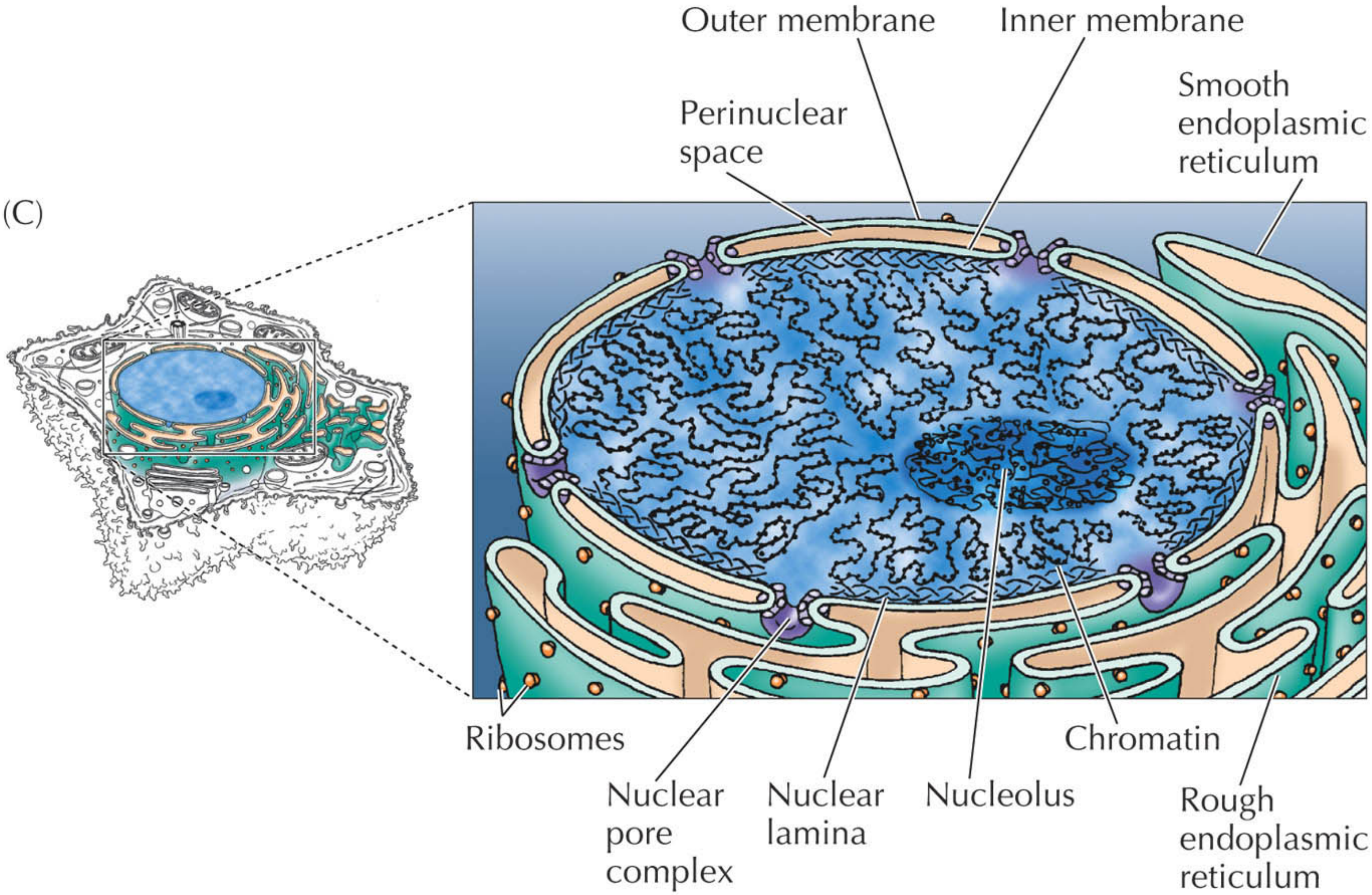
Nucleus
&
Genome Organization

Nucleus

- The nucleus was also described by **Franz Bauer in 1804**
- **Robert Brown** is known to discover in 1831 (Scottish botanist in a talk at the Linnean Society of London.
- Nucleus is a membrane-enclosed organelle found in mostly type of cells. It contains most of the cell's genetic material, organized as multiple long linear DNA molecules in complex form of chromosomes.
- The function of the nucleus is to maintain the integrity of these genes and to control the activities of the cell by regulating gene expression.
- The nucleus is, therefore, the control center of the cell.
- The nucleus is the largest cellular organelle in animal cells.
- In **mammalian cells**, the average diameter of the nucleus is **approximately 6 micrometers (μm)**, which occupies about 10% of the total cell volume.
- It appears as a dense, roughly spherical organelle.

(C)



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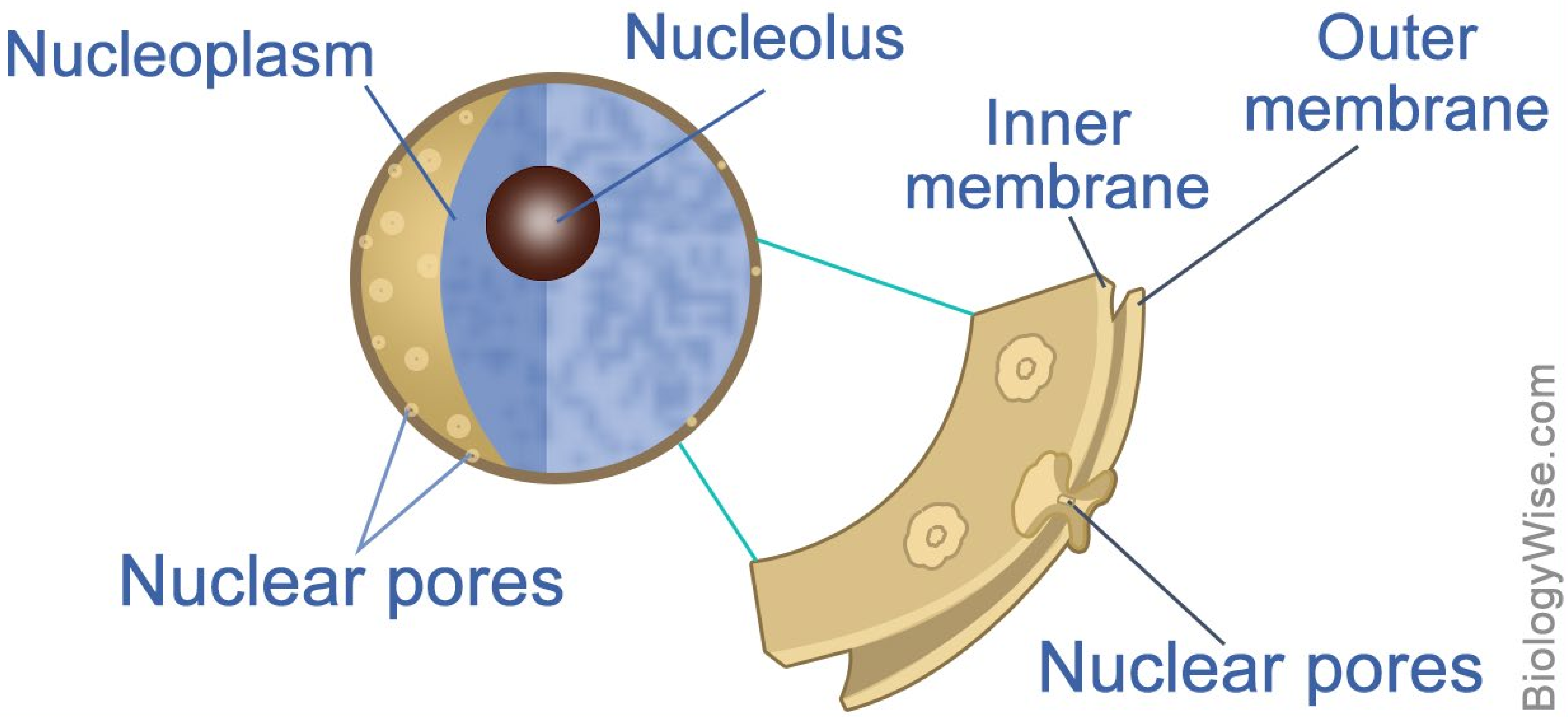
NUCLEUS


Nucleoplasm
Nucleolus
Outer membrane
Inner membrane
Nuclear pores
Nuclear pores
BiologyWise.com

Components of the nucleus

1. **Nuclear envelope** / membrane (made-up of lipid bilayer): The nuclear membrane covers the nucleus. It allows materials to flow in and out of small pores.
2. **Nuclear pore** (pores on the nuclear envelope): Allow small molecules to diffuse easily between nucleoplasm & cytoplasm. Controls passage of proteins & RNA protein complexes.
3. **Nucleoplasm:** the viscous liquid inside, similar in composition to the cytosol.
4. **Nucleolus:** subcellular organelle found inside nucleus, main function is to transcribe and modify ribosomal RNA (rRNA) and integrate ribosomal proteins to form immature ribosomes.
5. **Genomic contents**: chromosome/chromatin.

Nucleus chemical composition:

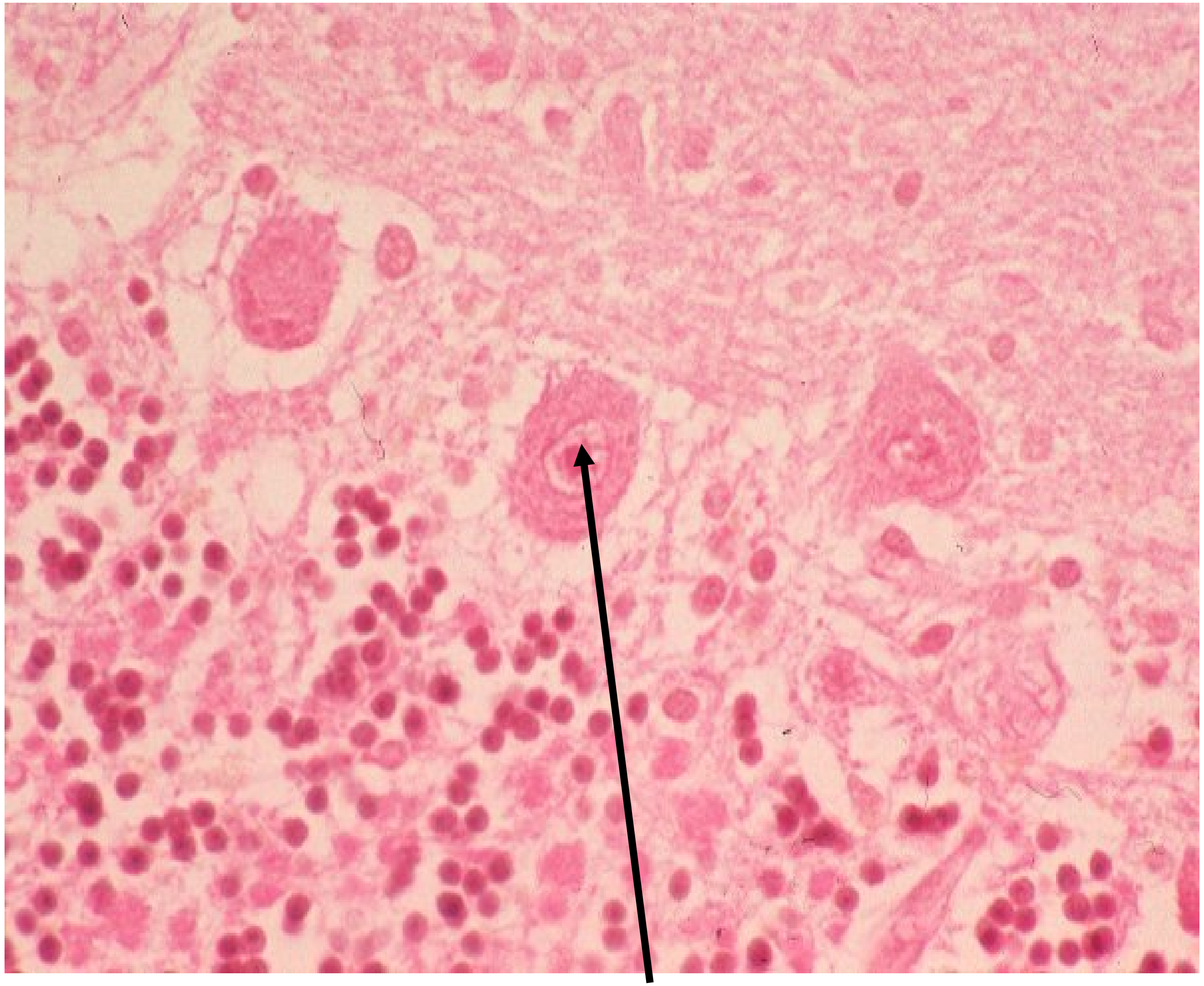
- 9-12 percent DNA
- 15 percent histone
- 65 percent enzymes, neutral proteins and acid proteins
- 5 percent RNA
- 3 percent lipids

Some of the main functions of the nucleus include:

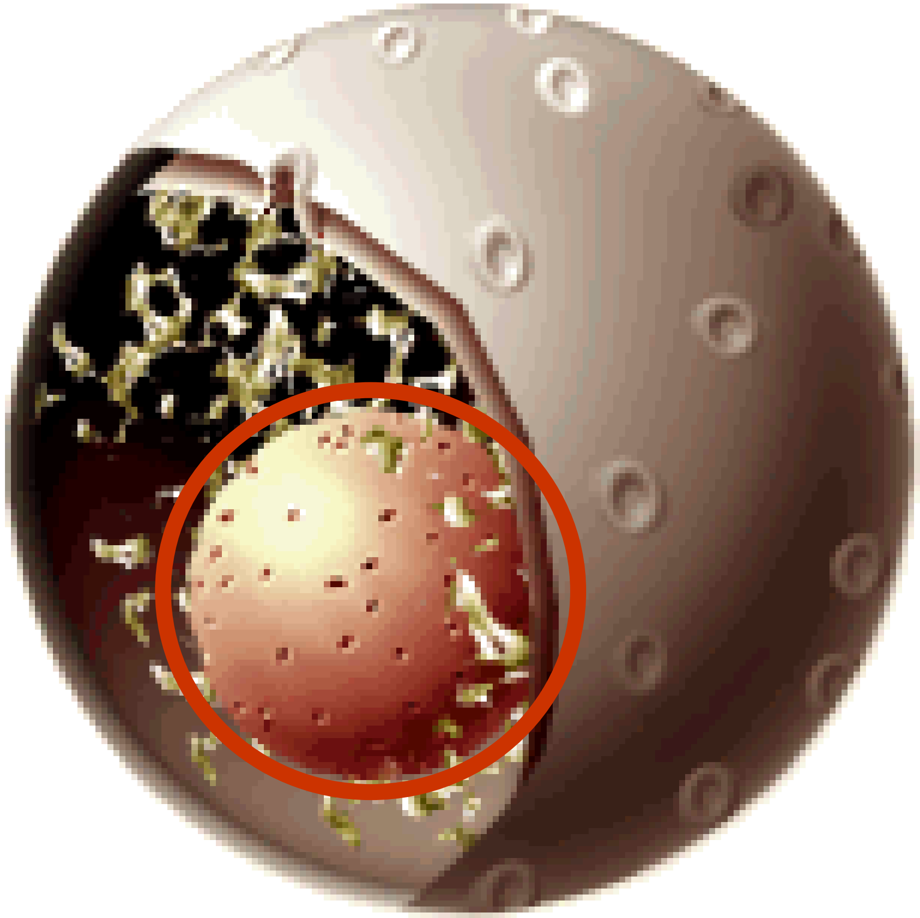
- Protein synthesis, cell division, and differentiation
- Control the synthesis of enzymes involved in cellular metabolism
- Controlling hereditary traits of the organism
- Store DNA strands, proteins, and RNA
- Site of RNA transcription - e.g. mRNA required for protein synthesis

Nucleolus

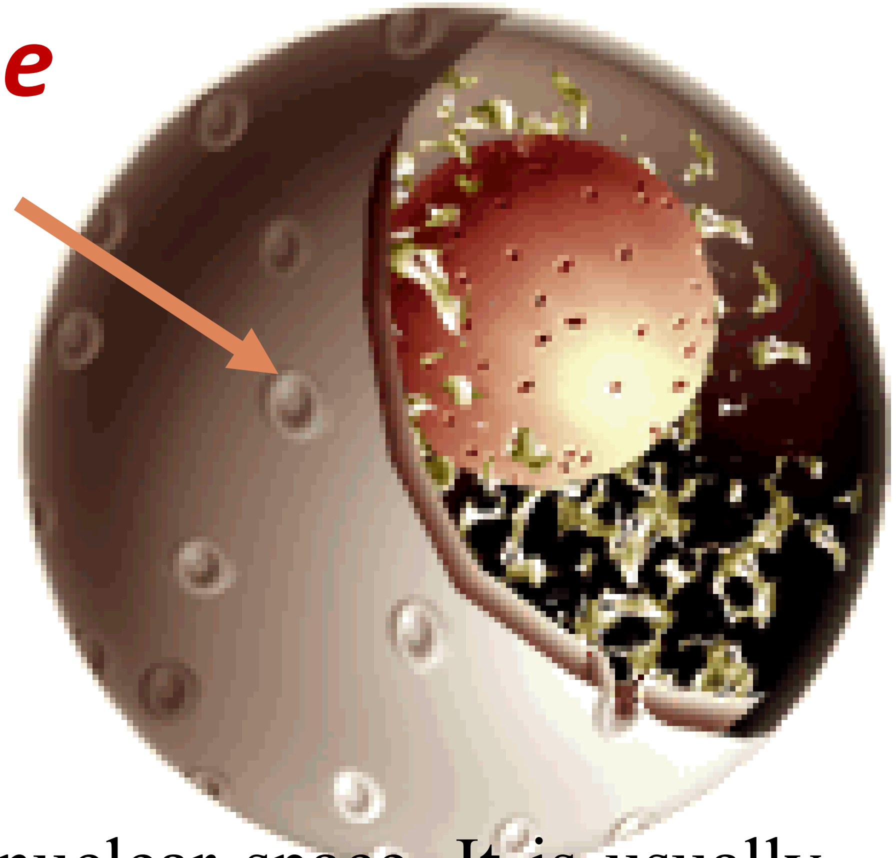
- This round structure appears as a dark dot in the nucleus.



Ribosomes are made here.



Nuclear Membrane

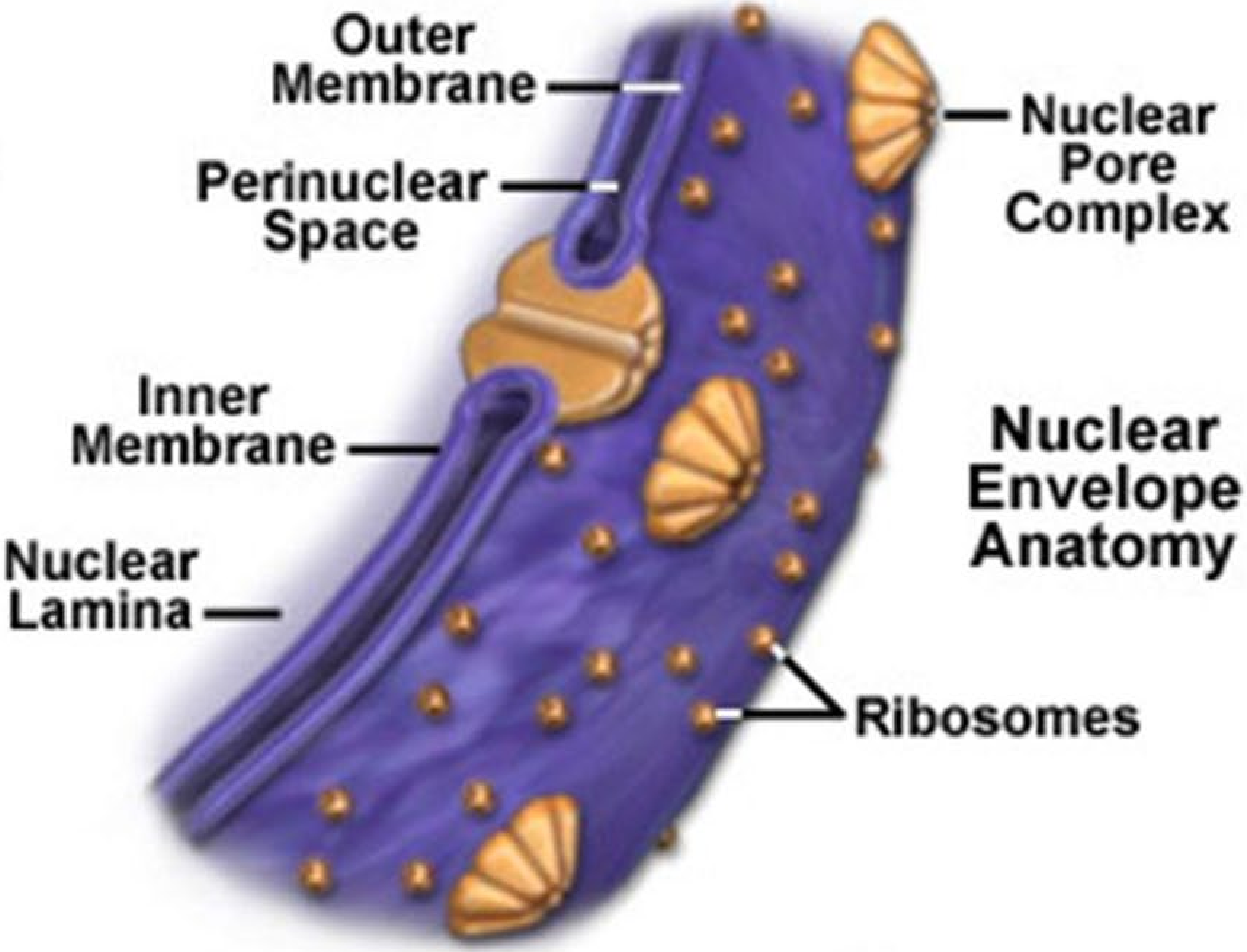


- The nuclear membrane covers the nucleus.
- It allows materials to flow in and out through small nuclear pores.
- The nuclear envelope/nuclear membrane is made up of two lipid bilayer membranes.
- The nuclear envelope consists of an inner nuclear membrane, and an outer nuclear membrane.

The space between the membranes is called the perinuclear space. It is usually about 20–40 nm wide. The outer nuclear membrane is continuous with the endoplasmic reticulum membrane. The nuclear envelope has many nuclear pores that allow materials to move between the cytosol and the nucleus. Intermediate filaments form a lamina internally to the inner nuclear membrane, and more loosely externally to the outer nuclear membrane to give structural support to the nucleus.

Nuclear membrane

- Also called the nuclear envelope
- Double membrane
- Porous



The Nuclear Membrane

The nuclear membrane is one of the aspects that distinguish eukaryotic cells from prokaryotic cells. Whereas eukaryotic cells have a nucleus bound membrane, this is not the case with prokaryotes (e.g. bacteria) that lack membrane-bound organelles.

As with the other cell organelles of eukaryotic organisms, the nucleus is a membrane-bound organelle. The nuclear membrane, like the cell membrane, is a double-layered structure that consists of phospholipids (forming the lipid bilayer nucleus envelope).
Present on the nuclear membrane are nuclear pores (made up of proteins) through which substances enter or leave the cell (RNA, proteins, etc). While the lipid bi-layers are separated by a thin space between them (perinuclear cisterna), studies have shown them to be fused at the pores. Nuclear membrane pores are occupied by dense granules/fibrillar material arranged in a cylindrical manner.

Fibrous lamina - The fibrous lamina is part of the nuclear cytoskeleton that is attached to the inner layer of the nuclear membrane. It consists of fine protein filaments and serves to provide mechanical reinforcement to the bilayer membrane.

Some of the other functions of the nuclear lamina include:
•Can play a role in regulating gene expression
•Serves as anchor sites for the pore complexes of the nuclear
•It regulates material entering or exiting the cell
* The nuclear membrane is connected to the endoplasmic reticulum in a manner that creates continuity between the nucleus and the external environment (through the lumen of the ER).

Nucleoplasm

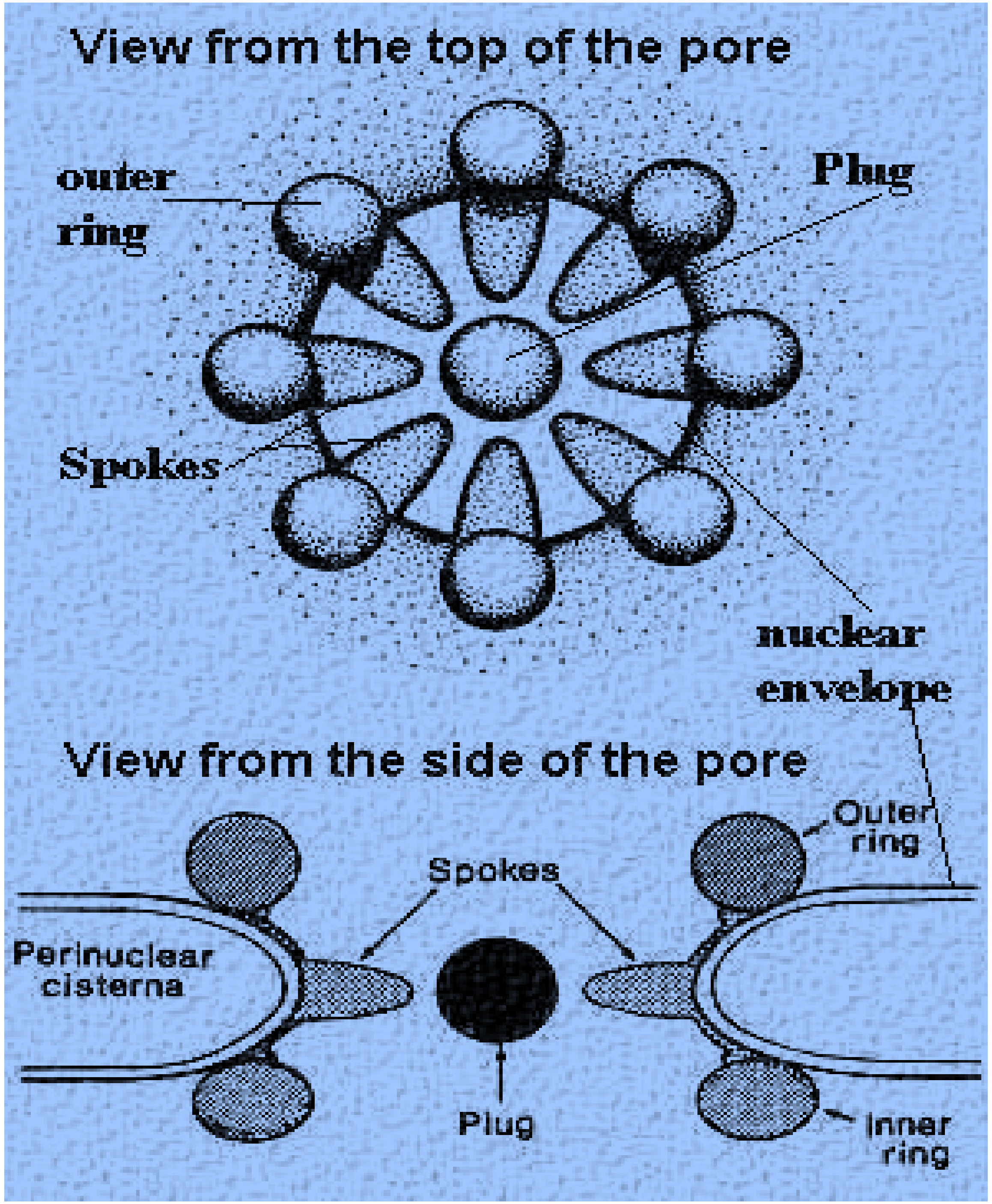
Also known as karyoplasm/nucleus sap, the nucleoplasm is a type of protoplasm composed of enzymes, dissolved salts, and several organic molecules. In addition, the nucleoplasm helps cushion and thus protect the nucleolus and chromosomes while also helping maintain the general shape of the nucleus.

Nucleolus

In the same way that the nucleus is the most prominent organelle of the cell, the nucleolus is the most prominent structure of the nucleus. Unlike the nucleus, however, this dense structure lacks its own membrane.

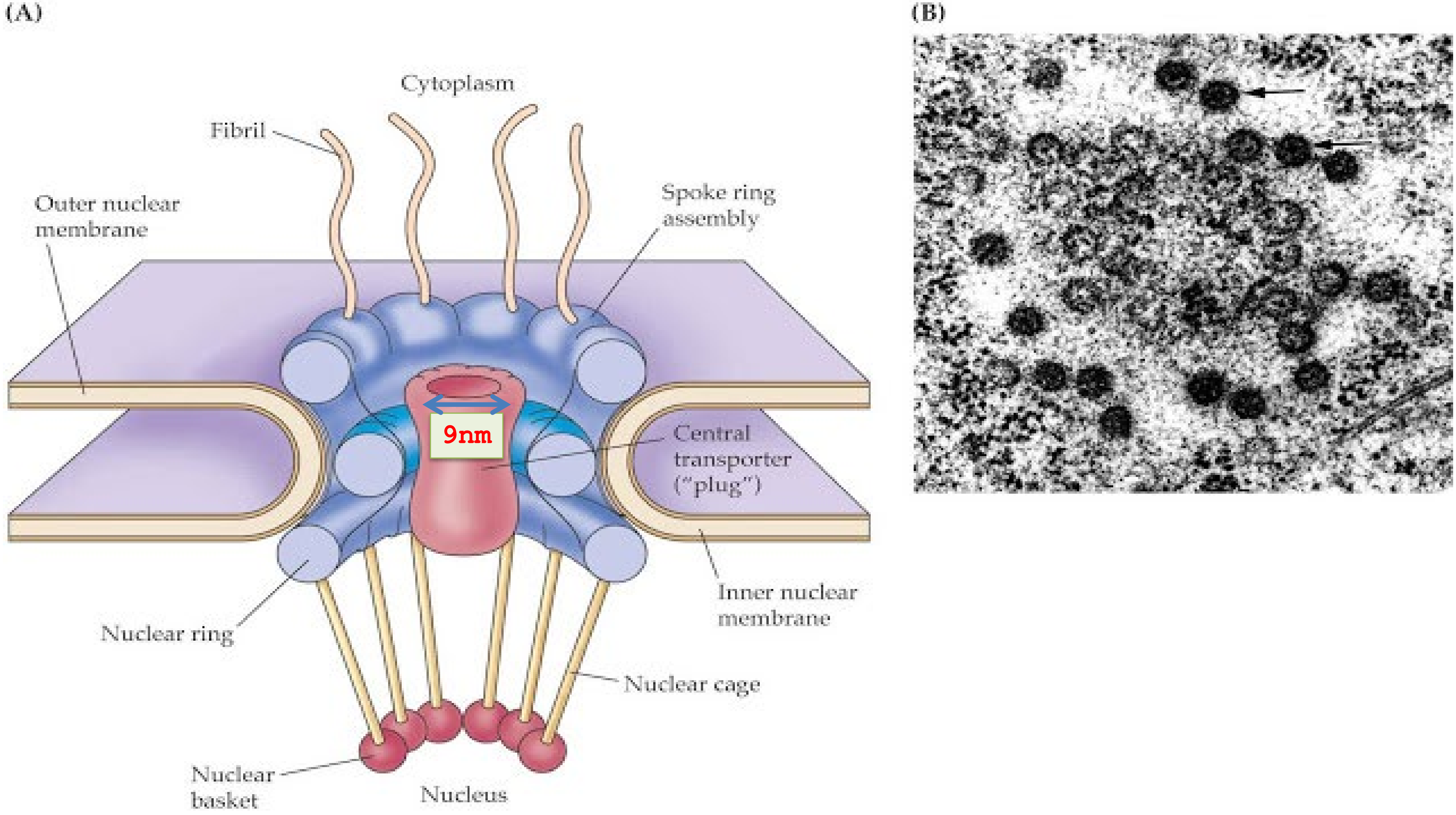
During cell division (mitosis), the nucleolus breaks up only to reform from specific sections of the chromosomes after mitosis.

* Although the nucleolus is the most prominent (and thus visible) structures of the nucleus, its size is largely dependent on the level of ribosome production as well as the different types of molecular processes that occur in the nucleus.
* The nucleolus is the site of transcription and processing of the ribosomal gene.
* In some organisms, the nucleus contains as many as four nucleoli.

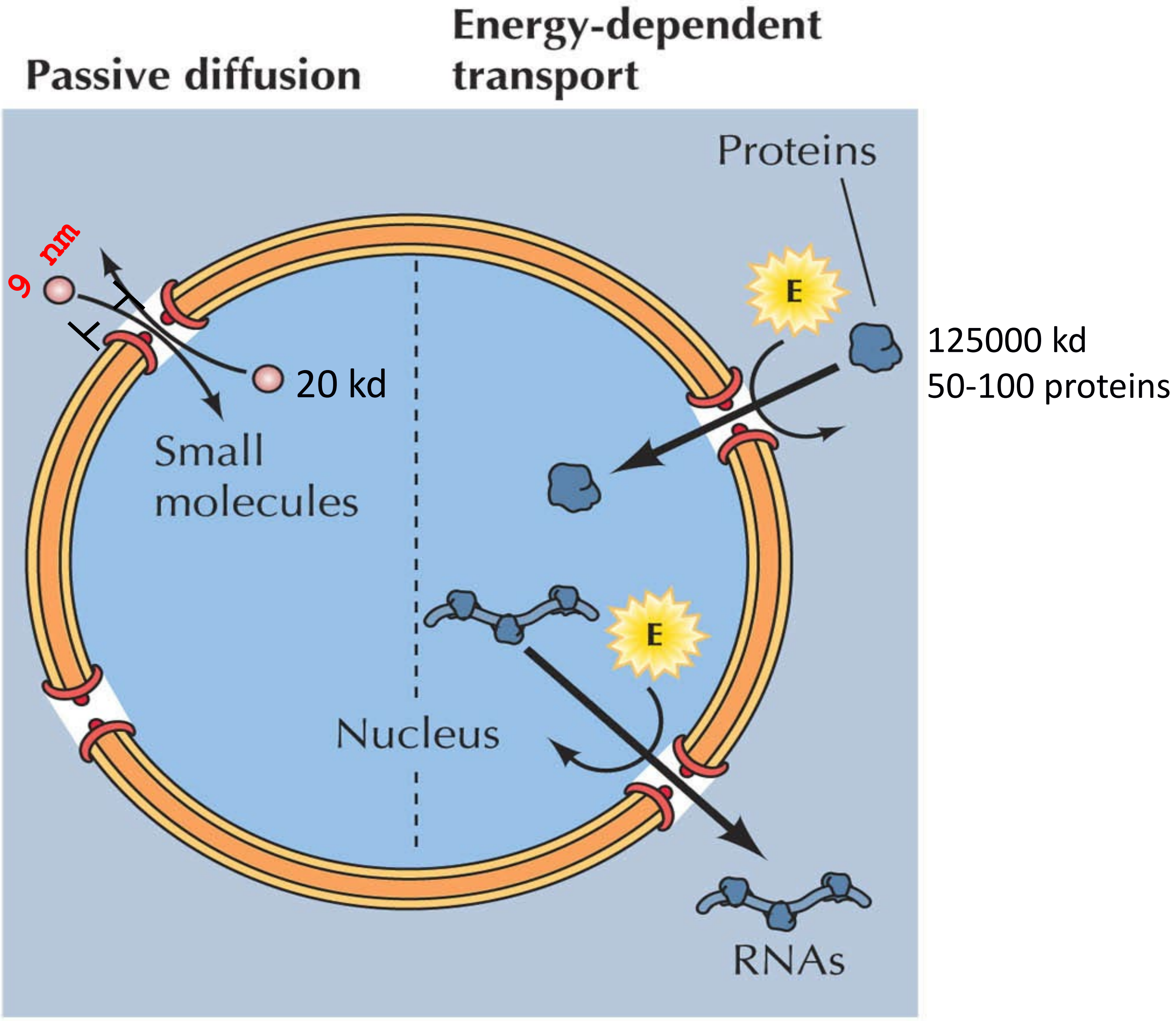


Nuclear Pore Complex

- Allow small molecules to diffuse easily between nucleoplasm & cytoplasm
- Control passage of proteins & RNA protein complexes
  - **Import**: proteins moving in to be incorporated into nuclear structure or to catalyze nuclear activities
  - **Export**: RNA / RNA-protein complexes to the cytoplasm


(A)
Cytoplasm
Fibril
Outer nuclear membrane
Spoke ring assembly
9nm
Central transporter ("plug")
Inner nuclear membrane
Nuclear ring
Nuclear cage
Nuclear basket
Nucleus
(B)

Molecular Traffic through Nuclear Pore Complexes



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Chromosome and Genome Organization

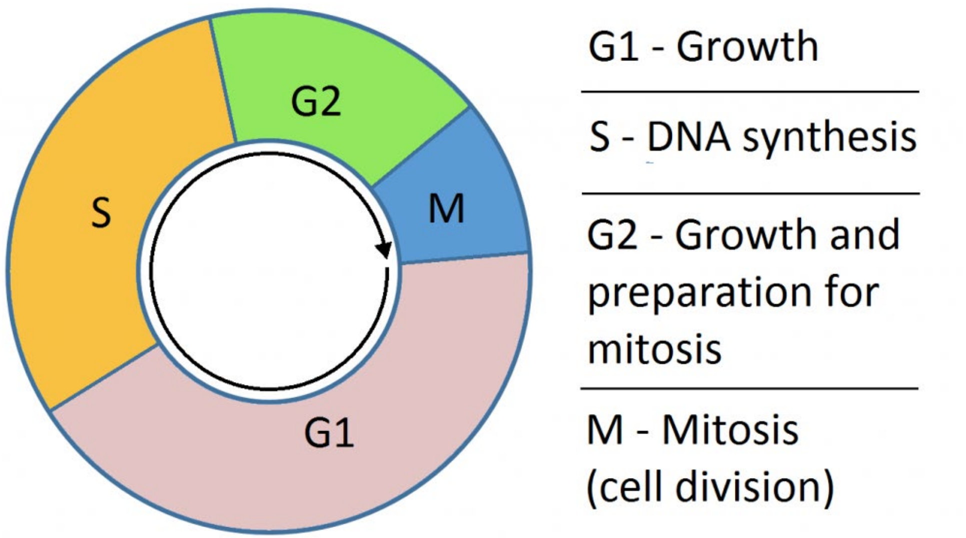
Genomic Materials

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.



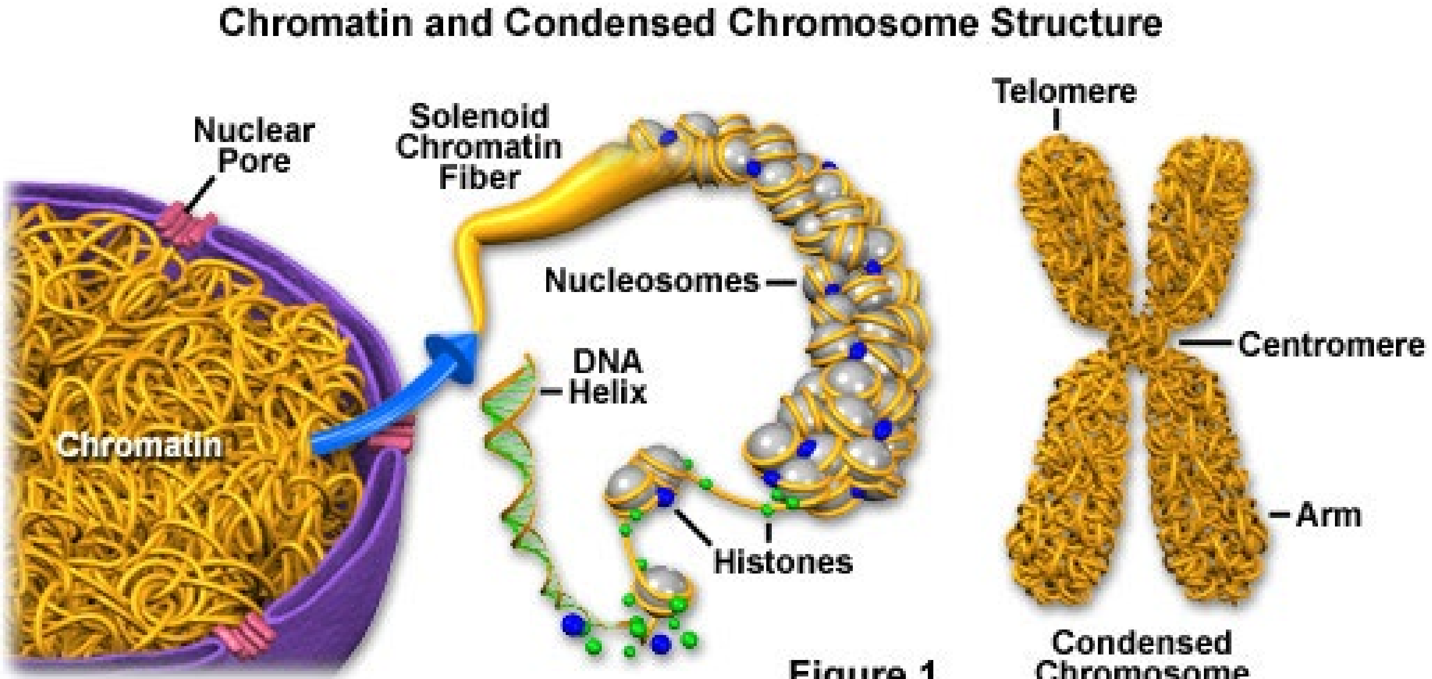
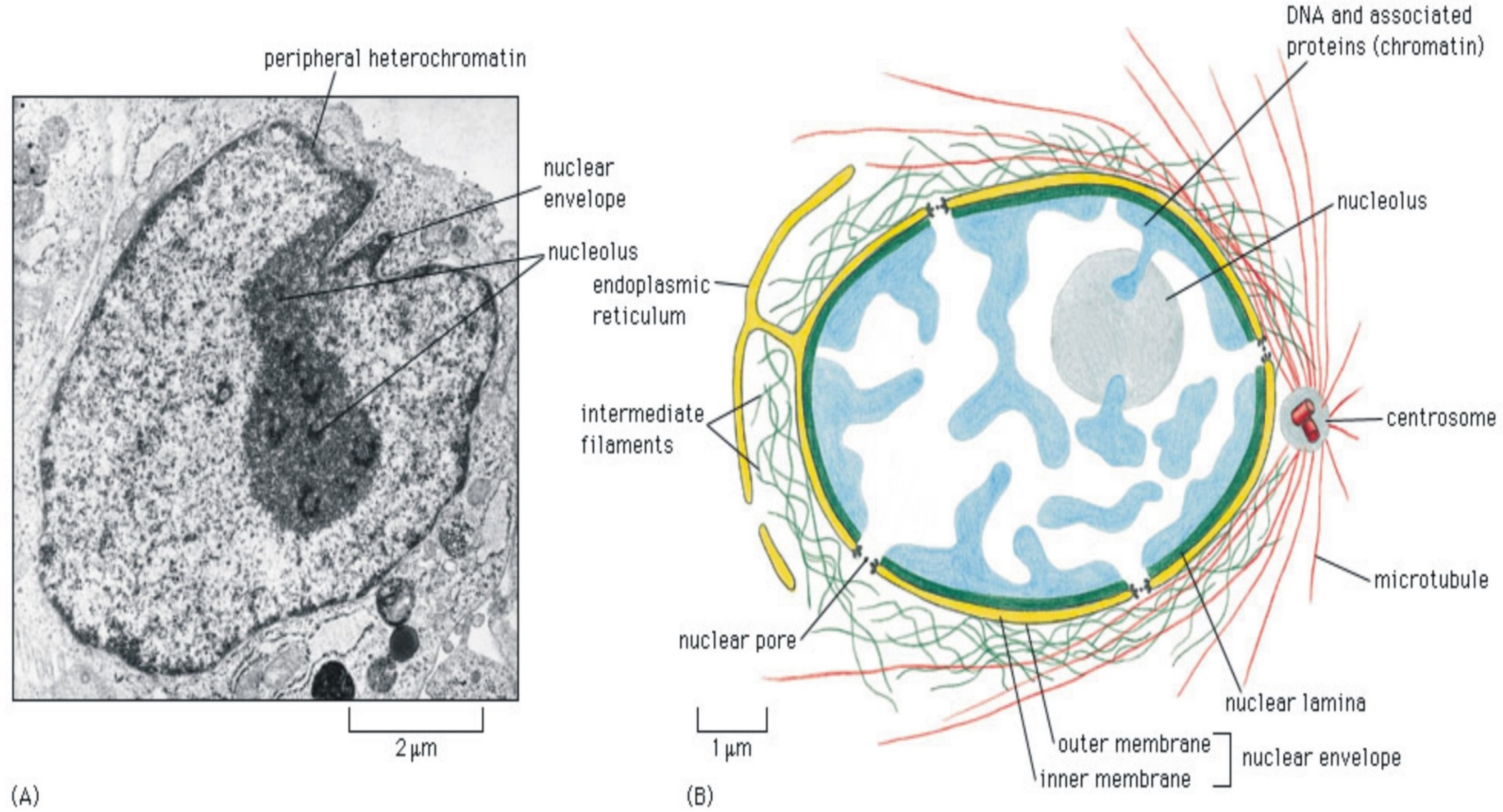


Figure 1

Interphase Nucleus

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



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

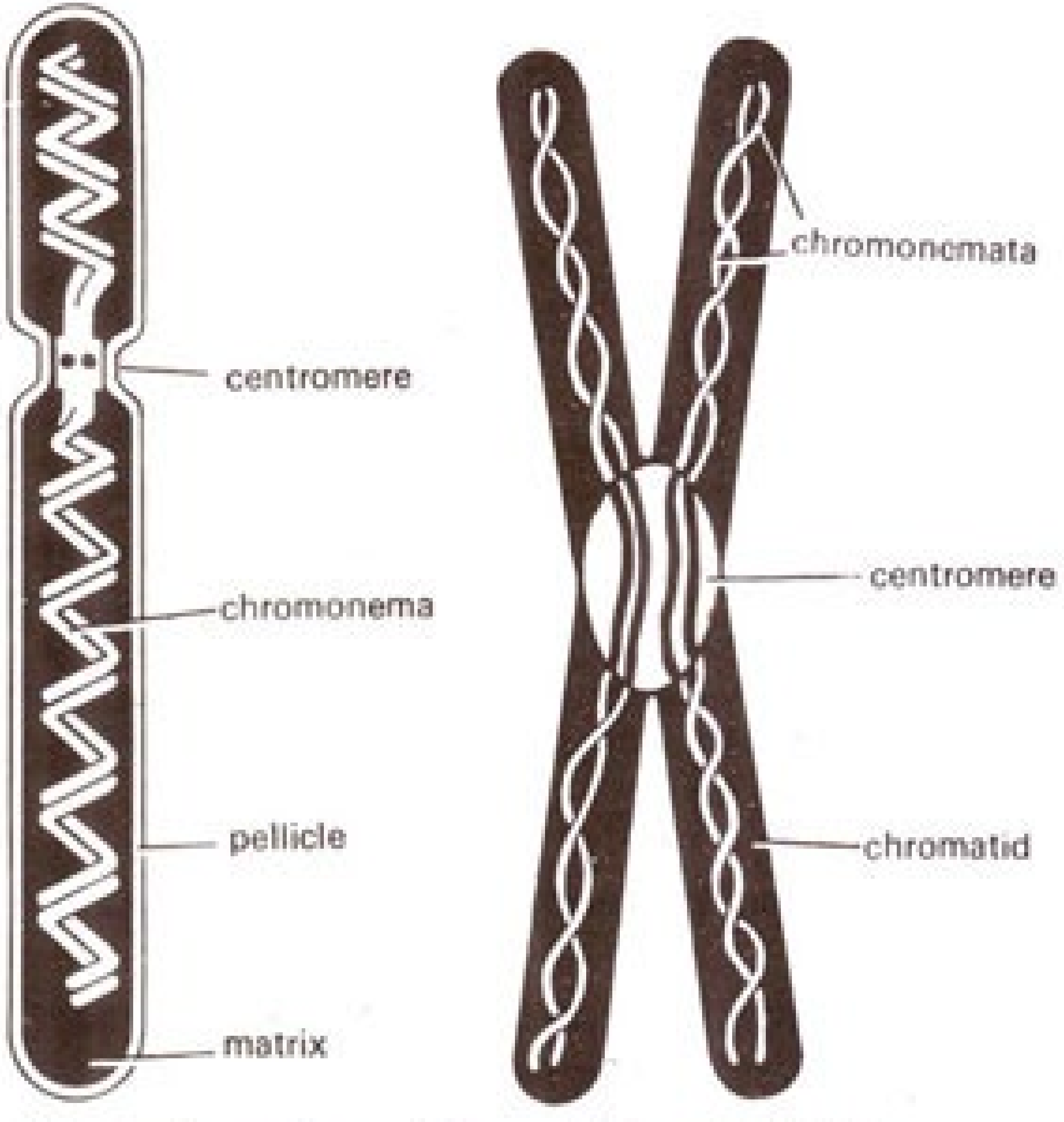
- Tightly packaged DNA
- Found only during cell division
- DNA is not being used for macromolecule synthesis

Chromatin

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

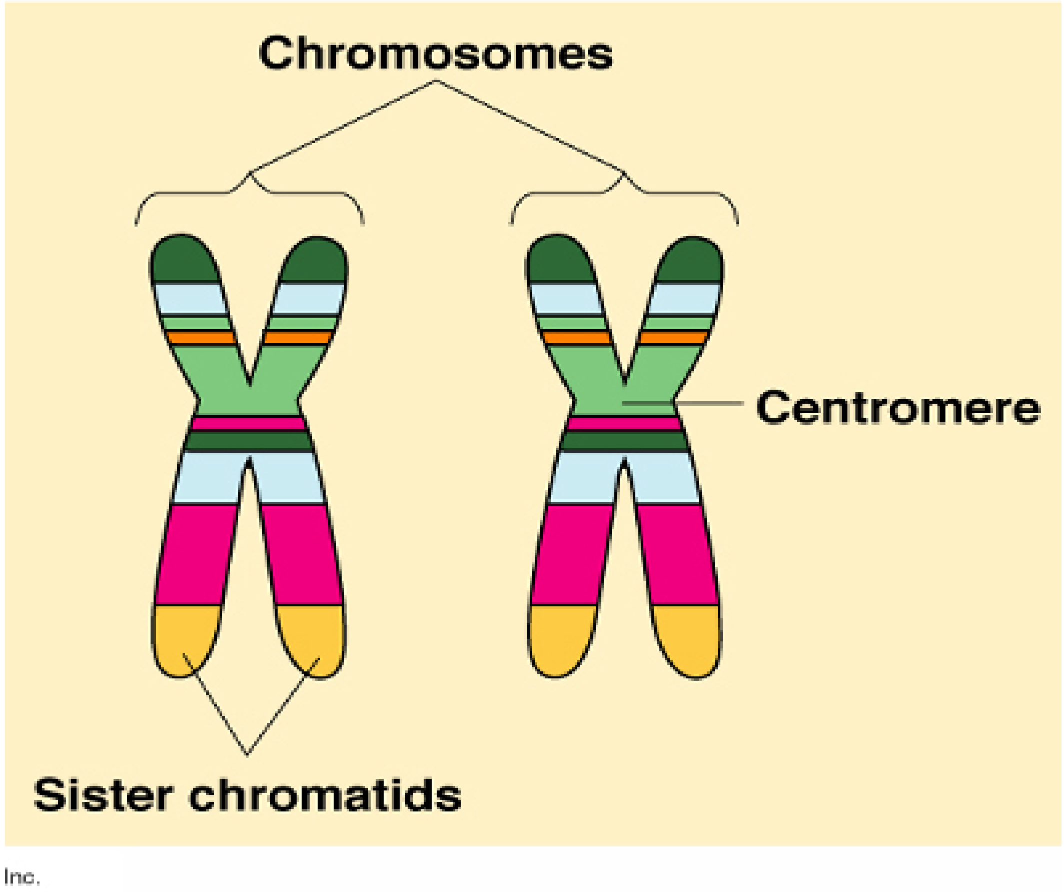
Chromatid:
one copy of a duplicated chromosome

Chromonema / Chromonemata:
central thread of a chromatid

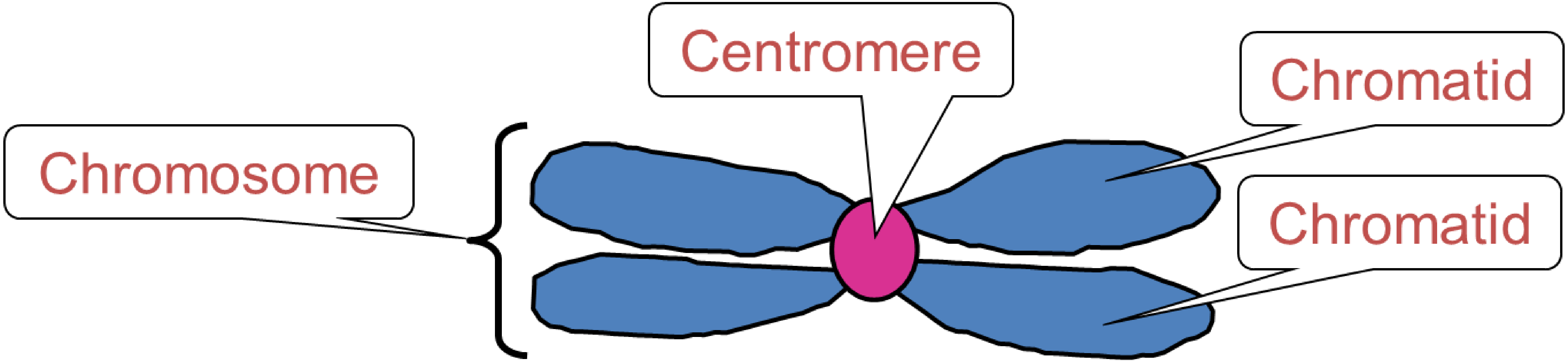


(A) structure of a chromosome

(B) a mitotic metaphase chromosome

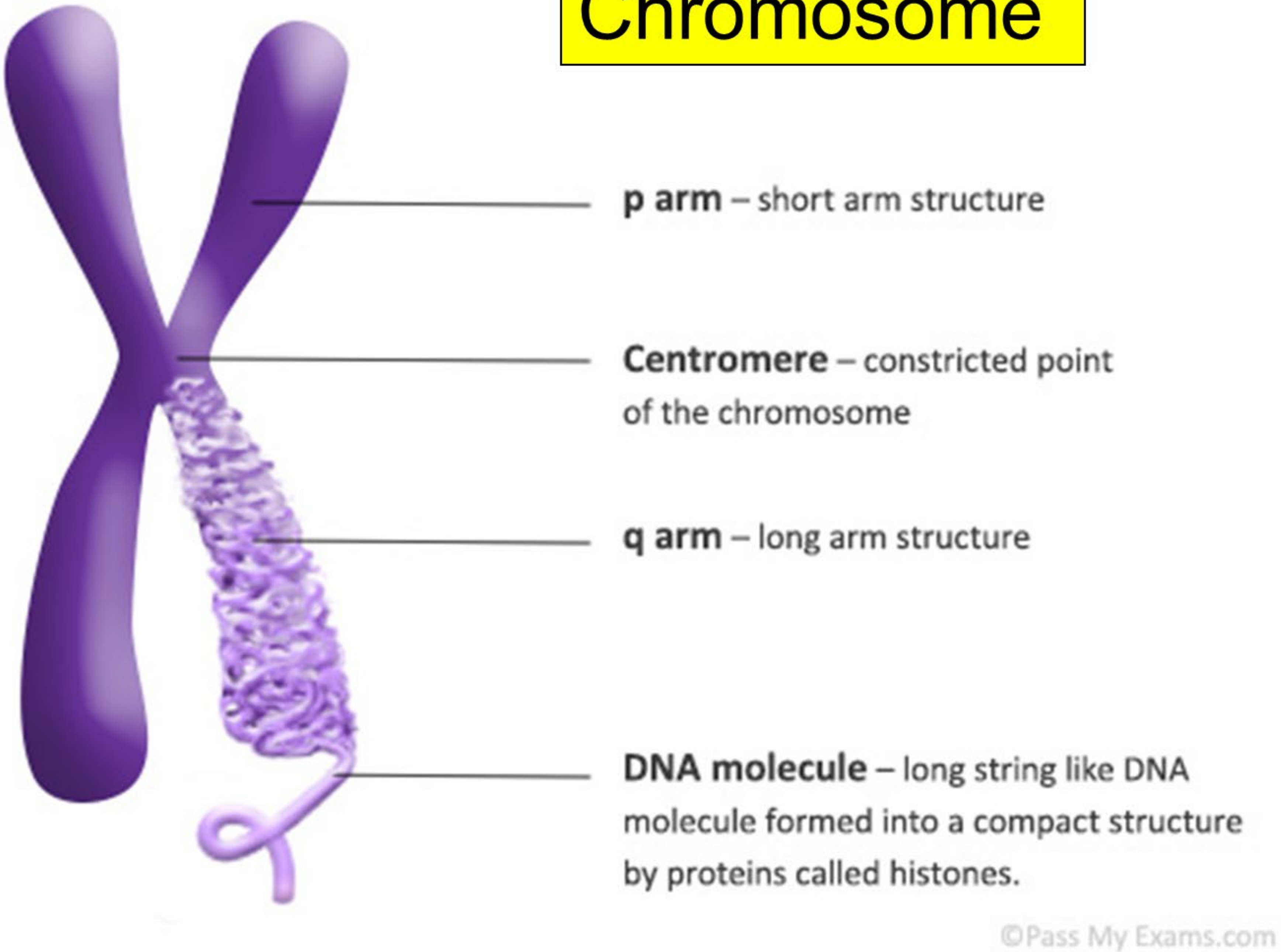


- A chromatid is a chromatid as long as it is held in association with a sister chromatid at the centromere



- 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.
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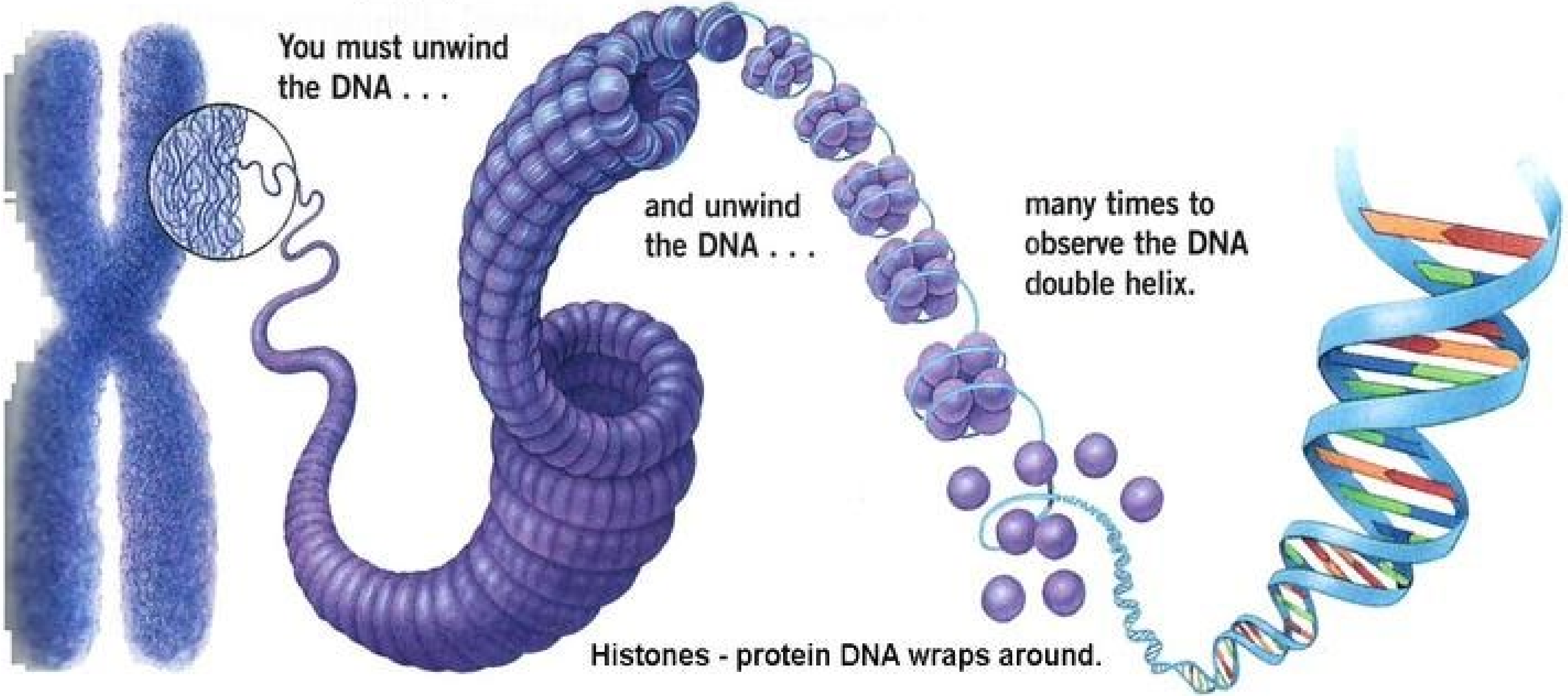
Components of chromosome:

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.

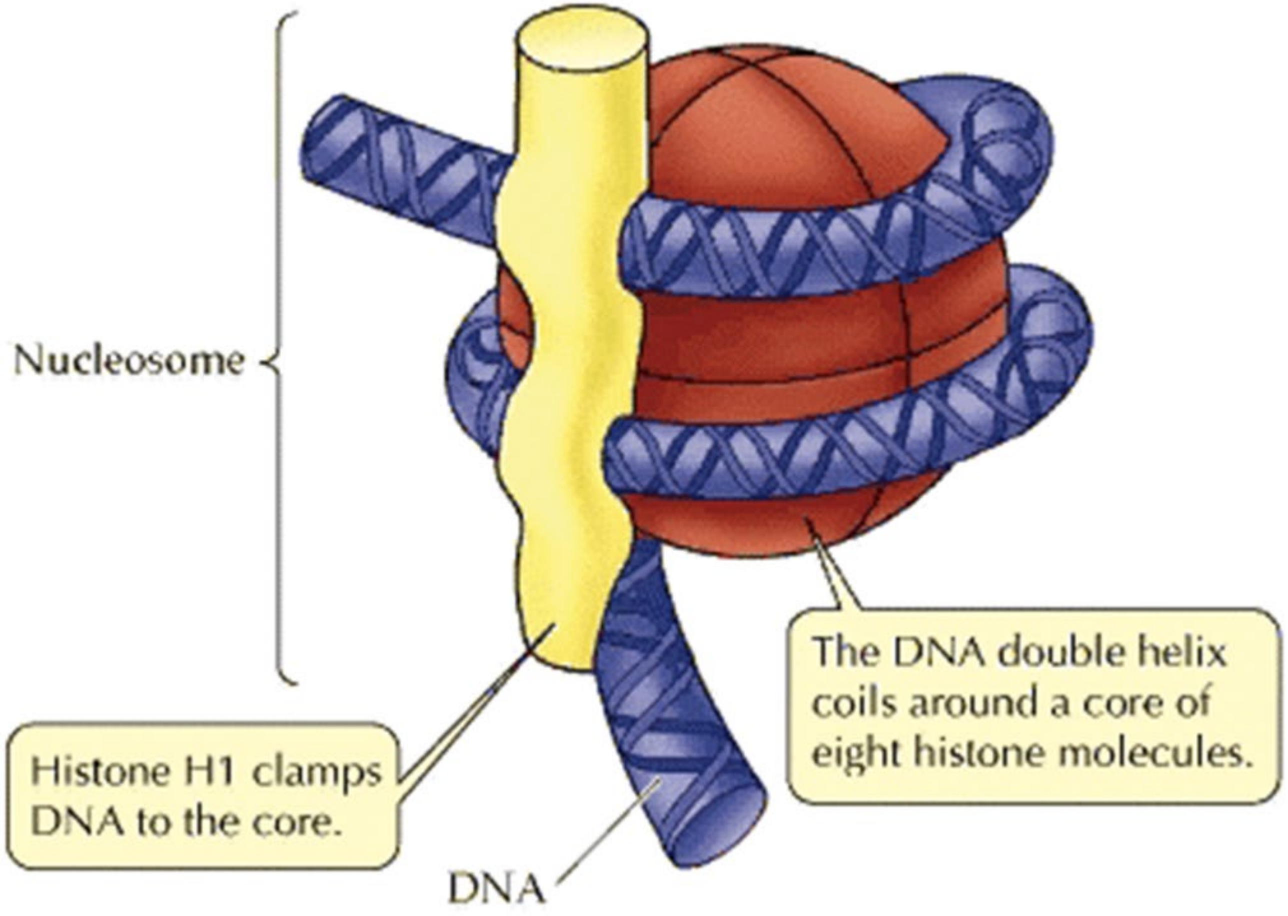
Three levels of chromatin organization

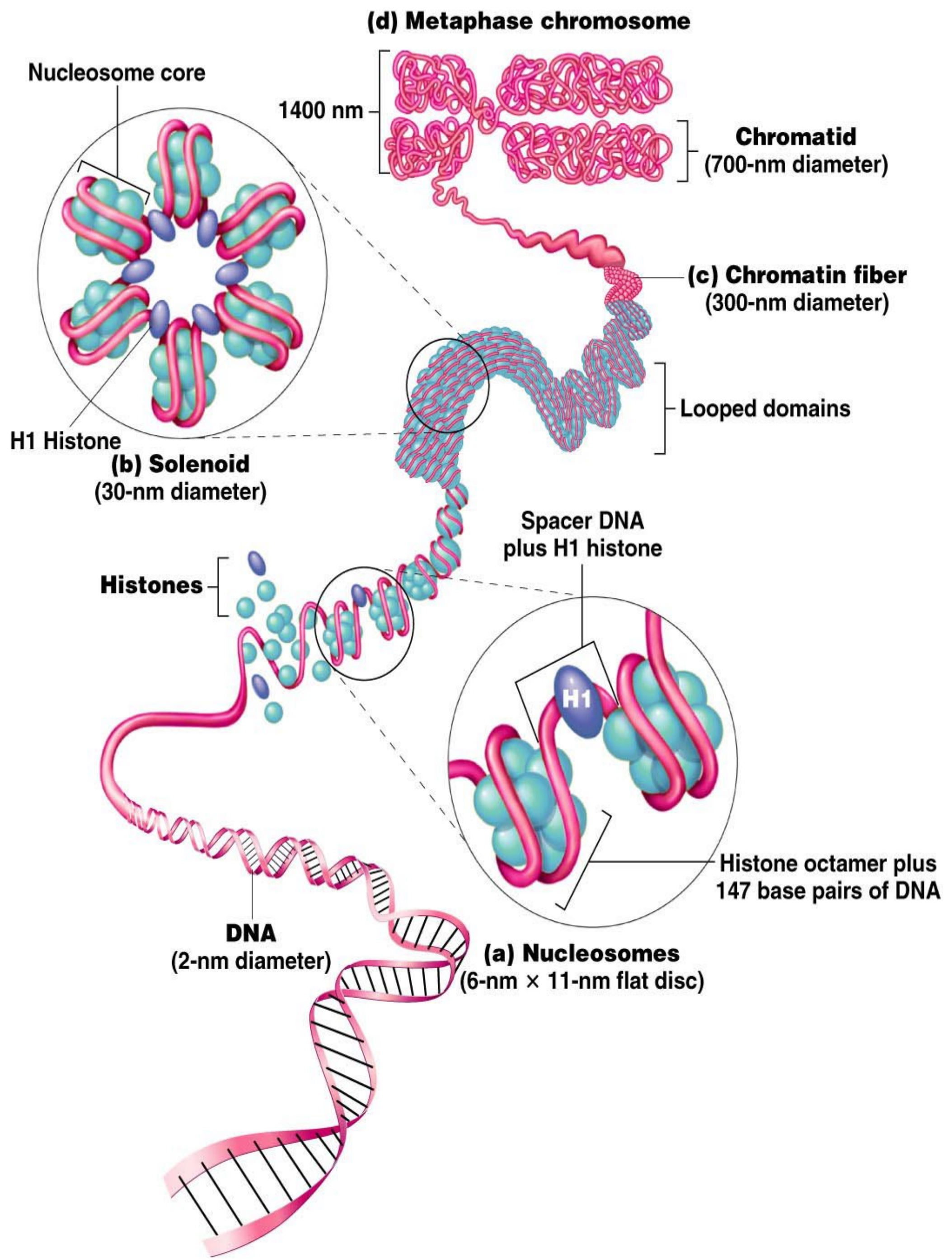
Level 1. DNA wraps around histone proteins forming **nucleosomes**: the "**beads on a string**" structure (euchromatin) **10 nm fiber**.

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).

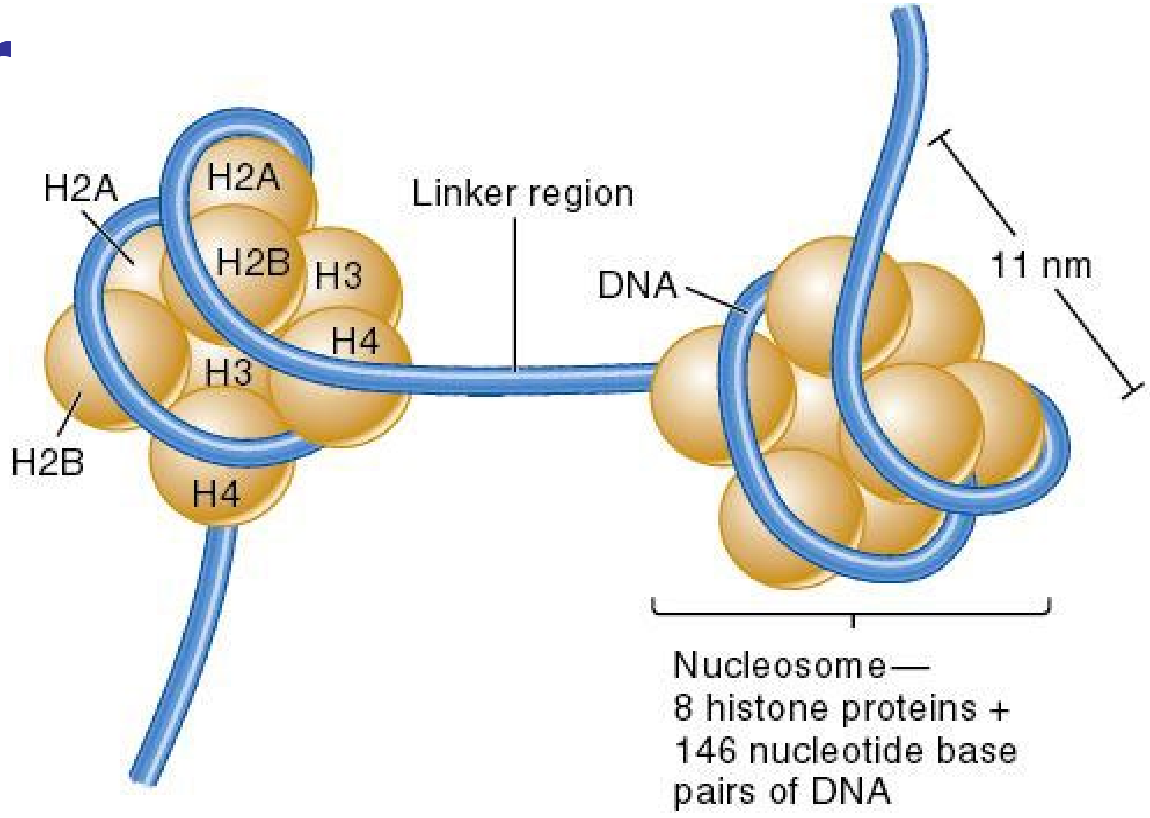
Nucleosomes are condensed several times to form the intact chromatids.

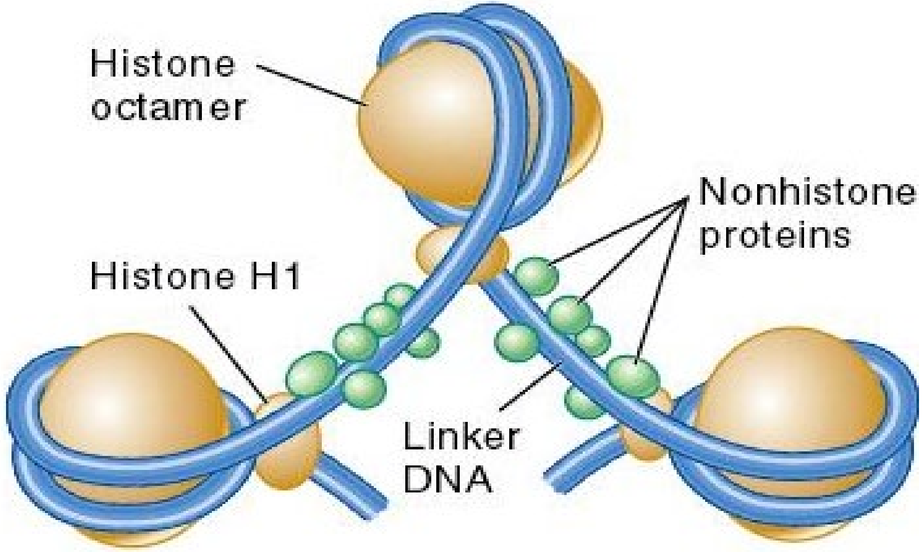




Nucleosomes – 10 nm fiber

- 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**

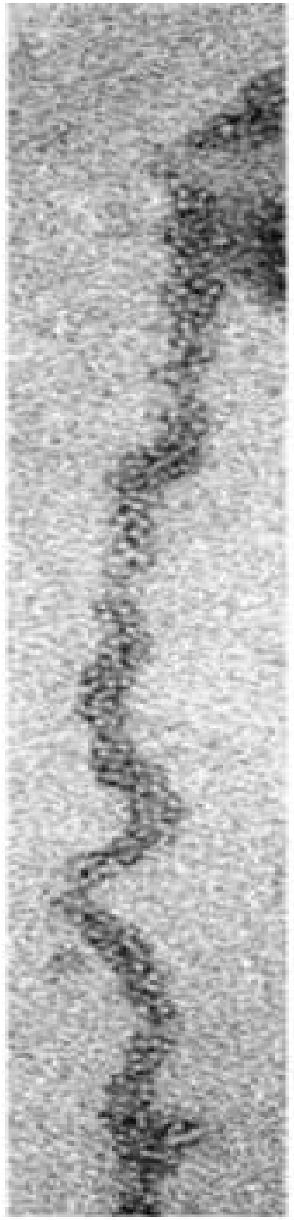
- Nucleosomes associate to form more compact structure - the **30 nm fiber**

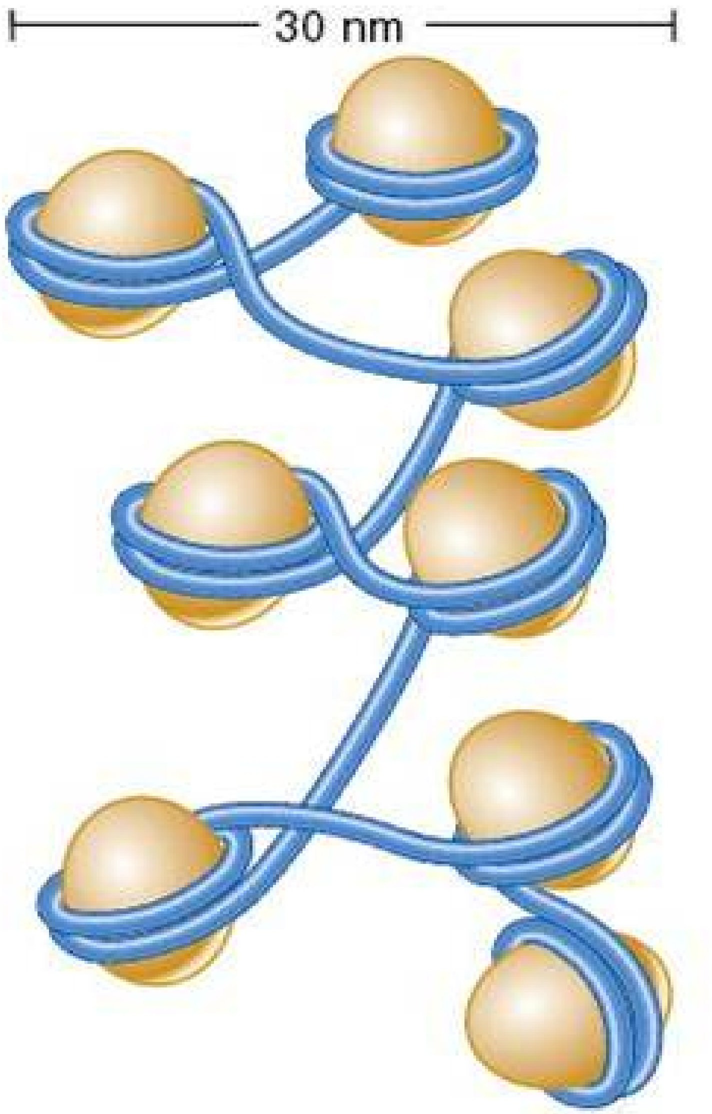
- Histone H1 plays a role in this compaction

Further Compaction of the Chromosome

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

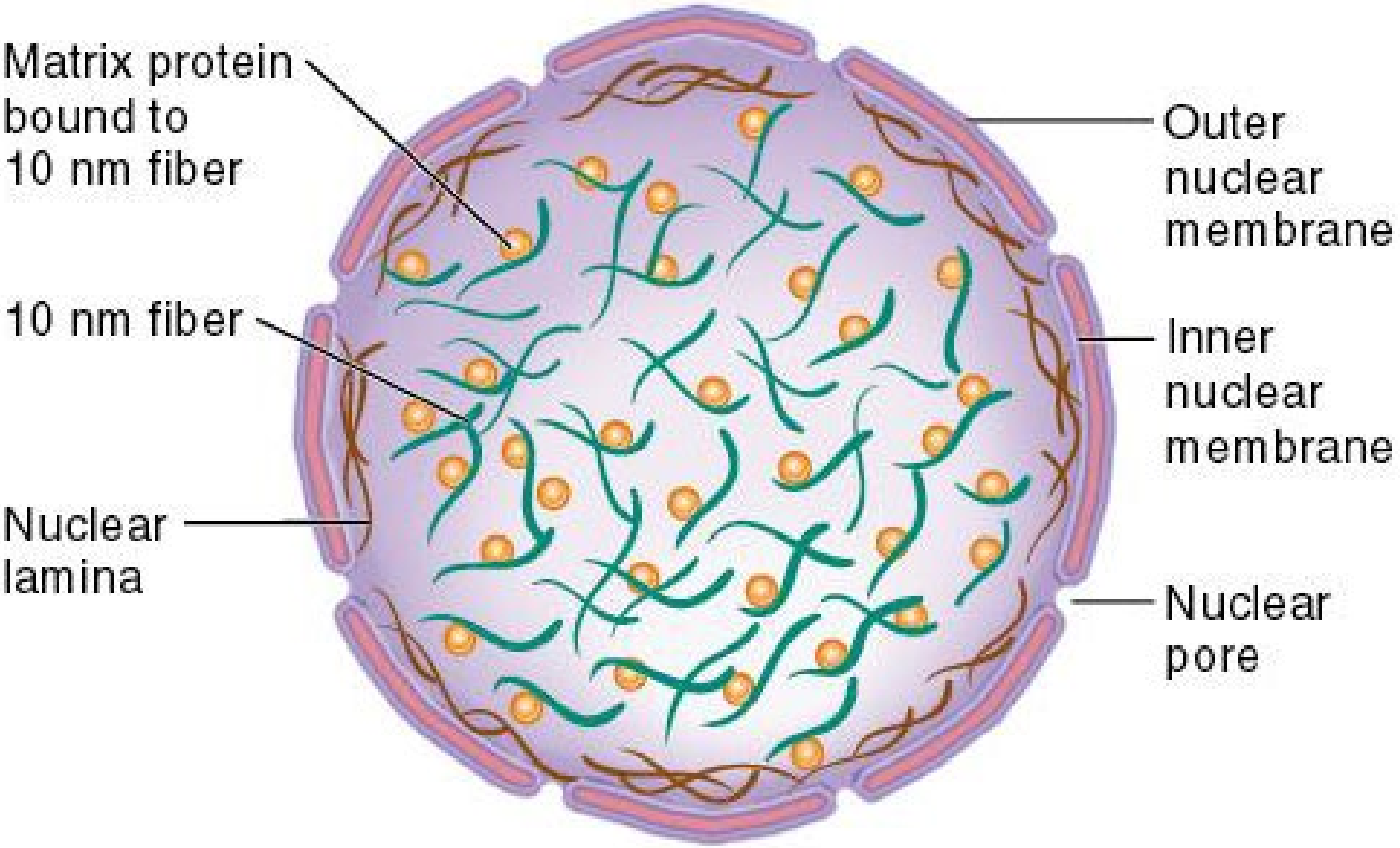
- A third level of compaction involves interaction between the 30 nm fiber and the **nuclear matrix**





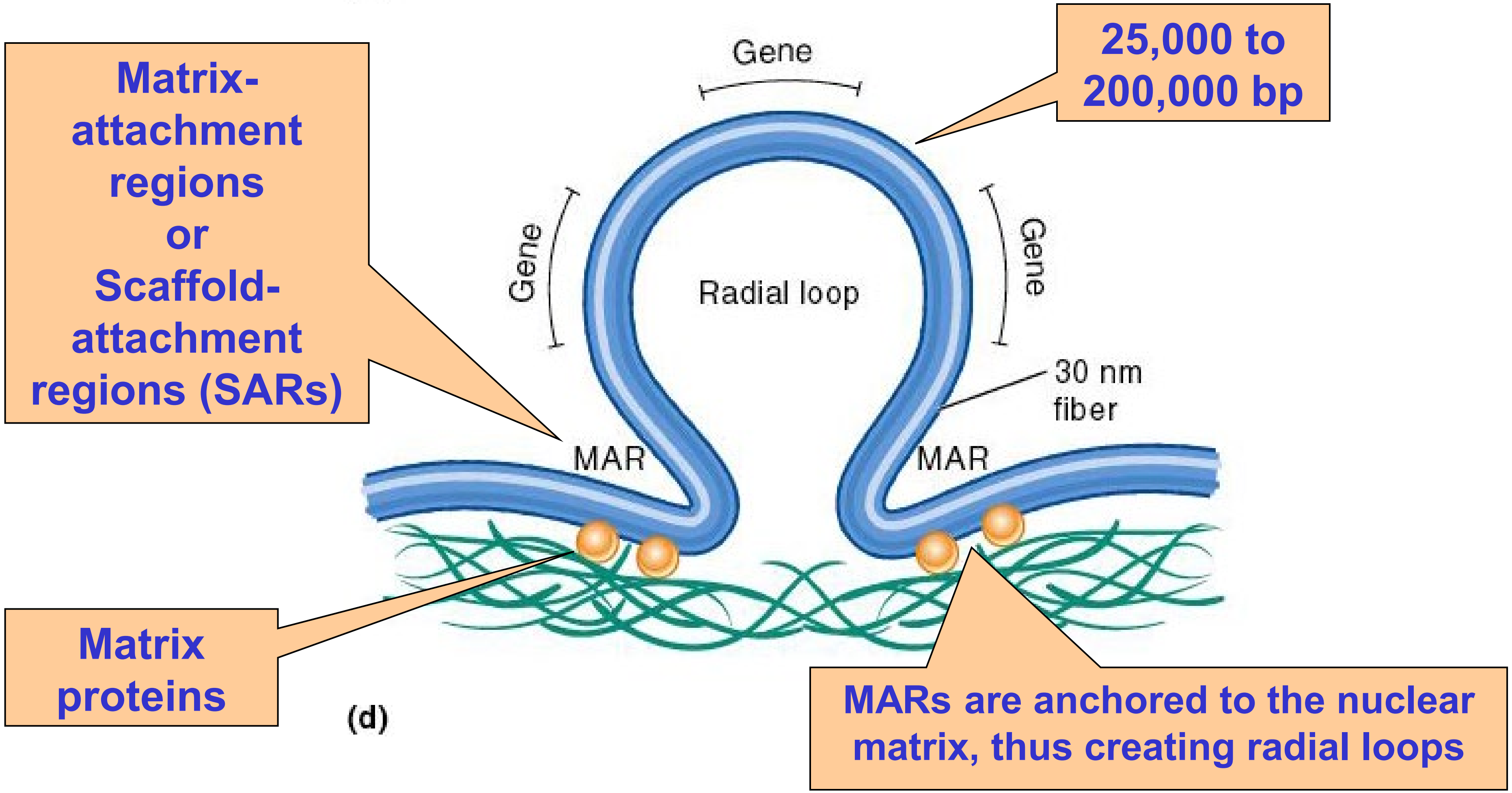
Nuclear Matrix Association

- 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**

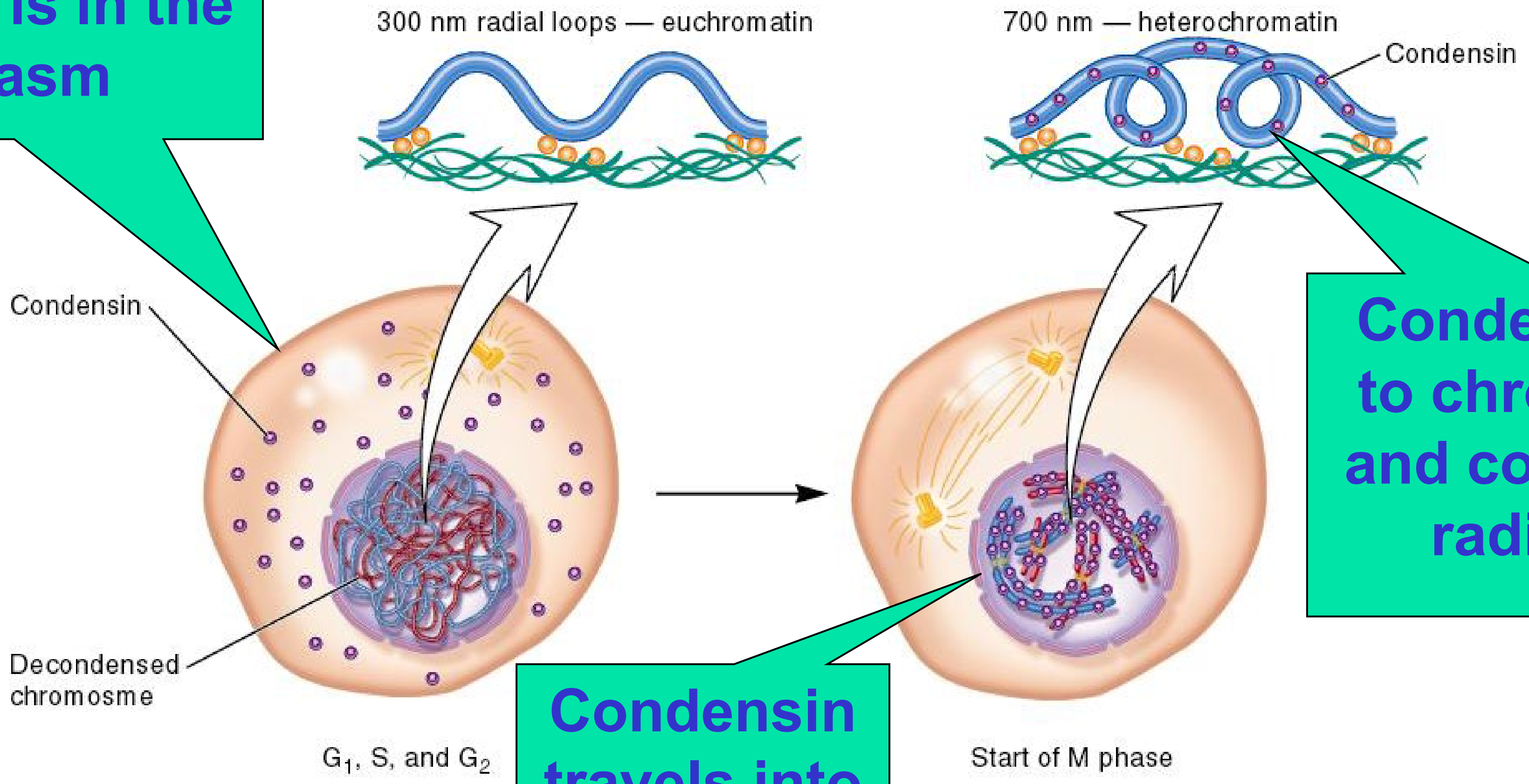
Metaphase Chromosomes

- 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

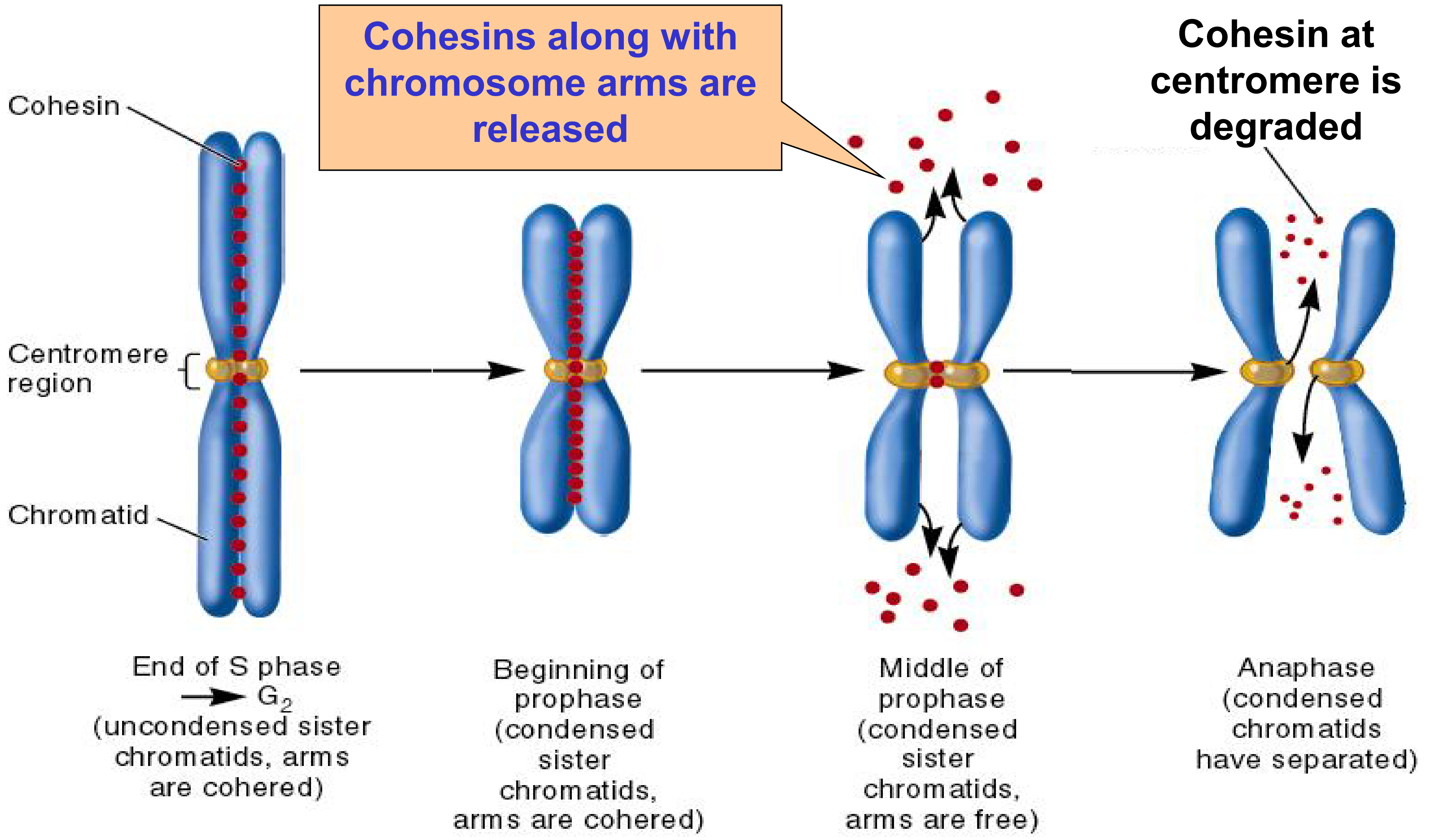


Condensin binds to chromosomes and compacts the radial loops

Condensin travels into the nucleus

The condensation of a metaphase chromosome by condensin.

Chromosomes During Mitosis



The alignment of sister chromatids via cohesin