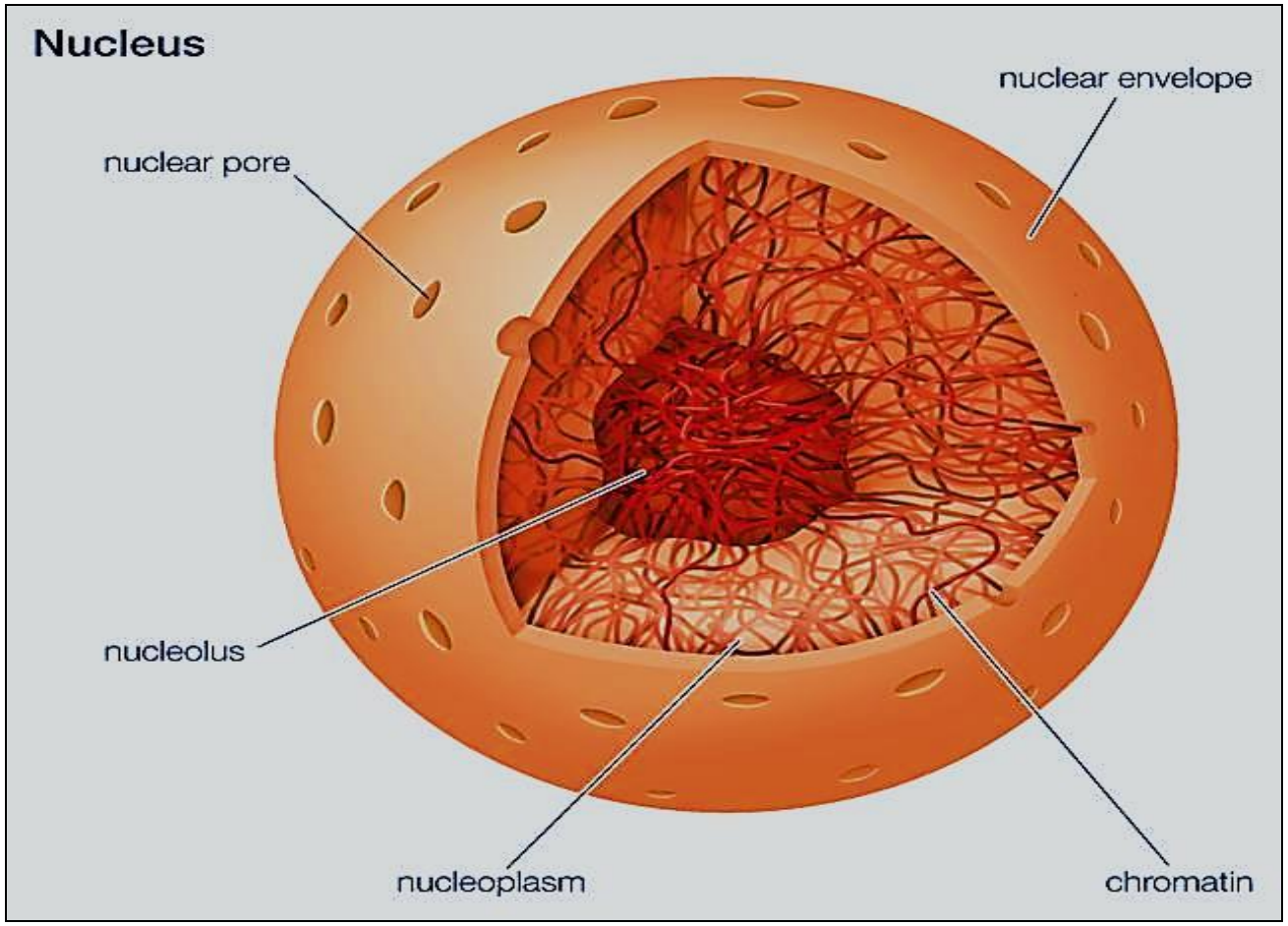
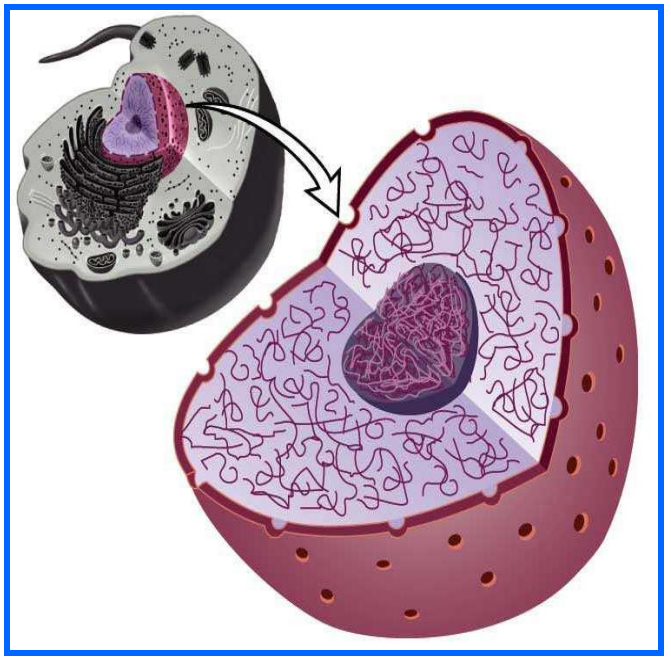
The Nucleus


Nucleus
nuclear envelope
nuclear pore
nucleolus
nucleoplasm
chromatin

The nucleus

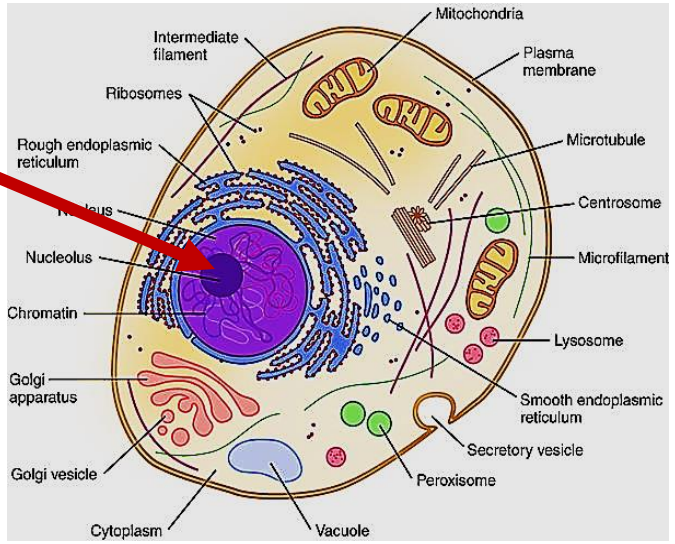
- The nucleus is the control center for all cell activities
- 5 µm in diameter, spherical
- Large, most obvious organelle
- is a membrane-enclosed organelle



- Contains most of the genetic information & regulatory machinery of the cell

Function:

- It **stores** the cell's **hereditary material** (DNA)
- Site of **DNA replication**
- Site of **DNA transcription** to mRNA



- **Ribosome formation** (Nucleolus within the nucleus contain r-RNA genes necessary for production of ribosomes)
- It **coordinates** the cell's activities, which include growth, metabolism, protein synthesis, and reproduction (cell division) by **regulating gene expression**

Gene expression:

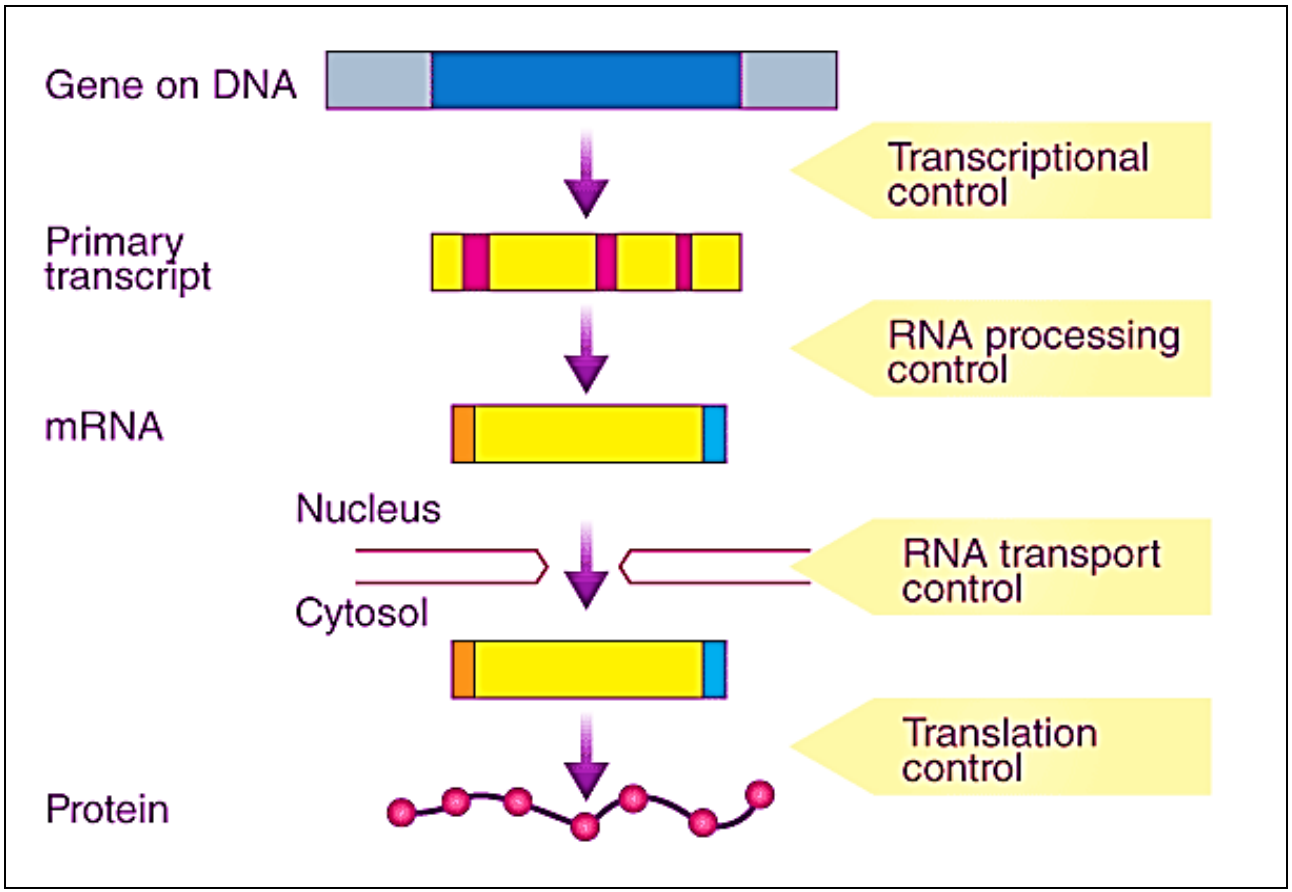
- Is the biological process by which information encoded in a gene is used to produce a functional product e.g. protein

Steps of gene expression

1- Transcription : DNA is transcribed into m-RNA, then it changed into mature m-RNA & become ready for translation

2- Translation: occur in the cytoplasm by the ribosomes , the ribosomes read the m-RNA sequence in codons (sets of 3 nucleotides) & assemble polypeptide chain using relating amino acids. t-RNA delivers amino acids to ribosomes

3- Post translational modifications : newly formed polypeptides become functional proteins



Process of gene expression

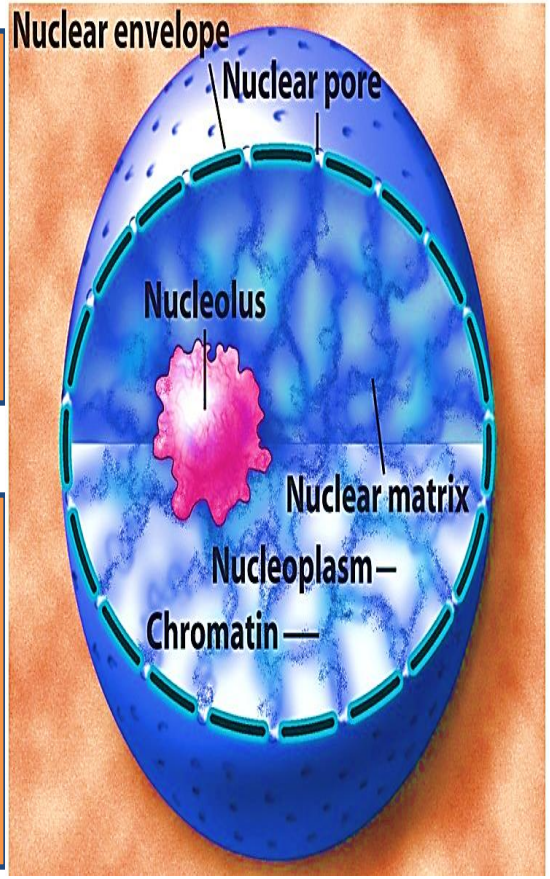
Structure of the nucleus

1- Nuclear envelope

2- Nucleoplasm

3- Chromatin

4- Nucleolus



The nuclear envelope/ membrane

- **Double layered membrane** surrounds the nucleus in eukaryotes **&** separates the nucleus from the cytoplasm
- Controls exchanges between nucleus and cytoplasm
- Protects the genetic material & maintain shape of nucleus
- **Structure** :
  - **External (outer) nuclear membrane**
  - **Internal (inner) nuclear membrane**
  - **Perinuclear space**
  - **Nuclear lamina**
  - **Nuclear pores (NPCs)**

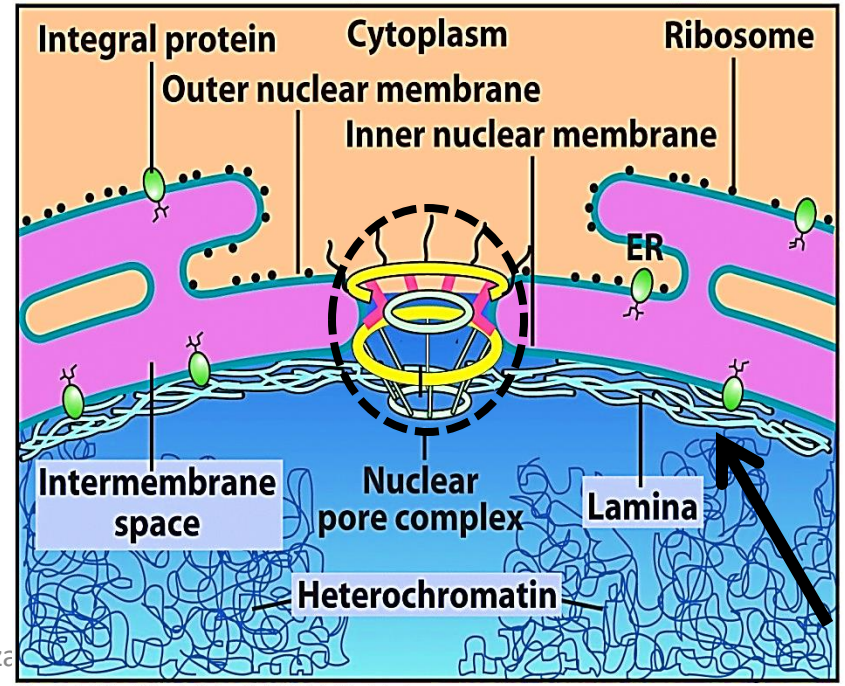
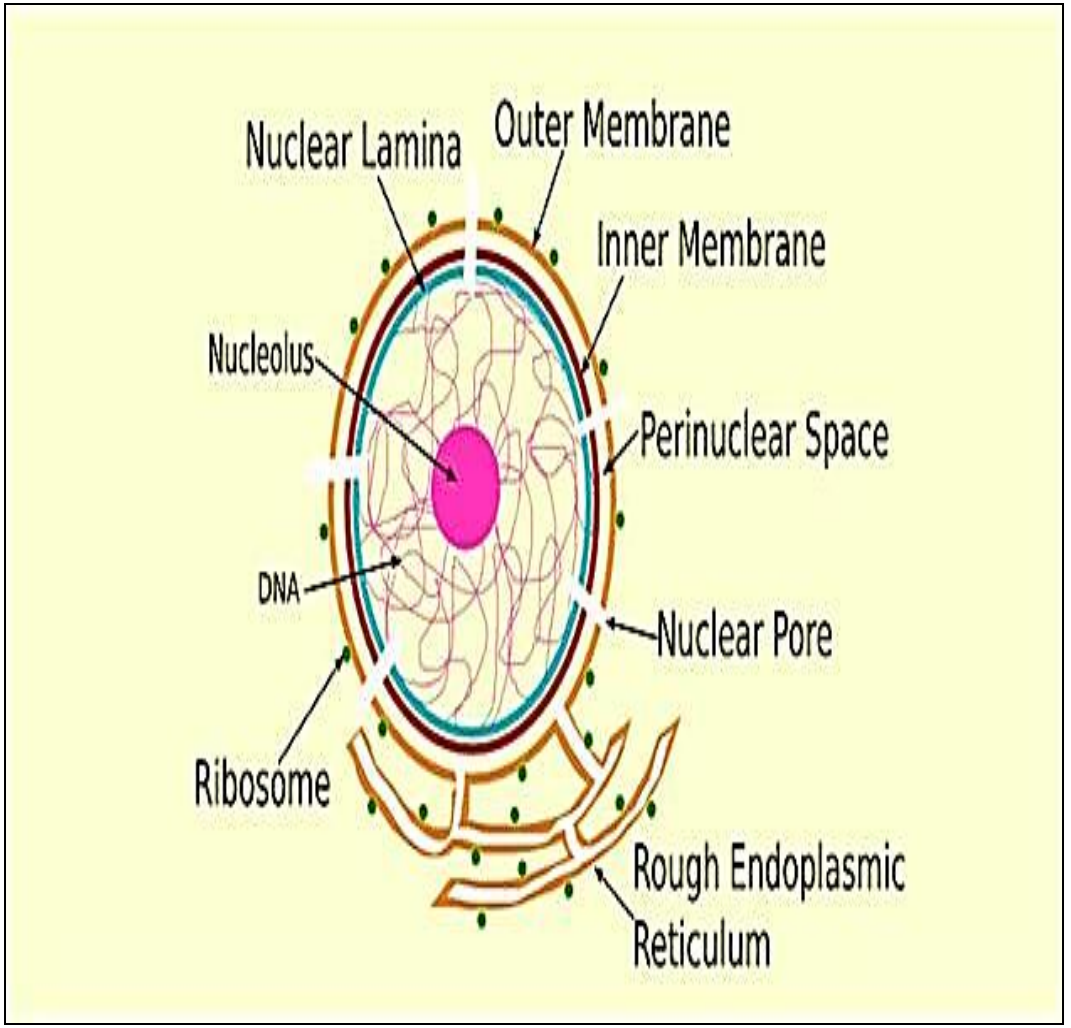


Figure 12-2a Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

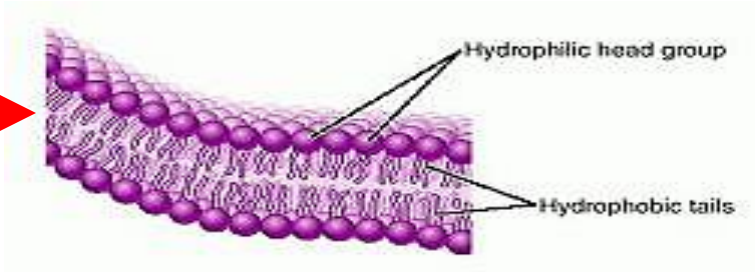
1. **External (outer) nuclear membrane**
2. **Internal (inner) nuclear membrane**
3. **Perinuclear space**
4. **Nuclear lamina**
5. **Nuclear pores (NPCs)**

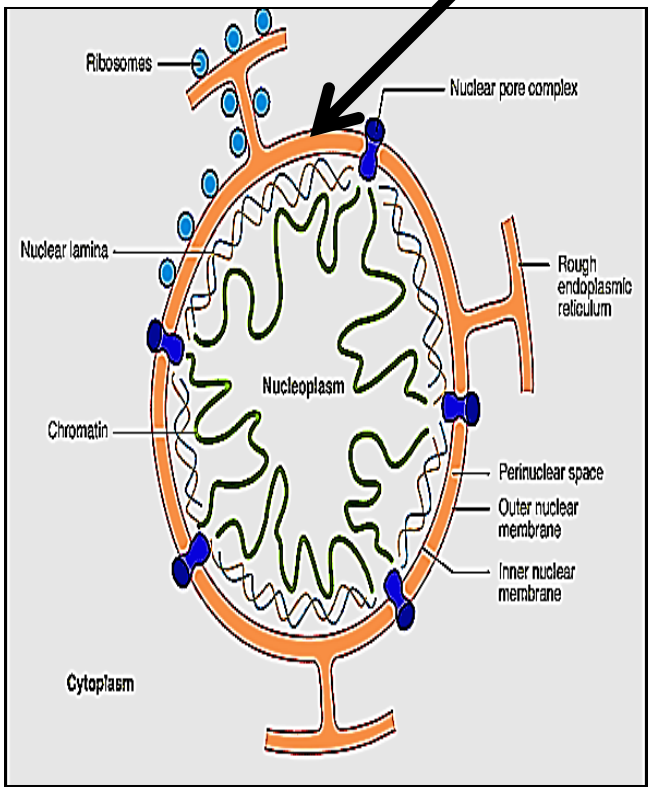


Structure of the nuclear membrane

1- Outer nuclear membrane

- Fluid mosaic (lipid bilayer of 7.5 nm thick with 70% proteins)
- Visible only by electron microscope
- It continues with RER membrane
- Ribosome attached on external face



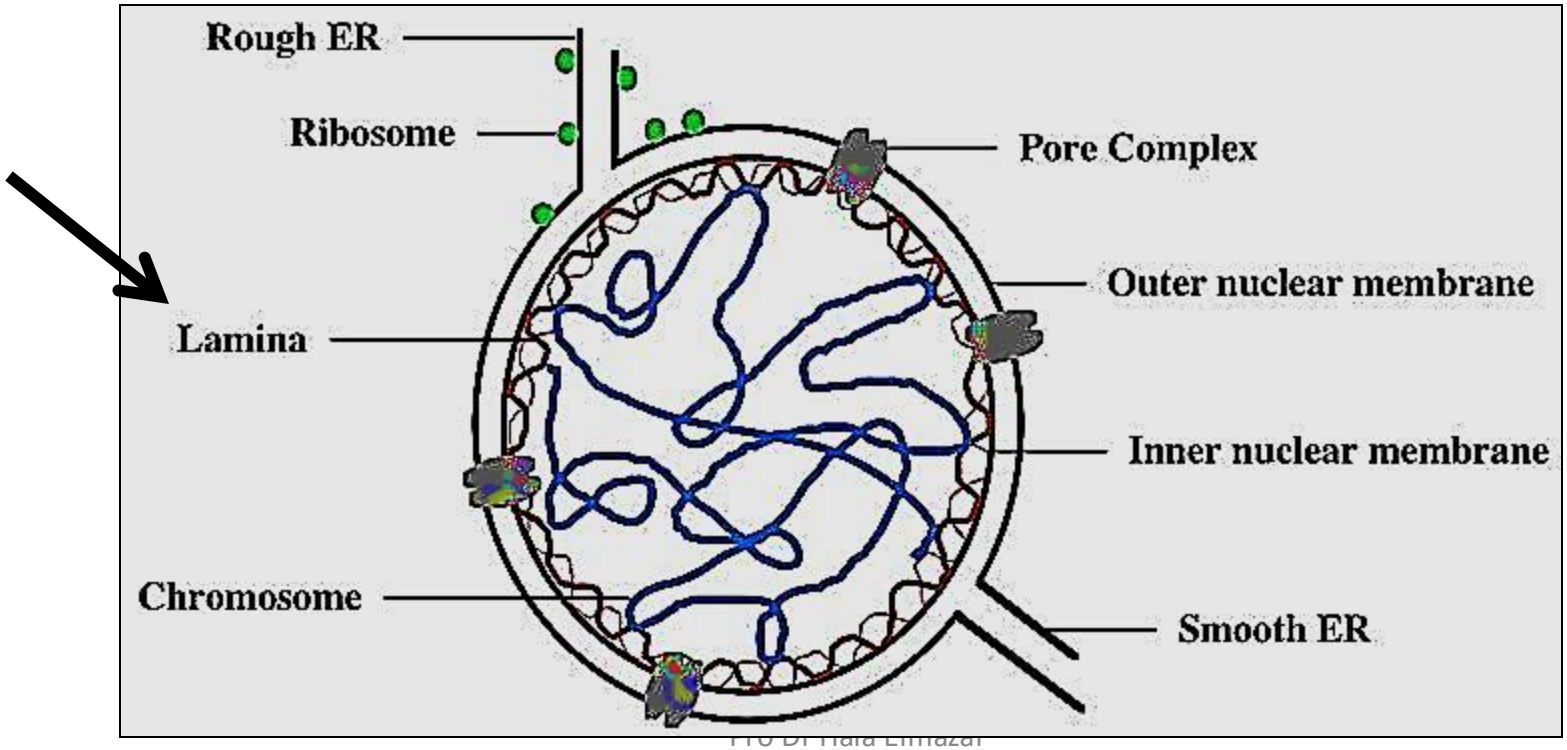


2- The perinuclear space

- 10-40 nm
- It communicates with the lumen of RER
- Contains the same molecules as RER
- Contains Ca^{+}

3- Internal nuclear membrane

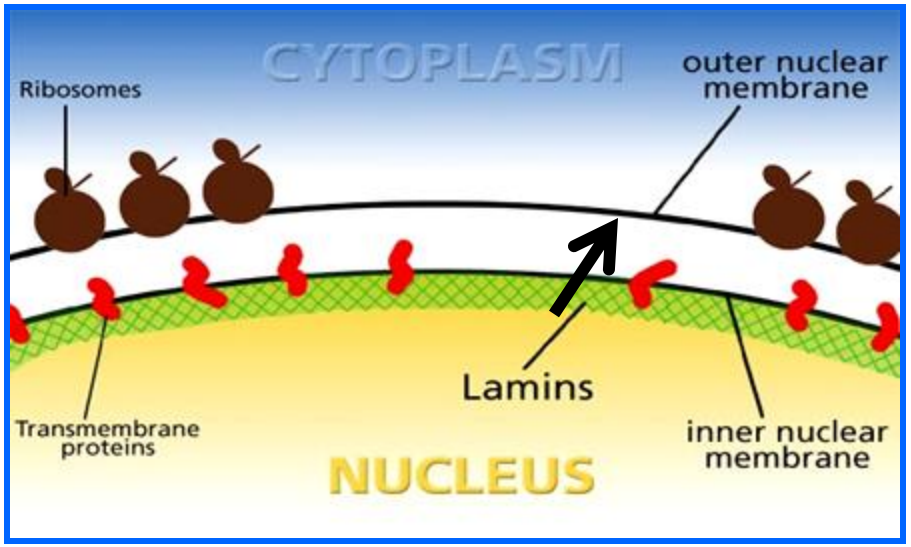
- Fluid mosaic (**lipid bilayer**), face the nucloplasm
- Visible only by electron microscope
- The inner surface of the nuclear envelop is attached to thin filamentous network (*lamins*) called the **nuclear lamina.** Lamins provide structural support

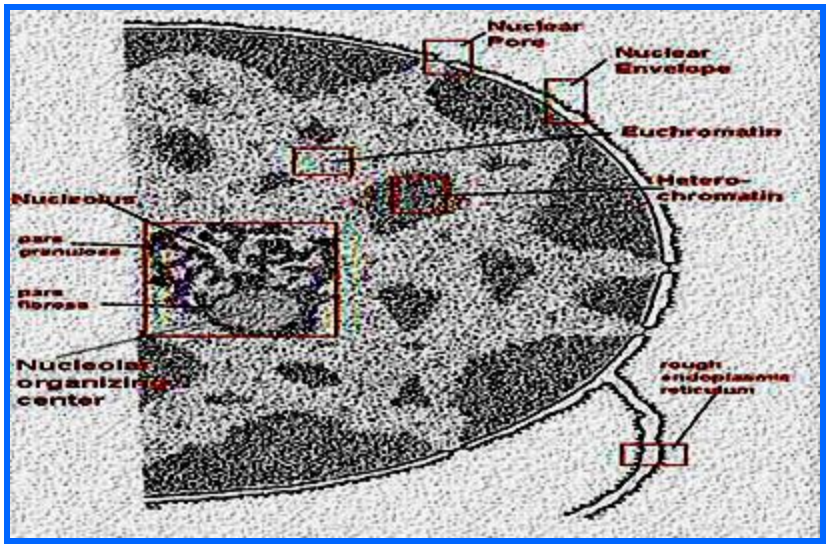


4- Nuclear lamina

- a network of intermediate filaments (lamins)
- The lamina acts as a site of attachment for chromatin
- provides structural strength & shape to the nucleus.

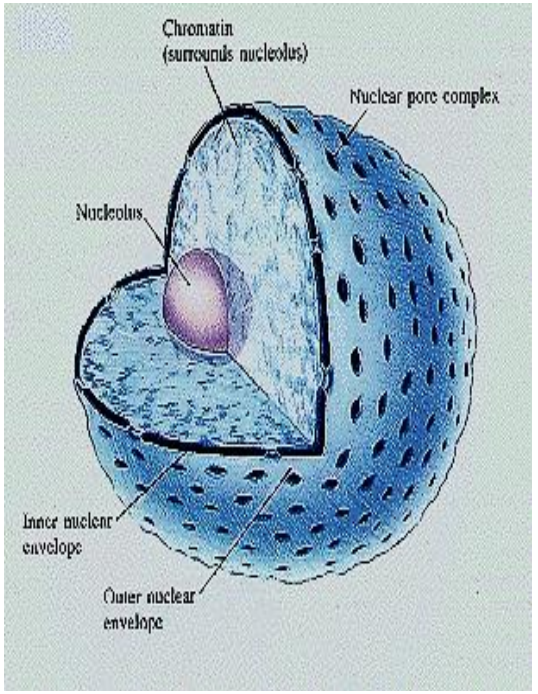
- Defect in Lamin → various genetic disorders collectively termed laminopathies (e.g. muscular dystrophy).





5- The nuclear pores (NPCs)

- **Gateways** in the nuclear envelope (3000- 4000 NP)
- Regulate exchanges between nucleus & cytoplasm
- Pores allow selective transport of molecules e.g. m-RNA, ribosomal subunits & proteins between nucleus & cytoplasm



- Proteins formed in the cytoplasm cross the nuclear envelop to initiate replication & transcription of genetic material.
- mRNA, tRNA & ribosomes formed in the nucleus then cross the nuclear pores to the cytoplasm

Structure of Nuclear pore complex (NPC)

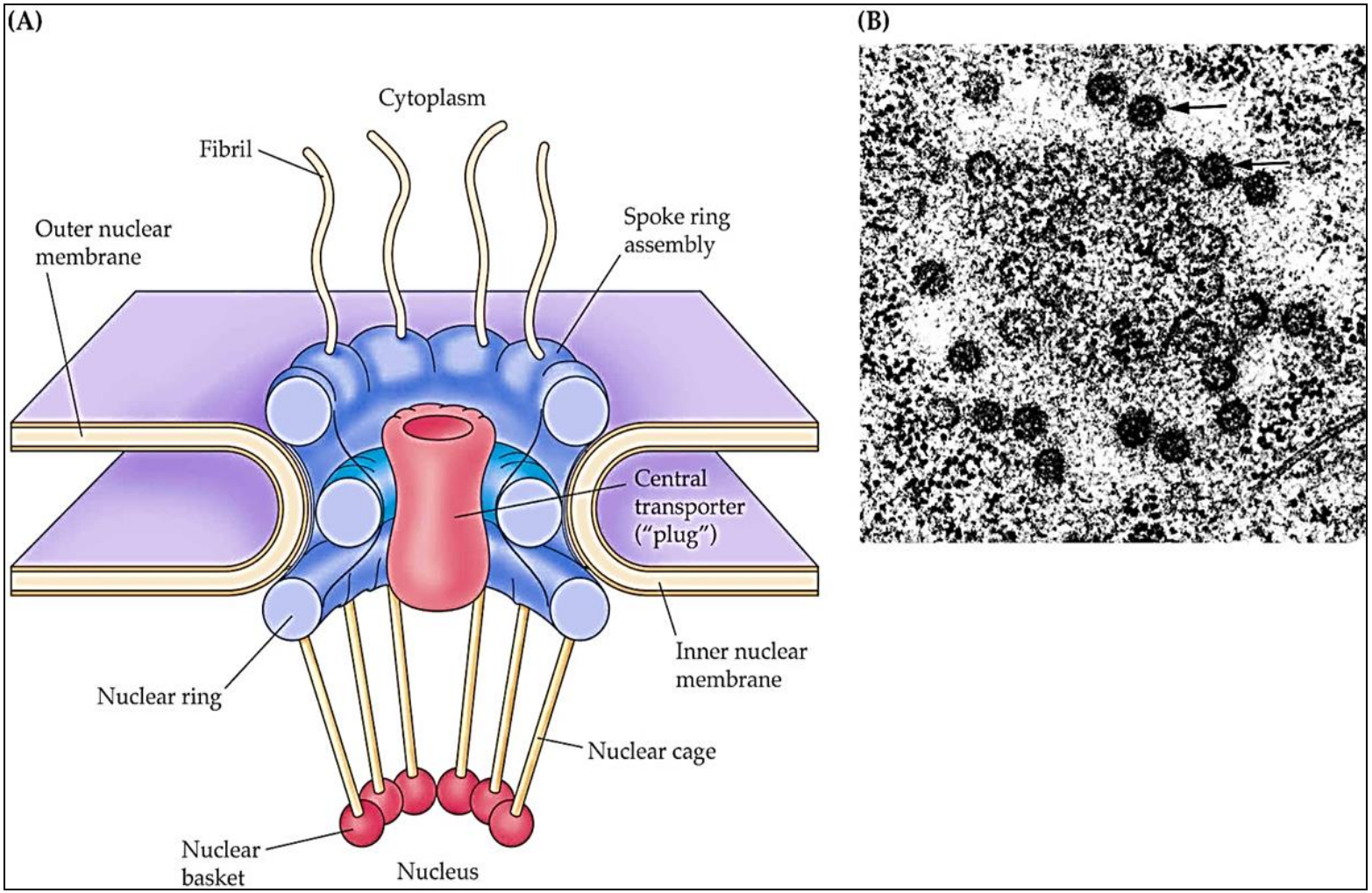
Is a large multiprotein structures embedded in the nuclear membrane around a central pore .NPCs regulate the exchange of molecules between the nucleus & the cytoplasm

Structure of NPCs:

- Each about 120 nm in diameter

- There are 3000-4000 nuclear pores. Dynamic structures they disassemble during mitosis then reassemble after & their number increase if is necessary

- Each NPC is formed of 3 rings : cytoplasmic , nuclear & luminal (membrane/inner) rings



Rings of the Nuclear pore complex (NPC)

Cytoplasmic ring:

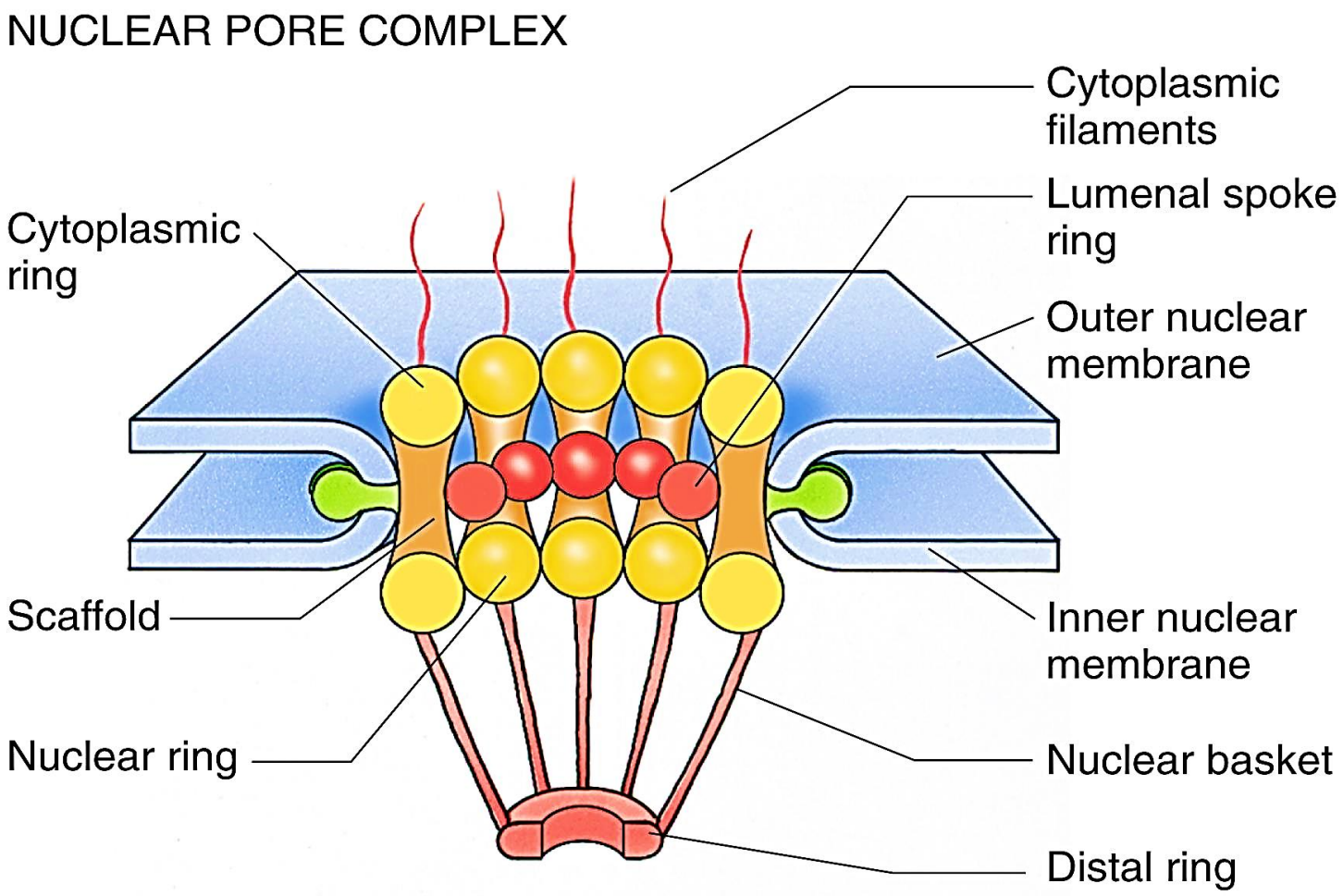
- Located at the cytoplasmic side of the nuclear membrane
- Anchors the cytoplasmic filaments that extend outwards & are involved in the Export process

Inner ring/ luminal (Spoke ring):

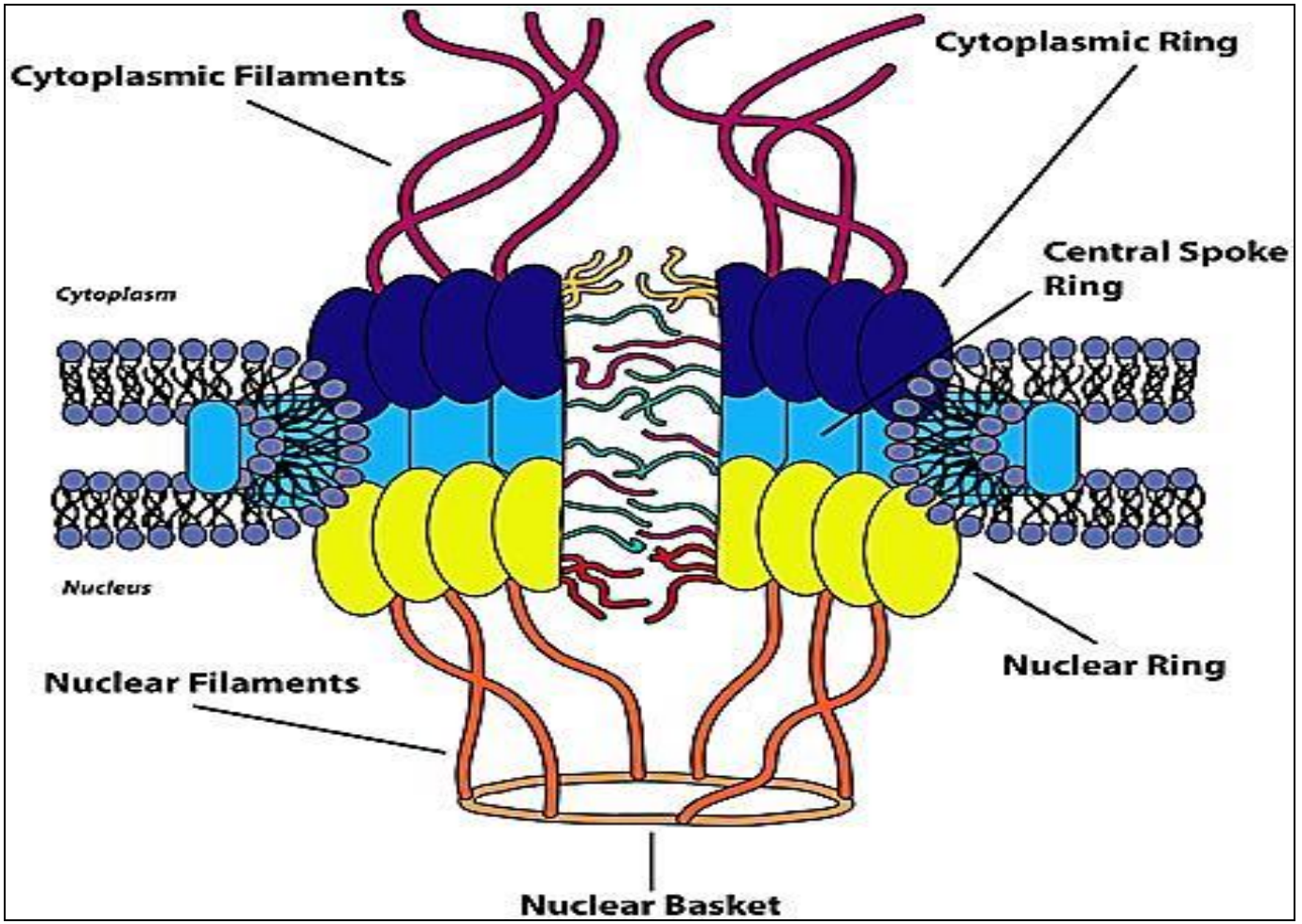
- Situated within the plane of the nuclear envelope
- Bridges the inner & outer membrane forming the central skeleton (scaffold) of the NPC & provide structural support

Nuclear ring:

- Found on the nuclear side of the nuclear membrane
- Anchors the nuclear basket



Inner ring Bridges the inner & outer membrane forming the central skeleton of the NPC & provide structural support



Nuclear pore complex

All together **the 3 rings + filaments + basket** contributes to the eightfold symmetry & function of the NPC

Structure of NPCs:

- They are made of 30 different **nucleoporins** (proteins that form the sub-structure of the NPC)
- Each NPC has 1000 protein subunits due to repetition of the nucleoporins in the complex

- Each ring is formed of 8 glycoprotein subunits **(nucleoporins (Nups))** form what is called **Octagonal symmetry**

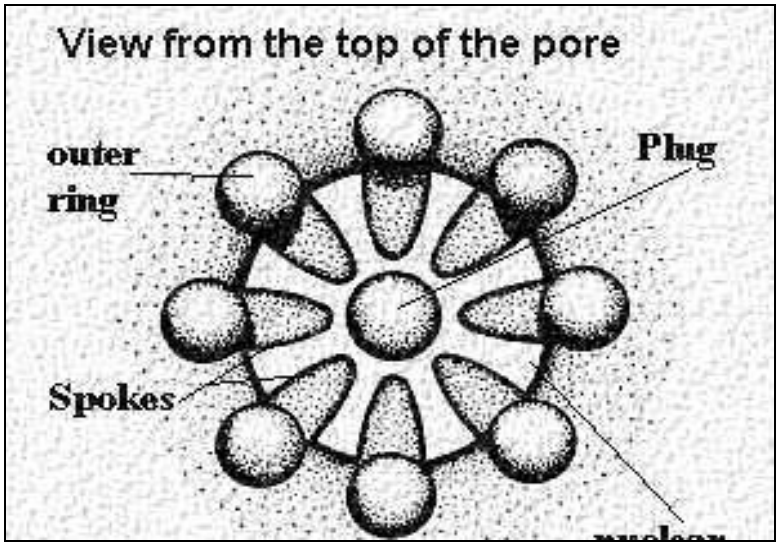
- Nucleoporins: are **symmetrical** on cytoplasmic and nuclear sides. This symmetry or the uniform distribution of the nucleoporins **ensure efficient transport across the NPC**

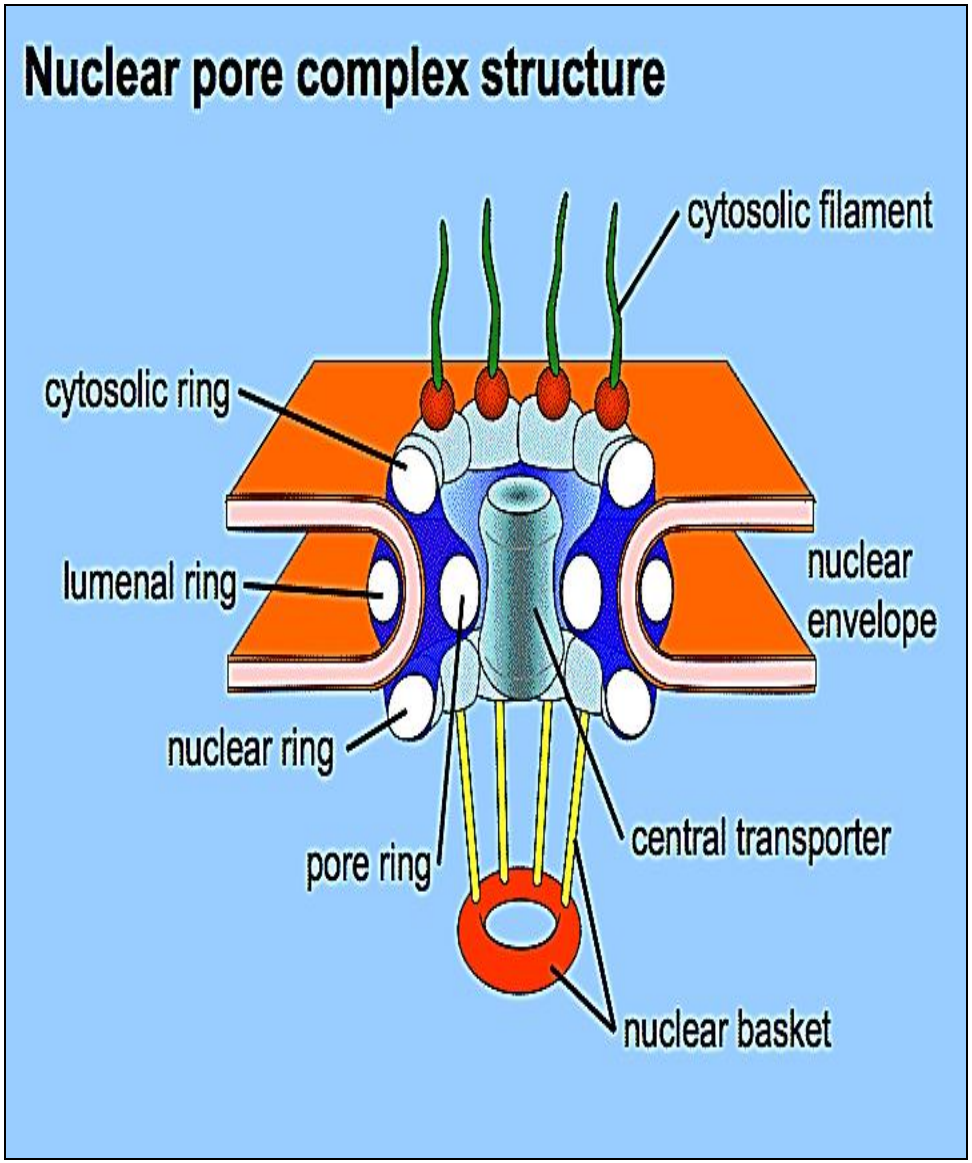
Octagonal symmetry

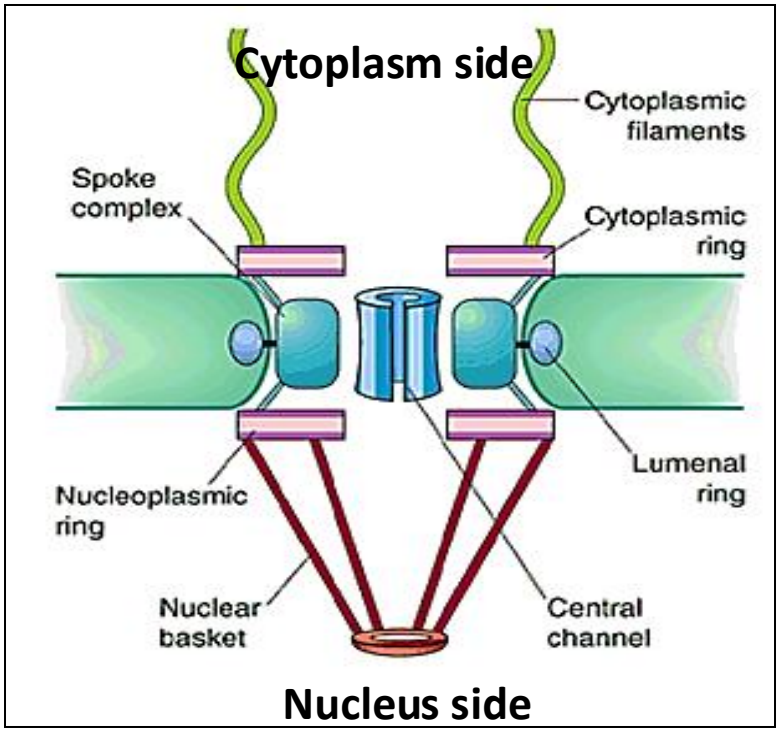
- Refers to the arrangement of the nucleoporins of the inner ring in radial pattern , with 8 repeating units organized around a central transport channel

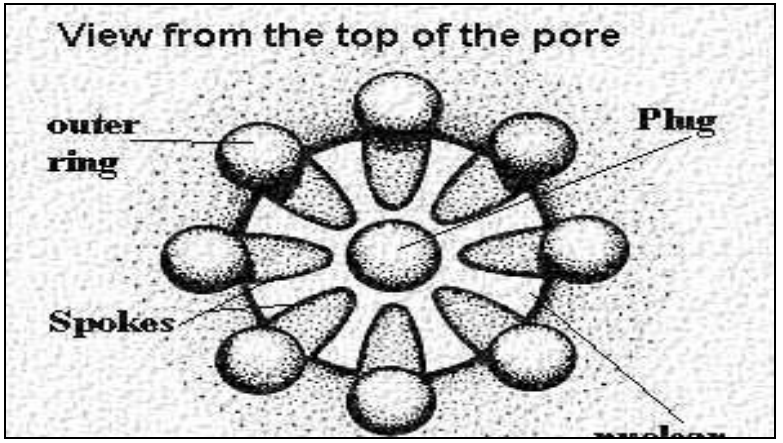
- When viewed from above that NPC looks like **octagonal wheel** with eight spokes radiating outward into the central channel

- This symmetry is essential for the NPC as a gateway between nucleus & cytoplasm




Nuclear pore complex structure
cytosolic filament
cytosolic ring
lumenal ring
nuclear envelope
nuclear ring
pore ring
central transporter
nuclear basket


Cytoplasm side
Cytoplasmic filaments
Spoke complex
Cytoplasmic ring
Lumenal ring
Nucleoplasmic ring
Nuclear basket
Central channel
Nucleus side


View from the top of the pore
outer ring
Plug
Spokes

Key features of Octagonal symmetry :

- **Cylindrical shape: NPC is arranged as cylindrical structure that spans across the nuclear membrane**

- **Eightfold radial symmetry: NPC has 8 repeating units called spokes which form a ring around the central transport channel. These spokes are part of the inner ring frame , which act as the structural core of the NPC**

- **Repeating subunits: nucleoporins are organized into repeating units within the octagonal symmetry. This organization is seen in all 3 rings**

- **Symmetry across both sides: The cytoplasmic & nuclear rings all has the same eightfold radial symmetry**

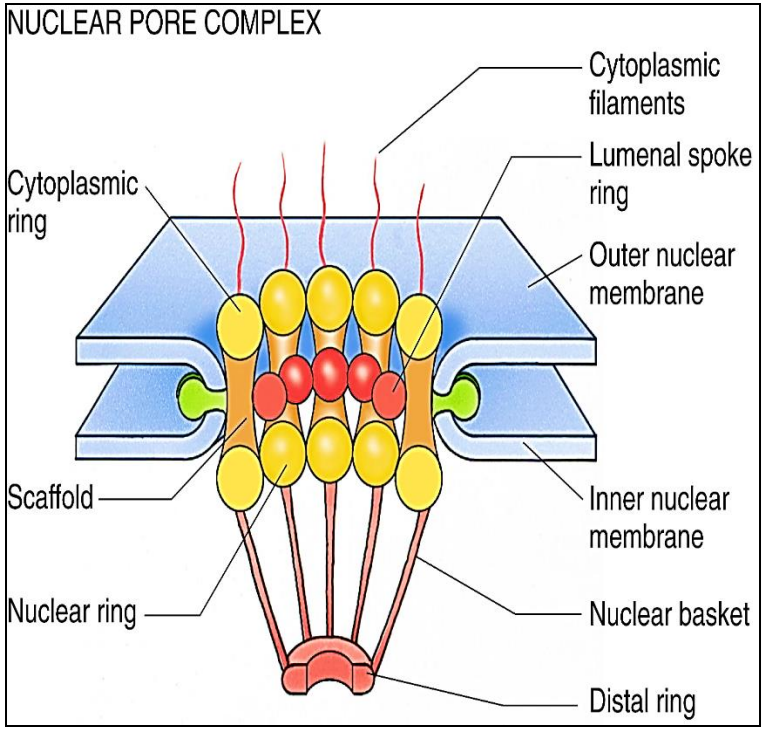
Structure of the luminal/inner ring

- This ring is embedded within the nuclear envelope composed of 2 parts luminal & inner rings

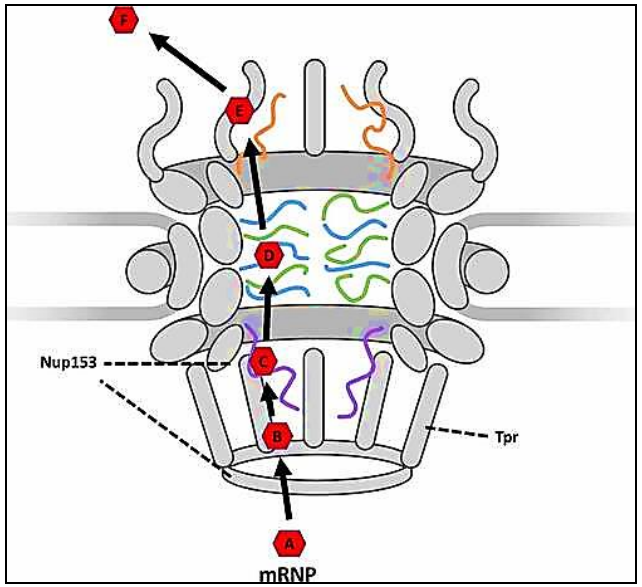
- Connects the outer & inner nuclear membrane→ stabilize the membrane structure

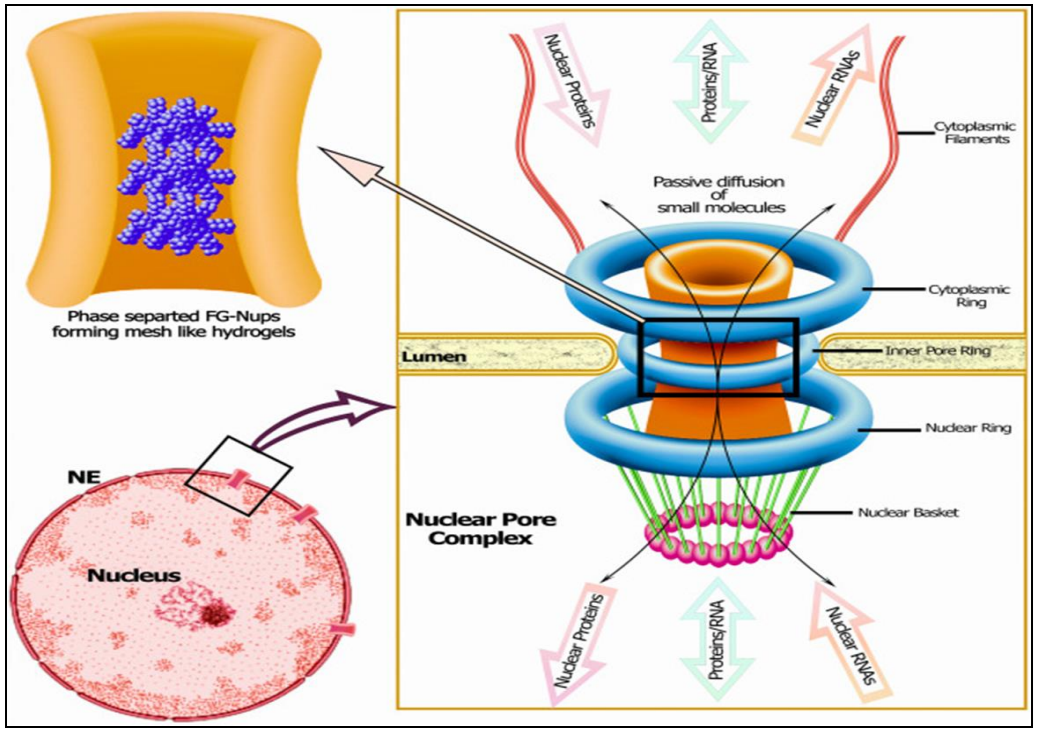
- It consists of nucleoporins
- that form the backbone of NPC

- It is composed of 8 repeating subunits organized radially to form a cylinder around central transport channel



- The inner ring defines the central transport channel & give attachment to **FG-nucleoporins** .
- FG -Nup form flexible barrier (plug) a dynamic structure that selectively permit the passage of macromolecules & allow free diffusion of small molecules





NPC plug

Nuclear basket:

- extend into the nucleoplasm from the nuclear ring of the NPC
- It is a long flexible filaments composed of specific nucleoporins that meet at the distal ring
- The basket plays role in nuclear transport e.g. RNA processing & export
- Chromatin organization within the nucleus
- Signal transduction : facilitate communication between cytoplasm & nucleus through interacting with signaling molecules imported to the nucleus

Types of Nuclear transport

- Passive diffusion: small molecules & ions diffuse freely into & out the nucleus (no energy or transport signals required)
- Active transport: proteins , RNA, ribosomal subunits require active transport, this process controlled **by the nuclear pore complexes (NPCs) & require energy**
- Large molecules need to link with proteins called **importins or exportins** to enter & exit the nucleus

➢ *Nuclear Import*:

Importins + nuclear localizing signal (NLS)+ protein → enter the nucleus

➢ *Nuclear export*:

Exportins + nuclear export signal (NES) + RNA → exit nucleus

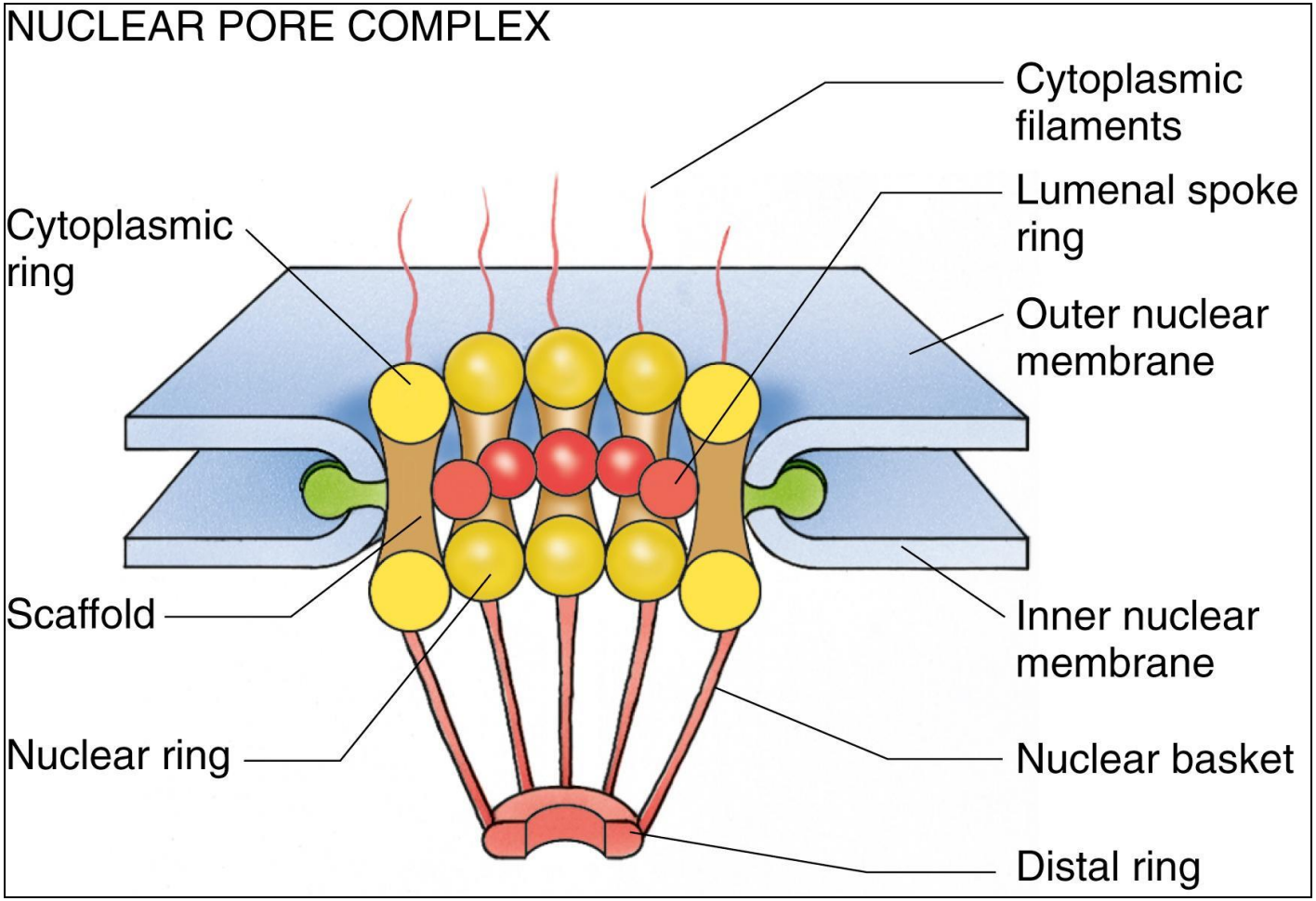
Importance of nuclear transport:

1- gene expression : transcription occurs in the nucleus and RNA must exported to the cytoplasm for translation

2- Nuclear organization: transport maintain the proper localization of nuclear proteins

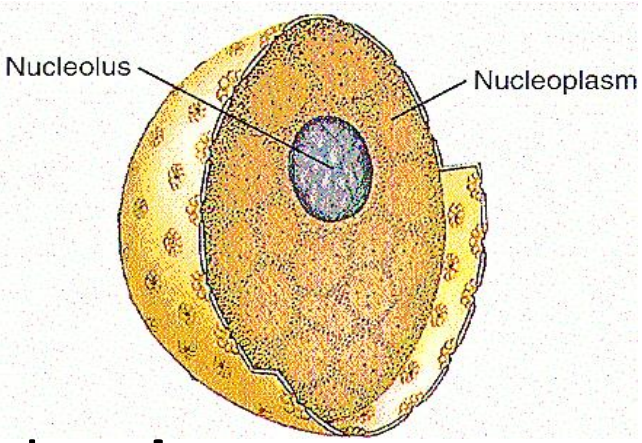
3- Cell cycle regulation

4- Signal transduction: import if signal molecules into the nucleus allows the nucleus to respond to extracellular signals

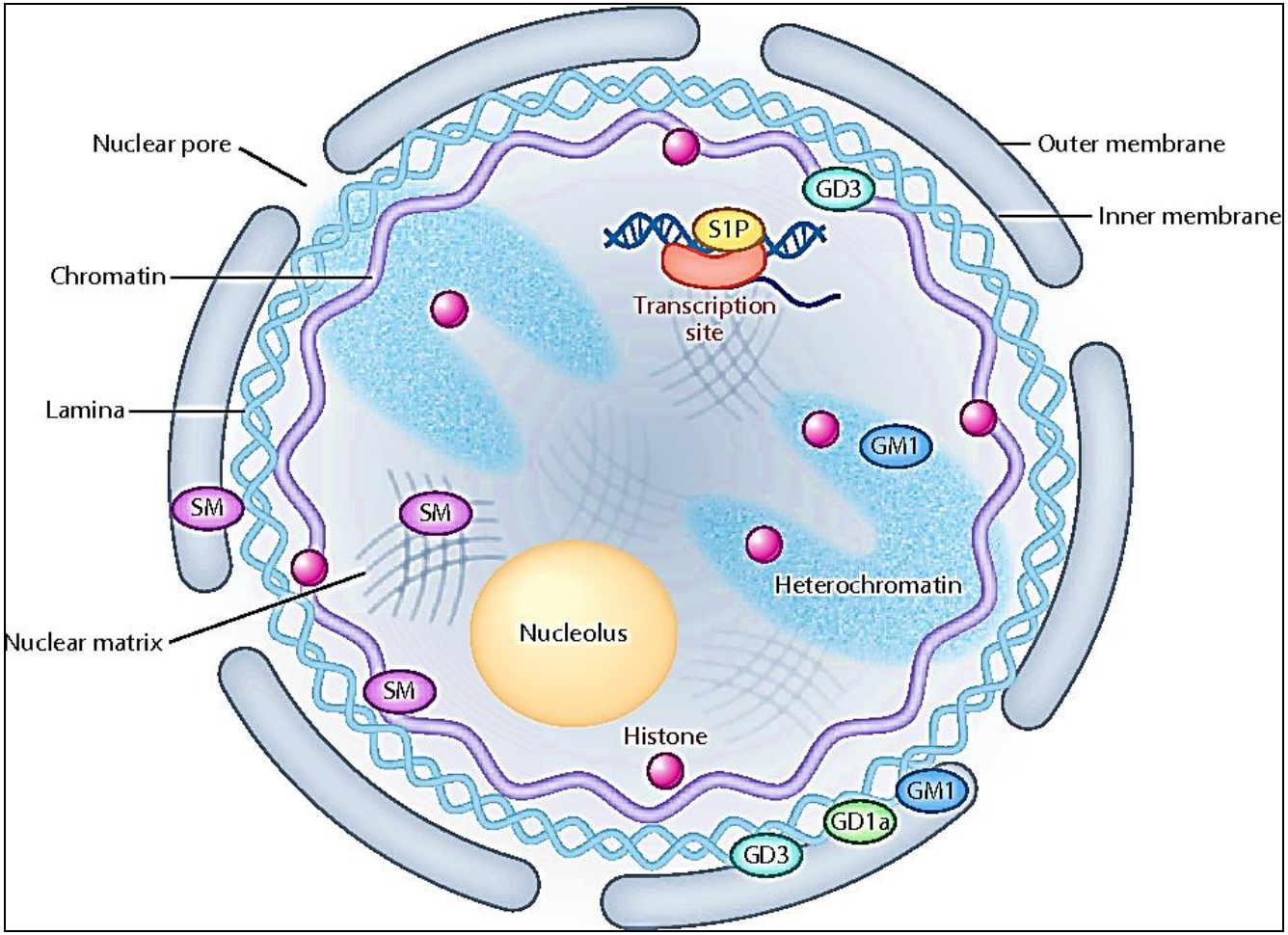


Nuclear basket

Nucloplasm



- Similar to cytoplasm also called nucleus sap or karyoplasm
- Highly viscous liquid that surrounds the **chromosomes** and **nucleolus**
- Composed of water, ions (pH of nucleus), macromolecules such as **nucleotides**, **enzymes, nuclear proteins (Histones), chromatin….** are found in the nucleoplasm
- A **network of fibers** known as the nuclear matrix can also be found in the nucleoplasm

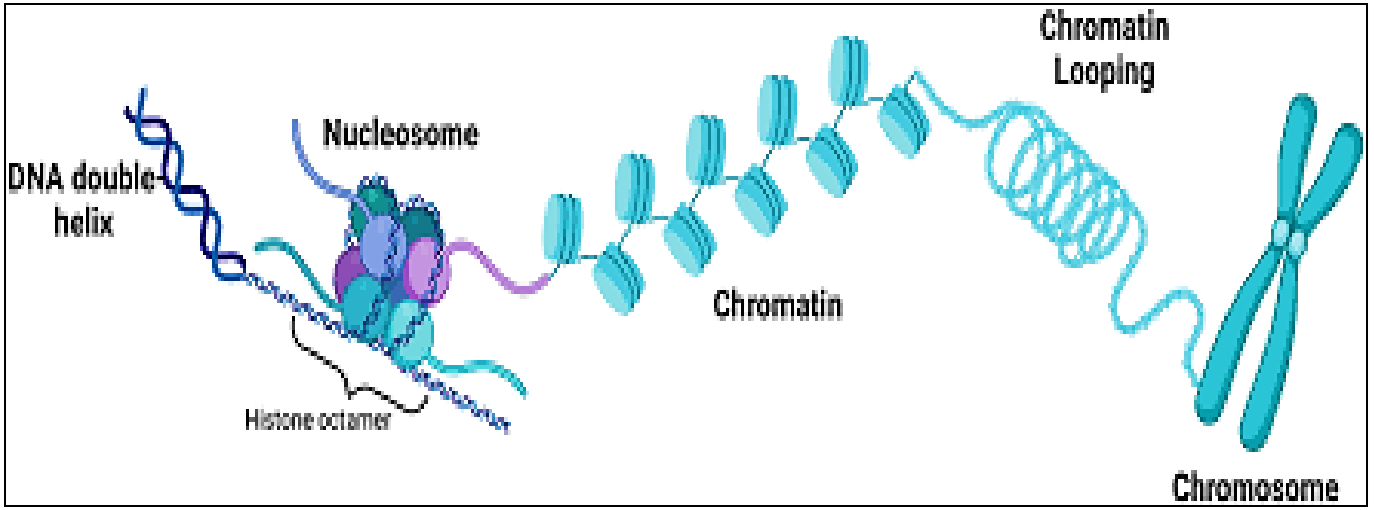


Content of nucleoplasm

Chromatin

- a complex of **DNA and proteins** that forms chromosomes within the nucleus

- It serves to pack the long DNA molecules into a compact structure
- Chromatin exist in a dynamic state which change depending on the cell's need



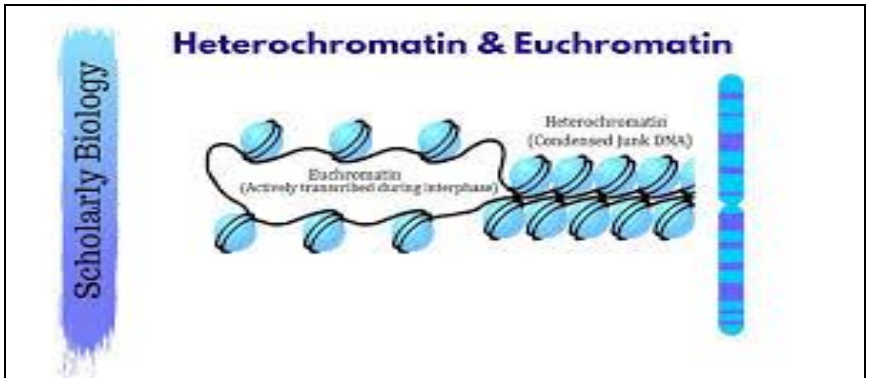
Types of chromatin

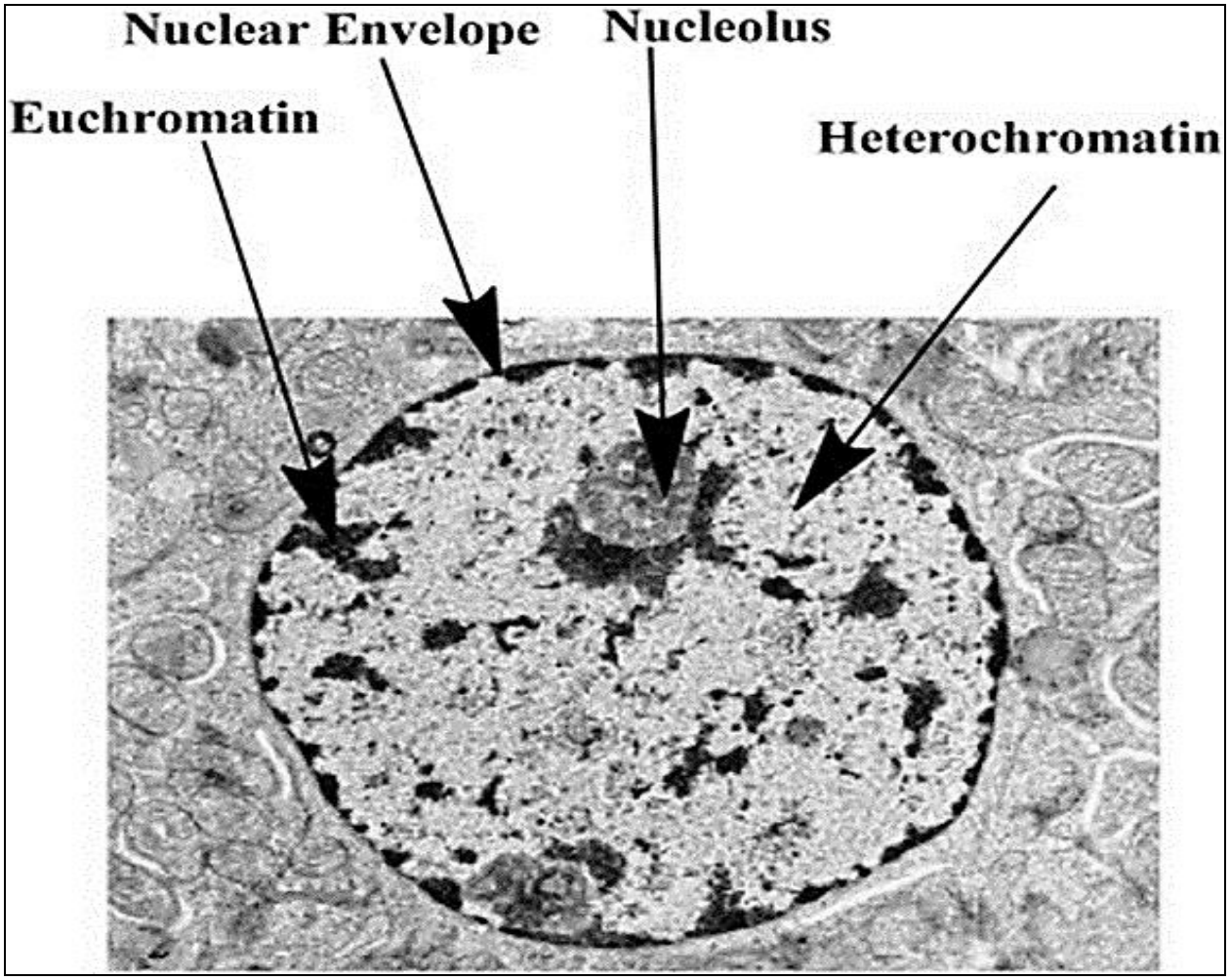
Dispersed

- Also called **euchromatin**
- less compacted
- Appear as lightly stained region in nucleus under microscope
- Transcription active, genes are exposed
- Function: gene expression & replication
- Interphase of cell cycle

Condensed

- Also called **heterochromatin**
- Highly compact form
- Dark stained region in nucleus under microscope
- Transcription inactive
- Two subtypes: constitutive & Facultative
- Function: structural role, maintain gene integrity
- Chromosomes

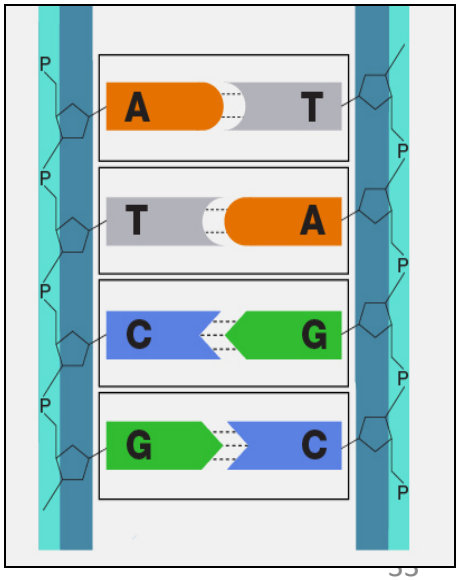




Euchromatin & Heterochromatin

Functions of chromatin:

- **Package DNA** into a smaller volume to fit in the nucleus
- **Regulation of DNA transcription & gene expression**
- **Chromosome Segregation :** during mitosis & meiosis chromatin condenses into chromosomes to ensure accurate separation of genetic material
- **DNA replication & repair**
- **To prevent DNA damage**



Levels of chromatin organization:

There are 3 levels of chromatin organization:

1. The "beads on a string"

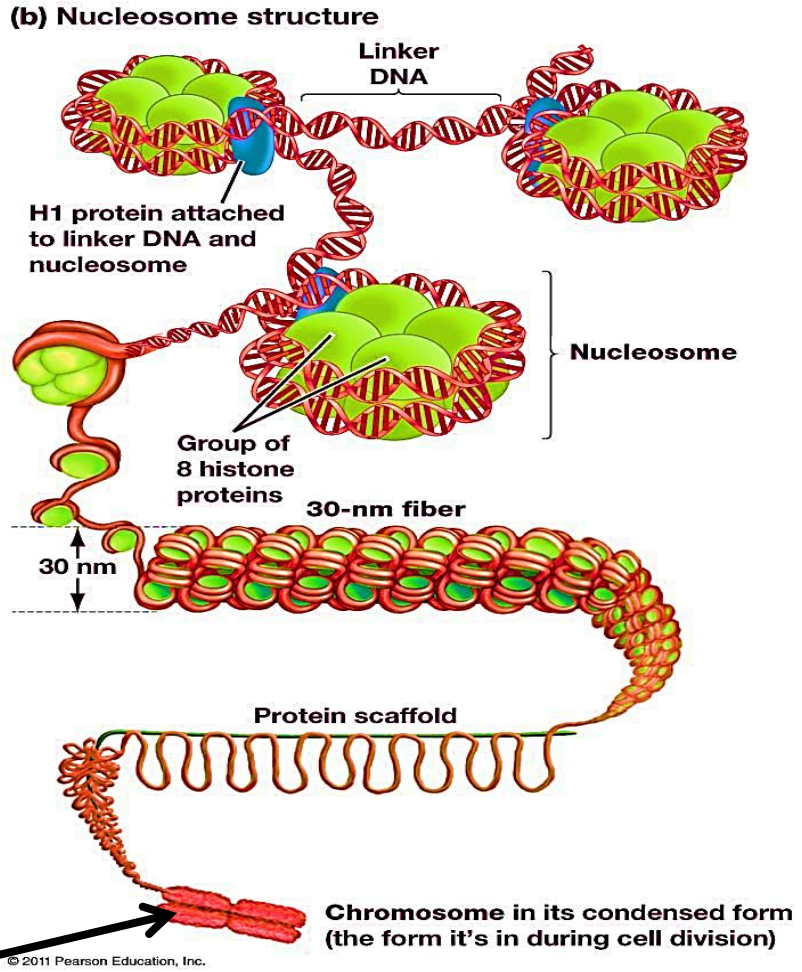
DNA wraps around **Histones** proteins forming nucleosomes

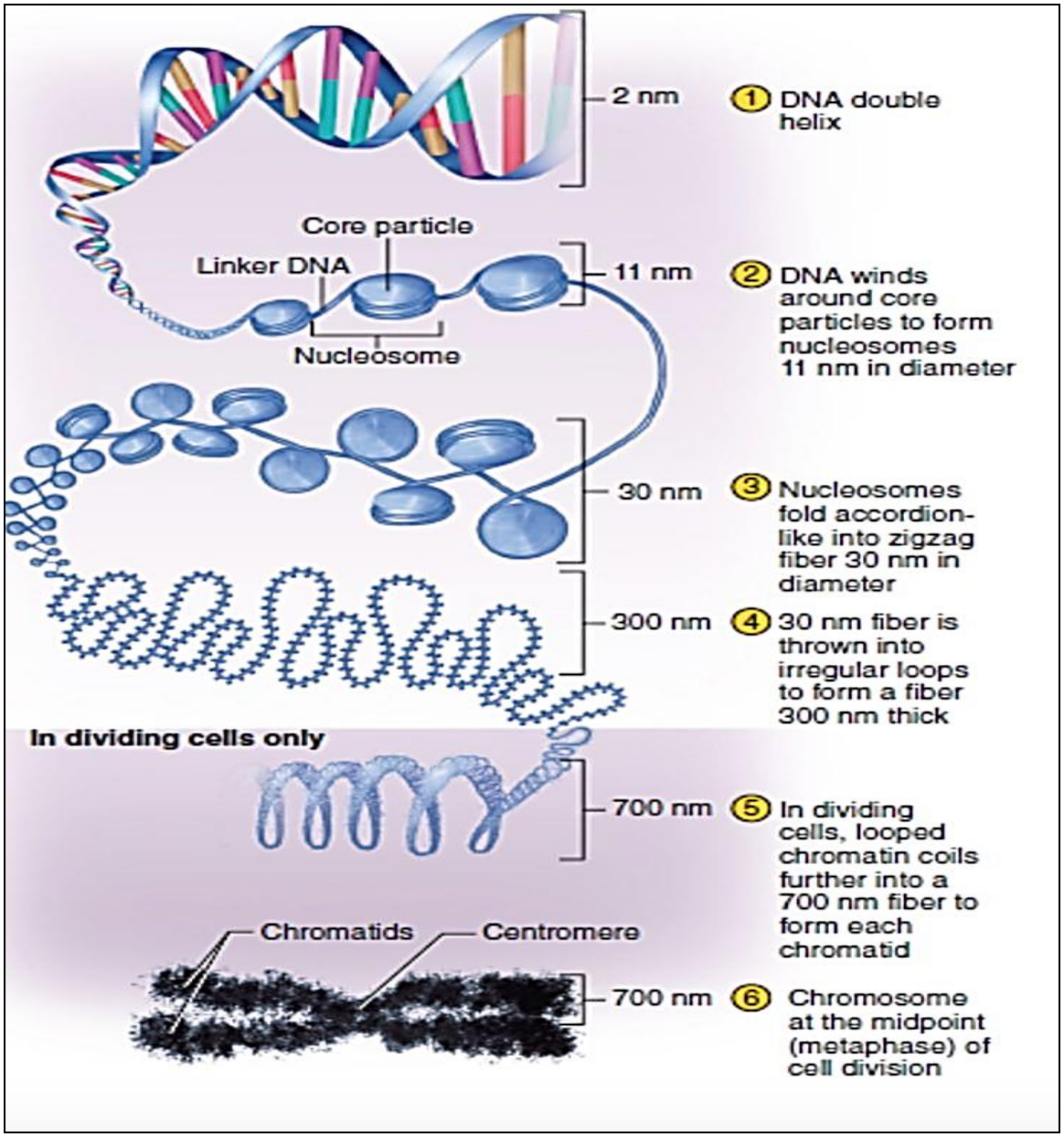
2. 10-30 nm fiber

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

3. Metaphase chromosome:

A higher organized level of DNA packaging of the 30 nm (during mitosis and meiosis).

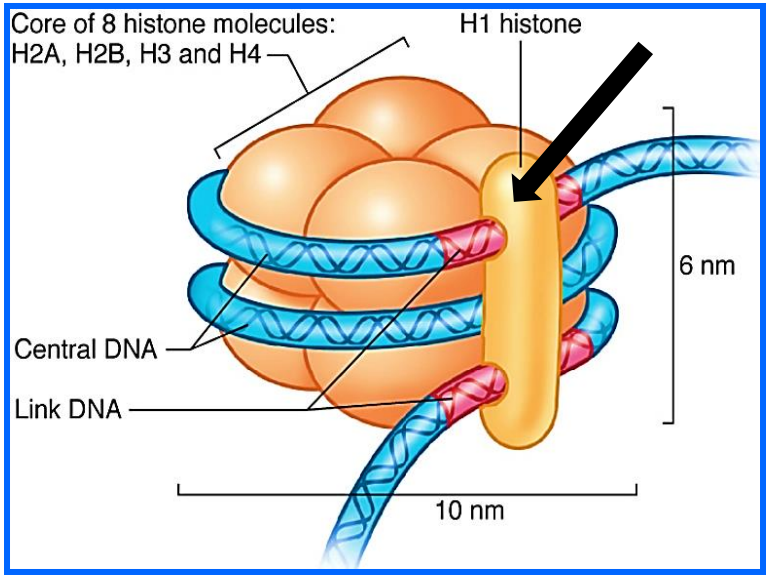




Levels of chromatin organization

1. the "beads on a string"

- DNA and histones are organized in repeating subunits called **nucleosomes**



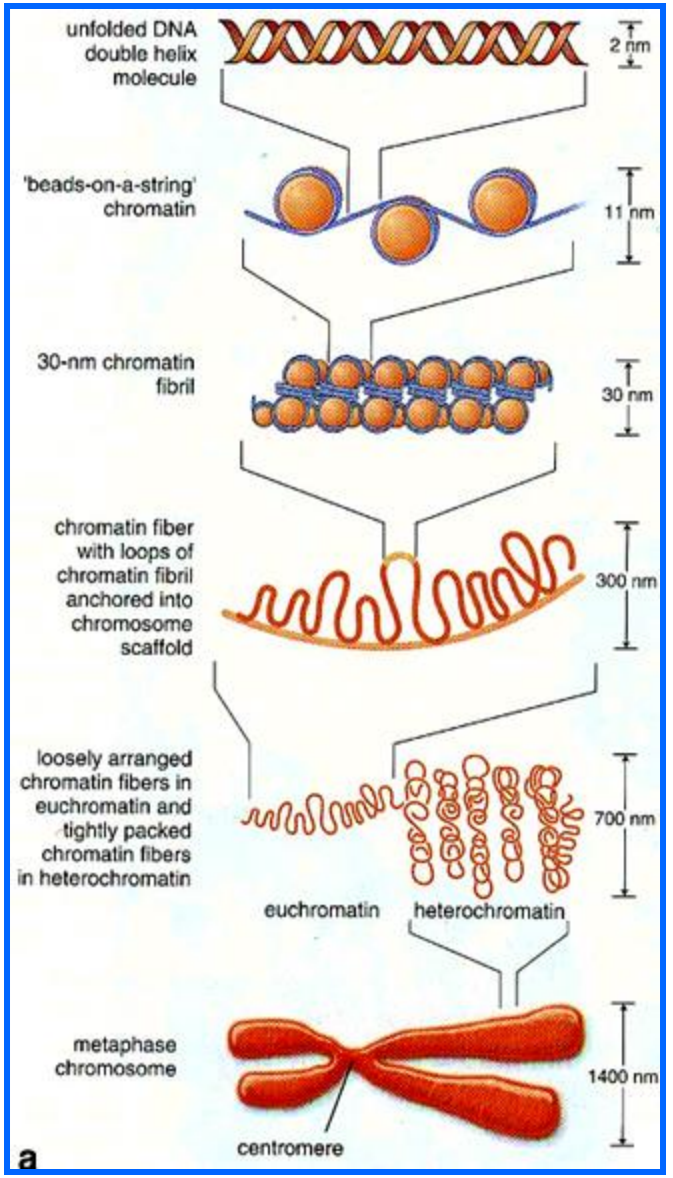
- **nucleosome** composed of **two loops** of DNA wrapped around a **protein core** (eight **histone** molecules, two copies of H2A, H2B, H3 and H4)
- A nucleosome core particle consists of **146 base pairs** of **DNA** wrapped in **two loops** around 8 histone molecules
- **H1 histone**, the **linker histone**, resides outside the nucleosome and binds to the **linker DNA** that connects one nucleosome to the next.

2. 10- 30 nm fiber:

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

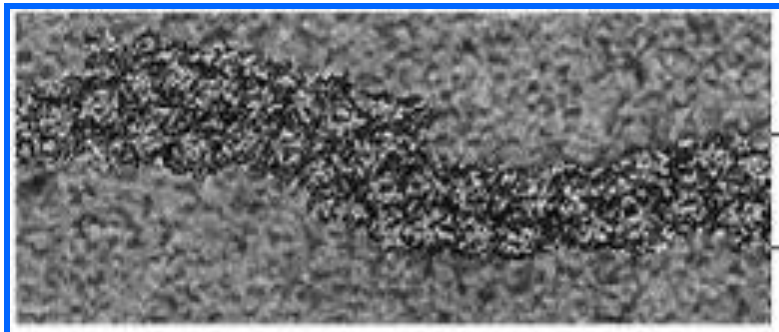
- The **30 nm fiber** gather into larger super-coiled loops

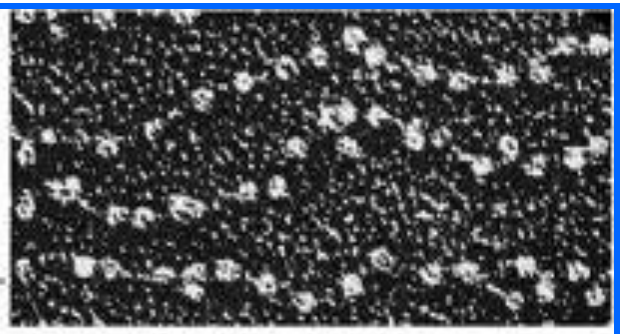
- The chromatin loops are anchored on a protein core (non-histone proteins).



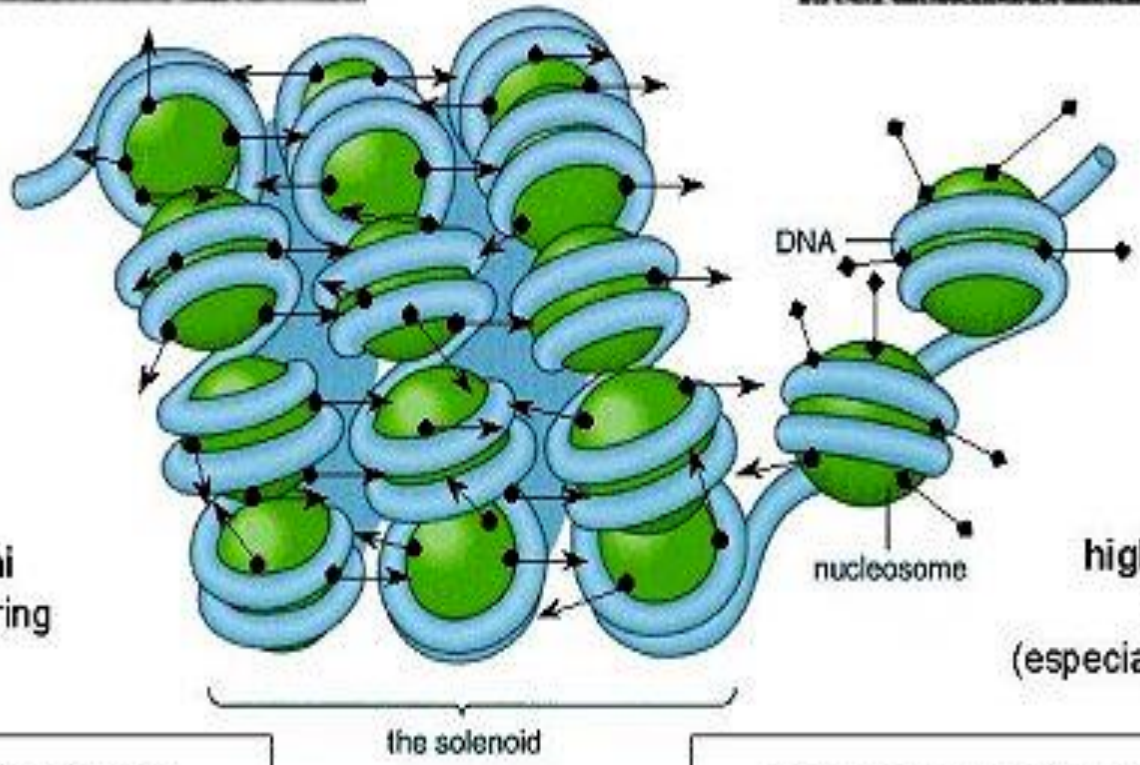
- Early during **mitotic** division chromatin fibers are highly condensed to form **chromosomes**

Chromatin fibers





30 nm chromatin fiber



11 nm (beads)

(+) charged N termini (bind DNA on neigboring nucleosomes)

highly acetylated core histones (especially H3 and H4)

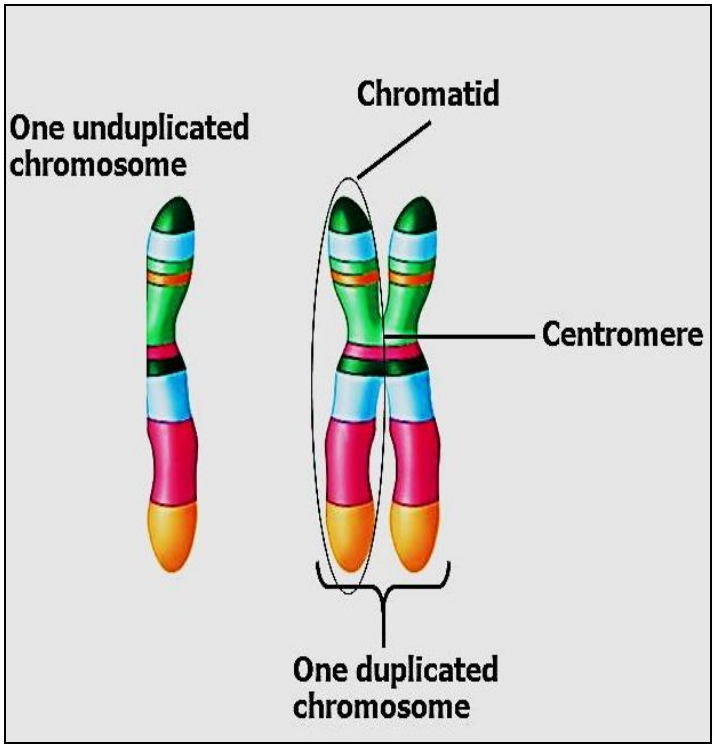
- HIGH level of histone H1
- NO gene transcription

- Reduced level of histone H1
- Gene transcription possible

3. Metaphase chromosomes:

- When cell prepares to **divide**, chromatin fibers coil up become more condensed forming **chromosomes**

- Predominantly heterochromatic



- Chromosomes may exist as either

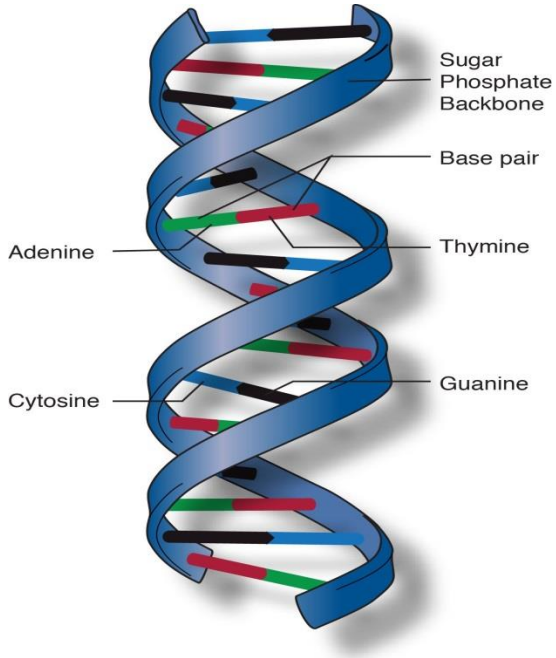
➢ **Unduplicated**: single strands

➢ **Duplicated:** two identical copies

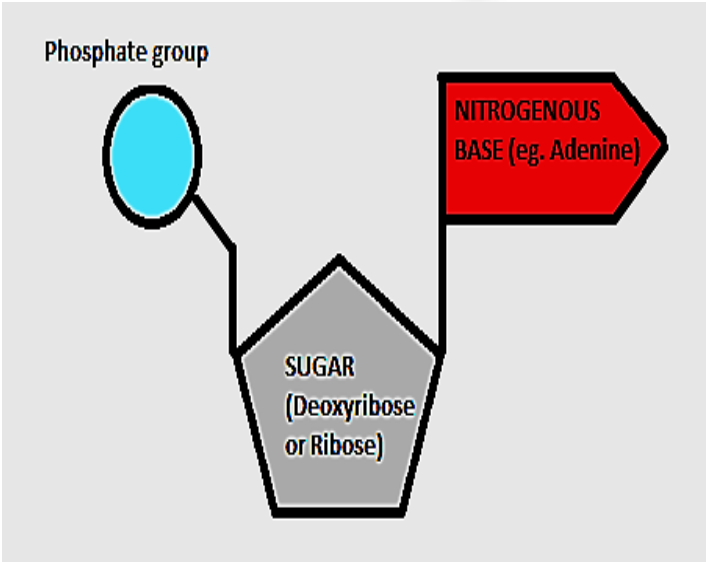
(called **chromatids**) joined by a **centromere**.

Structure of Deoxyribonucleic acid (DNA)

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



- DNA molecules consist of two strands coiled around each other to form a **double helix**



- Each DNA strand is composed of simpler units called **nucleotides**

- Each nucleotide is composed of a **nitrogen-base** either Adenine (A), Cytosine (C), Guanine (G), or Thymine (T) + **Sugar** (deoxyribose) + **phosphate** group.

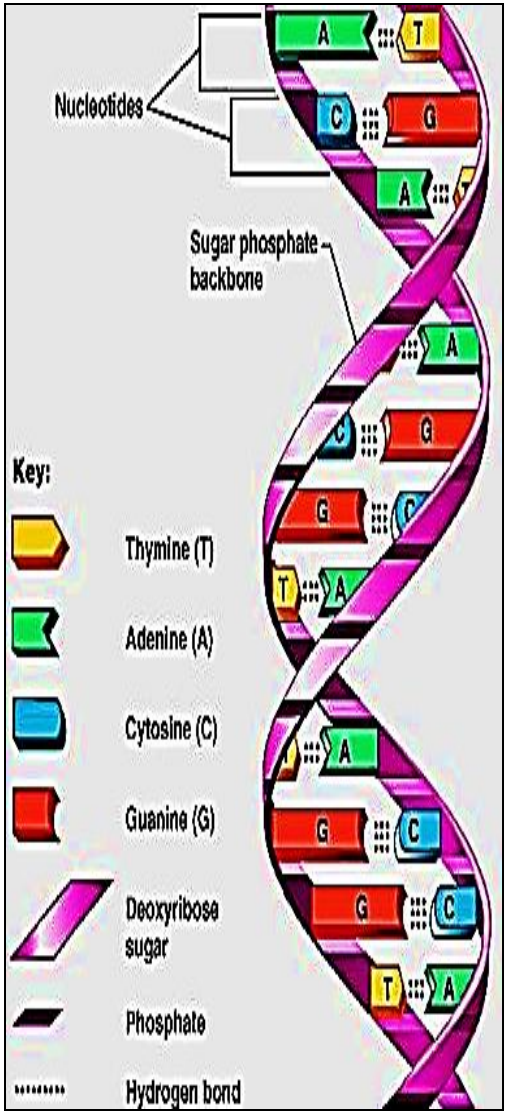
- According to base pairing rules

  (**A + T & C + G**)

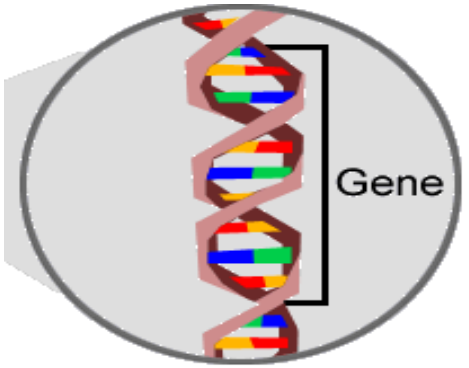
  Hydrogen bonds bind the nitrogenous bases of the two separate strands to make double-stranded DNA

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

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



Gene



- is a unit of heredity in living organisms.

  DNA consists of **thousands of genes**

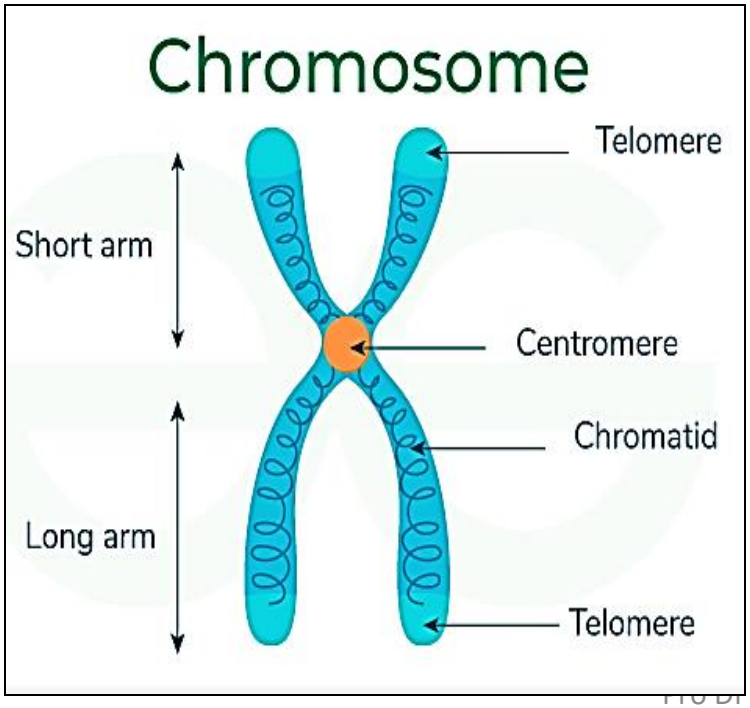
  It specifies everything that is needed for the maintenance, function, and replication of the cell

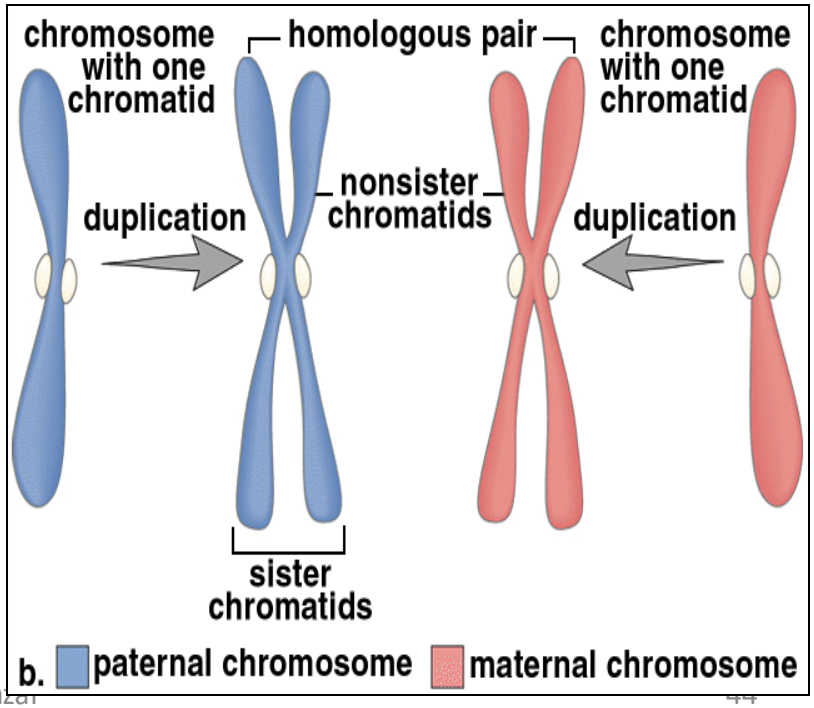
- ***Replication***: DNA making a identical copy of itself
- ***Transcription***: making of RNA from code of DNA
- ***Translation***: making of protein

chromosomes

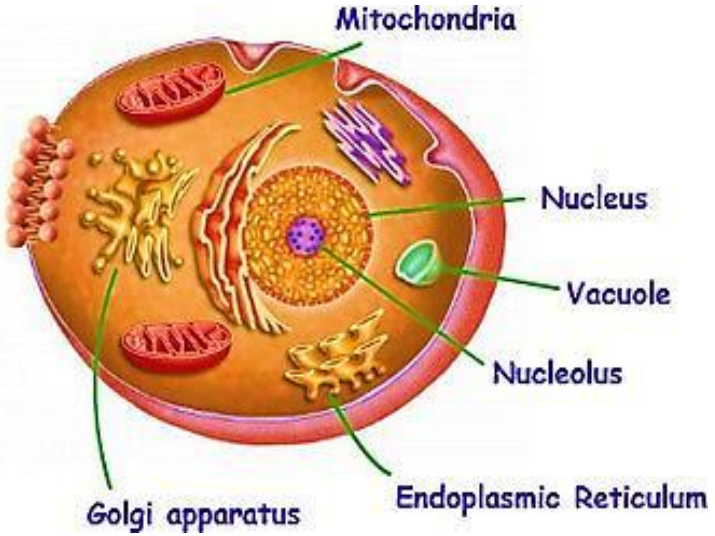
- A **chromosome** is an **organized** structure of **DNA** and **protein** found in nuclei of cells.
- Chromosomes carry the **genetic** information.
- The structure of chromosomes and chromatin **varies** through the **cell cycle** In human
- **Somatic cell** contains **23 pairs** i.e. **46 chromosomes** i.e. different chromosomes (**Diploid**).
- **Germ cell** (Gamete/sperm &egg cells) has one set of 23 chromosomes (**Haploid**).

- **One** of the chromosome pairs is the **sex chromosome (XX** or **XY)**, the other **22 pairs** of chromosomes are termed **autosomes**
- The members of each pair of autosomes are said to be **homologous**, because their DNA is very **similar**. The **X** and **Y** chromosomes are **not homologous**





Nucleolus



Plural: **nucleoli**

Is a **non-membrane** bounded structure found within nucleus

is the **most dense** (prominent) structure of the nucleus and frequently is located in its **center**

It contains parts of chromosomes carrying genes for ribosomal RNA & ribosomes (genes are transcribed & ribosomes are assembled { RNA + proteins}

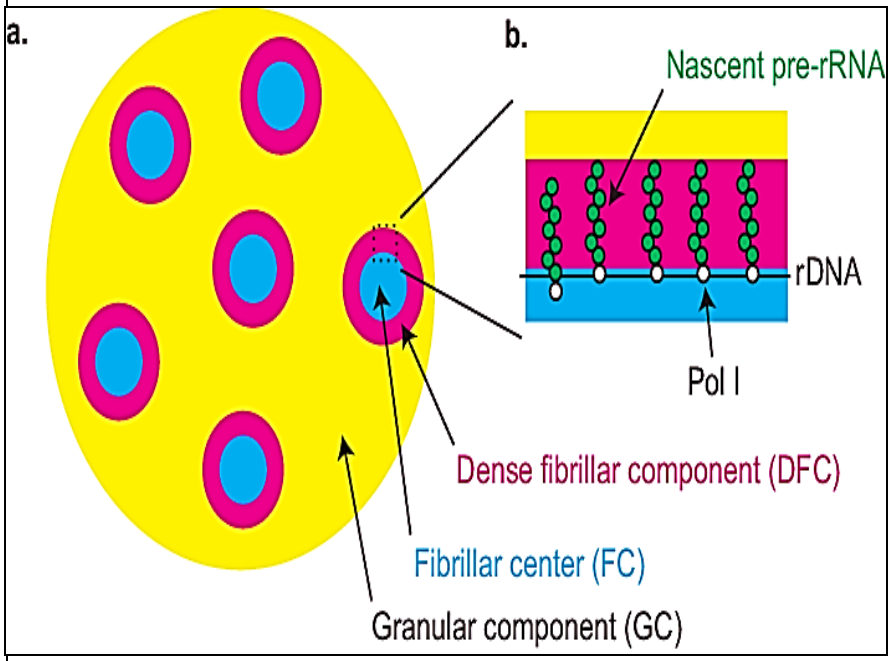
Function: synthesis & assembly of ribosomes

Structure of nucleolus:

The major components of the nucleolus are:

- **fibrillar center**: contain inactive ribosomal DNA (rDNA), is the site where rDNA is stored before transcription

- **Dense Fibrillar component**: surround the fibrillary center & contains newly transcribed rRNA + proteins
-
- **Granular component**: the outermost region where rRNA bound to ribosomal proteins & begin to **assemble** into ribosomal subunits



Thank you