Topic 8: Metabolism, cell respiration and photosynthesis (HL)

8.1 Metabolism

U1	Metabolic pathways consist of chains and cycles of enzyme-catalysed reactions.
U2	Enzymes lower the activation energy of the chemical reactions that they catalyse.
U3	Enzyme inhibitors can be competitive or non-competitive.
U4	Metabolic pathways can be controlled by end-product inhibition
A1	End-product inhibition of the pathway that converts threonine to isoleucine
A2	Use of databases to identify potential new anti-malarial drugs.

Definitions

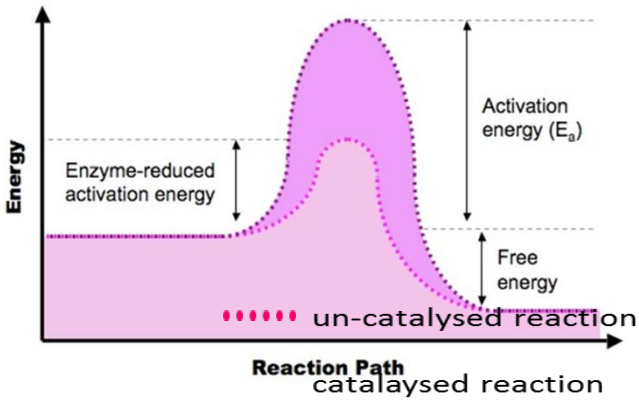
Metabolism: the sum total of all chemical reactions that occur within an organism.

Metabolic pathways: cycles or chains of enzyme catalysed reactions. The chemical change from one molecule to another often does not happen not in one large jump, but in a sequence of small steps. The small steps together form what is called a metabolic pathway, e.g. glycolysis is a metabolic chain and Calvin cycle is a metabolic cycle.

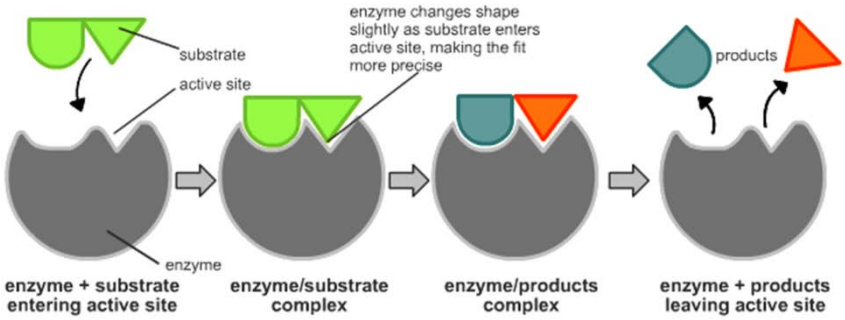
Metabolic chains and cycles

- Metabolism – the chemical reactions that occur in organisms in order for them to maintain life, such as the synthesis of ATP during cellular respiration.
- In metabolic pathways, enzymes catalyse each reaction along the pathway
- Some of these pathways are anabolic, which is building up of organic molecules (easy to remember as anabolic steroids help build muscle)
- The other pathways are catabolic, which means breaking down of large organic molecules into smaller ones (example – hydrolysis reactions during digestion)
- Some of these metabolic reactions are cycles (i.e. Krebs Cycle) and some are linear chains (i.e. Glycolysis)

Enzymes lower the activation energy



- The substrate binds to the enzymes' active site and the active site is altered to reach the transition state.
- Due to the binding the bonds in the substrate molecule are stressed/become less stable.
- The binding lowers the overall energy level of the transition state.
- The activation energy of the reaction is therefore reduced.
  Notice: the **net amount of energy released** by the reaction is unchanged
- Activation energy is the energy that must be overcome in order for a chemical reaction to occur.
- Activation energy more specifically can be defined as the **energy needed to weaken and break the chemical bonds of the substrate**.
- Enzymes work by lowering the activation energy needed for the reaction to occur.
- These reactions therefore occur faster and more substrates can be converted into more products (rate of reaction increases dramatically).



Enzyme inhibitors can be competitive or non-competitive

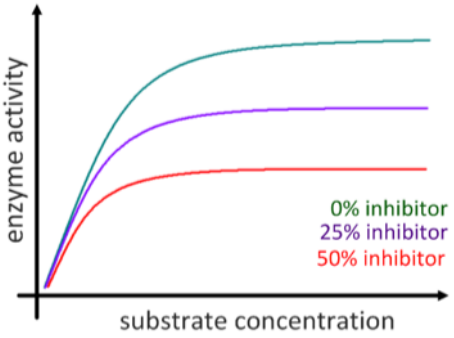
- Enzyme inhibition occurs when molecules bind to enzymes and decreases their activity.
- Two types of enzyme inhibition are competitive and non-competitive inhibition.

Definitions

Inhibitor: a molecule that binds to an enzyme and slows down or stops the enzyme's function.

Competitive inhibition

- Competitive inhibition occurs when a molecule that is structurally similar to the substrate competes directly with substrate for access to the active site, thus **decreasing the number of times a substrate interacts with an enzyme**.
- The inhibitor essentially blocks the substrate from binding to the enzyme.
- Since there is less enzyme/substrate interactions, the chemical reaction rate decreases.
- Competitive inhibition is usually **reversible** but can be irreversible in some cases.
- Competitive inhibition can be overcome by sufficiently increasing the concentrations of substrate, thereby out-competing the inhibitor.
- With **competitive inhibition**, the same maximum rate of reaction will be achieved if more substrates are added – because we haven't changed the number of available enzymes.



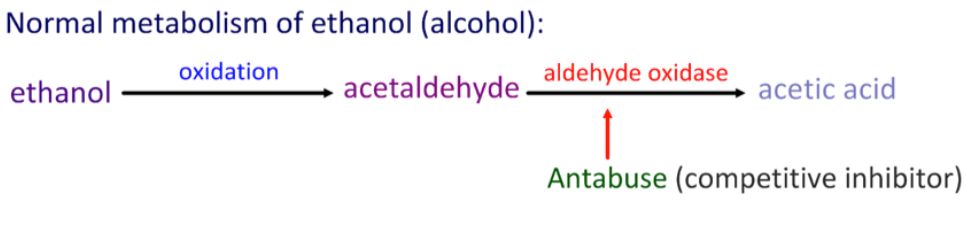
Non-competitive inhibition

- Non-competitive inhibition occurs when an inhibitor does not compete for the active site with the substrate, but instead binds to a separate site on the enzyme, binding to **allosteric site**
- When non-competitive inhibitor binds to the enzyme at the alternative site, it changes the conformational **shape of the enzyme** and thus the active site, so that the substrate can no longer bind to the enzyme for a reaction to occur.
- Non-competitive inhibition is usually reversible.
- Since the inhibitor binds to a site other than the active site, increasing the concentration of the substrate will not speed up the reaction or reduce the effect of the inhibitor.

As concentration of non-competitive inhibitor increases, the rate of reaction decreases. This is because there are fewer active sites available for reaction. The maximum rate of reaction is also reduced – with fewer functional active site, the enzyme has reduced ability to process the substrates, even if substrate concentration is increased.

Example

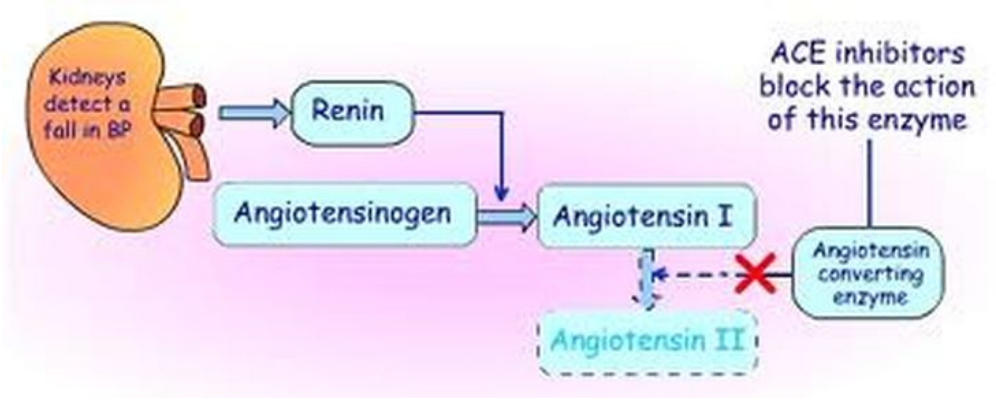
Overcoming alcoholism : an example of competitive inhibition.



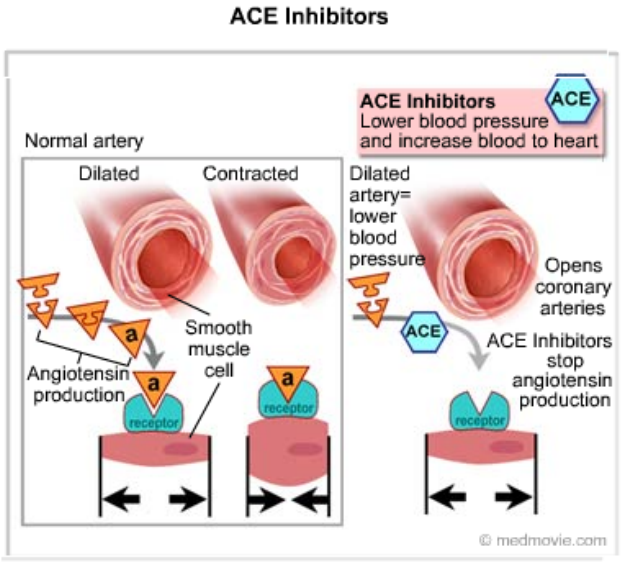
- **Antabuse** competes with **aldehyde oxidase** and prevents **acetaldehyde** from being converted into acetic acid.
- Acetaldehyde builds up and creates a good deterrent from drinking.
- Antabuse is a kind of daily pill, if patient stops taking it, he can drink again.
- Acetaldehyde is a kind of chemical which makes people hangover and sick.

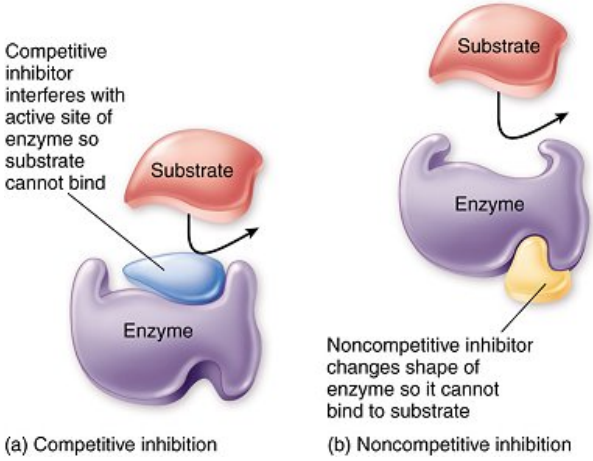
Example

ACE inhibitor (helping control blood pressure): an example of non-competitive inhibition.



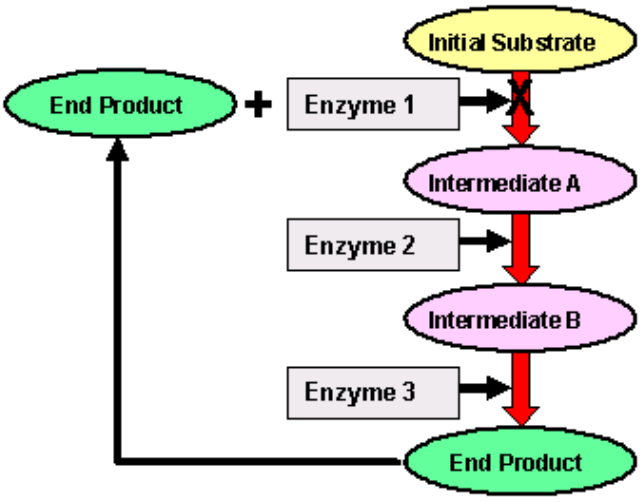
- The RAA system causes vasoconstriction (tightening of blood vessels) when blood pressure drops.
- In people with **hypertension** or heart failure, the Angiotensin II can make the condition worse.
- ACE Inhibitors are medications that inhibit Angiotensinogen Converting Enzymes – they prevent increasing blood pressure.
- ACE Inhibitors are non-competitive and reversible.





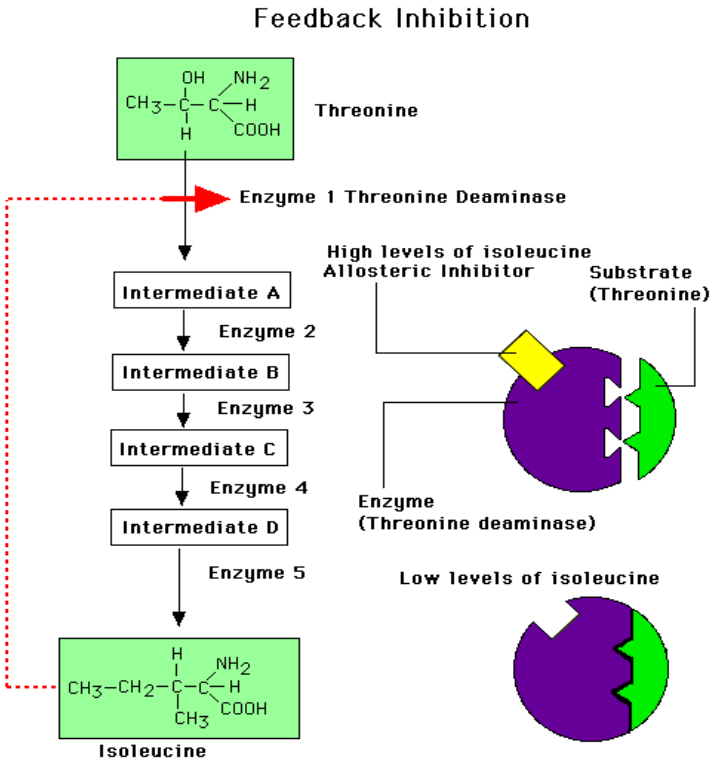
Metabolic pathways can be controlled by end-product inhibition (A.K.A. Feedback Inhibition)

- End-product inhibition prevents the cell from wasting chemical resources and energy by making more of a substance than it needs.
- If a cell is creating a specific product through a metabolic pathway and it makes too much of this product, this product will actually inhibit the first enzyme in the metabolic pathway, thus stopping the metabolic pathway from producing more unneeded product.
- Each step of the reaction is catalysed by a specific enzyme, and a specific end product is present.
- When product is in a sufficient quantity, it inhibits the 1st enzyme and slows down the reaction which means less product made.
- As concentration of product decreases, inhibition decreases and rate of reaction increases.



End-product inhibition of the pathway that converts threonine to isoleucine

- Isoleucine is an essential amino acid
- Bacteria synthesize **isoleucine** from **threonine** in a series of five enzyme-catalysed steps
- As the concentration of isoleucine increases, some of it binds to the allosteric site of threonine deaminase
- Isoleucine acts as a **non-competitive inhibitor** to threonine deaminase
- The pathway is then turned off, regulating isoleucine production.
- If the concentration of isoleucine later falls (as a result of its use) then the allosteric sites of threonine deaminase are emptied and the enzymes recommence the conversion of threonine to isoleucine takes place.



Use of databases to identify potential new anti-malarial drugs.

- Bioinformatics is an approach whereby multiple research groups can add information to a database enabling other groups to query the database.
- Bioinformatics has facilitated research into metabolic pathways is referred to as **chemogenomics**.
- Increasing drug resistance to **anti-malarial** drugs has lead to the use of bioinformatics and chemogenomics to try and identify new drugs.
- Malaria is a disease caused by the protist ***Plasmodium falciparum***
- The increased resistance of the pathogen ***P. falciparum*** to anti-malarial drugs such as chloroquine and the increasing global efforts to eradicate malaria have driven the need to produce new anti-malarial drugs
- P. falciparum strain 3D7 has been sequenced by scientists and is used to test chemicals for new possible medication
- One specific study tested over 300,000 chemicals against a chloroquine-sensitive 3D7 strain and a chloroquine-resistant K1 strain to determine if any of these chemicals inhibited metabolism
- The results showed that 19 new chemicals inhibited the enzymes normally targeted by anti-malarial drugs and 15 chemicals that bound to a total of 61 different malarial proteins.
- **This research provides starting points to produce possible new ant-malarial drugs**

8.2 Cell respiration

U1	Cell respiration involves the oxidation and reduction of electron carriers.
U2	Phosphorylation of molecules makes them less stable.
U3	In glycolysis, glucose is converted to pyruvate in the cytoplasm.
U4	Glycolysis gives a small net gain of ATP without the use of oxygen.
U5	In aerobic cell respiration pyruvate is decarboxylated and oxidized, andconverted into acetyl compound and attached to coenzyme A to form acetylcoenzyme A in the link reaction.
U6	In the Krebs cycle, the oxidation of acetyl groups is coupled to the reductionof hydrogen carriers, liberating carbon dioxide.
U7	Energy released by oxidation reactions is carried to the cristae of themitochondria by reduced NAD and FAD.
U8	Transfer of electrons between carriers in the electron transport chain in themembrane of the cristae is coupled to proton pumping.
U9	In chemiosmosis protons diffuse through ATP synthase to generate ATP.
U10	Oxygen is needed to bind with the free protons to maintain the hydrogengradient, resulting in the formation of water.
U11	The structure of the mitochondrion is adapted to the function it performs.
A1	Electron tomography used to produce images of activemitochondria.
S1	Analysis of diagrams of the pathways of aerobic respiration to deducewhere decarboxylation and oxidation reactions occur.
S2	Annotation of a diagram of a mitochondrion to indicate the adaptationsto its function.

Oxidation and reduction (OIL RIG)

Oxidation	Reduction
Lose electrons(energy)	Gain electron(energy)
Oxygen is gained	Oxygen is removed
Hydrogen is removed	Hydrogen is gained

Electron carrier in respiration

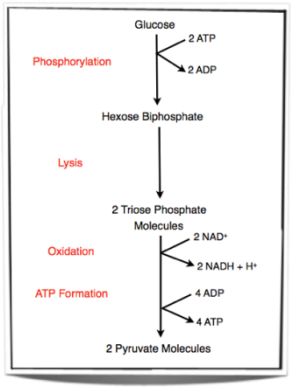
Electron carriers are substances that accept and give up electrons so they can transfer and save energy. There are two types of electron carriers involving in cell respiration

- NAD: $NAD^+ \leftrightharpoons NADH$(forward reaction in reduction)
- FAD: $FAD^+ \leftrightharpoons FADH_2$(forward reaction in reduction)
- During respiration NAD which actually exists as NAD^+ accepts 2 electrons and a proton (H^+) from the molecule being oxidized (like pyruvate) to form NADH with one extra H^+ leftover as a product, in which NAD^+ is reduced into NADH
- After the electron carriers are reduced, they will be transported to electron transport chain, in which, electron carriers will be oxidized and release protons and electrons into inter-membrane space

Glycolysis

Sequence of glycolysis	Explanation	Reaction	Energy
Phosphorylation	a phosphate molecule is added to an organic compound. Phosphorylation can make the molecule more reactive so unstable.	Glucose is added 2 phosphate group at each end (a.k.a. 2 times of phosphorylation) Glucose then is turned into hexose phosphate (6 carbon molecule)	2ATP→2ADP
Lysis	Splitting molecules	Hexose phosphate is splitted into 2 triose phosphate (3 carbon molecule)	n/a
ATP formation	Create ATP	Triose phosphate is turned into pyruvate	$2NAD^+ \rightarrow 2NADH$ 4ADP→4ATP

Summary of glycolysis



Net gain of ATP: 2

Site of reaction: cytoplasm

Link reaction

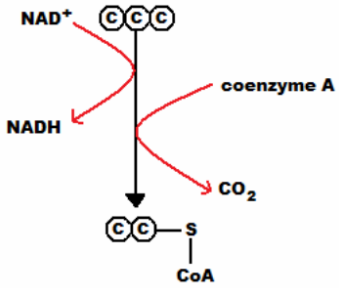
Pyruvate is not allowed to enter the mitochondria, so coenzyme A comes and breaks pyruvate (3 carbon molecule)

Into acetyl CoA (2 carbon molecule) and a single carbon molecule, which is eventually bind with 2 oxygen atoms to

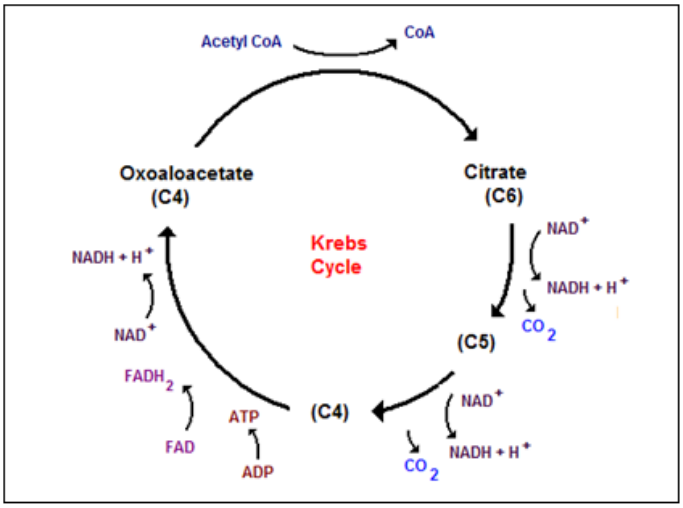
form carbon dioxide. For every glucose molecule, it will go through **twice** link reaction

- Decarboxylation is a chemical reaction that removes a carboxyl group and releases carbon dioxide (CO_2).
- Oxidation is the *loss* of electrons or an *increase* in oxidation state by a molecule, atom, or ion. Pyruvate is oxidized by the by the removal of pairs of hydrogen atoms (with their electrons), which are passed on the NAD^+ and FAD

Krebs cycle



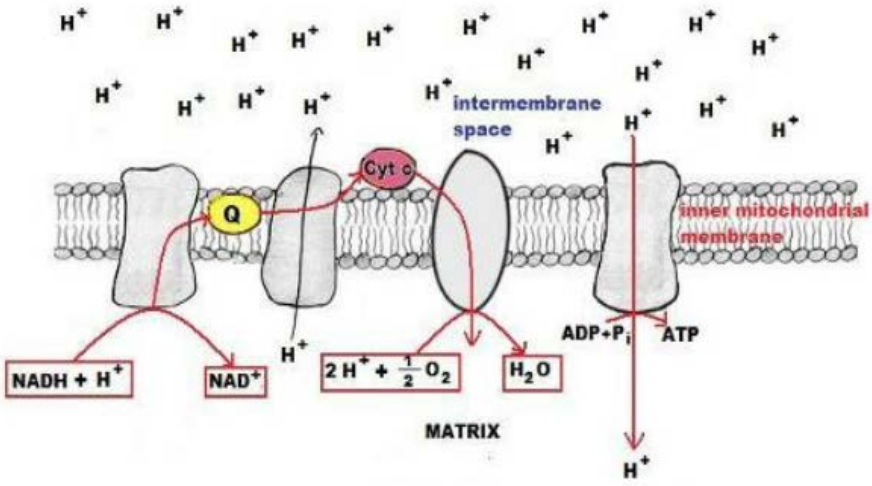
- Acetyl Co A is a two carbon molecule that transfers the acetyl group to the four carbon molecule oxaloacetate to form the six-carbon compound citrate (6C).
- Citrate is decarboxylated (released as carbon dioxide) and CO_2 is excreted as a waste product with the CO_2 from link reaction.
- Citrate is also oxidized and NAD^+ is reduced to form NADH.
- The C5 molecule formed is further oxidized and decarboxylated to form another CO_2 molecule (excreted as waste) and another NADH.
- At this point all the carbons from the original pyruvate molecule have been released as CO_2.
- The C4 molecule undergoes changes to regenerate the original oxaloacetate (C4) molecule, further producing a NADH, a $FADH_2$ and an ATP through a series of redox reactions.
- The products produced by the Krebs cycle are used in electron transport chain to make ATP.
- Final products for one glucose molecule: **2 ATP, 6 NADH, 2 $FADH_2$ and 4 CO_2(excreted).**
- For every glucose molecule, it will go through **twice** kerbs cycle



Electron Transport Chain and Chemiosmosis

- The chain is a series of electron carriers located in the inner membrane of mitochondria that pass electrons from one carrier to the next down an energy gradient.
- NADH supplies 2 electrons to the first carrier in the chain (reforming NAD^+). These electrons move along the chain of electron carriers giving up energy each time they pass from one carrier to the next.
- $FADH_2$ is also oxidized (forms FAD^+) releases its electrons a little later into the electron transport chain.
- Energy is released as the electrons are passed along the carrier proteins.
- This energy is used to pump H^+ ions across the inner mitochondrial membrane from the matrix to the inter-membrane space.
- This accumulation of H^+ ions in the inter-membrane space creates an H^+ concentration gradient between the matrix (less concentrated) and the inter-membrane space (more concentrated)
- Protons (H^+) flow back from the inter-membrane space to the matrix through special protein channels located in the inner mitochondrial membrane called **ATP synthase**.

- As the protons pass across the membrane, they release energy, which is used by the ATP synthase to produce ATP through a phosphorylation reaction.
- This process is called oxidative phosphorylation because oxygen is **the final electron acceptor** and the energy released by **reducing oxygen to water** is used to phosphorylate ADP and generate ATP.
- For each glucose molecule, about 32 molecules of ATP are produced.



Summative table of cell respiration

Reaction sequence	Location	Net Energy Gain per glucose	Enzyme	Waste production
Glycolysis	Cytoplasm	2 ATP,2 NADH	N/A	N/A
Link reaction	Cytoplasm	2 NADH	Coenzyme A	CO_2
Krebs cycle	Mitochondria	2 ATP, 6 NADH, 2 $FADH_2$	N/A	CO_2
Electron transport chain	Inner membrane of mitochondria	N/A	Protein carrier	N/A
Chemiosmosis	Inter-membrane space and matrix	32 ATP	ATP Synthase	H_2O
Respiration in general	Cell	36 ATP	N/A	CO_2,H_2O

Role of oxygen

- At the end of the ETC, electrons are given to oxygen. Oxygen accepts hydrogen ions and forms water (known as the terminal acceptor).
- If oxygen is not available, electron flow along the ETC stops and NADH + H^+ cannot be reconverted to NAD^+.
- Supplies of NAD^+ in the mitochondrion run out and the link reaction and Krebs cycle cannot continue.
- Glycolysis can continue because conversion of pyruvate into lactate or ethanol and carbon dioxide produces as much NAD^+ as is used in glycolysis.
- Therefore oxygen is necessary for aerobic respiration to take place.
- Also, by using up the hydrogen to form water, the proton gradient across the inner mitochondrial membrane is maintained.

Functions of different parts of mitochondria

Structure	Functions
Outer membrane	Separates the contents of the mitochondria from the rest of the cell creating a separate compartment
Inner membrane	Contains the ETC and the ATP synthase for oxidative phosphorylation reactions. The cristae membrane is highly folded to increase the surface area for these reactions

Inter-membrane space	The volume of the space is small to allow proton build-up to create a concentration gradient in order to create ATP through oxidative phosphorylation as the protons flow back into the matrix through ATP synthase
Matrix	Contains enzymes necessary for the reactions that take place; the Krebs cycle and the link reaction

8.3 Photosynthesis

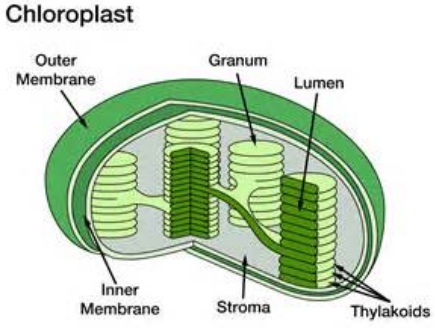
U1	Light-dependent reactions take place in the intermembrane space of thethylakoids.
U2	Light-independent reactions take place in the stroma.
U3	Absorption of light by photosystems generates excited electrons.
U4	Photolysis of water generates electrons for use in the light-dependentreactions.
U5	Transfer of excited electrons occurs between carriers in thylakoid membranes.
U6	Excited electrons from Photosystem II are used to contribute to generate aproton gradient.
U7	ATP synthase in thylakoids generates ATP using the proton gradient..
U8	Excited electrons from Photosystem I are used to reduce NADP.
U9	In the light-independent reactions a carboxylase catalyses the carboxylation of ribulose bisphosphate.
U10	Glycerate 3-phosphate is reduced to triose phosphate using reduced NADPand ATP.
U11	Triose phosphate is used to regenerate RuBP and produce carbohydrates.
U12	Ribulose bisphosphate is reformed using ATP.
U13	The structure of the chloroplast is adapted to its function in photosynthesis.
A1	Calvin's experiment to elucidate the carboxylation of RuBP.
S1	Annotation of a diagram to indicate the adaptations of a chloroplast toits function.

Structure of chloroplast

- The chloroplast has an outer membrane and an inner membrane
- The inner membrane encloses the interconnected membranes called the thylakoid membranes
- Chlorophyll molecules are grouped together into photosystems contained within the thylakoid membranes.
- The area within these thylakoid membranes is called the thylakoid space (lumen) and this is where the light-dependent reactions take place

Inside the thylakoid, green pigments can be found, which is mainly consisted ofhlorophyll A, chlorophyll B and carotenoids.

All those pigments are organized into photosystems



Structure	Function
Thylakoid membrane	Increased SA allows for greater absorption of light by the photosystems in the membrane
Stroma	Allows for the concentration of enzymes necessary for the Calvin cycle to occur
Thylakoid space (lumen)	Small space allows for the accumulation of protons to create a concentration gradient necessary for chemiosmosis to occur

Light-dependent reaction

Photosystem II:

- Photon of light is absorbed by pigments on photosystem II and the energy is transferred to chlorophyll A and excites one of its electron
- The electron is captured by an electron carrier to the electron transport chain (ETC)
- Water is splitted to replace lost electron, and produce H^+ ion, oxygen and electrons
- Water splitting process is called **photolysis**, which is happened in the enzymes called water splitting enzyme

Electron transport chain:

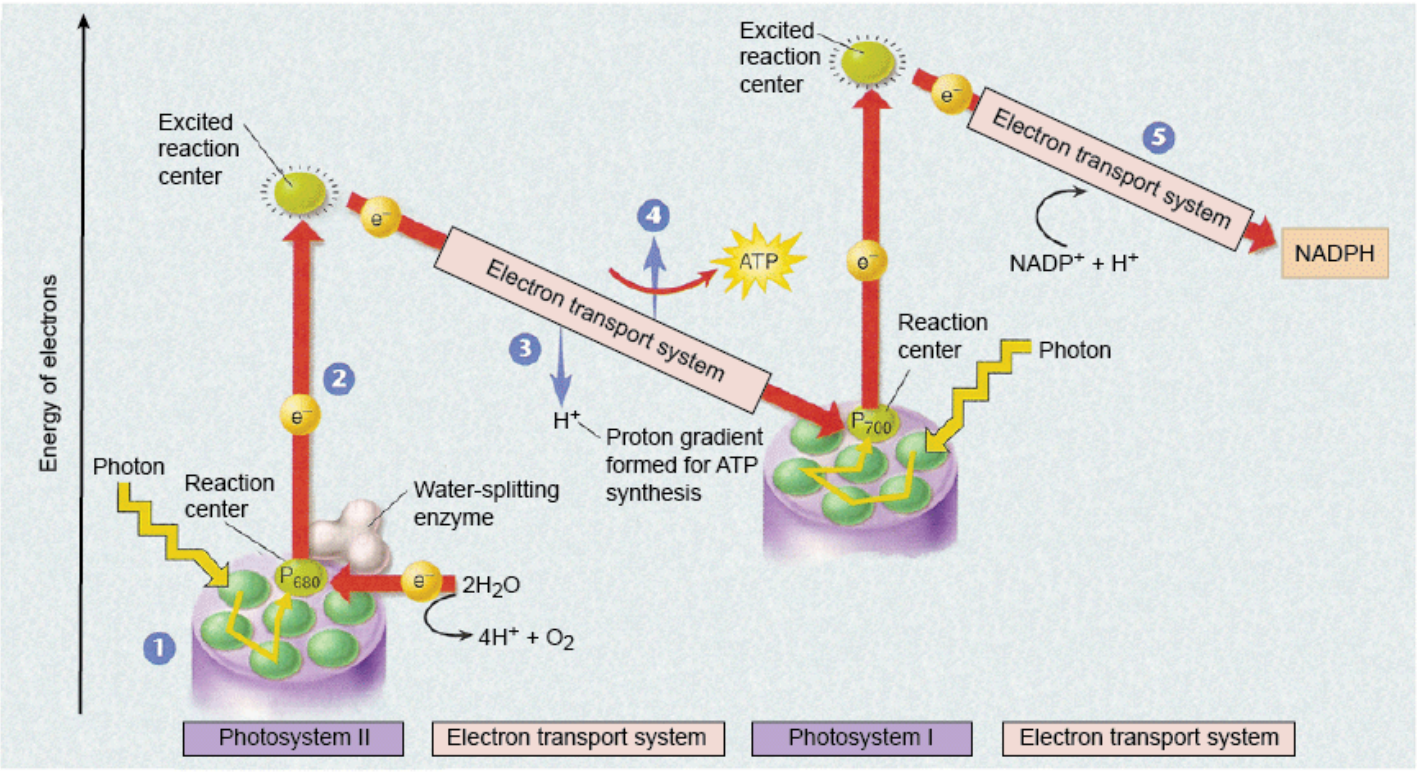
- Electrons (from photosystem II)are carried along the electron transport chain, actively transport H+ ion across the membrane. The de-energised electrons are passed to the photosystem I to replace lost electrons
- **Chemiosmosis**: H^+ ions create a concentration difference between the thylakoid space and stroma. Through normal diffusion along the concentration gradient, H^+ ions diffuse back into the thylakoid space (lumen) and then drive **ATP synthase** to produce ATP

Photosystem I:

- Photons excite electrons in photosystem I, moved by an electron acceptor to **ferredoxin**
- Lost electrons are replaced form electrons travelled from ETC, which is originally excited in photosystem II
- Electrons are used to reduce $NADP^+$ to NADPH by NADP reductase

Summative Light-dependent reaction table

Sequence of reactions	Products transfer	Site of reaction	Overall Products
Photosystem II	Electrons, oxygen, H^+ ions	Lumen (thylakoid space)	ATP, NADPH, O_2 (waste)
Electron transport chain	Electrons, H^+ ions (from photosystem II) → produce ATP by chemiosmosis	Thylakoid membrane	
Photosystem I	Get electrons from ETC, excites electron to ferredoxin then to NADP reductase, turing into NADPH	Lumen (thylakoid space)	



Light-independent reaction (Calvin Cycle)

- One CO_2 molecule enters the Calvin cycle and combines with a 5 carbon molecule called Ribulose bisphosphate (**RuBP**) to temporarily form a 6C molecule.
- This reaction is catalyzed by the enzyme **RuBP carboxylase (rubisco)**.
- This immediately breaks down into two 3C molecules called **glycerate-3-phosphate (G3P).**
- G3P molecules are reduced by adding hydrogen from NADPH using the energy from the breakdown of an ATP molecule, which will be turned into triose phosphate
- Two TP molecules are used to produce one six carbon glucose phosphate molecule, which can eventually be combined with other glucose phosphate to form starch.
- The other ten TP (3C) molecules are used to regenerate six RuBP (5C) using 6 ATP molecules for energy.
- So for every 6 triose phosphate molecules produced, 5 of these triose (3C) sugars are used to reform 3 RuBP (5C) molecules using 3 ATP molecules The one remaining triose phosphate forms half a glucose phosphate

Summative Light-independent reaction table

Sequence of reactions	Products transfer	Energy transfer	Overall Products
Carbon fixation	$6\ CO_2 + 6\ RuBP \rightarrow 12$ Glycerate-3-phosphate **RuBP carboxylase (Rubisco)**	N/A	1 Glucose (**1 glucose production per 6 carbon dioxide**)
Reduction	12 Glycerate-3-phosphate $\xrightarrow{\text{reduce}}$ 12 Triose phosphate	12 ATP + 12NADPH $\rightarrow$ 12 ADP, 12 H^+, 12$NAPD^+$	
Regeneration	12 Triose phosphate $\xrightarrow{\text{rearrange}}$ 6 RuBP ($\frac{1}{6}$ triose phosphate is used to produce glucose, others are used to rearrange to form RuBP, in this case 2 molecules)	6 ATP $\rightarrow$ 6 ADP