Cellular Organelles

Microfilament, Microtubules, Nucleus & Cell Cycle

Learning Objectives:

- Define the term " Cytoskeleton". Describe the structure & functions of microfilaments, intermediate filaments, and microtubules.
- Describe the structure (anatomy), contents and functions of the nucleus.
- Define the term "Cell Cycle" and describe **BREIFLY** its different phases.
- Match individual functions/events of the cell cycle with the phase in which such functions/events occur.

The Cytoskeleton:

- The cytoskeleton, literally, ***"cell skeleton"***, is an elaborate network of rods running through the cytosol and hundreds of accessory proteins that link these rods to other cell structures.

- It acts as a cell's ***"bones," "muscles," and "ligaments"*** by supporting cellular structures and providing the machinery to generate various cell movements.

- There are three types of rods in the cytoskeleton, ***non of them is membrane covered are:***

  - **Microfilaments**
  - **Intermediate filaments.**
  - **Microtubules.**

The Cytoskeleton - *Microfilaments:*

- Microfilaments ***The thinnest elements of the cytoskeleton***, microfilaments, are semiflexible strands of the protein actin ("ray").

- Each cell has its own unique arrangement of microfilaments, so no two cells are alike. However, nearly all cells have *a fairly dense cross-linked network of microfilaments, called the **terminal web***, attached to the cytoplasmic side of their plasma membrane. The web strengthens the cell surface, resists compression, and transmits force during cellular movements and shape changes.

- *Most microfilaments are involved in cell motility (movement) or changes in cell shape.* The cells move "when they get their actin together." ***e.g., actin filaments interact with another protein, unconventional myosin, to generate contractile forces in a cell.***

- This interaction also ***forms the cleavage furrow that pinches one cell into two during cell division***. Microfilaments attached to cell adhesion molecules are responsible for the crawling movements of ***amoeboid motion***, and for ***the membrane changes that accompany endocytosis and exocytosis.***

- ***Except in muscle cells, where they are highly developed, stable, and long-lived***, ***actin filaments are constantly breaking down and re-forming from smaller subunits whenever and wherever their services are needed.***

The Cytoskeleton – *Intermediate Filaments :*

- Intermediate filaments are ***tough, insoluble protein fibers*** that ***resemble woven ropes.***

- Made of twisted units of tetramer (4) fibrils, they ***have a diameter between those of microfilaments and microtubules.***

- ***Intermediate filaments are the most stable and permanent of the cytoskeletal elements and have high tensile strength***. They attach to desmosomes, and their main job is to act as internal guy-wires to resist pulling forces exerted on the cell.

- ***Because the protein composition of intermediate filaments varies in different cell types, there are numerous names for these cytoskeletal elements***—for example, ***they are called neurofilaments in nerve cells and keratin filaments in epithelial cells.***

The Cytoskeleton - *Microtubules:*

- ❖ The elements with ***the largest diameter***, microtubules, are hollow tubes made of spherical protein subunits called ***tubulins***. Most microtubules radiate from a small region of cytoplasm near the nucleus called ***the centrosome*** or ***cell center.***

- ❖ Microtubules are remarkably dynamic organelles, constantly growing out from the centrosome, disassembling, and then reassembling at the same or different sites.

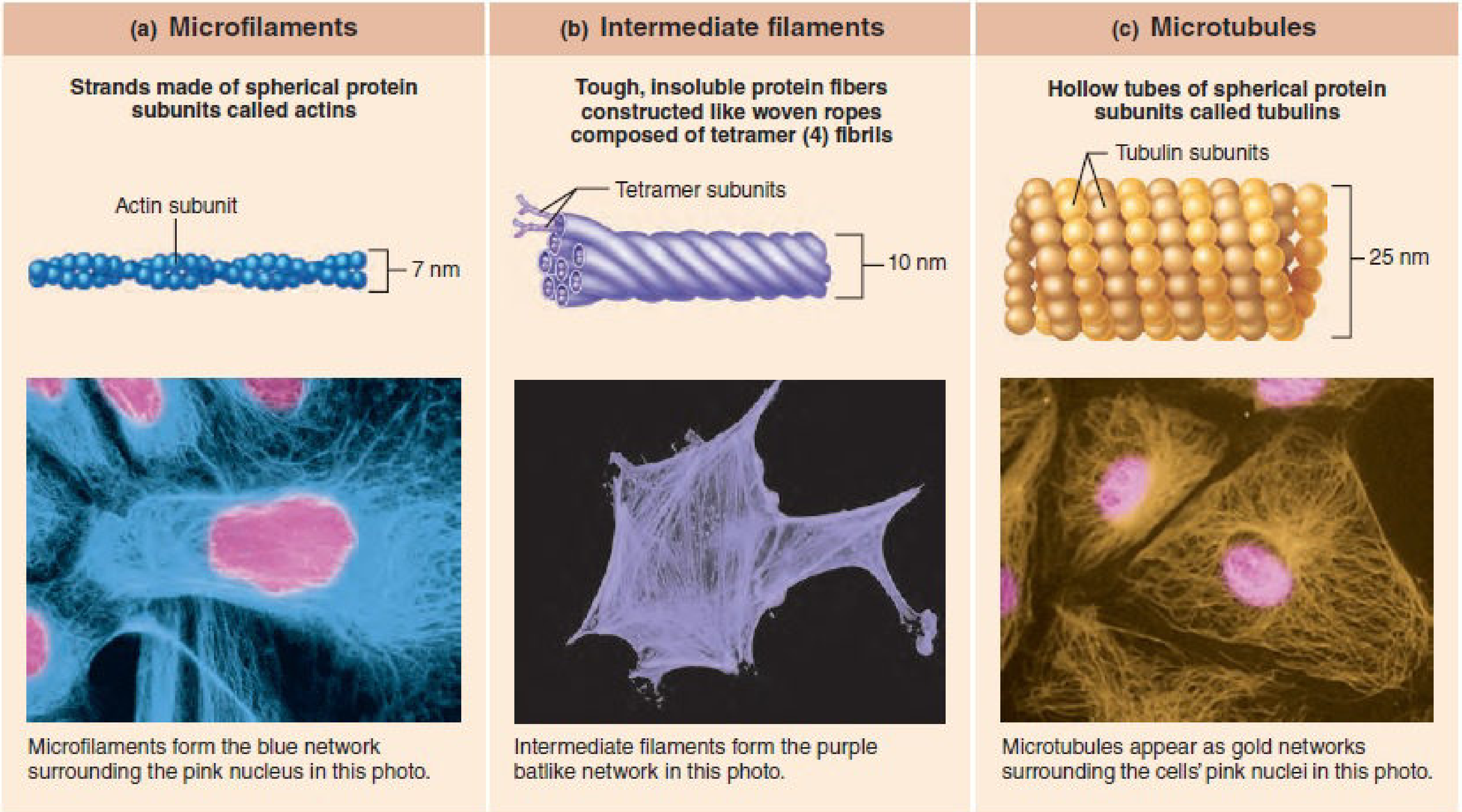
- ❖ The stiff but bendable ***microtubules determine the overall shape of the cell, as well as the distribution of cellular organelles.***

- ❖ Mitochondria, lysosomes, and secretory vesicles attach to the microtubules like ornaments hanging from tree branches. Tiny protein machines called ***motor proteins*** *(kinesins, dyneins, and others*) continually move and reposition the organelles along the microtubules.

- ❖ Motor proteins work by changing their shapes. Powered by ATP, some motor proteins appear to act like train engines moving substances along on the microtubular "railroad tracks."

- ❖ Others move "hand over hand" somewhat like an orangutan gripping, releasing, and then gripping again at a new site further along the microtubule.

The Cytoskeleton:



Cytoskeletal elements support the cell and help to generate movement. Diagrams (above) and photos (below). The photos are of fibroblasts treated to fluorescently tag the structure of interest.

The Cytoskeleton - *Centrioles:*

- As mentioned, microtubules are anchored at one end in an inconspicuous region near the nucleus called the ***centrosome*** or ***cell center.***

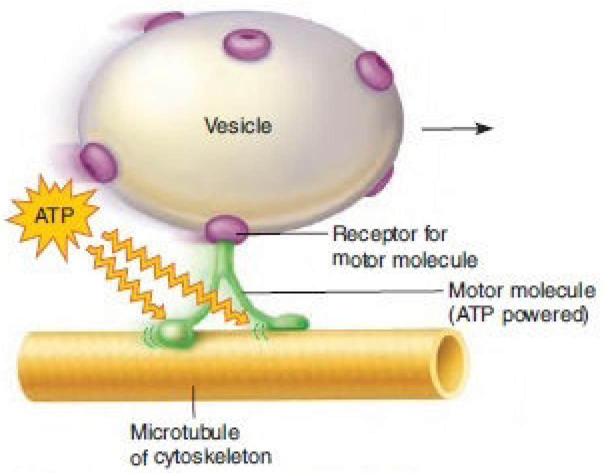
- The centrosome acts as a microtubule organizing center. It has few distinguishing marks other than a granular looking matrix that contains ***paired centrioles***, ***small, barrel-shaped organelles oriented at right angles to each other.***

- *The centrosome matrix (with centrioles) is best known for generating microtubules and* ***organizing the mitotic spindle in cell division****.*

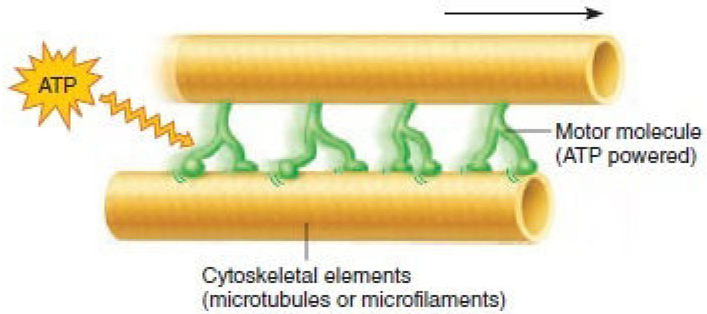
- Each centriole consists of ***a pinwheel array of nine triplets of microtubules, each connected to the next by non tubulin proteins and arranged to form a hollow tube***. Centrioles also form the bases of cilia and flagella.

The Cytoskeleton:

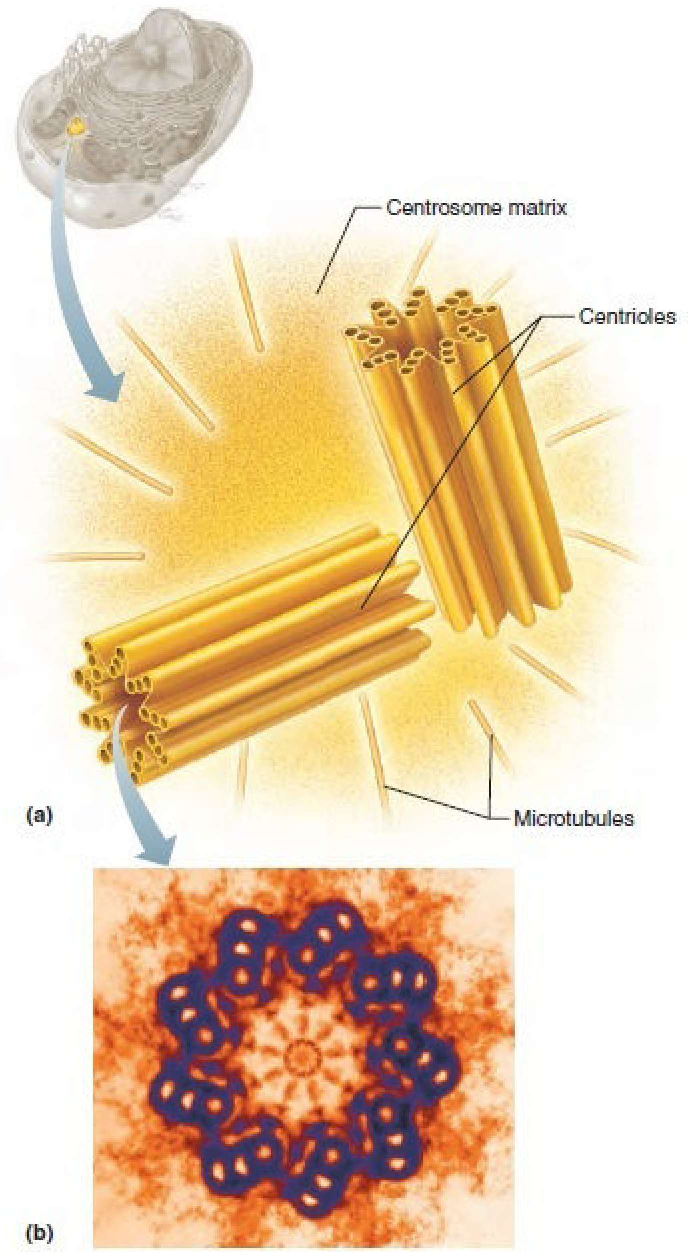
Microtubules and microfilaments function in cell motility by interacting with motor molecules powered by ATP.



(a) Motor molecules can attach to receptors on vesicles or organelles, and carry the organelles along the microtubule "tracks" of the cytoskeleton.



(b) In some types of cell motility, motor molecules attached to one element of the cytoskeleton can cause it to slide over another element, which the motor molecules grip, release, and grip at a new site. Muscle contraction and cilia movement work this way.



The Nucleus:

- Anything that works, works best when it is controlled. ***For cells, the control center is the gene-containing nucleus.*** The nucleus can be compared to a computer, design department, construction boss, and board of directors—all rolled into one.

- As the genetic library, ***it contains the instructions needed to build nearly all the body's proteins.*** Additionally, it dictates the kinds and amounts of proteins to be synthesized at any one time in response to signals acting on the cell.

- ***Most cells have only one nucleus***, but some, including ***skeletal muscle cells, bone destruction cells, and some liver cells, are multinucleated,*** that is, they have many nuclei. ***The presence of more than one nucleus usually signifies that a larger than usual cytoplasmic mass must be regulated***.

- ***Except for mature red blood cells, whose nuclei are ejected before the cells enter the bloodstream, all of our body cells are nucleated***. Anucleate cells cannot reproduce and therefore live in the blood stream for only three to four months before they deteriorate. Without a nucleus, a cell cannot produce mRNA to make proteins, and when its enzymes and cell structures start to break down (as all eventually do), they cannot be replaced.

The Nucleus:

- The nucleus, averaging ***5 µm in diameter, is larger than any of the cytoplasmic organelles.*** Although most often spherical or oval, its shape usually conforms to the shape of the cell.

- ***The nucleus has three recognizable regions or structures***: ***the nuclear envelope (membrane), nucleoli, and chromatin.***

- **Anatomy :**

  - **Nuclear envelope :**

    - ✓ Membranous structure separating nucleoplasm from cytoplasm.
    - ✓ Consists of 2 membranes, an inner membrane and an outer membrane.
    - ✓ 2 membranes separated by a perinuclear space, 20-40nm deep.
    - ✓ Nuclear envelope thought to be derived from rough ER. May be continuous with it.
    - ✓ ER cistemal space continuous with perinuclear space; ribosomes on nucleus.
    - ✓ Nuclear envelope is penetrated by many nuclear pores, = entrance into nucleus.

The Nucleus- *Anatomy:*

- **Nuclear pores:**

  - ✓ Channels providing direct contact between cytoplasm and nucleoplasm.
  - ✓ Each pore is made by fusion of the 2 membranes, strengthened by an annulus.
  - ✓ Annulus = octameric protein, located on cytoplasmic and nucleoplasmic sides .
  - ✓ Most cells have 10-12 pores per sq µm, giving 3,000 - 4,000 pores per nucleus.
  - ✓ Pores are 9nm diameter, so may occupy 2%- 25% of surface area of nucleus.

- **Nuclear cortex**, aka **nuclear lamina**, or **karyoskeleton**:

  - ✓ Made of a ***network of intermediate filaments***, of a type called ***lamins.***
  - ✓ Provides and maintains the shape of the nuclear envelope.
  - ✓ Funnels material to the nuclear pores for passage to the cytoplasm.

The Nucleus- *Anatomy:*

❖ **Contents of the nucleus:**

➢ **Chromatin & Chromosomes:**

✓ Consist of DNA and histones. DNA = blueprint for the cell.
✓ DNA is coiled around the histones, and the whole thing is coiled more.

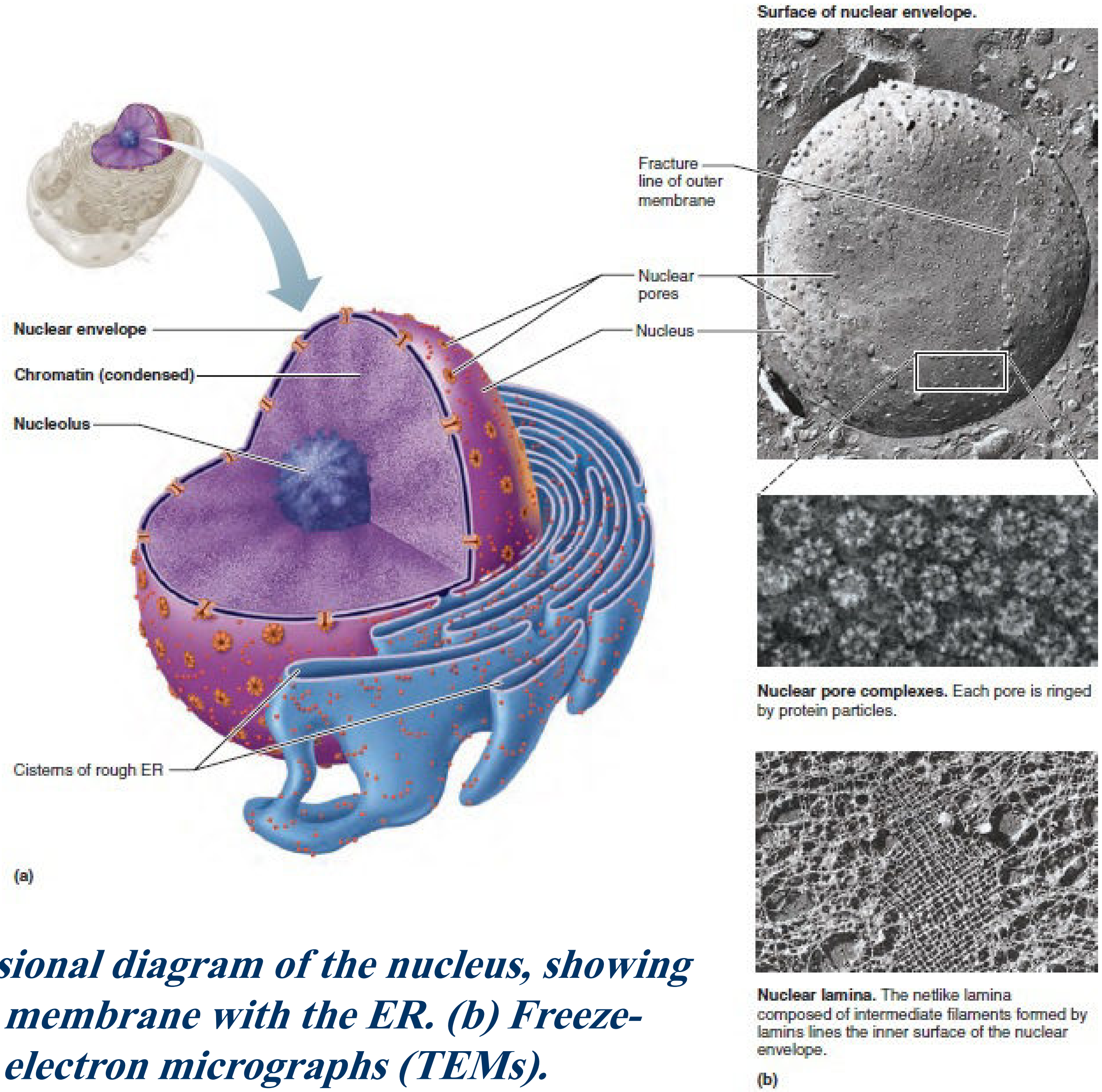
➢ **Nucleolus = ribosome factory:**

✓ Nucleoli are associated with ***nucleolar organizer regions, which contain the DNA that issues genetic instructions for synthesizing ribosomal RNA (rRNA).***
✓ As molecules of rRNA are synthesized, they are combined with proteins to form the ***two kinds of ribosomal subunits***.
✓ ***More metabolically active cells have a large nucleolus, making more subunits.***

❖ **Ribosomal subunits** go to cytoplasm via nuclear pores:

➢ Subunits are 15nm diameter, so have to be squished to fit through nuclear pores.
➢ Active cell makes 20,000 subunits per minute.
➢ With 3000-4000 pores, 5-6 subunits move through each pore each minute.
➢ Subunits come in 2 sizes, called **40S & 60S**, depending on sedimentation rate.

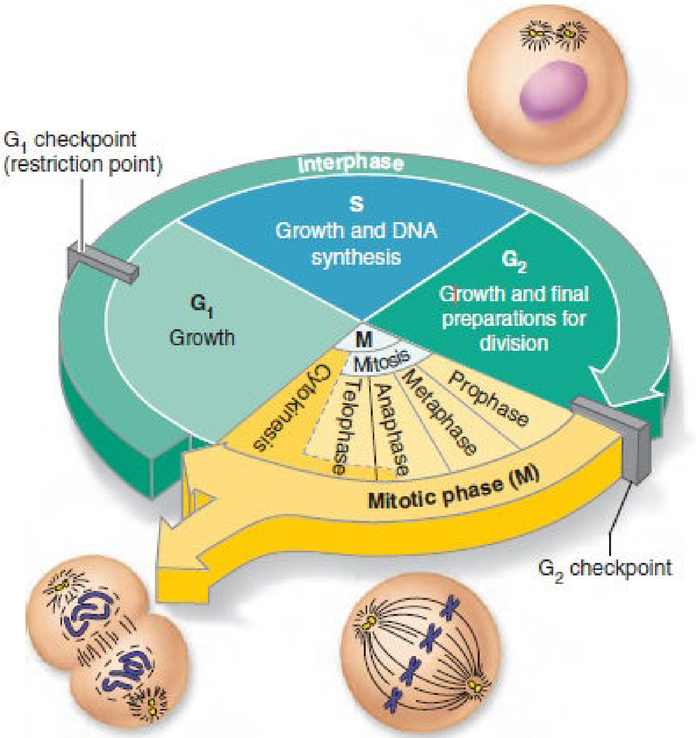
The Nucleus:



The nucleus. (a) Three-dimensional diagram of the nucleus, showing the continuity of its double membrane with the ER. (b) Freeze-fracture transmission electron micrographs (TEMs).

Nuclear Function & The Cell Cycle:

- The cell cycle is the series of changes a cell goes through from the time it is formed until it reproduces. There are two major periods of the cell cycle:
  - **Interphase,** in which the cell grows and carries on its usual activities.
  - **Cell division or the mitotic phase** , during which it divides into two cells.



The Cell Cycle - *Interphase:*

- **Interphase is the period from cell formation to cell division**: ***It is the metabolic phase or growth phase:***

  - **G1 phase = first phase of growth:**
    - ✓ Transcription: RNA is synthesized, using information from DNA.
    - ✓ The RNA is made in order to take genetic copies out of the nucleus.
    - ✓ After leaving the nucleus, RNA directs protein synthesis by translation.
    - ✓ Some of the proteins being made are ribosomal proteins, which go into the nucleus to join with ribosomal RNA to make ribosomal subunits.
    - ✓ New protein synthesis is directed into cell growth.
    - ✓ Towards the end of the G1 phase, histones are made, to prepare for S phase.

  - **S phase = DNA replication phase (S = synthesis):**
    - ✓ DNA is replicated, ensuring that the two future cells being created will receive identical copies of the genetic material. New DNA is synthesized, using information from the pre- existing DNA.
    - ✓ New histones are made and assembled into chromatin. One thing is sure, without a proper S phase, there can be no correct mitotic phase.
  - **G2 phase = second phase of growth:**
    - ✓ This is the same as the G1 phase regarding functions. The difference is that, towards the end of G2, the cell prepares for mitosis.

The Cell Cycle:

❖ **Transport through nuclear pores:** During the G phases, many macromolecules enter and leave the nucleus via the pores:

Inward transport	Outward transport
Enzymes for DNA and RNA synthesis	Molecules of RNA during G phases
Ingredients for DNA and RNA synthesis	Ribosomal subunits during G phases
Histones, at the end of G1 only	
Ribosomal proteins during G phases	

The Cell Cycle – *Cell Division (Mitotic Phase):*

- In most body cells, cell division, which is called the **M (mitotic) phase** of the cell cycle, ***involves two distinct events:***

    - **Mitosis*****, the division of the nucleus:***

        - **Prophase:** Nuclear membrane, nuclear cortex and nucleolus all disappear.
        - **Metaphase:** Nucleus absent. Chromosomes align on spindle equator.
        - **Anaphase:** Nucleus absent. Sister chromatids move to spindle poles.
        - **Telophase:** Nuclear membrane, nuclear cortex and nucleolus all reappear in the daughter cells.

    - **Cytokinesis*****, the division of the cytoplasm,*** *during late anaphase and is completed after mitosis ends.*

- A different process of nuclear division called ***meiosis*** produces sex cells (ova and sperm) with only half the number of genes found in other body cells. *We will discuss mitosis and meiosis in details in the upcoming lectures.*

The Cell Cycle – *Cell Division (Mitotic Phase):*

- Cell division is essential for body growth and tissue repair. ***According to the cells' potential of mitosis***, ***there are three types of cells:***

  - **Labile cells:** these are continuously dividing cells like those of the epithelia (GIT, respiratory tract, etc.), bone marrow.

  - **Stable cells:** these are cells that are quiescent and divide only when stimulated like parenchymal cells (liver, kidney, pancreas, etc.), mesenchymal cells (bone, cartilage, fibroblasts).

  - **Permanent cells**: these are cells that cannot divide like neurons, skeletal muscles, and heart muscles.