Biochemistry of Nucleic acids

3rd stage

Anbar University-College of Pharmacy-Clinical Laboratory Sciences Department
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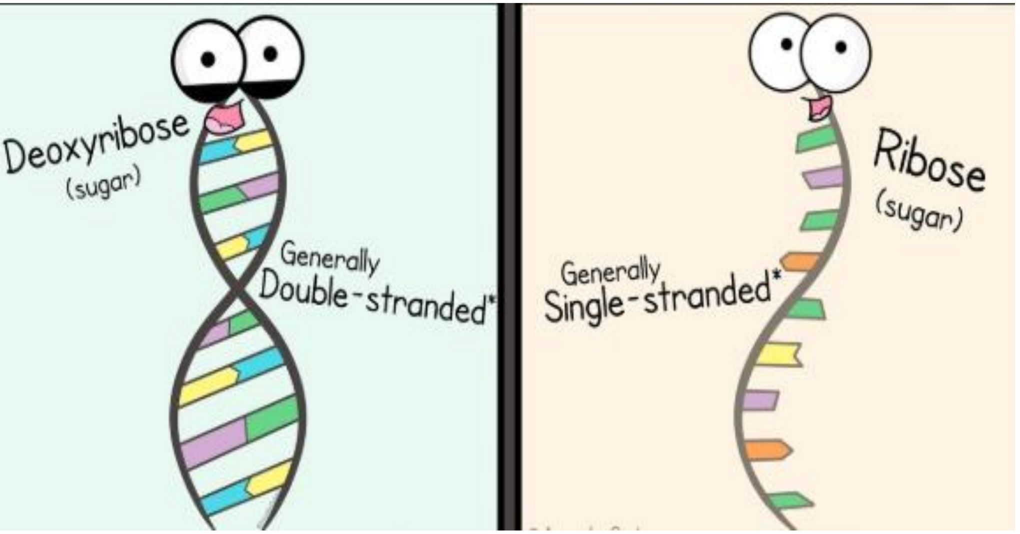


References

- ✓ Harper's Illustrated biochemistry, 26th edition
- ✓ Biochemistry – Berg, Tymoczko and Stryer, 6th edition
- ✓ Lippincott's Illustrated Reviews: Biochemistry 5th edition

Learning outcomes

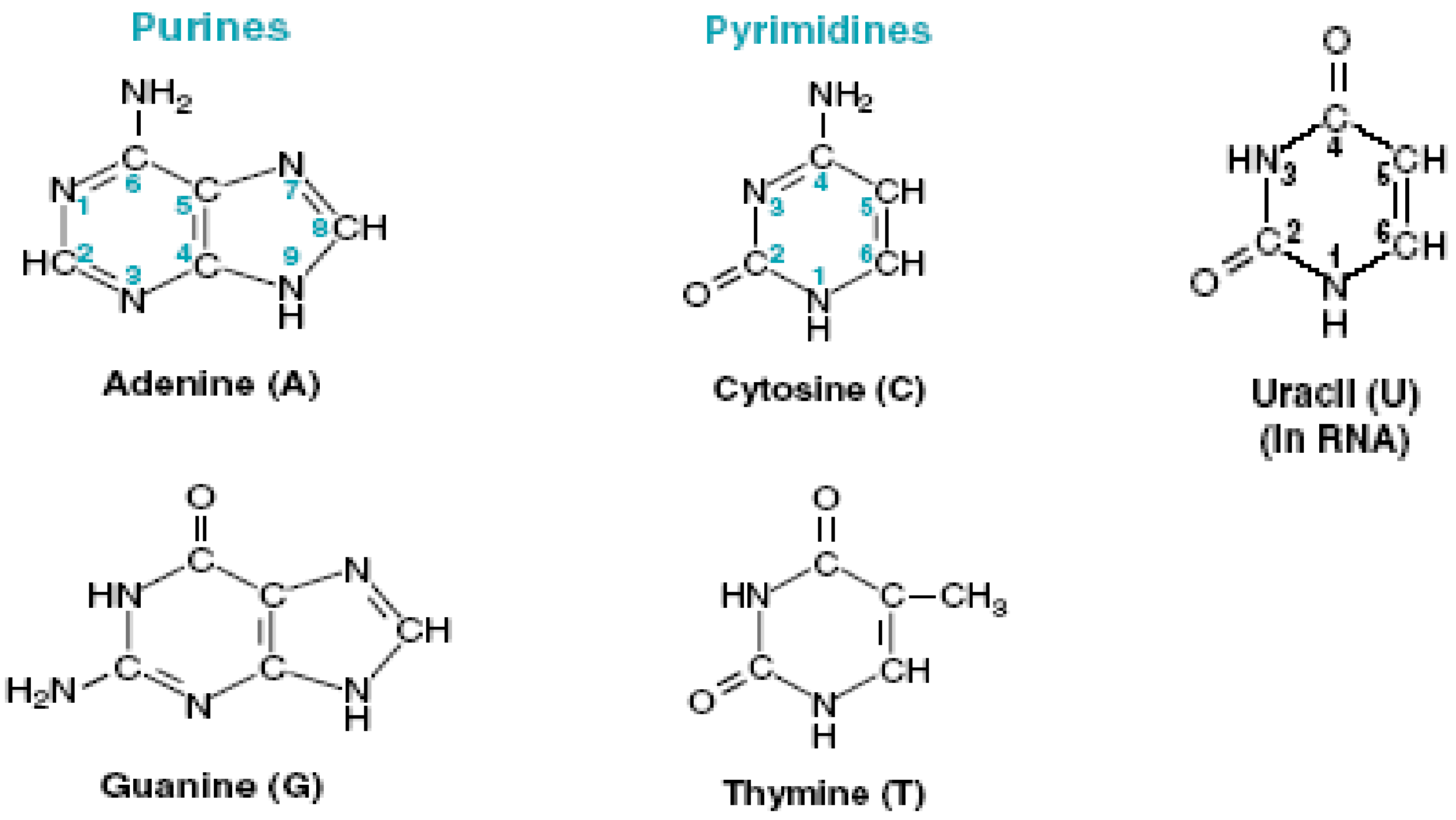
By the end of this lecture you will be able:

- To know the formation of Nucleic acids
- To know the differences between the Nucleosides and Nucleotides
- To understand the structural organisation of Nucleic acids
- To appreciate the various functions of Nucleic acids

- **Nucleic acids** are required for the storage and expression of genetic information.
- There are two chemically distinct types of Nucleic acids: Deoxyribonucleic acid (**DNA**) and ribonucleic acid (**RNA**).
- **DNA**: the storehouse of genetic information, is present not only in the nucleus of eukaryotic organisms, but also in mitochondria and the chloroplasts of the plants. The genetic information found in DNA is copied and transmitted to daughter cells through DNA replication.
- **Nucleotides**: are the monomeric units of the nucleic acids, DNA and RNA.
- Each **nucleotide** is consist of a **heterocyclic nitrogenous base**, a **sugar**, and one, two or three **phosphate**.
- **DNA** contains the **purine bases adenine (A) and guanine (G).** Also **the pyrimidine bases cytosine (C) and thymine (T)**, the sugar is **deoxyribose**.
- **RNA** contains **A, G**, and **C**, but it has uracil (**U**) instead of **T**, the sugar is **ribose**.

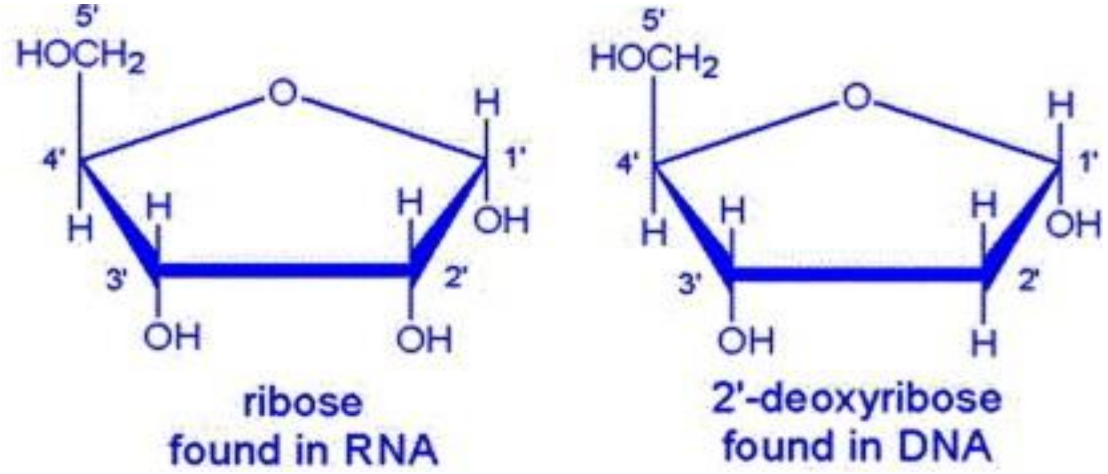
Bases present in DNA and RNA

- Both **DNA** and **RNA** contain the same purine bases: Adenine (**A**) and Guanine (**G**). Both DNA and RNA contain the pyrimidine cytosine (**C**), but they differ in their second pyrimidine base : DNA contains thymine (**T**) , while RNA contains uracil (**U**).
- The atoms in the rings of the bases are numbered **1 to 6 in pyrimidines** and **1 to 9 in purines.**
- Numbering of bases is unprimed



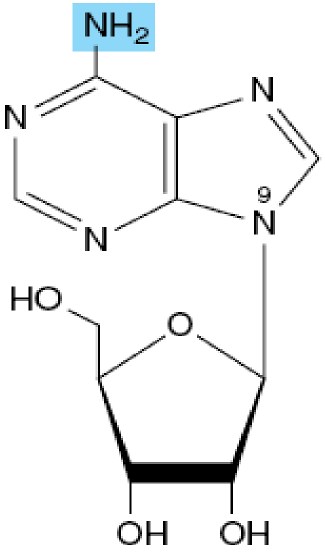
Sugars present in DNA and RNA

- Pentoses (5-C sugars)
- Numbering of sugars is primed

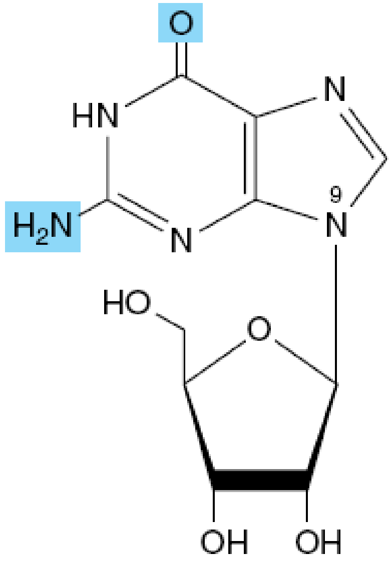


Nucleosides

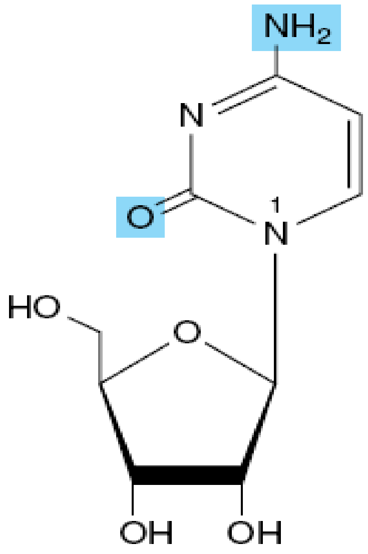
- Result from linking one of the sugars with a purine or pyrimidine base through an N-glycosidic bond
- **purines** are bonded to **C1** of the sugar at their **N9** atoms.
- **pyrimidines** are bonded to **C1** of the sugar at their **N1** atoms.
- If the sugar is D-ribose, a **ribonucleoside** is produced , if the sugar is 2-deoxyribose a **deoxyribonucleoside** is produced.
- In **DNA**: Deoxyadenosine, Deoxyguanosine, Deoxycytidine, and Deoxthymidine
- In **RNA**: Adenosine, Guanosine, Cytidine, and Uridine



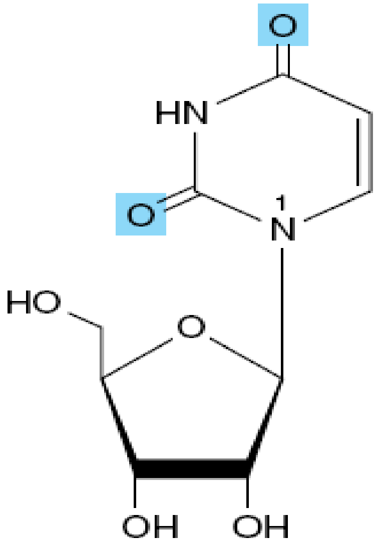
Adenosine



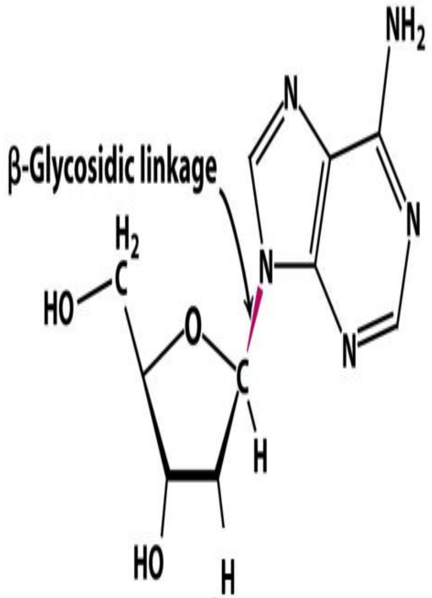
Guanosine



Cytidine



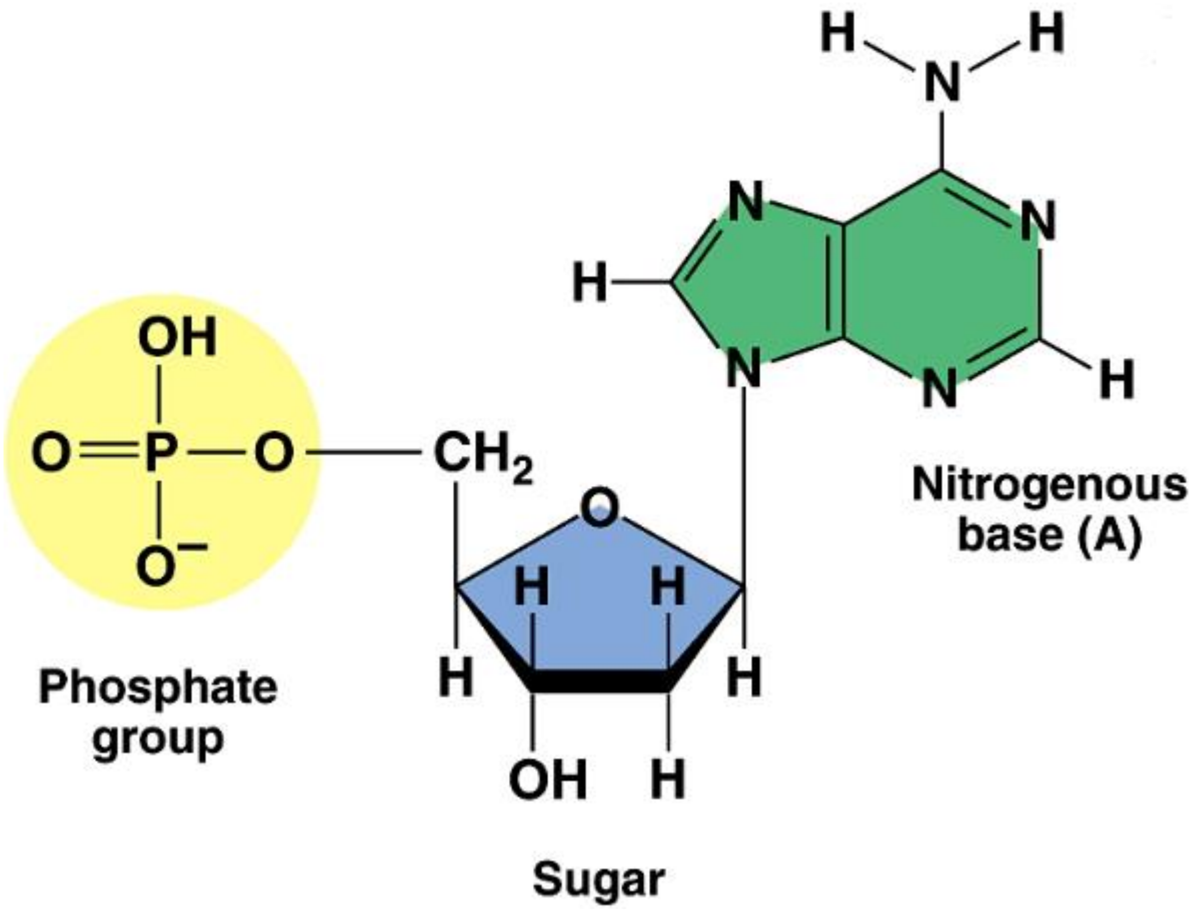
Uridine



Deoxyadenosine

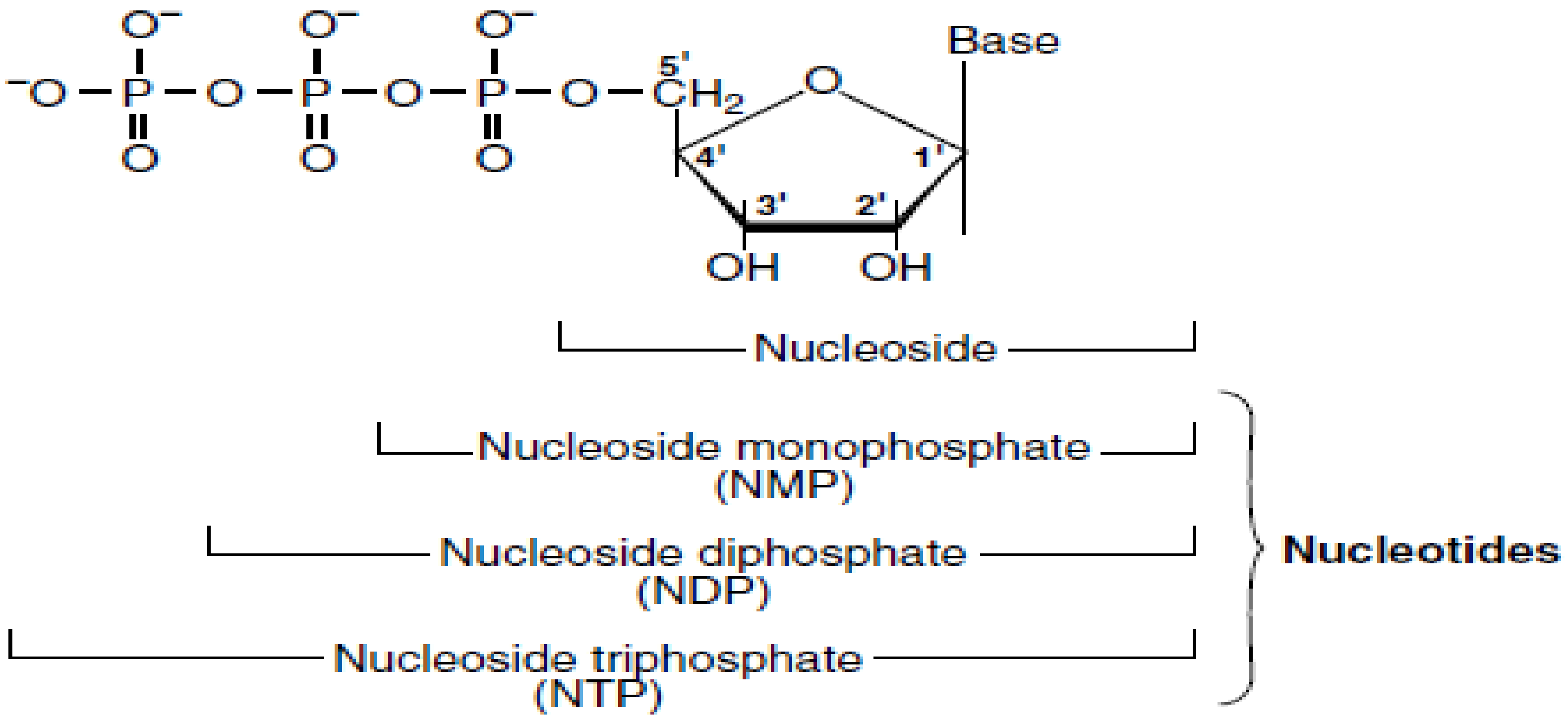
Phosphate Group

- Mono, di- or triphosphates
- Phosphates can be bonded to either C3 or C5 atoms of the sugar



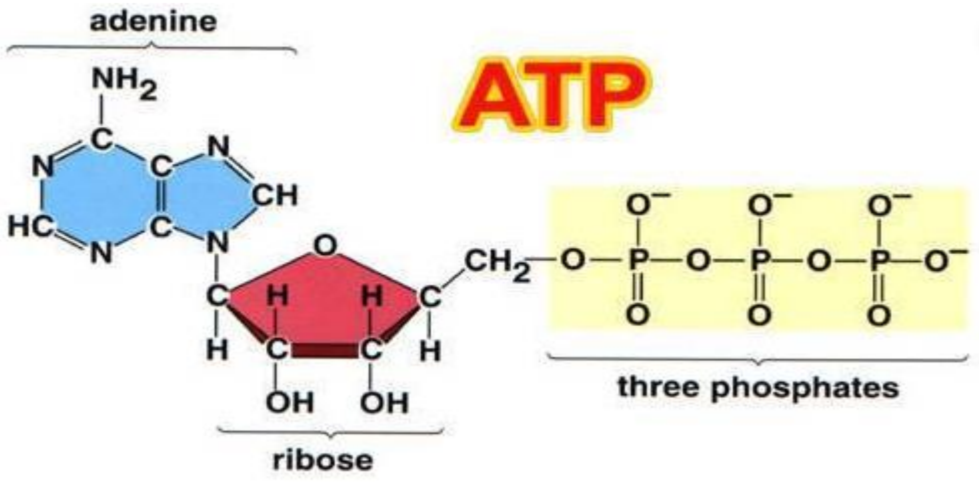
Nucleotides

- A nucleotide is a nucleoside with an inorganic phosphate attached to a 5-hydroxyl group of the sugar in ester linkage.
- The nitrogenous base is linked by an N-glycosidic bond to the anomeric carbon of the sugar, either ribose or deoxyribose
- The names and abbreviations of nucleotides specify the base, the sugar, and the number of phosphates attached.



Nucleotide

- In deoxynucleotides, the prefix “d” precedes the abbreviation. For example, ADP is Adenosine diphosphate (the base Adenine attached to a ribose that has two phosphate groups) and dATP is deoxyadenosine triphosphate (the base adenine attached to a deoxyribose with three phosphate groups).



DNA is a polymer of deoxyribonucleotide

- Deoxyadenosine triphosphate (dATP)
- Deoxyguanosine triphosphate (dGTP)
- Deoxycytidine triphosphate (dCTP)
- Deoxythymidine triphosphate (dTTP)

RNA is a polymer of ribonucleotide

Adenosine triphosphate (ATP)

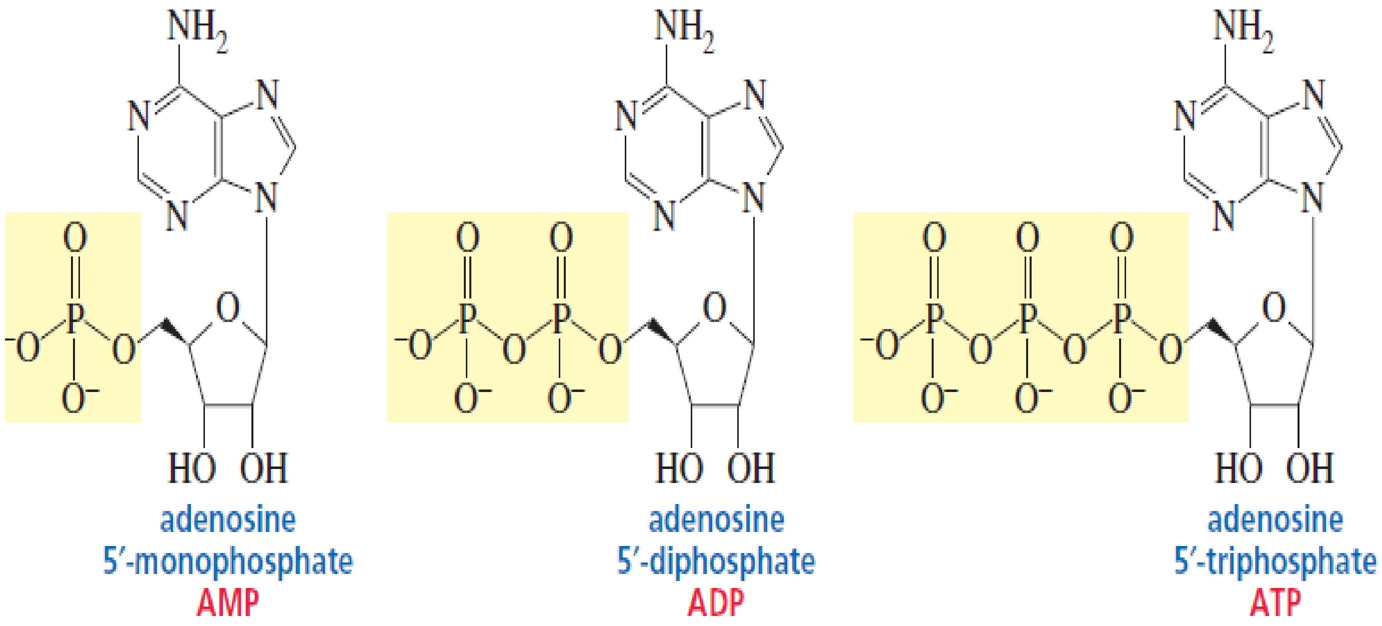
Guanosine triphosphate (GTP)

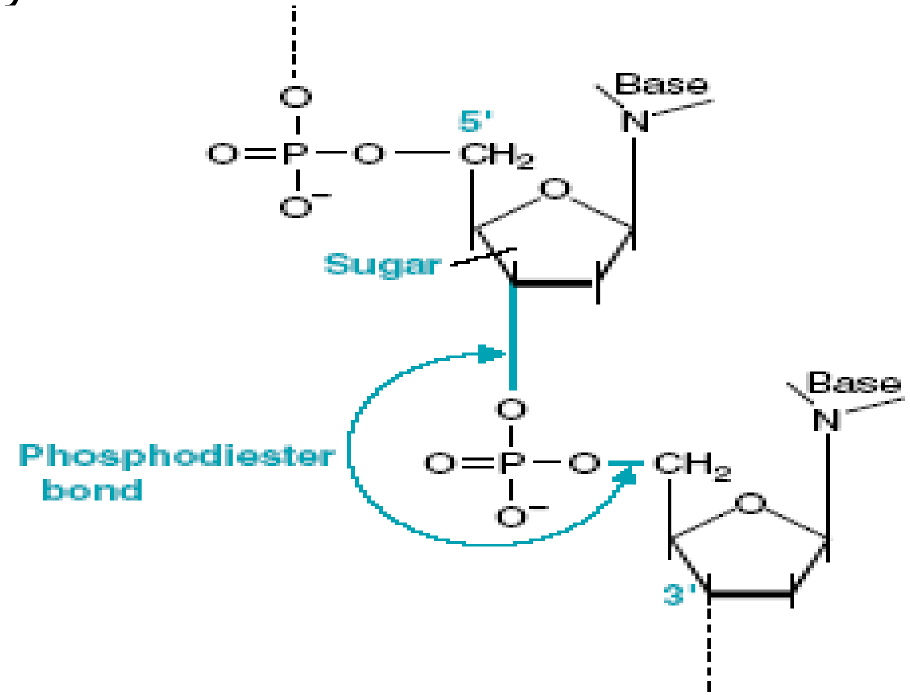
Cytidine triphosphate (CTP)

Uridine triphosphate (UTP)

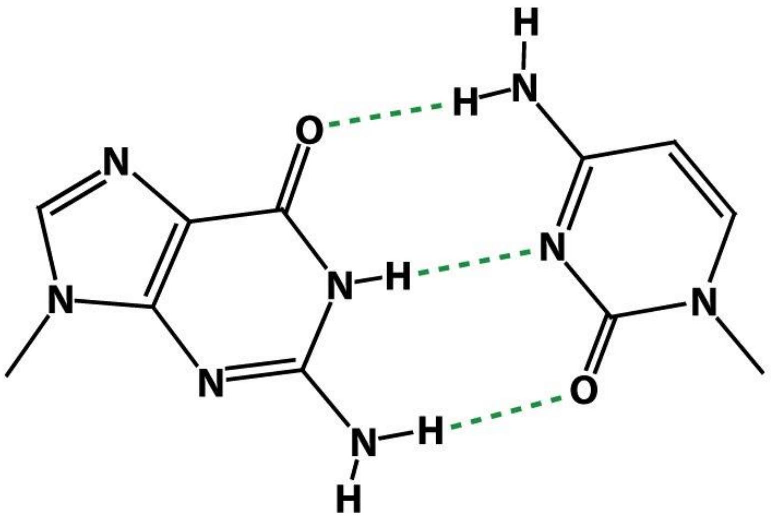
Nucleotide

- Nucleotide triphosphates are the building blocks of **DNA** and **RNA**.
- Polynucleotides such as DNA and RNA are linear sequences of nucleotides linked by 3- to 5-phosphodiester bonds between the sugars.
- All cells require energy to ensure their survival and reproduction. The cells get the energy by converting nutrients into a chemically useful form of energy. The most important form of chemical energy is adenosine triphosphate (**ATP**).
- Important components of coenzymes FAD, NAD and Coenzyme A



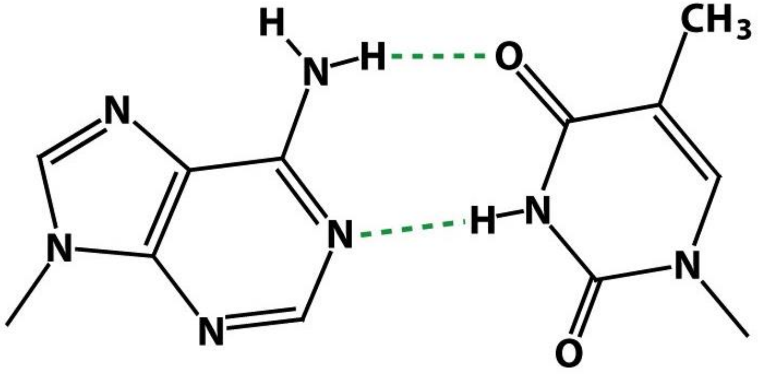


Bases in DNA make hydrogen bonds



Guanine　　Cytosine

PURINE　　PYRIMIDINE

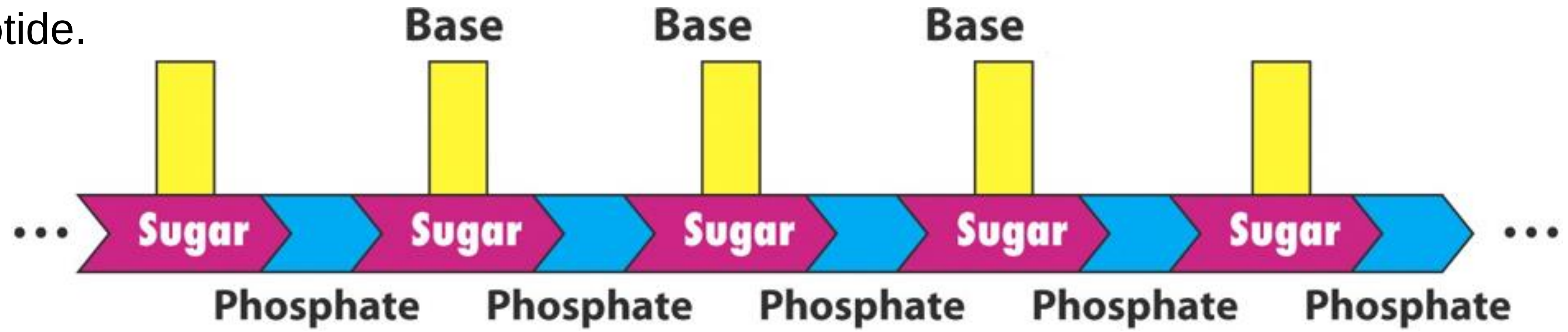


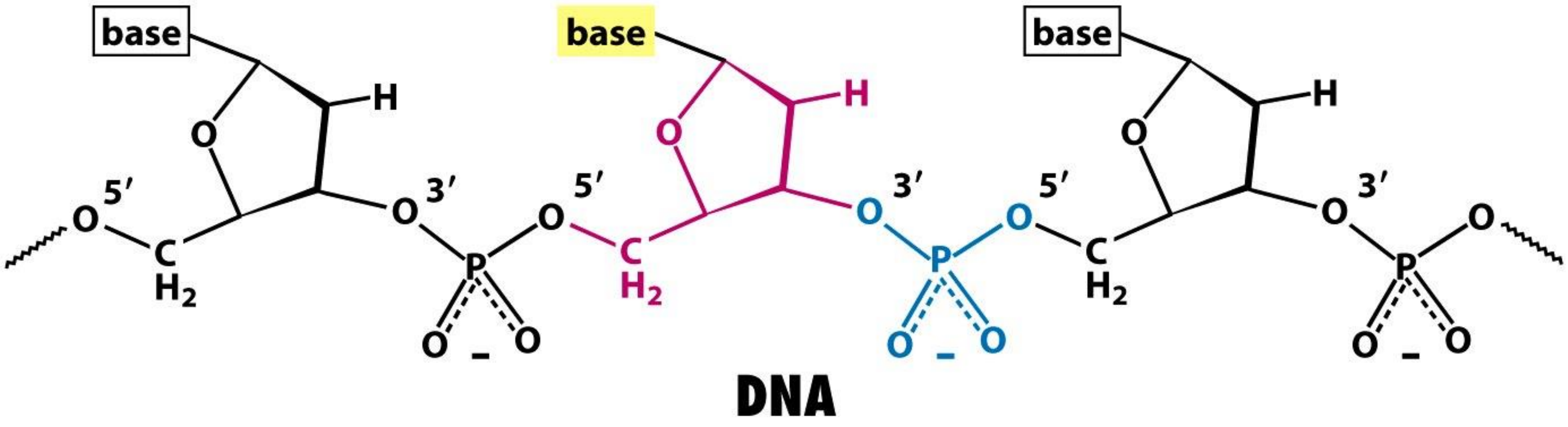
Adenine　　Thymine

PURINE　　PYRIMIDINE

DNA Structure

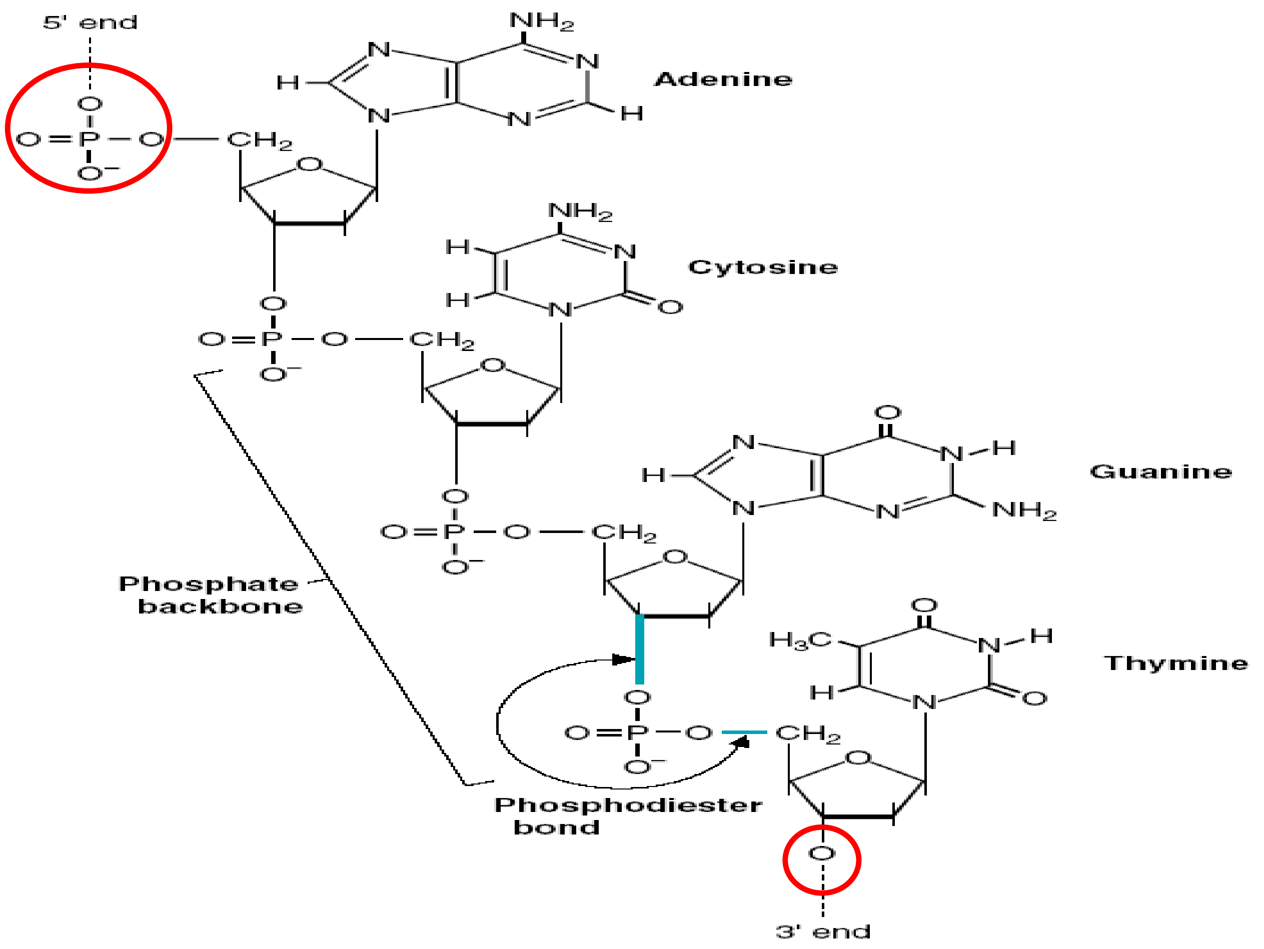
- DNA is a poly deoxyribonucleotide that contain many monodeoxyribonucleotide covalently linked by phosphodiester bonds.
- Phosphodiester bonds join the 3´-OH group of one nucleotide to the 5´-OH group of the next nucleotide.



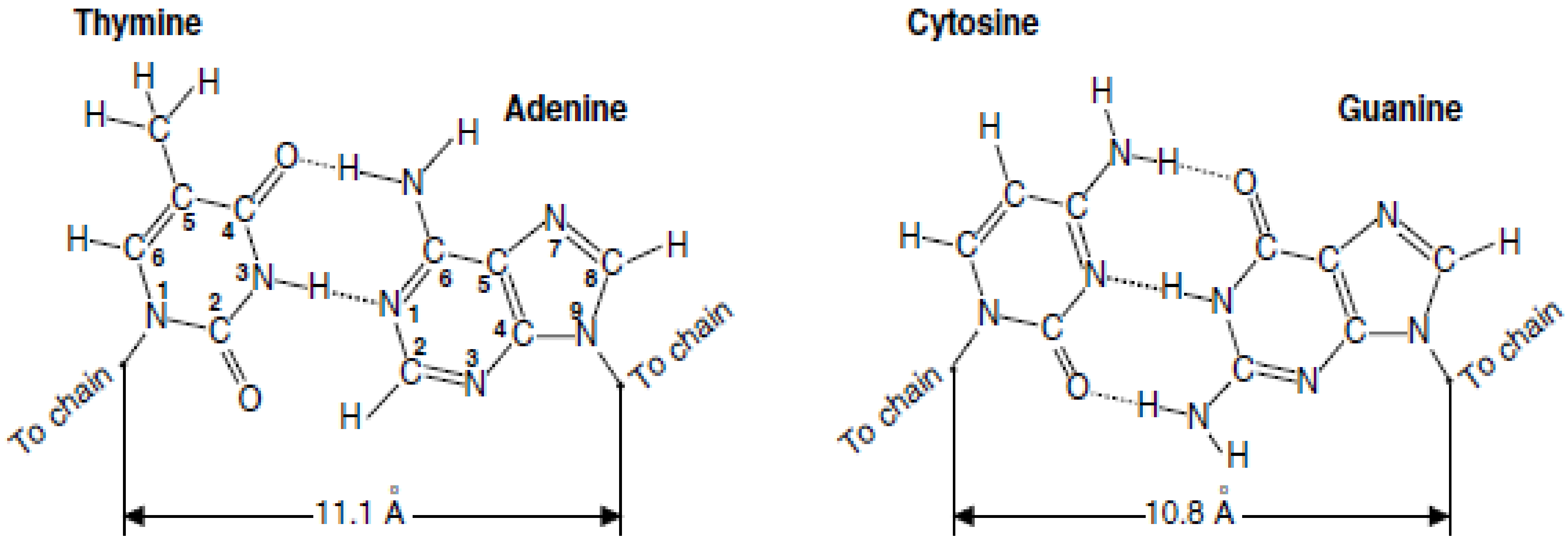


- With the exception of a few viruses that contain single-stranded DNA, DNA exist as a double-stranded molecules in which the two strands wind around each other forming a double helix.

A segment of one strand of a DNA molecule

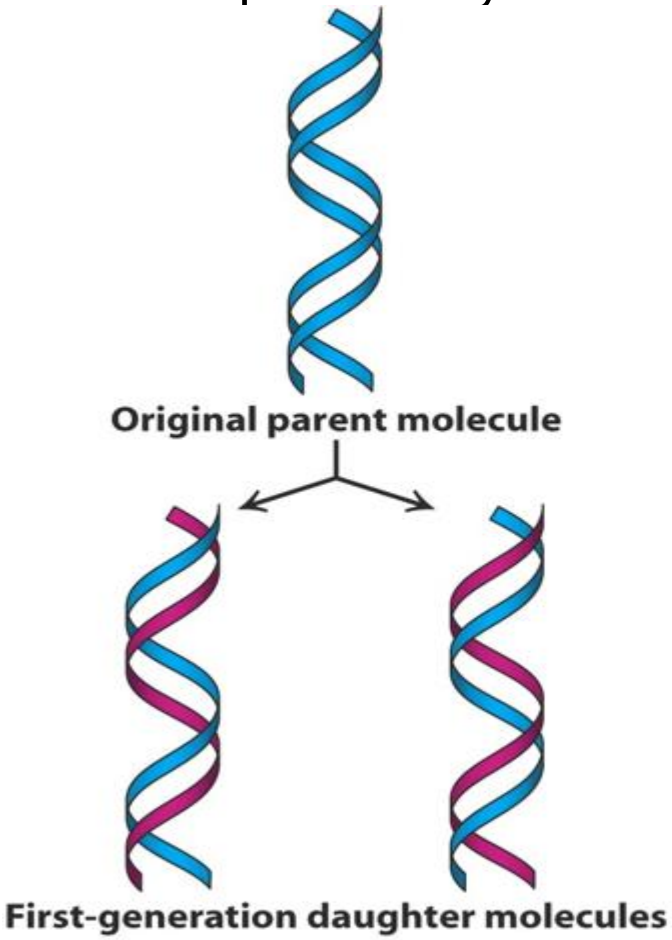


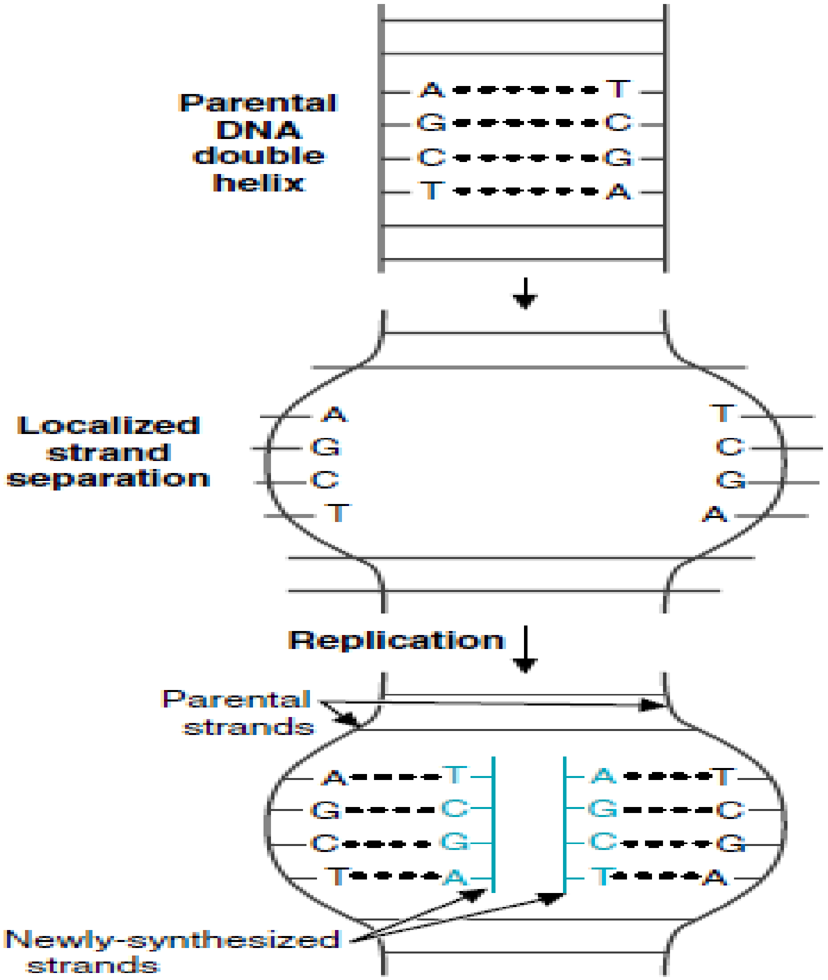
- As proposed by Watson and Crick, each DNA molecule consists of two polynucleotide chains joined by **hydrogen bonds** between the bases. In each base pair, a purine on one strand forms hydrogen bonds with a pyrimidine on the other strand. In one type of base pair, **adenine on one strand pairs with thymine on the other strand**.



- This base pair is stabilized by two hydrogen bonds. The other base pair, formed between guanine and cytosine, is stabilized by three hydrogen bonds. As a consequence of base-pairing, the two strands of DNA are complementary, that is, **adenine on one strand corresponds to thymine on the other strand,** **and guanine corresponds to cytosine.**

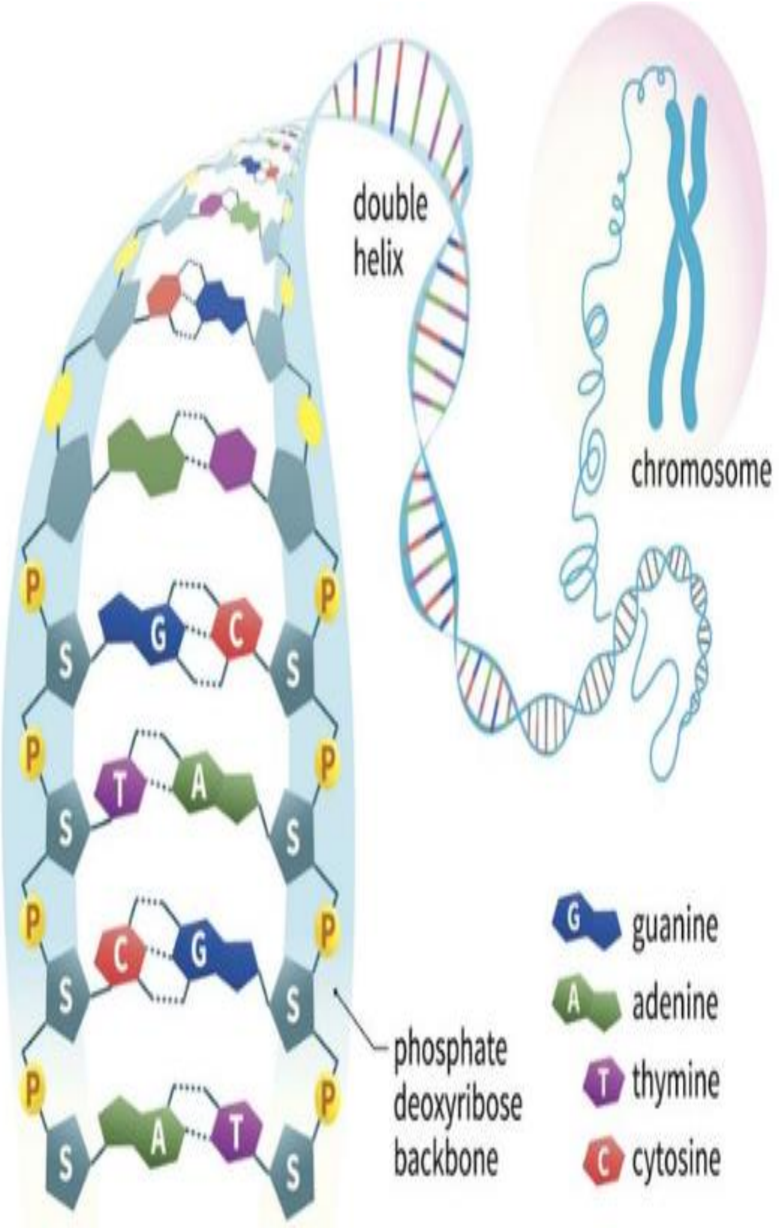
- The concept of base-pairing proved to be essential for determining the mechanism of **DNA replication** (in which the copies of DNA are produced that are distributed to daughter cells) and the mechanisms of **transcription** and **translation** (in which mRNA is produced from genes and used to direct the process of **protein synthesis**).
- Clearly, as **Watson and Crick** suggested, base-pairing allows one strand of DNA to serve as a template for the synthesis of the other strand. Base pairing also allows a strand of DNA to serve as a template for the synthesis of a complementary strand of RNA.





The DNA double helix

- Two helical polynucleotide chains, coiled about a common axis.
- The chains are **antiparallel** manner, the 5-end of one strand is paired with the 3- end of the other strand.
- The hydrophilic **deoxyribose-phosphate** of each chain is **on the outside** of the molecule, while the hydrophobic **bases** are stacked **on the inside.**



Base pairing

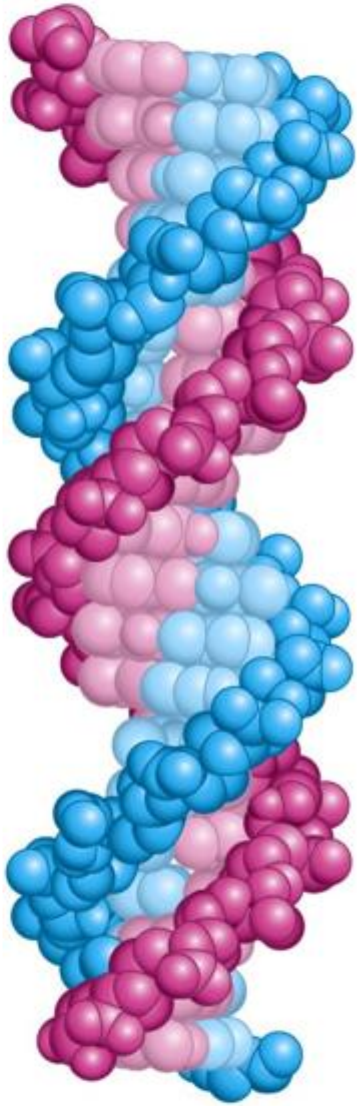
- The bases of one strand of DNA are paired with the bases of the second strand so that an **Adenine** is always paired with a **Thymine**, while a **Cytosine** is always paired with a **Guanine**. Therefore one polynucleotide chain of the DNA double helix is always the **complement of the other**. Given the **sequence of bases on one chain**, **the sequence of bases on the complementary chain can be determined**.

- The specific base pairing in DNA leads to **Chargaff's rules**: In any samples of duoble–strand DNA the amount of **Adenine** equals the amount of **Thymine** the amount of **Guanine** equals the amount of **Cytosine** and the **total amount of purines (A + G) equals the total amount of pyrimidines (T + C).**
- The base pairs are held together by hydrogen bonds: **two** between **A** and **T** and **three** between **G** and **C**. These hydrogen bonds plus the van der Waals forces between the stacked bases stabilize the structure of the double helix.

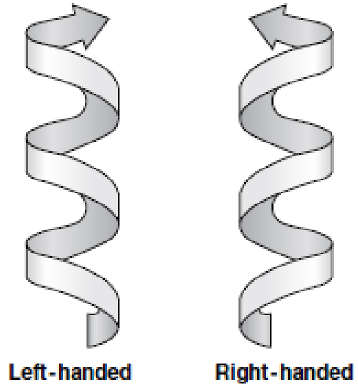
DNA can occur in different three-Dimensional (3D) Forms

DNA is a flexible molecule. Considerable rotation is possible around a number of bonds in the sugar–phosphate (phospho-deoxyribose) backbone. Many significant forms are described by Watson-Crick of DNA structure that are found in cellular DNA. These structural variations generally do not affect the key properties of DNA defined by Watson and Crick: strand complementarity, antiparallel strands, and the requirement for A=T and G = C base pairs.

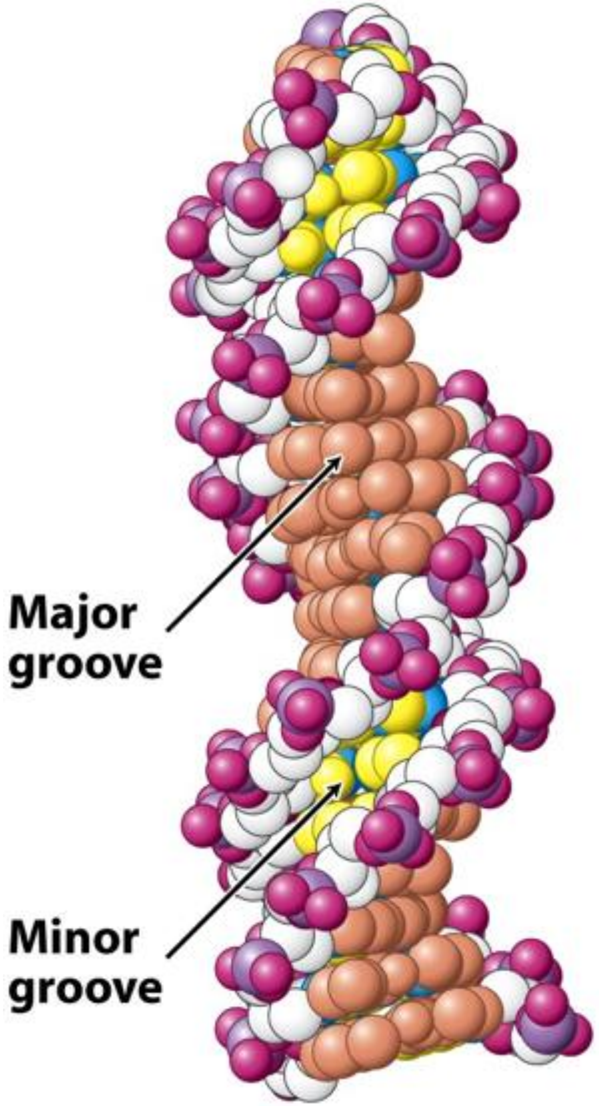
The B form (DNA double helix)



- Two helical polynucleotide chains, coiled about a common axis.



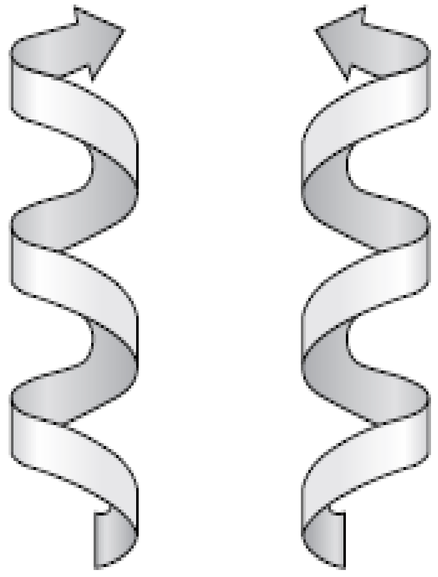
- Right-handed
- Chains are anti-parallel
- Sugar-phosphates on the outside; bases on the inside.
- Approx. 10 bases per helix turn and **0.34 nm** between base pairs.
- Rise/turn of helix = **3.57 nm**



Two structural variants that have been well characterized in crystal structures are the **A** and **Z** forms. These structural changes deepen the major groove while making the minor groove shallower.

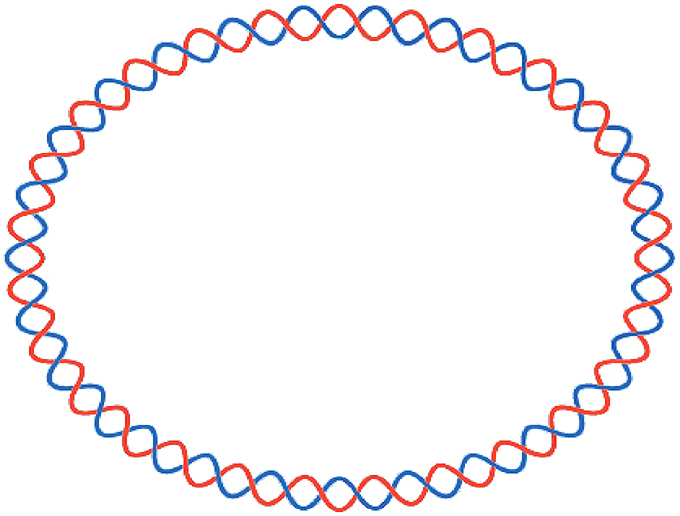
- **The A form** (Dehydration of DNA drives it into the A form).
  - Similar to the B form, but is more compact (**0.26 nm** between base pairs and **11** base pairs per turn).
  - Rise/turn of helix = **2.86 nm**

- **The Z form**
  - The bases of the two DNA strands are the **left-handed helix**.
  - **0.37 nm** between base pairs and **12** base pairs per turn.
  - Rise/turn of helix = **4.56 nm**

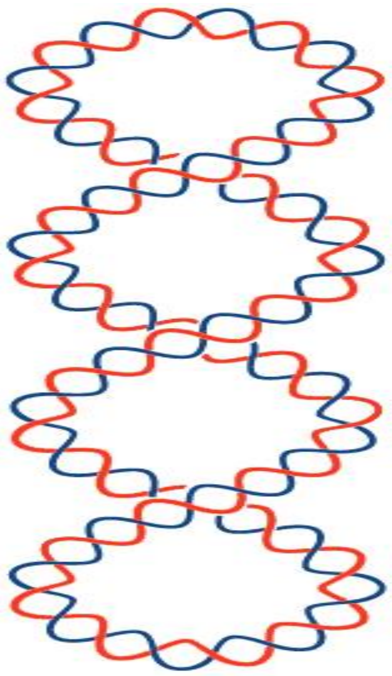


DNA Supercoiling

Supercoiling means the coiling of a coil. A telephone cord, for example, is typically a coiled wire. The path taken by the wire between the base of the phone and the receiver often includes one or more supercoils. DNA is coiled in the form of a double helix, with both strands of the DNA coiling around an axis. The further coiling of that axis upon itself produces DNA supercoiling. When there is no net bending of the DNA axis upon itself, the DNA is said to be in a **relaxed** state.



"relaxed" double-helical segment of DNA

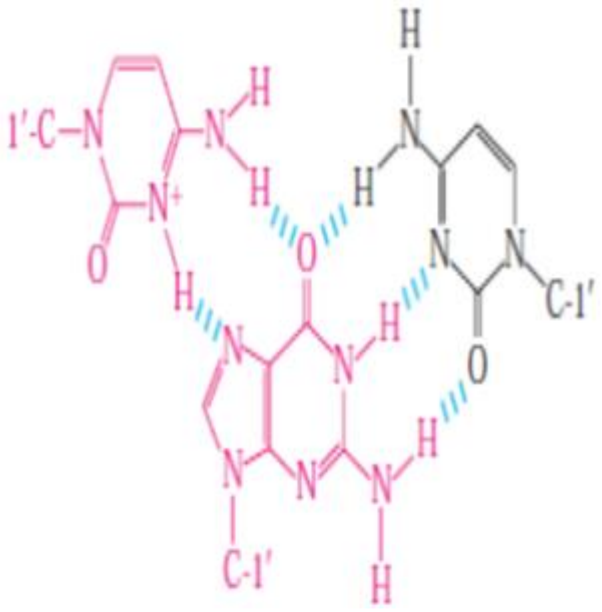


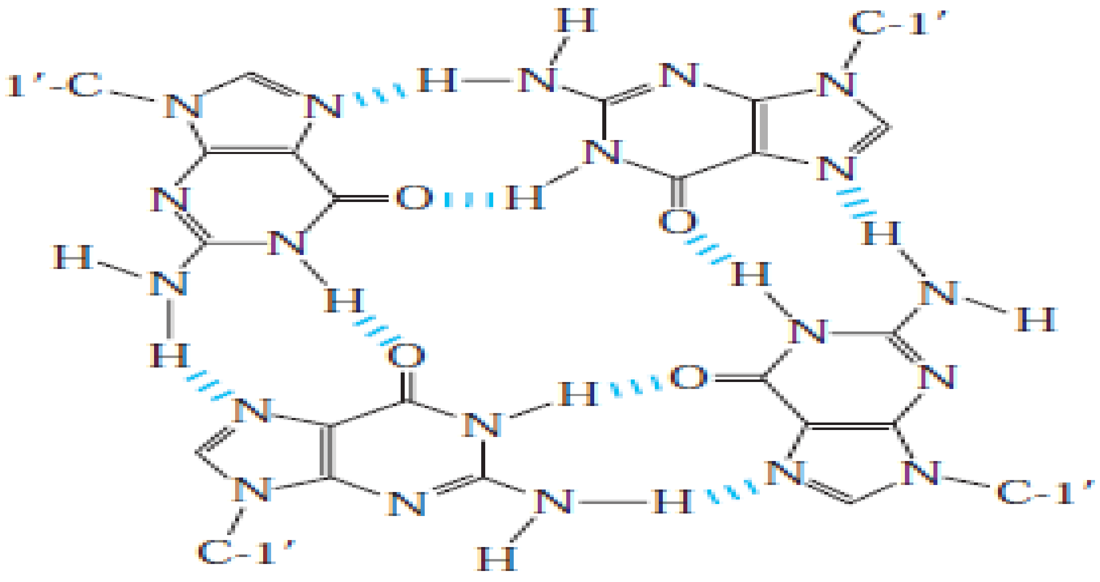
negative supercoiling

Alternative structures triplex and tetraplex (Quadruplex)

Watson-Crick base pair, can form a number of additional hydrogen bonds. For example, Cytidine can pair with Guanosine (G=C), and Thymidine can pair with Adenosine (A=T). The **N-7, O-6, and N-6 of purines**, the atoms that participate in the hydrogen bonding of triplex DNA, are often referred to as Hoogsteen positions, so called **Hoogsteen pairing**. Hoogsteen pairing allows the formation of triplex DNAs.

Four DNA strands can also pair to form a **tetraplex** (quadruplex), but this occurs only for DNA sequences with Guanosine. The guanosine tetraplex, is stable over a wide range of conditions.





Guanosine tetraplex

Several types of RNA and RNA polymerases

Messenger RNA (mRNA)

template for protein synthesis
RNA polymerase II (Pol II)

Transfer RNA (tRNA)

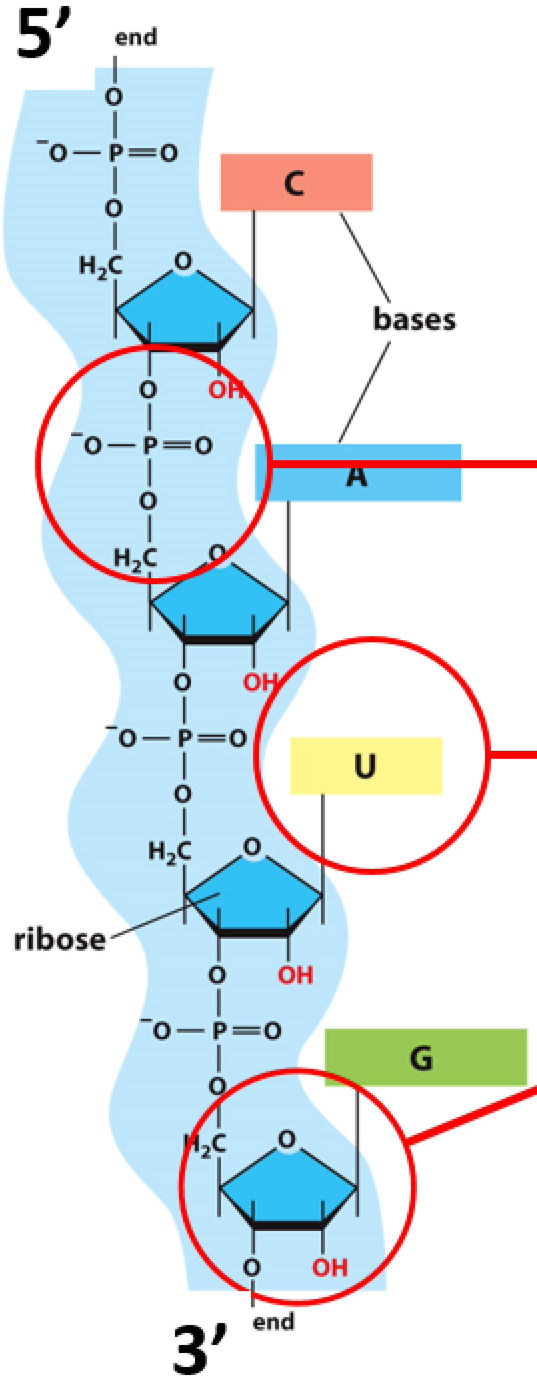
carries activated amino acids to ribosomes
RNA polymerase III (Pol III)

Ribosomal RNA (rRNA)

major component of ribosomes
RNA polymerase I (Pol I)

All require template DNA, ribonucleotides (ATP, GTP, UTP, CTP) and a divalent metal ion (Mg^{2+})

RNA



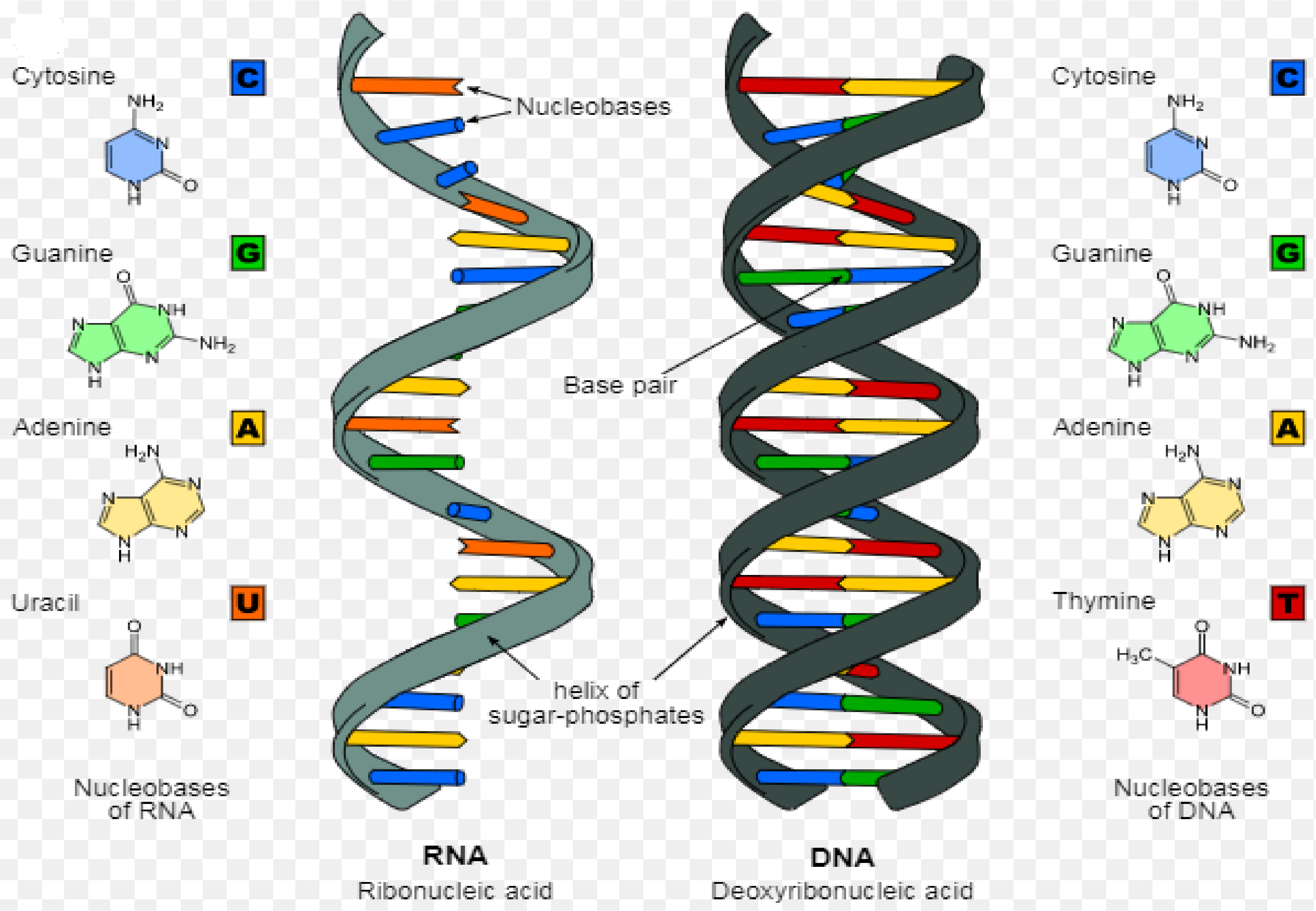
Phosphodiester link

Bases – C, A, G and U (not T)

Ribose; has OH group

Synthesised 5′ to 3′

RNA
DNA


Cytosine
C
Guanine
G
Adenine
A
Uracil
U
Nucleobases of RNA
Nucleobases
Base pair
helix of sugar-phosphates
Thymine
T
Nucleobases of DNA
RNA
Ribonucleic acid
DNA
Deoxyribonucleic acid