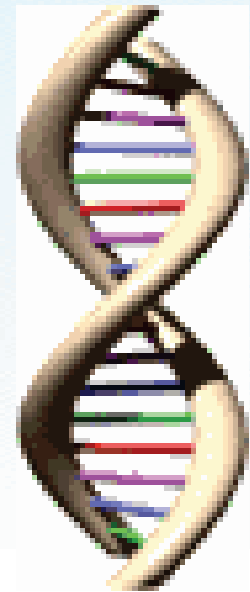
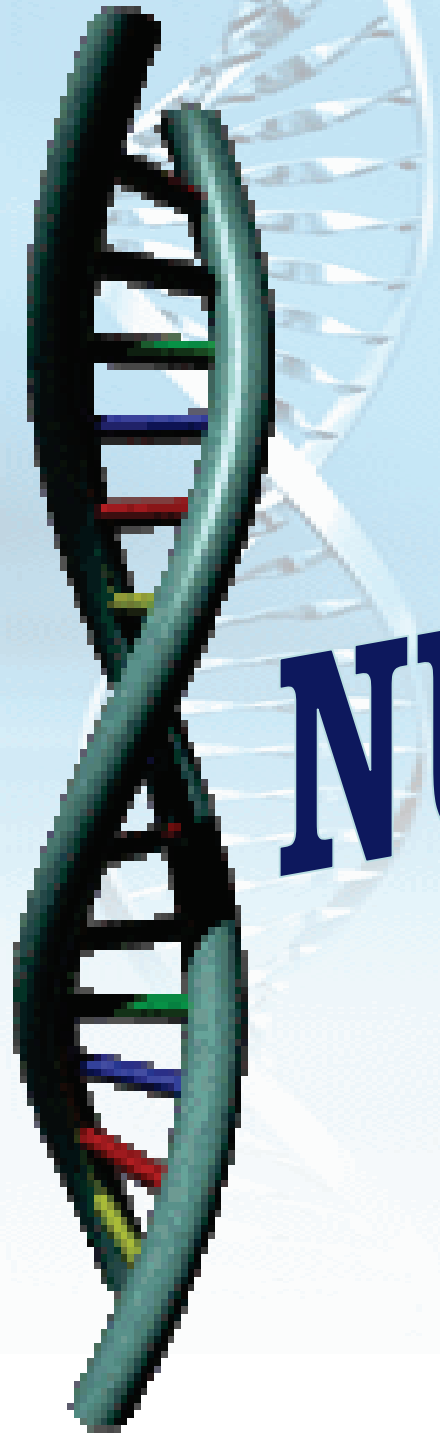
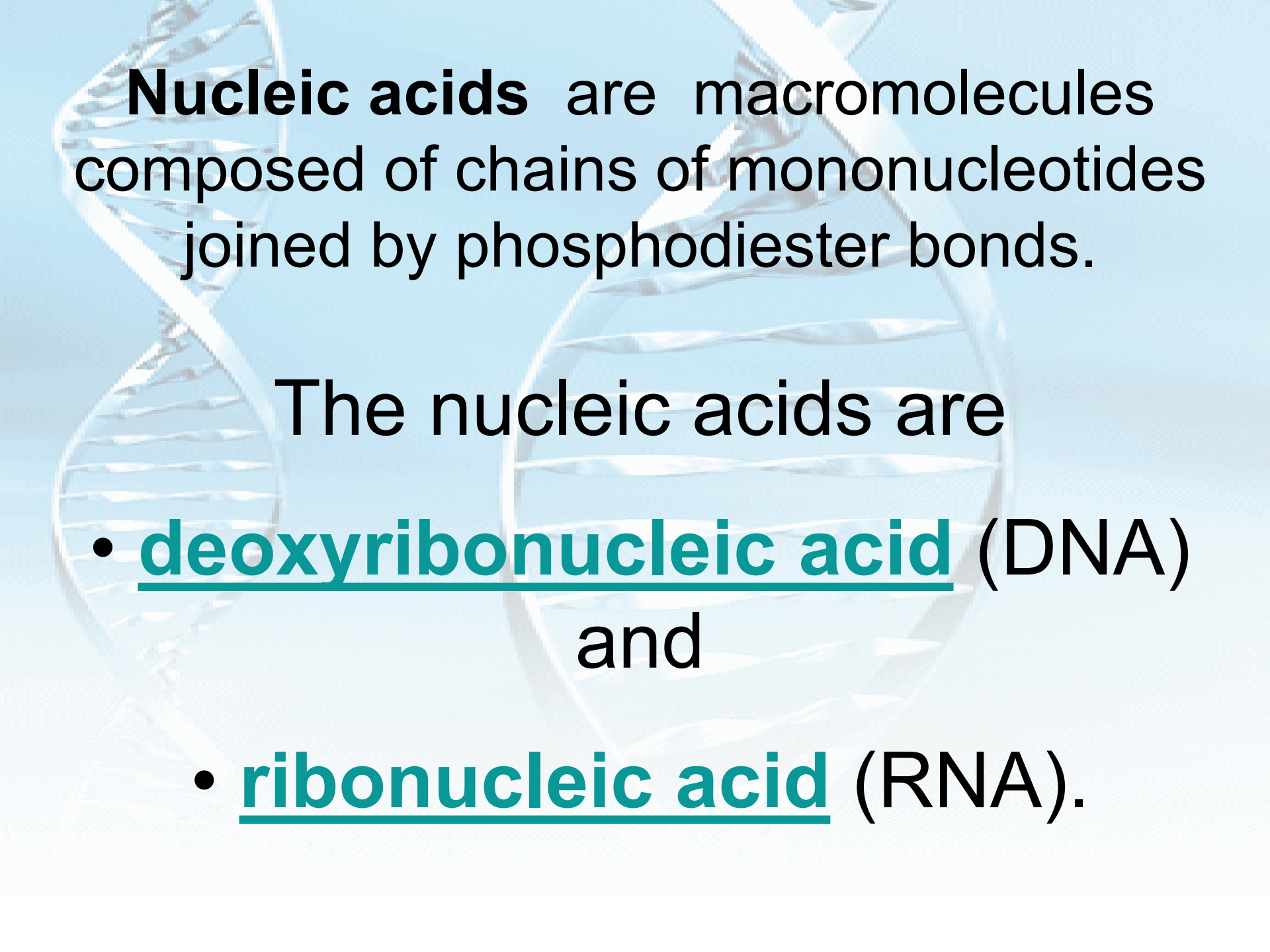


NUCLEIC ACIDS





Nucleic acids are macromolecules composed of chains of mononucleotides joined by phosphodiester bonds.

The nucleic acids are

- deoxyribonucleic acid (DNA)
and
- ribonucleic acid (RNA).



Nucleic acids are universal in living things, as they are found in all cells and viruses.

The role of nucleic acids is storage and expression of genetic information

Deoxyribonucleic acid (DNA) - functions in long-term information storage

Ribonucleic acids (RNAs) - are involved in most steps of gene expression and protein biosynthesis.

The distribution of the nucleic acids in the cell :

DNA

RNA

**97-99% in nucleus
1-3% in mitochondria**

**10% in nucleus
15% in mitochondria
50% in ribosomes
25% in cytoplasm**

Approximately 5-10% of the total weight of a cell is RNA. DNA is only about 1%

RNA exists in three major forms.

- **Ribosomal RNA - rRNA.** Combined with protein to form ribosomes, the site of protein synthesis.
- **Messenger RNA - mRNA.** Carries information about the order of amino acids in protein from a single gene from DNA to the ribosome.
- **Transfer RNA - tRNA.** Transport specific amino acids for use in protein synthesis.

The quantity of the RNA depends on the functional state of the cells, on the intensity of protein synthesis in cell.



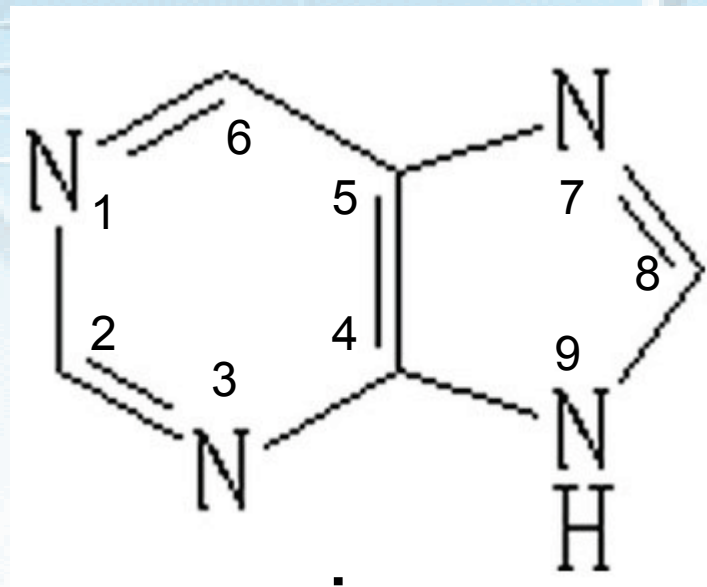
The structure of nucleic acids

All nucleic acids are made up from monomers called nucleotides which consist of

- nitrogenous base,*
- sugar,*
- phosphate residue.*

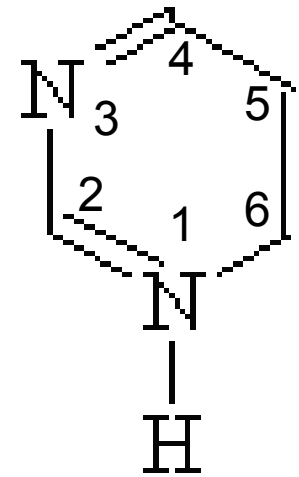
The nitrogenous bases

The nitrogenous bases that occur in nucleic acids are aromatic heterocyclic compounds derived from either **purine** or **pyrimidine**.



purine

A double ring (6 and 5 membered) structure



pyrimidine

A six membered ring structure



The nitrogenous bases

Purines

adenine

guanine

Pyrimidines

cytosine

uracil

thymine

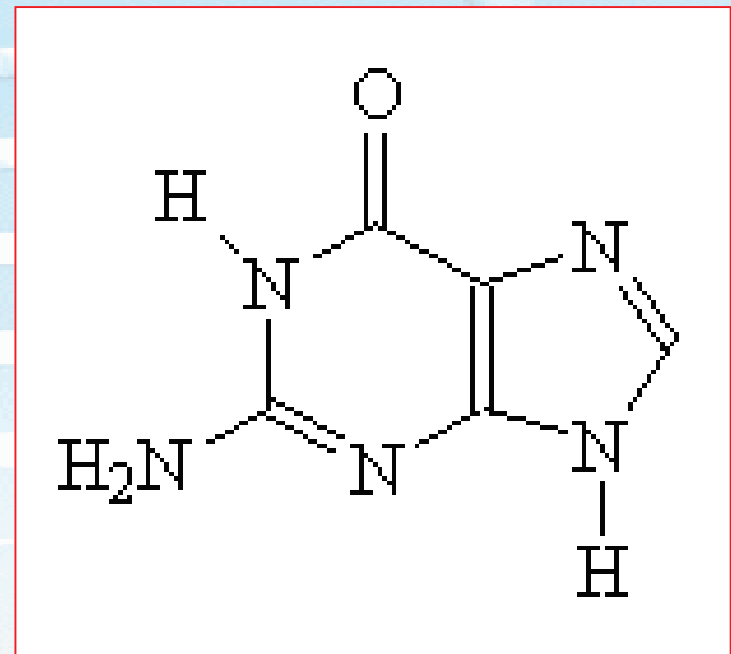
The purine bases **adenine** and **guanine** and the pyrimidine base **cytosine** are present in both **RNA** and **DNA**.

Uracil is only found in **RNA**.
Thymine is only found in **DNA**

The structure of purine bases

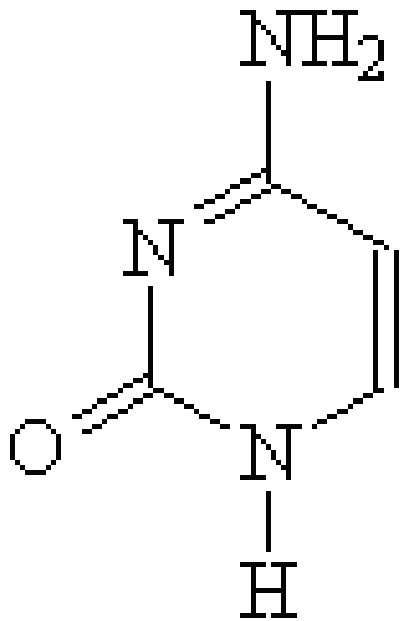


Adenine

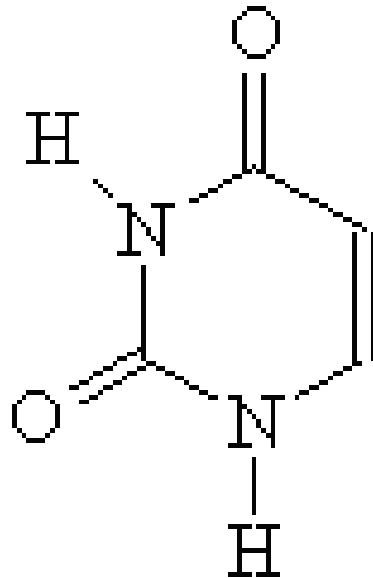


Guanine

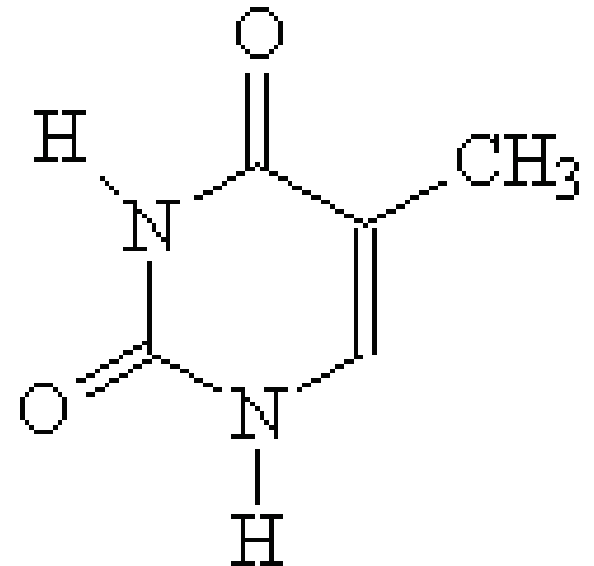
The structure of pyrimidine bases



cytosine



uracil

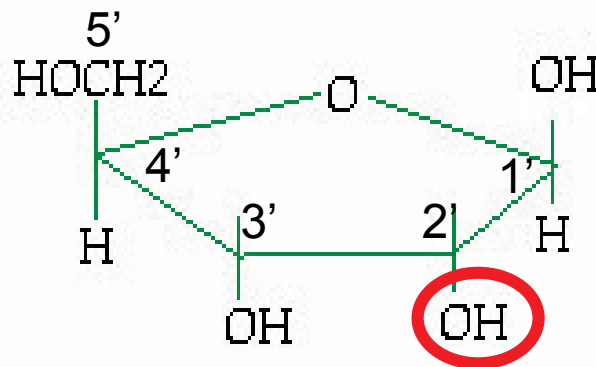


thymine

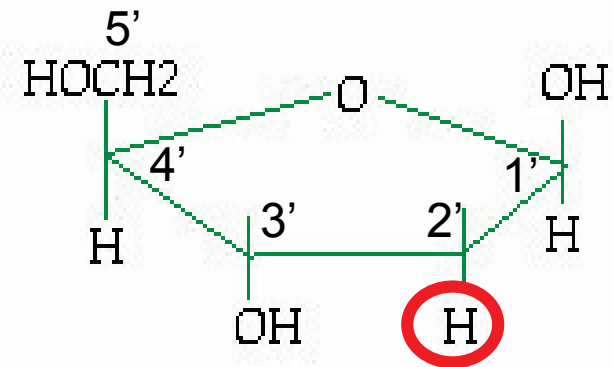
Sugars used

- Pentoses

ribose
used in RNA



2'- deoxyribose
used in DNA



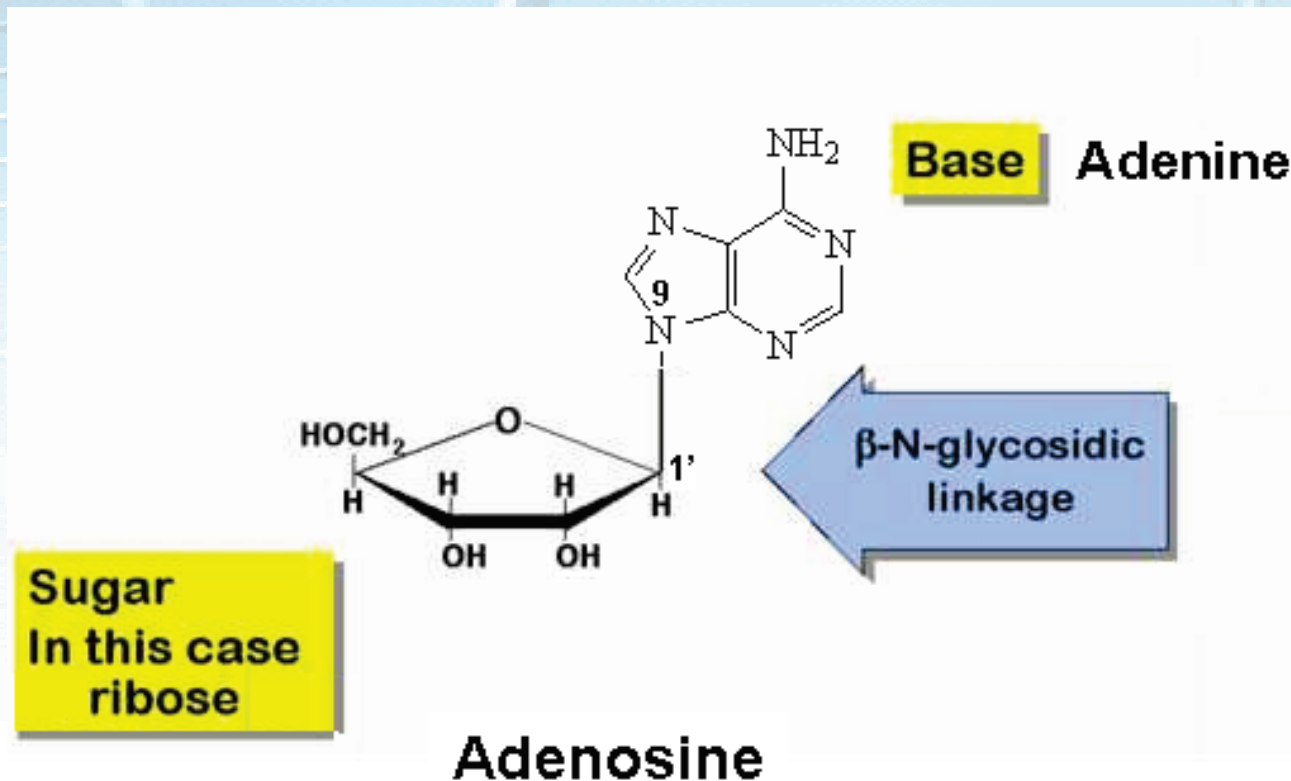
The "2'-deoxy-" notation means that there is no -OH group on the 2' carbon atom

Nucleoside

A sugar - base combination

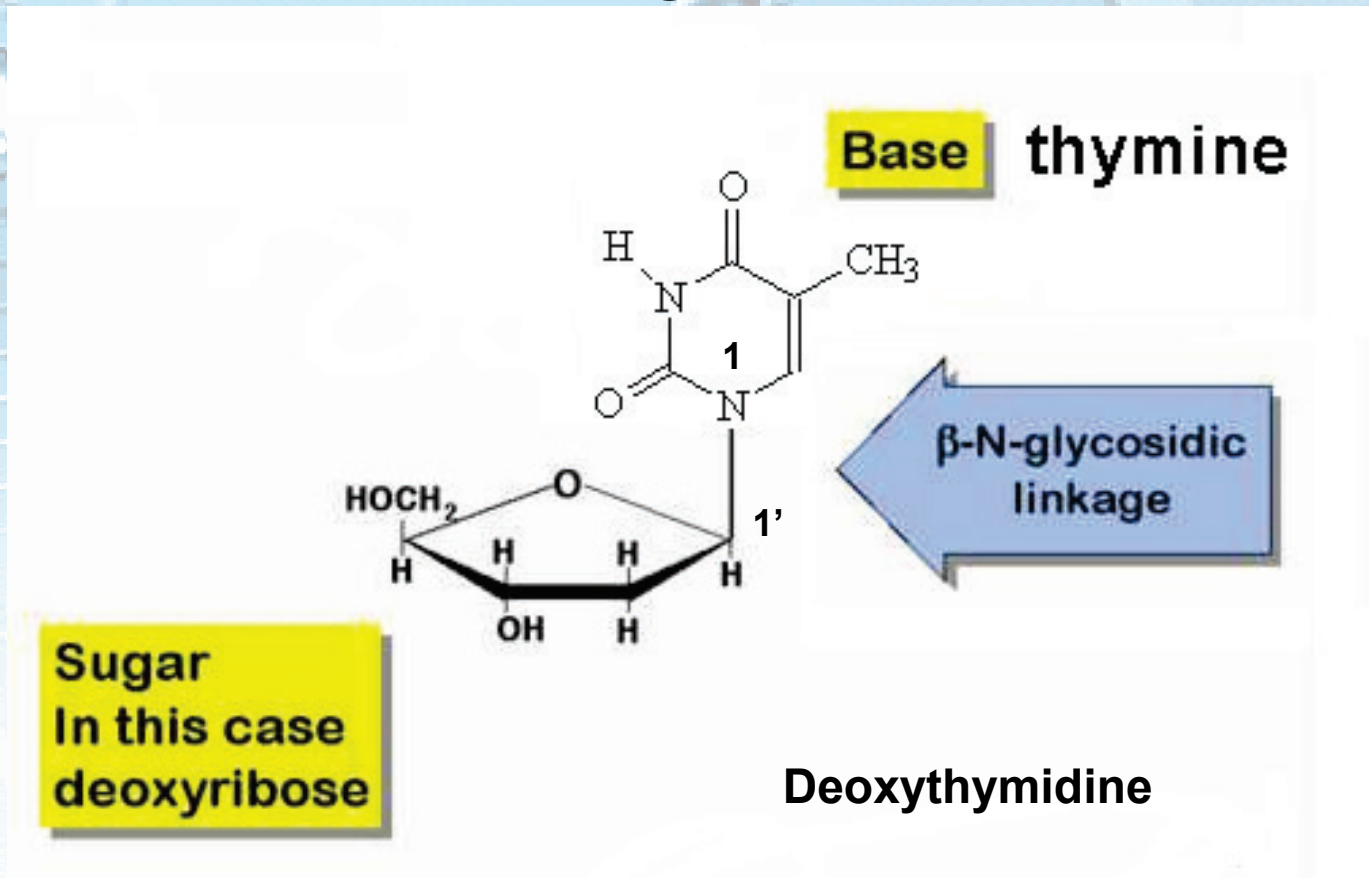
A **nucleoside** results from the linking of one of these 2 sugars with one of the purine- or pyrimidine-derived bases through an **N-glycosidic linkage**.

Purines bond to the C1' of the sugar at their N9 atoms



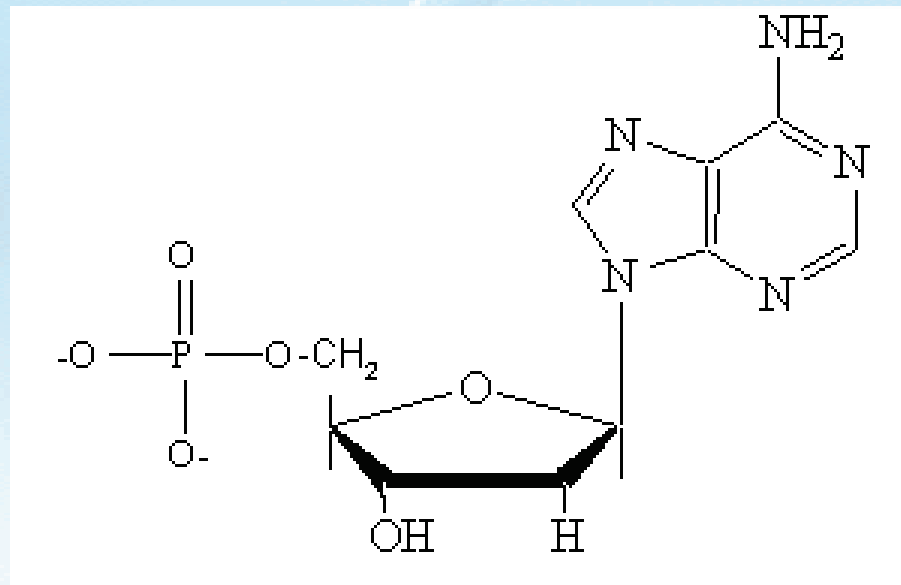
Nucleoside

Pyrimidines bond to the sugar C1' atom at their N1 atoms



Nucleotides

A nucleotide is a 5'-phosphate ester of a nucleoside.



deoxyadenosine monophosphate
(dAMP)

Nitrogenous base + pentose sugar + phosphate group(s)

The naming of the nucleosides and nucleotides

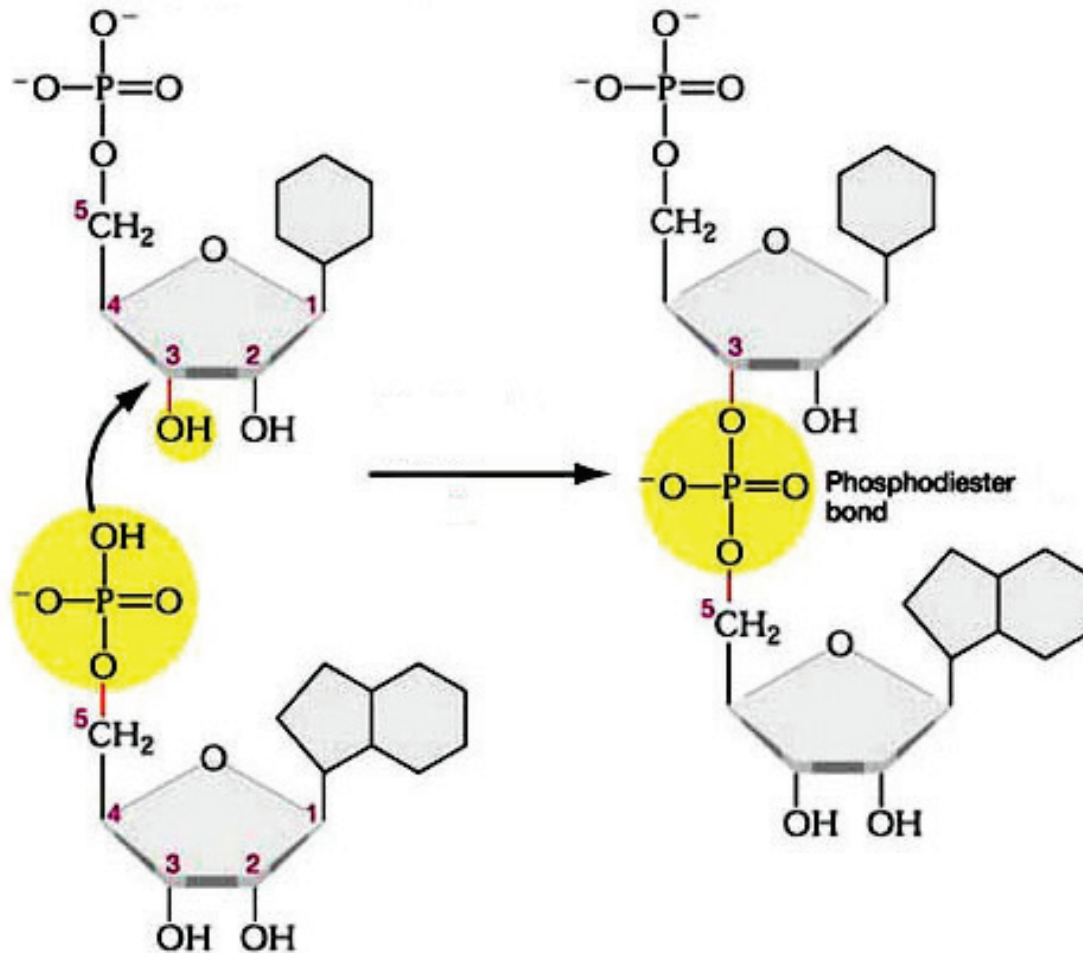
The purine nucleosides end in "***-sine***" :
adenosine and guanosine

The pyrimidine nucleosides end in "***-dine***" :
cytidine, uridine, deoxythymidine

To name the nucleotides, use the nucleoside name, followed by "mono-", "di-" or "triphosphate"

**adenosine monophosphate (AMP),
deoxythymidine diphosphate (dDTP),
guanosine triphosphate (GTP)**

In a nucleic acid chain, two nucleotides are linked by a 3'-5'-**phosphodiester bond**:

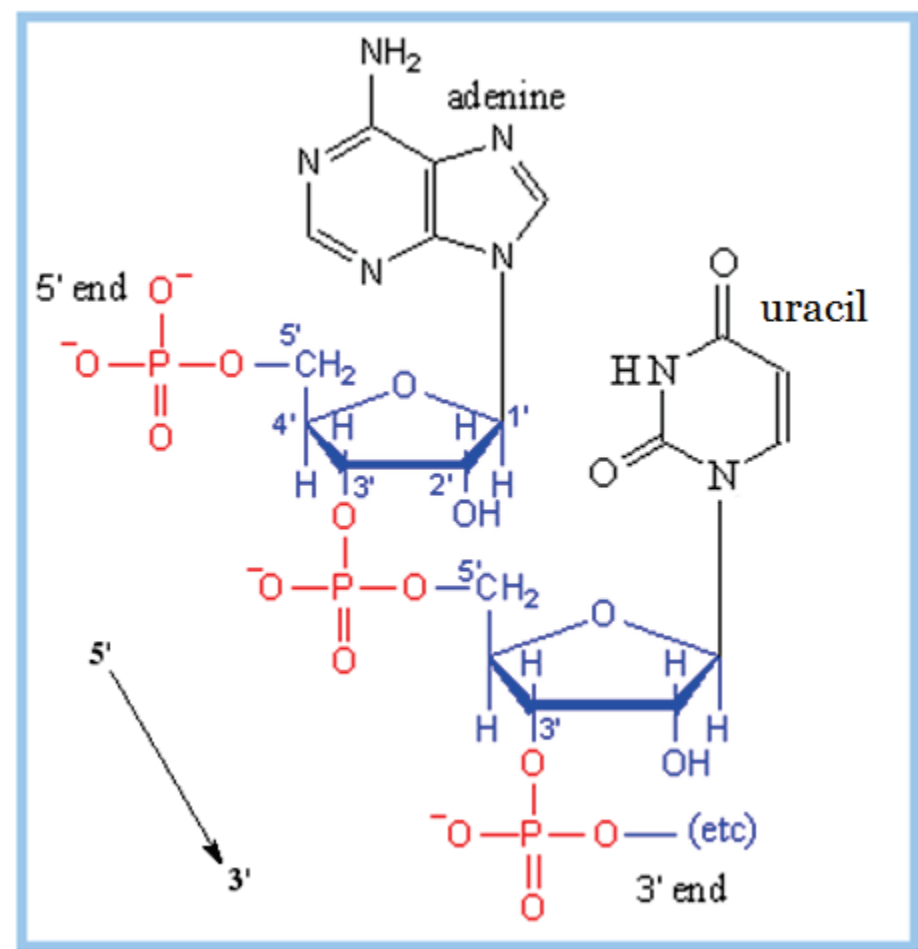


Phosphodiester linkages formation: the 5' phosphate of one nucleotide forms an ester linkage with the 3' hydroxyl of the adjacent nucleotide in the chain.

Primary structure

Nucleotides are link together by phosphodiester linkages to form a single strand

The **sequence** of nucleotides in the nucleic acid polymer is called **primary structure** of nucleic acid.



The single strand of nucleic acids have a **backbone of alternating phosphate and ribose** with **nitrogenous bases attached**.

A nucleic acid chain has orientation 5'-3': its 5' end contains a free phosphate group and 3' end contains a free hydroxyl group.

PRIMARY STRUCTURE

The sequence of nucleotide in the polynucleotide chain is called the **primary structure** of nucleic acids.

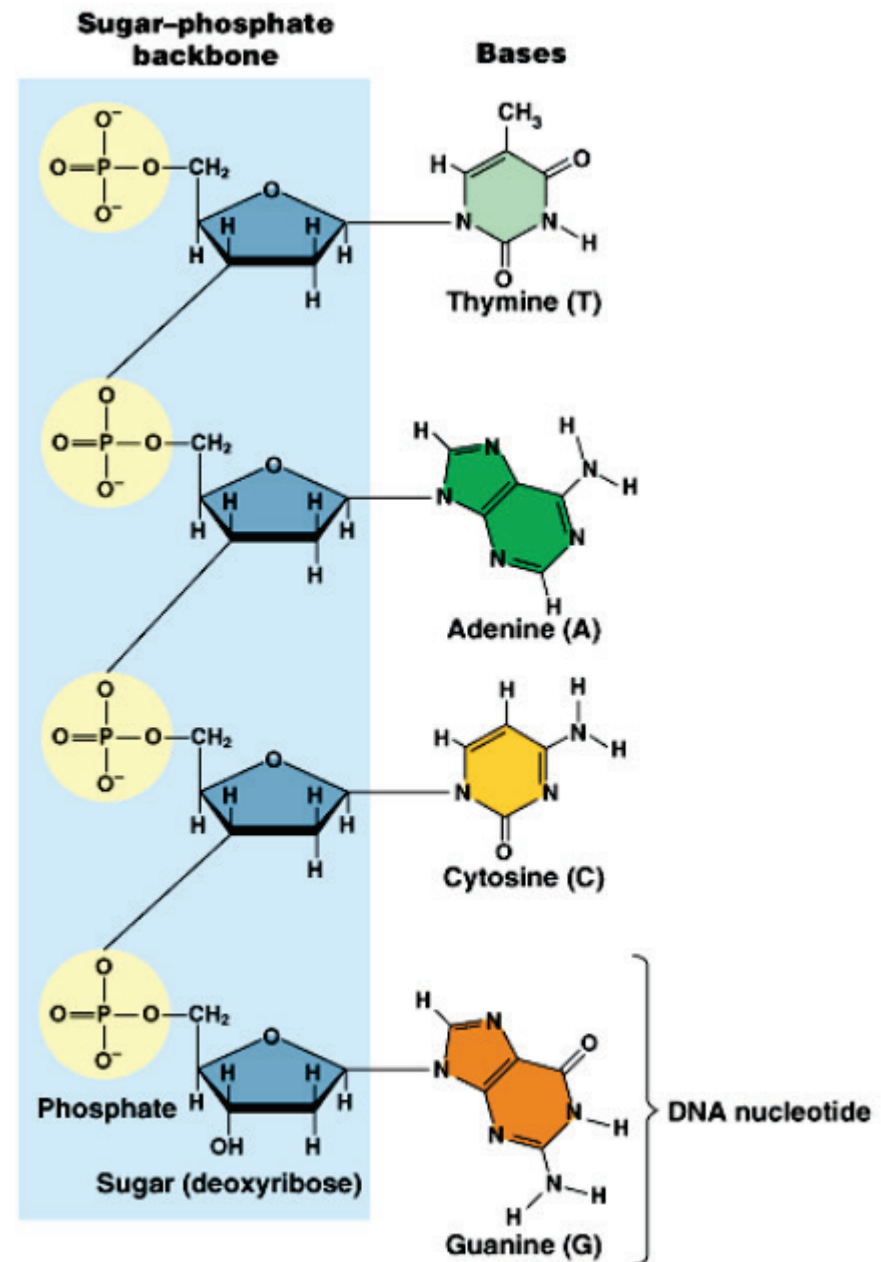
The differences between DNA and RNA primary structure:

1. nitrogenous bases composition:

in DNA – thymine, in RNA – uracil

2. pentose composition:

in DNA – deoxyribose, in RNA - ribose

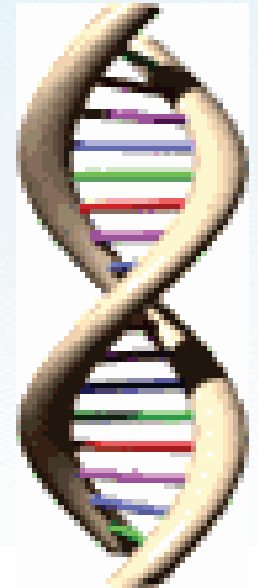


The secondary structure of DNA

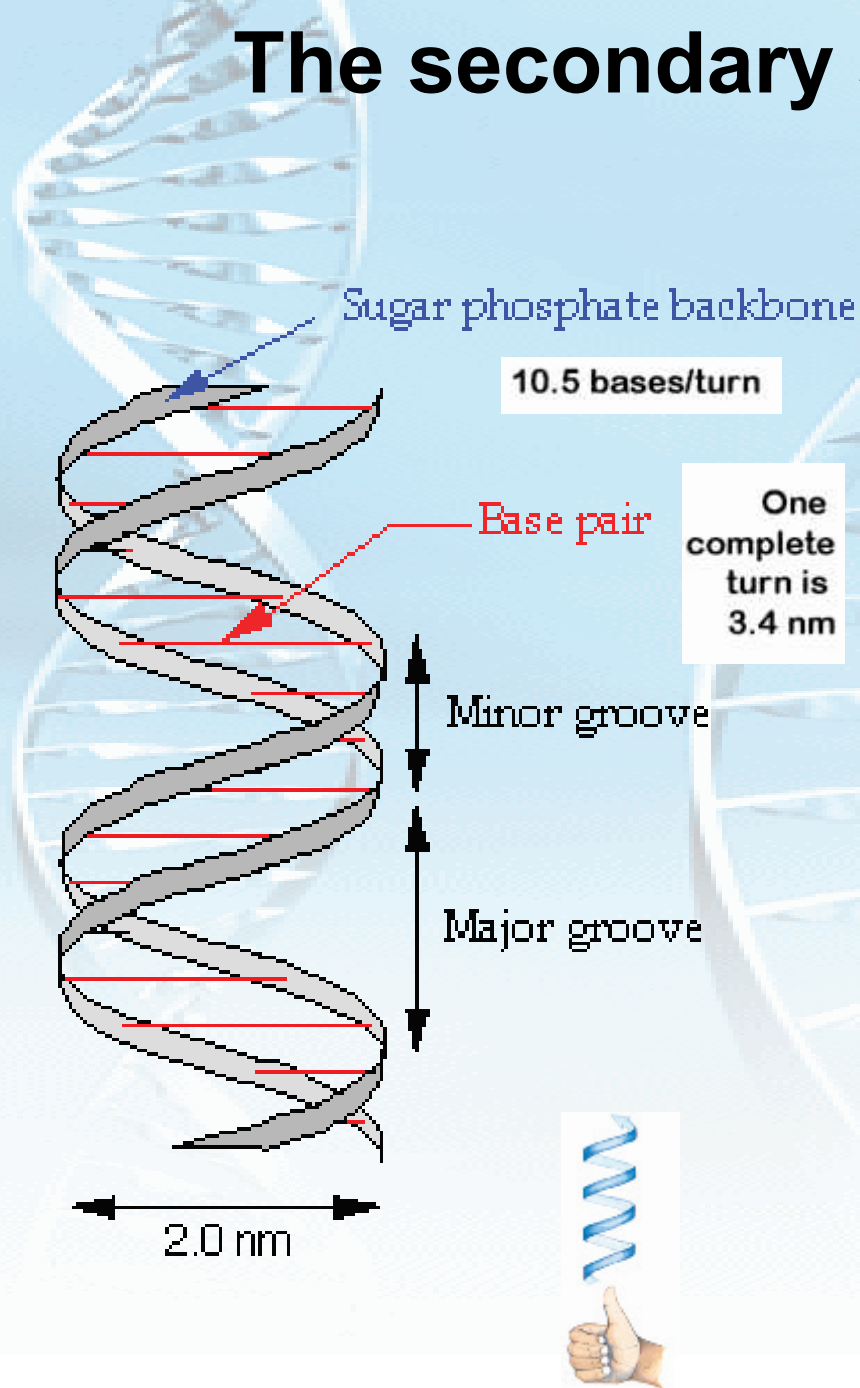
The DNA secondary structure is a double helix formed by 2 anti-parallel DNA strands bind together by hydrogen bonding between bases on opposite strands.

This model of secondary structure was proposed in 1953 by

Watson and Crick



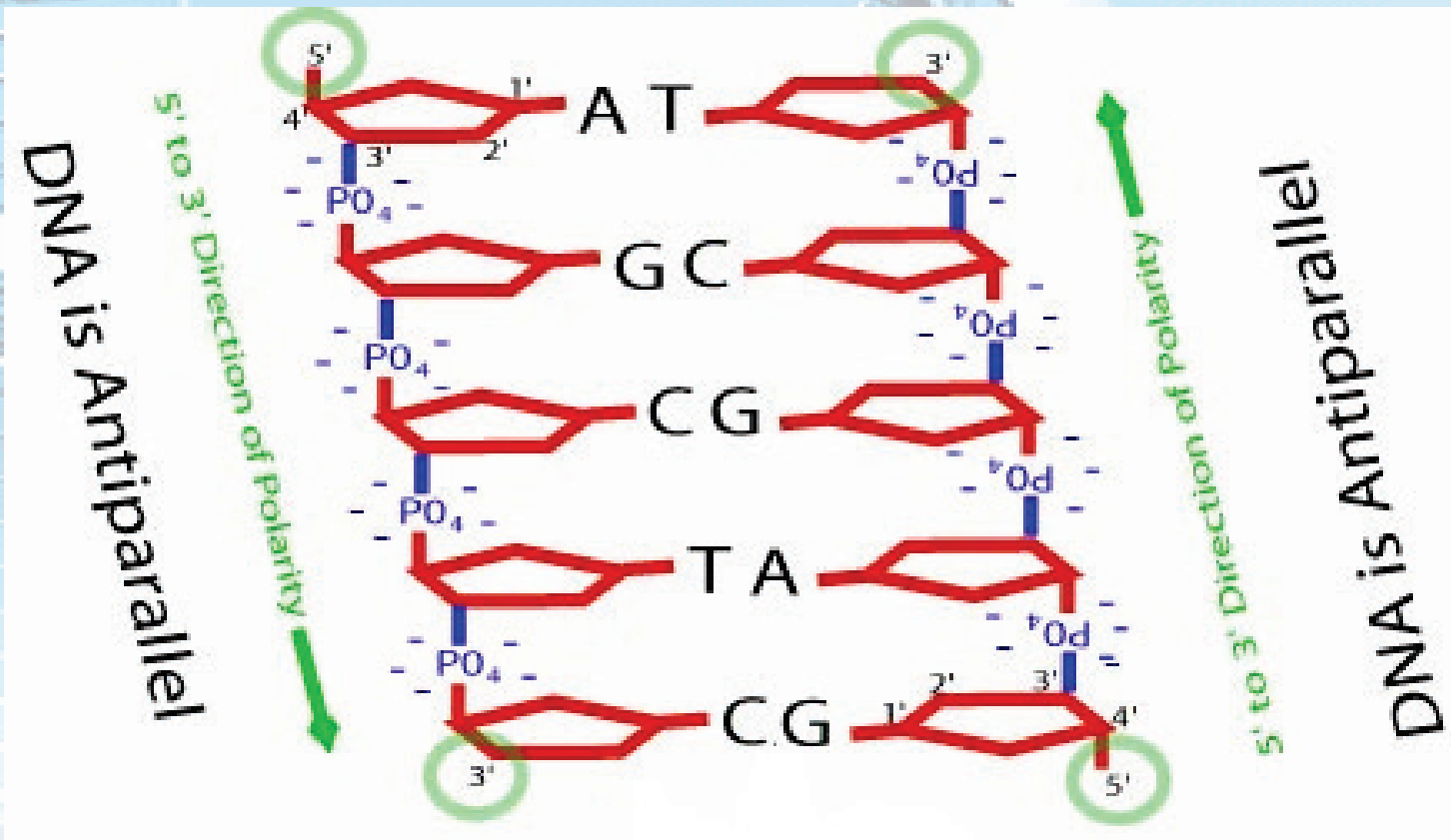
The secondary structure of DNA



Fundamental Properties of DNA secondary structure:

- **A right-handed double helix**
- **Two antiparallel and complimentary strands of deoxyribonucleic acid**
- **Hydrophilic polar external sugar-phosphate backbone**
- **Hydrophobic core of bases: Adenine, Thymine, Guanine, Cytosine**
- **a coil includes 10.5 base pairs and has a length of 3.4 nm**
- **width of the double helix - 2.0 nm**

Strands are antiparallel



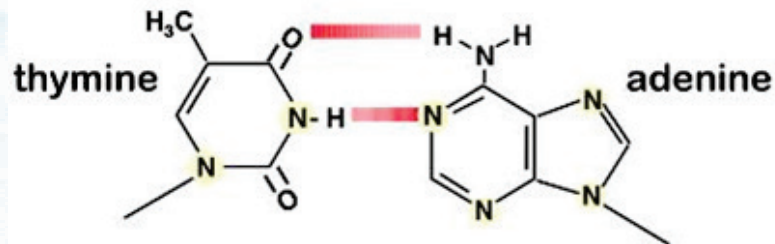
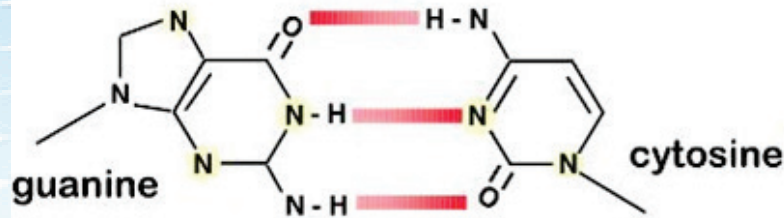
The two strands of DNA are arranged antiparallel to one another: one strand is aligned 5' to 3', while another strand is aligned 3' to 5'.

Strands are complementary

Pyrimidine and purine bases are located inside of the double helix in such a way that opposite a pyrimidine base of one chain is located a purine base of another chains and between them hydrogen bonds appear. These pairs are called **complementary** bases (T-A and C-G). Between adenine (A) and thymine (T) two hydrogen bonds appear, and between guanine (G) and cytosine – three:

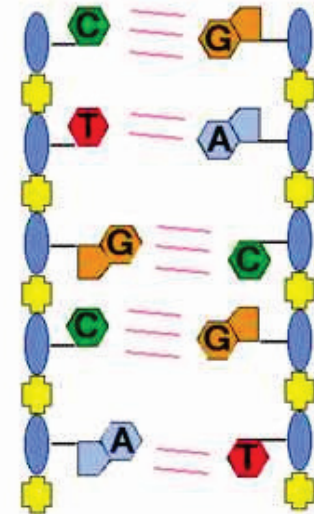


The G-C interaction is stronger (by about 30%) than A-T



Hydrogen bonds between complementary bases is one of the interaction forces that stabilize the double helix.

Hydrogen bonding

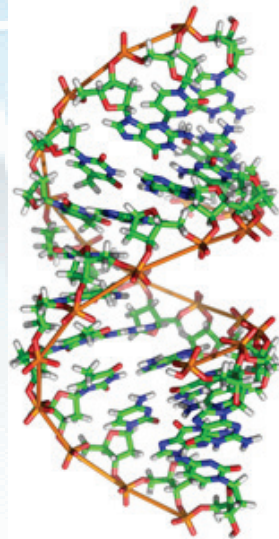


The original Watson and Crick model for the double helix, B-DNA, is one of several conformations.

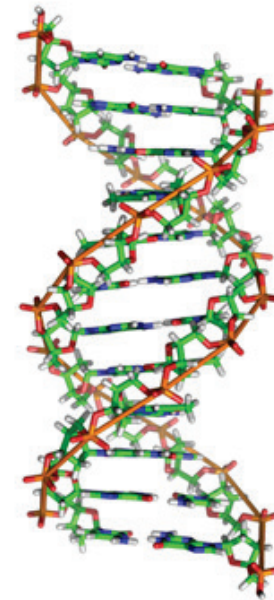
B-DNA - most stable form, predominating in physiological conditions. It has 10,5 base pairs per turn

A-DNA -occurs in DNA when dehydrated. It has 11 base pairs per turn.

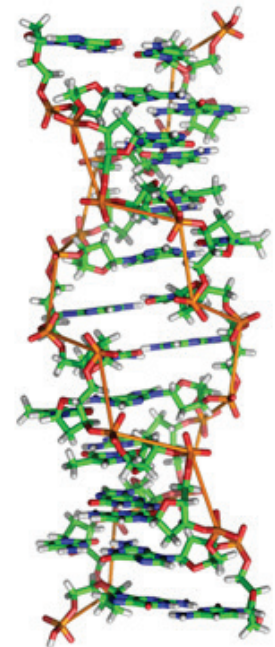
Z-DNA -Left handed helix with 12 base pairs per turn. It may play a role in regulation of gene expression



A-DNA



B-DNA

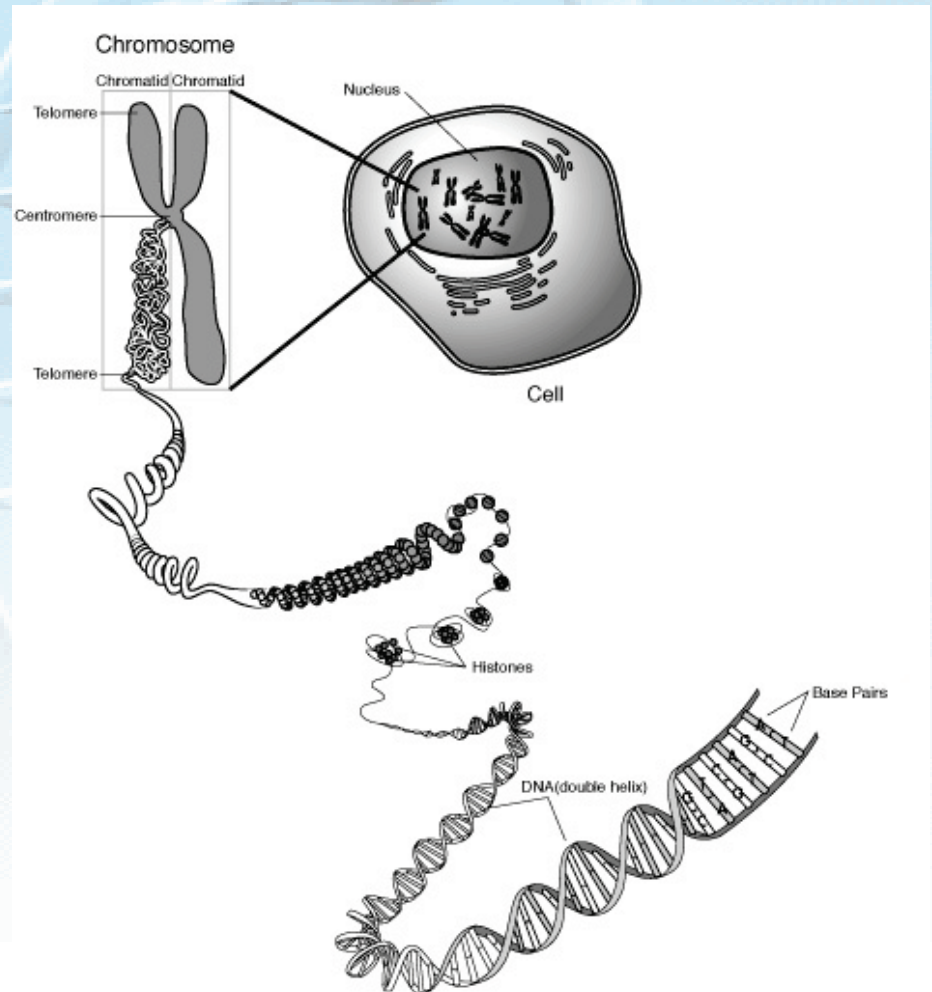


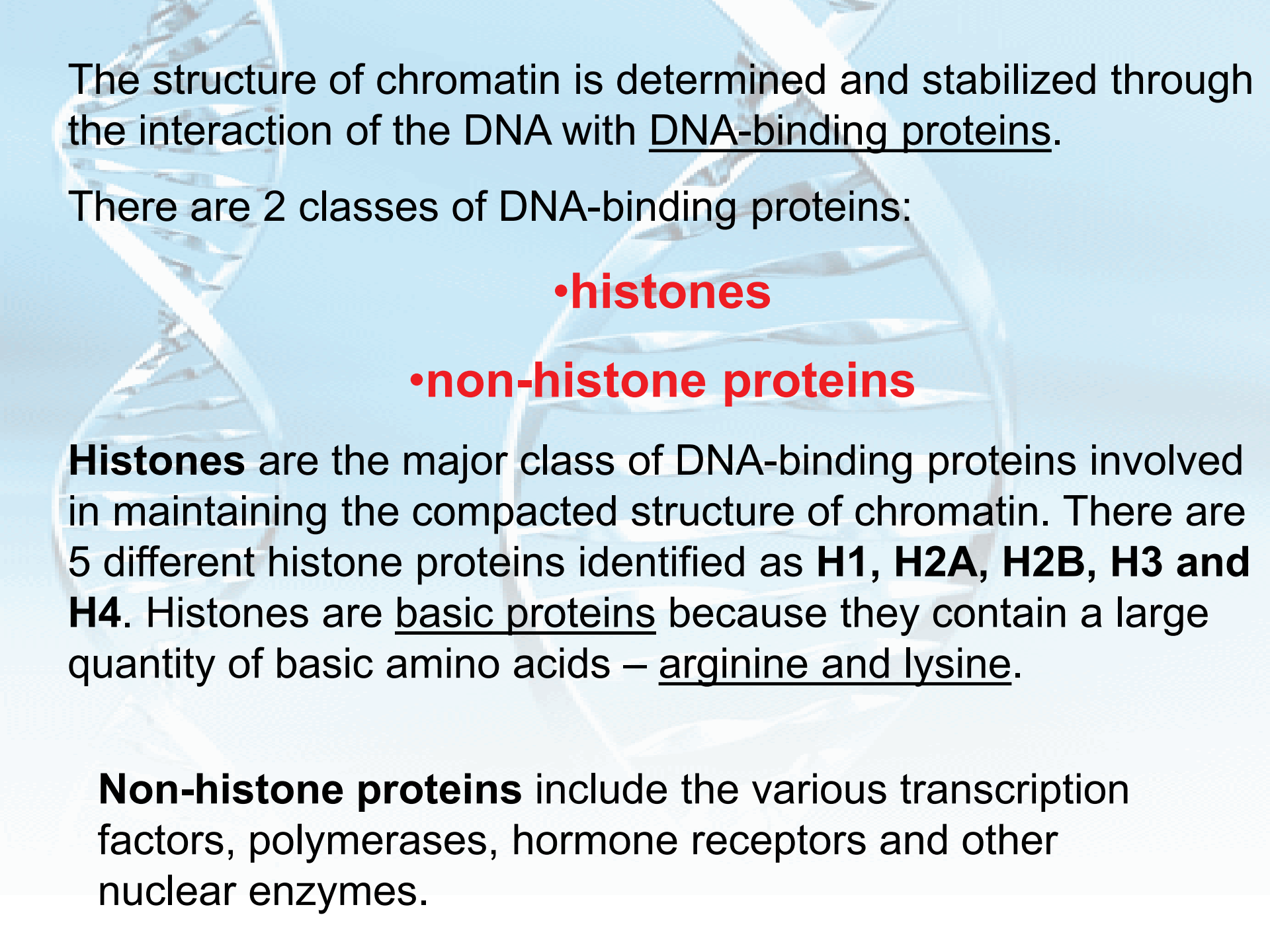
Z-DNA

The human genome contains about 3 billion nucleotide pairs organized as 23 chromosomes pairs. If uncoiled, the DNA contained in each chromosome would measure between 1.7 and 8.5 cm long. This is too long to fit into a cell.

DNA must become very compact to fit into the nucleus.

DNA has several level of compactization to form chromatin.





The structure of chromatin is determined and stabilized through the interaction of the DNA with DNA-binding proteins.

There are 2 classes of DNA-binding proteins:

- **histones**

- **non-histone proteins**

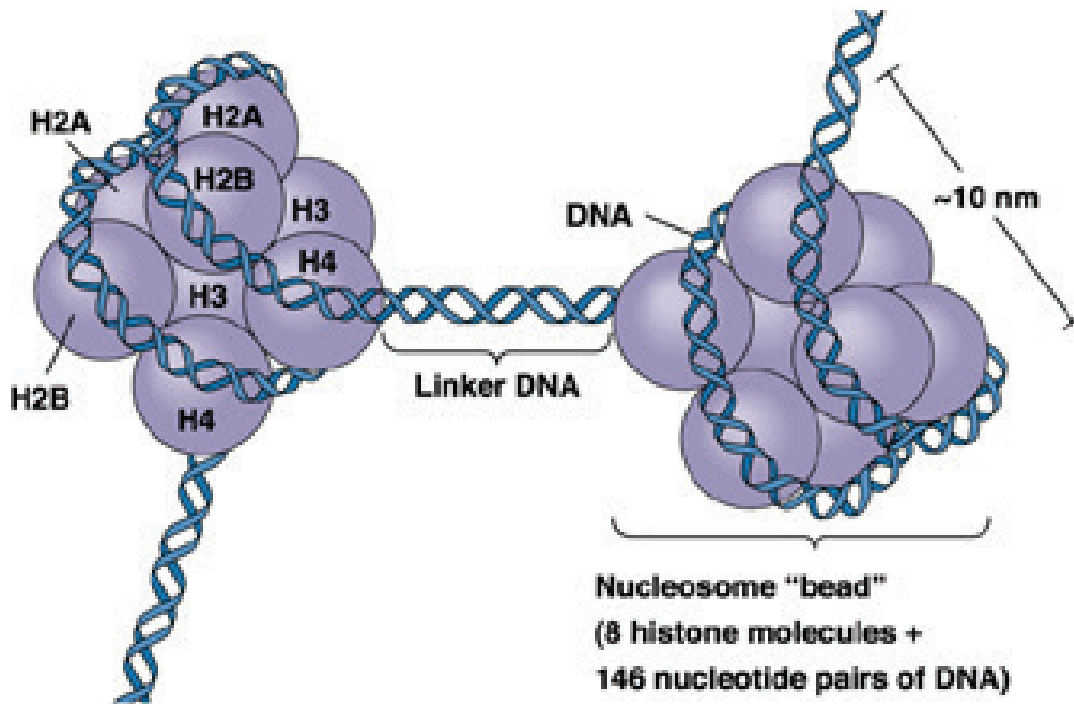
Histones are the major class of DNA-binding proteins involved in maintaining the compacted structure of chromatin. There are 5 different histone proteins identified as **H1, H2A, H2B, H3 and H4**. Histones are basic proteins because they contain a large quantity of basic amino acids – arginine and lysine.

Non-histone proteins include the various transcription factors, polymerases, hormone receptors and other nuclear enzymes.

Tertiary structure of DNA

The binding of DNA by the histones generates a structure called the **nucleosome**.

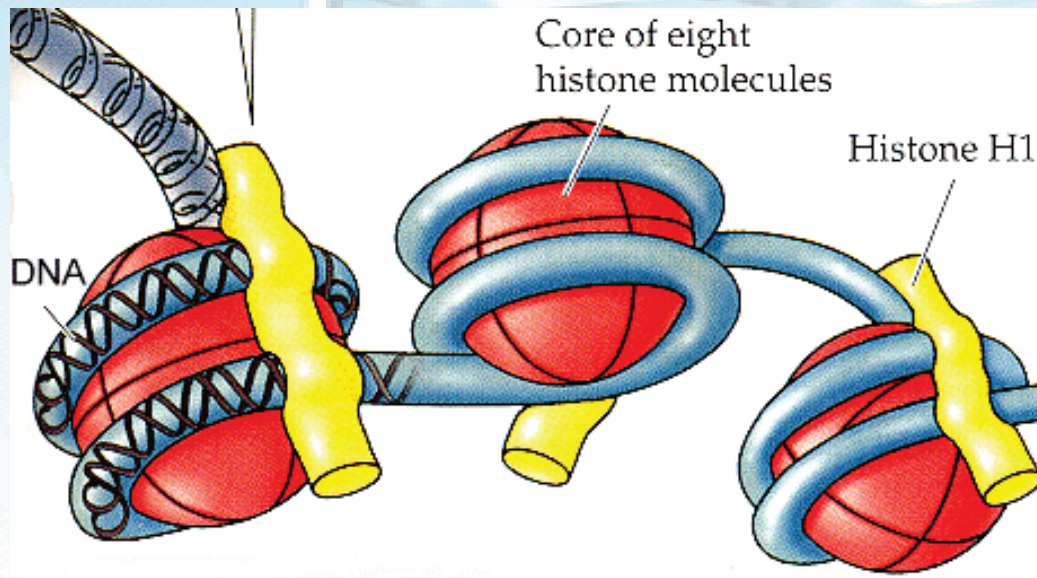
Nucleosome is a subunit of chromatin composed of a short length of DNA (**146 basepairs** of superhelical DNA) wrapped around a **core** of histone proteins.



The nucleosome **core** consists of 8 histone proteins - **H2A, H2B, H3 and H4** - two subunits of each, forming a histone octamer.

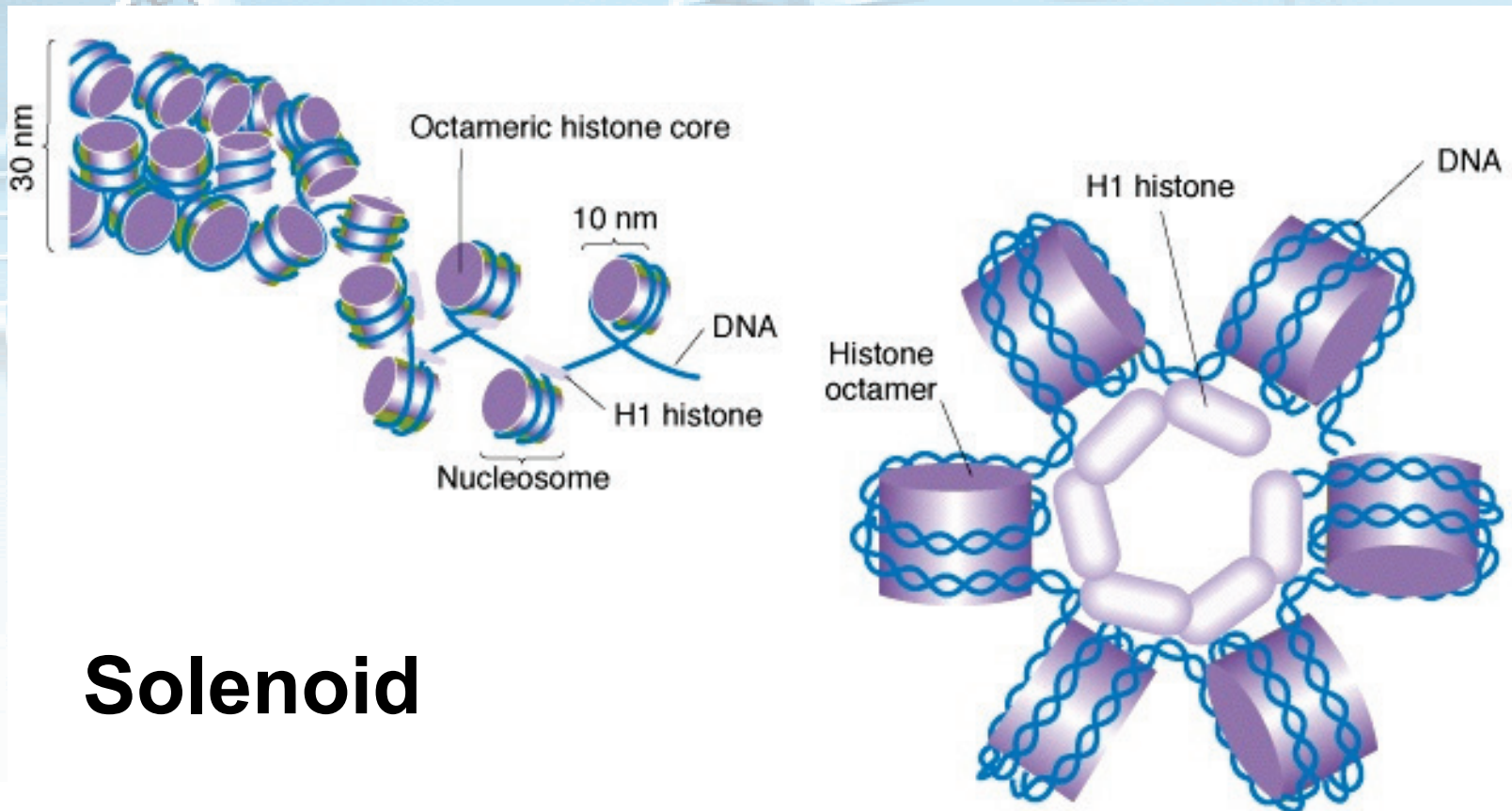
Tertiary structure of DNA

Histone H1 occupies the internucleosomal DNA (linker DNA) and is identified as the **linker histone**. The linker DNA between each nucleosome can vary from 20 to more than 200 basepairs.

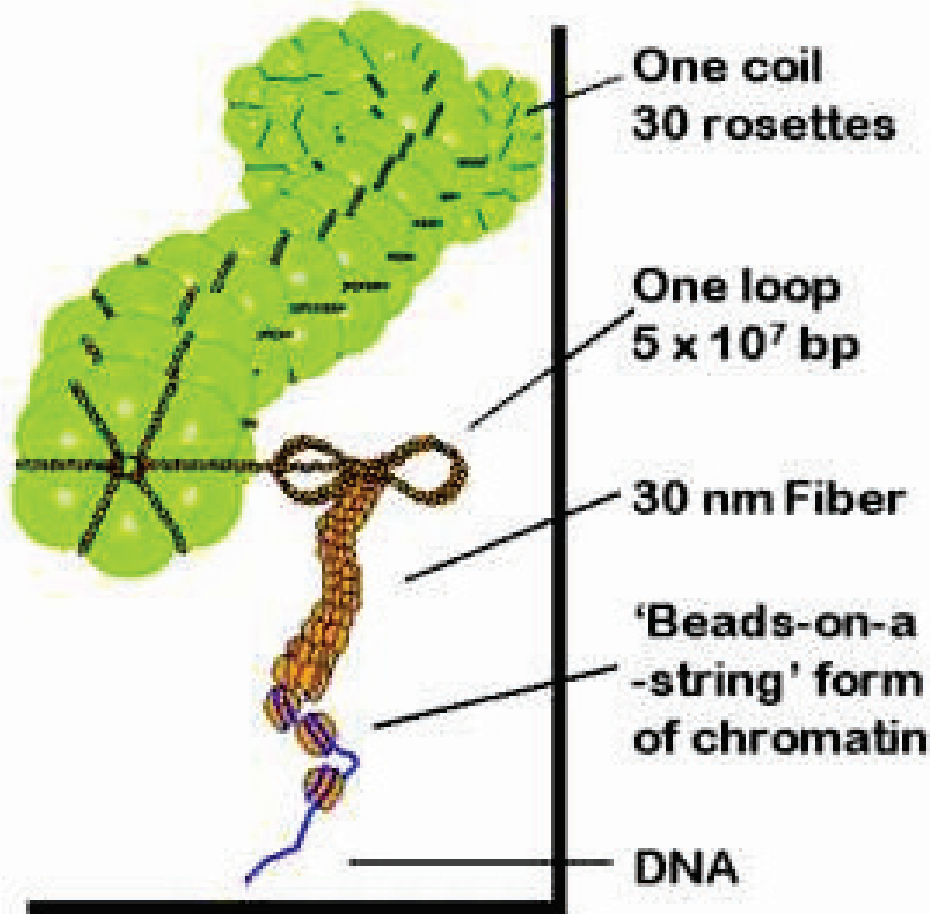


The nucleosomes, which at this point resemble beads on a string, are further compacted into a helical shape, called a **solenoid**.

The **solenoid** defines the packing of DNA as a **30 nm fiber** of chromatine and results from the helical winding of nucleosome strands.



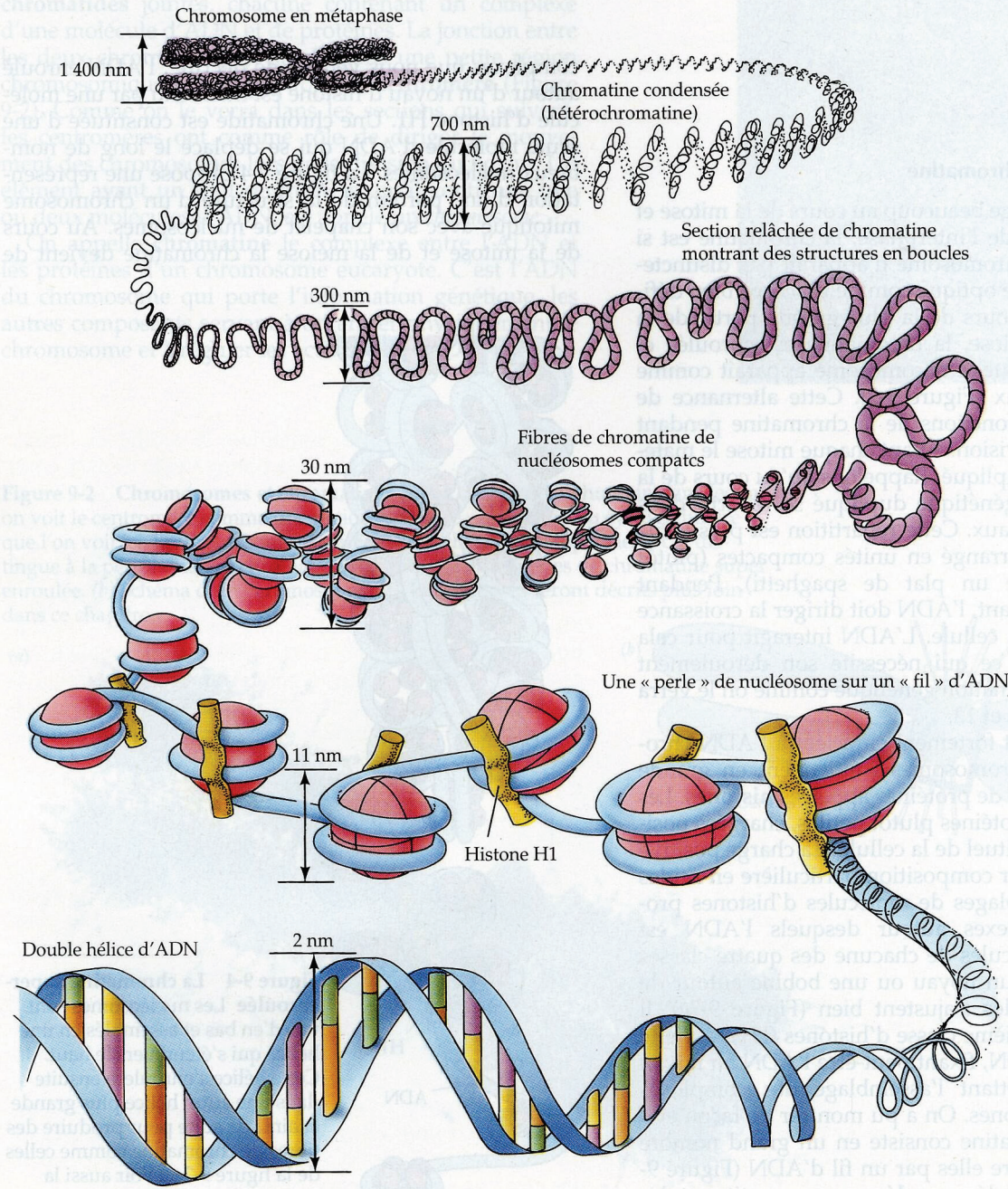
Coiling of DNA



With more packing, solenoids are able to become increasingly more packed, forming chromosomes.

Solenoids (30 nm fibers) coil around each other to form **a loop**, followed by **a rosette** (consisting of six connected loops), then **a coil** (consisting of 30 rosettes).

Figure 9-5 Niveaux d'empaqueté de l'ADN Schéma montrant comment l'ADN est « empaqueté » dans un chromosome en métaphase.



And at last,
two chromatids.
The end result is the
metaphase
chromosome.

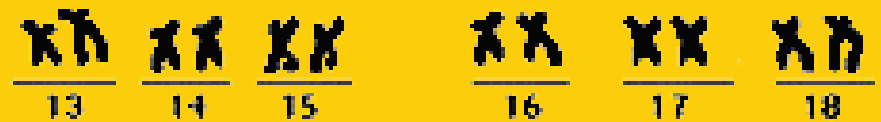
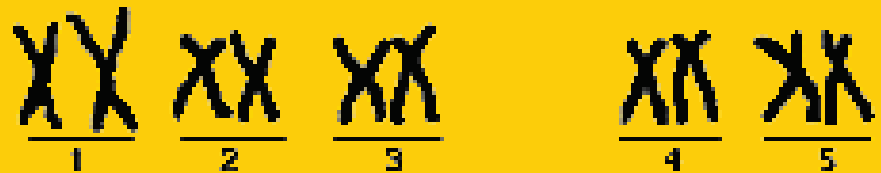
The completely
condensed
chromatin has a
diameter of up to 600
nm.

Human chromosomes!

centromere



chromatid



b

RNA Structure and function

There are 3 types of RNA:

- rRNA (ribosome RNA)
- tRNA (transfer RNA)
- mRNA (messenger RNA)

The role of RNA :

- **as a structural molecule (rRNA),**
- **as an information transfer molecule (mRNA),**
- **as an information decoding molecule (tRNA)**

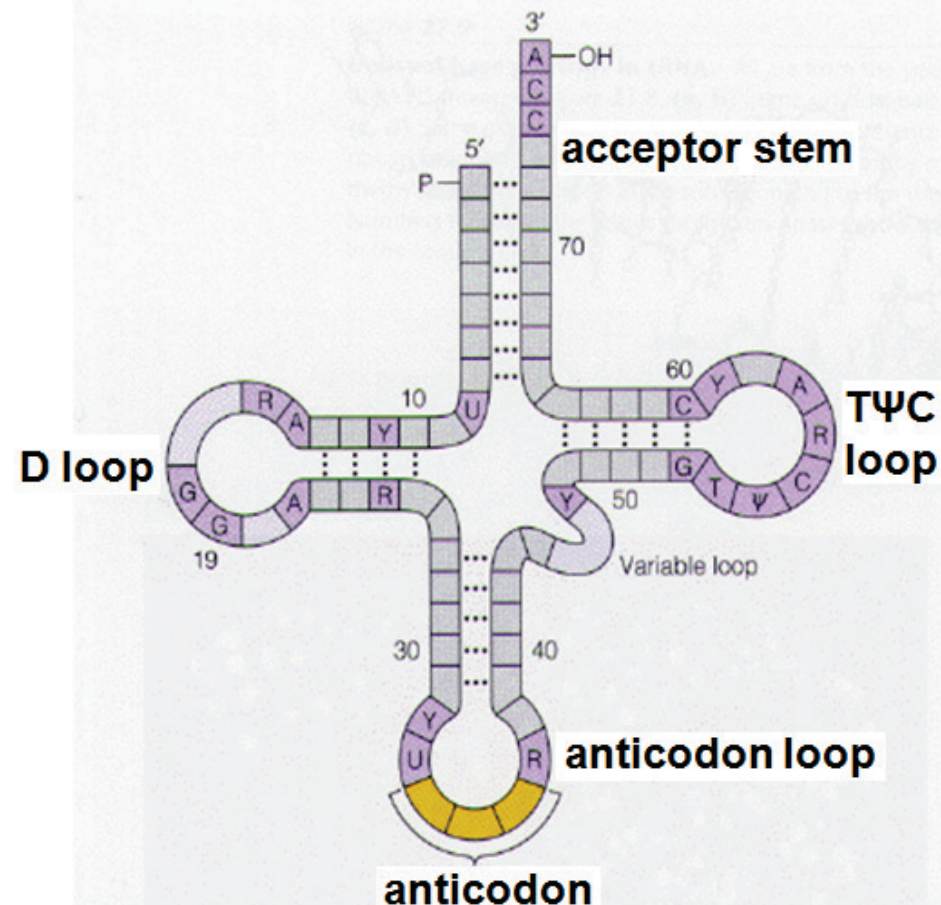
The structural, informational transfer and information adaptor roles of RNA are all involved in decoding the information carried by DNA

tRNA STRUCTURE

- tRNAs are the carriers of the 20 amino acids to the ribosomes where protein synthesis takes place. Each of the 20 amino acids has at least one specific tRNA molecule.
- tRNA - consists of 74-93 nucleotides;
- tRNA - contains some modified purine and pyrimidine nitrogenous bases (minor bases) eg.: dihydrouracil and pseudo uridine);

tRNA consist of:

- acceptor stem
- D-loop (dihydrouridilic)
- TΨC-loop (pseudouridine)
- anticodon loop.

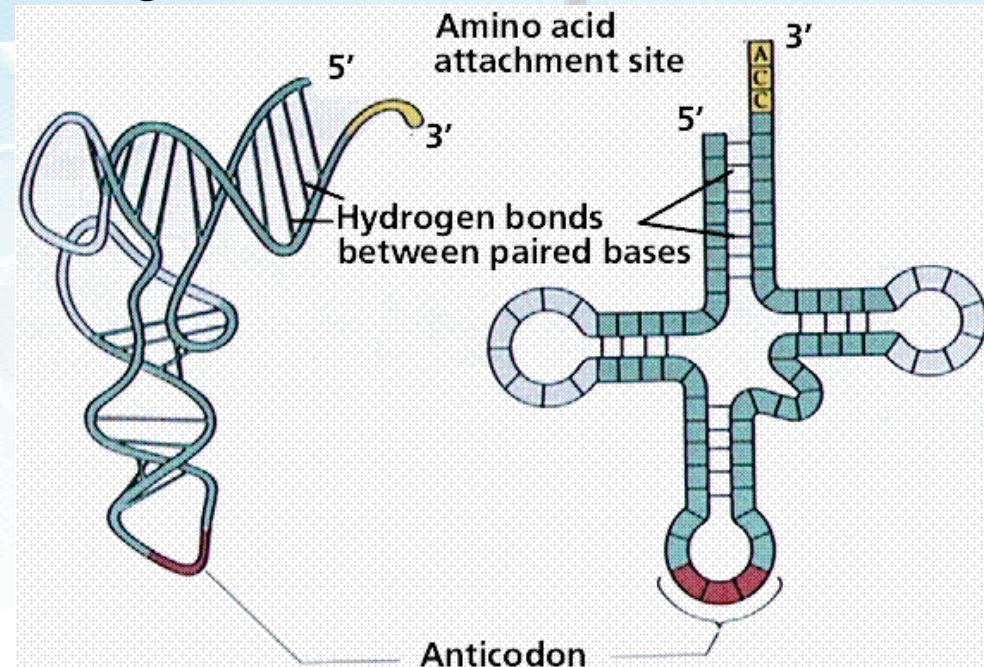


The acceptor stem is the site at which a specific amino acid is attached. **The 5' end** of acceptor stem is phosphorylated (usually phosphorylated G). At **the 3'-end** a sequence **CCA** is located (**CCA-terminus sequence**) that has a free 3'-OH group, where the activated amino acid is attached.

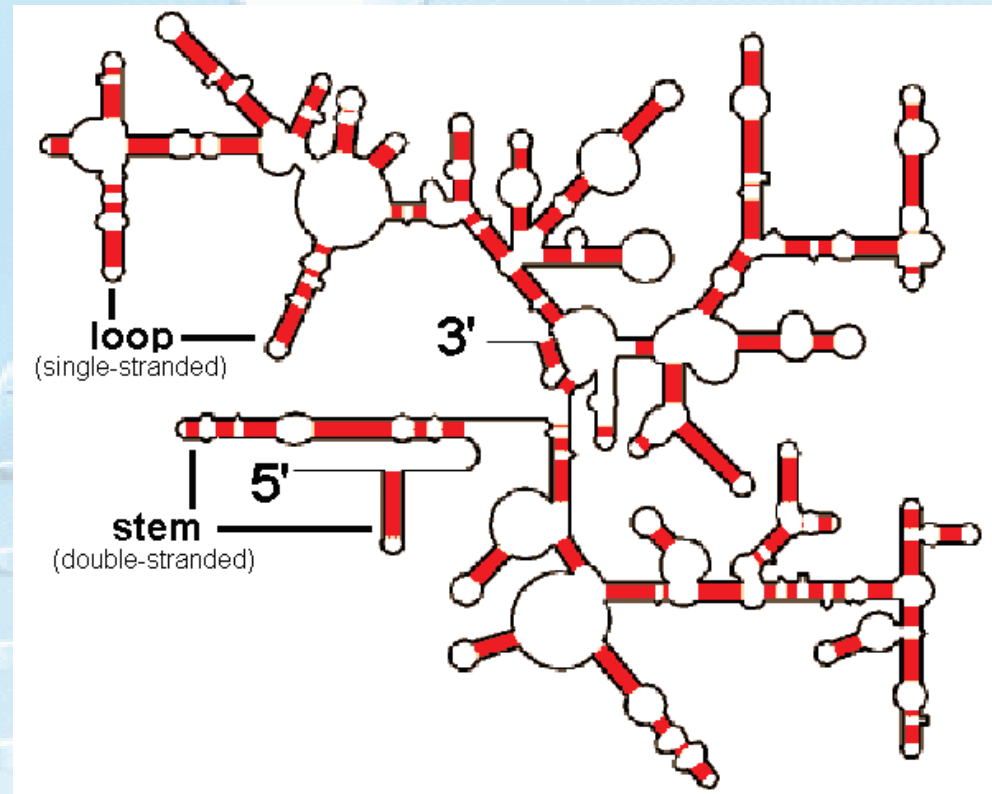
The anticodon reads the information in a mRNA sequence by base pairing.

D-loop (dihydrouridilic) - binds the aminoacyl-tRNA synthetase

TΨC-loop (pseudouridine)- interacts with ribosome



rRNA



Ribosomal RNA (rRNA) is a component of the ribosomes, the protein synthetic factories in the cell.

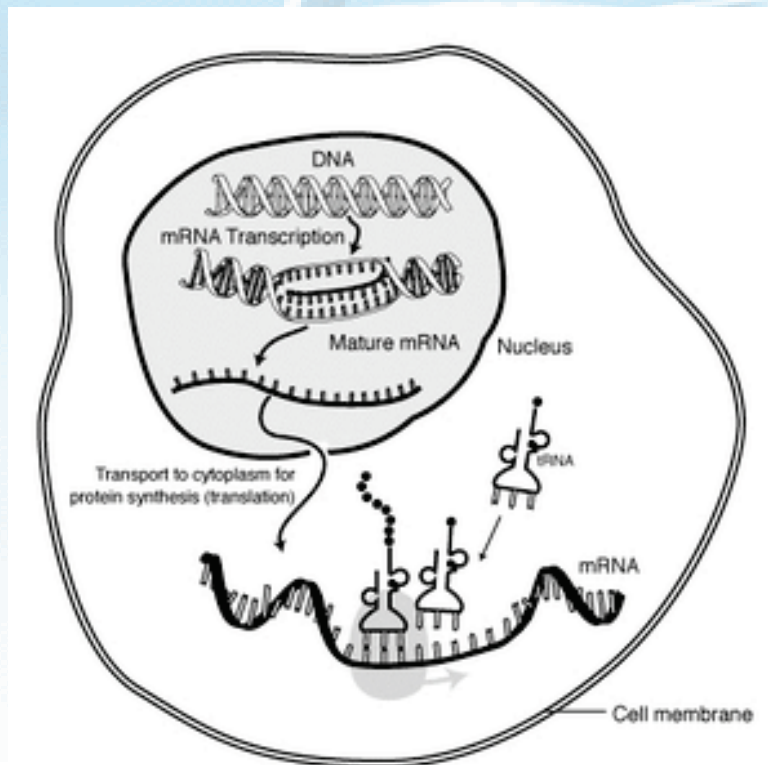
Eukaryotic ribosomes contain four different rRNA molecules: **18 S, 5,8 S, 28 S, and 5 S RNA.**

rRNA molecules combine with the ribosomal proteins to form **40 S and 60 S ribosomal subunits.**

mRNA

Messenger or mRNA is a copy of the information carried by a gene on the DNA.

The role of mRNA is to move the information contained in DNA to the translation machinery.



mRNA



mRNA is heterogeneous in size and sequence.

It always has a **5' cap** composed of a 5' to 5' triphosphate linkage between two modified nucleotides: a 7-methylguanosine and a 2' O-methyl purine. This cap serves to identify this RNA molecule as an mRNA to the translational machinery.

In addition, most mRNA molecules contain a **poly-Adenosine tail** at the 3' end.

Both the 5' cap and the 3' tail are added after the RNA is transcribed and contribute to the stability of the mRNA in the cell.