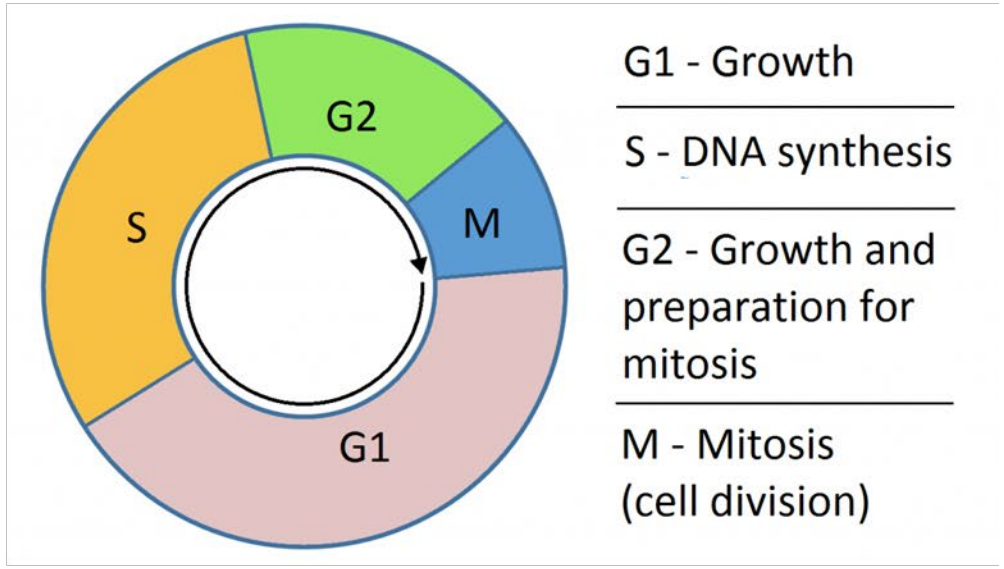
# MSc I Sem – Life Sciences

## Course – Cell Biology

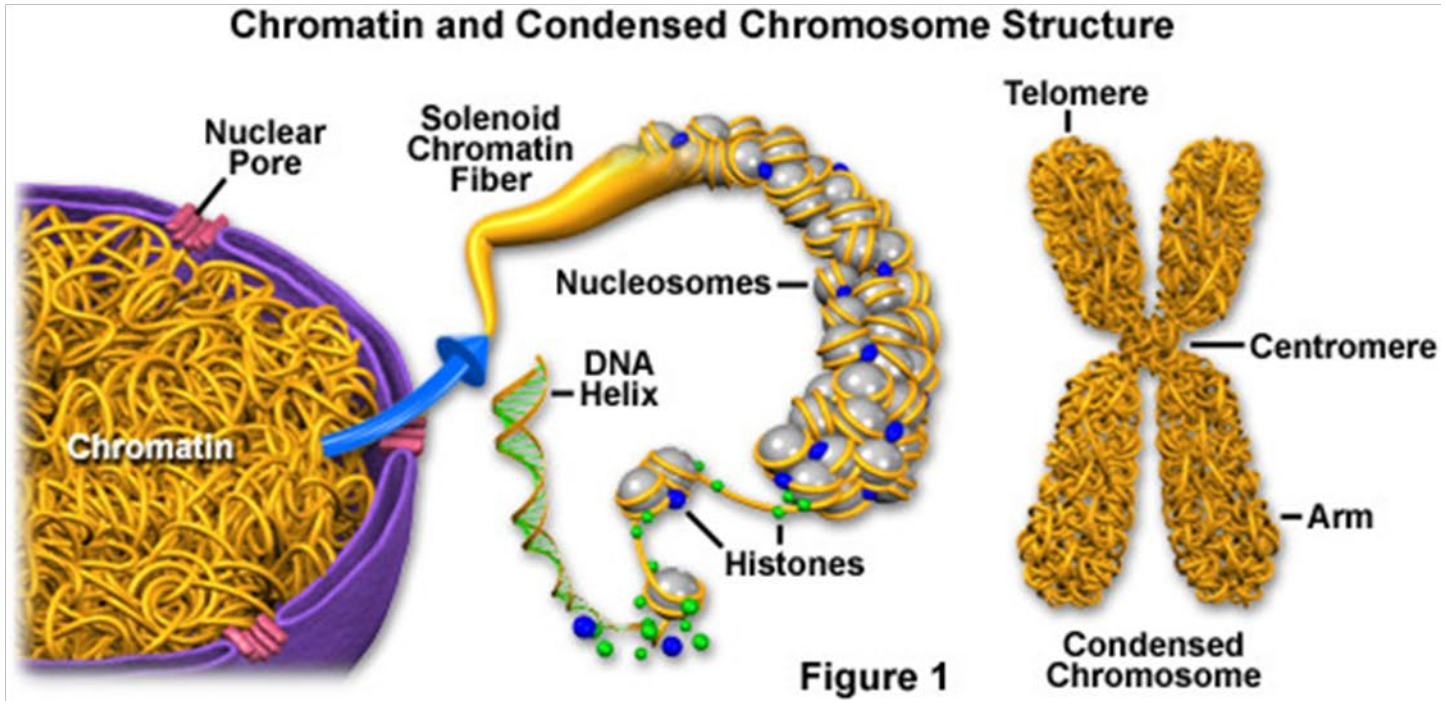
# Chromosome and Genome Organization

# Genomic Materials

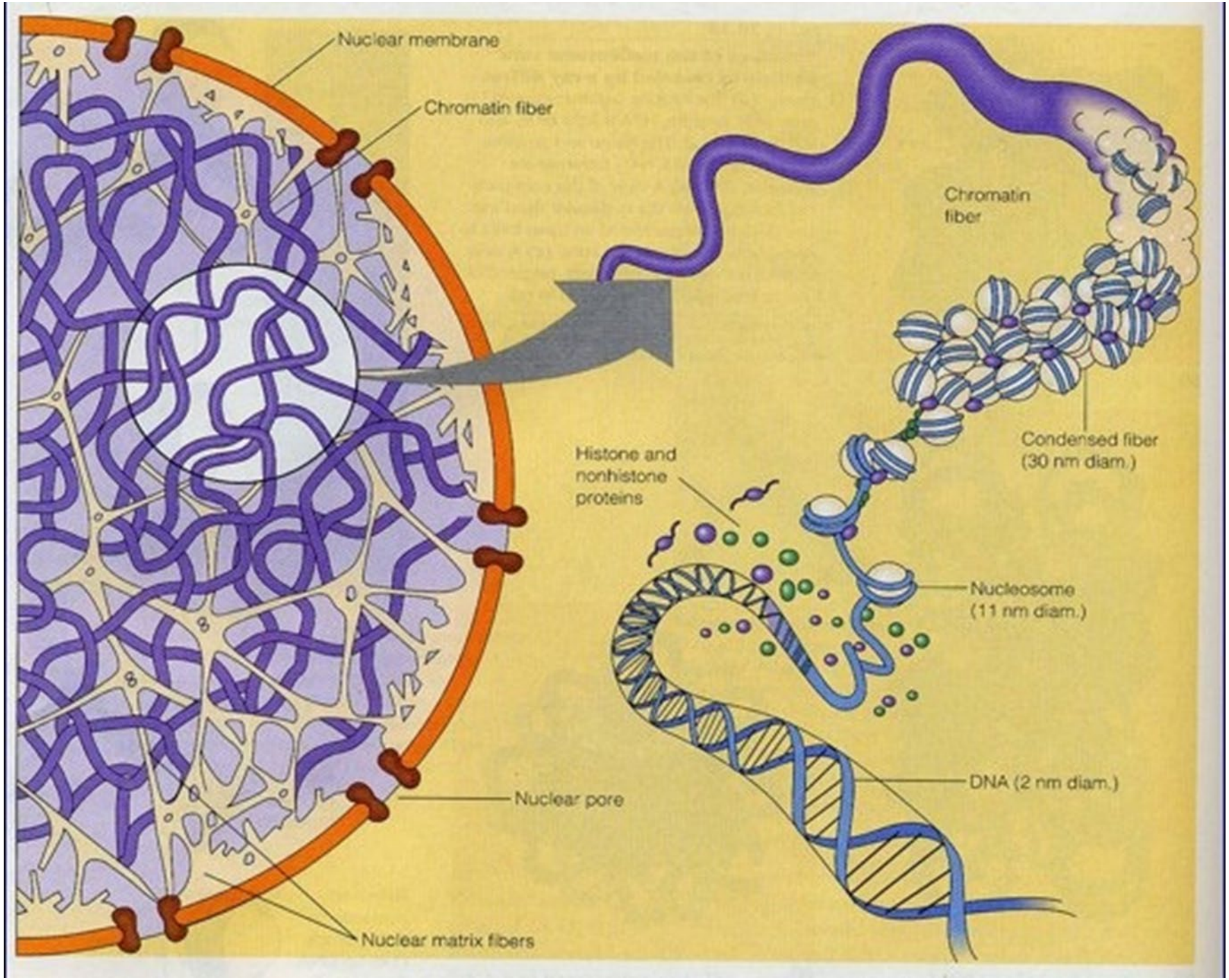
**Interphase Nucleus:**
In interphase, the chromatin is not yet condensed. Cell performs normal functions.




**Mitotic Metaphase Nucleus:** chromatin is condensed and organized in the form of chromosomes.

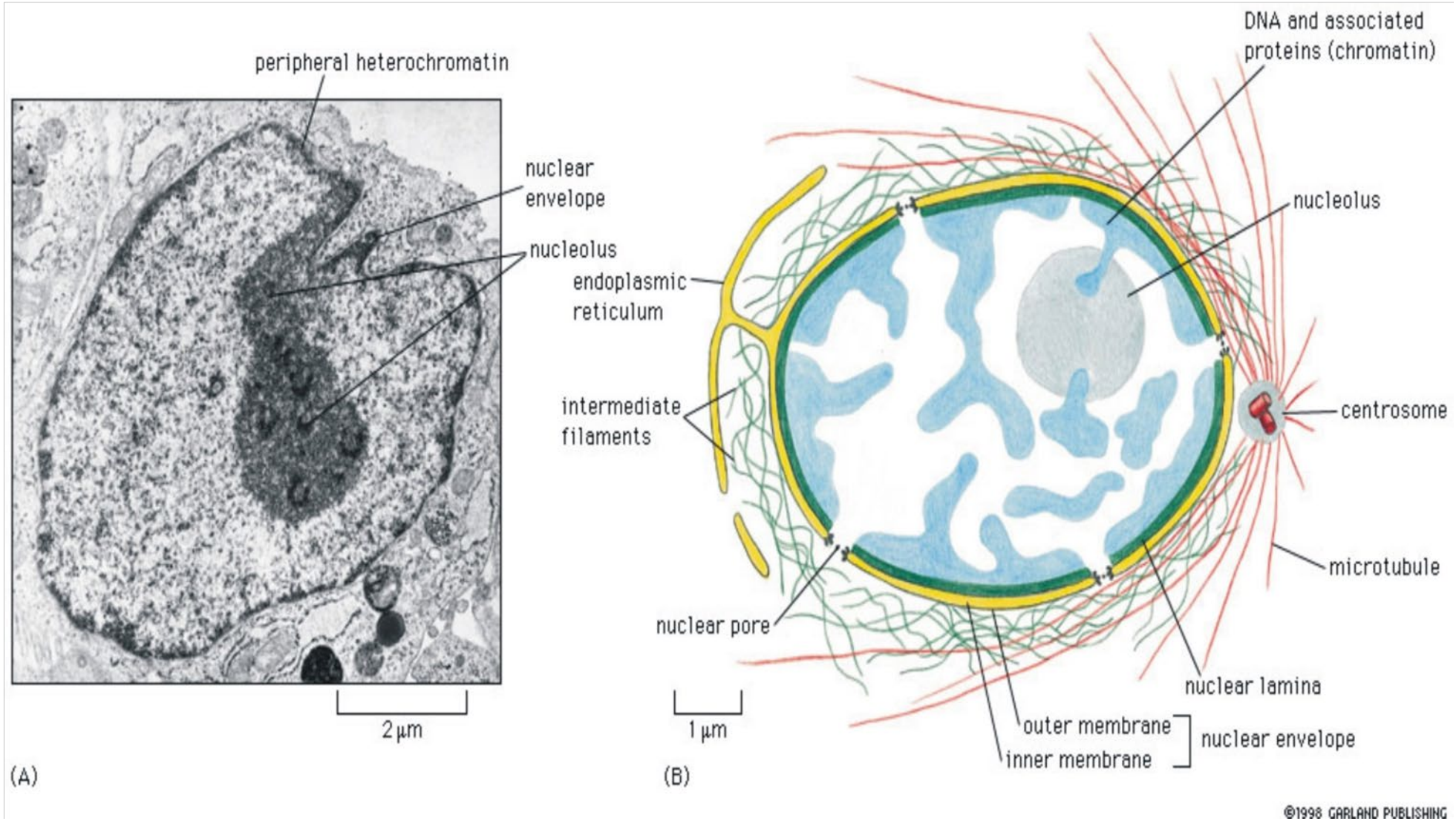


# Model for Organization of Chromatin in the Interphase Cell Nucleus



# Interphase Nucleus

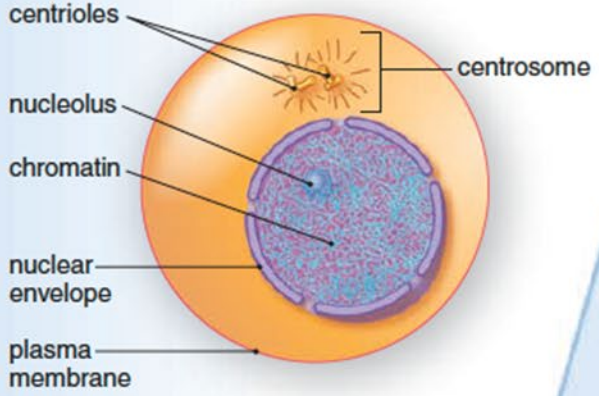
- In interphase, the **chromatin** is not yet condensed.
- Cell performs normal functions.



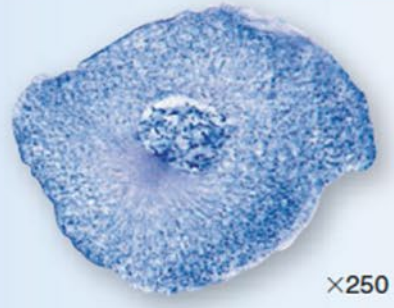
## Cell cycle $G_1$, S, $G_2$

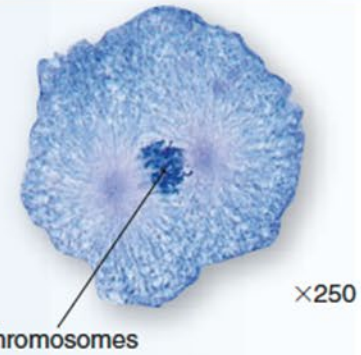
## Cell cycle M: Phases of mitosis

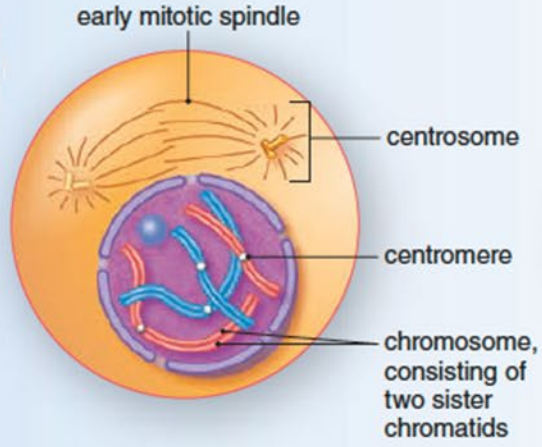
### Interphase

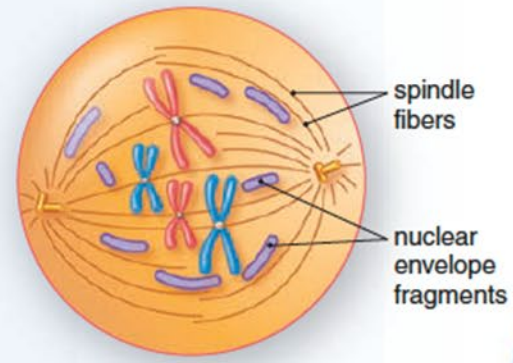



### Prophase




**Interphase**
During interphase, the eukaryotic cell duplicates the contents of the cytoplasm, and DNA replicates in the nucleus. The duplicated chromosomes are not yet visible. A pair of centrosomes is outside the nucleus.

**Prophase**
During prophase, the chromosomes are condensing. Each consists of two sister chromatids held together at a centromere. Outside the nucleus, the spindle begins to assemble between the separating centrosomes.

Prophase continues with the disappearance of the nucleolus and the breakdown of the nuclear envelope. Spindle fibers from each pole attach to the chromosomes at specialized protein complexes on either side of each centromere. During attachment, a chromosome first moves toward one pole and then toward the other pole.

# Chromosome

- Chromosomes were first discovered in 1842 by the Swiss botanist Karl Wilhelm von Nageli.
- The name "chromosomes," meaning "colored bodies," was coined by W. Waldeyer in 1888.
- Chromosomes are long string-like structures.
- They are coiled to fit into the nucleus.
- Chromosomes are made of DNA.
- They are the genetic information of the organism.

**Size: 05 – 30 µM length  0.2 – 3µM diameter**

**Chromosomes:**

- complexes of DNA and proteins – chromatin
- Viral – linear, circular; DNA or RNA
- Bacteria – single, circular
- Eukaryotes – multiple, linear

**Genome**

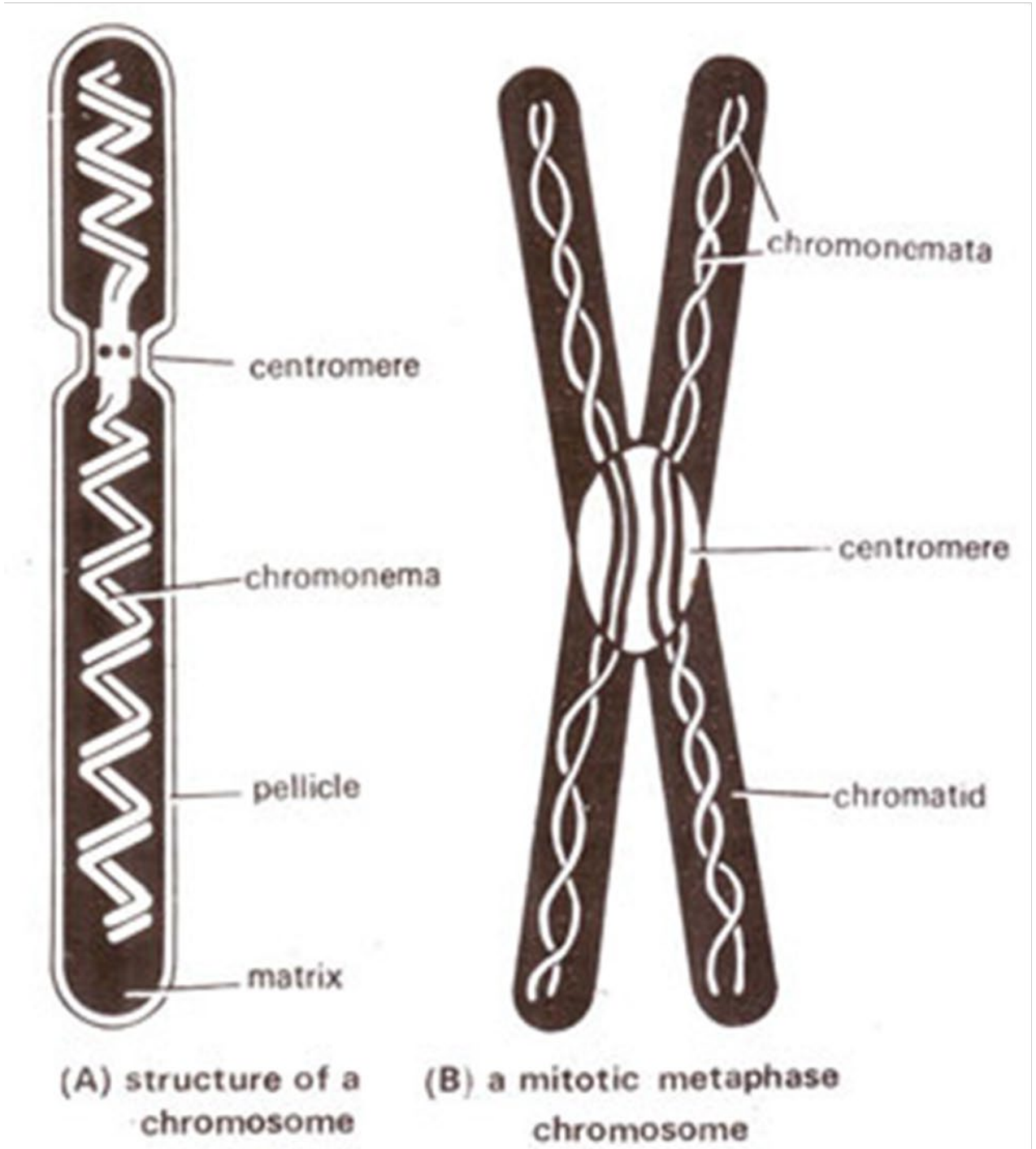
- The genetic material that an organism possesses
- Nuclear genome
- Mitochondrial & chloroplasts genome

**Chromosomes**

- Tightly packaged DNA
- Found only during cell division
- DNA is not being used for macromolecule synthesis

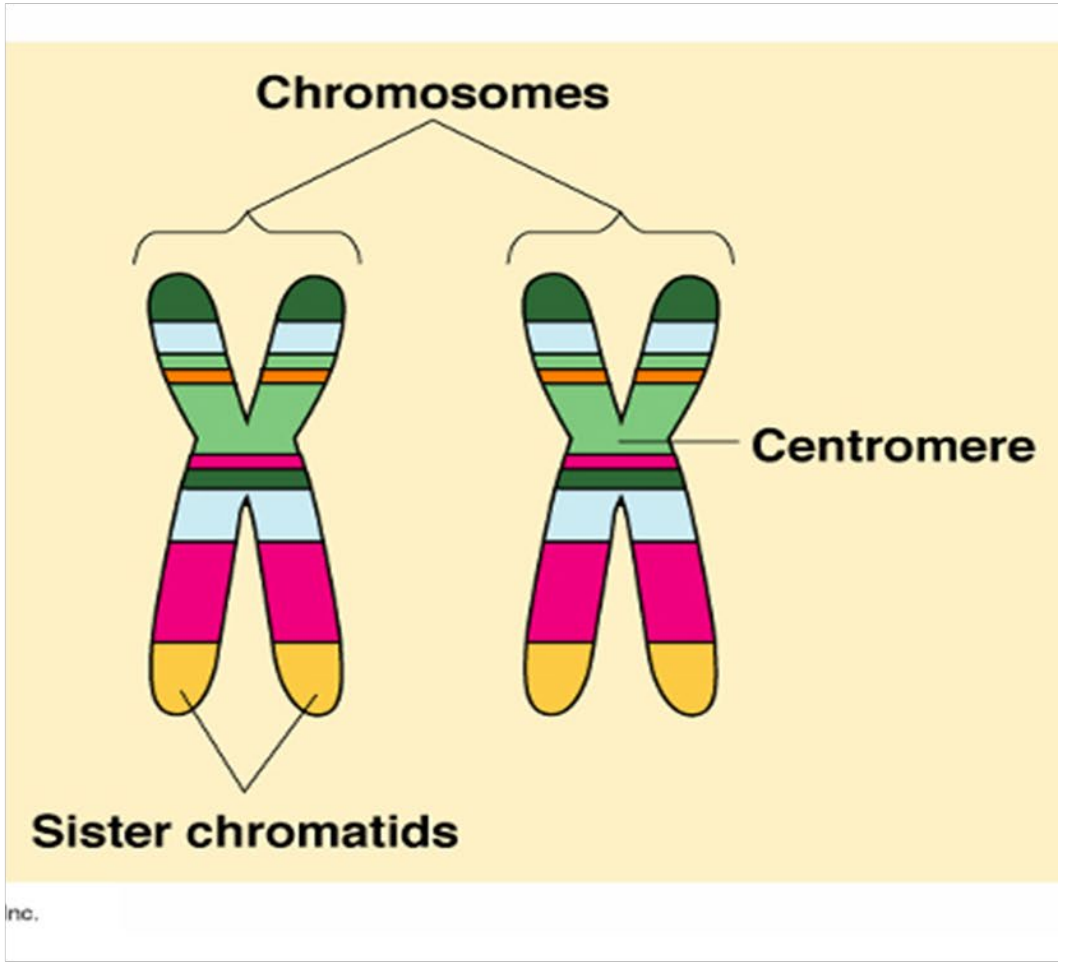
**Chromatin**

- Unwound DNA
- Found throughout Interphase
- DNA *is* being used for macromolecule synthesis

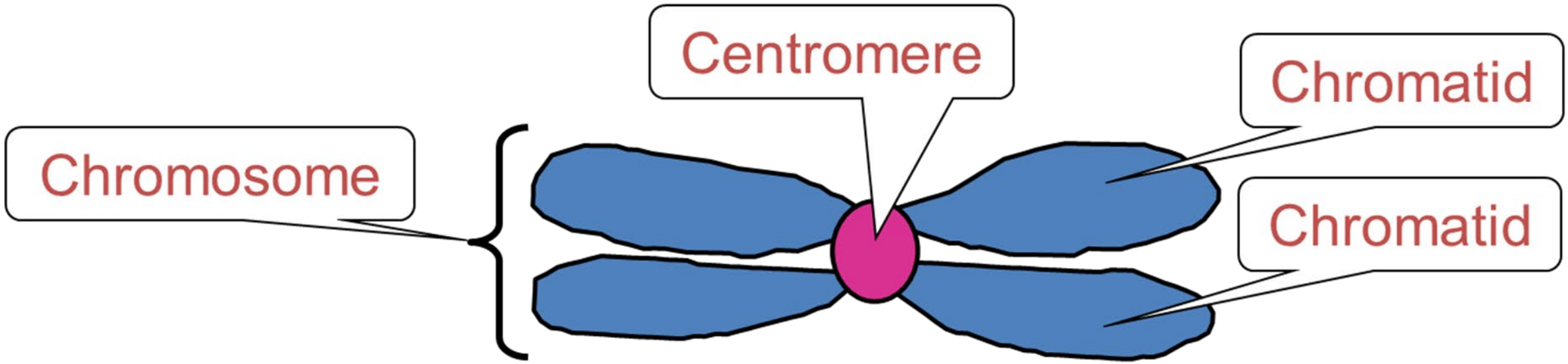



**Chromatid:**
one copy of a duplicated chromosome

**Chromonema / Chromonemata:**
central thread of a chromatid

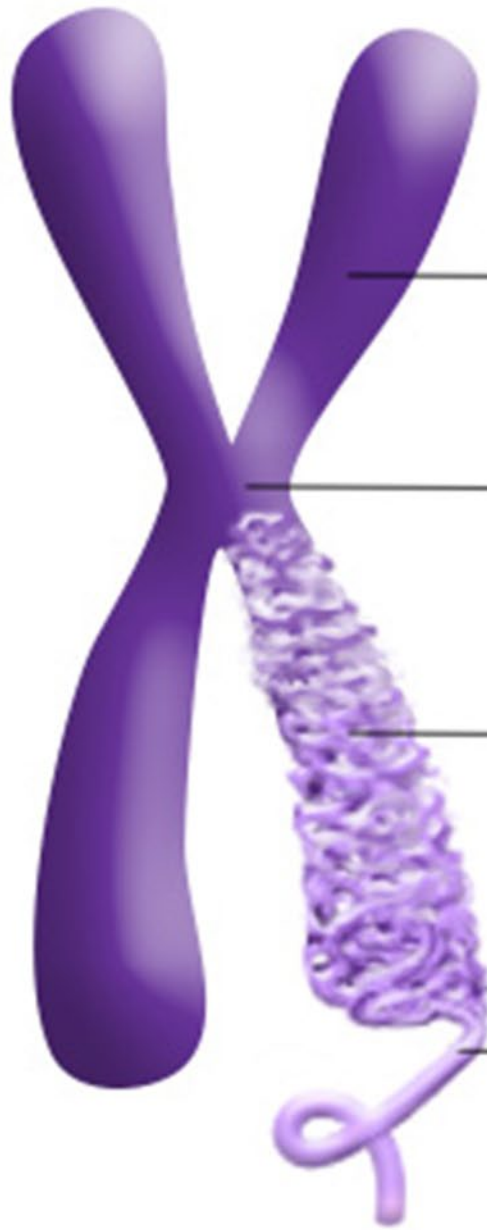


- A chromatid is a chromatid as long as it is held in association with a sister chromatid at the centromere




- When two sister chromatids separate (after metaphase) they go from being a single chromosome to being two different chromosomes

# Chromosome



**p arm** – short arm structure

**Centromere** – constricted point of the chromosome

**q arm** – long arm structure

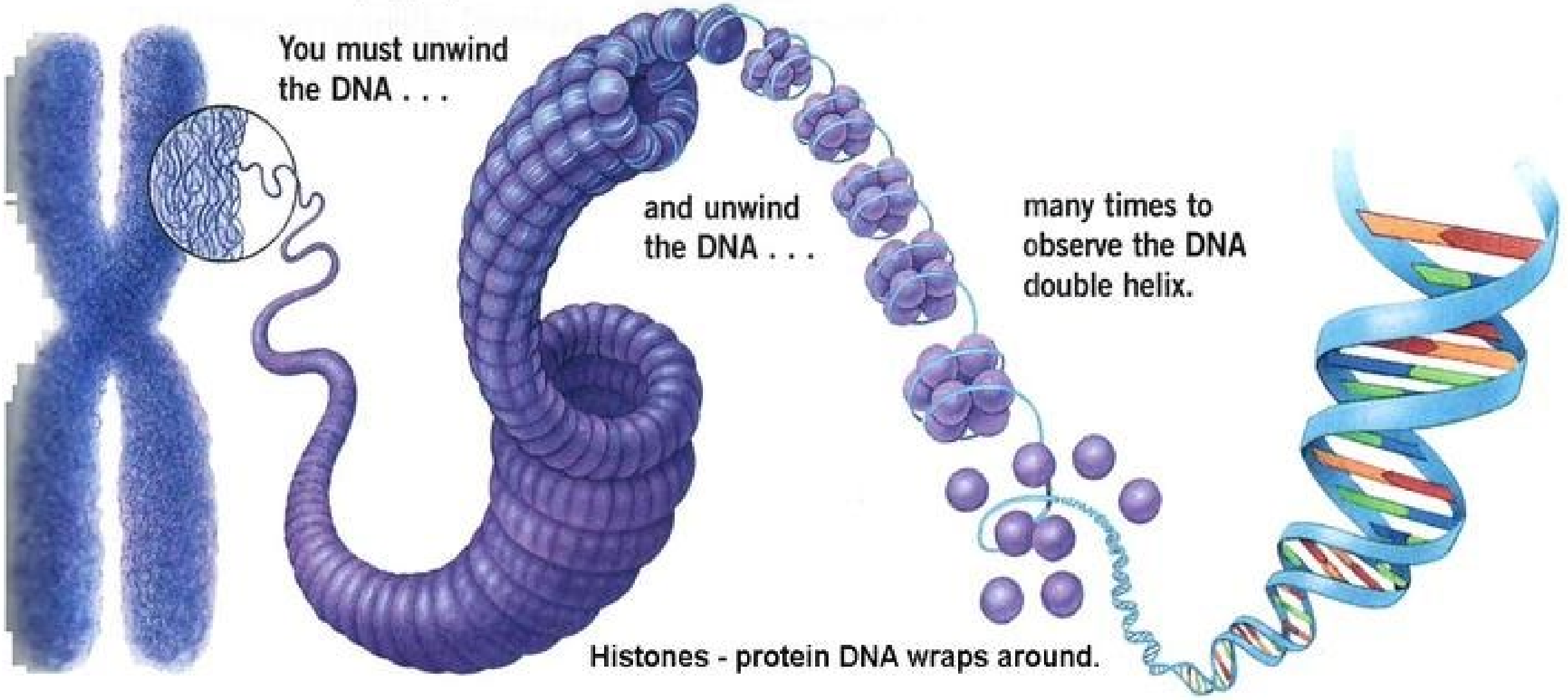
**DNA molecule** – long string like DNA molecule formed into a compact structure by proteins called histones.

## Components of chromosome:

1. Pellicle
2. Matrix
3. Chromonemata
4. Primary constriction (Centromere)
5. Secondary Constriction
6. Satellite
7. Telomere

FIGURE 7.7 **Chromosome Structure**

Chromosome contain very tightly wound DNA



# Eukaryotic Chromatin Compaction

- A single set of human chromosomes will be over 1 meter long
  - nucleus is only 2 to 4 μm in diameter
- The compaction of linear DNA in eukaryotic chromosomes involves interactions between DNA and various proteins
- Proteins bound to DNA are subject to change during the life of the cell
- These changes affect the degree of chromatin compaction

# Eukaryotic Genome Organization

- *DNA Is Organized into Chromatin in Eukaryotes*
- Eukaryotic chromosomes are complexed into a nucleoprotein structure called **chromatin**.
- Chromatin is bound up in nucleosomes with **histones proteins**.

**Categories and Properties of Histone Proteins**

| Histone Type | Lysine-Arginine Content | Molecular Weight (Da) |
|---|---|---|
| H1 | Lysine-rich | 23,000 |
| H2A | Slightly lysine-rich | 14,000 |
| H2B | Slightly lysine-rich | 13,800 |
| H3 | Arginine-rich | 15,300 |
| H4 | Arginine-rich | 11,300 |

# Histone Proteins

- Histones are highly alkaline proteins found in eukaryotic cell nuclei that package and order the DNA into structural units called nucleosomes.
- They are the chief protein components of chromatin, acting as spools around which DNA winds, and play a role in gene regulation.
- Without histones, the unwound DNA in chromosomes would be very long (a length to width ratio of more than 10 million to 1 in human DNA).
- For example, each human cell has about 1.8 meters of DNA, (~6 ft) but wound on the histones it has about 90 micrometers (0.09 mm) of chromatin, which, when duplicated and condensed during mitosis, result in about 120 micrometers of chromosomes.

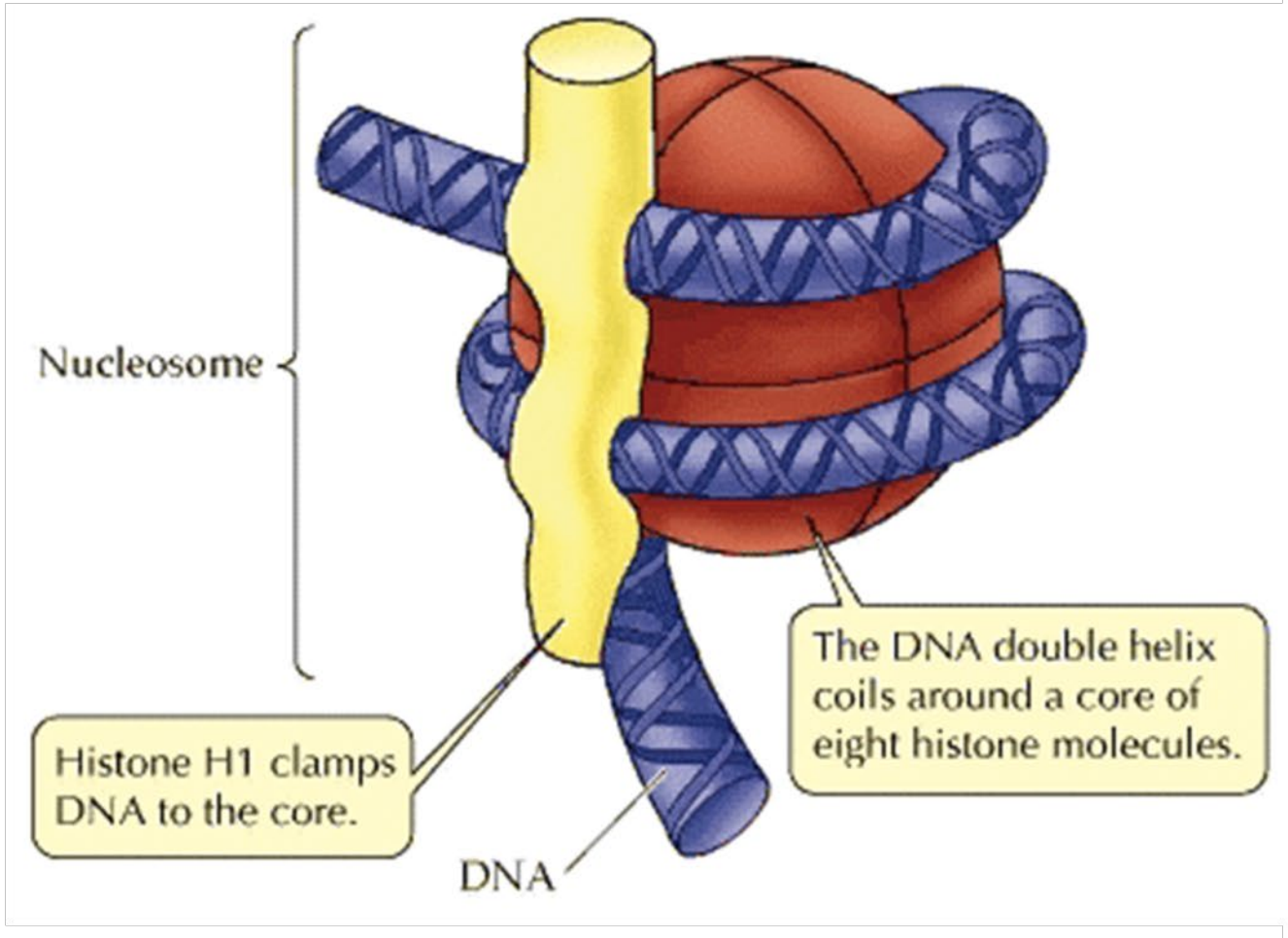
# Three levels of chromatin organization

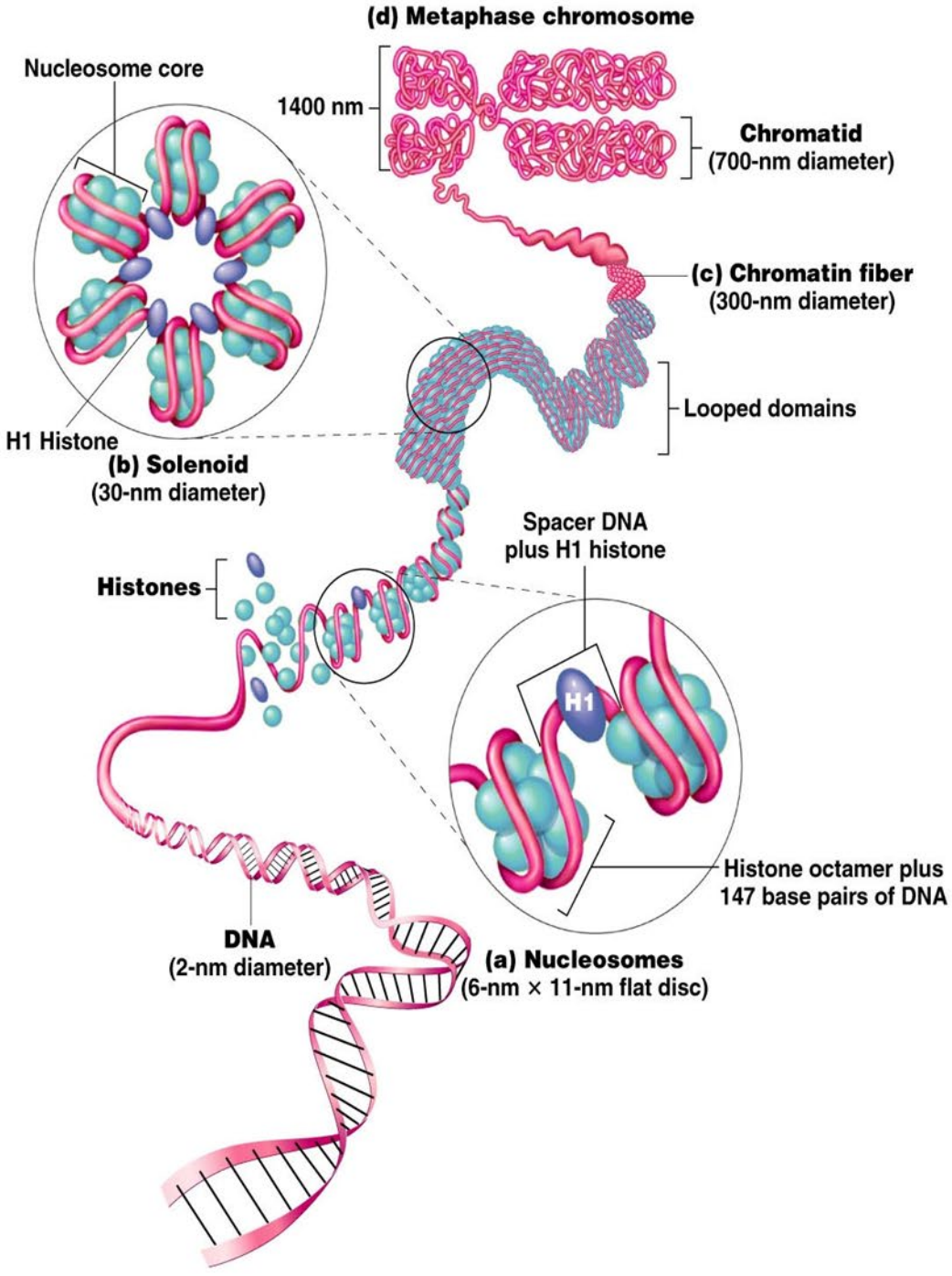
**Level 1.** DNA wraps around histone proteins forming **nucleosomes**: the "**beads on a string**" structure (euchromatin) **10 nm fiber**.

**Level 2.** Multiple histones wrap into a **30 nm fiber** consisting of nucleosome arrays in their most compact form (heterochromatin).

**Level 3.** Higher-level DNA packaging of the 30 nm fiber into the **metaphase chromosome** (during mitosis and meiosis).

**Nucleosomes** are condensed several times to form the intact chromatids.



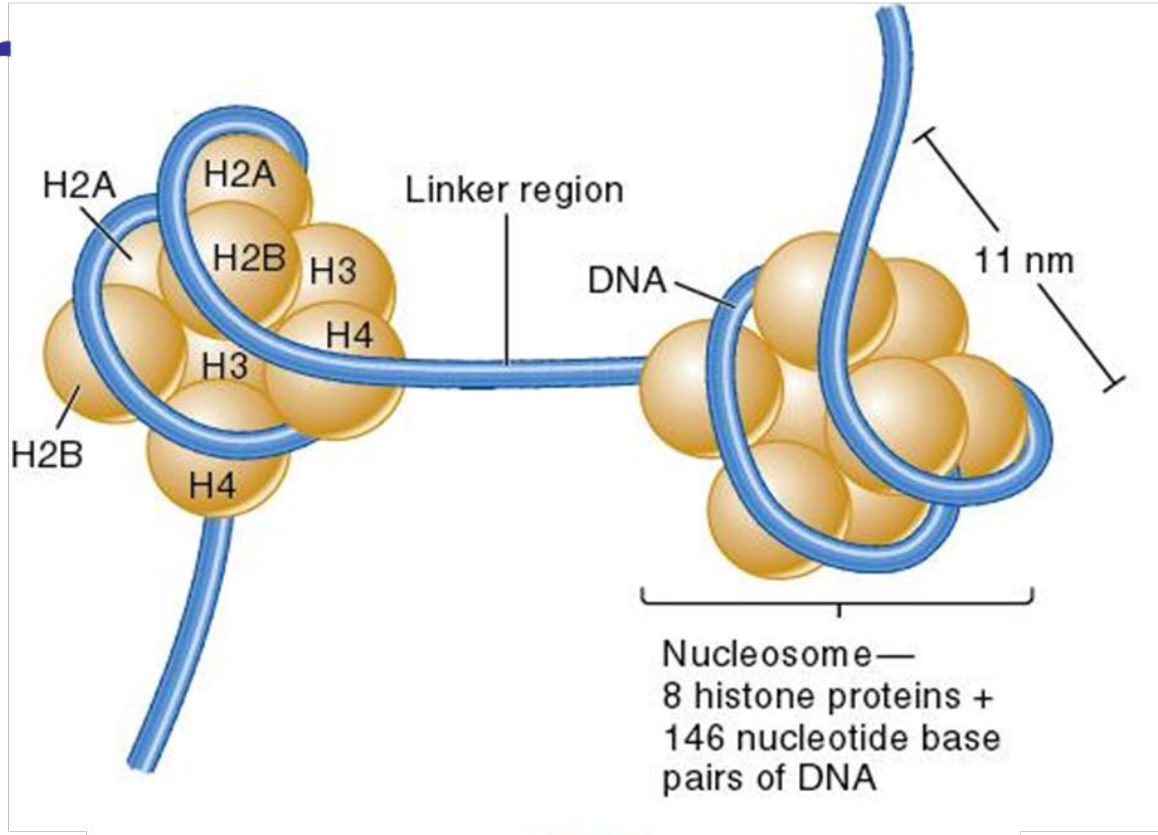



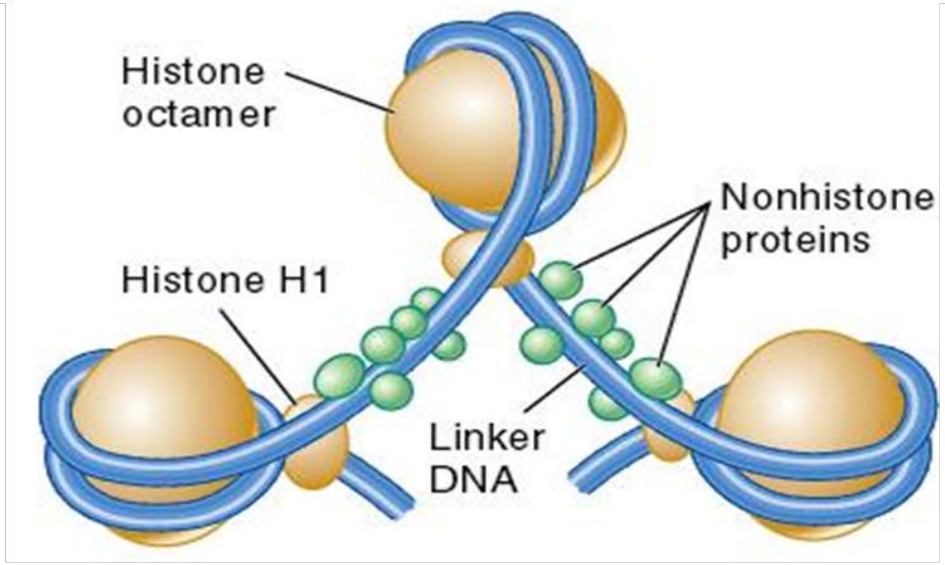
# Nucleosomes – 10 nm fiber

- 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



# Nucleosomes join to form **30 nm fiber**

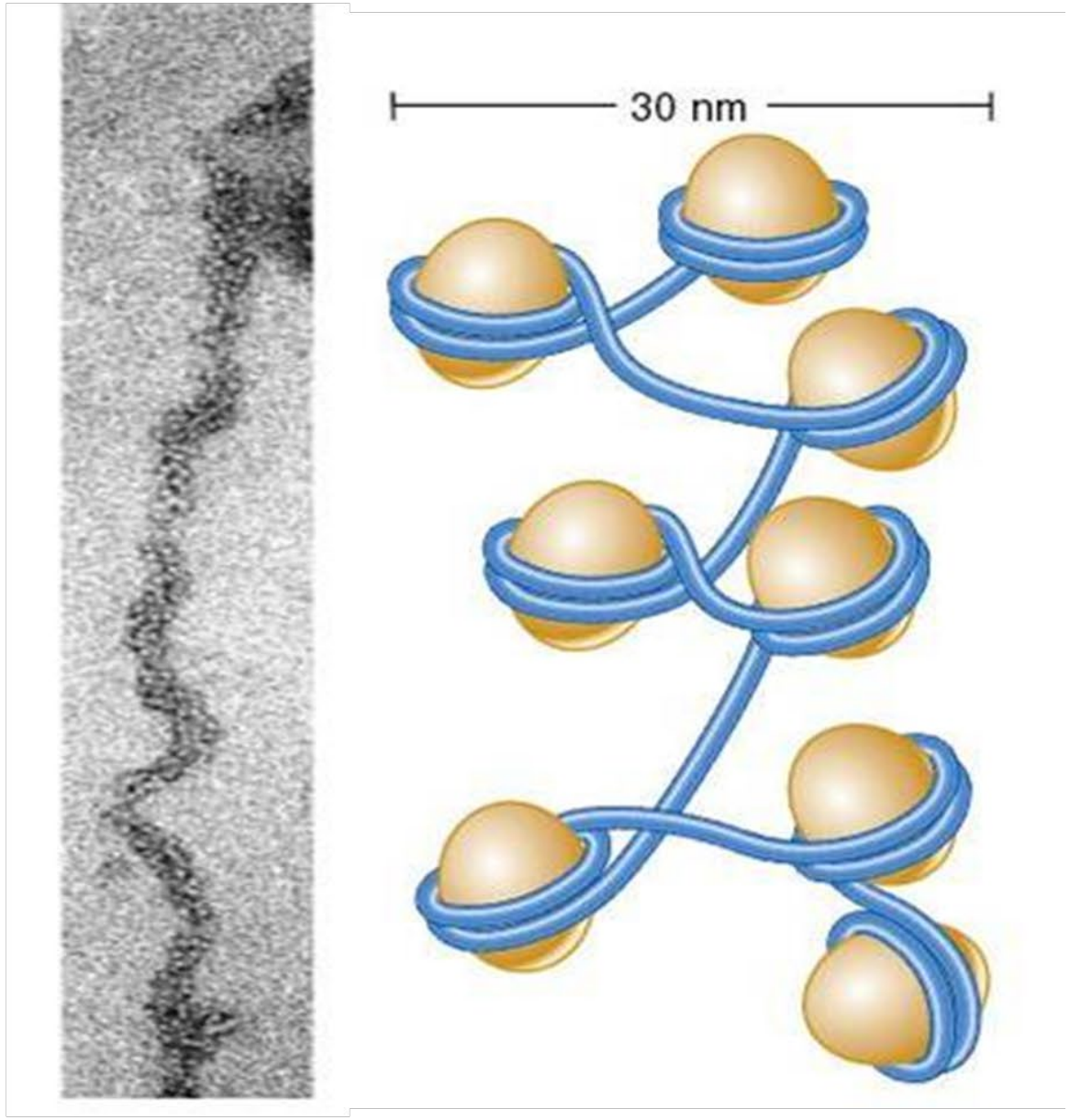
- Nucleosomes associate to form more compact structure - the **30 nm fiber**

- Histone H1 plays a role in this compaction

**Further Compaction of the Chromosome**

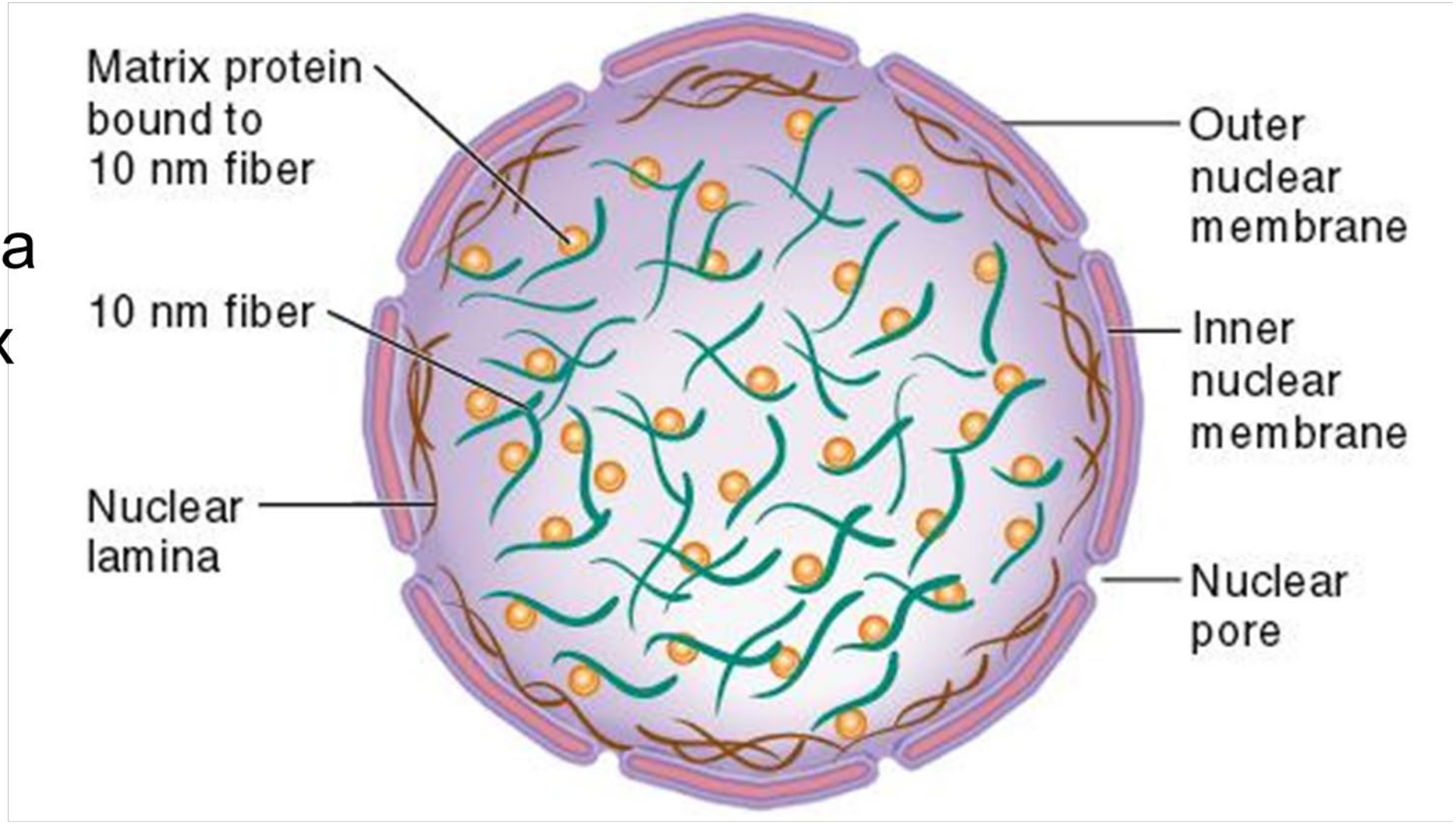
- The two events could shorten the DNA about 50-fold

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



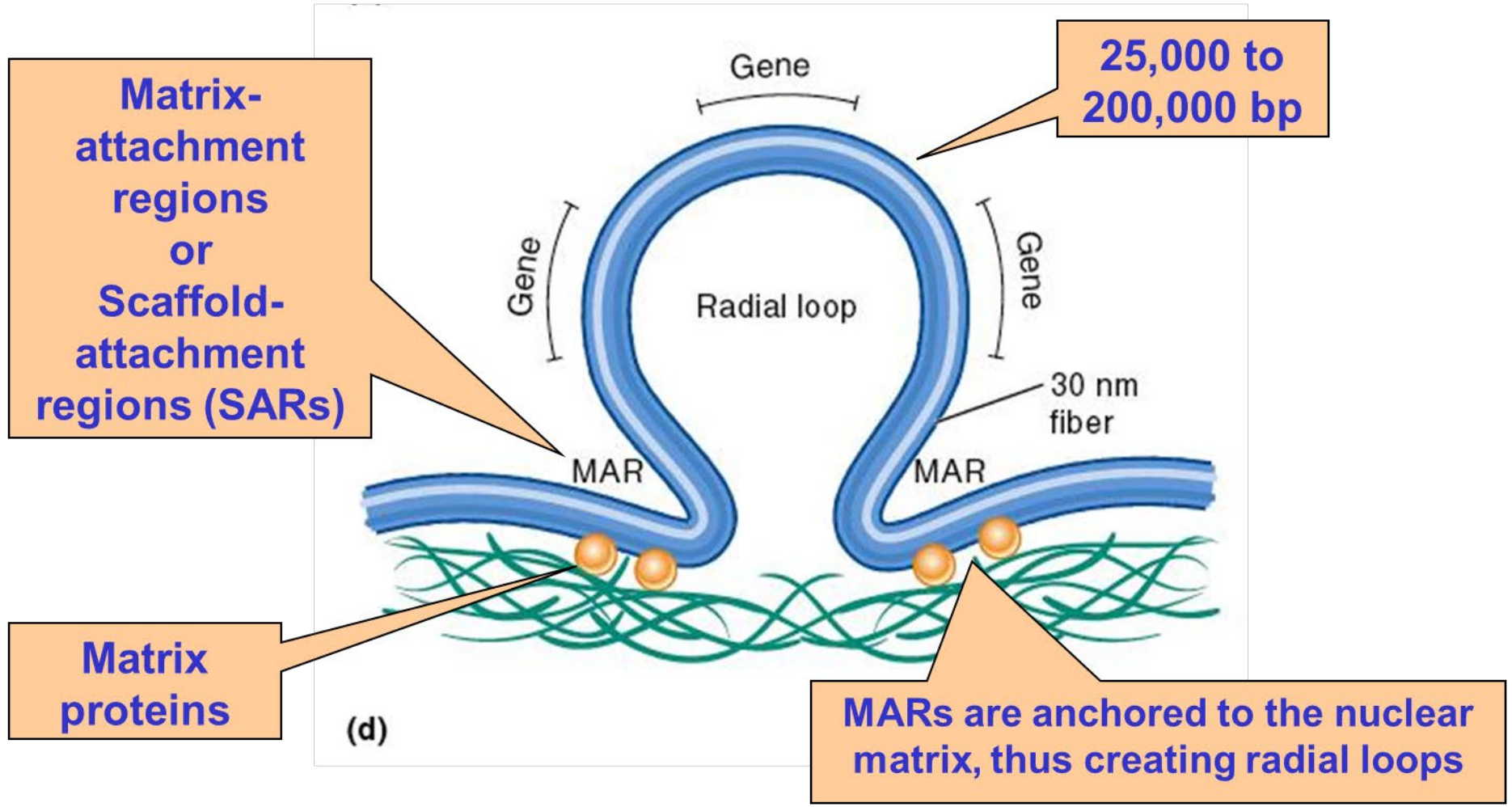
# Nuclear Matrix Association

- 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



# Further Compaction of the Chromosome

## 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

**Feulgen stain:** a staining technique discovered by Robert Feulgen

- used to identify chromosomal material or DNA in cell specimens
- **Higher stain – heterochromatin**

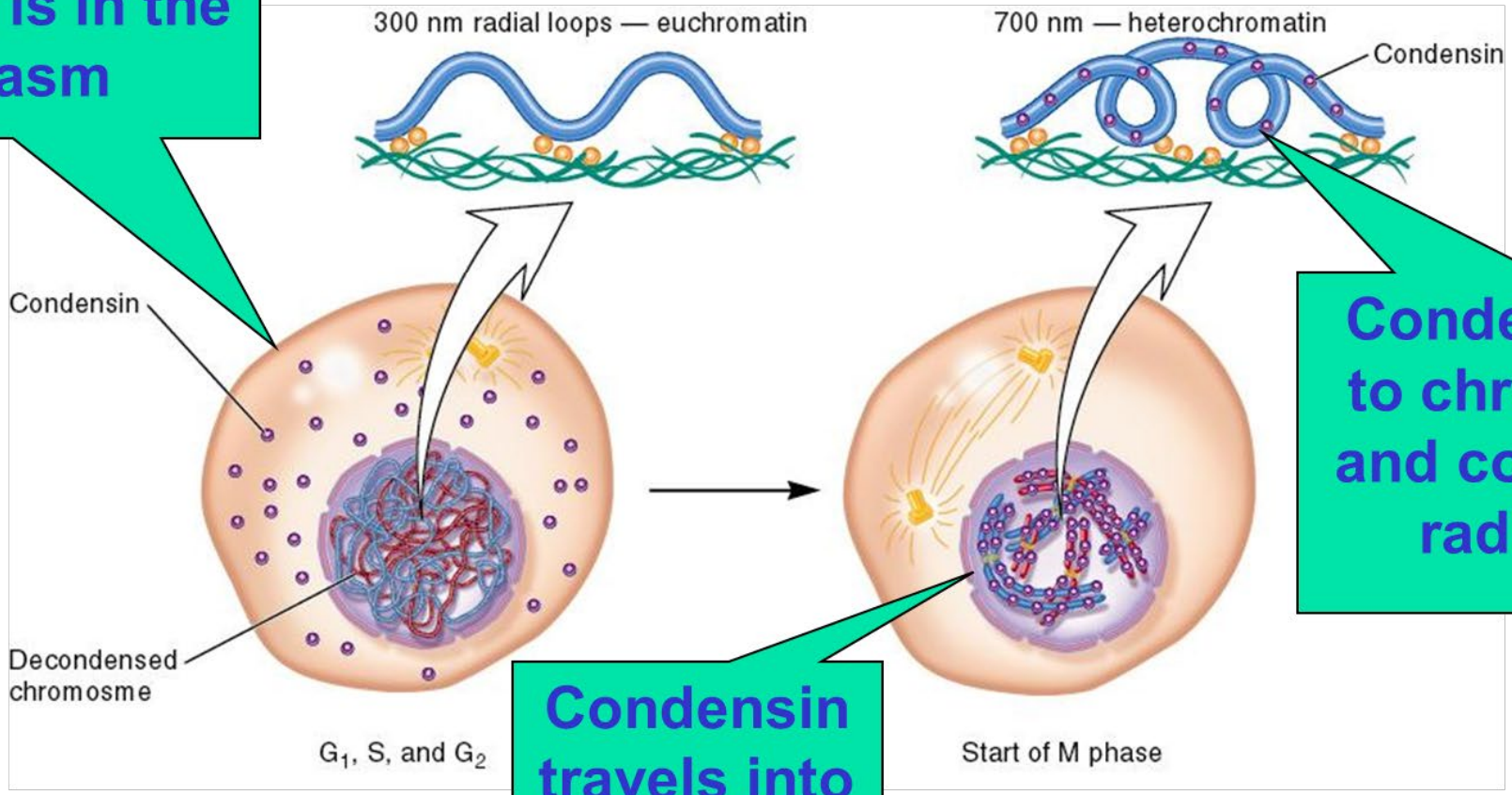
# Metaphase Chromosomes

- Condensed chromosomes are referred to as metaphase chromosomes
- During prophase, the compaction level increases
- By the end of prophase, sister chromatids are entirely heterochromatic
- These highly condensed metaphase chromosomes undergo little gene transcription
- In metaphase chromosomes, the radial loops are compacted and anchored to the nuclear matrix scaffold

# Chromosome Condensation

During interphase, condensin is in the cytoplasm

The number of loops has not changed
However, the diameter of each loop is smaller

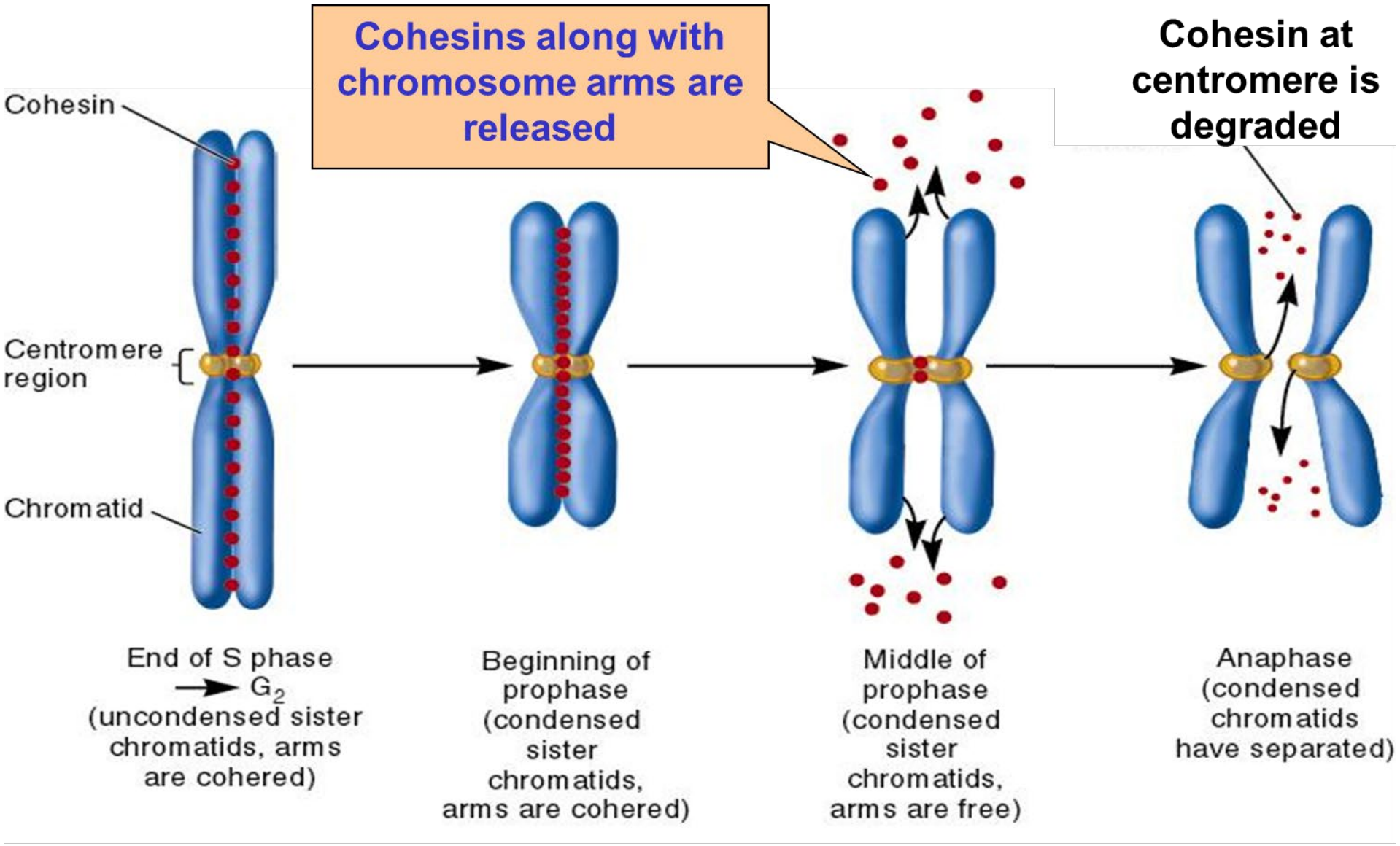



Condensin binds to chromosomes and compacts the radial loops

Condensin travels into the nucleus

**The condensation of a metaphase chromosome by condensin.**

# Chromosomes During Mitosis




**The alignment of sister chromatids via cohesin**

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