DNA and RNA are nucleic acids responsible for storing and transmitting genetic information.

1. DNA is the stably inherited code for proteins ("Book")
2. RNA is a partial copy ("Transcript") of that code used to instruct ribosomes how to make the proteins

NUCLEIC ACIDS IN CELLULAR PHYSIOLOGY

OUTLINE

15.1 Nucleotides and Nucleic Acids

15.2 DNA

15.3 RNA and Protein Synthesis

NUCLEOTIDES

- **Nucleic acids** are *polymers* of nucleotides:
  - Polymers are arranged in a linear sequence
  - Only 4 distinct building blocks (nucleotides) are used

- **Nucleotides** consist of:
  1. A base, a nitrogen-containing ring
  2. A \(\beta\)-D-pentose monosaccharide
  3. A phosphate group

- A **nucleoside** consists of only the base and monosaccharide components (no phosphate)
The monosaccharide in nucleic acids may be:

- **D-ribose** → for RNA (ribonucleic acids)
- **2-deoxy-D-ribose** → for DNA (deoxyribonucleic acids)

They differ only in the presence of an alcohol (-OH) at the 2-position.

Recall the numbering system for sugars when they are found in the ring form...

"What is the name for a 5-member ring sugar?"

The nitrogenous bases making up DNA are derived from either **purine** or **pyrimidine**:

- **Purines** contain a double ring (6 + 5 member)
- **Pyrimidines** contain a single ring (6 member)

The components of a nucleotide are connected together by specific bonds:

- Nitrogenous base → Sugar = **N-glycosidic bond**
- Phosphate → Sugar = **Phosphate ester**
NUCLEOTIDE USAGE IN BIOCHEMISTRY

- Nucleotides are utilized for biochemical purposes other than building nucleic acids:
  - Energy transfer (ATP & CoA)
  - Redox Coenzymes

NUCLEIC ACIDS

- **Nucleic acids** (DNA and RNA) are formed by polymerization of nucleotide triphosphates:
  - Polymerization of nucleotides is a form of condensation reaction between a phosphate & an alcohol
  - Note the charge on the phosphates

  - The sequence of a nucleic acid is determined by position on the sugar-phosphate backbone:
    - The 3’ position and the 5’ position are defined by monosaccharide carbon numbers
    - The sequence of bases is written from the 5’ end toward the 3’ end

NUCLEIC ACIDS: RNA vs. DNA

- DNA and RNA are both nucleic acids, but differ in several key ways:
  - Sugar: RNA (Ribose) vs. DNA (Deoxyribose)
  - Structure: Single stranded vs. Double stranded
  - Nucleotides: A-G-C-U vs. A-G-C-T

http://biobook.nerinxhs.org/bb/genetics/dna.htm
THE DOUBLE HELIX

DNA consists of two nucleic acid strands twisted around each other to form a double helix:

- Alternating phosphate/sugar backbone is to the outside
- The nitrogenous bases are located between the strands like rungs of a ladder
- The two strands run antiparallel to each other (5’ and 3’ ends located at opposite ends)

BASE PAIRING IN THE DOUBLE HELIX

The nitrogenous bases are positioned in pairs between the two strands of a DNA helix:

- Pairs = 1 purine + 1 pyrimidine
- The geometry of bases only permits specific pairing

Note hydrogen bonding patterns

2 H-bonds

3 H-bonds

G-C bonds are ~50% stronger than A-T bonds

DNA STRUCTURE IN THE NUCLEUS

Cellular DNA is organized into compact structures within the nucleus called chromosomes:

1. Each chromosome is one double stranded DNA double helix
2. The DNA is coiled around proteins called histones, in a unit called a nucleosome
3. Many nucleosomes coil up to create a larger structure, known as chromatin
• **DNA replication** is the process of forming new DNA strands prior to cell division.

• At the **replication fork**, each strand serves as template for a daughter strand.

• Several different enzymes are required to complete replication:
  1. **Helicase** – unwinds DNA double helix to separate strands
  2. **DNA polymerase** – adds matching bases to template strand & forms new phosphate esters in backbone
  3. **Ligase** – seals backbone into single strand

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**PROOFREADING DURING REPLICATION**

• DNA replication occurs **very quickly** with extremely high fidelity!!!
  - about 100 nucleotides per second by DNA polymerase on a growing DNA strand.
  - The overall error rate is less than 1 base per billion

• The low error rate is due to "proof-reading":
  - DNA polymerases have the capacity to detect mismatches
  - Corrected during replication process

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**SOURCES OF GENETIC MUTATIONS**

• DNA damage can be caused by **internal** sources of errors:
  1. Errors during **replication** result in genetic mutations
     - These errors are propagated during cell division
  2. **Reactive intermediates** from cellular metabolism (eg. O’ or H₂O₂) can also damage DNA

• There are also **external** sources of DNA damage:
  3. High energy **radiation** (ultraviolet light, X-rays & γ-rays)
  4. Chemical **carcinogens** (cigarettes smoke, heavy metals, highly reactive organic compounds)
A genetic mutation is a chemical change that:
1. makes a permanent alteration in DNA sequence
2. results in a change to the primary structure of a protein encoded by that DNA

There are two classes of genetic mutations:
1. Substitutions: one nucleotide is substituted for another
   - Leads to a change in a single amino acid in a protein
2. Insertions / Deletions: one or more nucleotides are added or subtracted from a DNA sequence:
   - Can have small changes in a few amino acids
   - Can cause a dramatic frameshift, in which all the remaining amino acids will be incorrect

**MUTATION EXAMPLES**

- Single amino acid change in protein primary sequence
- Frameshift – dramatic change in protein primary sequence

**PRACTICE PROBLEMS**

1. Below are sequences of nucleotides located on a segment of one DNA strand. Indicate the complementary sequence of base pairs on the other DNA strand.
   a. TTGGCA
   b. ATGCCA

2. For each property described below, name the part of the DNA double helix that has that property.
   a. is on the inside of the double helix.
   b. is on the outside of the double helix.
   c. interacts with the other strand through hydrogen bonding.
Two cellular processes are fundamental to the extraction of information from genomic DNA:

1. **Transcription**
   - DNA → mRNA
   - Occurs in the nucleus

2. **Translation**
   - mRNA → protein
   - Occurs on ribosomes in the cytosol

The process of extracting information from DNA requires several types of RNA as intermediates. The three major classes of RNA include:

1. **Messenger RNA** (mRNA) – information transmitting molecule (intermediate between DNA & protein)
2. **Ribosomal RNA** (rRNA) – structural molecule
3. **Transfer RNA** (tRNA) – “decoding” molecule

RNA is produced as single-stranded molecules, but can form intramolecular basepairs.

The identity of cells depends upon the array of genes they express at any given time:

- Genomic DNA is essentially identical between cells....
- ...but the expression of genes from genomic DNA varies widely between different cell types
- Genes may be either “turned on” (expressing their protein) or “turned off” (not expressing their protein)

**Gene expression** begins with transcription, where the DNA sequence of nucleotides is copied into an mRNA:

- Only one of the two strands (the “template strand”) is copied
- This is a polymerization reaction in which ribonucleotides are linked together by successive condensation reactions
TRANSCRIPTION: DNA TO mRNA

- Transcription of the DNA template to a messenger RNA (mRNA) is carried out by RNA polymerase.
- The newly formed RNA strand is complementary to the template strand read by RNA polymerase:
  - For example, if the DNA reads GATCAT, then the RNA strand is CUAGUA.
  - Note that uracil (U) is read in place of thymidine (T) on RNA.

TRANSLATION IS DONE BY RIBOSOMES

- Translation of the nucleotide code of nucleic acids into the amino acid code of proteins is a complex process carried out by ribosomes:
  - Ribosomes are huge, multi-component enzymes.
  - Function as protein-making factories in the cytoplasm.
- Ribosomes are composed of two parts:
  1. Ribosomal RNA (rRNA)
  2. About 50 different proteins.

THE GENETIC CODE

- Messenger RNA (mRNA) molecules are the transcripts that are "read" by ribosomes.
- Groupings of 3 nucleotides on the mRNA are called a codon.
- Each codon codes for an amino acid to be inserted into a growing protein.
- This "genetic code" is common to all living organisms.
Ribosomes translate mRNA sequence into proteins using transfer RNA (tRNA) “decoding keys”:

- Each tRNA contains two critical components that match codons to amino acids:
  1. The anticodon loop, that joins with the codon on the mRNA using rules of base-pairing
  2. The amino acid covalently linked to its 3’ end

Example: a tRNA with a GGC anticodon matches the GCC codon & adds alanine to the growing polypeptide chain

The process of translation proceeds as follow:

1. The ribosome recognizes & binds to an mRNA
2. The ribosome recruits a tRNA based on its ability to match with the first codon of the mRNA.
3. A second tRNA is recruited by binding to the second codon.
4. The ribosome joins the new amino acid to the first by forming a new peptide bond between them.
5. The second tRNA leaves the ribosome without its amino acid and the ribosome moves on to the third codon through translocation.
6. The process is repeated until the end when a stop codon is reached.
7. Finally the completed protein is ejected from the ribosome.
1. Using the table, determine the amino acid specified by the following codons:
   a. GGG
   b. AAA

2. Specify all the codons that code for the following amino acids:
   a. histidine
   b. leucine

3. What are the three stop codons? What is a stop codon?