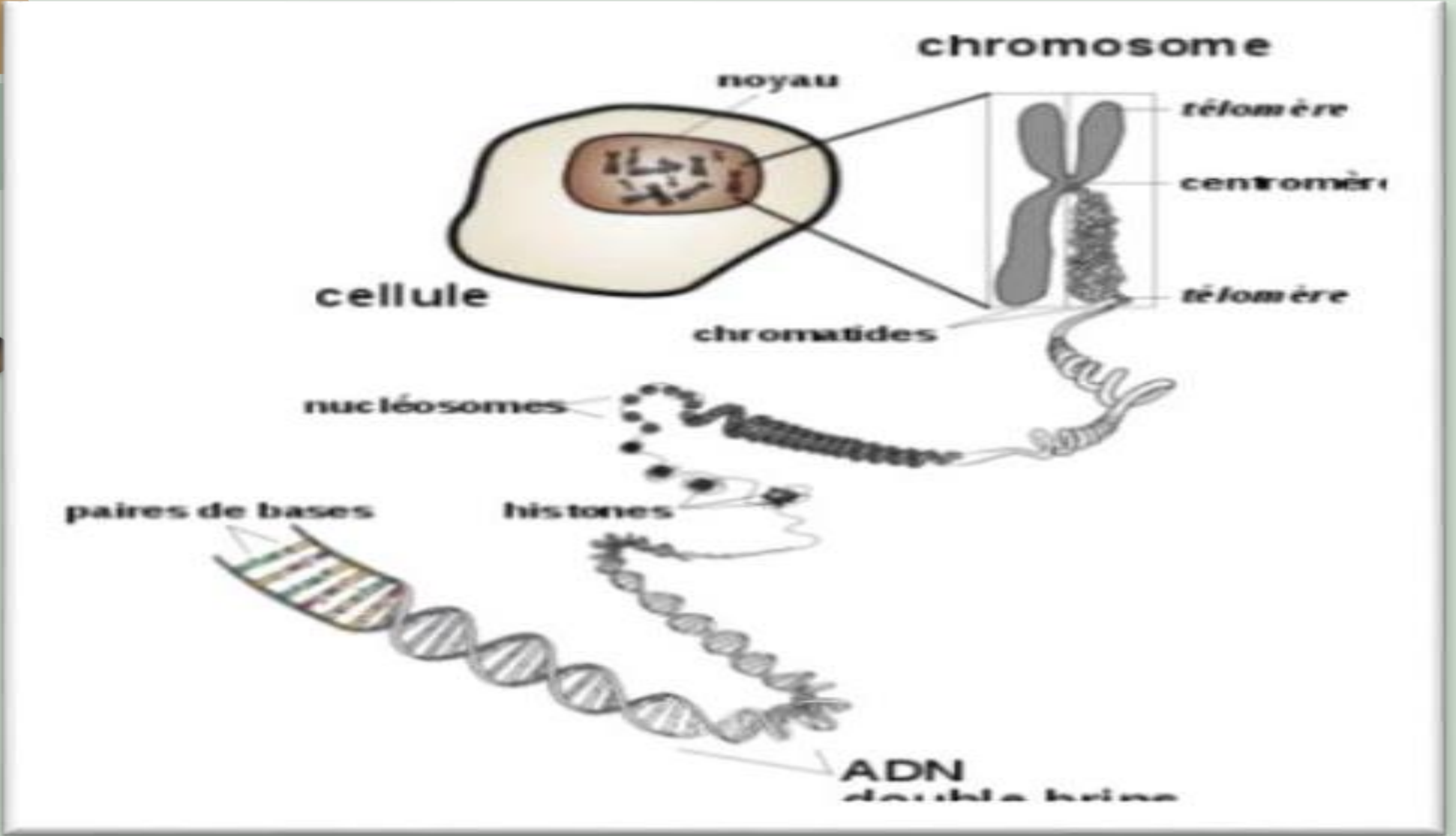
# Chapter 6:
# Chromatin, chromosome and cell nucleus

- Chromatin is the structure within which DNA is **packaged** and **compacted** in the limited volume of the nucleus of eukaryotic cells.
- Chromatin is made up of a combination of **DNA, RNA** and **proteins** of two types: **histones** and **non-histones**.
- It is **the main** constituent of eukaryotic chromosomes. Under microscopy, **two types** of **chromatin** are distinguished, corresponding to **different levels of compaction.**
- Euchromatin corresponds to a less condensed chromatin in which genes, more accessible, see their expression facilitated.
- **Heterochromatin corresponds to a denser chromatin with less easily accessible DNA.**

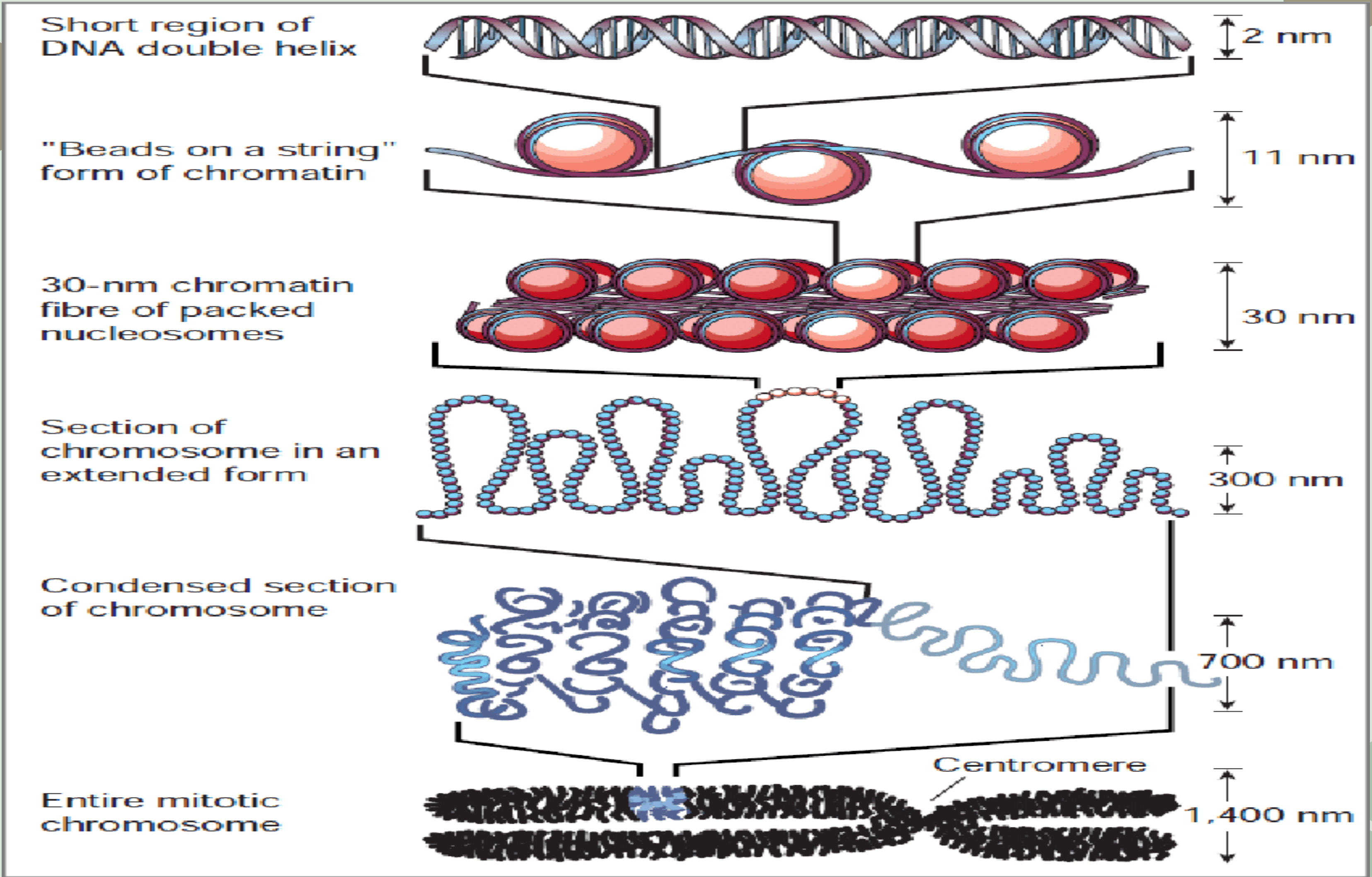

chromosome
noyau
télomère
centromèr
cellule
télomère
chromatides
nucléosomes
paires de bases
histones
ADN

**Heterochromatin :**

It is a condensed chromatin, fibers of **20 to 30 nm**, electron dense, located mainly at the periphery of the nucleus on the nucleoplasmic face of the internal nuclear membrane and in contact with the lamina. It is also found a little around the nucleolus, called perinucleolar heterochromatin

**Euchromatin:**

formed of fibers of 3.5 to 6 nm in diameter, very despiralized, weakly stainable, corresponding to active gene sites. It corresponds to DNA molecules in the process of transcription.


Short region of
DNA double helix
2 nm
"Beads on a string"
form of chromatin
11 nm
30-nm chromatin
fibre of packed
nucleosomes
30 nm
Section of
chromosome in an
extended form
300 nm
Condensed section
of chromosome
700 nm
Centromere
Entire mitotic
chromosome
1,400 nm

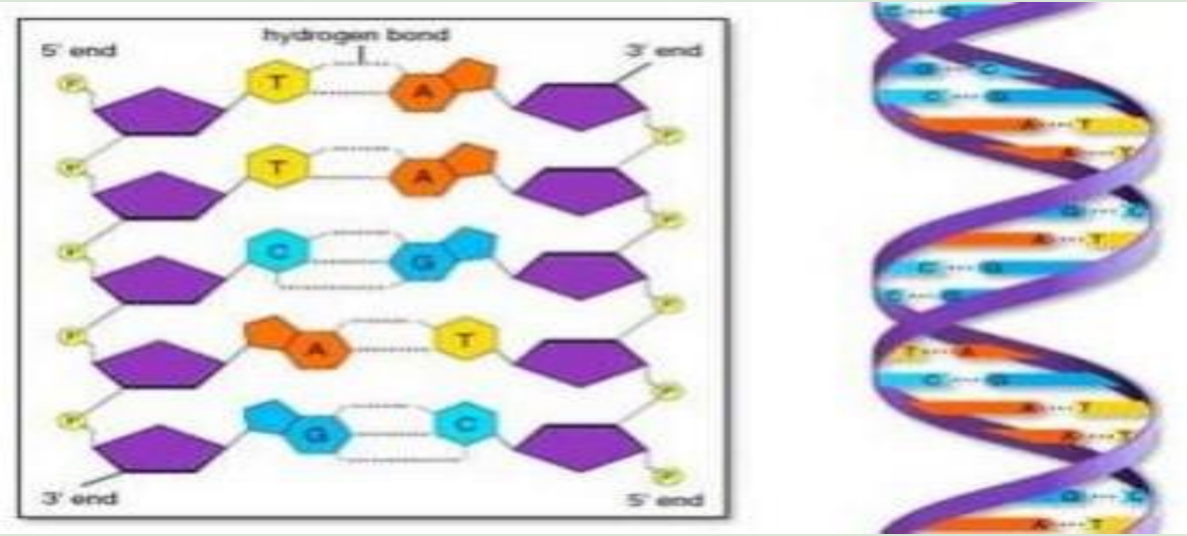
**When the cell enters mitosis the organization of the nucleus changes considerably. The chromatin threads coil and condense considerably to form these short rods called chromosomes ,**
**so chromatin and chromosome are two different morphological states of the same genetic material**

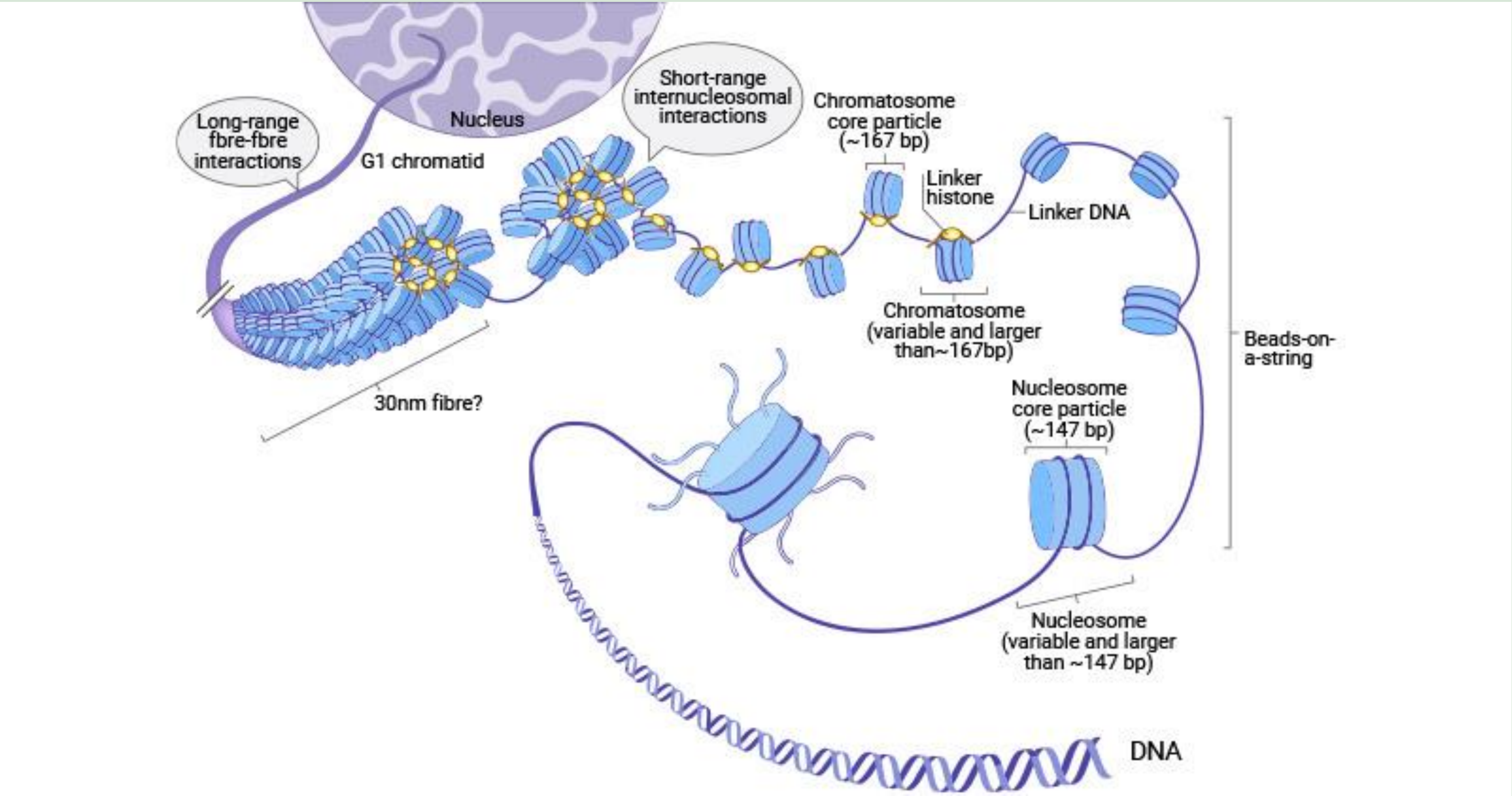
**Chromosomes:**

Chromosomes are individual molecules of DNA associated with proteins. They contain genes (made of DNA, the unit of hereditary information). Chromosomes carry all genetic information in the form of genes

**Chemical composition:**

**DNA:** It is a molecule formed of two long chains of nucleotides (double strand) wound in a double helix.Each strand is made up of a long chain of nucleotides.Each nucleotide is made up of a phosphoric acid, a deoxyribose (sugar) and a nitrogenous base.





Nucleus
Long-range fbre-fbre interactions
G1 chromatid
Short-range internucleosomal interactions
Chromatosome core particle (~167 bp)
Linker histone
Linker DNA
Chromatosome (variable and larger than~167bp)
Beads-on-a-string
30nm fibre?
Nucleosome core particle (~147 bp)
Nucleosome (variable and larger than ~147 bp)
DNA

## Organization of genetic material in eukaryotes: from chromatin to chromosomes:

The ADN of eukaryotic cells combines with **basic proteins** and **histone** cells to former structures called **nucleosomes**. In the course of the mitose of the chromatine, there is more and more of a complex with the participation of proteins and acids that make up a squelette from the base that drives the Fiber A (perle collar) that transforms into Fiber B (solénoïde) and then. Constitutes loops that condense more and more to reach the maximum hours of metaphase (chromosomal metaphase).

## 1. What Are Histones?

Histone was first discovered by Albrecht Kossel in 1884 [1]. Histones are a family of alkaline proteins found in the nuclei of eukaryotic cells and are the major structural components of chromosomes. They are rich in lysine and argin

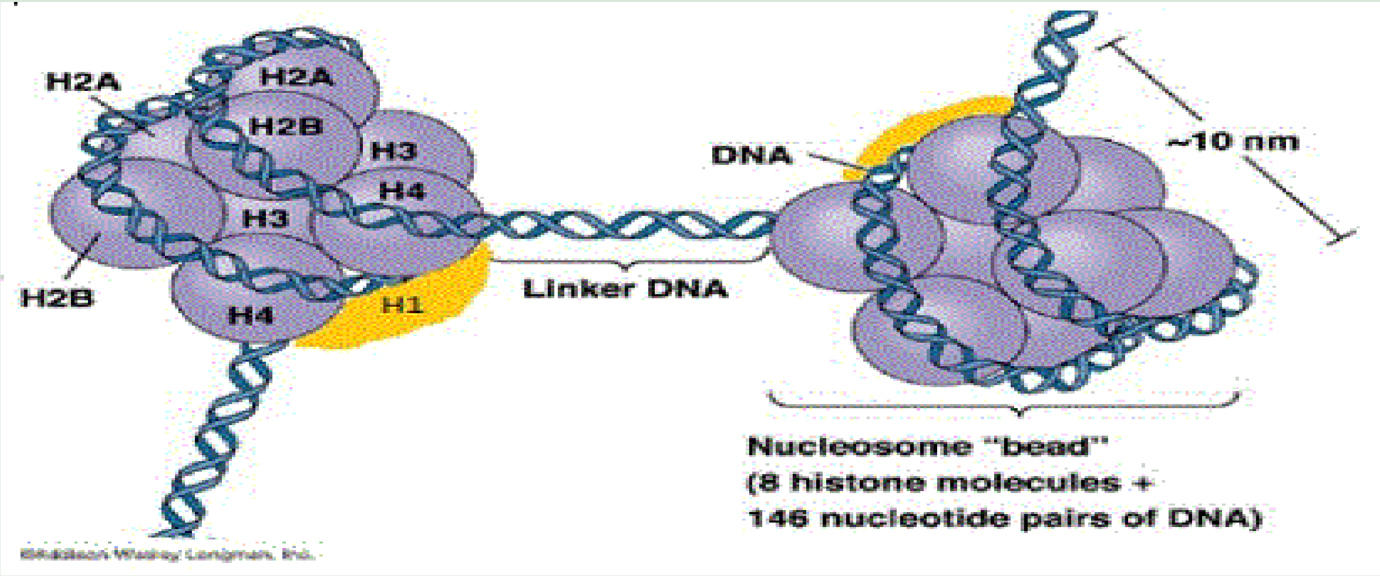
**2. Structure and Classes of Histones**

ely charged, enabling their tight binding to the negatively charged DNA to form chromatin.

**Histones:** are basic proteins of five types: H1, H2A, H2B, H3 and H4

The core of a nucleosome is a histone octamer composed of **2 histones H2A**, **2 histones H2B, 2 histones H3** and **2 histones H4**. Nucleosome = core particle = **146 bp** wrapped in a levorotatory helix around a histone octamer comprising two copies each of histones H3, H4, H2A, H3B.

**Histone H1** ('Linker histone') binds the DNA where it enters and exits the core particle over 20 bp, sealing the nucleosome.



The final passage from condensed chromatin to chromosome is done by the grouping of these loops into rosettes

This process allows to pass from a total length of 1.90 m for human DNA to a length of 220 µm corresponding to the total length of the chromosomes. This is a condensation of about 8000 times

**Metaphase chromosomes:**

chromosomes reach their maximum condensation during metaphase and are arranged on a single plane (equatorial plate). Their visibility is at its maximum at this stage and they appear split into two chromatids. They have a number of structural characteristics:

- The centromere or primary constriction: constrictions present at the level of all chromosomes. This is the last point of contact between the chromatids before their separation. It includes a complex of microtubules called kinetochore.The kinetochore is a supramolecular assembly of proteins at the level of the centromeric regions of mitotic chromosomes. There are two chinetochores per centromere which can, in mammals, interact with 20 to 40 microtubules

- **Secondary constriction:** constrictions present on certain chromosomes that correspond to the usual location of nucleolar organizers at rest during mitosis.
- **Telomeres:** These are special DNA sequences formed by numerous repetitions of short sequences (GGGTA in humans) and located at the ends of chromosomes. They are involved in the stabilization and protection of chromosome ends.

# Cell Nucleus

The nucleus plays a supporting rôle in the cell, but it is also the seat of our genetic program. Indeed, it contains our DNA in the form of a complex called chromatin.

What is the cell nucleus?
What is its composition?
What is its purpose?
What are its diseases and treatments.
We will learn everything about the cell nucleus.

# What is a cell nucleus?

**Definition of cell nucleus**

The nucleus is located at the center or periphery of the cell depending on the cell's function. It is present in eukaryotic cellular organisms , which are those that have a well-defined nucleus separated from the rest of the cell by a nuclear membrane . The nucleus contains and protects the genetic material of the cell, which is generally formed by DNA molecules.

## Shape of cell nuclei

The nucleus has a variable shape depending on the cell type (for example, it is spherical in neurons and ovoid in fibroblasts). Its diameter is a few micrometers (5 to 6 µm) and it generally represents less than 10% of the total cell volume.

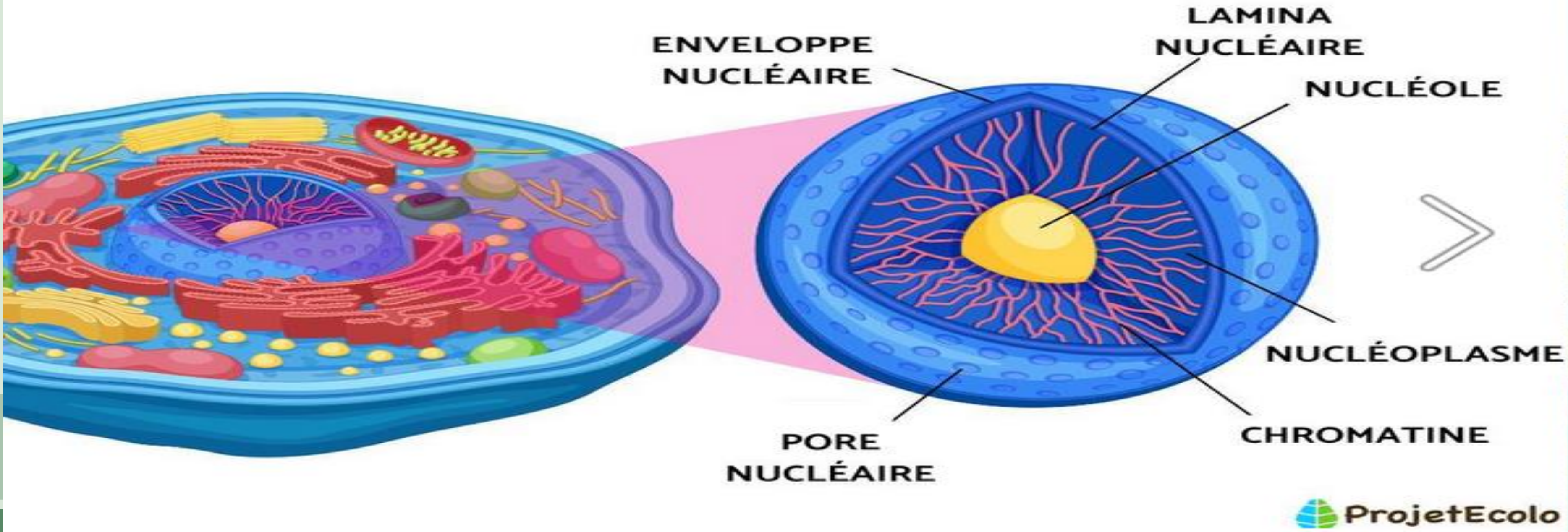
## Structure of cell nuclei

The nucleus is bathed in the cytoplasm, an aqueous gel found in the cell.The nucleus is separated from the cytoplasm by a nuclear envelope. This is composed of two spaced membranes that merge at certain points, forming openings or "nuclear pores".

The latter allow the passage of molecules between the nucleus and the granular endoplasmic reticulum that surrounds it.

The inner membrane merges with the nucleus while the outer membrane is an integral part of the rough endoplasmic reticulum.

# DÉFINITION ET SCHÉMA D’UN NOYAU CELLULAIRE



# Chapter 09/
# The interphase nucleus

**Definition**

The time interval between two successive cell divisions (mitoses) is called interphase. During this period, the nucleus is said to be interphase. Interphase is long in adult organisms, where divisions are rare.

Each cell has (or has during its development) a nucleus that contains almost all the genetic information. It characterizes eukaryotic cells.The nucleus or “vital center” of the cell is:Limited by a nuclear envelope during interphase. Indispensable to the life of eukaryotic cells.Carrier of the hereditary message in the form of DNA, which it preserves despite divisionsthanks to DNA replication.

Responsible for the synthesis of mRNA, tRNA, and ribosomal RNA.It represents the most visible element in a eukaryotic cell.

## II. Structure:

**A. Highlighting:**

1. **By standard staining:** Hematoxylin-eosin, the nucleus appears basophilic.
2. **2. By special staining:** Toluidine blue, Feulgen staining.

**B. Morphological characteristics of the nucleus:** The nucleus is limited by a nuclear envelope formed of two membranes separated by a perinuclear space, and contains:

- ➢ A poorly stainable nucleoplasm.
- ➢ Clusters of a highly chromophilic substance, chromatin.
- ➢ Spherical bodies, the nucleoli.

-Size: It varies according to the cell type.

**The Nucleo-cytoplasmic ratio(NCR) is the ratio:** volume of the nucleus / Cell volume-volume of the nucleus.This ratio is constant for each cell type and is specific to the species.

**-Shape:**

the shape of the nucleus differs depending on the shape of the cell.It can be rounded in cubic cells, ovoid in cylindrical cells,discoid or polylobed….

-**Position:** the nucleus can be:

✓ **Central:** lymphocytes, fibroblasts, endocrine gland cells.

✓ **Pushed back to the base of the cell:** mucous cells, exocrine glandular cells.

✓ **Peripheral**: striated muscle cells, adipocytes.

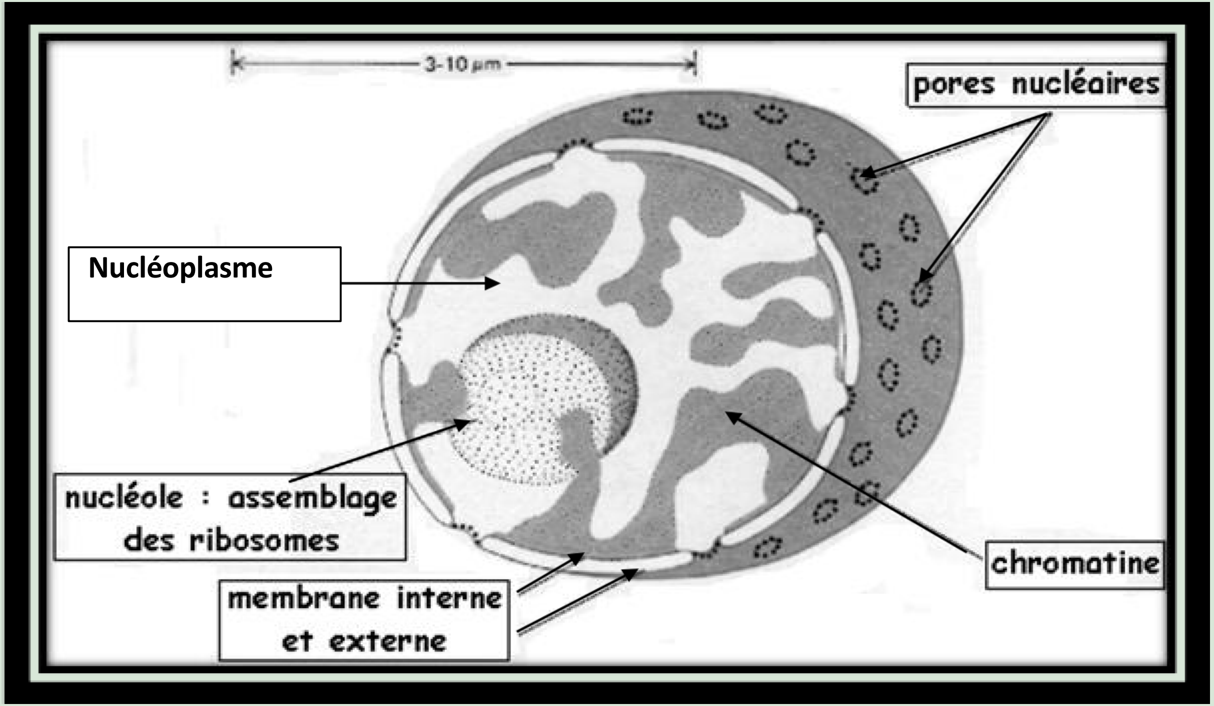
-Number: the majority of cells have a single nucleus, but there areexceptions:

-Red blood cells and keratinocytes (cells of the superficial layers of the epidermis)are anucleated cells.

-Hepatocytes (liver cells) most often have 02 or more nuclei.

-Osteoclasts, giant cells of bone tissue, have on average around ten nuclei.

# III. Ultrastructure:




**The interphase nucleus in electron microscopy**

**Le noyau interphasique en microscopie électronique**

**A. The nuclear envelope:**

is a complex membrane assembly characteristic of eukaryotic cells that:

 Separates chromatin from hyaloplasm during interphase.

 And controls exchanges in both directions between the nucleus and hyaloplasm.

**1. Ultra structure:**

-The nuclear envelope appears to be formed of two tri-stratified membranes, each 75A° thick.

-These two membranes are separated by a peri-nuclear space 200 to 400A° wide.

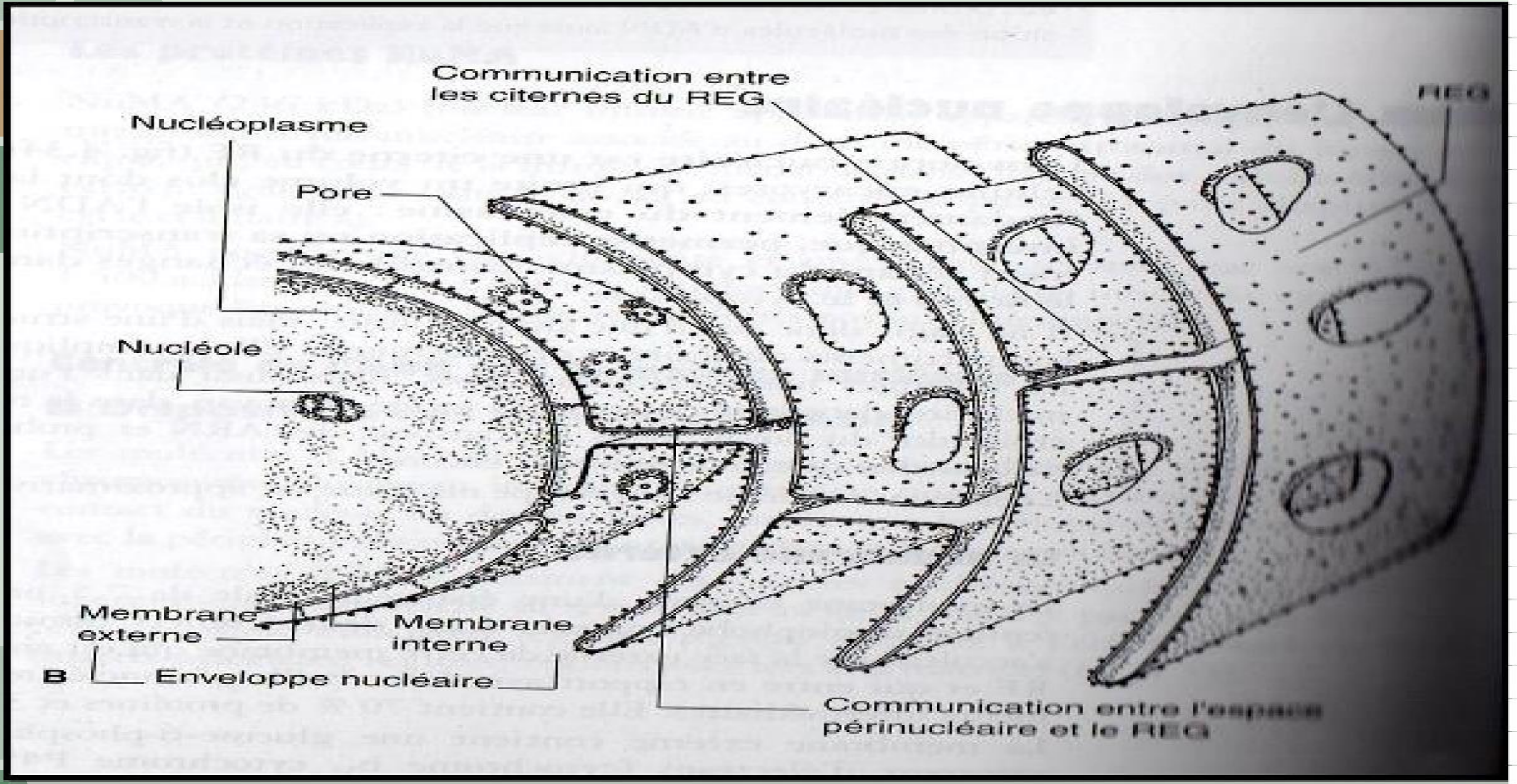
**a. The external membrane:**

**b.** • Is lined, on its hyaloplasmic face, with ribosomes and is continuous with the endoplasmic reticulum.

c. • Contains 70% proteins and 30% lipids.

d. • Is very rich in enzymes: glucose-6-phosphatase, two electron transport chains (cytochromes).

e. **b. The perinuclear space:** located between the two membranes, represents the storage site for calcium ions.




the nuclear envelope

**Enveloppe nucléaire (1)**

**d. Role of the nuclear envelope:**

it:

-  Plays the role of a barrier controlling the passage of water, ions and macromolecules.
-  Is involved in nucleocytoplasmic exchanges.
-  Participates in protein synthesis, through its external membrane which is lined with ribosomes.
-  Ensures the active transport of $Ca^{++}$, as well as its storage in the perinuclear space.

## B. The Nuclear Pore:

### 1. Definition:

Nuclear pores: are:

-  Complex structures, made up of zones of interruption of the nuclear envelope,
-  Formed by an assembly of positively charged proteins (about fifty) called: nucleoporins.
-  With a molecular weight of around 125 million Daltons, involved in exchanges between the nucleus and the cytoplasm.

## 2. Pore dynamics:

Pores are not permanent structures, but dynamic structures, likely to disappear during cell rest and reappear when nucleocytoplasmic exchanges are increased.The number of pores is approximately 3000 to 4000 per nucleus (5 to 15% of the envelope surface). It varies according to the physiological state of the cell, particularly during cell growth (embryogenesis).

## 3. three-dimensional structure:

It shows an organization in 8 subunits, these eight subunits form two rings,one cytoplasmic, the other nucleoplasmic. Each ring carries perpendicular filaments, the filaments located on the nucleoplasm side are connected at their end andform a nuclear basket. The whole is anchored in the nuclear envelope.Towards the pore each s/unit emits an arm, connected to the two rings. The arms leave betweenthem fine lateral tunnels of about 10nm. All the arms form a central tunnelof the order of 40nm. The central tunnel is closed by a diaphragm, its opening isdone during the passage of molecules in the presence of energy. 4. Role of the pore:

The pores control nucleocytoplasmic exchanges, in both directions, both in the cytoplasm-nucleus direction and in the nucleus-cytoplasm direction, and allow selective transit:

• Small molecules (nucleotides, proteins, etc.) with a molecular weight < 4OKda and ions pass through the pore without external intervention by passive diffusion: these exchanges use the lateral channels of the pore.

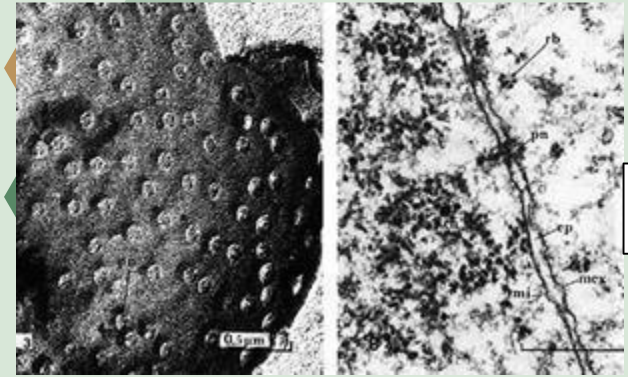
3**. structure tridimensionnelle :** Elle montre une organisation en 8 sous-unités, ces huit sous unités forment deux anneaux, l’un cytoplasmique, l’autre nucléoplasmique. Chaque anneau porte des filaments perpendiculaires, les filaments situés du coté du nucléoplasme sont reliés à leur extrémité et forment un panier nucléaire. L’ensemble est ancré dans l’enveloppe nucléaire. Vers le pore chaque s/unité émet un bras, reliés aux deux anneaux. Les bras laissent entre eux des tunnels latéraux fins de 10nm environ. L’ensemble des bras ménagent un tunnel central de l’ordre de 40nm. Le tunnel central est obturé par un diaphragme, son ouverture se fait lors du passage de molécules en présence d’énergie. 4. Rôle du pore : Les pores contrôlent les échanges nucléo cytoplasmiques, dans les 2 sens, aussi bien dans le sens cytoplasme-noyau que dans le sens noyau-cytoplasme, et permettent un transit sélectif:

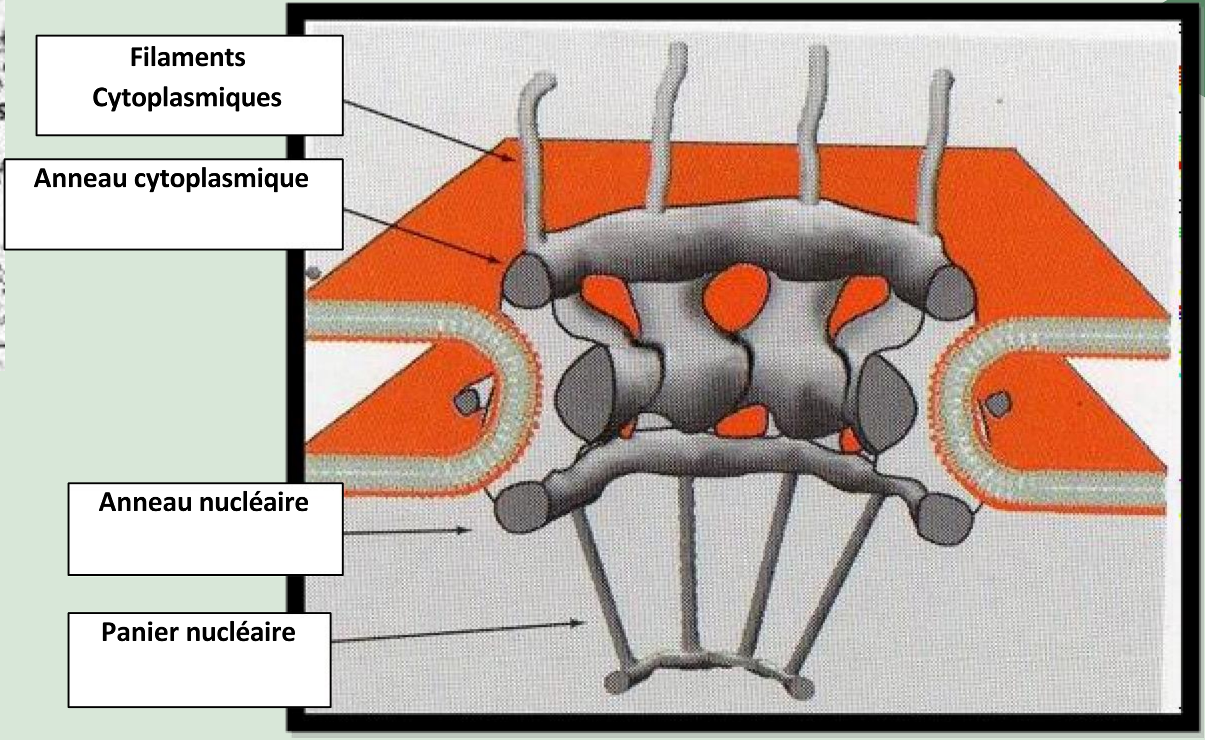
- Les petites molécules (nucléotides, protéines...) de poids moléculaire < 4OKda et les ions traversent le pore sans intervention extérieur par **diffusion passive**: ces échanges utilisent les **canaux latéraux** du pore.

Le transport des **grosses molécules** se produit à travers le **transporteur central** et s'assoient à des protéines spécialisées de transport, dont le transport nécessite de l**’énergie**:

Le transport met en jeu un système d’adressage basé sur l’existence de séquences spécifiques d’acides aminés. Seules les protéines portant ce signal seront transportées.

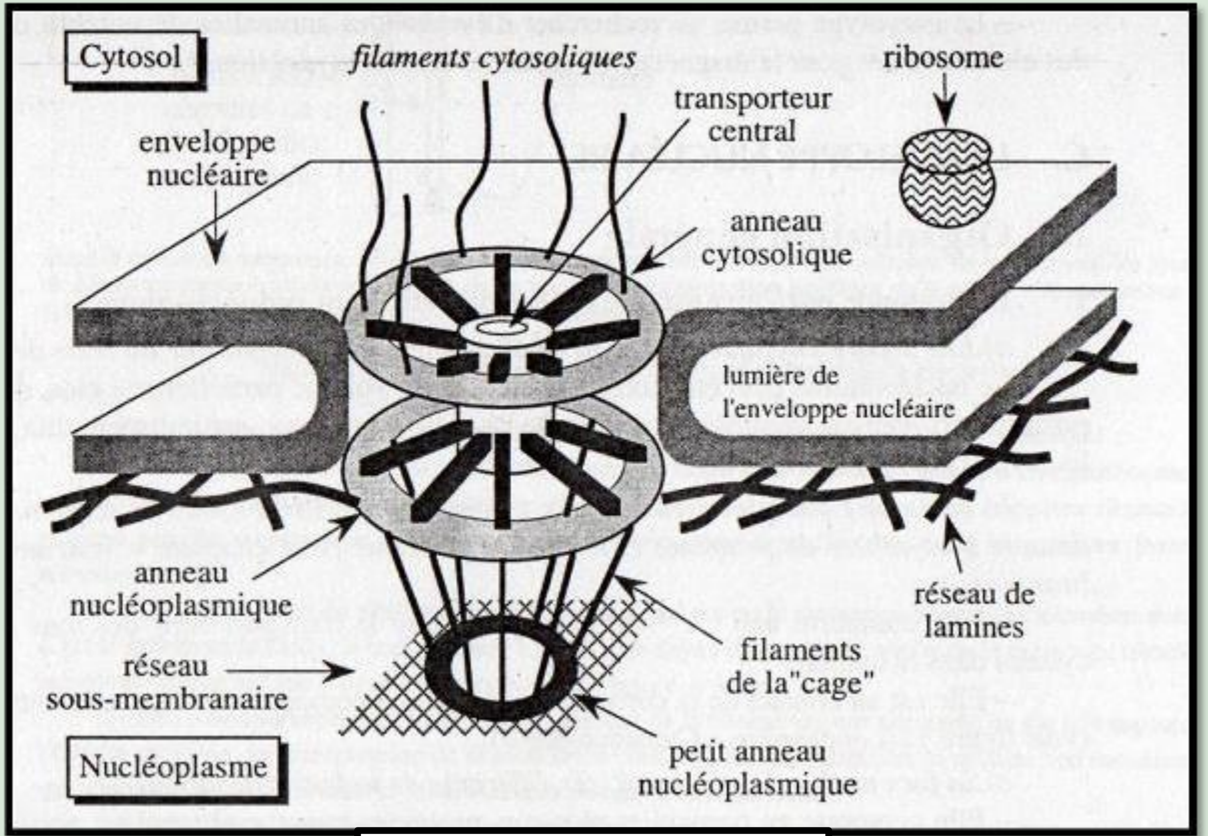
Le transport met en jeu un adaptateur (importine, exportine) reconnaissant un système d’adressage.






Section of a nuclear pore (2)

**Coupe d’un pore nucléaire (2)**




**Le complexe du pore nucléaire**

**Vue de Face (4)**

## E. Chromatin:

**Definition:**

chromatin represents the content of the nucleoplasm observable by optical or electron microscopy in the nuclei of cells in interphase (outside of mitosis).
Chromatin has two aspects:

**(see chapter 6)**

**C. The lamina:** is a dense protein fibrillar network, closely linked to the inner faceof the envelope.
The lamina is made up of fibrous polypeptides, called lamins, proteinsof the cytoskeleton of the intermediate filament family (lamins A, B and C).
The lamina dissociates at the beginning of mitosis and finally reorganizes itself during cell division.

-  **Roles:** constitutes a scaffold that gives the nucleus its shape and maintains the rigidityof the nuclear envelope.
-  **Pathology:** Progeria: -is an extremely rare genetic disease, characterizedby premature aging. - Due to a mutation of the gene that codes for lamins, located on chromosome 1.