ADVANCED MOLECULAR BIOLOGY
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Block 1: Unit 2

Histone proteins and its structure

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HISTONE PROTEINS AND ITS STRUCTURE

LECTURE NO- 5

Objective-

- **Definition of histone**
- **Structure of histone**
- **Types of Histone protein**
- **Concept of Nucleosome**
- **Function of Histone Protein**

HISTONE PROTEIN

- **Histones** belong to a family of highly basic proteins whose primary job is to associate with DNA and condense the chromatin.
- Histones are rich in positively charged amino acids such as lysine and arginine. They are alkaline or basic pH proteins, and their positive charges allow them to associate with the negatively charged DNA with greater affinity.
- Histones are found in the nucleus of a eukaryotic cell where nuclear DNA resides, and they form the major protein within the chromatin of a eukaryotic cell. Chromatin is the complex of DNA and proteins that form the chromosomes of a eukaryotic cell nucleus

- The length of nuclear DNA is too large to be fitted in the tiny space of a nucleus as linear strands; instead, DNA is wrapped around complexes of histone proteins that allow the compaction of DNA into chromosomes.
- Condensed or compact chromatin fits inside the nucleus with histones providing structural support to the chromosomes. The linear DNA undergoes gradual condensation with hierarchy starting from the basic structural units of chromatin, **nucleosomes**.
- A nucleosome consists of a segment of DNA (around 147 base pairs in length) wrapped around a complex of eight histone proteins.
- A nucleosome is the basic and repeating unit of the eukaryotic chromatin, giving it an appearance like beads on a string under the microscope, where each "bead" is one nucleosome.

The consecutive nucleosomes are separated by around 50 base pairs of long DNA segments called the linker DNA. These nucleosomes further fold into a higher order of condensation, ultimately resulting in the compact chromosome structure.

Histones prevent the tangling or damage of DNA strands. Moreover, histones and their modifications play a crucial role in the regulation of eukaryotic gene expression

Types of Histone Proteins

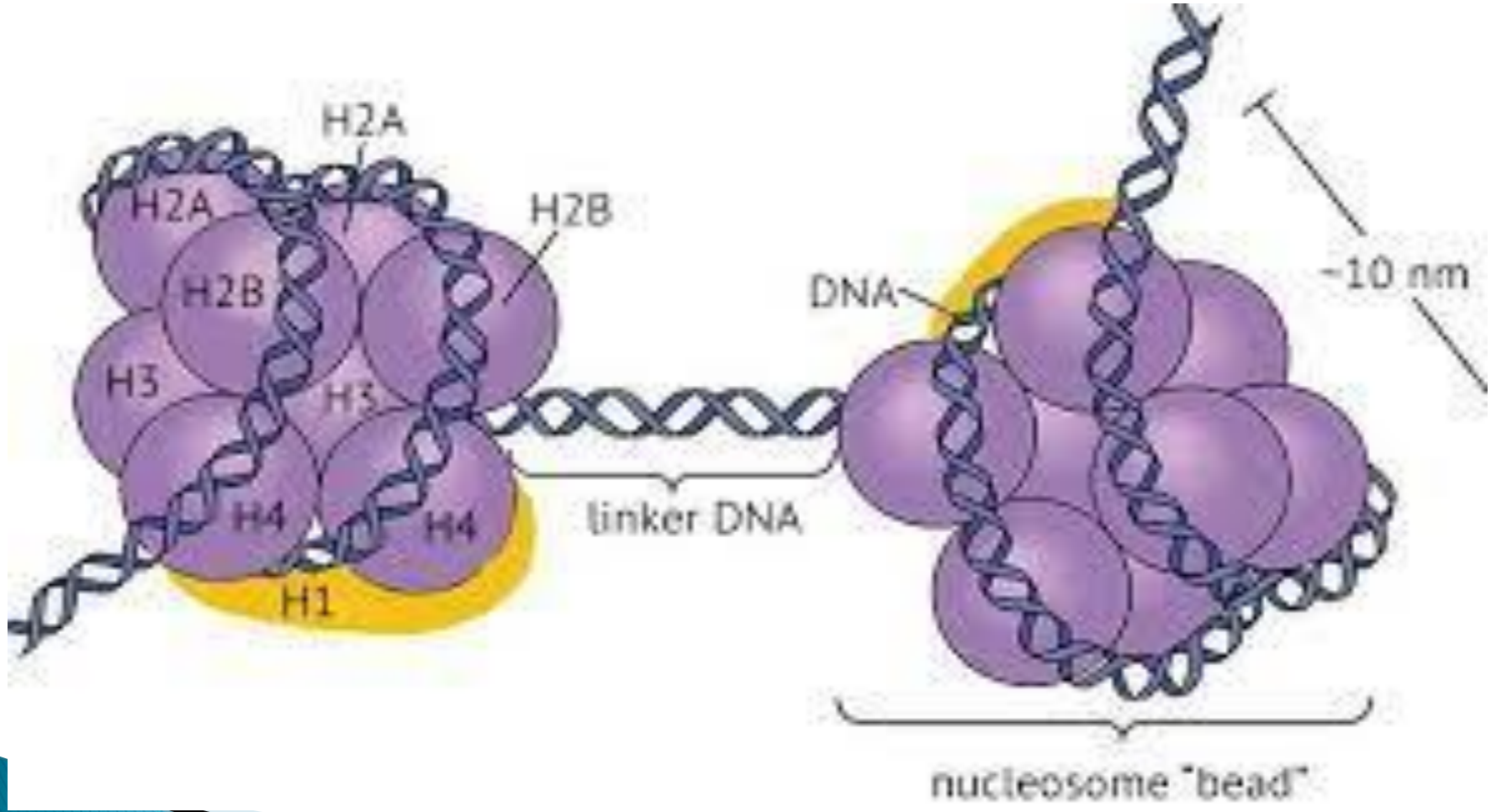
- Histone proteins fall into two major categories: **core histones** and **linker histones.**
- These categories include five types of histone proteins.
- H1 and its homologous protein H5 belong to the linker histone protein family, while H2A, H2B, H3, and H4 are known as core histones.
- Core histones are the part of the nucleosome; H2A, H2B, H3, and H4 complex together and act as a spool which the DNA wraps around.
- Linker histones on the other hand bind to linker DNA and are involved in the higher-order condensation of the chromatin. Several variants for both core and linker histones can be found in a eukaryotic cell.

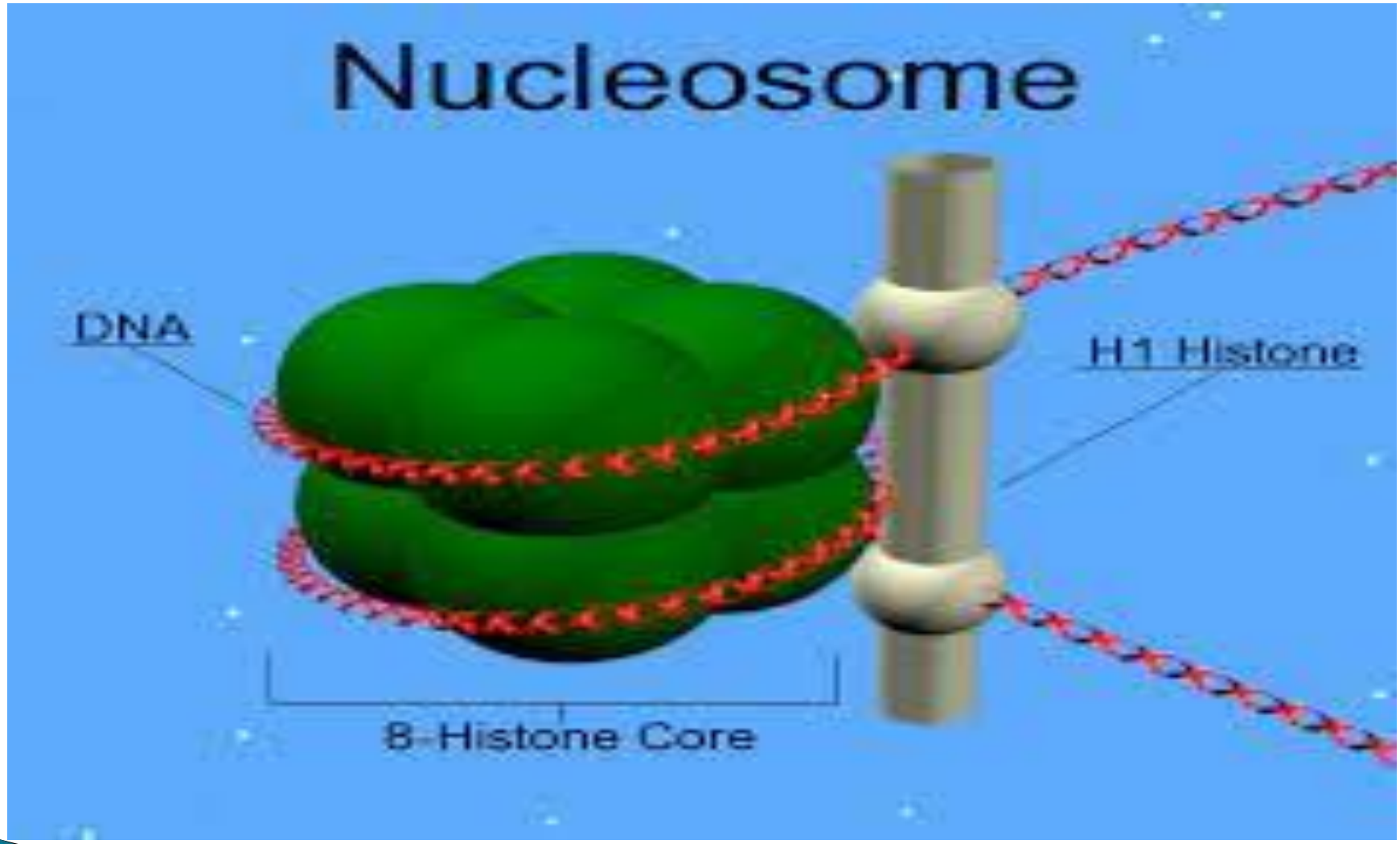
Structure of Histones

All core histones share two common structural domains:

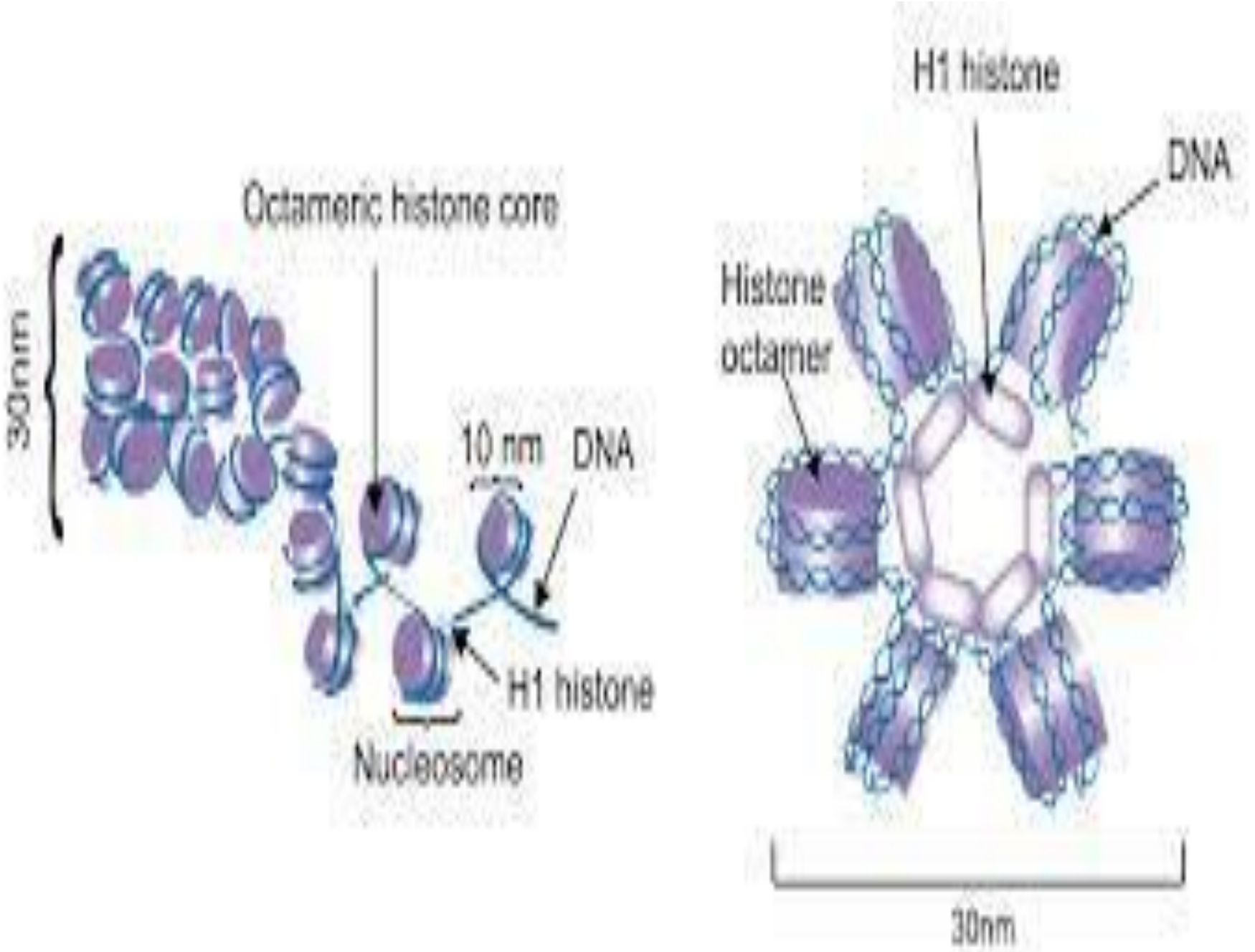
1. The histone fold domain
2. The histone tail, rich in lysine residues

Structure of Histone protein




Nucleosome
DNA
H1 Histone
8 Histone Core

- The histone core of the nucleosome is made up of histone **dimers** and **tetramers.**
- Dimers are formed by two histones joined together while tetramer consists of four histones.
- Core histones H2A and H2B together form dimers (one H2A and one H2B protein joined together) and histones H3 and H4 join to form tetramers consisting of two H3 and two H4 proteins.
- Two H2A–H2B dimers and one H3–H4 tetramer combine to form the octamer (consists of eight histone proteins) histone core of the nucleosome.
- Approximately 147 base pairs of long DNA segment are wrapped in 1.6 turns around this octameric histone core.
- Since nucleosomes are the basic unit, this makes histones the main proteins of the chromatin.


Octameric histone core
30nm
10 nm
DNA
H1 histone
Nucleosome
H1 histone
DNA
Histone octamer
30nm

What Do Histones Do?

- Histones perform the following major functions in the cell:
- Compacting DNA or DNA packaging
- Providing structural support to the chromosomes
- Regulating gene expression or gene regulation
- Histone proteins provide structural support to the chromosomes and help in DNA packaging. With the structural support, chromosomes achieve their distinct X-shaped structure.
- Histones associated with the DNA prevent them from being intertwined and damaged.
- DNA packaging is essential for the high-order compaction of the DNA so that it is able to fit into a tiny nucleus. Apart from these structural and physical associations, histones also play a crucial role in the regulation of gene expression.
- Histones undergo several chemical modifications and can remodel chromatin through these modifications. Such chromatin remodeling by histone modifications results in the regulation of several genes.