Organization of eukaryotic DNA

By

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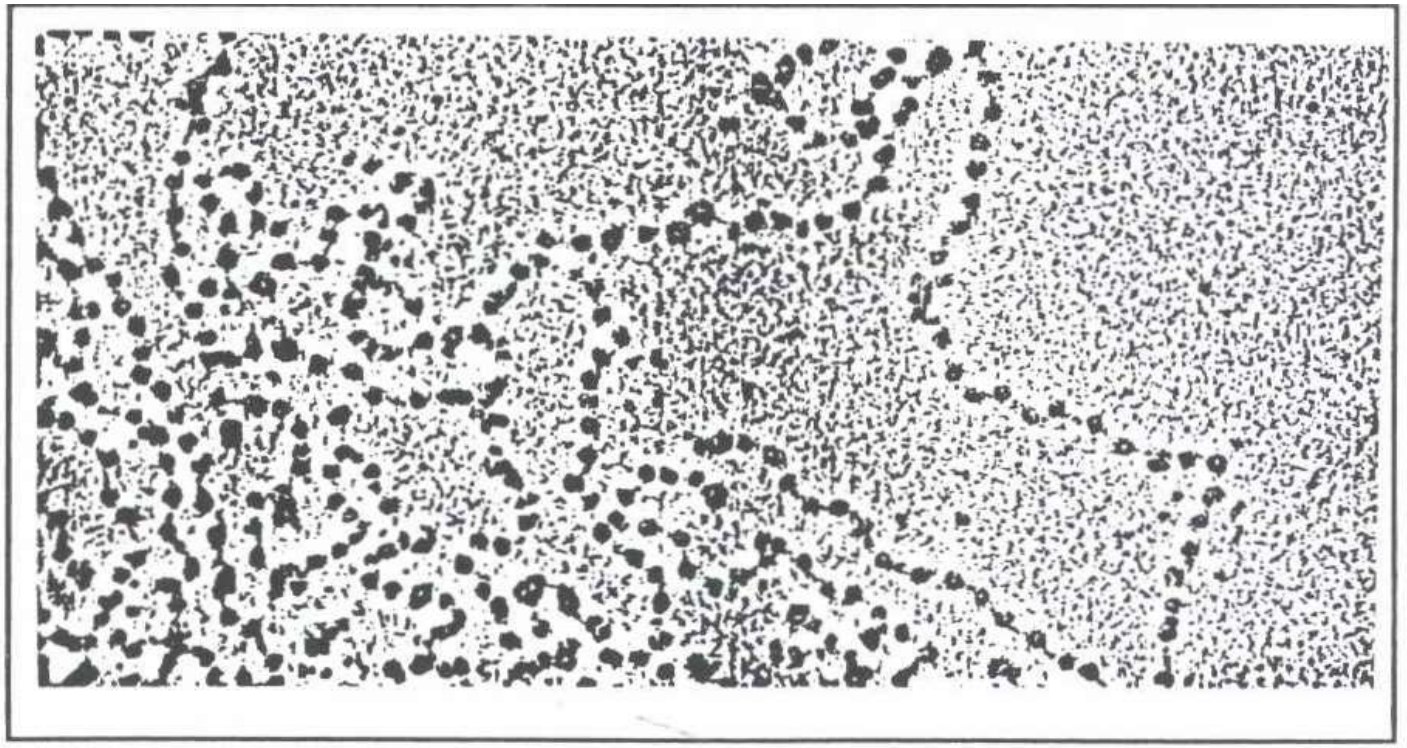
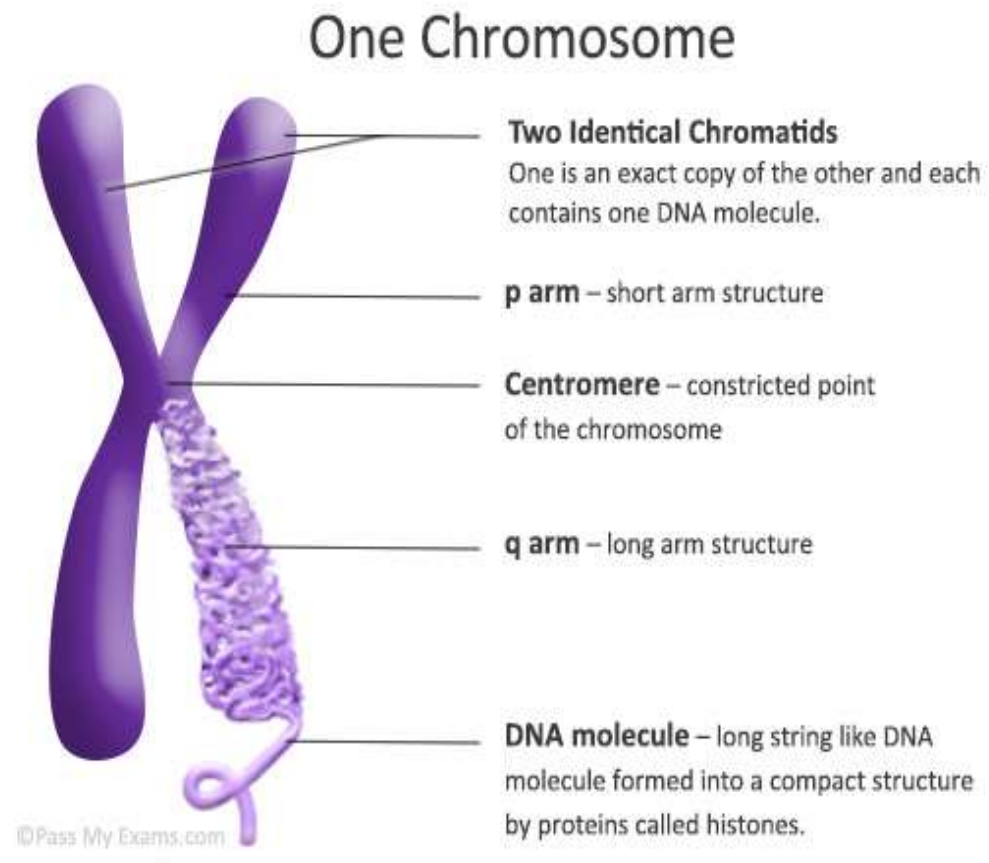
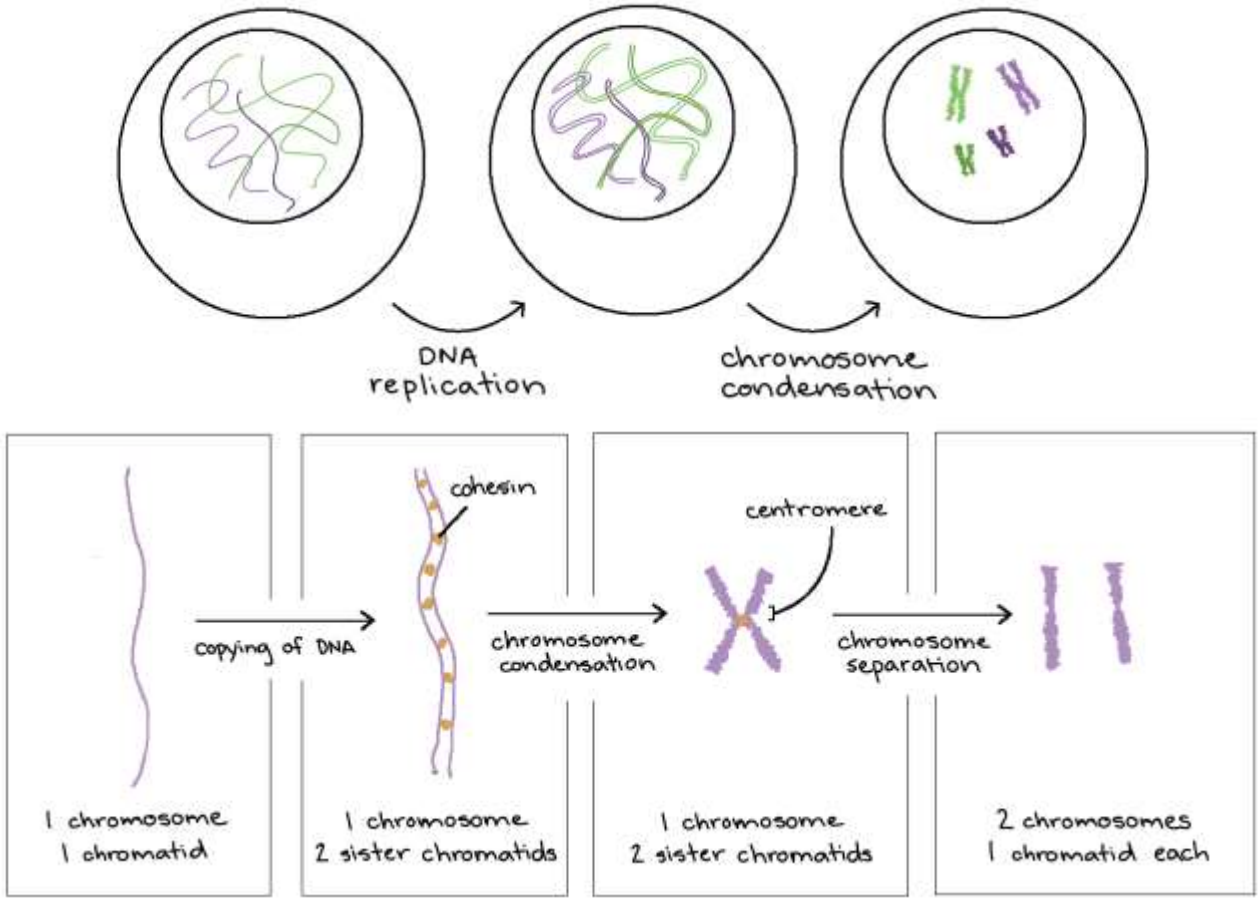
- **Chromatin**
- The simplest form of chromatin is present in non dividing eukaryotic cells, when chromosomes are not sufficiently condensed to be visible by light microscope.
- Chromosomes are normally visible under a light microscope only when the cell is undergoing the **metaphase** of cell division, when the **chromosome is in its most condensed state.**

- In electron microscope, chromatin resembles a regularly beaded thread.



- Before cell division, all DNA molecules are replicated or doubled, the chromatin is **supercoiled** in the form of chromosomes and each chromosome is formed of two identical chromatids.
- A chromatid is one of the two identical halves of a chromosome that has been replicated in preparation for cell division.





As long as the sister chromatids are connected at the centromere, they are still considered to be one chromosome. However, as soon as they are pulled apart during cell division, each is considered a separate chromosome.

- **Each chromatid consists of :**

1- A single DNA molecule.

2- Histone proteins: they are **basic proteins** rich in lysine and arginine (positively charged), that are united to the **DNA which is acidic** (negatively charged) due to the presence of phosphate groups.

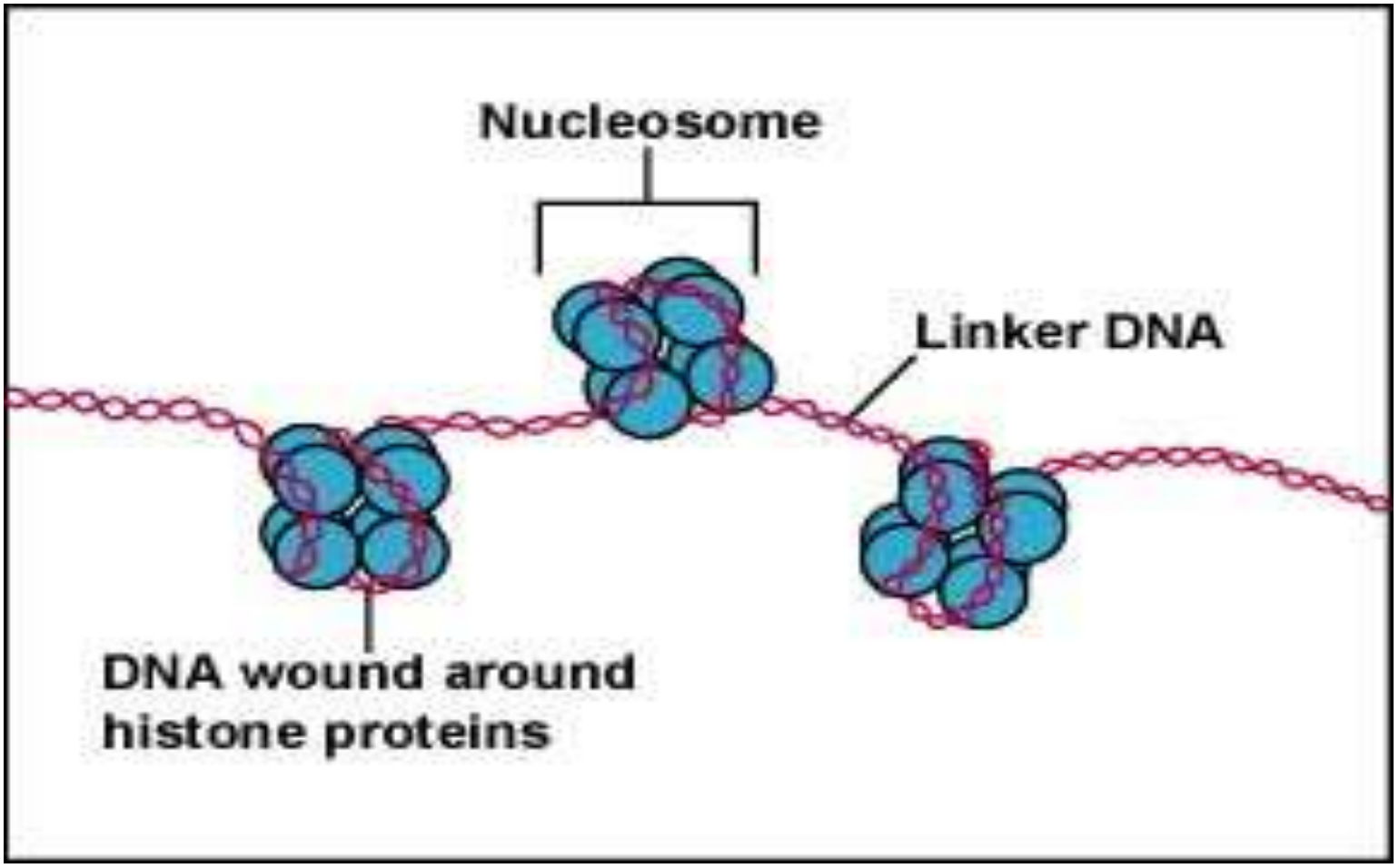
- Five major types of histones (H1, H2A, H2B, H3 and H4) are present in eukaryotic chromosomes.
- Histones play an **important role in DNA supercoiling** and **regulation of gene expression**.

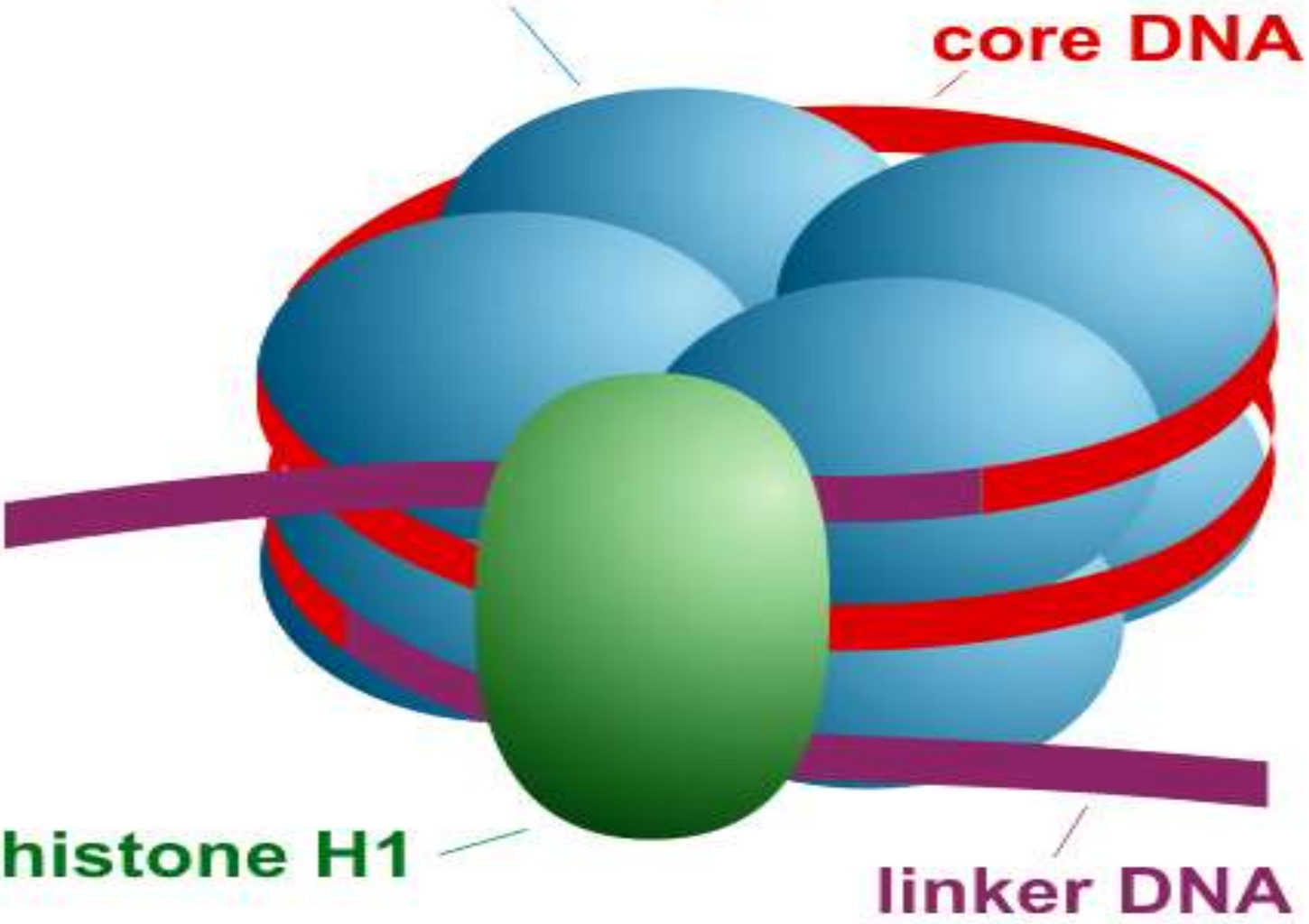
3- Non-histone proteins: include enzymes involved in DNA replication and transcription as well as proteins regulating these two processes.

- The two identical chromatids of each chromosome are connected at the **centromere**, which is rich in A---T and is about 130 bp long. The centromere is connected to specific proteins to form a complex known as **kinetochore**, which is connected to the mitotic spindle.

- Each chromatid has two ends or **telomeres**, that are characterized by the presence of variable repeat number of specific sequence of several kilobases long, which is (TTAGGG)n in humans

- Each chromatid is formed of many **nucleosomes**.
- Each nucleosome is formed of eight histones (histone octomer or histone core) or two copies of each of H2A, H2B, H3 and H4.
- Around the histone octomer is wrapped 1.75 left – handed turns of DNA (contains average **140** bp).
- Linker or spacer DNA (contains average **60** pb) connects the different nucleosomes like beads on a string. **H1 histones are connected to these linker DNA segments**.
- Linker histones such as H1 and its isoforms are involved in chromatin compaction and sit at the base of the nucleosome near the DNA entry and exit binding to the linker region of the DNA.


Nucleosome
Linker DNA
DNA wound around
histone proteins


octamer of core histones:
H2A, H2B, H3, H4 (each one ×2)
core DNA
histone H1
linker DNA

- **Supercoiling of DNA:**

- Supercoiling of DNA is important for its packing within the small nucleus. (in mammalian cells approximately 2 m of linear DNA have to be packed into a nucleus of roughly 10 µm diameter).

- **The first level** of supercoiling (packing ratio of 10) around histone octomer in the form of nucleosomes produces a ten fold shortening of the length of DNA to form **the 10-nm fibril** (10 nm in diameter)

- **The second level of supercoiling** (packing ratio of 50):

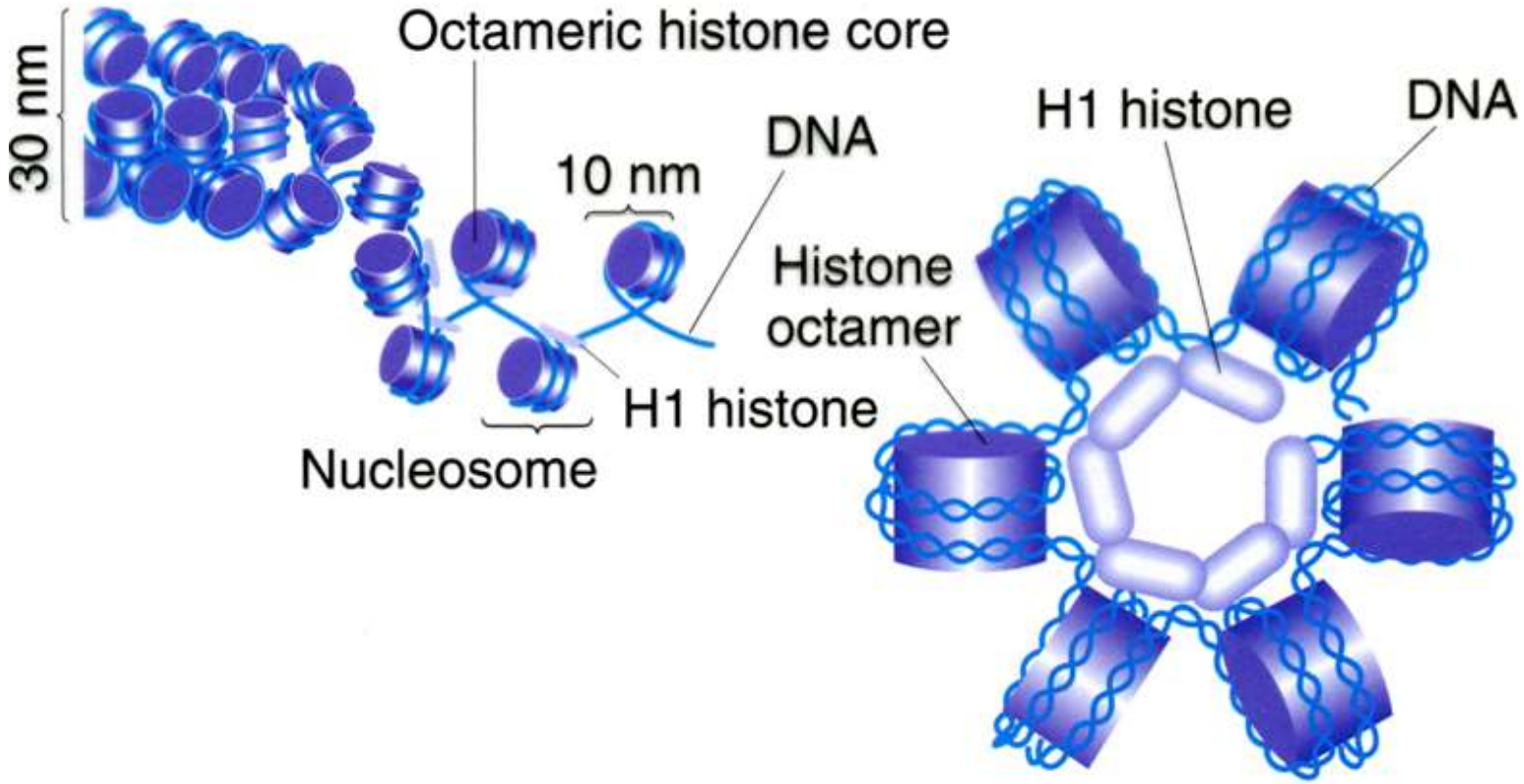
  Requires the presence of H1, this leads to 50-fold shortening of the DNA and it looks like a solenoid (cylindrical coil), **each turn contains 6 nucleosomes** that form **the 30-nm fiber** (30 nm in diameter).

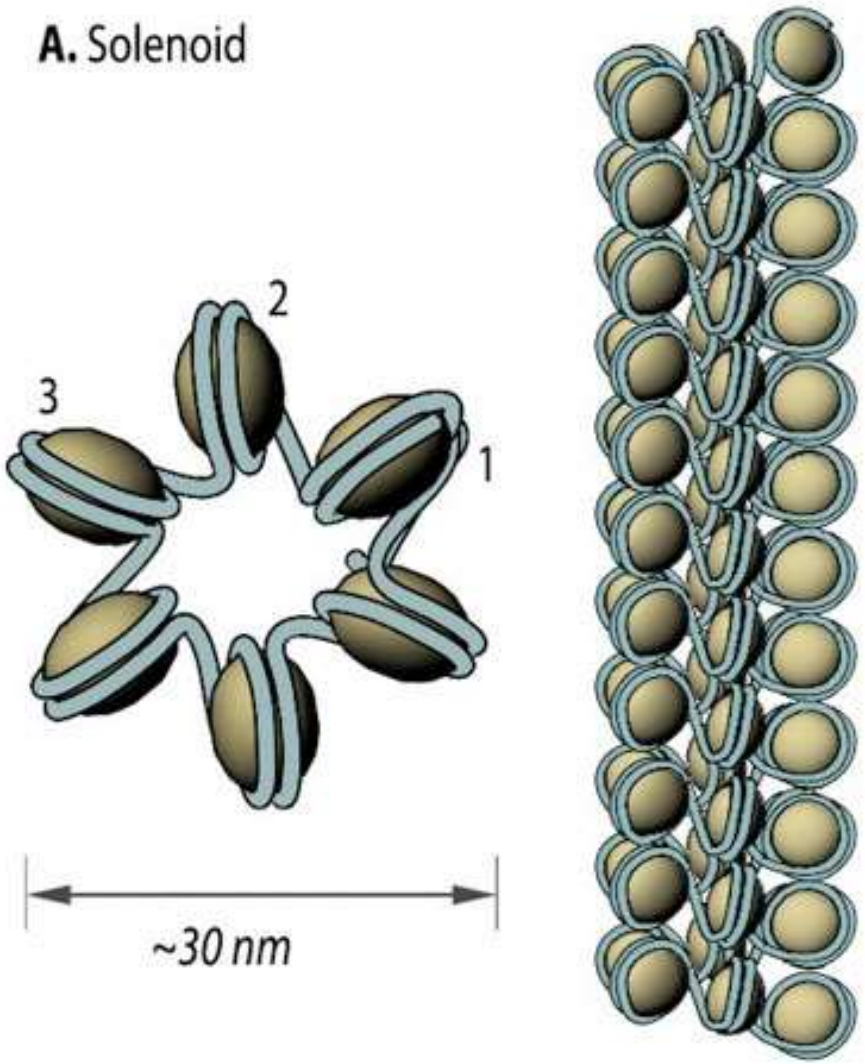
- **The third level of supercoiling** (packing ratio of 8000):

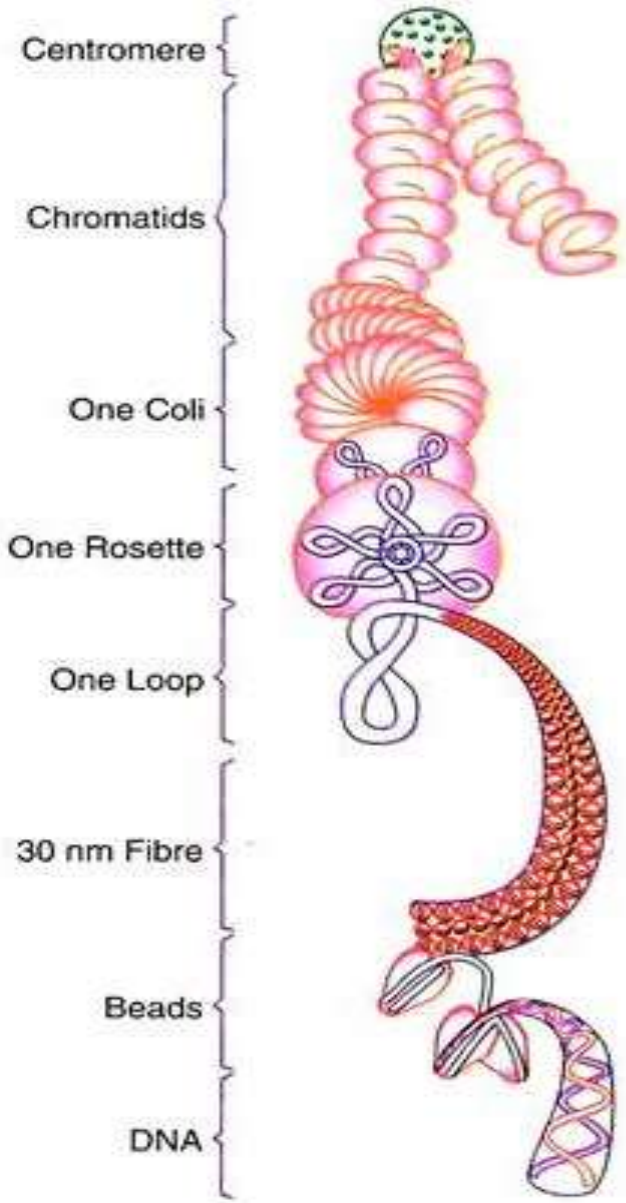
  Coiling of the 30nm fiber into **twisted-looped structure** attached to a protein scaffold in the form of rosettes. Each rossette contains 6 loops.

  The rosettes are arranged in the form of a coil to form each chromatid, each turn of the coil is composed of about **30 rosettes.**

30 nm fibers


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


A. Solenoid
2
3
1
~30 nm



Packaging of eukaryotic DNA

Compaction of DNA in a eukaryotic chromosome