

College and Medical Sciences Department of Medical Laboratory Science

12/18/25

LESSON ONE



□ **Chapter One: Introduction**

- Define terms in molecular biology
- Historical overview of molecular biology
- Overview of cellular structure and function, Biologically important molecule

Introduction

Molecular biology:

- Molecular is the science that study all life processes within cells and at the molecular level.
- It overlaps with genetics & biochemistry.

□ **Biochemistry:**

- It is the study of the chemical substances & vital processes occurring in living organisms

□ **Genetics**

- It is study of heredity & the effect of genetic variation among generation of organisms.
- Thus, Molecular biology use specific techniques native to molecular biology, but increasingly combine these techniques with techniques & ideas of genetics & biochemistry.

Molecular Biology History overview

- 1866, Gregor Mendel provide the fundamental principle of heredity.
- 1909, Johannse coined the term gene to denote the basic unit of heredity.
- 1910, Morgan describe the gene is contained in chromosome.
- In 1944, Oswald Avery demonstrated that genes are made up of DNA

History Over View Cont...

- In 1953, James Watson & Francis Crick discovered the double helical structure of the DNA molecule.
- 1956, number of chromosomes in humans (46) understood.
- In 1961, Francois Jacob & Jacques Monod hypothesized the existence of an intermediary between DNA & its protein products, which they called mRNA

CONT....

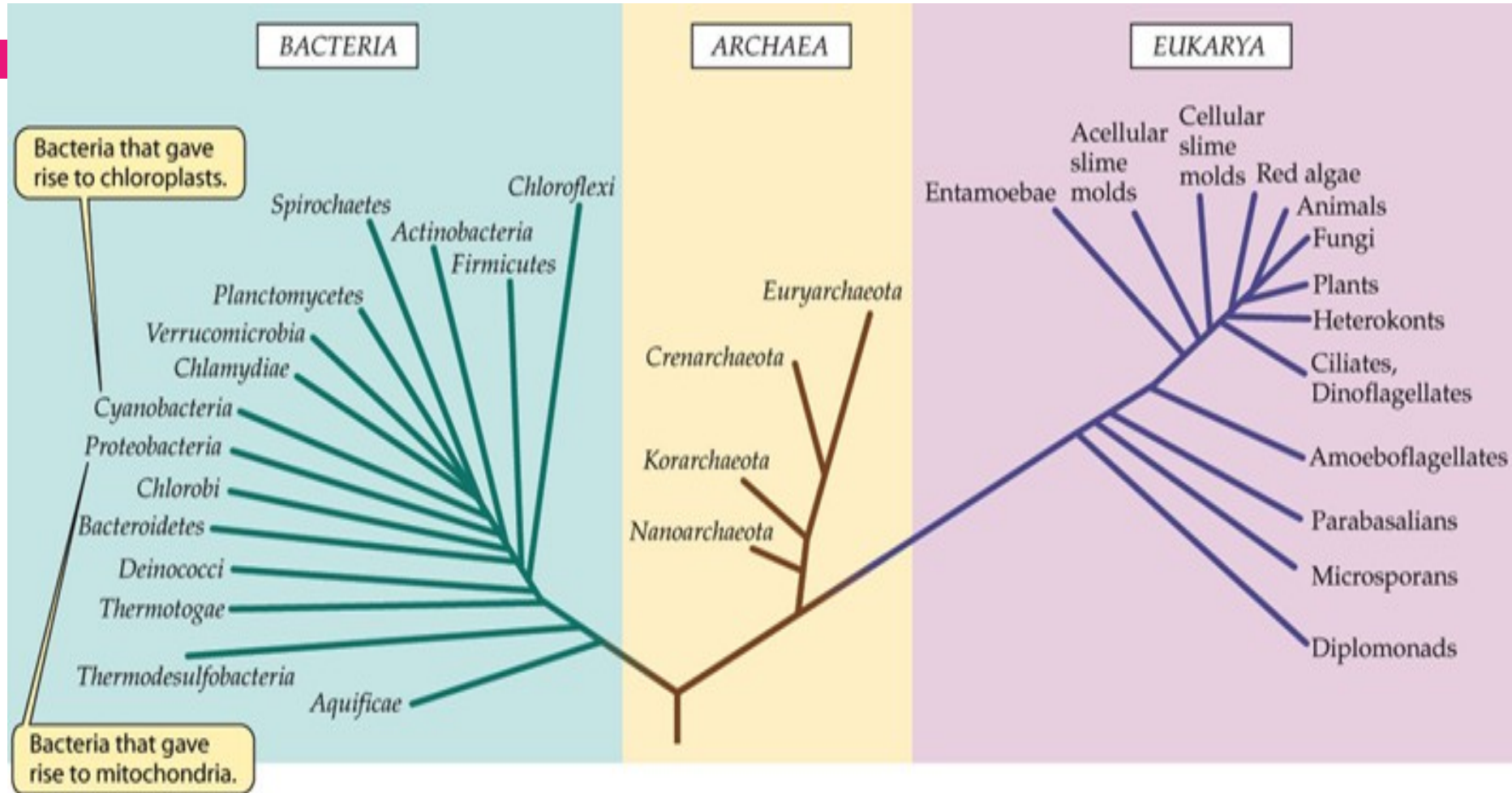
- 1961 - 1965, the relationship between the information contained in DNA & the structure of proteins was determined:
 - Correspondence between nucleotides in the sequence & a series of amino acids in proteins.
- In 1966, gene transcription described
- In 1975, Edward Southern discovered Southern blotting
- In 1977, DNA sequencing methodology discovered

- 
- In 1981, Kan & Chang shown genetic diagnose of sickle cell anemia
 - In 1985, PCR developed by Millis & co-workers
 - In 2001 Draft of human genome sequence was revealed
 - In 2003, Human Genome Project was launched

Overview of cells & Macromolecules

- Cells
- All genetic diseases involve defects at the level of the cell
- For this reasons, one must understand the basic cell biology to understand genetic diseases.

The three domains of life



The biological universe consists of two types of cells

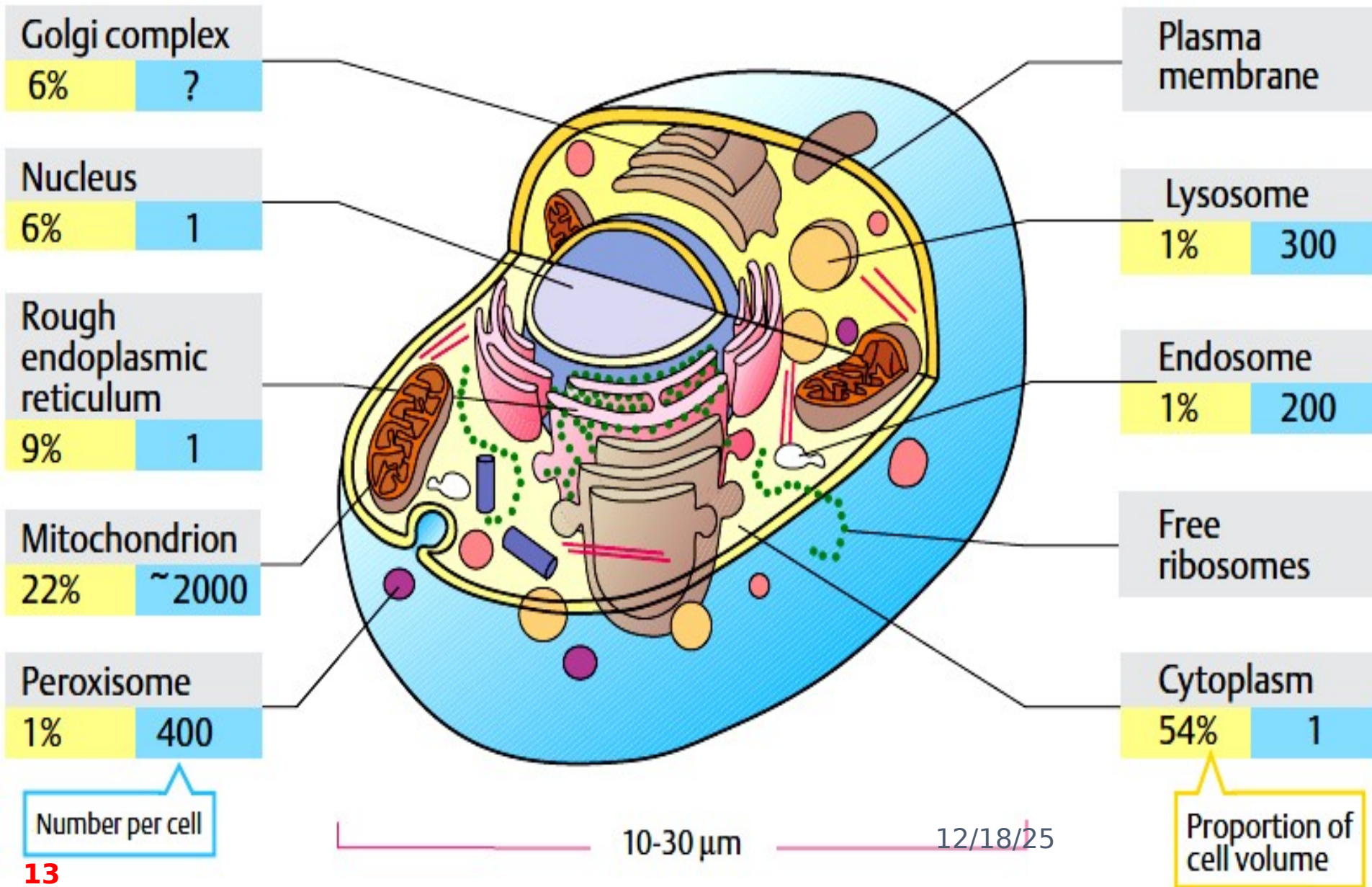
Prokaryotes

- Archaea and Bacteria
- Simplified internal organization
- A distinct nucleus is absent/Nuclear material dispersed
- DNA is in the form of a single circular chromosome.
- Additional DNA is carried in plasmids.
- Transcription and translation can be carried out simultaneously

Eukaryotes

- Unicellular and Multi-cellular
- DNA is carried on several chromosomes within a nucleus.
- The nucleus is bounded by a nuclear membrane.
- Transcription requires formation of messenger RNA (mRNA) & movement of mRNA out of the nucleus into the cytoplasm.
- The cytoplasm is rich in membrane-bound organelles (mitochondria, endoplasmic reticulum, Golgi apparatus, lysosomes) which are absent in prokaryotes.

Structure of an Animal Cell



Metabolic Processes Occur in a Variety of Spaces within Cells

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□ Most metabolism occurs;

- within the complex ecosystem of the cell,
 - in subcellular organelles

□ Compartmentalization of metabolic processes

- is important for several reasons:

- to protect from **autodigestion**,
- to **concentrate** pathways & metabolites in **space**,
- to enable different pathways, such as;
 - **synthesis & degradation** of proteins,
- to operate at the same time

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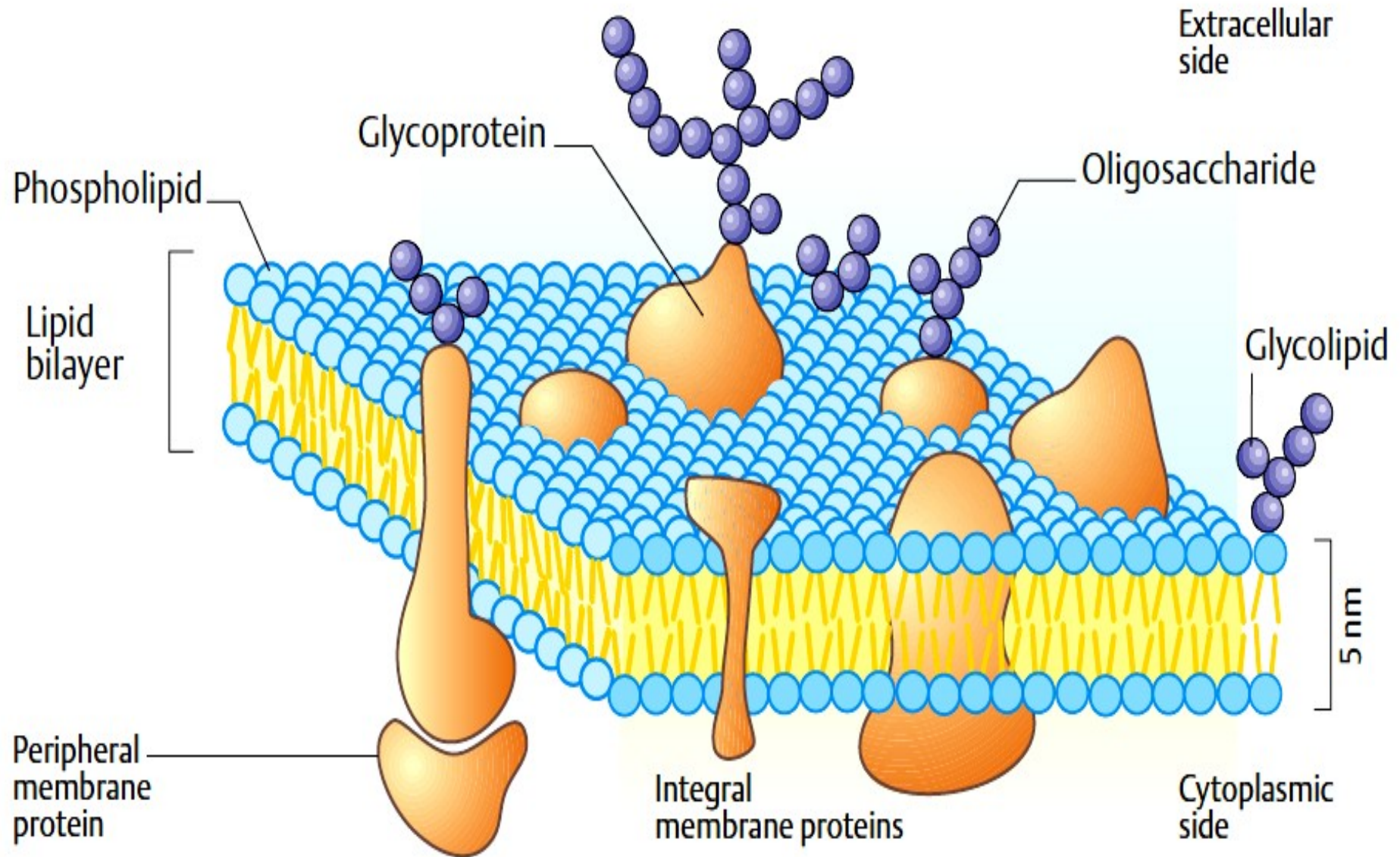
□ Containment:

- Plasma (cell) membrane
- Cell wall
- All cells have an oily, lipid cell membrane
- Inside of this membrane exists a marvelous chemical system that allows each cell to:
 - grow, divide, fight off intruders,
 - take in important reagents, &
 - excrete other materials that are either:
 - waste products or
 - important products of this particular cell's metabolism

□ **Structure of the Plasma (Cell) Membrane:**

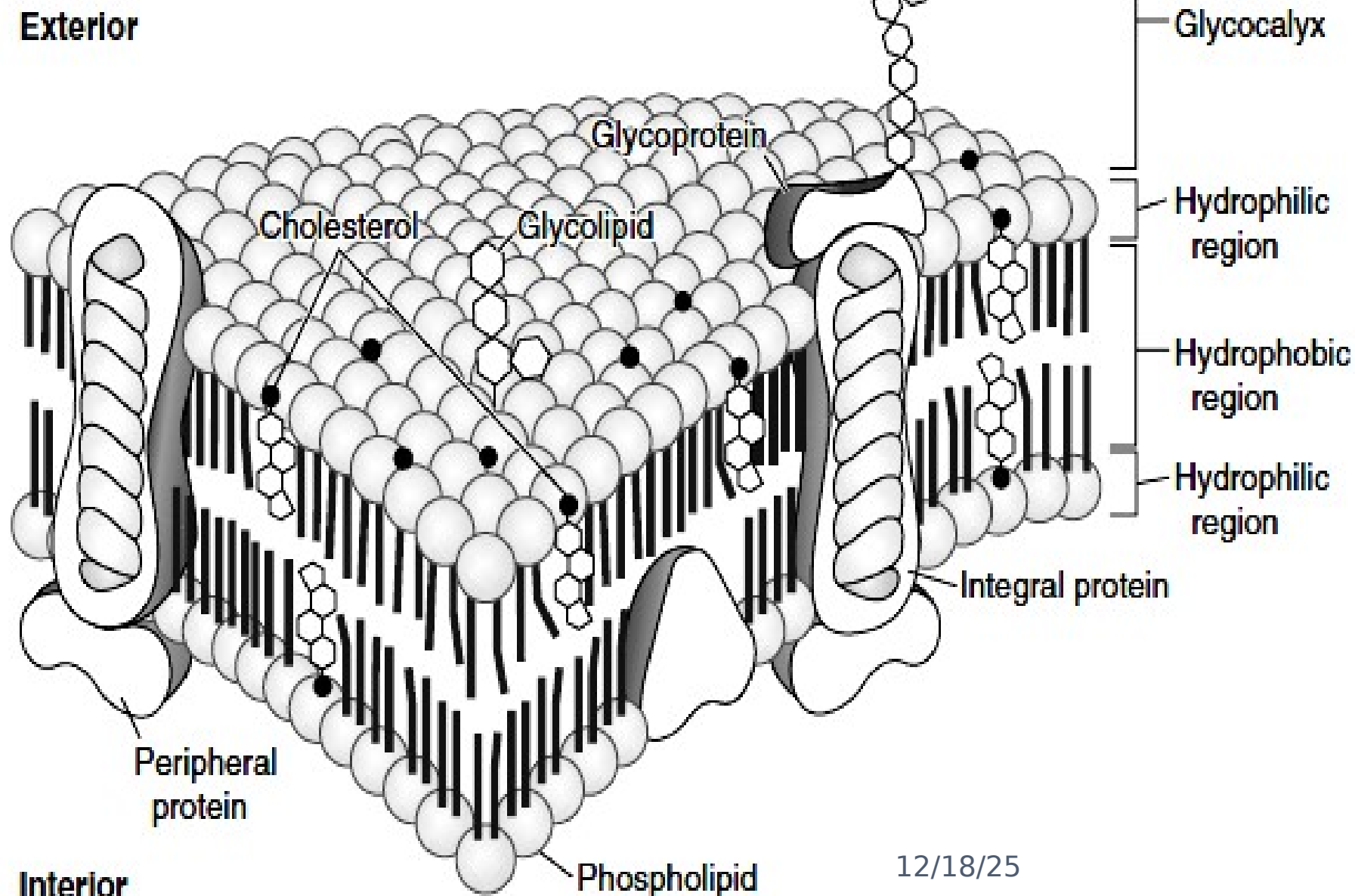
- **Consist of a continuous bilayer of amphipathic lipids $\approx 5\text{nm}$ thick,**
 - **proteins are embedded**
 - **also carry carbohydrates (mono- & oligosaccharides)**
- **The proportions of lipids, proteins, & carbohydrates**
 - **differ markedly depending on the type of cell & membrane**
- **Membrane lipids are strongly **amphipathic** molecules with:**
 - **a polar hydrophilic “**head group**” &**
 - **an apolar hydrophobic “**tail**”**
- **The **fluidity** of membranes primarily depends on their:**
 - **lipid composition &**
 - **temperature**

Structure of the Plasma Membrane



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Basic structure of an animal cell membrane with composition

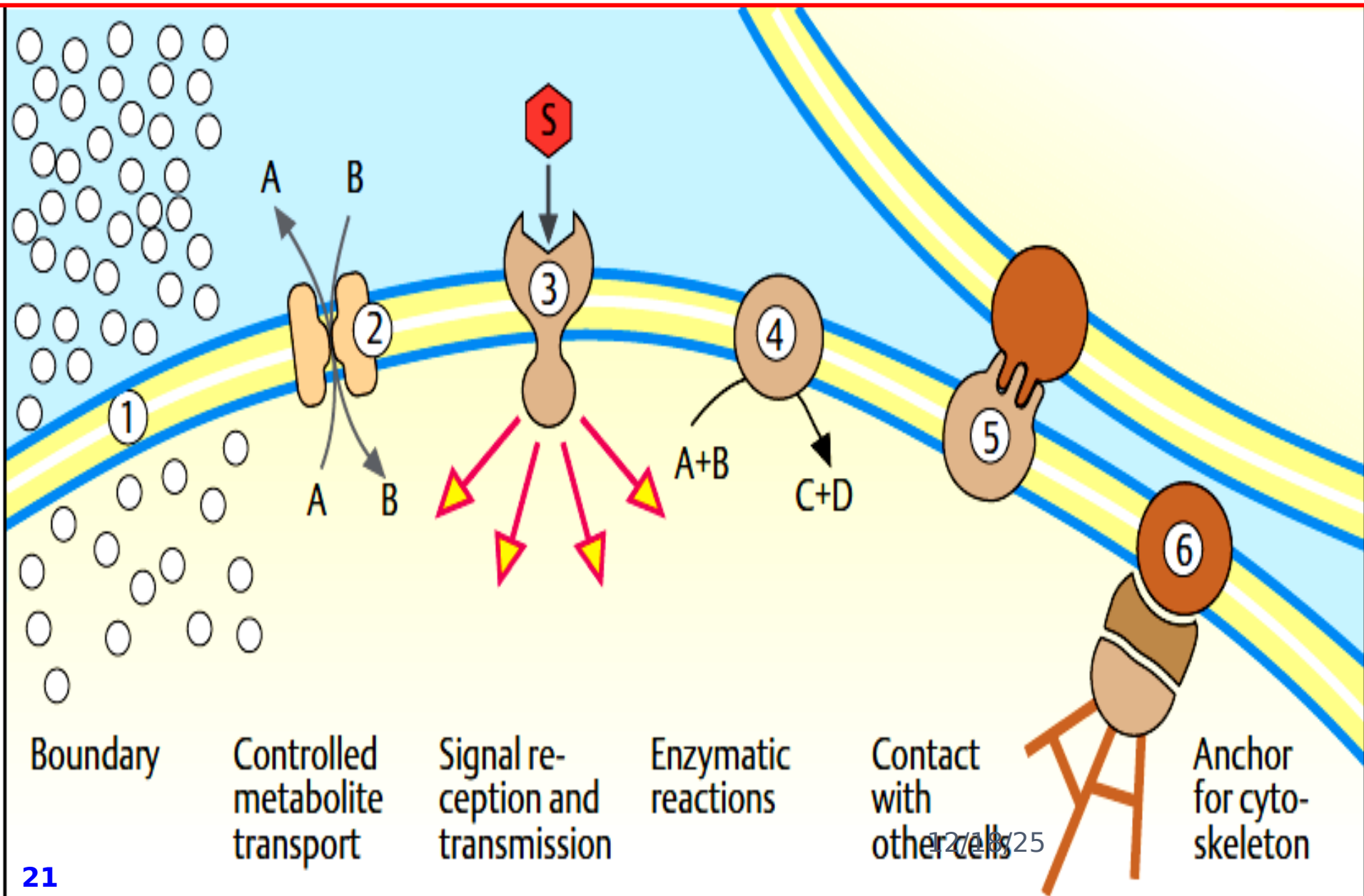


- **The most important membranes in animal cells are the:**
 - plasma membrane,
 - inner & outer nuclear membranes,
 - membranes of the ER & Golgi apparatus,
 - inner & outer mitochondrial membranes
- **Lysosomes, peroxisomes, & various vesicles;**
 - are also separated from the cytoplasm by membranes
- **In plants, additional membranes are seen in the:**
 - plastids & vacuoles
- **All membranes show polarity:**
 - i. e., there is a difference in the composition of the:
 - inner layer &
 - outer layer

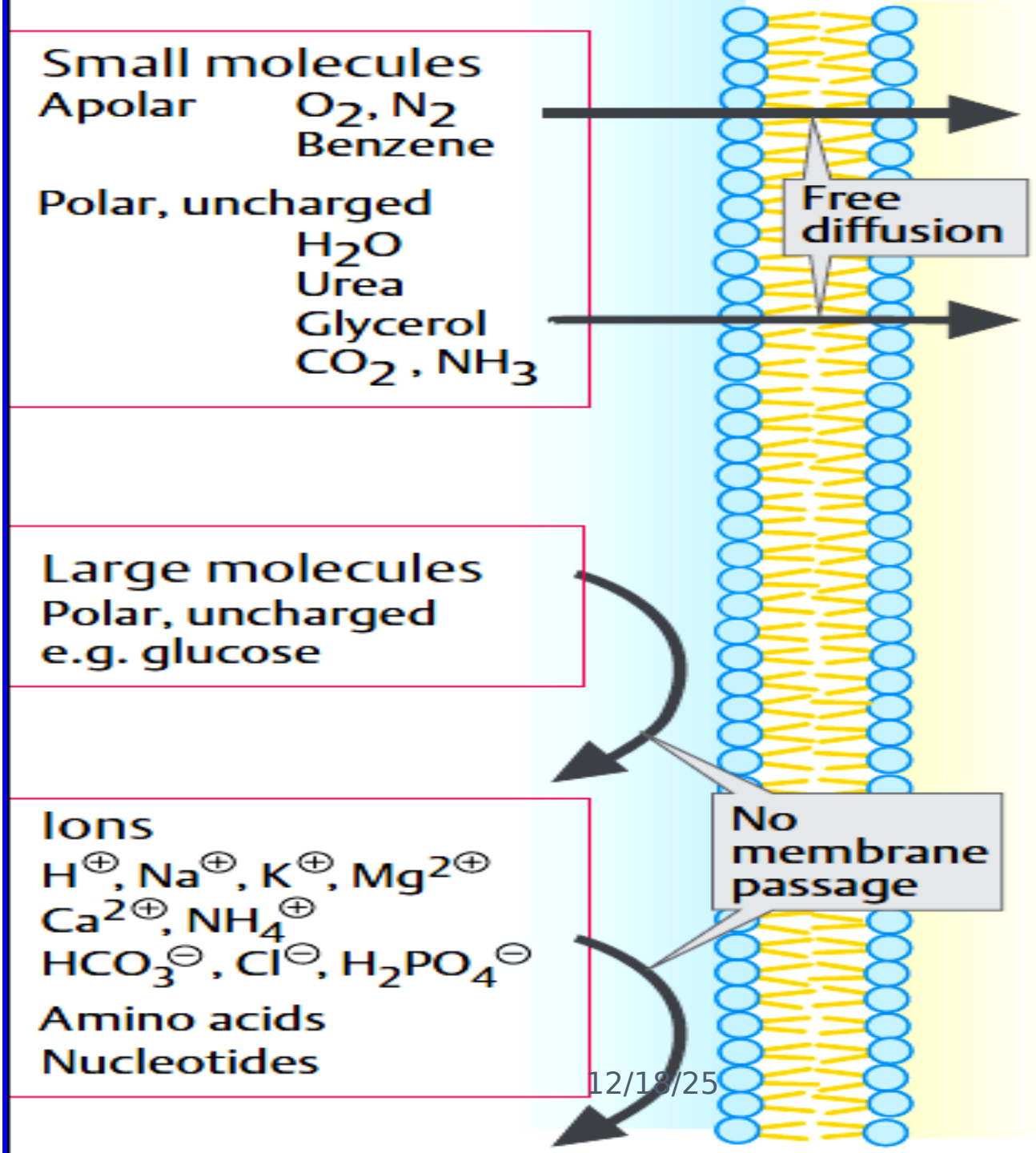
□ **Membranes & their components have the following Functions:**

- 1. Enclosure & insulation of cells and organelles**
- 2. Regulated transport of substances;**
 - **selective barrier (charged & polar molecules)**
- 3. Reception of EC signals & transfer of these signals**
 - **to the inside of the cell, as well as the production of signals**
- 4. Enzymatic reactions**
- 5. Interactions with other cells for the purposes of:**
 - **cell fusion & tissue formation, as well as communication with the EC matrix**
- 6. Anchoring of the cytoskeleton**
 - **to maintain the shape of cells & organelles**
 - **to provide the basis for movement processes**
- **Energy (*prokaryotes*)***

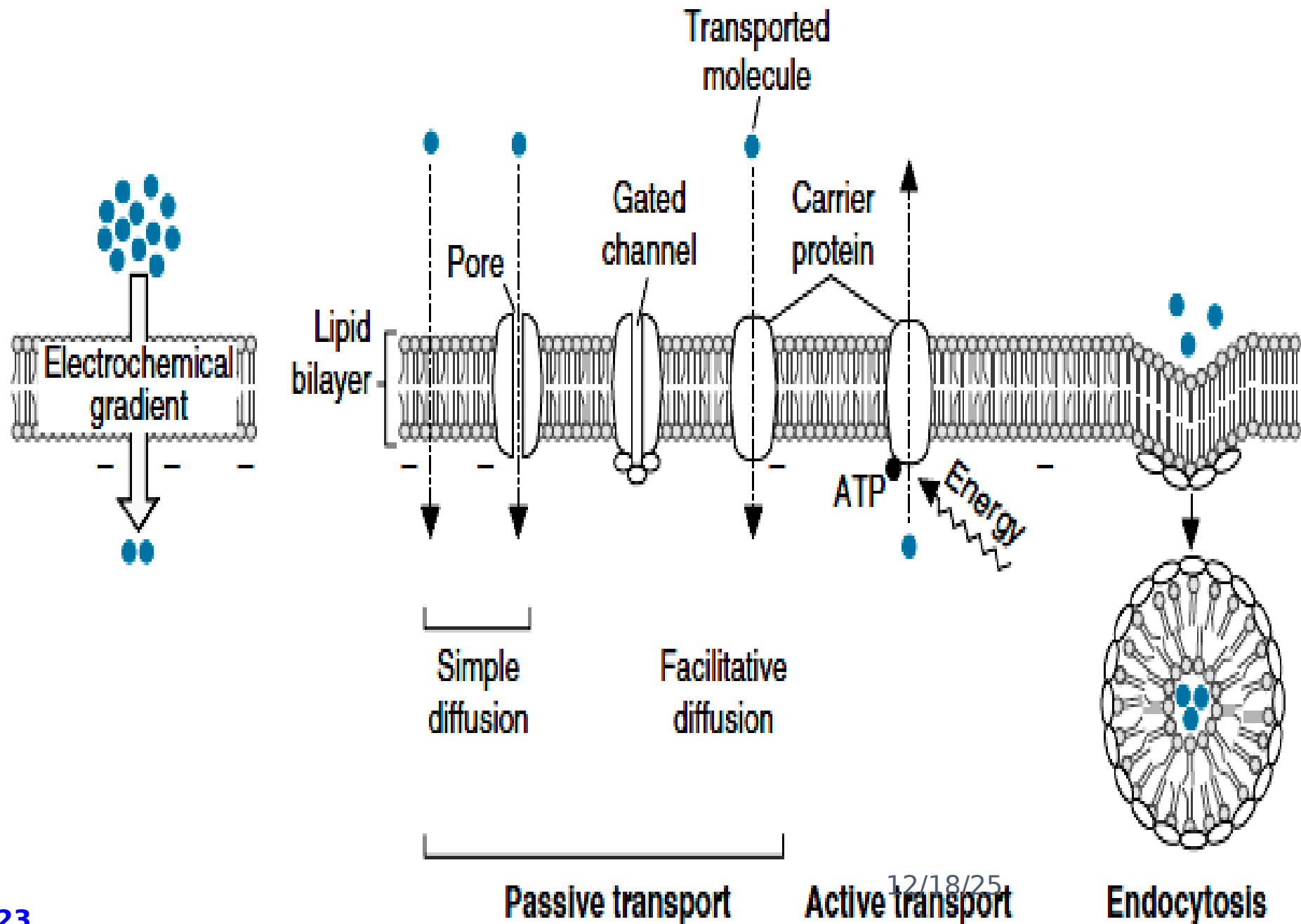
Functions of Membranes



Permeability of Membranes



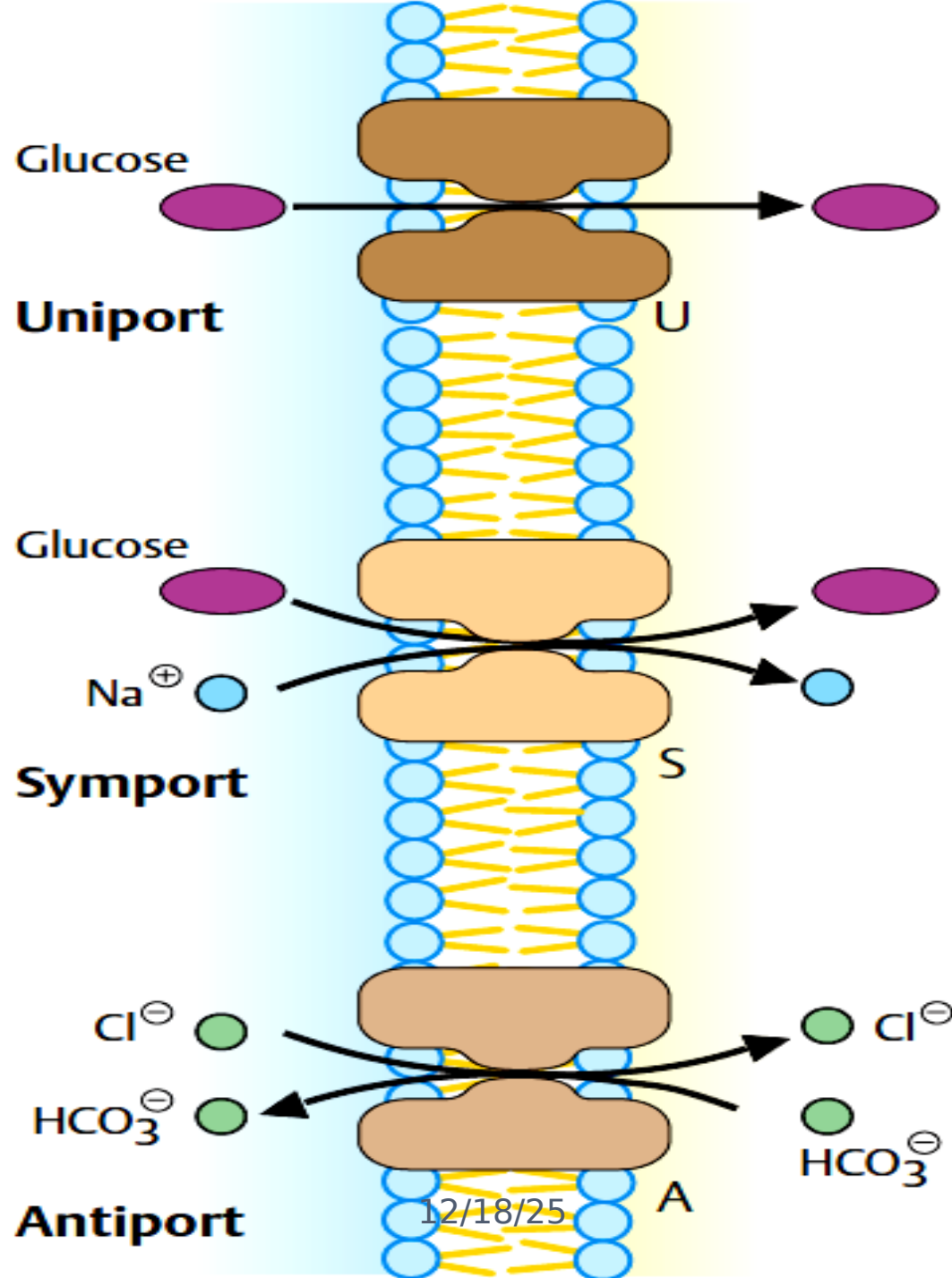
Common types of transport mechanisms for human cells.



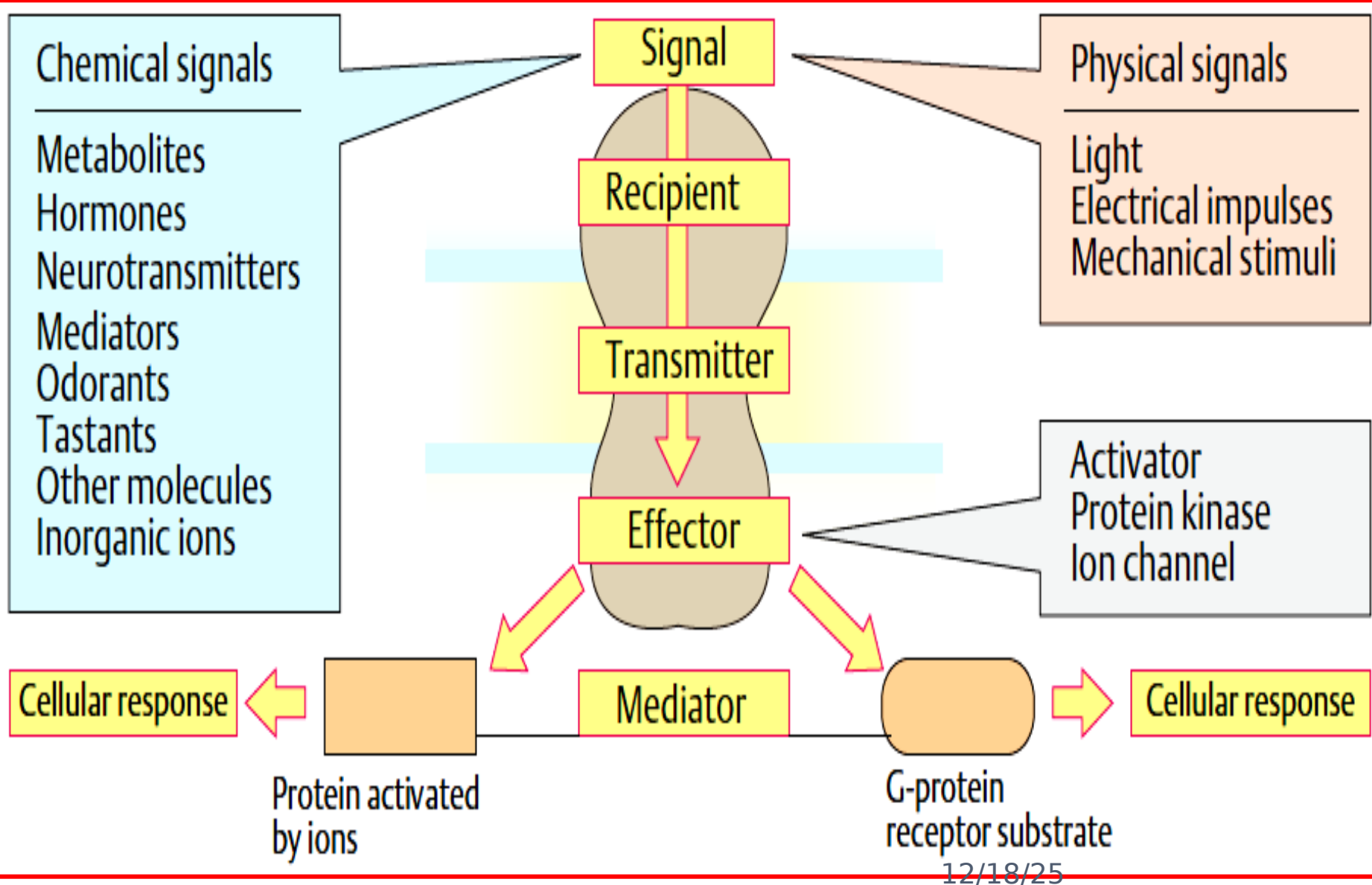
Transport Processes

□ Another classification of transport processes is based on the:

- number of particles transported &
- direction in which they move



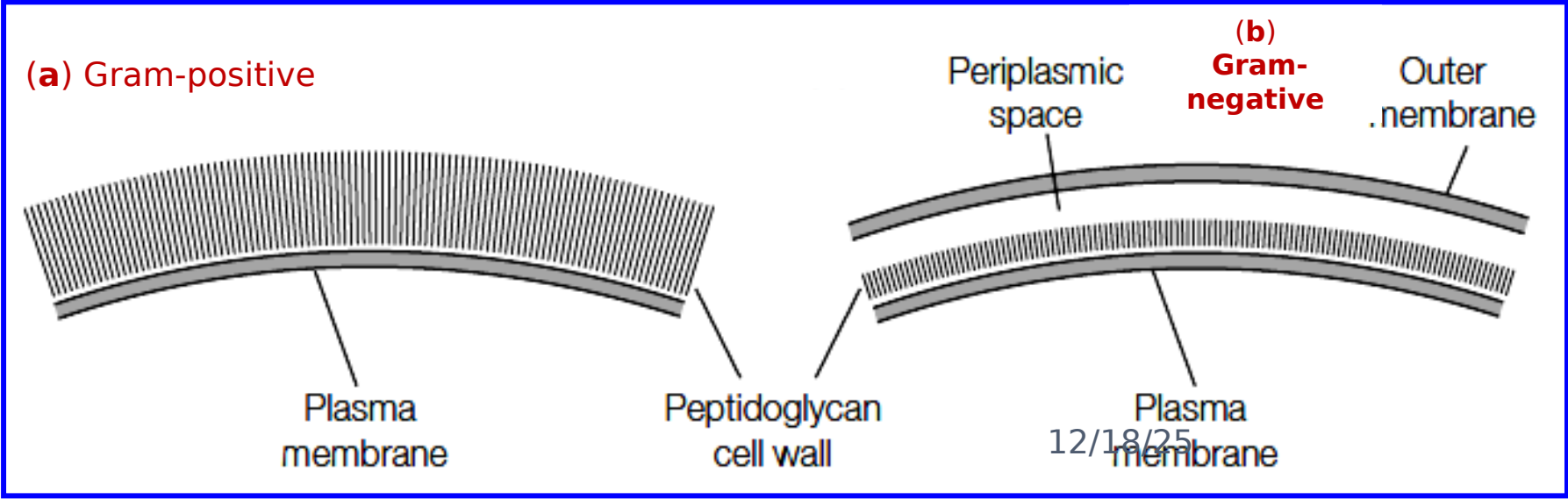
Principle of Receptor Action



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□ **Cell wall:**

- **most bacteria, archaea, algae, fungi, & plants**
- **a rigid 3-25 nm thick**
- **composed of peptidoglycan, a complex of oligosaccharides & proteins**
- **protects the prokaryotic cell from mechanical & osmotic pressure**
- **A Gram-positive bacterium has a **thick** cell wall**
- **Gram-negative bacteria have a **thinner** cell wall & an **outer membrane**, b/n w/c is the **periplasmic space****



Biochemical Functions of the Cytoplasm

- In eukaryotes, the cytoplasm,
 - representing slightly more than 50% of the cell volume,
 - is the most important cellular compartment
- It is the central reaction space of the cell
 - many important pathways of the intermediary metabolism take place—e.g.,
 - *glycolysis, pentose phosphate pathway,*
 - *the majority of gluconeogenesis, & fatty acid synthesis*
 - *protein biosynthesis*
- By contrast,
 - *fatty acid degradation, Kreb's cycle, & oxidative phosphorylation*
 - are located in the mitochondria

Biochemical Functions of the Cytoplasm

Pentose phosphate cycle

Gluconeogenesis

Schematic net of the reactions in the cytoplasm

Protein biosynthesis

Fatty acid biosynthesis

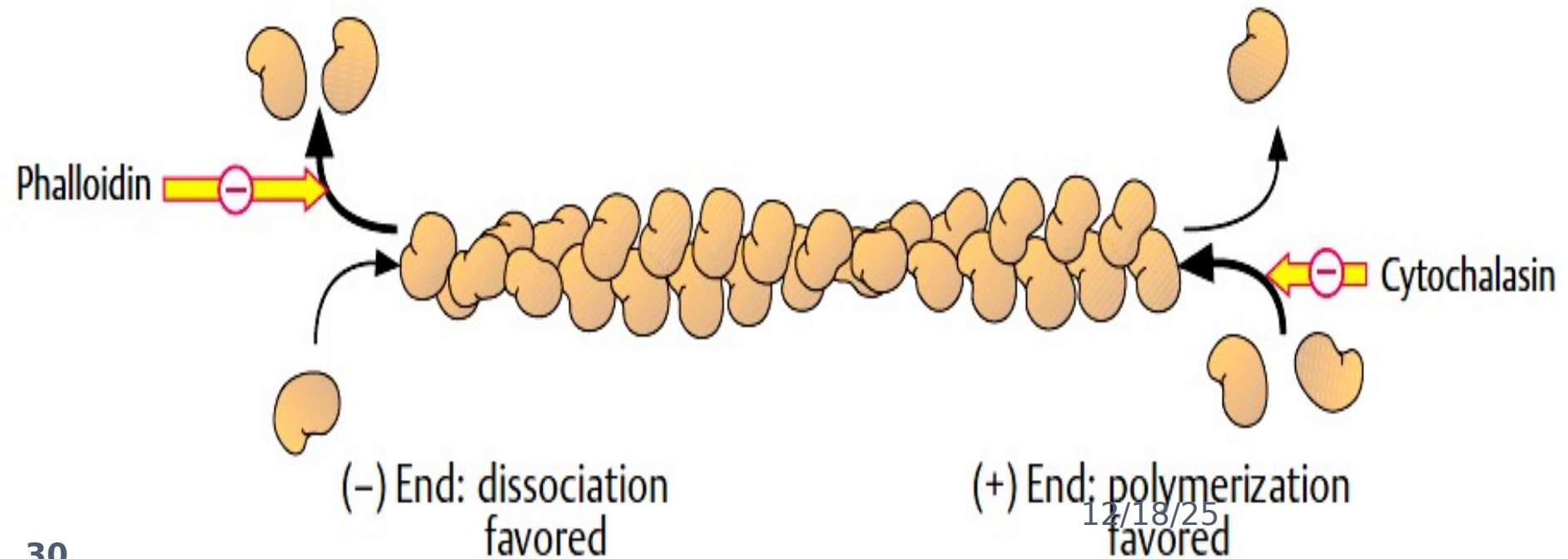
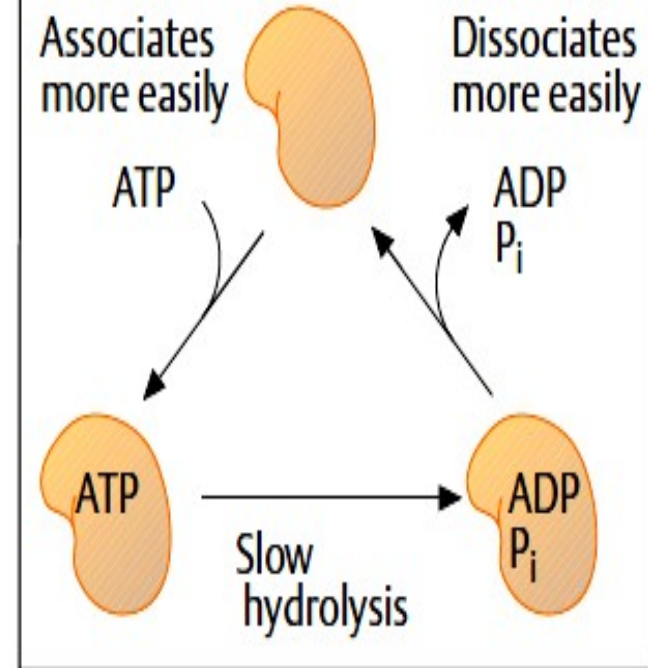
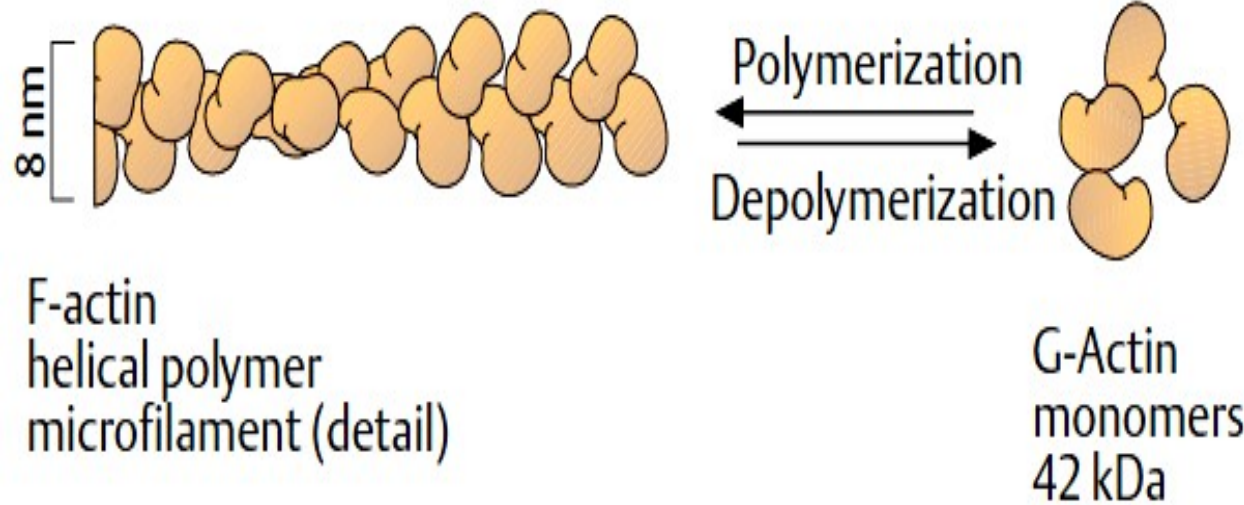
Glycolysis

And many other reactions

□ Cytoskeleton:

- The cytoplasm of eukaryotic cells is traversed by 3D scaffolding structures;
 - consisting of **filaments** (long protein fibers),
 - w/c together form the cytoskeleton
- These filaments are divided into **three** groups,
 - based on their diameters:
 - **Microfilaments** (6–8 nm)
 - **Intermediate filaments** (ca. 10 nm)
 - **Microtubules** (ca. 25 nm)
- All of these filaments are polymers assembled from **protein** components

Actin

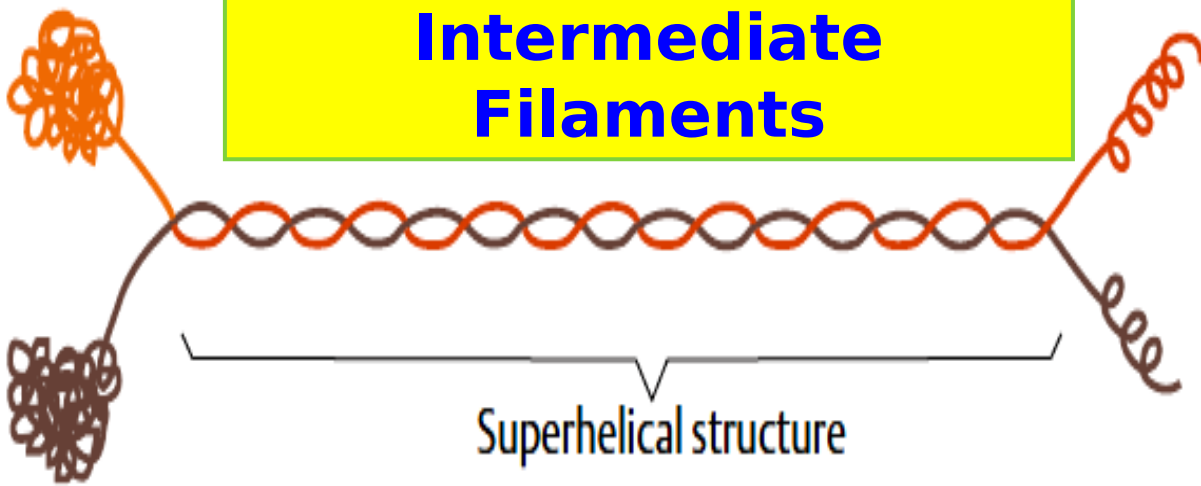


Intermediate Filaments

IF Proteins:
Cytokeratins
Desmin
Vimentin
Glial fibrillary
acidic protein
Neurofilaments
Lamins

S-50

Dimer



Tetramer



Protofilament



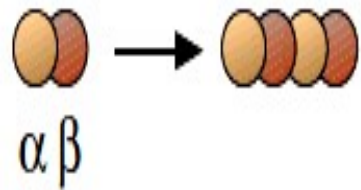
Intermediate filament



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Tubulins

binds GTP and slowly hydrolyzes it



Tubulin
53 and 55 kDa
heterodimer

Protofilament

25 nm

Microtubule
(cylindrical polymer)

(-) End: stabilized by binding
to the centromere

(+) End: grows
or shortens

Plant
alkaloids:
Vinblastine,
vincristine,
colchicine

Taxol

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□ The cytoskeleton carries out three major tasks:

1. It represents the cell's *mechanical scaffolding*,

- w/c gives it its typical shape &
- connects membranes & organelles to each other

2. It acts as the *motor for movement* of animal cells

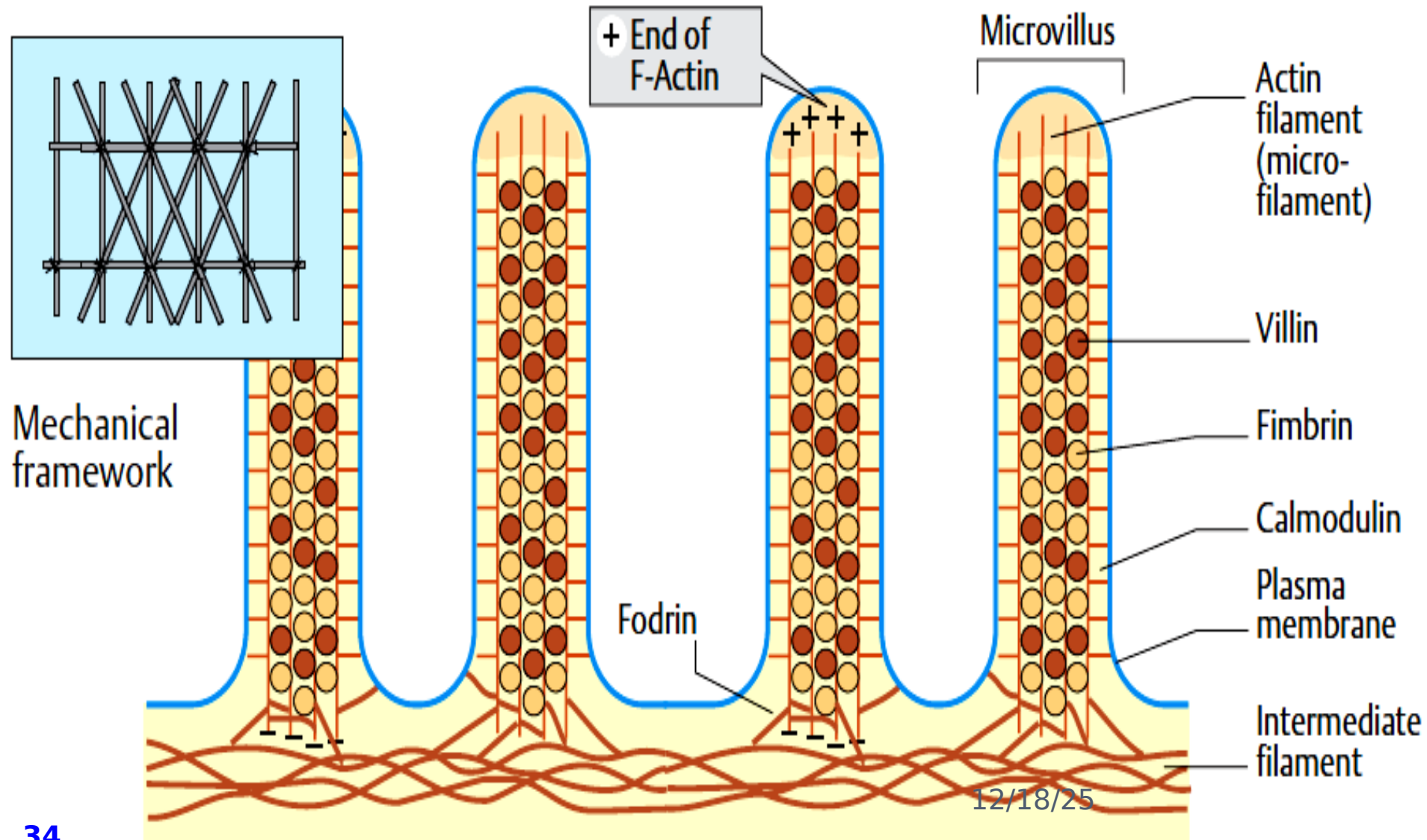
- cell movement, shape changes during growth, cytoplasmic streaming, & cell division;
 - *are all made possible by components of the cytoskeleton*

3. It serves as a *transport track* within the cell;

- organelles & other large protein complexes can move along the filaments with the help of the motor proteins

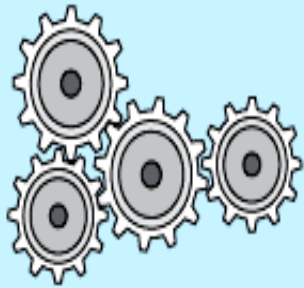
STRUCTURE & FUNCTIONS

► Microfilaments & Intermediate Filaments

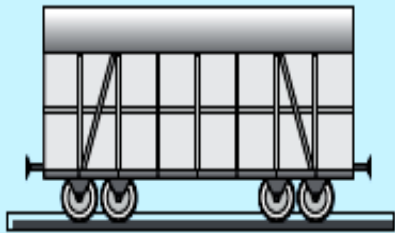


STRUCTURE & FUNCTIONS

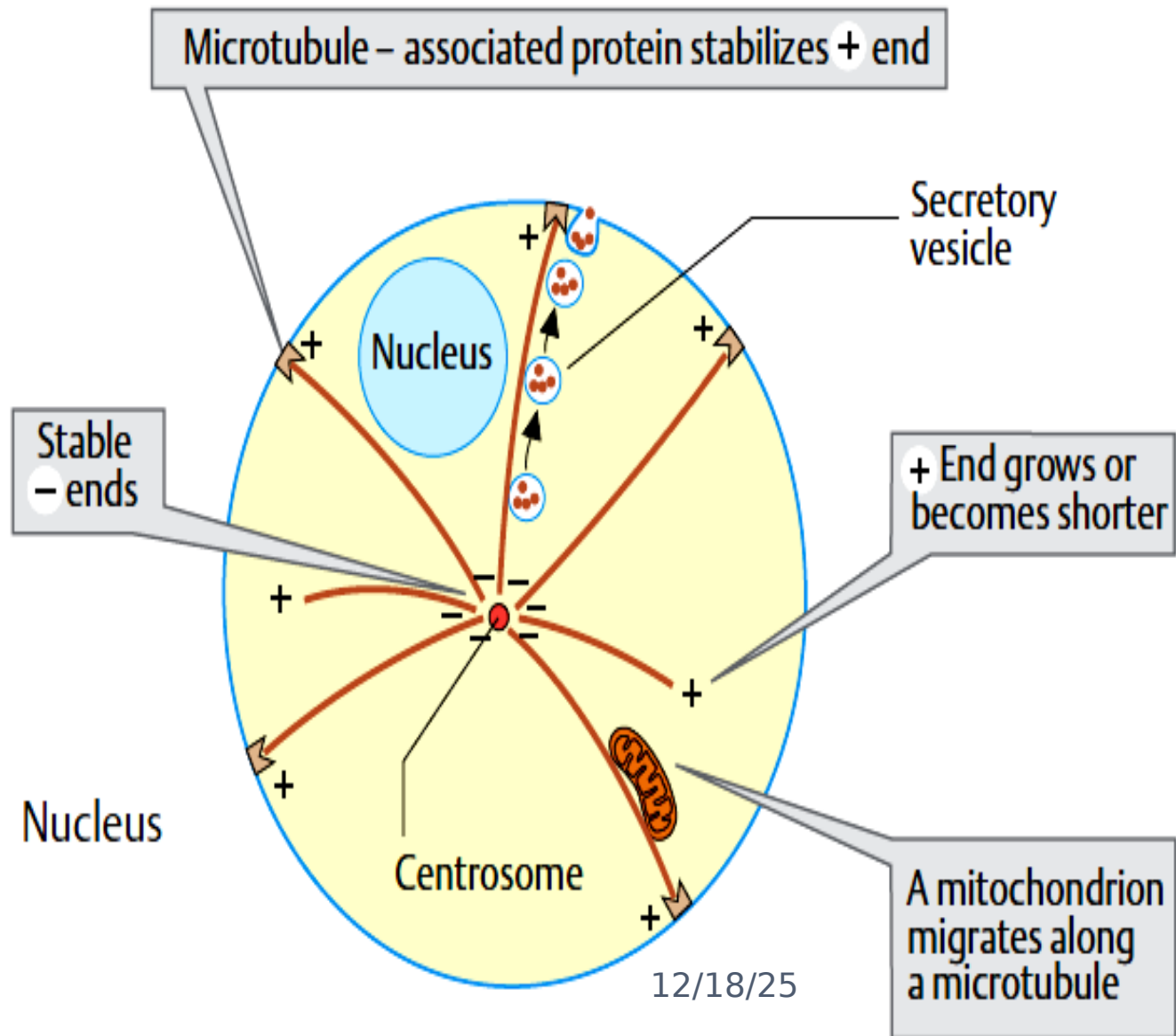
► Microtubules



Motor for movement



Rail for transport



Introduction to Cell Organelles

- The interior of living cells is as compact as a submarine;
 - within the interior, biomolecules whirl around rapidly in a random fashion
- The achievement of chemical processes,
 - whereby specific reagents must come together in an orderly fashion
- This is especially true for prokaryotic cells,
 - which have few options to isolate different processes
- The eukaryotic cell is able to conduct certain bioprocesses more efficiently than prokaryotes b/c:
 - different functions are packaged within interior structures, called organelles;
 - that are rather like simplified cells themselves

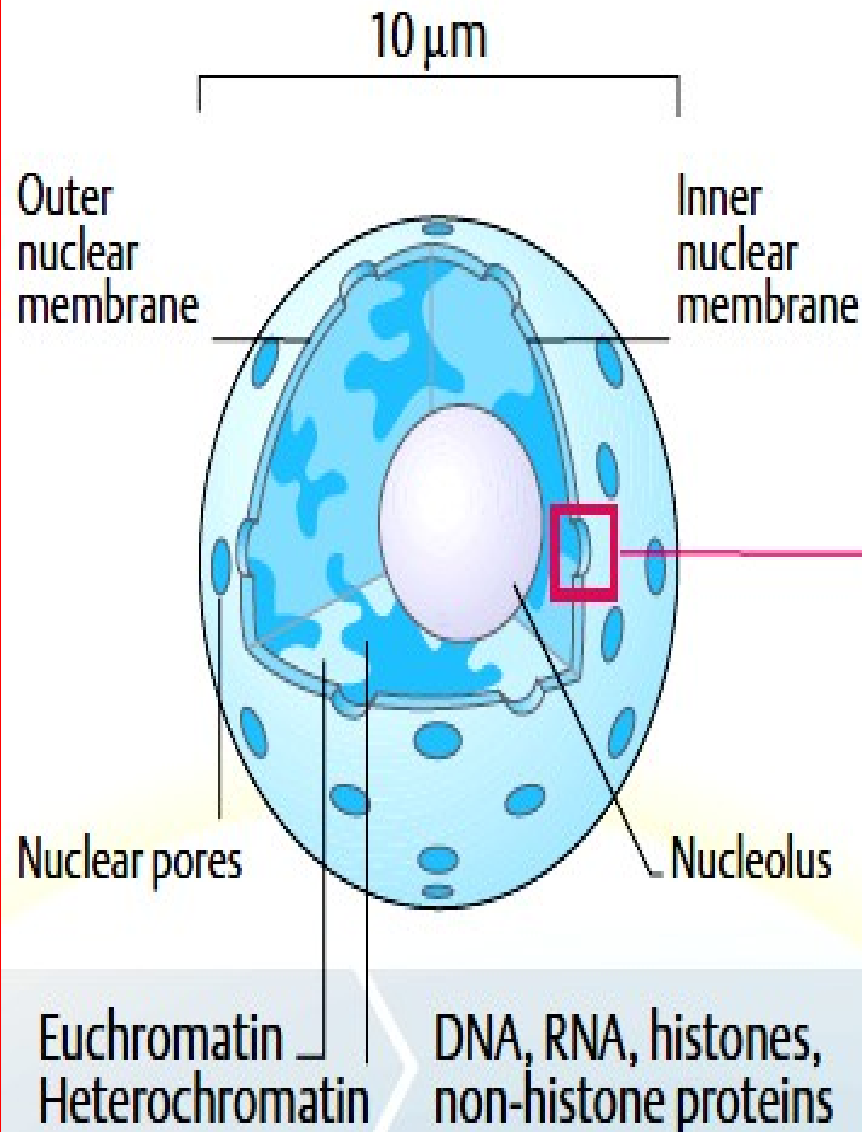
□ Cell Organelles:

- Nucleus
- Ribosomes
- Endoplasmic reticulum
- Mitochondria → *Prokaryotes living within eukaryotes?*
- Chloroplasts
- Golgi apparatus
- Peroxisomes
- Vacuoles & lysosomes
- Proteasomes

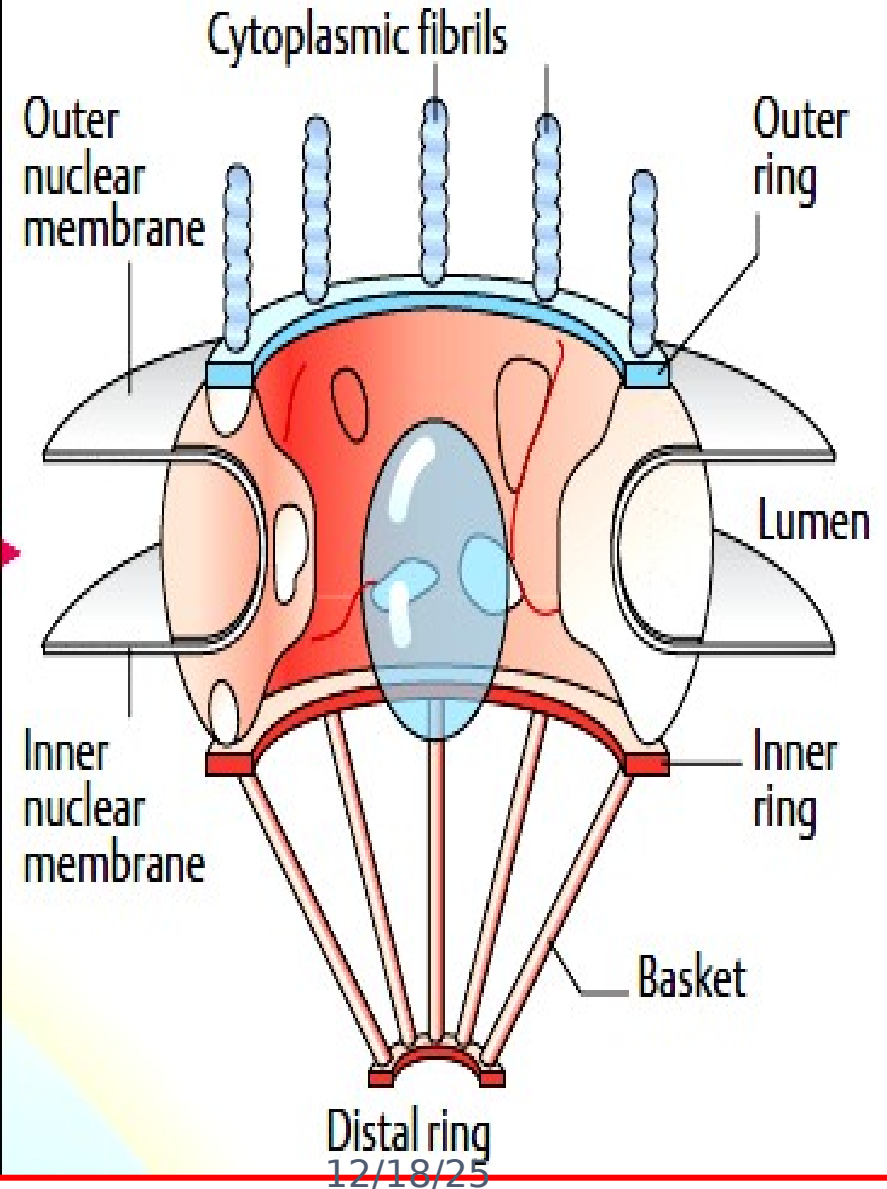
□ **Nucleus:**

- **the largest organelle in the eukaryotic cell**
- **with a diameter of about 10 μm ,**
- **is the location for:**
 - **storage, replication, & expression of genetic information**
- **Nuclear envelope**
 - **the nucleus is separated from the cytoplasm**
 - **w/c consists of the outer & inner nuclear membranes**
 - **the membranes are separated from each other**
→ perinuclear space
- **Nuclear pores:**
 - **w/c traverse the nuclear membrane**
 - **exchange of substances b/n the nucleus & the cytoplasm**

Nucleus

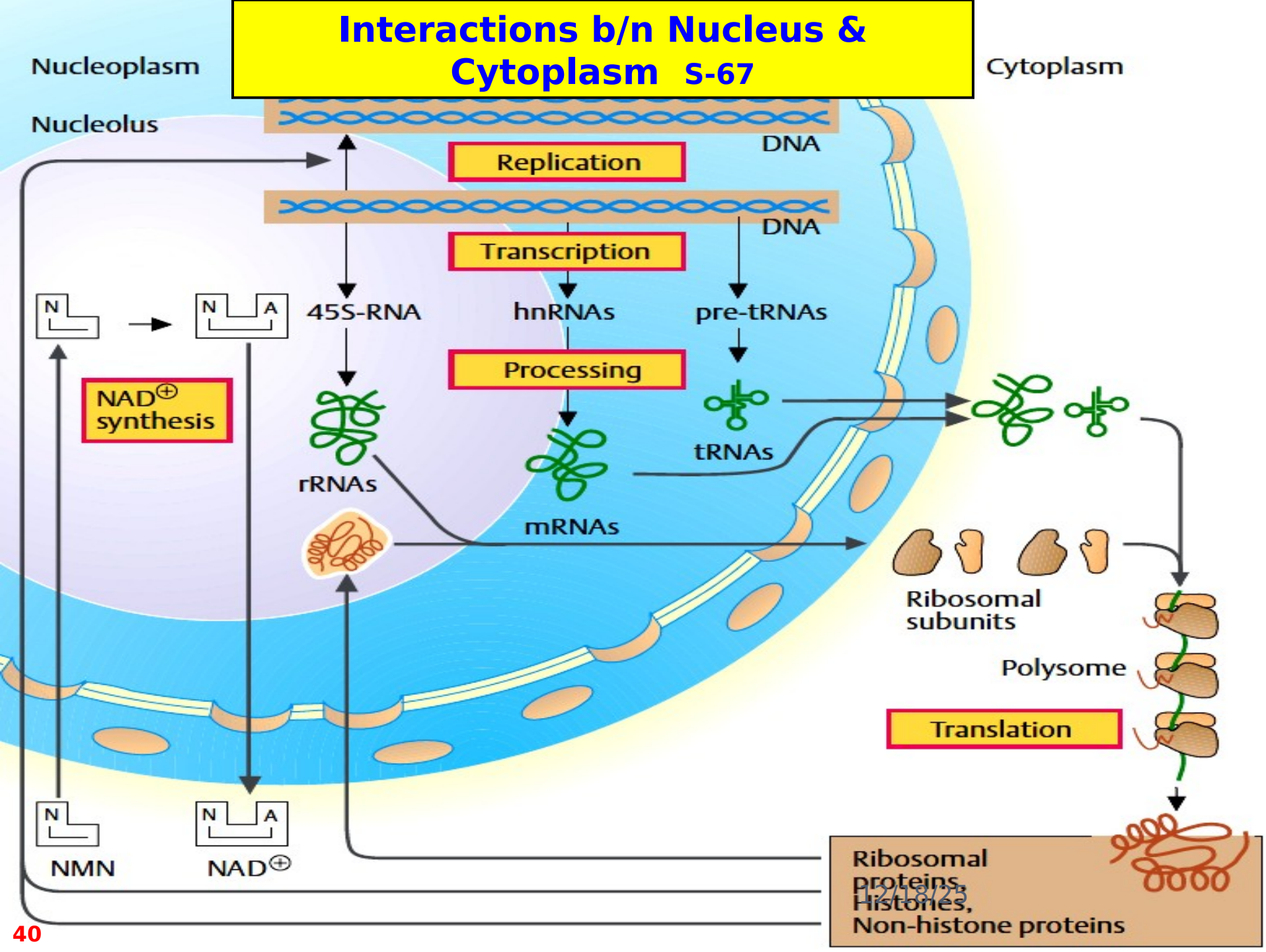


Nuclear Pores



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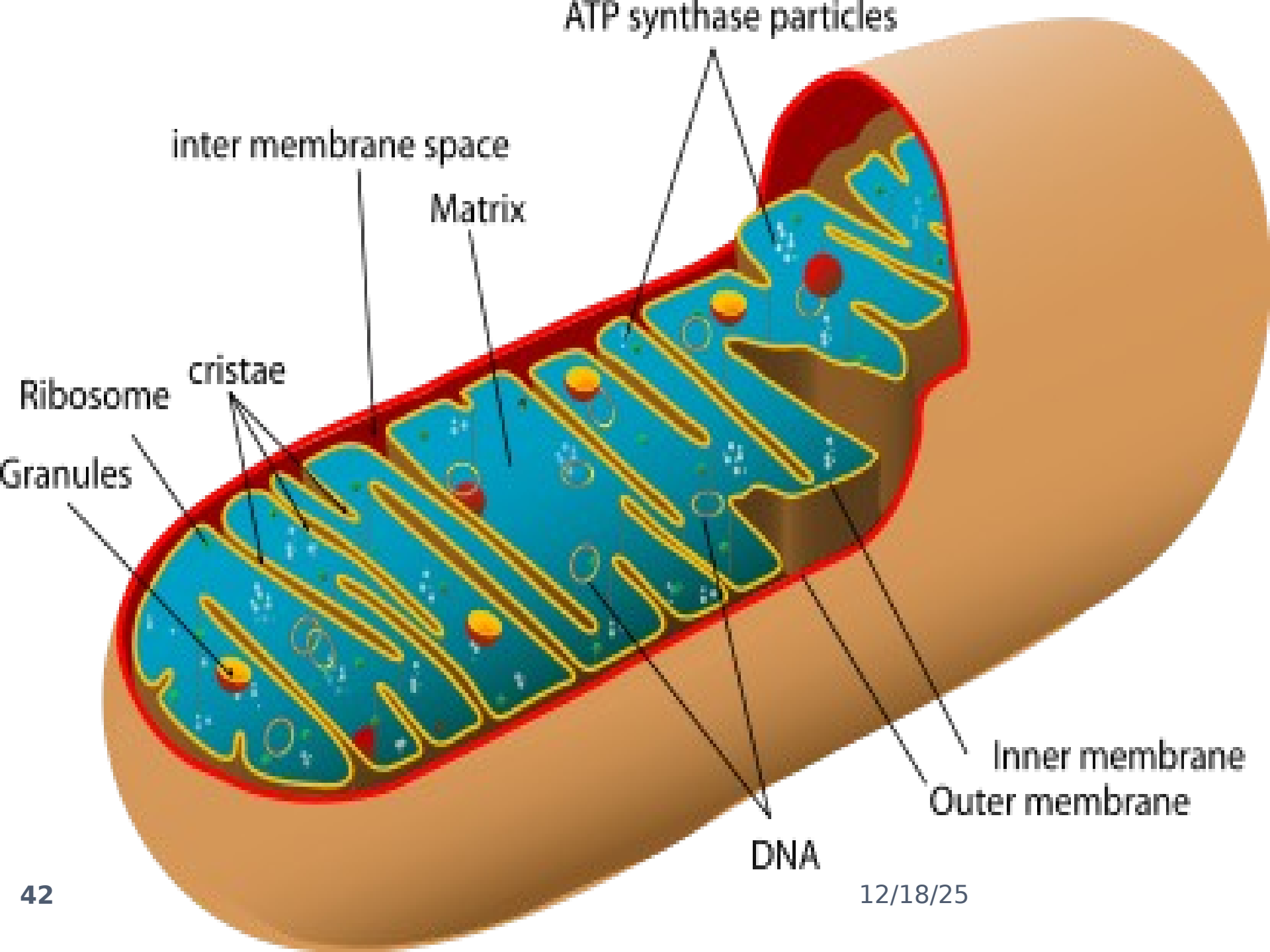
Interactions b/n Nucleus & Cytoplasm s-67



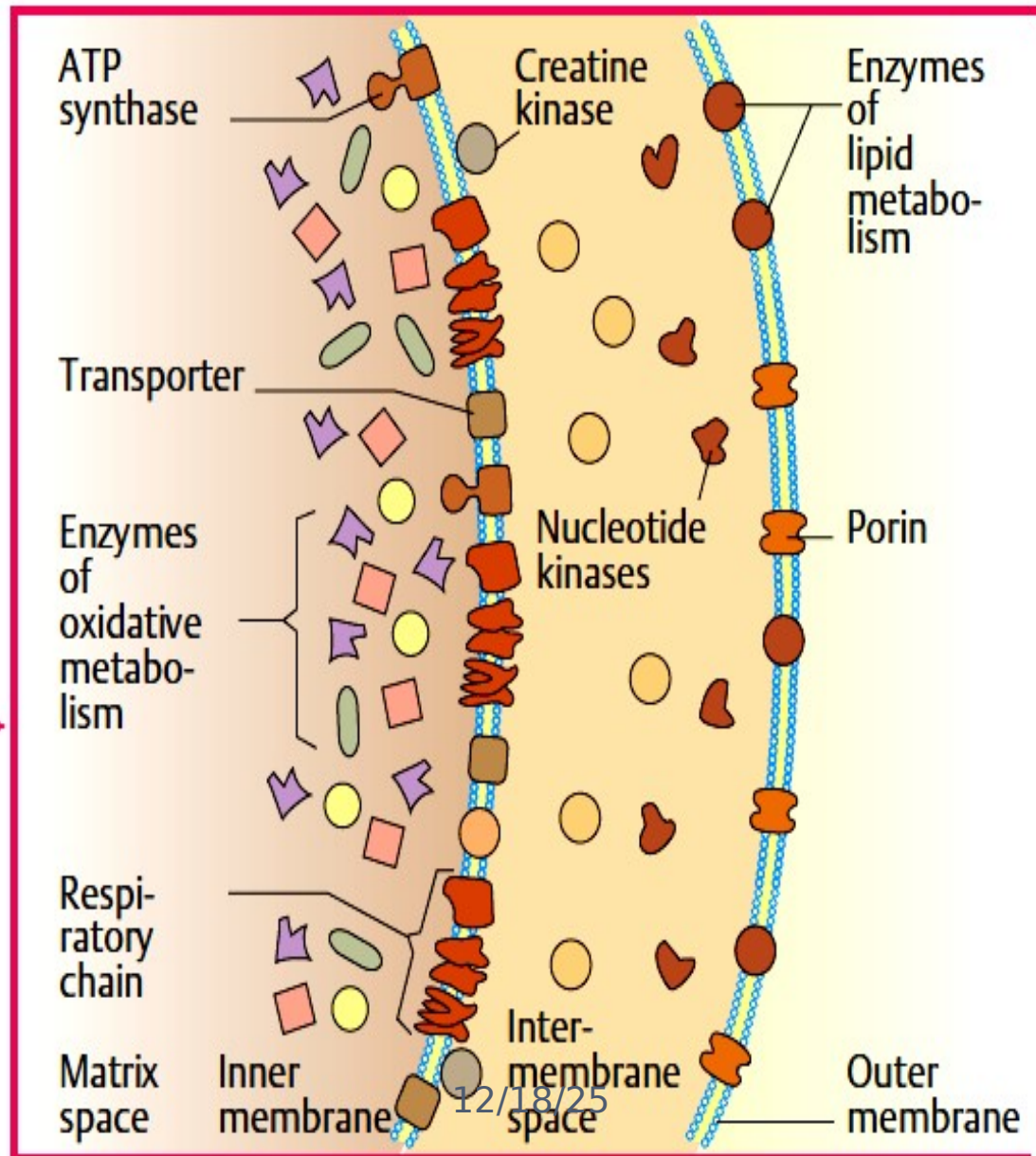
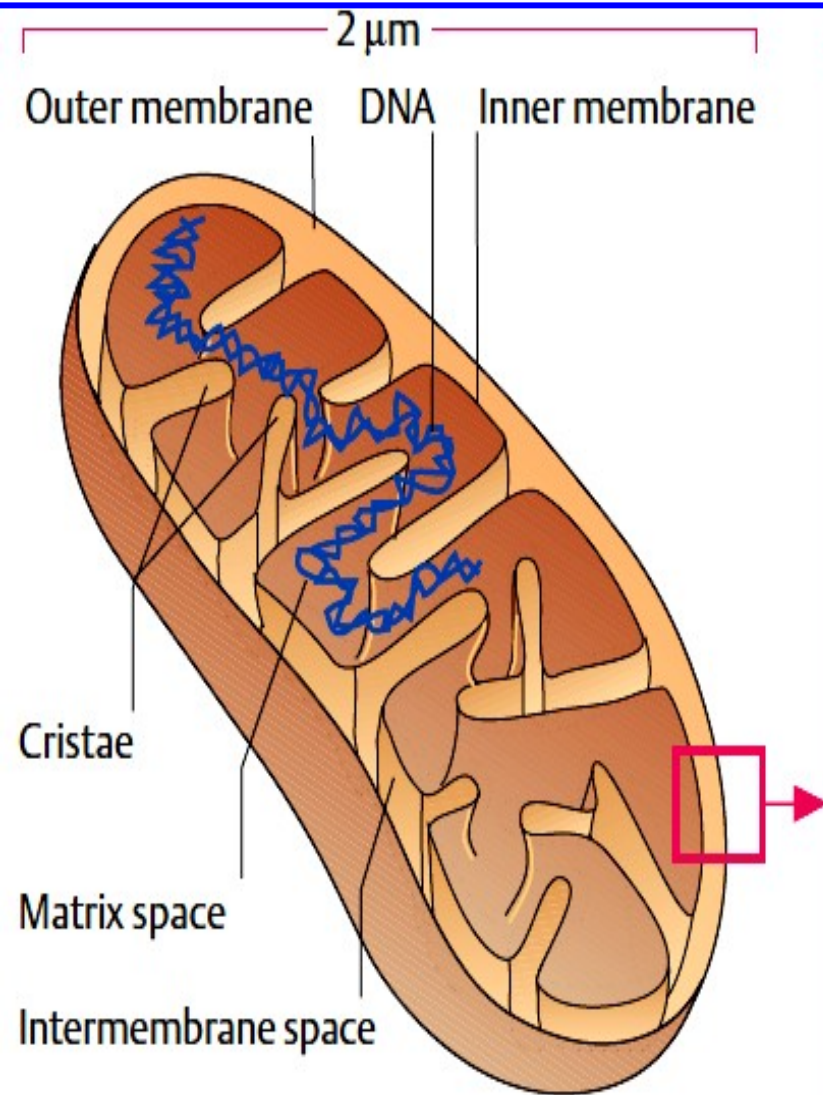
Mitochondrial Structure & Functions

■ Mitochondrial structure:

- Are bacteria-sized organelles (about 1 x 2 μm in size),
- w/c are found in large numbers in almost all eukaryotic cells
- typically, there are about 2000 mitochondria per cell,
 - representing around 25% of the cell volume
- Mitochondria are enclosed by two membranes:
 - a smooth outer mmb.
 - a markedly folded or tubular inner mitochondrial mmb.,
 - w/c has a large surface & encloses the **matrix** space
- The folds of the inner membrane are known as **cristae**,
 - tube-like protrusions are called **tubules**
- The intermembrane space:
 - is located b/n the inner & the outer membranes



Mitochondrial Structure



□ Metabolic Functions:

□ Mitochondria are also described

- as being the cell's biochemical powerhouse,
- since—through oxidative phosphorylation;
 - they produce the majority of cellular ATP

□ located in the matrix are:

- Pyruvate dehydrogenase (PDH) complex, Krebs's cycle,
- β -oxidation of fatty acids, & parts of the urea cycle

□ Inner membrane associated with:

- the respiratory chain, ATP synthesis, &
- enzymes involved in heme biosynthesis

□ In addition to the endoplasmic reticulum, the mitochondria;

- also function as an intracellular calcium reservoir

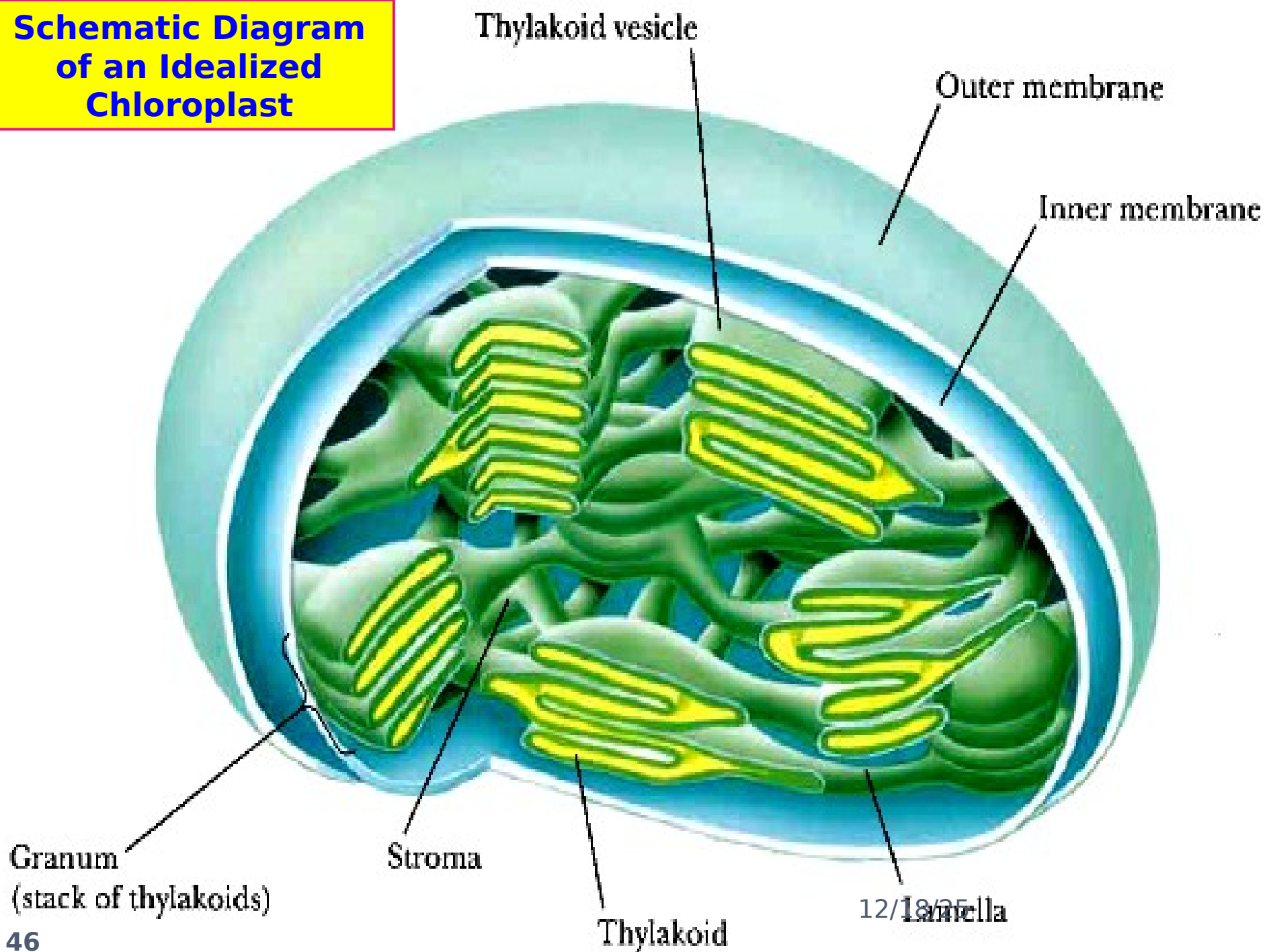
□ The mitochondria also play an important role in;

- “programmed cell death”—apoptosis

□ Chloroplasts:

- Photosynthesis
- Also have inner & outer membranes
- In addition, there is an extensive internal membrane system made up of;
 - **thylakoid vesicles** (interconnected vesicles flattened to form discs)
 - stacked upon each other to form **grana**
- Within the thylakoid vesicles is the green pigment chlorophyll,
 - along with the enzymes that trap **light energy** & convert it into chemical energy in the form of **ATP**
- The **stroma**, the space surrounding the thylakoid vesicles,
 - is the site of **CO₂ fixation**
- Chloroplasts, like mitochondria, contain **DNA**;
 - w/c encodes some of the chloroplast proteins

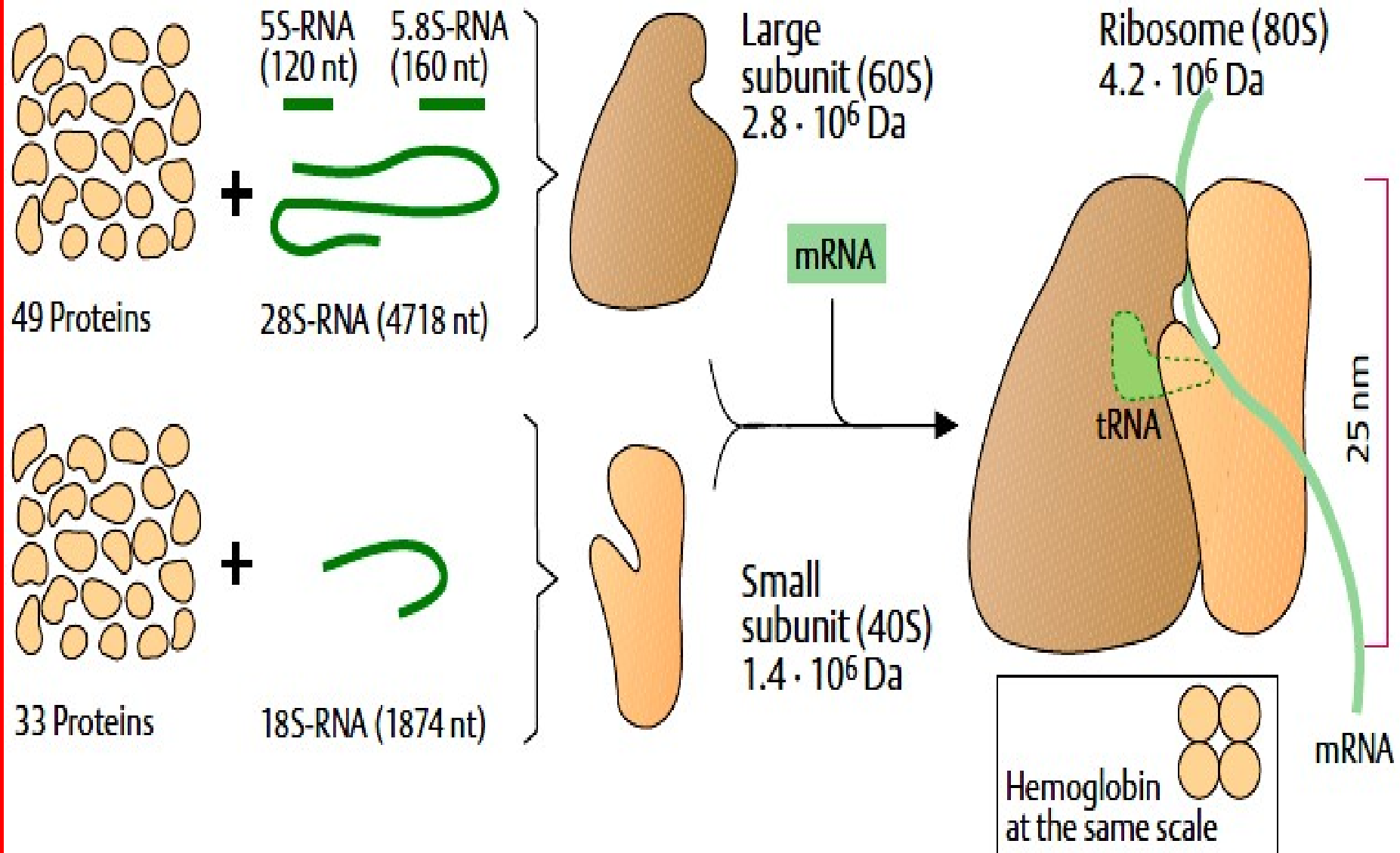
Schematic Diagram of an Idealized Chloroplast



□ **Ribosomes :**

- Ribosomes are found in all forms of life & are similar with all
- The base sequences on the RNA within ribosomes formed the basis for;
 - the definition of the three domains of life
- Looking through a microscope, ribosomes look like;
 - pebbles distributed within the cytoplasm
- Ribosomes are the factory units for the **production of proteins**
- In both types of cells, the ribosomes come in two subunits,
 - one large and one small
- There are small differences b/n ribosomes of eukaryotes & prokaryotes,
 - but both contain proteins & a few molecules of RNA

Structure of Eukaryotic Ribosomes

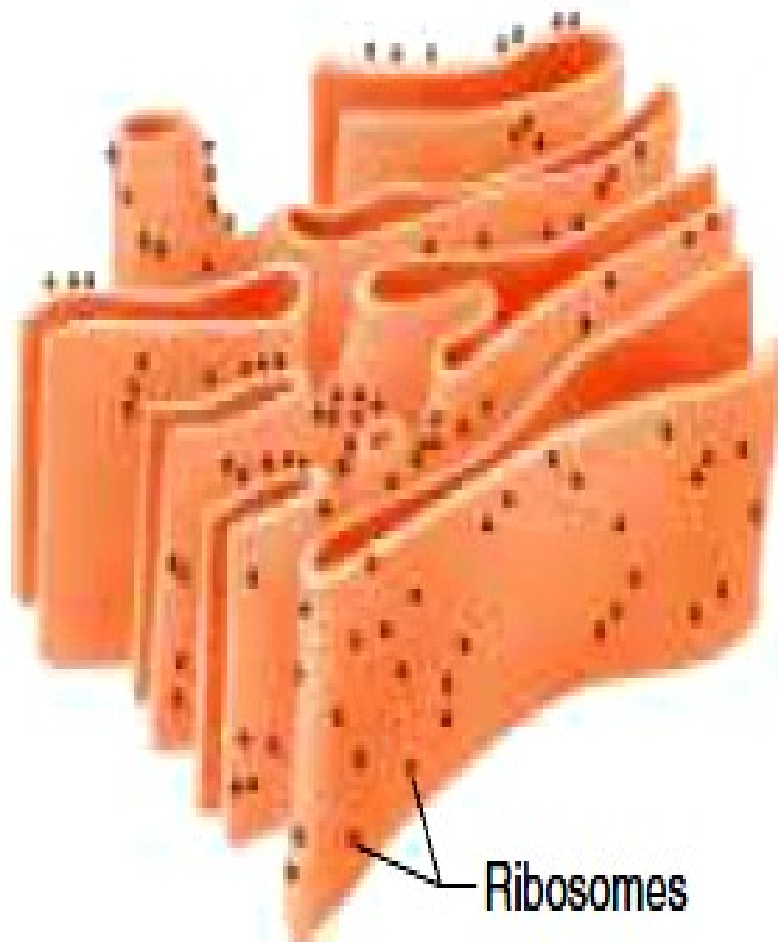


□ **ER: Structure & Function**

- **ER is an extensive closed membrane system consisting of tubular & saccular structures**
 - **In the area of the nucleus, the ER turns into:**
 - **the external nuclear membrane**
- **This interconnected network of membrane vesicles is divided into two distinct parts:**
 - **Rough ER (RER), w/c is studded with ribosomes,**
 - **is the site of membrane & secretory protein biosynthesis & their post-translational modification**
 - **Smooth ER (SER) is rich in membrane bound enzymes,**
 - **w/c catalyze partial rxn's in the lipid metabolism as well as biotransformations**
 - **SER also functions as an IC calcium store,**
 - **w/c normally keeps the Ca^{2+} level in the cytoplasm low**
 - **Sarcoplasmic reticulum ➔ SER in muscle cells**

Rough (Granular) ER & Smooth (Agranular) ER.

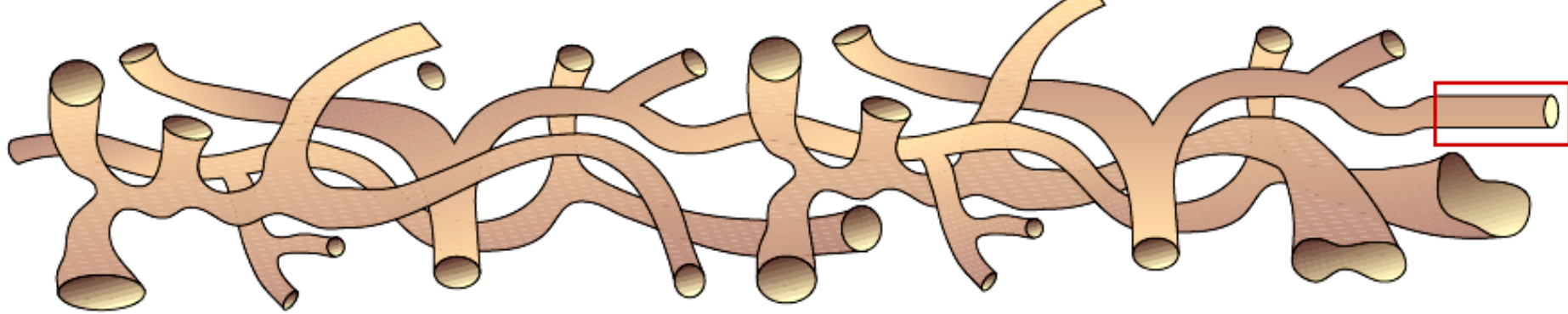
Granular endoplasmic reticulum



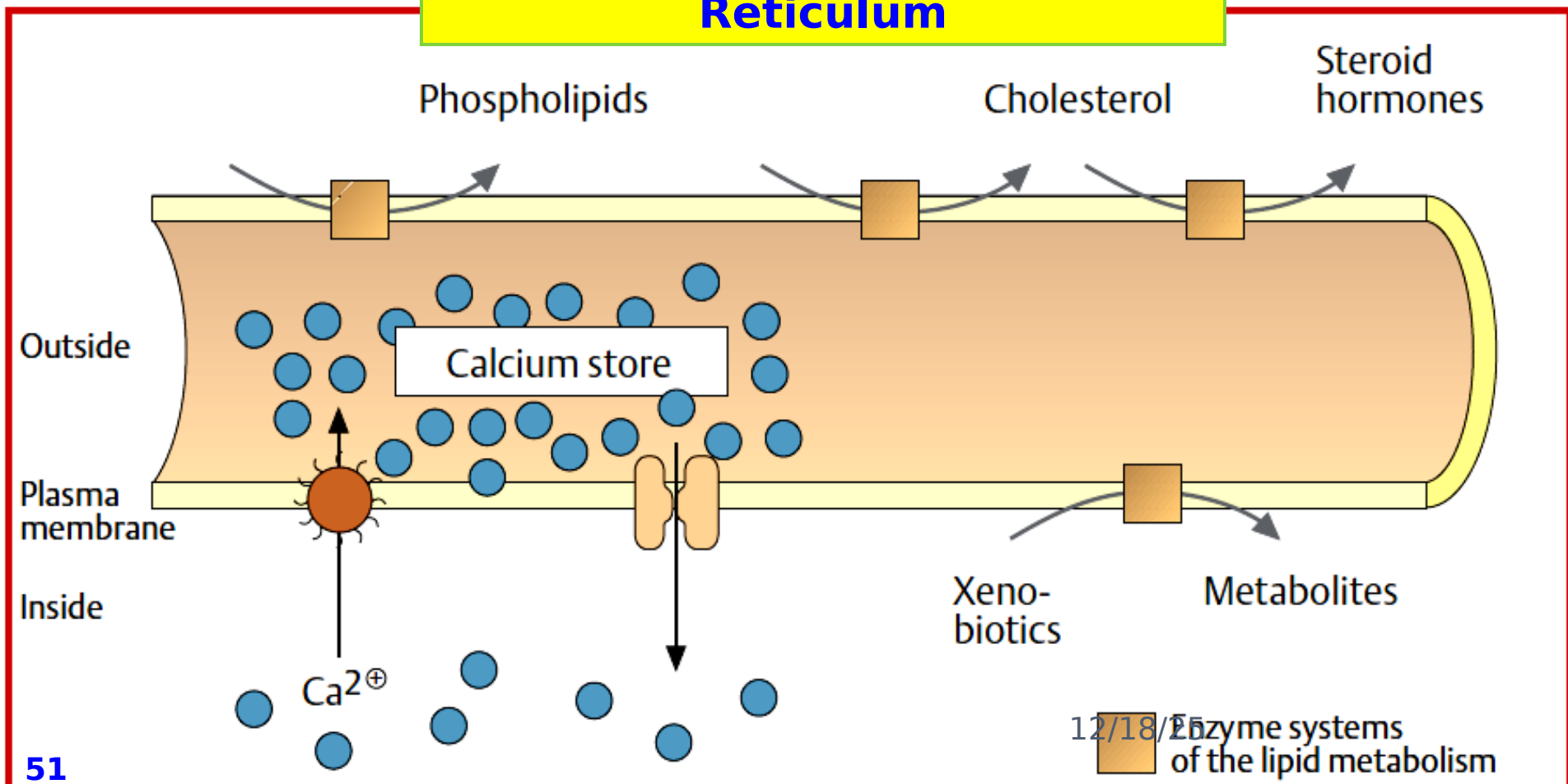
Agranular endoplasmic reticulum



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Smooth Endoplasmic Reticulum



□ Golgi Apparatus:

- *Dr. Camillo Golgi in 1898*

- a system of flattened membrane-bound sacs,
- is the sorting & packaging center of the cell

- Like the ER, the Golgi apparatus is composed of;

- small internal compartments or sacs called **cisternae**

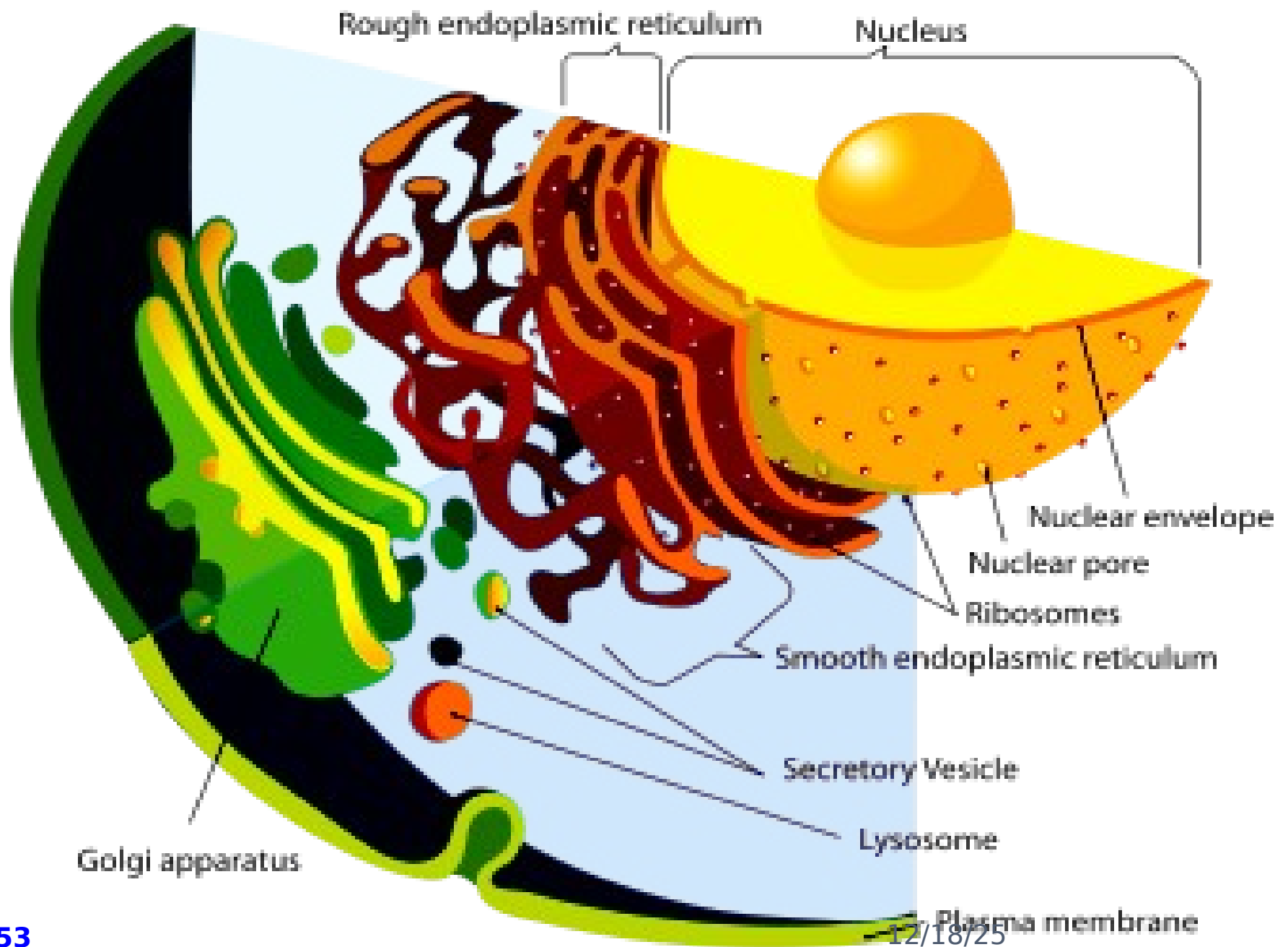
- It has a role in the:

- production, processing, & destruction of lipid
- production of lysosomes &
- processing of protein;

- It receives membrane vesicles from the RER,

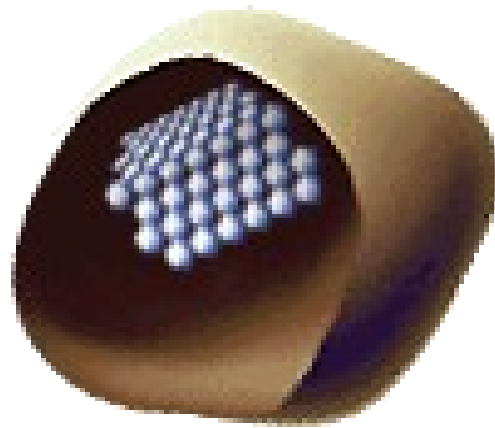
- Further modifies the proteins within them, &
- Then packages the modified proteins in other vesicles
- w/c eventually fuse with the plasma membrane or other subcellular organelles





□ Peroxisomes (microbodies)

- Site for synthesis and degradation of H_2O_2
 - e.g. oxidation of longer chain fatty acids generates H_2O_2
- Contain:
 - Oxidases produce H_2O_2
 - Catalase degrade H_2O_2



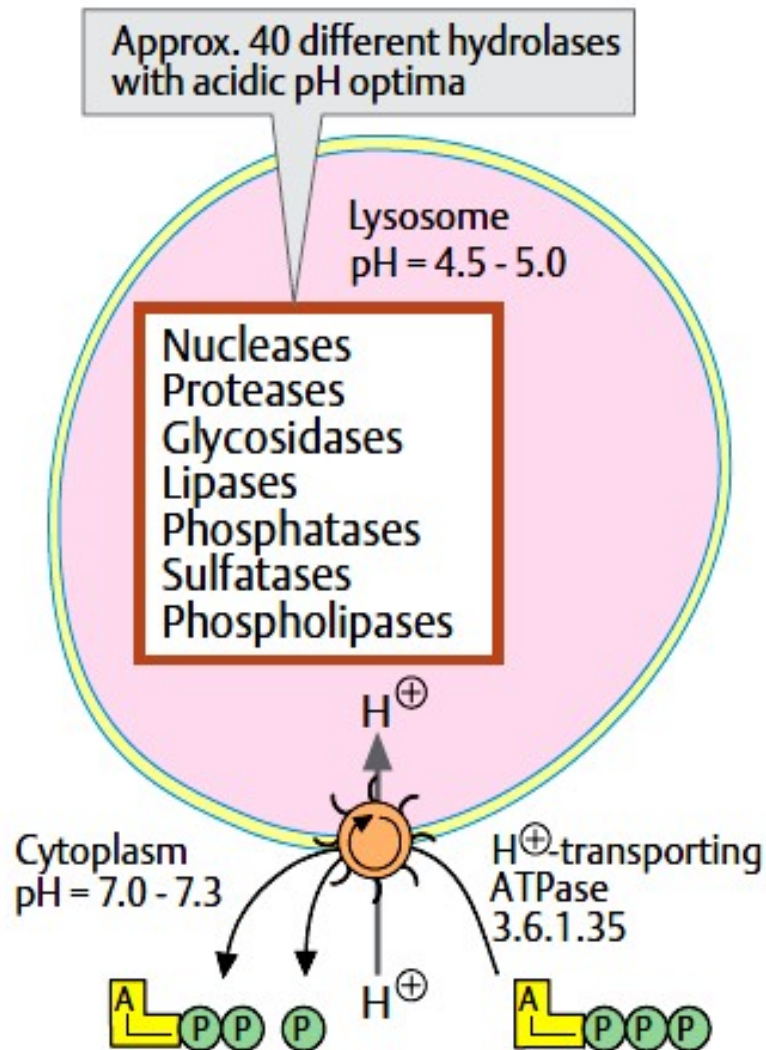


□ Lysosomes

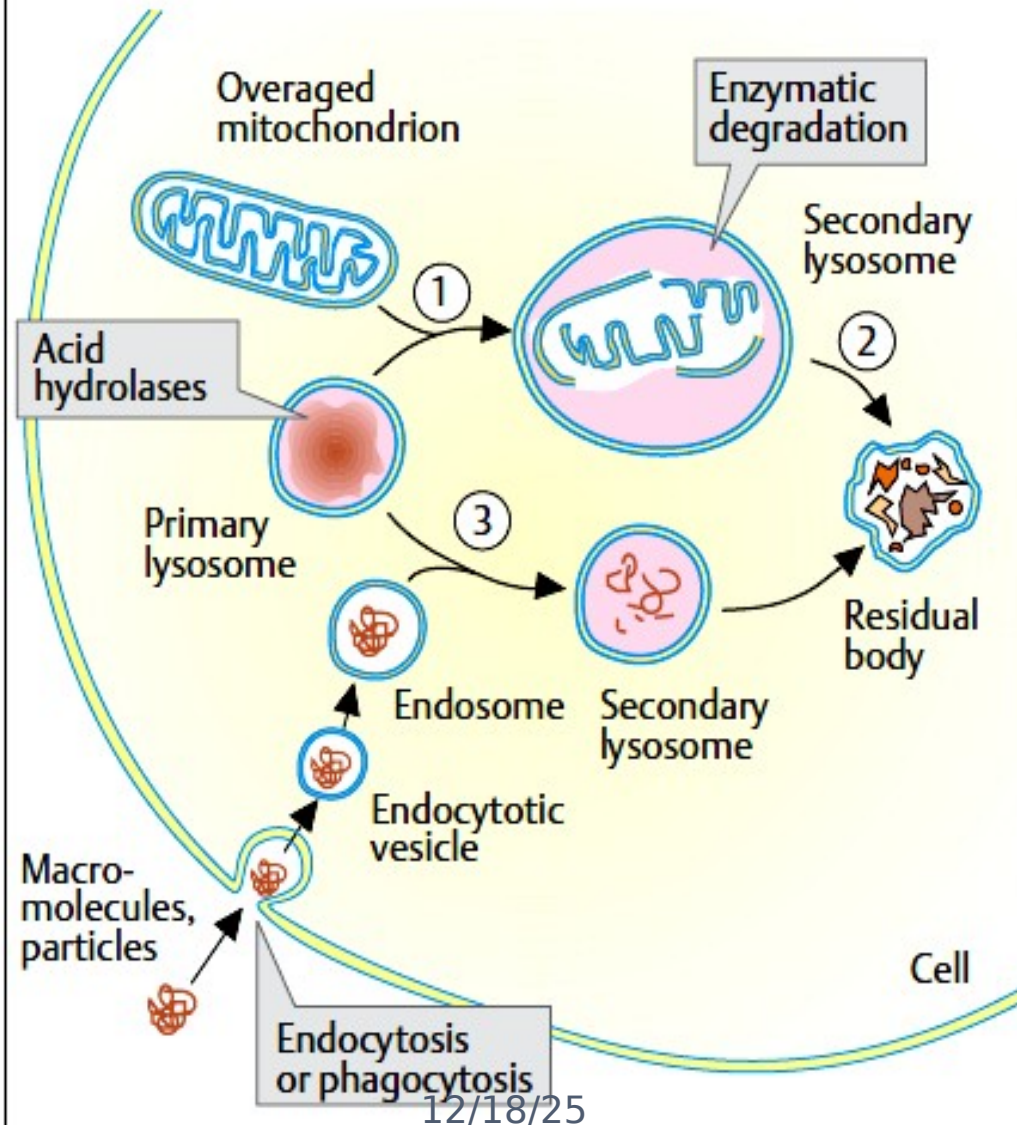
- **Organelles with a diameter of 0.2-2.0 μm**
 - with various shapes that are surrounded by a single membrane
 - there are usually several hundred lysosomes per cell
- **ATP-driven V-type proton pumps are active in their membranes;**
 - these accumulate H^+ in the lysosomes,
 - the content of lysosomes with pH values of 4.5-5 is much more acidic than the cytoplasm (pH 7-7.3).
- **The lysosomes are the cell's "stomach,"**
 - serving to break down various cell components
- **For this purpose, they contain some 40 different types of hydrolases,**
 - w/c are capable of breaking down every type of macromolecule

Lysosomes

A. Structure and contents



B. Functions



Cellular genetic components

❑ **Chromosomes** are made of long strands of DNA nucleotides wrapped around histone proteins.

1. The smallest of the 46 human chromosomes contains 30 million (that's 30,000,000) base pairs.
2. There is 1 meter of DNA in each typical cell nucleus in the human body
3. Tightly wrapped histones and DNA form

Cellular genetic components

4. Chromatin generally exists as a long coiled thread, but during mitosis/meiosis it becomes even more coiled, **this is what is seen during Prophase through Anaphase and is called a chromosome.**



DNA

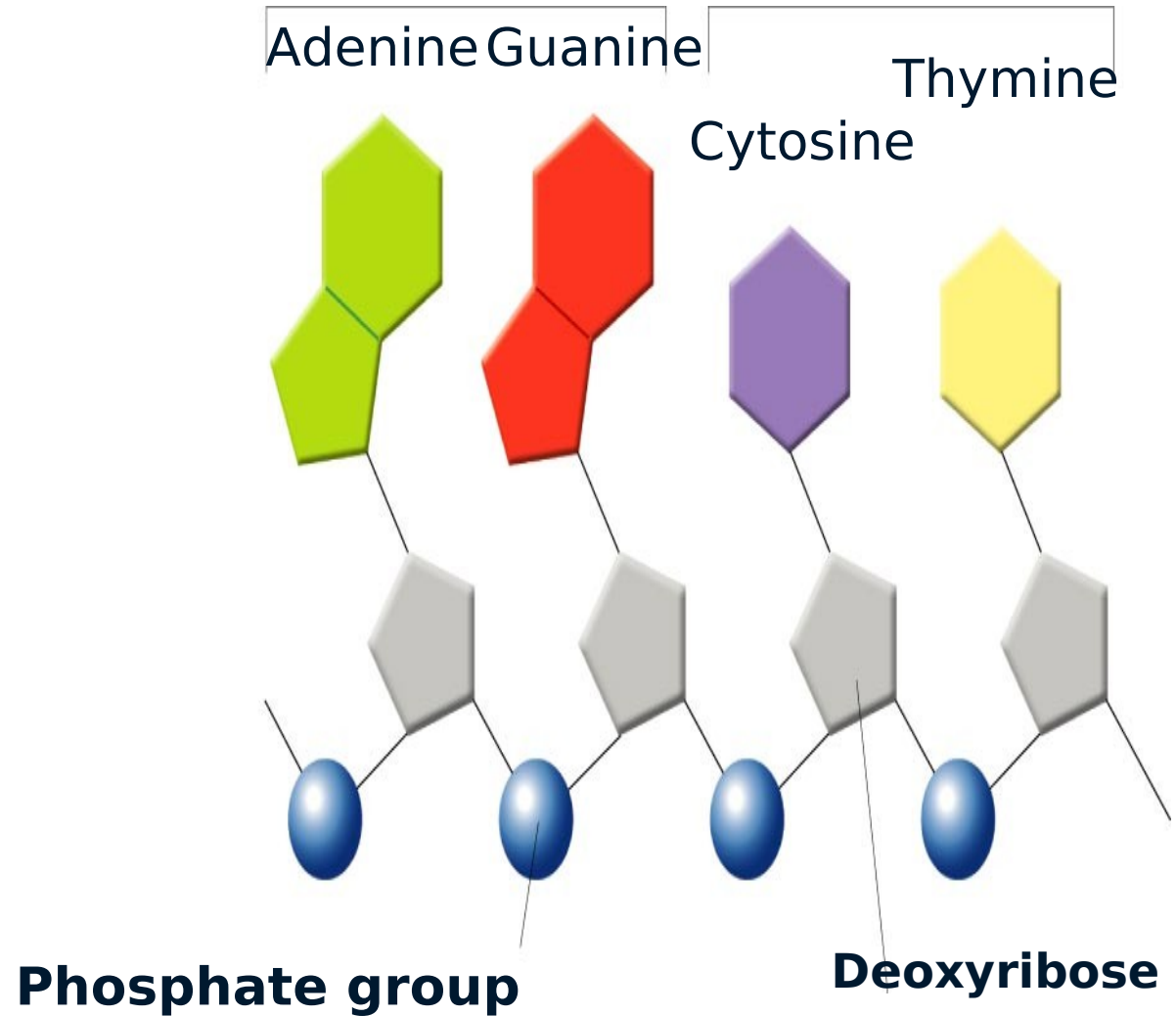
DNA is a Special molecule:

- 1.DNA stores and carries genetic information from one generation to the next.
- 2.DNA determines heritable characteristics of organisms.
- 3.DNA is easily copied since it is replicated during cell division.

Made of units called nucleotides.

- a. Deoxyribose (a sugar)
- b. A Phosphate Group
- c. One of four possible
Nitrogenous Base

1. Adenine
2. Thymine
3. Guanine
4. Cytosine



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Nucleotide Use

- Like letters in the alphabet, these four nitrogenous bases are strung together in many different arrangements **in order to *code for* and *carry* genetic information.**

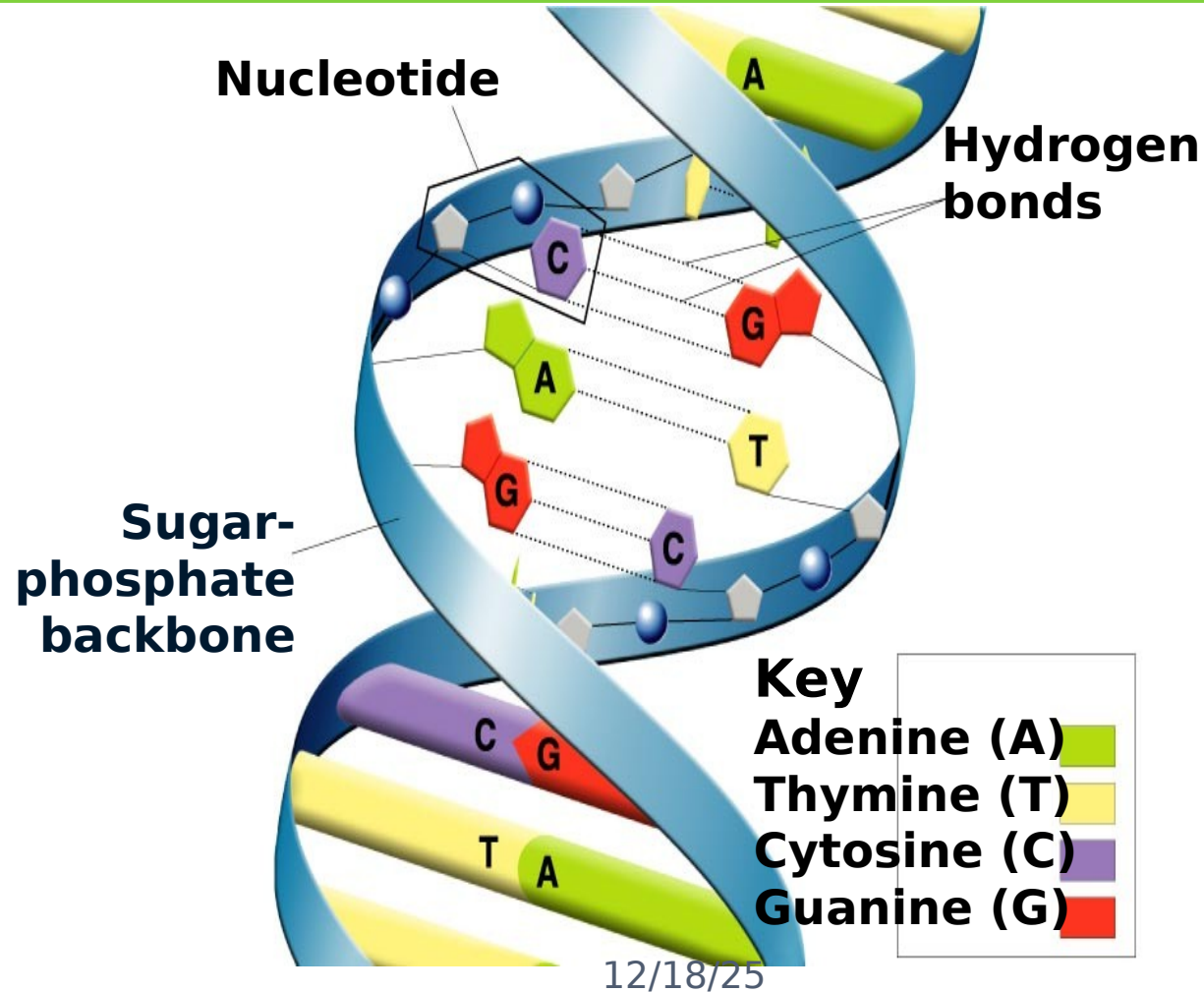
The Structure of DNA

The Double Helix:

- A. “A twisted ladder” forms when adenine and thymine attract to each other.
- Cytosine and Guanine attract as well.
- So $A=T$ and $G=C$ in a DNA molecule
- This attraction (called Base Pairing) is caused by hydrogen bonds between the bases.

More on the double helix

- Two ***separate*** and ***opposite*** strands wrap around each other to form a stable twisting molecule



RNA



- The main role of RNA is to aid in Protein Synthesis
- RNA is similar to DNA in that both are made of nucleotides

RNA is different than DNA:

- Sugar backbone in RNA is **Ribose** (not **Deoxyribose**)
- RNA is **single stranded** while DNA is **double stranded**
- RNA contains **Uracil** in place of **Thymine**.

(U in place of T)

- DNA always stays in the nucleus, **while RNA can be found in the nucleus and cytoplasm.**

The Central Dogmas of Molecular Biology

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1. The concept of genes is historically defined on the basis of genetic inheritance of a phenotype. (Mendelian Inheritance)
 2. The DNA an organism encodes the genetic information. It is made up of a double stranded helix composed of ribose sugars. Adenine(A), Cytosine (C), Guanine (G) and Thymine (T).
- [note that only 4 values need to be encoded ACGT.. Which can be done using 2 bits.. But to allow redundant letter combinations (like N means any 4 nucleotides), one usually resorts to a 4 bit alphabet.]

3) Each side of the double helix faces its complementary base.

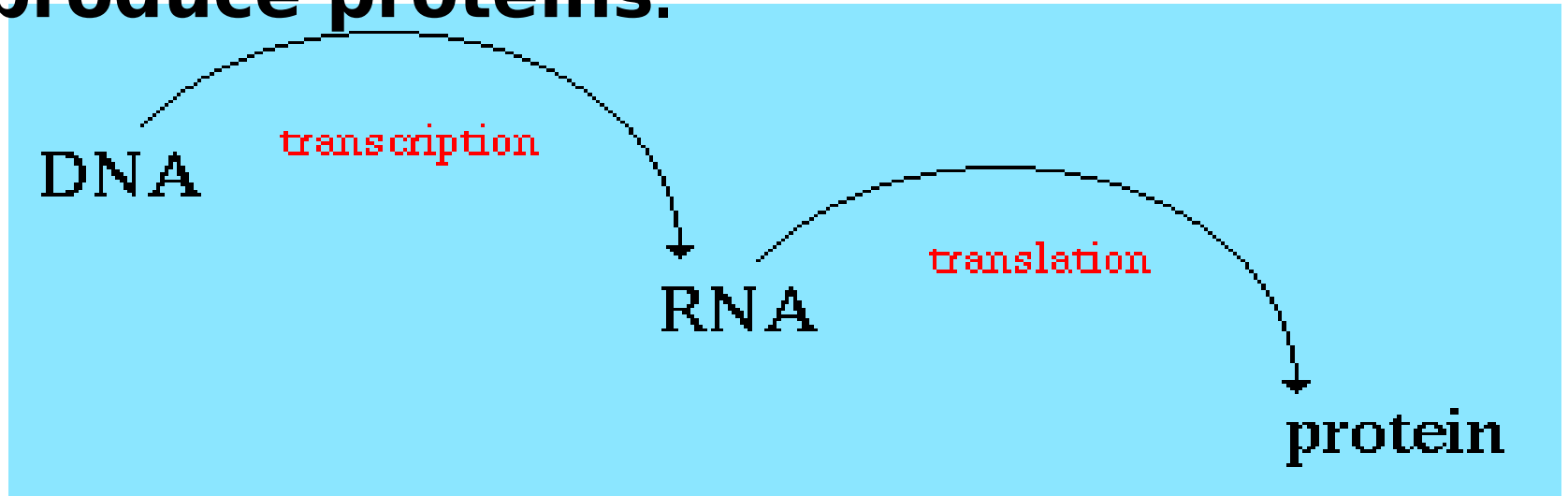
$A \leftrightarrow T$, and $G \leftrightarrow C$.

4) Biochemical process that read off the DNA always read it from the 5' side towards the 3' side. (replication and transcription).

5) A gene can be located on either the 'plus strand' or the minus strand. But rule 4) imposes the orientation of reading .. And rule 3 (complementarity) tells us to complement each base E.g. If the sequence on the + strand is **ACGTGATCGATGCTA**, the - strand must be read off by reading the complement of this sequence going 'backwards'

Central Dogmas of Molecular Biology

6) DNA information is copied over to mRNA that acts as a template to produce proteins.



We often concentrate on protein coding genes, because proteins are the building blocks of cells and the majority of bio-active molecules. (but let's not forget the various RNA genes)

