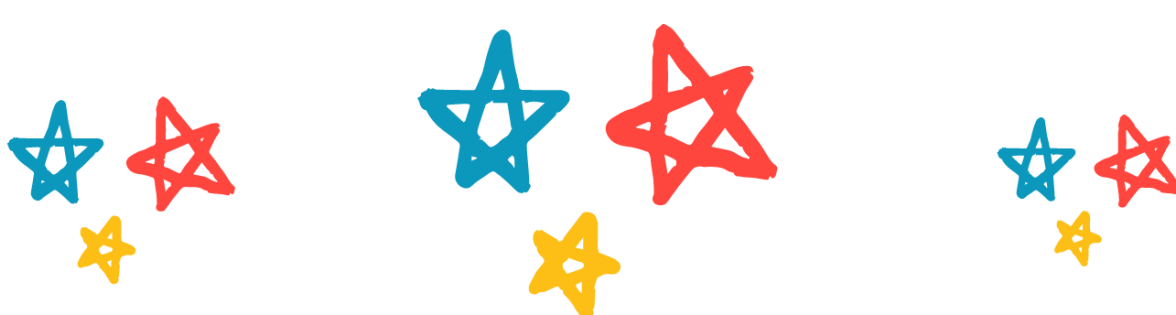




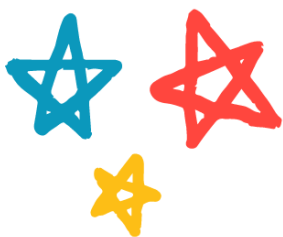
Higher Human Biology



UNIT 1



Revision notes



1.Somatic/Germline Stem cells

Stem Cells

Unspecialised cells that:

1. Reproduce themselves to produce more stem cells and remain undifferentiated.
2. Differentiate into specialised cells.

Somatic cells

Cells in the body that are not involved in reproduction (e.g. muscle, skin, bone, blood etc).

They have two sets of chromosomes (**diploid** cells).

Somatic stem cells divide by mitosis to form more somatic cells.

Germline cells

Haploid gametes (sperm and ova) & stem cells that divide to form gametes.

Germline stem cells can divide by:

1. MITOSIS

To produce more germline stem cell to maintain the diploid chromosome number.

Diploid cells have 23 pairs of homologous chromosomes (46 single chromosomes).

2. MEIOSIS

To produce haploid gametes. The nucleus undergoes two divisions.

First division: separates homologous chromosomes (diploid to two haploid cells).

Second division: separates chromatids to produce more haploid gametes.

Haploid gametes contain 23 single chromosomes.

1. Stem Cells

Cell differentiation

The process by which a cell expresses certain genes to produce specific proteins characteristic for that type of cell.

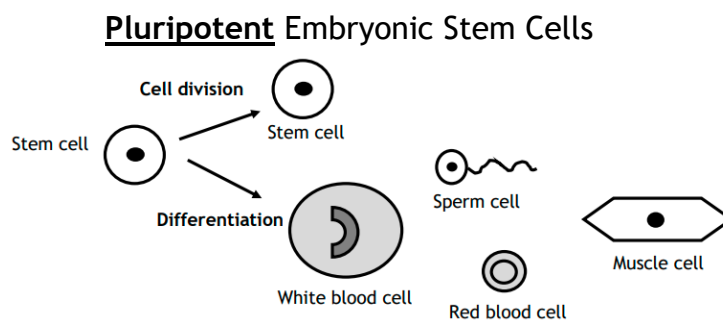
This allows a cell to carry out specialised functions. This saves ATP/resources.

Types of Stem Cells

1. Embryonic Stem Cells

Cells in the very early embryo can differentiate into all the cell types that make up the individual

All the genes in embryonic stem cells can be switched on so these cells can differentiate into any type of cell aka pluripotent.

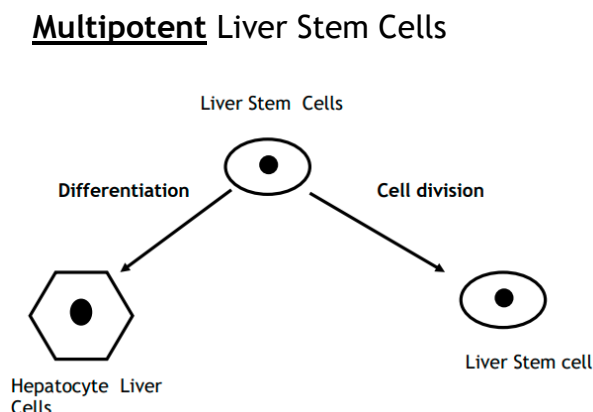


2. Tissue stem cells

Involved in the growth, repair and renewal of the cells found in one tissue and so are called multipotent.

Example 1: Blood stem cells in bone marrow can give rise to ONLY a few types of blood cells.

Example 2: Liver Stem Cells produce only 1 type (liver hepatocytes)



1. Therapeutic/Research uses & Cancer Cells

Research Uses of Stem Cells

1. Provide information of cell growth/cell differentiation
2. Model cells for studying how diseases develop.
3. Model cells for drug testing

Therapeutic Uses of Stem Cells

Involve the repair of damaged/ diseased organ or tissues.

1. Corneal Repair
2. Regeneration of damaged skin

Ethics surrounding Embryonic Stem Cell

Embryonic stem cells can self renew under right conditions in the lab and be used as a potential therapeutic use of stem cells.

Advantage

Offer effective treatment for disease/injury.

Disadvantage

Involves destruction of the embryo.

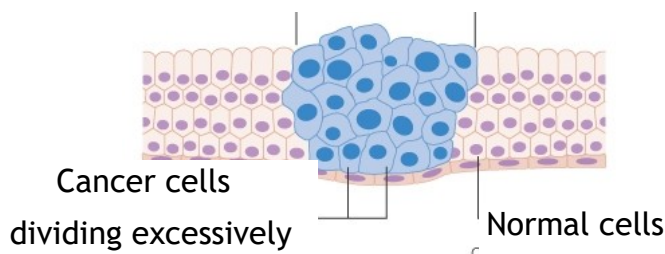
Cancer Cells

Divide excessively as they fail to respond to **regulatory signals**.

This results in a mass of abnormal cells called a tumour.

If **tumour cells** fail to attach to each other they can **spread throughout the body** causing a secondary tumour.

Tumour forms (mass of abnormal cells)

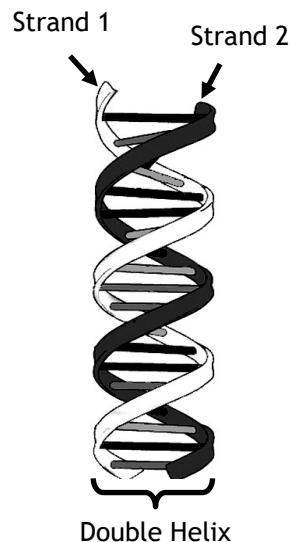


2. Structure of DNA

The base sequence of DNA forms the genetic code for producing specific proteins.

3D Structure

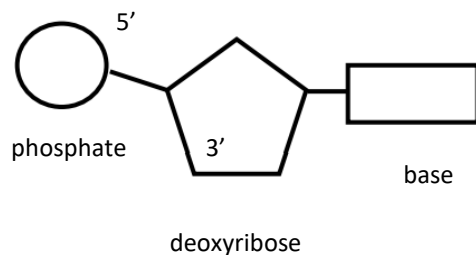
DNA is made of 2 strands of nucleotides that coil up to form a 3D structure called a double helix.



Nucleotide

Smallest individual unit of DNA made up of:

1. **Phosphate** on carbon 5 (C5)
2. **Deoxyribose sugar** on carbon 3 (C3)
3. **Base** (Adenine, Thymine, Guanine or Cytosine)

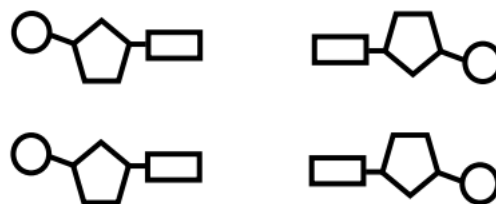


Complementary Base Pairing

Adenine pairs with Thymine.

Guanine pairs with Cytosine.

* ALWAYS USE FULL NAMES *

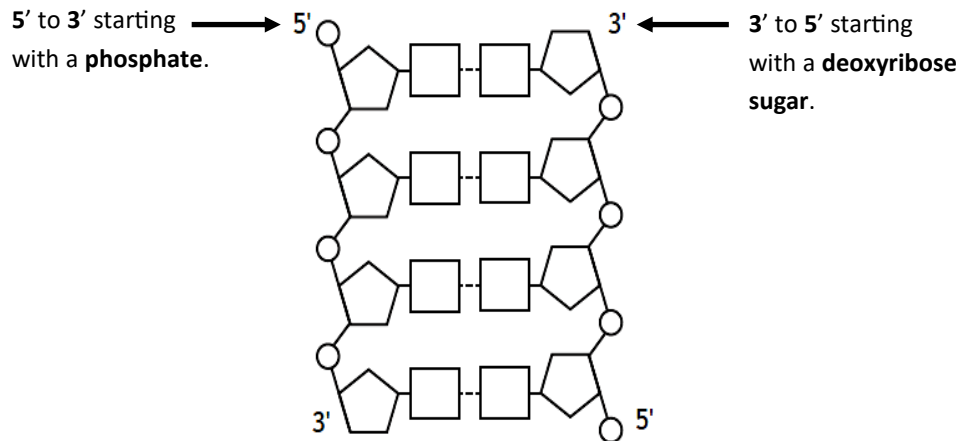


2. Structure of DNA

Antiparallel Structure

One strand runs from **5' to 3'** starting with a phosphate.

The other strand runs from **3' to 5'** starting with a deoxyribose sugar.

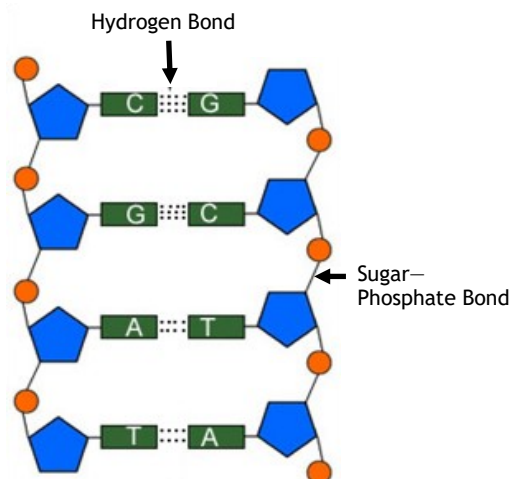


Hydrogen Bonds

Bonds between complementary bases hold the two strands together.

Sugar Phosphate Backbone

Sugar-phosphate bond between C3 on Deoxyribose sugar and C5 on phosphate creates the DNA backbone.



DNA Calculations

1. If there are 300 bases in total and 20% are guanine, calculate the number that are Adenine.

Adenine - 30% Thymine - 30%
Guanine - 20% Cytosine - 20%

Adenine - 30% of 300

$300/100 = 3$ (1%)

$3 \times 30\% = \underline{90 \text{ bases}}$

2. There are 300 bases in total. On the original strand there are 50 Adenine and 40 Guanine bases. On the complementary strand there are 30 Guanine bases. How many thymine bases are there on the original strand?

A 50	50 T
T	A
G 40	40 C
C 30	30 G

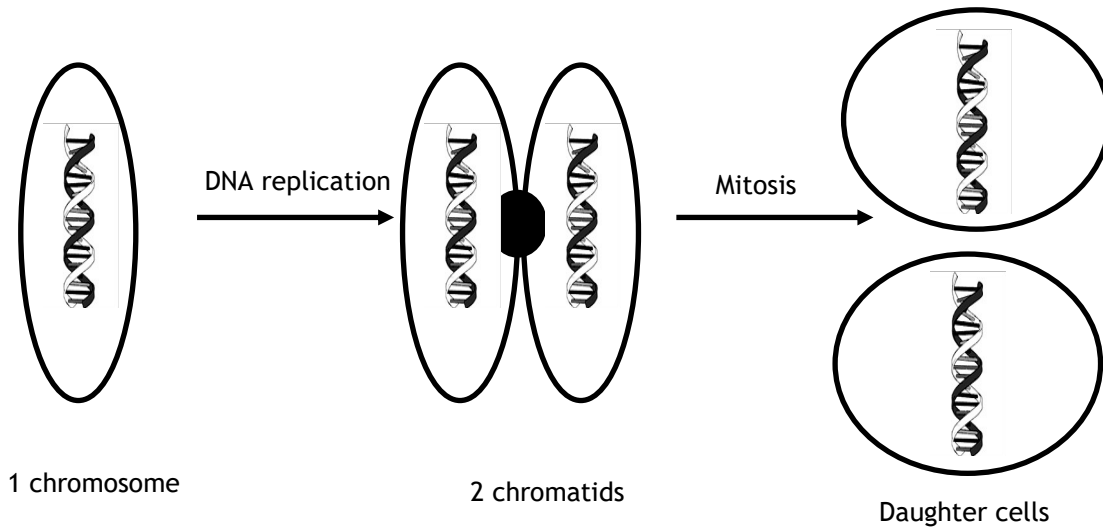
= 240 bases

$300 - 240 = 60 \text{ bases}$

Thymine = 30 bases

2. Replication of DNA

DNA is replicated before cell division occurs to form two identical DNA double helixes.



Importance of DNA Replication

To ensure that each daughter cell has the correct number of chromosomes to ensure that no genetic information is lost.

DNA Replication - Requirements

1. Primers
2. Enzymes (DNA Polymerase and Ligase)
3. DNA Template
4. Free complementary DNA nucleotides
5. ATP

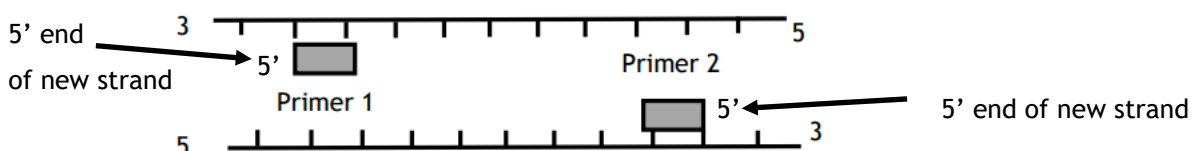
Primers

Short strand of nucleotides complementary to target DNA.

Function of Primers

Start DNA replication by binding to 5' end of newly synthesised strand.

This allows DNA polymerase to start replication of the new DNA strand.



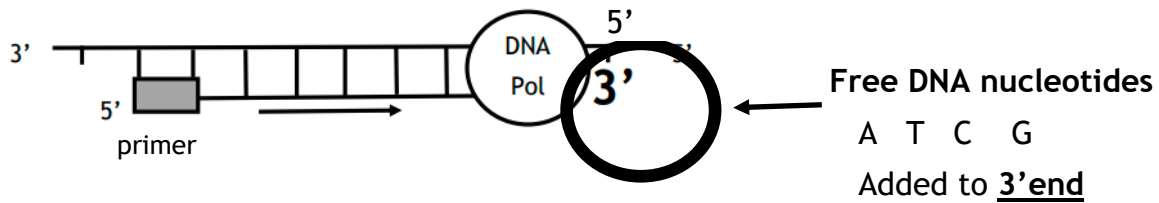
2. Replication of DNA

DNA Polymerase (enzyme)

Adds free complementary DNA nucleotides to the 3' end of the new DNA strand

Free Complementary DNA Nucleotides

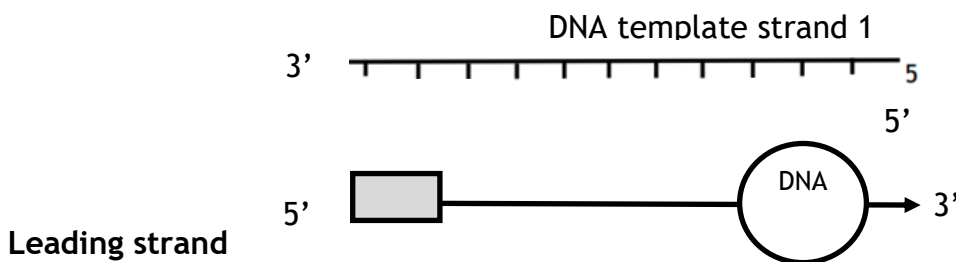
Added to the 3' end to create the new strand.



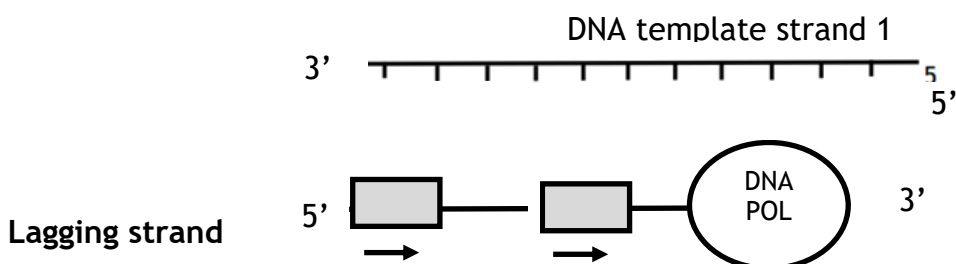
Leading & Lagging Strand

Leading strand replicated continuously

Lagging strand replicated in fragments



Newly synthesised single leading strand from 5' to 3'



Newly synthesised DNA fragments in lagging strand from 5' to 3'

Ligase (enzyme)

Joins fragments of DNA together.

2. Replication of DNA

DNA Replication

Stage 1

DNA unwinds and separates into two template strands, breaking hydrogen bonds between the bases.

Stage 2

Primers bind to the 5' end of the new strand, starting DNA replication by allowing DNA polymerase to add DNA nucleotides.

Stage 3

DNA polymerase adds free complementary DNA nucleotides to the 3' end of the new DNA strand.

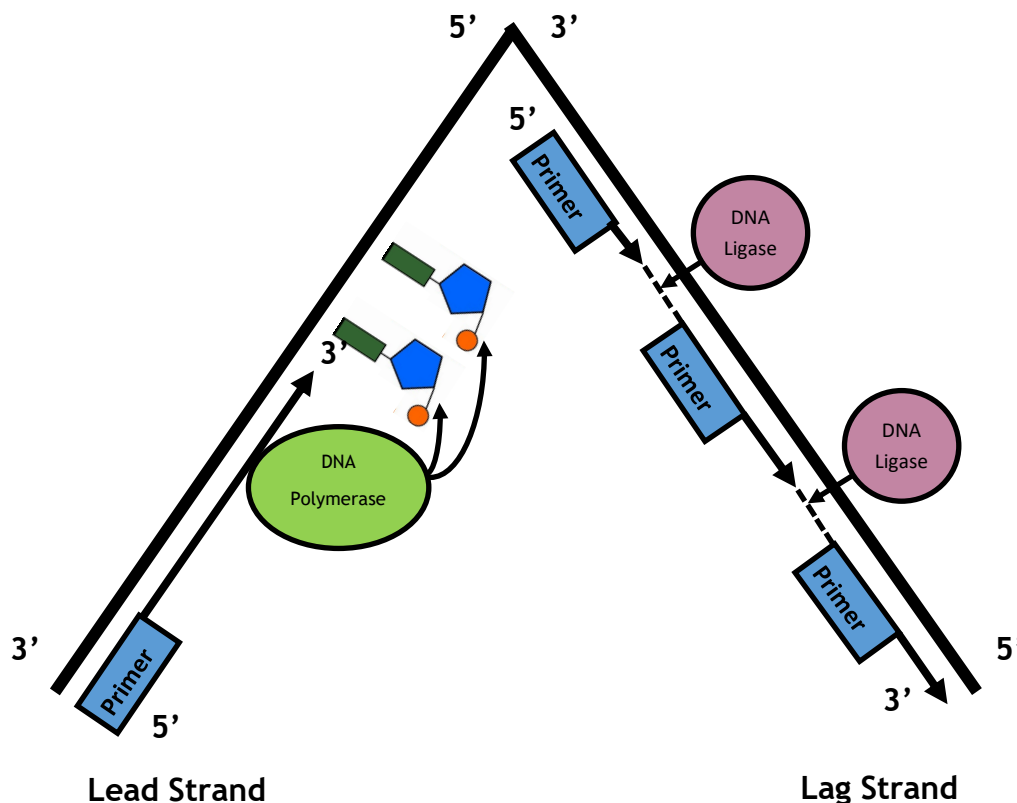
Stage 4

DNA polymerase only adds nucleotides from 5' to 3' on the new strand and as DNA is antiparallel

1. The leading strand being replicated continuously
2. The lagging strand replicated in fragments.

Stage 5

Fragments in the lag strand are joined by the enzyme ligase.



2. PCR

Polymerase Chain Reaction (PCR) Function

Amplifies target DNA.

Practical Applications (Uses)

1. Help solve crimes
2. Settle paternity suits
3. Diagnose genetic disorders

Requirements for PCR

1. Template DNA sample
2. Free complementary DNA nucleotides
5. ATP
3. Primers
4. Heat Tolerant DNA Polymerase

Stages of PCR.

There are 3 stages per cycle of PCR with 30-60 cycles needed.

Repeated heating and cooling occurs in each cycle to double DNA content.

Stage of Cycle	Description	Temperature Range
Heating	Separate the DNA strands	92° C and 98° C
Cooling	Allow primers to bind to target sequences to <u>start DNA replication</u> .	50° C and 65° C
Heating	Heat-tolerant DNA polymerase <u>replicates the DNA</u>	70° C and 80° C

2. PCR

Primers

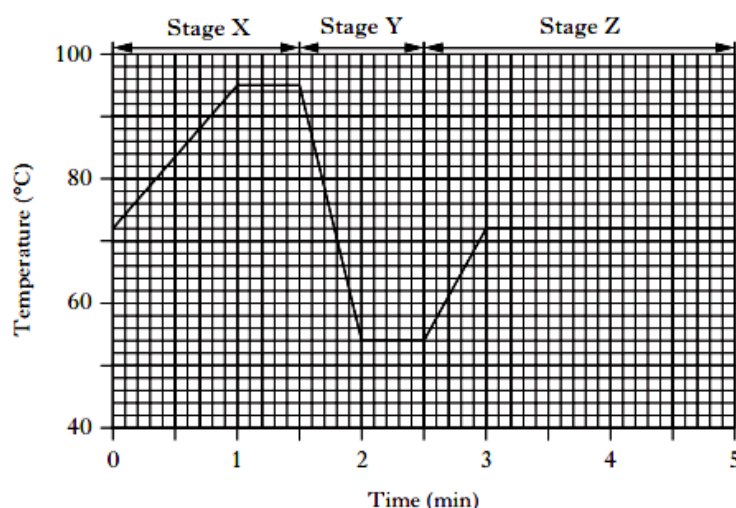
Short sequences of DNA which bind to complementary target sequences on one end of each template strand.

Two types of primers are needed per PCR reaction. One for each of the two template strands.

Heat Tolerant DNA Polymerase

To ensure enzymes do not denature at high temperatures of PCR

Easy Graphs



PCR Calculations

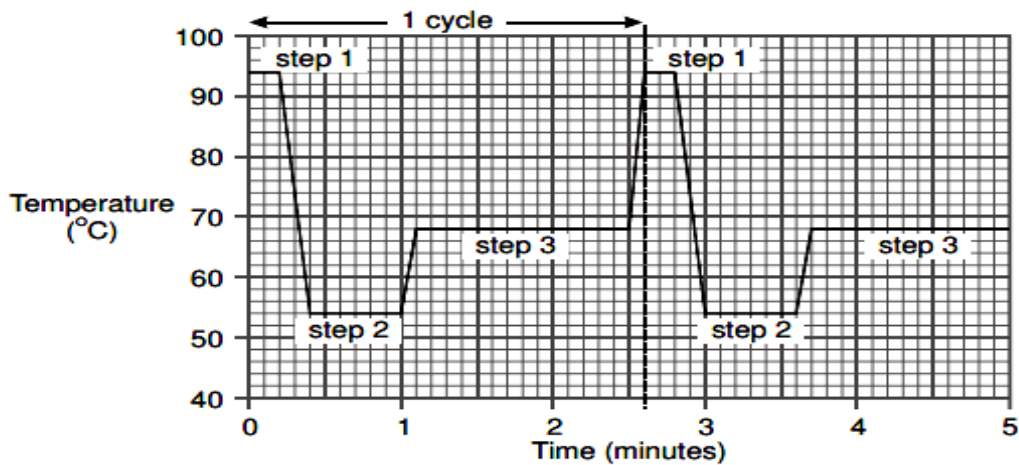
- How long does one cycle of PCR last from the graph above.
5 minutes
- How long will it take to make four DNA molecules from one original DNA molecule using graph 2 above.
5 minutes **10 minutes**
1 → 2 → 4 DNA molecules
- During step Z, DNA polymerase extends the DNA rate of 500 base pairs per minute. Calculate the length of the DNA fragment produced each time from the graph.

Step Z is 2.5 minutes in length from graph.

$2.5 \times 500 \text{ base pairs} = 1250 \text{ base pairs}$

2. PCR

Difficult Graphs



PCR Calculations

- How long does one cycle of PCR last from the graph above.

2.6 minutes

- How long will it take to make four DNA molecules from the original DNA molecule using graph 2 above.

5.2 minutes

- During step 3, DNA polymerase extends the DNA rate of 500 base pairs per minute. Calculate the length of the DNA fragment produced each time from the graph.

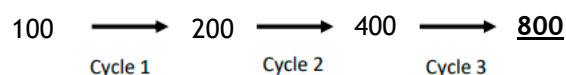
Step 3 is 1.5 minutes in length from graph.

$$1.5 \times 500 \text{ base pairs} = 750 \text{ base pairs}$$

PCR calculation (non graph)

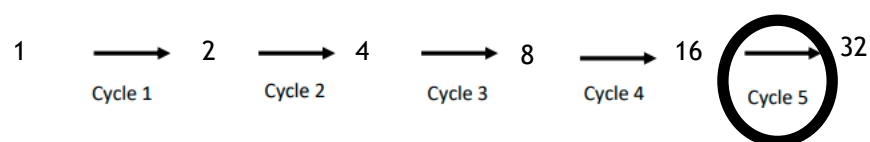
Calculate how many copies of DNA would be produced from **100 molecules** of DNA.

(i) 3 cycles



Calculate the number of cycles needed to produce the following number of DNA molecules from a single molecule.

(ii) 24 molecules



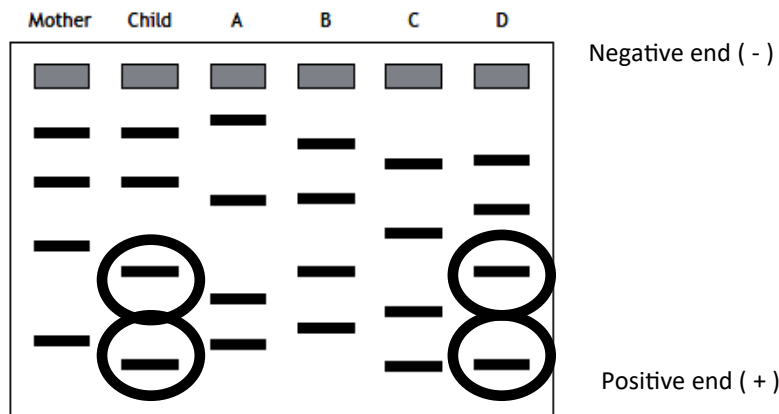
2. Gel Electrophoresis

Gel electrophoresis separates DNA fragments by size.

DNA is negatively charged and moves through the gel to the positive end

Smaller fragments move further through the gel to the positive end.

Paternity test Gel Electrophoresis



Q. Identify the father of the child from the options above.

A. **Parent D** as the last two bands of the child not belonging to the mum match up.

The first two bands of the child belong to their mother.

Solving Crimes Gel Electrophoresis

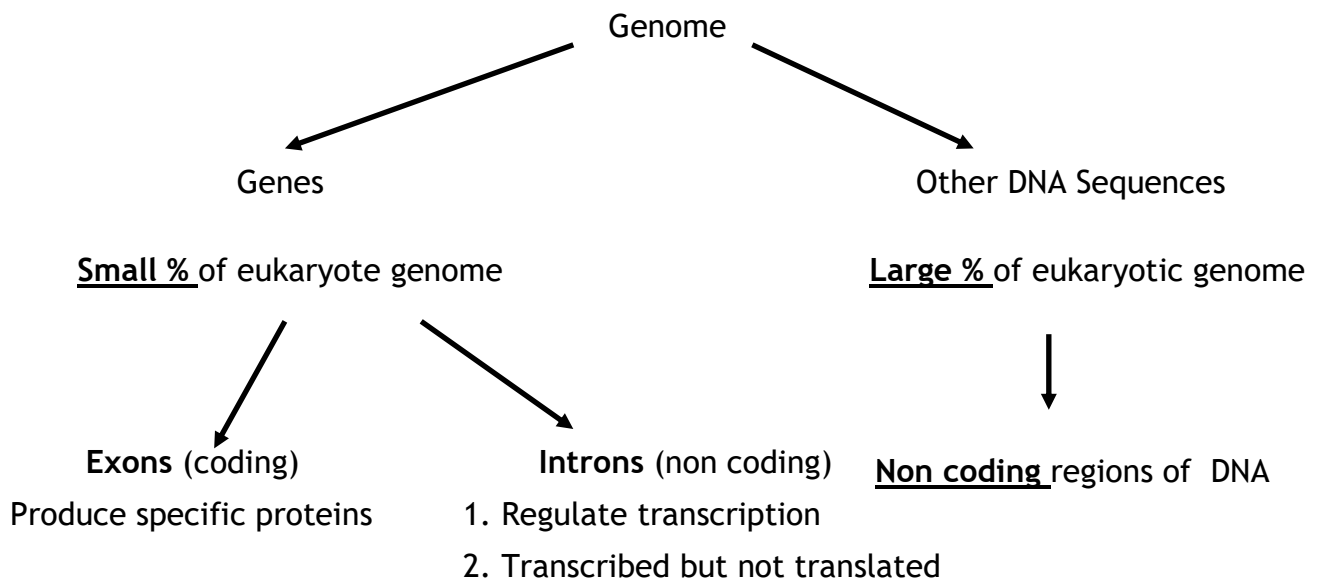
Crime Scene	Suspect X	Suspect Y	Suspect Z

Only suspect Z's DNA is found at the crime scene.

The other two suspects can be eliminated from enquires.

3. The Genome & RNA

The genome is the entire hereditary information in our DNA.



Differences between DNA and RNA

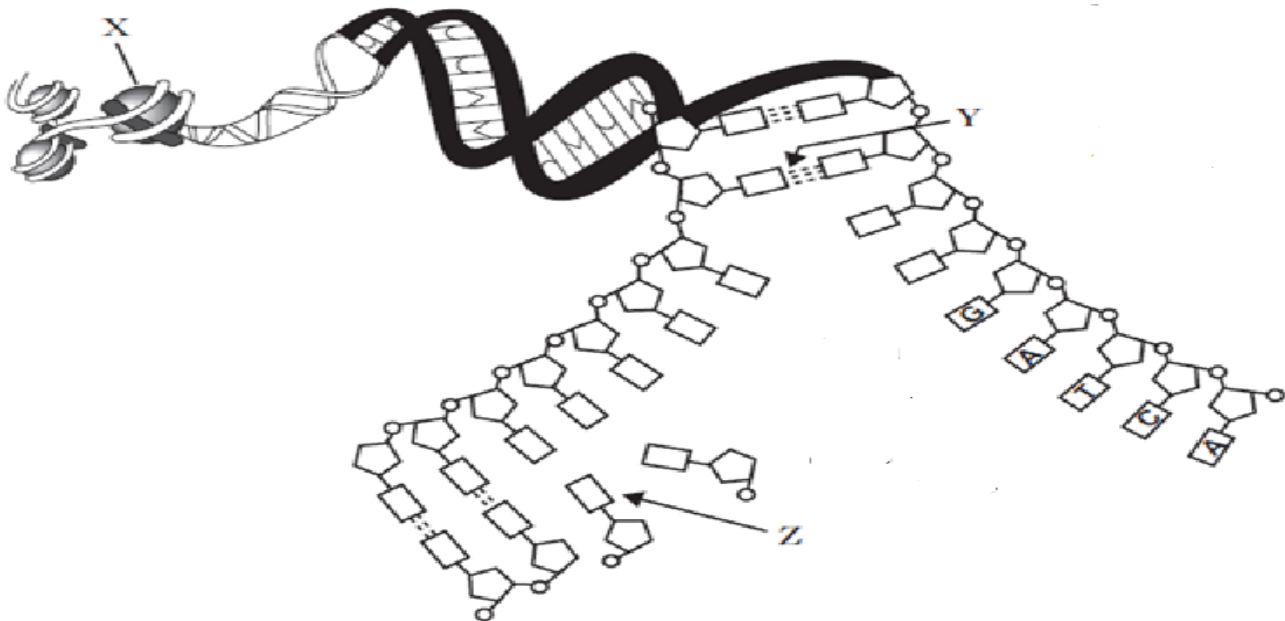
DNA	RNA
Double stranded	Single stranded
Deoxyribose sugar	Ribose sugar
2 strands of nucleotides	1 strand of nucleotides
Base Thymine	Base Uracil

Types of RNA	Function	3 bases are called	Coding/ Non-coding for protein
mRNA	Carries a complementary copy of the DNA code from nucleus to ribosome.	CODON for 1AA	CODING
tRNA	1. binds to a specific amino acid 2. takes the amino acids to the ribosome.	ANTI CODON for 1 AA	NON– CODING
rRNA	Part of the ribosome along with protein.		NON– CODING

3. Transcription

RNA polymerase (enzyme) has two roles in transcription of DNA into primary mRNA transcripts.

1. RNA polymerase unwinds double helix & breaks hydrogen bonds between the bases on the two strands of the double helix.
2. RNA polymerase attaches free complementary RNA nucleotides to make the primary mRNA transcript.



Transcription occurs in the Nucleus of the cell.

DNA code → primary transcript → mature transcript

Primary Transcript contains:

- A) Introns which are non - coding regions of the gene
- B) Exons which are coding regions of the gene

Mature transcript contains:

Only exons, as the introns are removed during a process called RNA splicing.

Introns have 2 key roles in protein synthesis.

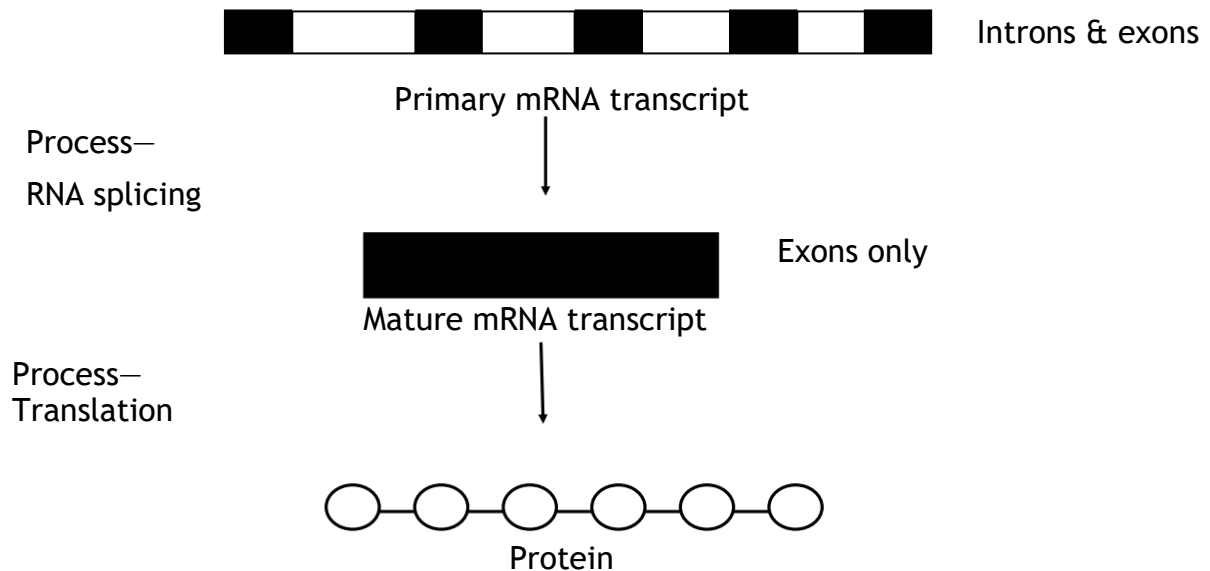
1. Transcribed but not translated.
2. Regulate transcription.

3. RNA Splicing

RNA Splicing

Introns removed from the primary transcript

The exons are joined together to form mature mRNA transcript.

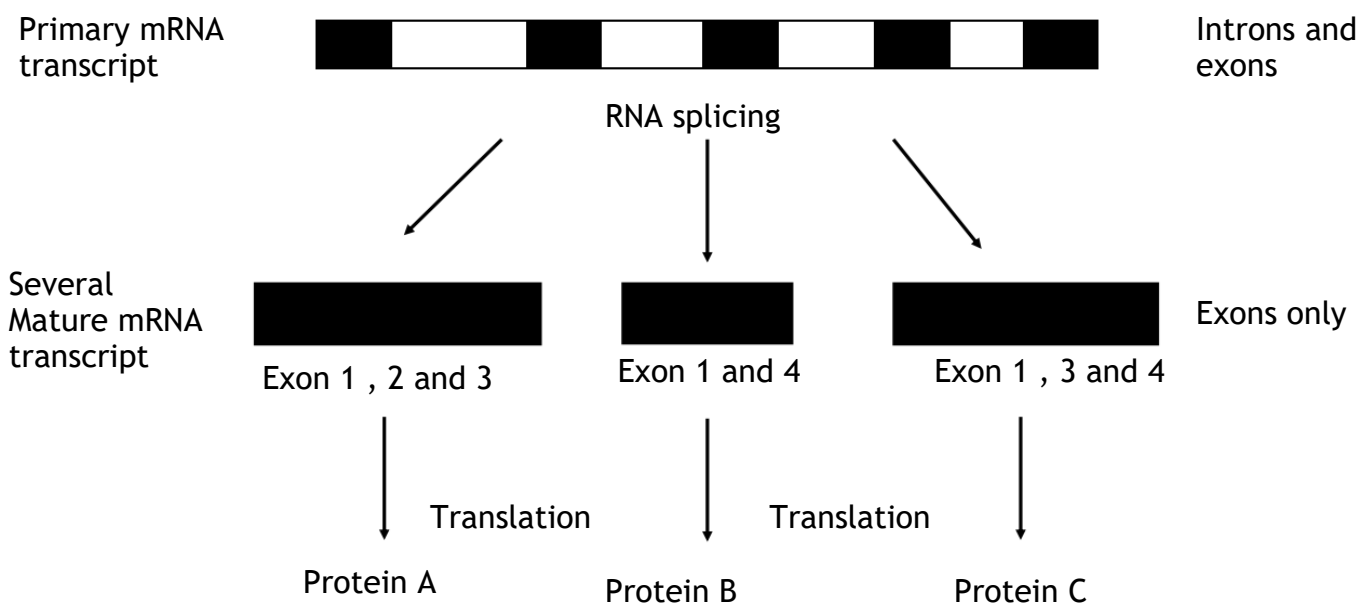


Alternative RNA Splicing

Different proteins can be expressed from one gene.

The introns are removed and different combinations of exons are spliced together, forming alternative mature transcripts.

Note: Note the order of the exons is unchanged during splicing.



3. Types of RNA

There are three types of RNA.

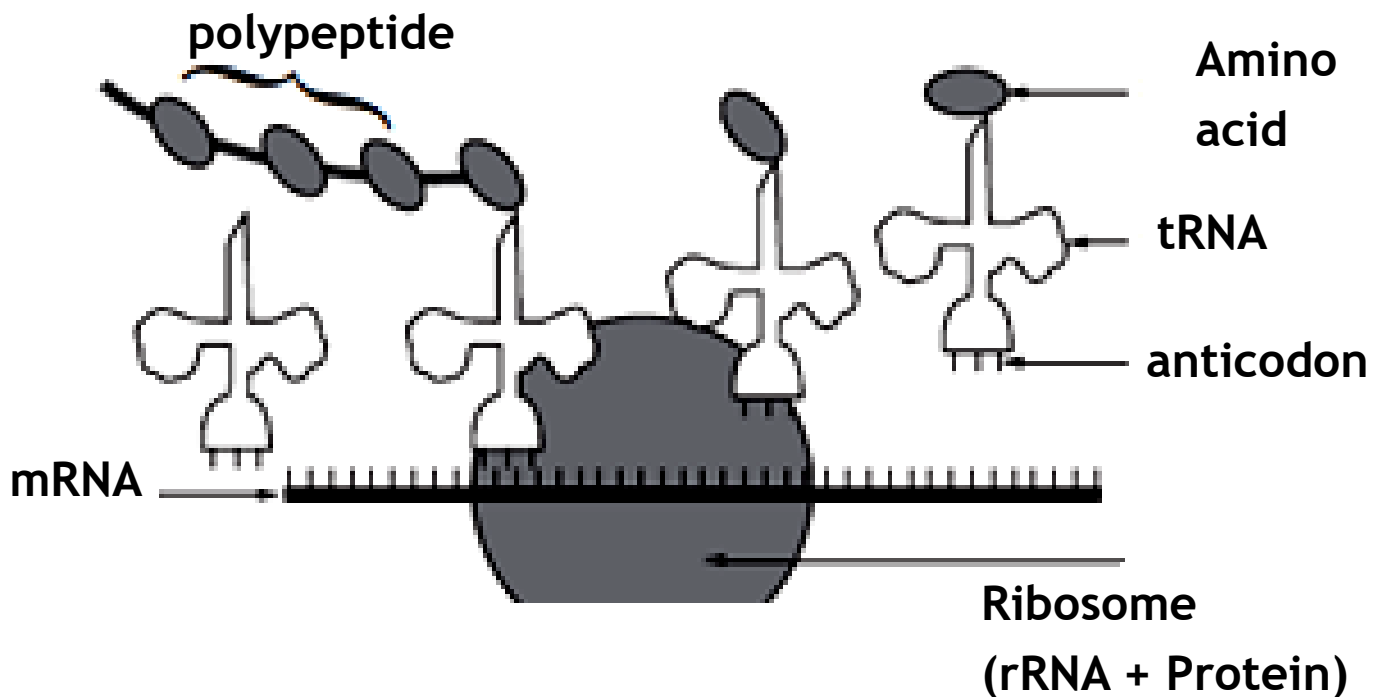
1. mRNA → Made from coding regions called **exons**
2. rRNA } Made from non - coding regions called **introns**
3. tRNA }

1. mRNA

Messenger RNA (mRNA) carries a complementary copy of the DNA code from the nucleus to the ribosome.

2. rRNA

Ribosomal RNA (rRNA) and proteins form the ribosome.



3. Types of RNA

There are three types of RNA.

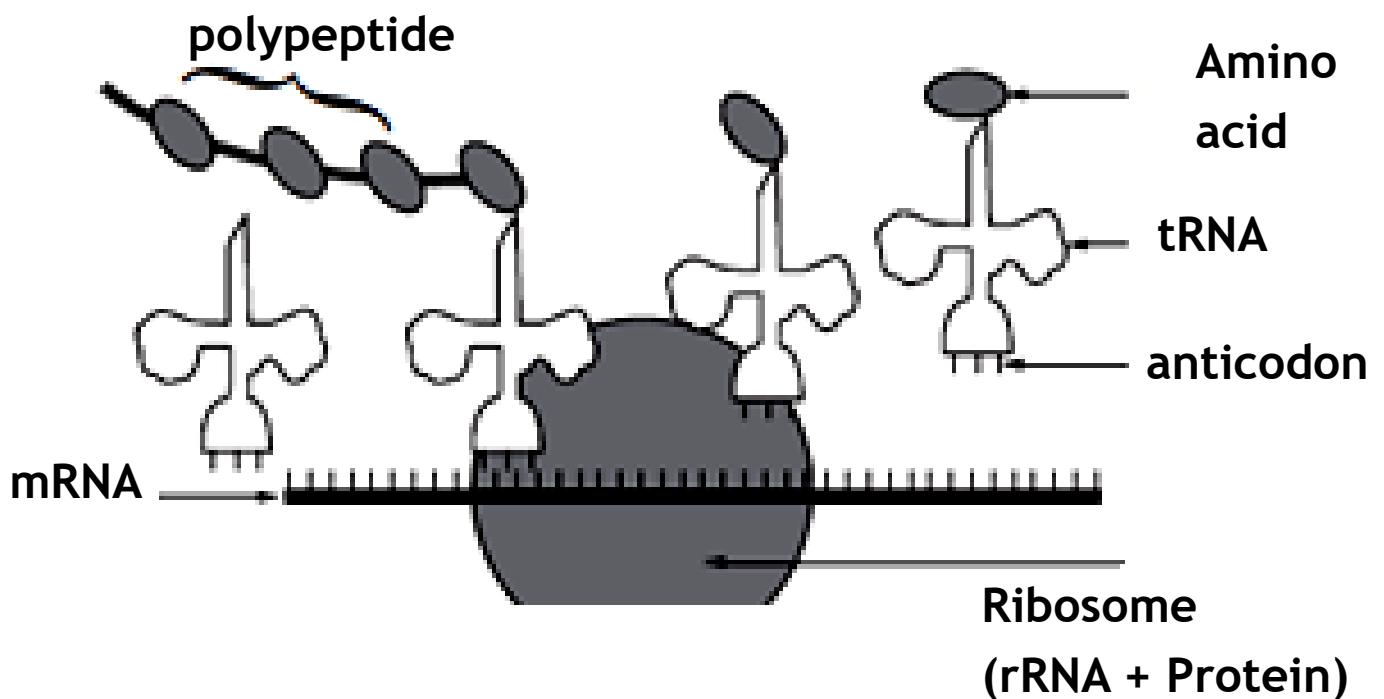
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1. mRNA

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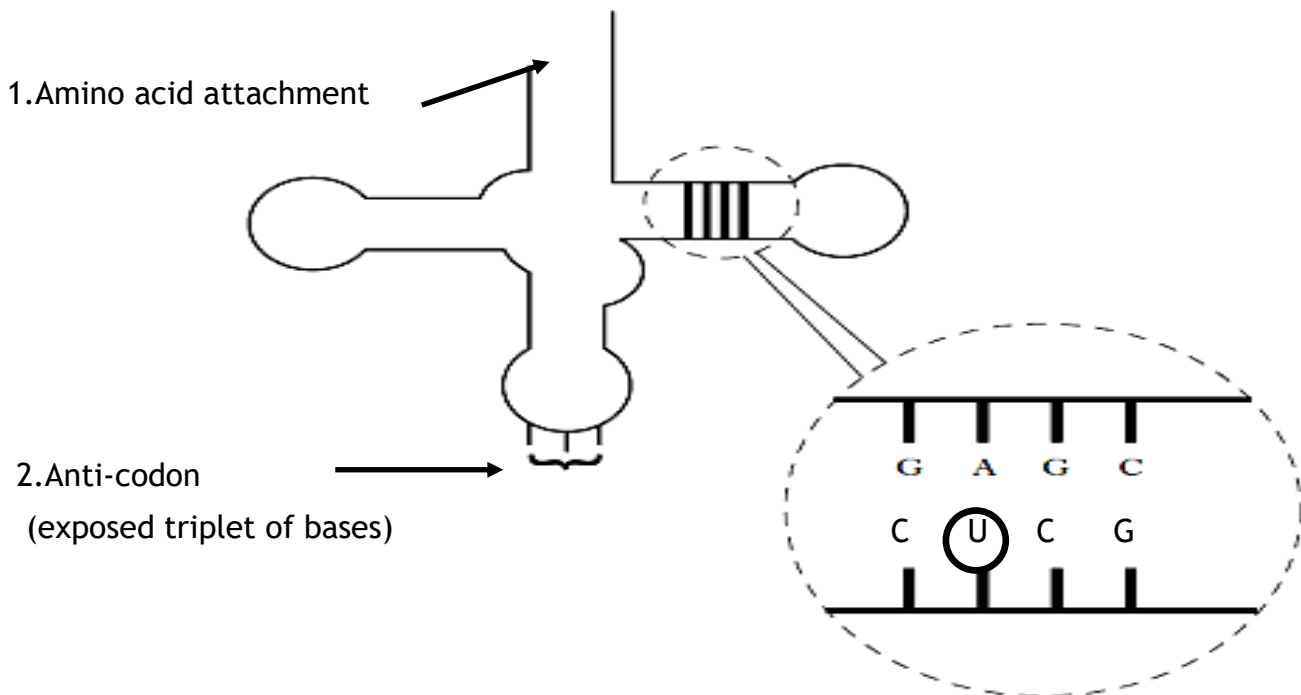


3. Types of RNA

3. tRNA

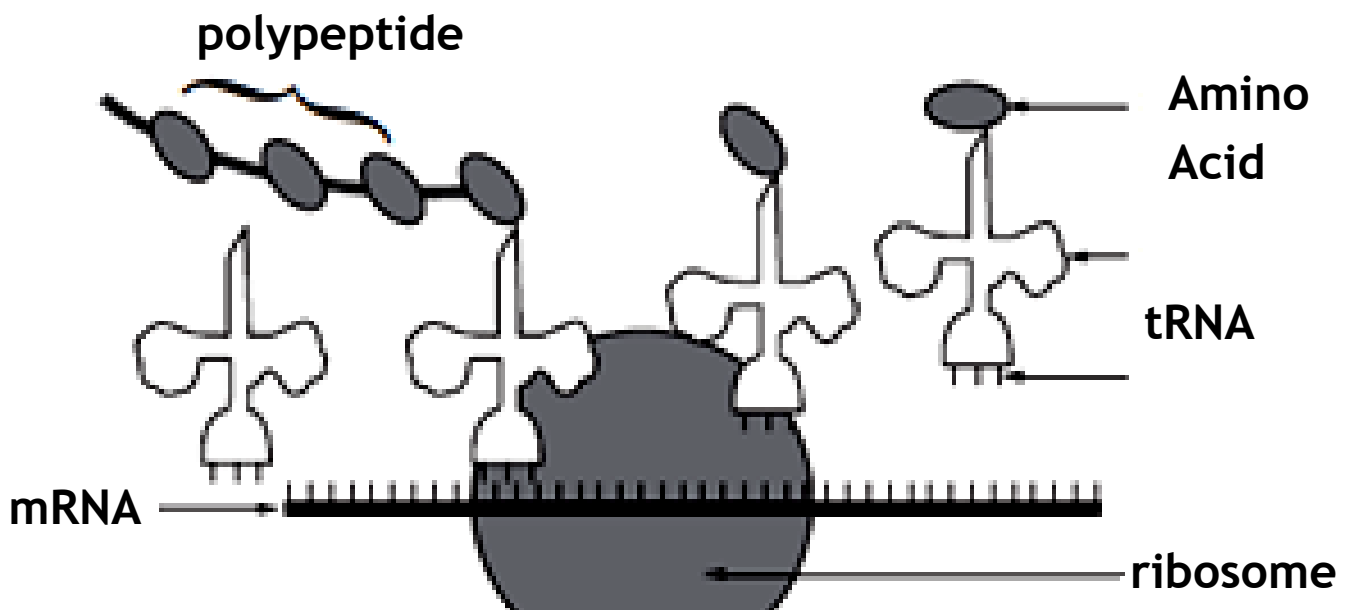
A single stranded molecule which is folded and held together by complementary base pairs.

tRNA is made up of 2 parts—



tRNA Function

1. Binds to a specific amino acid AND carries it to the ribosome.
2. tRNA anticodons complementary base pair with mRNA codons forming a polypeptide

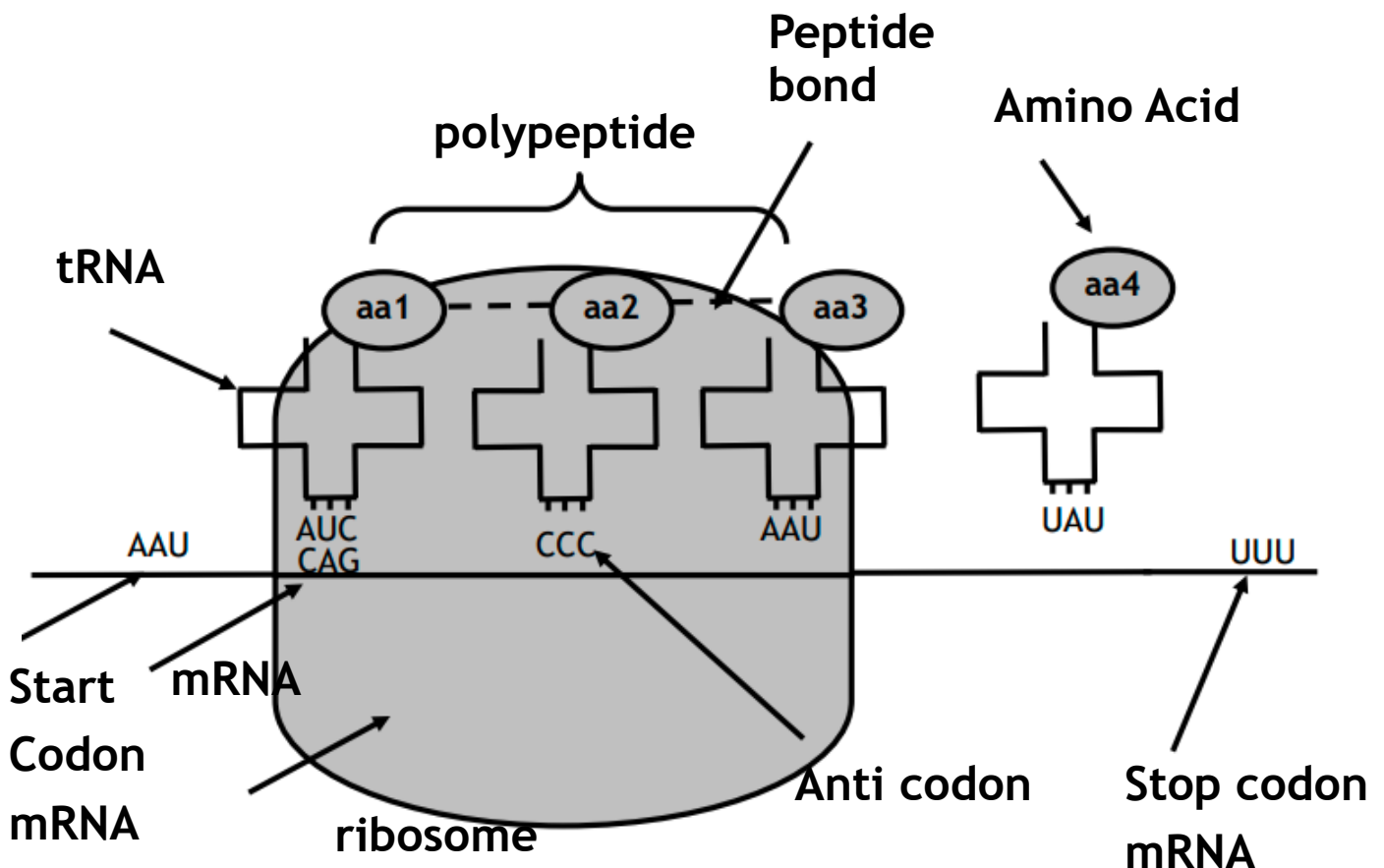


3. Translation

Translation

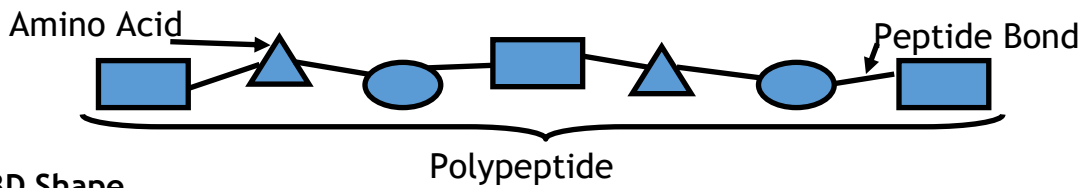
This involves the mature mRNA transcript directing protein synthesis at the ribosome.

1. mRNA attaches onto ribosome
2. tRNA binds to a specific amino acid and takes it to the ribosome
3. Translation begins at a start codon and ends at a stop codon.
4. Anticodons on tRNA bond to codons on mRNA by complementary base pairing
5. This lines the amino acid in a specific sequence forming a polypeptide.
6. Peptide bonds join the amino acids together.
7. Each tRNA then leaves the ribosome as the polypeptide chain is formed.



3. Protein Folding

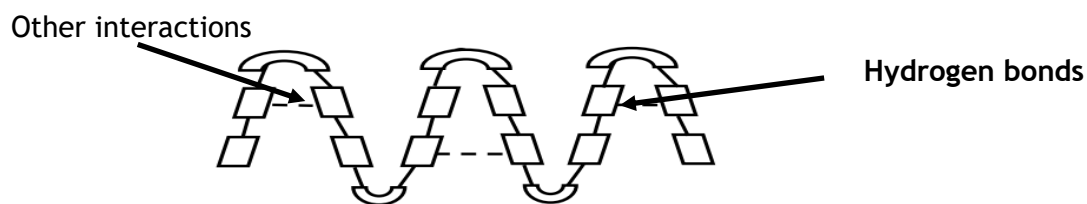
Amino acids are linked by peptide bonds to form **polypeptides**.



3D Shape

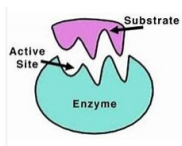
Polypeptide chains fold to form the 3D shape of a protein.

These 3D shapes are held together by hydrogen bonds OR other interactions between individual amino acids.

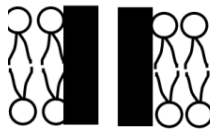


Proteins have a large variety of shapes which determines their functions.

Enzymes



Pore (diffusion)



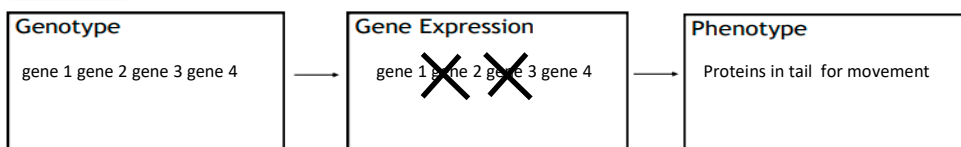
Pump (active transport)



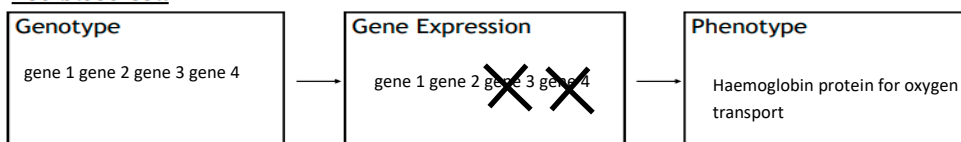
Gene Expression

All cells contain the same genes. However, only a small percentage are actually expressed in any one cell through a process called cellular differentiation

Sperm cell



Red blood cell



Phenotype is determined by

1. Proteins produced as a result of gene expression
2. Environmental factors also affect gene expression

4. Mutations

Mutations

Changes in the DNA that can result in no/altered protein being synthesised.

1. **Single gene mutations** - Changes to the DNA nucleotide base sequences
2. **Chromosome structure mutations** - Changes to a section of a chromosome (gene order).

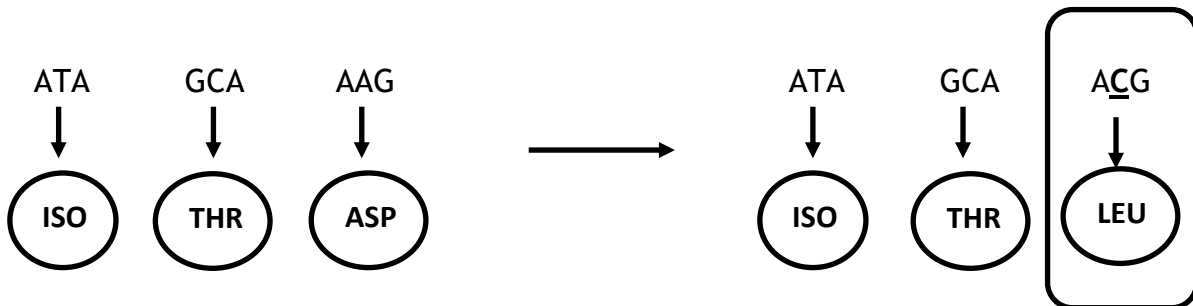
Single gene mutations (SID)

1. Substitution—3 types

1.1 Missense mutation

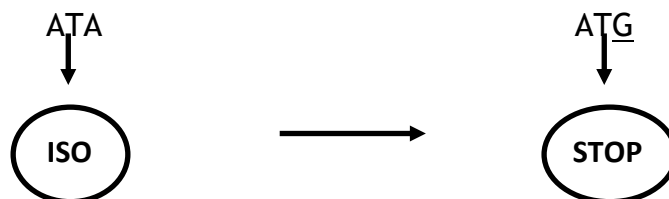
Affects one codon/amino acid.

Result - non-functional OR little effect on the protein.



1.2 Nonsense mutation

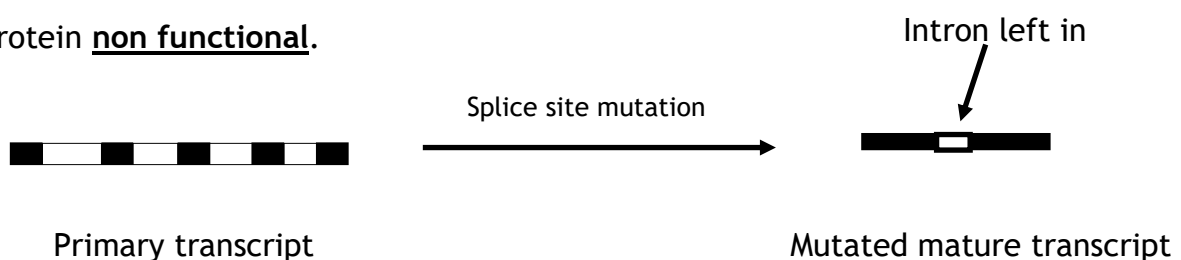
Results in a premature stop codon being produced which results in a protein that is too short. Protein non functional.



1.3. Splice-site Mutation

Result in some introns being retained and/or exons not being included in the mature transcript.

Protein non functional.



4. Single gene Mutations

2. Insertion mutation frameshift

A base has been added into the base sequence.

ATA GCU GAT TAA

ATA GCU GCA TTA A

3. Deletion mutations frameshift

A base is removed from the base sequence

ATA GCU GAT TAA

ATA GCU GTT AA

Frameshift mutations

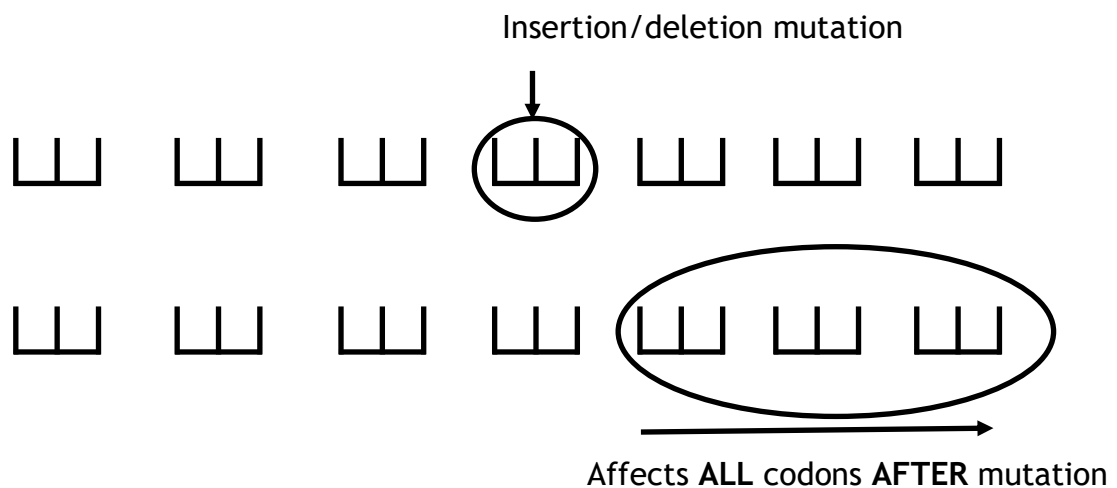
Cause—insertion or deletion mutations

Effect on base sequence

All of the codons/amino acids after the mutation are changed.

This has a major effect on the structure of the protein produced & is non functional.

****Remember 1 codon (triplet of bases) codes for 1 amino acid****



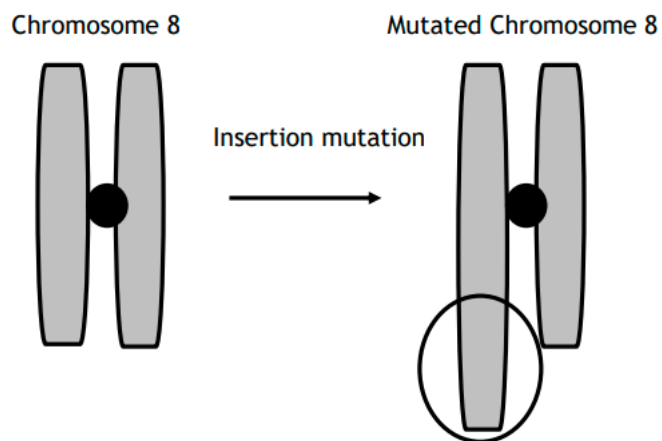
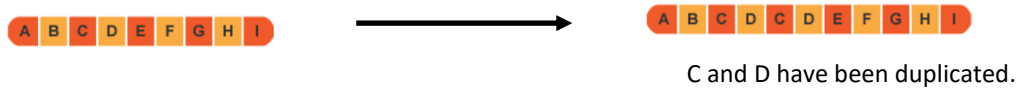
4. Chromosome Structure Mutations

Chromosome Mutations (TIDD)

The substantial changes in chromosome mutations often make them lethal.

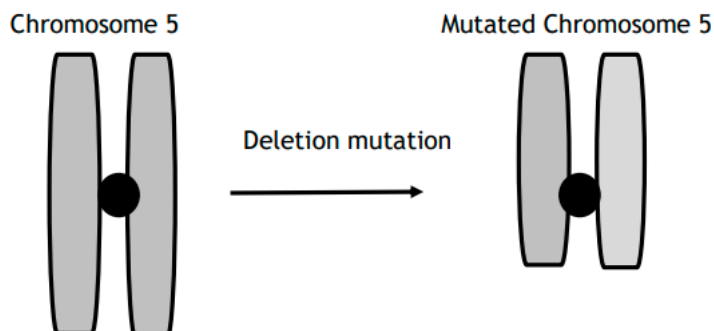
Duplication

A section of a chromosome is added from its homologous partner.



Deletion

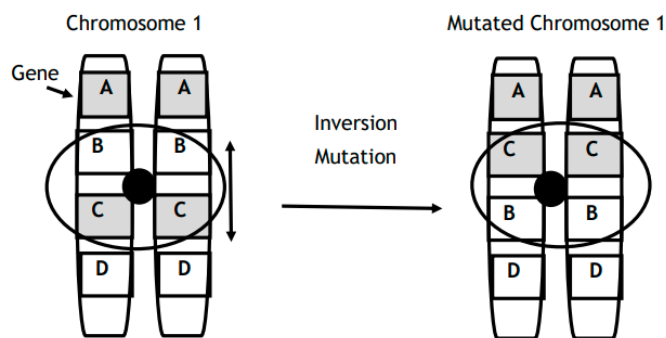
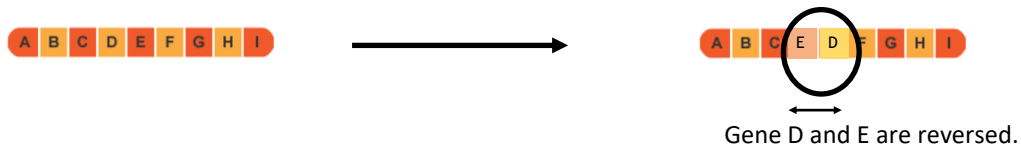
Deletion is where a section of a chromosome is re- moved.



4. Chromosome Structure Mutations

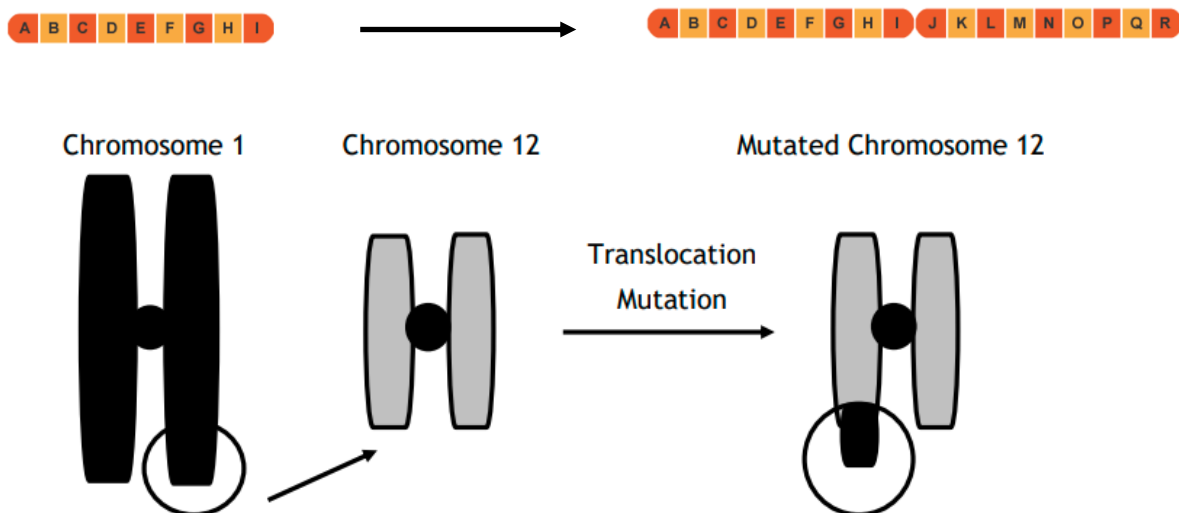
Inversion

Inversion is where a section of chromosome is reversed.



Translocation

A section of a chromosome is added to a chromosome from a NON homologous partner.



Duplication - Importance in Evolution

Allows potential beneficial mutations to occur in a duplicated gene whilst the original gene can still be expressed to produce its protein.

5. Genomic Sequencing

Genomic Sequencing

The sequence of nucleotide bases can be determined for individual genes or entire genomes.

Bioinformatics

To compare sequence data, computer and statistical analyses (bioinformatics) are required.

Bioinformatics

Computer programs can be used to identify base sequences by looking for sequences similar to known genes.

Pharmacogenetics

Analysing an individuals genome.

This allows personalised medicine to be created to;

1. Determine the likelihood of developing certain diseases.
2. Used to choose the most appropriate drug and dosage to treat disease (pharmacogenetics).

Side effects

Personalised medicine is needed to make sure that patients have no side effects and the drug is beneficial to the patient.

Side effects Beneficial	No side effect Beneficial
Side effects Not Beneficial	No side effect Not Beneficial

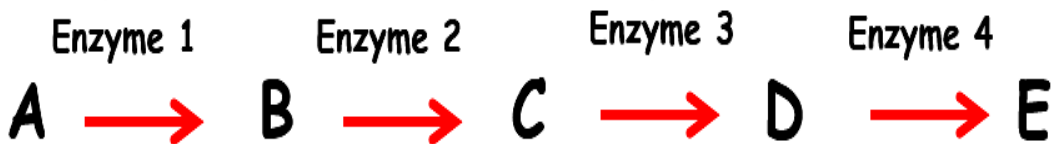
6. Metabolic Pathways

Metabolic Pathways

Integrated and controlled pathways of enzyme-catalysed reactions within a cell.

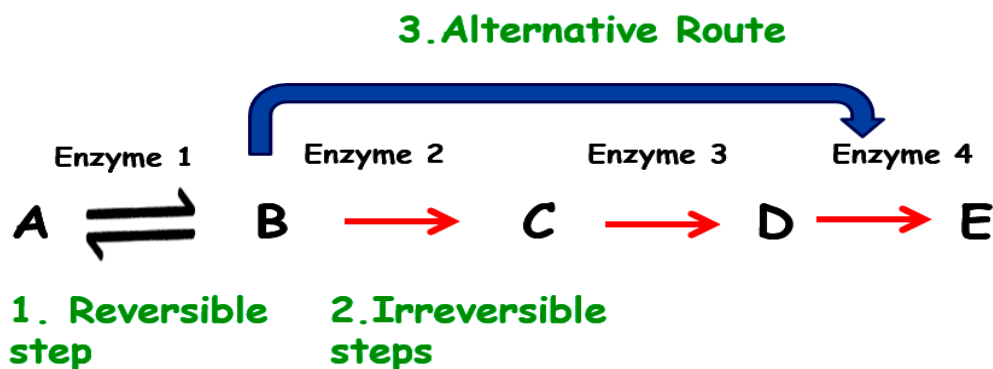
Metabolic Pathways

Each step in a metabolic pathway requires a specific enzyme.



Three Steps in a metabolic Pathway

1. Reversible Step (2 way arrow allowing forward and backward reaction)
2. Irreversible Step (1 way reaction)
3. Alternative route (skips certain steps but produces same molecule regardless)

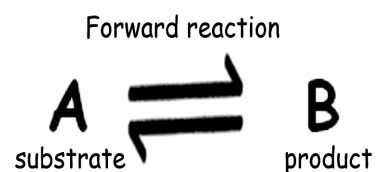


Substrate & Product Concentration in Reversible reactions

Forward Reaction of A to B is promoted by:

High substrate concentrations (A)

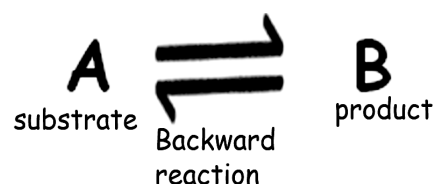
Low product concentration (B)



Backward Reaction of B to A is promoted by:

High product concentrations (B)

Low substrate concentration (A)

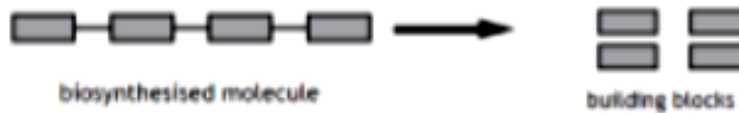


6. Metabolism and Enzymes

Types of Metabolic Reactions

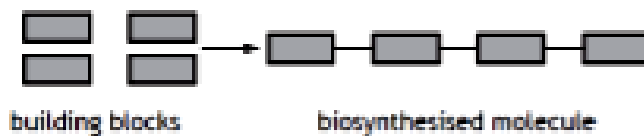
1. Catabolic reactions **breakdown** larger molecules into smaller ones **RELEASING** energy.

Example glycogen/starch → glucose protein → amino acids



2. Anabolic reactions involve the **BIOSYNTHESIS** of larger molecules into smaller ones **REQUIRING** energy to undertake this process.

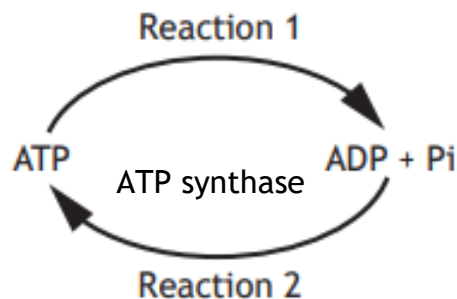
Example glucose → starch amino acids → polypeptides (proteins)



ATP Example

Reaction 1: ATP is broken down is **catabolic** and **releases** energy.

Reaction 2: ATP is synthesized by the enzyme ATP synthase. **Anabolic** and **requires** energy.

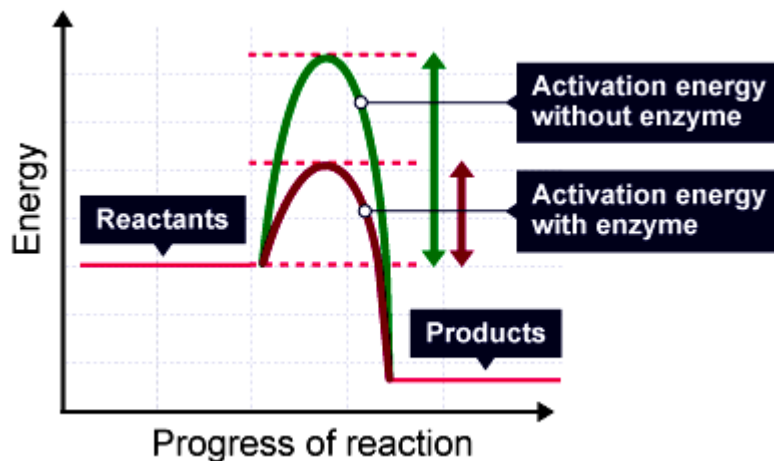


6. Enzymes

Activation Energy

The energy required to BREAK chemical bonds in the reactants to allow products to be made.

Enzymes speed up reactions as they lower the activation energy required to form products .



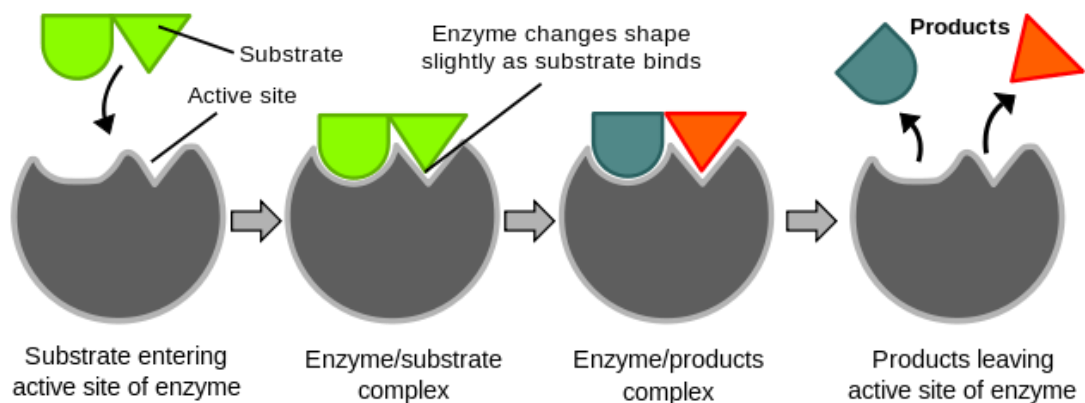
Induced Fit model

After the substrate has bound to the active site, the ACTIVE site changes shape to better fit the substrate.

Affinity for Active site

Substrate—**high affinity** for active site

Product—**low affinity** for active site



6. Substrate Concentration Graphs

Substrate Concentration

1. Low substrate concentration = Low enzyme activity

There are not enough substrate molecules to fill all the active sites.

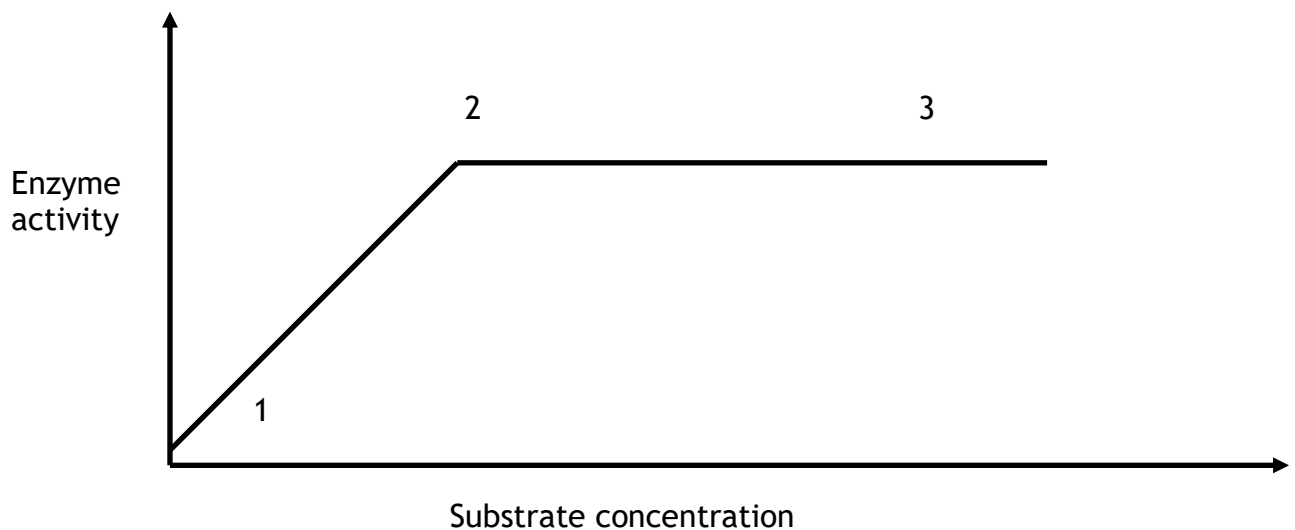
2. High substrate concentration = Higher enzyme activity

All active sites are filled by substrates due to increased concentration of substrates.

3. Very High substrate concentrations = No further increase in enzyme activity

Enzyme working at maximum and all active sites are filled by substrates.

No further increase in reaction rate.



6. Inhibitors

Inhibitors

Inhibitors reduce enzyme activity.

3 types of enzyme inhibitors

1. Competitive Inhibitors
2. Non Competitive Inhibitors

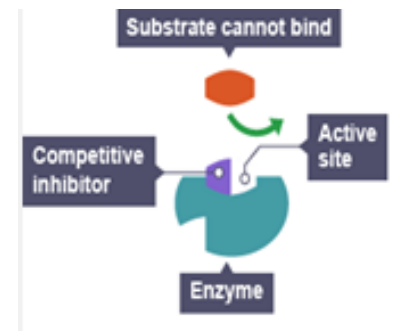
3. Feedback Inhibition

Competitive Inhibitors

Bind at the active site and prevent substrate from binding.

Competitive inhibitor molecule resembles substrate.

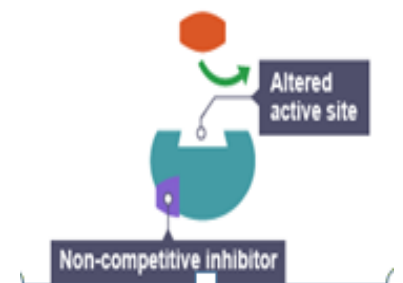
Inhibition reversed with increasing substrate concentration.



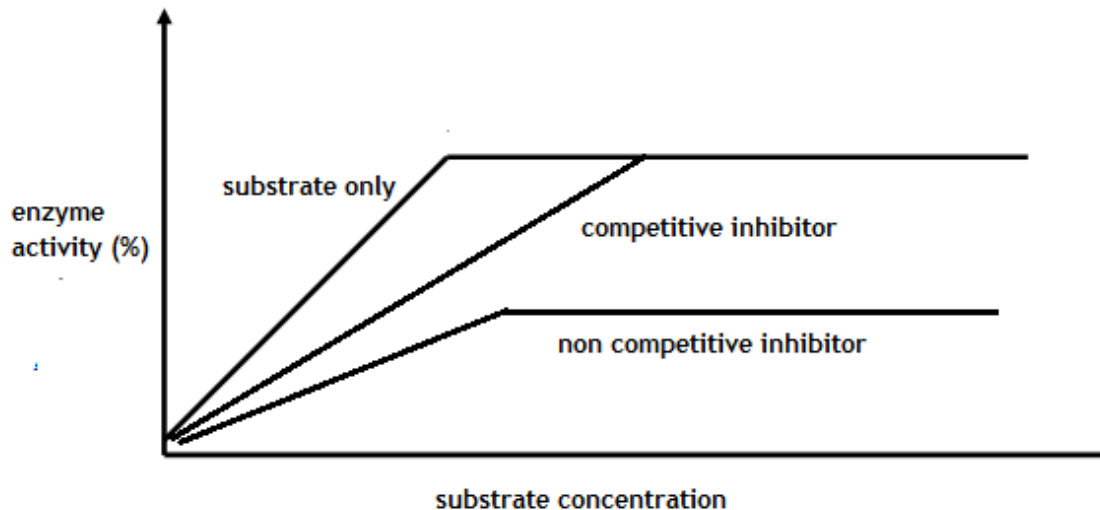
Non competitive Inhibitors

Bind AWAY from active site and change shape of active site preventing substrate from binding.

Action irreversible—no effect when increasing substrate concentration.

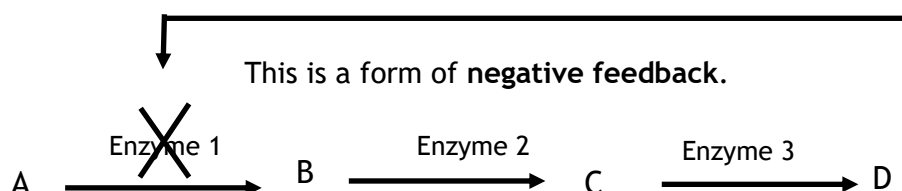


Enzyme Inhibitor Graph



Feedback Inhibition

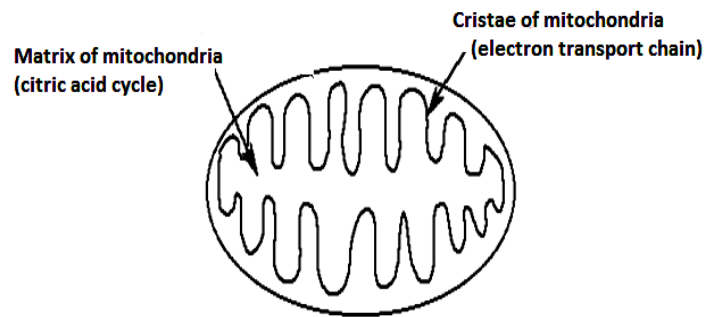
When the end product concentration reaches a critical concentration (too high), it binds to an earlier enzyme in the pathway, preventing its own synthesis. Saves ATP.



7. Respiration

Stages of respiration

1. Glycolysis (cytoplasm)
2. Citric Acid Cycle (Kreb Cycle)
(matrix of mitochondria)
3. Electron Transport Chain
(cristae/inner mitochondria membrane)



ATP production

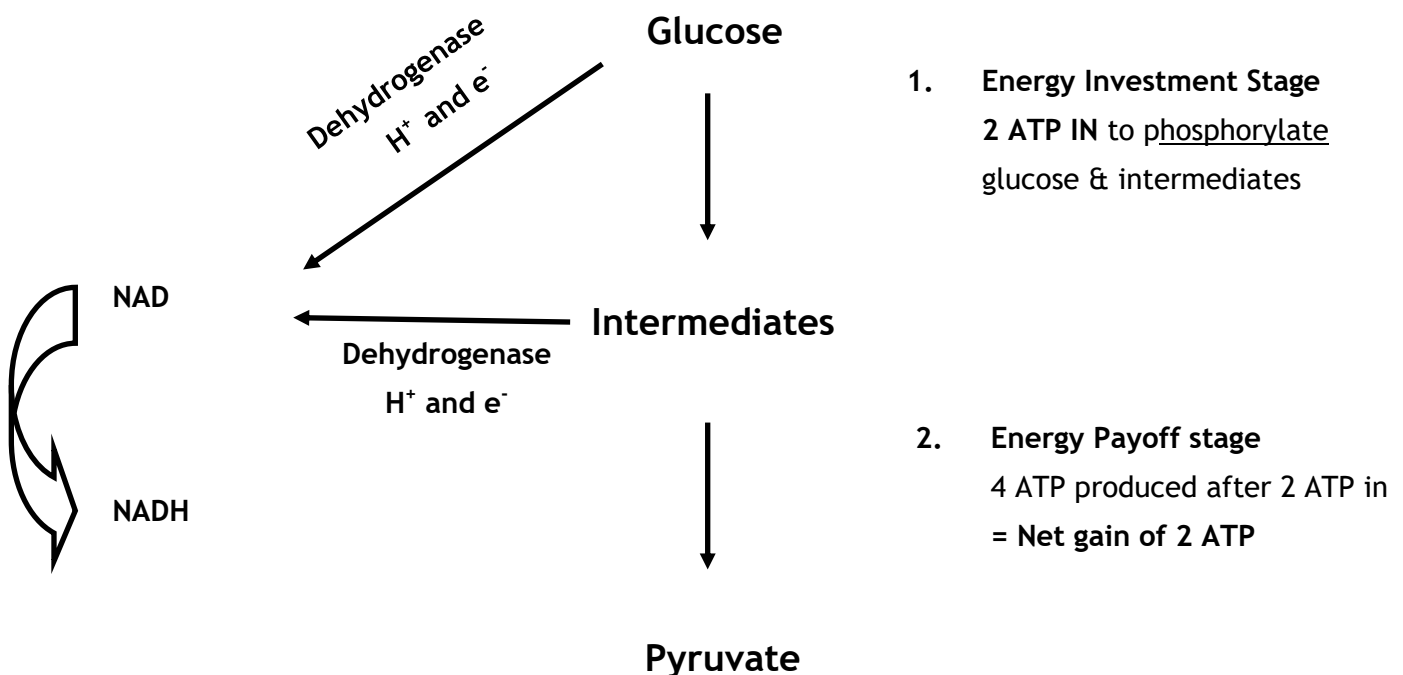
The majority of the ATP is produced during the electron transport chain although **ALL** stages generate some ATP.

Glycolysis

Location—cytoplasm

Process does not require oxygen

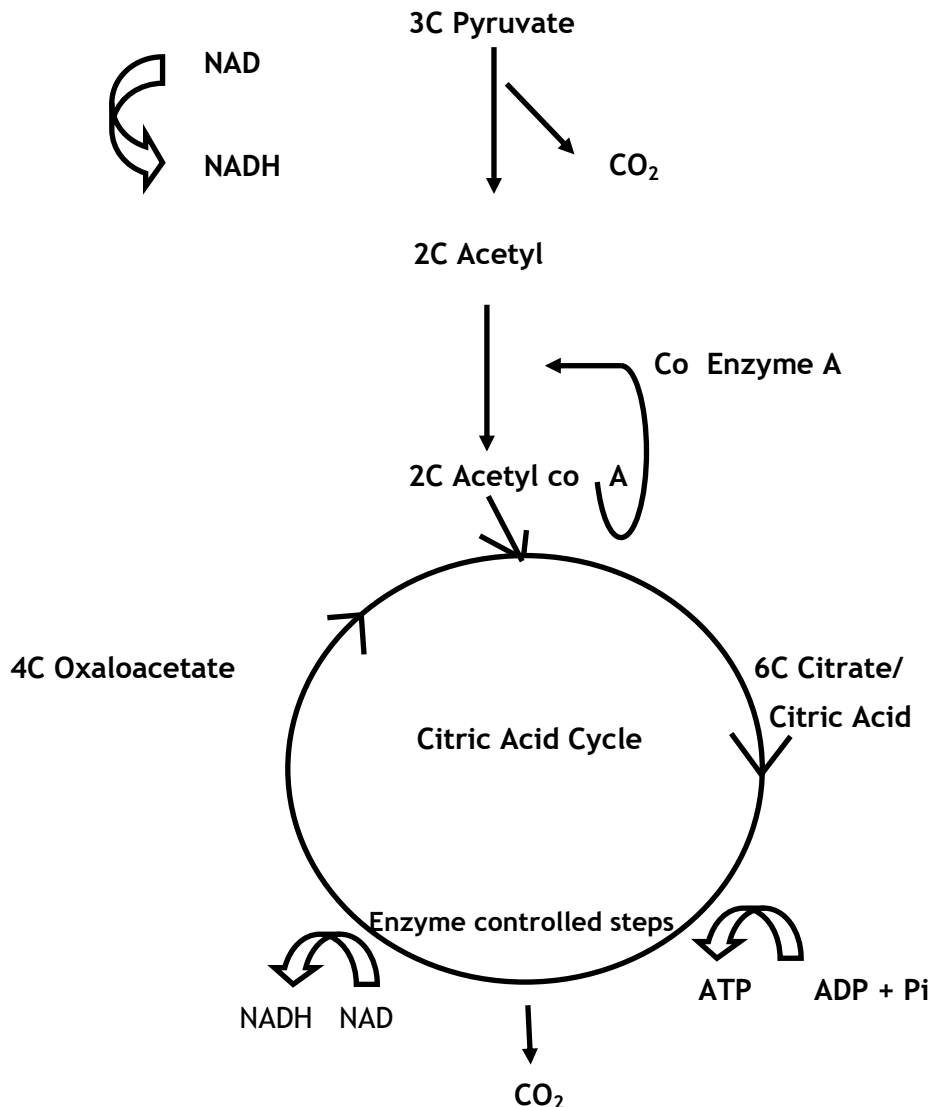
Net gain of 2ATP



7. Aerobic Respiration

Aerobic Stage of Respiration

Process requires oxygen to move beyond pyruvate and is controlled by enzymes called dehydrogenases.



Summary of steps

1. In aerobic conditions, pyruvate is broken down to an acetyl group.
2. Acetyl combines with recycled coenzyme A forming acetyl coenzyme A.
3. In the citric acid cycle, the acetyl group from acetyl coenzyme A combines with oxaloacetate to form citrate.
4. During a series of enzyme-controlled steps, citrate is gradually regenerated back into oxaloacetate.
5. ATP, NADH and CO₂ are all produced during these enzyme-controlled steps.

7. Dehydrogenases and Co enzymes

Role of dehydrogenase

Removes hydrogen ions and electrons from substances and passes to coenzyme NAD to form NADH.

Location—Glycolysis and Citric Acid Cycle.

Role of Co enzymes

Accepts hydrogen ions and electrons and takes them to the electron transport chain on inner mitochondrial membrane.

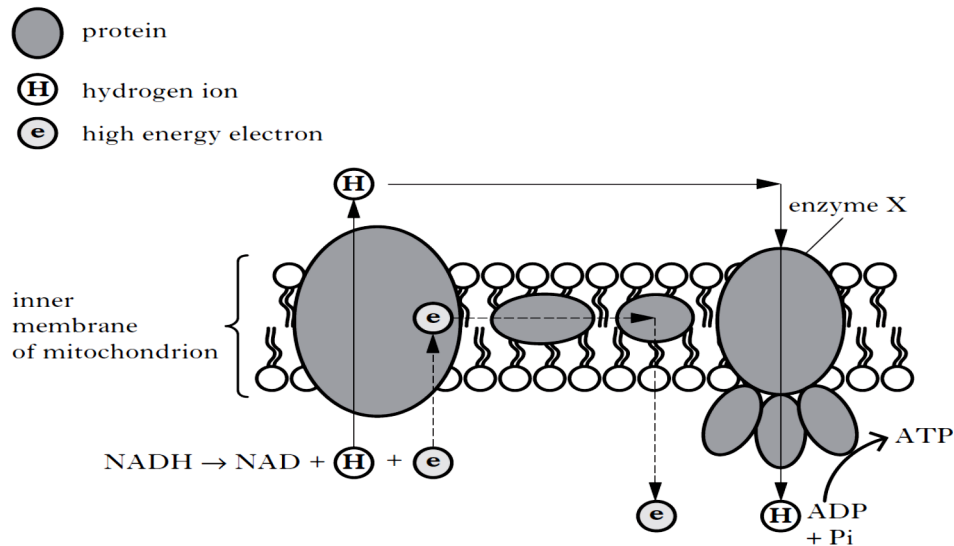
Location—Glycolysis, Citric Acid Cycle and Electron Transport Chain

7. Electron Transport Chain

Electron Transport Chain

The electron transport is a series of **carrier proteins** attached to the **inner mitochondrial membrane**.

Location—Inner membrane of mitochondria (Cristae).



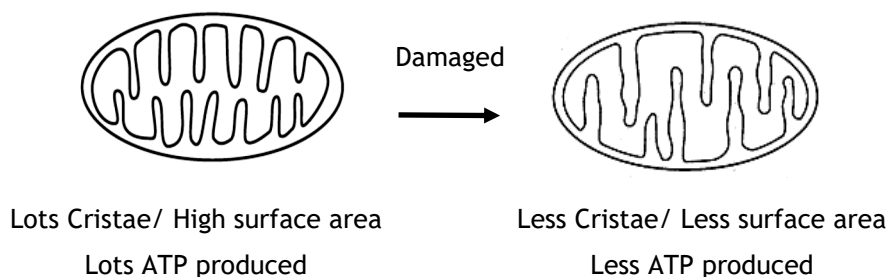
Summary of Process

1. The co enzyme NADH releases electrons and hydrogen ions in the inner mitochondrial membrane.
2. Electrons pass along the electron transport chain and release energy.
3. The energy released by electrons pumps H ions across the membrane by active transport.
4. H diffuses back across ATP synthase causing it to rotate to make ATP from ADP + Pi.
5. Oxygen is the final hydrogen ions and electron acceptor forming water.
1. Most of the ATP produced during respiration occurs during this stage.

High/Low Cristae

Lots of folds in the inner mitochondrial membrane are needed for active cells as they need lots of ATP e.g. muscle/brain/sperm cells.

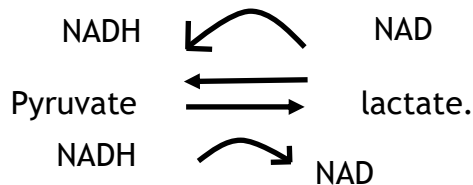
More folds/cristae mean more electrons pass down chain/more H is released & more ATP is produced by ATP synthase.



8. Energy systems in muscles

Vigorous exercise

Muscle cells get insufficient oxygen to support the electron transport chain.



To compensate, muscle cells convert pyruvate into lactate via the transfer of H⁺ ions from NADH which regenerates NAD.

NAD is needed to maintain ATP production through glycolysis.

Lactate accumulates & muscle fatigue occurs, creating an oxygen debt.

The oxygen debt is repaid when exercise stops. This allows respiration to provide the energy to convert the reverse reaction of



Types of Skeletal muscle fibres

1. Slow-twitch muscle fibres

Contract relatively slowly, but can sustain contractions for longer.

Rely on aerobic respiration to generate ATP.

For endurance activities such as long-distance running, cycling or cross-country skiing

Features of slow twitch muscle fibres

- (a) Many mitochondria
- (b) Large blood supply
- (c) High concentration of myoglobin (O₂ storing protein).

8. Muscle Fibres

2. Fast- Twitch Muscle Fibres

Fast-twitch muscle fibres contract relatively quickly, over short periods.

Generate ATP through glycolysis only

Useful when sprinting or weightlifting

Features of Fast-Twitch Muscle Fibres

- (a) **Fewer** mitochondria
- (b) **Lower** blood supply compared to slow-twitch muscle fibres.
- (c) **Lower** concentration of myoglobin
- (d) **Glycogen** is major storage fuel

Muscle Fibre Composition

Most human muscle tissue contains a mixture of both slow & fast-twitch muscle fibres.

Athletes show distinct patterns of muscle fibres that reflect their sporting activities.