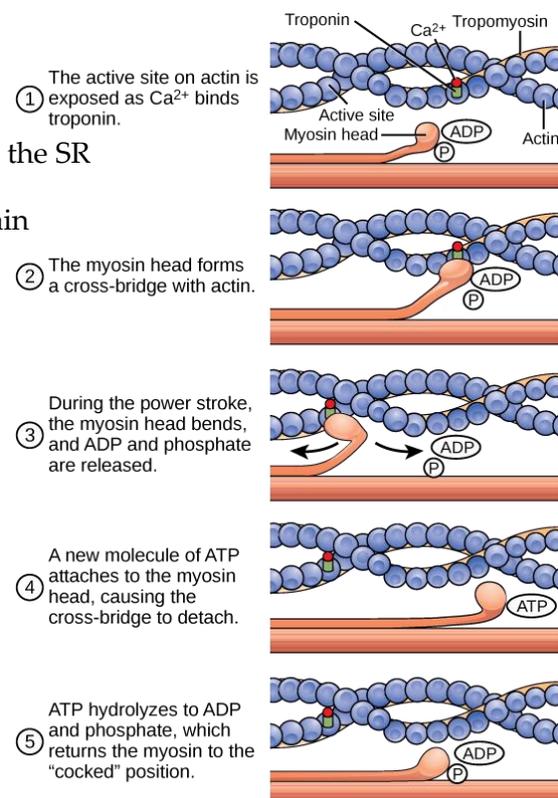
- The sarcoplasmic reticulum (SR) can regulate contraction by either transporting  $Ca^{2+}$  into storage during muscle relaxation, or releasing  $Ca^{2+}$  during excitation-contraction coupling (muscle contraction)



Once an End-Plate-Potential has been reached, the action potential will propagate through the T-tubules, the DHP (dihydropyridine) receptor will trigger  $Ca^{2+}$  to be released from the SR

Myosin consists of two heavy chain segments and two light chain segments → they heavy chain has two myosin heads and a tail → the head has an actin binding site

The thin filaments are made up of actin, as well as two other proteins: troponin, and tropomyosin → the calcium released by the SR will bind to troponin, pulling tropomyosin away from the actin filament → this uncovers the active binding sites so that the myosin heads can travel from one spot to the next by pulling the actin filament (contracting the muscle)



The above cycle is called the crossbridge cycle, and utilises many ATP molecules at once in order to contract muscle fibres in an efficient matter: it is important to note that:

- Neither actin nor myosin change length during contraction (the filaments overlap)
- In the presence of no ATP, the muscles are essentially stuck at a fixed length until the fibres themselves degrade (this is the cause of rigor mortis; stiffness after death)
- $\text{Ca}^{2+}$  is a crucial ion for both muscle contraction and neurotransmitter release

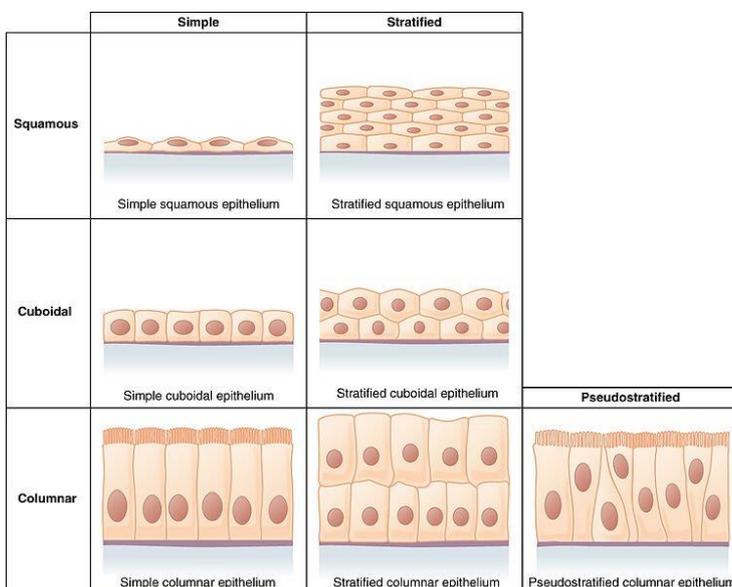
### Cardiac Muscle

- Cardiac muscle has striations and myofibrils similar to skeletal muscle
- Contraction of cardiac muscle, however, is involuntary and is innervated by the autonomic nervous system (skeletal muscle contraction is voluntary)
  - Cardiac muscle fibres are branched and have centrally based nuclei, and large numbers of mitochondria → they are attached at their ends via intercalated disks → these contain membrane junctional complexes (i.e. gap junctions)
- Cardiac muscle cells do not regenerate (they are repaired by fibrous connective tissues)
- Cardiac muscle cell depolarisation is facilitated by cell-cell contact at the gap junction → this permits electrical propagation of an action potential across the entire heart

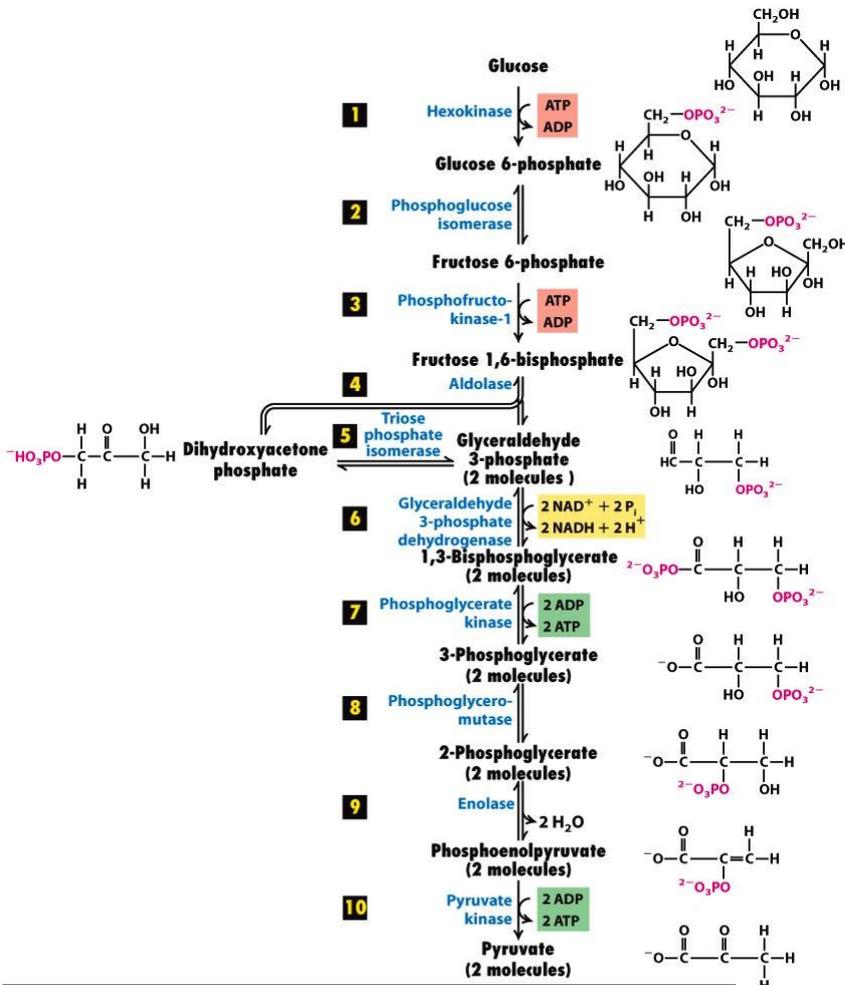
### 5.3 Epithelial Cells and Tissues

Epithelia Tissues have the following characteristics:

- They cover all body surfaces (skin and organs)
- They are the tissues that make up glands
- Their cells are anchored by a nonliving 'basement' membrane or layer
- They lack blood vessels (they are nourished via diffusion of material)
- Epithelial tissues are classified according to the characteristics of their cells → elongated cells are columnar, flattened cells are squamous, and cube-shaped cells are cuboidal
- They are also classified as simple if they have a single layer, or stratified if they have multiple layers of cells; a pseudostratified epithelium has an unusual layering of individual cells



Importantly, cuboidal cells generally are present in secretory glands, while stratified squamous epithelium is for protection (e.g. the skin)



To the left is a summary of glycolysis and all the enzymes required to produce each intermediate in the pathway

Step 1 is irreversible and utilises 1 ATP molecule to convert glucose to G-6-P using hexokinase

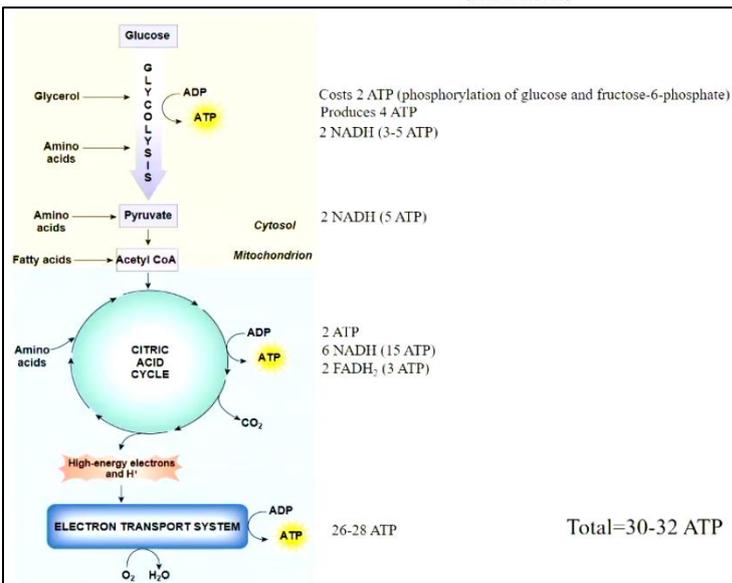
Step 2 converts G-6-P to F-6-P, and Step 3 utilises a 1 more ATP molecule to turn F-6-P into F,1-6,bis-P using the enzyme phosphofructokinase-1 (PFK1) (step 3 is the rate limiting step of glycolysis)

Step 4 Converts the single F,1-6,bis-P into 2 GA-3-P molecules (as two products can form, Triose Phosphate Isomerase will convert any incorrect molecules into GA-3-P; This is Step 5)

Step 6 utilises 2 NAD<sup>+</sup> molecules and 2 phosphate molecules to convert the two GA-3-P into two 1,3-BPG (2 NADH and 2H<sup>+</sup> are produced)

Step 7 converts the two 1,3-BPG into two 3PG molecules → 2 ADP molecules are converted into 2 ATP molecules in this step

Step 8 converts the two 3PG into two 2PG, in Step 9, enolase dehydrates the two 2PG into two PEP (two H<sub>2</sub>O are released)



Step 10 converts the 2 PEP into two pyruvate molecules → 2 more ADP molecules are converted into ATP molecules

Overall, we have a net gain of 2 ATP per glucose molecule broken down

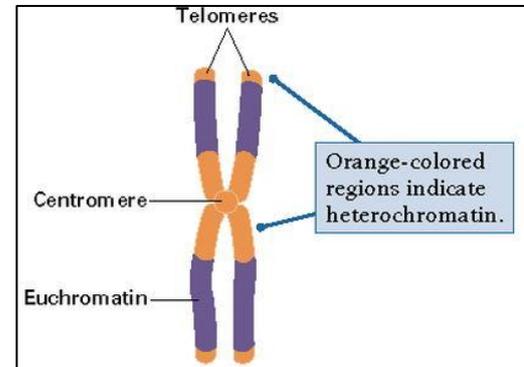
(a) Anaerobic Metabolism		$C_6H_{12}O_6 \rightarrow 2 C_3H_7O_3^- + 2 H^+$			
	GLYCOLYSIS	NADH	FADH <sub>2</sub>	ATP	CO <sub>2</sub>
1 Glucose		2		4	
2 Pyruvate		-2			
2 Lactate					
<b>TOTALS</b>		<b>0 NADH</b>		<b>2 ATP</b>	

(b) Aerobic Metabolism		$C_6H_{12}O_6 + 6 O_2 \rightarrow 6 CO_2 + 6 H_2O$			
	GLYCOLYSIS	NADH	FADH <sub>2</sub>	ATP	CO <sub>2</sub>
1 Glucose		2*		+4	
2 Pyruvate		2		-2	
2 Acetyl CoA		2			2
Citric acid cycle		6	2	2	4
6 O <sub>2</sub>					
<b>TOTALS</b>		<b>6 H<sub>2</sub>O</b>		<b>30-32 ATP</b>	<b>6 CO<sub>2</sub></b>

\* Cytoplasmic NADH sometimes yields only 1.5 ATP/NADH instead of 2.5 ATP/NADH.

The part of the chromosome containing active genes which can be transcribed into proteins is called euchromatin, the inactive genes which are rarely or not transcribed are called heterochromatin → transcription of chromatin produces mRNA



### 1.3 DNA and RNA

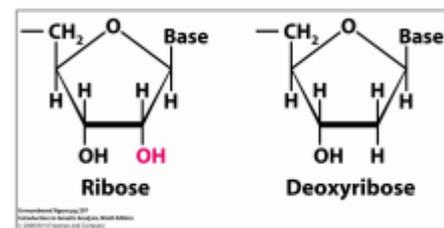
- DNA (Deoxyribonucleic Acid) is a double stranded molecule made up of C, N, H, O, and P. It is made up of numerous nucleosides (sugar + base) (making it a polynucleotide) linked together through phosphodiester bonds (P-O). The phosphate group connects to the C5' of the above sugar and the base connects to C1' of the next sugar. The next P connects to the C3' -OH group. Thus, DNA runs in a 5' → 3' direction.
- DNA nucleotides consist of 3 parts: Nucleotide bases (G, C, A, and T), a deoxyribose (Sugar group) and a phosphate Group
- Each nucleotide has a conjugate pair. These 2 pairs are A=T and C≡G. The AT bonds are held together by 2 h-bonds whereas the CG base pair is held together by 3 h-bonds. CG is therefore stronger than AT.

Adenine and Guanine are PURINES (2 ringed) Thymine, Cysteine, and Uracil are PYRIMIDINES (1 ring)

- The strands of DNA are antiparallel (run in opposite directions) and complementary → meaning if you have one strand you can figure out the sequence of the other → we write DNA in order of 5' to 3'

There are three (3) main differences between DNA and Ribonucleic Acid (RNA) molecules:

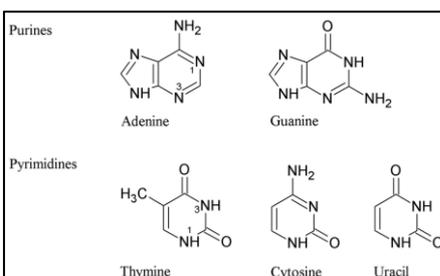
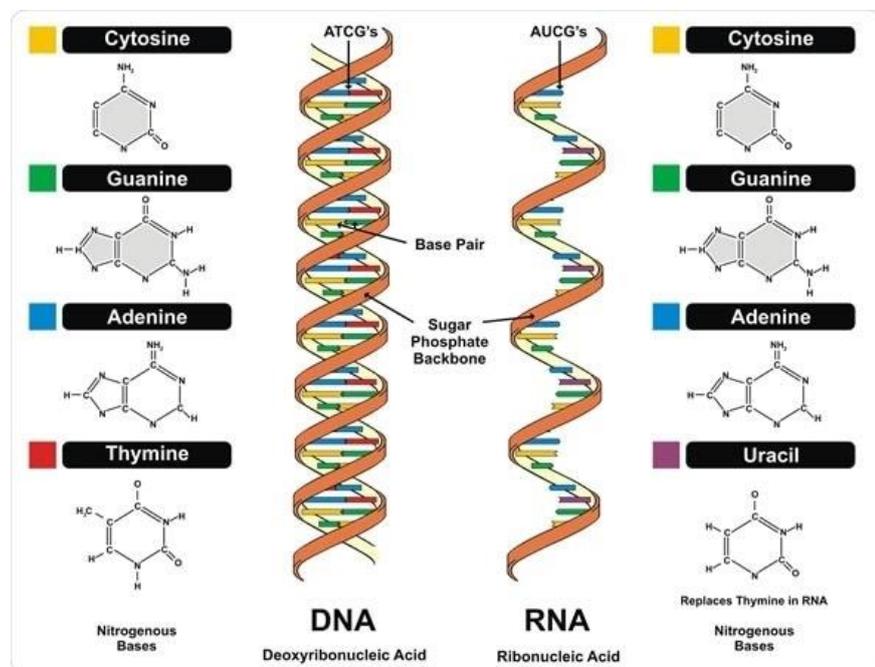
1. DNA contains the sugar deoxyribose (carbon 2 has -H), whereas RNA contains ribose (carbon 2 has -OH). This is the biggest difference between the 2 molecules.
2. Number of strands. DNA is a double stranded molecule (in a helix formation), whereas RNA is a single stranded molecule.
3. Adenine's conjugate base pair. Whilst DNA uses the nucleotide base Thymine (T), RNA pairs adenine with the base Uracil (U).



DNA → A=T

RNA → A=U

- RNA is involved in both transcription and translation, and primers made up of RNA are involved in DNA replication. Viruses use RNA as their genome rather than DNA.



### 13.3.5 Column Chromatography

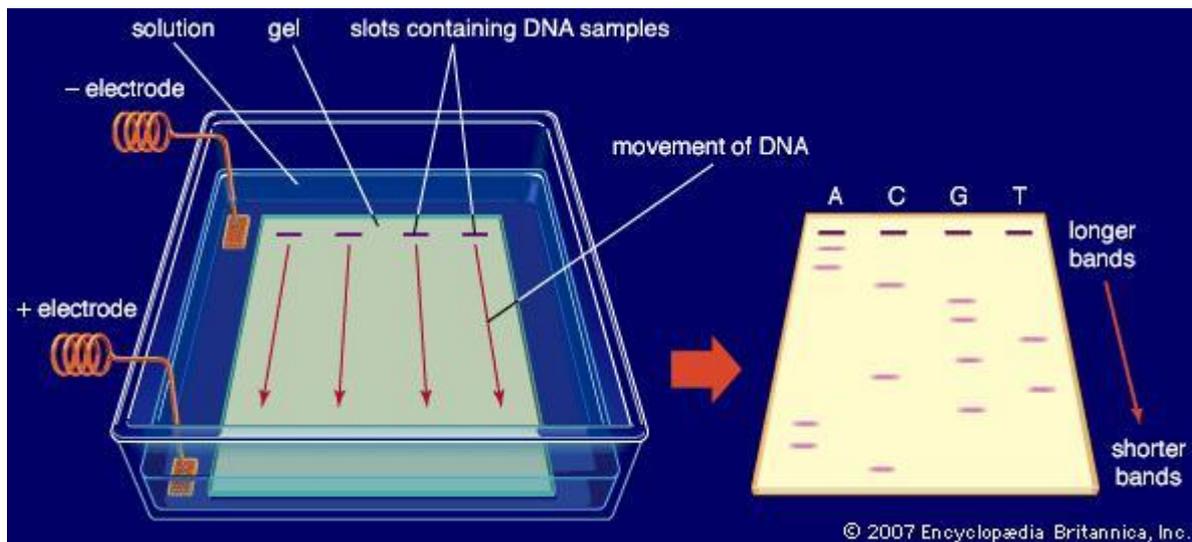
- Column Chromatography is similar to gas-liquid chromatography, where the mobile phase is passed over a stationary phase → however there is no pressurised gas forcing the fluid through the stationary phase, only gravity pulling the mobile phase down through the column
  - The solvent will drip down through the column to a collecting tap at the bottom, the various constituents can be collected at the bottom

There are many different column chromatography techniques such as:

- Ion exchange → the column is full of beads coated in charged substances that will attract compounds of the opposite charge
- Size exclusion → the column is filled with porous beads that will allow small molecules to spend more time in the column whilst larger ones are eluted faster
- Affinity chromatography → the column is customised to bind a specific substance that passes through the column, allowing for high selectivity

### 13.4 Gel Electrophoresis

Gel electrophoresis is an important method of separating biological molecules such as protein and DNA based on their size and/or charge → molecules will move through a gel which is under an electric current



DNA is uniformly negatively charged under biological conditions, so when placed at the top of the electrophoresis chamber, they will move towards the positively charged end

- The negative electrode is the anode, the positive electrode is the cathode
- As the mass of the DNA increases, the more difficulty it will face whilst migrating through the gel → lighter DNA will travel a shorter distance

We use 3 common types of gel electrophoresis

1. Agarose Gel Electrophoresis to separate DNA/RNA based on charge
2. SDS-Polyacrylamide Gel Electrophoresis (SDS-PAGE) → separates proteins based on their mass (SDS, sodium dodecyl sulphate will make all proteins equally negative)
3. Isoelectric focusing → separation of proteins based on their pI using a low pH end and a high pH end with an appropriate electric field

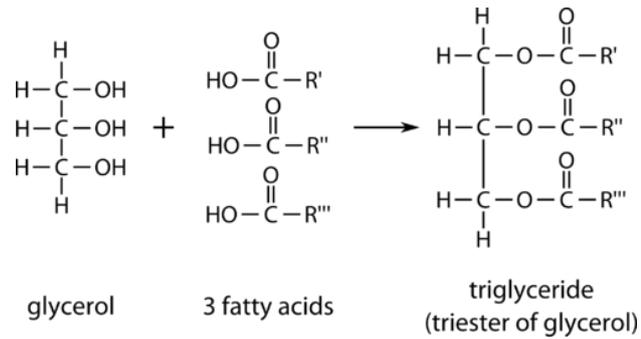
## 12.4.1 What are Lipids?

Lipids are a broad class of molecules containing substances such as: fatty acids, fats, waxes, triglycerides, terpenes, and steroids → the main biological function of lipids is to store energy, and act as structural components of cell membranes

- Lipids are highly non-polar, and hence hydrophobic and insoluble in water
- Lipids can be cyclic, linear, or even aromatic
- Some lipids (e.g. phospholipids) have a polar head and a long non-polar tail, which gives them amphipathic (hydrophobic + hydrophilic) properties

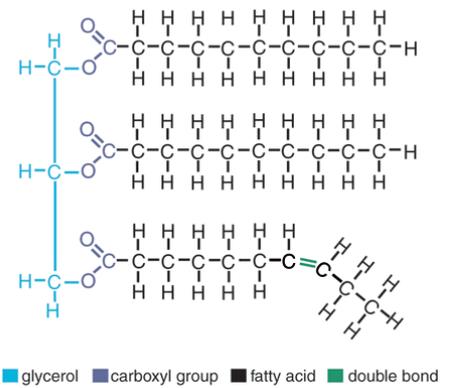
Triglycerides are oils and fats derived from plants or animals → generally, fats are solid at room temperature, and oils are liquid

- Typically, the fatty acid side chains of the triglyceride are very long, and can all be the same or different, giving rise to different kinds of fats
- We often hear terms such as trans fats, saturated fats, monounsaturated and polyunsaturated fats'



The example to the right would be a monounsaturated fat, as it only contains one double bond, a fat with multiple double bonds (in each chain) would be a polyunsaturated fat

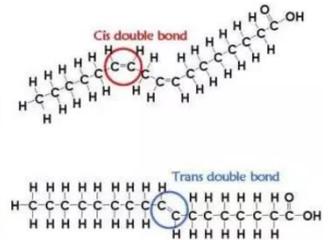
- Fats that only consist of single bonds are saturated fats
- Saturated fats have higher melting points than unsaturated



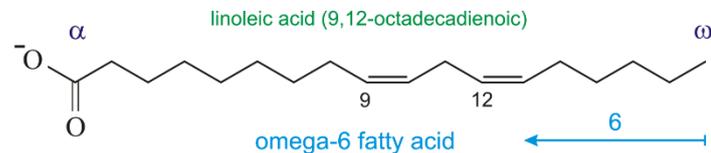
Usually the double bond is in the cis conformation, however, trans conformation fats are very difficult for the human body to process and end up as storage fat (which is why we want to avoid them!)

Essential fatty acids are unable to be produced in the body, and must be acquired through the diet (alpha-linolenic acid and linoleic acid)

The 'acid' end of a fatty acid is called the alpha end, the fatty acid tail has an omega end, notice that omega-3 and omega-6 fatty acids are named such that they represent the distance of the nearest double bond to the omega carbon

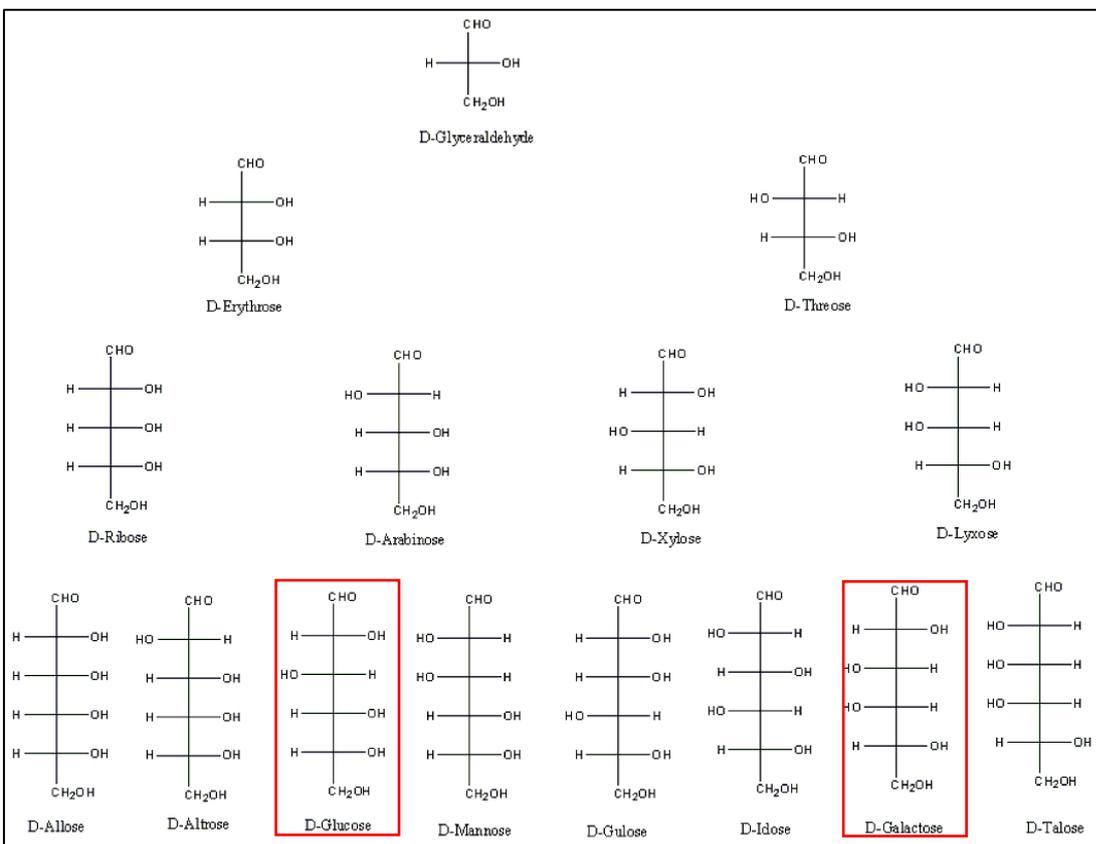


Waxes are simple esters of a fatty acid and a long chain alcohol in a condensation reaction – they usually serve as protective coatings



### 12.3.2 Epimers of Aldoses

- The example we have been looking at has been the interconversion of the 6 membered hexose D-glucose to its pyranose form → but our knowledge of chirality would suggest that if we swapped the OH and H on carbons 2 through 5, we would end up with multiple diastereomers of the glucose!
- We call these specific OH and H swaps, epimers

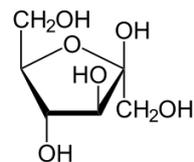


The rather daunting chart to the left gives all the epimers of D-aldoses of length 3 to 6 carbons

The number of epimers for a given aldose sugar is simply  $2^n$ , where n is the number carbon atoms minus 3  
Hexose →  $2^{6-3} = 2^3 = 8$

You do not need to memorise the structure of any sugar, but ideally, you should recognise glucose and galactose and its

anomeric forms without any labelling or colour coding. You should also recognise fructose.



### 12.3.3 Formation of Disaccharides via Hemiacetal Reaction

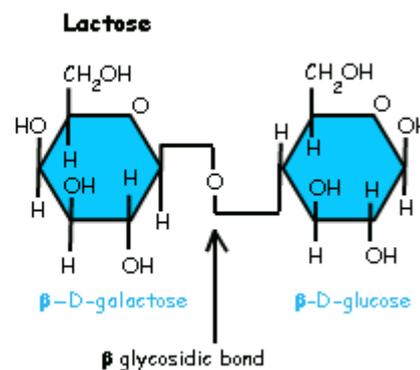
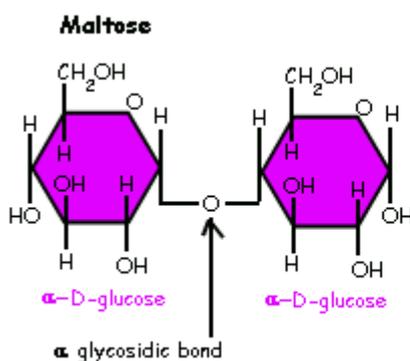
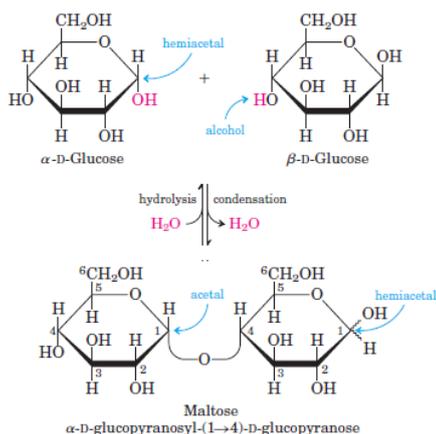
#### Hemiacetal Reaction

- We have discussed the conversion of the straight chain sugar to its cyclic form, and the mechanism behind it is a nucleophilic addition reaction → this will form the cyclic hemiacetal
  - We have also observed the C1 group position prerequisites to form the  $\alpha$  and  $\beta$  anomers → in the cyclic form, this carbon is called the anomeric carbon and it is a new chiral centre
- The  $\alpha$  anomer is in the trans conformation (it is axial, all other OH are equatorial)
- The  $\beta$  anomer is in the cis conformation (it is equatorial like the other OH groups)

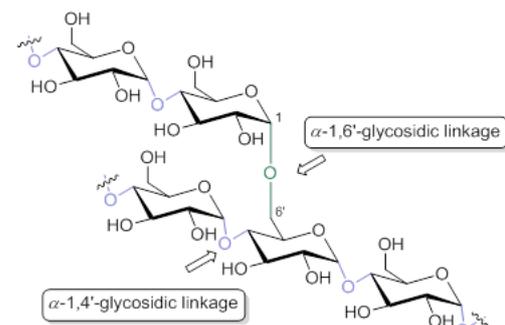
When exposed to water, a sugar can interconvert between  $\alpha$  and  $\beta$  anomers in a process called mutarotation

## Glycosidic Bond (Linkage) Formation

- A disaccharide is a molecule formed by the condensation of two cyclic monosaccharides (water is released as a by-product)
- This bond forms between the hemiacetal carbon (C1) of one sugar with the hydroxyl group of another (C4) → as the hydroxyl group can be in two anomeric positions:  $\alpha$  or  $\beta$ , we get two types of bonds →  $\alpha$ 1-4 and  $\beta$ 1-4 (we usually do not state if the adjoined molecule is an alpha or beta anomer as that hydroxyl group has no impact on the bond formed; but you should be able to recognise it)



Sometimes, we can even get  $\alpha$ 1-6 or  $\beta$ 1-6 linkages, which are easily distinguishable from 1-4 linkages (note that a  $\beta$ 1-6 linkage will be more horizontal than its alpha counterpart, but visibly there should be a hydrogen to hint at the conformation)

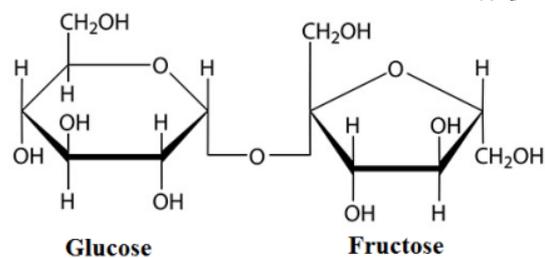
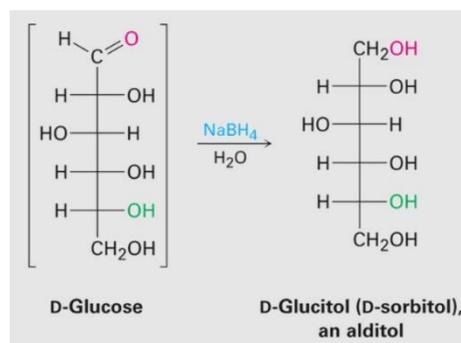


Some common disaccharides include:

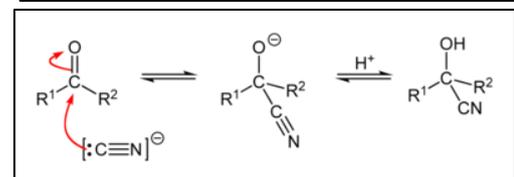
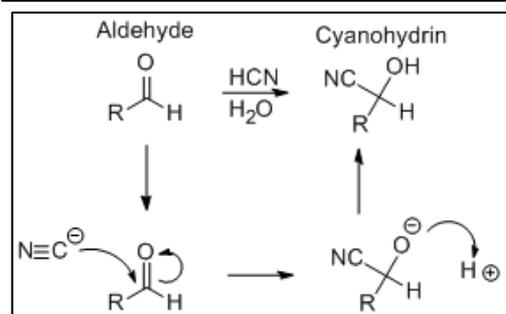
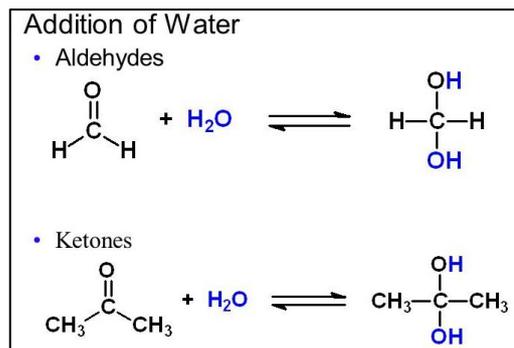
- Sucrose (glucose + fructose)
- Lactose (glucose + galactose in a  $\beta$ 1-4)
- Maltose (glucose + glucose in an  $\alpha$ 1-4 bond)

### 12.3.4 Other Reactions of Carbohydrates

- Monosaccharides with acid chlorides/anhydrides will form esters, also the hydroxyl groups can be esterified → OH will become OC(=O)R
- Monosaccharides with alkyl halides (with a silver oxide catalyst) will form ethers, and similar all the hydroxyl groups can be converted from OH to OR groups
  - Alcohols in the form of ROH can substituted their R group onto the sugar (essentially the ROH and sugar-OH swap, forming  $H_2O$  and sugar-OR)
- Monosaccharides can be reduced by  $NaBH_4$  to form a polyalcohol (CHO group becomes  $CH_2OH$ )



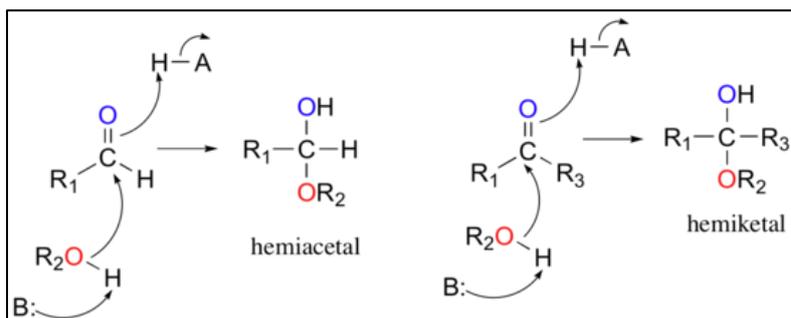
- Aldehydes and ketones react with water in the presence of a strong acid or base catalyst to form 1,1-diols or a geminal diol ( $\text{RC}(\text{OH})_2\text{R}$ )
- Aldehydes and ketones react with HCN to form cyanohydrins  $\rightarrow$   $\text{CN}^-$  attacks the carbonyl C and the protonation of O forms the tetrahedral cyanohydrin product
- Reduction of aldehydes and ketones with Grignard reagents ( $\text{RMgX}$ )  $\rightarrow$  see section 6.5
  - With formaldehyde  $\rightarrow$  primary alcohol
  - With other aldehydes  $\rightarrow$  secondary alcohol
  - With ketones  $\rightarrow$  tertiary alcohol
- Other reducing agents like  $\text{LiAlH}_4$  and  $\text{NaBH}_4$  will react similar to  $\text{RMgX}$  to produce alcohols (see 6.5)



### 7.7 Acetal (ketal) and Hemiacetal (hemiketal) Formation

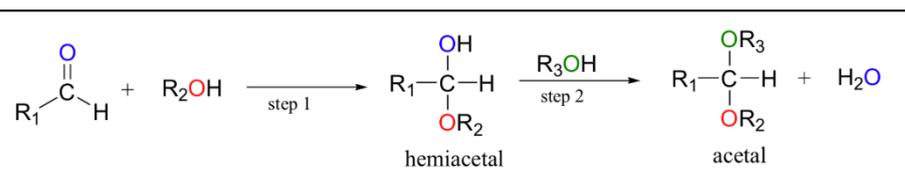
#### Aldehydes form Hemiacetals, Ketones form Hemiketals

- This reaction will occur when an aldehyde/ketone is dissolved in a primary alcohol with a small amount of acid catalyst



If the hemiacetal or hemiketal is allowed to react further with the primary alcohol, the hemiacetal  $\rightarrow$  acetal, and the hemiketal  $\rightarrow$  ketal

Note that an acetyl is just a hemiacetal with an extra group opposite the group bound to the oxygen atom introduced by the first round of primary alcohol



To compare, a ketal is the exact same thing, except the central carbon is a quaternary carbon, rather than a tertiary (no lone H)

Notice that in hemiacetal formation, the electrophile is the carbonyl O, which attracts the electrophilic H to form a carbocation  $\rightarrow$  this attracts the O in the primary alcohol to bind itself and the R group to form the hemi-compound

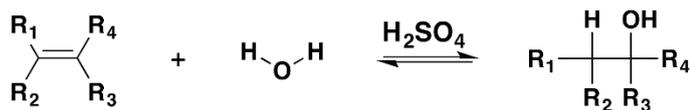
- In the diagram, the lost proton from  $\text{R}_2\text{OH}$  reacts with the catalyst ( $\text{B} + \text{H} \rightarrow \text{H-A}$ )
  - Note that B is the conjugate Base of the Acid catalyst, represented by A)
- In acetal formation, the same thing occurs where the oxygen will attract the acid more strongly as it has an OH group  $\rightarrow$  the leaving group will be protonated ( $\text{OH} \rightarrow \text{H}_2\text{O}$  which is a good leaving group)  $\rightarrow$  the third R group can join

Note that the reactions spoken about in 7.7 are all fully reversible!

## 6.5 Synthesis of Alcohols

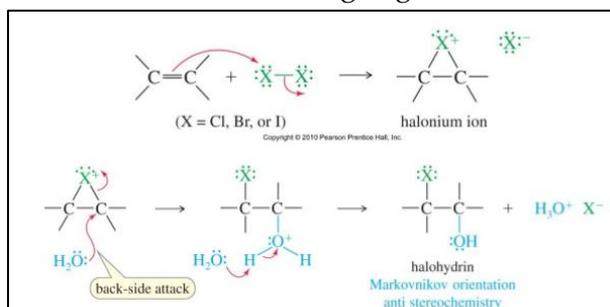
### 1. Hydration of Alkenes

- By combining an alkene with water under acidic conditions, an alcohol group can be formed

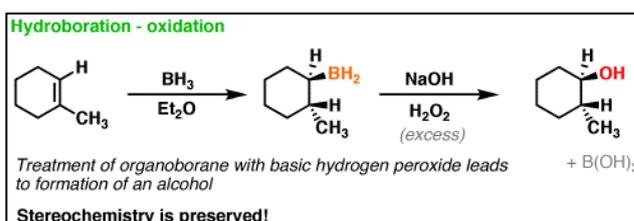


Note that we can create these alcohols through addition of an alkene with water and:

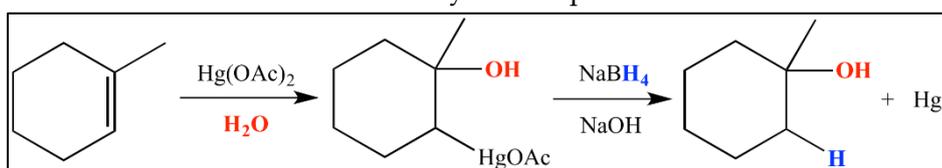
- A halohydrin can be formed (i.e. an alcohol with an adjacent halide) by reacting an alkene with a halogen gas in water



A hydroborate ( $\text{BH}_3$ ) can produce an anti-Markovnikov product (OH on least substituted carbon)



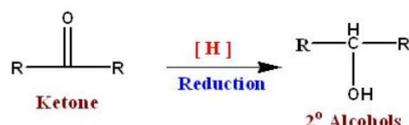
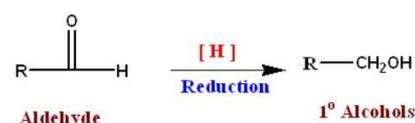
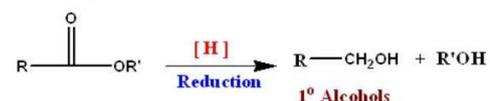
- Oxymercuration-Reduction yields another Markovnikov hydration product



### 2. Reduction of Carbonyl Compounds

Reducing an aldehyde, ketone, carboxylic acid, or an ester will produce an alcohol

- Aldehydes from primary alcohols
- Ketones (with a reducing agent like  $\text{NaBH}_4$  or  $\text{LiAlH}_4$ ) form secondary alcohols
- Reacting  $\text{NaBH}_4$  with esters or carboxylic acids will form primary alcohols (in the image, the ester is  $\text{RCOOR}'$ )



### 3. Addition Reaction with a Grignard Reagent

A Grignard reagent is simply ( $\text{RMgX}$ ), where R is anything that isn't H, and X is a halogen  $\rightarrow$  these reagents are produced by reacting Mg with alkyl (aryl or vinyl) halides

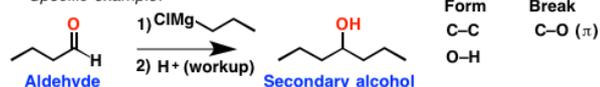
Note that carboxylic acid ( $\text{RCOOH}$ ) +  $\text{RMgX}$  will just produce a magnesium salt of the acid

Here we can see that aldehyde will form a secondary alcohol, while ketones, and esters form tertiary alcohols  $\rightarrow$  formaldehyde ( $\text{HCOH}$ ) will form a primary alcohol

Quick Review: 3 key reactions of Grignards with carbonyl compounds

#### Key Reaction #1: Addition of Grignards to aldehydes

Specific example:



#### Key Reaction #2: Addition of Grignards to ketones

Specific example:



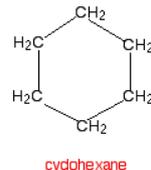
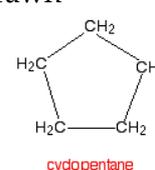
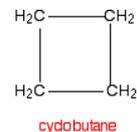
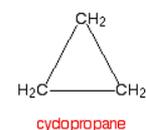
#### Key Reaction #3: Addition of Grignards to esters

Specific example:



### 3.2.3 Cyclic Alkanes

- The cyclic alkanes all have the prefix cyclo- and are shorthand simply drawn as the n-sided shape corresponding to the number of carbon atoms → cyclopropane is just a triangle, cyclooctane would be an octagon



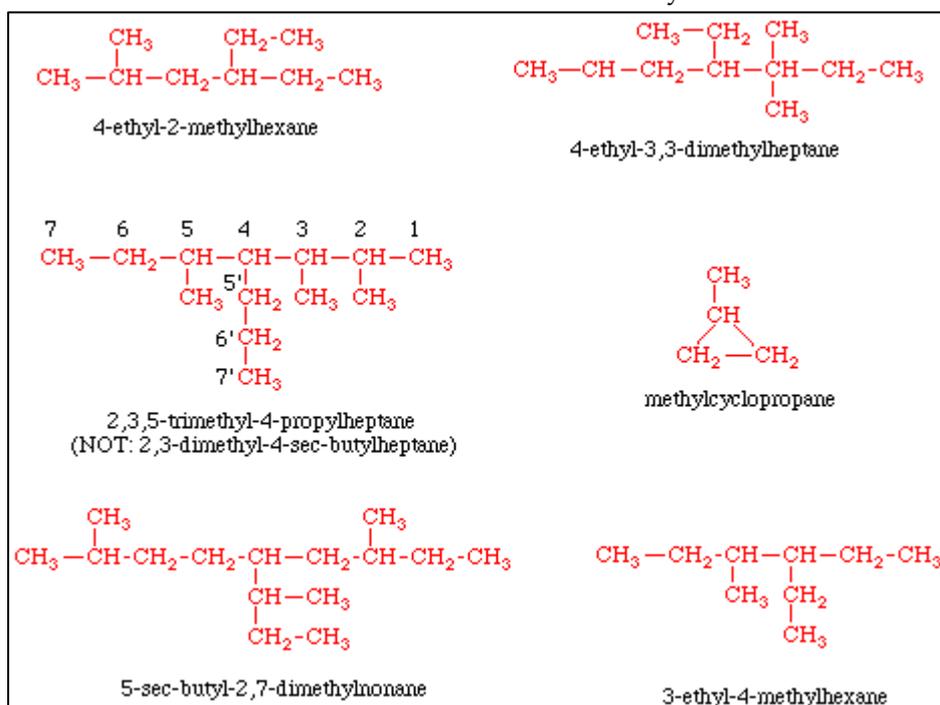
### 3.2.4 Types of Carbon Atoms

- When looking at shorthand hydrocarbon drawings, you should be able to identify a primary, secondary, tertiary, or quaternary carbon atom
  - A primary carbon (1°) is bound to one other carbon
  - A secondary carbon (2°) is bound to two other carbon atoms
  - A tertiary carbon (3°) is bound to three other carbon atoms
  - A quaternary carbon (4°) is bound to four other carbon atoms

### 3.2.5 Naming Branched Chain Hydrocarbons

With our knowledge of alkyl groups and prefix nomenclature, we can now name a presented branched alkane

- First, we must determine the longest straight chain → this is simply the longest number of connected carbon atoms in a row
- Now we can assign each straight chain carbon a number, we describe each functional or alkyl group relative to the number of the carbon they branch off of
  - Note that we try to use the Lowest numbers possible, so look at the examples below on how we ideally name branched alkanes



Take a look at the set of branched alkanes here, notice how a branched CH<sub>3</sub> is noted as methyl

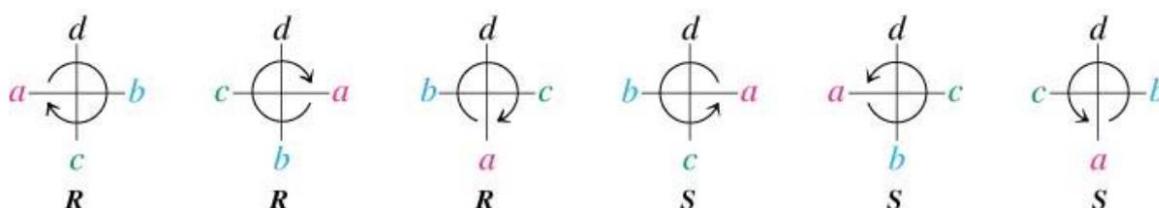
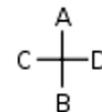
Also note how we deal with multiple groups on a single carbon, and also how we describe the overall number of groups (3,3-dimethyl or 2,3,5-trimethyl)

Ideally, we number from the side which has the closest functional group, we also do not state "1-" if an alkyl group is on the first carbon

Please take the time to look at other examples online to further deepen your understanding of how we name these hydrocarbons!

To determine the chirality of a Fischer projection:

1. Assign priorities to the 4 groups
2. Shift the groups to get the lowest priority group to the top
  - a. Note that to retain identity of the stereoisomer, group shifting must be done TWICE moving any two groups at a time → moving once forms a mirror image, moving again undoes this and the original molecule is retained
  - b. For example, using the molecule to right: to move C to the top while maintaining chirality → swap C with A, and then B with D
3. Now we can assign R/S nomenclature → if the priority order is clockwise, (R), if anticlockwise, (S)



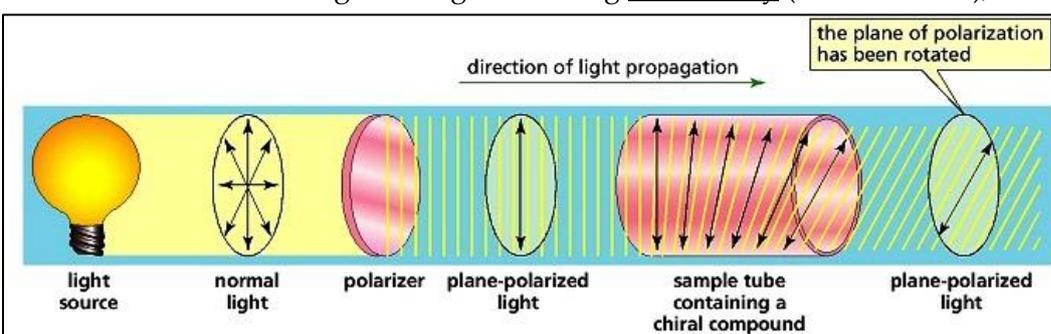
Have a go moving a group around while maintaining chirality → not that you can swap any two groups, as long as you swap groups TWICE, chirality is maintained

### 2.3.3 Optical Isomers

- Optical isomers are enantiomers that only differ by the orientation of atoms around the chiral carbon atom
  - When we pass plane-polarised light (light waves that oscillate in one plane) through a solution containing a pure enantiomer → the light will emerge rotating clockwise or anticlockwise based on the chirality of the substance

Optical isomers only differ due to the effect they have on plane polarised light:

- If light emerges vibrating dextrorotary (clockwise), it is denoted d- or (+)
- If light emerges vibrating laevorotary (anticlockwise), it is denoted l- or (-)



In this example, the light has twisted clockwise (it would be denoted as a d- isomer)  
The angle at which the light is twisted is called the plane shift ( $\alpha$ )

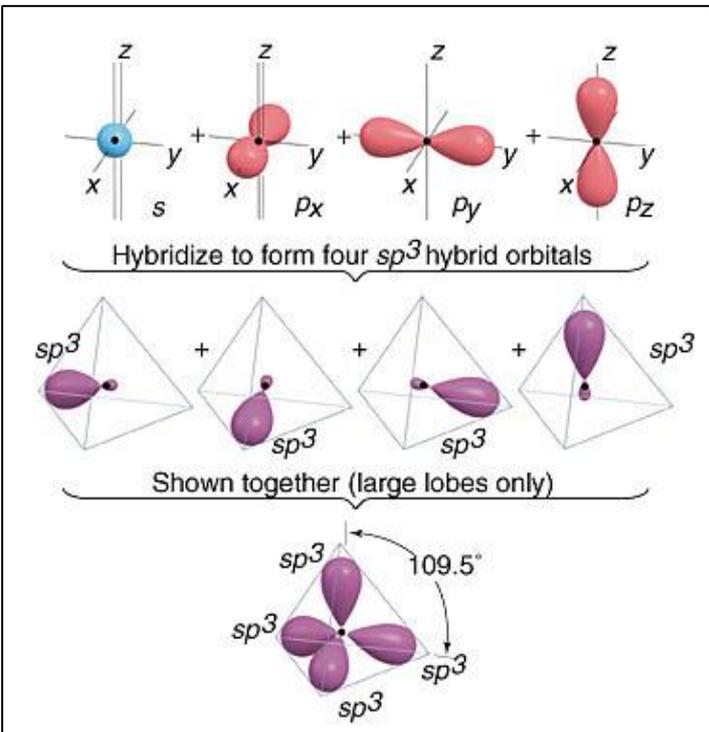
The rotation will increase as the length of the tube or the sample concentration increases

A racemic mixture (ray-see-mick) will show no rotation of polarised light → a racemic mixture contains equal amounts of d- and l- isomers and hence there is no net rotation

- The designation of d- and l- has nothing to do with D and L isomers and nor can we use d- and l- to determine if a molecule is in its R or S configuration
- Optical rotation can only be determined via experiment

## 1.4 Hybrid Orbitals of Carbon

- From our previous look at orbitals from inorganic chemistry, we recall that there are s and p orbitals, and they can combine in various ways to form hybrid orbitals
- This concept is rather tricky to understand, but we will start by recalling that carbon has 1 s and 3 p orbitals

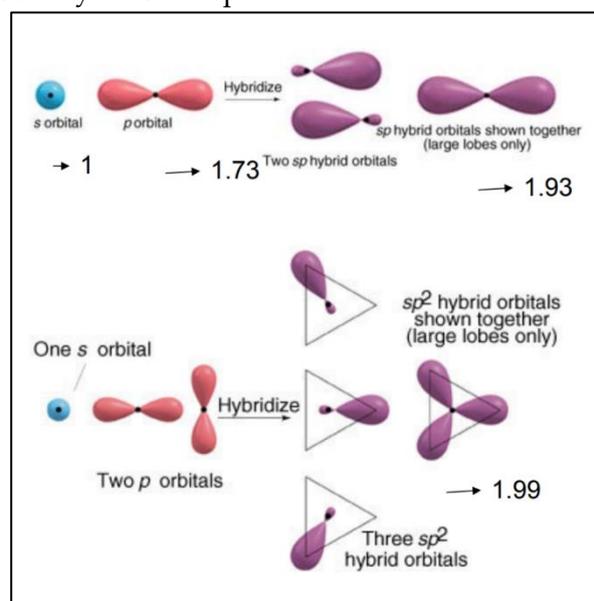


The image to the left shows the most common type of carbon hybridisation to form the tetrahedral form (note that the p orbitals exist in the x, y, and z planes)

Here we can see the  $s + 3p \rightarrow 4 sp^3$  hybrids  $\rightarrow$  the hybridised orbitals represent the space the orbital electrons may be, so they must be spaced

equidistant as they are all equally repelled by their negative charge!

This will occur when carbon is bonded 4 times (e.g.  $CH_4$ )



If only two of the p orbitals combine, we get  $s + 2p \rightarrow 3 sp^2$  hybrids (and one leftover p). The hybrid orbitals here all space out at  $120^\circ$  angles to form a triangular separation  $\rightarrow$  this occurs when Carbon is bonded 3 times (e.g.  $CH_2O$ )

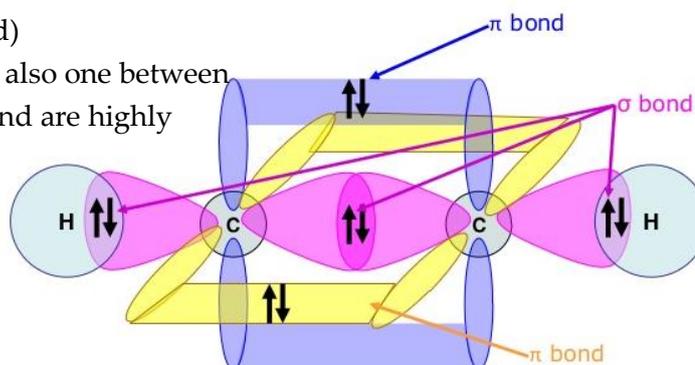
- If only one p orbital is combined with the s orbital, we get  $s + p \rightarrow 2sp$  (and two leftover p orbitals). The hybrid orbitals split linearly and the angle across the bond is  $180^\circ \rightarrow$  this occurs when carbon is bonded 2 times (e.g.  $CO_2$ )

## 1.5 Sigma and Pi Bonds

When single, double, or triple bonds are formed, we use sigma and pi bonds to describe the approximate location and density of the electrons in these bonds

- The sigma bond represents the location of electrons in the SINGLE bond  $\rightarrow$  the sigma bond lies directly between the two atoms and forms a circular tube that is fully rotatable about its axis
- The pi bond represents the location of the electrons in a DOUBLE or TRIPLE bond  $\rightarrow$  the pi bond is unusual as it wraps around the carbon atoms like a rubber band around a block of wood
- Ethyne is  $C_2H_2$  or  $H-C\equiv C-H$  (it has a triple bond)

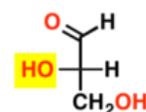
Notice that there is a sigma bond between the CH and also one between the CC  $\rightarrow$  the pi bonds wrap around the sigma bond and are highly rigid and NOT rotatable



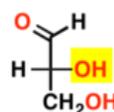
## 2.3 Absolute and Relative Configuration of Chiral Centres

We use the absolute and relative configuration nomenclature to describe a chiral centre

- The relative configuration uses the D/L system which compares a given pair enantiomers to the glyceraldehyde enantiomers
- The more common absolute configuration uses the R/S system which is a reformatting of D/L
- Note that D became R || and L became S
- Sometimes we call the D/R enantiomer the clockwise enantiomer → this means the L/S enantiomer is the anticlockwise enantiomer



L - glyceraldehyde



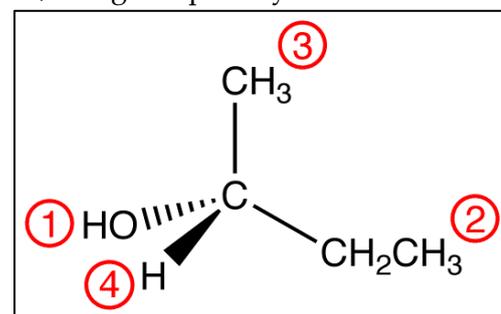
D - glyceraldehyde

### 2.3.1 The R/S System

- We define chiral centres as either R or S (originally D or L)
- Note that as enantiomers come in pairs → there is an R and an S enantiomer

Steps in Determining the Chirality of a Chiral Centre

1. Identify the asymmetric carbon and its 4 attached groups
2. Assign priorities to the 4 groups using the Cahn-Ingold-Prelog CIP rule:
  - a. Atoms of higher atomic number have highest priority (Cl > O > C)
  - b. Isotopes of higher atomic mass (C14 > C12) have higher priority
  - c. The groups with the atoms of highest atomic mass (OH > CH<sub>3</sub>) will get higher priority or highest overall mass/number of atoms (CH<sub>2</sub>CH<sub>3</sub> > CH<sub>3</sub>)
  - d. The group with the most bonds (C=O > C≡C > C=C) and/or highest priority atom will have the highest overall priority
3. Once groups are assigned priority, the atom must be arranged so that the lowest priority group is pointed away from the reader → the image to the right needs to be inverted

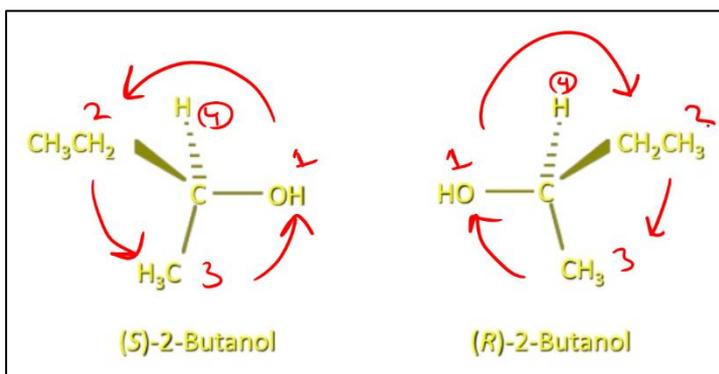


Now we can determine if the molecule is R or S by seeing if the order of the top 3 priority groups

forms a clockwise or anticlockwise circle

- Clockwise → Twisting Right → R
- Anticlockwise → Twisting Left → S

The molecule in the box above is (R)-2-butanol



### 2.3.2 R/S Fischer Projections

- A Fischer Projection shows the 3D nature of an atom in 2D geometric structure → the diagram on the right shows that vertical axis groups point away, and horizontal groups point forward
- To determine if 2 given Fischer projections are identical you can invert one projection 180° or keep on group in place while you shift the other three in a circle (e.g. C moves to D, D to B, and B to C) and see if the projections match → this will let you determine if two molecules are enantiomers or diastereomers

