

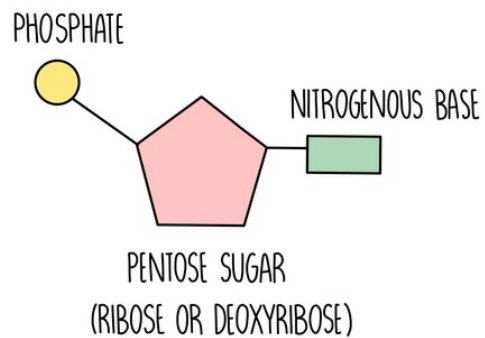
# Module 2: Foundations in Biology

## Nucleic Acids

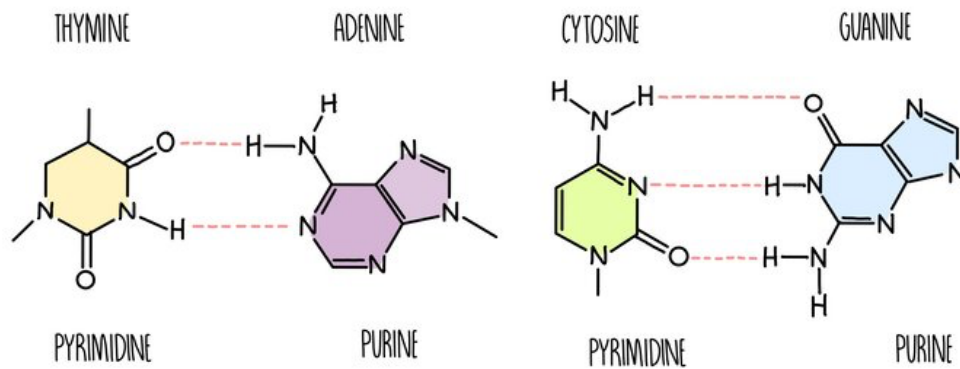
### Nucleotide structure

Nucleic acids are long chains (polymers) of lots of **nucleotide** monomers joined together by **phosphodiester bonds**. Each nucleotide is made up of three components:

1. **Pentose sugar** (either deoxyribose or ribose),
2. **Nitrogenous base** (guanine, cytosine, adenine, thymine or uracil)
3. **Phosphate**



DNA consists of two nucleic acid strands bonded together by **complementary base pairing**, the strands twisted around each other to form a **double helix**. The two strands have the same sequence running in **opposite directions** so we say they are **anti-parallel**. The bonding between bases is predictable, since **guanine always pairs with cytosine** with three hydrogen bonds holding them together. **Adenine always bonds with thymine** (in DNA) or **uracil** (in RNA) with two hydrogen bonds between them. **Adenine and guanine** are **purines**, which mean they have a large double ring structure. **Cytosine and thymine** are **pyrimidines**, which are smaller as they are composed of a single ring. Notice that a purine always base pairs with a pyrimidine - this happens because it's the only way DNA can keep a regular shape and not become too bulky or narrow.



There are some important **differences** between a molecule of DNA and RNA:

1. They contain **different sugars** - the pentose sugar in DNA is **deoxyribose** and in RNA is **ribose**. The difference is that deoxyribose has one less oxygen atom.
2. RNA contains **uracil** instead of thymine
3. DNA is **double-stranded** whereas RNA is **single-stranded**
4. DNA has **hydrogen bonds** between the two complementary strands

During DNA and RNA synthesis, nucleotides are connected through the formation of **phosphodiester bonds** (a type of covalent bond) between the **phosphate group** on one nucleotide and the **pentose sugar** of the next nucleotide. It is a **condensation reaction** which means that water is formed during the reaction and it is catalysed by an enzyme called **DNA polymerase** or **RNA polymerase** depending on whether a DNA or RNA strand is being synthesised. Breaking phosphodiester bonds requires the addition of a water molecule, so it is a **hydrolysis reaction**.

### Adenine triphosphate (ATP)

ATP is a **phosphorylated nucleotide**. Its structure consists of a **ribose** sugar and **adenine** attached to **three phosphate groups**. Hydrolysis of ATP to ADP removes one of the phosphate groups and releases **energy** in a single reaction. It also releases energy in **small, manageable quantities** which means less is wasted.



- When ATP is hydrolysed, it is converted into adenine diphosphate (ADP) and inorganic phosphate ( $P_i$ ). This reaction is catalysed by the enzyme **ATP hydrolase**.
- As well as releasing energy, the **phosphate can be attached to other molecules** to make them more reactive. Enzymes and other proteins can be phosphorylated to convert them from an inactive to an active form.
- ATP is re-synthesised in a condensation reaction, joining ATP and  $P_i$  to reform ATP. This reaction is catalysed by the enzyme **ATP synthase**.

## Purifying DNA

You can purify DNA from any living material (strawberries work well because their DNA is really big and stringy). To do so, carry out the following method:

- **Blend** the fruit to break cells apart.
- Mix together **detergent** (e.g. washing up liquid), **salt** and distilled **water** and the blended fruit in a test tube.
  - The detergent **breaks down the cell membranes** to release the DNA.
  - The salt binds to the DNA, causing it to **clump together**.
- Place in a **water bath at 60°C** for 15 minute – this **denatures enzymes**, preventing them from degrading the DNA.
- Place in an **ice bath** to cool then **filter** the mixture. Transfer a sample to a fresh test tube.
- Add **proteases** to the test tube – these **break down proteins** (histones) bound to the DNA.
- Slowly add cold **ethanol** so that it forms a layer on top of the mixture.
- The DNA will **precipitate** out of the solution and can be removed with a **glass rod**.

## Semi-conservative DNA replication

During cell division, cells need to make a complete copy of their genetic information. When DNA is replicated, the new DNA molecule is made up of **one strand of the original DNA** whereas the other strand is made of freshly made DNA. Since half of the DNA is preserved from the previous round of DNA replication, we describe the process as **semi-conservative**. It takes place in the following stages:

- **DNA helicase** unwinds the double helix, **breaking the hydrogen bonds** between complementary base pairs to separate the strands. One of the strands will act as a **template** for synthesis of the other strand.
- **Complementary nucleotides** will attach to the template strand by **hydrogen bonding**.
- **DNA polymerase** catalyses the formation of **phosphodiester bonds** between nucleotides, forming a complementary strand alongside the template parent strand.
- **Two** daughter DNA molecules are formed, each containing **half** of the **original DNA molecule**.

It is important that DNA polymerase **accurately copies** the template strand to avoid placing the wrong DNA nucleotide in the incorrect position. To avoid this, DNA polymerase '**proofreads**' the complementary strand as it moves along the DNA. If it detects a mismatch, it can 'snip out' the wrong nucleotide and replace it with the right one. DNA polymerase has an accuracy rate of about 99%, which means that mistakes do occur every once in a while. A mistake results in a change to the DNA base sequence, which is known as a **mutation**. DNA mutations can have detrimental effects to the organism, since an altered base sequence can **change the sequence of amino acids** in a protein, causing it to **fold differently** and possibly **lose its function**.

## Types of RNA

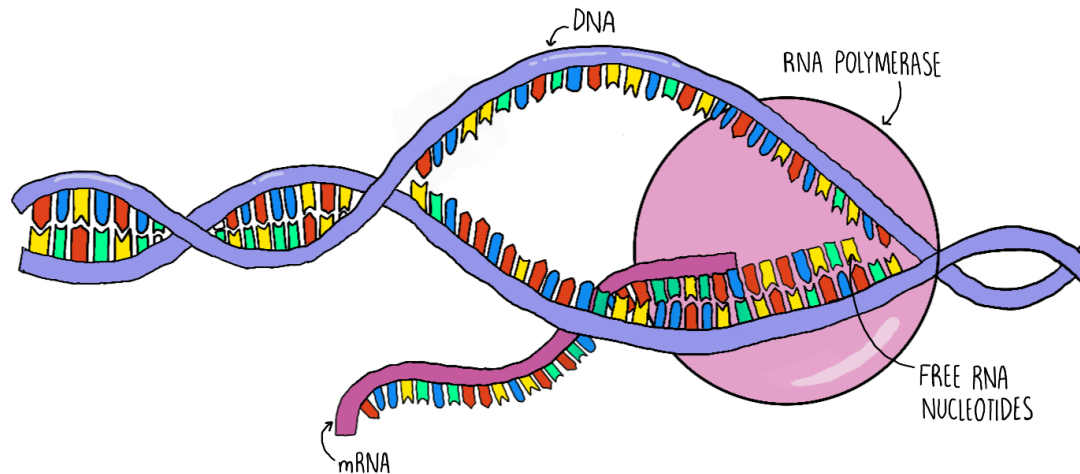
- **Messenger RNA (mRNA)**
  - Produced during transcription – RNA polymerase uses DNA as a template to provide mRNA strand
  - Carries the genetic code from the nucleus to the cytoplasm – provides the instructions for making a protein on the ribosome in translation
  - Made up of triplets of bases called codons
- **Transfer RNA (tRNA)**
  - Carries amino acids to the ribosome during translation
  - Contains an amino acid binding site at one end and an anticodon at the opposite end
  - Anticodons bind to complementary codons on mRNA to convert the mRNA sequence into a protein's primary sequence
- **Ribosomal RNA (rRNA)**
  - Associates with proteins to form the two subunits that make up the ribosome
  - The ribosome moves along mRNA during translation, catalysing the formation of peptide bonds between amino acids to form a polypeptide chain.

## Protein synthesis

DNA is too large to leave the nucleus (and too precious to be damaged), so it is first converted into messenger RNA in transcription, which moves into the cytoplasm and binds to a ribosome. Here, it is used to synthesise a protein in the process of translation.

## Transcription

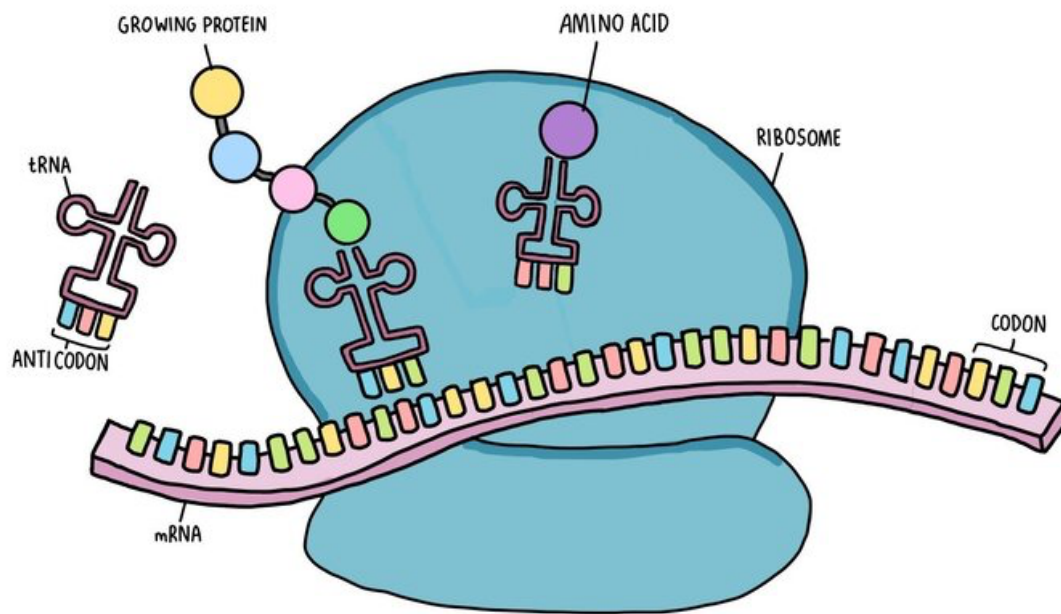
For a gene to produce a protein, the DNA within the gene must first be copied into **RNA** in a process called **transcription**. During transcription, **RNA polymerase** binds to the beginning of a gene in an area known as the **promoter region**. The promoter region is a regulatory region which does not code for amino acids but facilitates the process of transcription by **helping RNA polymerase bind** to the gene. RNA polymerase **separates the DNA strands**, producing a single DNA template for transcription. As RNA polymerase moves along one of the DNA strands (the **template strand**), it adds complementary nucleotides and connects them through the formation of **phosphodiester bonds**. The other strand is referred to as the **coding strand** and will have an identical sequence to the newly synthesised RNA, except for the presence of thymine instead of uracil. Eventually RNA polymerase will reach a codon which does not code for an amino acid but tells the enzyme to stop transcribing (these are called stop codons). A molecule of **messenger RNA (mRNA)** has been formed which will leave the nucleus and enter the cytoplasm.



## Translation

- Once in the cytoplasm, the messenger RNA finds its way to structures called **ribosomes**.
- The ribosome attaches itself to the RNA and slides along it (this is known as *translocation*). The ribosome 'reads' the mRNA in a series of **three bases** (such as AUG, CCA, GCU) called **codons**. Each codon corresponds to a particular **amino acid**.
- As the ribosome reads the codons, a **transfer RNA (tRNA)** molecule which has a complementary **anticodon** carries an **amino acid** to the ribosome. Once the ribosome has read through the length of the mRNA, a series of different amino acids will have been dropped off by several tRNA molecules.
- The ribosome catalyses **peptide bond** formation (condensation reaction) between the amino acids to form a polypeptide.

**tRNA** molecules have an unusual **clover-shaped structure**, formed by a single RNA strand folded over on itself through **hydrogen bonding**. At one end of the molecule, there is an **amino-acid binding site** and at the other there is an **anticodon**, which contains a **complementary base sequence** to the mRNA **codon**.



## The Nature of the Genetic Code

The genetic code can be described in a number of ways - it is a **triplet** code, **non-overlapping**, **degenerate** and **universal**.

- **Triplet code:** three nucleotide bases make up a **codon**, which code for a particular **amino acid**.
- **Non-overlapping code:** the codons **do not overlap**. Once the ribosome has 'read' one codon and the appropriate amino acid has been recruited, the ribosome moves onto a new codon.
- **Degenerate code:** **different codons** can code for the **same amino acid**. For example, the codons CUU and CUC both code for the amino acid leucine. This means that **some mutations** will have **no effect** on the organism since the same protein will still be produced.
- **Universal code:** **all organisms** use the **same genetic code**. Bacteria, bonobos and bananas all contain DNA made up of the four nitrogenous bases that are found in humans.