2. Chromatin structure

2.1 Chromatin

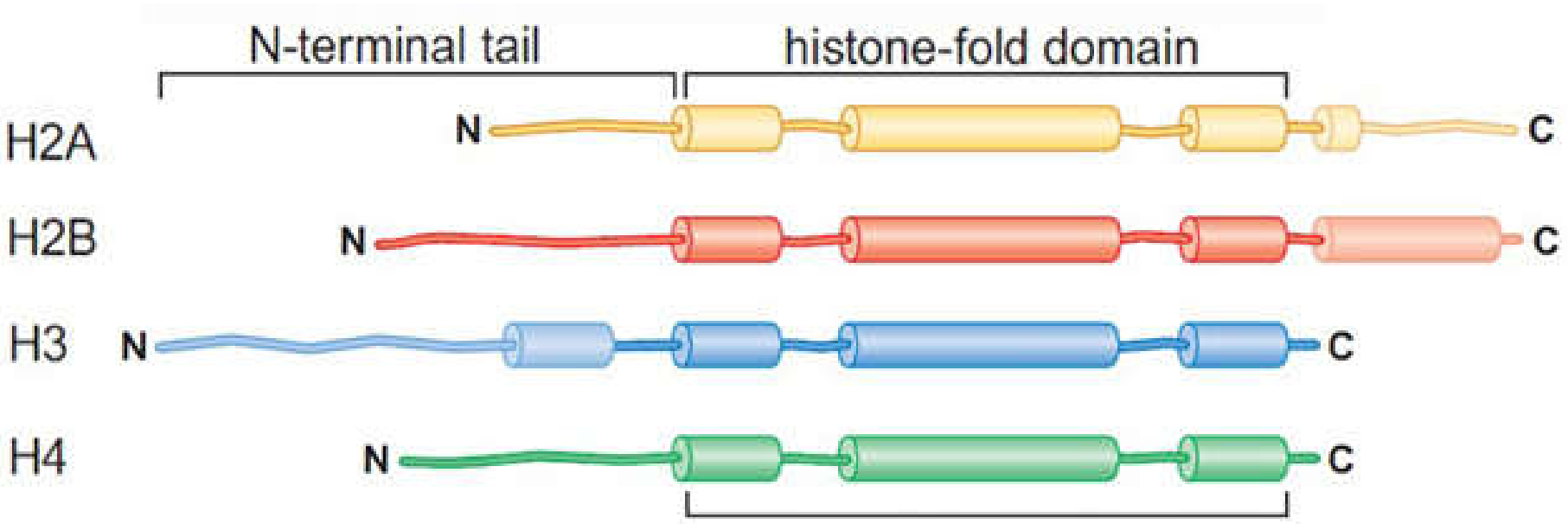
- **Chromatin** is the highly ordered DNA-protein complex which makes up the eukaryotic chromosomes.
  染色质是组成真核生物染色体的高度有序的DNA-蛋白质复合物。
- The chromatin undergoes **further condensation** to form the chromosome.

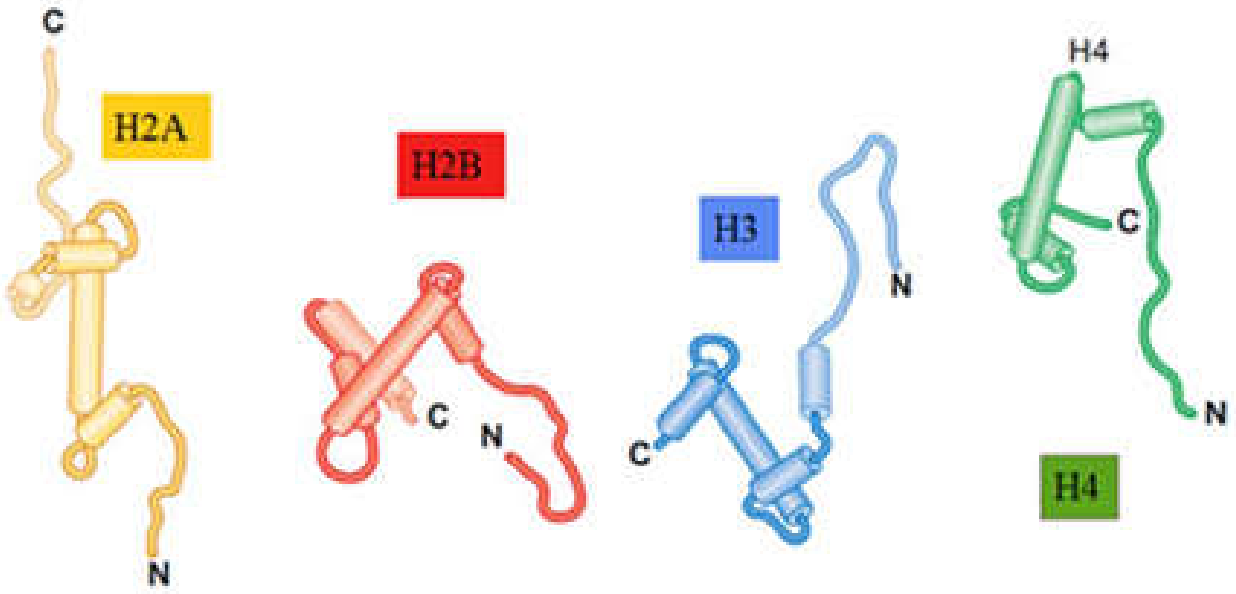
2.2 Histones (组蛋白)

- The major protein components of chromatin are the histones.
- Small, basic (positively charged) proteins which bind tightly to DNA

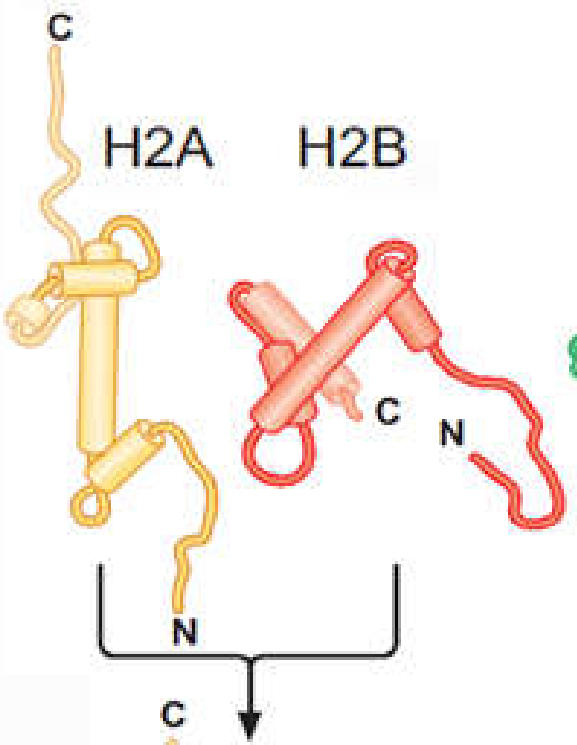
20%-30% Lys, Arg

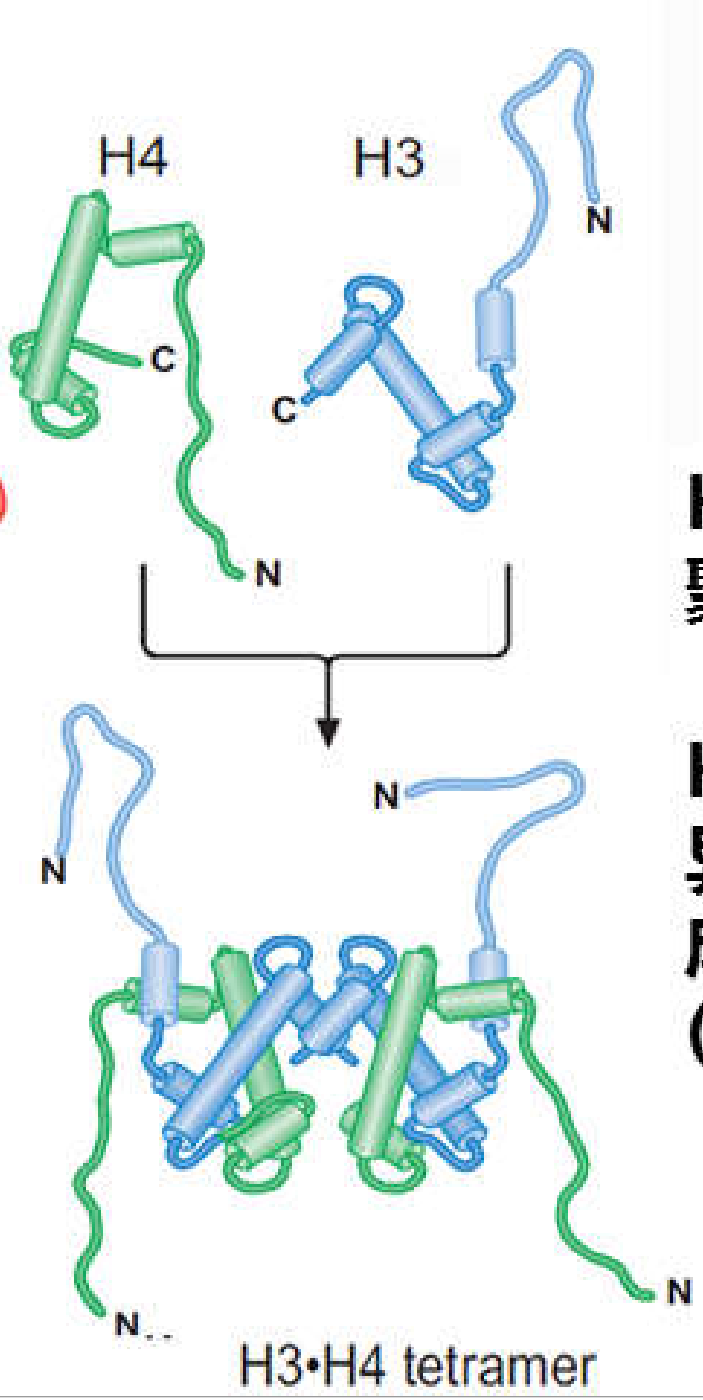
Histones
- Core histones 核心组蛋白: H2A, H2B, H3, H4; 11-15 kD, structurally similar and highly conservative (保守)
- Linker histone 连接组蛋白: H1 (H5 in some cell types); ~21 kD, more variation in sequences





Composed of 3 α-helical regions separated by 2 short loops



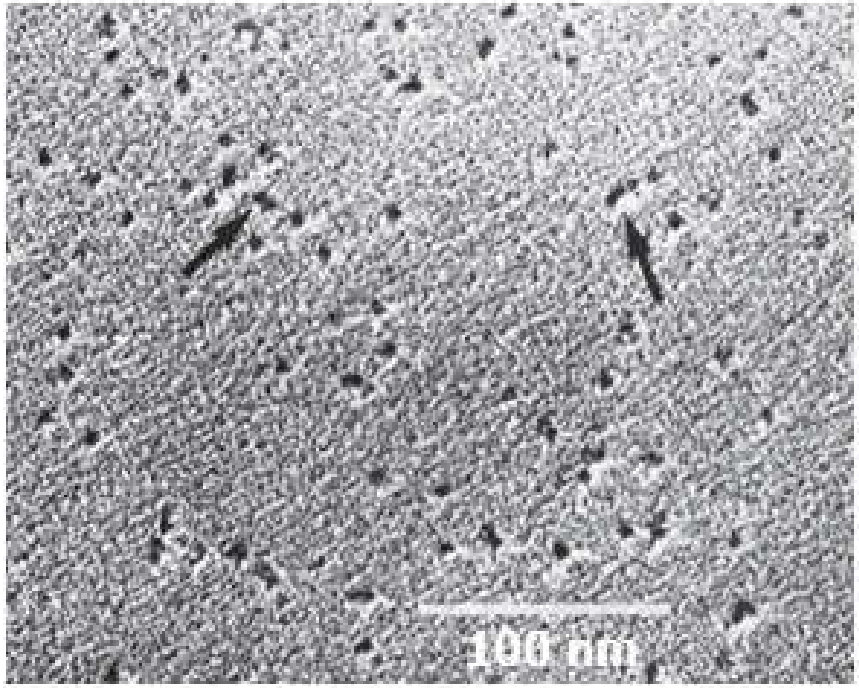


H2A-H2B异二聚体(heterodimer)

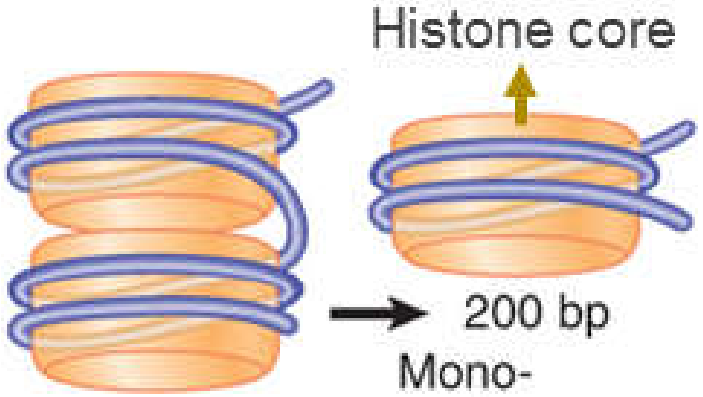
H3-H4先形成异二聚体，再组成四聚体(tetramer)

2.3 Nucleosomes (核小体)

- **Nucleosome is the basic unit of chromatin structure, consisting of ~200 bp of DNA and histone proteins.**



Digestion of chromatin with micrococcal nuclease (微球菌核酸酶)



Nucleases

Hydrolyze the phosphodiester bonds of nucleic acids

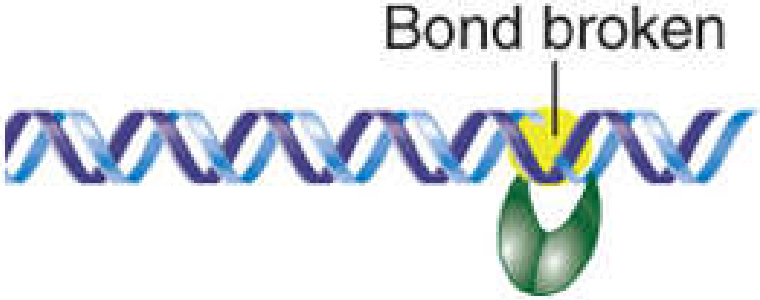
Exonucleases (外切核酸酶)

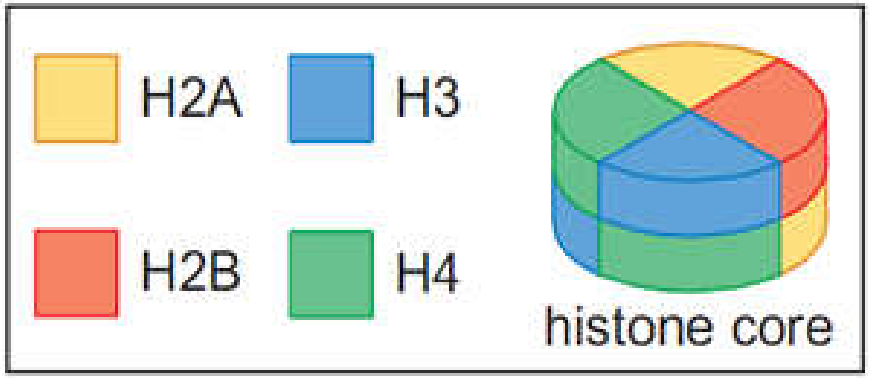
Release single nucleotides from the ends of nucleic acids

Endonucleases (内切核酸酶)

Cleave internal phospho-diester bonds of nucleic acids

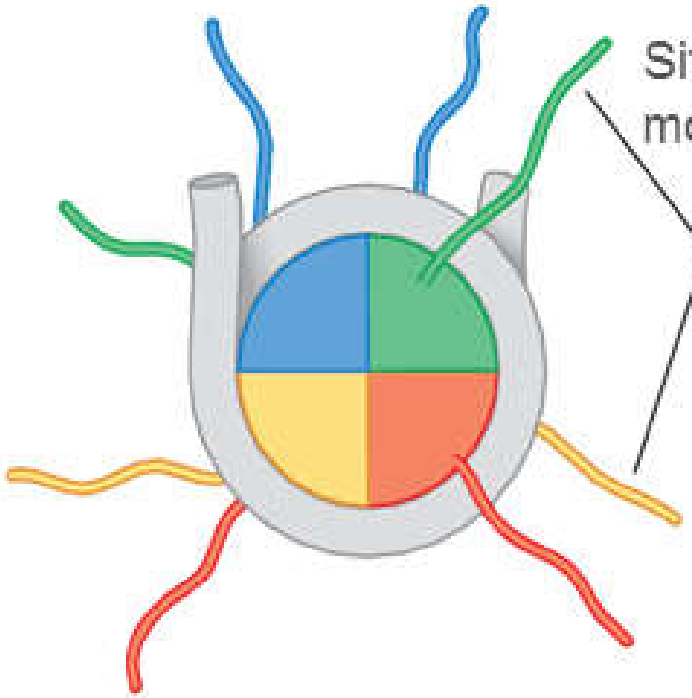
e.g. restriction endonuclease **(限制性内切核酸酶)**

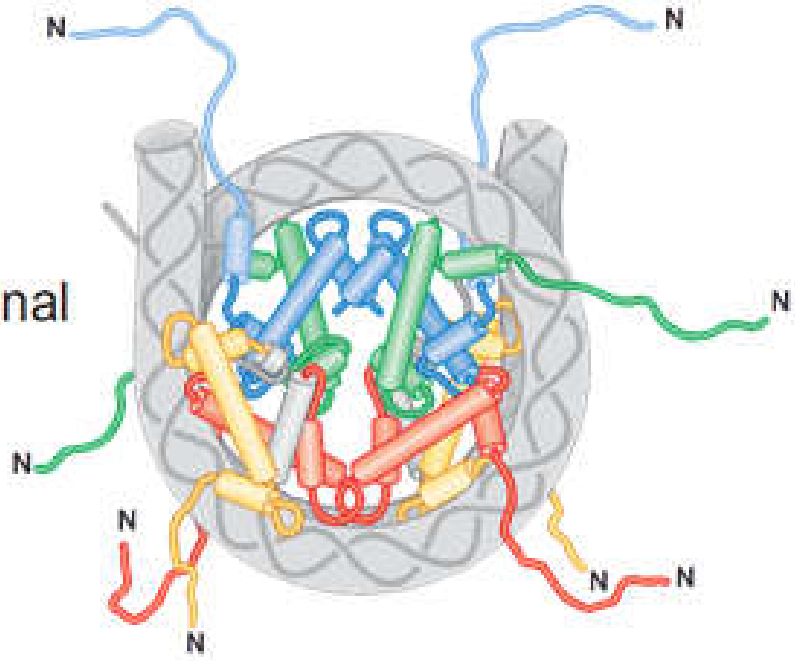




Histone octamer (八聚体)

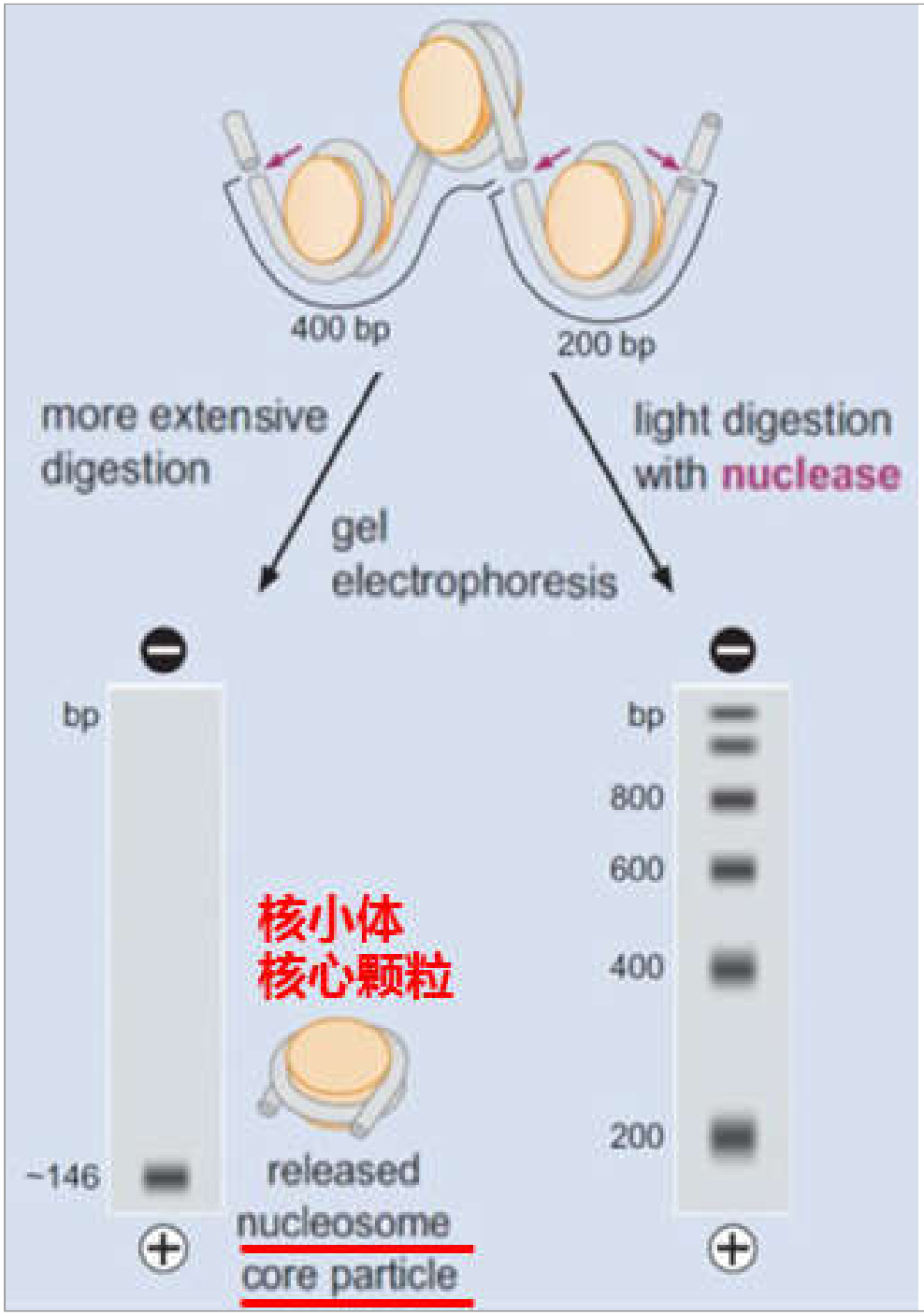
$(H2A)_2(H2B)_2(H3)_2(H4)_2$

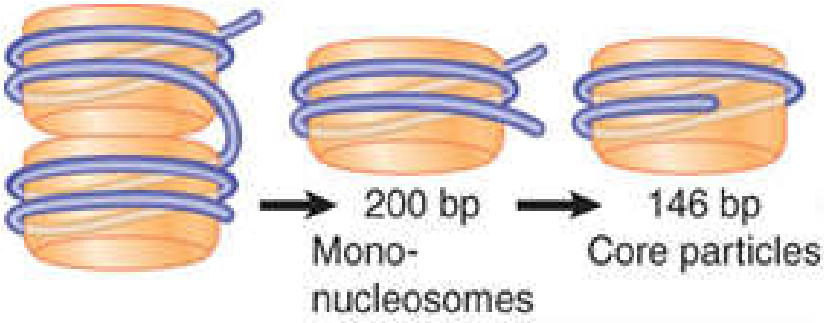




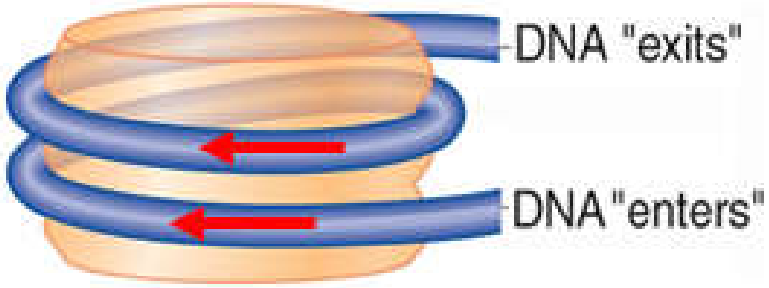
$(H2A \bullet H2B)_2(H3 \bullet H4\text{-}H3 \bullet H4)$

二聚体　　四聚体

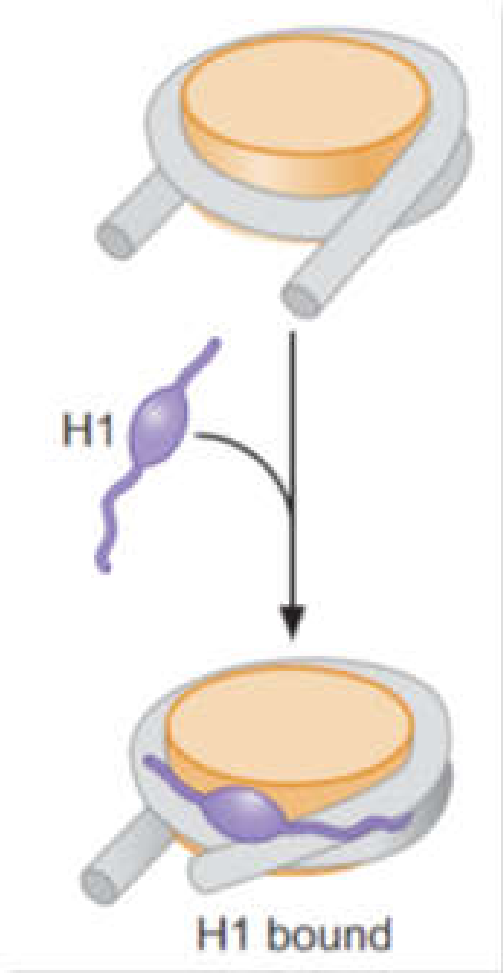




- **Nucleosome core** = **Histone core + ~146 bp DNA**



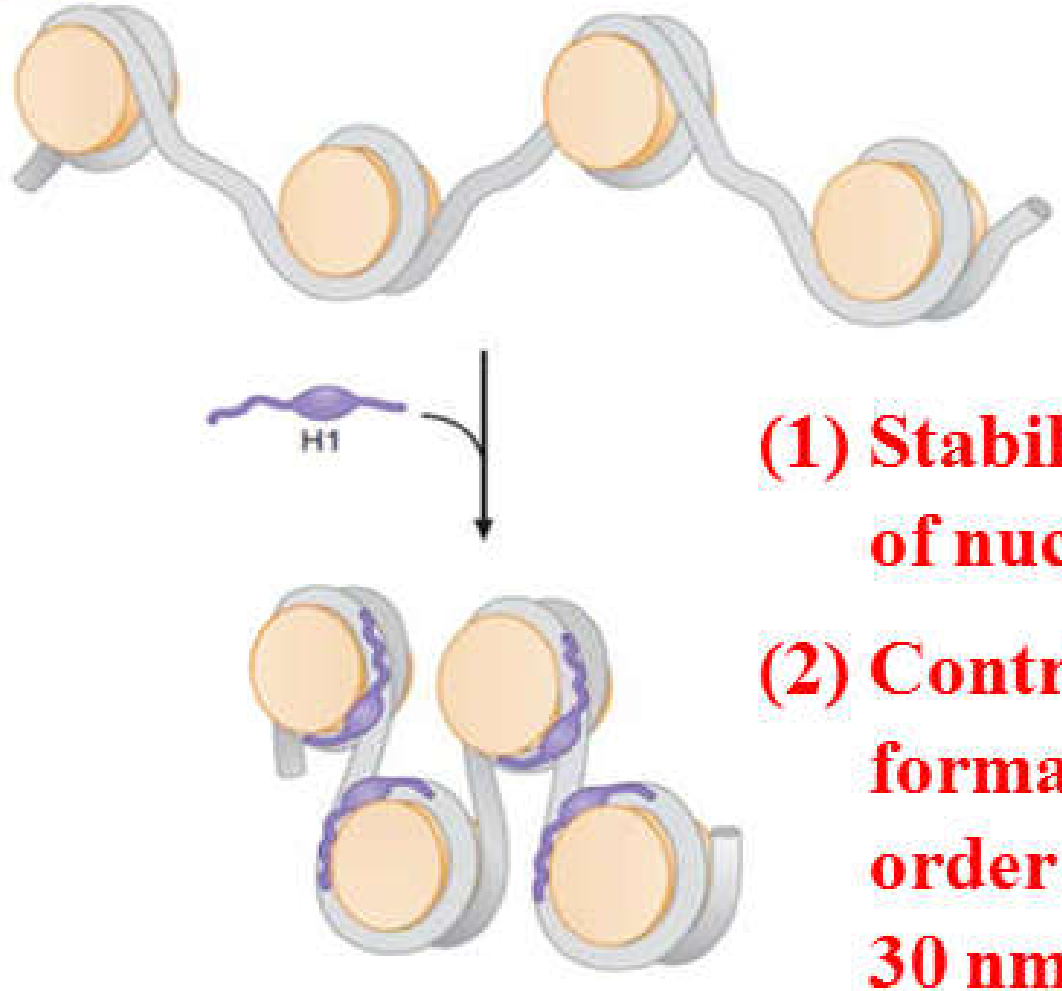
The left-handed wrapping of the DNA around the nucleosome corresponds to negative supercoiling.



- **Chromatosome (染色小体) = Nucleosome core + histone H1 + ~20 bp DNA**

H1 may interact with either the entry or exit DNA in addition to the central turn of DNA on the nucleosome.

• Functions of histone H1

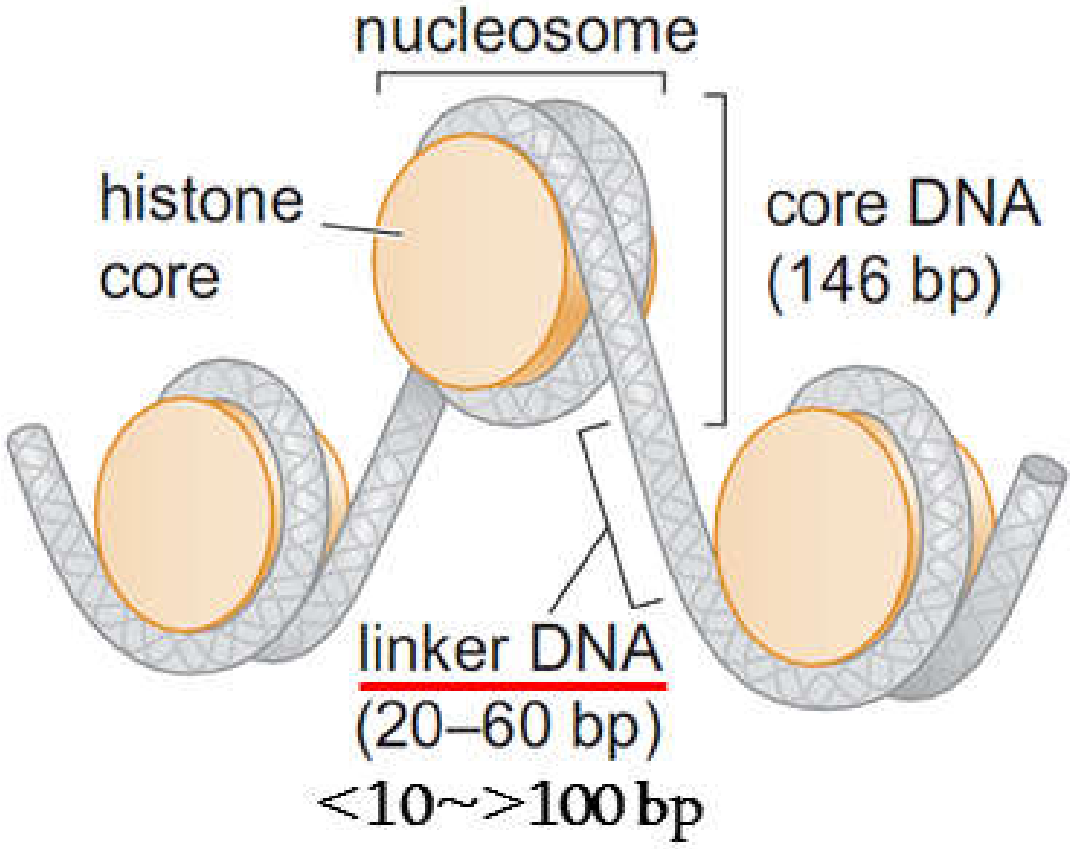


(1) Stabilizes the structure of nucleosome

(2) Contributes to the formation of higher order structures (the 30 nm fiber)

• Linker DNA (连接DNA)

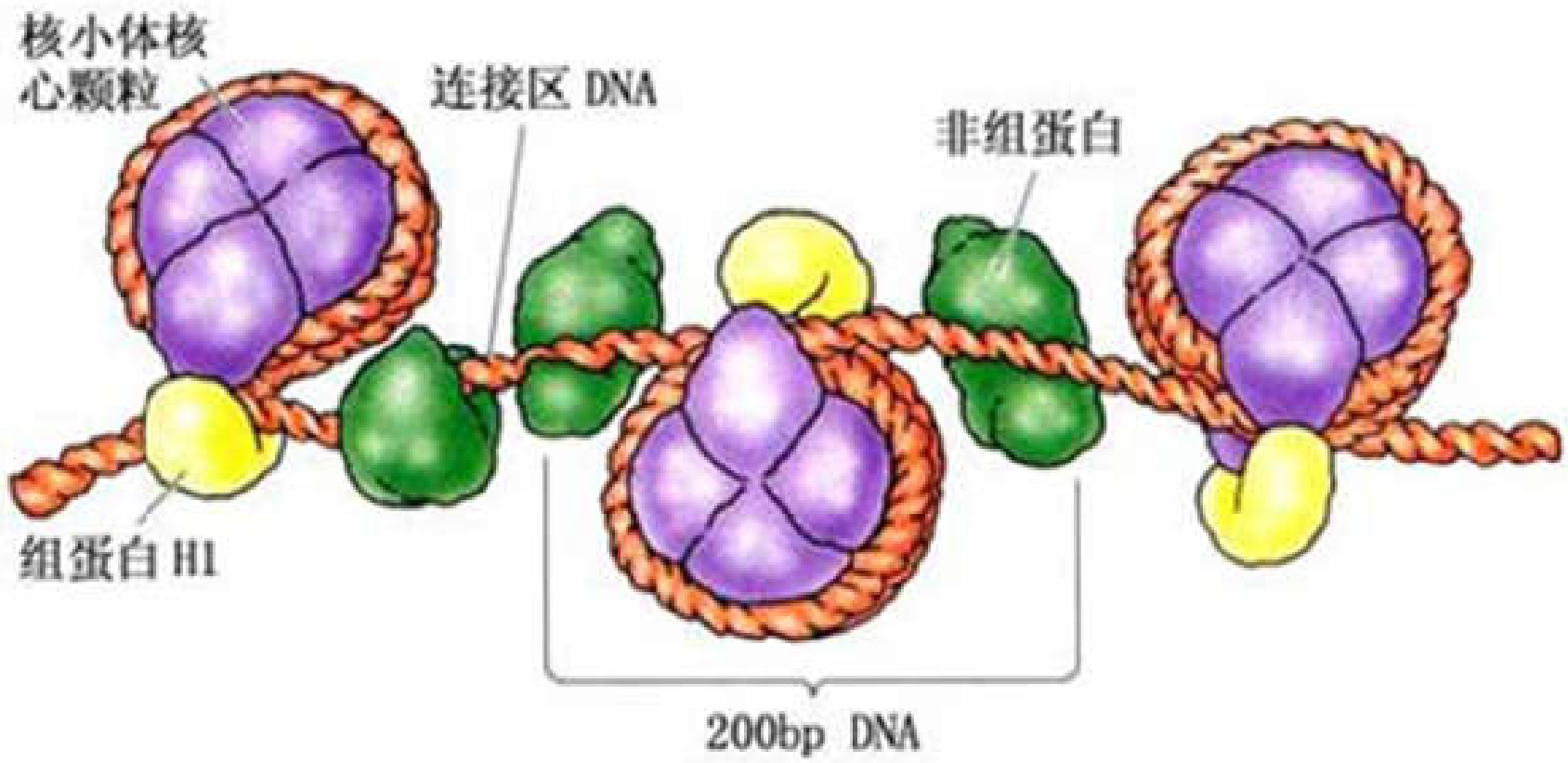
The DNA between each nucleosome (the "string" in the "beads on a string"串珠) is called linker DNA.



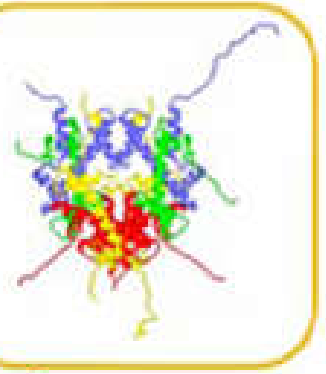
核小体核心

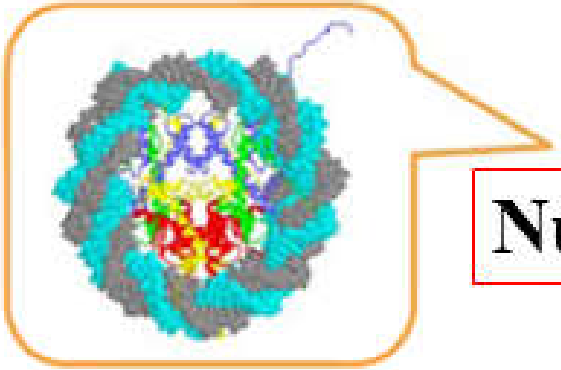
核小体 = 组蛋白八聚体+146 bp DNA
(~200 bp DNA) +组蛋白H1+ 20 bp DNA (核心外)
+ 连接DNA

染色小体



DNA+ Histone octamer

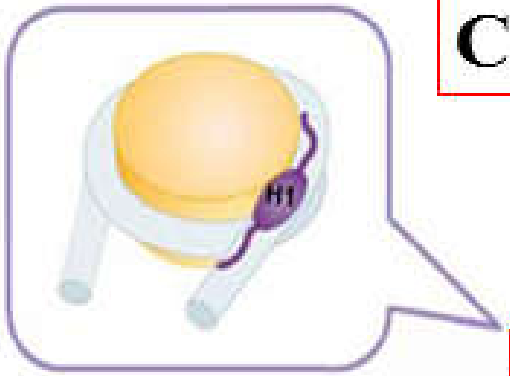




Nucleosome core (146 bp DNA)

Histone H1

Chromatosome (166 bp DNA)

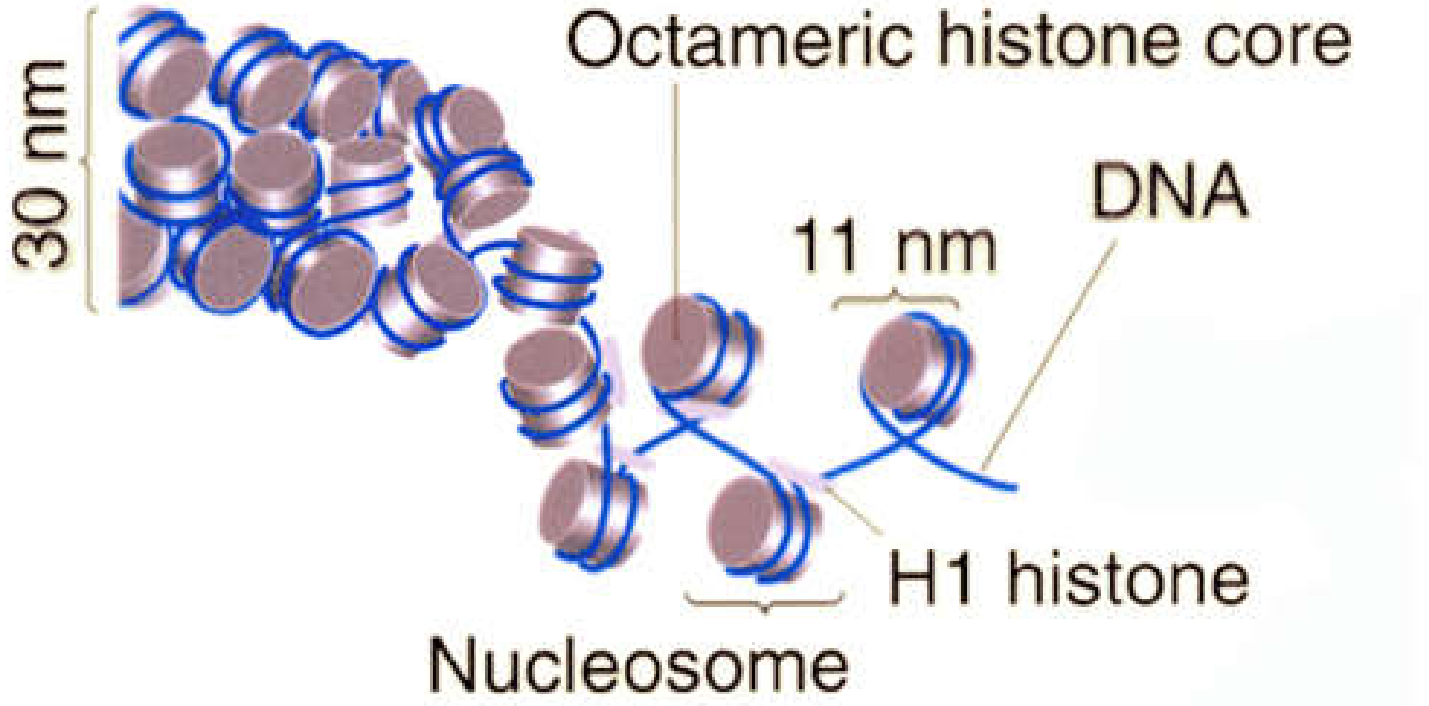


Linker DNA

Nucleosome (~200 bp DNA)

2.4 The 30-nm fiber (纤丝)

- **Histone H1, histone tails, and increased ionic strength all promote the formation of the 30-nm fiber.**

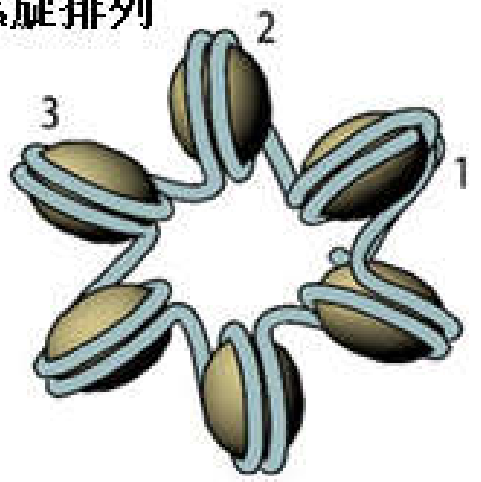


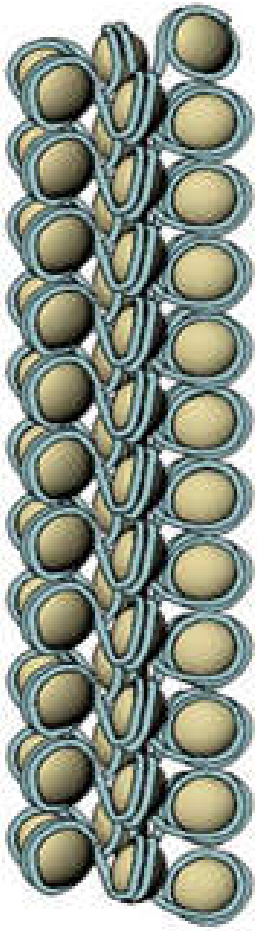
Two models for the 30-nm chromatin fiber

螺线管

A. Solenoid

linker DNA弯曲，不穿过中心轴；核小体依次相邻，螺旋排列

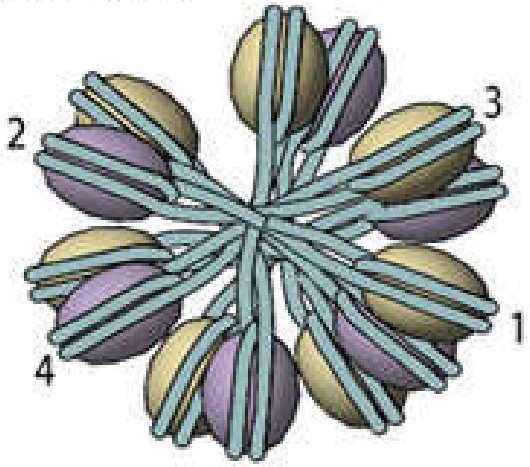


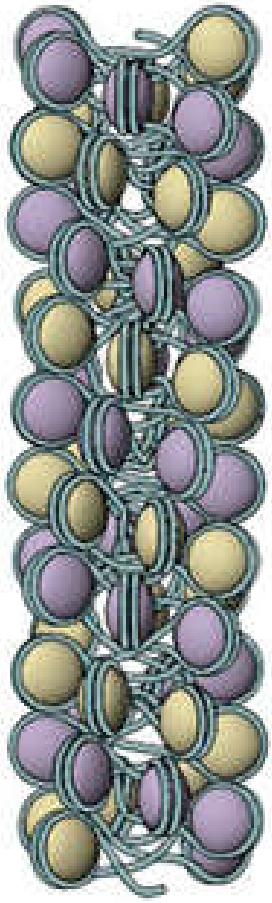


锯齿形

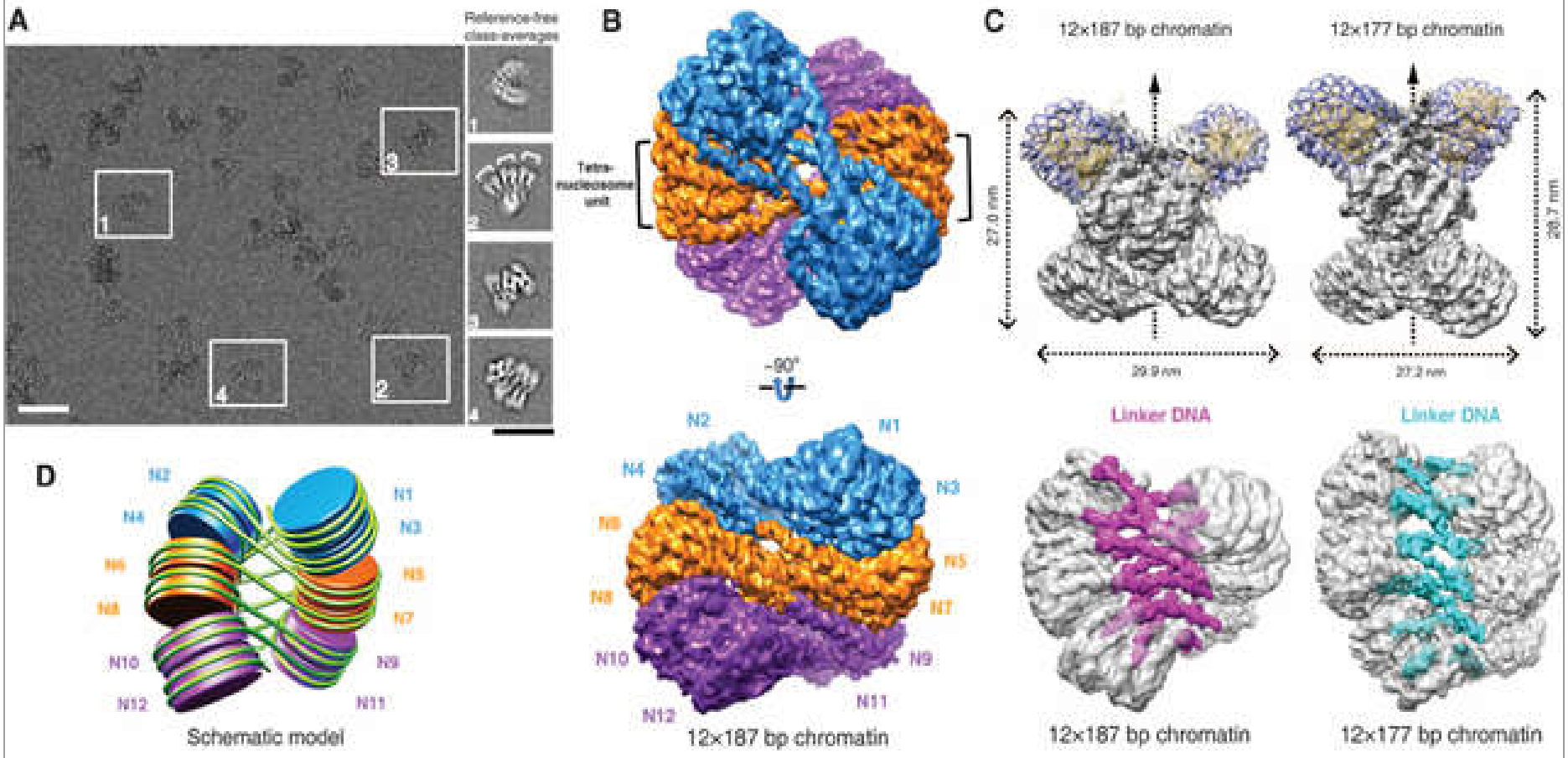
B. Zigzag

linker DNA拉直，频繁穿过中心轴；核小体间隔相邻，交错排列





Six nucleosomes per turn



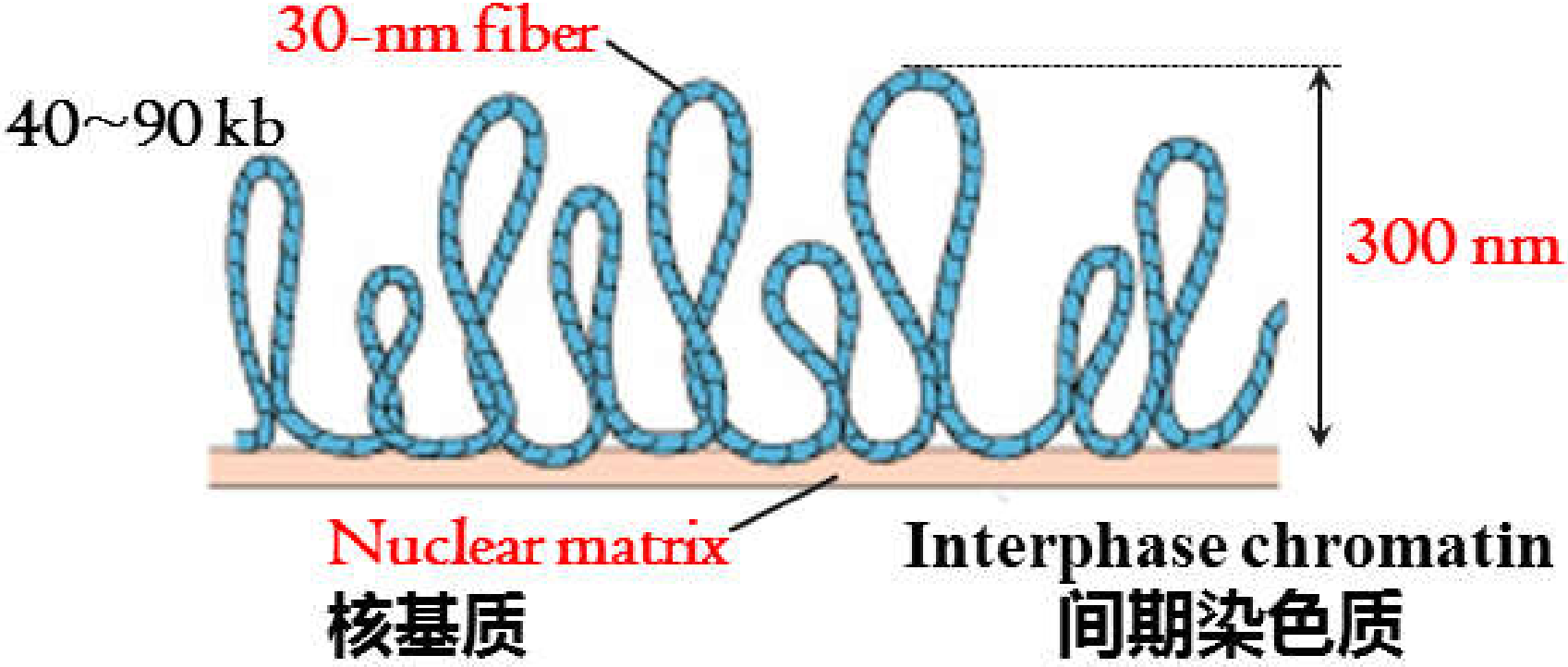
Repeating tetranucleosomal structural units

四核小体

Song F et al. Cryo-EM study of the chromatin fiber reveals a double helix twisted by tetranucleosomal units. *Science*, 2014, 344(6182):376-80.

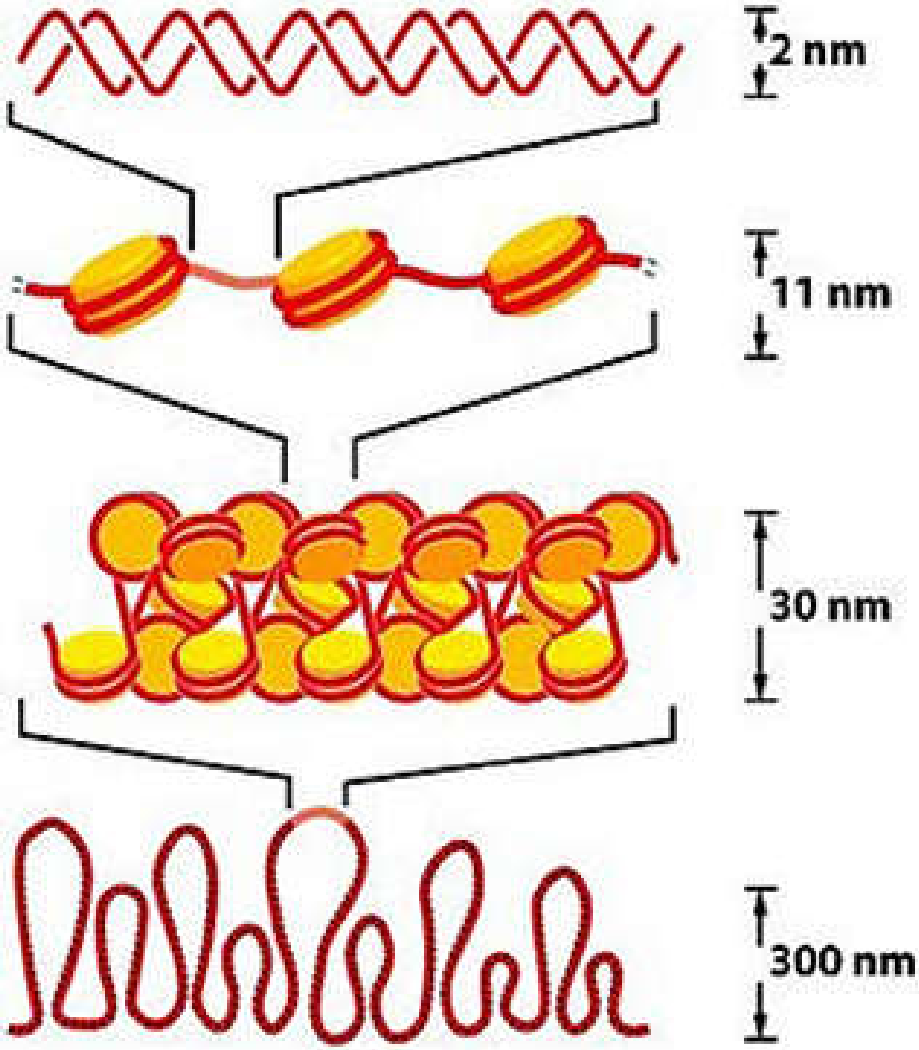
2.5 Higher order structure

- Chromosomal DNA is organized into **loops** of up to 100 kb in the form of 30-nm fiber, constrained by interaction with a protein complex known as the **nuclear matrix**.



Chromatin packing

Packing ratio

Short region of DNA double helix	1	
"Beads on a string" form of chromatin	6	
30-nm chromatin fiber of packed nucleosomes	40	
Section of chromatin in an extended form	680	