DNA, Chromosomes, and Genes

• When a cell is not actively dividing, its nucleus is occupied by chromatin, which is a compact tangle of **DNA (a polymer of deoxyribonucleic acid)**, the carrier of genetic information, twisted around proteins (known as histones).

• During cell division, chromatin organizes itself into **chromosomes**. Each chromosome contains a different DNA molecule, and the DNA is duplicated so that each new cell receives a complete copy.

Each DNA molecule, in turn, is made up of many **genes**—individual segments of DNA that contain the instructions that direct the synthesis of a single polypeptide.
What is DNA?

• DNA is a long polymer made up repeating units of nucleotides

• Each repeating unit is very small (nm scale) but the entire molecule is very long, i.e. it contains millions of nucleotides.

• A DNA molecule is made of a deoxyribose (sugar), a phosphate ester group and a base. (this is a base made up of C, N and H and NOT NaOH, KOH etc)

• A DNA strand has a double helix structure. The double helical structure is from Hydrogen bonding between the bases.

Facts about Nucleotides

• Nucleic acids are polymers of nucleotide subunits.

• Nucleotides are made up of a ribose or deoxyribose sugar unit having a phosphate group attached, usually at the 5’ end, and a purine or pyrimidine base attached at the 1’ position.

• There are two types of nucleic acids, DNA and RNA. They differ in that DNA contains deoxyribose, while RNA contains ribose, and DNA contains a thymine base, while RNA contains uracil. Both DNA and RNA also contain phosphate, cytosine, adenine, and guanine. The total mass of RNA in a cell is usually much larger than the mass of DNA.
The bases are heterocyclic amines (named purines and pyrimidines)

Thymine (T) is present only in DNA, Uracil (U) only in RNA

Adenine (A), Guanine (G) and Cytosine (C) are present in both nucleic acids
Naming Nucleotides

1. Name the base (compound that has lots of Nitrogen atoms within a ring)
2. Locate the position of the phosphate ester (on Carbon 1 or Carbon 2 etc..)
3. Specify the location of the phosphate
4. You can decide if it is a ribonucleotide or a deoxyribonucleotide by looking at the –OH position? (Is there an error in this diagram?)

Structure of a Nucleotide

A nucleotide

Adapted from McMurry et al; GOB Chemistry; 5th Ed.
Writing Nucleotide Chains

For a single chain, the sugars are connected through phosphate ester linkages between the C-3 (3’, 3' prime end) and C-5 (5’ 5 prime end). 3’ is free –OH group.

Reading a nucleotide sequence:

Start at the 5’ end and work toward the 3’ end.

The base abbreviations (ATGC) denote the sequence. This sequence is T-A-G.

A = Adenine
C = Cytosine
G = Guanine
T = Thymine
**Nucleotides**

- A combination of a purine or pyrimidine base, sugar, and phosphate is called a nucleotide.
- Nucleotide subunits are the building blocks of polynucleotide DNA and RNA.
- Nucleotides also are sometimes found as diphosphate or triphosphate esters.
- Adenosine triphosphate (ATP) is the source of a great deal of biochemical energy.

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**What is a Nucleoside?**

It is a nucleotide without a phosphate group; has a 5 carbon sugar bonded to a base.

Note the β-N-glycosidic bond.

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Adapted from McMurry et. Al; GOB Chemistry; 5th Ed.
Purine/Pyrimidine Bases

If the nucleoside has a purine base, such as Adenine or Guanine

A purine (double ringed). How are the lone pairs located in this ring?

If the nucleoside has a pyrimidine base, such as Cytosine, Thymine, Uracil

A pyrimidine ring

Base Pairing in DNA

DNA is double helical

The two strands run antiparallel to each other; one in the 5'-3' direction and the other 3'-5' direction

Note that the base pairs are perpendicular to the backbone
Hydrogen bonding is present between the bases of the opposing strands, Adenine with Thymine and Cytosine with Guanine. These H-bonds provide stability to the structure and the bases are always complementary.

Base Pairing

- **Base Pairing in DNA: The Watson-Crick Model**
  - Complementary pairs of polynucleotides form hydrogen bonds which stabilize the chains.
  
  - The strands are said to be antiparallel (their polarity runs in opposite directions) and complementary (they fit together by hydrogen bonding).
  
  - In native DNA, the percentage of cytosine is always equal to the percentage of guanine, and the percentage of adenine is always equal to the percentage of thymine. (This is known as Chargaff’s rule.)
Nucleic Acids and Heredity

• Heredity is transfer of characteristics from parents to their offsprings through their Genes.

• Within a cell, information is stored in the DNA, every time cell division occurs, its DNA gets copied.

• DNA or RNA has three fundamental processes, Replication, Transcription and Translation.

  Replication: The process by which a DNA makes a copy of itself when a cell divides.

  Transcription: The process by which information is read from DNA and used for synthesizing RNA.

  Translation: The process by which RNA synthesizes proteins.
Step 1. The first major step for the DNA Replication is the breaking of hydrogen bonds between bases of the two antiparallel strands.

The unwinding of the two strands is the starting point.

The splitting happens in places of the chains which are rich in A-T. That is because there are only two bonds between Adenine and Thymine (there are three hydrogen bonds between Cytosine and Guanine).

Helicase is the enzyme that splits the two strands.
The initiation point where the splitting starts is called "origin of replication".
The structure that is created is known as "Replication Fork".

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Step 2. One of the most important steps of DNA Replication is the binding of RNA Primase in the initiation point of the 3′-5′ parent chain. This is also known as the RNA Primer.

RNA Primase can attract RNA nucleotides which bind to the DNA nucleotides of the 3′-5′ strand due to the hydrogen bonds between the bases.

RNA nucleotides are the primers (starters) for the binding of DNA nucleotides.
Step 3. Only the leading strand grows continuously from 5’ to 3’ towards the fork.

The lagging strand is replicated from 5’ to 3’ in short segments called Okazaki fragments.

These short sections are joined later by DNA ligase.

The diagram on the left shows linear view of the Okazaki fragments. The DNA Polymerase cannot read the 3’-5’ template. That is why the replication of this strand (The lagging strand) is complicated and fragments are formed. An enzyme called DNA Pol α is used to read this strand.

The Okazaki fragments are read using a different DNA enzyme (DNA Pol I Exonuclease).

The short gaps between the fragments are joined later with the help of DNA polymerase and DNA ligase.
Each new double helix consists of one Parent chain and one complementary chain. This is known as **Semiconservative Replication**.

Snapshot of DNA replication showing Initiation and Elongation

There is a 3rd step known as **Termination** where the duplicated chromosomes separate from each other, this is not part of our course.

Adapted from McMurry et. al; GOB Chemistry, 5th Ed.

Image source: www.DNAreplicationinfo.org
Ribosomal RNAs: Outside the nucleus but within the cytoplasm of a cell are the ribosomes, small granular organelles where protein synthesis takes place. Each ribosome is a complex consisting of about 60% ribosomal RNA (rRNA) and 40% protein, with a total molecular weight of approximately 5,000,000 amu.

The transfer RNAs (tRNA) are smaller RNAs that deliver amino acids one by one to protein chains growing at ribosomes. Each tRNA carries only one amino acid.

The messenger RNAs (mRNA) carry information transcribed from DNA. They are formed in the cell nucleus and transported out to the ribosomes, where proteins will be synthesized. These polynucleotides carry the same code for proteins as does the DNA.

### Structure and Function of RNA

<table>
<thead>
<tr>
<th>TABLE 26.3</th>
<th>Comparison of DNA and RNA</th>
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</thead>
<tbody>
<tr>
<td><strong>SUGAR</strong></td>
<td><strong>BASES</strong></td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribose</td>
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<td></td>
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<td>RNA</td>
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Facts about Transcription

- Transcription is the process of biosynthesis mRNA from DNA
- The mechanism is very similar to DNA replication
- A single stranded copy of mRNA is produced from DNA (i.e., only one of the DNA strands is used as a template)
- The DNA strand that is transcribed is the template strand
- The transcribed mRNA molecule is an exact complementary of the DNA strand.
- The only difference is Thymine will be replaced by Uracil in the mRNA.

RNA transcription: Initiation

The transcription process begins when RNA polymerase recognizes a control segment in DNA that precedes the nucleotides to be transcribed.

The sequence of nucleic acid code that corresponds to a complete protein is known as a **gene**.
RNA transcription: Elongation

The RNA polymerase moves down the DNA segment to be transcribed, adding complementary nucleotides one by one to the growing RNA strand as it goes.

The bubble formation on the template DNA strand is from the unraveling of helical DNA.

RNA Transcription: Termination

Transcription ends when the RNA polymerase reaches a codon triplet that signals the end of the sequence to be copied.
The Genetic Code

- **Codon**: A sequence of three ribonucleotides in the messenger RNA chain that codes for a specific amino acid; also a three-nucleotide sequence that is a stop codon and stops translation.

- **Genetic code**: The sequence of nucleotides, coded in triplets (codons) in mRNA, that determines the sequence of amino acids in protein synthesis.

### TABLE 26.4 Codon Assignments of Base Triplets in mRNA

<table>
<thead>
<tr>
<th>FIRST BASE (5' END)</th>
<th>SECOND BASE</th>
<th>THIRD BASE (3' END)</th>
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<tbody>
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<td>U</td>
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<td>U</td>
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<td>Phe</td>
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<tr>
<td>C</td>
<td>Ser</td>
<td>Ser</td>
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<tr>
<td>A</td>
<td>Tyr</td>
<td>Tyr</td>
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<tr>
<td>G</td>
<td>Cys</td>
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<td>G</td>
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</tbody>
</table>

Adapted from McMurry et. Al; GOB Chemistry, 5th Ed.
Chapter Summary

- Nucleic acids are polymers of nucleotides. Each nucleotide contains a sugar, a base, and a phosphate group. A nucleoside contains a sugar and a base, but not the phosphate group. Nucleotides are connected by phosphate diester linkages between the 3’ –OH group of one and the 5’ phosphate group of the next.
- DNA consists of two polynucleotide strands twisted together in a double helix. The sugar–phosphate backbones are on the outside, and the bases are in the center of the helix. The bases are complementary, opposite every T is an A, opposite every G is a C. The base pairs are connected by hydrogen bonds.

Chapter Summary Cont.

- Replication requires DNA polymerase enzymes. The enzymes copy only in the 3’ to 5’ direction of the template strand, so that one strand is copied continuously and the other strand is copied in segments as the replication fork moves along. In each resulting double helix, one strand is the original template strand and the other is the new copy.
- mRNA carries the genetic code to the ribosomes in the cytosol, where tRNAs bind to amino acids and deliver them for protein synthesis. rRNAs are incorporated into ribosomes.
Chapter Summary Cont.

• In transcription one DNA strand serves as the template and the other, the informational strand, is not copied.
• Nucleotides carrying bases complementary to the template bases between a control segment and a stop codon are connected one by one to form mRNA. The primary transcript mRNA (or hnRNA) is identical to the matching segment of the informational strand, but with uracil replacing thymine.
• Introns, which are base sequences that do not code for amino acids in the protein, are cut out before the final transcript mRNA leaves the nucleus.

Chapter Summary Cont.

• 61 codons specify amino acids and 3 are stop codons. Each tRNA has at one end an anticodon consisting of three bases complementary to those of the codon that specifies the amino acid it carries.
• Initiation of translation is the coming together of the large and small subunits of the ribosome, an mRNA, and the first amino acid–bearing tRNA.
• Elongation proceeds as the next tRNA arrives at the second binding site, its amino acid is bonded to the first one, and the first tRNA leaves. These steps repeat until the stop codon is reached and the two ribosome subunits, the mRNA, and the protein separate.