Molecular biology (1)

(Foundation Block)

By

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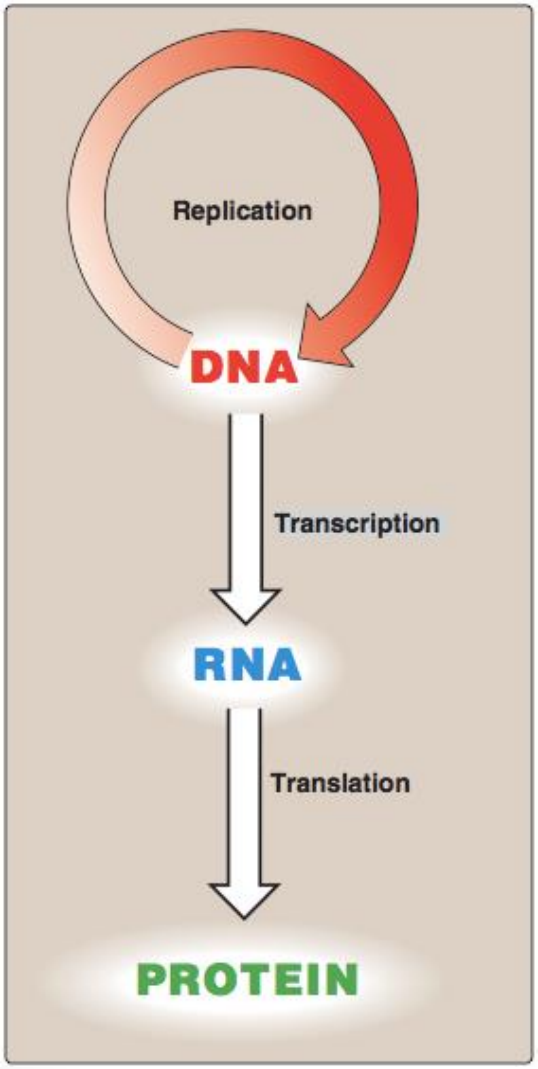
Objectives

By the end of this lecture, the students should be able to:

- Know the central dogma of molecular biology.
- Understand the composition, types and structure of DNA and RNA.
- Describe the organization of DNA in the chromosome and the role of histone proteins.

The central dogma of Molecular Biology



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

*RNA is translated into **proteins**.*

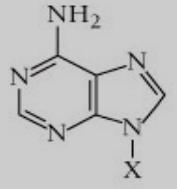
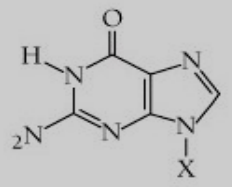
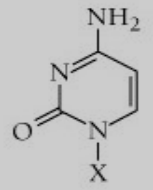
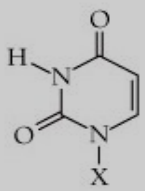
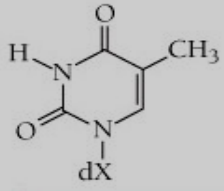
Human genome contains about 35,000 genes

Nucleic acids

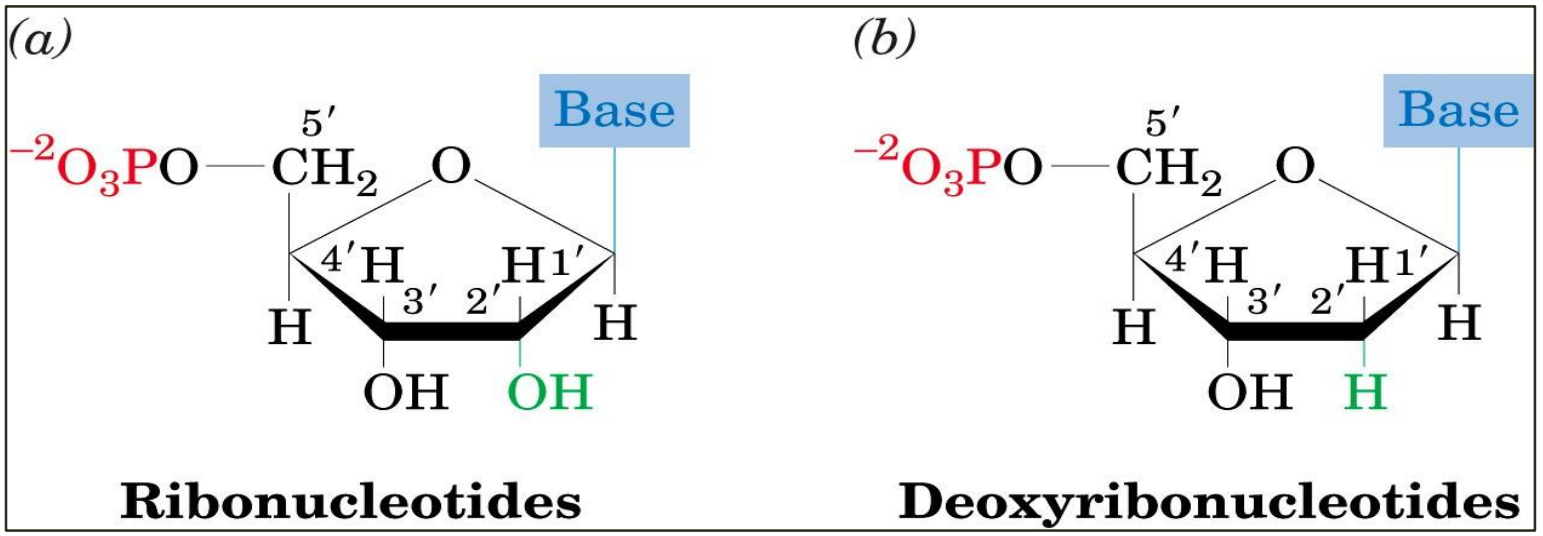
- Required for the storage and expression of genetic information.
- **Two types:**
  - DNA (Deoxyribonucleic acid).
  - RNA (Ribonucleic acid).
- Building blocks of nucleic acids are nuclueoside triphosphates (**nucleotides**).

Nucleotides

- **Nucleotides are composed of:**
  1. **Nitrogenous base:**
     - Purines: **A**denine (**A**) and **G**uanine (**G**)
     - Pyrimidines: **C**ytosine (**C**), **T**hymine (**T**) and **U**racil (**U**).

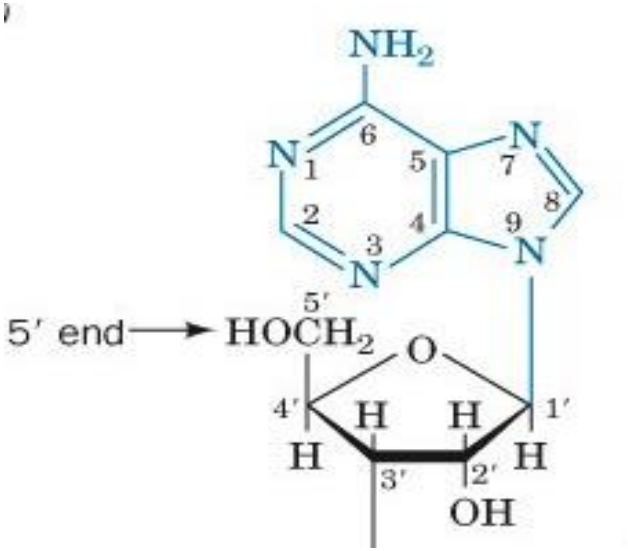
Base Formula	Base (X = H)	Nucleoside (X = ribose[a])	Nucleotide[b] (X = ribose phosphate[a])
	Adenine Ade A	Adenosine Ado A	Adenylic acid Adenosine monophosphate AMP
	Guanine Gua G	Guanosine Guo G	Guanylic acid Guanosine monophosphate GMP
	Cytosine Cyt C	Cytidine Cyd C	Cytidylic acid Cytidine monophosphate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

2. **Sugar: pentose with 5 carbon ring:**
   a) Ribose (with –OH at C_2).
   b) Deoxyribose.

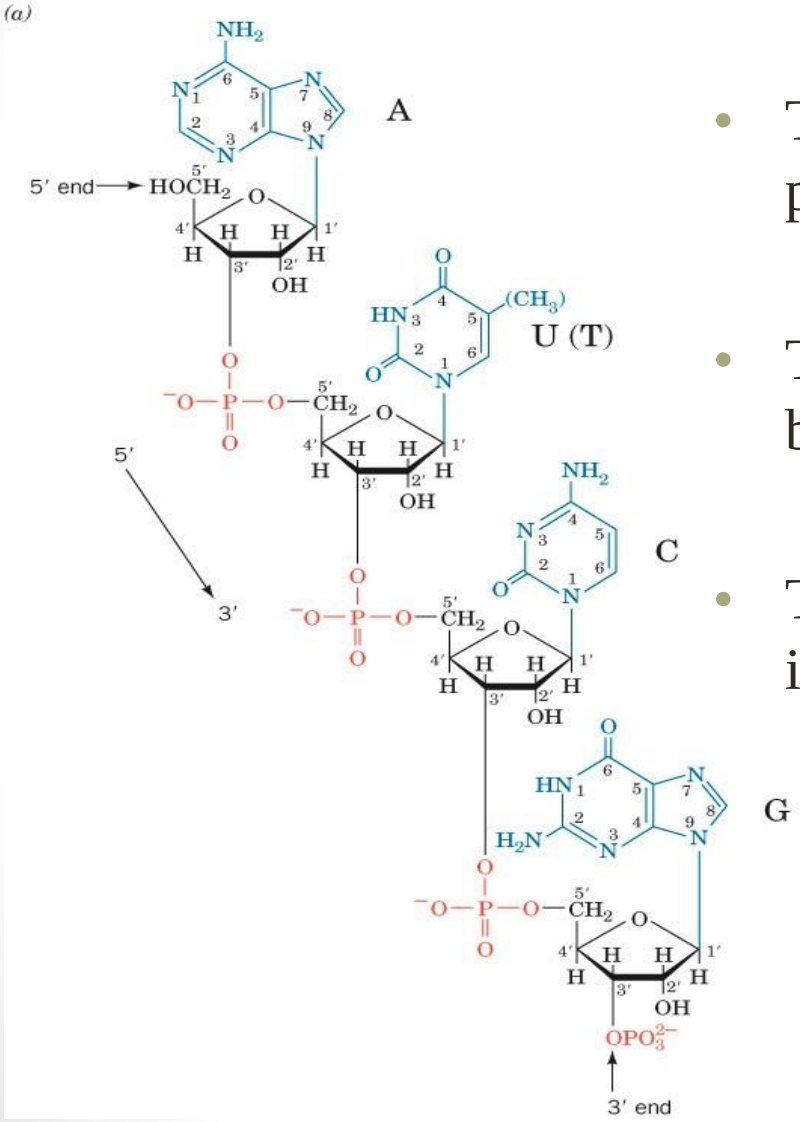


3. **Phosphate groups.**

- The **sugar carbon** numbers are primed (1’ 2’ 3’ etc.), while **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.



Chemical structure of DNA & RNA



- 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 linkage between the nucleotides is called **phosphodiester bond**

Function of nucleotides

- Polymers of nucleotides (as DNA or RNA) store and transfer genetic information.
- Free nucleotides and their derivatives perform various metabolic functions not related to genetic information.
- Other nucleotides: FAD, NAD, CoA.

The double helix DNA

- The structure of DNA was first determined by James Watson and Francis Crick in 1953.

- Commonly known as Watson-Crick structure.

Features of Watson-Crick DNA structure

1. Two polynucleotide chains wind around a common axis to form a double helix.

1. The two strands are anti-parallel (run in opposite direction).

1. Each strand is a right-handed helix.

2. The nitrogenous bases are in the center of the double helix and the sugar-phosphate chains are on the sides.

- The surface of the double helix contains 2 grooves: the major and minor grooves.

- Each base is hydrogen bonded to a base in the opposite strand to form a base pair (A-T and G-C), known as complementary base pairing.

- The helix has 10 base pairs (bp) per turn.

Watson-Crick base pairs

Adenine (A) = Thymine (T)

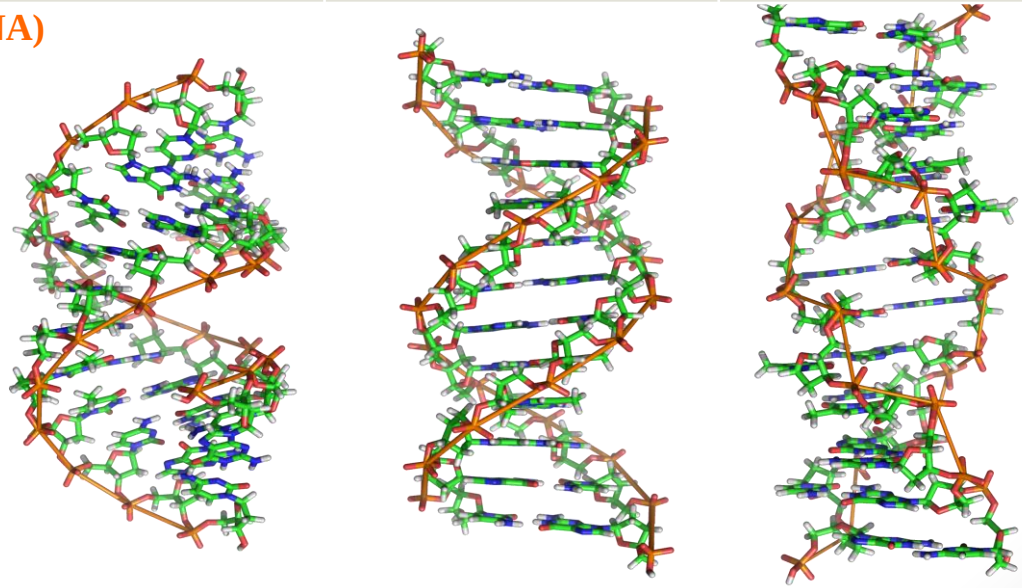
Guanine (G) ≡ Cytosine (C)

In RNA, Thymine is replaced by Uracil (U)

Types of DNA structure

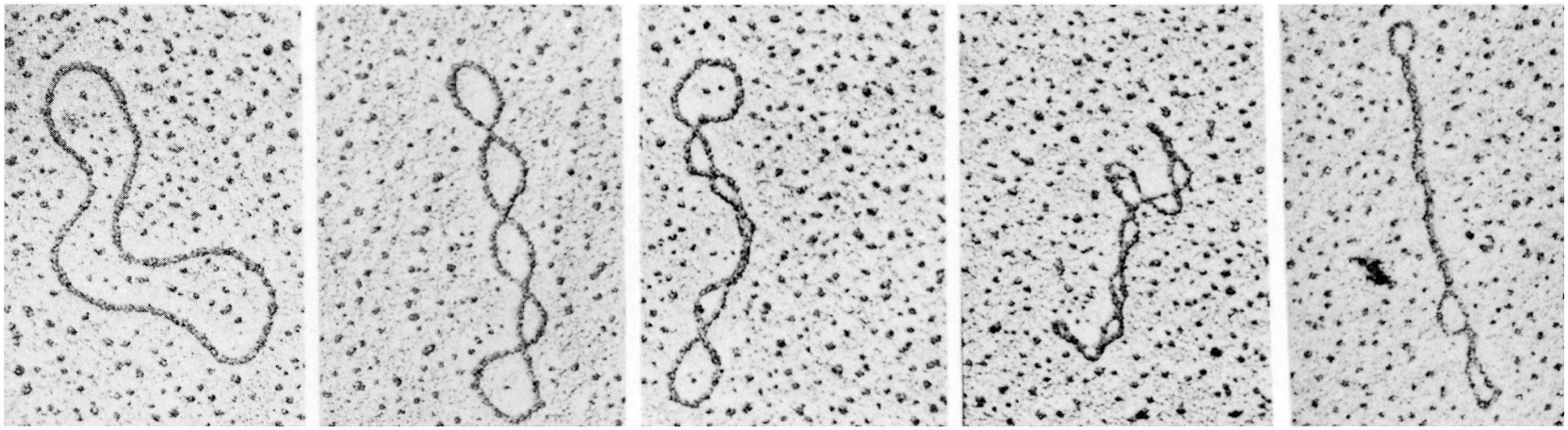
	A-DNA	B-DNA*	Z-DNA
Direction	Right-handed	Right-handed	Left-handed
Helix length	Short	Elongated	More elongated
Major groove	Deep and narrow	Wide	Not real groove
Minor groove	Wide	Narrow	Narrow
Placement of bp	Displaced away from the helical axis	Centred over the helical axis	Zig-zag pattern (nearly perpendicular to the helical axis)
bp per turn	11	10	12
Conformation of deoxyribose	C_3	C_2	G (C_2) ; C (C_3)

*** Watson-Crick model (B-DNA)**



DNA supercoiling

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

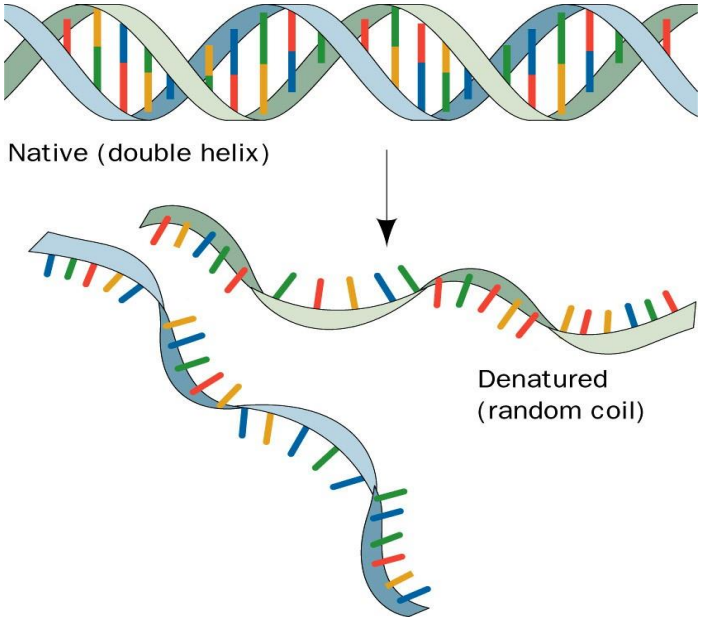


Electron micrographs by Laurien Polder. From Kornberg, A. and Baker, T.A., DNA Replication (2nd ed.), p. 36, W.H. Freeman (1992). Used with permission

Melting temperature (MT)

- The temperature at which the double-stranded DNA is separated into two single strands.

- MT of DNA depends on nitrogenous base content (A-T and G-C). G-C has 3 hydrogen bonds ➔ stronger than A-T.



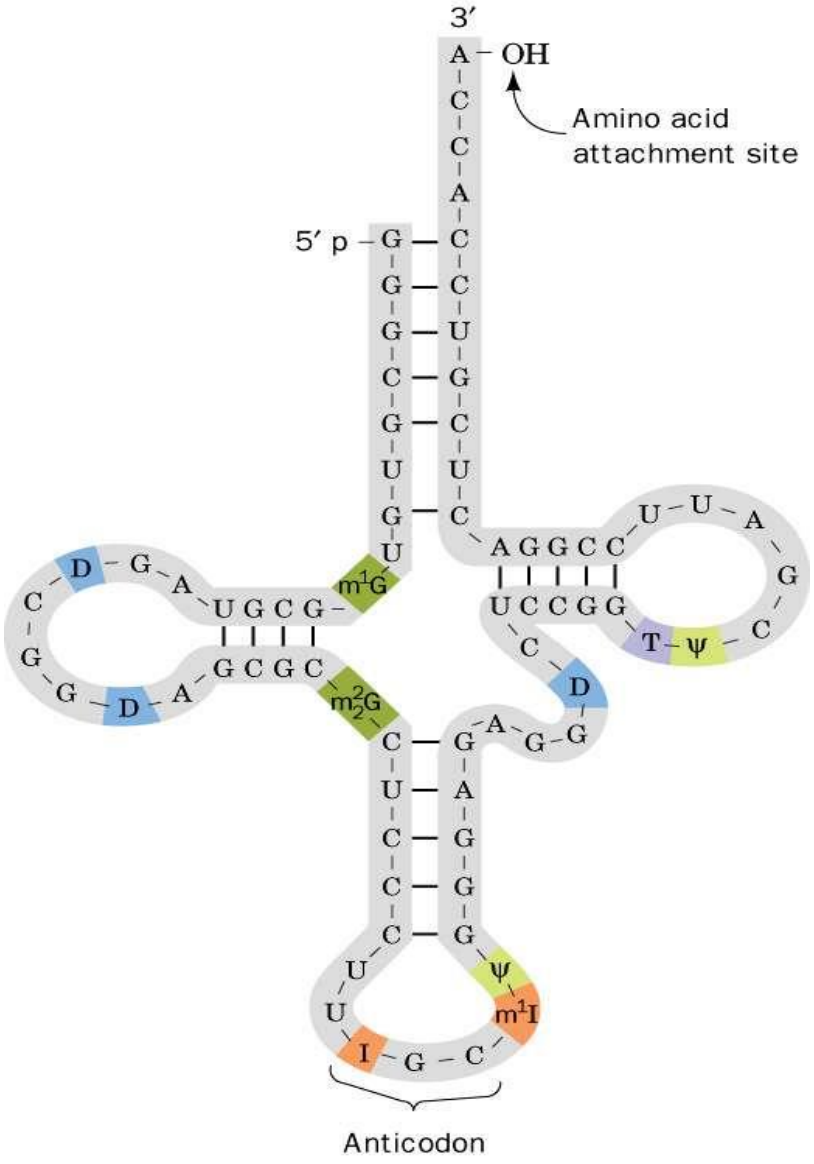
RNA (Types and function)

- **RNA is a single-stranded polymer of ribonucleotides.**

- **Types of RNA:**
  - *mRNA (messenger RNA)* ➔ *Function*: Transcription process (from DNA to mRNA).

  - *tRNA (transfer RNA)* ➔ *Function*: Recognition and transferring. It recognizes amino acids' codons and transfers the selected amino acids to the growing protein chain.

  - *rRNA (ribosomal RNA)* ➔ *Function*: Site of protein synthesis (factory).



Structure of a tRNA

How DNA is organized in a chromosome?

- The human genome contains 3.5 billion base pairs and more than 95% is non-coding or “junk” DNA.
- 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?
- Each chromosome is a complex of a single linear DNA molecule and protein called **chromatin**.
- 50% of chromatin consists of proteins called **histones**.

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.

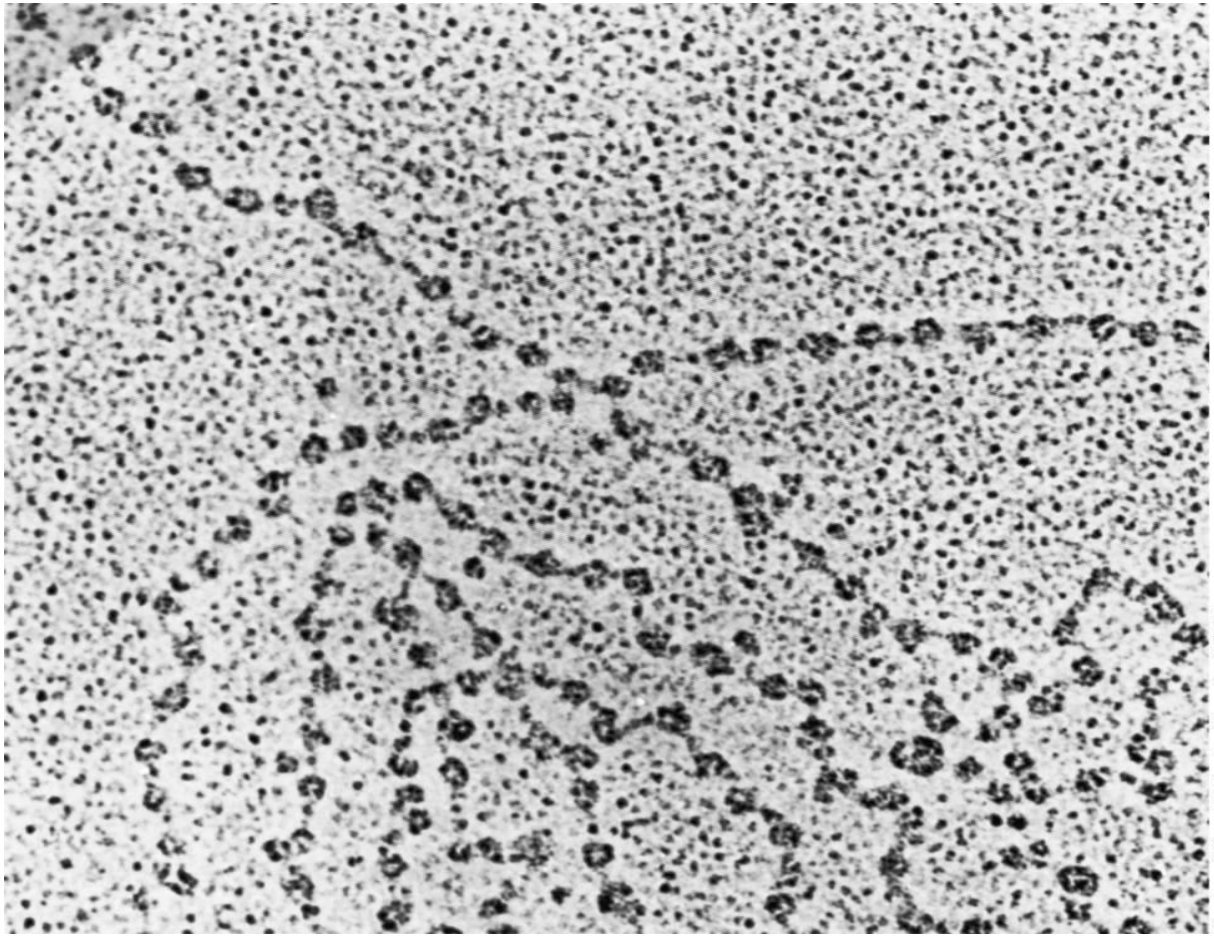
Nucleosomes

- Nucleosomes are particles consisting of DNA and histones connected by thin strands of naked DNA (like beads on a string; Sibhah in Arabic).

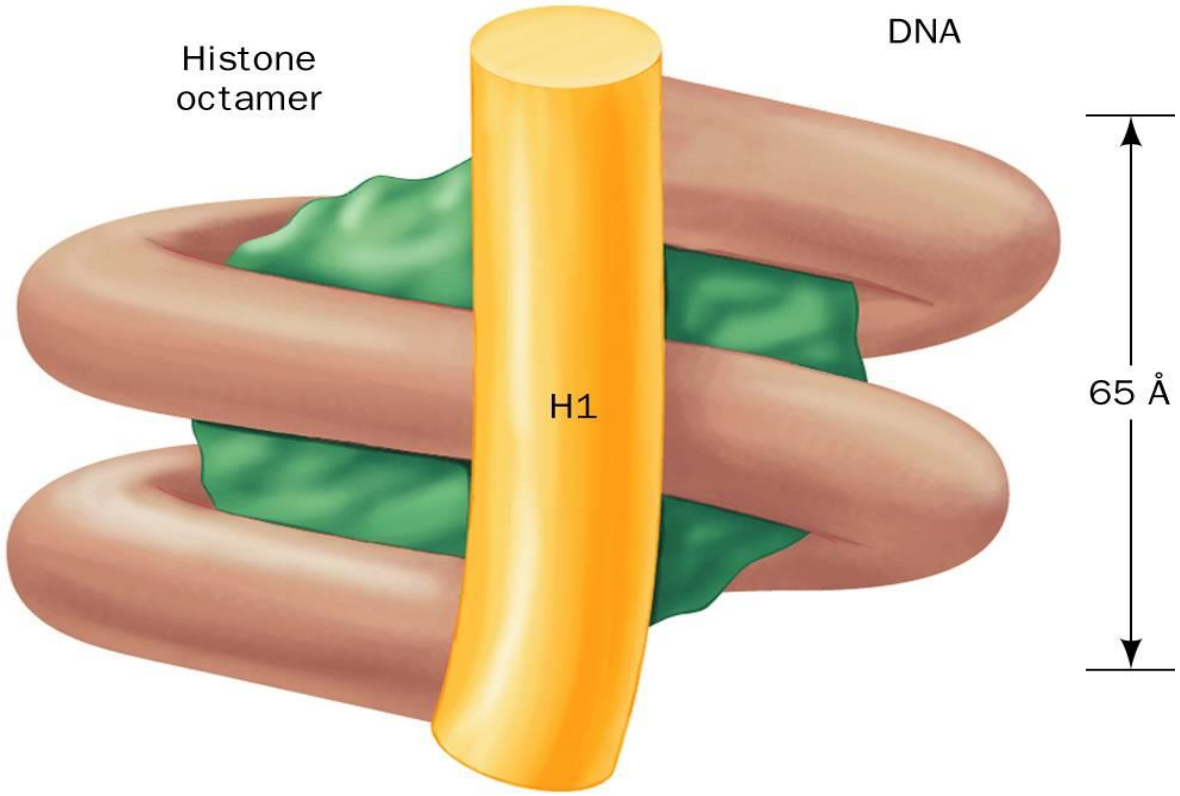
- Nucleosomes consist of the histone octamer (eight) and DNA

$$(H2A)_2(H2B)_2(H3)_2(H4)_2$$

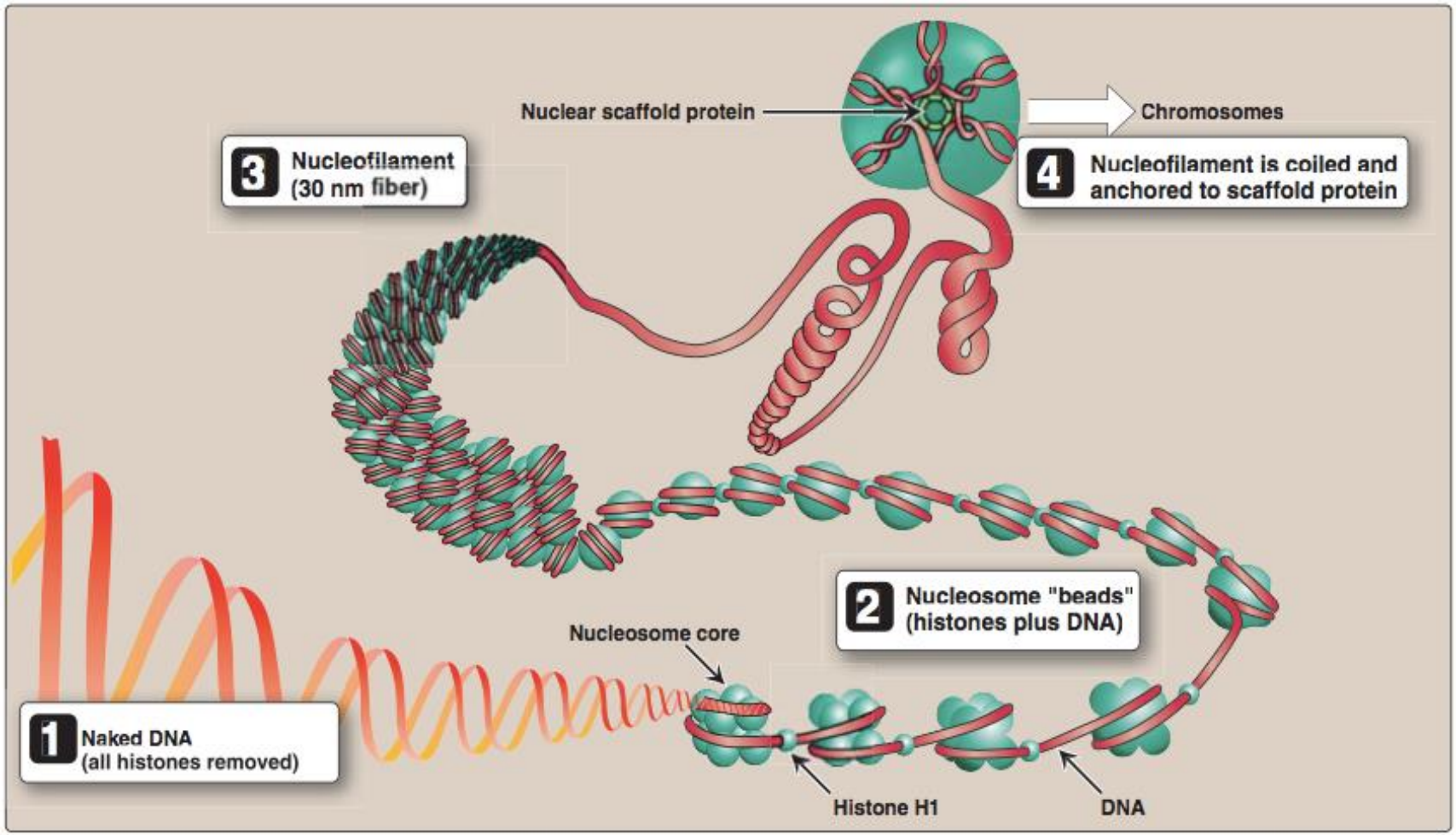
- H1 binds to 2 complete helical turns of DNA.



Electron micrograph of chromatin showing nucleosomes



A nucleosome showing interaction of histones with the DNA



Chromatin filament with nucleosomes and naked DNA

Take home messages

- The central dogma of molecular biology involves three components: DNA, RNA and protein.
- There are two chemically distinct types of nucleic acids: DNA and RNA, which perform several crucial functions.
- To package the long sequence of the genomic DNA, it is highly organized into chromosomes.

Reference

- Lippincott's Illustrated reviews: Biochemistry 6th edition, Unit 6, Chapter 29 and 30, Pages 395-430.

- Biochemistry by Voet and Voet 3rd edition.

- http://www.tulane.edu/~biochem/nolan/lectures/rna/bzcomp2.htm

- http://biowiki.ucdavis.edu/Genetics/Unit_I%3A_Genes,_Nucleic_Acids,_Genomes_and_Chromosomes/Chapter_2._Structures_of_nucleic_acids/B-Form,_A-Form,_Z-Form_of_DNA