Lecture 11

Genome organization

Eukaryotes

Readings (chapter 7)

Course 371

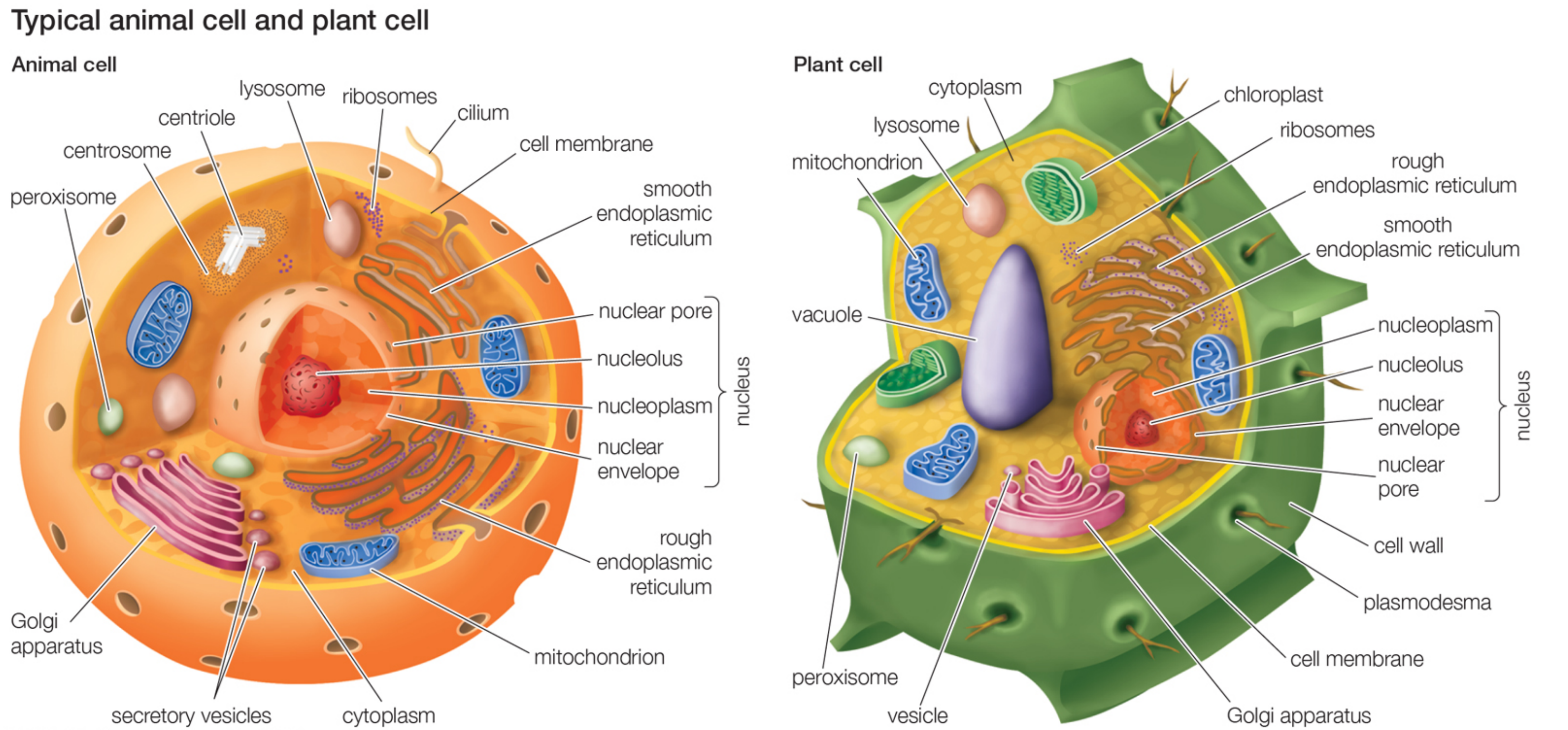
AIMS

- Introduce the locations where DNA can be found in a eukaryotic cell.
- Introduce the genome organization of the mitochondrial and chloroplast genomes.
- Introduce the nuclear genome organization.
- Explain the histone proteins and their involvement in higher organization of the nuclear genome.

Eukaryotic genomes

Where is the eukaryotic genome located?

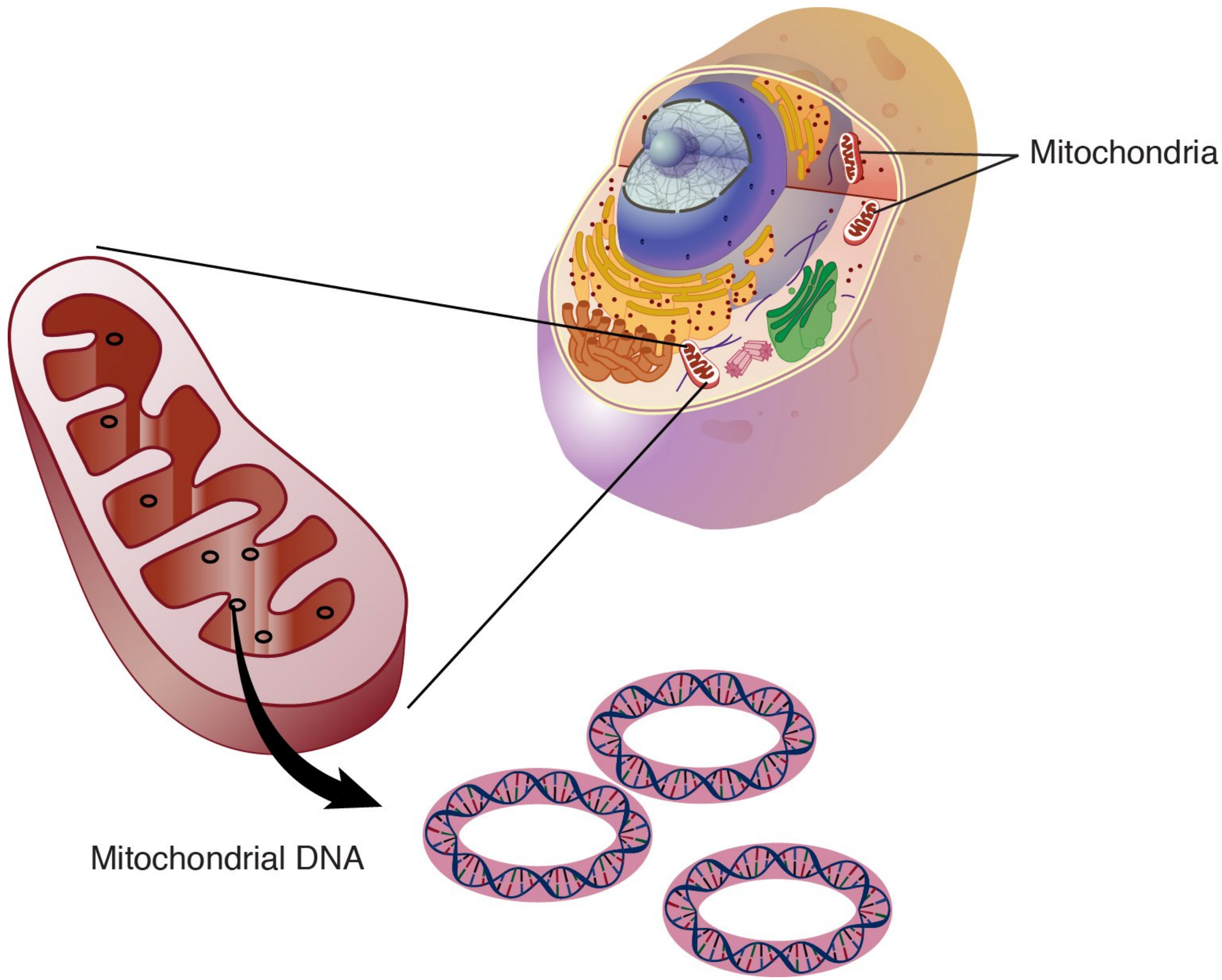
Eukaryotic genomes



Nuclear genome, mitochondrial genome, chloroplast genome

Mitochondrial genome

The mitochondria has its own genetic material

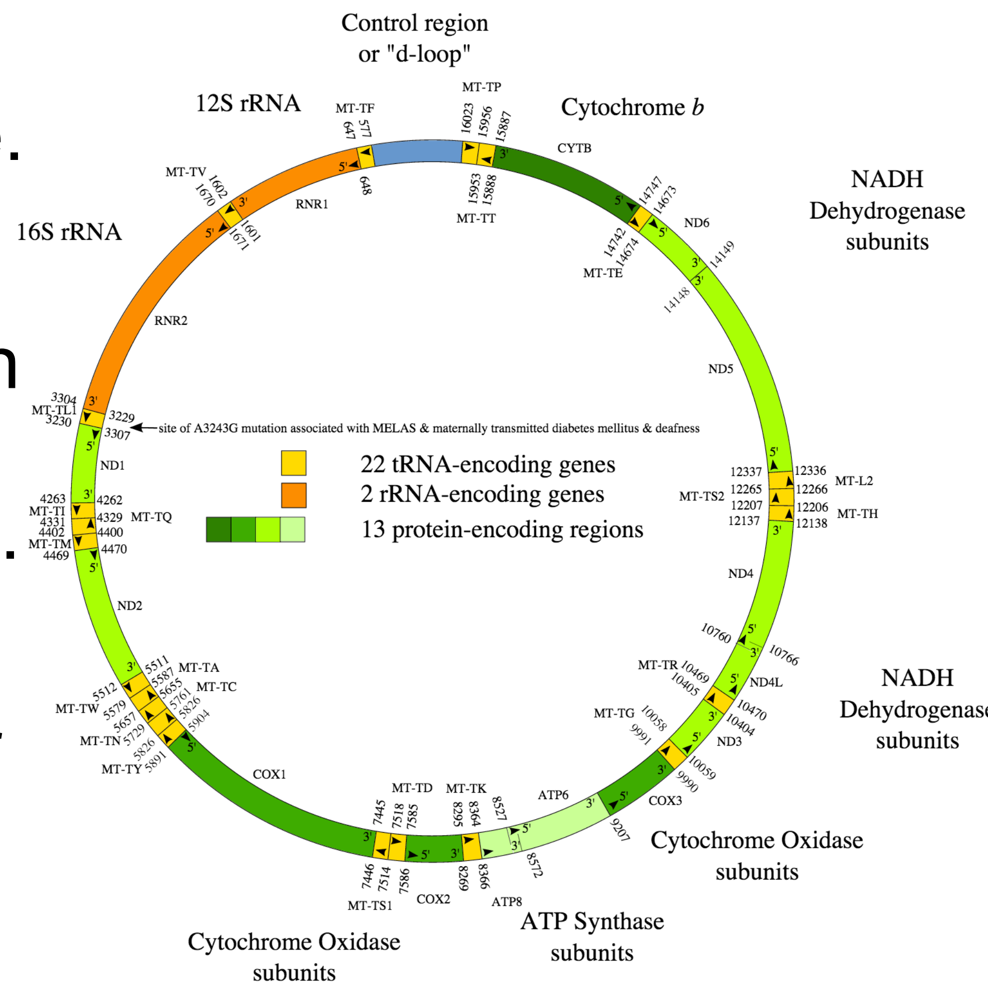


What is the function of the mitochondria?

How many copies of the genetic material a mitochondria has?

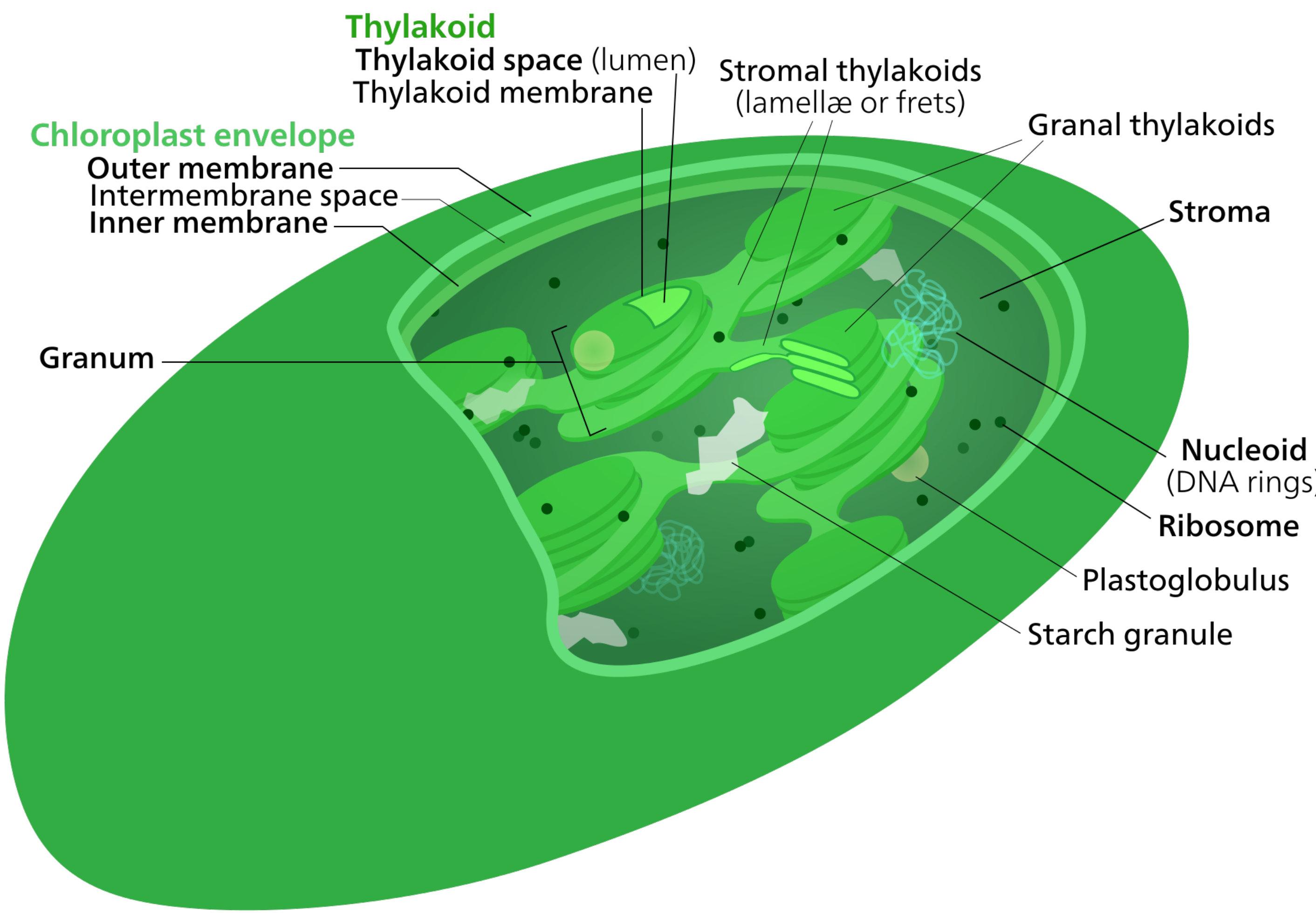
Mitochondrial genome

- The mitochondrial genome is a small circular one genome.
- Genome organization is similar to prokaryotic genomes.
- Notice the number of genes in the mitochondrial genome and their functions



Chloroplast genome

Chloroplast has its own genetic material

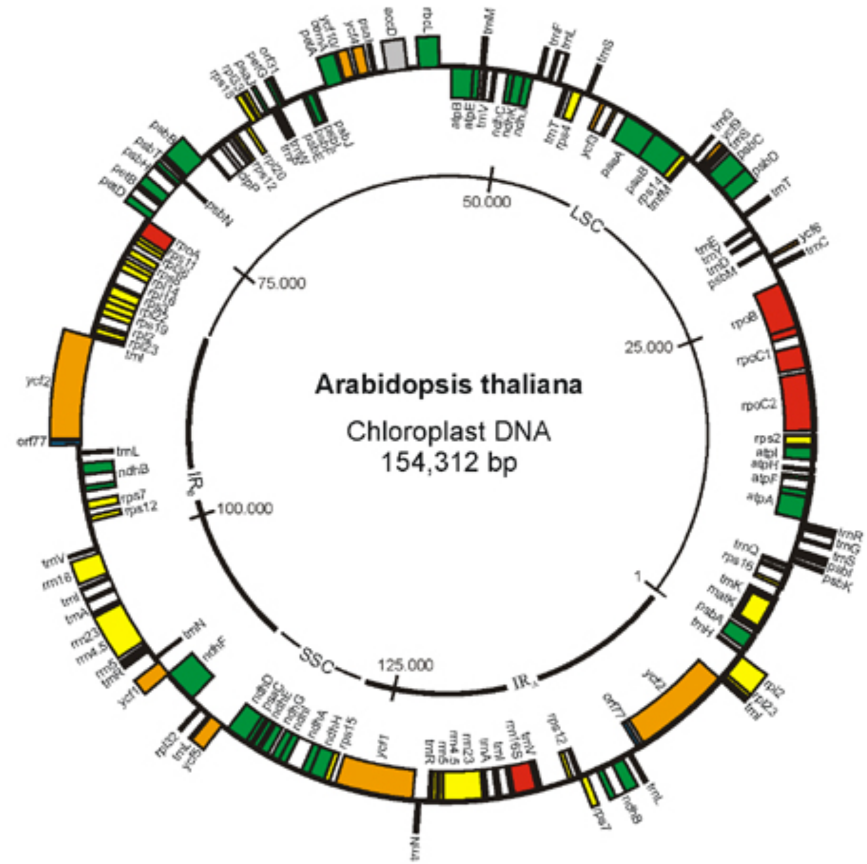


What is the function of the chloroplast?

How many copies of the genetic material a chloroplast has?

Chloroplast genome

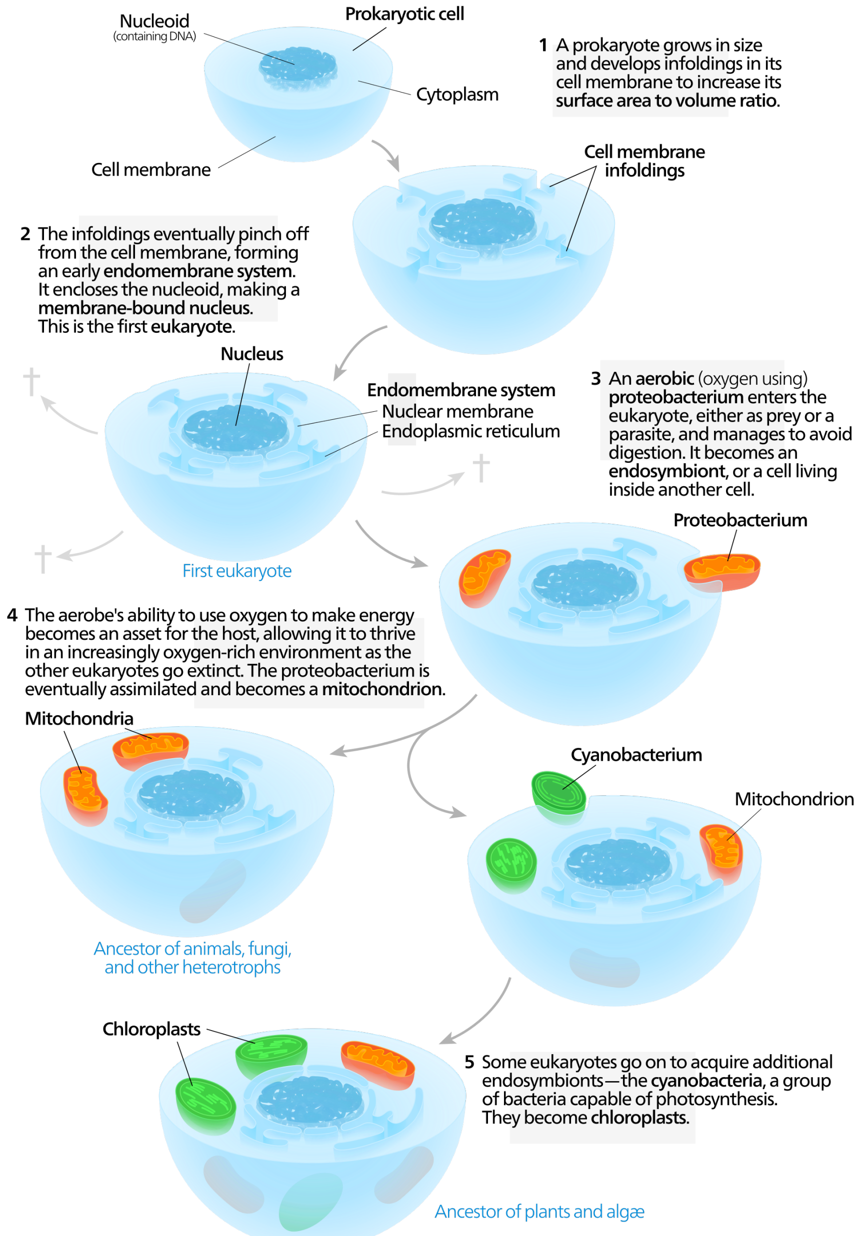
- The chloroplast genome is a small circular one genome.
- Genome organization is similar to prokaryotic genomes.



A. thaliana chloroplast DNA (inner circle: clockwise, outer: counter-clockwise). Function: transcription (red), translation (yellow), photosynthesis (green), tRNA (black), other (gray), unknown (orange). Sequence: AP000423 (see Sato et al., DNA Res 6: 283-290, 1999).

Why the mitochondria and chloroplast have similar genomes to prokaryotes?

Endosymbiosis



The mitochondrial and chloroplast are a result of an endosymbiotic relationships between various prokaryotic cells.

Aerobic proteobacterium

Cyanobacterium

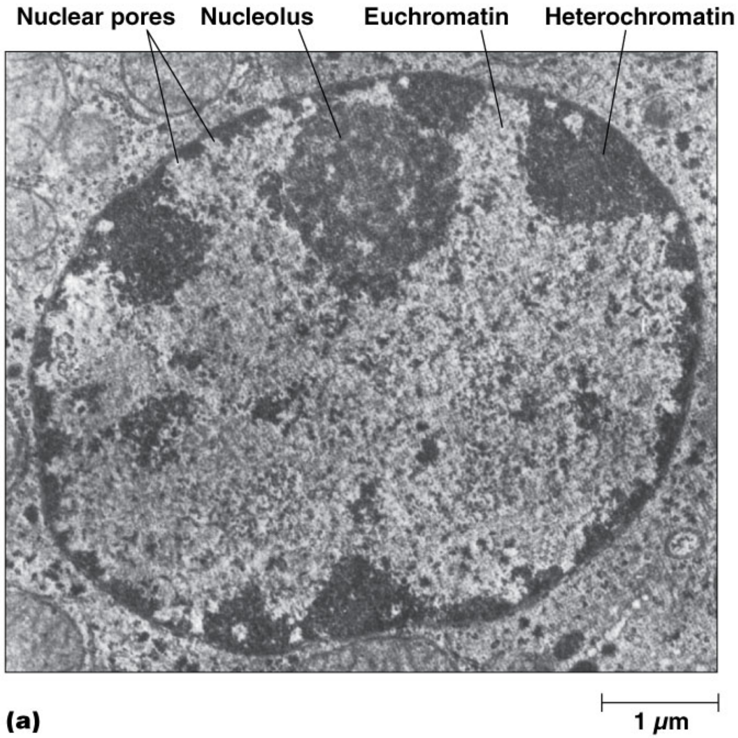
How is the mitochondrial genome organized?

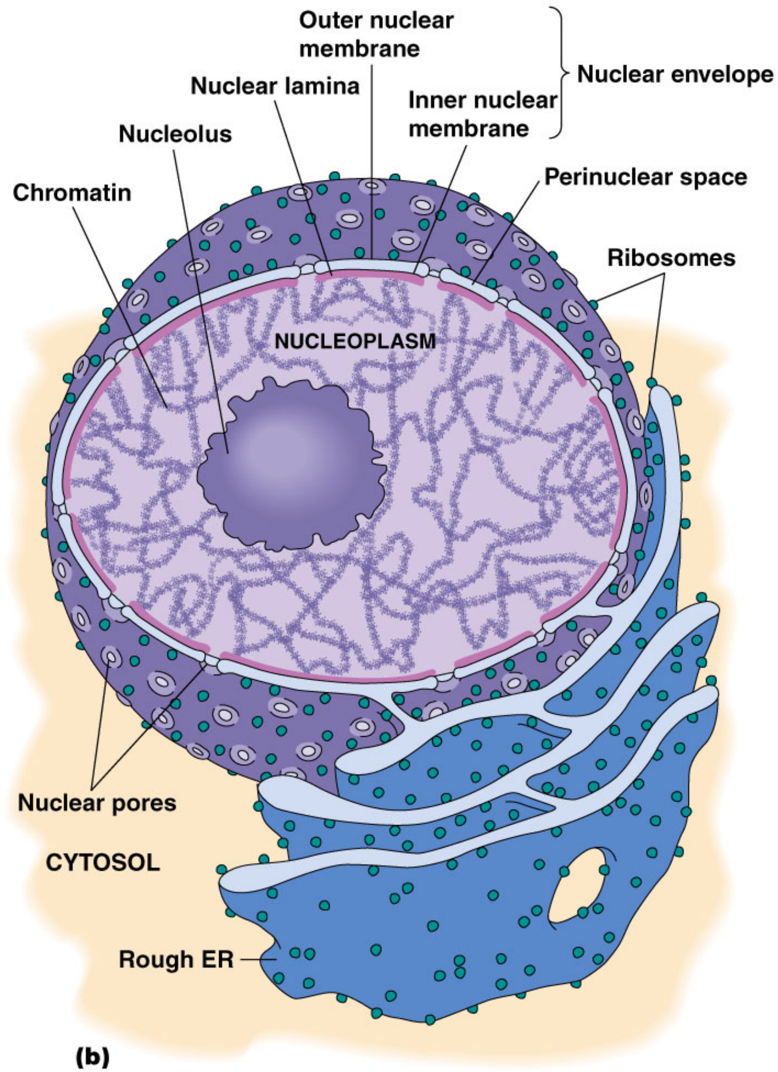
How is the chloroplast genome organized?

Do plants have mitochondrial genomes?

Nuclear genome

Where is the nuclear genome located?





Nuclear genomes

• Characteristics eukaryotic nuclear genomes are:

1. Genome is a double stranded DNA.

2. Genome arranged in several linear packages called **chromosomes** through interactions with several proteins.

Nuclear genomes

• The chromosomes in their most condensed form are called metaphase chromosomes.

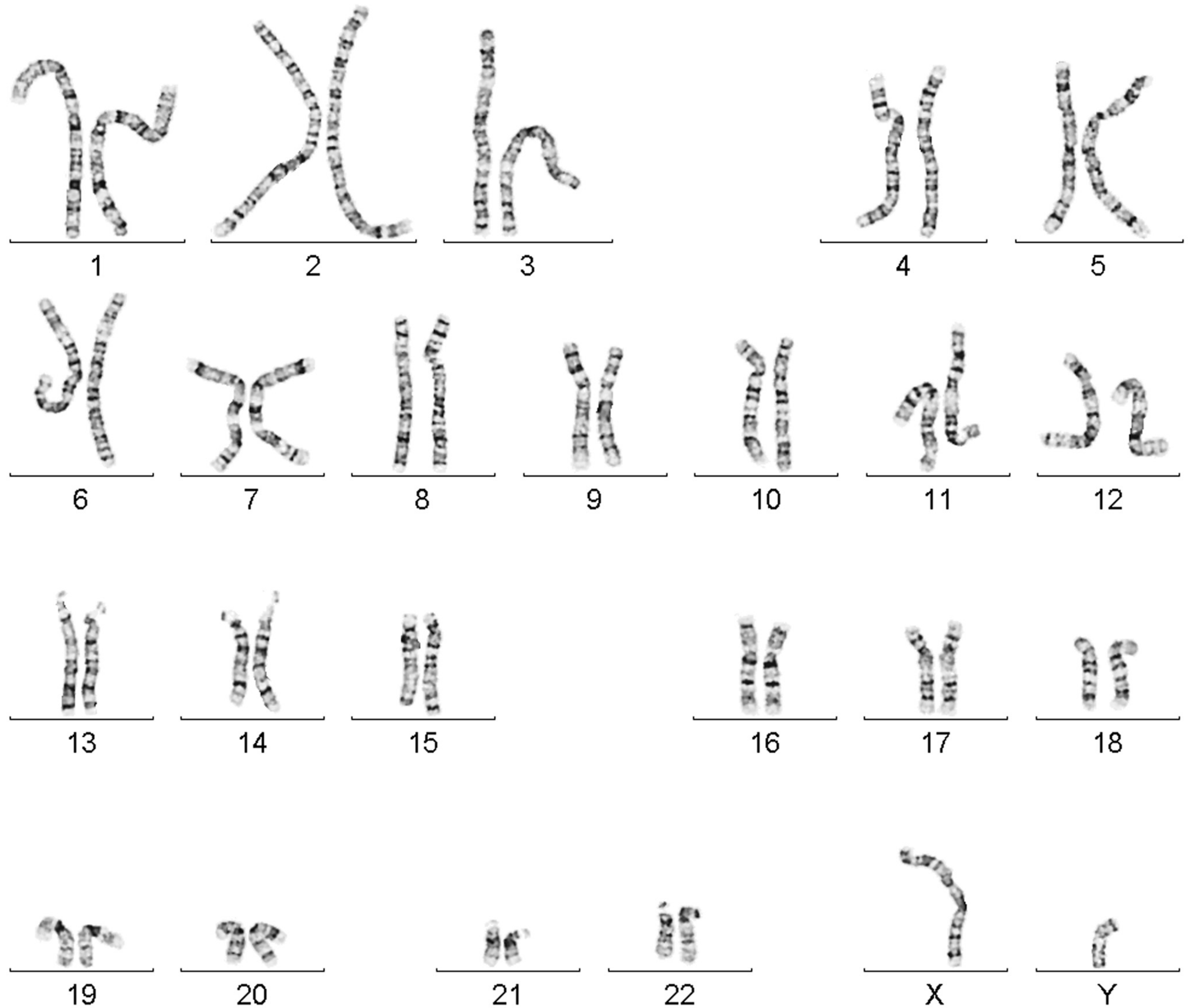
• The entire genome represented by metaphase chromosomes is called **karyotype**.

• The number of sets of chromosomes in a given eukaryotic cell is referred to as the level of ploidy.

What is your level of ploidy?

The genome packaged into chromosomes

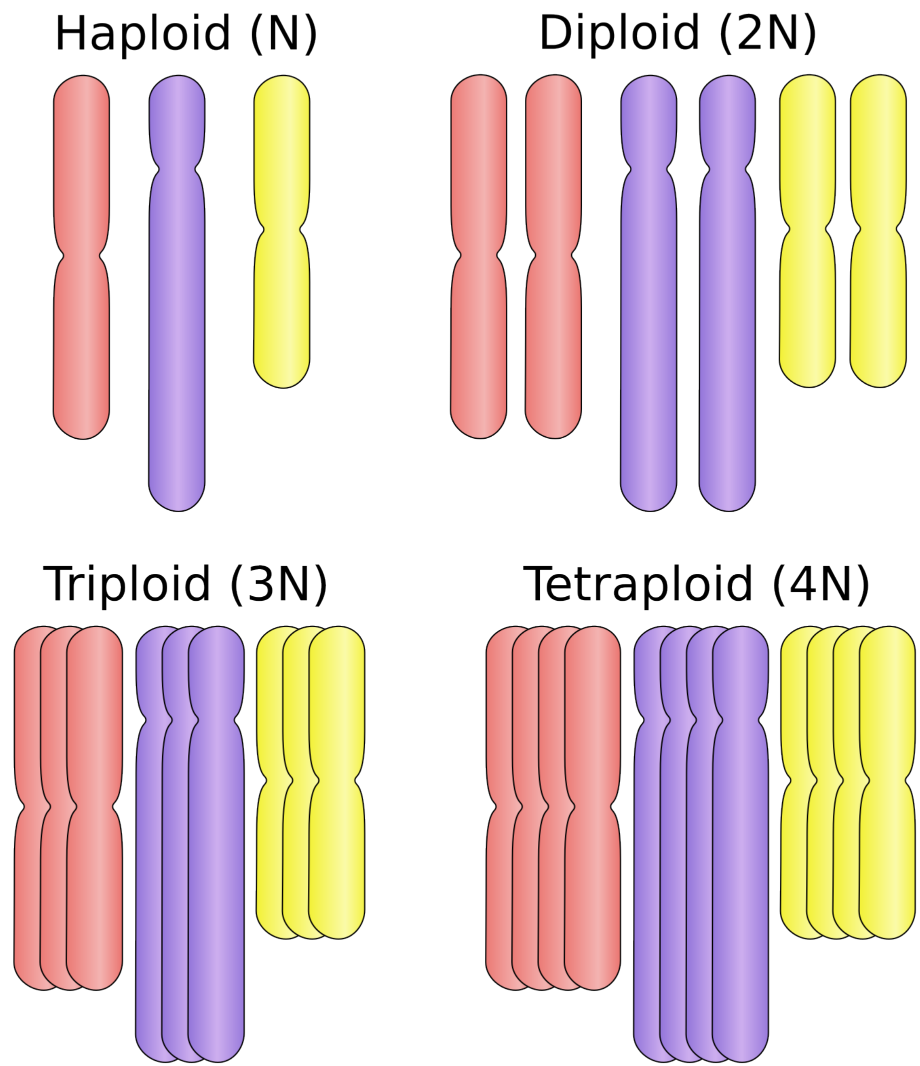
Karyotype



Ploidy

- **Haploid (1N):** cells that contain one set of chromosomes. Which of human cells are haploid and what 1N = ?

- **Diploid (2N):** cells that contain two sets of chromosomes. Which of human cells are haploid and what 2N = ?



The genome packaged into chromosomes

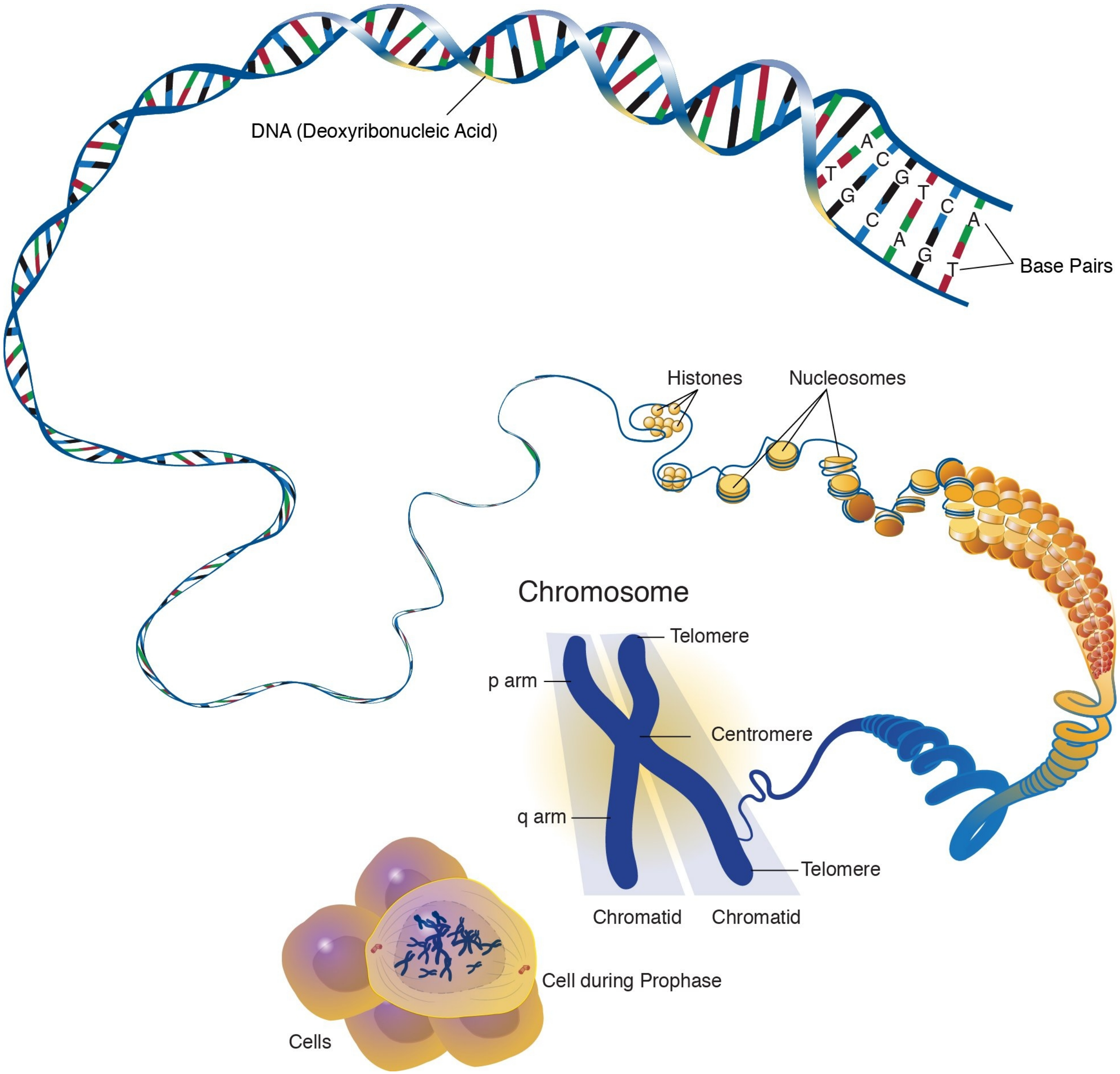
Eukaryotic nuclear chromosomes are linear with different chromosome copy numbers

TABLE 7-1 Variation in Chromosome Makeup in Different Organisms

Species		Number of Chromosomes	Chromosome Copy Number	Form of Chromosome(s)	Genome Size (Mb)
Prokaryotes					
Mycoplasma genitalium		1	1	Circular	0.58
Escherichia coli K-12		1	1	Circular	4.6
Agrobacterium tumefaciens		4	1	3 circular 1 linear	5.67
Sinorhizobium meliloti		3	1	Circular	6.7
Eukaryotes					
Saccharomyces cerevisiae (budding yeast)		16	1 or 2	Linear	12.1
Schizosaccharomyces pombe (fission yeast)		3	1 or 2	Linear	12.5
Caenorhabditis elegans (roundworm)		6	2	Linear	97
Arabidopsis thaliana (weed)		5	2	Linear	125
Drosophila melanogaster (fruit fly)		4	2	Linear	180
Tetrahymena thermophilus (protozoa)	Micronucleus	5	2	Linear	125
	Macronucleus	225	10–10,000	Linear	
Fugu rubripes (fish)		22	2	Linear	393
Mus musculus (mouse)		19 + X and Y	2	Linear	2,600
Homo sapiens		22 + X and Y	2	Linear	3,200

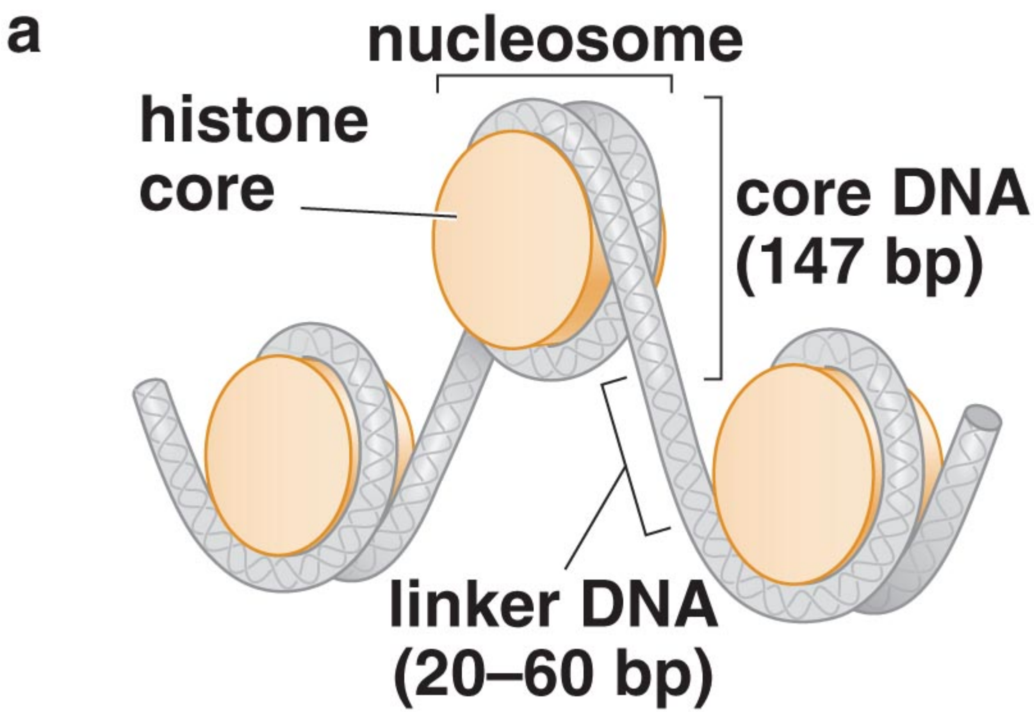
How is the nuclear genome organized and packaged?

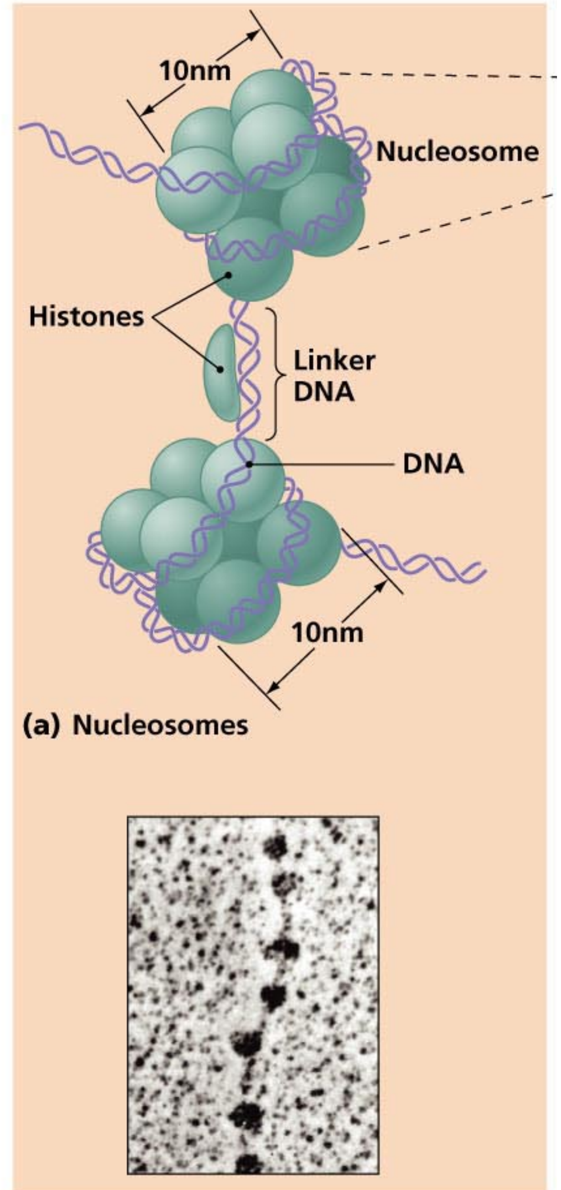
Eukaryotic genome packaging



1. Double stranded DNA + histones

- DNA interacts with **histone** proteins to form **Nucleosomes**.

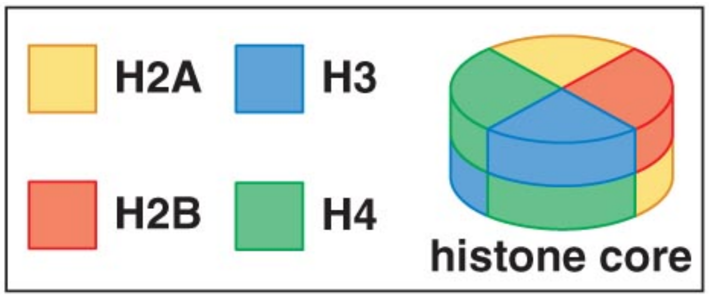


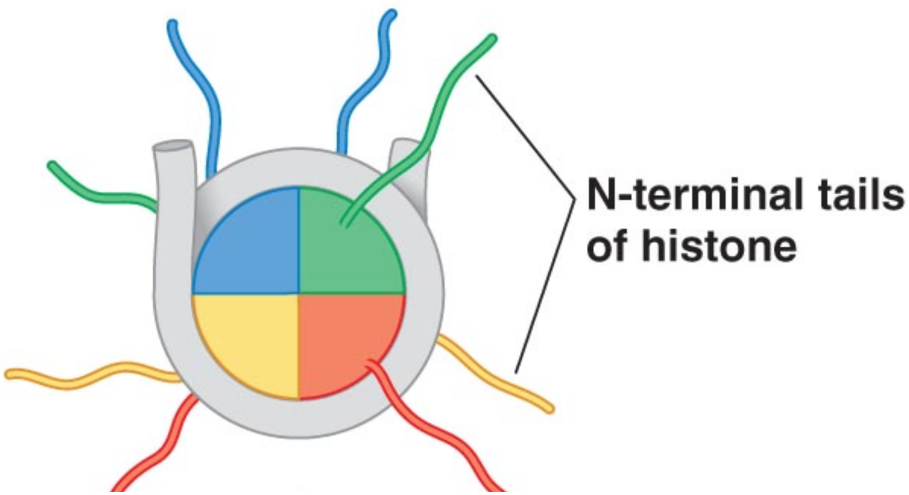


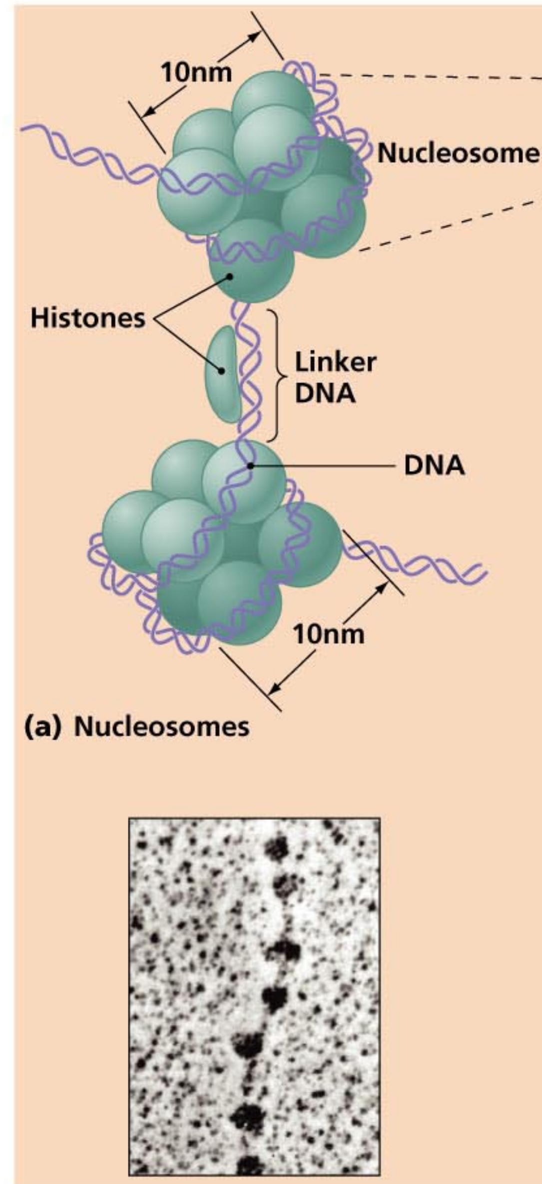
(a) Nucleosomes

1. Double stranded DNA + histones

A histone octamer (H2A, H2B, H3, H4) x 2 interacts with DNA to form a nucleosome.







(a) Nucleosomes

Histone proteins

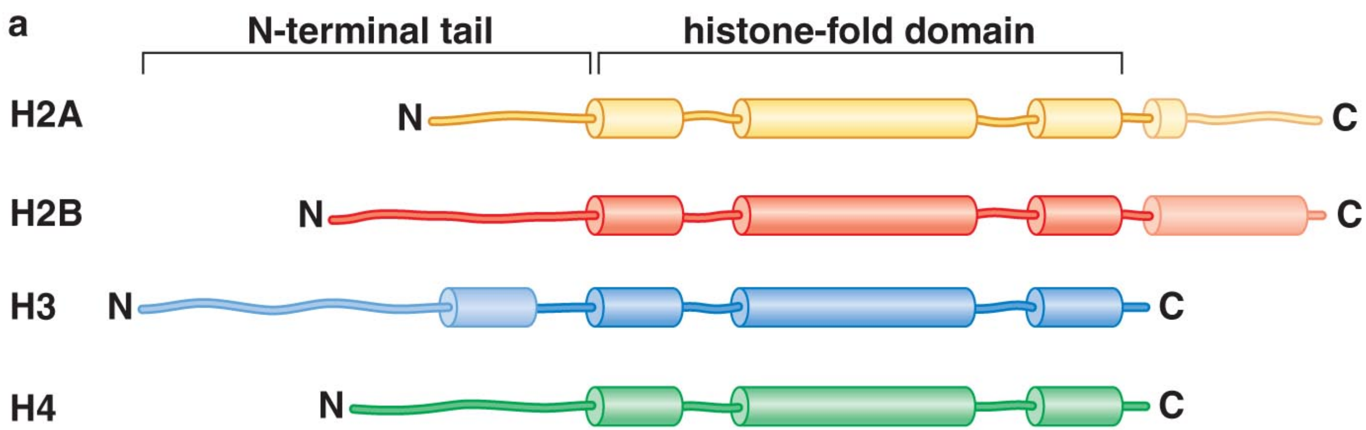


TABLE 7-5 General Properties of the Histones

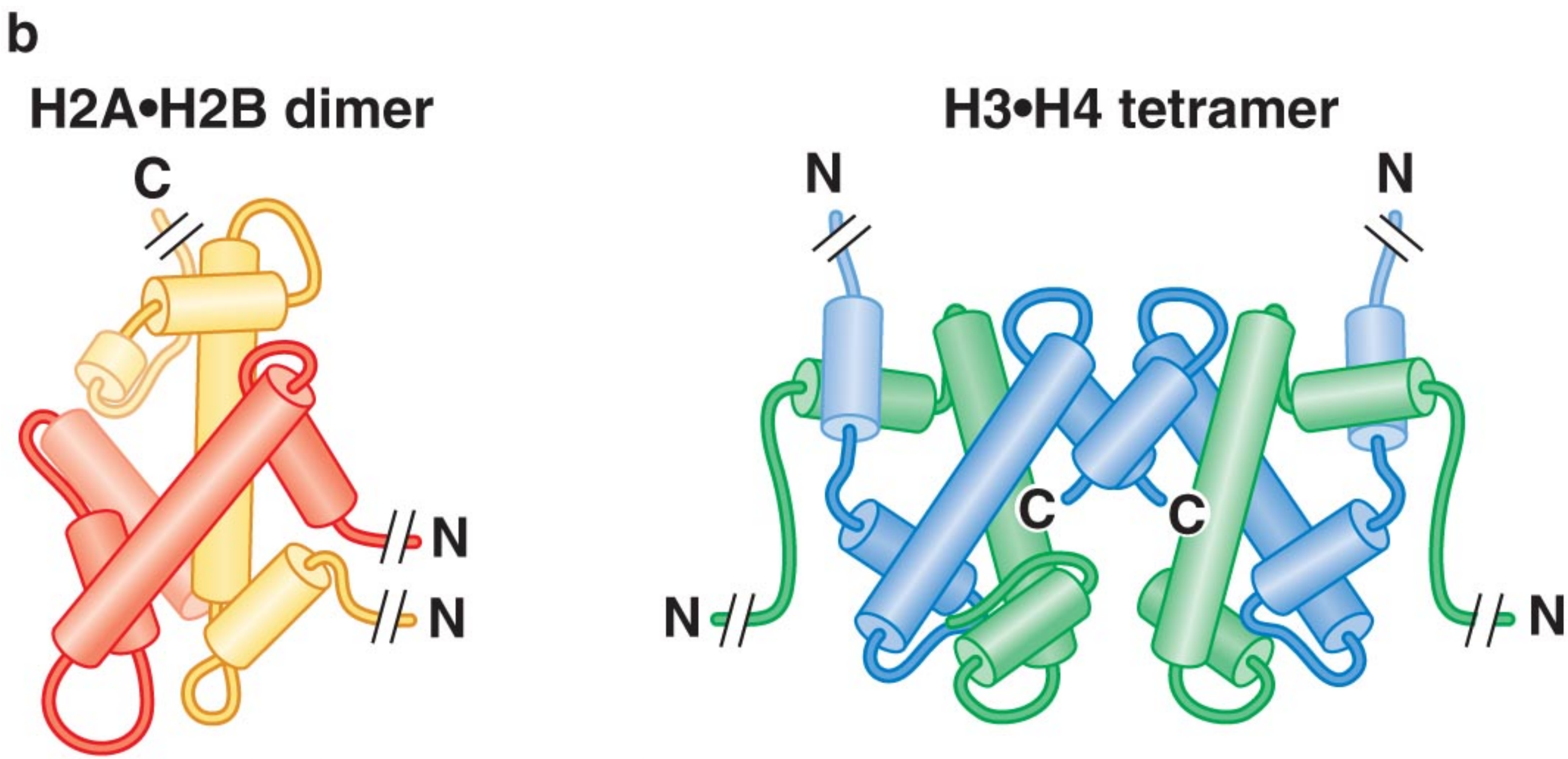
Histone Type	Histone	Molecular Weight (M_r)	% of Lysine and Arginine
Core histones	H2A	14,000	20
	H2B	13,900	22
	H3	15,400	23
	H4	11,400	24
Linker histone	H1	20,800	32

Histone proteins

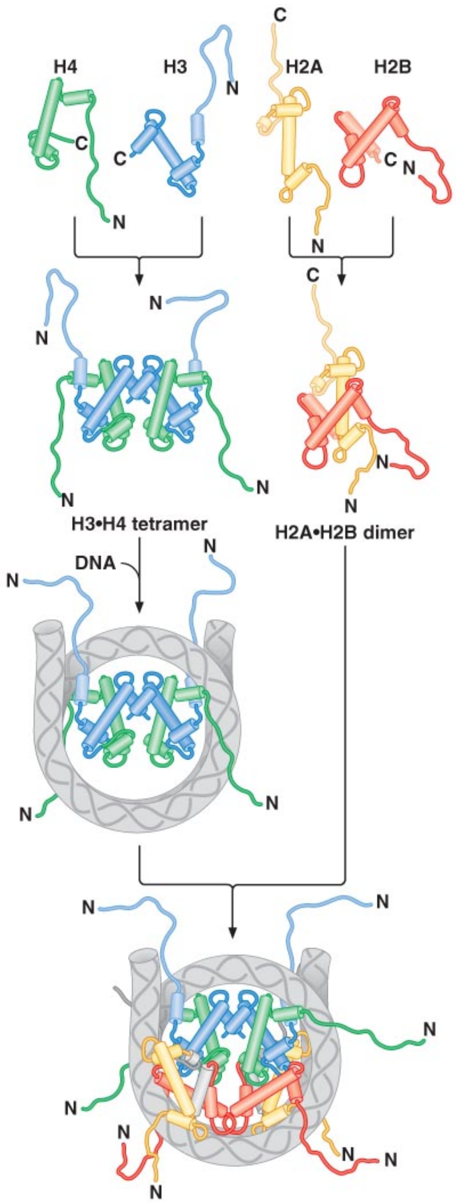
Where do histone proteins come from?

Histone proteins

- H2A and H2B form a dimer
- H3 and H4 form a tetramer (two H3 and two H4)



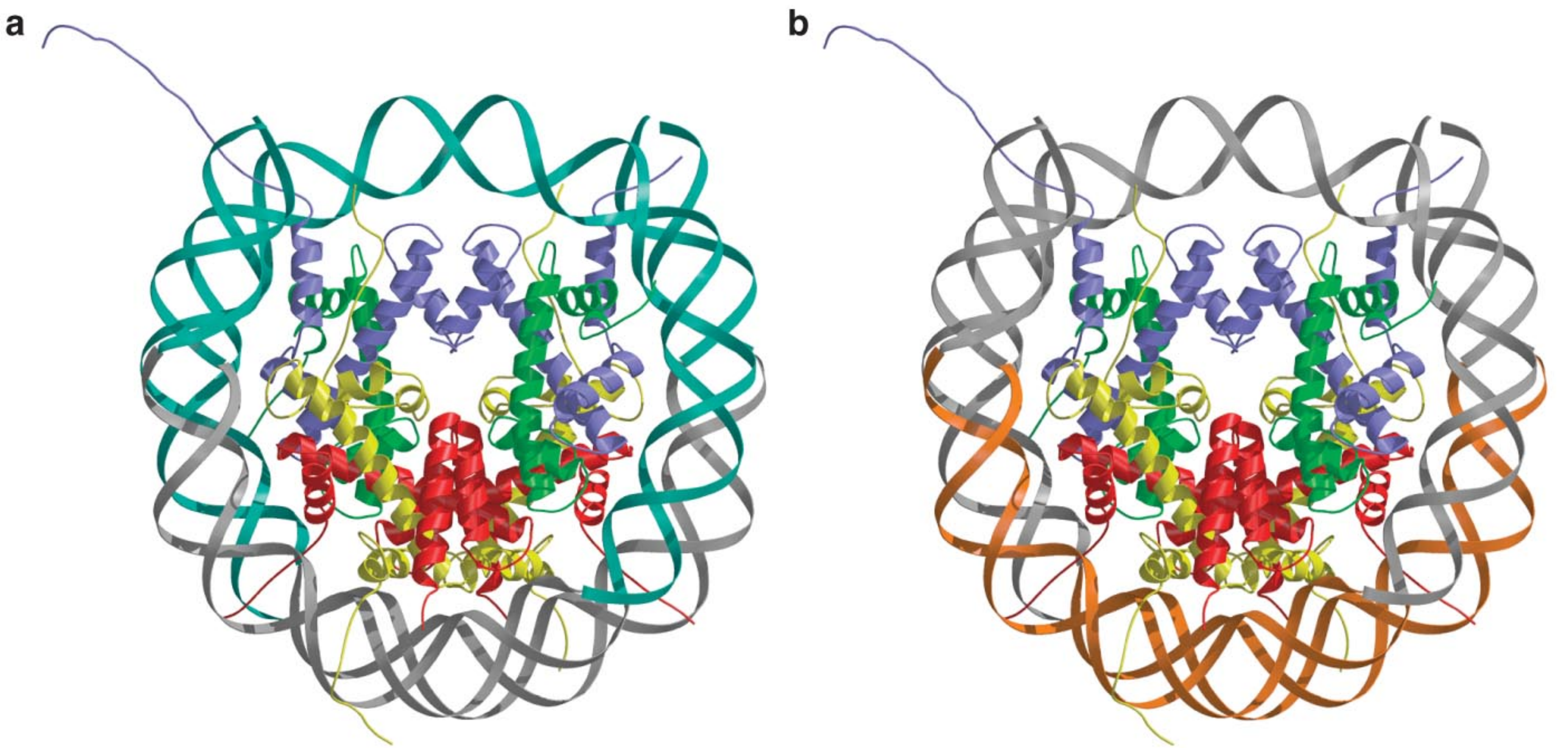
Histone proteins



- H3 and H4 tetramer first bind to DNA.
- two units of the H2A, H2B dimers then binds to DNA to form the histone core (nucleosome).

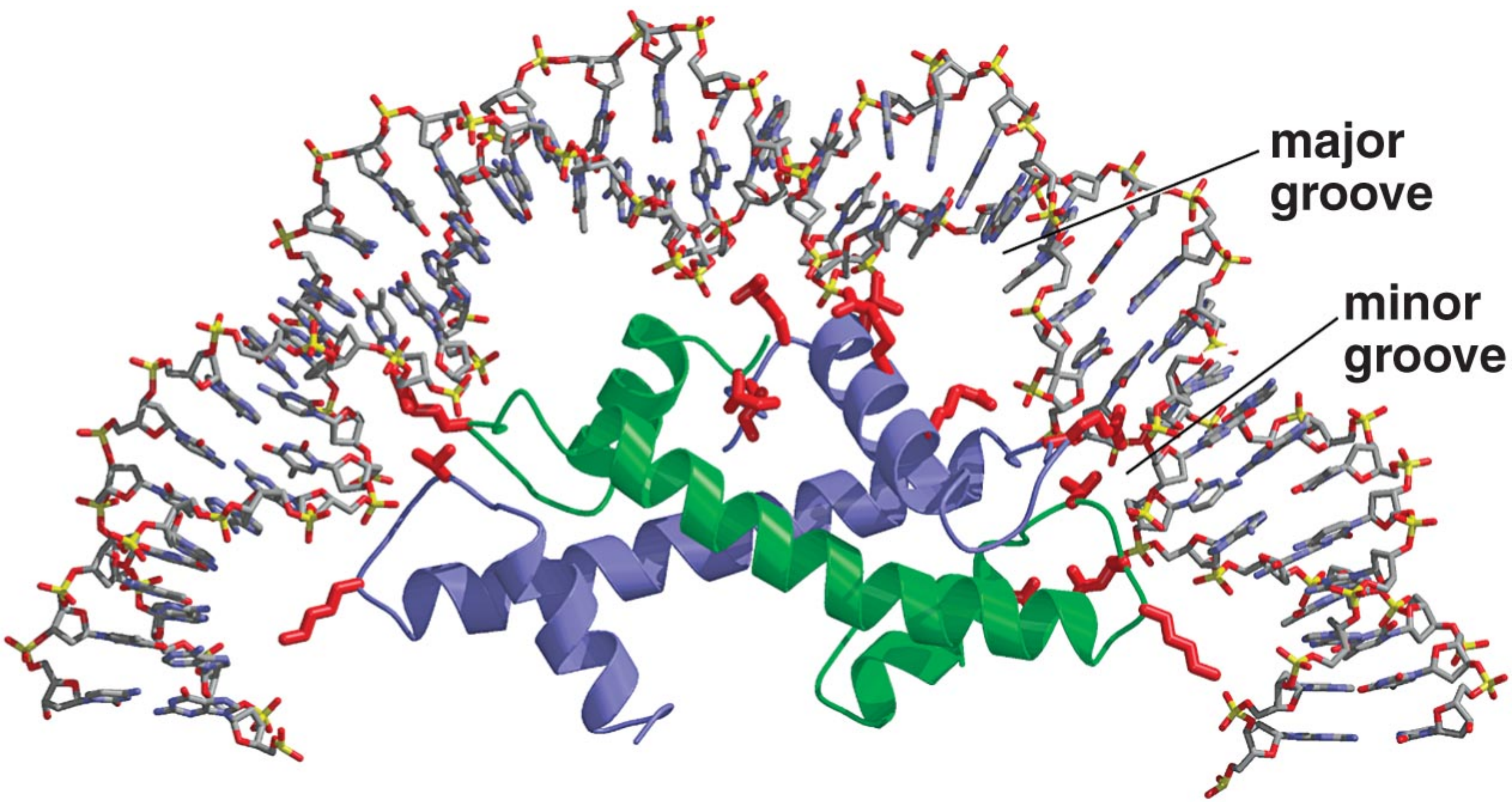
Histone proteins

How do histone proteins bind to DNA?



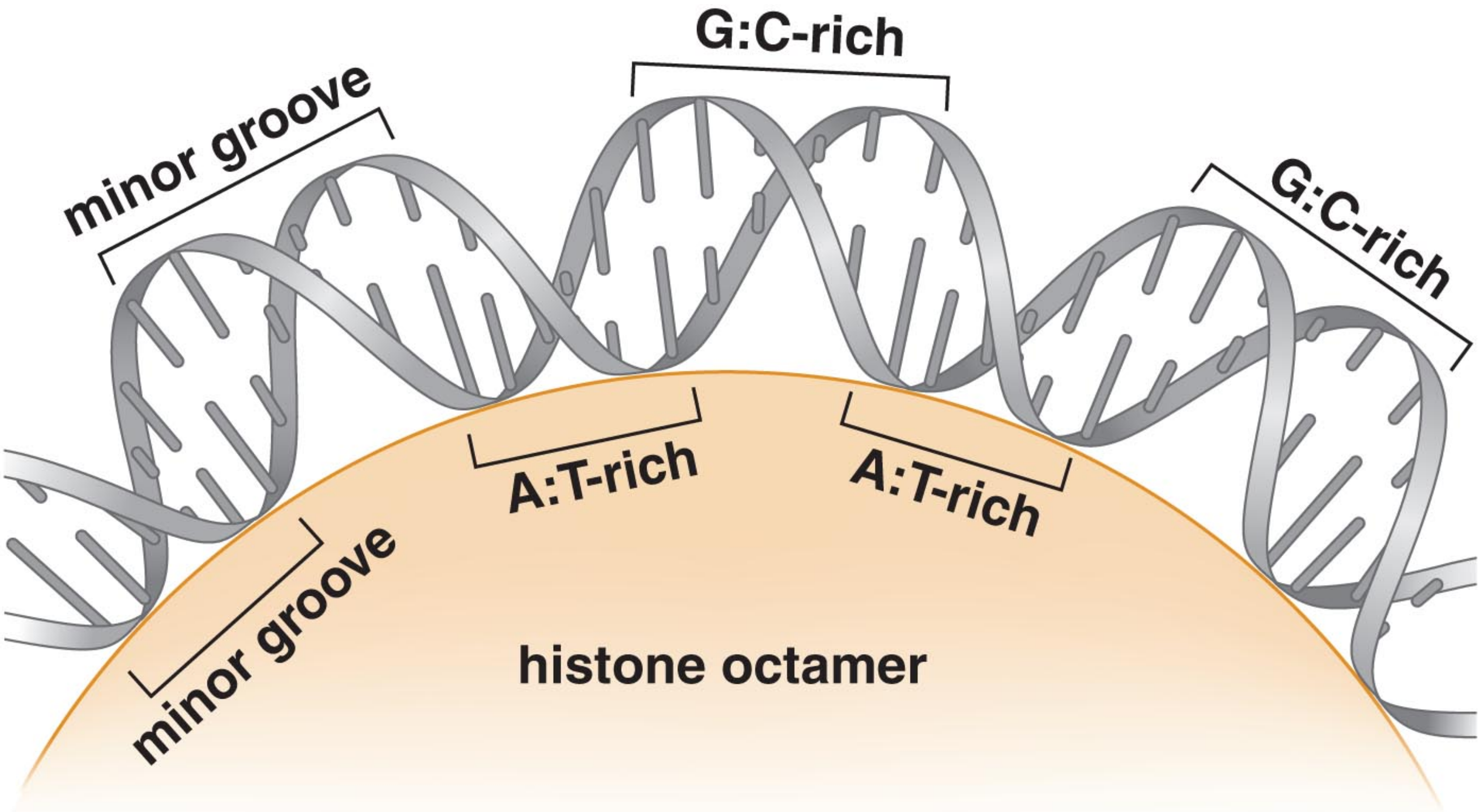
Histone proteins

The interactions between the amino acids of histone proteins and the bases of DNA



Histone proteins

Specific DNA sequences allow DNA to bend around histone octamer



1. Double stranded DNA + histones

147 bp of DNA goes around each histone octamer around 1.65 times.

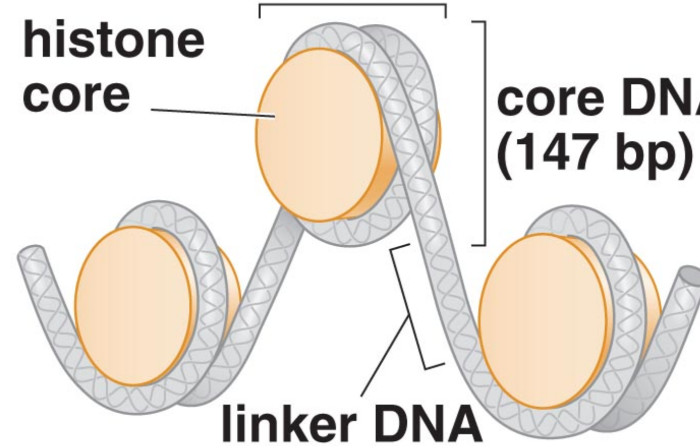
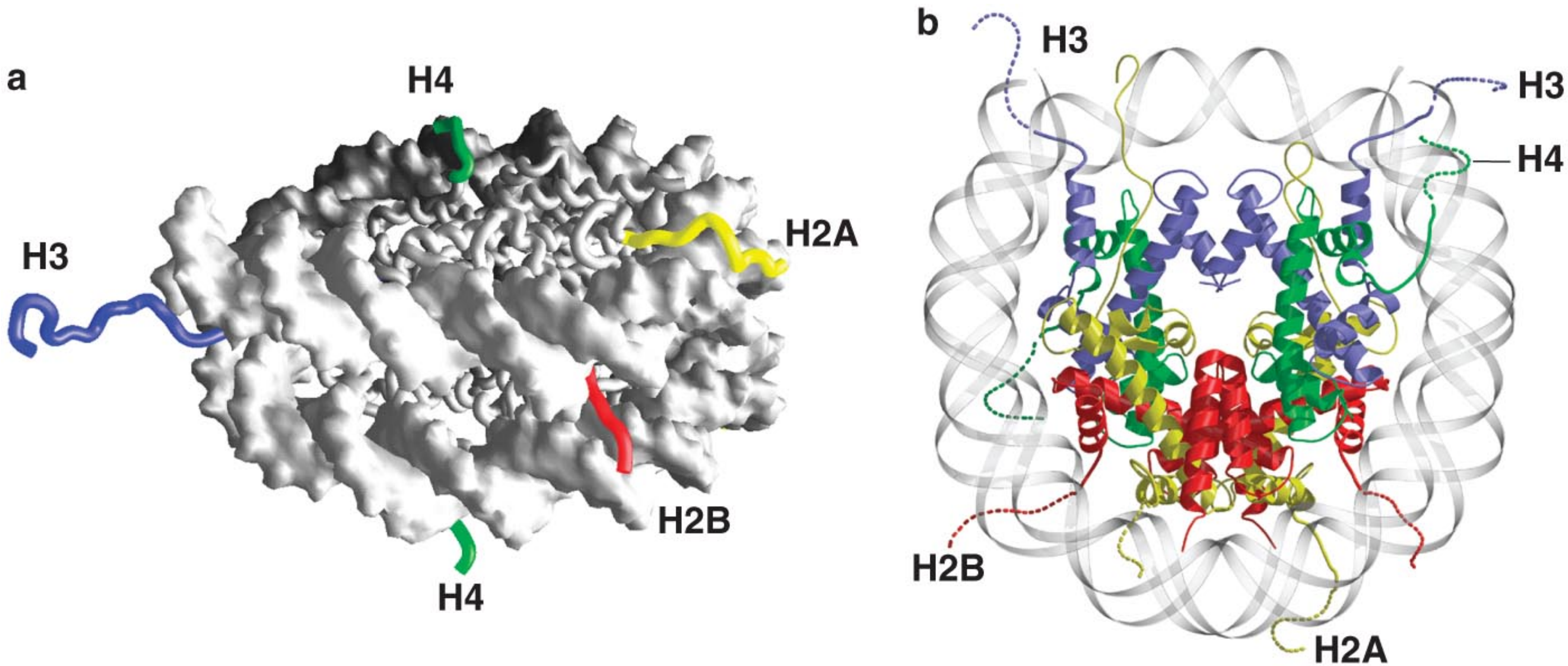


TABLE 7-4 Average Lengths of Linker DNA in Various Organisms

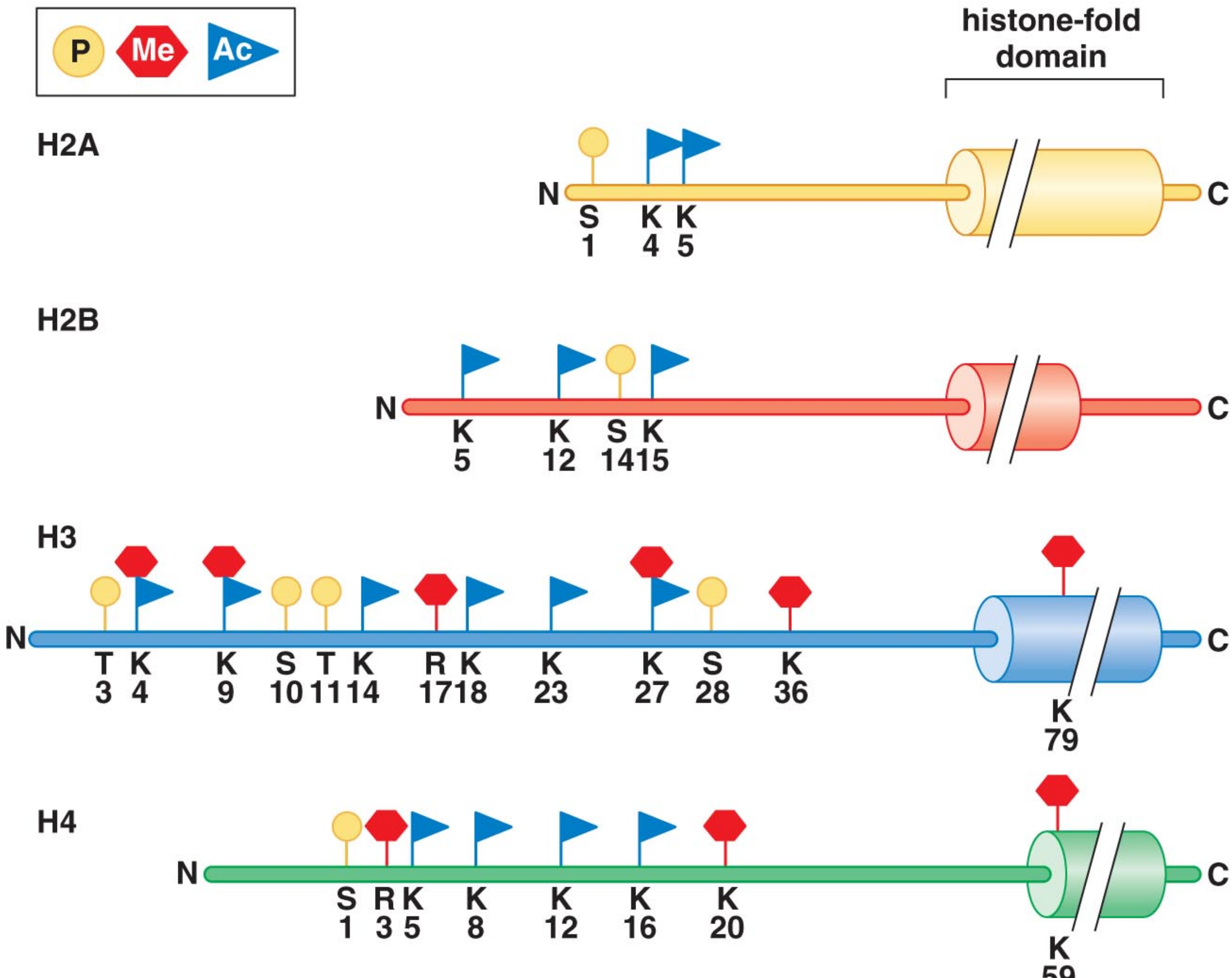
Species	Nucleosome Repeat Length (bp)	Average Linker DNA Length (bp)
Saccharomyces cerevisiae	160–165	13–18
Sea urchin (sperm)	~260	~110
Drosophila melanogaster	~180	~33
Human	185–200	38–53

Histone tails

What is the function of histone tails?



Histone tail modification



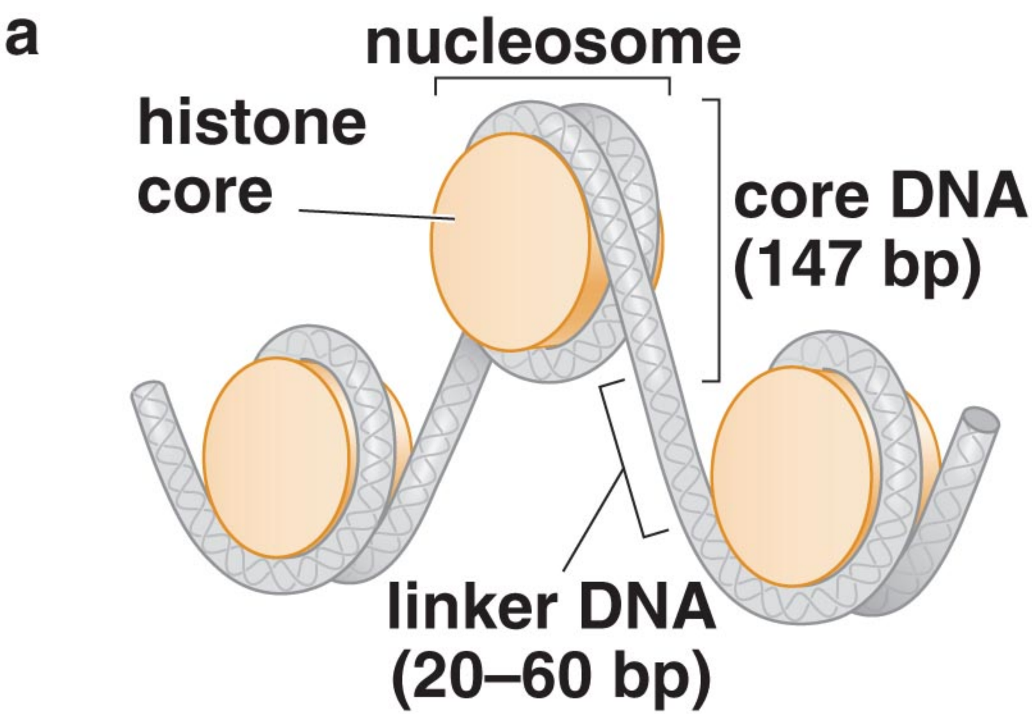
Histone tail modification

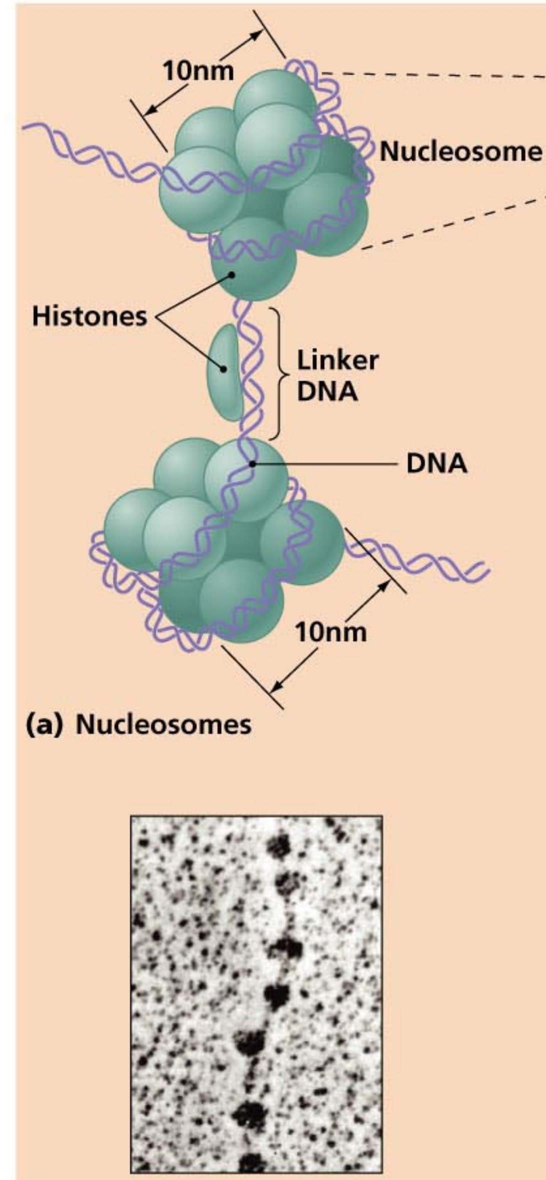
TABLE 7-7 Histone Modifications

Histone Subunit Residue	Modification	Consequence(s)
H2A		
Serine 1	Phosphorylation	Mitosis, transcriptional repression
Lysine 4	Acetylation	Transcriptional activation
Lysine 5	Acetylation	Transcriptional activation
Lysine 7	Acetylation	Transcriptional activation
H2B		
Lysine 5	Acetylation	Transcriptional activation
Lysine 12	Acetylation	Transcriptional activation
Serine 14	Phosphorylation	Apoptosis
Lysine 15	Acetylation	Transcriptional activation
H3		
Threonine 3	Phosphorylation	Mitosis
Lysine 4	Acetylation, methylation	Acetylation: transcriptional activation Methylation: active euchromatin
Lysine 9	Acetylation,methylation	Acetylation: transcriptional activation Methylation: transcriptional repression
Serine 10	Phosphorylation	Transcriptional activation
Threonine 11	Phosphorylation	Mitosis
Lysine 14	Acetylation	Transcriptional activation/elongation
Arginine 17	Methylation	Transcriptional activation
Lysine 18	Acetylation	Transcriptional activation, DNA repair
Lysine 23	Acetylation	Transcriptional activation, DNA repair
Lysine 27	Methylation, acetylation	Transcriptional silencing
Serine 28	Phosphorylation	Mitosis
Lysine 36	Methylation	Transcriptional elongation
Lysine 56	Acetylation	DNA repair
Lysine 79	Methylation	Transcriptional elongation
H4		
Serine 1	Phosphorylation	Mitosis
Arginine 3	Methylation	Transcriptional activation
Lysine 5	Acetylation	Histone deposition
Lysine 8	Acetylation	Transcriptional activation
Lysine 12	Acetylation	Histone deposition, telomeric silencing
Lysine 16	Acetylation	Transcriptional activation, DNA repair
Lysine 20	Methylation	Transcriptional silencing

1. Double stranded DNA + histones

Between two nucleosomes there is a linker DNA that is ~ 40-50 bp.





(a) Nucleosomes

1. Double stranded DNA + histones

Is the length of linker DNA the same across different species?

TABLE 7-4 Average Lengths of Linker DNA in Various Organisms

Species	Nucleosome Repeat Length (bp)	Average Linker DNA Length (bp)
Saccharomyces cerevisiae	160–165	13–18
Sea urchin (sperm)	~260	~110
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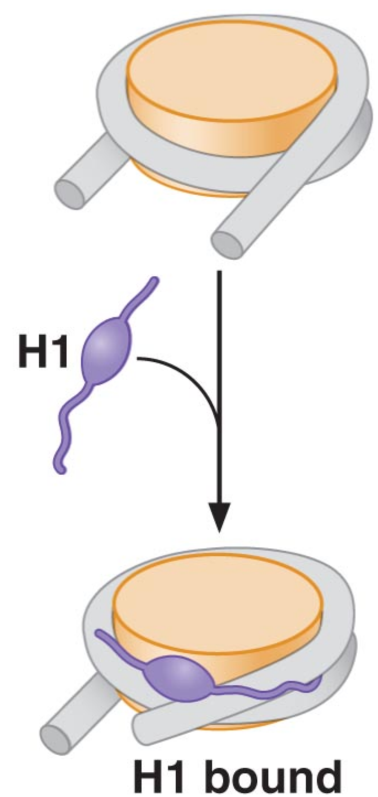
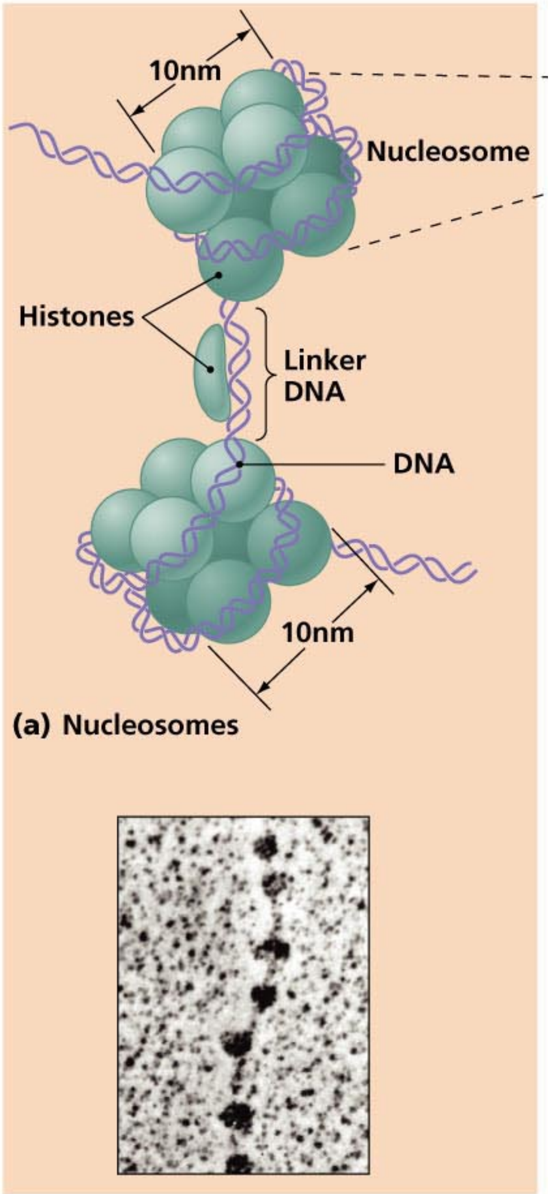
1. Double stranded DNA + histones

Another histone protein (H1) also facilitate into further condensation.

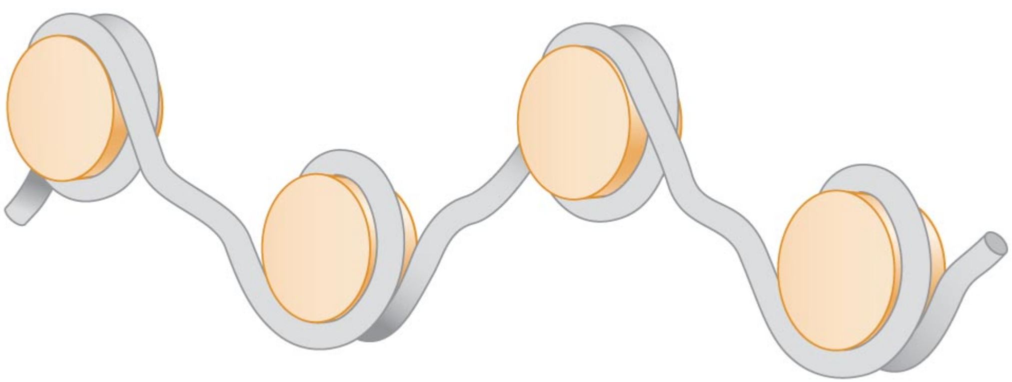


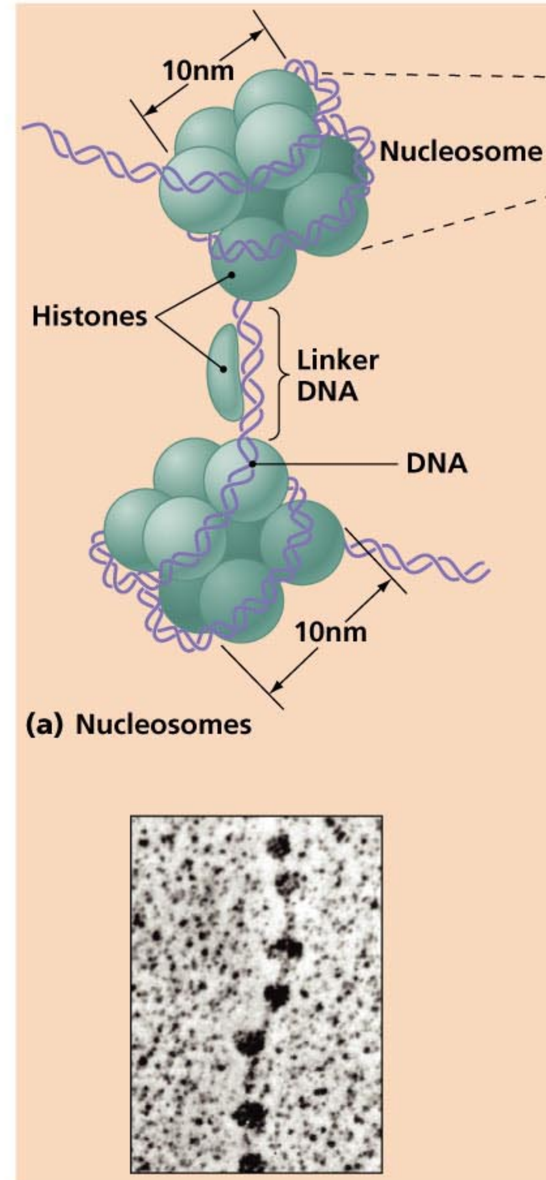


(a) Nucleosomes

1. Double stranded DNA + histones

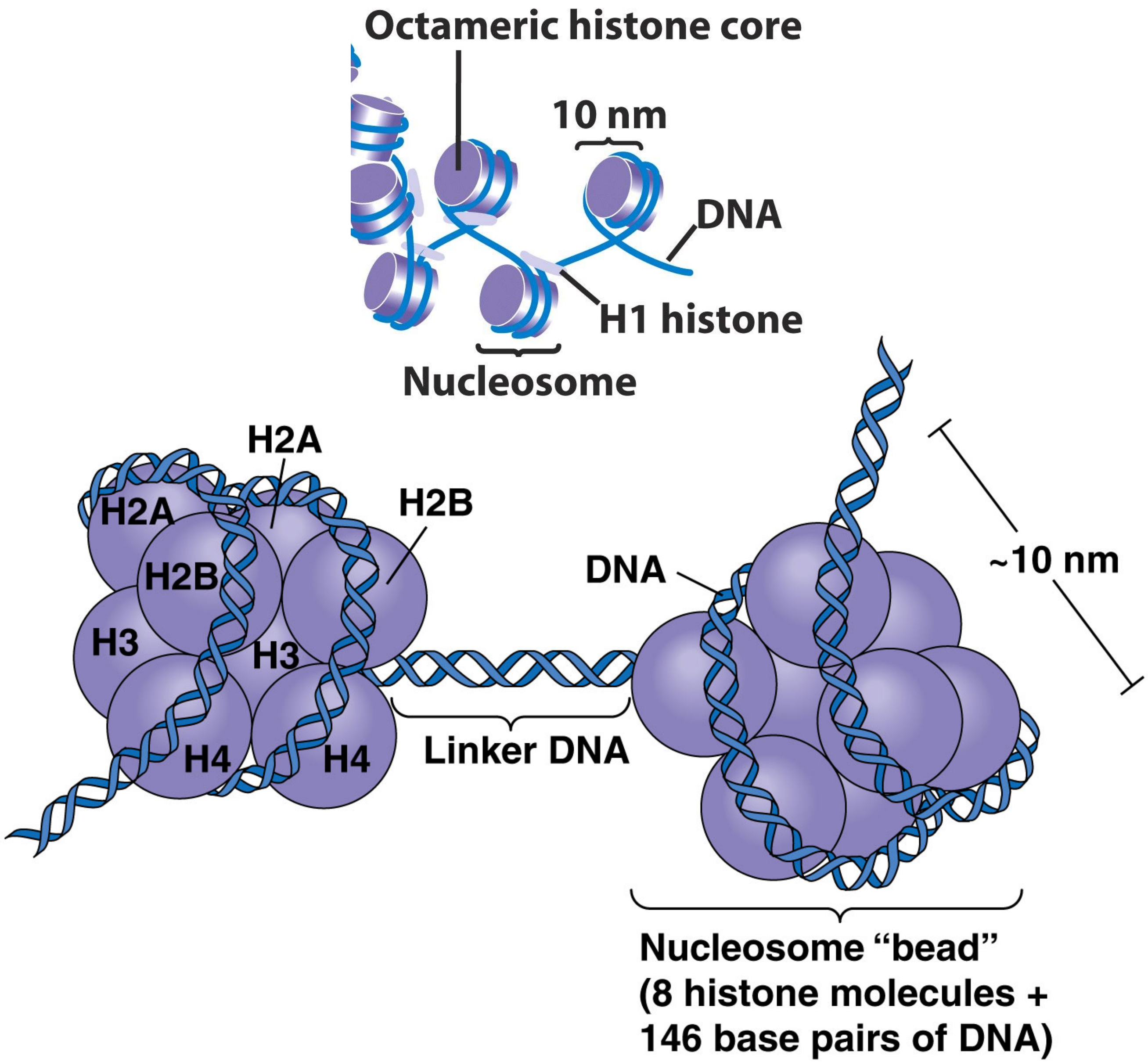
This structure is referred to as **beads-on-a-string**.





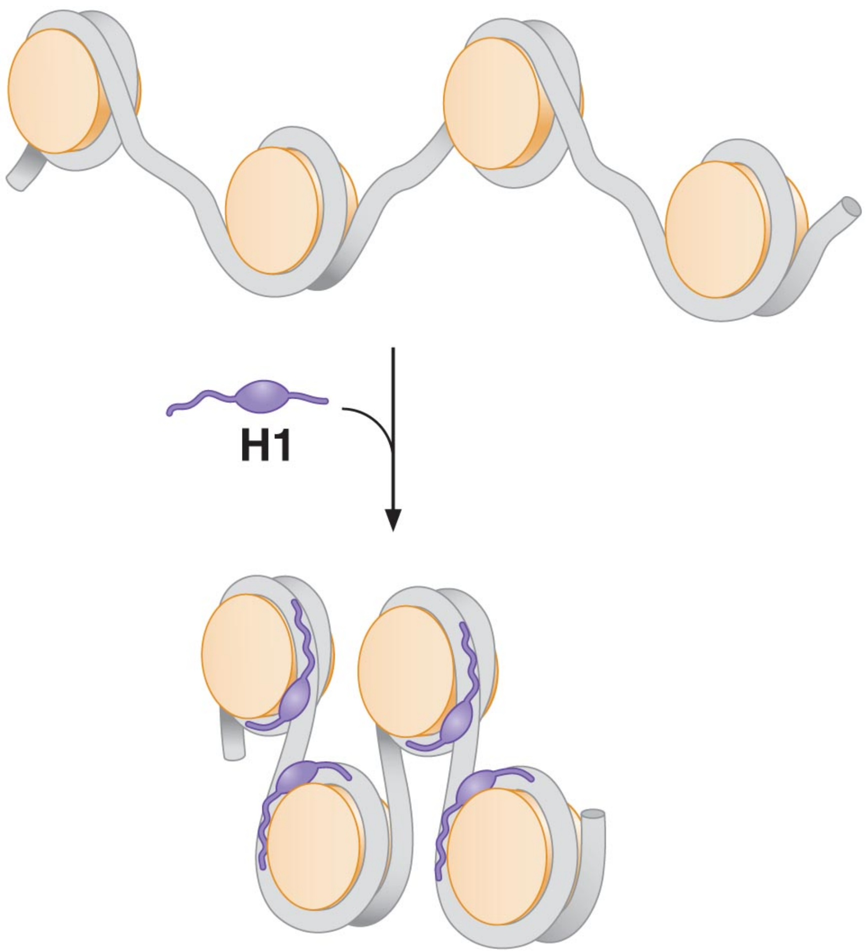
(a) Nucleosomes

Nucleosome summary



2. Nucleosomes to chromatin fiber

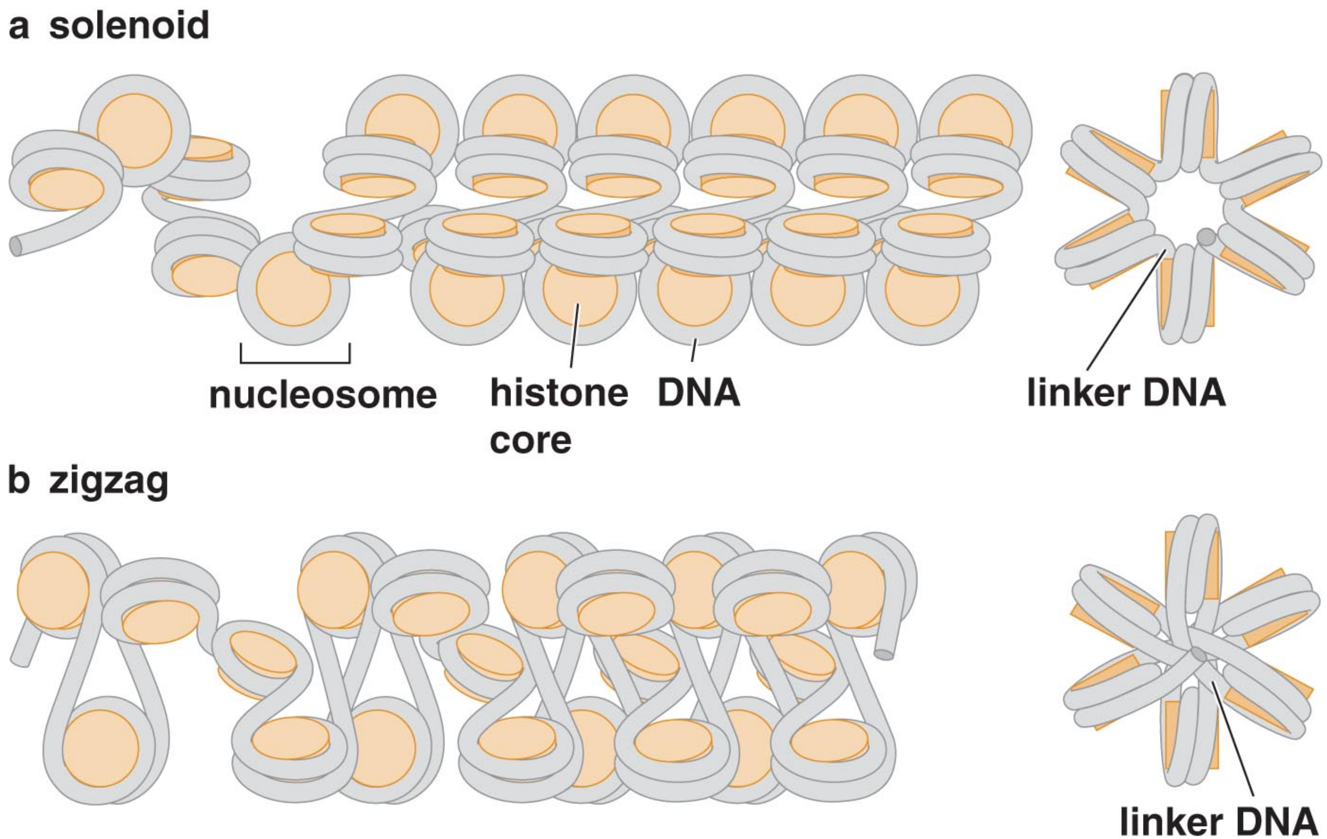
Nucleosomes condense to form the **Solenoid or the 30nm fiber.**



Histone H1 facilitates further condensation of nucleosomes

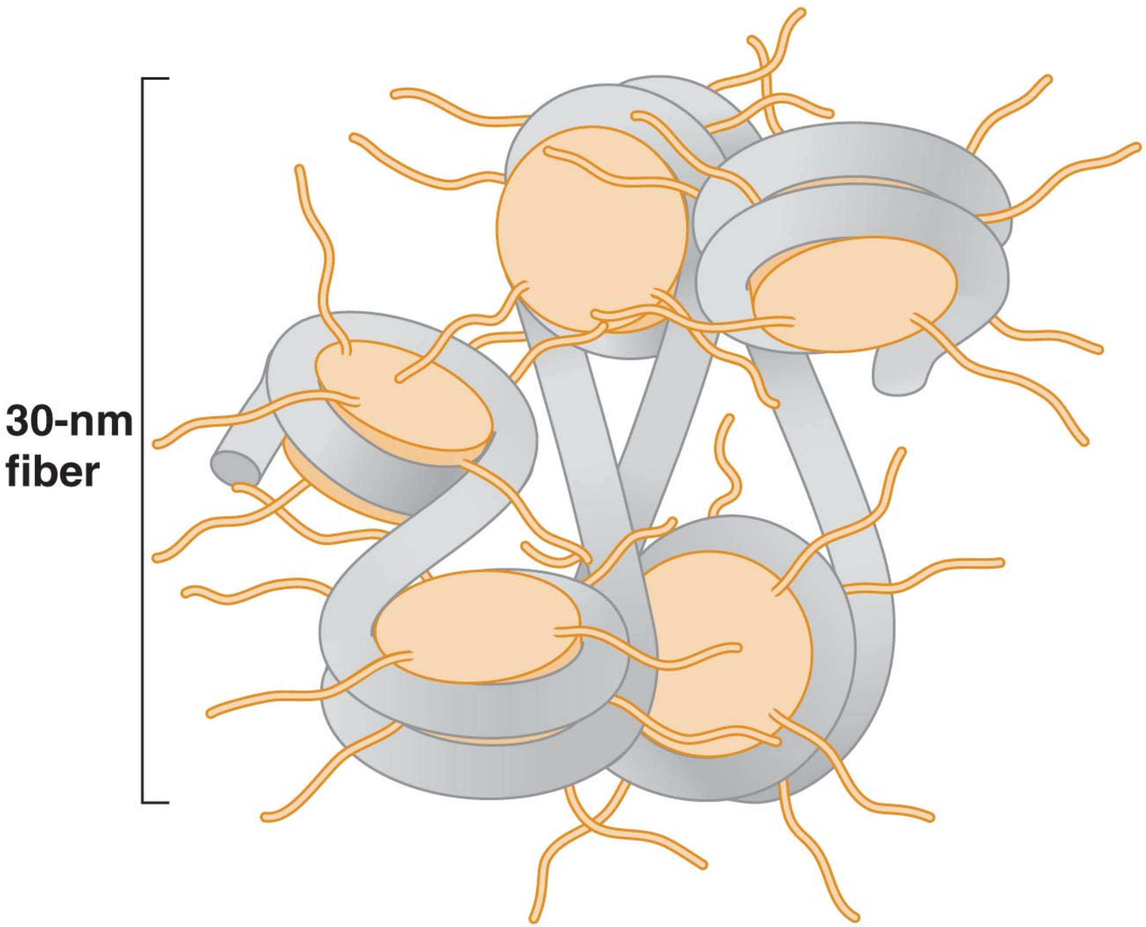
2. Nucleosomes to chromatin fiber

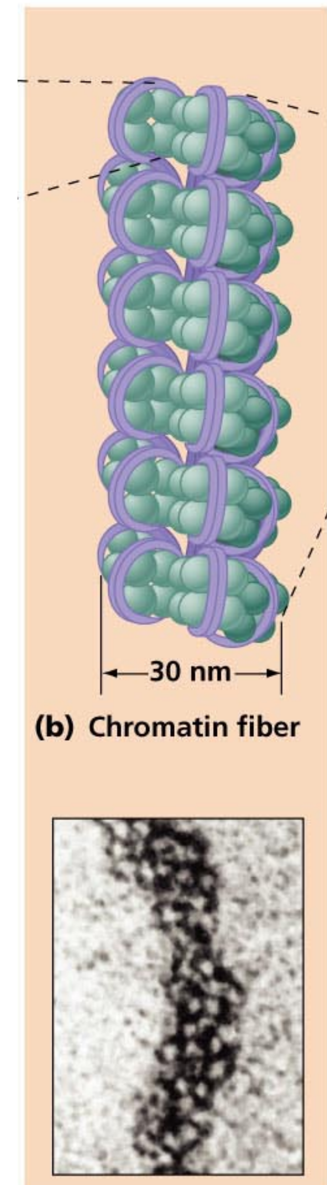
Two models of the condensation of nucleosomes into chromatin



2. Nucleosomes to chromatin fiber

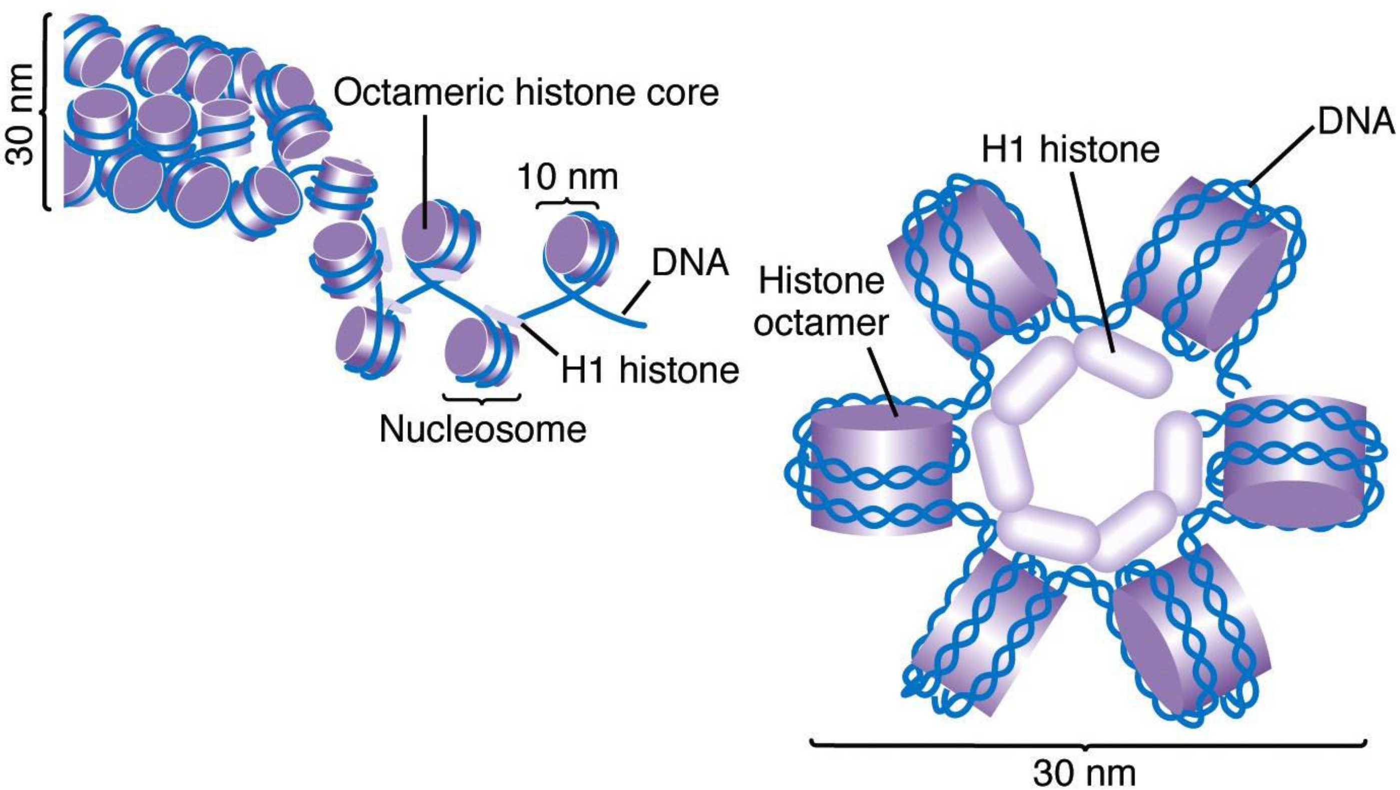
• Nucleosomes condense to form the **Solenoid or the 30nm fiber.**





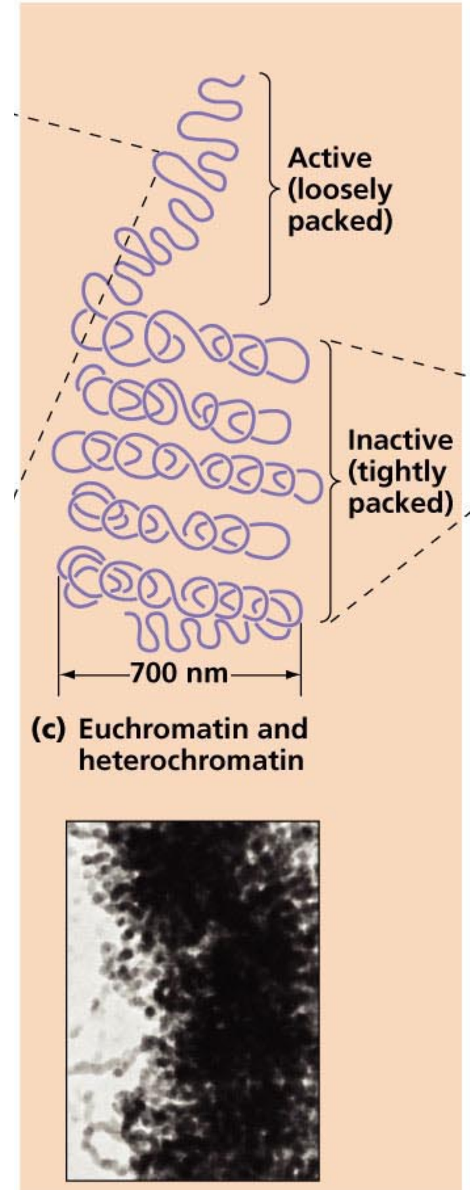
2. Nucleosomes to chromatin fiber

- Nucleosomes condense in a spiral orientation.
- As the name indicates the width of the molecule is 30nm.



3. Chromatin to Euchromatin and Heterochromatin

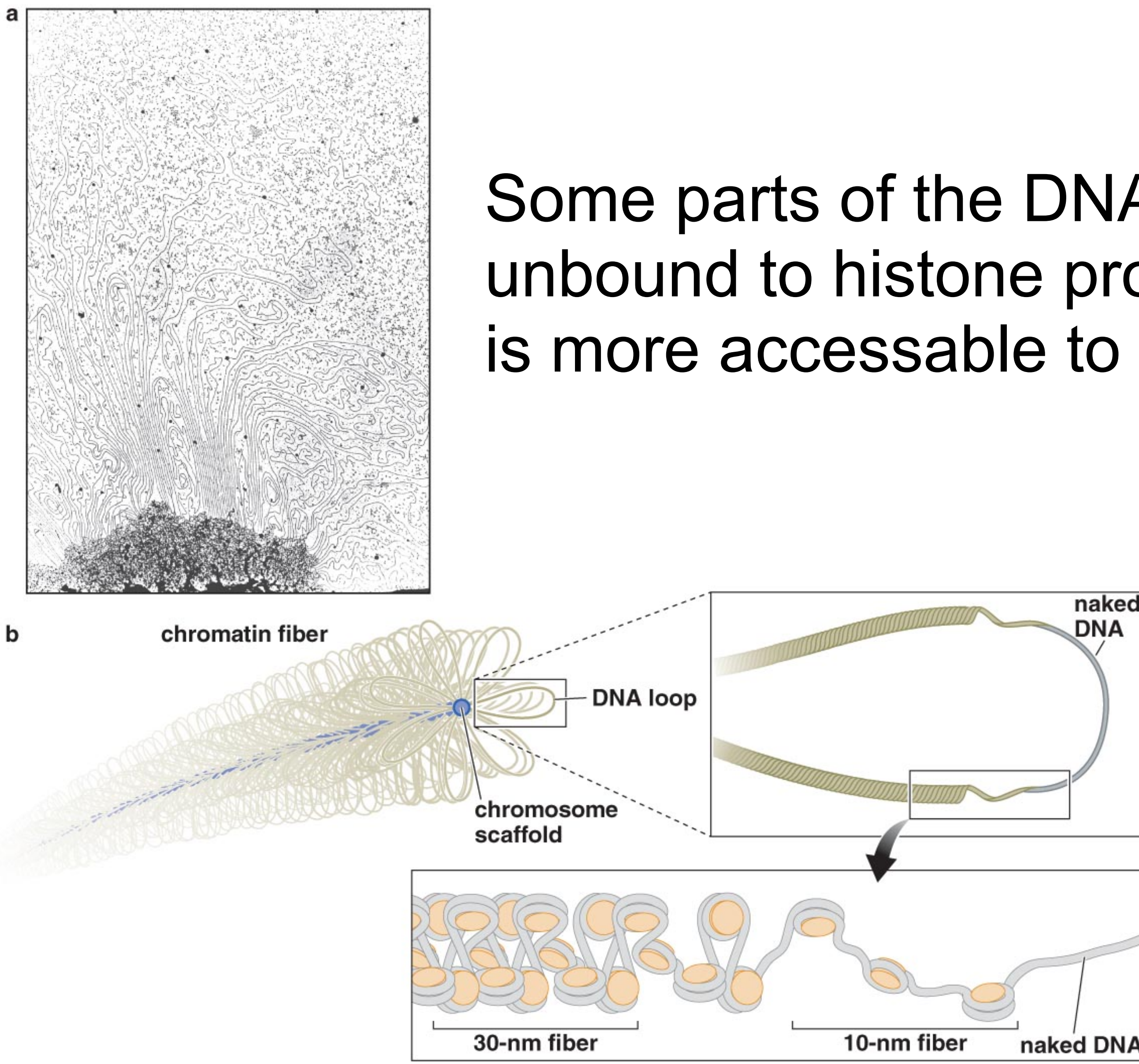
- Chromatin packs into:
  - **Euchromatin**
  - **Heterochromatin.**



(c) Euchromatin and heterochromatin

3. Chromatin to Euchromatin and Heterochromatin

Some parts of the DNA remains unbound to histone proteins and is more accessable to enzymes.



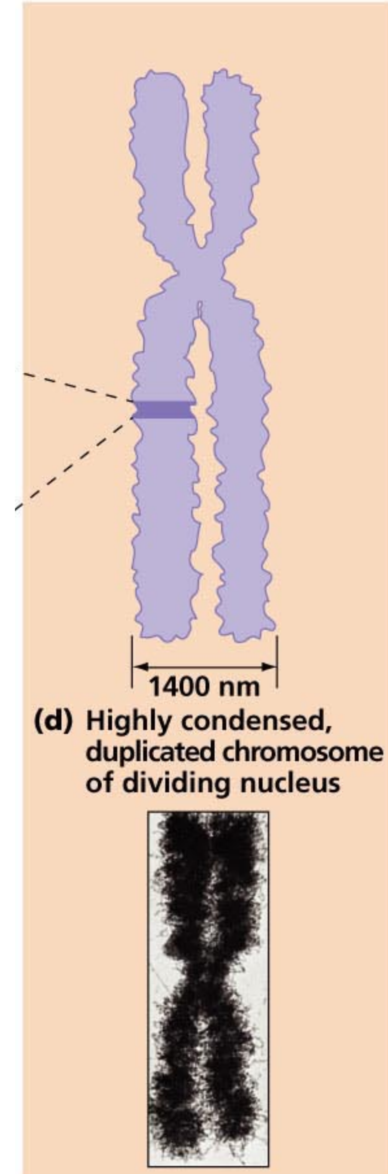
3. Chromatin to Euchromatin and Heterochromatin

- **Euchromatin:** regions that condense and decondense during the cell cycle and normally represent active (loosely packed) regions because:
  - The regions are transcribed
  - The regions do not have a lot of repeat sequences.

- **Heterochromatin:** regions that is condensed throughout the cell cycle.
  - These regions do not have genes or have genes that are not transcribed.

4. Chromosome formation

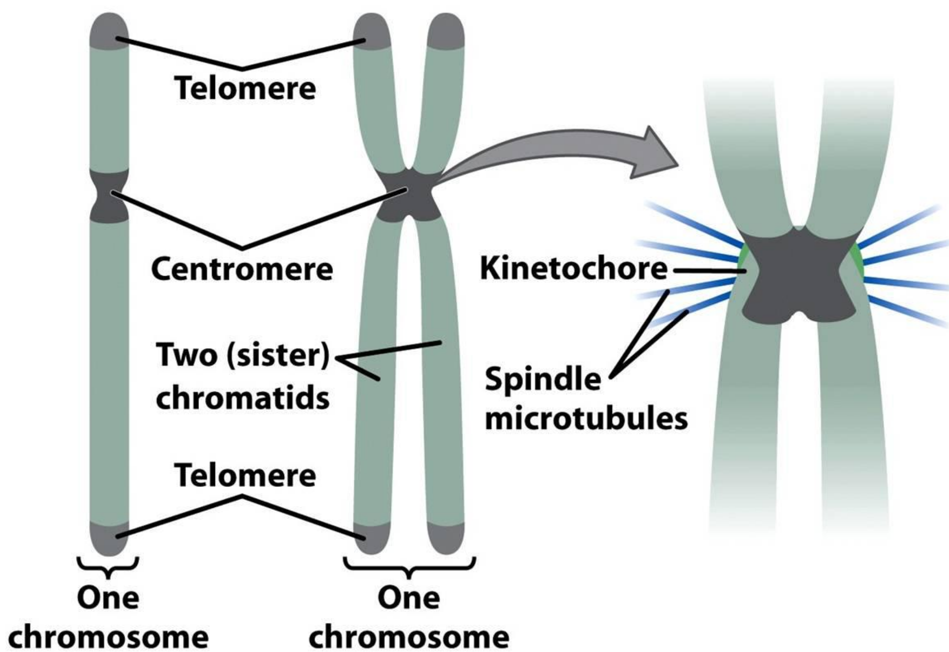
The genome in its most condensed form is represented by chromosomes.



4. Chromosome formation

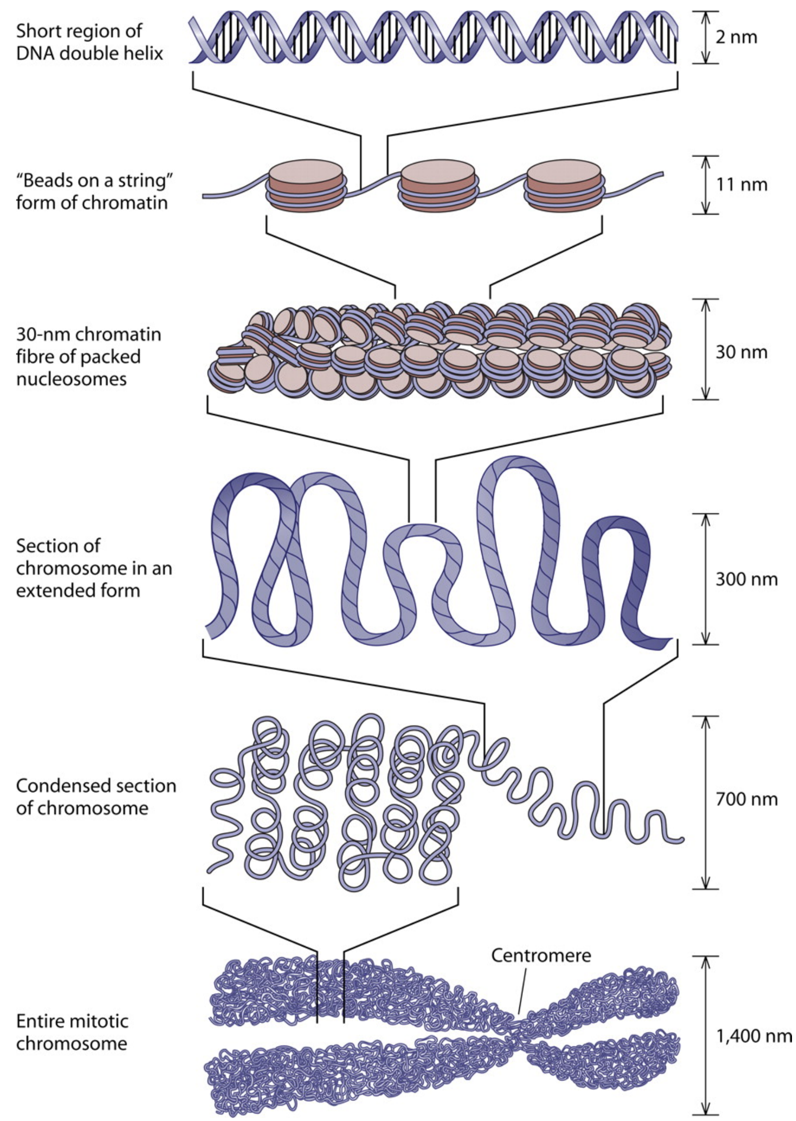
- Metaphase chromosomes have:

    1. Two arms (short p, long q) and separated by centromere.
    2. Centromere (region holds the arms).
    3. telomeres (ends of the chromosome).



Review of genome condensation

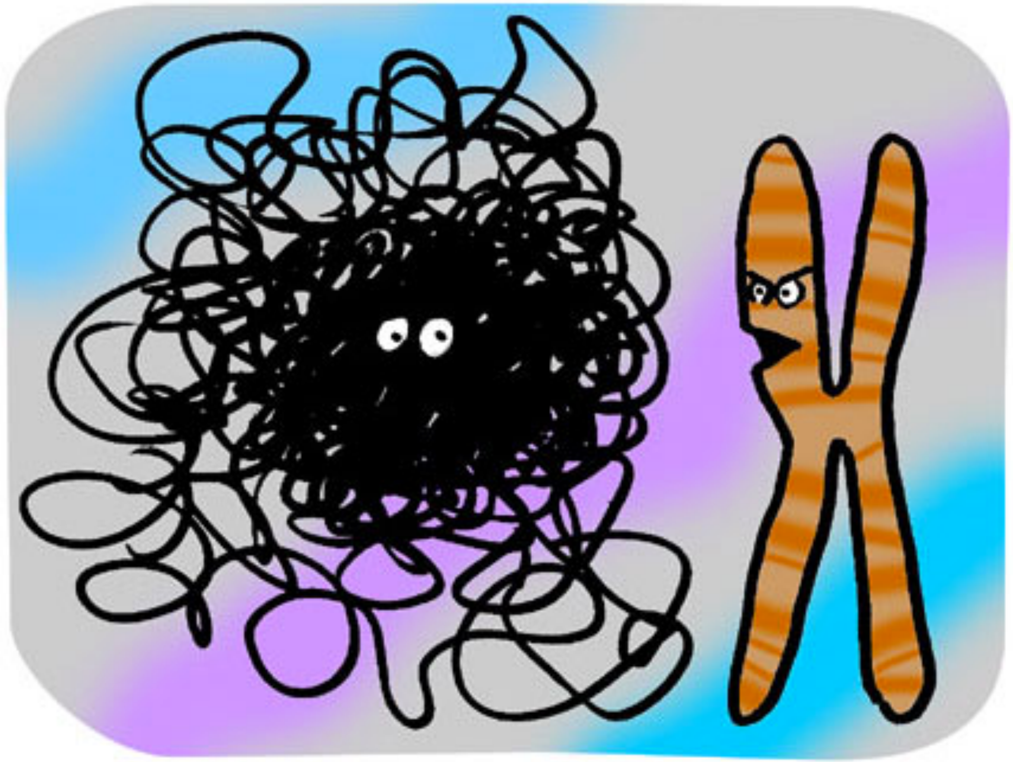
- Double helix.
    - Nucleosomes (DNA histones).
        - Beads on a string.
            - 30 nm chromatin fiber/ solenoid.
                - Eu/Heterochromatin.
                    - Metaphase chromosome.



Expectations

- You know the locations of DNA in eukaryotic cells.
- You know why the mitochondrial and chloroplast genomes are similar to that of prokaryote.
- You are familiar with the nuclear genome organization.
- You know how histone proteins interact with DNA to form nucleosomes and condensed genome.

For a smile



Dude, mitosis starts in five minutes...
I can't believe you're not condensed yet.

http://www.promega.com/