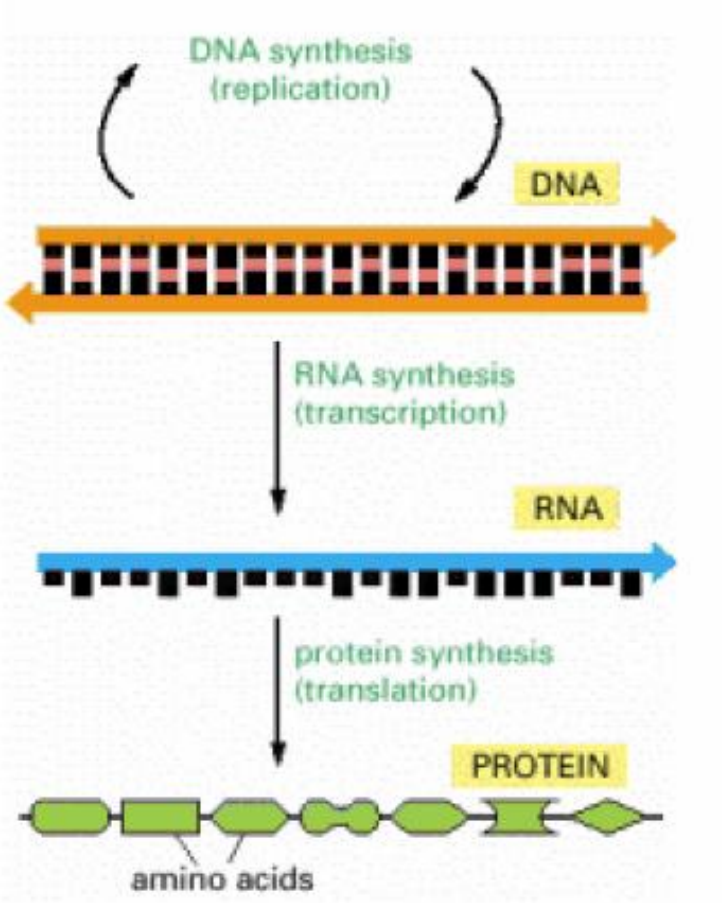
Molecular Biology I-II

Objectives :

- **The central dogma of molecular biology**
- **Nucleotide chemistry**
- **DNA, RNA and Chromosome Structure**
- **DNA Replication**
- **Gene Expression**
  - **Transcription**
  - **The genetic code**
  - **Translation**

“Dogma means organization”

The Central Dogma of Molecular Biology



Replication is the synthesis of DNA from DNA
Transcription is the synthesis of RNA from DNA
Translation is the protein synthesis from RNA

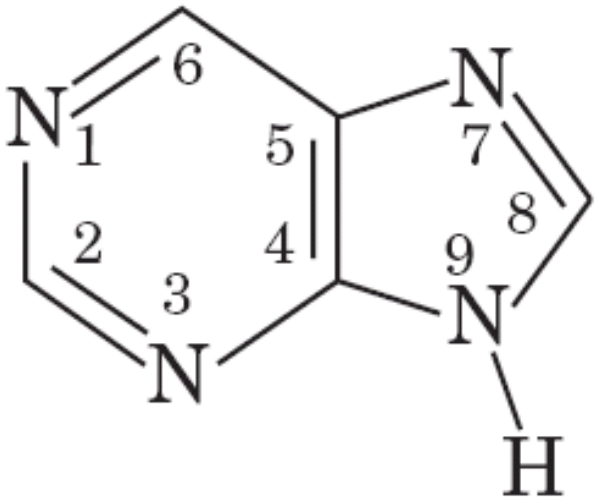
A portion of ***DNA,*** called a ***gene,*** is ***transcribed*** into ***RNA.***
RNA is ***translated*** into ***proteins.***

- Human genome contains about 35,000 genes

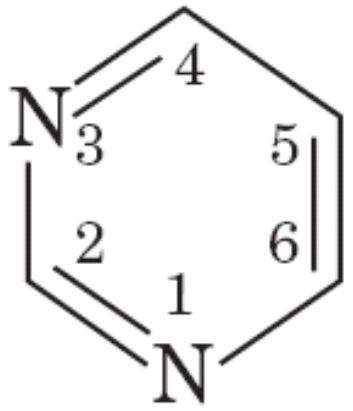
Nucleotides

- Nucleotides are composed of a nitrogenous base, sugar, and phosphate group(s)
- The nitrogenous bases are of two types:
  - Purine
  - Pyrimidine

- The most common purines are:
  - Adenine (A)
  - Guanine (G)
- The most common pyrimidines are:
  - Cytosine (C)
  - Uracil (U)
  - Thymine (T)

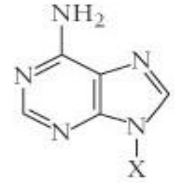
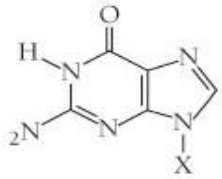
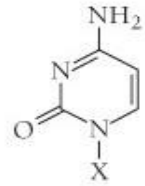
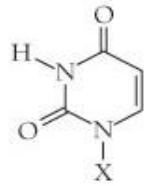
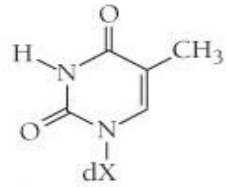


Purine



Pyrimidine

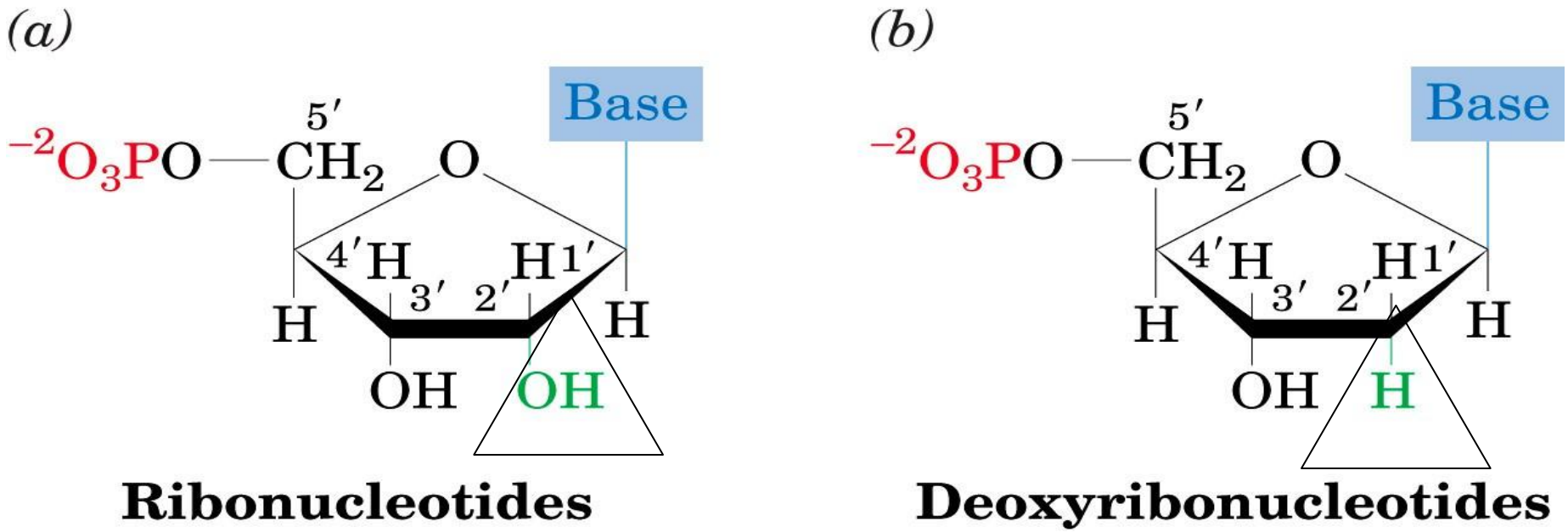
Base+suger =nucleoside Nucleoside+ phosphat group=nucle otide

Base Formula	Base (X = H)	Nucleoside (X = ribose[a])	Nucleotide[b] (X = ribose phosphate[a])
	Adenine Ade A	Adenosine Ado A	Adenylic acid Adenosine monophosphate AMP
	Guanine Gua G	Guanosine Guo G	Guanylic acid Guanosine monophosphate GMP
	Cytosine Cyt C	Cytidine Cyd C	Cytidylic acid Cytidine monophosphate CMP
	Uracil Ura U	Uridine Urd U	Uridylic acid Uridine monophosphate UMP
	Thymine Thy T	Deoxythymidine dThd dT	Deoxythymidylic acid Deoxythymidine monophosphate dTMP

Names and Abbreviations of Nucleic Acid Bases, Nucleosides, and Nucleotides

Ribose Sugar

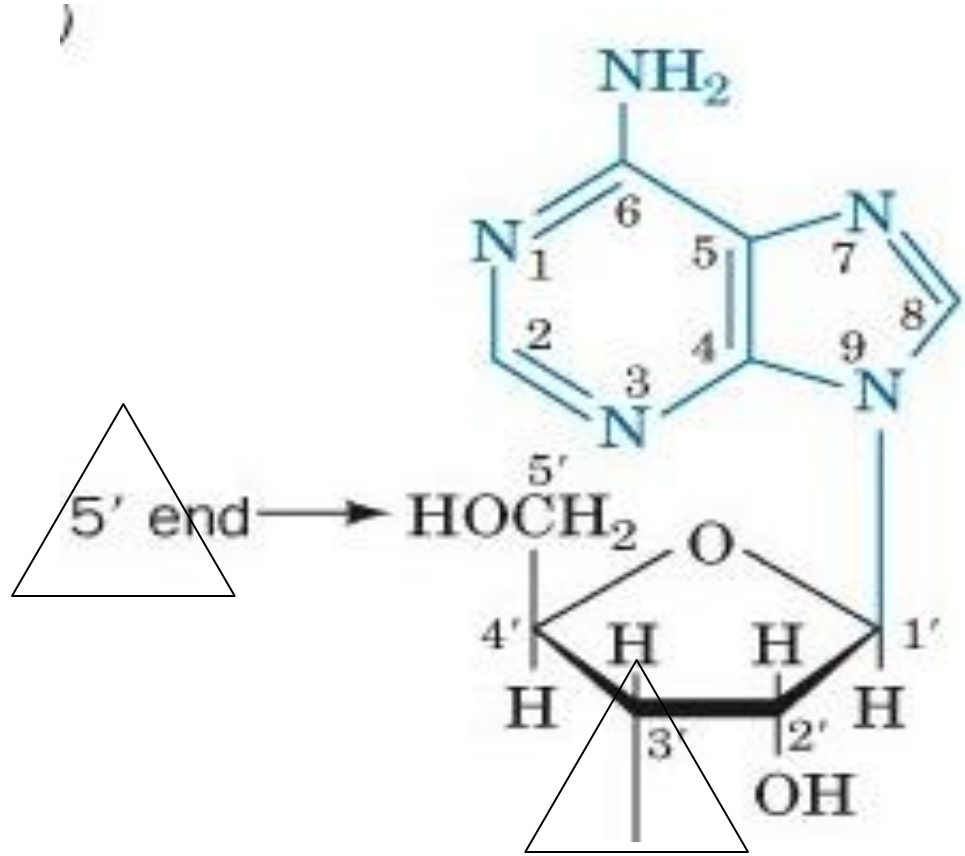
- Ribose sugar is a pentose sugar (with 5 carbon ring)
- Two types of ribose sugar:
  - Deoxyribose (no OH at C_2)
  - Ribose (with OH at C_2)



Chemical structures of (*a*) ribonucleotides and (*b*) deoxyribonucleotides

- In ribonucleotides, the sugar is ribose
- In deoxyribonucleotides, the sugar is deoxyribose
- The sugar carbon numbers are primed (1’ 2’ 3’ etc.)
- The nitrogenous base atoms are unprimed
- The nitrogenous base is bonded to C_1’ of sugar
- The PO_4 group is bonded to C_3’ or C_5’ of sugar

The NA contain 3 phosphate group



Structure of a nucleotide

The possible places of phosphate

Functions of Nucleotide

- Nucleotides in DNA and RNA store and transfer genetic information
- Free nucleotides have metabolic functions only
  - Other nucleotides: ATP, FAD, NAD, CoA

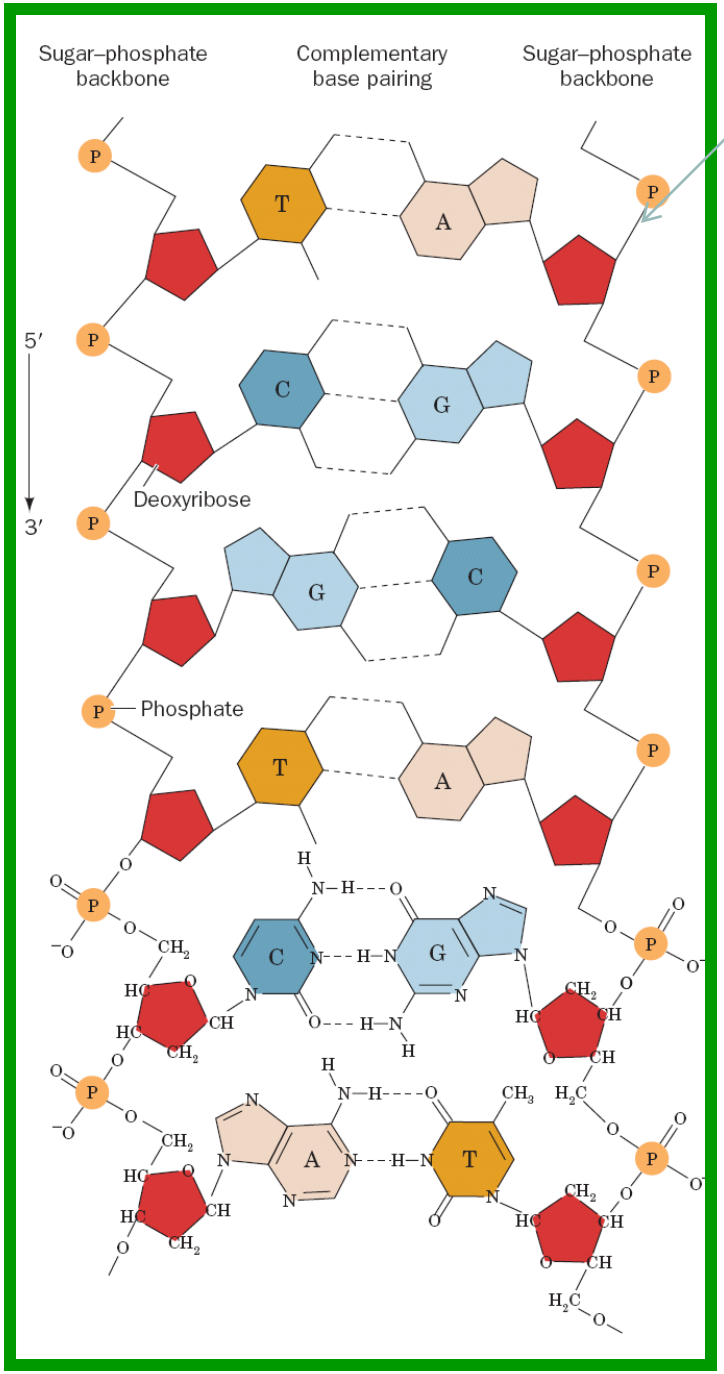
The functions of NA are storage of genetic information + metabolism

Types of Nucleic acids

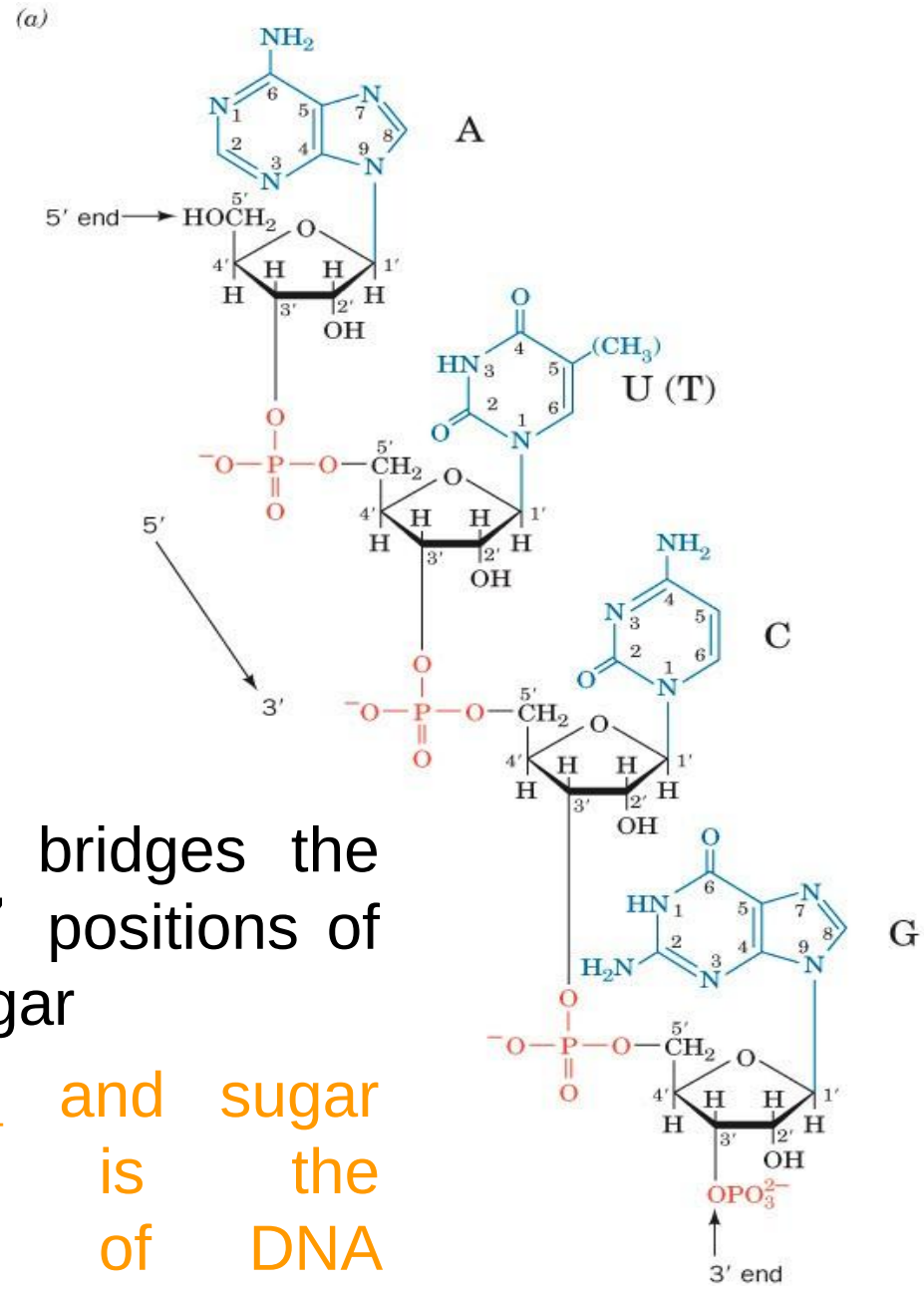
- DNA (Deoxyribonucleic acid)
- RNA (Ribonucleic acid)

Structure of DNA

- DNA is a double-stranded, helical polymer of deoxyribonucleotides



The phosphatediester bond between the sugar and the phosphate group

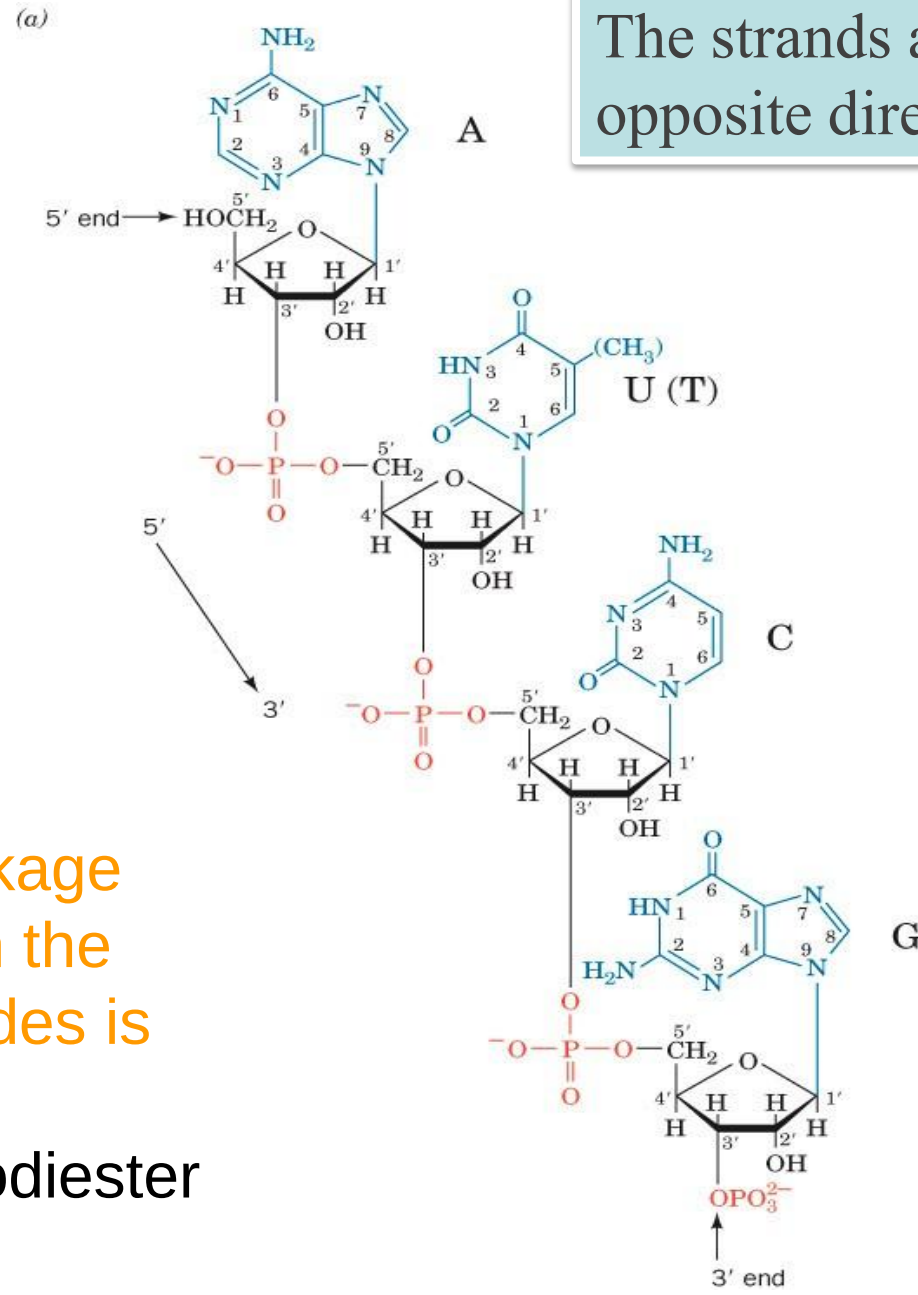


Chemical structure of a nucleic acid

- The PO_4 bridges the 3’ and 5’ positions of ribose sugar
- The PO_4 and sugar bonding is the backbone of DNA structure

The strands are antiparallal (in opposite direction)

Chemical structure of a nucleic acid

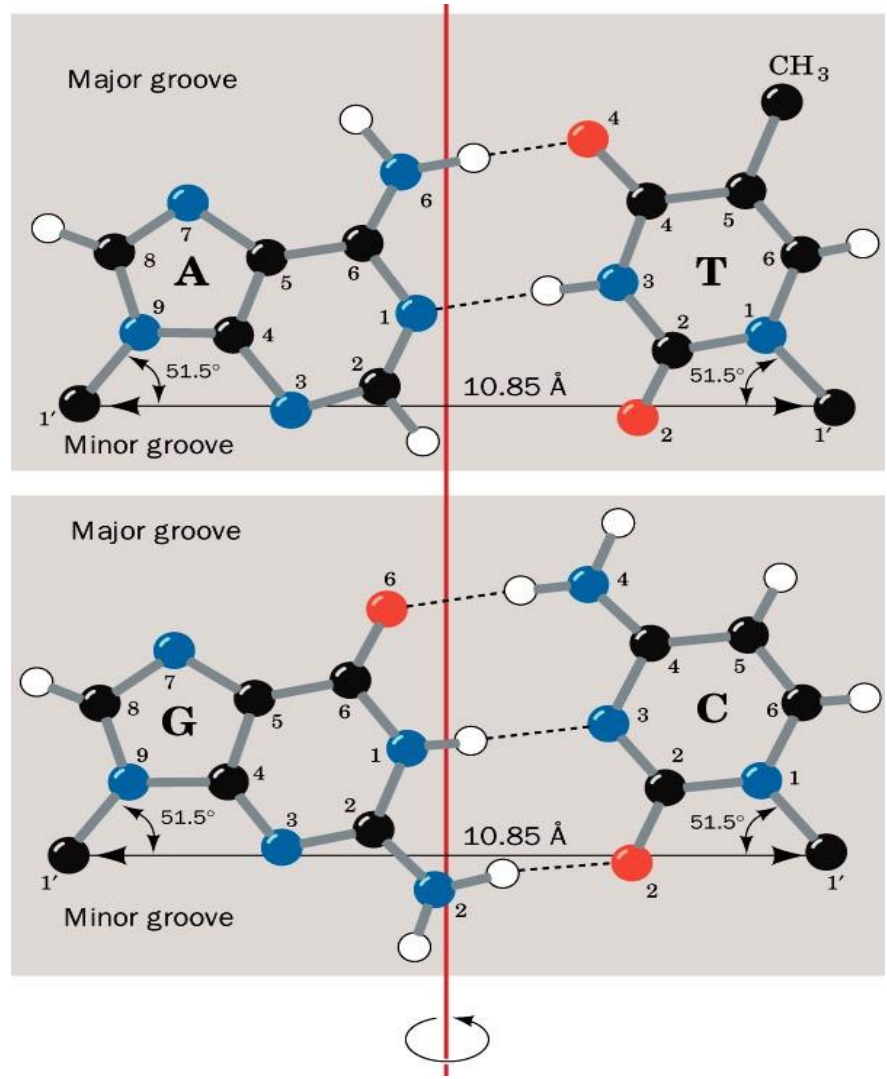


- The linkage between the nucleotides is called phosphodiester bond

Base pairing in DNA

- Adenine(A) = Thymine (T)
- Guanine (G) = Cytosine (C)
- The bonds between the bases are hydrogen bond

- In RNA there is no Thymine (T)
  - Adenine (A)
  - Uracil (U) instead of thymine (T)
  - Guanine (G)
  - Cytosine (C)



Watson-Crick base pairs

The reason of (the 2 bonds between A & T) and (3 between G & C) is that the atoms that responsible for the third bond in G & C is too far in A&T

The double helix DNA

- The first DNA structure was determined by James Watson and Francis Crick in 1953
- Commonly known as Watson-Crick structure

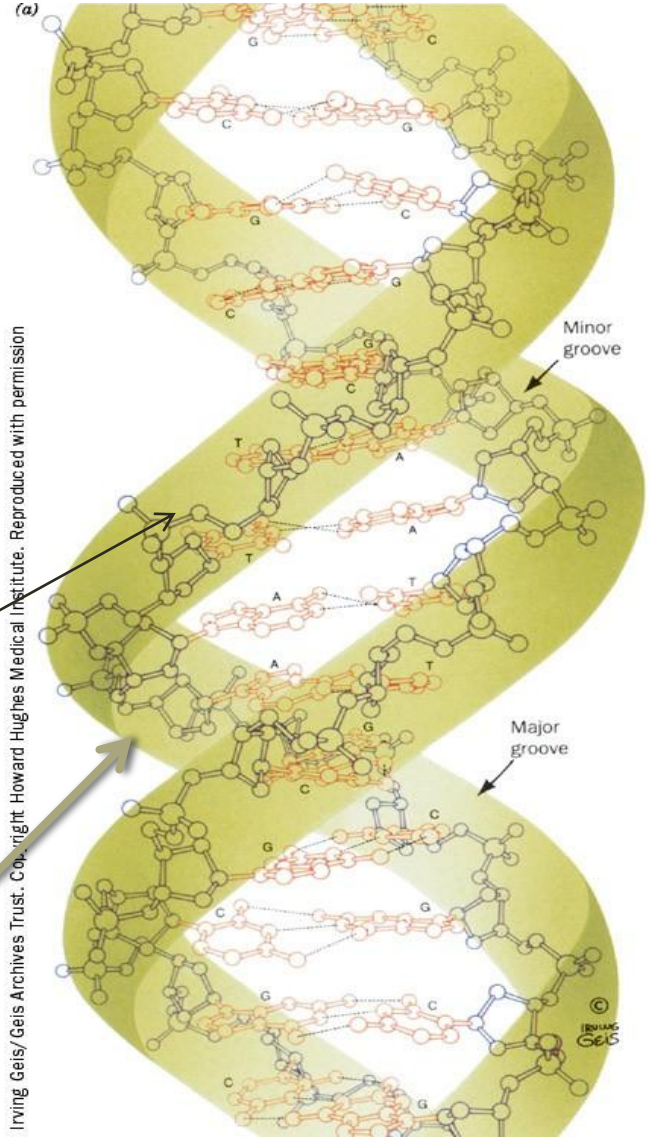
James Watson and Francis Crick

The Features of Watson-Crick DNA structure

- Two polynucleotide chains wind around a common axis to form a double helix
- The two strands are anti-parallel (run in opposite direction) one of the strand from 5'to 3'
- And the other one is from 3'to5'
- Each strand is a right-handed helix
- The nitrogenous bases are in the center of the double helix and the sugar-phosphate chains are on the sides

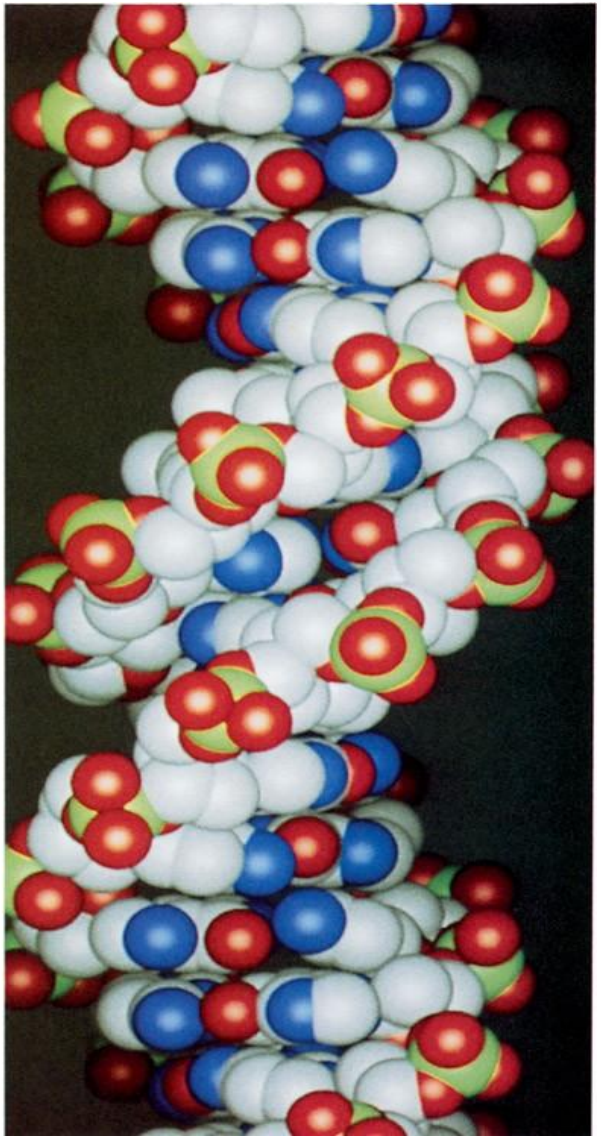
The Features of Watson-Crick DNA structure

- The surface of the double helix contains 2 grooves: the major (large) and minor(small) grooves (the grooves are the area where the proteins come to bind and interact with the DNA, depending on the shape of protein if it bind to the minor or the major)
- Each base is hydrogen bonded to a base in the opposite strand to form a planar base pair (A-T and G-C), known as complementary base pairing
- The helix has 10 base pairs (bp) per turn
- Thargaff's is the amount of purine = the amount of pyrimidine



major

minor

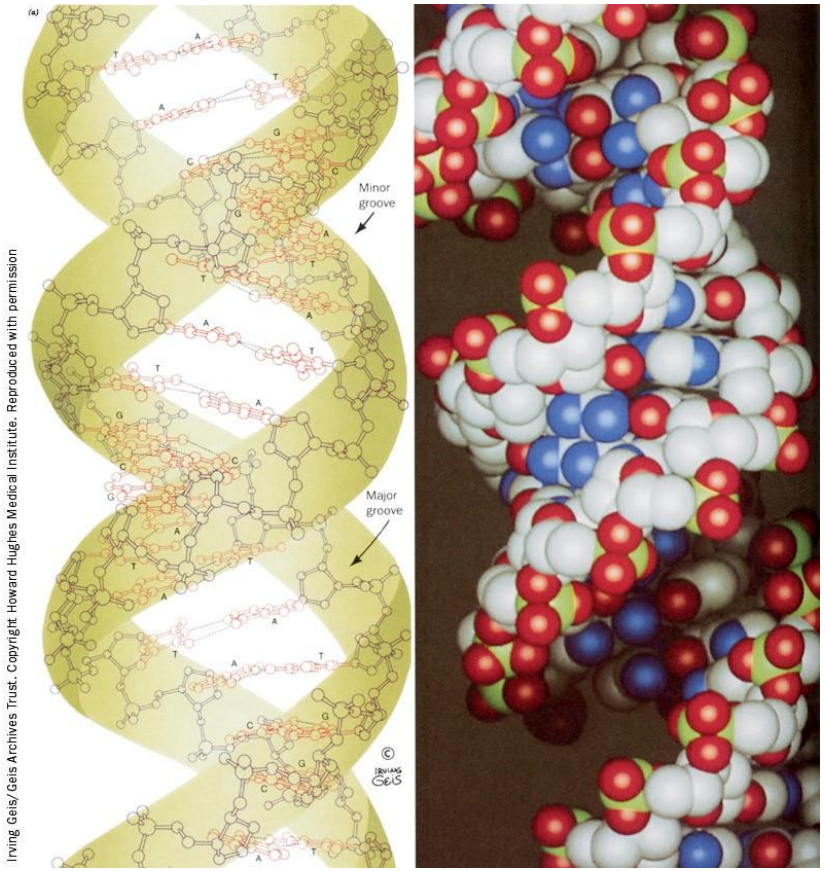


Structure of B-DNA

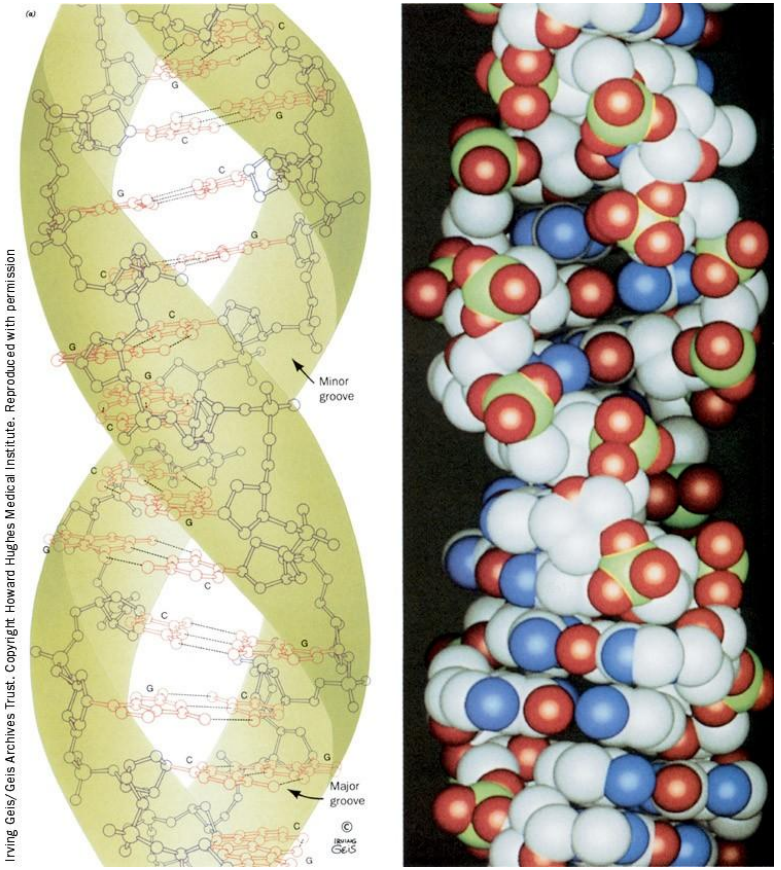
Types of DNA Structure

- A-DNA
- B-DNA (Watson-Crick DNA) is the major one
- Z-DNA

1)Has 11 base pairs per turn
2)It is the dehydration form of B-DNA



Structure of A-DNA

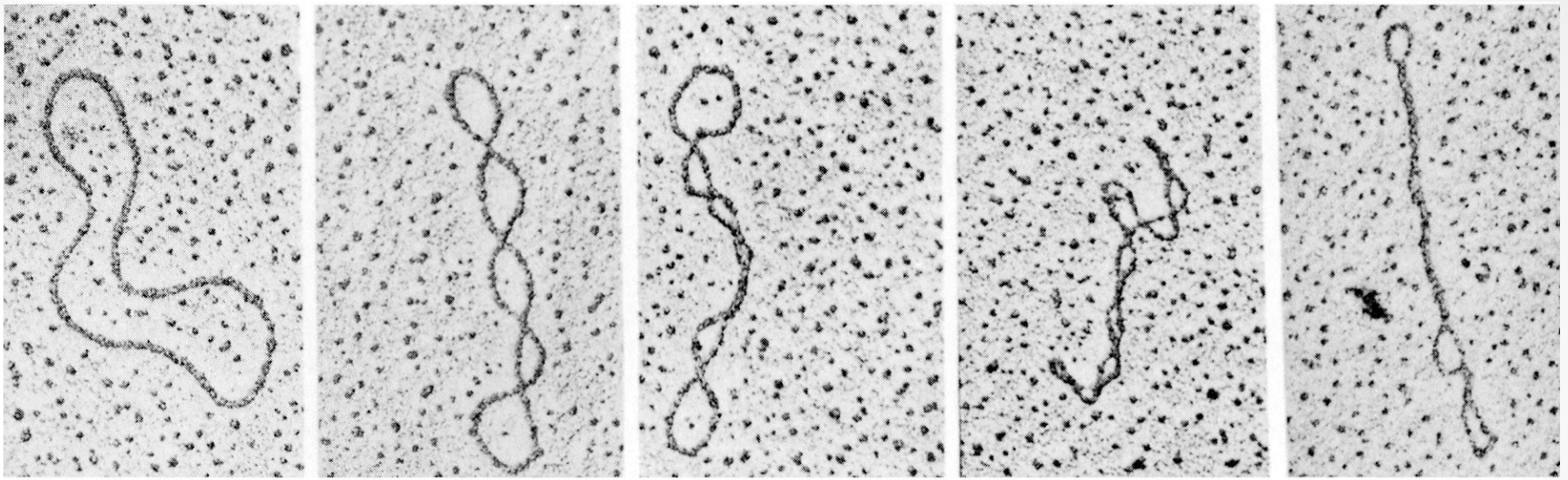


1)The purine alternates with pyridine
2)Has 12 base pairs per turn
3) It isn't regulare in it is structure

Structure of Z-DNA

DNA Supercoiling

- The chromosomes of many bacteria and viruses contain circular DNA which is supercoiled

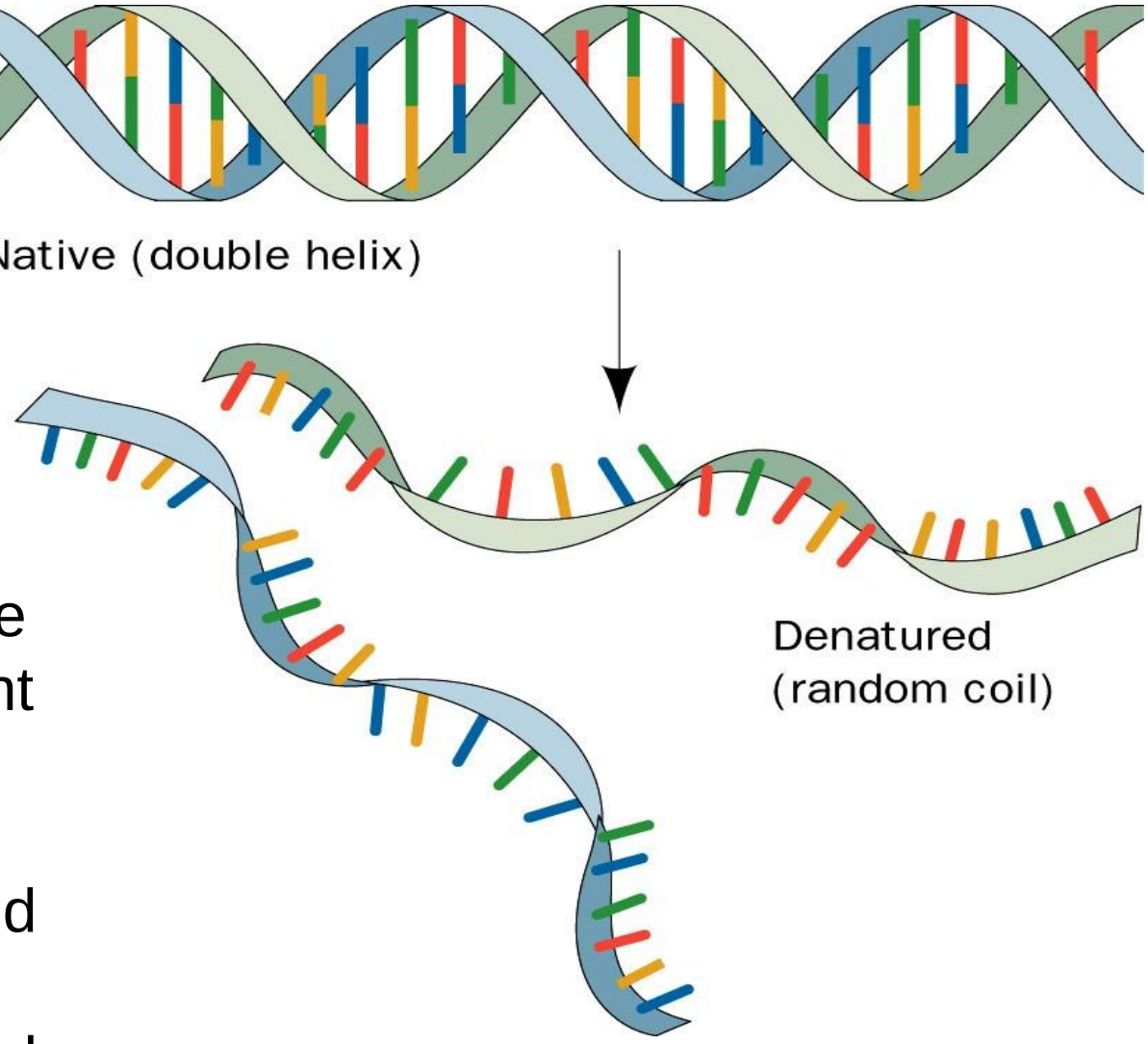


Electron micrographs by Laurien Polder. From Kornberg, A. and Baker, T.A., DNA Replication (2nd ed.), p. 36, W.H. Freeman (1992). Used with permission

DNA Supercoiling in bacteria and viruses

Melting Temperature (Tm)
melting of DNA means break down of its bonds between the bases

- The temperature at which the double-stranded DNA is separated into two single strands
- Melting temp. of DNA depends on nitrogenous base content (A-T and G-C)
- G-C has 3 hydrogen bonds (stronger than A-T)
- DNA with more G_C(high melting)
- DNA with more A_T(low melting temprature)



If we low the melting point again the strands will come to bind again (redenatured or reaneling)

DNA melting due to heat

Structure of RNA

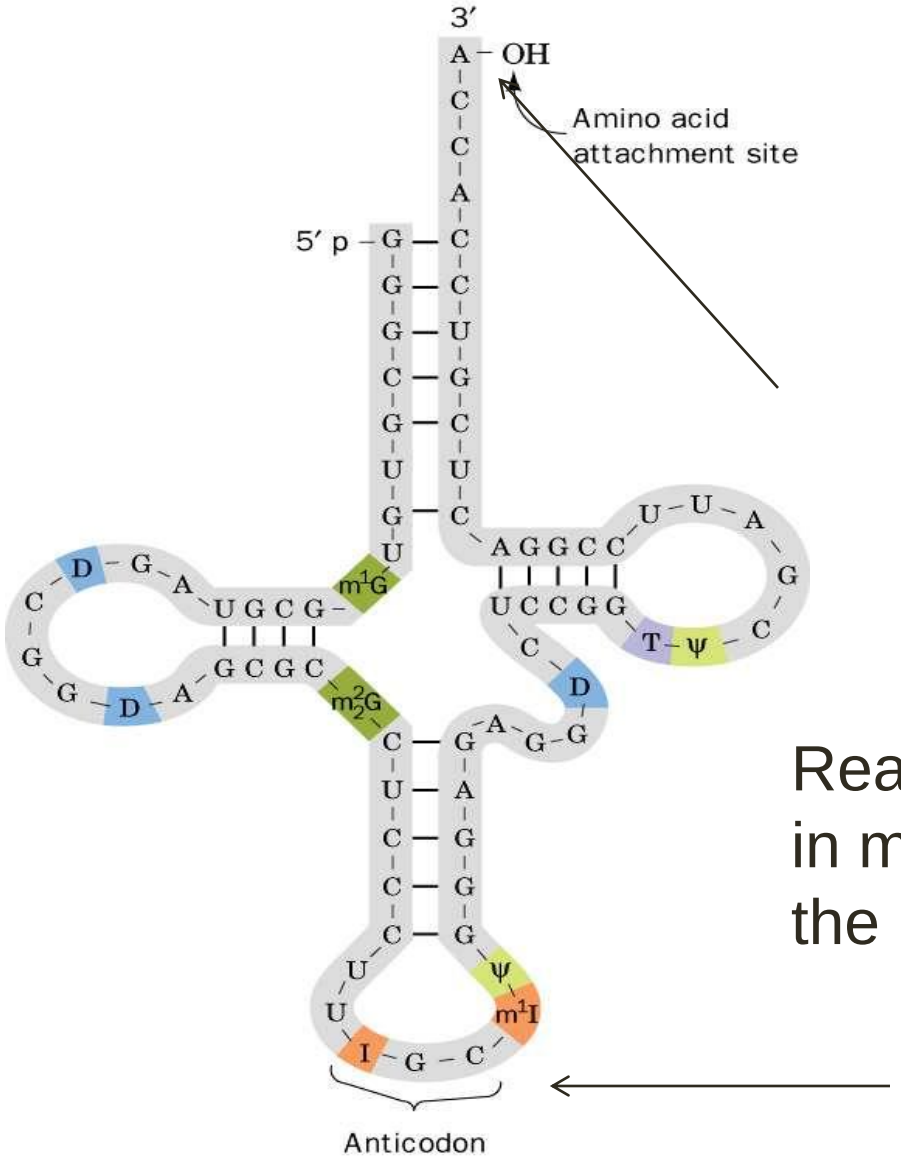
- RNA is a single-stranded polymer of ribonucleotides

Types of RNA

- mRNA carries the information (messenger RNA)
  - *Function*: Transcription process (from DNA to mRNA) takes the message from DNA in the nucleus into the ribosome in the cytoplasm

Types of RNA

- tRNA (transfer RNA) called adaptor molecule
  - *Function*: Translation process (from mRNA to protein synthesis)
  - It transfers amino acids to the growing protein chain



Read what is written in mRNA to choice the right aa

Structure of a tRNA

Types of RNA

- rRNA (ribosomal RNA)makes the ribosomal units
  - *Function*: Site of protein synthesis (factory)

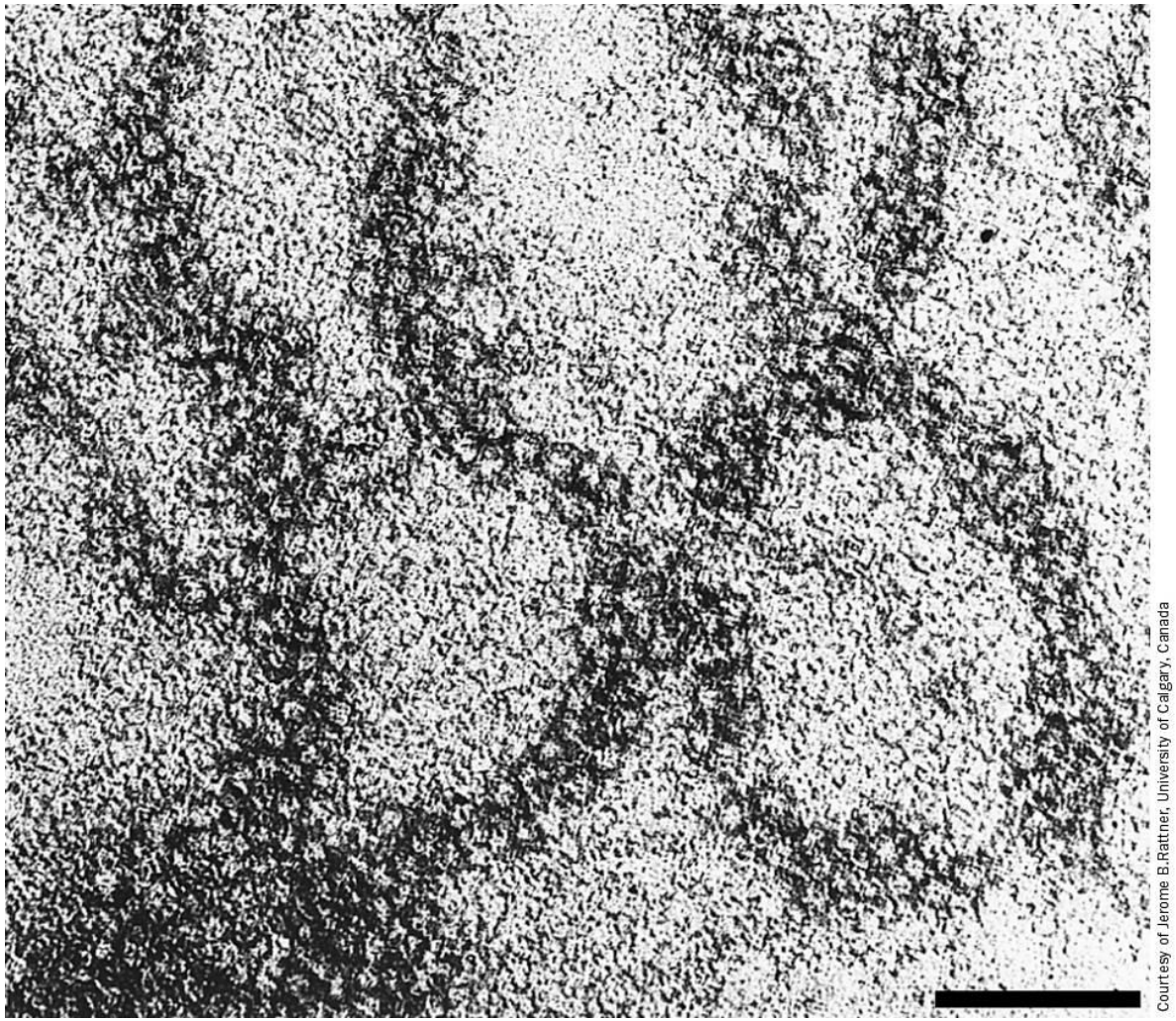
Chromosome Structure: How DNA is organized in a chromosome?

- The human genome contains 3.5 billion base pairs and more than 95% is non-coding(means not code fro aa to synthesis proteins) or "junk" DNA but they have another functions
- The DNA from single 23 human chromosomes have a length of 1 meter
- How such large quantities of DNA are packed into a single cell?

The DNA of a human chromosome

- Chromatin: Each chromosome is a complex of a single linear DNA molecule and histone proteins called chromatin

- Chromatin consists of:
  - 50% DNA
  - 50% histones (primary protein bind to DNA)



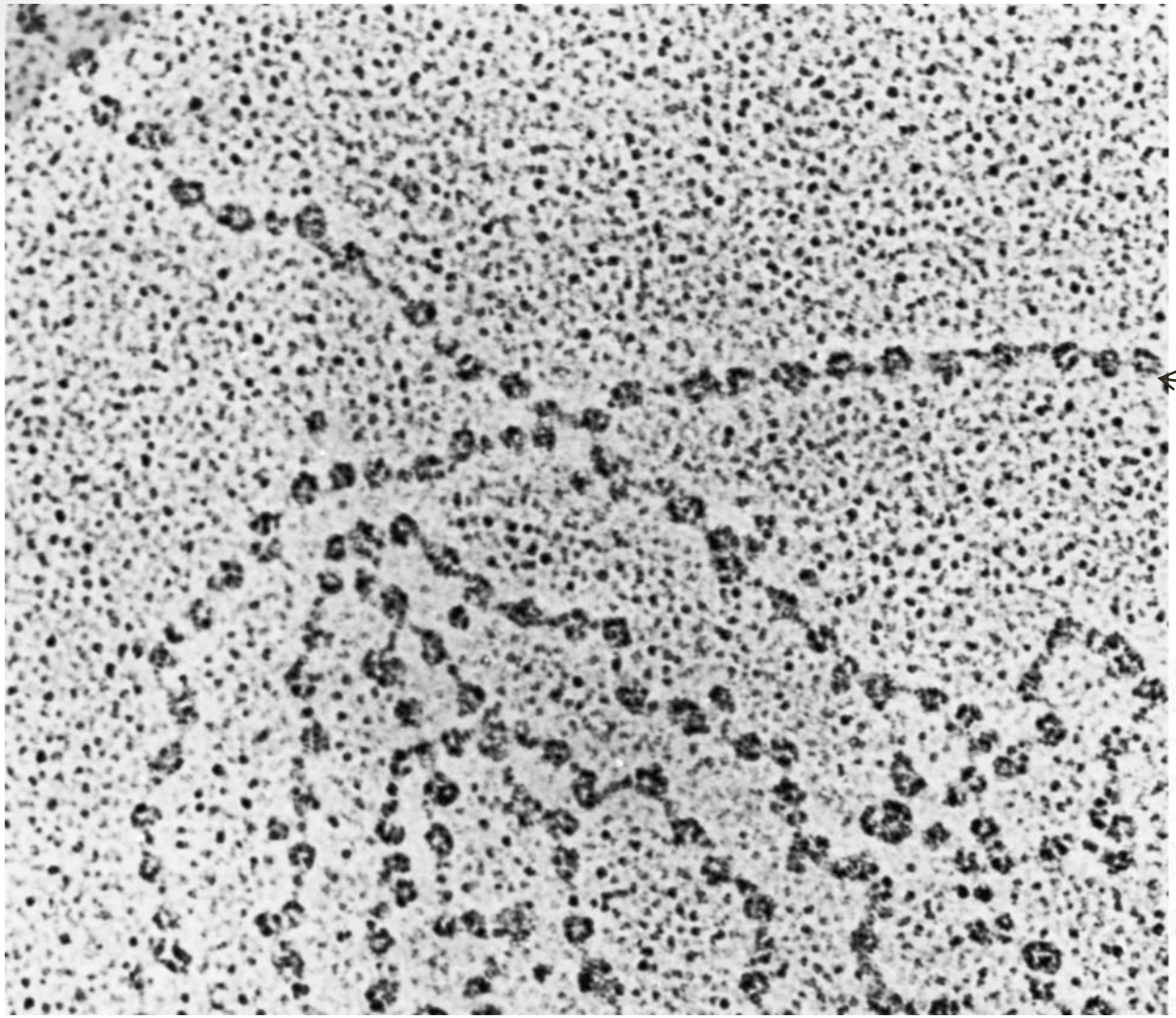
Electron micrograph of chromatin filaments

Histones

- Five major types of histones:
  - H1 H2A H2B H3 H4
- Histones have positively charged amino acids (arginine and lysine)
- These proteins bind to negatively charged PO_4 groups of DNA to stabilize the chromatin structure

Nucleosomes

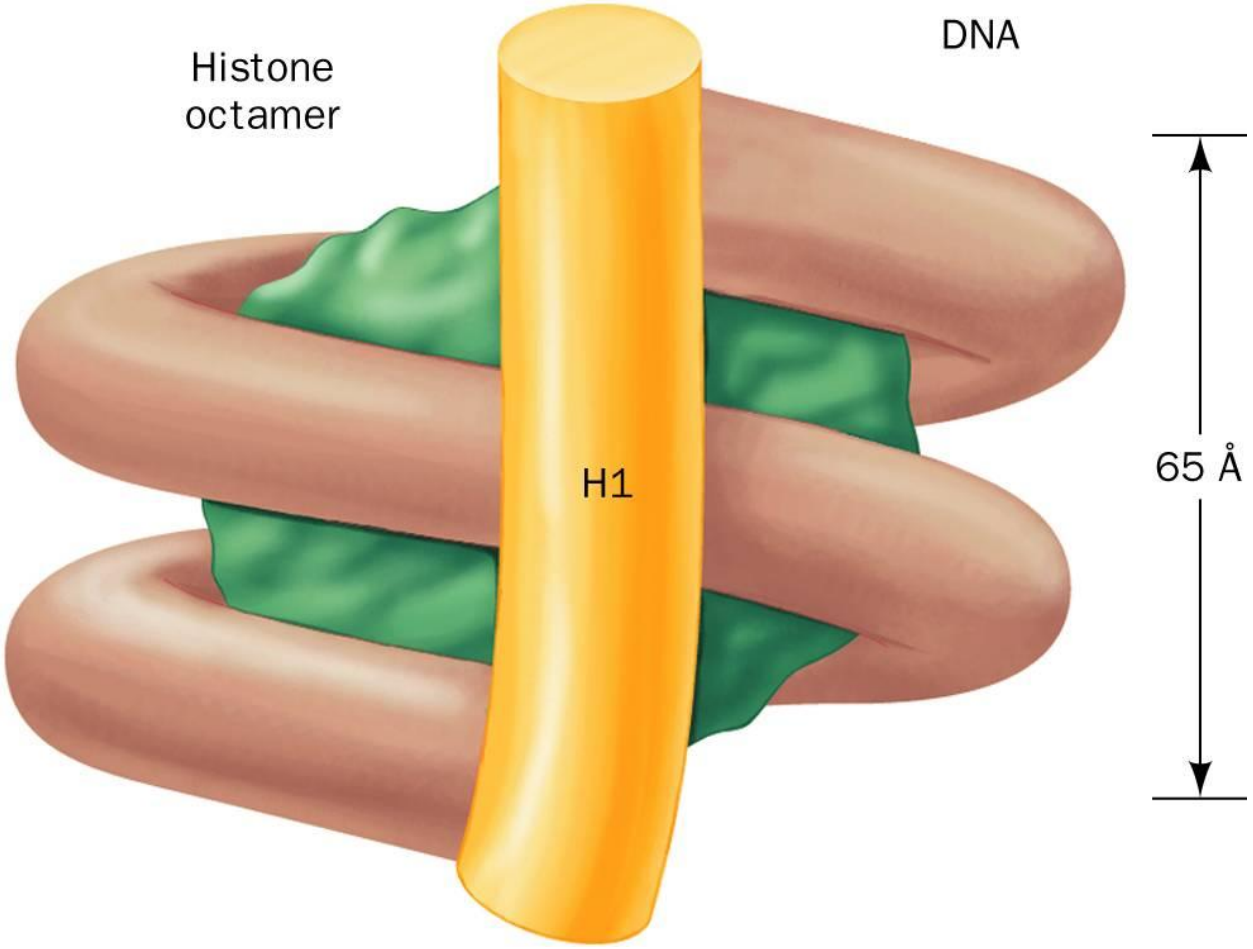
- Nucleosomes are particles consisting of DNA and histones connected by thin strands of naked DNA (like beads on a string; Sibhah in Arabic)
- Nucleosomes consist of the histone octamer 2*(H2AH2B H3 H4) (eight) and DNA
  - $(H2A)_2(H2B)_2(H3)_2(H4)_2$
- H1 binds to 2 complete helical turns of DNA
- And it secure by H1



Courtesy of Oscar L. Miller, Jr., University of Virginia

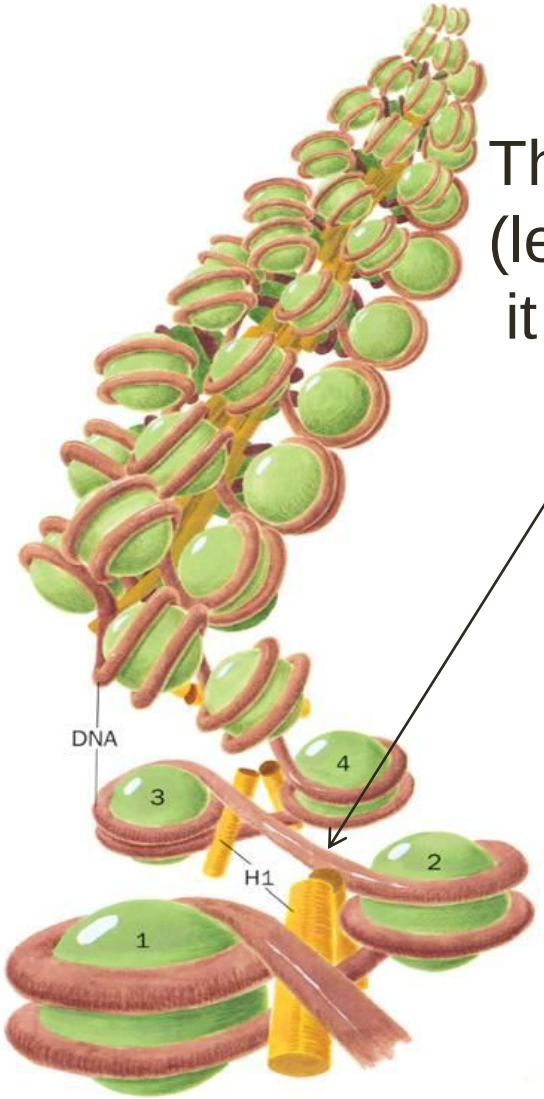
The round thing is the nucleosom e

Electron micrograph of chromatin showing nucleosomes



A nucleosome showing interaction of histones with the DNA

The naked DNA
(leaved with out histone)
it consists of 50 base pairs



Chromatin filament with nucleosomes and naked DNA