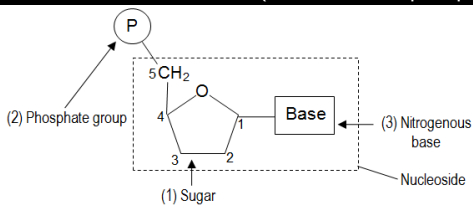
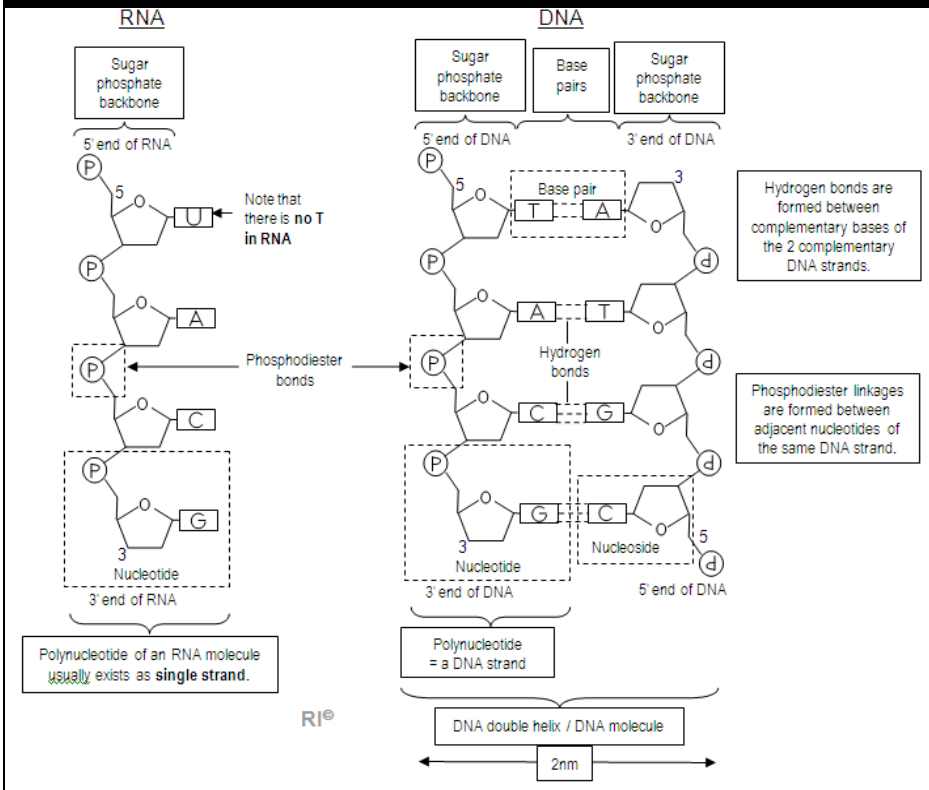
Nucleic acid		RNA (mRNA, tRNA & rRNA)	DNA
Pentose (five carbon) sugar		Ribose	Deoxyribose
Nitrogenous bases	Purines (2 rings)	Adenine & Guanine	Adenine & Guanine
	Pyrimidines (1 ring)	Cytosine & Uracil	Cytosine & Thymine
Complementary base pairing occurs between		Adenine & Uracil (2 H bonds) Cytosine & Guanine (3 H bonds)	Adenine & Thymine (2 H bonds) Cytosine & Guanine (3 H bonds)
Structure		Single Stranded	Double Stranded
Found in (location)		Cytoplasm, Nucleus	Nucleus

Structure of a nucleotide (a nucleoside + phosphate group = nuceloside monophosphate)



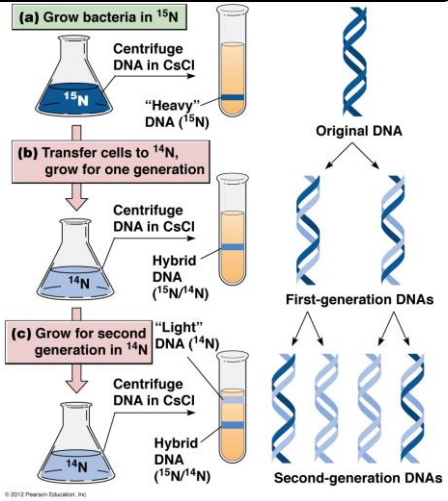
Nitrogenous base: attached to C1
Phosphate group: attached to C5
OH group attached to C3: involved in phosphodiester bond formation
If H is attached to C2 ➔ deoxyribose sugar
If OH is attached to C2 ➔ ribose sugar

Structure of RNA and DNA



In DNA
* A:T = 1:1 and C:G = 1:1
* (A+G) = (C+T)
  i.e. no.of purines = no.of pyrimidines
* Purines: 2 rings (baby's are pure & go googooGAGA)
* Pyrimidines: 1 ring (CUT food on dinner plate)
* Constant width between sugar phosphate backbone = 2nm
* 2 strands are anti-parallel: one strand runs in the 5' to 3' direction, while the other strand runs in the 3' to 5' direction➔ DNA is said to have directionality
* 1complete turn of the double helix has 10 base pairs and spans a distance of 3.4nm
* 1 DNA molecule is made up of 2 strands of DNA

Evidence for semi-conservative replication



(a) A stock of parental *E. coli* were grown for many generations in **^{15}N medium as the only source of nitrogen** until ^{15}N was incorporated into the nitrogenous bases of all bacterial DNA.

(b) The *E.coli* containing ^{15}N-^{15}N were then **transferred into a medium containing only ^{14}N.** The transferred *E. coli* were allowed to **divide once and were then collected**. The DNA extracted and centrifuged in CsCl were **all hybrid (^{14}N-^{15}N) DNA**. This excluded conservative replication in which no hybrids form.

(c) Some of these cells were then allowed to **divide once more**. The DNA extracted and centrifuged in CsCl were **half hybrid (^{14}N-^{15}N) DNA** and **half "light" (^{14}N-^{14}N) DNA.** This excluded dispersive replication in which no pure ^{14}N-^{14}N can be obtained.

<u>3 hypotheses for DNA replication mechanism:</u>

1) <u>Semi-conservative replication</u>
➔both strands separate by the **breaking of hydrogen bonds** and each strand acts as a **template** for the synthesis of a new strand through **complementary base pairing**.
Thus each DNA molecule formed is a **hybrid** consisting of **1 original strand and 1 newly synthesized strand**.

2) <u>Conservative replication</u>
➔2 parental strands re-associate after acting as templates, thus restoring the original double helix. The other DNA molecule consists of 2 newly synthesized strands.

3) <u>Dispersive replication</u>
➔Parental DNA molecule is fragmented and dispersed. Daughter molecules are madeup of a mixture of old and newly synthesized parts.

Gene Mutations

A gene mutation is an **alteration in the sequence of nucleotides** which may change the **sequence of amino acids** in a polypeptide chain. This may change the **3D shape of the protein**, affecting the **protein function** and subsequently affect the **characteristics (phenotype)** of the organism.

Type of mutation	Substitution	Inversion	Insertion	Deletion
Description	**Replacement** of one nucleotide by another	A segment of nucleotides separates from the allele and rejoins at the original position but is inverted	One or several nucleotides are inserted into a sequence	One or several nucleotides are removed from a sequence
Result of mutation	1 codon changed	1 or more codons changed	Shifts reading frame from point of mutation	Shifts reading frame from point of mutation
Effect on protein	Minor/Major	Minor / Major, depending on whether a frameshift occurs	Usually Major	Usually Major
			If the number of nucleotides inserted or deleted are a **multiple of three**, there will change the primary sequence but a **frame shift will not result.**	

1. **Frame-shift mutation:**
   - ➔ due to **insertion or deletion of a number of nucleotides that is not divisible by 3**. Hence due to the triplet code, this would disrupt the reading frame and produce a **different and non-functional polypeptide**
2. **Silent mutation:**
   - ➔ is a **point mutation** that **does not change the amino acid sequence** in a polypeptide
   - ➔ it can occur in the either **coding** or **non-coding** regions
   - ➔ due to the **degeneracy of the genetic code**, **more than one codon can code for the same amino acid**, and hence even if the mutation occurs in the **coding** sequence of a gene, the **same polypeptide** will be synthesized
   - ➔ if the mutation occurs in the **non-coding** region, the **same polypeptide** will be synthesised.
3. **Missense mutation**
   - ➔ is a **point mutation** in which a single nucleotide change results in a **codon that codes for a different amino acid**
   - ➔ if the new amino acid has **similar biochemical properties (e.g. charge, size)** to the one that was replaced, the mutation is said to be **conservative**
   - ➔ if the new amino acid has **different biochemical properties (e.g. charge, size)** to the one that was replaced, the mutation is said to be **non-conservative**
4. **Nonsense mutation**
   - ➔ is a **point mutation** which results is a **premature stop codon (UAG, UAA, UGA),** causing the **polypeptide to be truncated and non-functional**

Example of a disease due to a substitution mutation:

Name of disease	Sickle-cell anaemia
Protein affected	Beta-globin chain of haemoglobin (From **HbA** to **HbS)**
Description of change	Change in **DNA** : **CTC** to **CAC** (substitution) Change in **mRNA** : **GAG** to **GUG** Change in amino acid : **glutamate** to **valine**
Effect of the change	Charged and **hydrophilic glutamate** changed to non-polar and **hydrophobic valine** in HbS. **<u>At low oxygen concentrations</u>**, HbS undergoes a **conformation change** which will cause the **hydrophobic patches on different HbS to stick together**. This **polymerization** of **HbS** results in the formation of abnormal, rigid, **rod-like fibres**. Shape of **red blood cell distorted** – **sickle shaped.**
Effects of disease	Sickle red blood cells are more **fragile** and **break easily**. This results in **shortage of red blood cells** and **poor oxygen transport**. This leads to **anaemia**, lack of **energy and heart failure**. Sickle red blood cells may also **lodge in small blood vessels** and **interfere with blood circulation**. This will lead to **organ damage**.

Chromosomal aberrations

- Chromosomal aberrations can be due to variation in (A) **<u>chromosomal structure:</u>**

1. A **deletion removes** a chromosomal segment.
2. A **duplication repeats** a chromosomal segment.
3. An **inversion reverses** a segment within a chromosome.
4. A **translocation moves** a segment from **one chromosome to another**, **non-homologous** one.

Chromosomal deletions and **duplications** can result in **phenotypic abnormalities** due to the **reduced or additional genes** respectively.
Chromosomal inversions and **reciprocal translocations** can result in disease although the **amount of genetic material remains the same as** the expression of a gene can be influenced by its new location.

- Chromosomal aberrations can also be due to variation in (B) **<u>chromosomal number:</u>**

1. **Aneuploidy** is a condition where the cell does not have a chromosome number that is a multiple of the haploid number. Chromosomes are present in either extra or fewer copies than the wild type.
2. Aneuploidy is a result of a **non-disjunction** event where:
   a) **Homologous chromosomes do not move properly to opposite poles** during **meiosis I** OR
   b) **When sister chromatids fail to separate properly to opposite poles** during **meiosis II**.

So one gamete receives two of the same type of chromosome and another gamete receives no copy. If either of the aberrant gametes fuse with a normal gamete at fertilisation, the zygote will have an abnormal number of chromosomes i.e. **aneuploidy.** Mitosis will subsequently transmit the anomaly to all embryonic cells.

Non-disjunction can also occur during **mitosis**. If such an error occurs early in embryonic development, then the aneuploid condition is passed on to a large number of cells where the severity of the effect is more pronounced.

- **<u>Down syndrome (Trisomy 21)</u>** is result of an **extra chromosome 21** (a total of 3 copies), so each body cell has a total of **47 chromosomes**. Most cases result from non-disjunction during meiosis I. Individuals with Down syndrome have characteristic facial features, short stature, heart defects, susceptibility to respiratory infection and mental retardation. Most individuals are sexually underdeveloped and sterile.

Process	Replication	Transcription	Translation
Location	Nucleus (also in mitochondria and chloroplasts)	Nucleus	Cytoplasm
Begins at Ends at	**Origin of replication** Where 2 adjacent replication bubbles meet / Telomeres	**Promoter** **Termination sequence**	**Start codon** (AUG) (AUG: **A**re **U** **G**ood?) **Stop codon** (UAG, UAA, UGA) (UAG: **U** **A**re **G**ood UAA: **U** **A**re **A**wful UGA:**U** are **G**ood & **A**wful)
Template	DNA (both strands)	DNA (template / non-coding strand)	mRNA
Monomers	**Deoxyribonucleotides**	**Ribonucleotides**	**Amino acids**
Complementary base-pairing	Adenine & Thymine Cytosine & Guanine	Adenine & Uracil Thymine & Adenine Cytosine & Guanine Guanine & Cytosine	Complementary pairing between codon and anti-codon
Enzymes Involved	**DNA polymerase, Helicase, Primase, DNA Ligase, Topoisomerase**	**RNA polymerase** (Poly A polymerase & endonuclease in eukaryotes)	**Aminoacyl – tRNA synthetase** **Peptidyl transferase (a ribozyme)**
Bonds within molecule formed	**Phosphodiester bonds, Hydrogen bonds**	**Phosphodiester bonds**	**Peptide bonds**
Ribosomes involvement	No	No	Yes
Template strand is read in	3' to 5' direction	3' to 5' direction	5' to 3' direction
Molecule is synthesized in	5' to 3' direction	5' to 3' direction	from the amino end to the carboxyl end
Proof reading	Yes	-	-
Product (s)	2 DNA molecules	mRNA,tRNA rRNA,snRNA etc.	Polypeptide chain
Product destination	Nucleus	Cytoplasm	Cytoplasm/ Cell membrane/Outside cell

Role of DNA

The main role of DNA is to <u>store information</u> and <u>pass it on from one generation to the next</u>.

It is a suitable store of information as:

a) It can be **replicated accurately** ➔ daughter cells have identical copies of DNA as the parent cell

Weak hydrogen bonding between the two strands allow them to separate and act as a template for new strand synthesis

(Adenine forms 2 hydrogen bonds with thymine and cytosine forms 3 hydrogen bonds with guanine through complementary base pairing)

b) It is a **stable** molecule ➔ can be passed on to the next generation without loss of the coded information

Collectively, numerous hydrogen bonds hold the two strands of DNA together and adjacent nucleotides in each strand are joined by strong covalent phosphodiester bonds

c)There is a **backup of code**

DNA is double stranded and one strand to serve as a template for the repair of the other if a mutation occurs on either one.

d) Coded information can be **readily utilised/accessed**

Weak hydrogen bonding allows the template strand to separate from the non-template strand allowing transcription to take place

Complementary base pairing allows the faithful transfer of info from DNA to RNA in transcription, which will be translated to protein subsequently

Role of mRNA:

1) Messenger RNA (mRNA) serves as a 'messenger' that, in eukaryotes, **takes the information out of the nucleus** via the nuclear pore **to the cytoplasm** where **translation** takes place.
2) mRNA acts as a **template for translation**
3) As each codon within the coding region of the mRNA represents an amino acid in a polypeptide, the **sequence of codons** will **determine the polypeptide sequence**.

Role of tRNA:

They **bring in specific amino acids in a sequence corresponding to the sequence of codon in mRNA** to the growing polypeptide.

It can facilitate translation due to:

1) its ability to **bind to a specific single amino acid**
2) the ability of the **anticodon to base-pair with the mRNA codon**

Role of rRNA:

1) rRNA **associates with a set of proteins to form ribosomes**.
2) rRNA is the main constituent of the interface between the large and small subunits of the ribosome
   Thus the **small ribosomal subunit can bind to the mRNA** as complementary base pairing can occur between the **rRNA in the mRNA binding site of the small ribosomal subunit and the mRNA.**
3) rRNA is the main constituent of the P site (peptidyl-tRNA binding site) and A site (amino-acyl tRNA binding site) on the large ribosomal subunit
   Hence rRNA **enables the binding of aminoacyl-tRNAs to the P site and A site**
4) An rRNA molecule (peptidyl transferase) on the large ribosomal subunit also **catalyses the formation of the peptide bond** between the amino group of the new amino acid in the A site and the carboxyl end of the growing polypeptide in the P site.