Chapter 10: DNA and RNA structure and function

DNA is the cell’s master repository of genetic information. It is consists of two strands of linked nucleotides.

DNA → RNA → proteins → cell structure and function

DNA: adenine (A), thymine (T), guanine (G), cytosine (C)
RNA: adenine (A), guanine (G), cytosine (C), uridine (U)

\[ G = C, \ A = T, \ A = U \]

Component of nucleotides

Nucleotides are phosphate esters of pentoses in which a nitrogenous base is linked to C1 of the sugar residue.

1. An aromatic cyclic compound containing carbon and nitrogen atoms (base).
2. A five-carbon carbohydrate (ribose or deoxyribose)
3. One, two or three phosphate groups.

The nitrogenous bases are planar, aromatic, heterocyclic molecules which, for the most part, are derivatives of either purine or pyrimidine.

The major purine components of nucleic acids are adenine and guanine residues.
The major pyrimidine residues are those of cytosine, uracil (RNA) and thymine (DNA).

If the phosphate group is absent in the nucleotide structure, the compound is known as a nucleoside.

The covalent linkage in nucleosides forms between N9 of purines or N1 of pyrimidines and C1 of sugar ring by elimination of water.

Nomenclature for nucleosides and nucleotides in DNA and RNA

<table>
<thead>
<tr>
<th>Base</th>
<th>Nucleoside</th>
<th>Nucleotide (Abbreviation)</th>
<th>Nucleic Acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purine</td>
<td>Adenosine, deoxyadenosine</td>
<td>Adenosine 5'-monophosphate (5'-AMP)</td>
<td>RNA</td>
</tr>
<tr>
<td></td>
<td>Guanosine, deoxyguanosine</td>
<td>Guanosine 5'-monophosphate (5'-GMP)</td>
<td>DNA</td>
</tr>
<tr>
<td></td>
<td>Cytosine, deoxycytidine</td>
<td>Cytidine 5'-monophosphate (5'-CMP)</td>
<td>DNA</td>
</tr>
<tr>
<td></td>
<td>Thymine, deoxythymidine</td>
<td>Thymidine 5'-monophosphate (5'-TMP)</td>
<td>DNA</td>
</tr>
<tr>
<td></td>
<td>Uracil, deoxyuridine</td>
<td>Uracil 5'-monophosphate (5'-UMP)</td>
<td>RNA</td>
</tr>
</tbody>
</table>

Guanosine triphosphate (GTP), uridine triphosphate (UTP), deoxyguanosine triphosphate (dGTP), and deoxyuridine triphosphate (dUTP) are important in biosynthetic processes including the synthesis of nucleic acids.

Nucleotide forms when phosphoric acid reacts with a carbohydrate hydroxyl group on the nucleoside.

The most important and abundant mononucleotide in the cell is 5'– AMP.

ATP is the principal carrier of chemical energy in the cell.
Nucleic Acids

Nucleic acids are, with few exceptions, linear polymers of nucleotides whose phosphate bridge the 3’ and 5’ positions of successive sugar residues.

The phosphate of these polynucleotides, the phosphodiester groups, are acidic so that, at physiological pH’s, nucleic acids are polyanions.

Nucleosides are represented as:

C1’ and position of N-glycosidic bond.

The standard format for drawing an oligonucleotide begins with the 5’ end on the left. 5’ AGCT(U)3’
DNA structural elements

Like most other types of biological macromolecules, nucleic acids adopt highly organized 3-dimensional structures.

In 1953 Watson and Crick postulated a unique, double-stranded helical structure for the DNA.

The detailed features of the DNA double helix are as follows:

1- Two-right handed, helical, polynucleotide chains are coiled around a common axis to form an ~20-Å-diameter double helix.

2- The two strands are antiparallel and wrap around each other such that they cannot be separated without unwinding the helix.
3- Bases occupy the core of the helix and sugar-phosphate chains are coiled about its periphery, minimizing the repulsions between charged phosphate groups.

4- Double helix is stabilized by two types of forces:
   - Hydrogen bonds between pairs of complementary bases on opposite strands.
   - Van der Waals and hydrophobic interactions.

   The planes of bases are nearly perpendicular to the helix axis and stabilize the helical structure by stacking interactions.

   The most remarkable feature of Watson-Crick structure (B-DNA) is that it only can accommodate two types of base pairs:
   1- Maximum number of hydrogen bonds
   2- Maximum stability
   3- Distance between two strands

   10.5 base pairs per turn for B-DNA
A-DNA: 11 bases per helix turn and more compact structure.
Common structural features:
1- both right-handed
2- antiparallel strands
3- complementary base pairs: A-t, G-C

Z-DNA: 12 bases per helix turn.
The line joining successive phosphate groups on a polynucleotide strand of Z-DNA follows a zigzag path around the helix

Physical and biological properties of the double helix

Each strand of double helix is used as a template to make complementary daughter strands.
Hyperchromic effect: UV absorption increases during denaturation process of DNA due to change in the arrangement of valence (π) electrons in the aromatic rings.

Renaturation or annealing

Tertiary structure of DNA

The chromosomal DNA of many microorganisms is a closed circle, a result of covalent joining of the two ends of a linear double helix.

Closed, circular, duplex DNA has a unique structural feature. It is found twisted into a new conformation, known as supercoiled DNA.

Topoisomerases catalyze the interconversion of relaxed form to supercoiled DNA.

RNA structural elements

RNA and DNA are both long, unbranched polymers composed of nucleotide monomers.

Two fundamental structural differences between RNA and DNA

1- RNA contains the carbohydrate ribose rather than deoxyribose. Extra hydroxyl group in RNA makes it more susceptible to hydrolysis.

2- one of the major bases in RNA is uracil instead of thymine in DNA.

All classes of RNA, no matter what their size or biological function, are synthesized as single-stranded molecules.
Single strands of RNA arrange themselves into conformations containing several structural elements.

1. **Hairpin turns**: Bring together complementary stretches for base pairing.

2. **Right-handed double helix**: Complementary hydrogen bonding and stacking interactions hold the double helix together.

3. **Internal loops and bulges**: Structural features that disrupt the formation of continuous double helix regions.

**tRNA structure**
1. There is at least one corresponding tRNA for each amino acid.
2. They all have between 74 and 93 nucleotides in a single chain.
3. All have a common secondary and tertiary structure.

rRNA is much larger than tRNA and contains regions with extensive double-helix features.

**Cleavage of DNA or RNA by nucleases**

Enzyme *nuclease* catalyze the hydrolysis of phosphodiester bonds.

Enzymes that only work on RNA are called ribonucleases or RNases.

Enzymes that only work on DNA are called deoxyribonucleases or DNase.

**Exonucleases** catalyze the hydrolytic removal of terminal nucleotides.

Hydrolytic cleavage of internal phosphodiester bonds is carried out by endonucleases.
DNA restriction enzymes

Systematic breakdown of duplex DNA requires restriction enzymes (restriction endonuclease) that cleave DNA at specific recognition sequences.

Hundreds of restriction enzymes with different specificities are available, giving a great deal of choice in where to cut the genome.

Most of these enzymes recognize a sequence of either four or six successive base pairs.

No analogous enzymes have yet been found that catalyze the cleavage of RNA into well-defined fragments by cutting at predicted sites.

Chromosomes

DNA contains the genetic information transmitted to each daughter cell when cells divided. The DNA usually exists in the form of nucleoprotein (DNA-protein) complexes called chromosomes.

Chromatin is one of the nucleoprotein complexes in the eukaryotic cell nucleus.

Components of chromatin:
1- histone chromosomal proteins
2- nonhistone chromosomal proteins