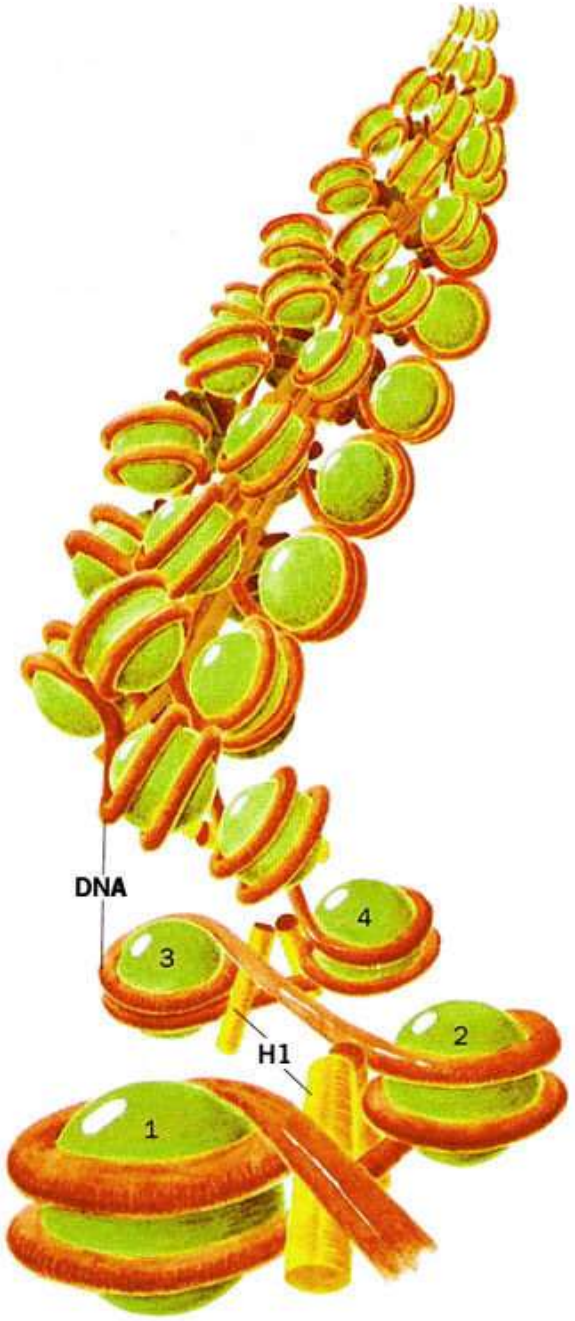
Nucleosomes & Higher Order Chromatin Structure



- Introduction
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  - N-terminal tails
- Higher Order Chromatin Structure
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  - Importance of Histone N-terminal tails
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- Regulation of Chromatin structure
  - DNA – Histone dynamic interaction
  - Nucleosome remodeling complexes
  - Nucleosome positioning
  - Modifications of Histone N-terminal tails
  - Nucleosome modification and Remodeling – increase DNA accessibility

- Nucleosome assembly
  - Immediately after replication
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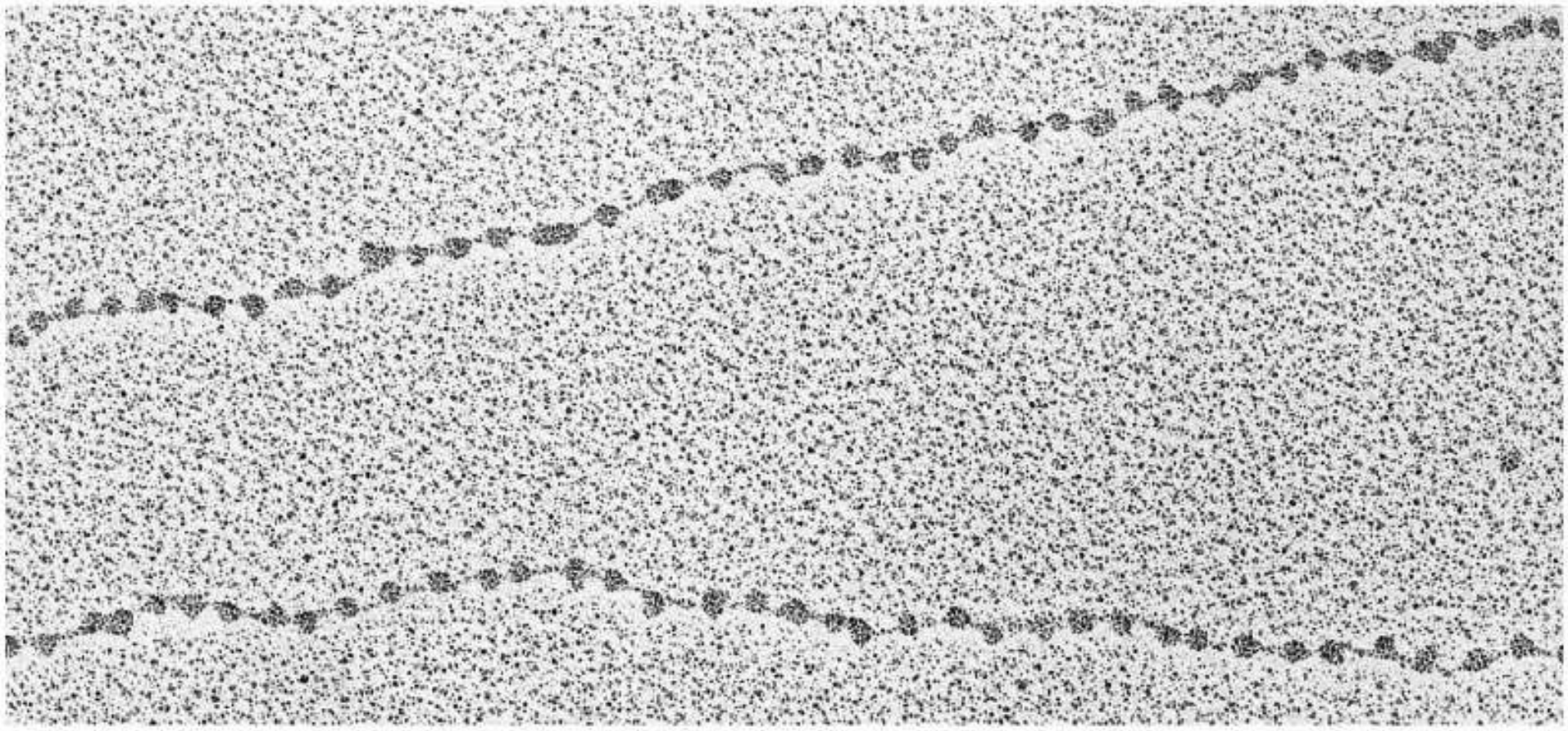
INTRODUCTION

- Within the cell DNA is associated with proteins and each DNA and its associate protein is called **Chromosome**.
- Functions played on packaging of DNA
  - Compact - fits inside nucleus
  - Protect DNA from damage.
  - Only packaged DNA transferred to daughter cells.
- In eukaryotic cells, a given region of DNA with its associated protein is called **chromatin**.
- Majority of these associated proteins are small basic proteins called **histones**. Others called non histone proteins.
- Association of DNA with histones - forms structure called **Nucleosomes**.

Chromosome Structure

- Human DNA's total length is ~2 meters!
- This must be packaged into a nucleus that is about 5 micrometers in diameter
- This represents a compression of more than 100,000!
- It is made possible by wrapping the DNA around protein spools called nucleosomes and then packing these in helical filaments

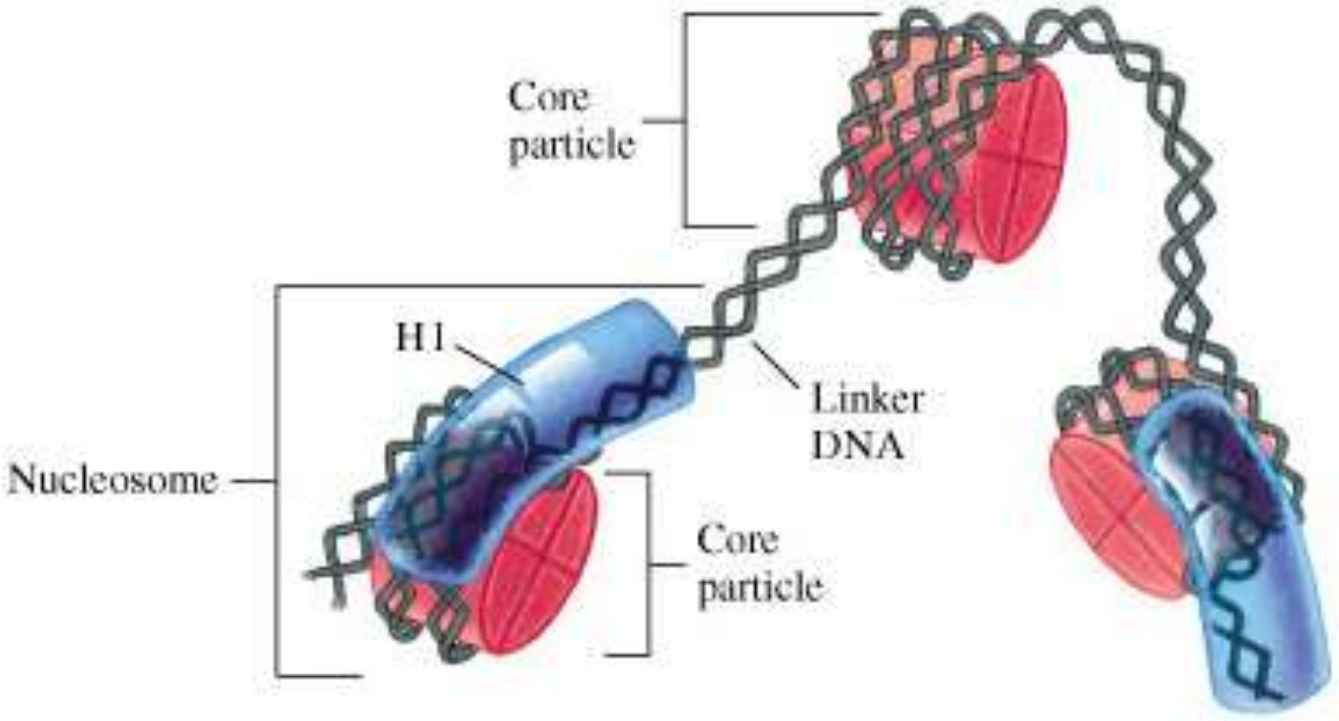
Micrograph of extended chromatin



Electron micrograph of extended chromatin showing "beads-on-a-string" organization. The "beads" are DNA-histone complexes called nucleosomes, and the "string" is double-stranded DNA.

NUCLEOSOME STRUCTURE

- Four pairs of Histone protein monomers namely H2A, H2B, H3, H4 make up the histone core (octamer).



- **Histones**

Nucleosome Structures

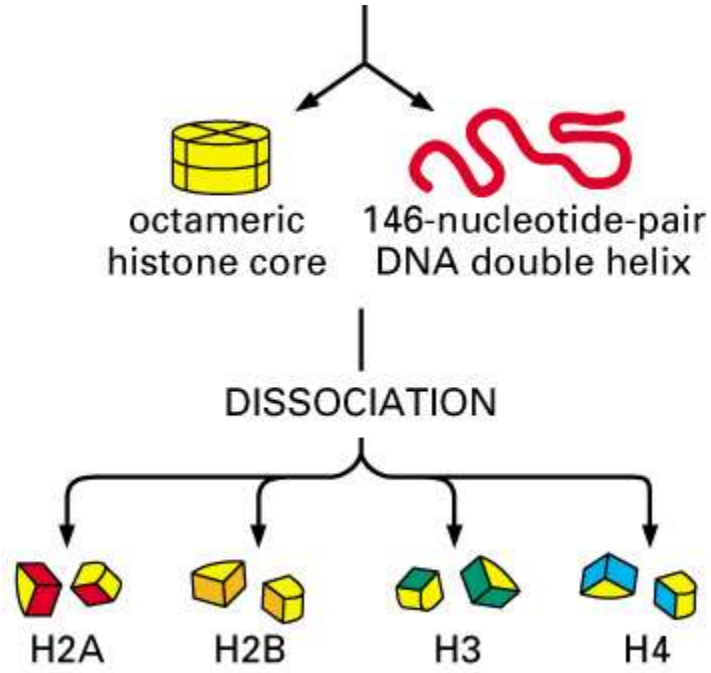
Histone octamer

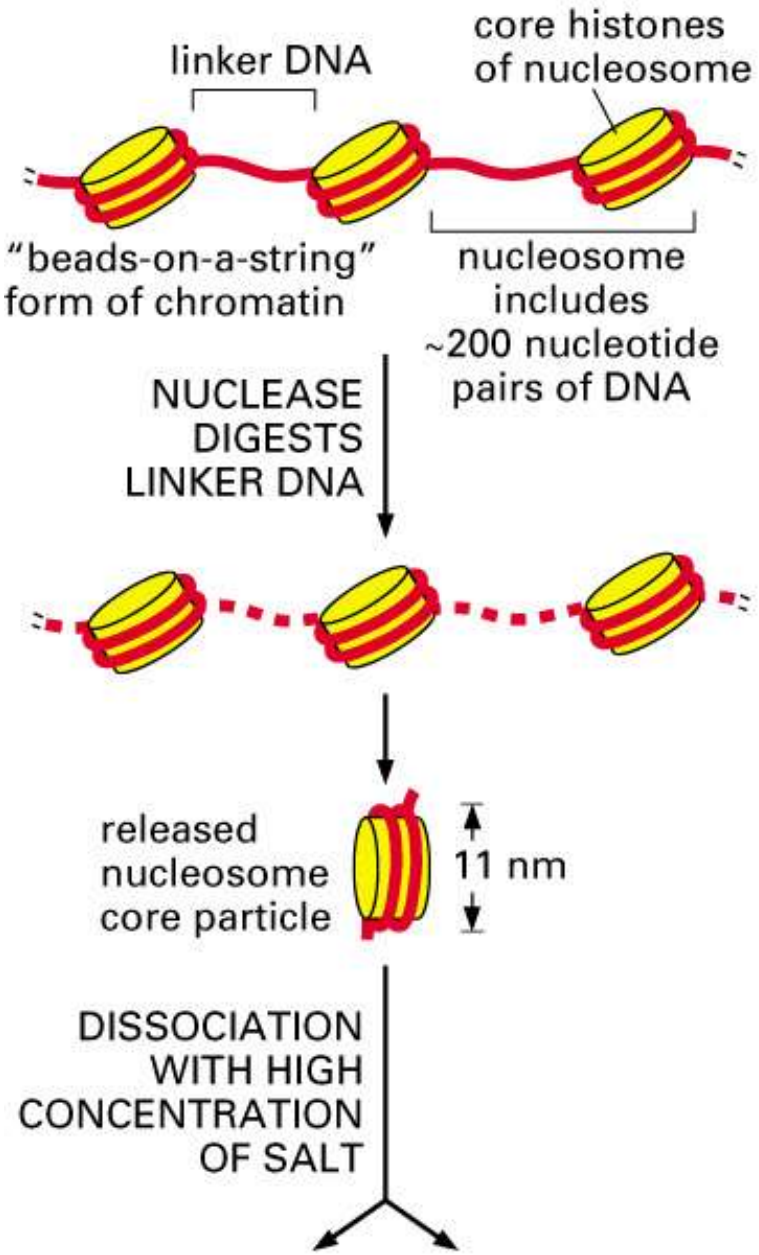
2 H2A

2 H2B

2 H3

2 H4



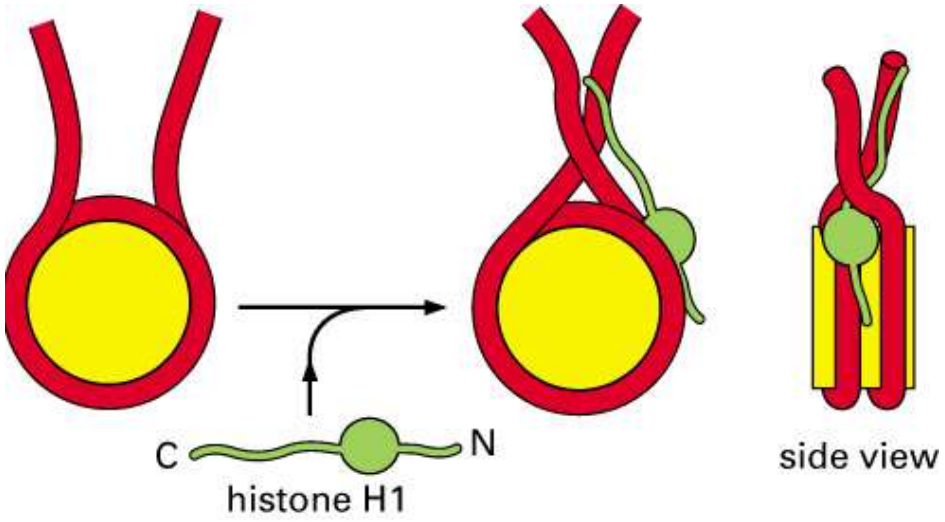


Each nucleosome is composed of a

- core (octamer) particle,
- histone H1 and
- linker DNA.

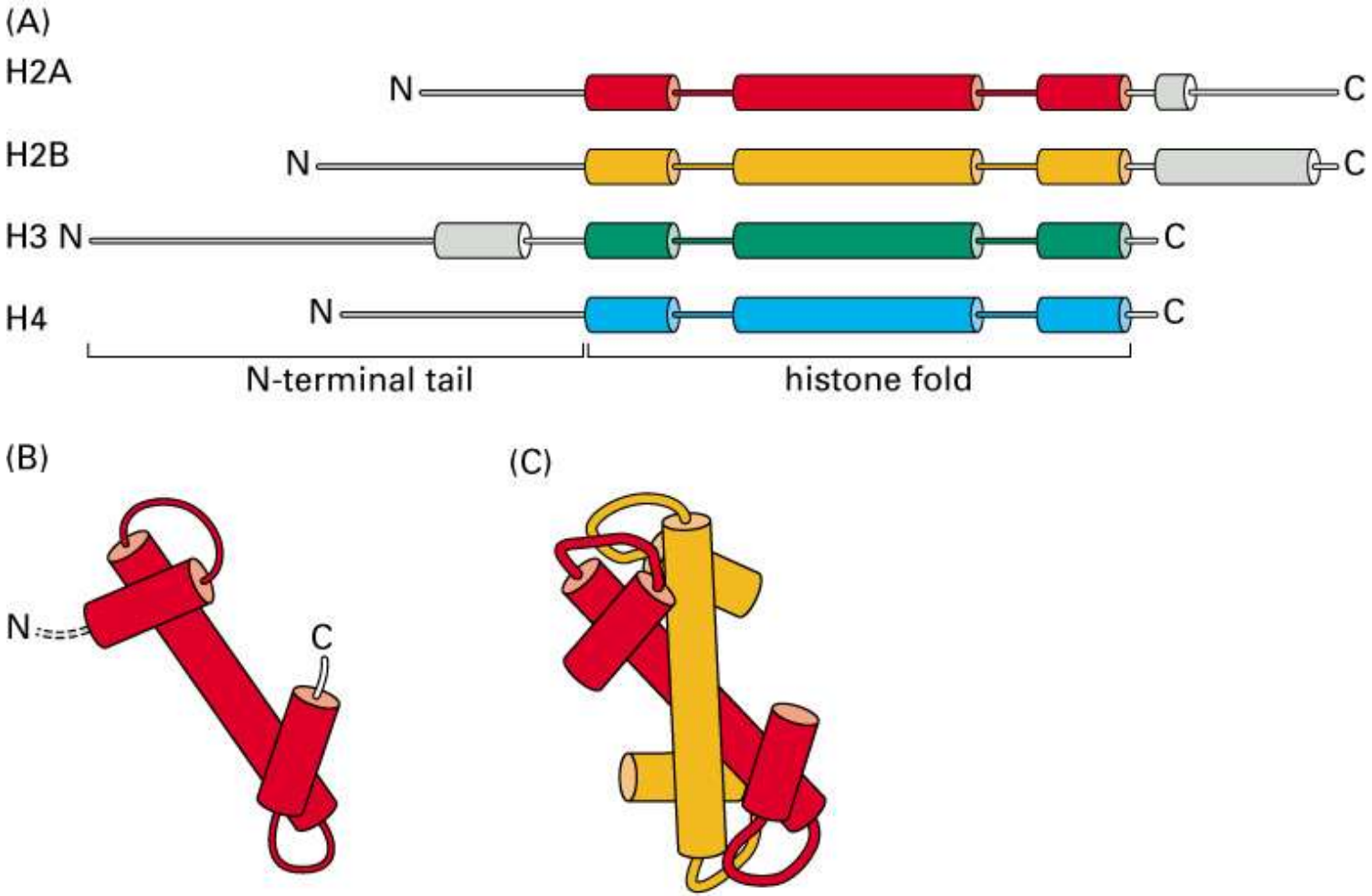
Nucleosome core particle is composed of

- histone octamer and
- 146 base pairs of DNA.

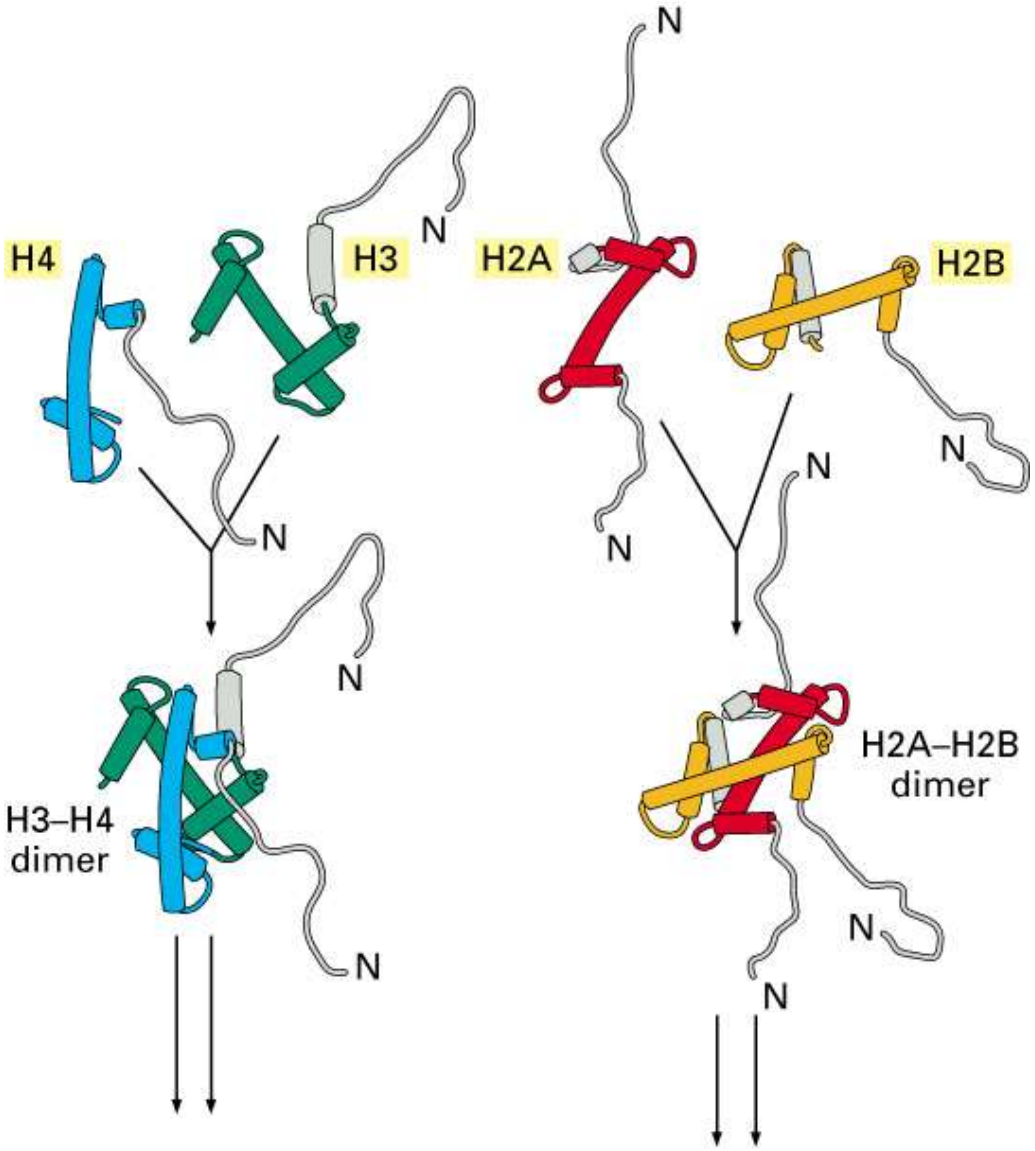


- Histone H1 binds to core particle and linker DNA.
- DNA forms left-handed wraps around the histone octamer.
- These coils are topologically equivalent to negative super coils.

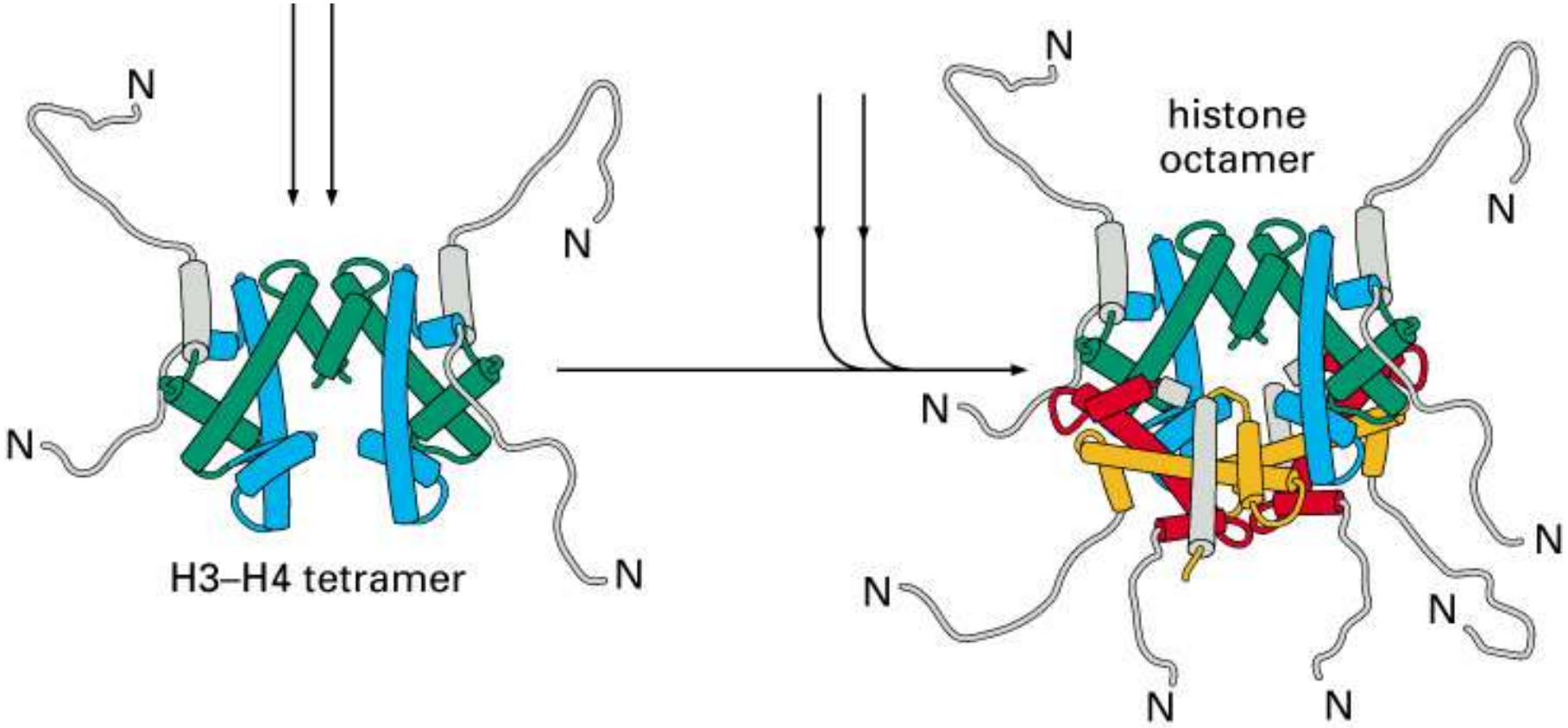
- **Structural Organization of the Core Histones**



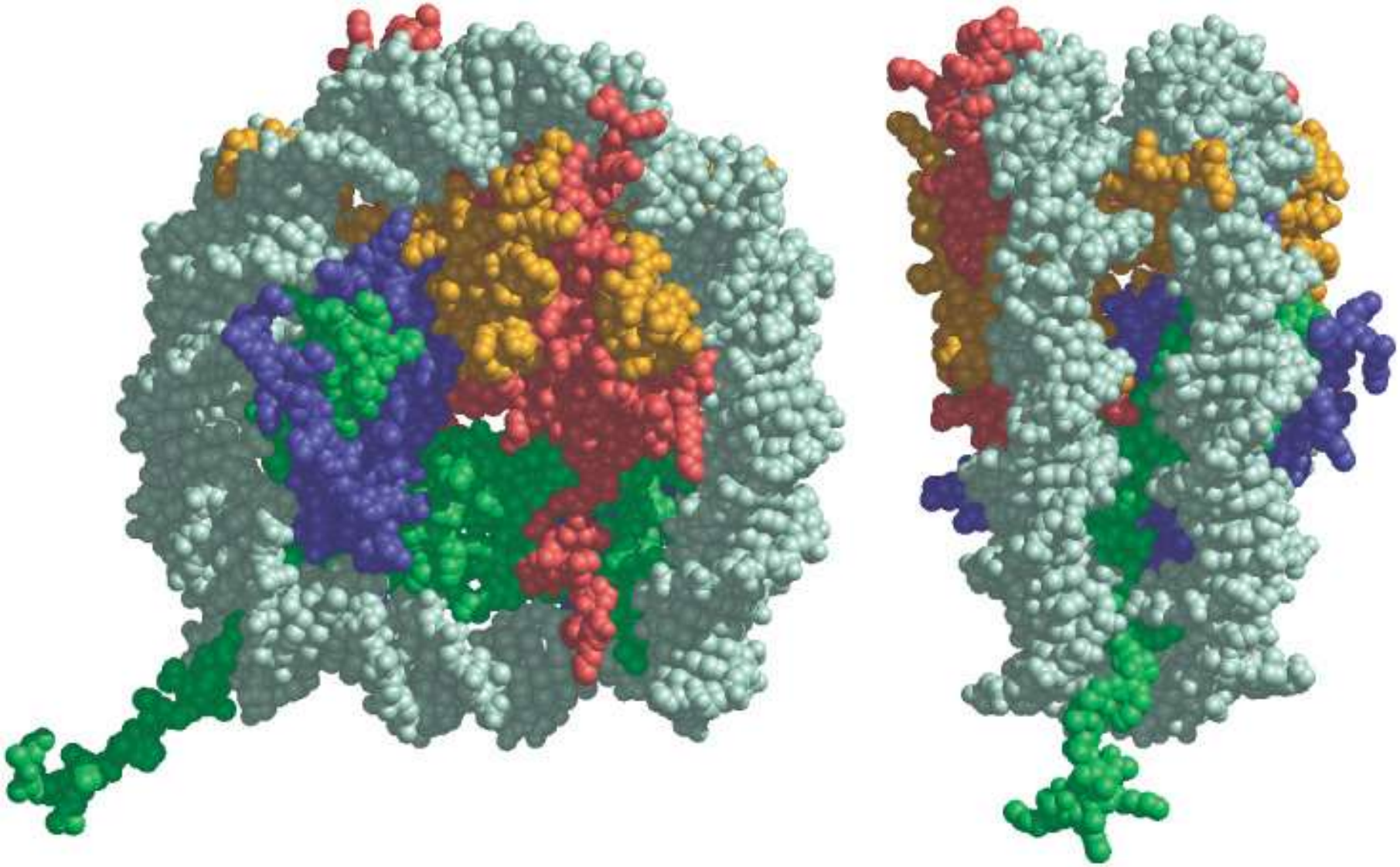
The Assembly of the Core Histones



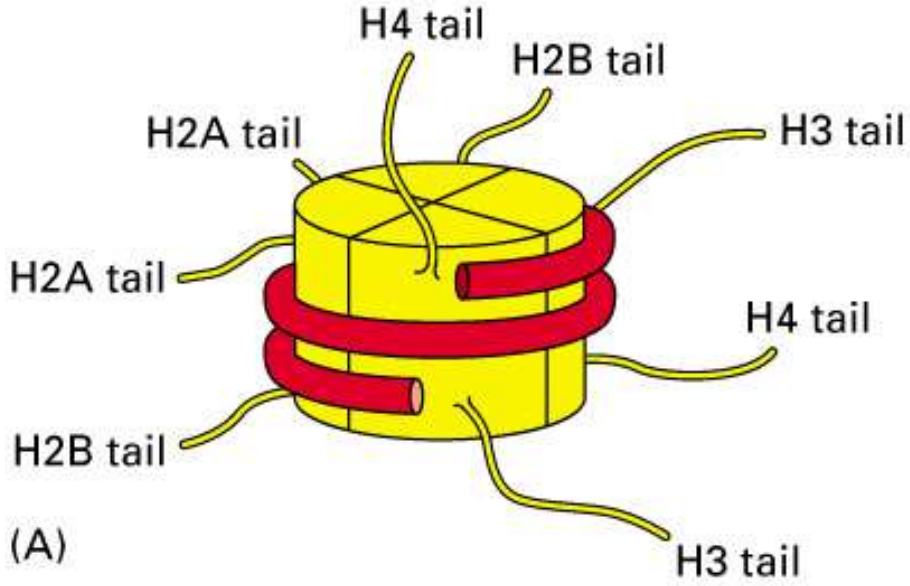
Notice the long tails of the octamer

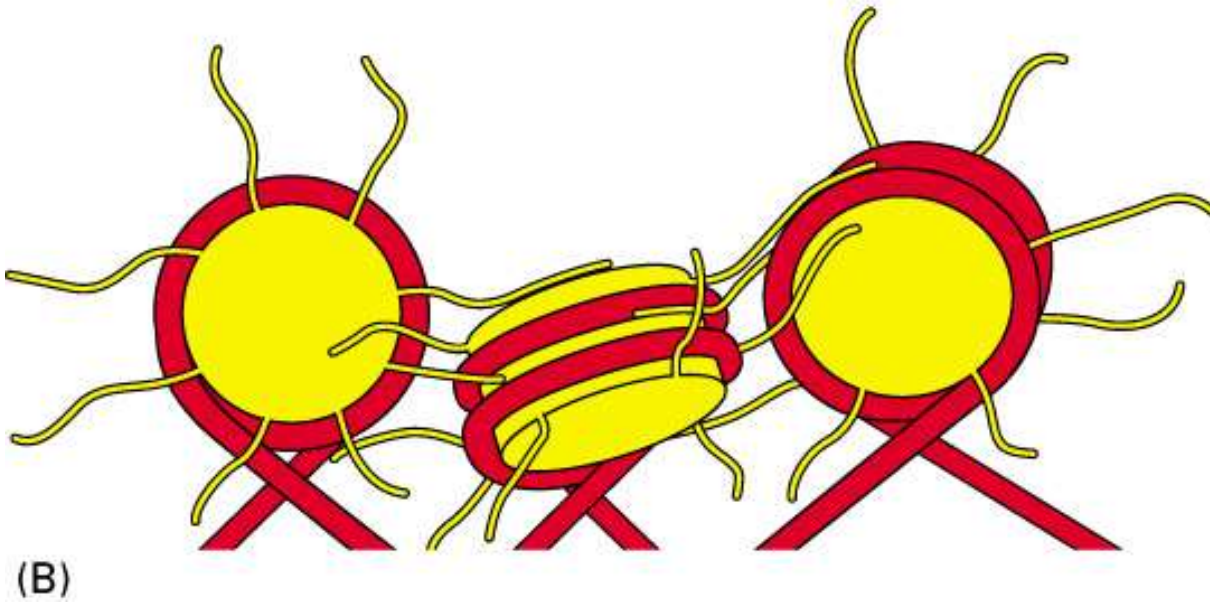


X-ray diffraction analyses of crystals
Structure of a nucleosome core particle



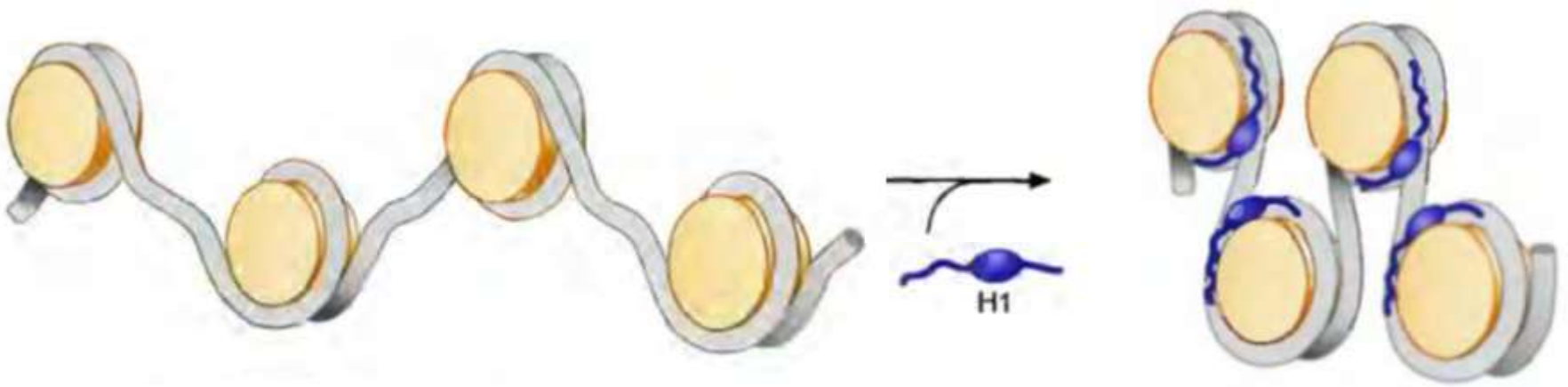
The function of Histone tails





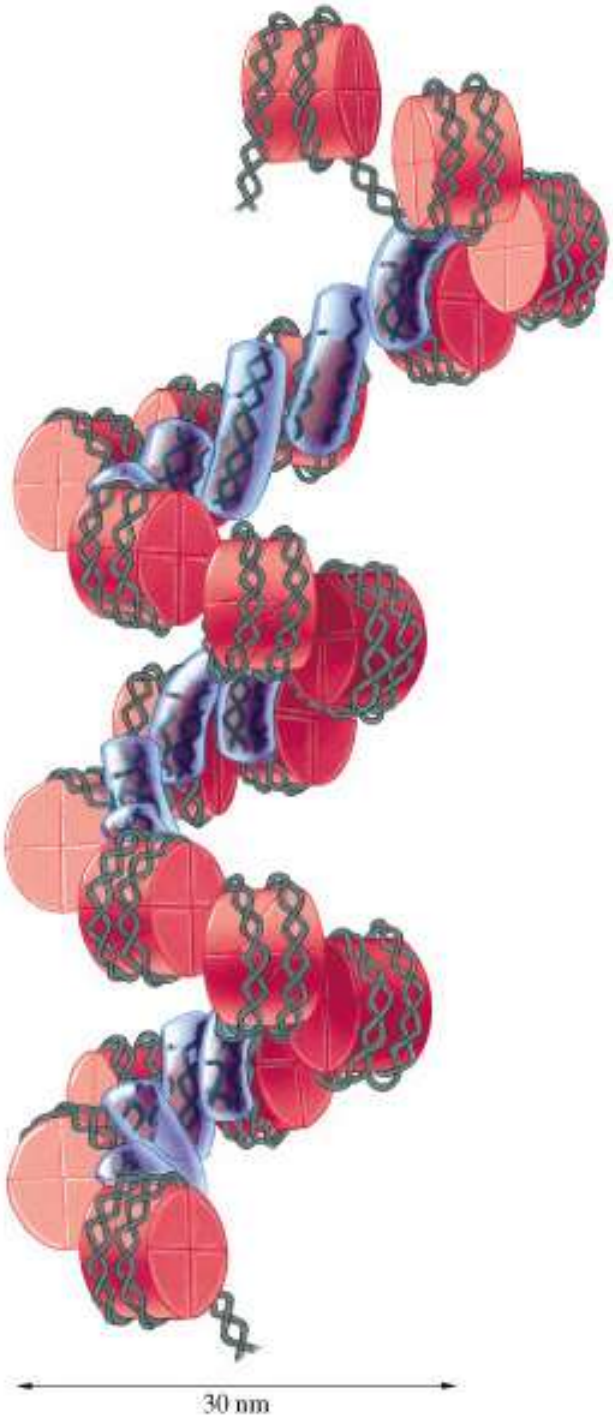
HIGHER ORDER CHROMATIN STRUCTURE

- **Wrapping of DNA in presence and absence of H1**



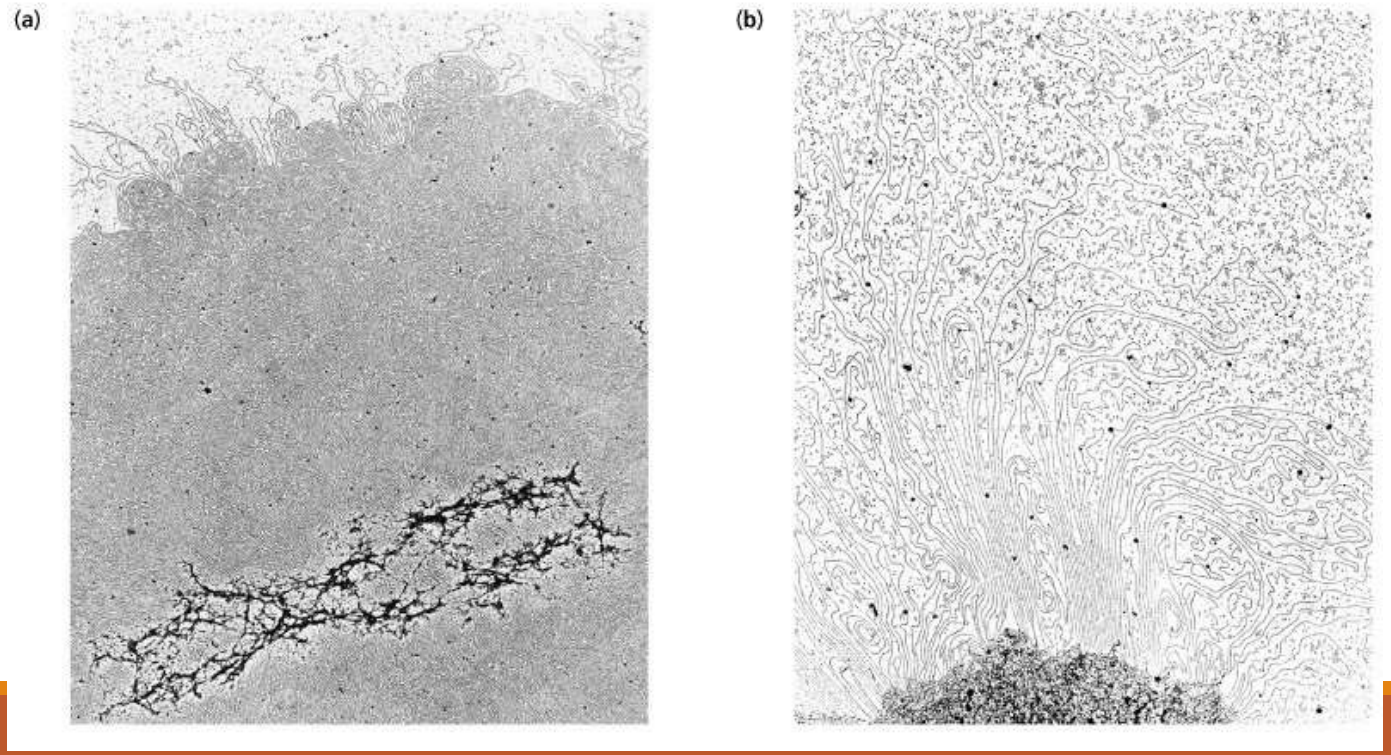
- **30 nm chromatin fiber**

30nm chromatin fiber model shown as a solenoid, or helix, formed by individual nucleosomes. The nucleosomes associate through contacts between adjacent histone H1 molecules. This solenoid is left handed, with net topological effect of introducing negative super coils into the DNA. The 30nm fiber attaches to an RNA-protein scaffold that holds the fibers in large loops.



Electron micrographs of a histone-depleted chromosome

(a) Entire protein scaffold of the histone-depleted chromosome is visible. The swirls are DNA double-helices. (b) Magnification of a portion of (a), individual loops attached to the protein scaffold can be seen. Each loop would form a solenoid attached to the protein scaffold. The degree of compacting of DNA by formation of nucleosomes is significant.



Zigzag model of the 30-nm chromatin fiber

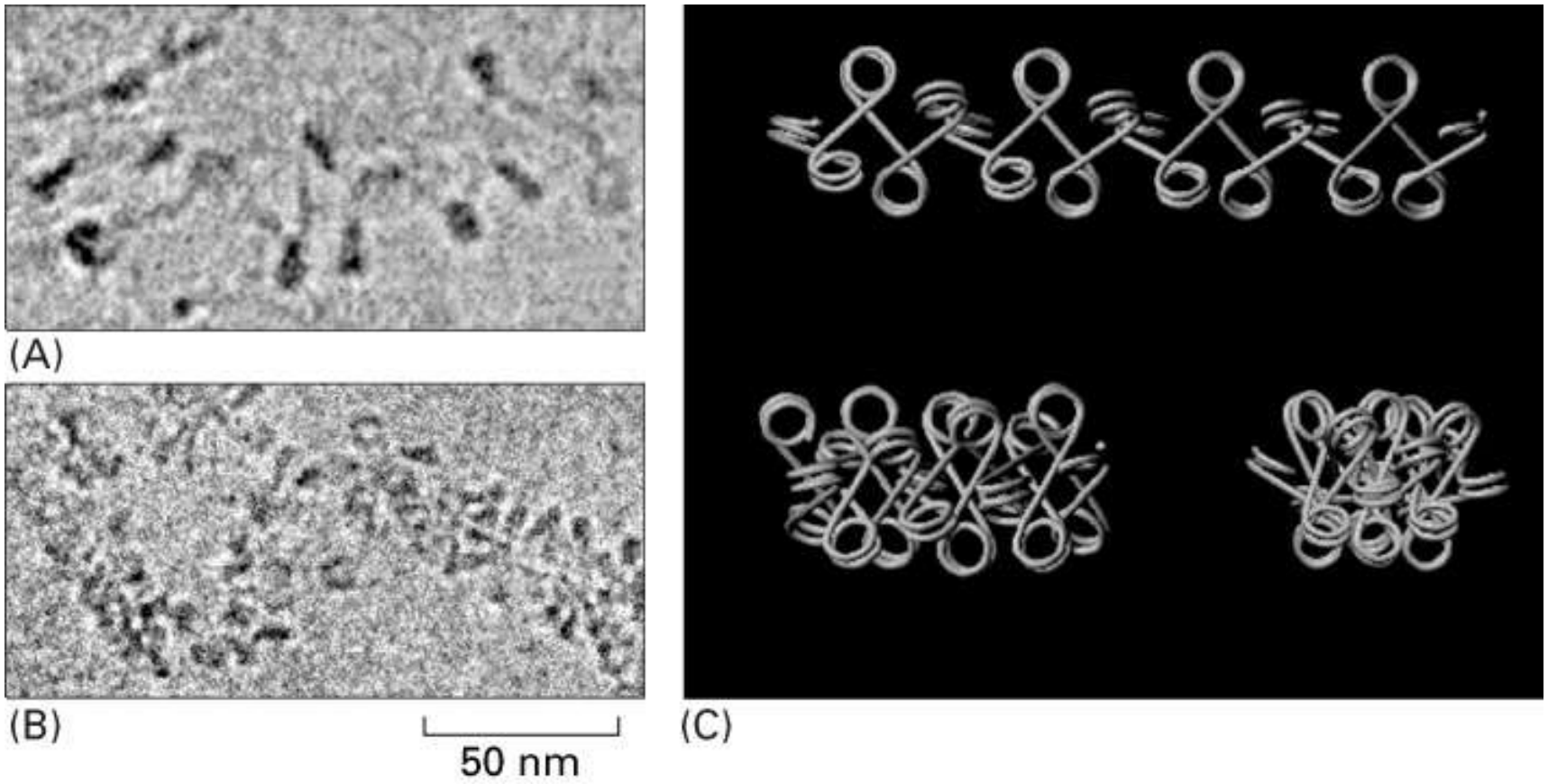
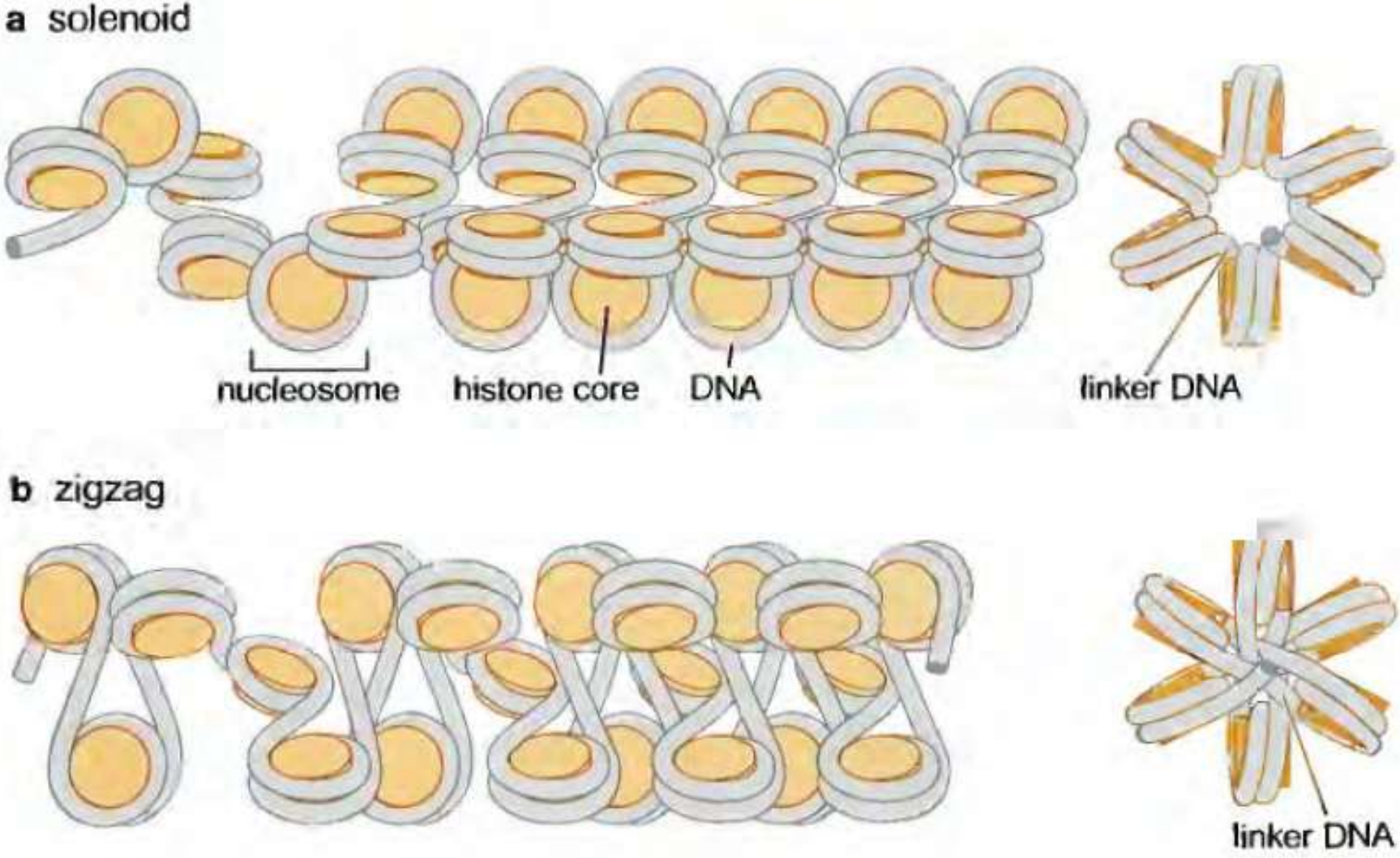
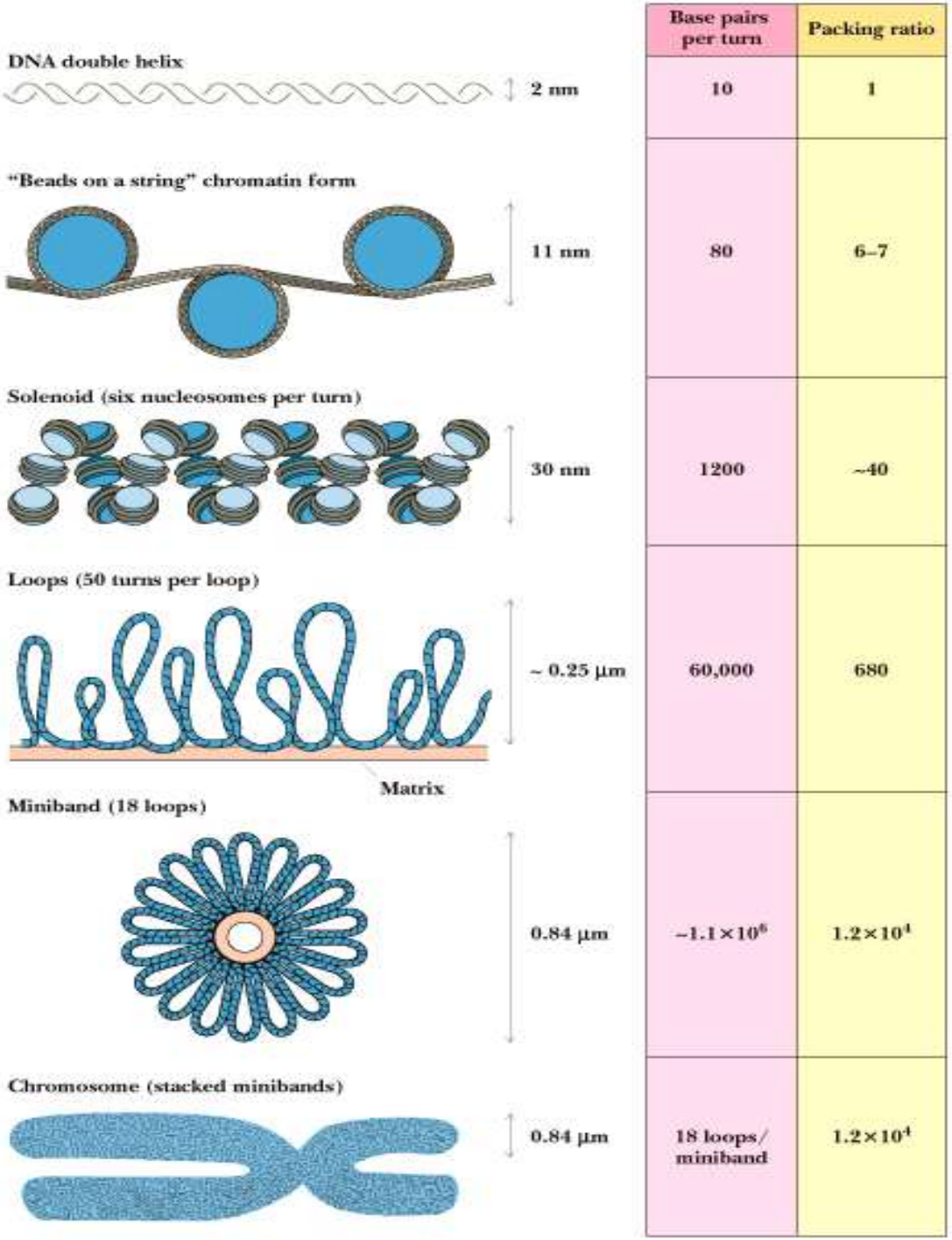


Figure 4–29. Molecular Biology of the Cell, 4th Edition.


a solenoid
nucleosome
histone core
DNA
linker DNA
b zigzag
linker DNA



Base pairs per turn	Packing ratio
10	1
80	6–7
1200	~40
60,000	680
$\sim 1.1 \times 10^6$	1.2×10^4
18 loops/ miniband	1.2×10^4

The bending of DNA in a nucleosome

1. Flexibility of DNAs: A-T riched minor groove inside and G-C riched groove outside
2. DNA bound protein can also help

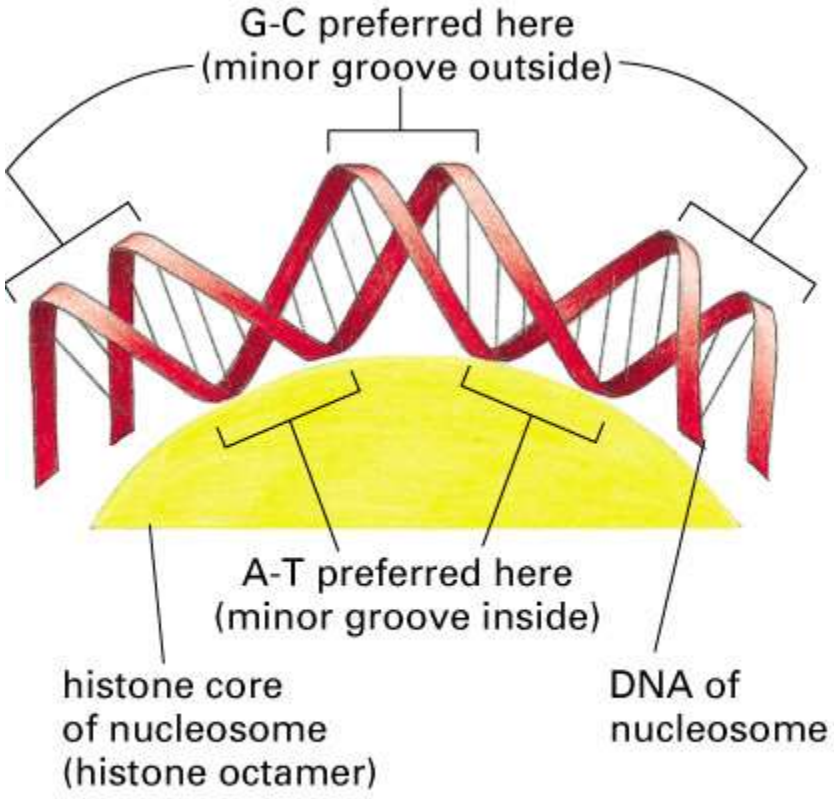


Figure 4–28. Molecular Biology of the Cell, 4th Edition.

Chromosome structures