ORGANIZATION OF EUKARYOTIC CHROMOSOMES

Eukaryotic chromosomal organization

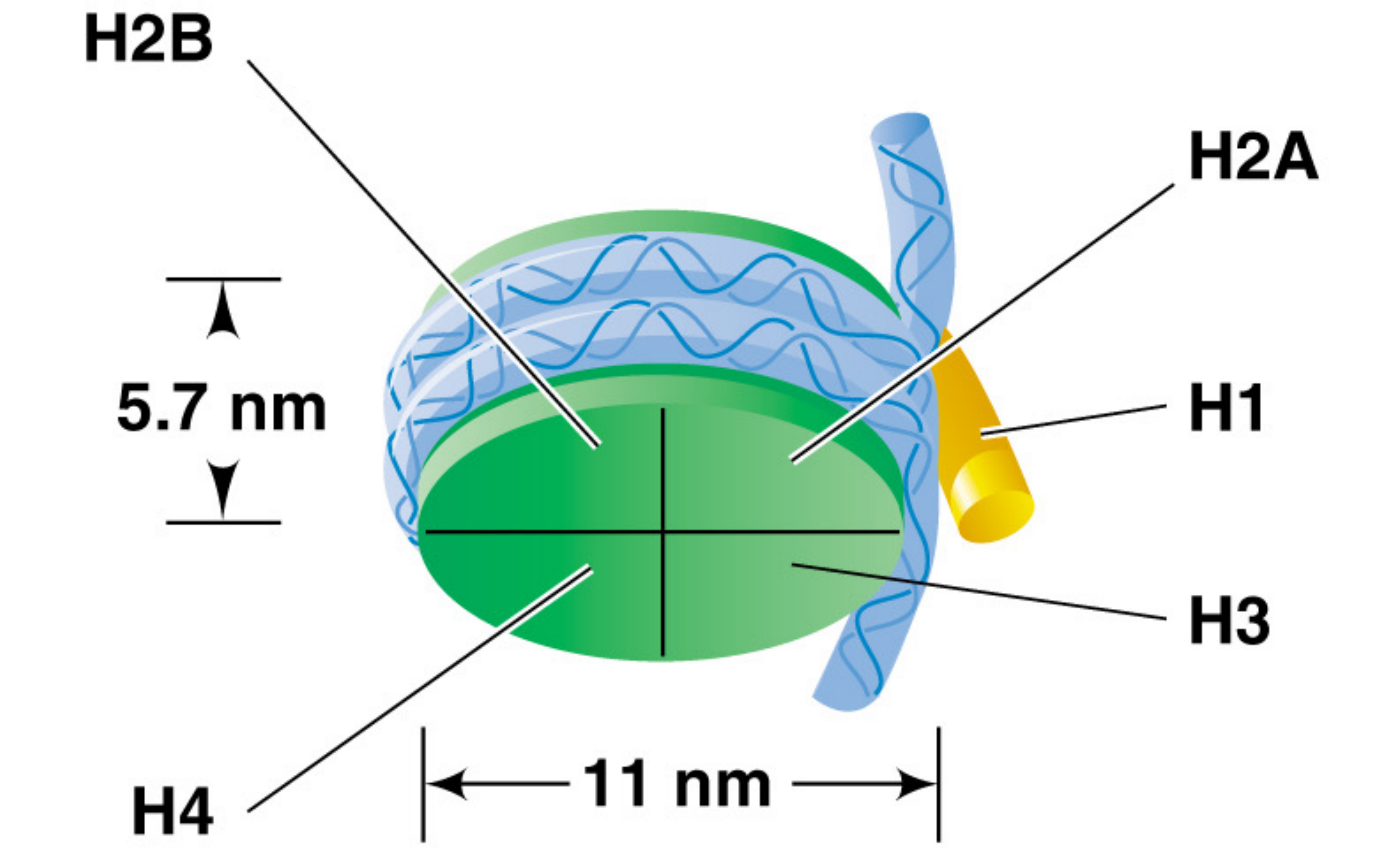
- Histone proteins
  - Abundant
  - Histone protein sequence is highly conserved among eukaryotes—conserved function
  - Provide the first level of packaging for the chromosome; compact the chromosome by a factor of approximately 7
  - DNA is wound around histone proteins to produce nucleosomes; stretch of unwound DNA between each nucleosome
- Nonhistone proteins
  - Other proteins that are associated with the chromosomes
  - Many different types in a cell; highly variable in cell types, organisms, and at different times in the same cell type
  - Amount of nonhistone protein varies
  - May have role in compaction or be involved in other functions requiring interaction with the DNA
  - Many are acidic and negatively charged; bind to the histones;

Eukaryotic chromosomal organization

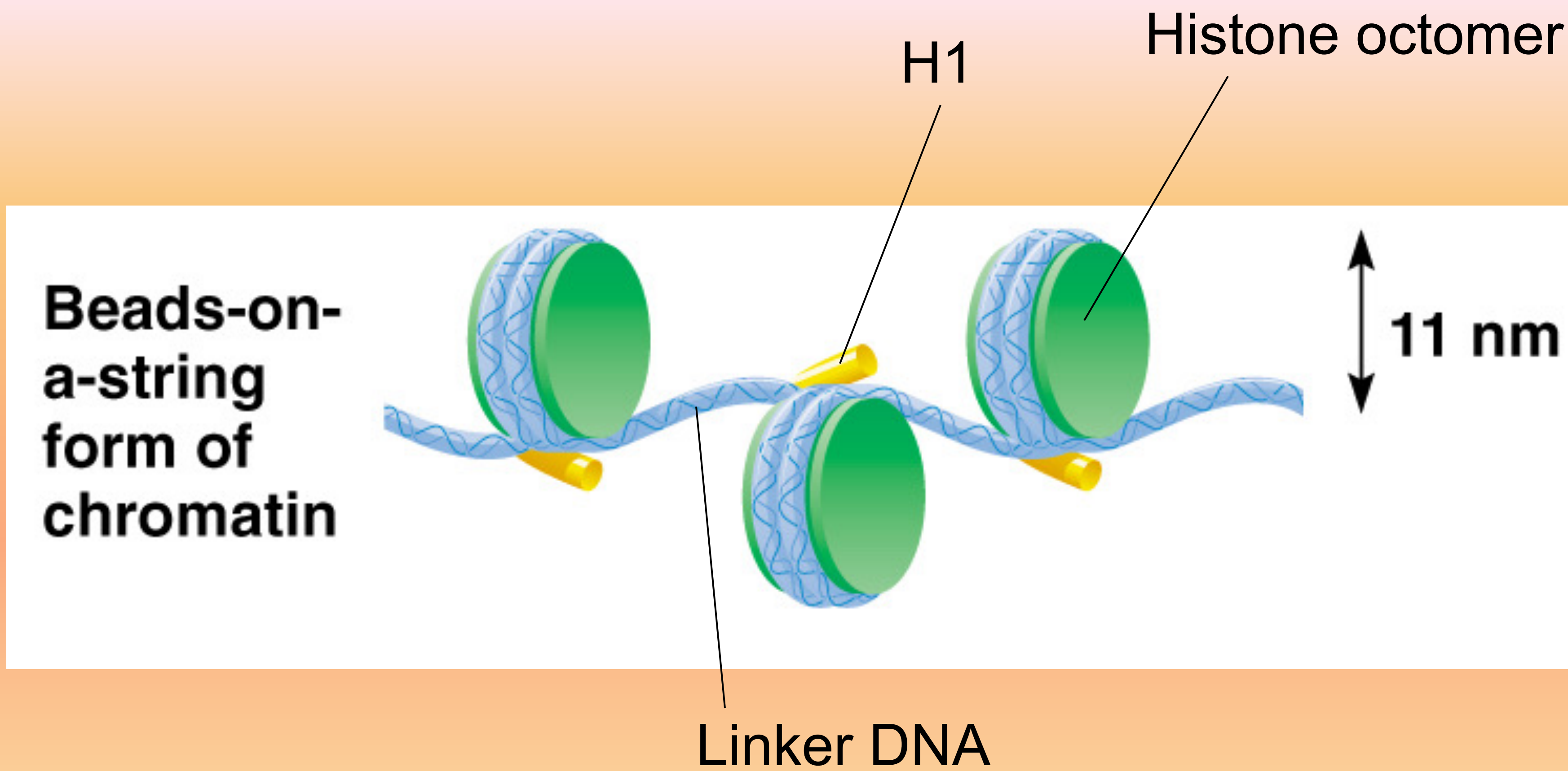
- Histone proteins
  - 5 main types
    - H1—attached to the nucleosome and involved in further compaction of the DNA (conversion of 10 nm chromatin to 30 nm chromatin)
    - H2A
    - H2B
    - H3
    - H4

    Two copies in each nucleosome 'histone octomer'; DNA wraps around this structure1.75 times
  - This structure produces 10nm chromatin

A possible nucleosome structure

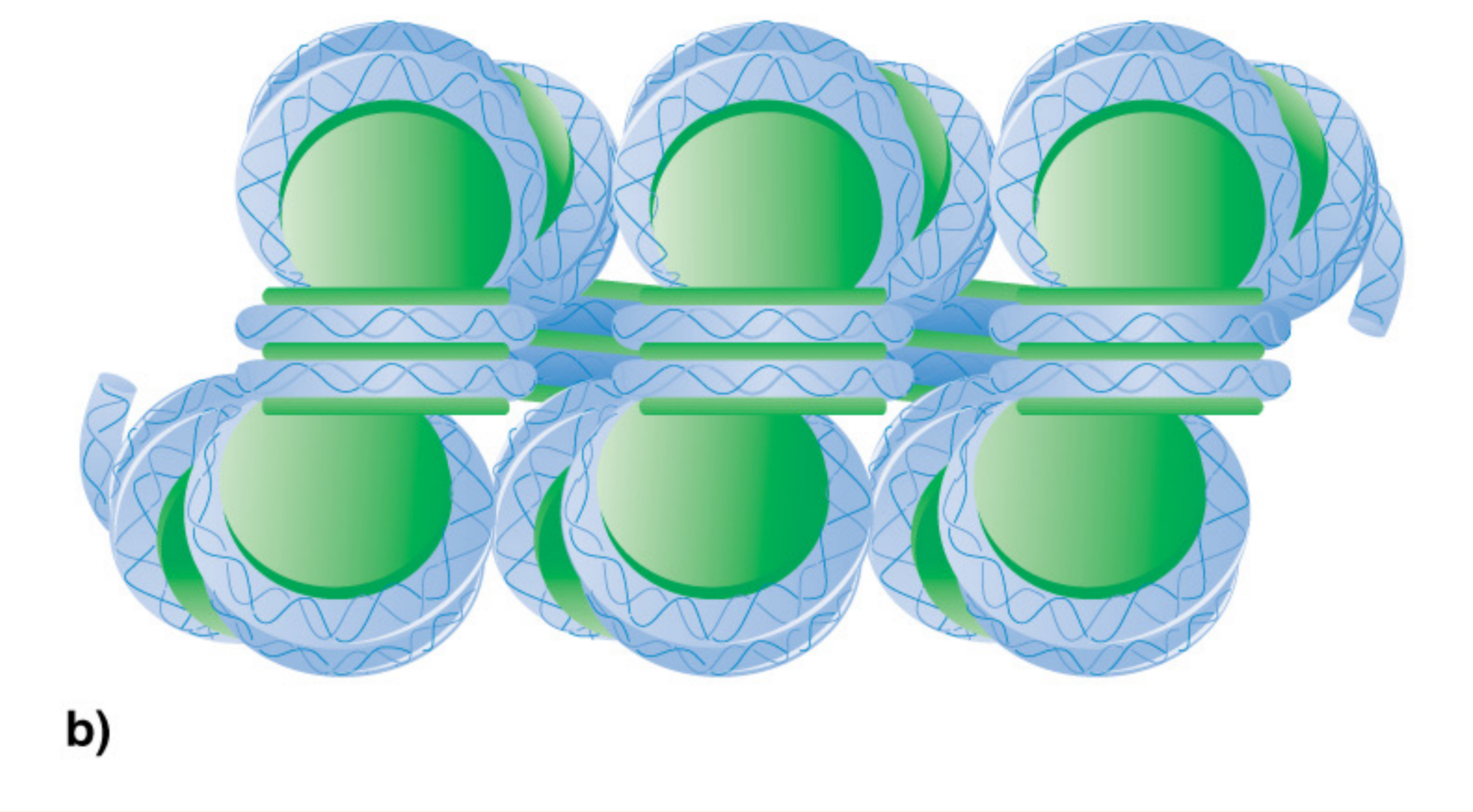


Nucleosomes connected together by linker DNA and H1 histone to produce the "beads-on-a-string" extended form of chromatin



10 nm chromatin is produced in the first level of packaging.

Packaging of nucleosomes into the 30-nm chromatin fiber

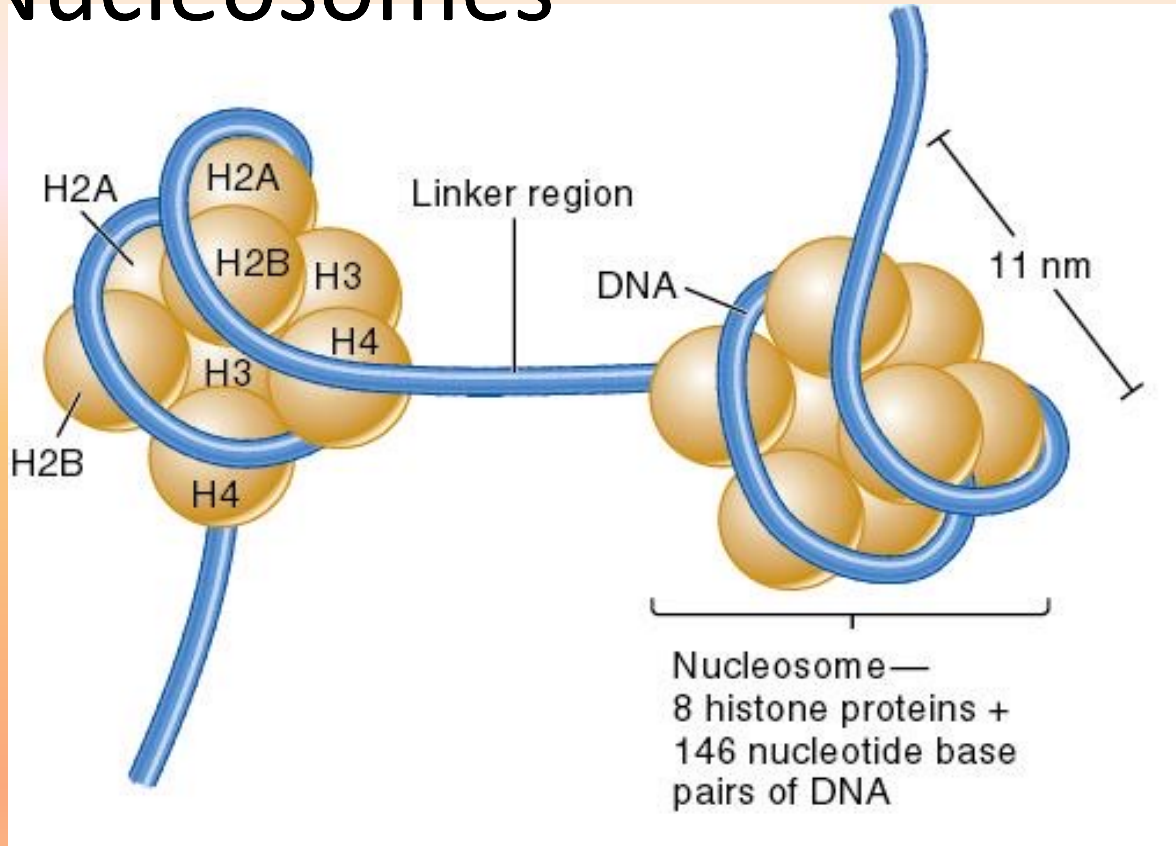


Nucleosomes

- Histone proteins basic (+ charged lysine & arginine) amino acids that bind DNA backbone

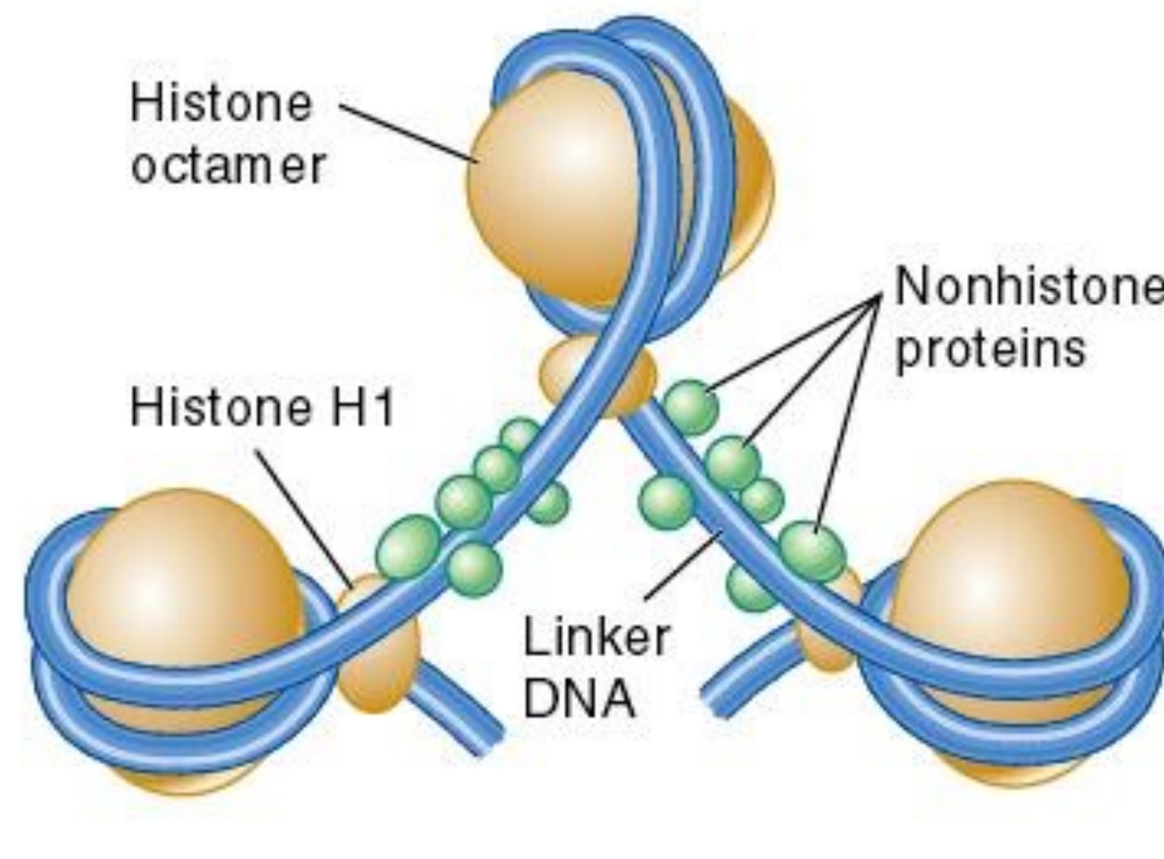
- Four core histones in nucleosome
  - Two of each of H2A, H2B, H3 & H4

- Fifth histone, H1 is the linker histone



(a) Nucleosomes showing core histones

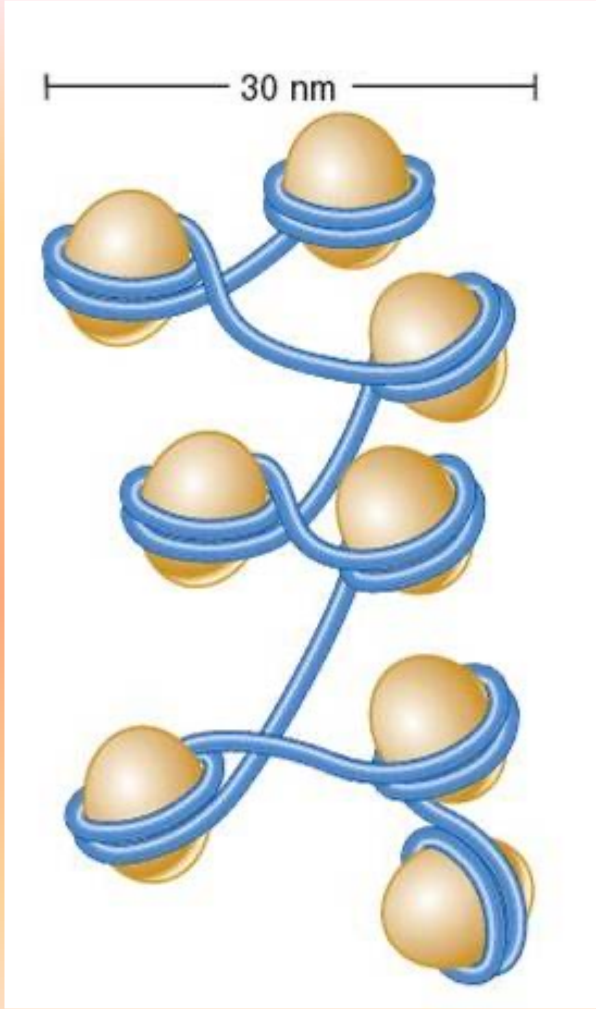
Nucleosomes



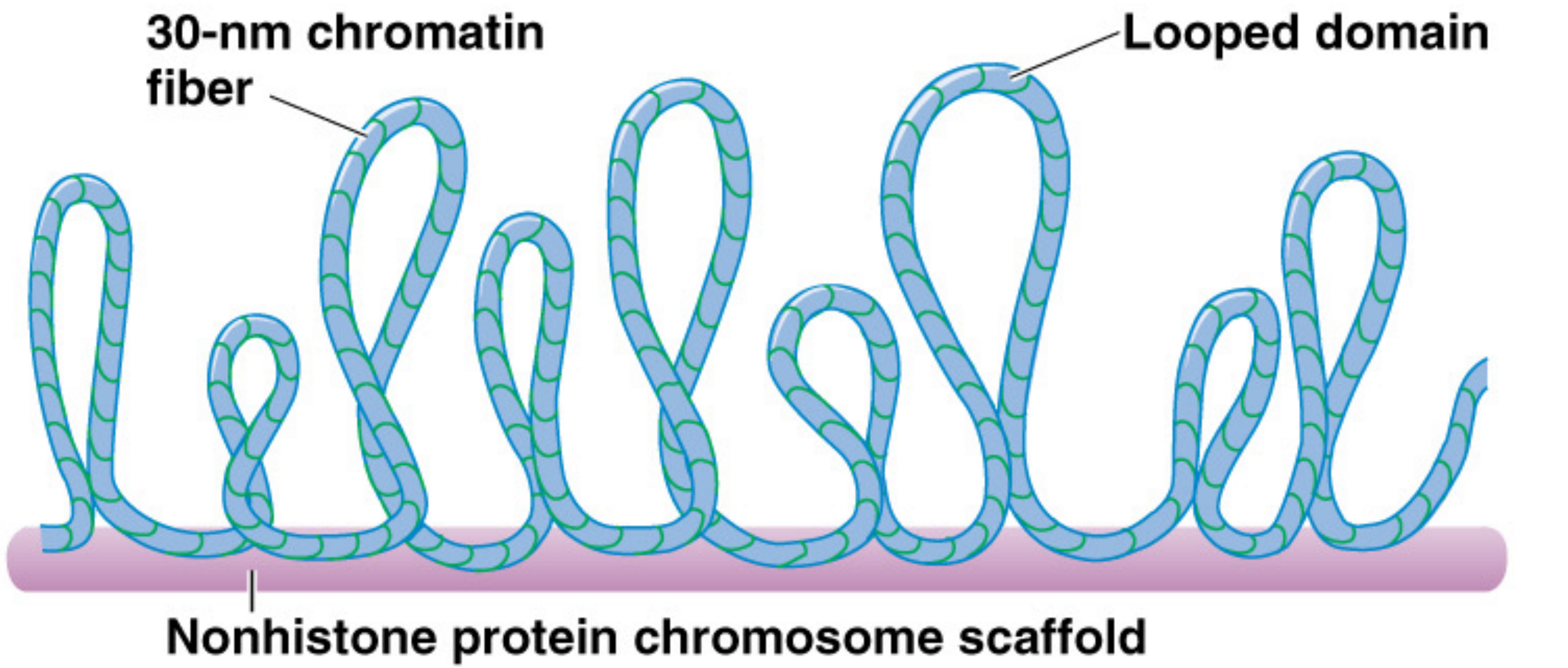
(b) Nucleosomes showing linker histones and nonhistone proteins

Nucleosomes Join to Form 30 nm Fiber

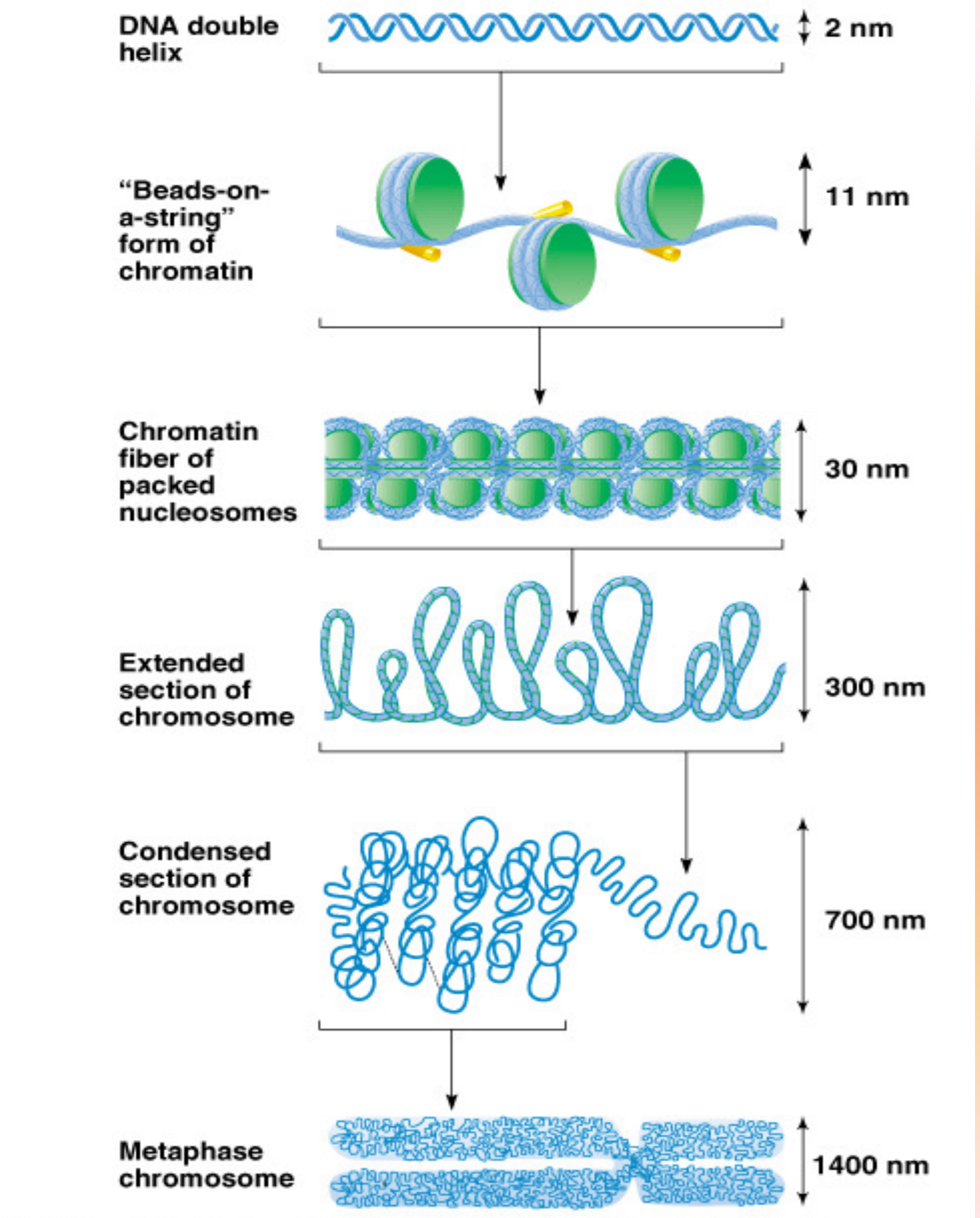
- Nucleosomes associate to form more compact structure - the 30 nm fiber
- Histone H1 plays a role in this compaction



Model for the organization of 30-nm chromatin fiber into looped domains that are anchored to a nonhistone protein chromosome scaffold



The many different orders of chromatin packing that give rise to the highly condensed metaphase chromosome



Eukaryotic chromosomal organization

- Compaction continues by forming looped domains from the 30 nm chromatin, which seems to compact the DNA to 300 nm chromatin
- Human chromosomes contain about 2000 looped domains
- 30 nm chromatin is looped and attached to a nonhistone protein scaffolding
- DNA in looped domains are attached to the nuclear matrix via DNA sequences called MARs (matrix attachment regions)
- MARs are known to be near regions of the DNA that are actively expressed
- Loops are arranged so that the DNA condensation can be independently controlled for gene expression

DNA compaction

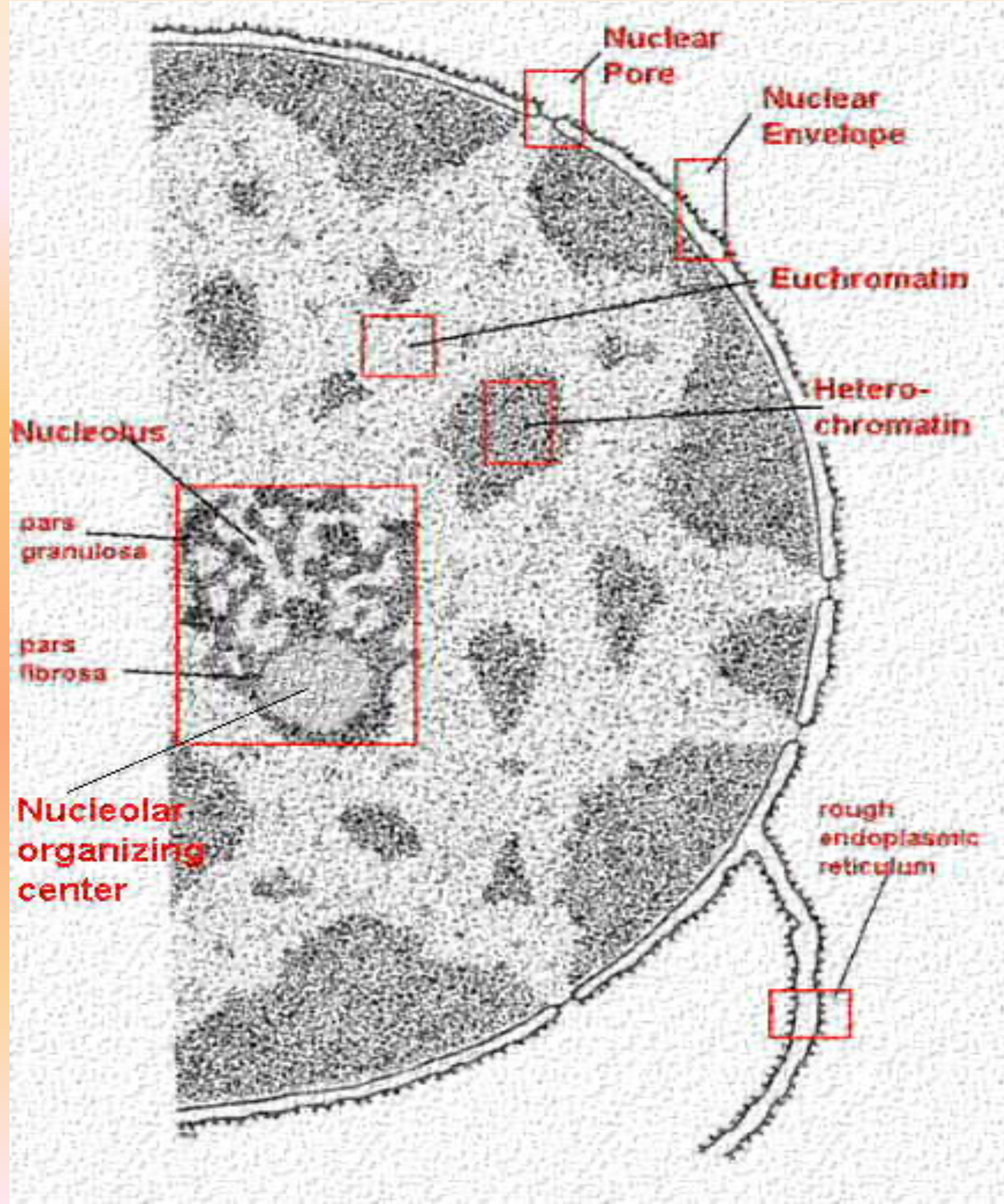
- Level of DNA compaction changes throughout the cell cycle; most compact during M and least compact during S
- 2 types of chromatin; related to the level of gene expression
  - Euchromatin—defined originally as areas that stained lightly
  - Heterochromatin—defined originally as areas that stained darkly

DNA compaction

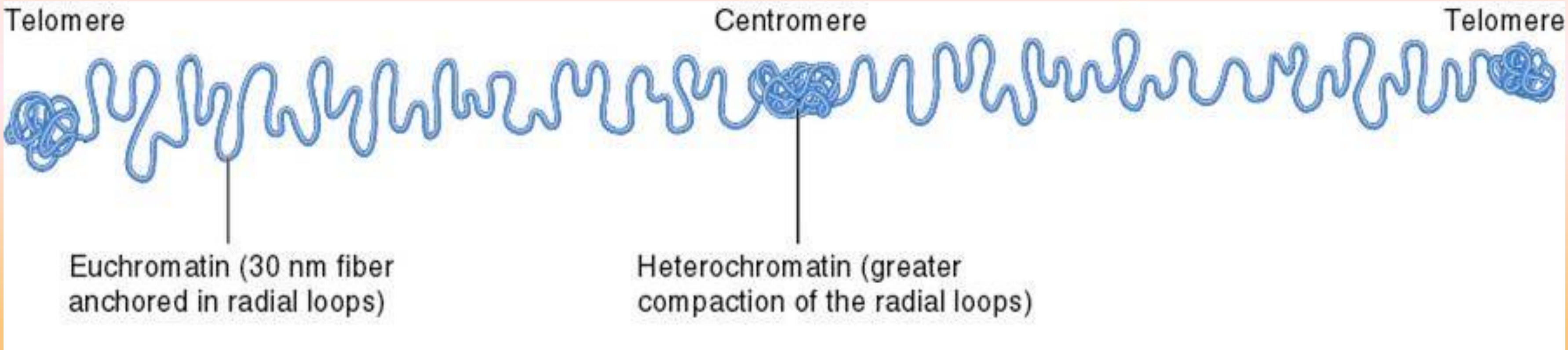
- Euchromatin—chromosomes or regions therein that exhibit normal patterns of condensation and relaxation during the cell cycle
  - Most areas of chromosomes in active cells
  - Usually areas where gene expression is occurring

- Heterochromatin—chromosomes or regions therein that are condensed throughout the cell cycle
- Provided first clue that parts of eukaryotic chromosomes do not always encode proteins.

Euchromatin is uncoiled and active, whereas **heterochromatin** remains condensed and is inactive.



Heterochromatin *vs* Euchromatin



- Compaction level of interphase chromosomes is not uniform
- Euchromatin
  - Less condensed regions of chromosomes
  - Transcriptionally active
  - Regions where 30 nm fiber forms radial loop domains

- Heterochromatin
  - Tightly compacted regions of chromosomes
  - Transcriptionally inactive (in general)
  - Radial loop domains compacted even further

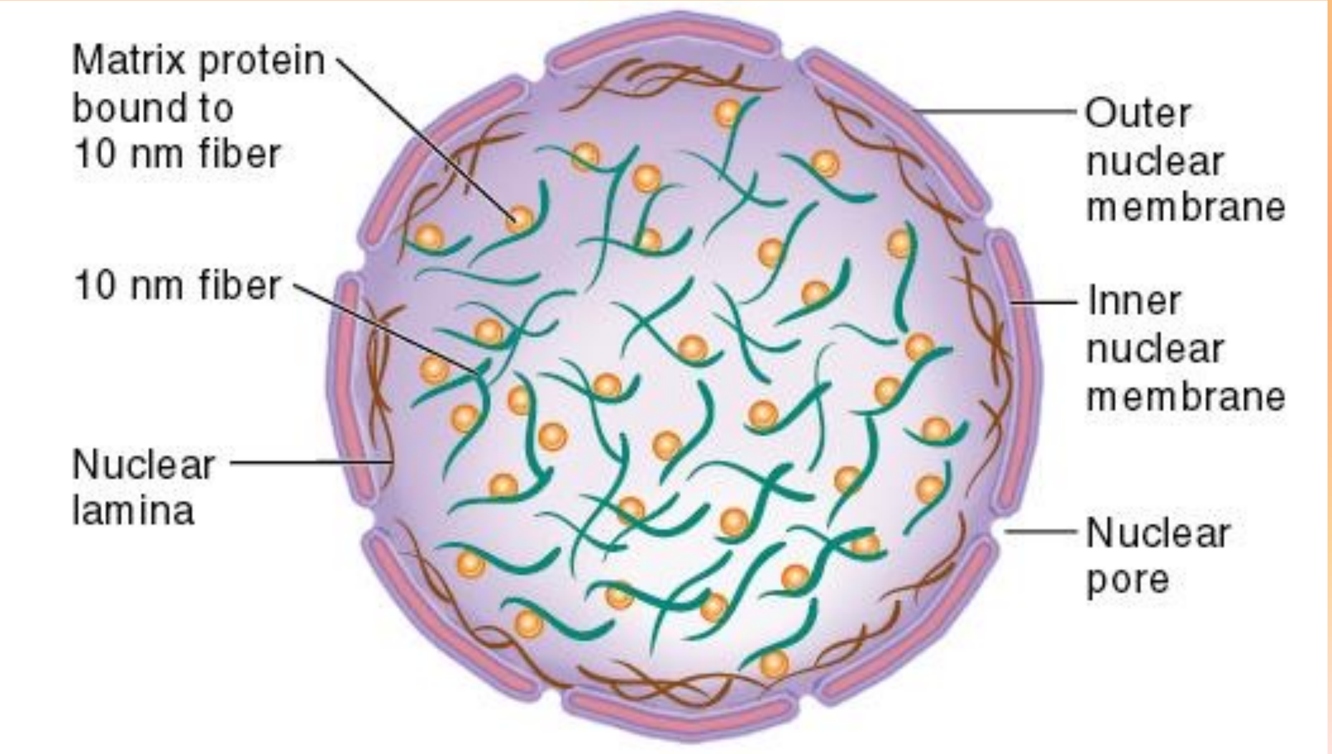
Further Compaction of the Chromosome

- The two events we have discussed so far have shortened the DNA about 50-fold

- A third level of compaction involves interaction between the 30 nm fiber and the nuclear matrix

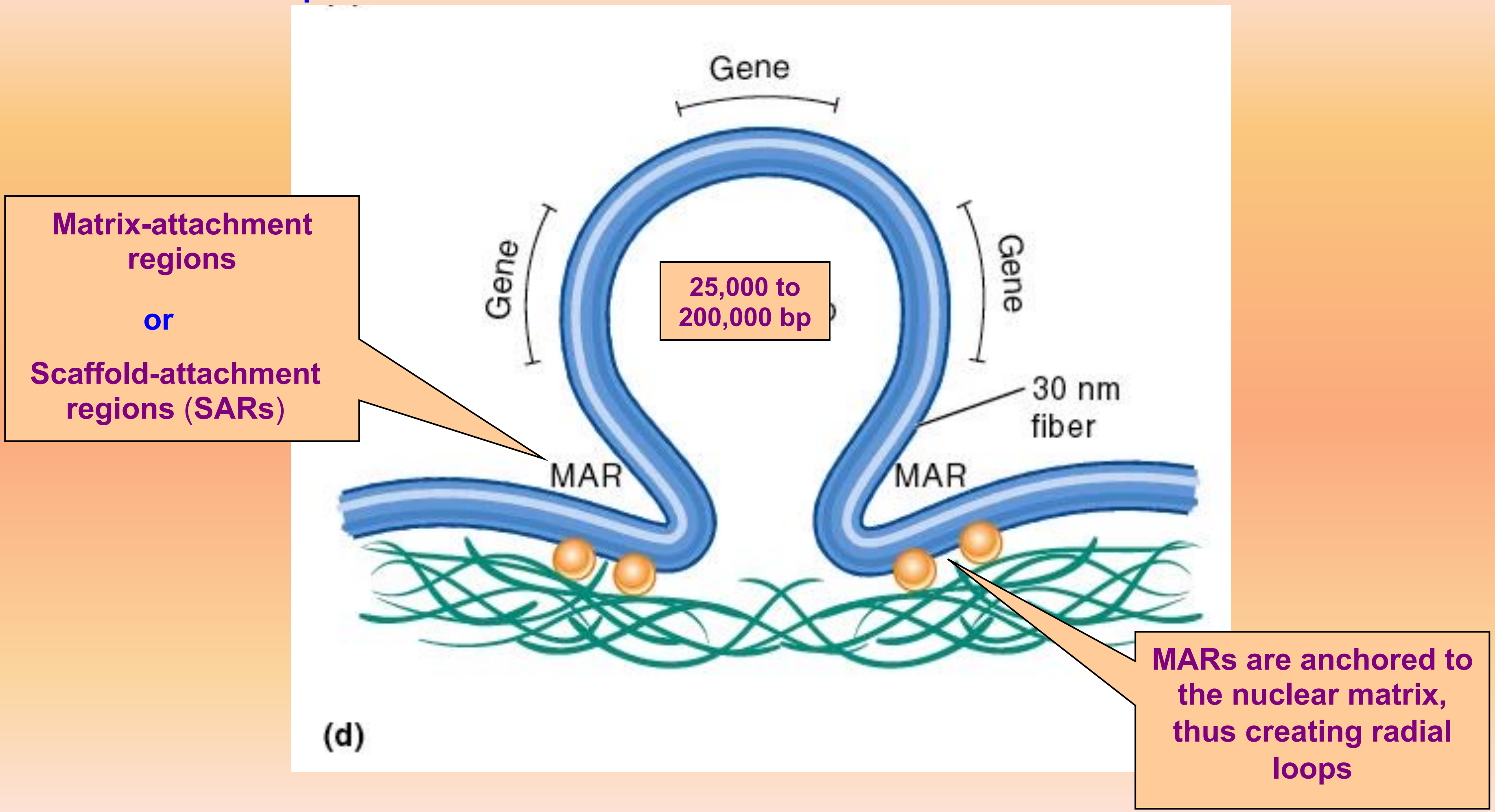
Nuclear Matrix Association

- Nuclear matrix composed of two parts
  - Nuclear lamina
  - Internal matrix proteins
    - 10 nm fiber and associated proteins



DNA Loops on Nuclear Matrix

- The third mechanism of DNA compaction involves the formation of radial loop domains



Chromatin Packing

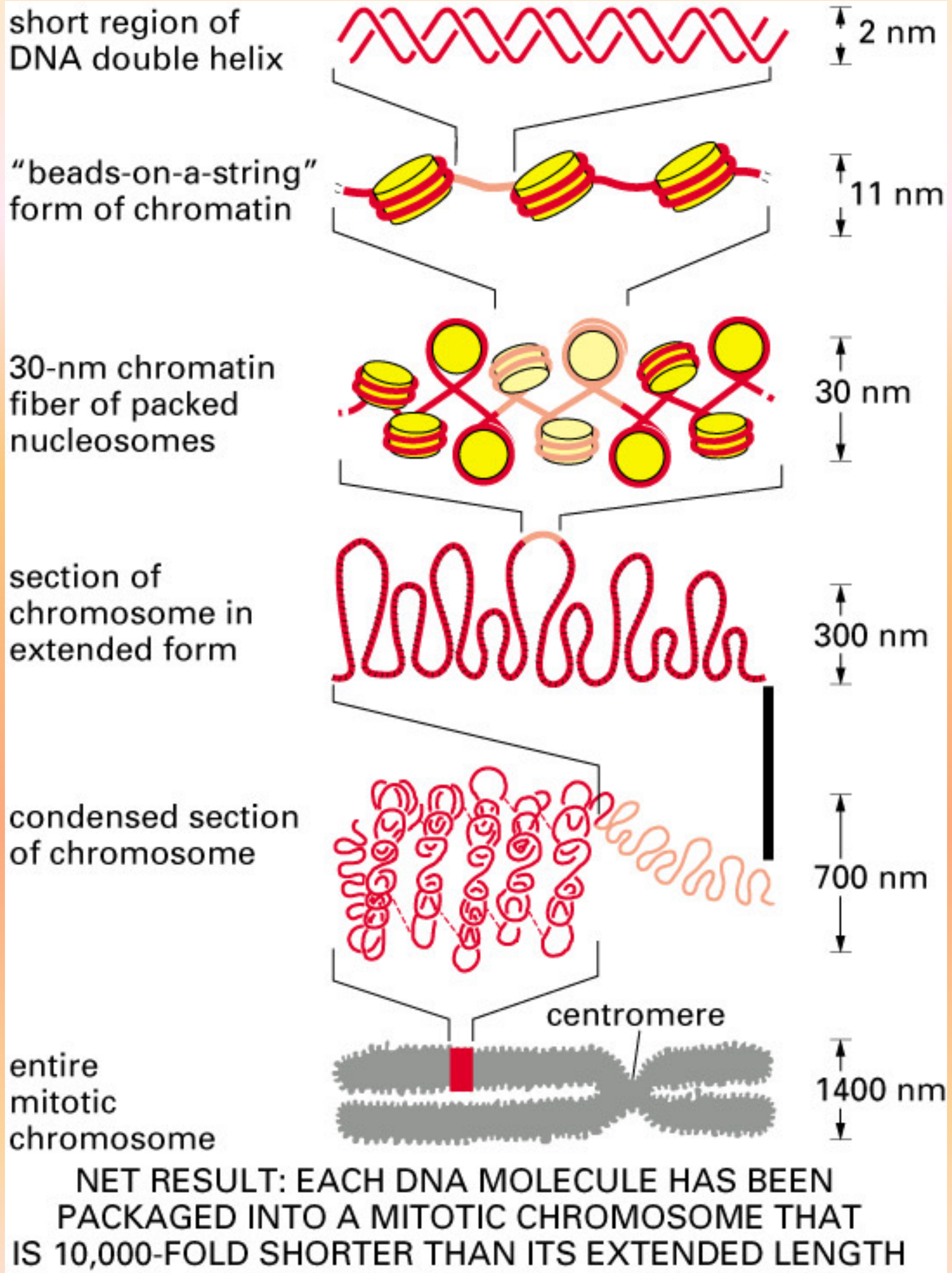


Figure 4–55. Molecular Biology of the Cell, 4th Edition.

Summary

- Life depends on stable and compact storage of genetic information.
- Genetic information is carried by very long DNA molecules and encoded in the linear sequence of nucleotides A, T, G, and C.
- A molecule of DNA is in the form of a double helix composed of a pair of complementary strands of nucleotides held together by hydrogen bonds between G-C and A-T base pairs.
- Each strand of DNA has a chemical polarity due to the linkage of alternating sugars and phosphates in its backbone. The two strands of the DNA double helix run antiparallel—that is, in opposite orientations.
- The genetic material of a eukaryotic cell is contained within one or more chromosomes, each formed from a single, enormously long DNA molecule that contains many genes.
- The DNA in a eukaryotic chromosome contains, in addition to genes, many replication origins, one centromere, and two telomeres. These sequences ensure that the chromosome can be replicated efficiently and passed on to daughter cells.

Summary

• Chromosomes in eukaryotic cells consist of DNA tightly bound to a roughly equal mass of specialized proteins. These proteins fold the DNA into a more compact form so that it can fit into a cell nucleus. The complex of DNA and protein in chromosomes is called chromatin.
• Chromosomal proteins include the histones, which pack DNA into a repeating array of DNA–protein particles called nucleosomes.
• Nucleosomes pack together, with the aid of histone H1 molecules, to form a 30-nm fiber. This fiber can be further coiled and folded, producing more compact chromatin structures.
• Some forms of chromatin are so highly compacted that the packaged genes cannot be expressed into protein.
• Chromatin structure is dynamic: by temporarily altering its structure—using chromatin remodeling complexes and enzymes that modify histone tails—the cell can ensure that proteins involved in gene expression, replication, and repair have rapid, localized access to the necessary DNA sequences.

The global organization of chromosome

- *Specialized Chromosomes Reveal Variations in the Organization of DNA*
- Chromosomes are decondensed during interphase and hard to visualize
- Lampbrush chromosomes of vertebrate oocytes and polytene chromosomes in the giant secretory cells of insects are exceptions, revealing the global organization of chromosome
- **Polytene chromosomes** and **lampbrush chromosomes** are very large and can be visualized by light microscopy.

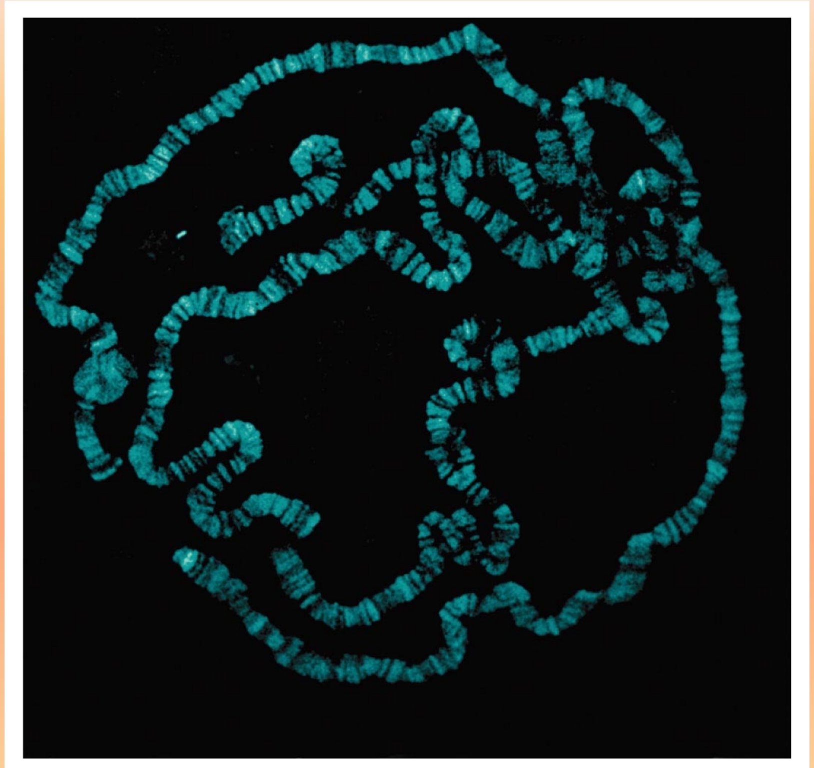
○ Studies of these two types of interphase chromosomes suggest that each long DNA molecule in a chromosome is divided into a large number of discrete domains that are folded differently.

○ In both lampbrush and polytene chromosomes the regions that are actively synthesizing RNA are least condensed.

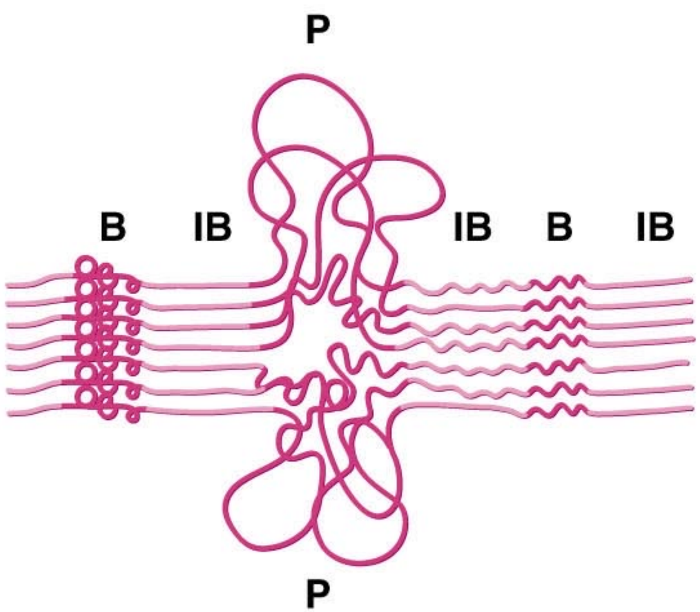
○ Likewise, as judged by nuclease sensitivity, about 10% of the DNA in interphase vertebrate cells is in a relatively uncondensed conformation that correlates with DNA transcription in these regions.

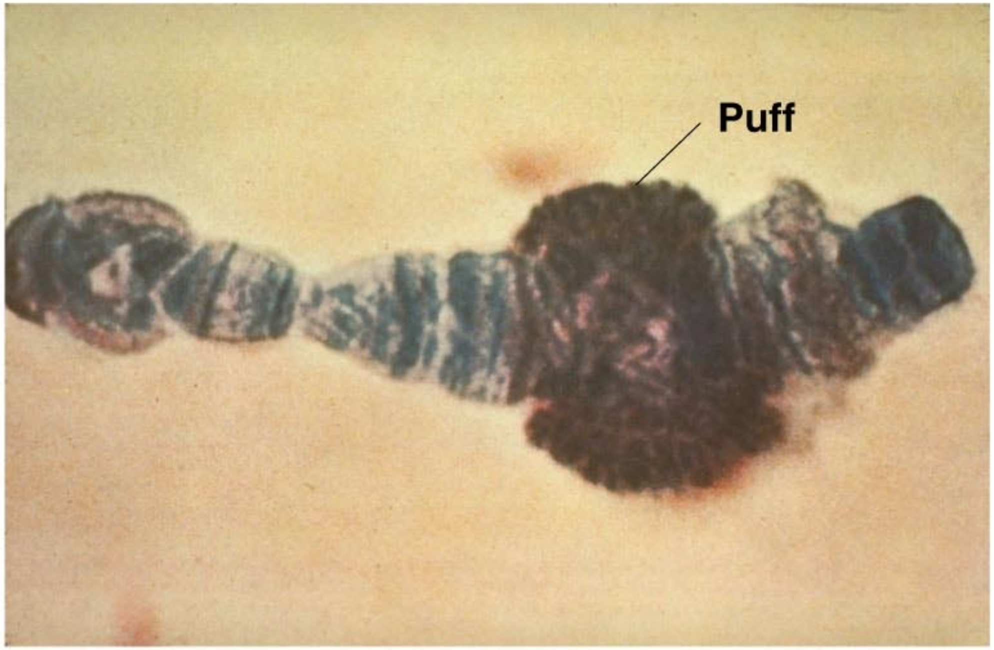
○ Such "active chromatin" is biochemically distinct from the more condensed inactive regions of chromatin.

- **Polytene chromosomes**:
  - have distinctive banding patterns
  - represent paired homologs
  - are composed of many DNA strands



- Polytene chromosomes have **puff** regions where the DNA has uncoiled and are visible manifestations of a high level of gene activity.





A polytene chromosome from Drosophila salivary gland
Dark bands and interbands

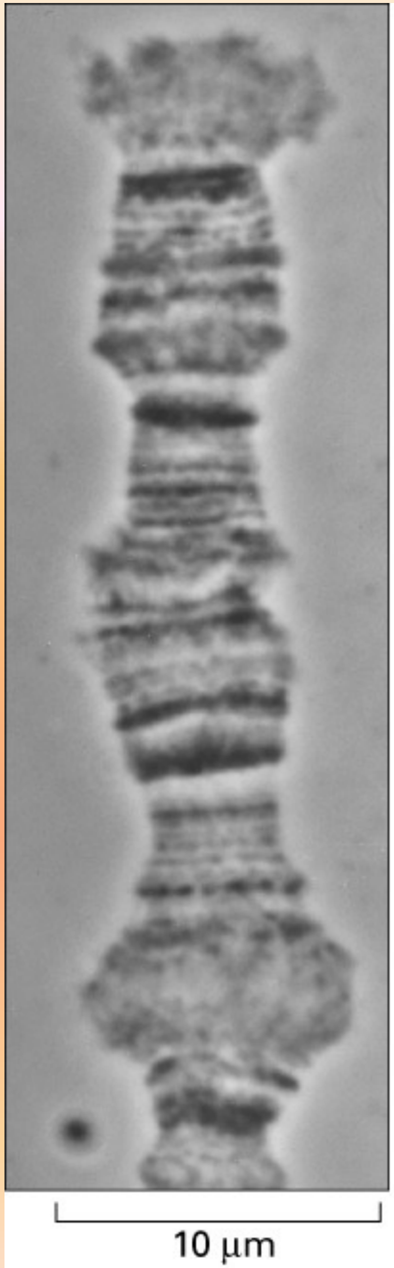


Figure 4–39. Molecular Biology of the Cell, 4th Edition.

Chromosome puffs
Folding and refolding at a time course of 22 hours

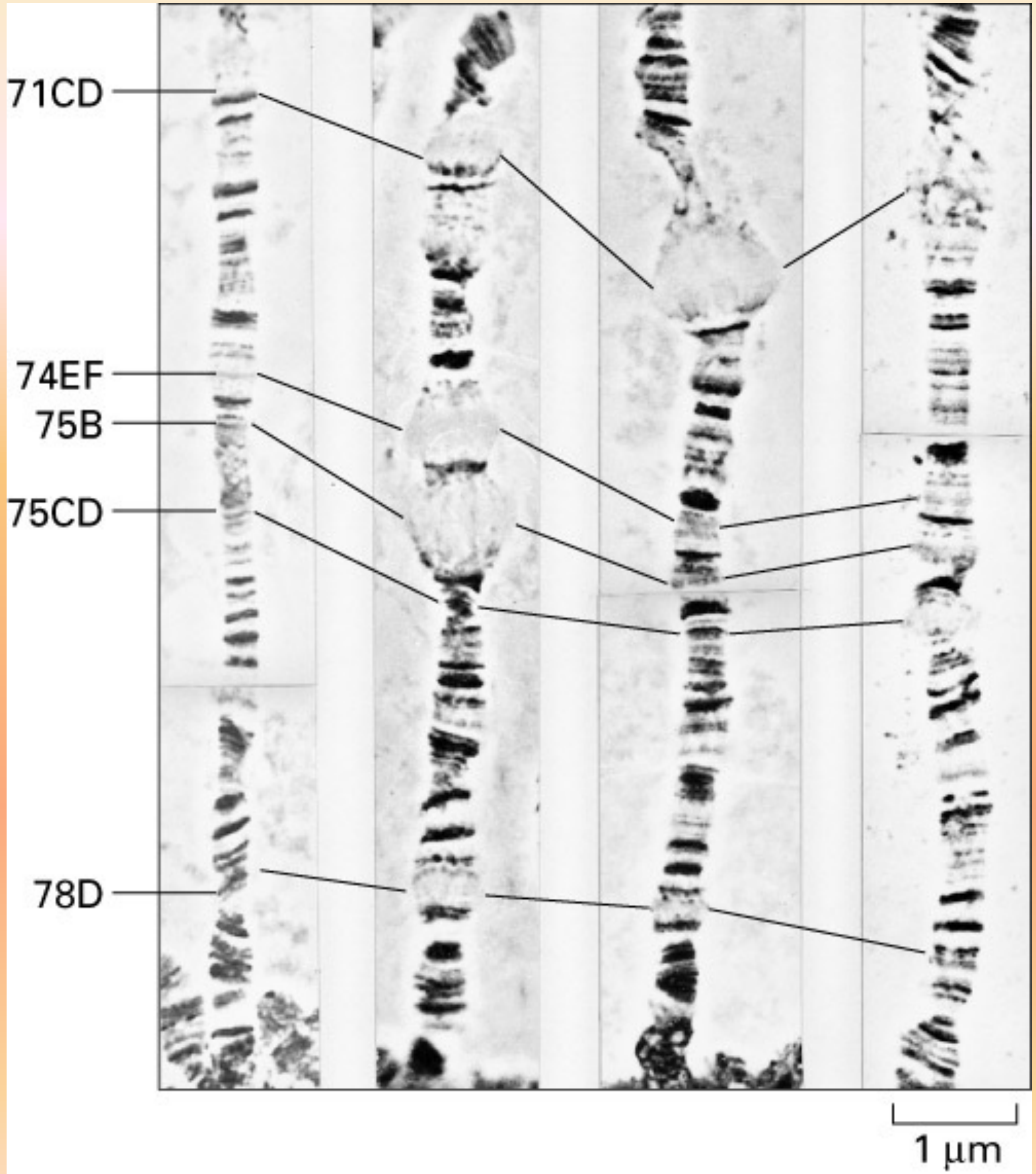
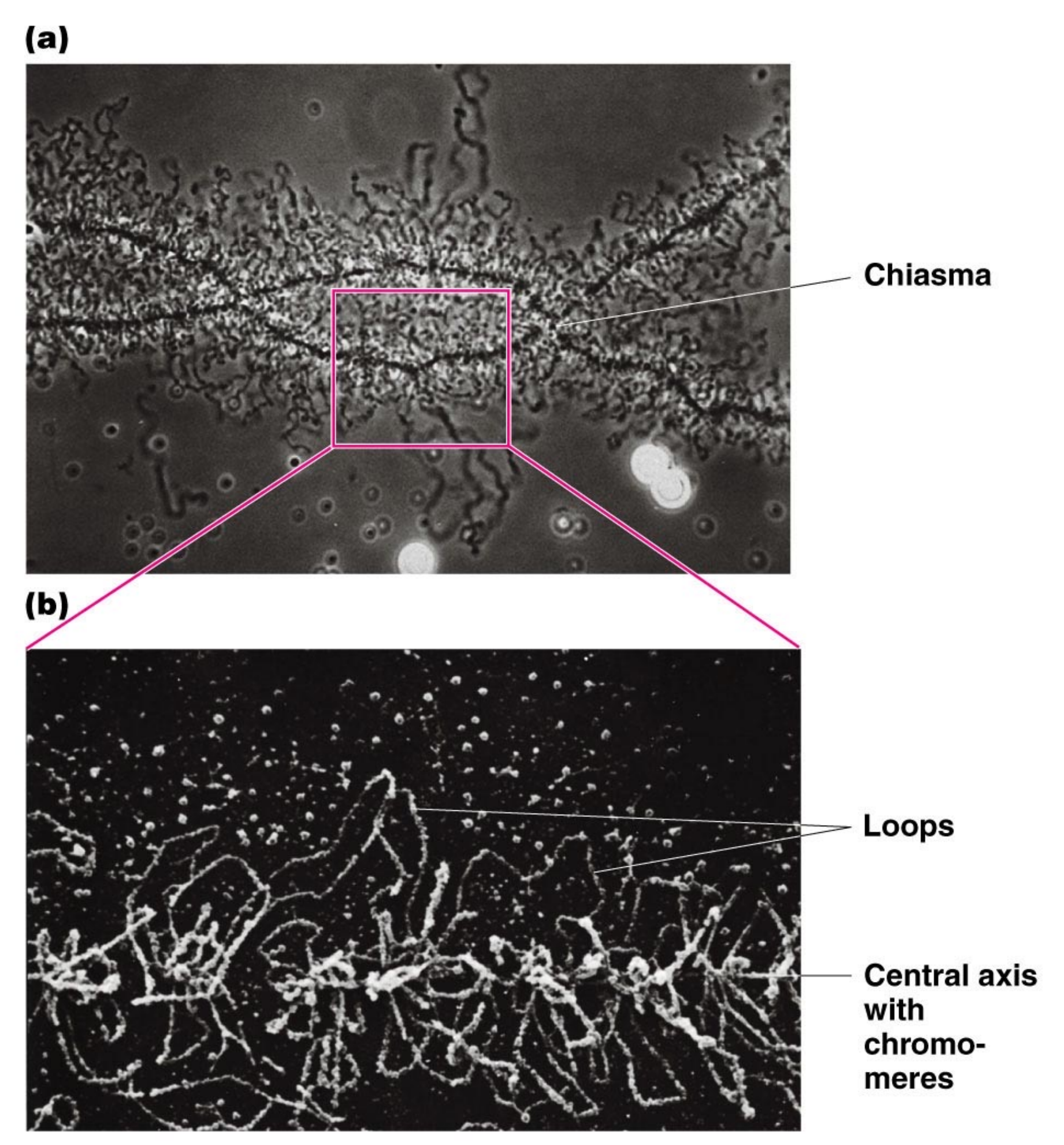
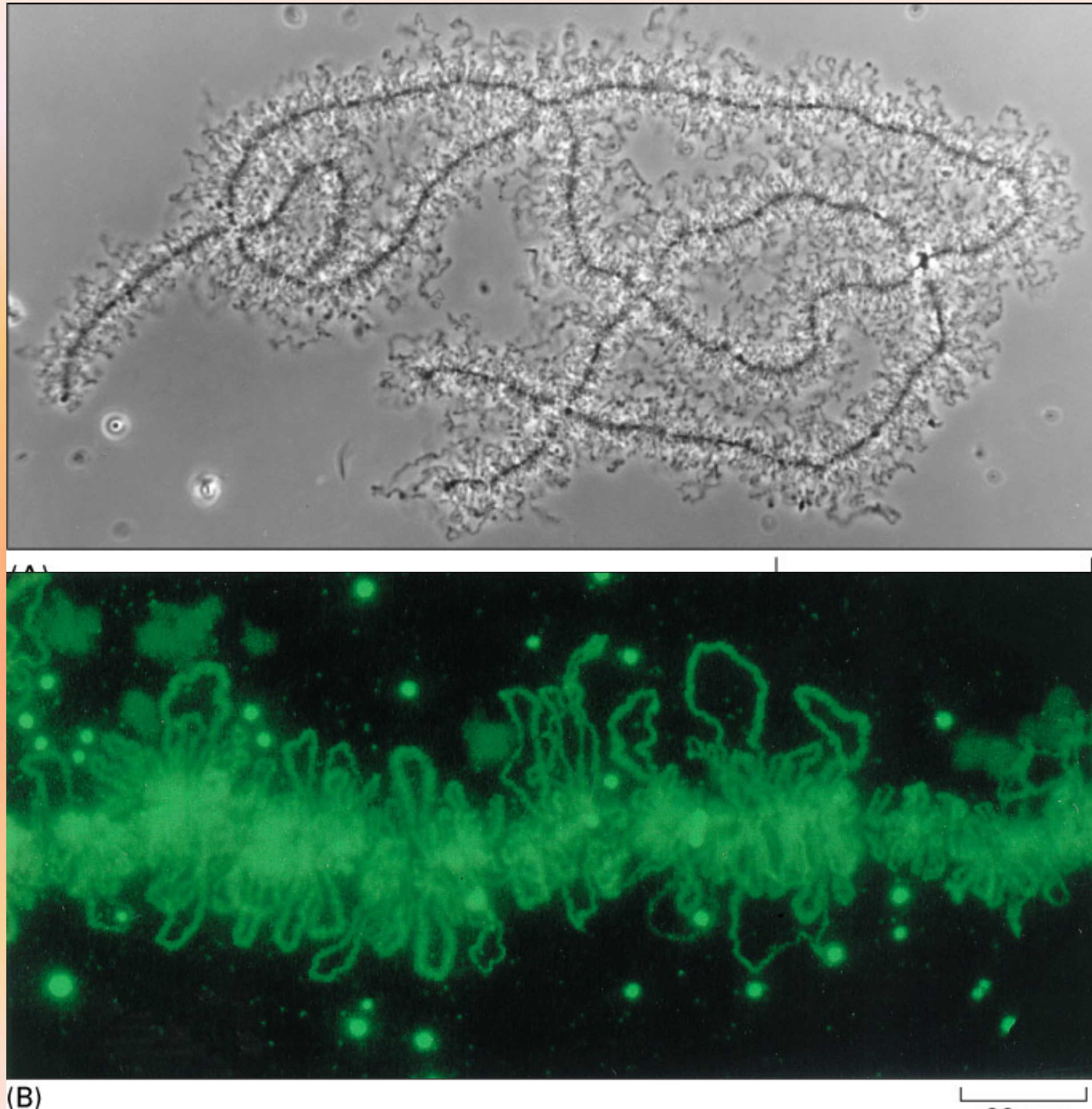


Figure 4–41. Molecular Biology of the Cell, 4th Edition.

- **Lampbrush chromosomes** - large and have extensive DNA looping.
- Found in oocytes in the diplotene stage of meiosis.



Lampbrush chromosomes (amphibian oocyte, immature eggs)



A model for the structure of a lampbrush chromosome
Chromomeres: highly condensed and in general not expressed until unfolding

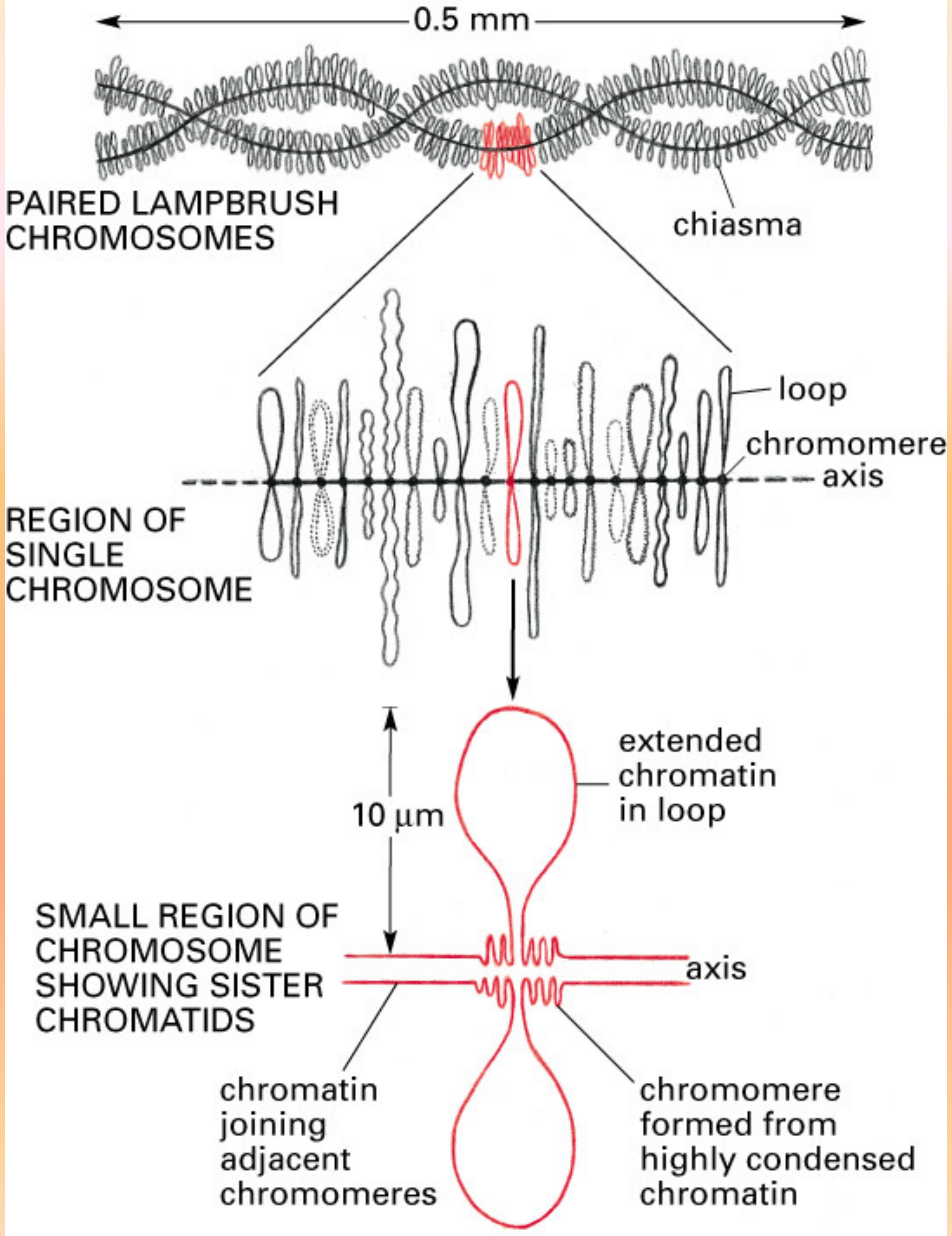


Figure 4–37. Molecular Biology of the Cell, 4th Edition.