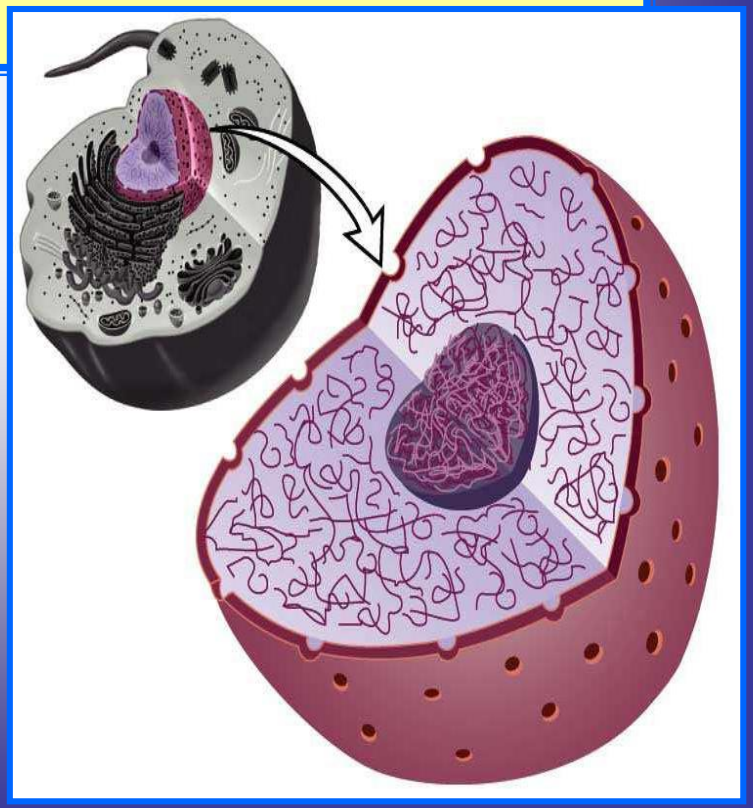
Nucleus

~ 5 µm in diameter

The nucleus is the **headquarters** (**controls** all cell activity) of the cell. It is the most **obvious** organelle

The Nucleus is a **membrane-enclosed** organelle which house most of the **genetic** information and regulatory machinery responsible for providing the cell with its unique characteristics

It is **absent** in mature **erythrocyte**

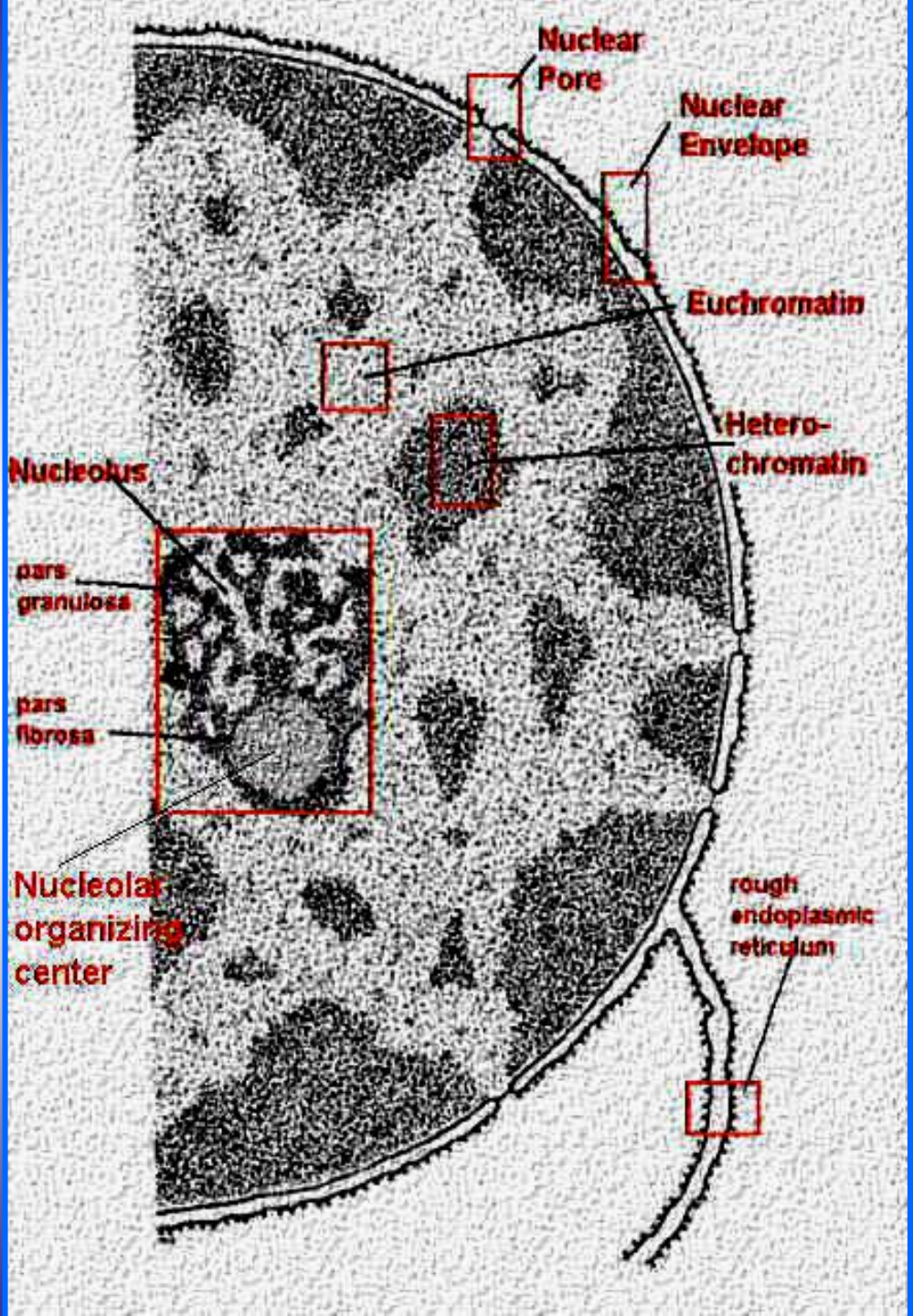


Functions

- It stores the cell's hereditary material (DNA)
- Site of DNA replication
- Site of DNA transcription to mRNA
- Ribosomal formation
  - **Nucleolus**: RNA & protein required for ribosomal synthesis
- It coordinates the cell's activities, which include growth, intermediary metabolism, protein synthesis, and reproduction (cell division) by regulating gene expression.

STRUCTURE

1. **Nuclear envelope, double membrane and nuclear pores**
2. **Nucleoplasm**
3. **Chromatin** Chromatin, Chromosome, DNA and RNA
4. **Nucleolus (concentrated area of chromatin, RNA and proteins)**

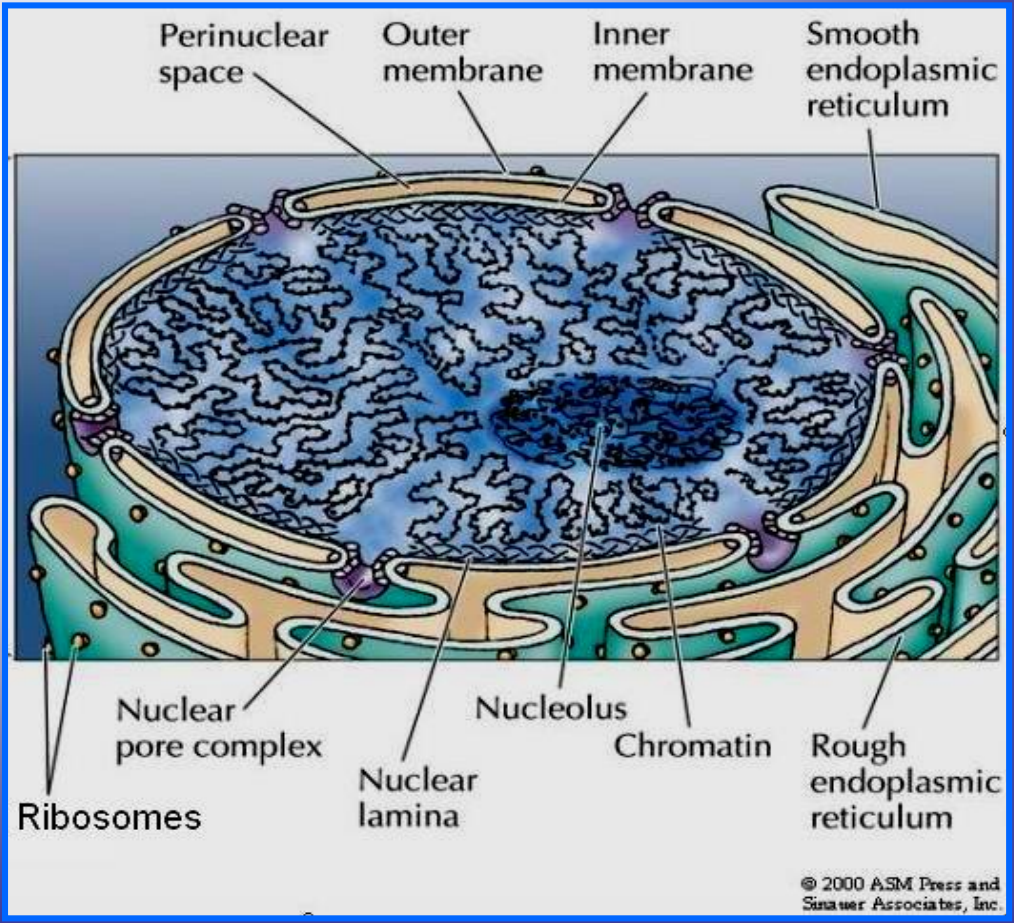


Nuclear envelope (Nucleolemm)

- Separates the enclosed nuclear compartment from cytoplasm
- Maintains the shape of nucleus
- Controls exchanges between nucleus and cytoplasm
- Important role in organization of nucleus content

Structure

- External (outer) nuclear membrane
- Internal (inner) nuclear membrane
- Perinuclear space
- Lamina densa (nuclear lamina)
- Nuclear pores



External nuclear membrane

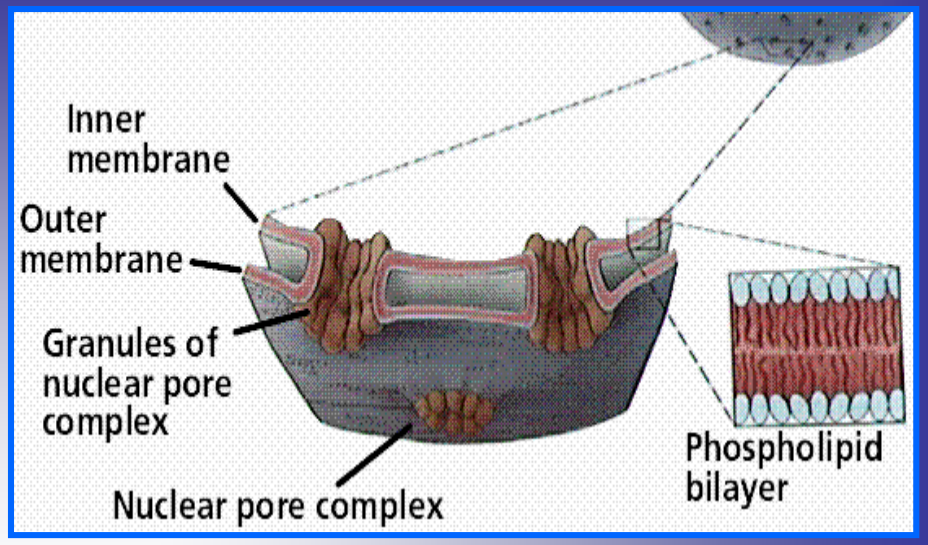
- Fluid mosaic (**lipid bilayer** of ~ 7 nm thick with **70% proteins**)
- Visible only by electron microscopy
- Ribosome attached on external face
- It **continues** with RER membrane

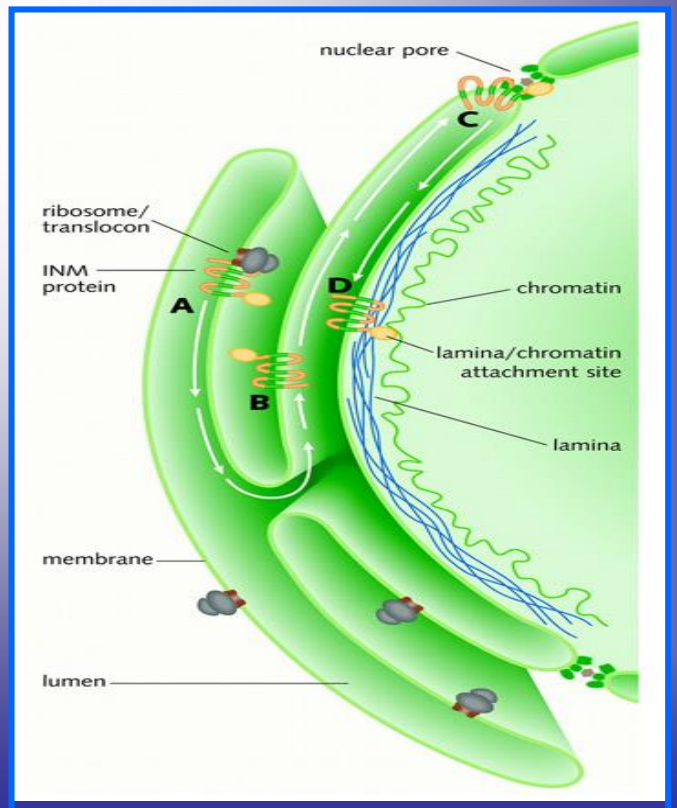
The perinuclear space

- 10-40 nm
- It **communicates** with the RER internal space
- Contains the same molecules as RER
- Contains **Ca2**+

Internal nuclear membrane

- Fluid mosaic (**lipid bilayer**)
- Visible only by electron microscopy;
- The inner surface of the nuclear envelop is bound to a thin filamentous network (*lamins polypeptides*) called the **nuclear lamina.**

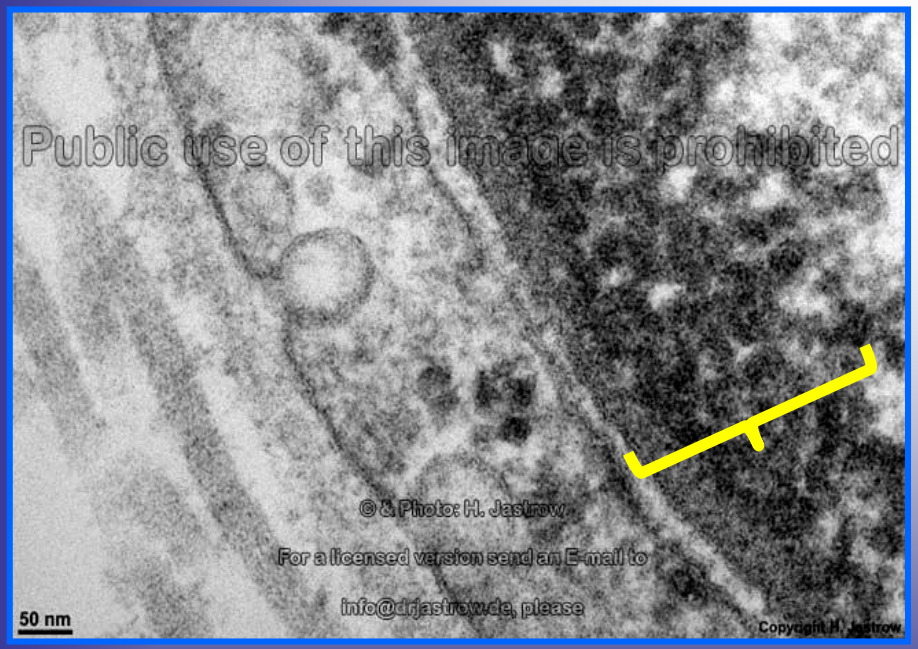


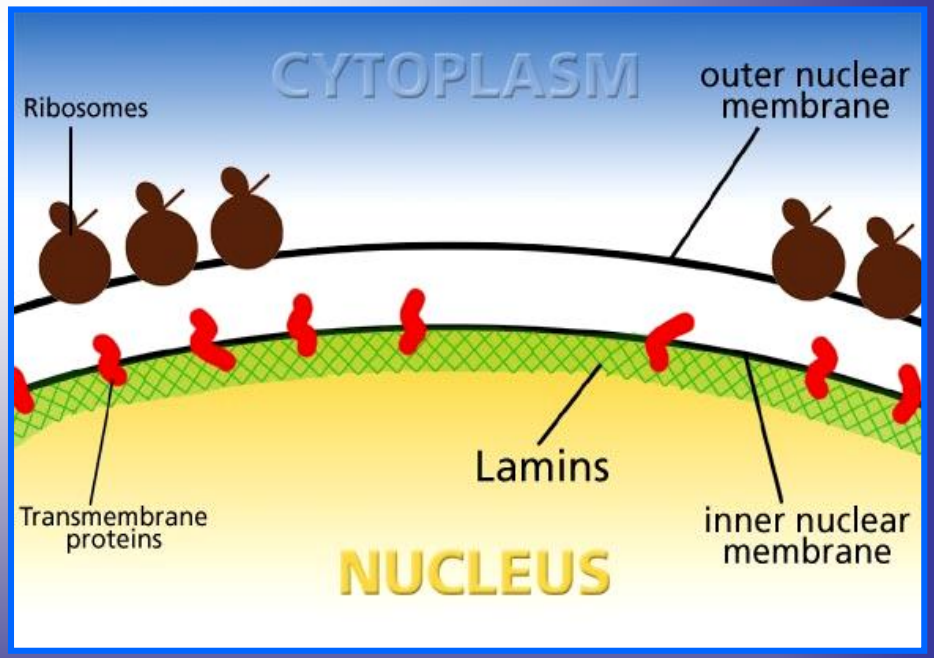


Nuclear lamina

a network of **intermediate filaments** composed of various **lamins**

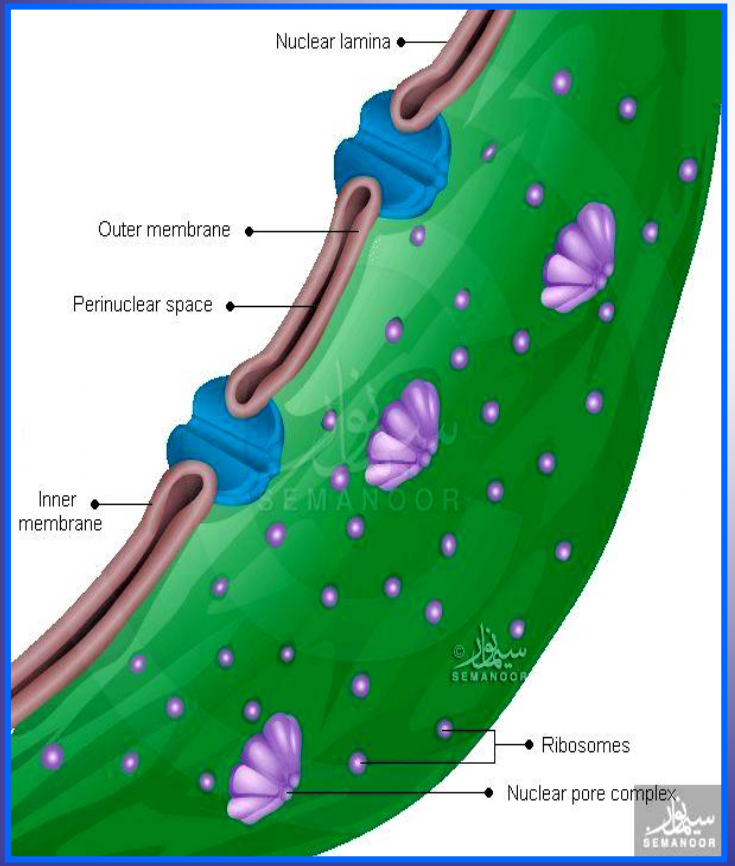
The lamina acts as a site of **attachmen**t for chromosomes and provides structural **stability** to the nucleus. The lamins have been associated with **various genetic** disorders collectively termed **laminopathies (**e.g. a rare form of muscular dystrophy).

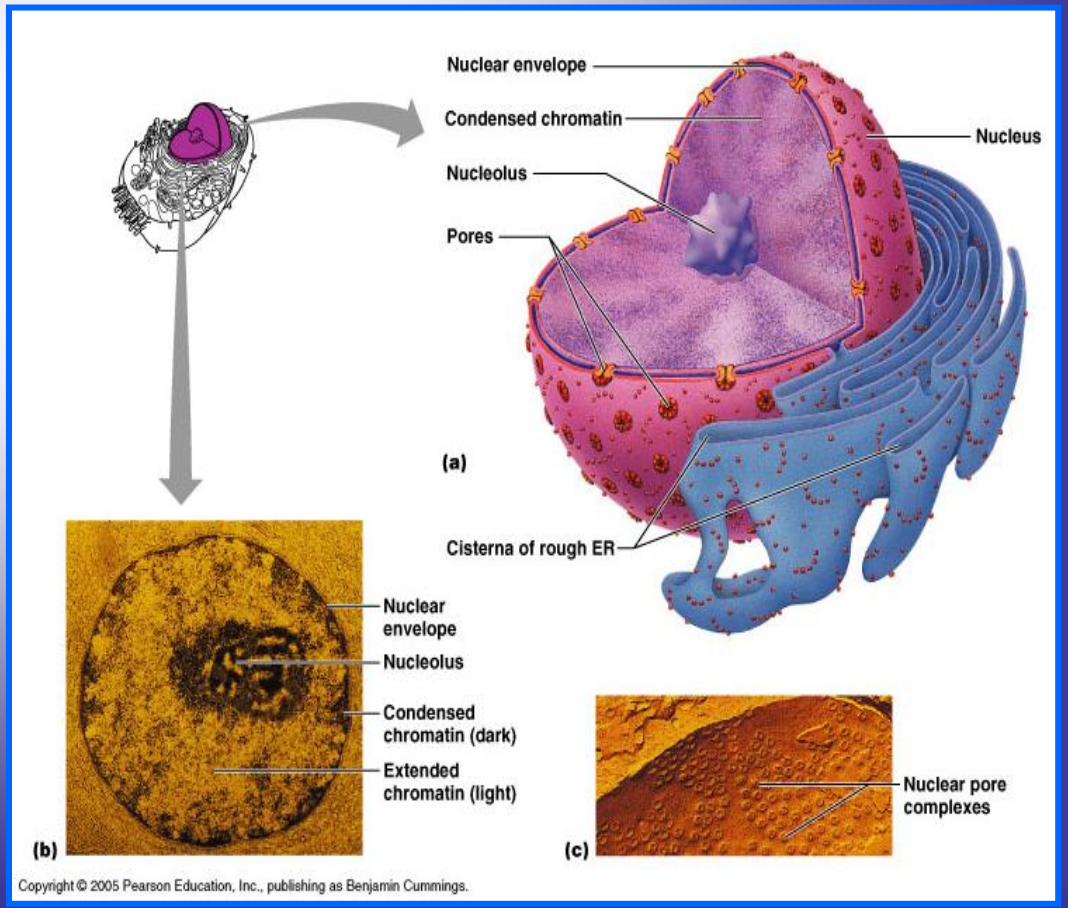


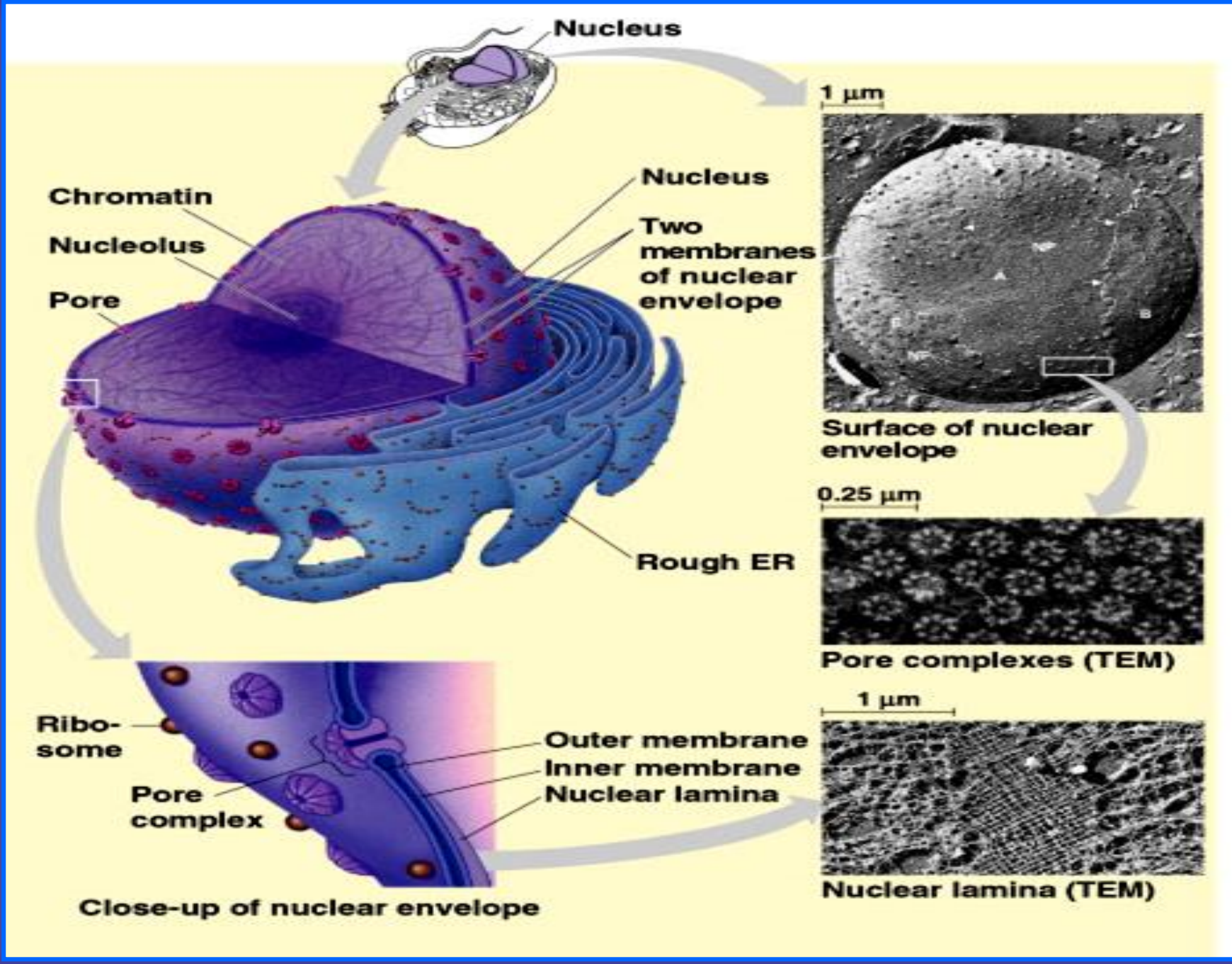


THE NUCLEAR PORE

- Openings in the nuclear envelope, diameter about **10nm**
- Area where the nuclear envelope is **interrupted**
- Regulates **exchanges** between nucleus and cytoplasm
- Ensures the selective **transport** for big molecules
- There are 3000-4000 nuclear pores (10 pores/μm2)
- **Dynamic** structures – their number grows if it's necessary

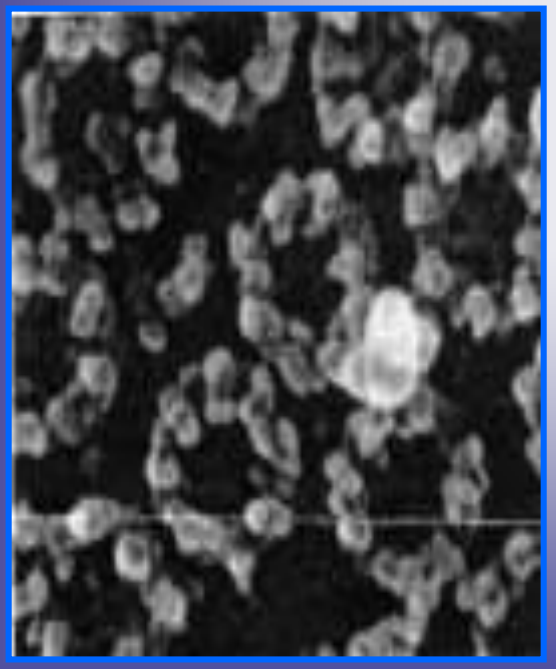




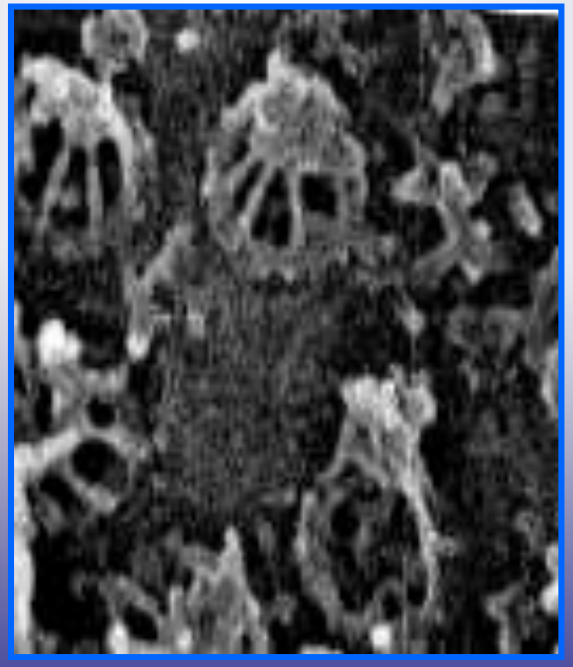

Nucleus
Chromatin
Nucleolus
Pore
Nucleus
Two membranes of nuclear envelope
Rough ER
1 µm
Surface of nuclear envelope
0.25 µm
Pore complexes (TEM)
Ribo-some
Pore complex
Outer membrane
Inner membrane
Nuclear lamina
Close-up of nuclear envelope
1 µm
Nuclear lamina (TEM)

•The nuclear pores are the gateways across which movement of **RNAs** and **proteins** takes place between the nucleus and cytoplasm in both direction.
•Proteins synthesized in the cytoplasm cross the nuclear envelop to initiate replication and transcription of genetic material. Similarly, mRNA, tRNA and ribosomal subunits built in the nucleus cross through the nuclear pores to the cytoplasm**.**

The Nuclear Pore Complex



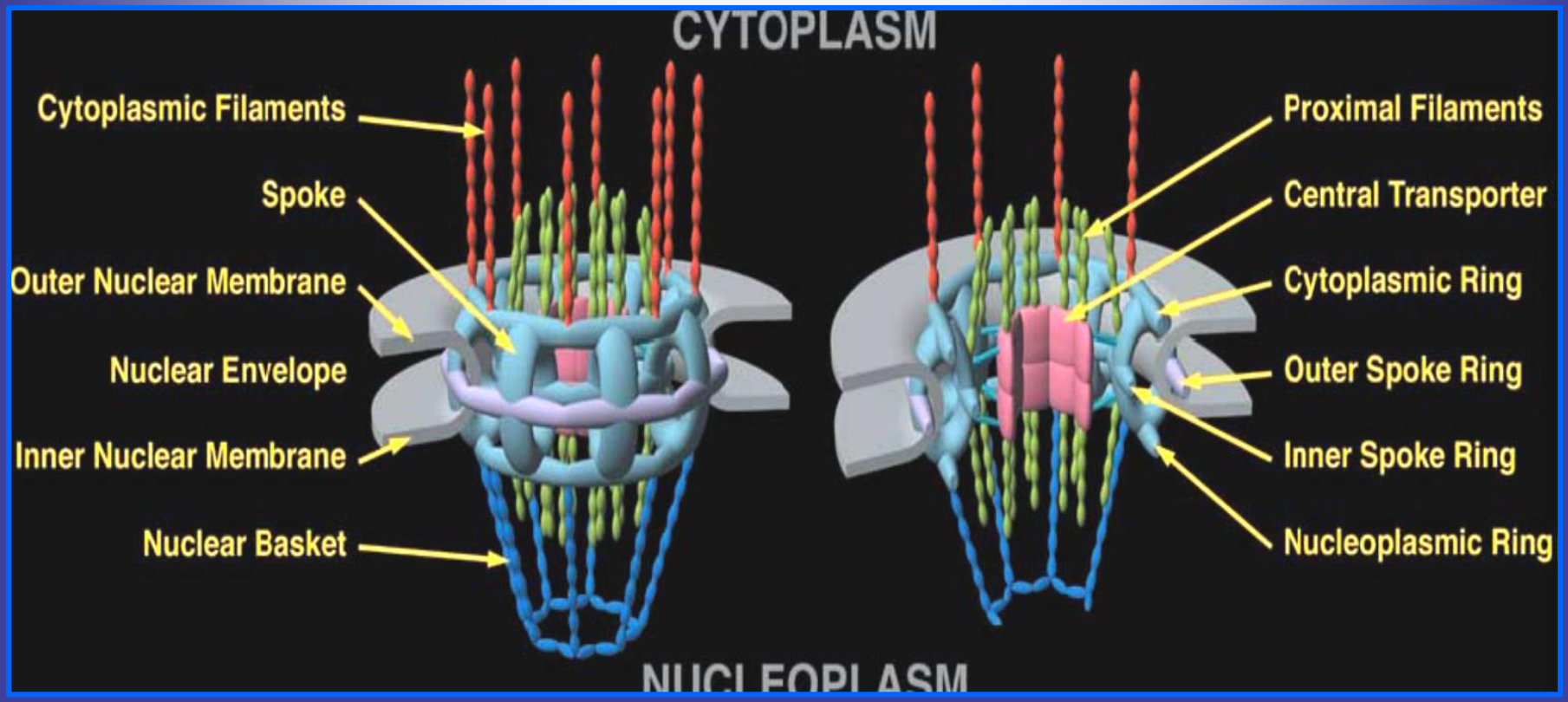
Cytoplasmic face



Nuclear face

- **Octagonal** symmetry
- **8** (octagonal) fold repetition of **glycoprotein** subunits (**Nucleoporins** or **Nups**)
- Nucleoporins: **symmetrical** on cytoplasmic and nuclear sides

Nucleoplasm	**Nuclear Membrane**	**Cytoplasm**
Nuclear Basket	Central Transporter	Cytoplasmic Ring
Nuclear Ring	Spoke Ring (inner & outer)	Cytoplasmic Filaments
Filaments		



Nuclear transport

The entry and exit of **large** molecules from the cell nucleus is **tightly controlled** by the nuclear pore complexes (NPCs). Although **small molecules** can enter the nucleus **without** regulation. Macromolecules such as RNA and proteins require association with **importins** proteins to enter the nucleus and **exportins** to exit

Nuclear Import

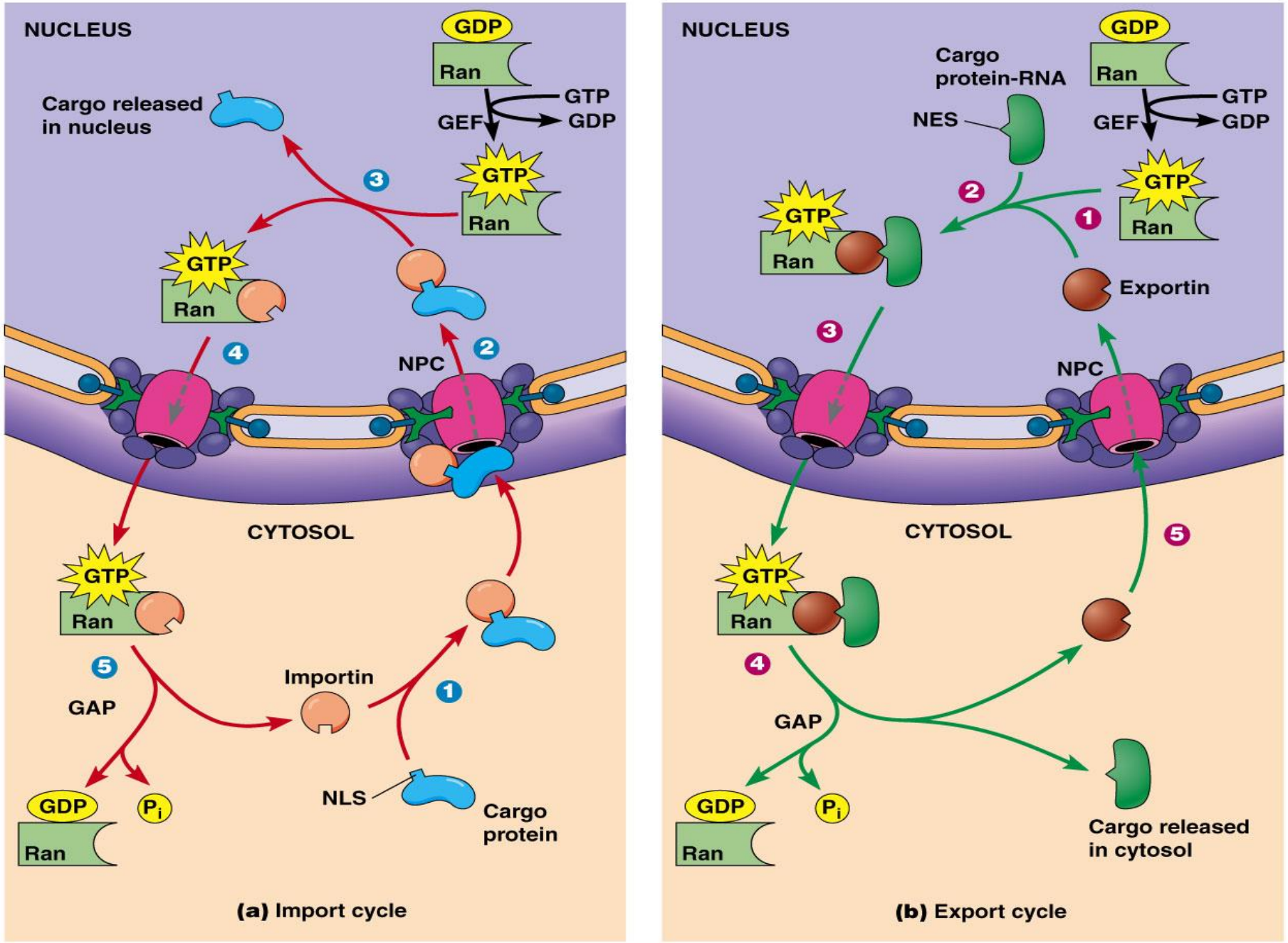
To get materials into the nucleus there is amino acid tag (zip code) called **nuclear localization signals** (NLS) added onto molecules and are assisted by proteins called **importins**

Once inside the nucleus, **interaction** with Ran-GTP causes a conformational change in the importin that causes it to **dissociate** from its cargo

{RANs are hydrolase enzymes that can bind and hydrolyze guanosine triphosphate (GTP)} ***Ran*** *(**RA**s-related **N**uclear protein)*

Nuclear Export

Nuclear export roughly **reverses** the import process; in the nucleus, the **exportin** binds the **cargo** and **Ran-GTP** and diffuses through the pore to the cytoplasm carrying **nuclear export signals** (NES) or the zip code bound by **exportins**. The complex can diffuse to the cytoplasm where GTP is hydrolyzed and the NES-protein is released
Hence, whereas **importins** depend on Ran-GTP to **dissociate** from their cargo, **exportins** require Ran-GTP in order to **bind** to their cargo.

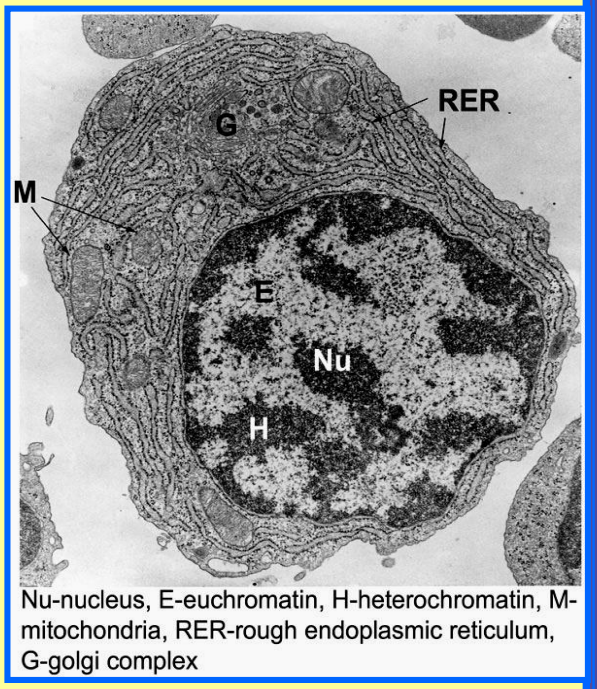


Nucleoplasm **(nucleus sap) or karyoplasm**

- **Analogy** with cytoplasm, that part of the nuclear contents other than the nucleolus.
- Highly **viscous** liquid that surrounds the chromosomes and nucleolus
- Many substances such as **nucleotides** and **enzymes** are dissolved in the nucleoplasm
- A network of **fibers** known as the **nuclear matrix** can also found in the nucleoplasm

CHROMATIN

Is the combination of **DNA** and **proteins** (**ratio 1:1**) that make up the contents of the nucleus of a cell, that is usually **dispersed** in the **interphase** and condensed to form **chromosomes** in mitosis and meiosis.



Nu-nucleus, E-euchromatin, H-heterochromatin, M-mitochondria, RER-rough endoplasmic reticulum, G-golgi complex

Functions

- Package DNA into a smaller volume to fit in the cell
- Strengthen and repair the DNA to allow mitosis and meiosis i.e. prevent DNA damage
- Regulate gene expression (transcription) and DNA replication

Types (During **interphase** // **no** cell division)

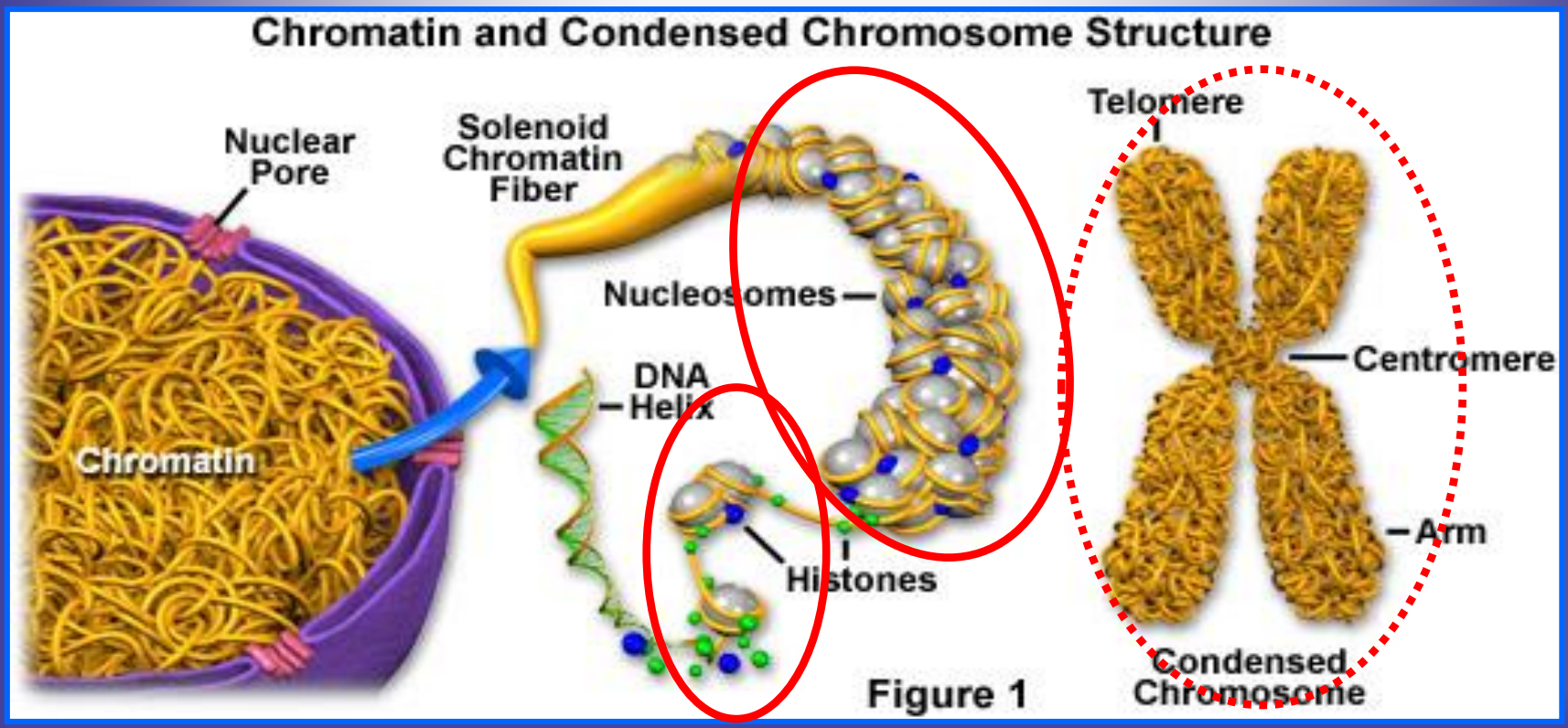
1- Euchromatin: is a **lightly packed** (**less dense**) form of chromatin that is **rich** in gene concentration, and is often under **active transcription**. It is found in both eukaryotes and prokaryotes.

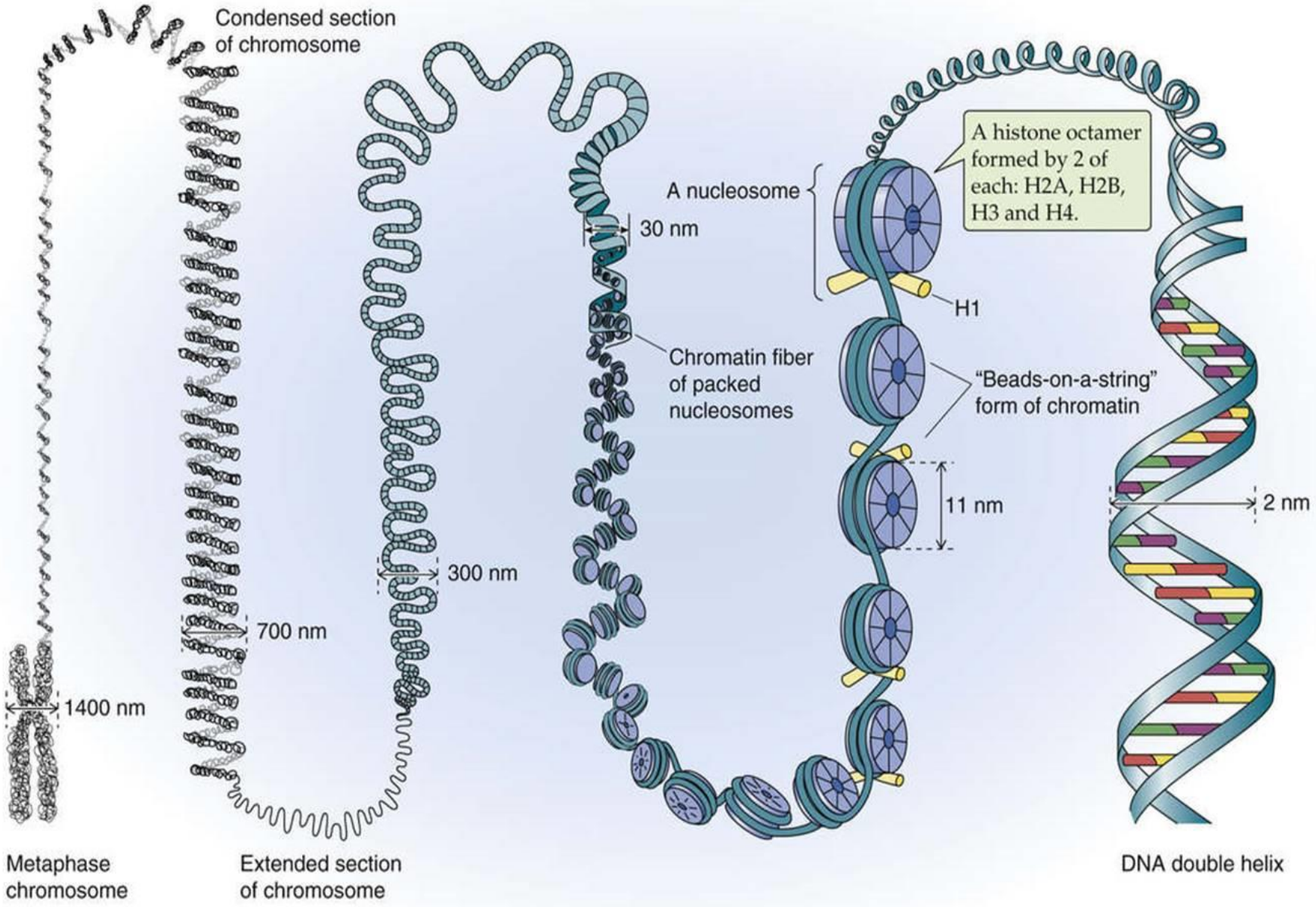
2- Hetrochromatin: is a **tightly packed** (**dense**) form of DNA that is **inactive (no transcription)** and remains compact during interphase. Heterochromatin plays a role in **gene regulation** and the **protection** of the integrity of chromosomes

LEVELS OF CHROMATIN ORGANIZATION (Chromatin Packing)

In general terms, there are three levels of chromatin organization:

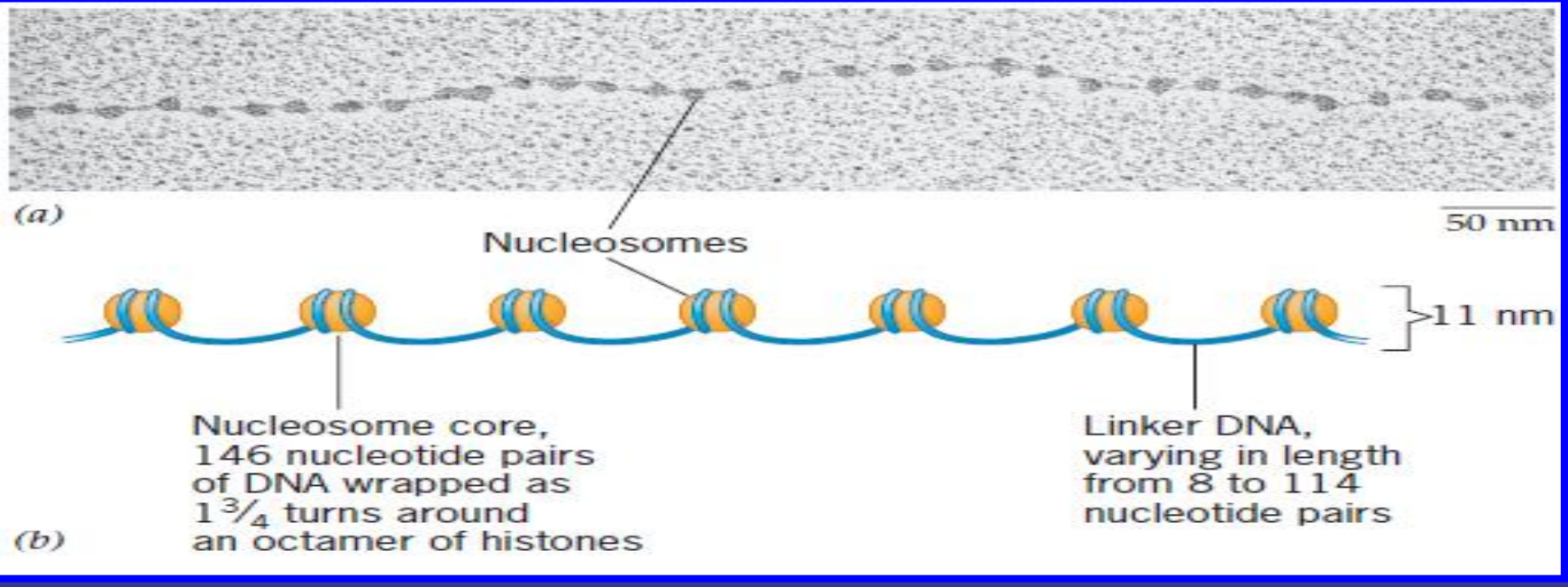
1. the "**beads on a string**" structure, **DNA** wraps around **histone** proteins forming **nucleosomes**
2. **30 nm fiber**, chromatin appears in **interphase** cells as tiny dots and fibers of 30 nm thickness
3. Higher-level DNA packaging of the 30 nm fibre into the **metaphase chromosome** (during mitosis and meiosis).

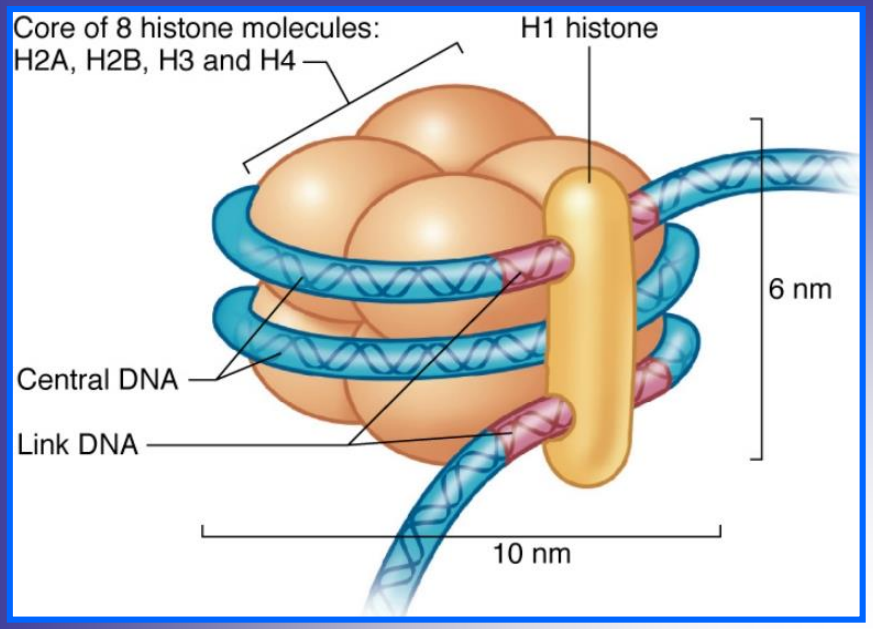


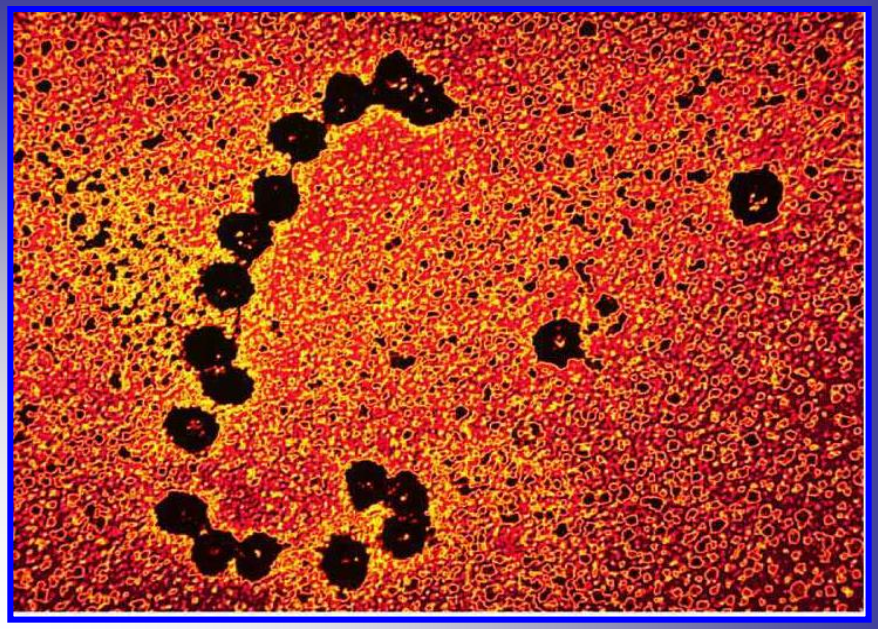

Condensed section of chromosome
1400 nm
700 nm
300 nm
30 nm
A nucleosome
A histone octamer formed by 2 of each: H2A, H2B, H3 and H4.
H1
Chromatin fiber of packed nucleosomes
"Beads-on-a-string" form of chromatin
11 nm
2 nm
Metaphase chromosome
Extended section of chromosome
DNA double helix

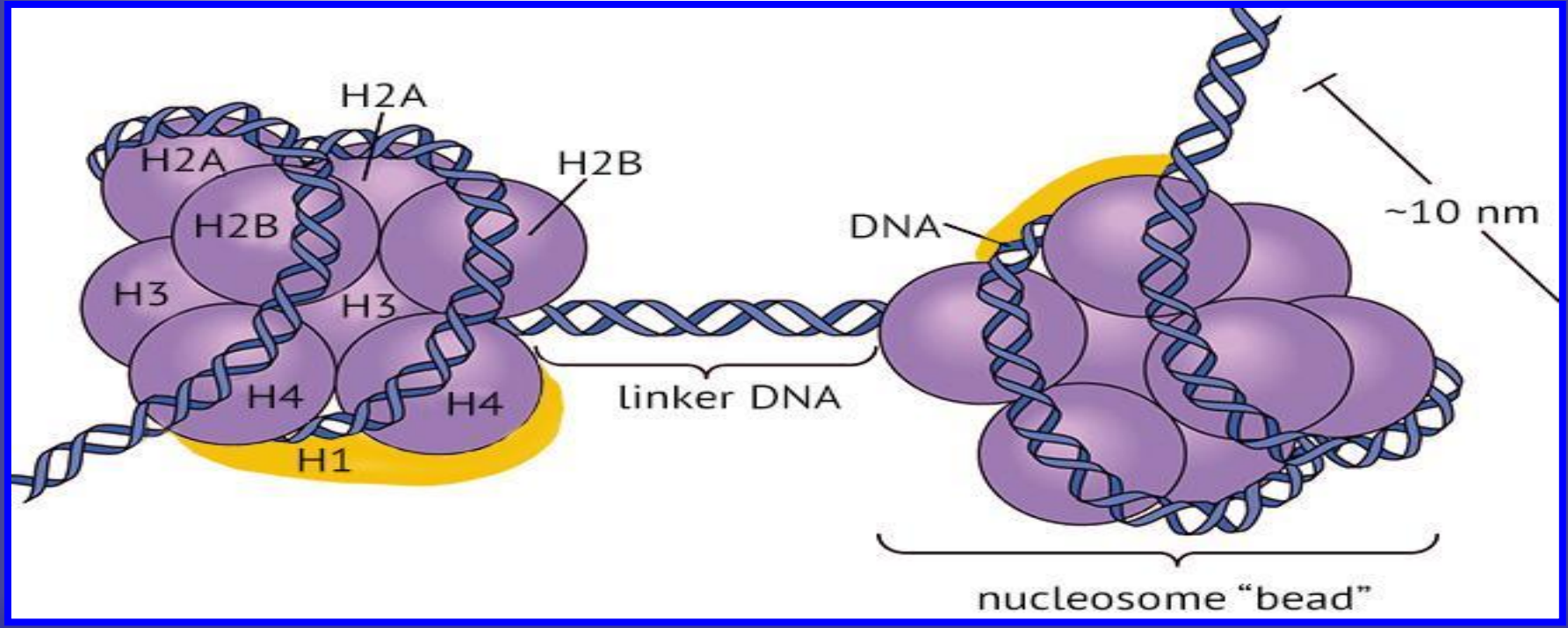
1. The "beads on a string"

- DNA and histones are organized into repeating subunits called **nucleosomes**
- **nucleosomes** composed of **two loops** of DNA wrapped around a **protein core** (eight **histone** molecules, two copies of H2A, H2B, H3 and H4)
- A **nucleosome core** particle consists of **146 base pairs** of supercoiled DNA wrapped **almost twice** around disk shaped complex of 8 histone molecules
- **H1 histone**, the **linker** histone, resides outside the nucleosome and binds to the linker DNA that connects one neucleosome to the next.




Core of 8 histone molecules:
H2A, H2B, H3 and H4
H1 histone
6 nm
Central DNA
Link DNA
10 nm




H2A
H2A
H2B
H2B
H3
H3
H4
H4
H1
DNA
~10 nm
linker DNA
nucleosome "bead"

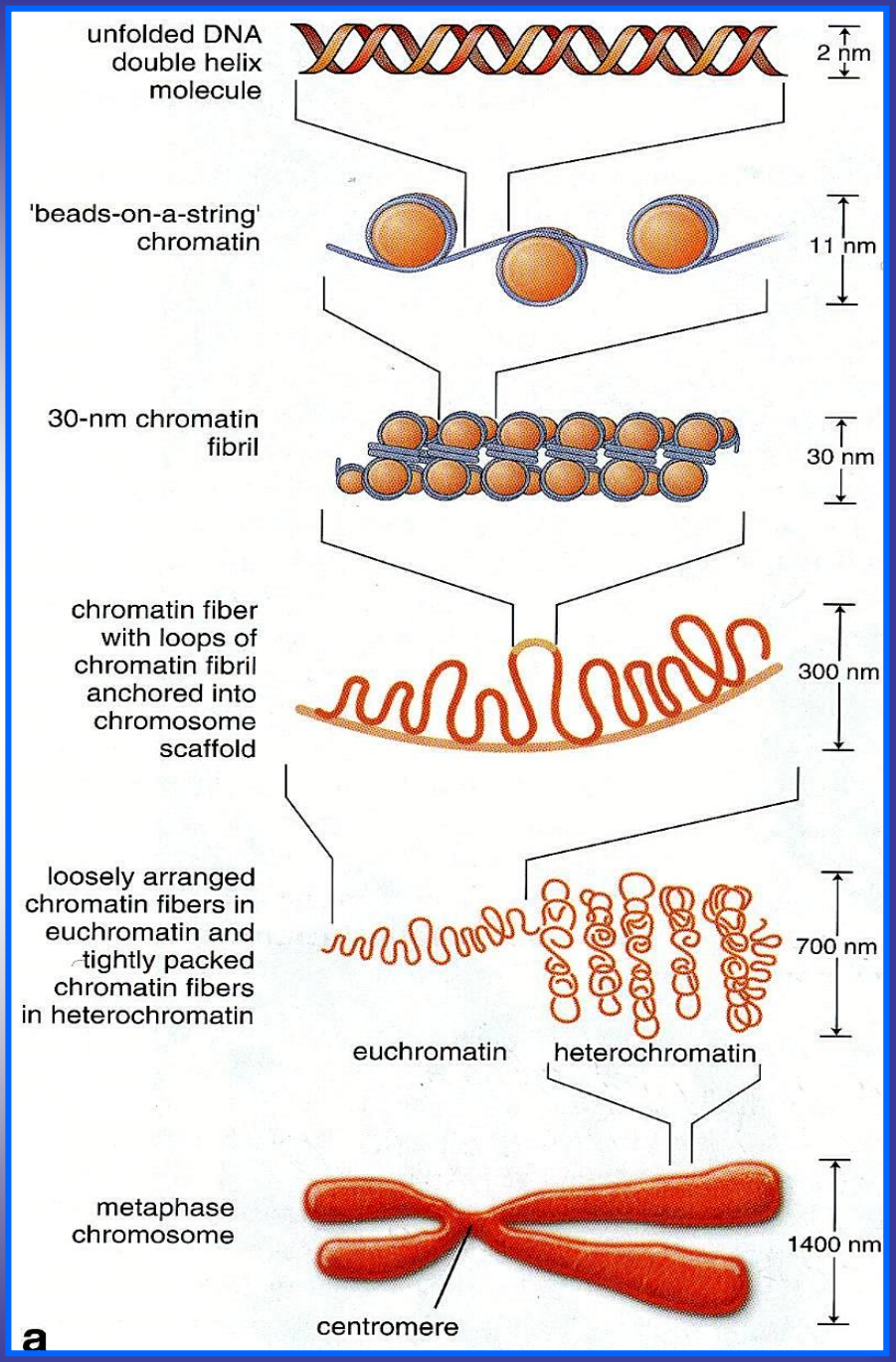
2. Fibers of 30 nm thickness

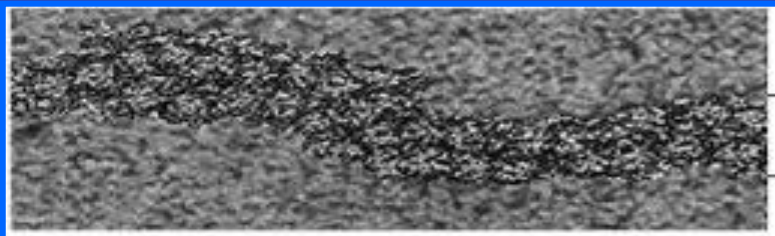
The **30 nm fibers** gather into larger supercoiled loops of thick fibers which normally spread through the **interphase** nucleus

Strand of nucleosomes is coiled to produce 30-nm **chromatin fibril**

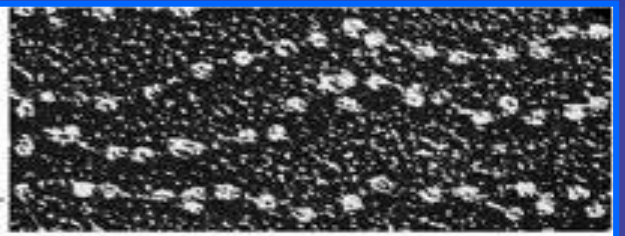
Chromatin fiber is composed of the loops of chromatin fibril anchored into **protein core** of chromosome (composed of non-histone proteins).

During **mitotic** division chromatin fibers are highly condensed and form **chromosomes**

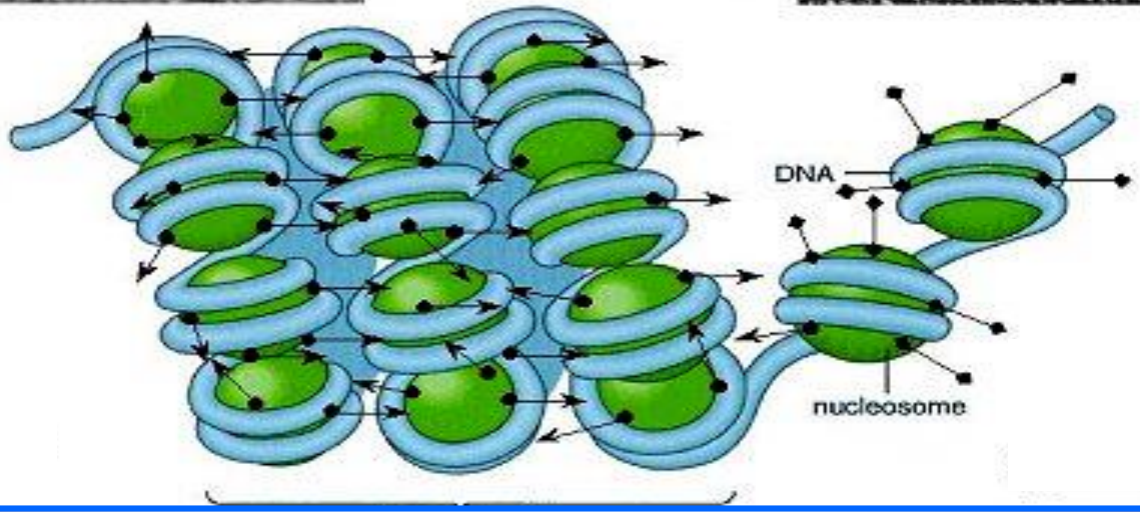




Chromatin fibers

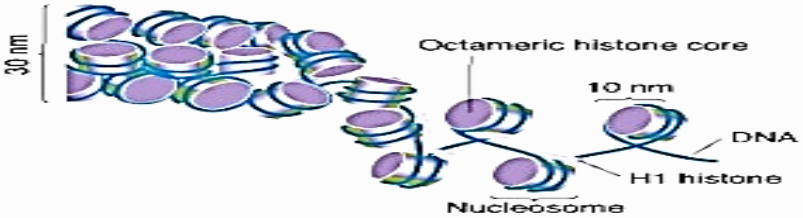


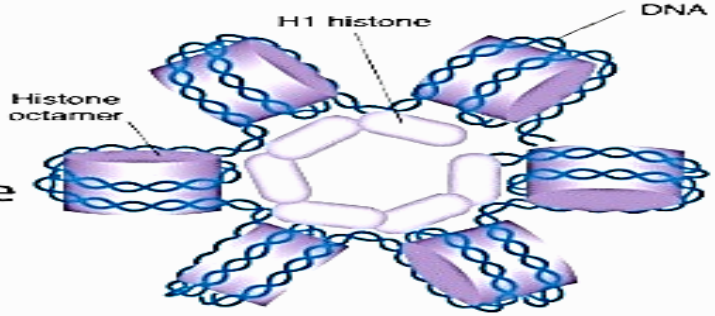
30 nm chromatin fiber



11 nm (beads)

Second level of packing: Solenoids / chromatin





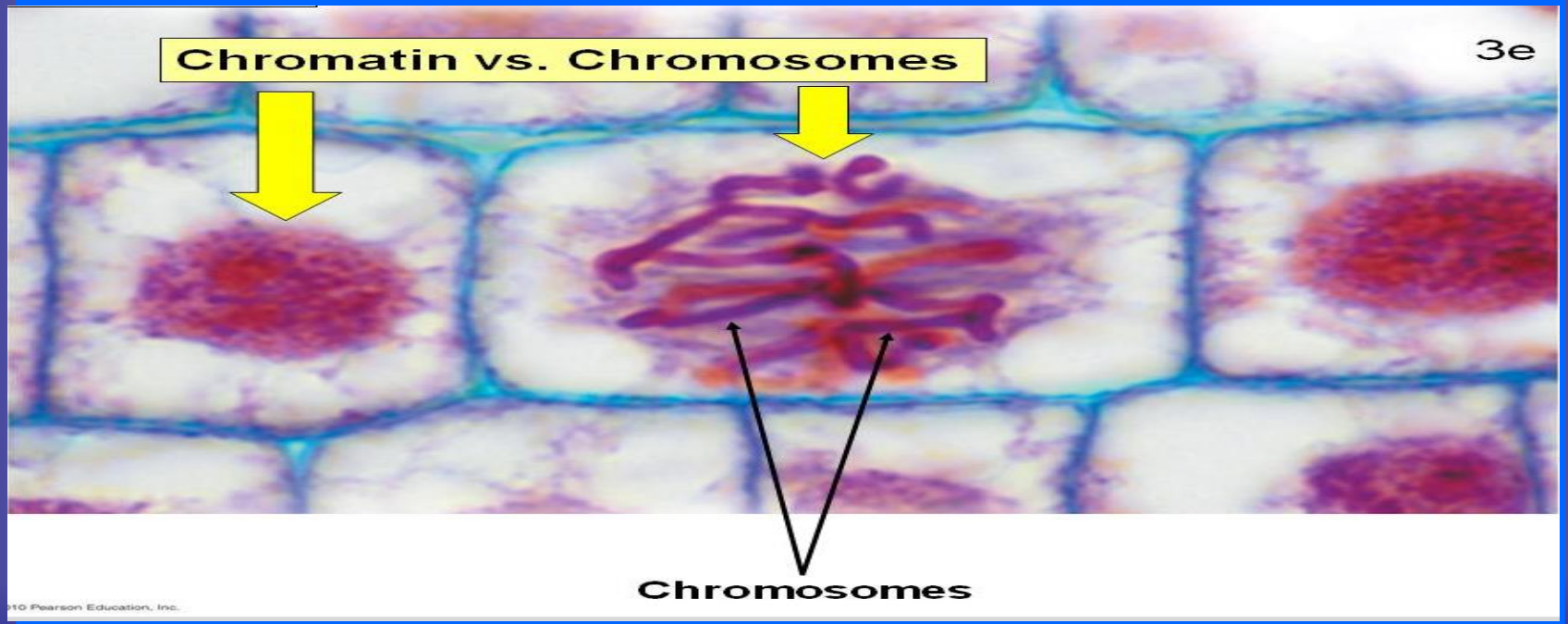
- Solenoid: H1 histones aggregate causing 6 nucleosomes to coil together
- 30 nm in diameter
- stack on top of each other forming the chromatin fiber

http://www.bio.miami.edu/dana/104/nucleosome.jpg

3. metaphase chromosome

When cell prepares to **divide**, chromatin fibers coil up as separate structures, **chromosomes** In the early stages of mitosis or meiosis (cell division/ **metaphase**), the chromatin strands become more and more condensed. They cease to function as accessible genetic material (**transcription stops**)

Chromosomes may exist as either **duplicated** or **unduplicated**. Unduplicated chromosomes are single linear strands, whereas duplicated chromosomes contain two identical copies (called **chromatids**) joined by a **centromere**.



Chromosome

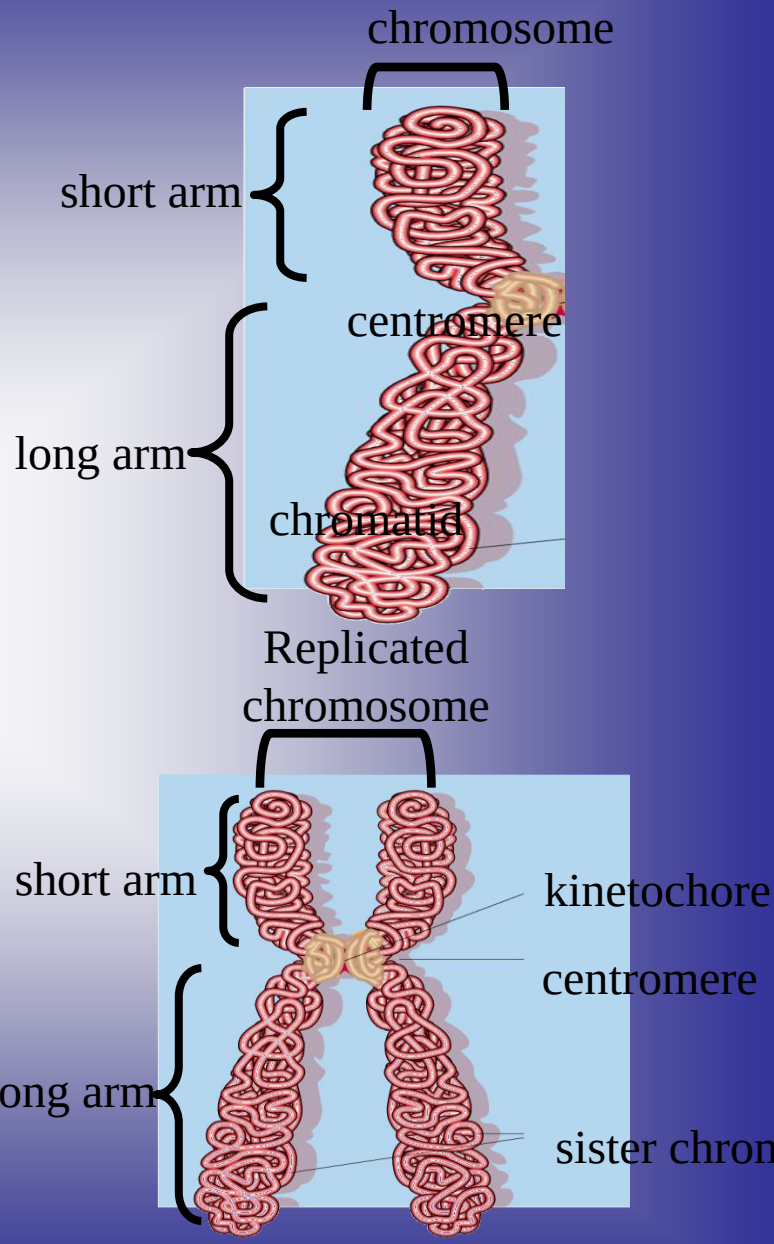
•A **chromosome** is an **organized** structure of **DNA** and **protein** found in cells.

• Chromosomes are the physical carriers of **genetic** information.

•The structure of chromosomes and chromatin **varies** through the **cell cycle**

•Each human **somatic** cell contains **23 pairs** i.e **46 chromosomes** of different chromosomes (**Diploid** cells). **GAMETES** (sperm and egg cells) have one set of 23 chromosomes (**Haploid** cells).
One of the chromosome pairs consists of the **sex chromosomes (X** and **Y)**, the other **22 pairs** of chromosomes are termed **autosomes**

•The members of each pair of autosomes are said to be **homologs**, or **homologous**, because their DNA is very **similar**. The **X** and **Y** chromosomes are **not** homologs of one another.



	Chromatin	Chromosome
Definition	The DNA molecules in the genome are packaged with histones, forming chromatin.	The highest packaged structure of DNA appears in the metaphase of the cell division.
Structure	Chromatin is composed of **nucleosomes**. Condensed **50 times than** the normal DNA doublehelix	Chromosomes are condensed into **chromatin fibres.** Condensed **10,000 times** the normal DNA doublehelix.
Appearance	Chromatin fibres are **thin**, **long**, uncoiled structures	Chromosomes are **thick**, **compact**, ribbonlike structures.
Pairs	Chromatin is a **single**, **unpaired** fibres	Chromosome exists as a **pair**.
Metabolic activity	Chromatin allows DNA **replication**, gene expression and recombination.	Chromosomes do **not** show any metabolic activity
Presence/ Period	Chromatin appears in the **interphase** of the cell cycle	Chromosomes appear during the **metaphase** and exist in the **anaphase** of the nuclear division
Conformation	Chromatin consists of two confirmations: euchromatin and heterochromatin.	Chromosome is usually heterochromatic.
Visualization	Chromatin can be observed under the **electron microscope** as a bead and string structure	Chromosome can be observed under **the light microscope** in its classic four arm structure

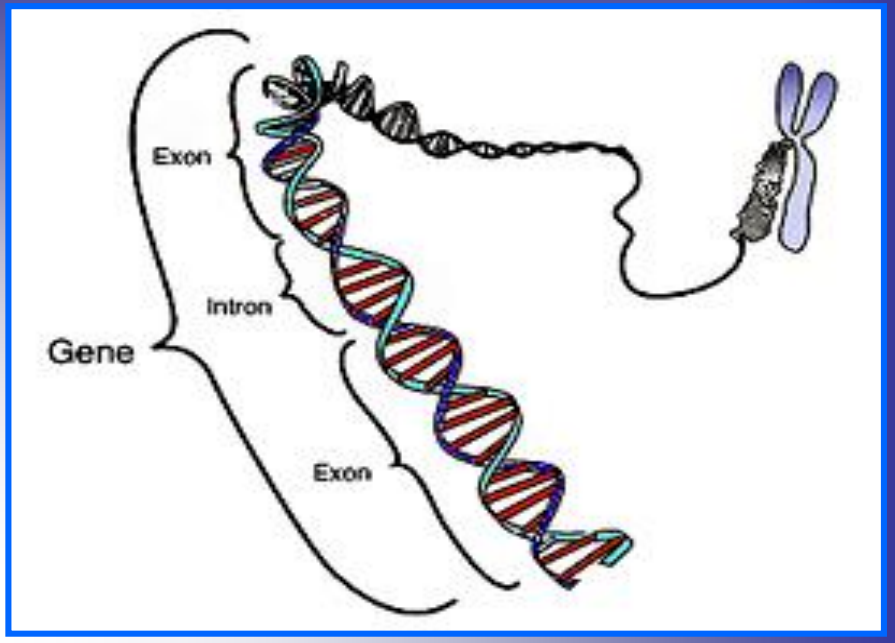
Deoxyribonucleic acid (DNA)

DNA is a **nucleic acid** that contains the **genetic** instructions used in the development and functioning of all known living organisms.

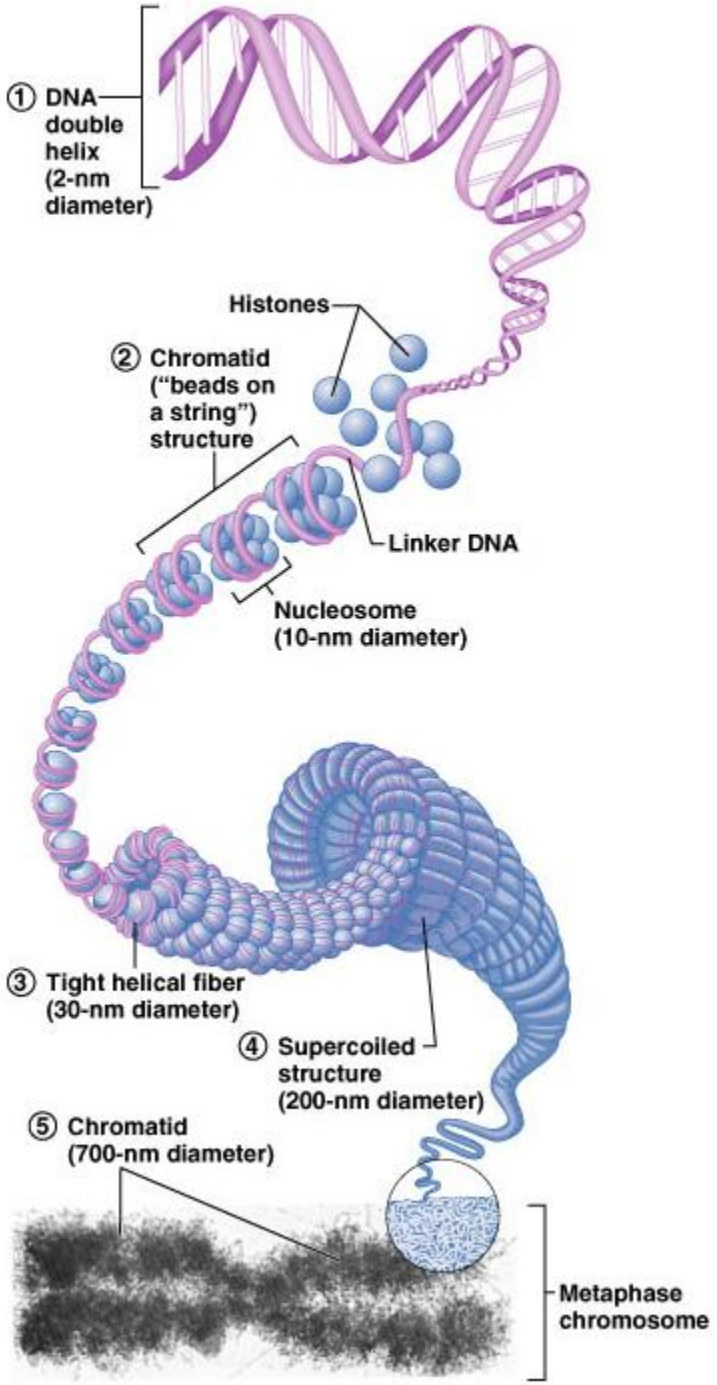
A **gene** is a **unit of heredity** in living organisms. DNA consists of thousands of genes. It specifies everything that is needed for the maintenance, function, and replication of the cell

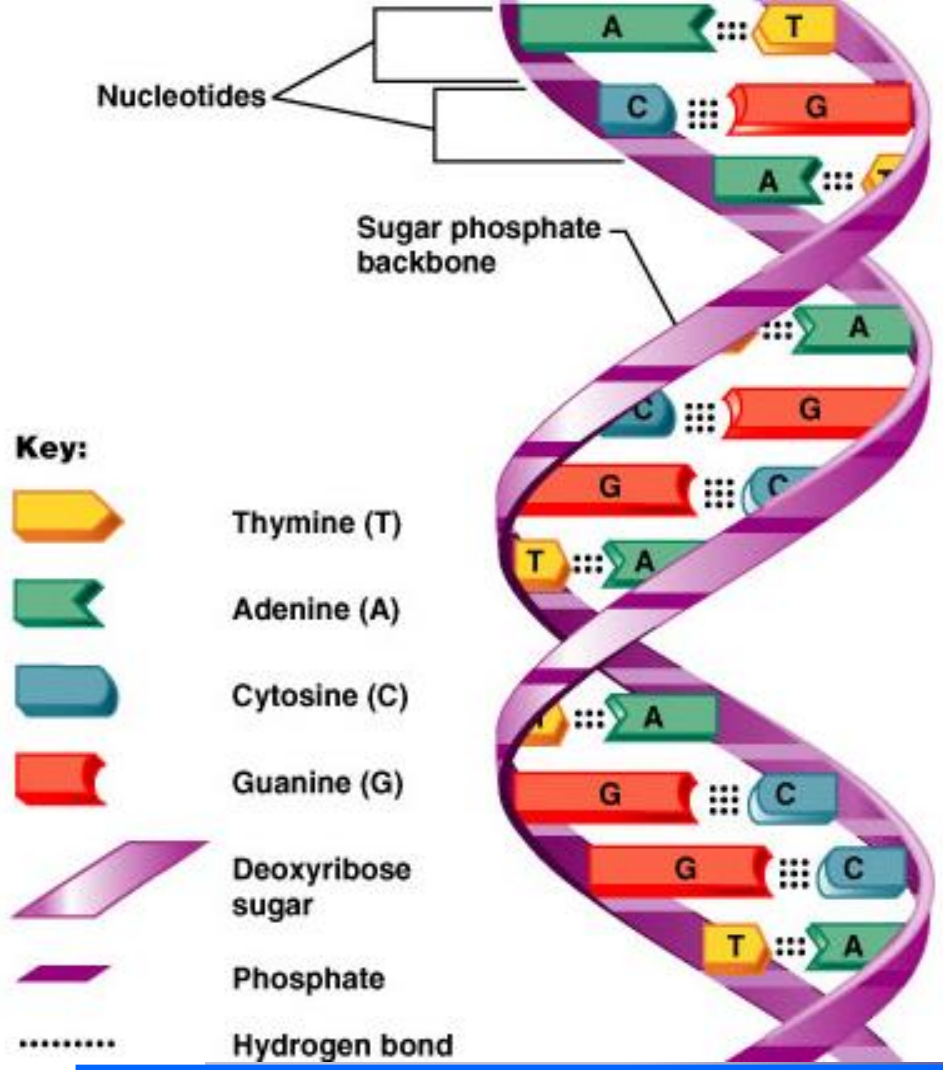
DNA consists of **two** (**double helix**) long **polymers** of simple units called **nucleotides**, with backbones made of **sugars** and **phosphate** groups joined by **ester** bonds.

Nucleotides are molecules that, when joined together, make up the structural units of RNA and DNA. = **nucleobase** + sugar+ phosphate group



Replication: DNA making a copy of itself
Transcription: making of RNA from code of DNA
Translation: making of protein coded by tRNA via mRNA via DNA





DNA "bases" – **T**, A, C, G (thymine, adenine, cytosine, guanine)

RNA "bases" – **U**, A, C, G (uracil instead of thymine)

The Nucleolus

The **nucleolus** (plural **nucleoli**) is a **non-membrane** bound structure composed of **proteins** and **nucleic acids** found within the nucleus/ **1-2 µm**

It is the **most dense** (prominent) structure of the cell, and frequently is located in central area of nucleus

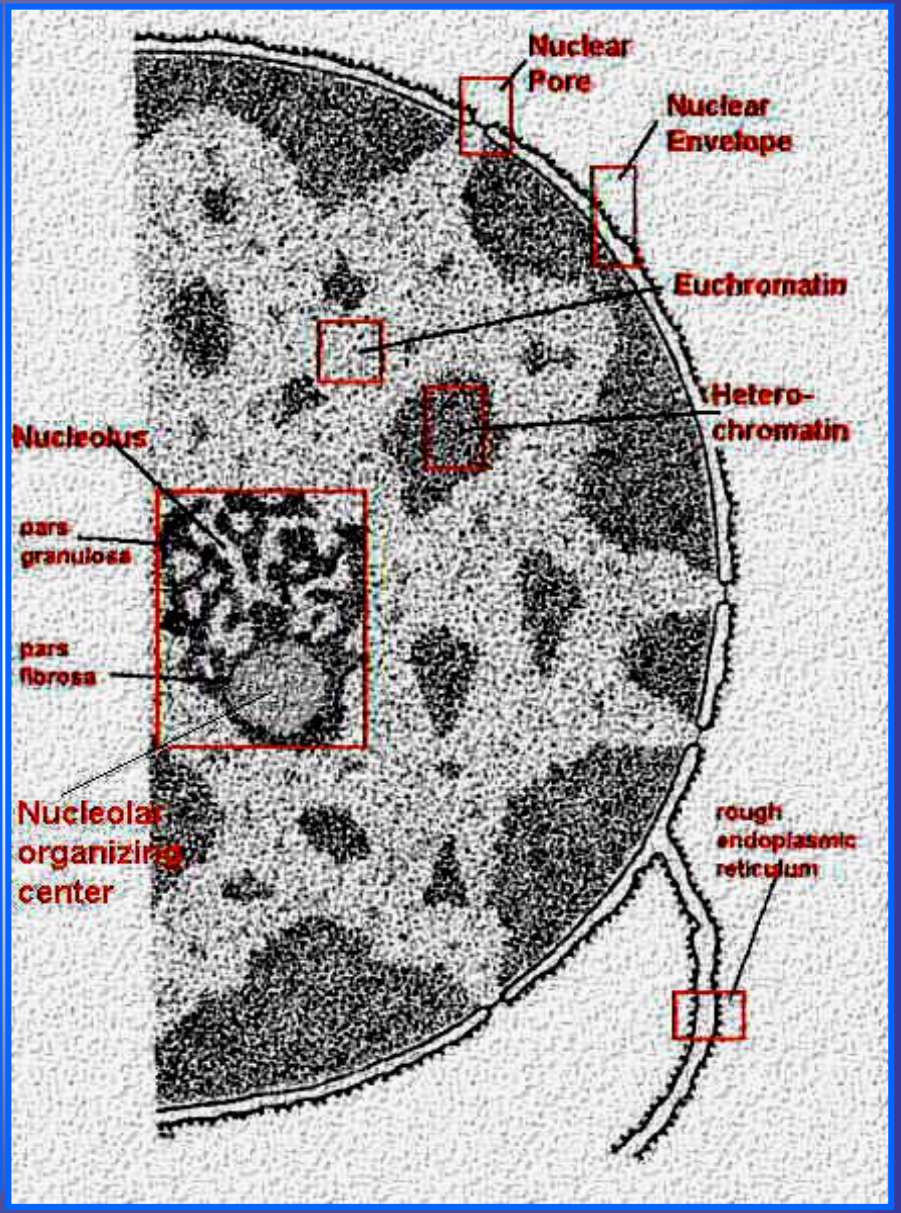
<u>Function</u>, site of **rRNA synthesis,** initial ribosomal **assembly**

<u>Structure</u>,

-fibrillar centers, filaments of chromatin

-pars fibrosa, newly transcribed rRNA

-pars granulosa, rRNA bound to ribosomal proteins that are beginning to **assemble** into ribosomes



Ultrastructure of the nucleolus