Open Elective Subject

EBTY183L Biological Machines

(L-T-P = 3-0-0)

BENNETT UNIVERSITY
TIMES OF INDIA GROUP

Lecture 1

Prof. N.Latha

Head, Department of Biotechnology

BIOLOGICAL MACHINES

Detailed Syllabus

Module 1 (15 hours)

Cell as a Machine

Introduction to Prokaryotic & eukaryotic cells, Different cell components as individual machines: Plasma membrane, Cell wall, Nucleus, Nucleolus, Ribosomes, Mitochondria, Chloroplast, Vacuoles, Centrioles, Glyoxisomes, Peroxisomes Endoplasmic reticulum, Golgi apparatus and Lysosomes, Cytoskeleton: Role in transport of cells and Organelles. Proteins as major functional molecules: Introduction to amino acids and protein synthesis. Machinery for the protein Transport to their site of action.

Module 2 (15 hours)

Cellular Transport Machinery

Cellular Transport machinery: Simple diffusion, Active and passive transport of molecules across membrane, Electrical properties of membranes and Action potential, Muscle contraction: motor proteins, myosin and actin, kinesin and dynein. The GroEL/GroEs Chaperonin machine, ATP synthase – a paradigmatic molecular machine, ATP-dependent proteases: The degradation machines.

Module 3 (12 hours)

Malfunctioning of Cellular Machinery and their effects

Malfunctioning of protein synthesis/transport mechanisms/folding mechanisms: Cause and effects of Progeria, Diabetes, Cystic Fibrosis, Sickle Cell Anemia, Parkinson, Prion Diseases, Kuru, Alzheimer's disease, Schizophrenia.

LIVING WORLD
BIOSPHERE

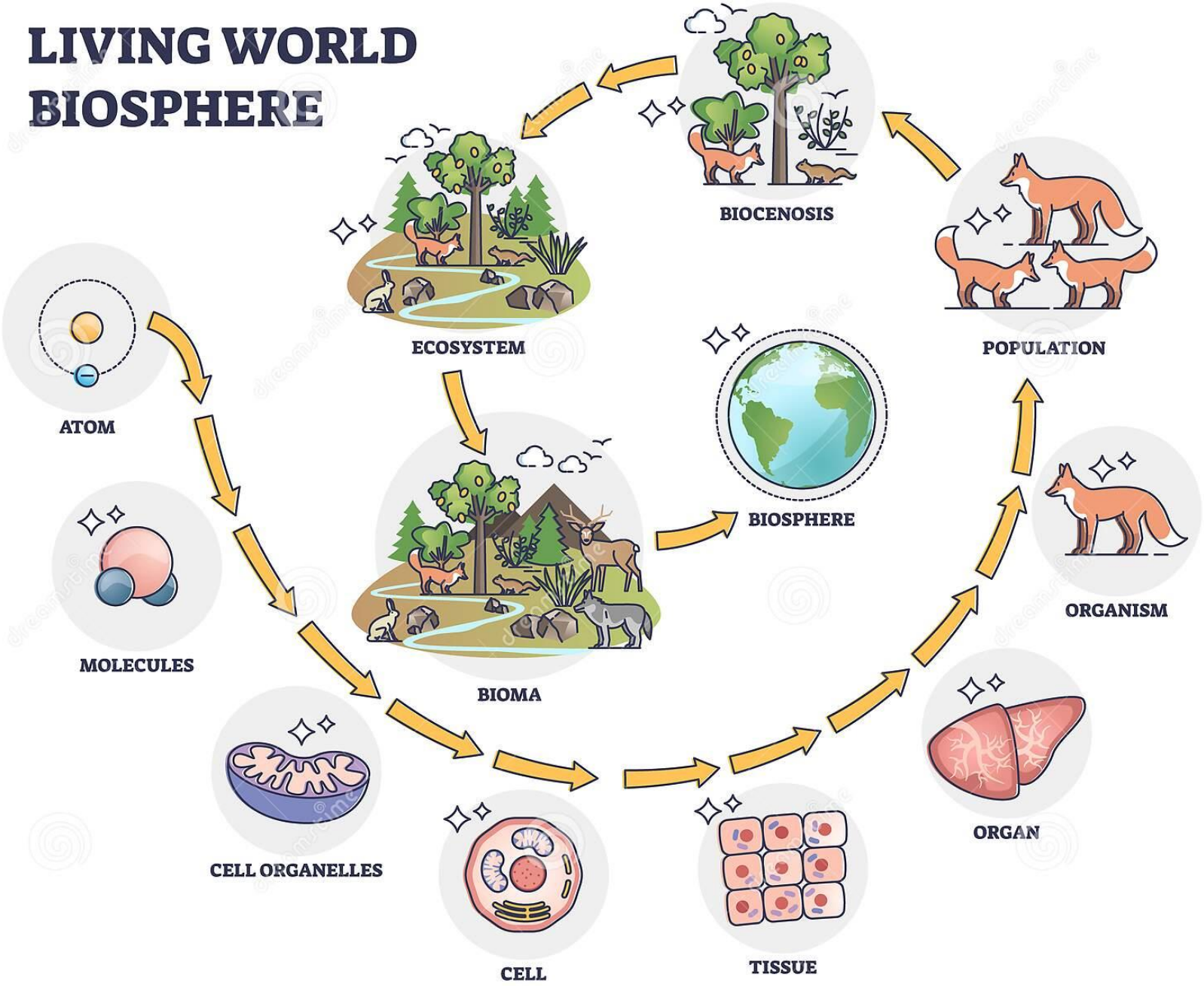


Figure 1 | **Marcello Malpighi** (from the *Opera Postuma*, 1798 Venetian In Folio edition). Malpighi, a prominent scientist in the seventeenth century, was one of the first to attribute body function to an organized series of minute 'organic machines'. The concept underlying his metaphor of the 'angel and the mill' prompted anatomical investigations, which laid the foundation for modern microscopic anatomy. (Image courtesy of the library *G. Romiti* of the Anatomical Institute of the University of Pisa.)

Marcello Malphigi

…one of the greatest 17th century life scientist

"Nature in order to carry out marvellous operations in plants and animals, has been pleased to construct their organized bodies with a very large number of machines, which are of necessity made of extremely minute so shaped and situated, such as to form a marvellous organ, the composition of which are usually invisible to the naked eye, without the aid of a microscope".

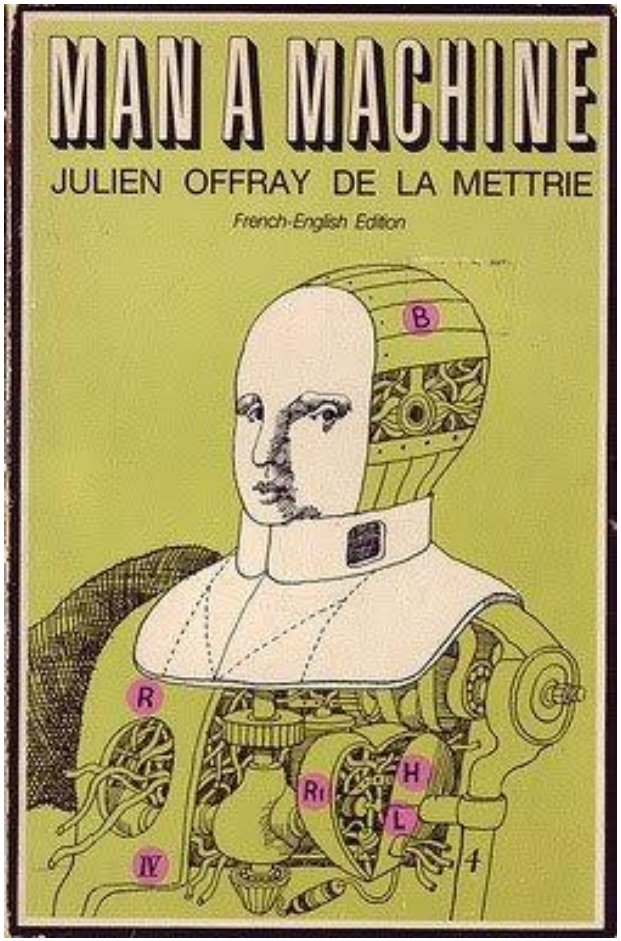
Box 2 | **Modern molecular machines**

Today, biology is revealing the importance of 'molecular machines' and of other highly organized molecular structures that carry out the complex physico-chemical processes on which life is based. There are many diverse molecular machines:

- The photosynthetic system and complex devices that produce ATP.
- DNA replication and protein translation apparatus.
- Enzymatic cascade of phototransduction.
- The integrated membrane system, involving ionic pumps and channels, that produces ionic gradients and generates electric differences across membranes; this underlies the production of electric signals in nerve fibres.
- Machines that convert chemical energy into mechanical energy during muscle contraction or flagellar motion.
- Finely integrated metabolic cycles and networks, including the system involved in antigen recognition and antibody production, the integrated system of hormones, extracellular molecules and intracellular messengers that are connected by many control pathways.

M. Piccollino , Nature Reviews Molecular Biology, Nov 2000, Vol 1, 140-152

Are humans only machines?



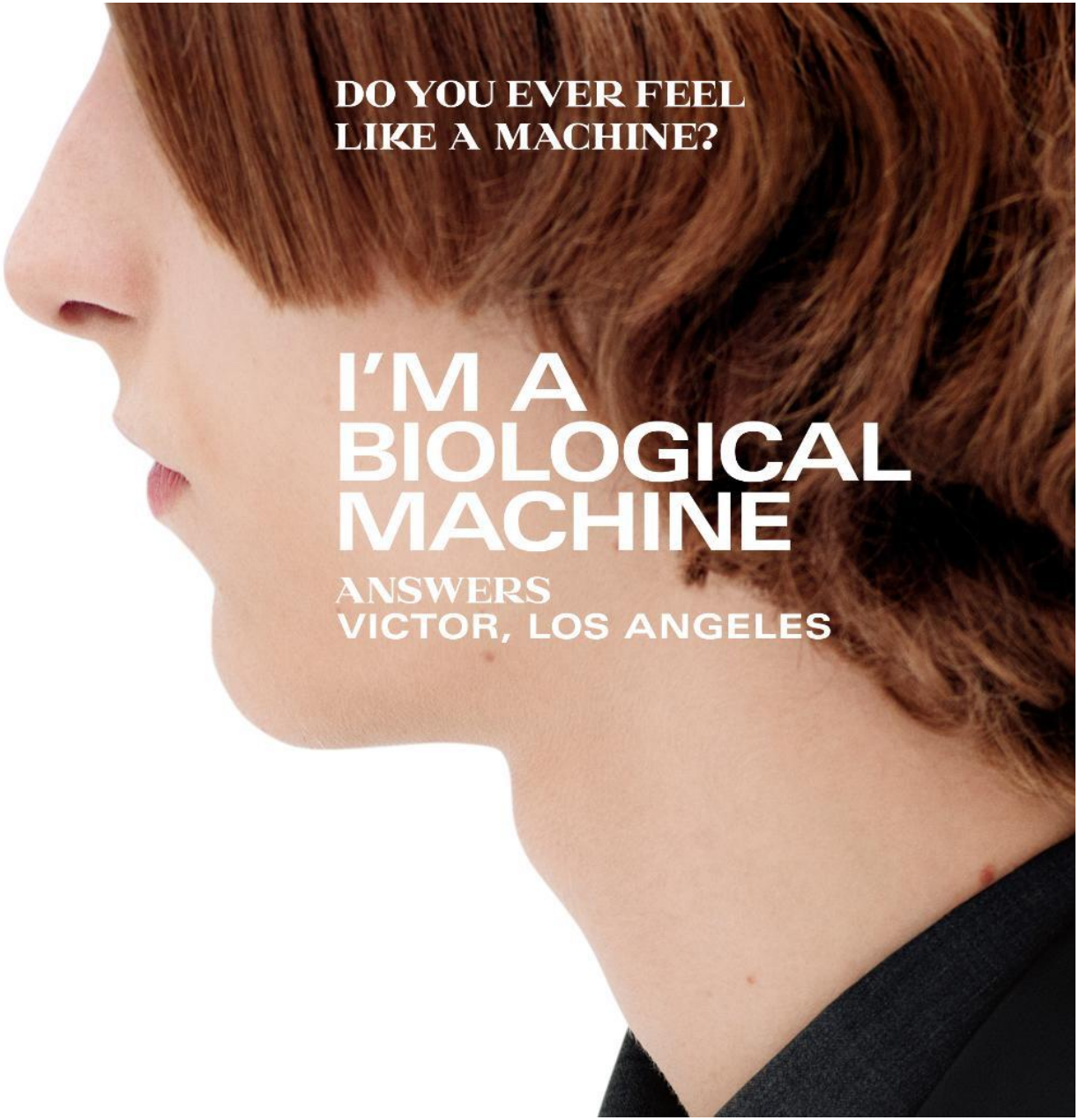
Two schools of thought

- Humans are machines.
  They were created via Evolution.

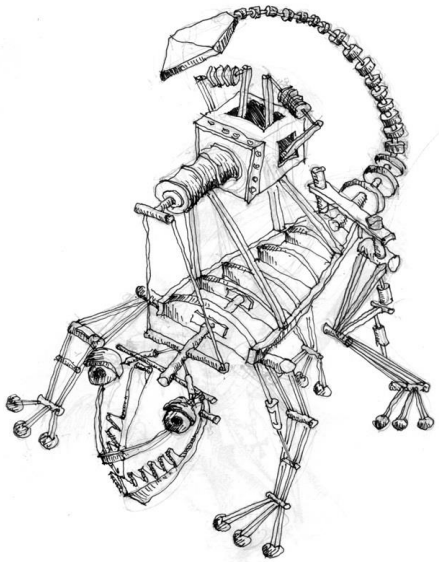
- Only in a loose metaphorical sense. Anyone who has tried to "scientifically" mechanistically explain the human species however fails.

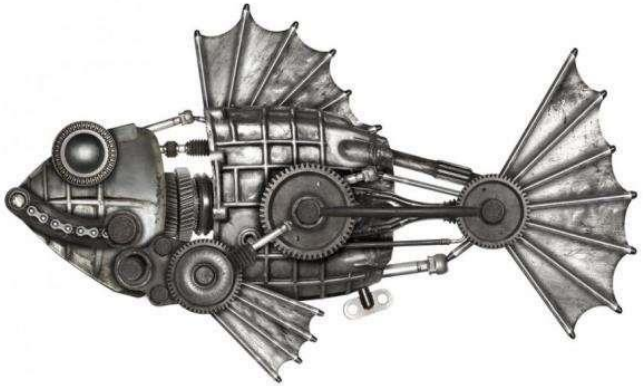
Man vs Machines

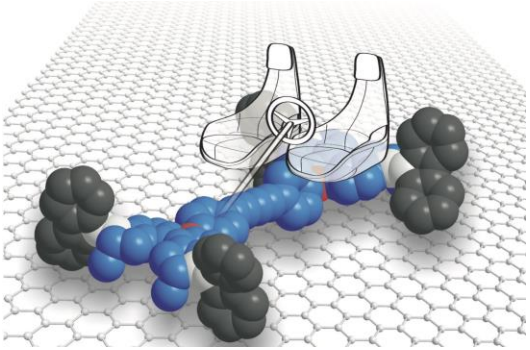
- How do machines compare to humans
- What are things human have, not possessed by machines
- What are some examples that machines can perform better than humans

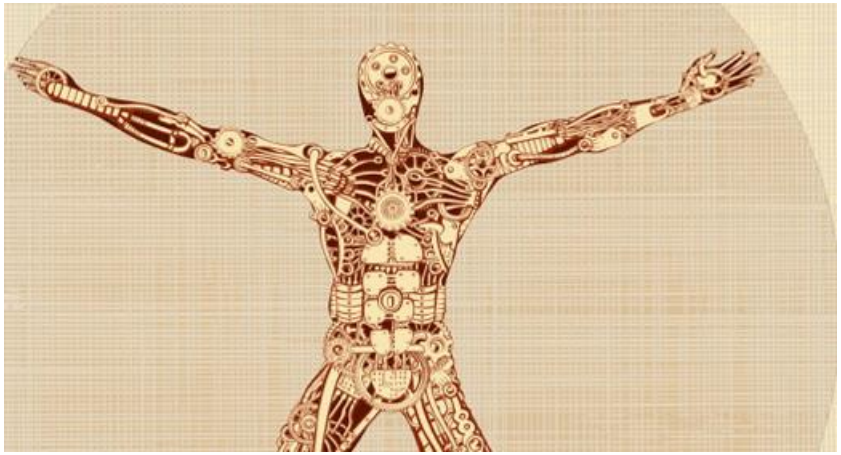

DO YOU EVER FEEL
LIKE A MACHINE?
I'M A
BIOLOGICAL
MACHINE
ANSWERS
VICTOR, LOS ANGELES

ARE LIVING ORGANISMS A MACHINE ?

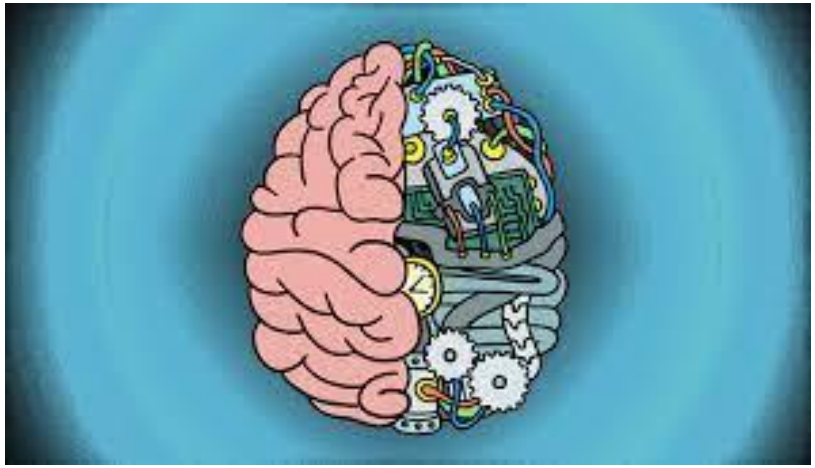








BIOLOGICAL MACHINES AT TISSUE/ORGAN LEVEL

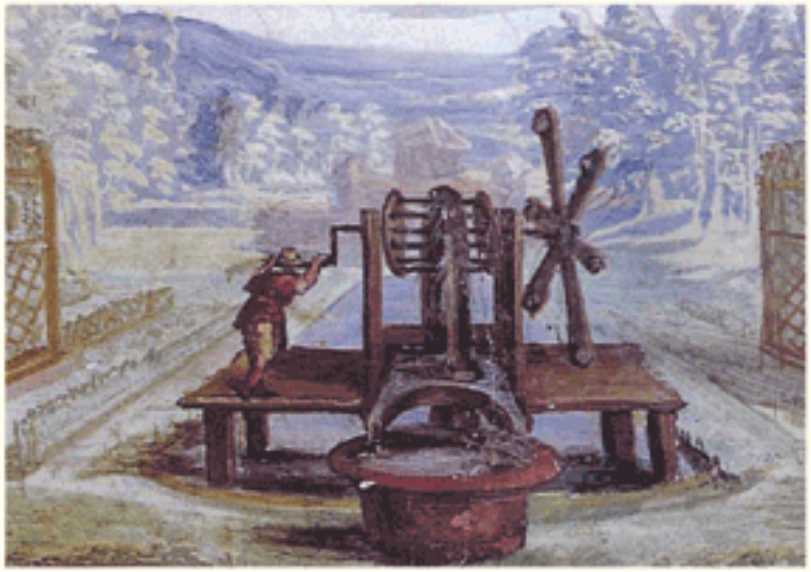


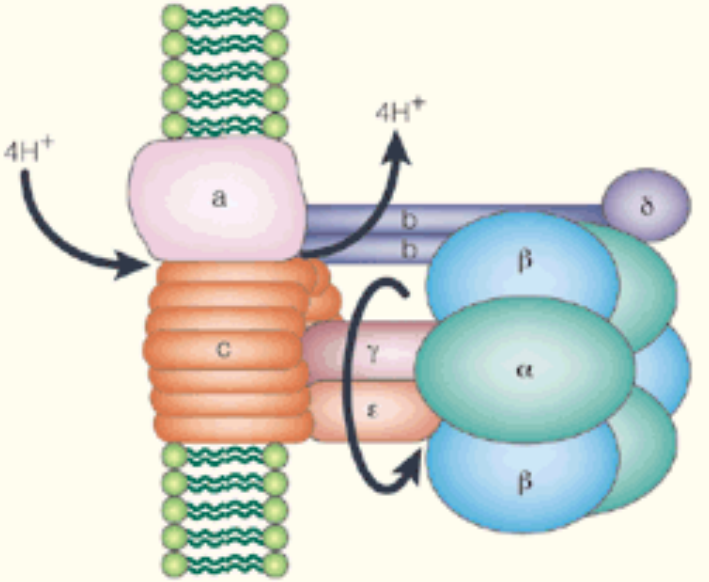
Cell as Machines

https://www.1088press.it/en/molecular-machines/2-natural-molecular-machines/

The Inner Life of the Cell. A myriad of molecular machines at work within a cell. Courtesy BioVision, Harvard University. Copyright © 2006 The President and Fellows of Harvard College.

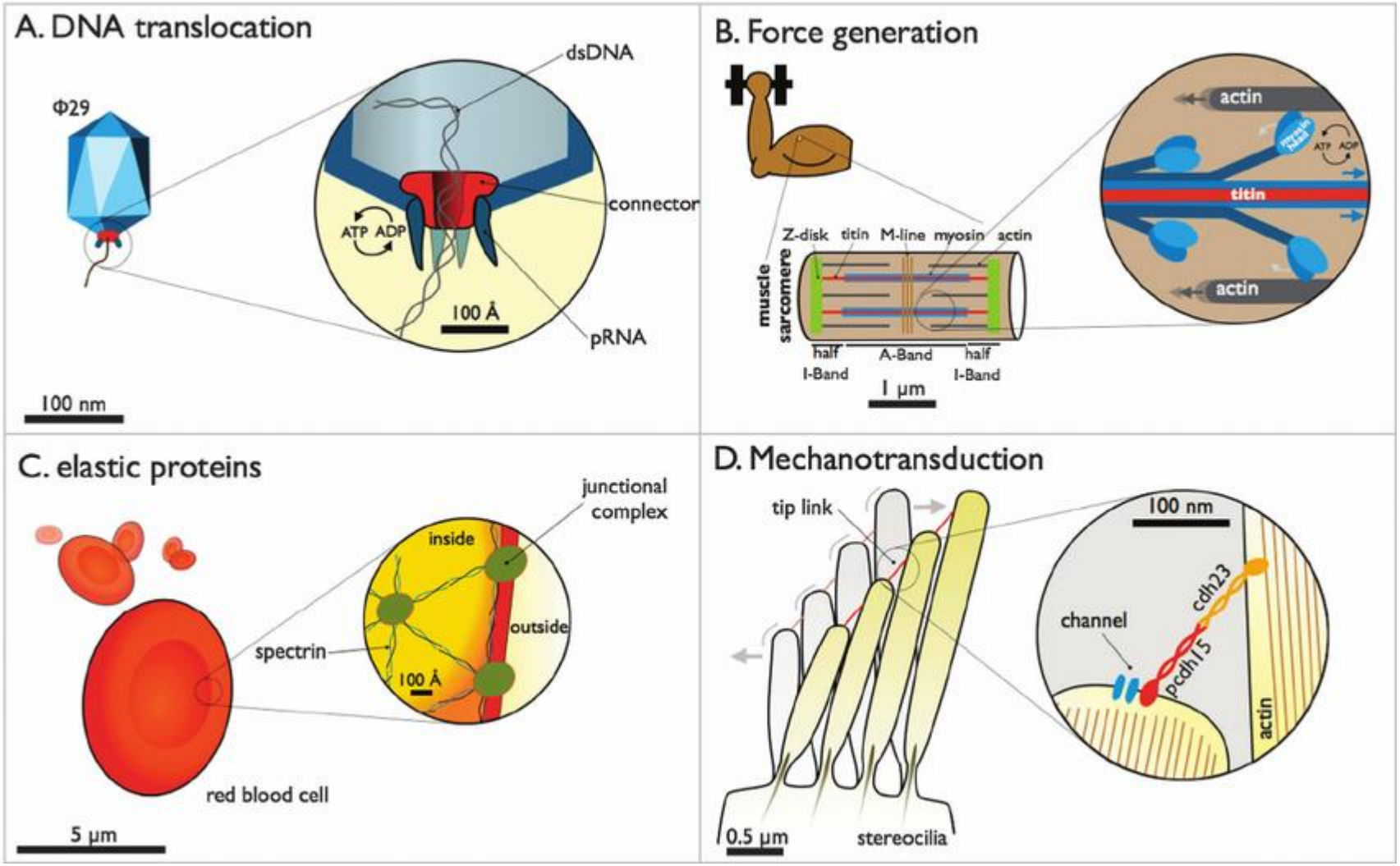
Biological machines: from mills to molecules





Nature Reviews | Molecular Cell Biology

PROTEINS AS MOLECULAR MACHINES



Shape Change

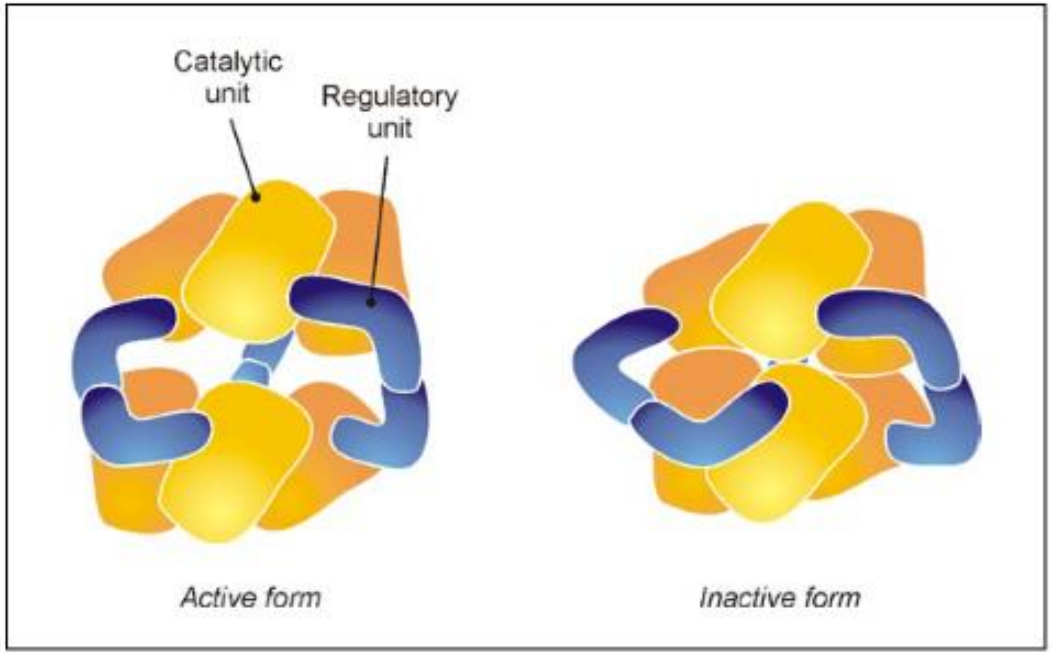


Fig. 16. The enzyme *aspartate transcarbamylase* is present in bacteria, where it is responsible for the synthesis of two important molecules, thymine and cytosine. This enzyme is able to self-regulate: an excess of synthesized molecules causes a change in shape (allosteric mechanism) that blocks the activity of the enzyme.

INTERFACE

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Review

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Reviews

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Keywords:
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Simple mechanics of protein machines

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[2]Department of Physical Chemistry, Fritz Haber Institute of the Max Planck Society, Faradayweg 4-6, 14195 Berlin, Germany

HF, 0000-0003-4984-9294

While belonging to the nanoscale, protein machines are so complex that tracing even a small fraction of their cycle requires weeks of calculations on supercomputers. Surprisingly, many aspects of their operation can be however already reproduced by using very simple mechanical models of elastic networks. The analysis suggests that, similar to other self-organized complex systems, functional collective dynamics in such proteins is effectively reduced to a low-dimensional attractive manifold.

1. Introduction

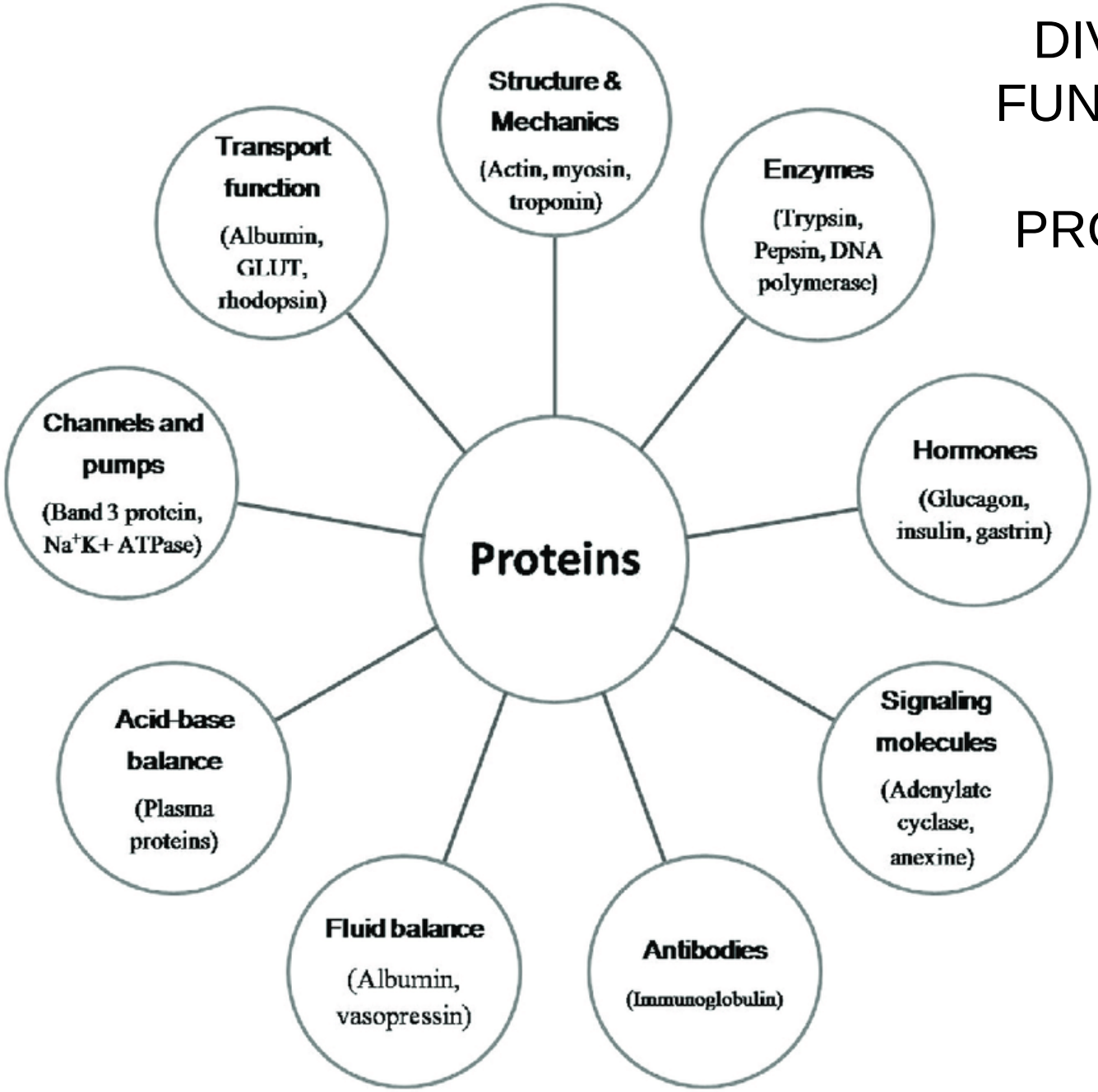
To a large extent, the living cell is a population of interacting molecular machines [1]. These protein machines, acting as motors and pumps or performing operations with other biomolecules, such as DNA, underlie basic functions of the cell. Understanding of their mechanisms is essential for molecular biology and for prospective biotechnology applications. Single-molecule experiments could provide much information on the dynamics of protein machines [2–5]. More recently, high-speed atomic force microscopy methods have allowed direct visualization of conformational motions at nanoscale resolution in real time [6].

Molecular structures and equilibrium conformations of almost all proteins are known. They are determined through a combination of X-ray diffraction experiments, cryo-electronic microscopy and other techniques, and can be found in the Protein Data Bank (PDB). Moreover, conformational dynamics of proteins is sufficiently well reproduced in all-atom molecular dynamics (MD) simulations. Hence, it may seem that just some special MD simulations have to be performed in order to unveil the operation mechanisms of protein machines. In practice, severe difficulties are encountered if one attempts to do this.

All-atom MD simulations of proteins are extremely demanding in terms of the computation time. Even with the most powerful supercomputers, the dynamics of a protein can be traced only up to microsecond times. The best achievement so far has been that, by employing special hardware and for a very small protein, a trajectory of a millisecond duration could be obtained [7]. This is frustrating because

Proteins act as motors and pumps or performing operations with other biomolecules

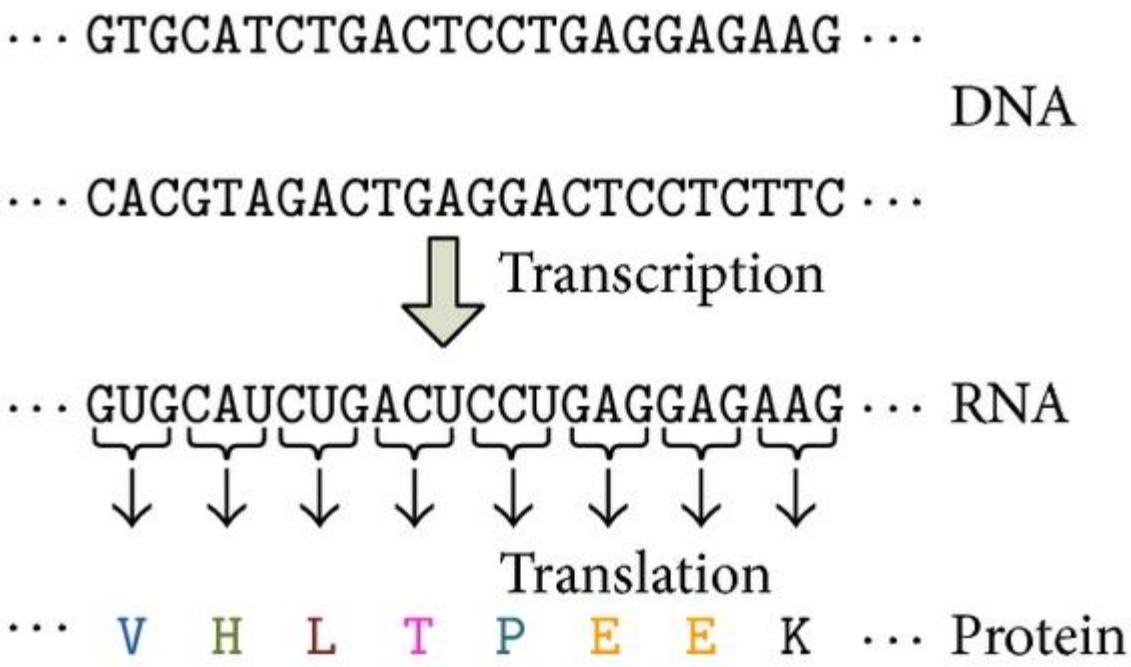
DIVERSE FUNCTIONS OF PROTEINS

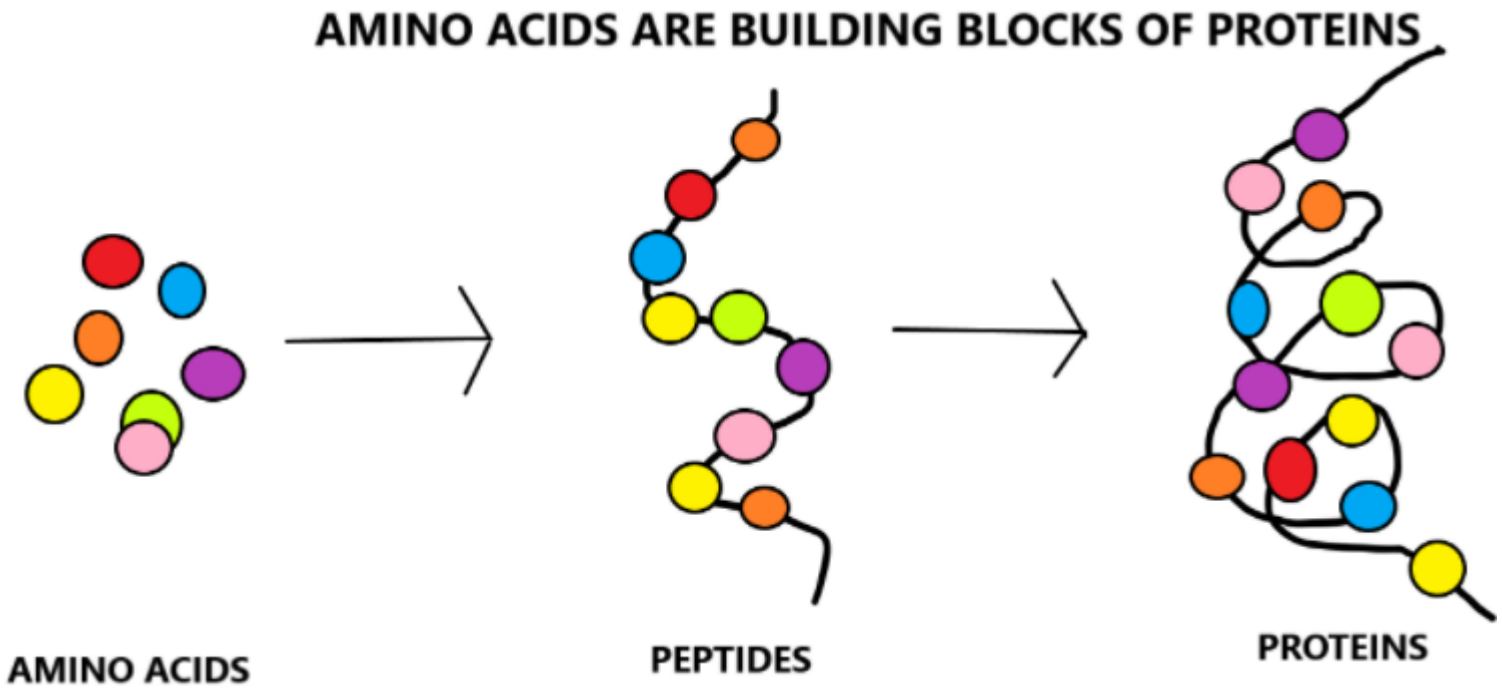


The diverse functions of proteins

Function	Example
Structural	Muscle fiber (myos**in**) Rhino horn (kerat**in**)
Hormonal	Insul**in**, lept**in**, hGH
Binding	Antibodies (γ-globul**in**), receptors, snake venom
Transport	Na+/K+ pump, hemoglob**in**, HDL
N storage	Gluten, ze**in,** alum**in**
Enzymes/ catalytic	Sucr**ase**, amyl**ase**, prote**ase**, nucle**ase**
Misc.	Antifreeze
Infectious	Mad cow disease (prion)

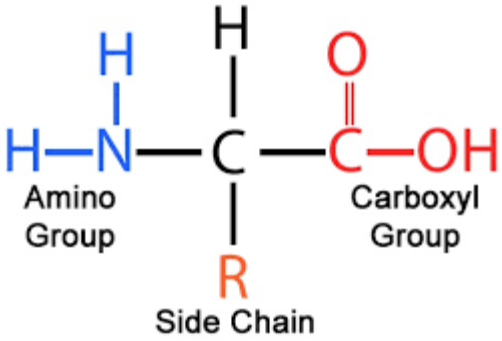
Central Dogma

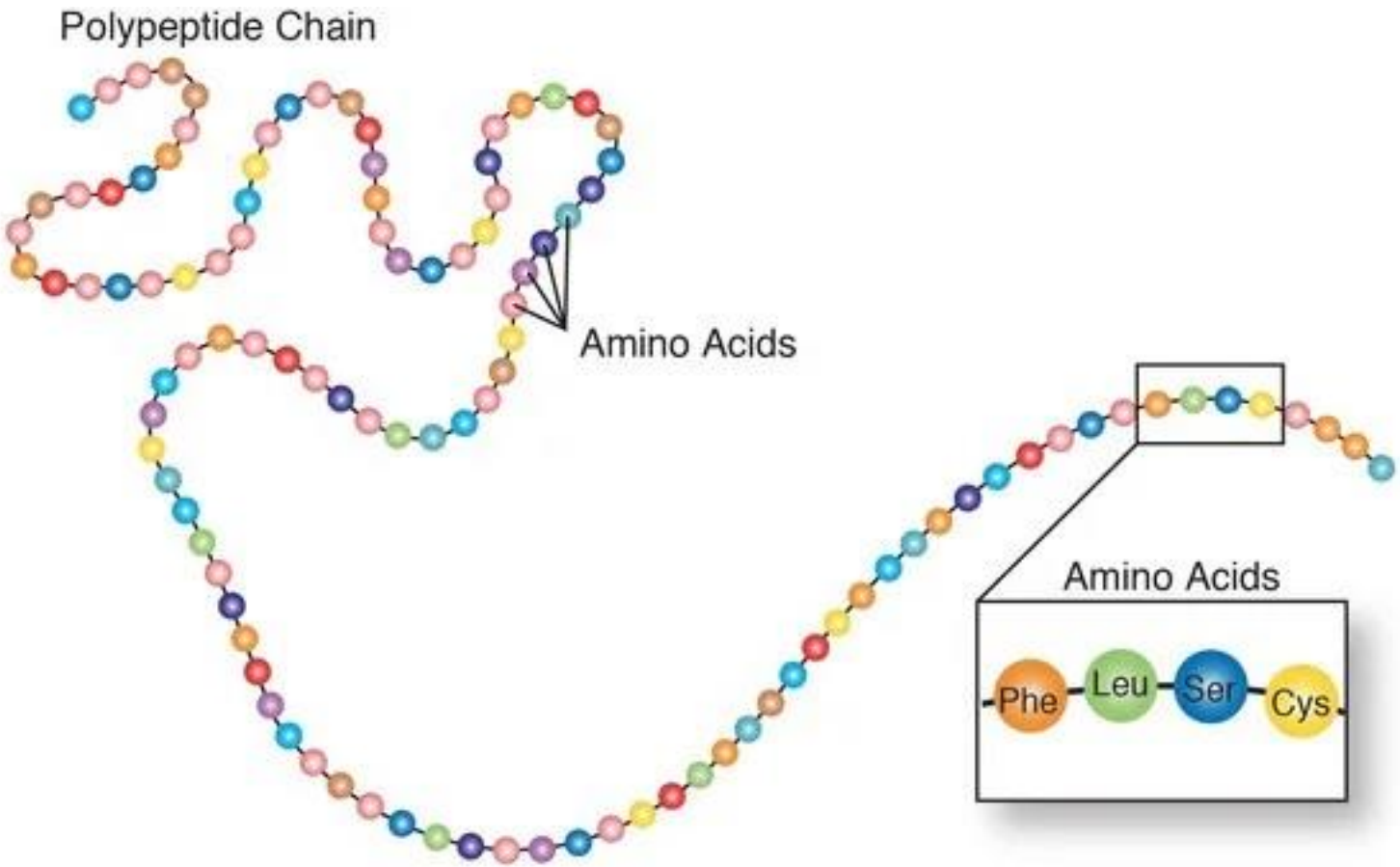




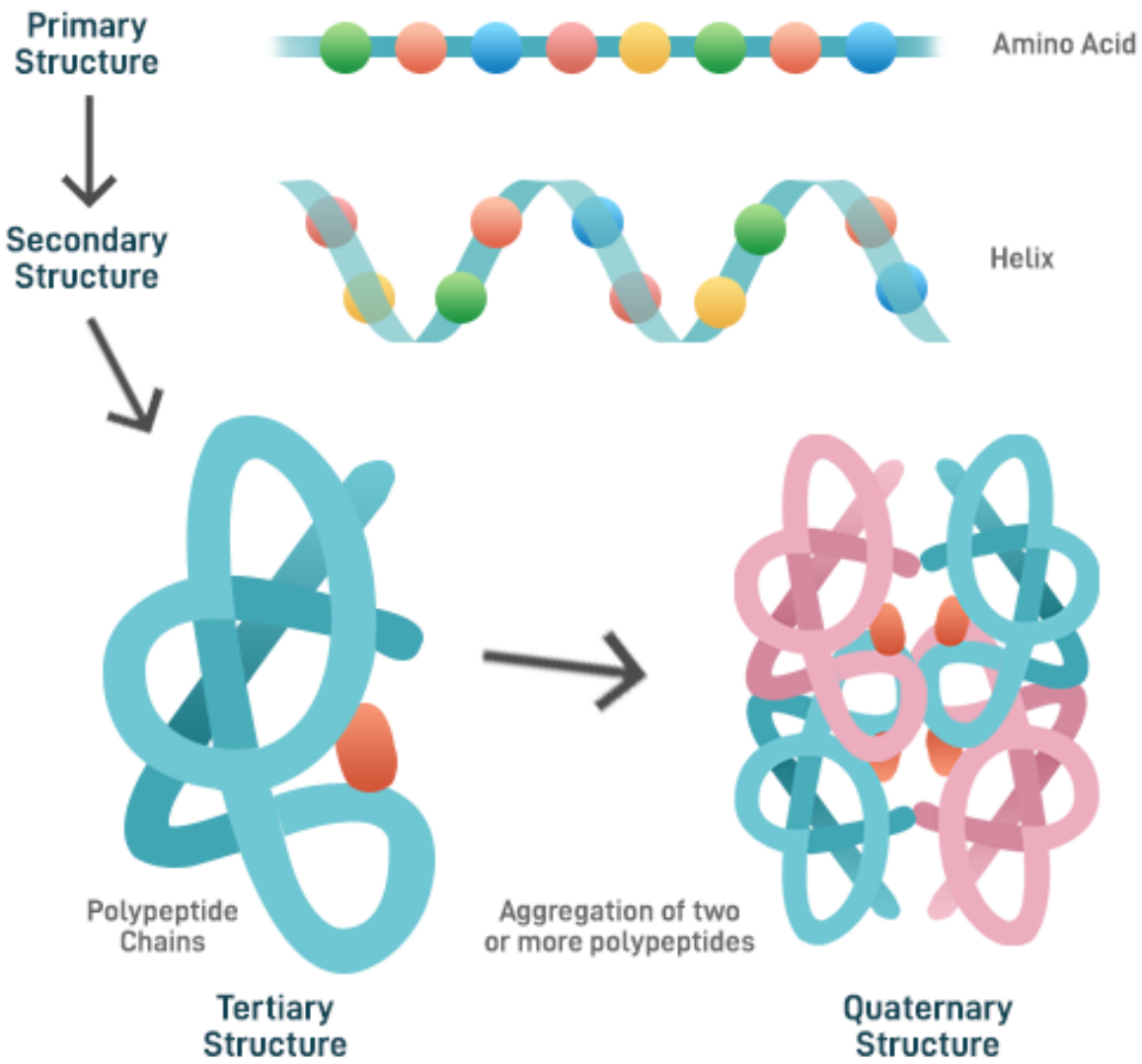
There are 20 naturally occurring amino acids

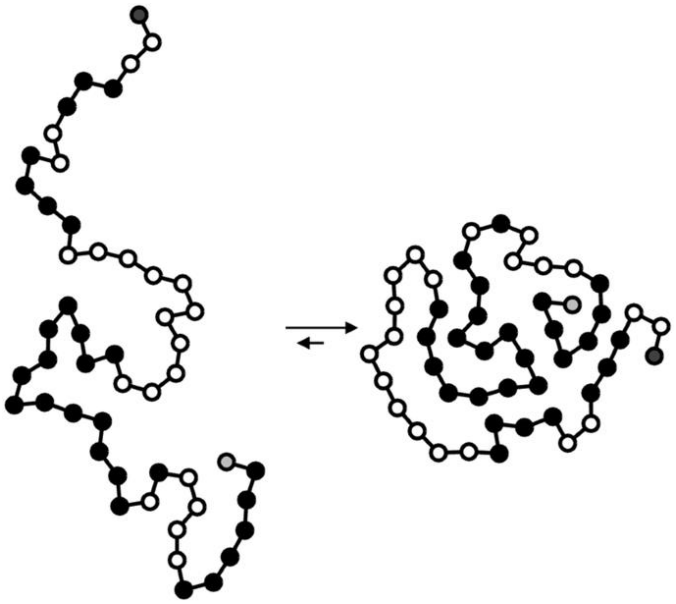
Amino-Acid	*3-Letter Name*	*Symbol*
Alanine	Ala	**A**
Arginine	Arg	**R**
Asparagine	Asn	**N**
Aspartic Acid	Asp	**D**
Asparagine or Aspartic Acid	Asx	**B**
Cysteine	Cys	**C**
Glutamine	Gln	**Q**
Glutamic Acid	Glu	**E**
Glutamine or Glutamic Acid	Glx	**Z**
Glycine	Gly	**G**
Histidine	His	**H**
Isoleucine	Ile	**I**
Leucine	Leu	**L**
Lysine	Lys	**K**
Methiodine	Met	**M**
Phenylalanine	Phe	**F**
Proline	Pro	**P**
Serine	Ser	**S**
Threonine	Thr	**T**
Tryptophan	Trp	**W**
Tyrosine	Tyr	**Y**
Valine	Val	**V**

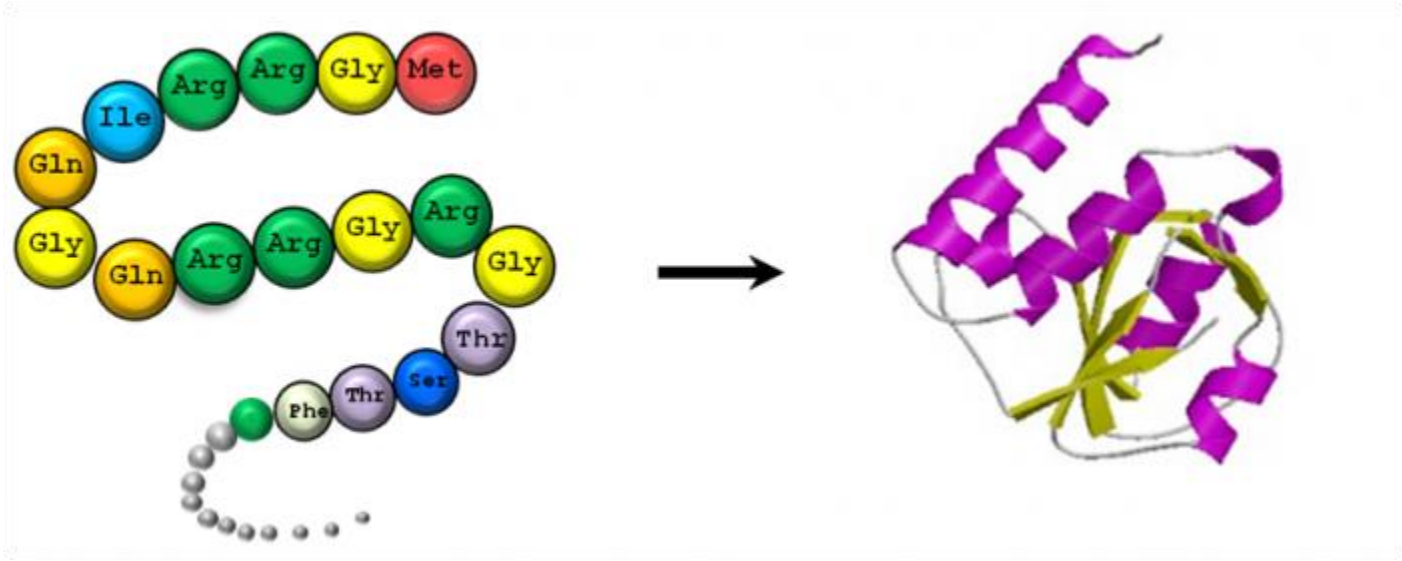



Polypeptide Chain
Amino Acids
Amino Acids
Phe
Leu
Ser
Cys

PROTEIN STRUCTURE






Met
Gly
Arg
Arg
Ile
Gln
Gly
Gln
Arg
Arg
Gly
Arg
Gly
Thr
Ser
Thr
Phe

Mutation in protein sequence will change the shape of the protein

PROTEIN DISORDERS
(Module 3)

Protein Mutations – (1) Sickle cell anemia
(2) Cystic Fibrosis
(3) Progeria

Protein Metabolic Disorder
(1) Diabetes Mellitus

Protein Aggregates – (1) Alzheimer's
(2) Schizophrenia
(3) Parkinson Disease

Infectious Protein – (1) Prion
(2) Kuru

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BENNETT UNIVERSITY
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Lecture 2

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Department of Biotechnology

MODULE 1

Introduction to Cell

The history of the cell theory

Hooke gives the cell its name

Ramón y Cajal studies nervous tissue

Microscopes are perfected

Malpighi develops microscopy

Brown defines the nucleus

17th Century | 19th Century | 20th Century

Leeuwenhoek observes microorganisms

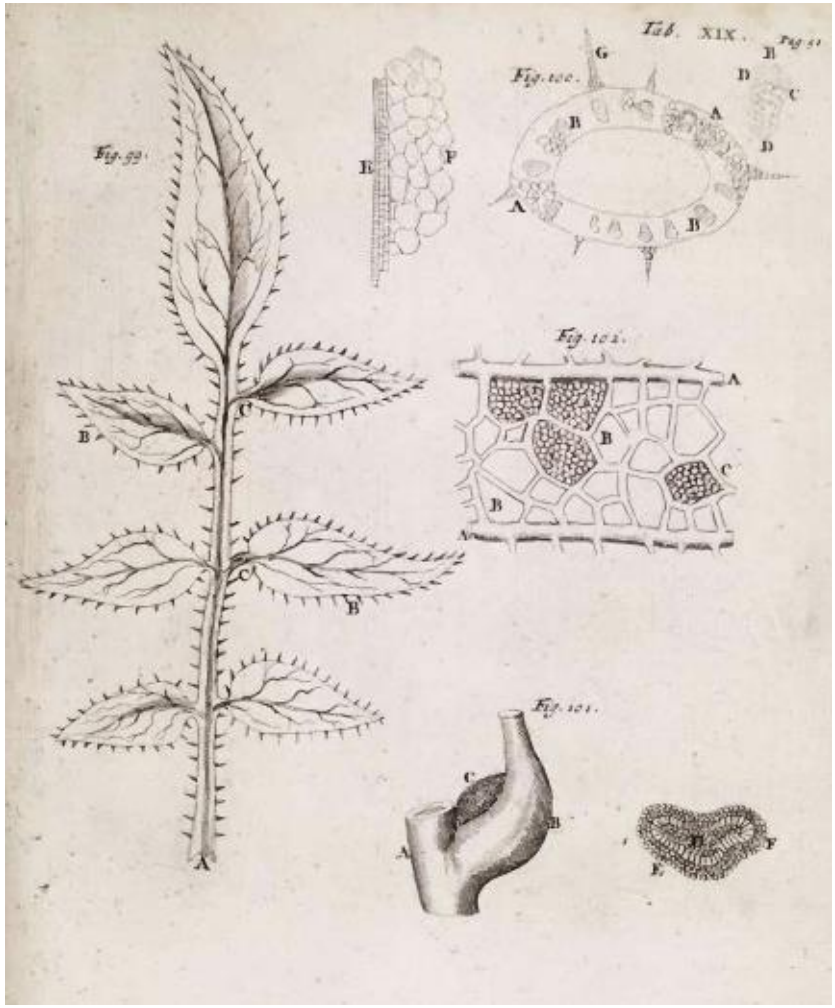
Schleiden, Schwann and Virchow develop the cell theory.

The history of the cell theory

Marcelo Malpighi

- An Italian doctor and naturalist, born in 1628.
- He is considered to be the father of microscopy, as he carried out many observations of tissues taken from living things using simple microscopes.
- He died in Rome in 1694.

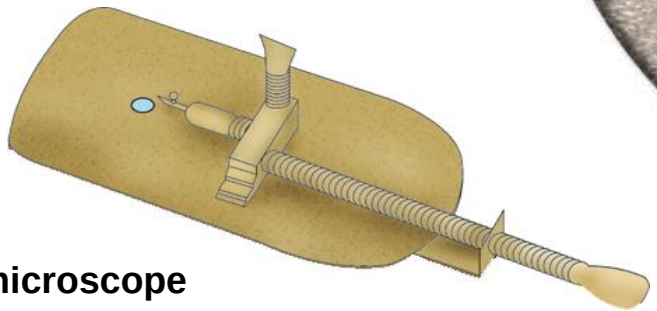
The history of the cell theory



- Malpighi made many drawings of his observations, like the ones in the engraving on the left.
- In this Malpighi drawing some of the observations he made of plant tissues can be seen.

Anton van Leeuwenhoek

- A Dutch scientist and tradesman, born in 1632. He died in 1723.
- He manufactured many microscopes and used them to observe microorganisms.

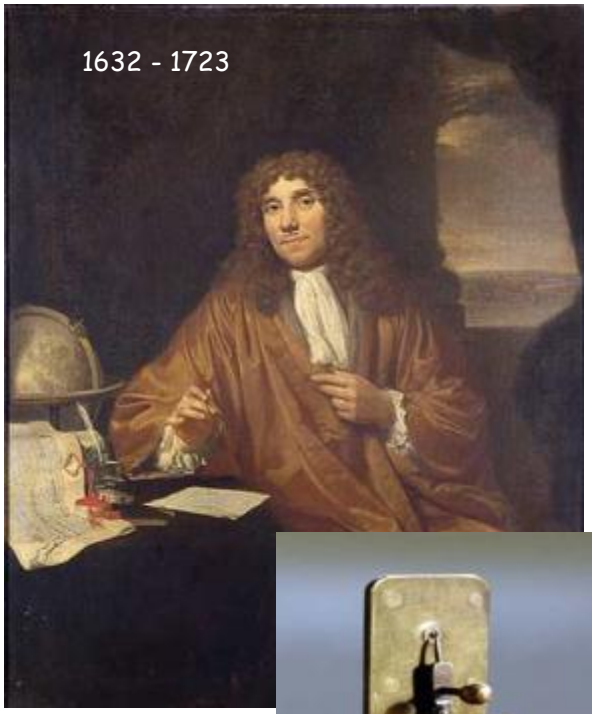


Leeuwenhoek's microscope

Anton van Leeuwenhoek: "Animalcules"

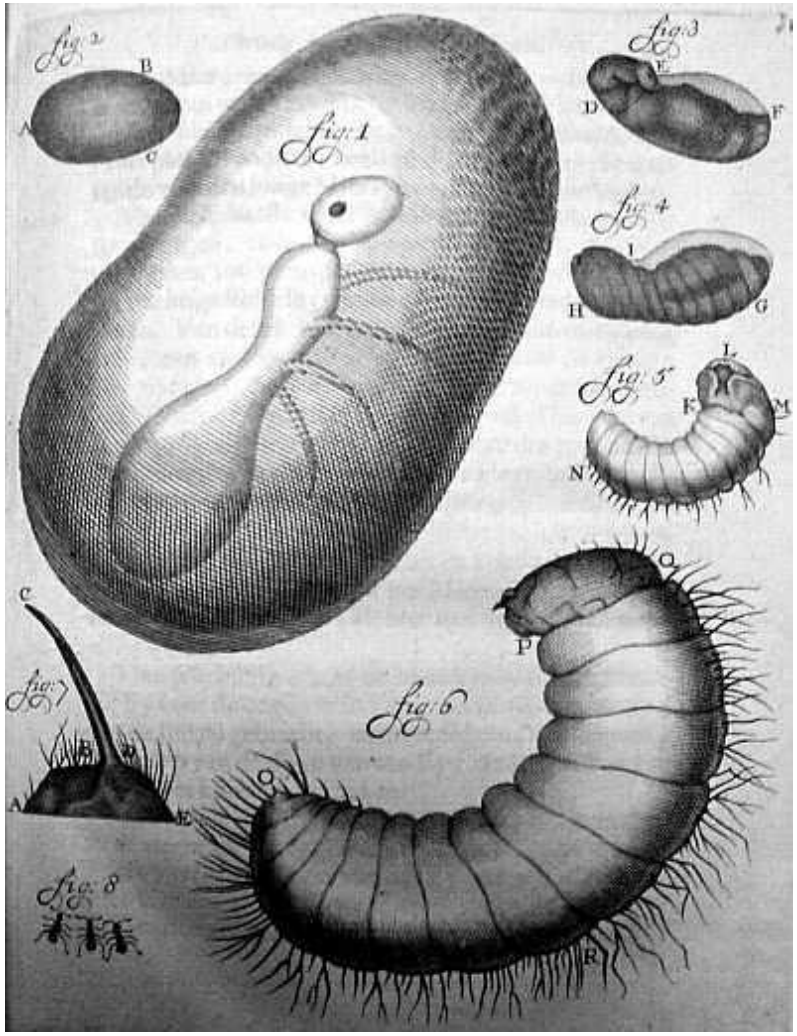
(Pronounced Lay-when-hook)

- As a tailor, used lenses to examine cloth. It was probably this that led to his interest in lens making.
- He assembled hundreds of microscopes, some of which magnified objects 270 times.
- As he looked at things with his microscopes, he discovered "micro" organisms - organisms so tiny that they were invisible to the naked eye.
- He called these tiny living organisms "animalcules". He first described bacteria and the protozoans.



Images: Leeuwenhoek portrait 1680, Jan Verkolje (I);. Replica of Leeuwenhoek microscope, Jacopo Werther; Man with scope, source unknown

The history of the cell theory



- The engraving on the left shows some drawings of the microorganisms that Leeuwenhoek observed using microscopes he made himself.

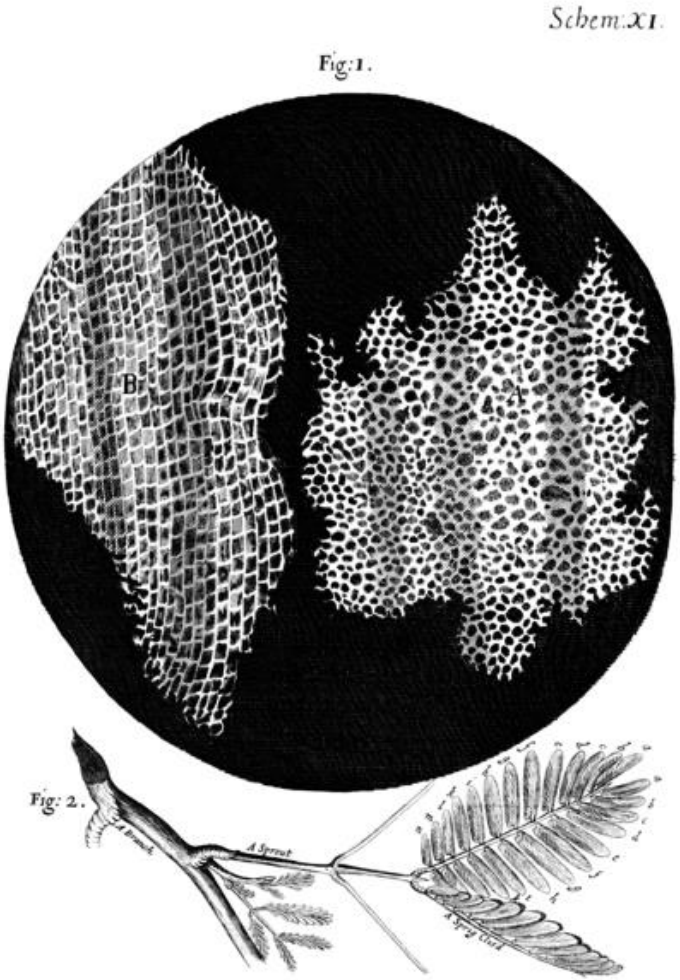
The history of the cell theory

Robert Hooke

- An English scientist, born in 1635. He died in 1703.
- In 1665, he studied a sheet of cork with a simple microscope like the one you see in the picture below.

Hooke's microscope

The history of the cell theory



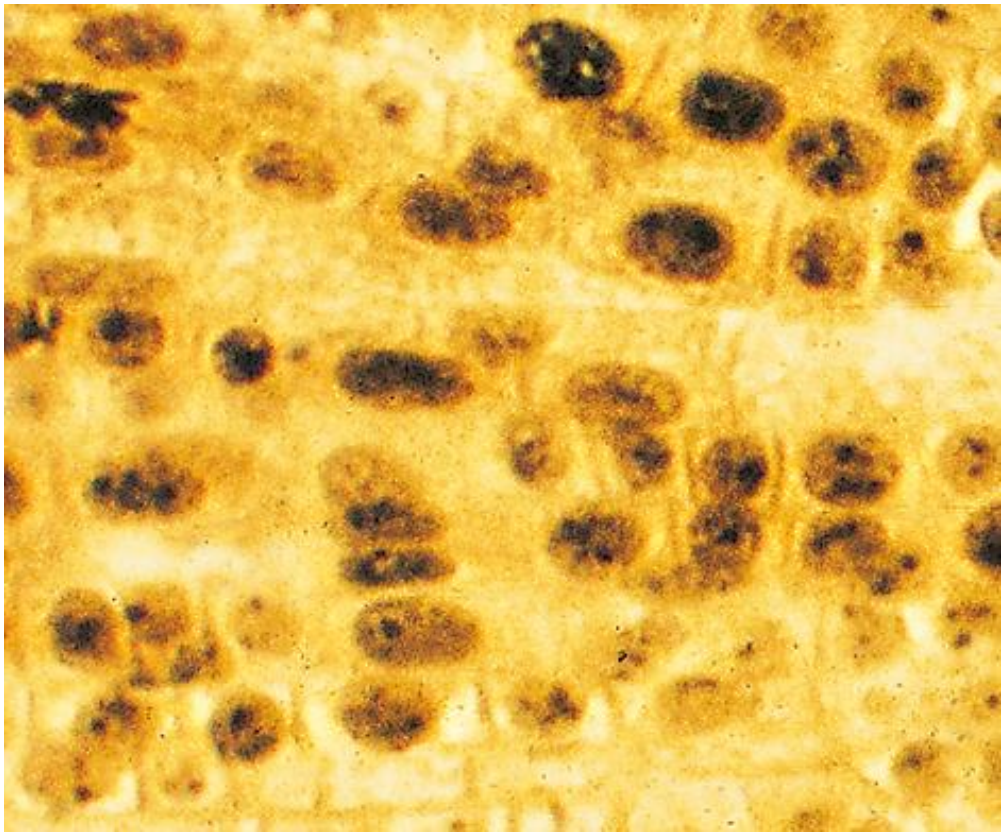
- The engraving on the left shows one of Hooke's drawings of his observations of a sheet of cork.
- When he saw the small, honeycomb-like compartments on the sheet, Hooke called them "cells" (from the Latin word for small room).

The history of the cell theory

Robert Brown

- A Scottish botanist, born in 1773. He died in 1858.
- Thanks to developments in microscopes, he was able to observe the inside of plant cells in more detail.

The history of the cell theory



- Brown discovered that there was a structure in plant cells: he called it the “nucleus.”
- Scientists would later discover that this structure is present in all eukaryotic cells.

The history of the cell theory

Matthias Schleiden

- A German botanist (1804-1881)

Theodor Schwann

- A German physiologist and anatomist (1810-1882)

Rudolf Virchow

- A German doctor (1821-1902)

The history of the cell theory

- In 1937, Schleiden came to the conclusion that the cell is the unit of structure in plants. In other words, that all plants are made of cells.

- A year later, Schwann concluded that this is also true for animals. In other words, that all animals are also made of cells.

Based on both scientists' findings, the first principle of the cell theory was developed:

The cell is the unit of structure of living organisms.

The history of the cell theory

- Virchow studied the physiology of cells and concluded that every cell carried out the three vital functions.

His work led to the completion of the other two principles of the cell theory:

1. The cell is the unit of function of living organisms.

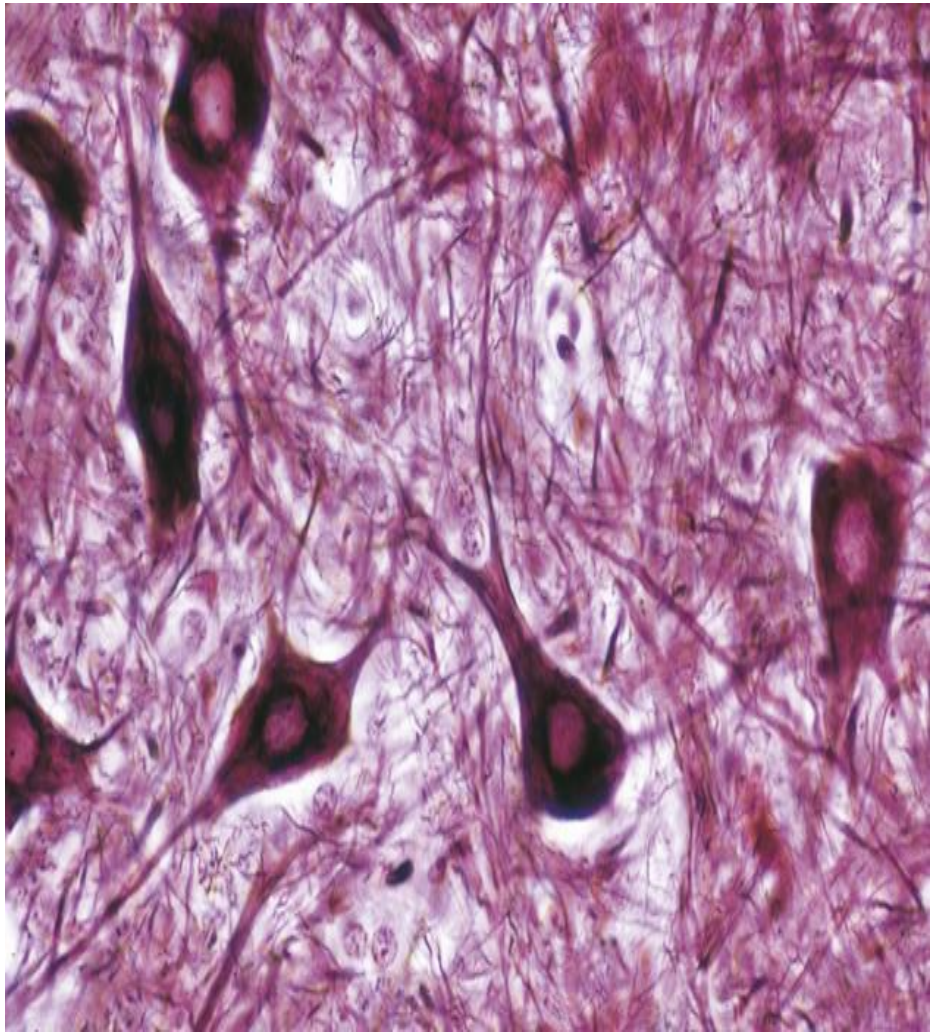
2. All cells come from preexisting cells.

The history of the cell theory

Santiago Ramón y Cajal

- A Spanish doctor, born in 1852. He died in 1934.
- He proved that the cell theory also applied to nervous tissue. Previously it was thought that nervous tissue was not made up of cells.

The history of the cell theory



- Ramón y Cajal studied tissue samples obtained from embryos and infants using a revolutionary method of staining with silver salts, developed by the Italian scientist Golgi.
- With this method, he was able to observe that this tissue, which appeared to be fibrous and not cellular, is, in fact, made up of cells (neurons).
- In recognition of his work, he was awarded the Nobel Prize, together with Golgi.

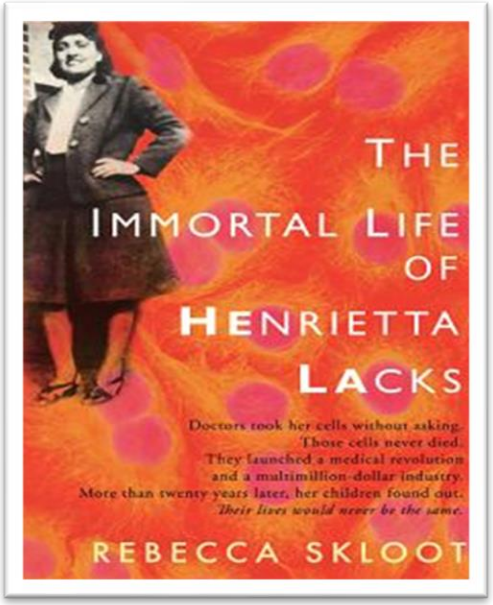
Everyday Cell Biology

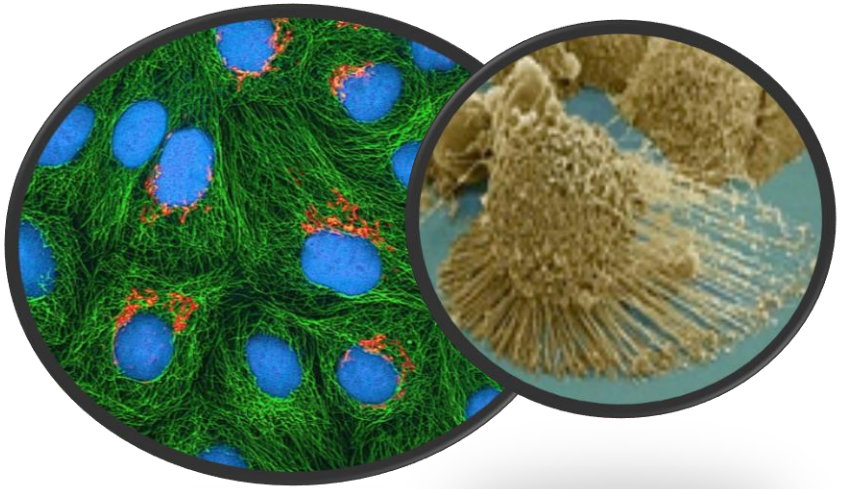
Who was Henrietta Lacks and why were her cells so important to medical science?

Let's explore the amazing story of Henrietta Lacks and her immortal cells.

Q: *What does the Henrietta Lacks story have to do with cell biology?*

https://www.youtube.com/watch?v=T3kR2dMCfOM





Images: Book, "The Immortal Life of Henrietta Lacks by Rebecca Skloot; Apoptotic HeLa cell, Wiki; Fluorescence image of cultured HeLa cells, Wiki

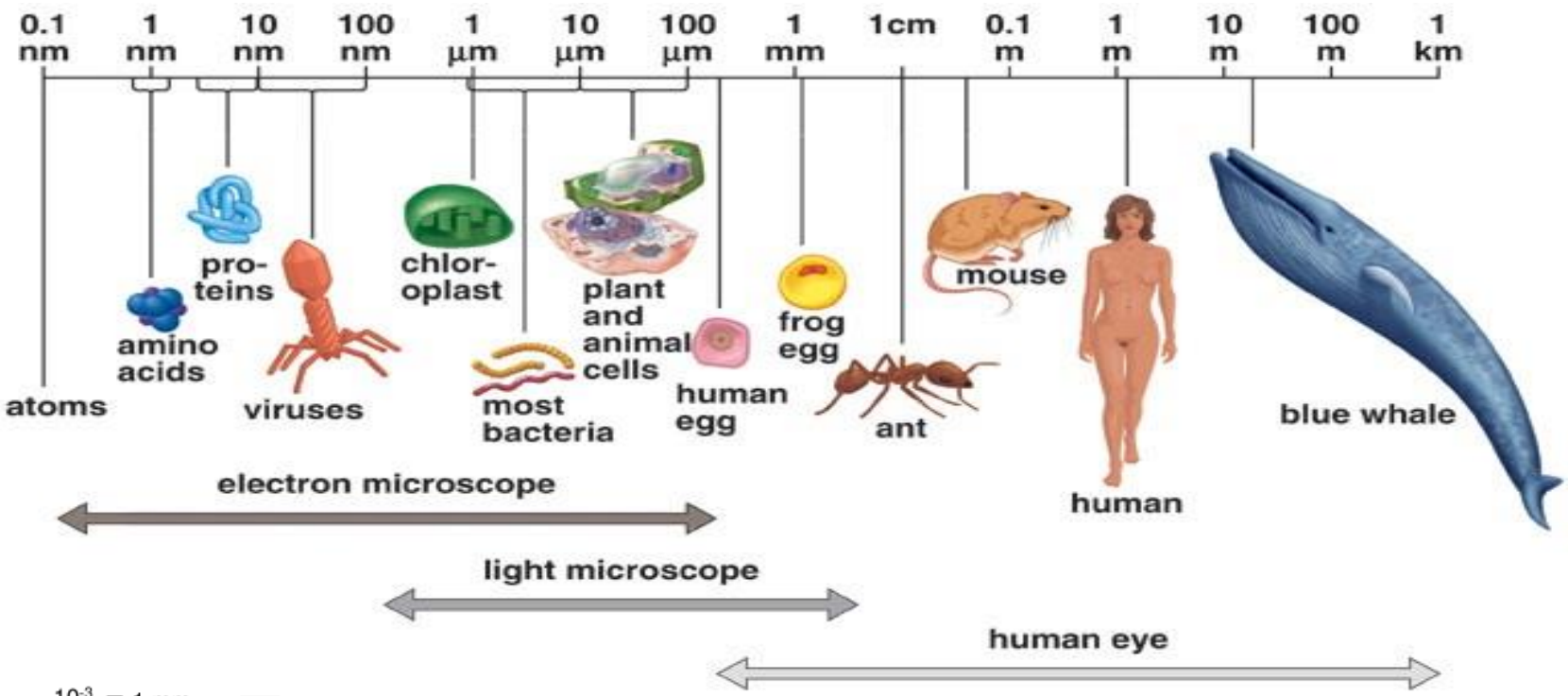
The Cellular Level of Organization

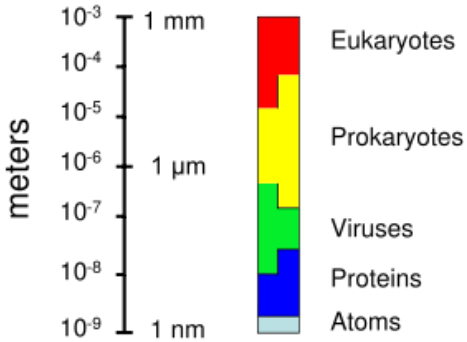
- Living things are constructed of **cells**.
- Living things may be **unicellular** or **multicellular**.
- Cell structure is diverse but all cells share common characteristics.
- Cells are **small** so they can exchange materials with their surroundings.
  - Surface area relative to the volume decreases as **size** of cell increases.
  - This limits the size of cells.
- **Cell Theory states:**

1. All organisms are composed of one or more cells.
2. Cells are the basic unit of structure and function in organisms.
3. All cells come only from other cells.

From the Virtual Cell Biology Classroom on ScienceProfOnline.com

Size of Living Things





1 m = 100 cm = 1,000mm = 1,000,000 μm = 1,000,000,000nm

1mm = 1000 μm = 1000000nm

1 μm = 1000nm

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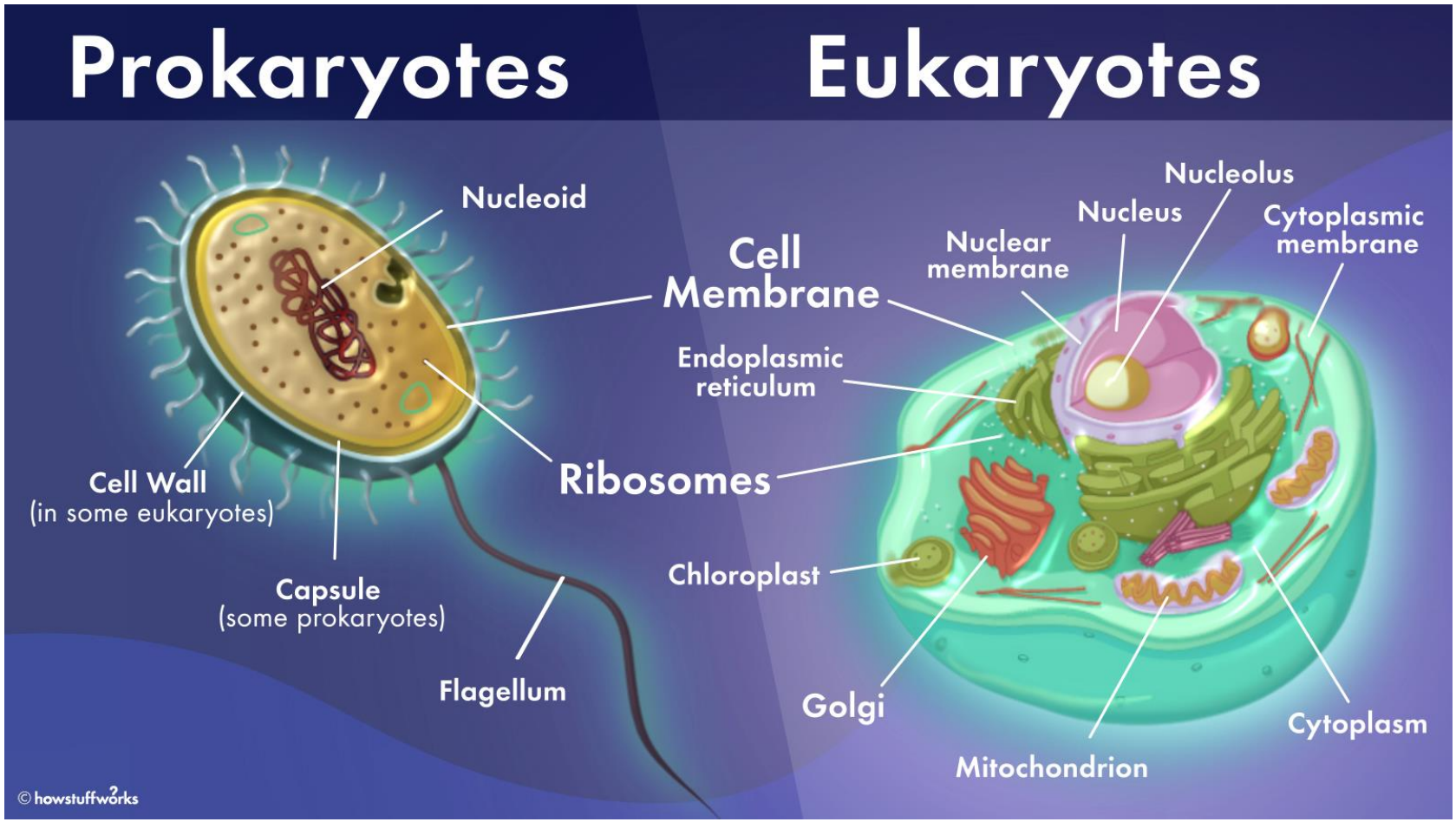
Only TWO Basic Types of Cells

All living organisms can be grouped into two types based on their fundamental cell structure. They are prokaryotes and eukaryotes, and the cells they possess are called prokaryotic cells and eukaryotic cells.



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Images: Prokaryotic Cell Diagram & Eukaryotic Cell Diagram, M. Ruiz

Prokaryotes…The "studio apartment" of cells.

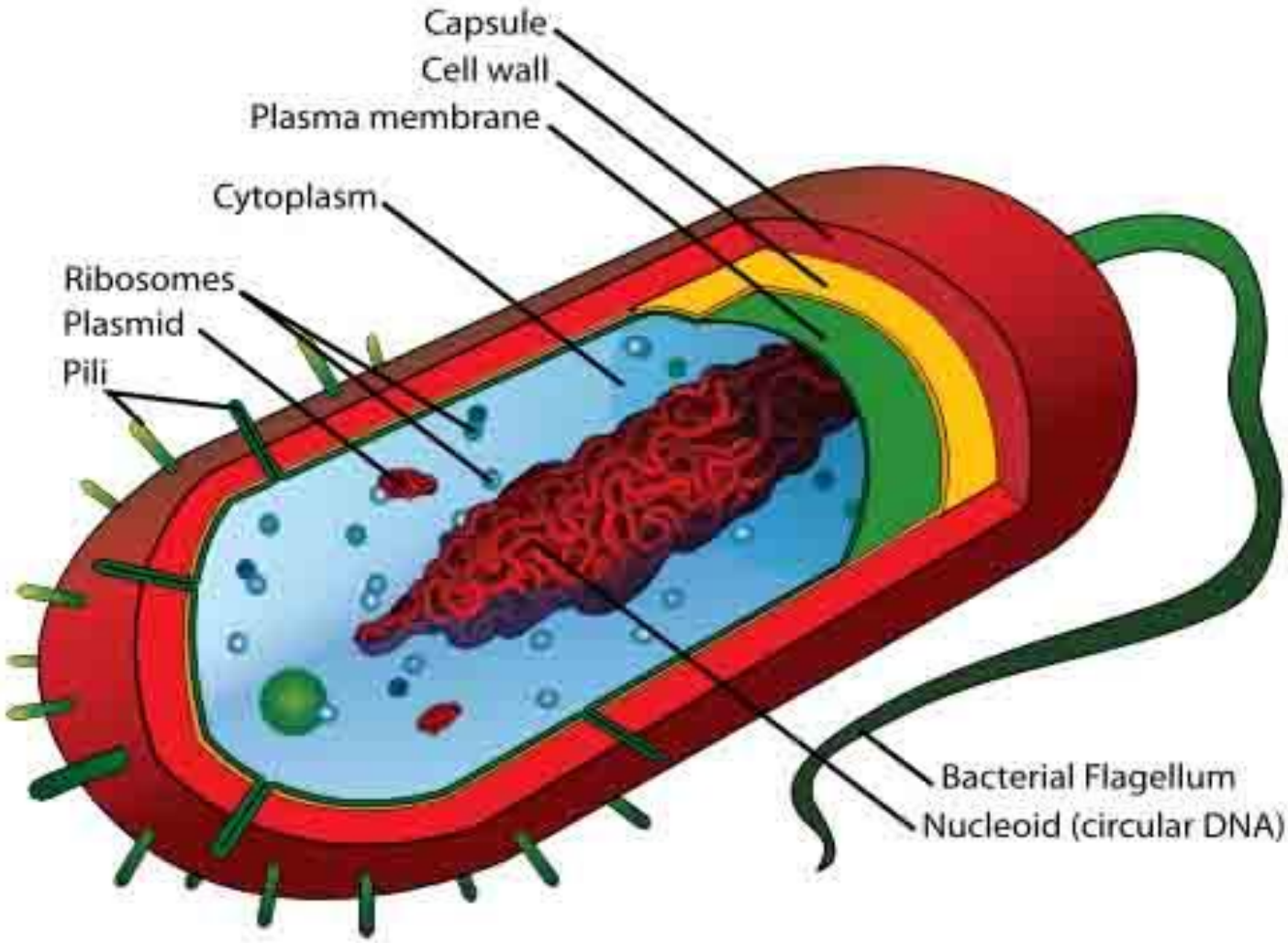

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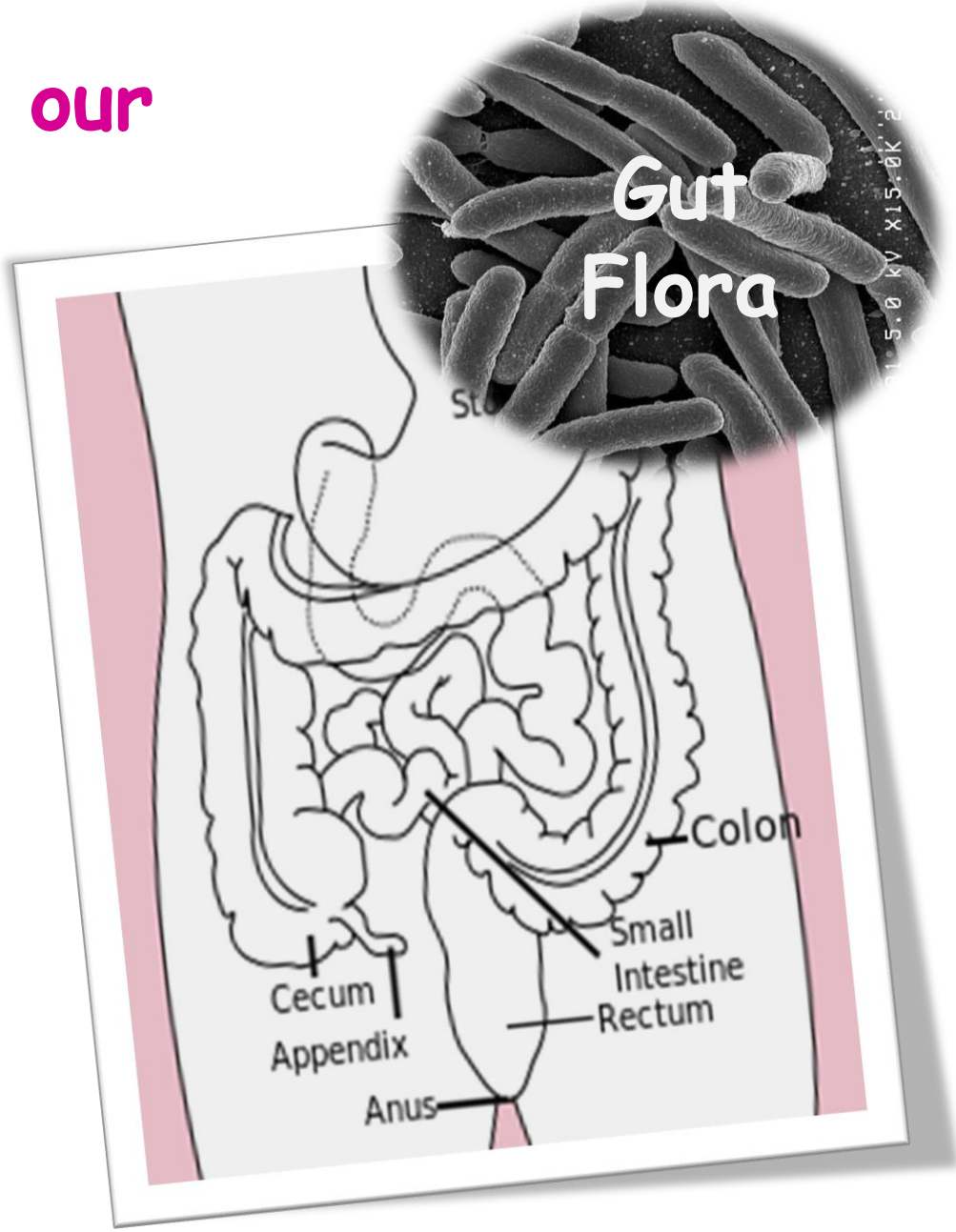
Image: Prokaryotic cell diagram, M. Ruiz,

Prokaryotes can be our friends…

- Human body has ~ 100 trillion microbes in intestines (10x more than the total number of human cells in the body).
- Bacteria that live on and in us without usually causing harm are called **normal flora**.
- Bacteria = ~ 60% of the dry mass of poo.
- Relationship between gut flora and humans **mutualistic** … win/win.
- Gut microbes perform many useful functions:
  - preventing growth of harmful, pathogenic bacteria
  - producing vitamins for host (such as biotin and vitamin K)
  - producing hormones to direct host to store fats
  - keeping our immune system on its toes



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Images: *E. coli*, Rocky Mountain Laboratories, NIAID, NIH; Human Gastrointestinal Tract, Wiki

Prokaryotes can be our foes…

Clostridium

- Members of this genus have a couple of bacterial weapons that make them particularly tough pathogens.
- Vegetative cells are **obligate anaerobes** killed by exposure to O2, but their endospores are able to survive long periods of exposure to air.
- Known to produce a variety of toxins, some of which are fatal.

  - *Clostridium tetani* = agent of tetanus

  - *C. botulinum* = agent of botulism

  - *C. perfringens* = one of the agents of gas gangrene

  - *C. difficile* = part of natural intestinal flora, but resistant strains can proliferate and cause pseudomembranous colitis.

Images: Man with Tetanus, Sir Charles Bell; Clostridium botulinum, PHIL #2107; Wet Gangrene, Wiki

Prokaryotes

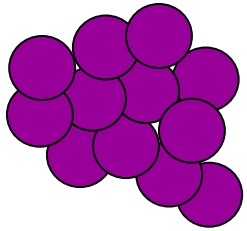
Bacterial "cousins"… one friend, one foe…

Staphylococcus

GRAM-POSITIVE

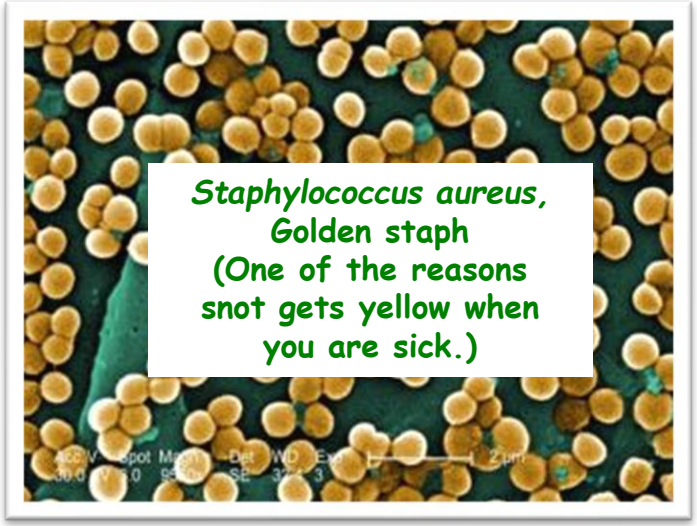
Facultative anaerobe

coccus-shaped



Coccus-shaped bacteria, which divides in a way that results in grape-like clusters.

- ***Staphylococcus aureus*** (golden staph), most common cause of staph infections.
- Approximately 20–30% of general population "Staph carriers."
- *S. aureus* can cause illnesses ranging from minor skin infections to life-threatening diseases, such as meningitis, toxic shock syndrome (TSS) & septicemia.
- One of the four most common causes of **nosocomial infections**, often causing postsurgical wound infections.
- ***S. epidermidis*** is normal flora which inhabits the skin of healthy humans.



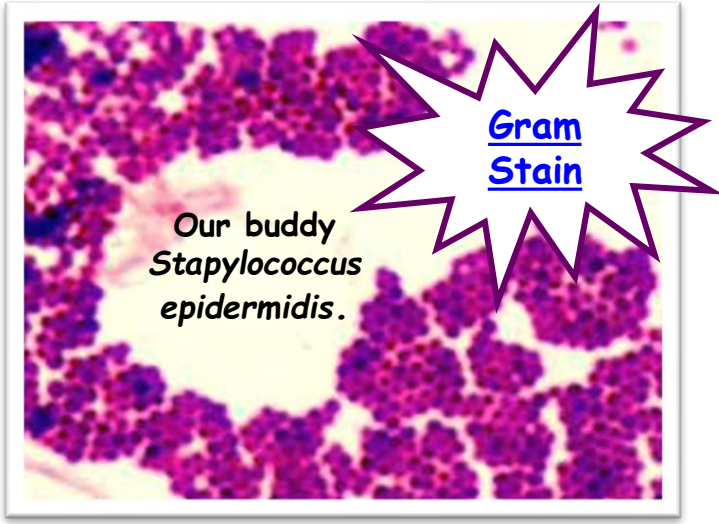
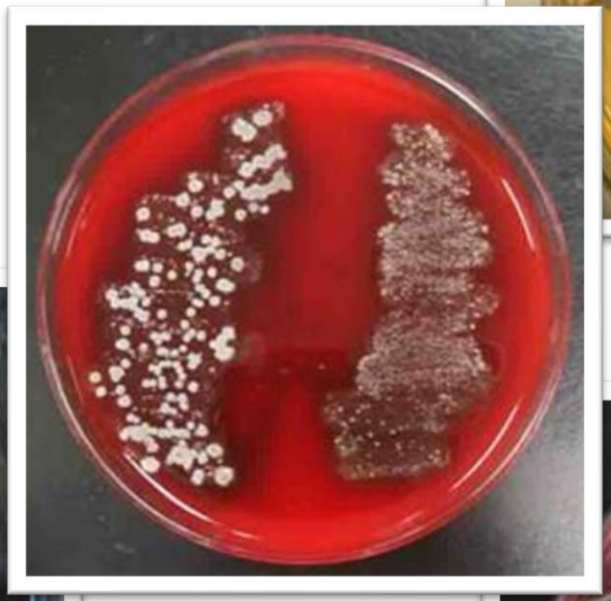
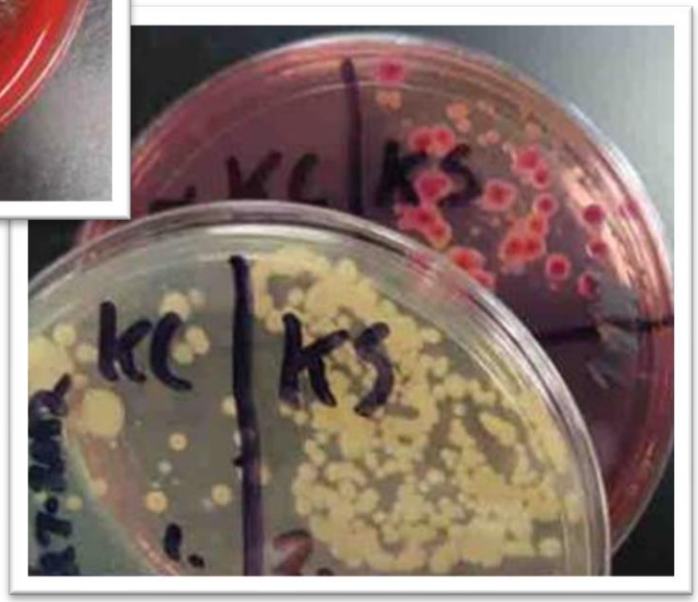


Image: Mannitol salt plates, T. Port; *S. aureus*, Janice Haney Carr , PHIL #10046; Gram stain *Staph*, T. Port

Prokaryotes

Bacteria
are
EVERYWHERE!





Images: Various types of bacterial growth media inoculated with different types of samples, T. Port

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Eukaryotes…The "mansion" of cells.

EUKARYOTIC CELL

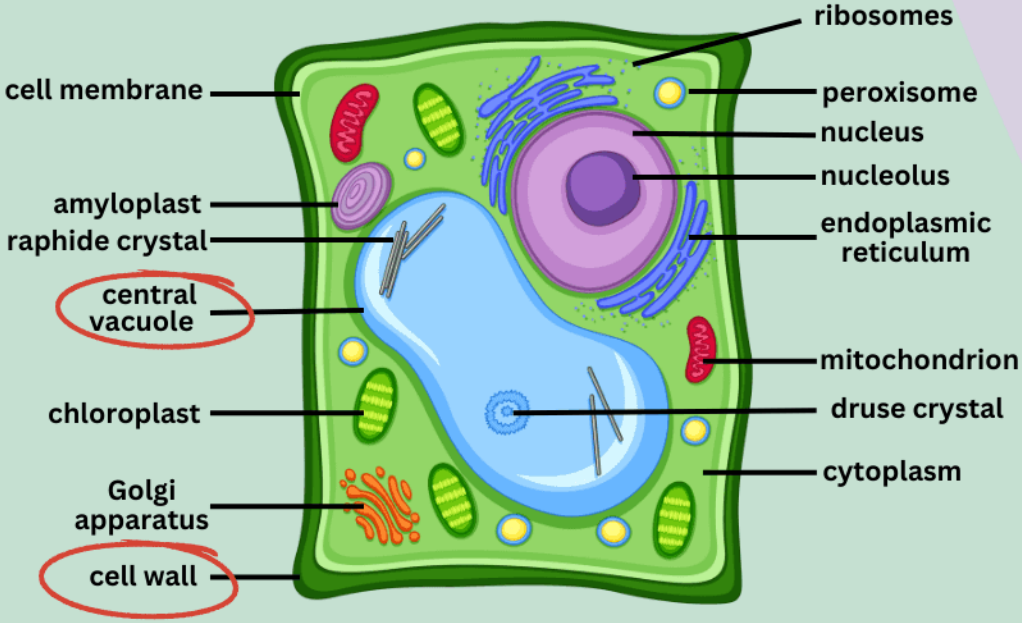
- Large & complex cells
- It has a clearly defined Nucleus, Nuclear membrane, Mitochondria, Golgi apparatus, Endoplasmic Reticulum and Lysosomes.
- A eukaryotic cell is a cell that has a membrane-bound nucleus and other membrane-bound compartments or sacs, called **organelles**, which have specialized functions.
- Size ranges from 10mm – 500 mm.
- There are four types of eukaryotes: **Animals, Plants, Fungi, and Protists.**

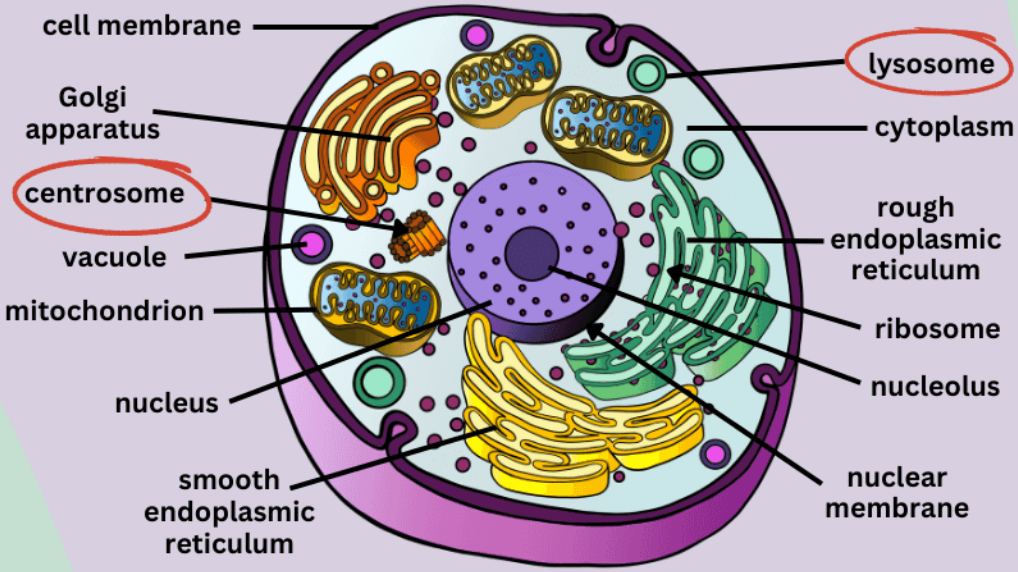
- **Animals-** this is the most familiar group of eukaryotes. Animals have cells with cell membranes, but no rigid cell walls like those of plants, fungi and some protists. Ex; humans, house cats, arthropods, whales and fish
- **Plants-** Plant cells have cellulose-bearing cell walls and chloroplasts. Plants use chloroplasts to turn sunlight into fuel to produce oxygen for their cells. Plants produce more oxygen than they use, adding oxygen to the atmosphere.
- **Fungi-** fungi have cell walls like plants, but their cell walls contain a protein called chitin, which is found in animals like beetles but not in plants. Ex; yeasts, mushrooms and truffles.
- **Protists-** Protists are one-celled eukaryotes. Examples of protists include amoebas, paramecium and kelp. All algae, except blue-green algae (now known as cyanobacteria) are eukaryotes.

PLANT CELL VS ANIMAL CELL

- Cell wall (rigid shape)
- Large central vacuole
- Chloroplasts (autotroph)
- Lack centrosomes
- Lack lysosomes

Plant Cell





Animal Cell

- No cell wall (irregular shape)
- Numerous small vacuoles
- No chloroplasts (heterotroph)
- Centrioles / centrosomes
- Lysosomes

sciencenotes.org

Eukaryotic vs. Prokaryotic Cells

Characteristics	Eukaryotic Cells	Prokaryotic Cells
Definition	Any cell that contains a clearly defined nucleus and membrane bound organelles	Any unicellular organism that does not contain a membrane bound nucleus or organelles
Examples	Animal, plant, fungi, and protist cells	Bacteria and Archaea
Nucleus	Present (membrane bound)	Absent (nucleoid region)
Cell Size	Large (10-100 micrometers)	Small (less than a micrometer to 5 micrometers)
DNA Replication	Highly regulated with selective origins and sequences	Replicates entire genome at once
Organism Type	Usually multicellular	Unicellular
Chromosomes	More than one	One long single loop of DNA and plasmids
Ribosomes	Large	Small
Growth Rate/Generation Time	Slower	Faster
Organelles	Present	Absent
Ability to Store Hereditary Information	All eukaryotes have this ability	All prokaryotes have this ability
Cell Wall	Simple: Present in plants and fungi	Complex: Present in all prokaryotes
Plasma Membrane	Present	Present
Cytoplasm	Present	Present

Open Elective Subject

EBTY183L Biological Machines

(L-T-P = 3-0-0)

BENNETT UNIVERSITY
TIMES OF INDIA GROUP

Lecture 3

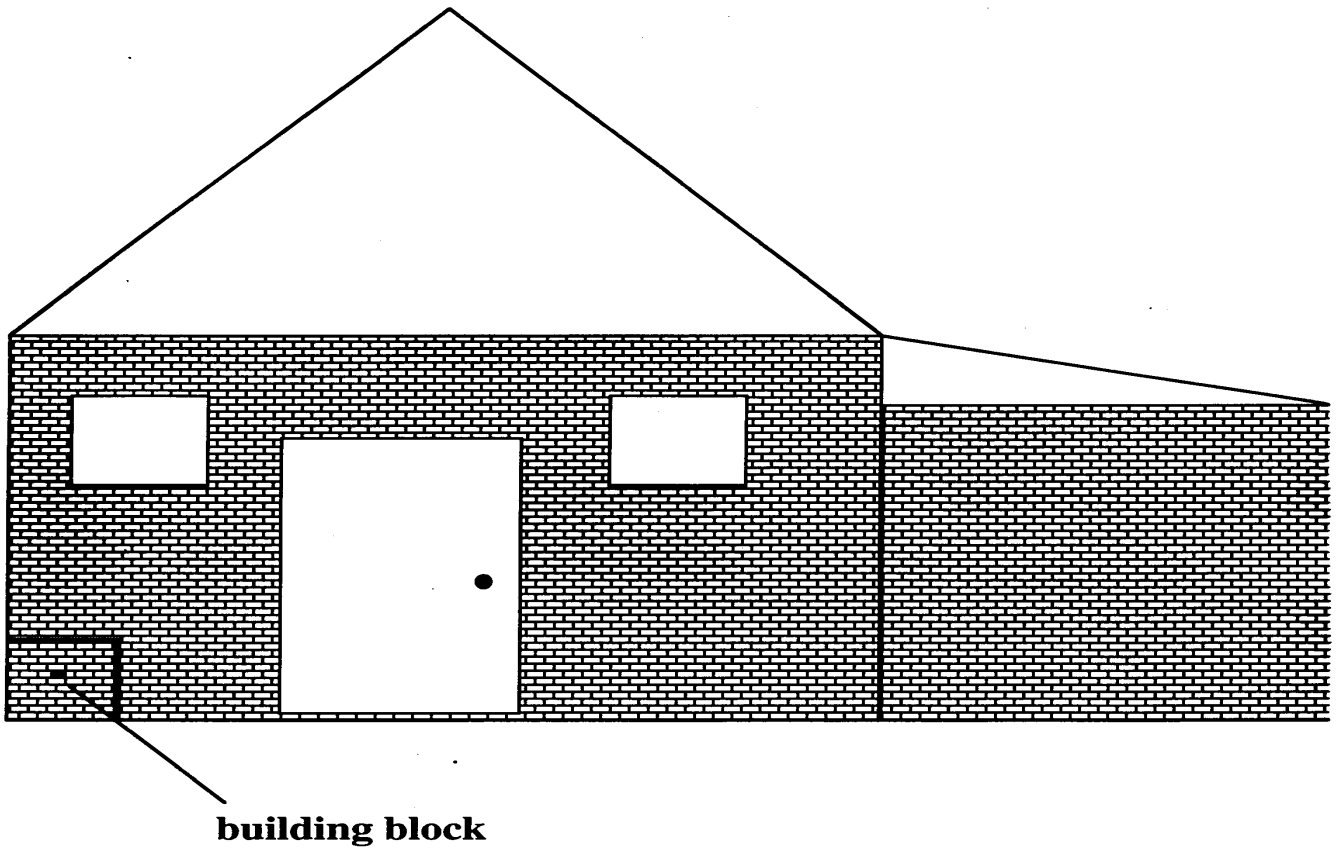
Prof. N.Latha

Head, Department of Biotechnology

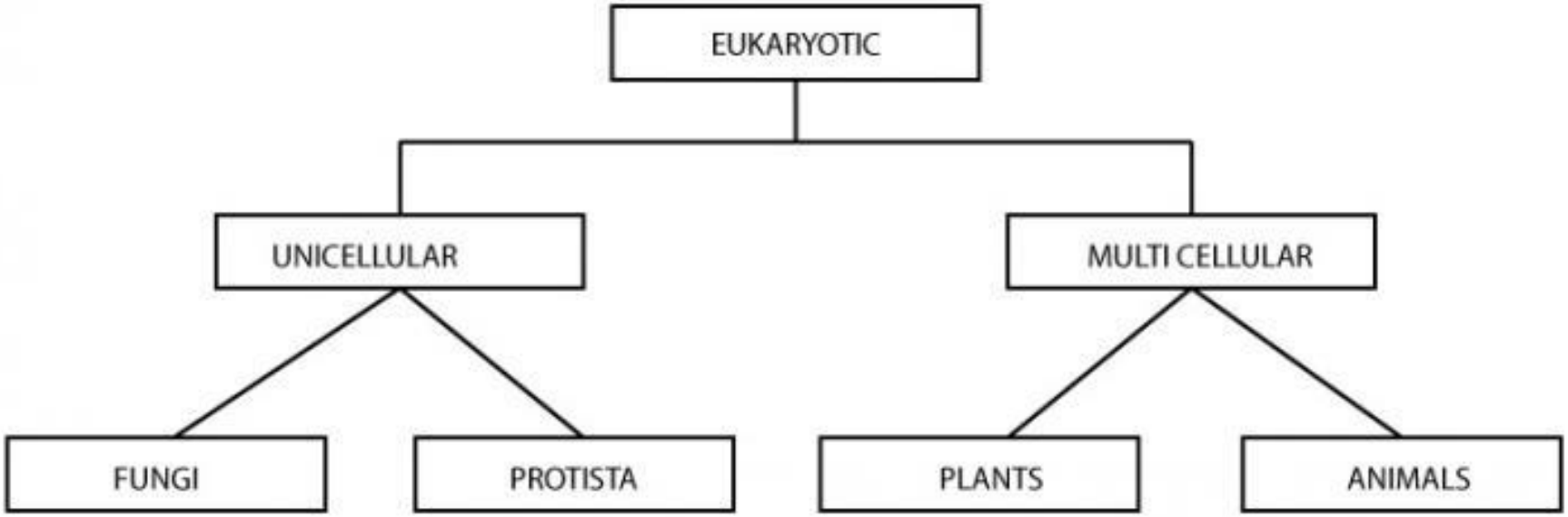
THE UNIVERSE INSIDE OUR CELLS

- Zoom into your own body to see the different cells that make up your heart, brain and bones.
- These trillions building block of cells are communicating with each other every moment of our lives.
- As the house is made by BRICKS…so are we made of cells

Consider how a house is built from bricks



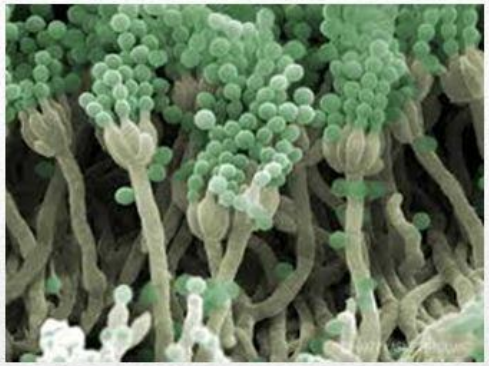
Eukaryotic Cell



UNICELLULAR EUKARYOTES - Fungi

FUNGI

- Include both unicellular and multicellular organisms
- Examples: bread mould, mushrooms, athlete's foot
- Yeast is a unicellular fungus that feeds on other organisms

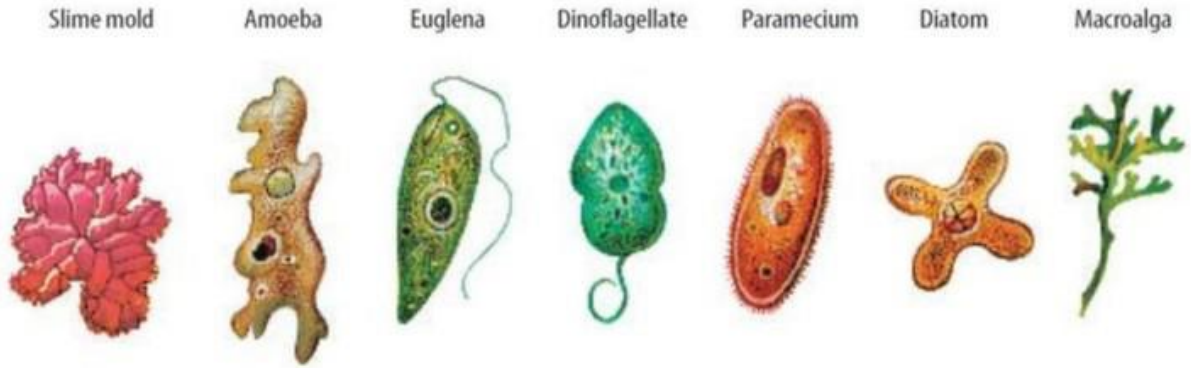


Bread Mold

Yeast budding

UNICELLULAR EUKARYOTES - Protista

Protists are simple eukaryotic organisms that are neither plants nor animals or fungi. Protists are unicellular in nature but can also be found as a colony of cells. Most protists live in water, damp terrestrial environments or even as parasites.

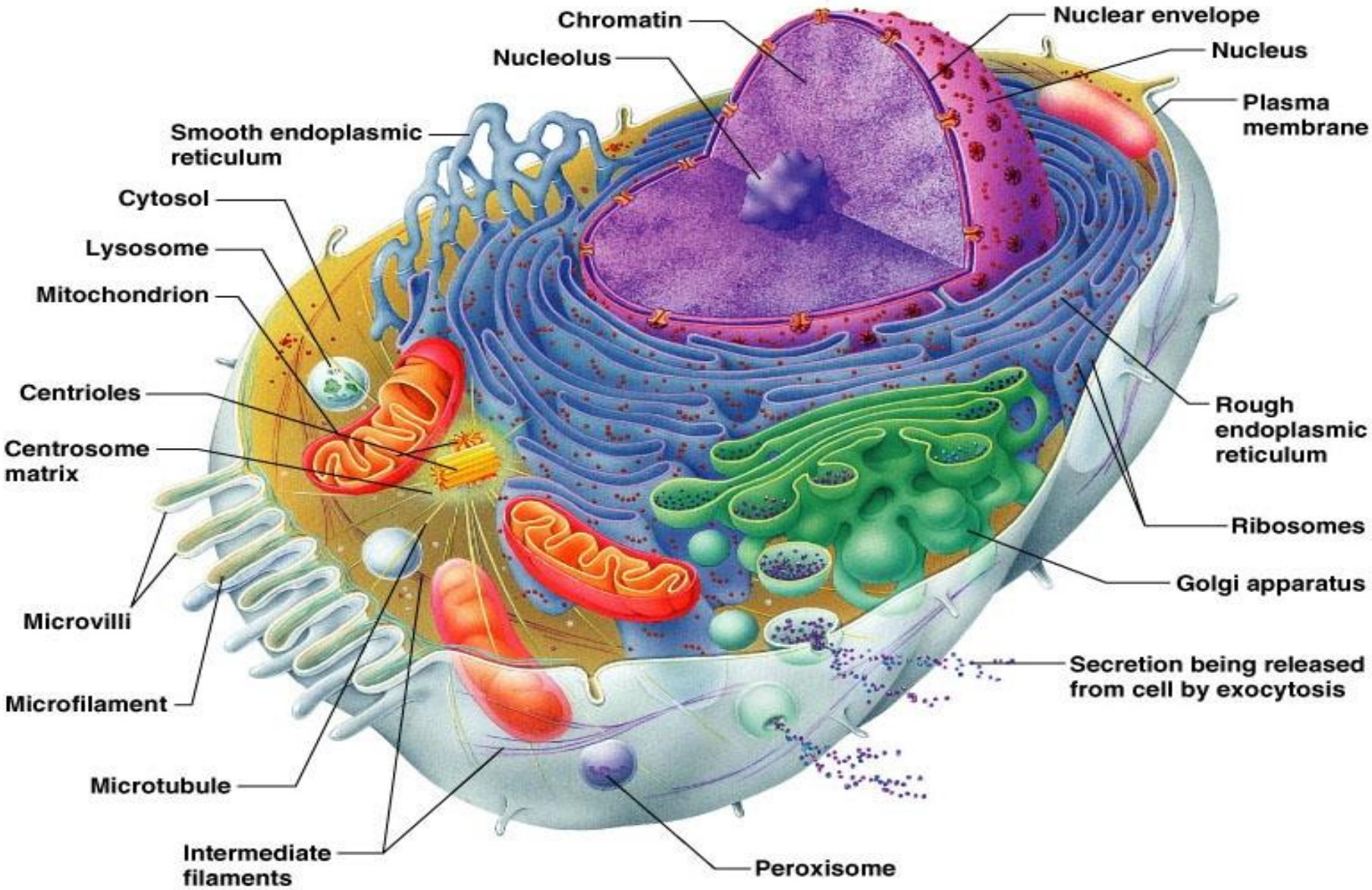


Kingdom: PROTISTA

Remember, protists are

EUKARYOTIC **UNICELLULAR**

ANIMAL CELL



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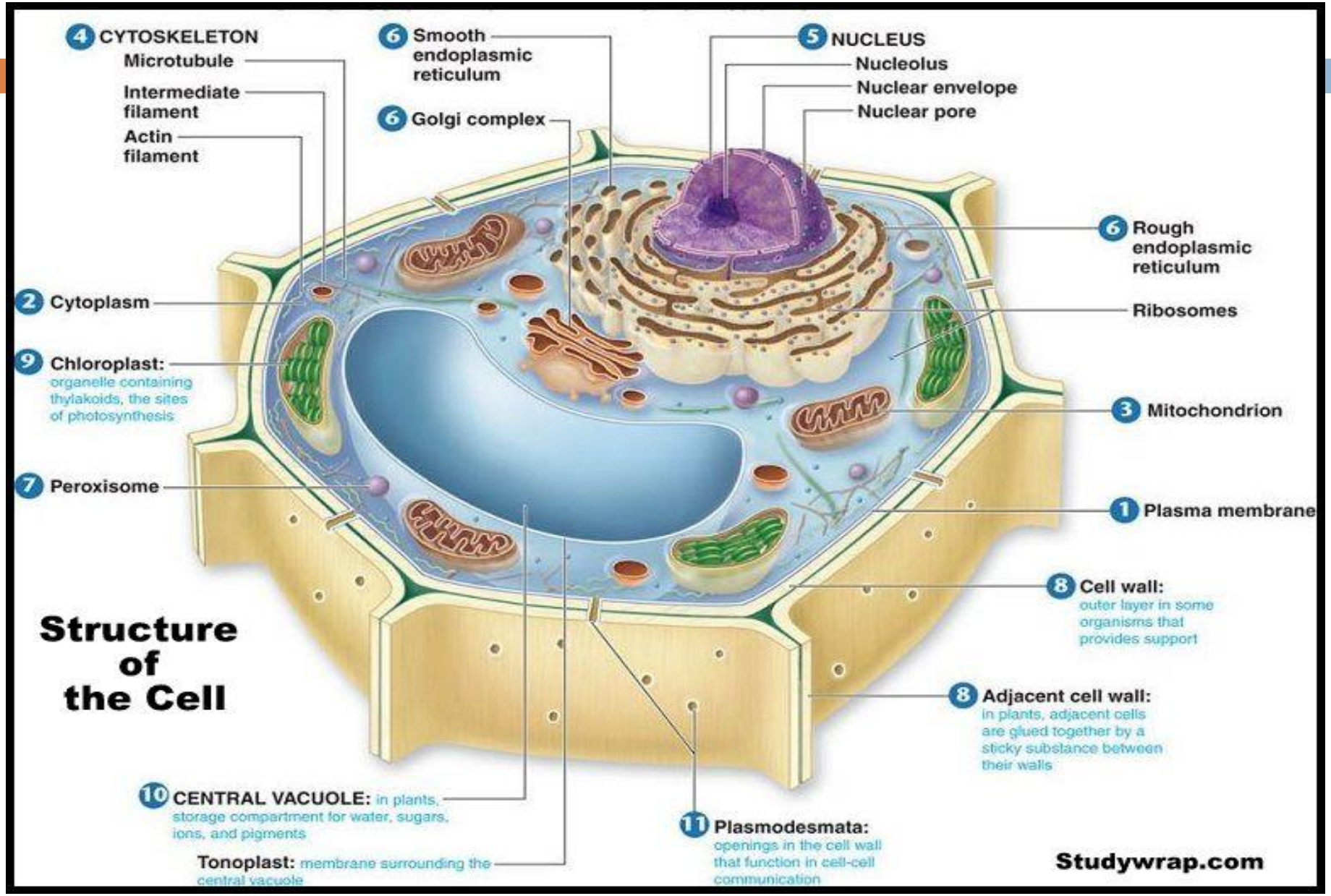
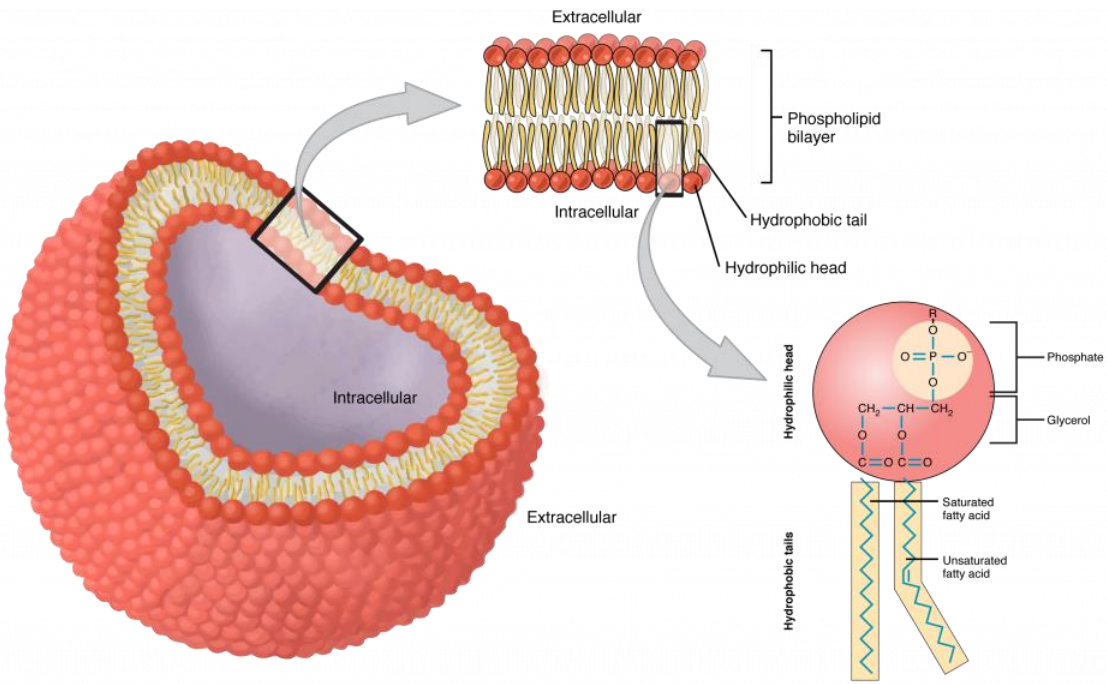
PLANT CELL


4 CYTOSKELETON
Microtubule
Intermediate filament
Actin filament
6 Smooth endoplasmic reticulum
6 Golgi complex
5 NUCLEUS
Nucleolus
Nuclear envelope
Nuclear pore
6 Rough endoplasmic reticulum
Ribosomes
2 Cytoplasm
9 Chloroplast: organelle containing thylakoids, the sites of photosynthesis
3 Mitochondrion
7 Peroxisome
1 Plasma membrane
8 Cell wall: outer layer in some organisms that provides support
Structure of the Cell
8 Adjacent cell wall: in plants, adjacent cells are glued together by a sticky substance between their walls
10 CENTRAL VACUOLE: in plants, storage compartment for water, sugars, ions, and pigments
Tonoplast: membrane surrounding the central vacuole
11 Plasmodesmata: openings in the cell wall that function in cell-cell communication
Studywrap.com

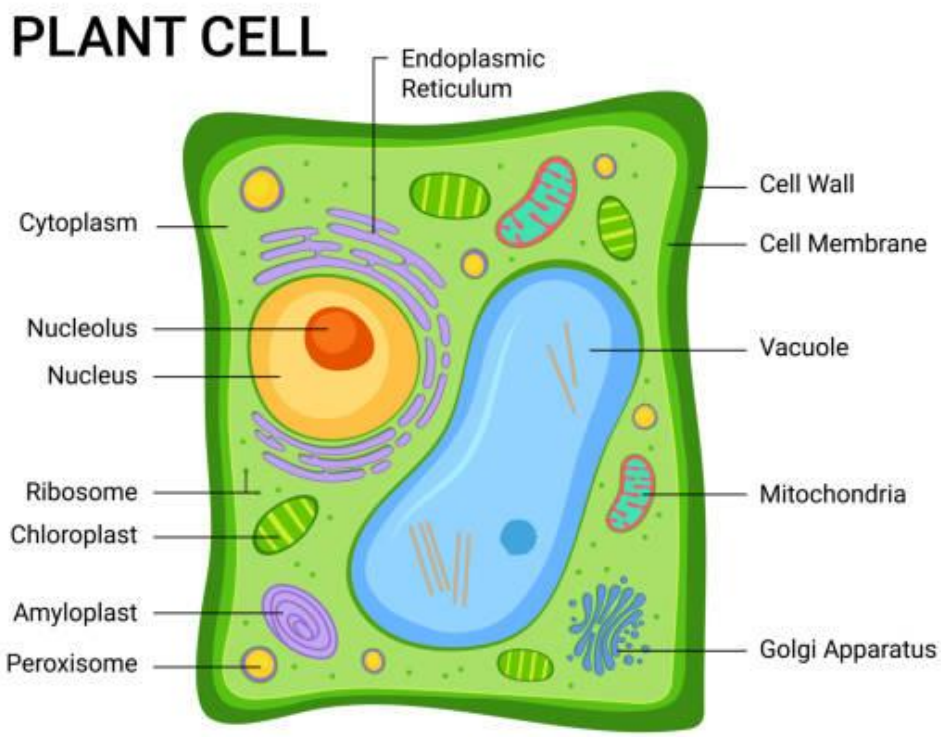
SURROUNDING THE CELL

Cell Membrane



- Provides shape, protects the inner organelle of the cell and acts as a selectively permeable membrane
- Outer membrane of cell that controls movement in and out of the cell
- Double layer

Cell Wall



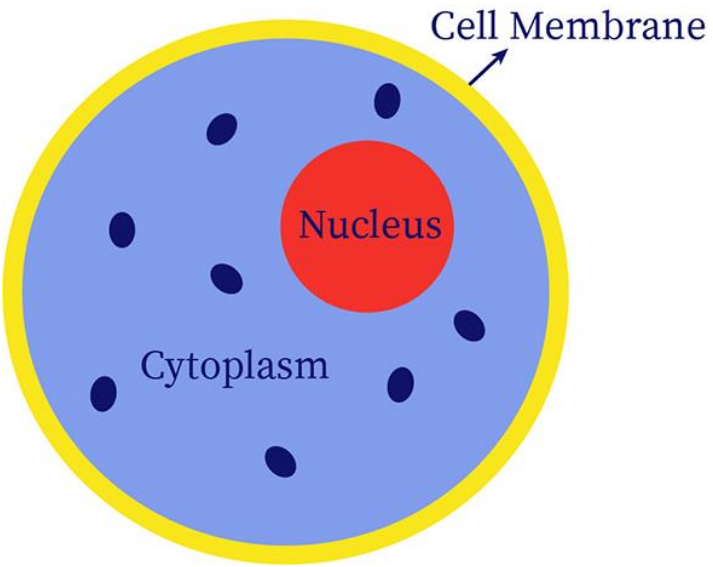
- Most commonly found in plant cells & bacteria
- Supports & protects cells

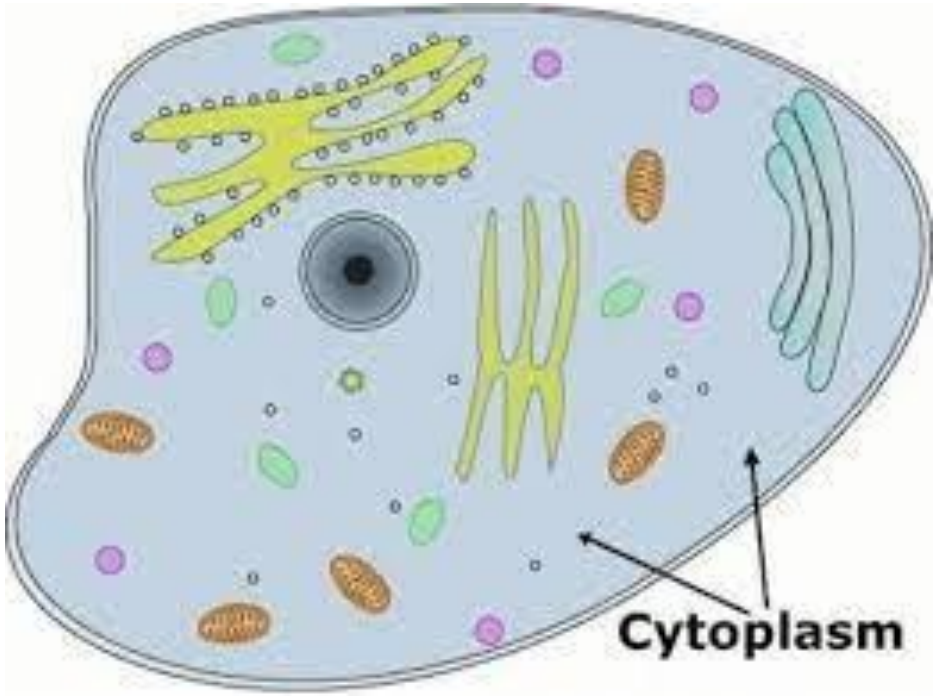
Cell Wall

- Found in plants, fungi, & many protists
- Surrounds plasma membrane

INSIDE THE CELL

CYTOPLASM





What is cytoplasm ?

- The cytoplasm is a jelly like material which is mostly made out of water
- site where most cell activities are carried out
- a mandatory part of the cells attached between the plasma membrane and the nucleus, divided into :
- cytosol (the main substance of the cytoplasm),
- organelles (the permanent component of the cytoplasm) and

Consists of :

- **Cytosol (Hyaloplasm)**

→ the main substance of the cytoplasm

→ colorless, slimy, thick and transparent colloidal solution

a) 90% of water and solutes

eg : Sugar, amino acids, enzymes, fatty acids, nucleotides, ATP and dissolved gases.

b) large molecules

eg : Proteins which form colloids

c) microfilament and microtubules

d) site for many biochemical reactions

- Organells

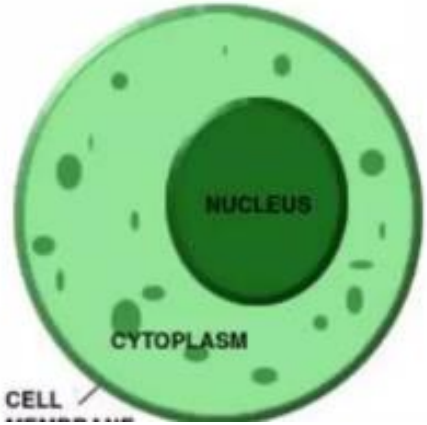
→ the permanent component of the cytoplasm

→Structure in the cell that carry out specialised functions

eg : mitochondrian, lysosomes, chloroplast, endoplasmic reticulum

Function of the cytoplasm

- It prevents the grouping of organelles in places due to gravity that would prevent their function.
- It acts as a buffer and protects the genetics material of the cell from damage caused due to movement and collision with other cells.
- It aids in metabolic activity.



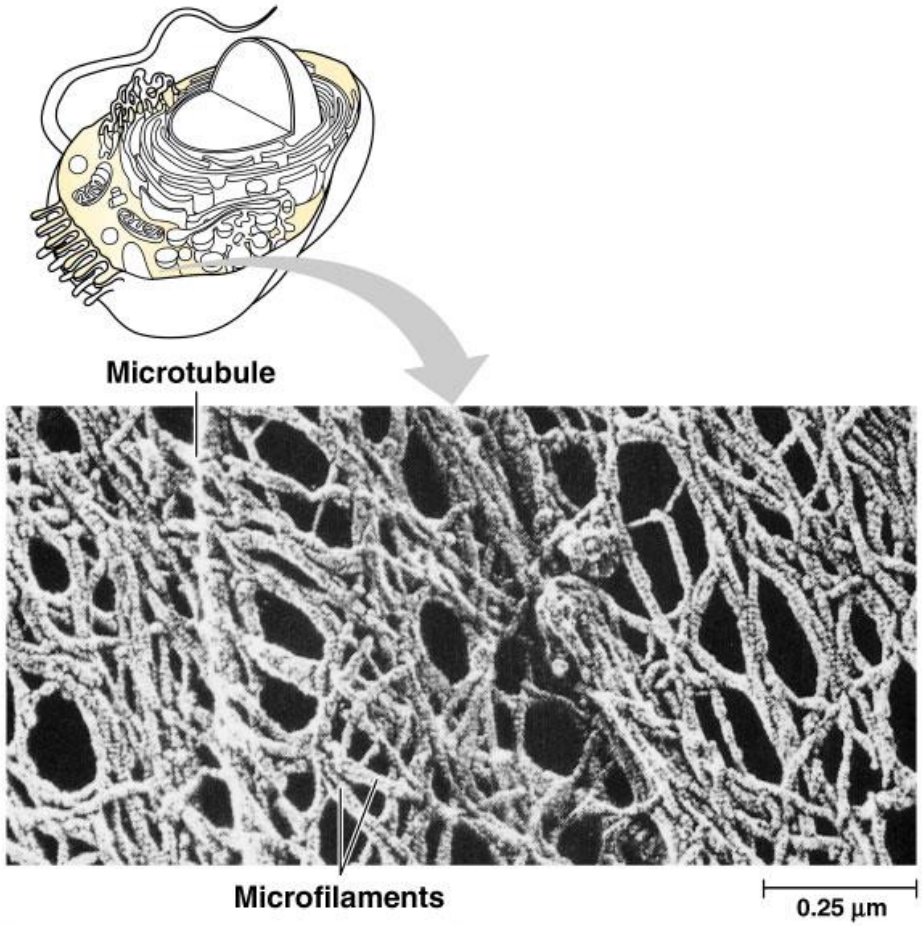
Cytoskeleton

- Means “cell skeleton”
- Internal framework of cell
- Has many functions
  - Anchoring cell organelles
  - Provide cell shape
  - Aids in cell motility
  - Response to environmental signals
- Comprises
  - Microtubules
  - Microfilaments
  - Intermediate filaments

Structural Support

- Mechanical support
  - Maintains shape
- Fibers act like a geodesic dome to stabilize and balance opposing forces
- Provides anchorage for organelles
- Dynamic
  - Dismantles in one spot and reassembles in another to change cell shape

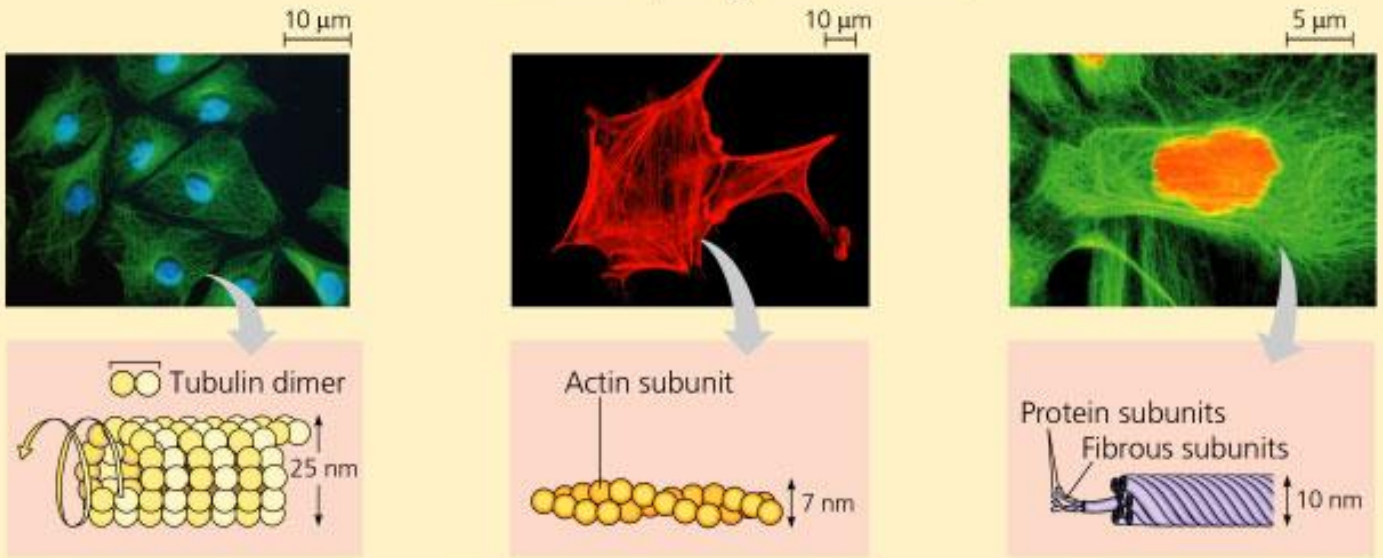
- The **cytoskeleton** is a network of fibers extending throughout the cytoplasm.
- The cytoskeleton organizes the structures and activities of the cell.



- There are three main types of fibers in the cytoskeleton: **microtubules, microfilaments,** and **intermediate filaments.**

Table 7.2 The Structure and Function of the Cytoskeleton

Property	Microtubules	Microfilaments (Actin Filaments)	Intermediate Filaments
Structure	Hollow tubes; wall consists of 13 columns of tubulin molecules	Two intertwined strands of actin	Fibrous proteins supercoiled into thicker cables
Diameter	25 nm with 15-nm lumen	7 nm	8–12 nm
Protein subunits	Tubulin, consisting of α-tubulin and β-tubulin	Actin	One of several different proteins of the keratin family, depending on cell type
Main functions	Maintenance of cell shape (compression-resisting "girders") Cell motility (as in cilia or flagella) Chromosome movements in cell division Organelle movements	Maintenance of cell shape (tension-bearing elements) Changes in cell shape Muscle contraction Cytoplasmic streaming Cell motility (as in pseudopodia) Cell division (cleavage furrow formation)	Maintenance of cell shape (tension-bearing elements) Anchorage of nucleus and certain other organelles Formation of nuclear lamina



SOURCE: Adapted from W. M. Becker, L. J. Kleinsmith, and J. Hardin, *The World of the Cell*, 4th ed. (San Francisco, CA: Benjamin Cummings, 2000), p. 753.

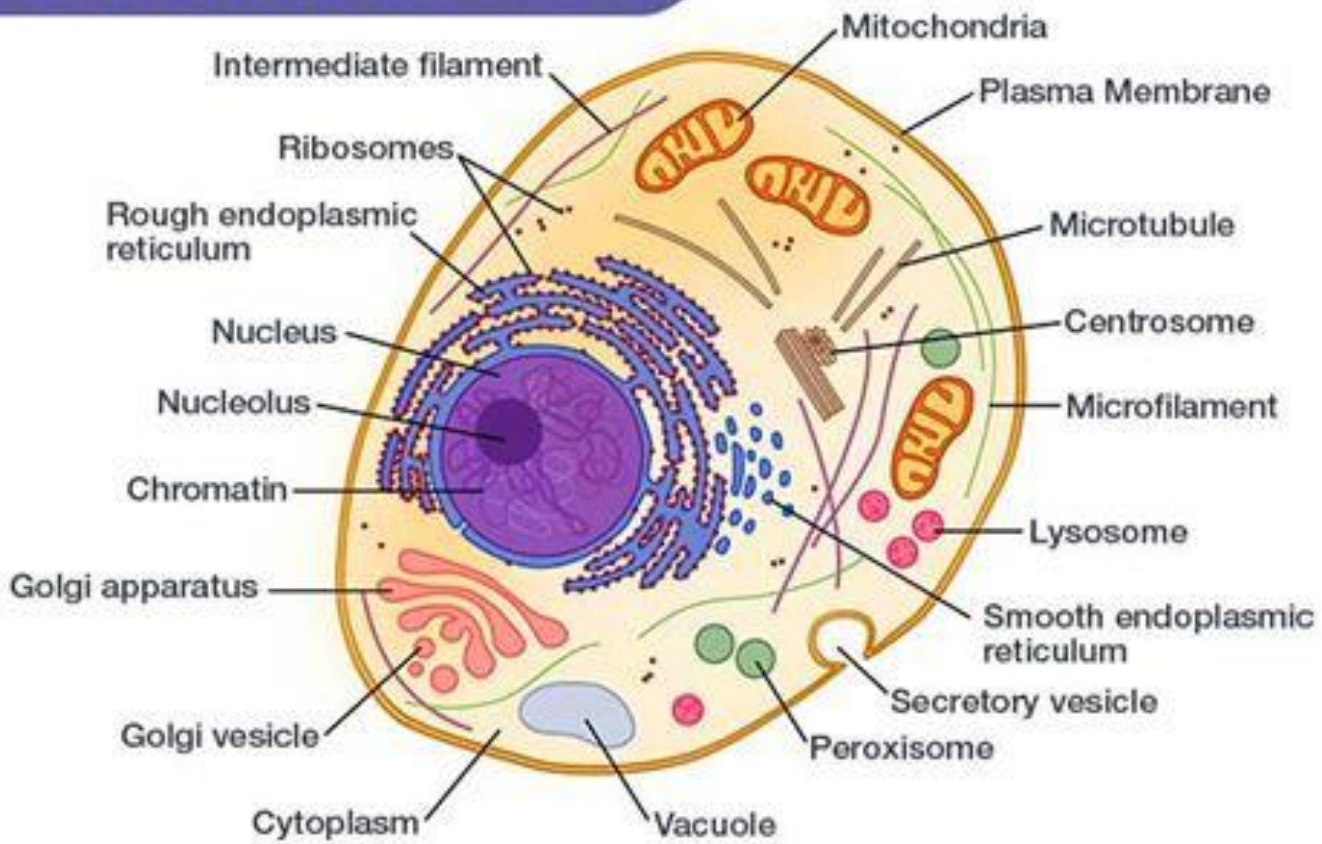
CELL ORGANELLES

- The cellular components are called the Cell Organelles.
- These cell organelles are generally membrane-bound, present within the cells and are distinct in their structures and functions.
- They coordinate with their functions efficiently for the normal functioning of the cell.
- There are various organelles present within the cell and are classified into three categories based on the presence or absence of membrane.

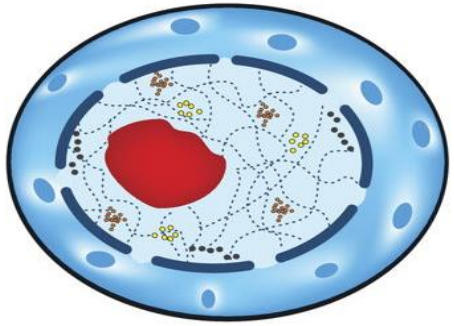
TYPES OF CELL ORGANELLES

- **Organelles without membrane:** The Ribosomes, Centrosome and Cytoskeleton are without membrane-bound cell organelles.
- **Single membrane-bound organelles:** Vacuole, Lysosome, Golgi Apparatus, Endoplasmic Reticulum are single membrane-bound organelles present only in a eukaryotic cell.
- **Double membrane-bound organelles:** Mitochondria and chloroplast are double membrane-bound organelles present only in a eukaryotic cell.

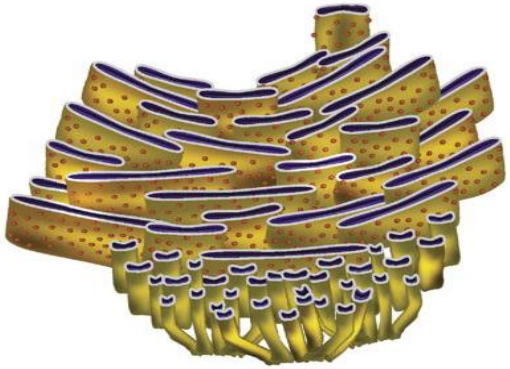
CELL ORGANELLES



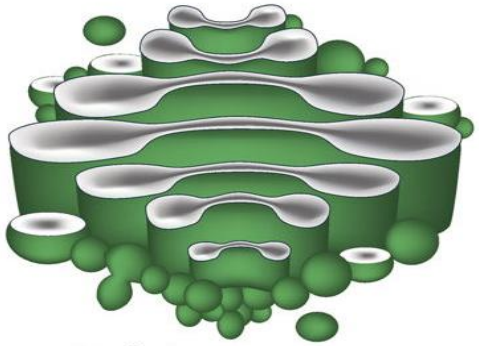
CELL ORGANELLES



Nucleus



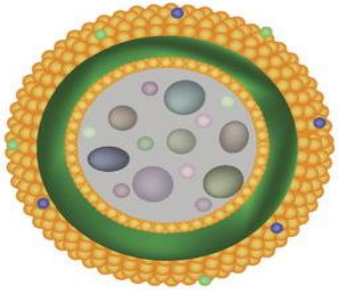
Endoplasmic reticulum



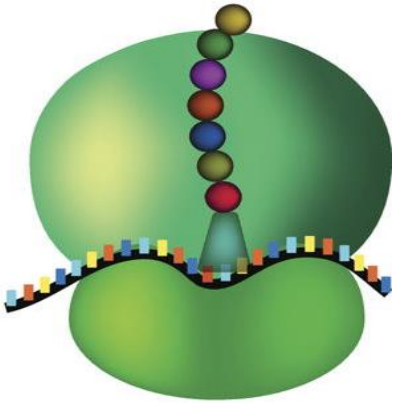
Golgi apparatus

Mitochondrion

Centrosome



Lysosome



Ribosome

Nucleus

- Control center of the cell
- Contains **DNA**
- Surrounded by a double membrane
- Usually the easiest organelle to see under a microscope
- Usually one per cell

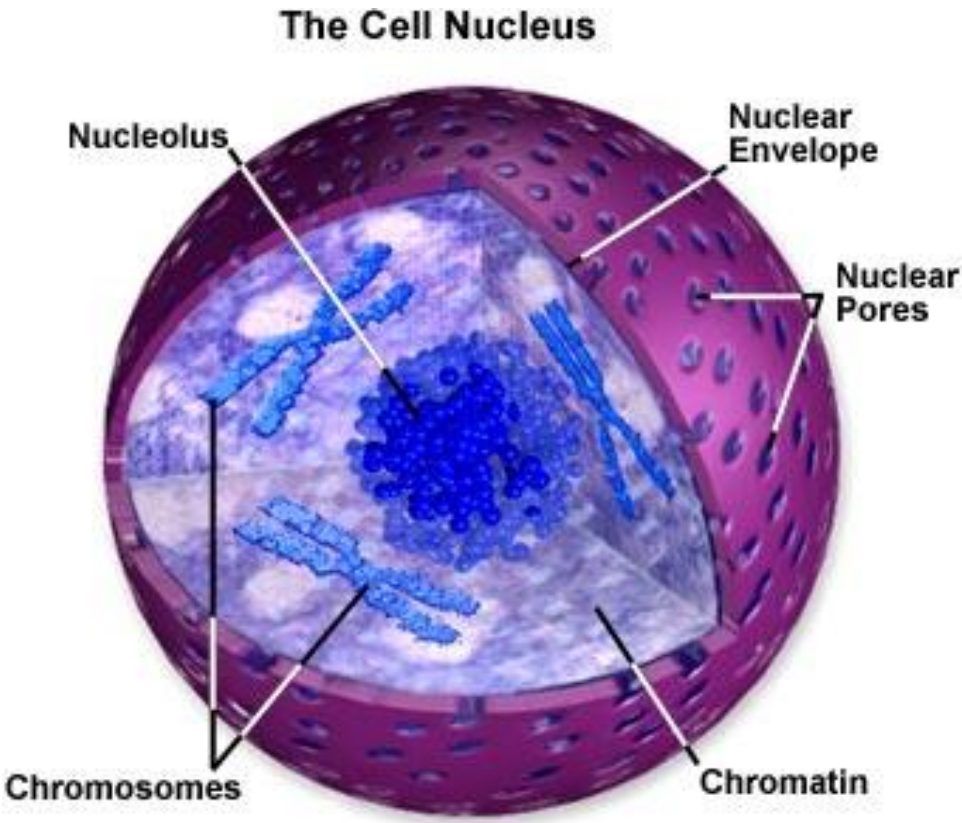
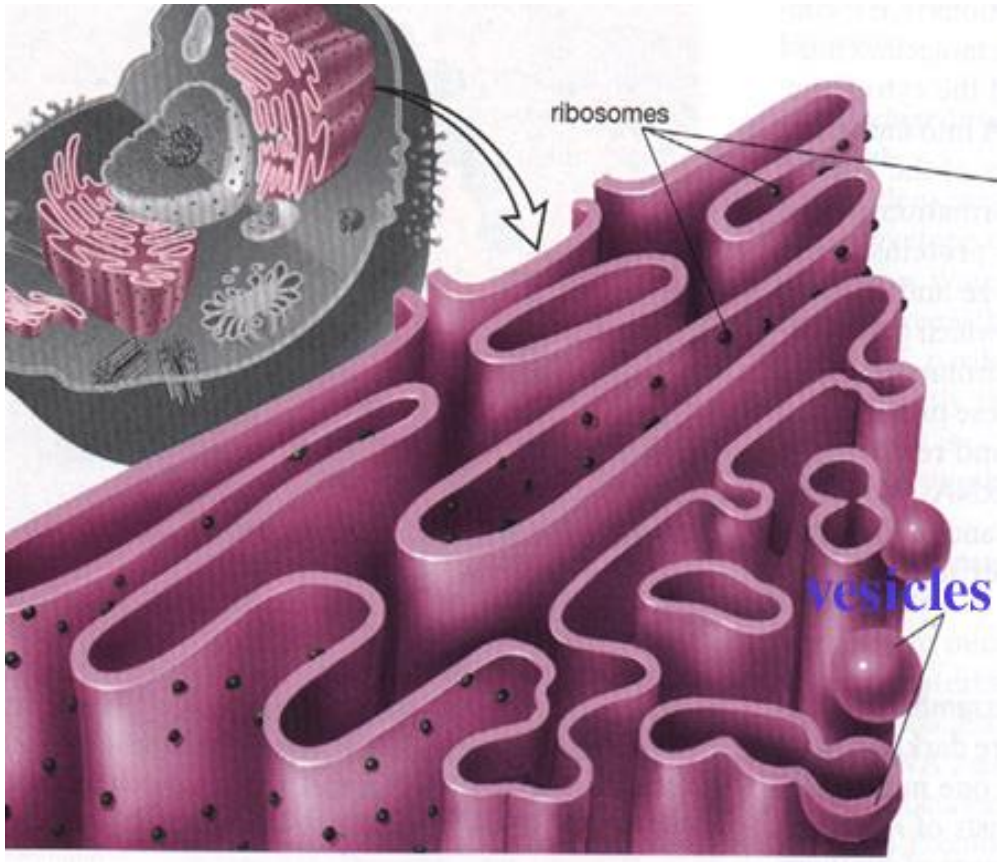


Figure 1

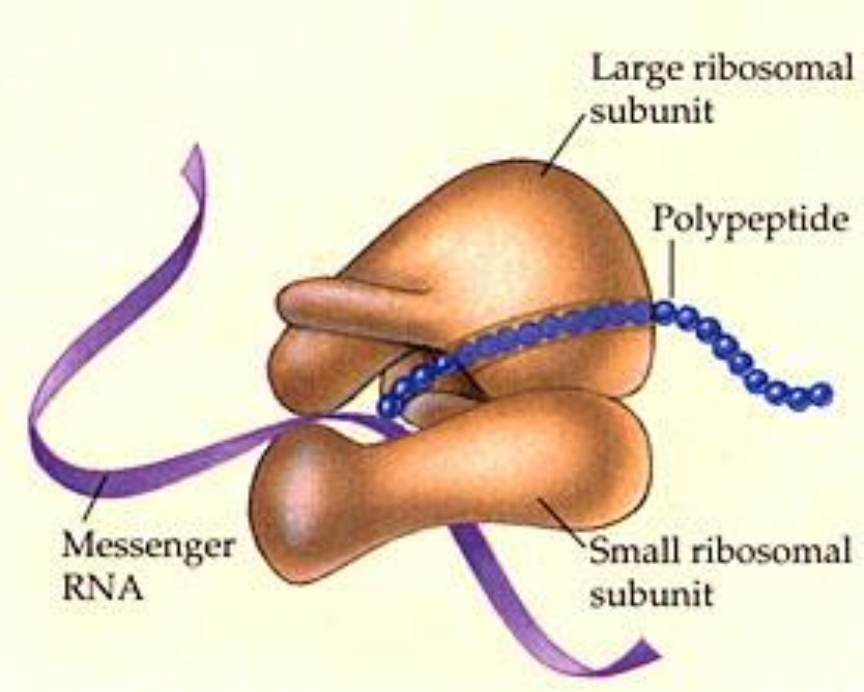
Endoplasmic Reticulum

- A.k.a. "ER"
- Connected to nuclear membrane
- Highway of the cell
- Rough ER: studded with ribosomes; it makes proteins
- Smooth ER: no ribosomes; it makes lipids



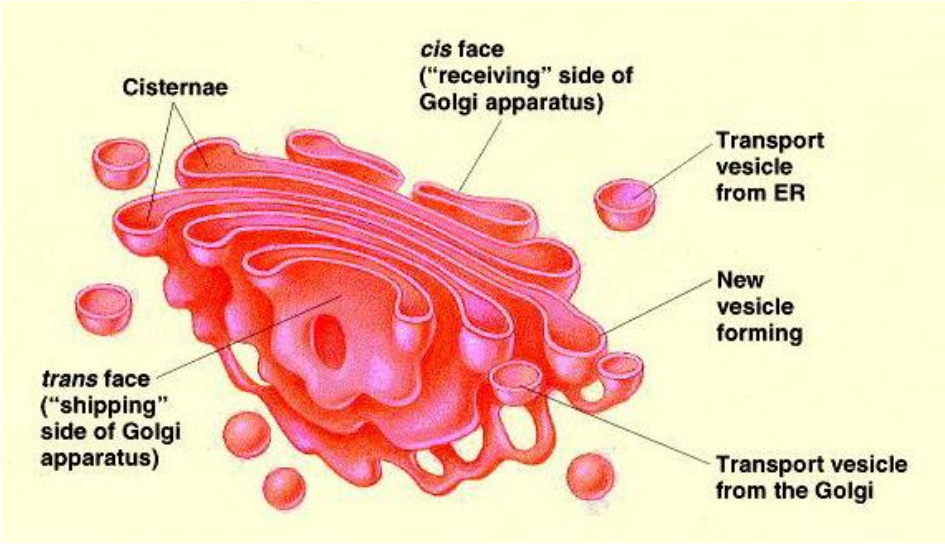
Ribosome

- Site of protein synthesis
- Found attached to rough ER or floating free in cytosol
- Produced in a part of the nucleus called the nucleolus



Golgi Apparatus

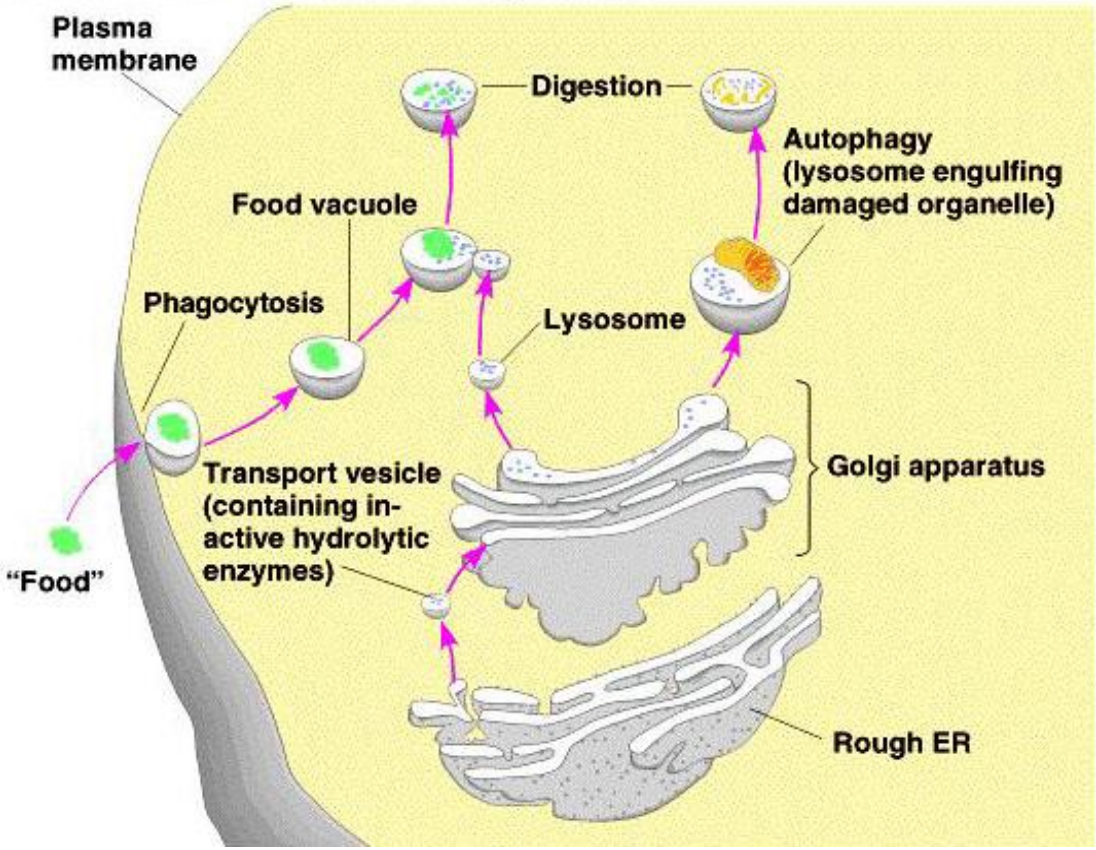
- Looks like a stack of plates
- Stores, modifies and packages proteins
- Molecules transported to and from the Golgi by means of vesicles



Lysosomes

- Garbage disposal of the cell
- Contain digestive enzymes that break down wastes

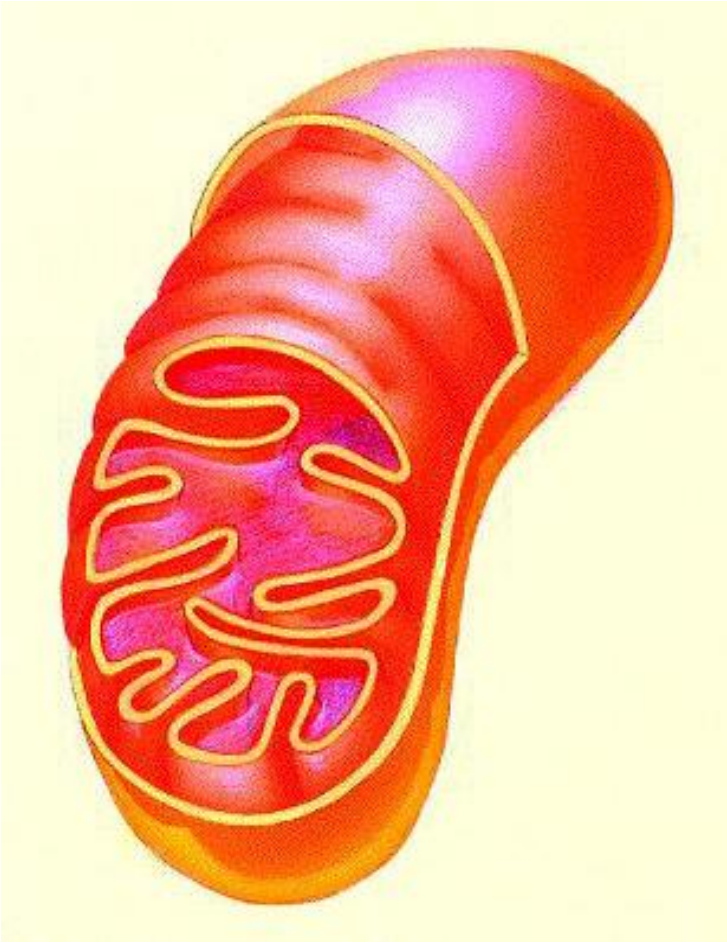
Figure 7.14 Formation and functions of lysosomes



Which organelles do lysosomes work with?

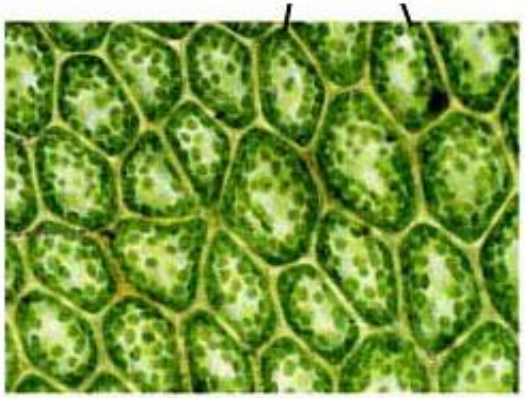
Mitochondria

- "Powerhouse of the cell"
- Cellular respiration occurs here to release energy for the cell to use
- Bound by a double membrane
- Has its own strand of DNA

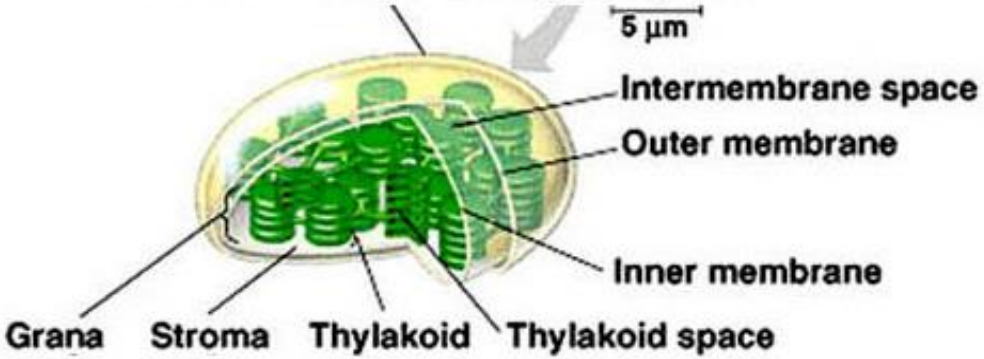


Chloroplast

- Found only in plant cells
- Contains the green pigment chlorophyll
- Site of food (glucose) production
- Bound by a double membrane

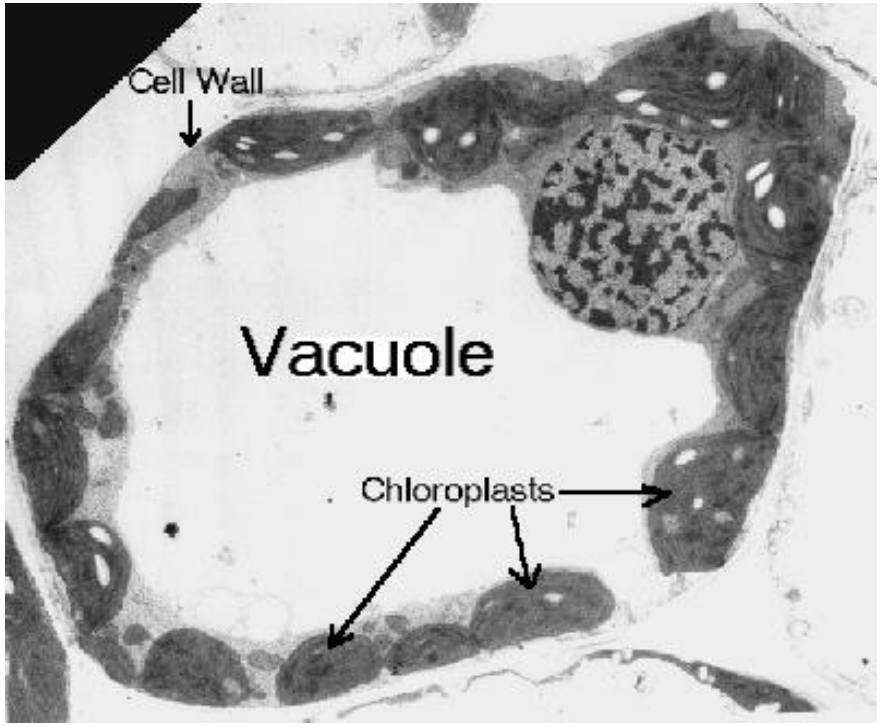


Cells containing chloroplasts



Vacuoles

- Large <u>central</u> vacuole usually in plant cells
- Many smaller vacuoles in animal cells
- Storage container for water, food, enzymes, wastes, pigments, etc.



Centriole

- Aids in cell division
- Usually found only in animal cells
- Made of microtubules

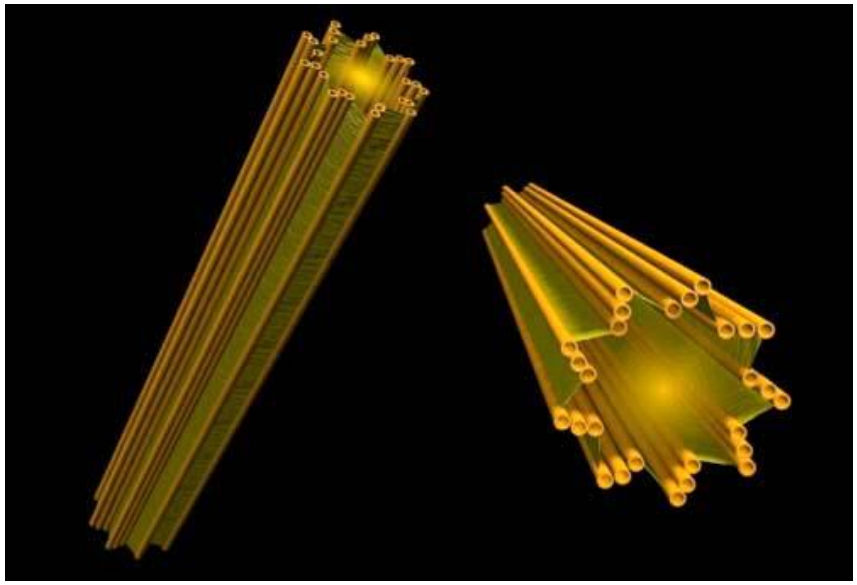


TABLE 5.2 A Comparison of Bacterial, Animal, and Plant Cells

	Bacterium	Animal	Plant
Exterior Structures			
Cell wall	Present (protein polysaccharide)	*Absent*	Present (cellulose)
Plasma membrane	Present	Present	Present
Flagella (cilia)	Sometimes present	Sometimes present	Sperm of a few species possess flagella
Interior Structures and Organelles			
Endoplasmic reticulum	*Absent*	Usually present	Usually present
Microtubules	*Absent*	Present	Present
Centrioles	*Absent*	Present	*Absent*
Golgi apparatus	*Absent*	Present	Present
Nucleus	*Absent*	Present	Present
Mitochondria	*Absent*	Present	Present
Chloroplasts	*Absent*	*Absent*	Present
Chromosomes	A single circle of naked DNA	Multiple units, DNA associated with protein	Multiple units, DNA associated with protein
Ribosomes	Present	Present	Present
Lysosomes	*Absent*	Present	Present
Vacuoles	*Absent*	*Absent* or small	Usually a large single vacuole in mature cell

Open Elective Subject

EBTY183L Biological Machines

(L-T-P = 3-0-0)

BENNETT UNIVERSITY
TIMES OF INDIA GROUP

Lecture 4

Prof. N.Latha
Head, Department of Biotechnology

EVALUATION

Mid Semester Examination - 20%
End Semester Examination - 35%
Quiz - 25%
Assignment – 20 %

Plasma membrane

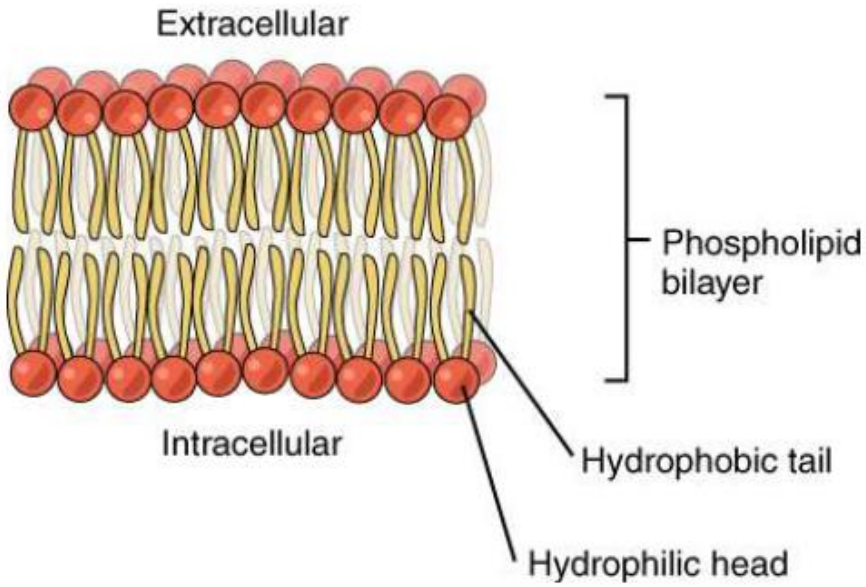
- All cells - both prokaryotic and eukaryotic - are surrounded by a plasma membrane, which defines the boundary of the cell and separates its internal contents from the environment.
- By serving as a selective barrier to the passage of molecules, the plasma membrane determines the composition of the cytoplasm.
- This ultimately defines the very identity of the cell, so the plasma membrane is one of the most fundamental structures of cellular evolution.
- Has a “railroad track” appearance under electron microscope

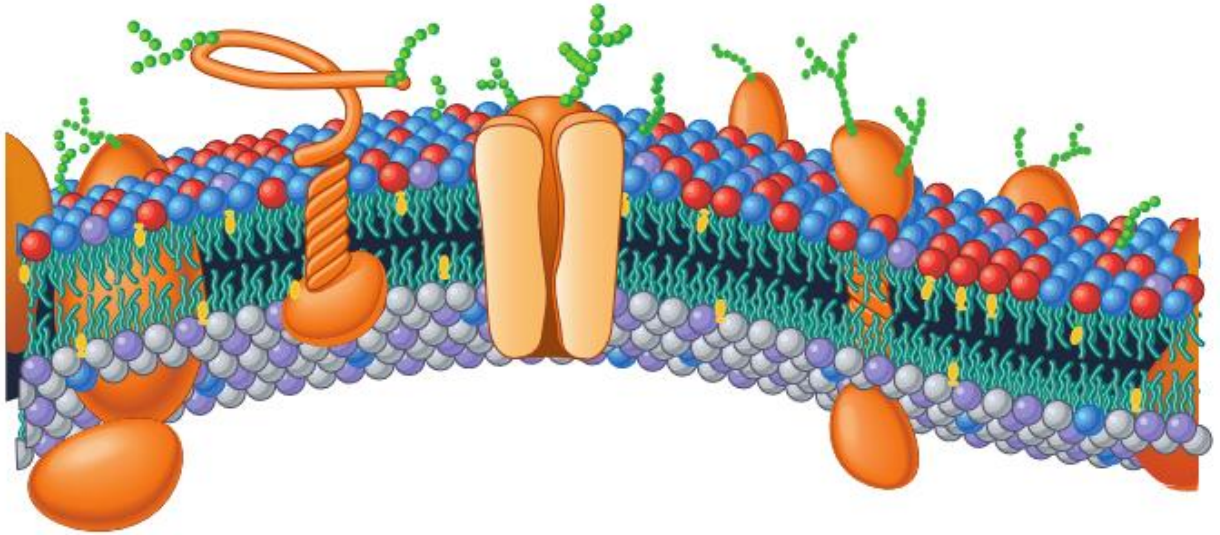
In 1925, two Dutch scientists (Evert Gorter and François Grendel) explained that the membranes consisted of lipid bilayers rather than
monolayers.

 Concept of membrane structure --- the fluid-mosaic model proposed in 1972 by S. Jonathan Singer and Garth Nicolson of the University
of California, San Diego.

 In the fluid-mosaic model, the membrane is present in a fluid state, and individual lipid molecules can move laterally within the plane of
the membrane.

 The fluid-mosaic model presents cellular membranes as dynamic structures in which the components are mobile and capable of coming together to engage in various types of transient or semipermanent interactions.





Functions of plasma membrane

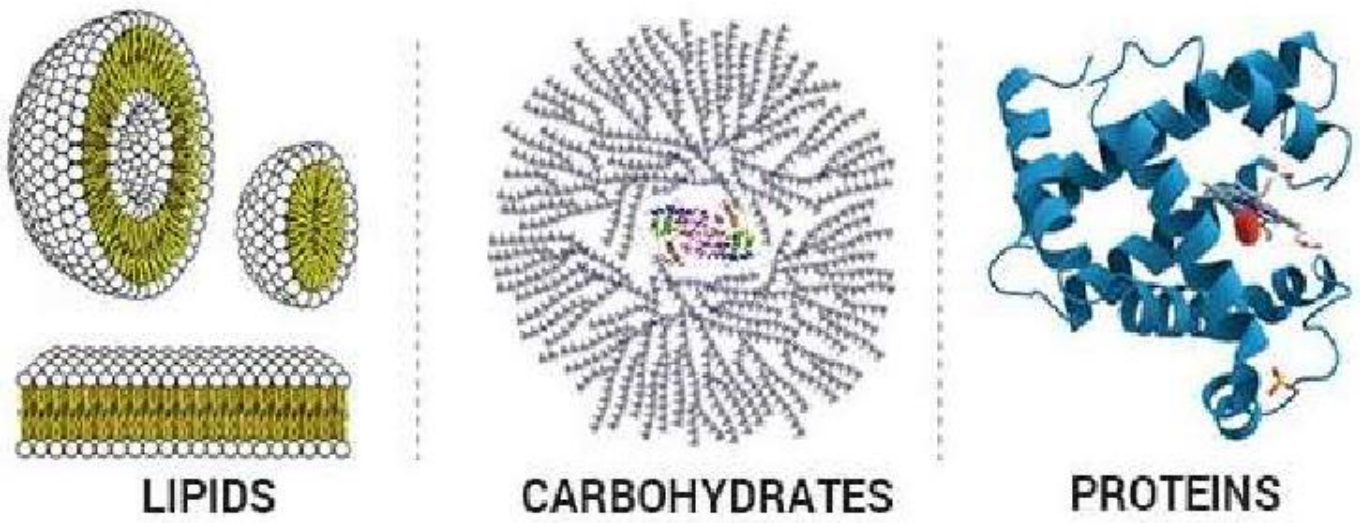
1. Compartmentalization: allows specialized activities to proceed without external interference and enables cellular activities to be
regulated independently of one another.
2. Scaffold for biochemical activities: Membranes provide the cell with an extensive framework or scaffolding within which components
can interact.
3. Providing a selectively permeable barrier: Membranes prevent the unrestricted exchange of molecules from one side to the other.
4. Transporting solutes: The plasma membrane contains the machinery for physically transporting substances from one side of the
membrane to another, often from a region where the solute is present at low concentration into a region where that solute is present
at much higher concentration.
5. Responding to external signals: The plasma membrane plays a critical role in the response of a cell to external stimuli, a process known
as signal transduction
6. Intercellular interaction

Chemical composition of Plasma membrane

Plasma membrane is made of 3 major components:

1. Lipids
2. Proteins
3. Carbohydrates

The proportion of these molecules varies depending on the cell type and its function



Membranes contain a wide diversity of lipids, all of which are amphipathic; that is, they contain both hydrophilic and hydrophobic regions

There are three main types of membrane lipids:

1. Phospholipids
2. Sphingolipids
3. Cholesterol

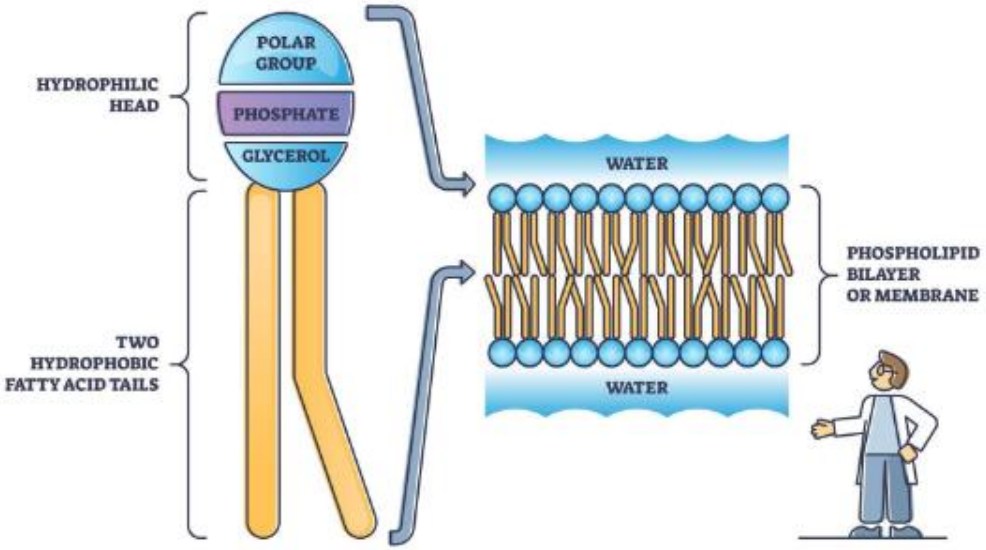
Phospholipids

 diglycerides—only two of the hydroxyl groups of the glycerol are esterified to fatty acids; the third is esterified to a hydrophilic phosphate
group.

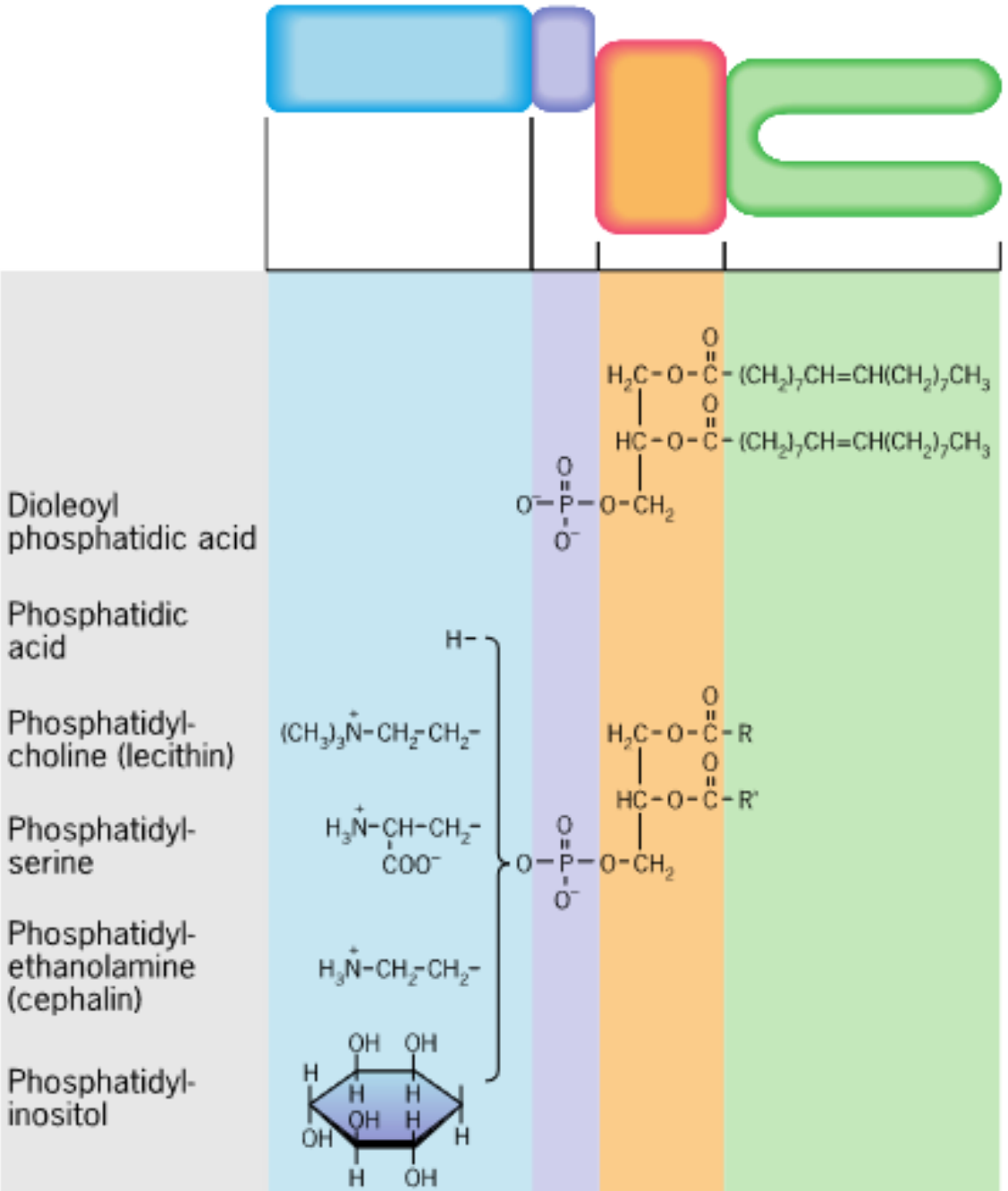
 Without any additional substitutions beyond the phosphate and the two
fatty acyl chains, the molecule is called phosphatidic acid.

 Phosphoglycerides often contain one unsaturated and one saturated
fatty acyl chain.

 Have an additional group linked to the phosphate, most commonly
either choline (phosphatidylcholine, PC), ethanolamine (phosphatidylethanolamine, PE), serine (phosphatidylserine, PS), or
inositol (phosphatidylinositol, PI)

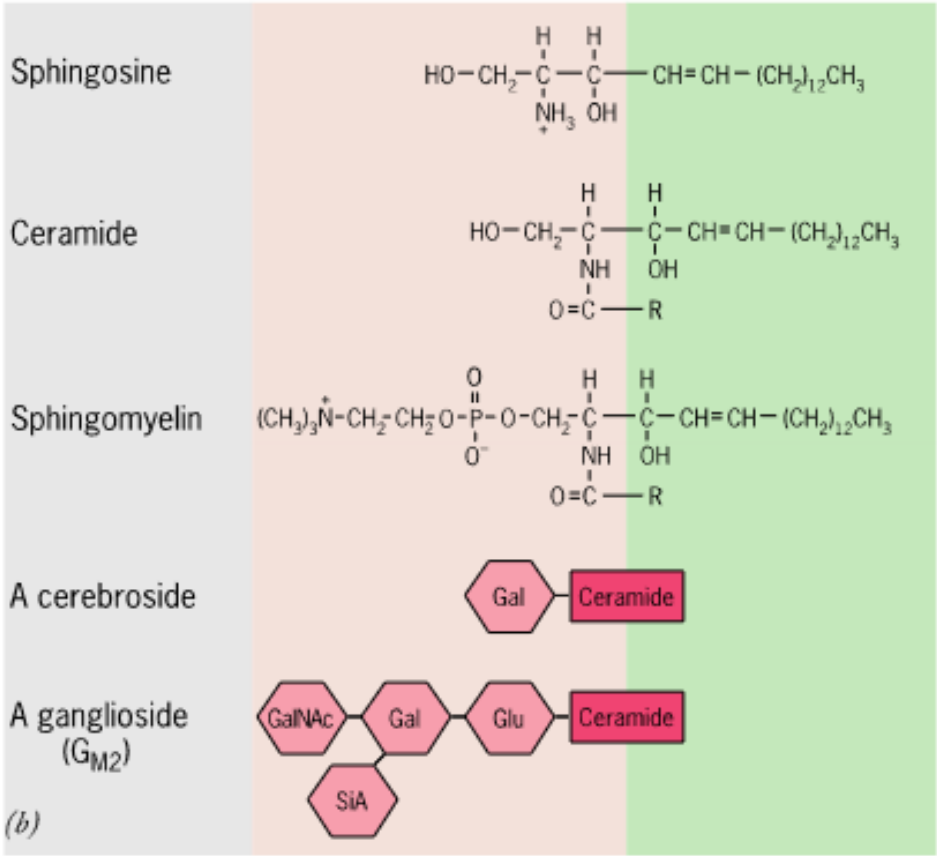


TYPES OF PHOSPHOLIPIDS



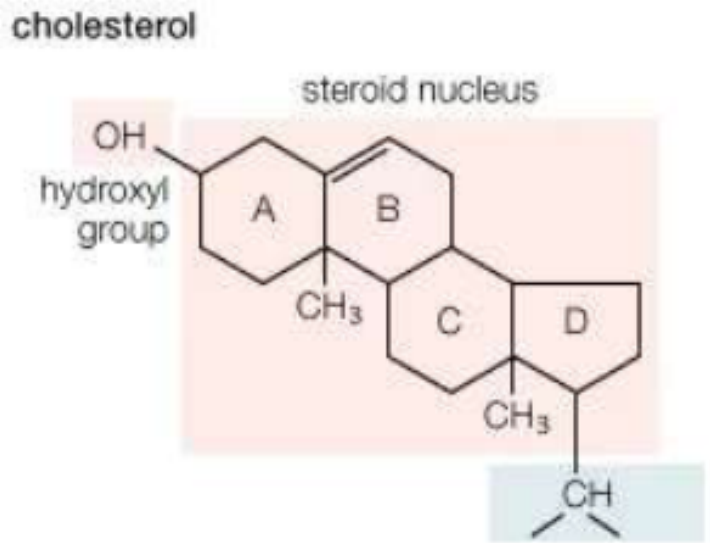
Sphingolipids

- Derivatives of **sphingosine**, an amino alcohol that contains a long hydrocarbon chain.
- **Sphingolipids** consist of sphingosine linked to a fatty acid by its amino group. This molecule is a ***ceramide***.
- If the substitution is phosphorylcholine, the molecule is ***sphingomyelin***, which is the only phospholipid of the membrane that is not built with a glycerol backbone.
- If the substitution is a carbohydrate, the molecule is a **glycolipid**.
- If the carbohydrate is a simple sugar, the glycolipid is called a ***cerebroside***; if it is a small cluster of sugars, the glycolipid is called a ***ganglioside***.
- Since all sphingolipids are also amphipathic



Cholesterol

- Certain animal cells may constitute up to 50 percent of the lipid molecules in the plasma membrane.
- Cholesterol is absent from the plasma membranes of most plant and all bacterial cells.
- Cholesterol molecules are oriented with their small hydrophilic hydroxyl group toward the membrane surface and the remainder of the molecule embedded in the lipid bilayer.
- The hydrophobic rings of a cholesterol molecule are flat and rigid, and they interfere with the movements of the fatty acid tails of the phospholipids.

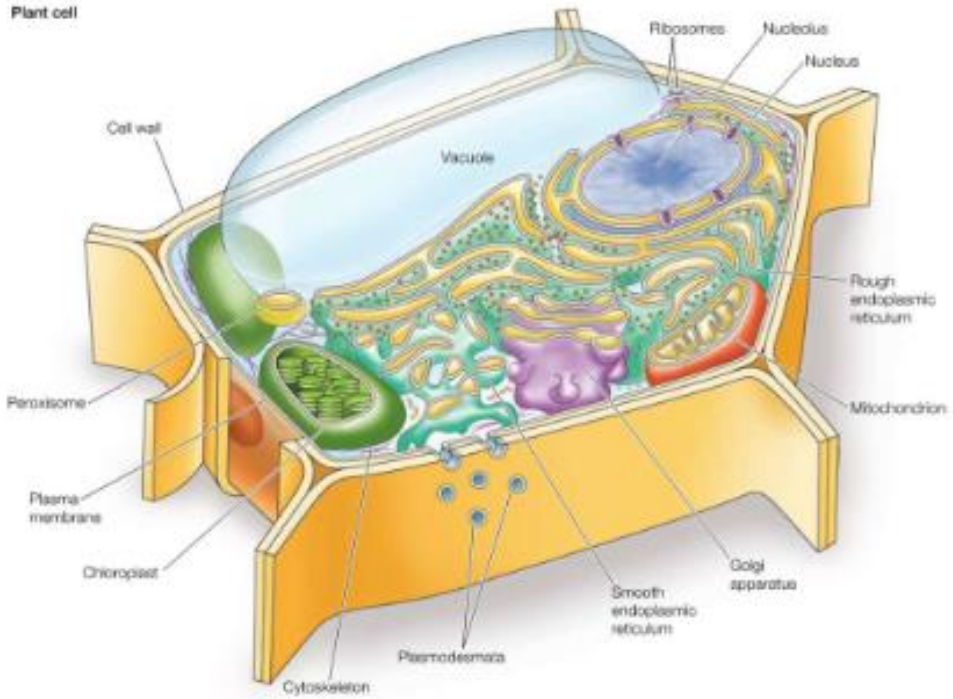


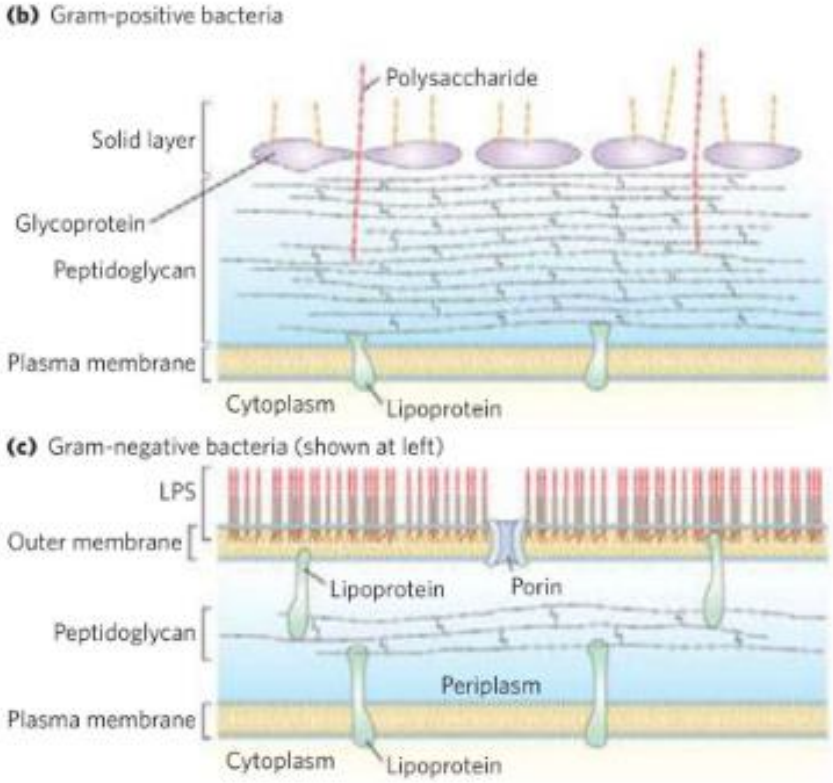
Cell wall

The cell wall surrounds the plasma membrane of plant and bacterial cells

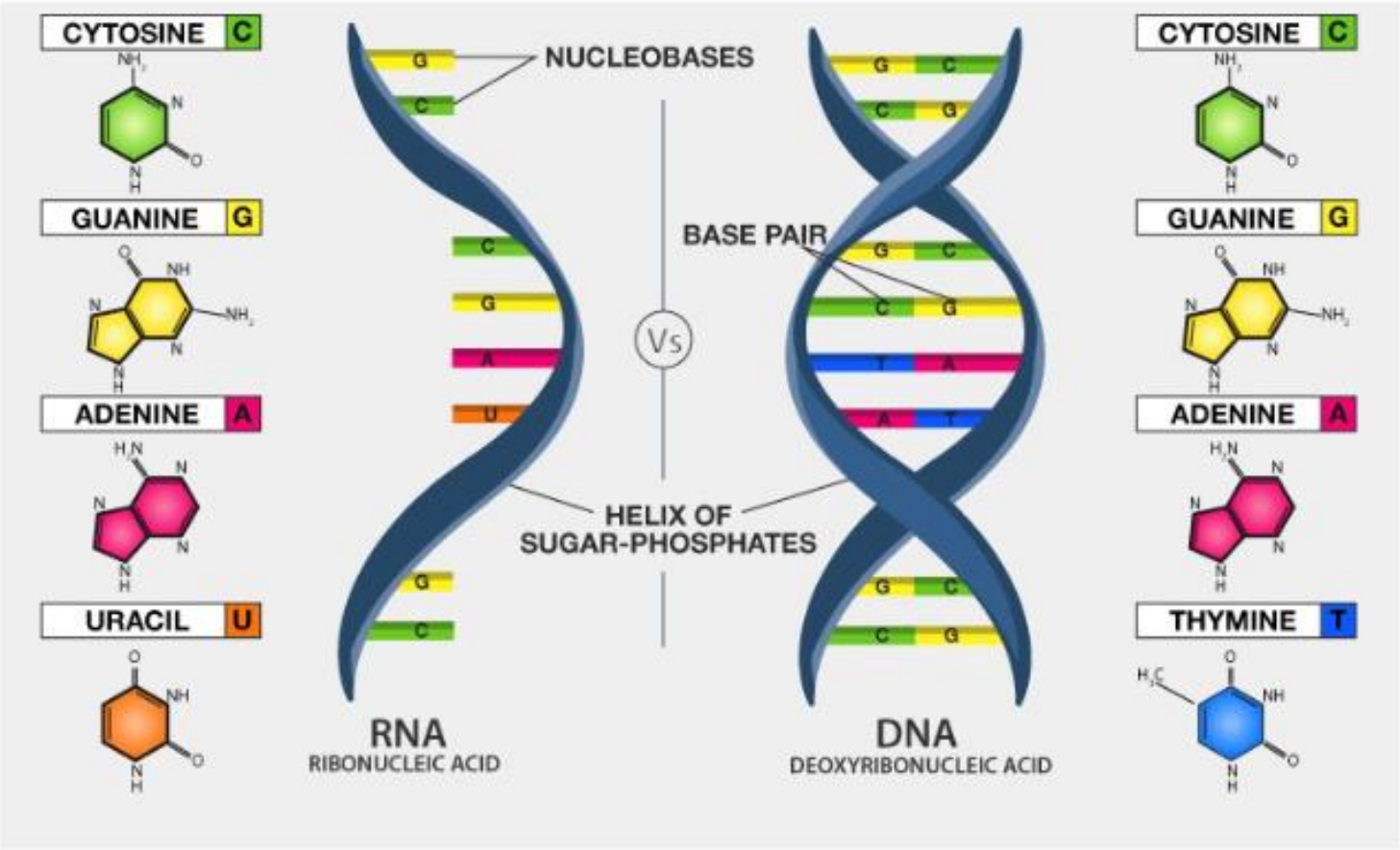
- Peptidoglycan
- Lipopolysaccharides
- Cellulose, Pectin

Why? Provides tensile strength and protection against mechanical and osmotic stress.

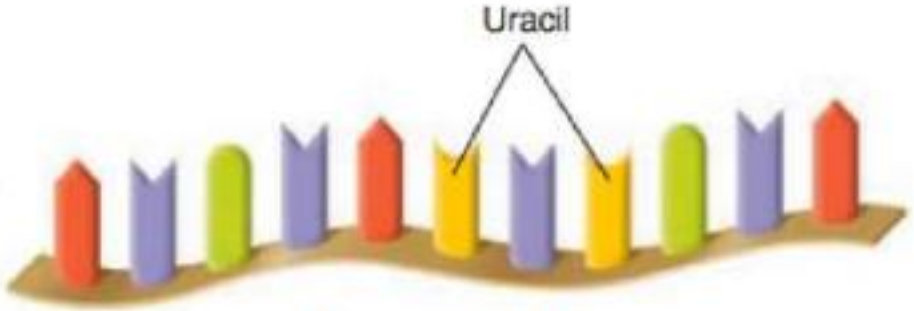




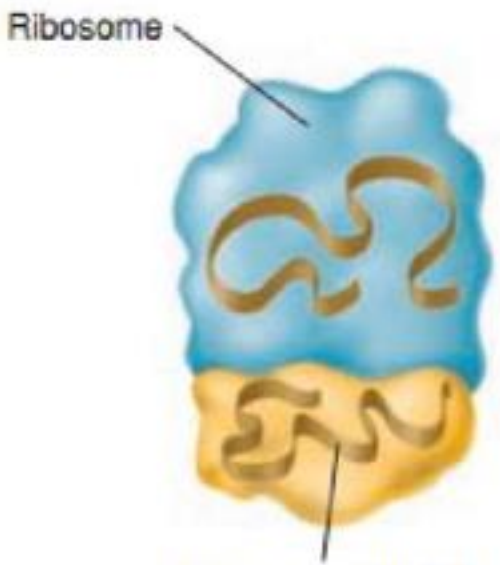
DNA versus RNA



Types of RNA



Messenger RNA

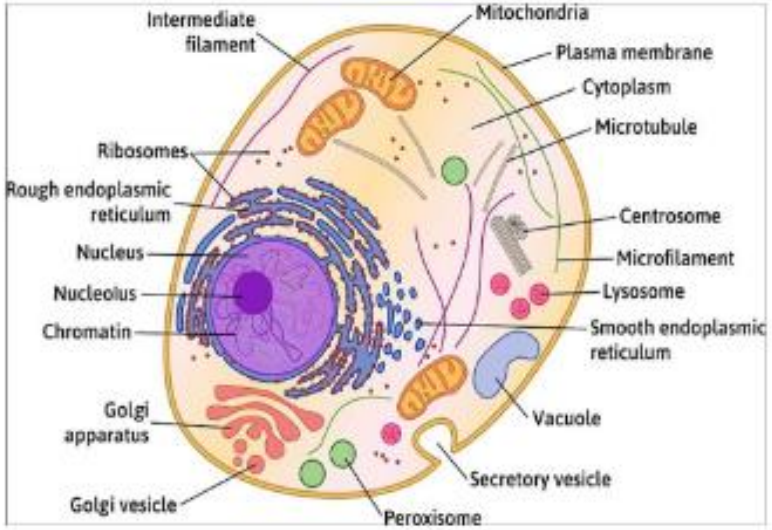


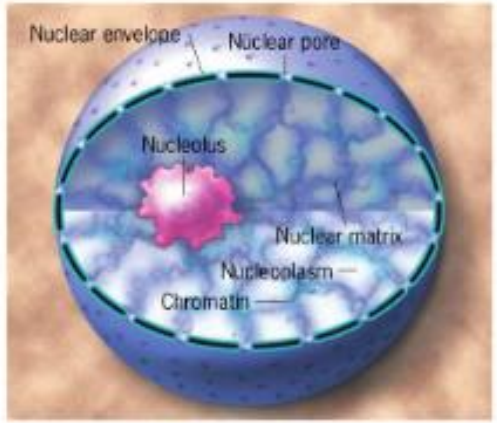
Ribosomal RNA

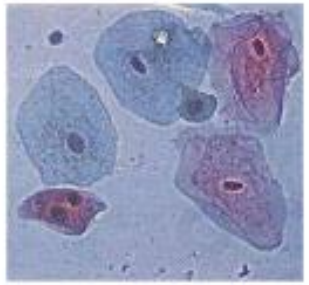
Transfer RNA

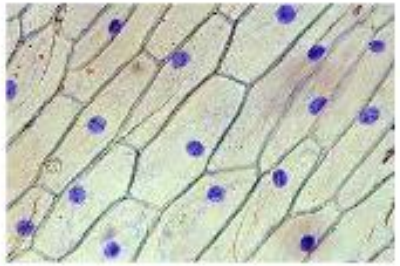
Nucleus

- The presence of a nucleus is the principal feature that distinguishes eukaryotic from prokaryotic cells.
- By housing the cell's genome, the nucleus serves both as the repository of genetic information and as the cell's control center.
- DNA replication, transcription, and RNA processing all take place within the nucleus, with only the final stage of gene expression (translation) localized to the cytoplasm.
- **Why is it needed?**
- By limiting the access of selected proteins to the genetic material, the nuclear envelope provides a control of gene expression at the level of transcription.



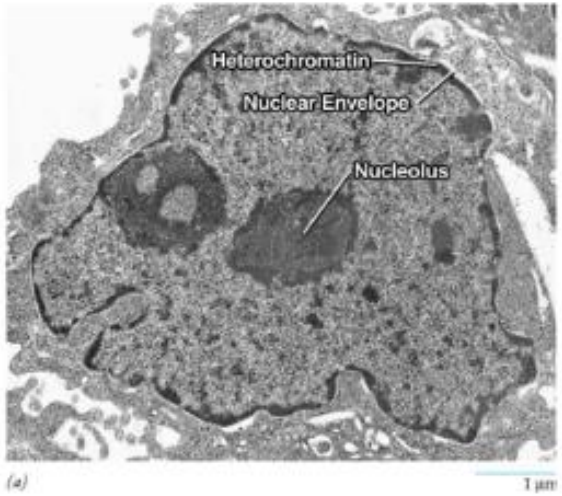


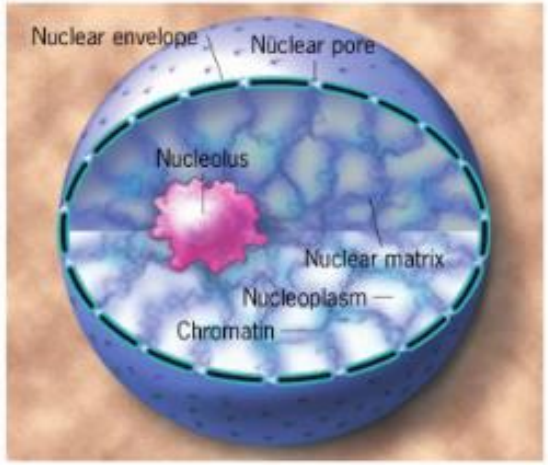




Nucleolus

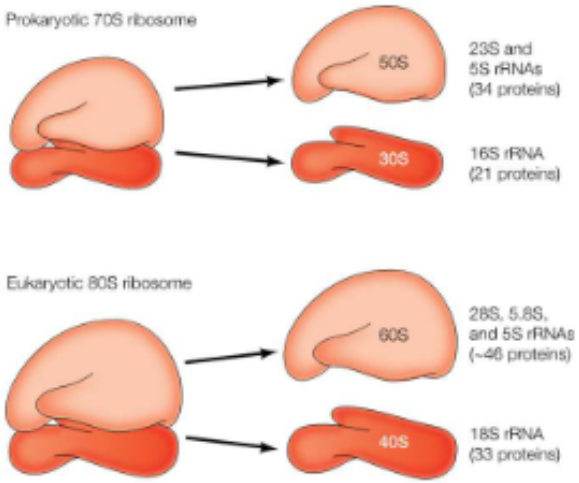
- **Nucleolus** is the site of rRNA transcription and processing as well as ribosome assembly.
- Cells require large numbers of ribosomes to meet their needs for protein synthesis.
- Actively growing mammalian cells, for example, contain approximately 10 million ribosomes that must be synthesized each time the cell divides.
- The nucleolus is a ribosome production factory, designed to fulfill the need for regulated and efficient production of rRNAs and assembly of the ribosomal subunits.

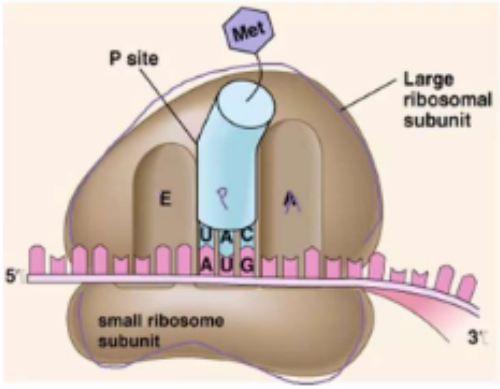




Ribosomes

- **Ribosomes** are the sites of protein synthesis in both prokaryotic and eukaryotic cells.
- First characterized as particles detected by ultracentrifugation of cell lysates, ribosomes are usually designated according to their rates of sedimentation: 70S for bacterial ribosomes and 80S for the somewhat larger ribosomes of eukaryotic cells.
- Both prokaryotic and eukaryotic ribosomes are composed of two distinct subunits, each containing characteristic proteins and **rRNAs**.
- The fact that cells typically contain many ribosomes reflects the central importance of protein synthesis in cell metabolism.
- *E. coli*, for example, contain about 20,000 ribosomes, which account for approximately 25% of the dry weight of the cell, and rapidly growing mammalian cells contain about 10 million ribosomes.
- The general structures of prokaryotic and eukaryotic ribosomes are largely similar.





In 2009, Thomas Steitz, the Sterling Professor of Molecular Biophysics & Biochemistry, was awarded the Nobel Prize in Chemistry for "studies of the structure and function of the ribosome," along with Venkatraman Ramakrishnan of the MRC Laboratory of Molecular Biology and Ada Yonath.

Open Elective Subject

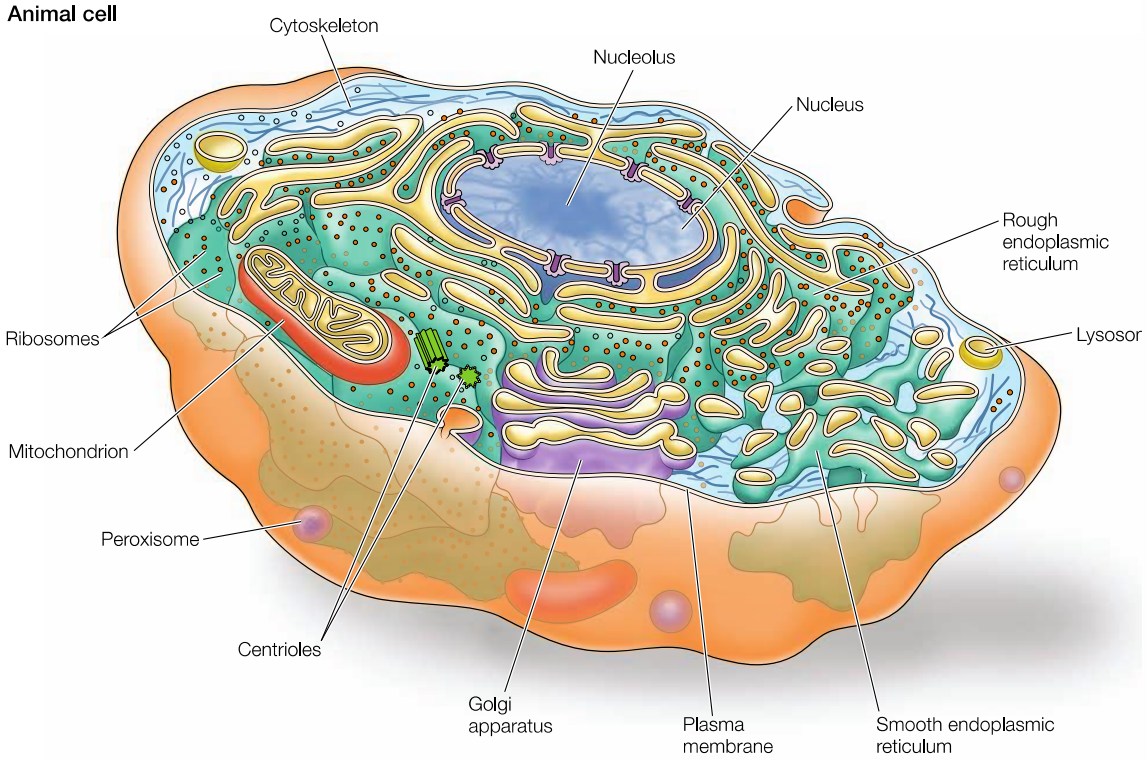
EBTY183L
Biological Machines
(L-T-P = 3-0-0)

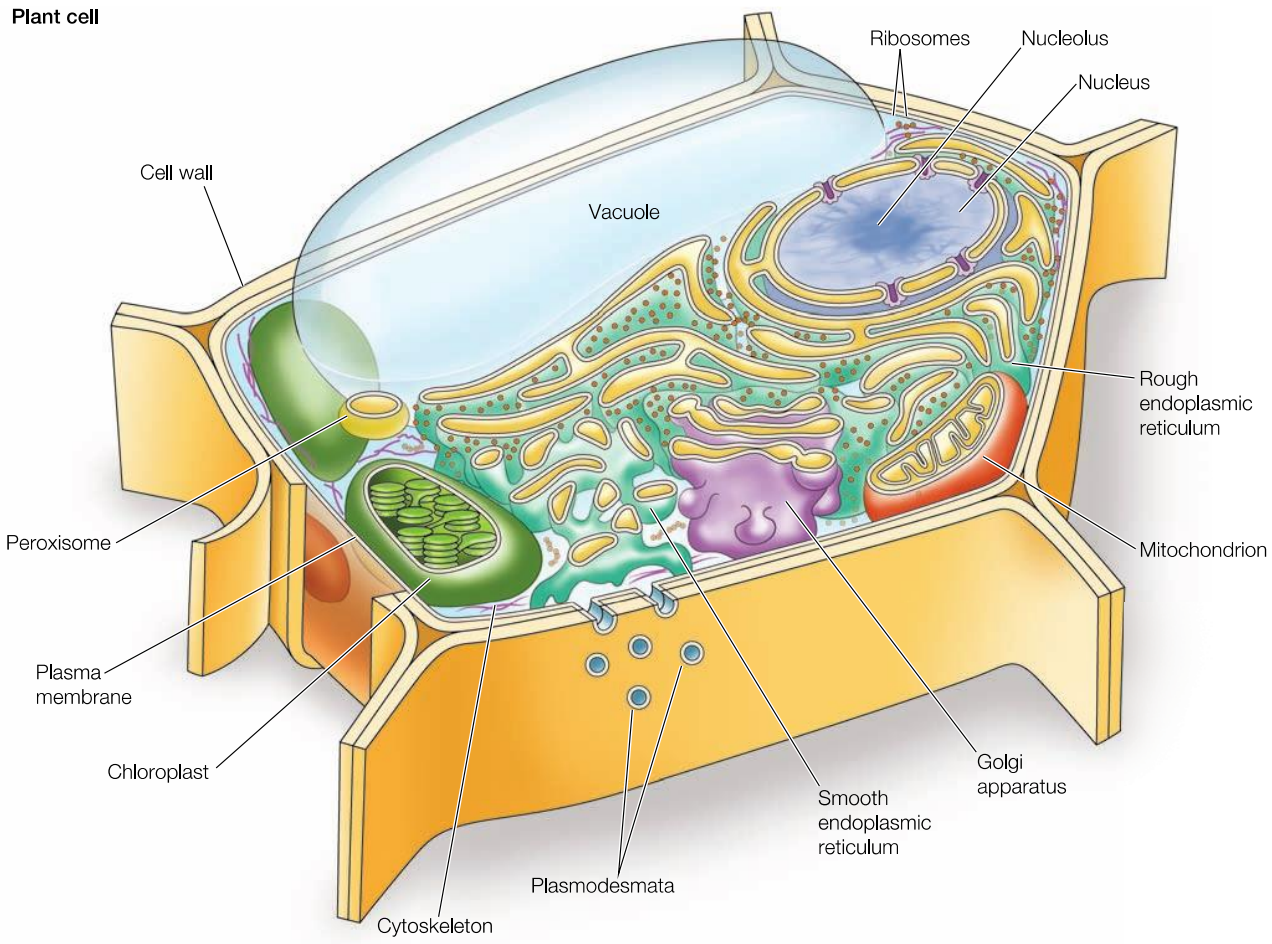
BENNETT UNIVERSITY
THE TIMES GROUP

Department of Biotechnology

Different cell components as individual machines

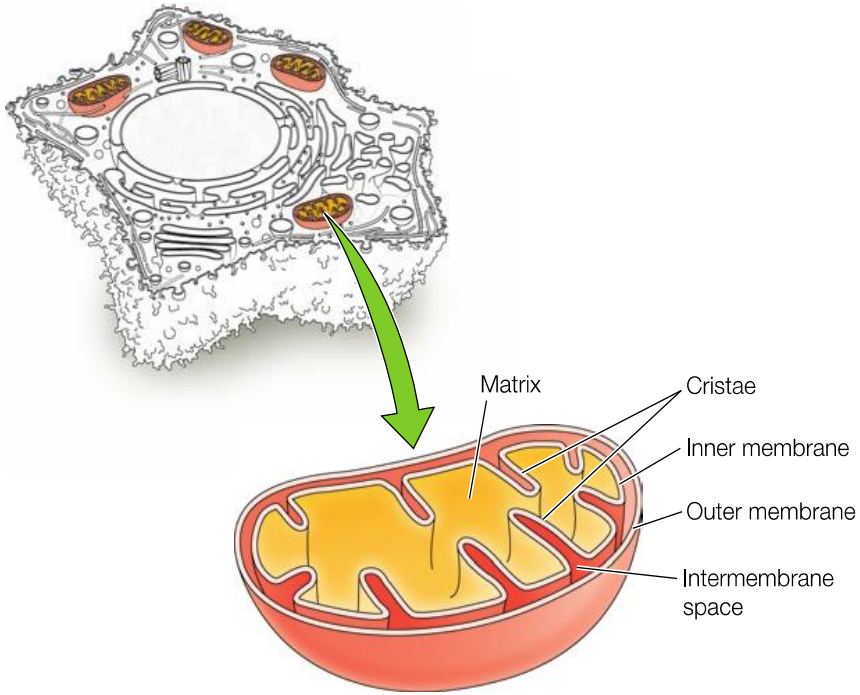
Plasma membrane, Cell wall, Nucleus, Nucleolus, Ribosomes, Mitochondria, Chloroplast, Vacuoles, Centrioles, Glyoxisomes, Peroxisomes Endoplasmic reticulum, Golgi apparatus and Lysosomes, Cytoskeleton: Role in transport of cells and Organelles

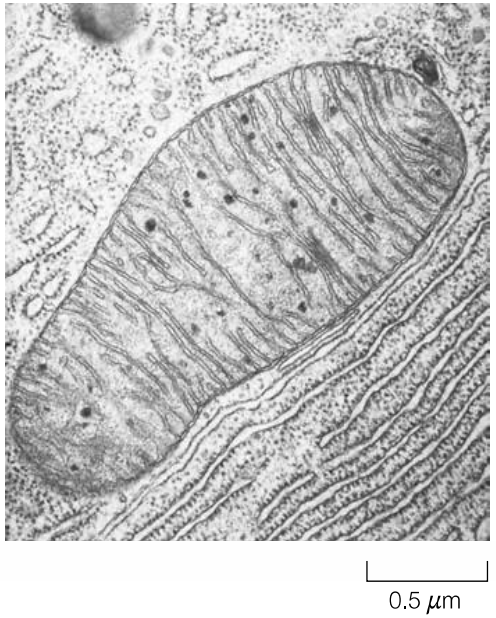




Mitochondria and Chloroplast

- The generation of metabolic energy is a major activity of all cells, and two cytoplasmic organelles are specifically devoted to energy metabolism and the production of ATP.
- **Mitochondria** are responsible for generating most of the useful energy derived from the breakdown of lipids and carbohydrates, which is converted to ATP by the process of oxidative phosphorylation.
- **Chloroplasts** use energy captured from sunlight to generate both ATP and the reducing power needed to synthesize carbohydrates from CO2 and H2O.





Mitochondria are the site of ATP production in aerobic non-photosynthetic cells – The power-house

- Mitochondria occupy 15 to 20 percent of the volume of an average mammalian liver cell and contain more than a thousand different proteins.

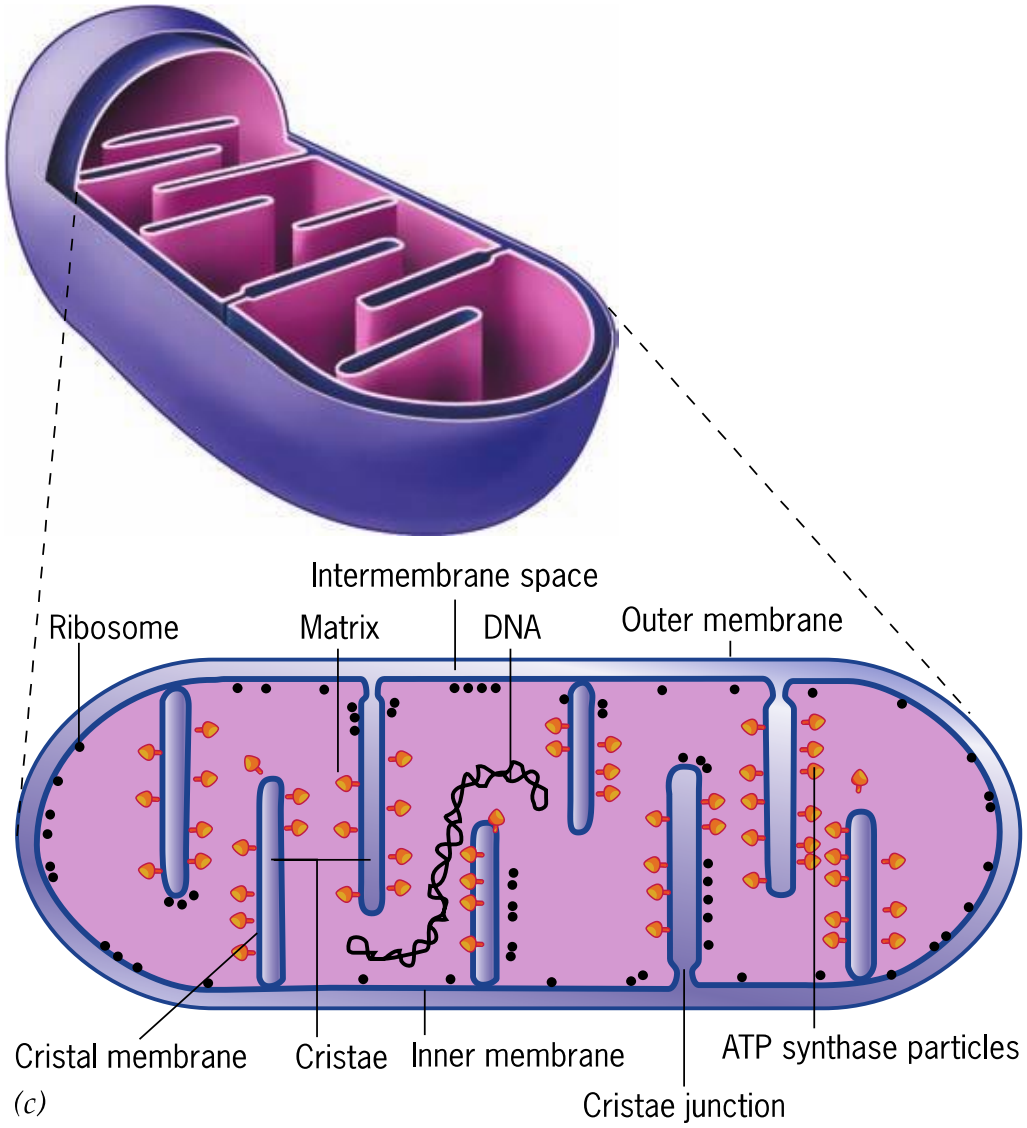
- The outer boundary of a mitochondrion contains two membranes:

  - **Outer mitochondrial membrane** completely encloses the mitochondrion, serving as its outer boundary.

  - **Inner mitochondrial membrane** is subdivided into two interconnected domains.

    - **Inner boundary membrane**, lies just inside the outer mitochondrial membrane, forming a double-membrane outer envelope.

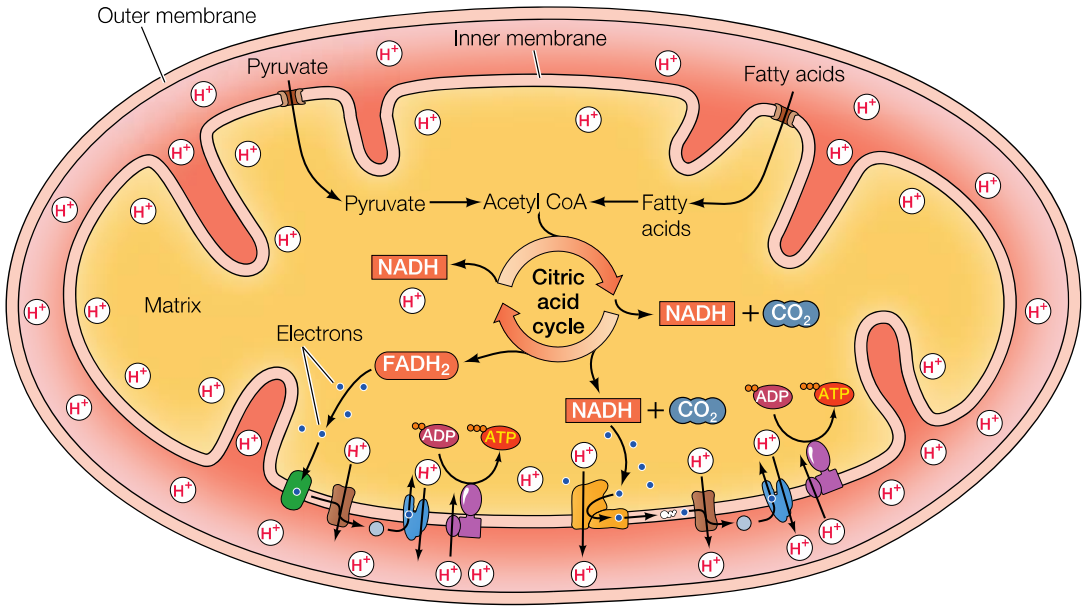
    - The other domain of the inner mitochondrial membrane is present within the interior of the organelle as a series of invaginated membranous sheets, called **cristae**

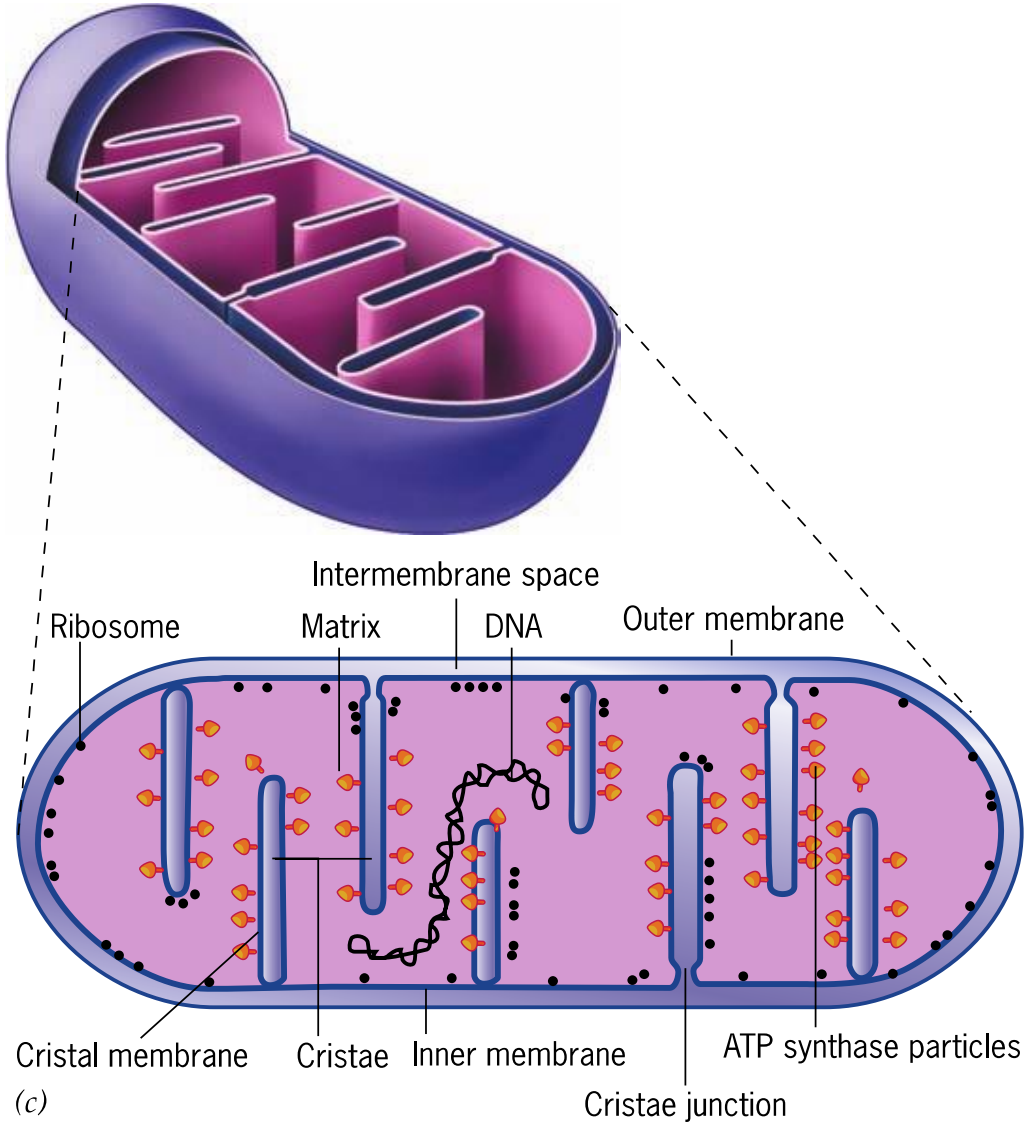


What is the importance of this kind of structure????

Houses the machinery needed for aerobic respiration and ATP formation.

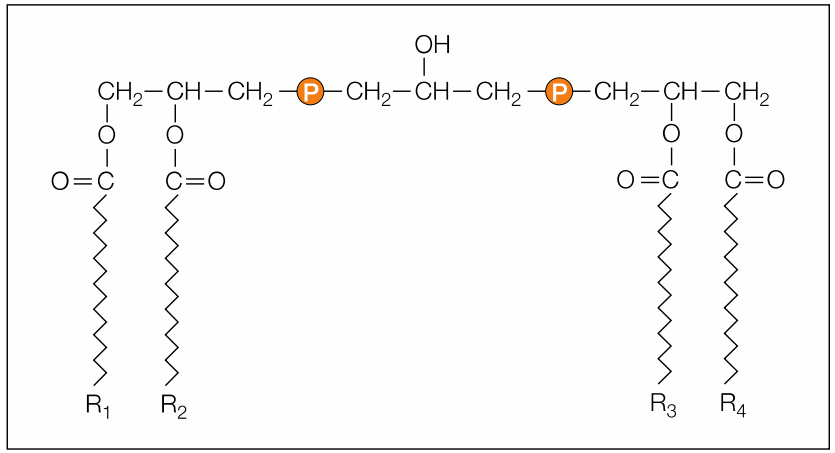
Cristae increase the surface area available for energy production.

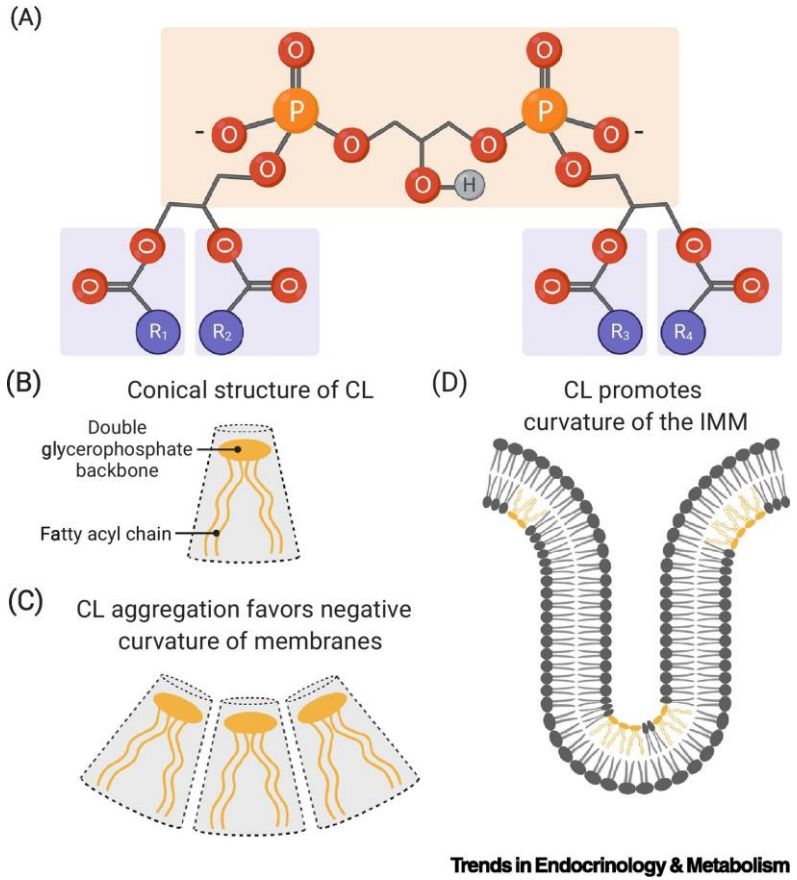




The outer and inner membranes have very different properties

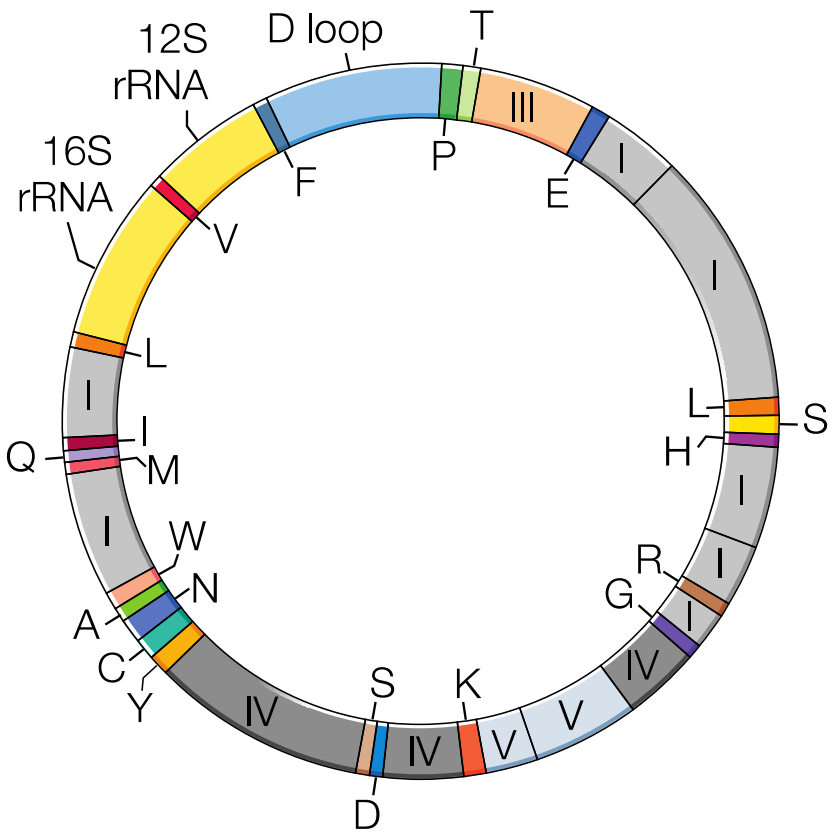
- The outer membrane is composed of approximately 50 % lipid by weight
- The inner has a very high protein/lipid ratio (more than 3:1 by weight, which corresponds to about one protein molecule for every 15 phospholipids). – Location of energy synthesis machinery!
- The inner membrane is rich in an unusual phospholipid, **cardiolipin** (diphosphatidylglycerol)
- **Cardiolipin** maintains structural integrity of membrane thereby facilitating the activity of the proteins involved in ATP synthesis.



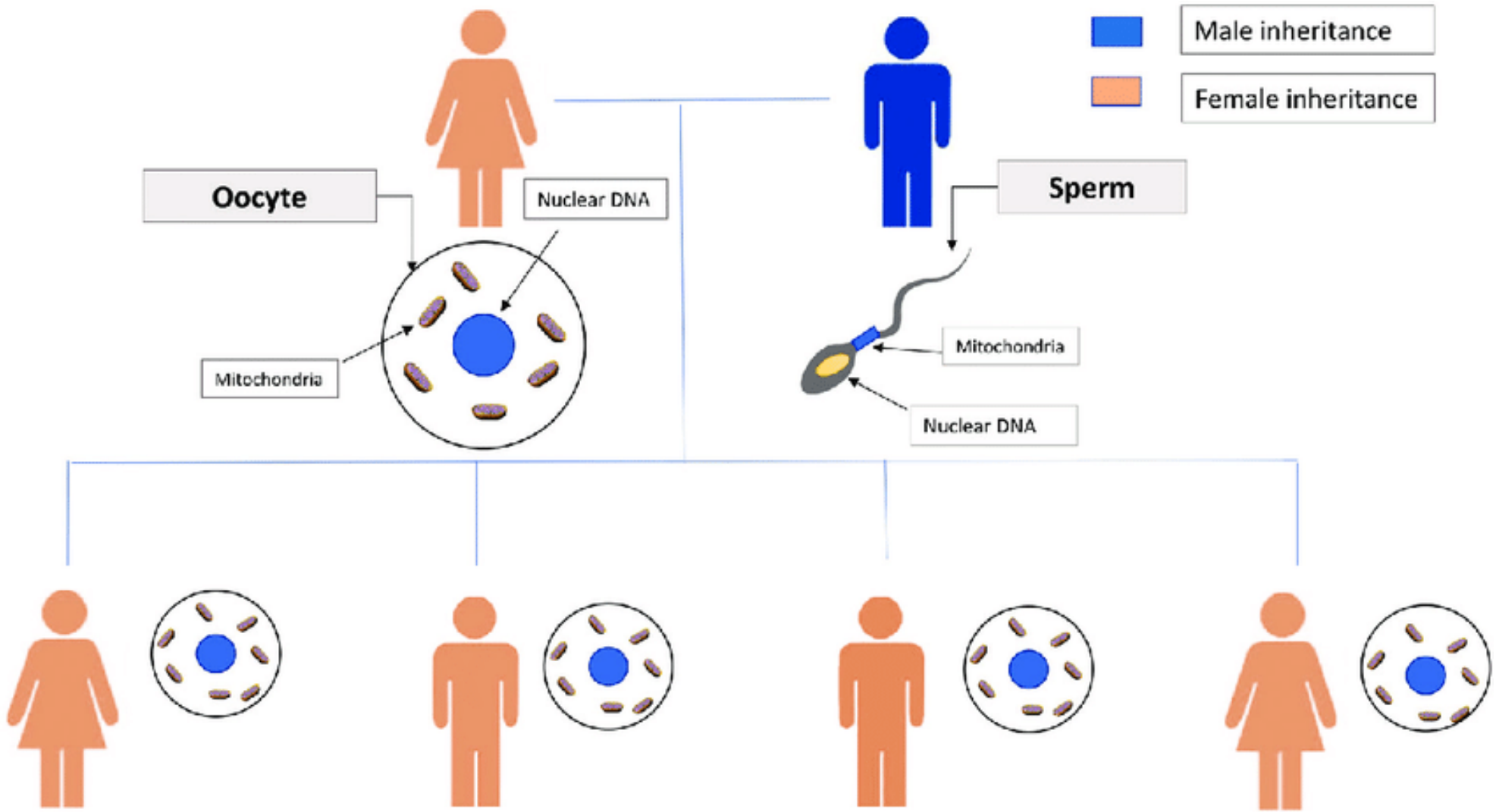


Mitochondria have their own DNA which can replicate independently – Semi Autonomous

- Mitochondria contain their own genetic system, which is separate and distinct from the nuclear genome of the cell.
- Mitochondrial genomes are usually circular DNA molecules like those of bacteria, which are present in multiple copies per organelle.
- They vary considerably in size between different species.
- Most present-day mitochondrial genomes encode only a small number of proteins that are essential components of the oxidative phosphorylation system.
- In addition, mitochondrial genomes encode all of the ribosomal RNAs and most of the transfer RNAs needed for translation of these protein-coding sequences within mitochondria.
- Other mitochondrial proteins are encoded by nuclear genes, which have been transferred to the nucleus from the ancestral mitochondrial genome.

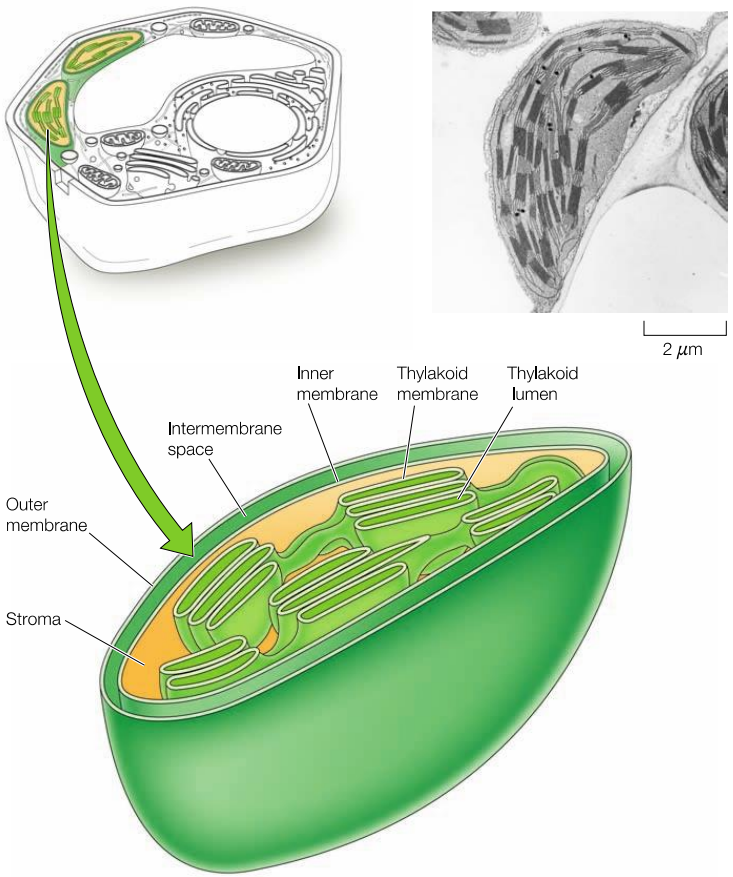


Maternal Inheritance – Importance in Forensics



Chloroplasts

- **Chloroplasts** were identified as the site of photosynthesis in 1881 in an ingenious experiment by the German biologist **T. Engelmann.**
  - Engelmann illuminated cells of the green alga *Spirogyra* and found that actively moving bacteria would collect outside the cell near the site of the large ribbon-like chloroplast.
  - The bacteria were utilizing the minute quantities of oxygen released during photosynthesis in the chloroplast for their aerobic respiration.
- Chloroplasts of higher plants are generally lens-shaped, approximately 2 to 4 um wide and 5 to 10 um long, and typically numbering 20 to 40 per cell.
- The outer covering of a chloroplast consists of an envelope composed of two membranes separated by a narrow space.
- The internal membrane of the chloroplast, which contains the energy-transducing machinery, is organized into flattened membranous sacs, called **thylakoids**.
- Thylakoids are arranged in orderly stacks called **grana.**
- The space inside a thylakoid sac is the *lumen*, and the space outside the thylakoid and within the chloroplast envelope is the **stroma**, which contains the enzymes responsible for carbohydrate synthesis.



Much of the photosynthetic machinery of the chloroplast— including light-absorbing pigments, a complex chain of electron carriers, and an ATP-synthesizing apparatus—is part of an internal membrane system that is physically separate from the double-layered envelope.

Mitochondria and chloroplasts, are assumed to have arisen by endosymbiosis—one cell living inside another:

Mitochondria are thought to have evolved from aerobic bacteria living inside the archaeal ancestor of eukaryotes and **chloroplasts** evolved from photosynthetic bacteria, such as cyanobacteria, living inside the ancestor to plants and green algae.

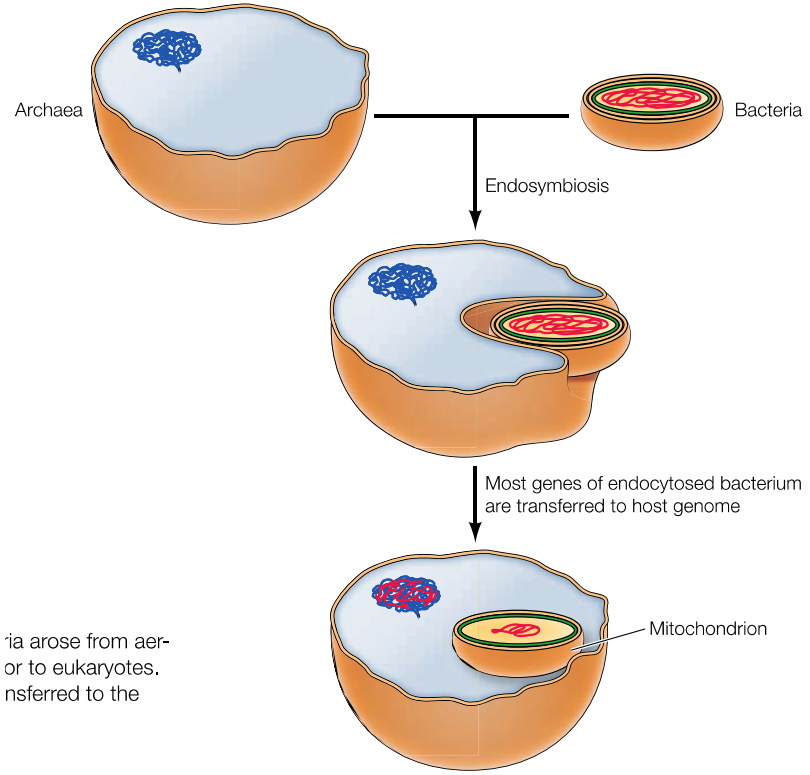
How?

- Both mitochondria and chloroplasts are similar to bacteria in size and, like bacteria, they reproduce by dividing in two.
- Mitochondria and chloroplasts contain their own genetic systems, which are distinct from the nuclear genome of the cell
- The sequence of genome is more closely related to the genomes of bacteria than to the nuclear genomes of eukaryotes.

Why?

- The acquisition of aerobic bacteria would have provided an anaerobic cell with the ability to carry out oxidative metabolism.
- The acquisition of photosynthetic bacteria would have provided the ability to perform photosynthesis, thereby affording nutritional independence.

Thus, these endosymbiotic associations were highly advantageous to their partners and were selected for in the course of evolution.



ia arose from aer-
or to eukaryotes.
nsferred to the

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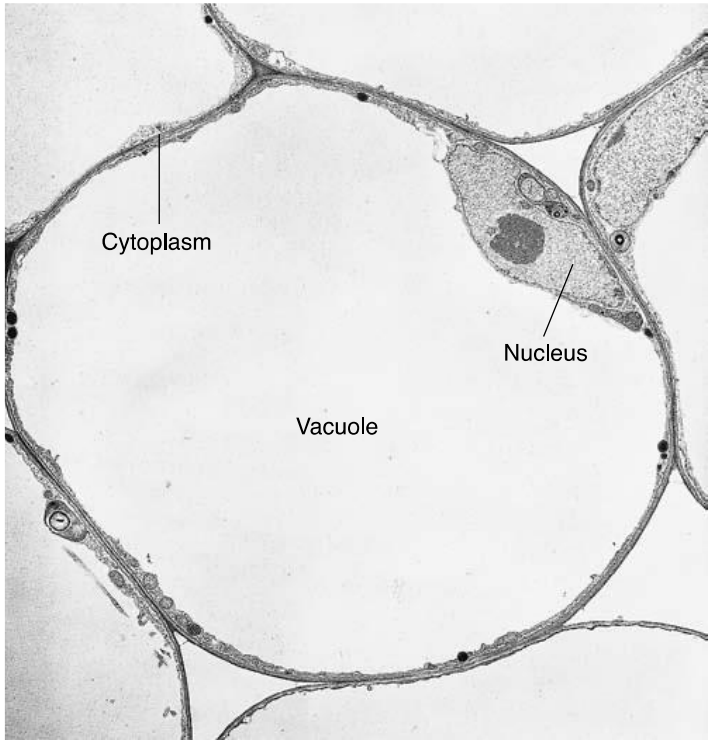
Vacuoles

Around 90 percent of the volume of many plant cells is occupied by a single membrane-bound, fluid-filled central **vacuole**.



Plant vacuoles carry out a wide spectrum of essential functions:

1. Many of a cell's solutes and macromolecules, including ions, sugars, amino acids, proteins, and polysaccharides, are stored temporarily in the vacuole.

2. **Vacuoles may also store a host of toxic compounds.** Some of these compounds (such as cyanide-containing glycosides) are part of an arsenal of chemical weapons that are released when the cell is injured by an herbivore or fungus.

   - Other toxic compounds are simply the by-products of metabolic reactions.

3. The membrane that surrounds the vacuole, the **tonoplast**, contains a number of active transport systems that pump ions into the vacuolar compartment to a concentration much higher than that in the cytoplasm or the extracellular fluid.

   - Because of its high ion concentration, water enters the vacuole by osmosis. Hydrostatic (turgor) pressure exerted by the vacuole not only provides mechanical support for the soft tissues of a plant, it also stretches the cell wall during cell growth.

4. Plant vacuoles are also sites of intracellular digestion, not unlike lysosomes, which are absent in plants.

Open Elective Subject

EBTY183L Biological Machines

(L-T-P = 3-0-0)

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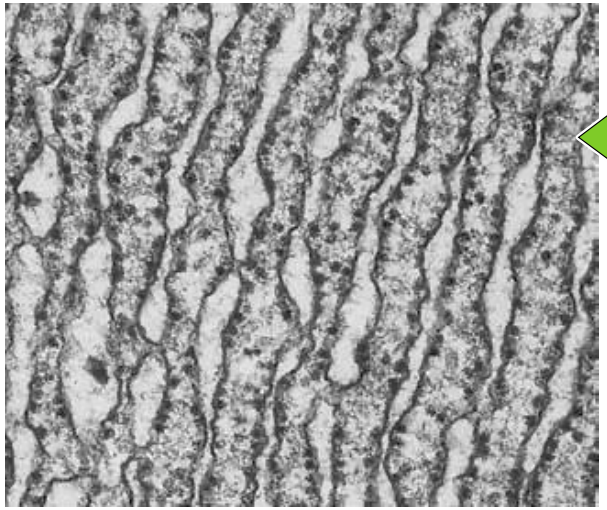
Lecture 6

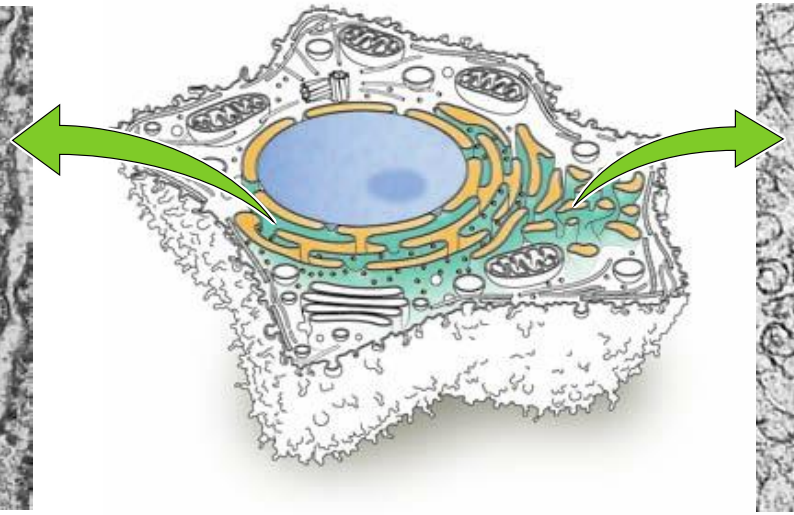
Dept of Biotechnology

Endoplasmic reticulum

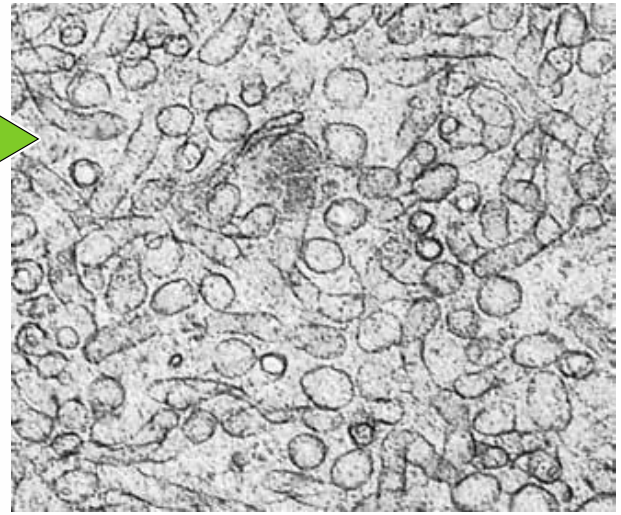
- The **endoplasmic reticulum (ER)** is a network of membrane-enclosed tubules and sacs (cisternae) that extends from the nuclear membrane throughout the cytoplasm.
- The entire ER is enclosed by a continuous membrane and is the largest organelle of most eukaryotic cells.
- Its membrane may account for about half of all cell membranes, and the space enclosed by the ER (the lumen, or cisternal space) may represent about 10% of the total cell volume.
- There are two contiguous membrane domains within the ER that perform different functions within the cell.
  - The **rough ER**, which is covered by ribosomes on its outer (cytosolic) surface, functions in protein processing.
  - The **smooth ER** is not associated with ribosomes and is involved in lipid, rather than protein, metabolism.

(A) Rough endoplasmic reticulum

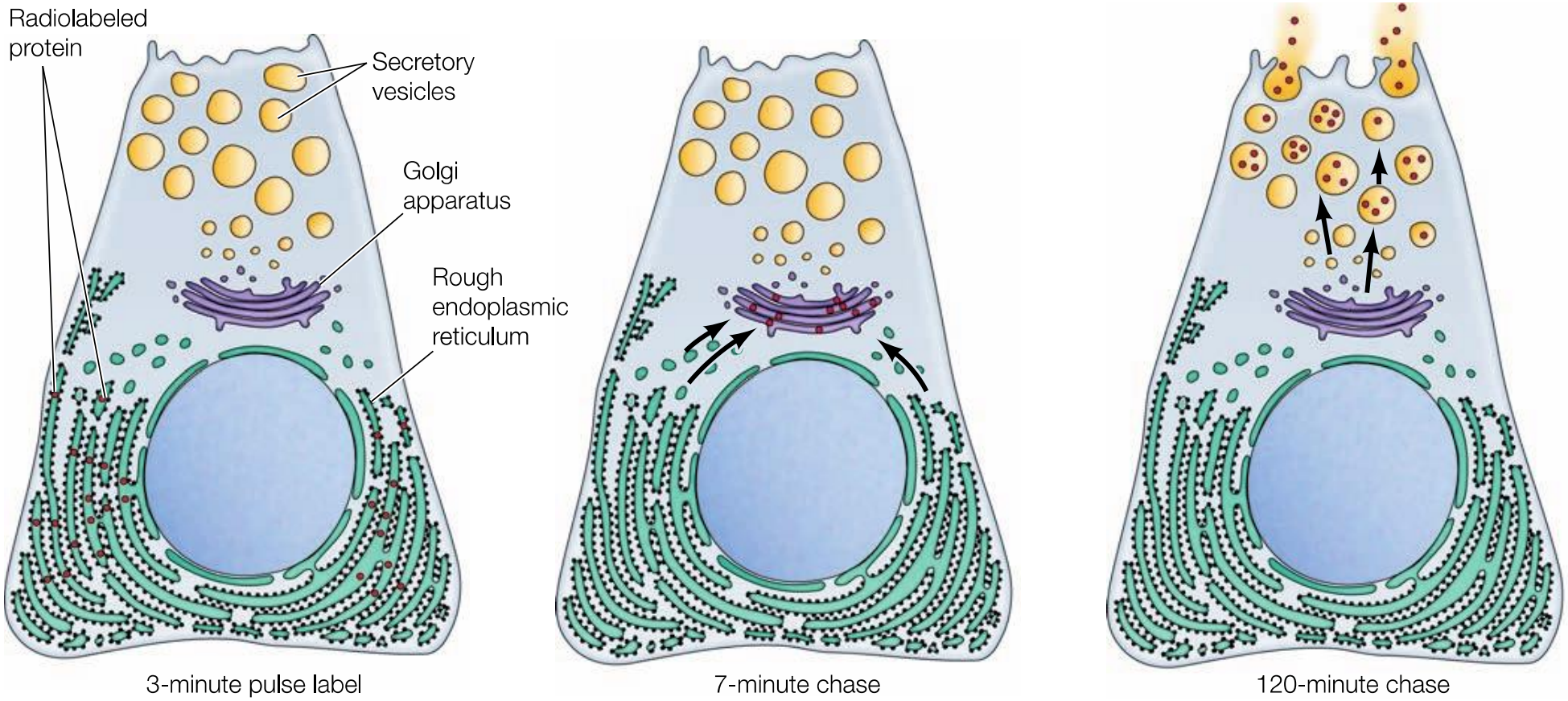




(B) Smooth endoplasmic reticulum

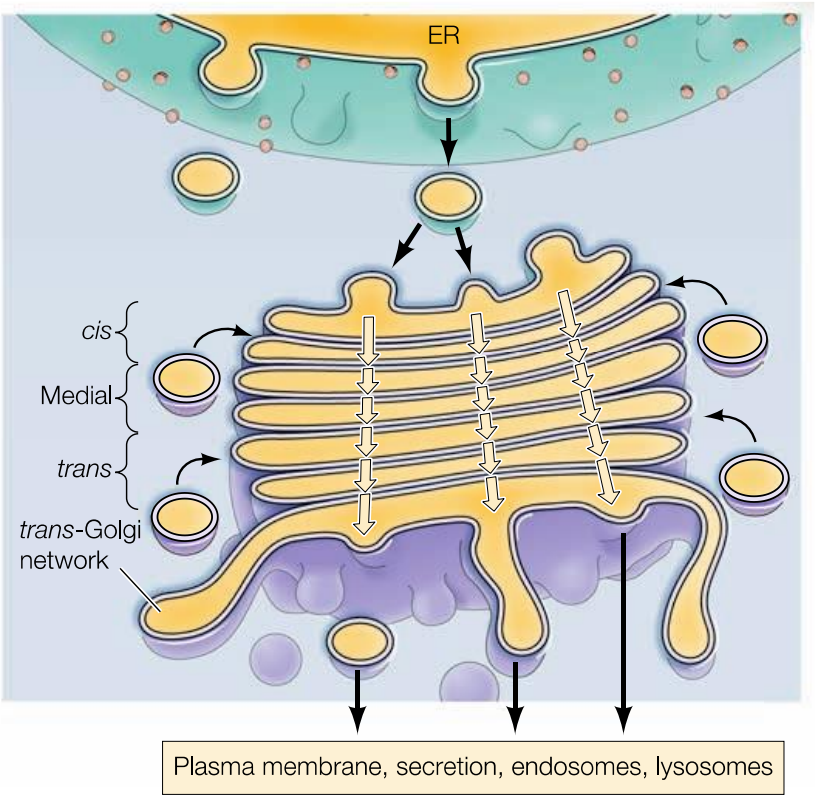


- **The rough ER is the starting point of the biosynthetic pathway: it is the site of synthesis of the proteins, carbohydrate chains, and phospholipids that journey through the membranous compartments of the cell.**
- **The role of the ER in protein processing and sorting was first demonstrated by George Palade and his colleagues in the 1960s.**
- They studied the fate of newly synthesized proteins in specialized cells of the pancreas (pancreatic acinar cells) that secrete digestive enzymes into the small intestine.



Golgi apparatus

- In 1898, Camillo Golgi applied a metallic stain to nerve cells from the cerebellum and discovered a darkly stained reticular network located near the cell nucleus.
- This network, which was later identified in other cell types and named the **Golgi complex**, helped earn its discoverer the Nobel Prize in 1906.
- The Golgi complex consists primarily of flattened, disklike, membranous cisternae with dilated rims and associated vesicles and tubules.
- The cisternae, whose diameters are typically 0.5 to 1.0 um, are arranged in an orderly stack, much like a stack of pancakes, and are curved so as to resemble a shallow bowl.
- Typically, a Golgi stack contains fewer than eight cisternae. An individual cell may contain from a few to several thousand distinct stacks, depending on the cell type.
- The Golgi complex is divided into several functionally distinct compartments arranged along an axis from the *cis* or entry face closest to the ER to the *trans* or exit face at the opposite end of the stack.
- The bulk of the Golgi complex consists of a series of large, flattened cisternae, which are divided into ***cis***, ***medial***, and ***trans*** **cisternae**.



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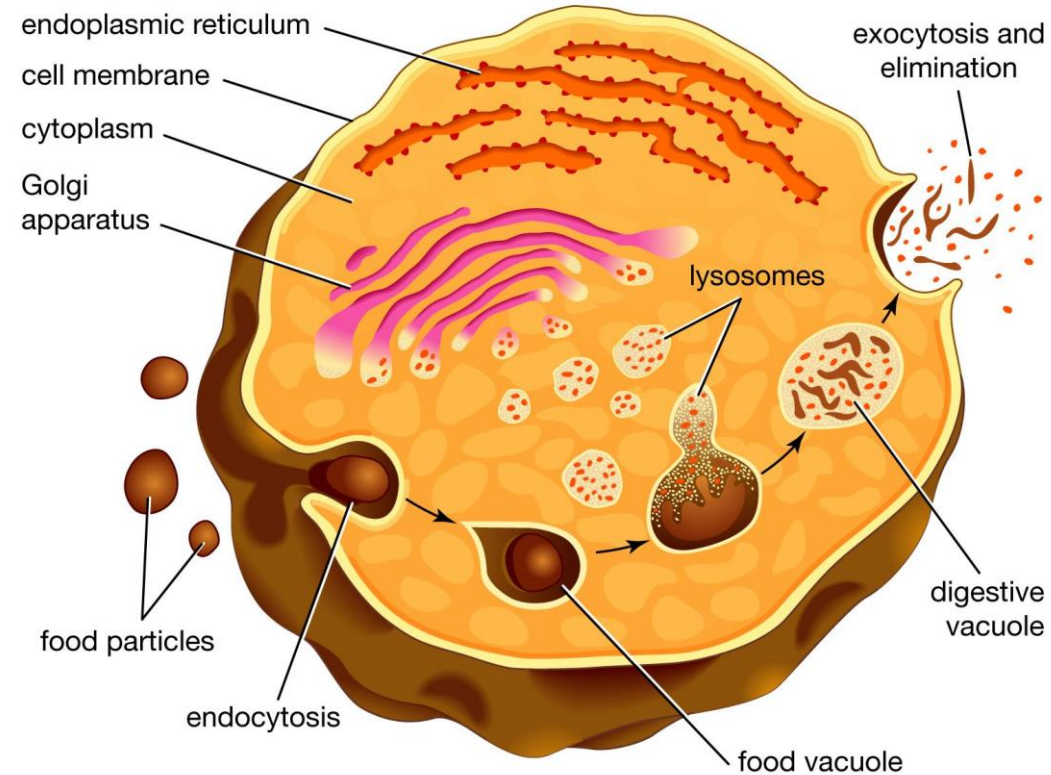
The SER is extensively developed in a number of cell types, including those of skeletal muscle, kidney tubules, and steroid-producing endocrine glands. SER functions include:

- Synthesis of steroid hormones in the endocrine cells of the gonad and adrenal cortex
- Detoxification in the liver of a wide variety of organic compounds, including barbiturates and ethanol
- Sequestering calcium ions within the cytoplasm of cells. The regulated release of Ca2+ from the SER of skeletal and cardiac muscle cells (known as the *sarcoplasmic reticulum* in muscle cells) triggers contraction.

Lysosomes

- Lysosomes are an animal cell's digestive organelles.
- A typical lysosome contains at least 50 different hydrolytic enzymes produced in the rough ER and targeted to these organelles.
- Lysosomal enzymes can hydrolyze virtually every type of biological macromolecule.
- The enzymes of a lysosome share an important property: all have their optimal activity at an acid pH and thus are **acid hydrolases**.
- The pH optimum of these enzymes is suited to the low pH of the lysosomal compartment, which is approximately 4.6.



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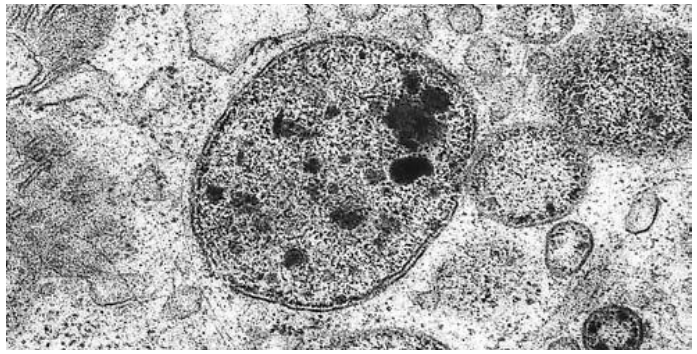


TABLE 8.1 A Sampling of Lysosomal Enzymes

Enzyme	Substrate
Phosphatases	
Acid phosphatase	Phosphomonoesters
Acid phosphodiesterase	Phosphodiesters
Nucleases	
Acid ribonuclease	RNA
Acid deoxyribonuclease	DNA
Proteases	
Cathepsin	Proteins
Collagenase	Collagen
GAG-hydrolyzing enzymes	
Iduronate sulfatase	Dermatan sulfate
β-Galactosidase	Keratan sulfate
Heparan *N*-sulfatase	Heparan sulfate
α-*N*-Acetylglucosaminidase	Heparan sulfate
Polysaccharidases and oligosaccharidases	
α-Glucosidase	Glycogen
Fucosidase	Fucosyloligosaccharides
α-Mannosidase	Mannosyloligosaccharides
Sialidase	Sialyloligosaccharides
Sphingolipid hydrolyzing enzymes	
Ceramidase	Ceramide
Glucocerebrosidase	Glucosylceramide
β-Hexosaminidase	G_{M2} ganglioside
Arylsulfatase A	Galactosylsulfatide
Lipid hydrolyzing enzymes	
Acid lipase	Triacylglycerols
Phospholipase	Phospholipids

Peroxisomes and Glyoxisomes

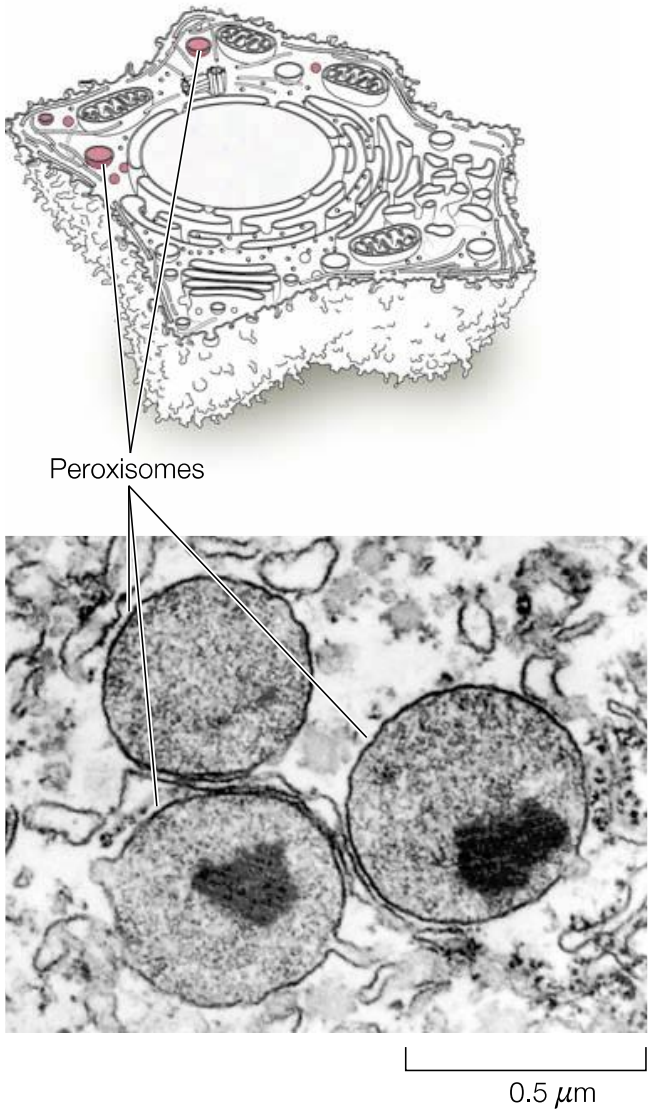
- Peroxisomes are small (0.1–1 μm), single-membrane-enclosed organelles that contain enzymes involved in a variety of metabolic reactions, including energy metabolism.
- Most human cells contain 100–1000 peroxisomes, depending on the metabolic activity of the cell.
- Peroxisomes do not have their own genomes and all their proteins are synthesized from the nuclear genome.

Similarity to mitochondria and chloroplasts

- Can replicate by division.

Difference:

- Single versus double membrane.
- While many mitochondrial proteins resemble those of prokaryotes, reflecting their endosymbiotic origin, the proteins of peroxisomes are typical eukaryotic proteins.



Human peroxisomes contain more than 50 different enzymes that play critical roles in several metabolic pathways, some of which are specific to particular tissues.

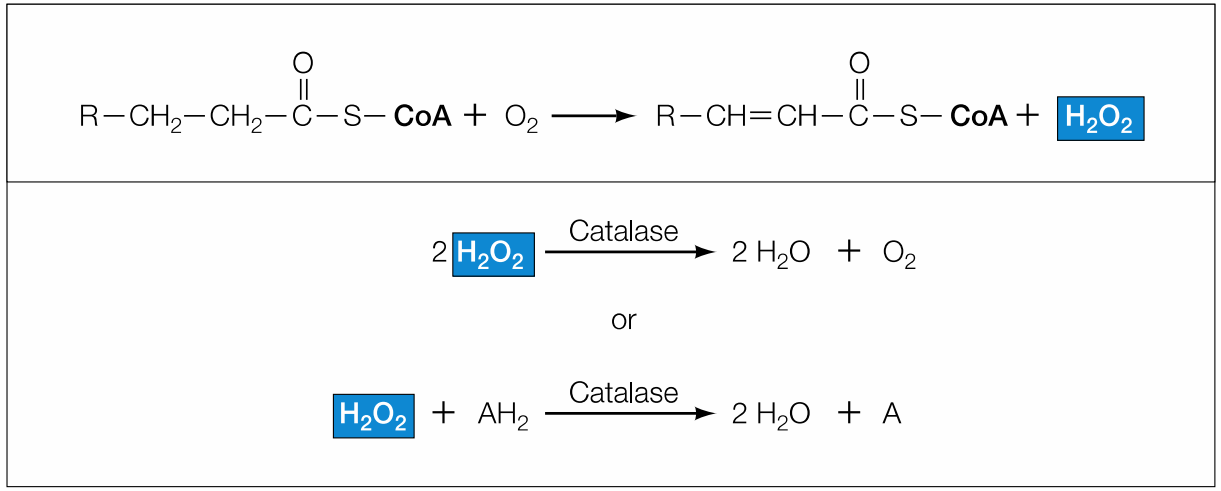
1. A variety of substrates are broken down by such oxidative reactions in peroxisomes, including uric acid, amino acids, purines, methanol, and fatty acids. The oxidation of fatty acids is a particularly important, since it provides a major source of metabolic energy.

2. Peroxisomes carry out oxidation reactions leading to the production of hydrogen peroxide.

3. H2O2 is harmful to the cell, peroxisomes also contain the enzyme **catalase**, which decomposes hydrogen peroxide either by converting it to water or by using it to oxidize another organic compound.

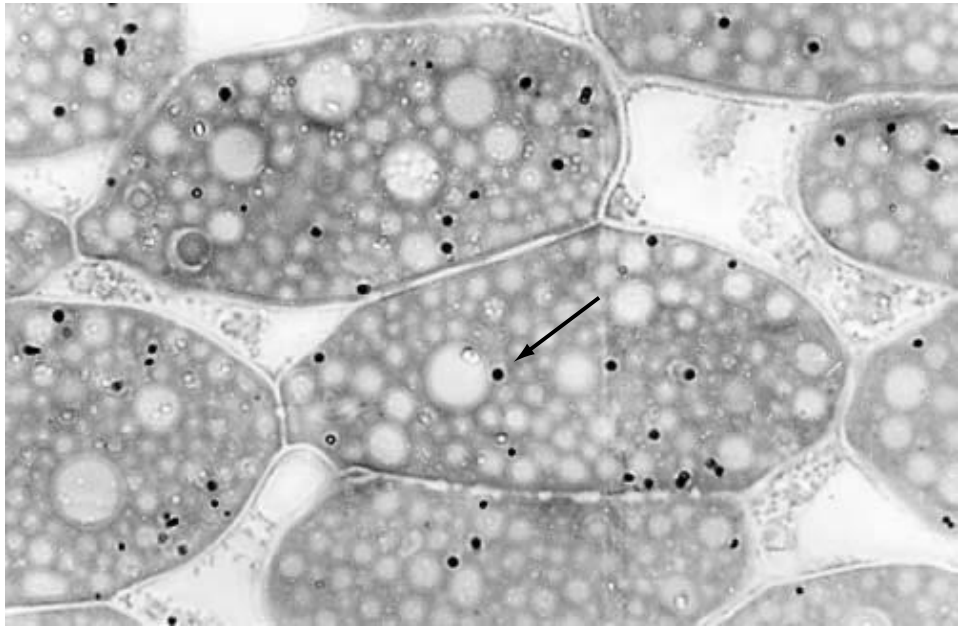
4. In addition to providing a compartment for oxidation reactions, peroxisomes are involved in biosynthesis of lipids.

5. Peroxisomes contain enzymes required for the synthesis of **plasmalogens**—a family of phospholipids in which one of the hydrocarbon chains is joined to glycerol by an ether bond rather than by an ester bond.



Glyoxisomes

- Peroxisomes are also present in plants.
- Plant seedlings contain a specialized type of peroxisome, called a **glyoxysome, that hydrolyze fatty acids.**
- Plant seedlings rely on stored fatty acids to provide the energy and material to form a new plant.
- One of the primary metabolic activities in these germinating seedlings is the conversion of stored fatty acids to carbohydrate.



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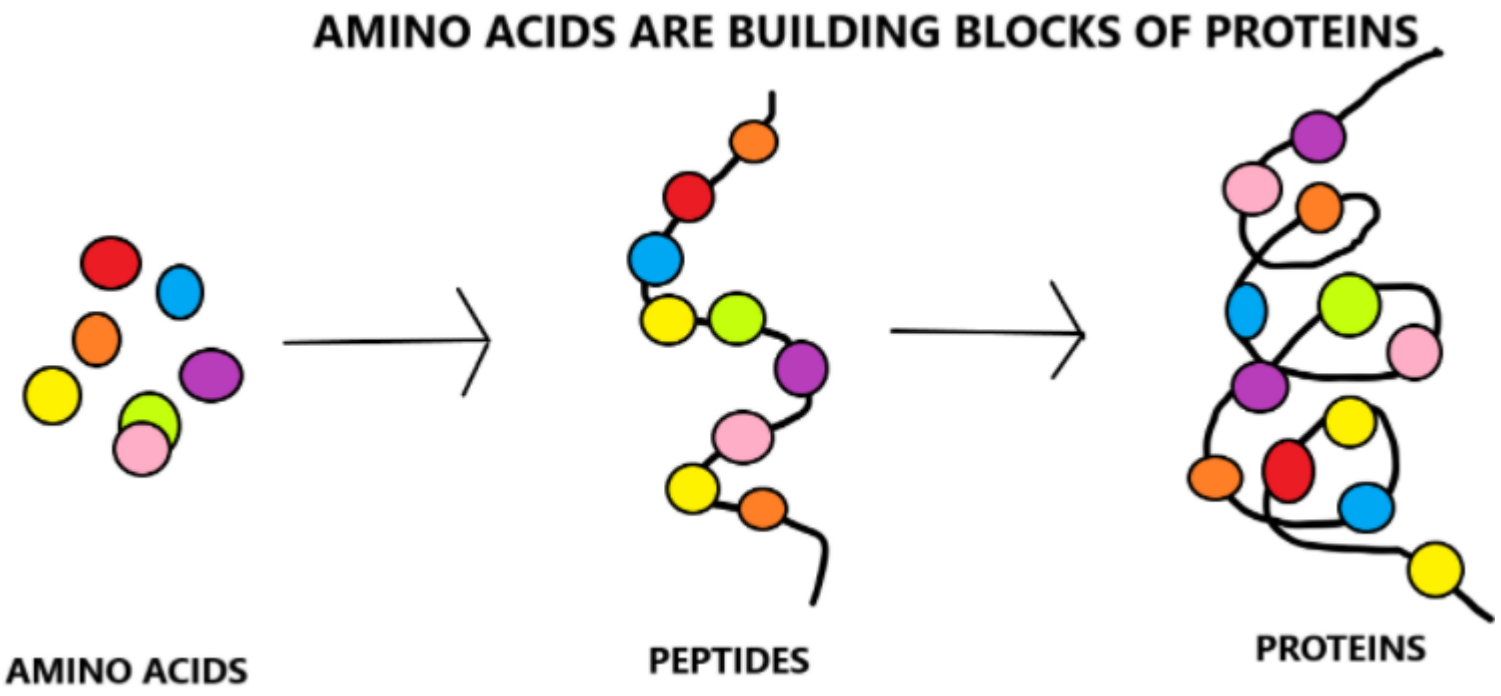
Lecture 7

Prof. N.Latha
Department of Biotechnology

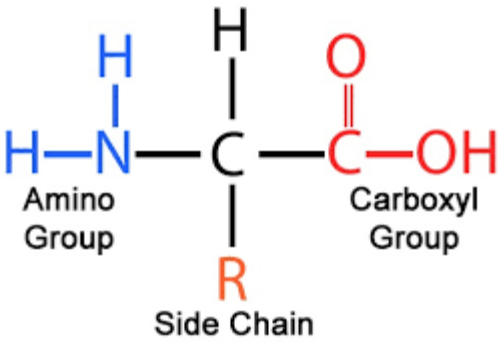
LECTURE 7

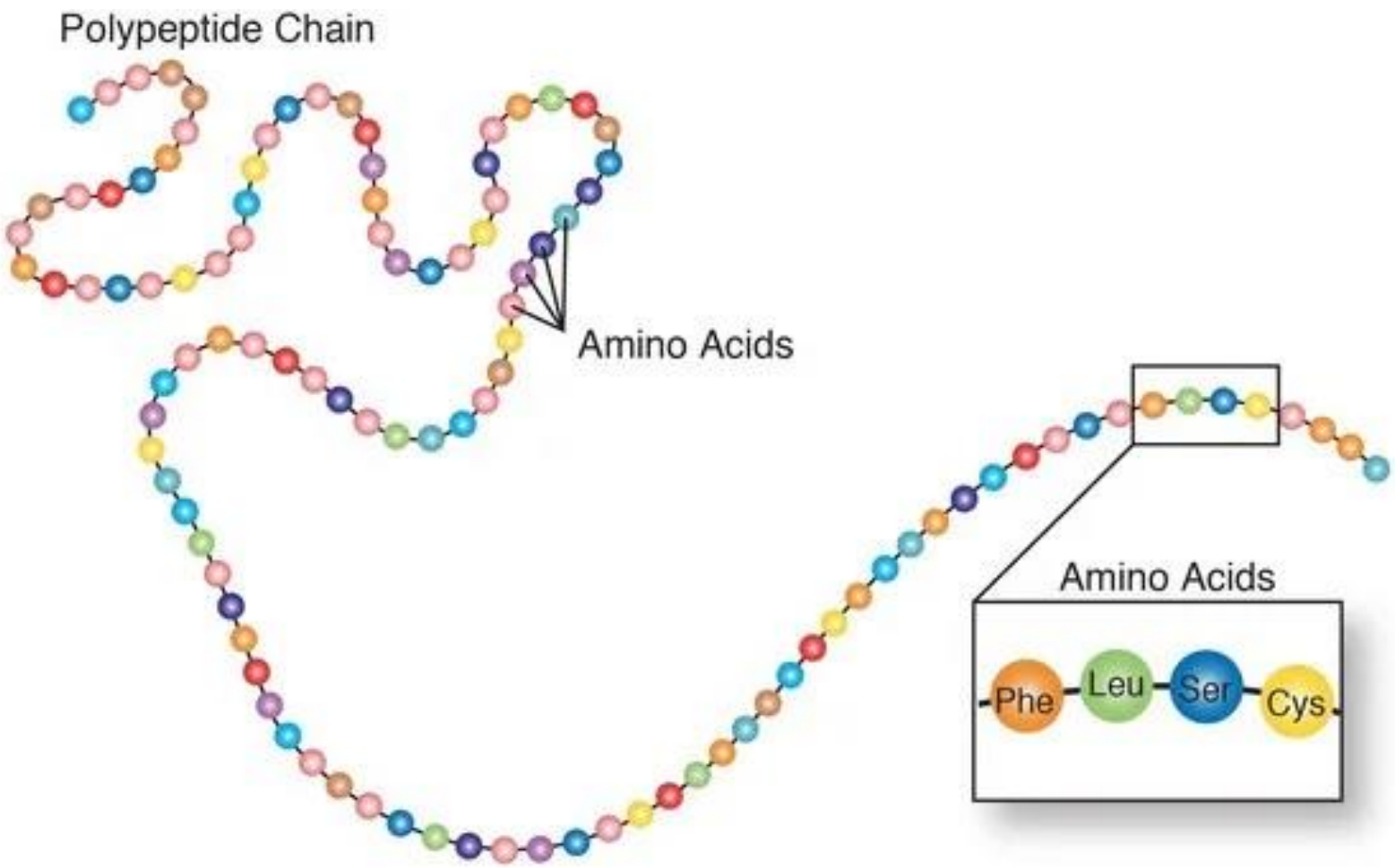
Introduction to amino acids and proteins



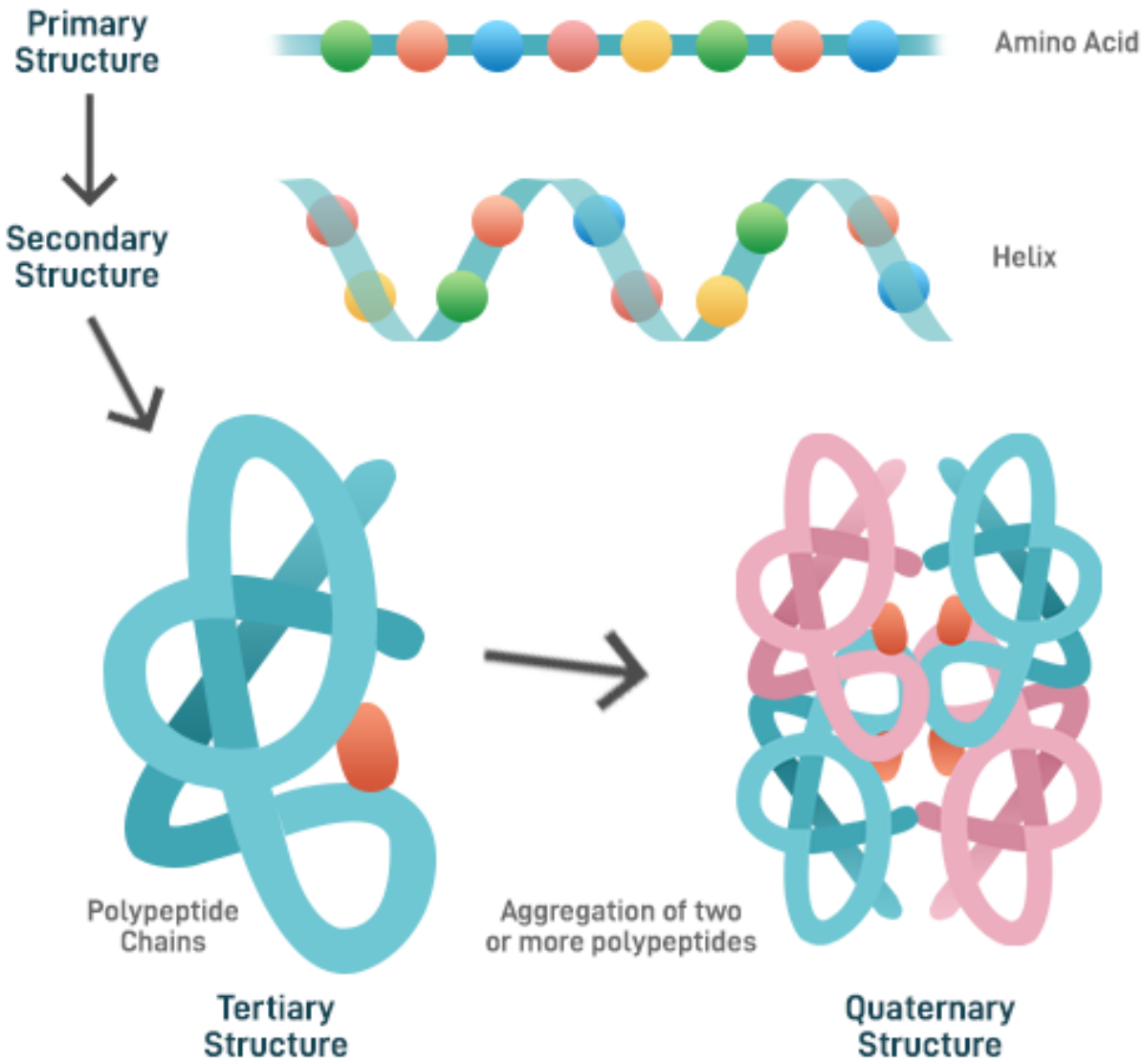
There are 20 naturally occurring amino acids

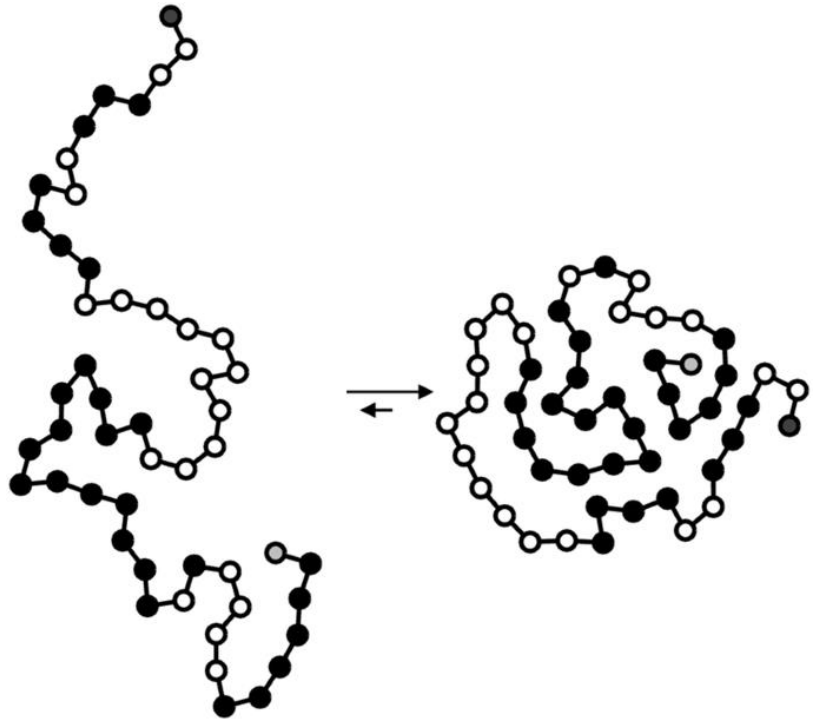
Amino-Acid	*3-Letter Name*	*Symbol*
Alanine	Ala	**A**
Arginine	Arg	**R**
Asparagine	Asn	**N**
Aspartic Acid	Asp	**D**
Asparagine or Aspartic Acid	Asx	**B**
Cysteine	Cys	**C**
Glutamine	Gln	**Q**
Glutamic Acid	Glu	**E**
Glutamine or Glutamic Acid	Glx	**Z**
Glycine	Gly	**G**
Histidine	His	**H**
Isoleucine	Ile	**I**
Leucine	Leu	**L**
Lysine	Lys	**K**
Methiodine	Met	**M**
Phenylalanine	Phe	**F**
Proline	Pro	**P**
Serine	Ser	**S**
Threonine	Thr	**T**
Tryptophan	Trp	**W**
Tyrosine	Tyr	**Y**
Valine	Val	**V**

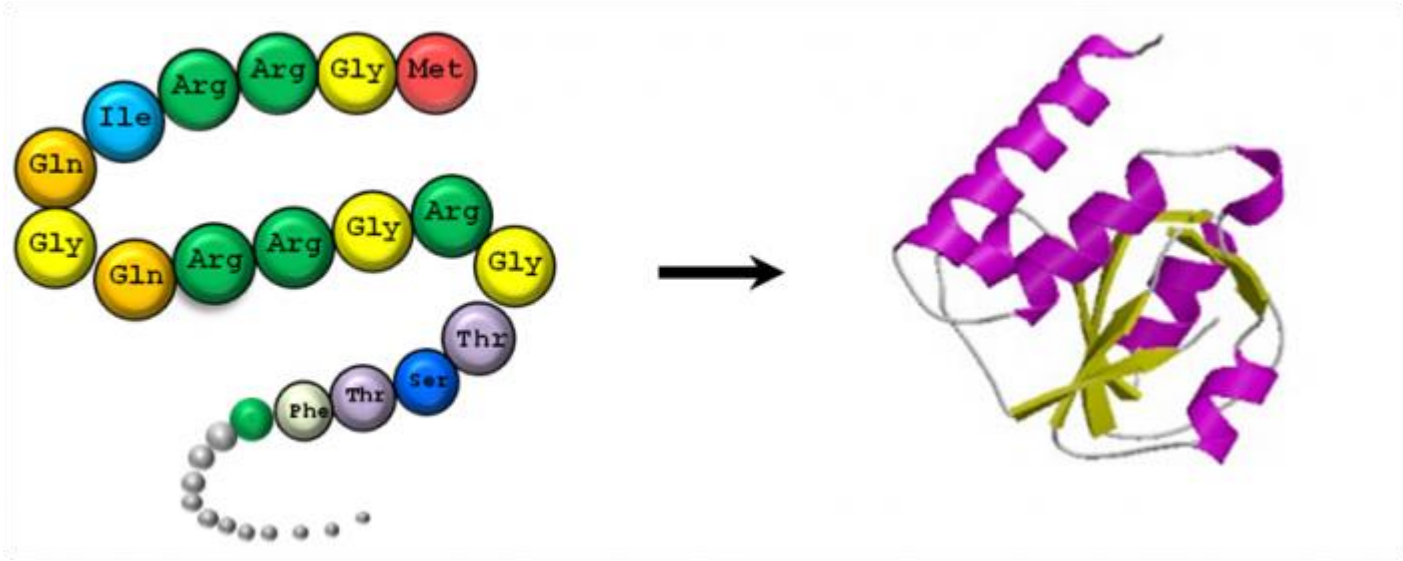



Polypeptide Chain
Amino Acids
Amino Acids
Phe
Leu
Ser
Cys

PROTEIN STRUCTURE






Met
Gly
Arg
Arg
Ile
Gln
Gly
Gln
Arg
Arg
Gly
Arg
Gly
Thr
Ser
Thr
Phe

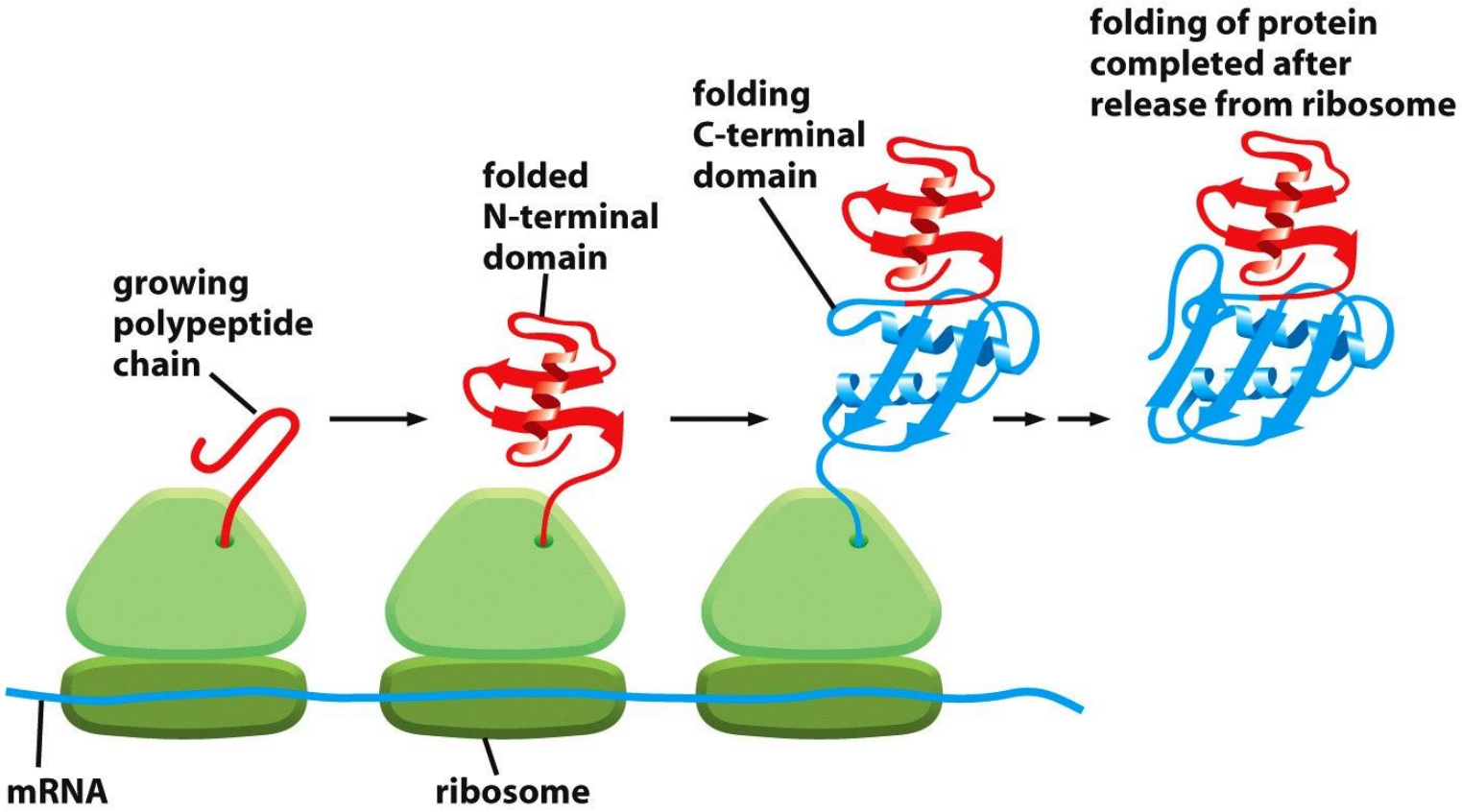
Mutation in protein sequence will change the shape of the protein

The Levinthal paradox

- Many proteins fold in seconds or less: how is this possible?
- Cyrus Levinthal tried to estimate how long it would take a protein to do a random search of conformational space for the native fold.
- Imagine a 100-residue protein with three possible conformations per residue. Thus, the number of possible folds = $3^{100} = 5 \times 10^{47}$.
- Let us assume that protein can explore new conformations at the same rate that bonds can reorient (10^{13} structures/second).
- Thus, the time to explore all of conformational space = $5 \times 10^{47}/10^{13} = 5 \times 10^{34}$ seconds = 1.6×10^{27} years >> age of universe
- This is known as the <u>Levinthal paradox</u>.

Protein Folding is not random hit & trial ,follows defined pathways

Co-translational protein folding



Some proteins begin to fold while still being synthesized.

Figure 6-84

How a protein folds into a compact conformation

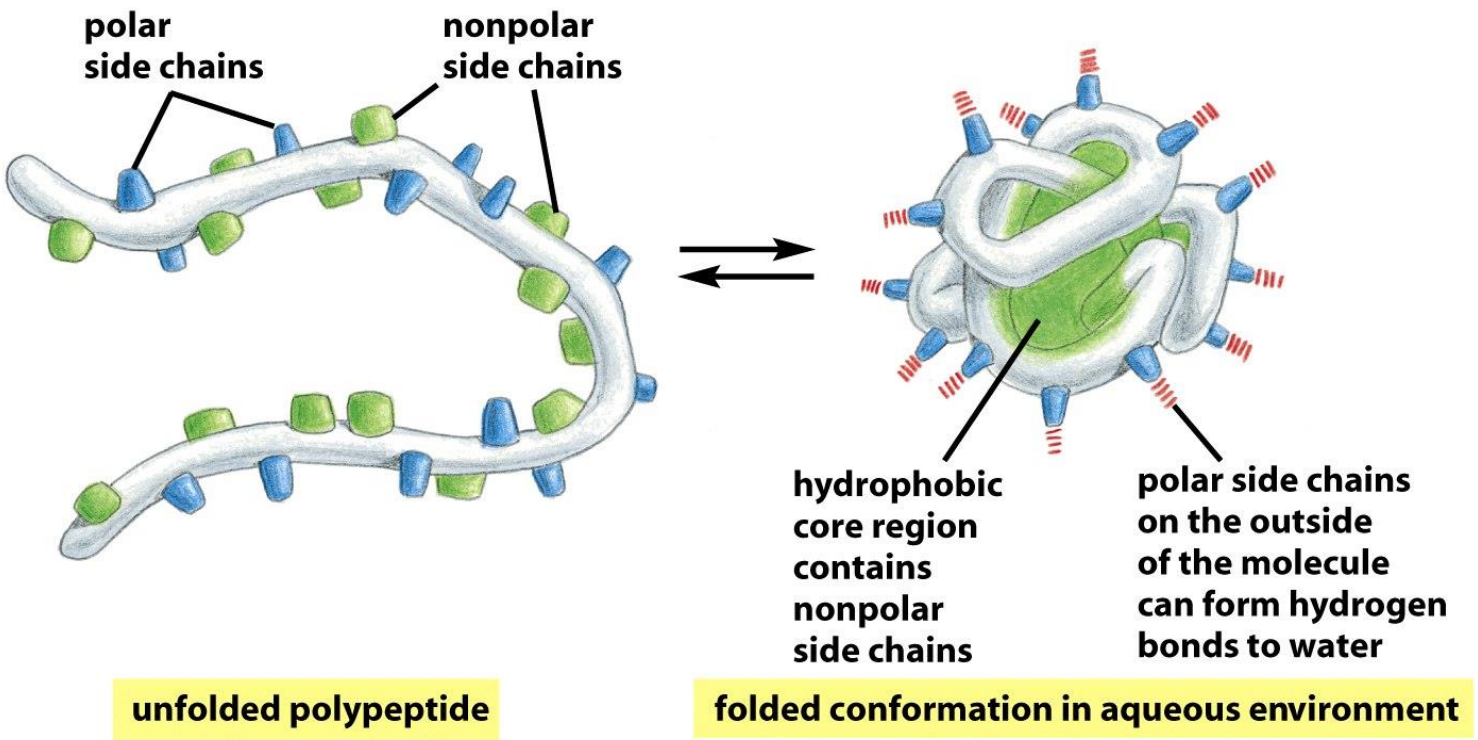


Figure 3-5

Three types of noncovalent bonds help proteins fold

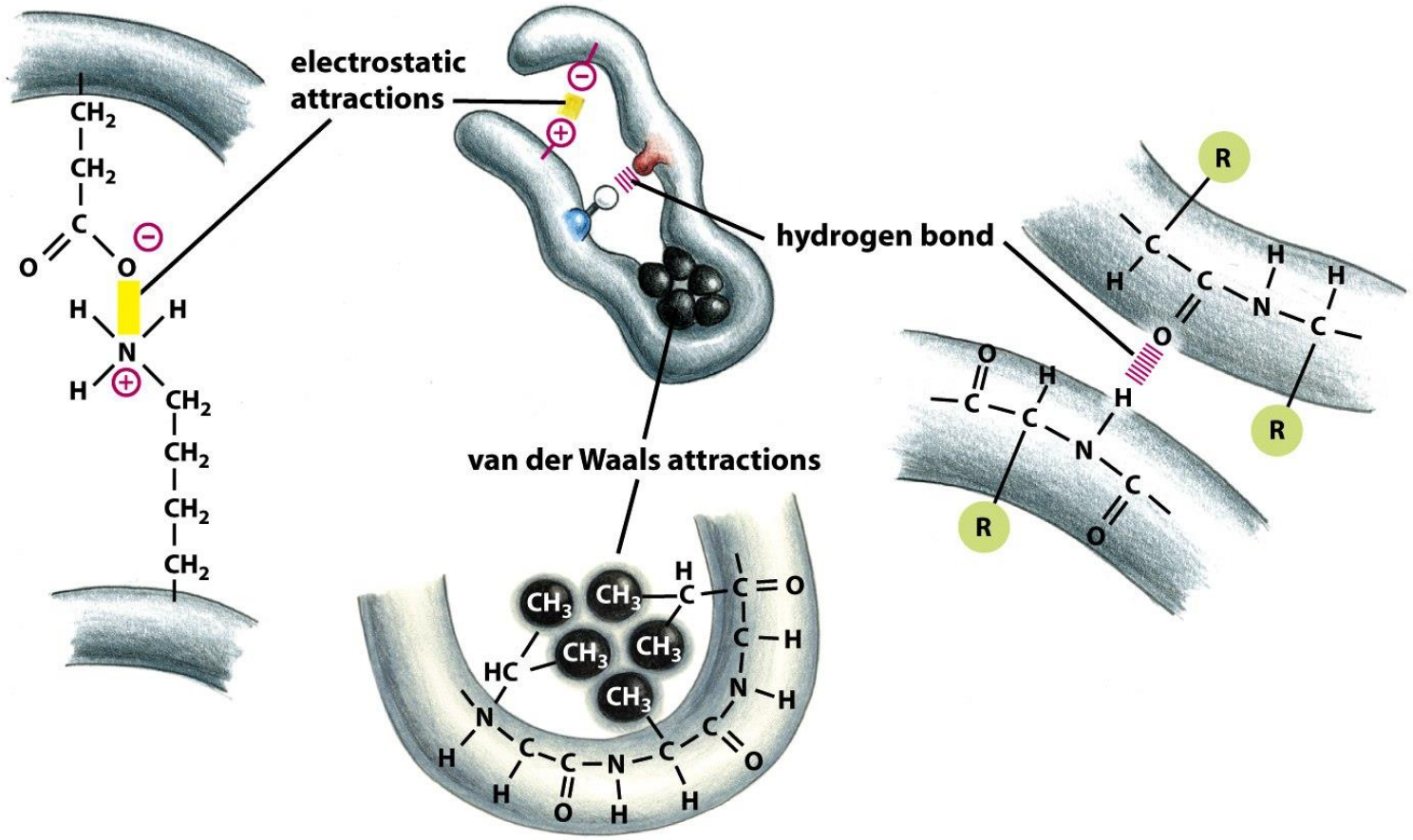


Figure 3-4

Protein Folding with Chaperons

* The production of a mature protein is a multistep process in eukaryotic cells.

* The final folded configuration, or shape, of a protein is determined by its amino acid sequence.

* Most proteins require the assistance of molecular chaperones, like Hsp70 & Hsp60, to reach their final folded form.

* These molecular chaperones bind to exposed hydrophobic patches on the surface of incompletely folded proteins.

* Hsp70 and Hsp60 act sequentially on proteins to help them achieve their correct folded state.

* Proteins that fail to be properly folded are ultimately targeted for destruction.

Potential fates of newly-synthesized proteins

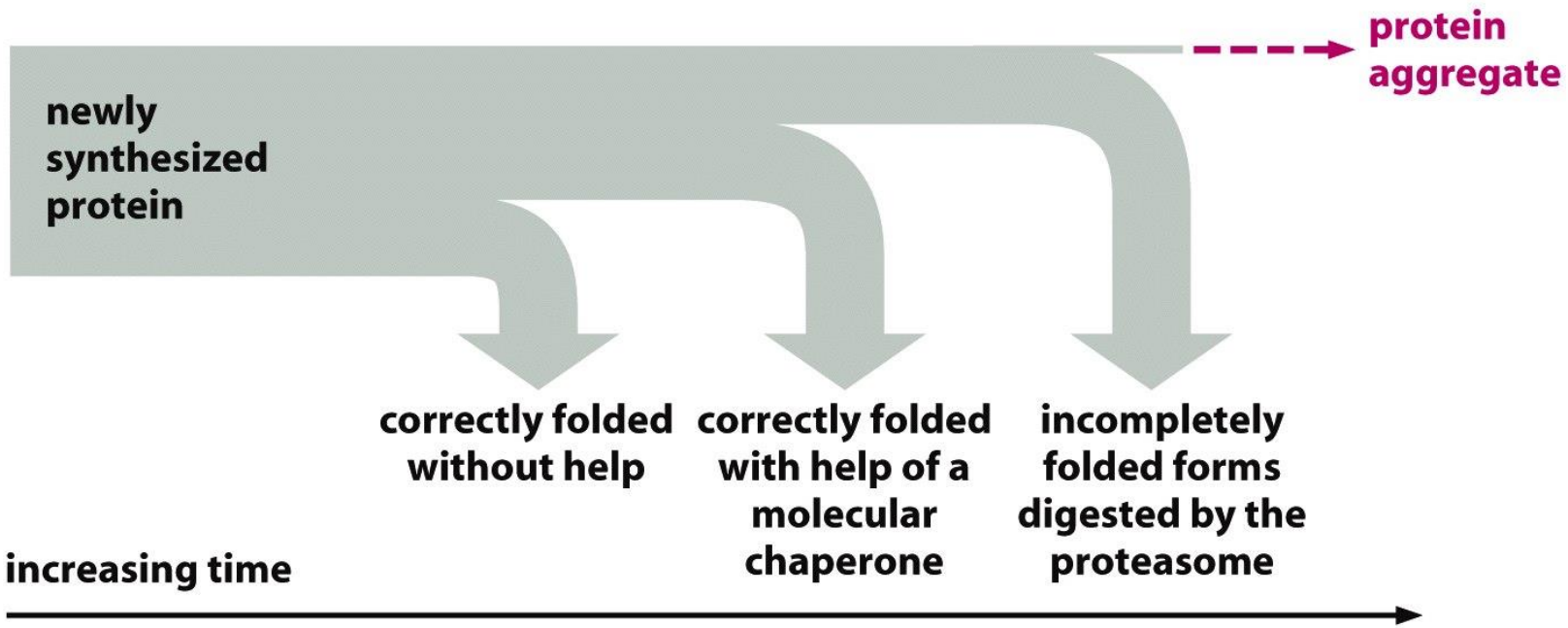
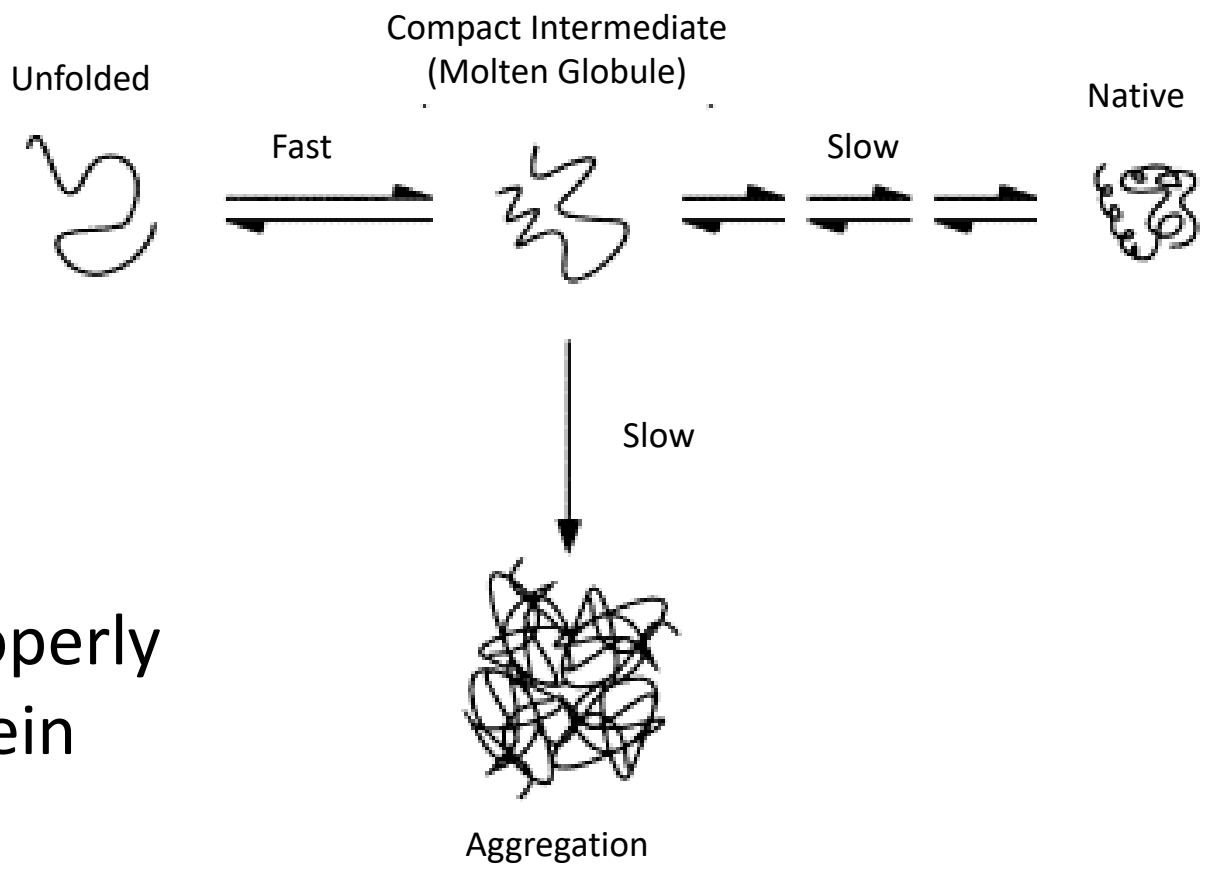


Figure 6-88 *Molecular Biology of the Cell* (© Garland Science 2008)



A failure to fold properly can lead to protein aggregation

Protein Misfolding Diseases (PMDs)

* Many inherited diseases result from mutant proteins that evade quality control processes, fold abnormally and ultimately form aggregates.

* The gradual decline of protein quality controls with age can also lead to disease by permitting normal proteins to form aggregates that can impair cellular functions.

* Many neurodegenerative diseases, including Huntington's and Alzheimer's, are associated with the presence of misfolded protein aggregates in neuronal tissue.

* The aggregates in patients can be intracellular (nuclear and/or cytoplasmic) or extracellular.

PROTEIN DISORDERS
(Module 3)

Protein Mutations – (1) Sickle cell anemia
(2) Cystic Fibrosis
(3) Progeria

Protein Metabolic Disorder
(1) Diabetes Mellitus

Protein Aggregates – (1) Alzheimer's
(2) Schizophrenia
(3) Parkinson Disease

Infectious Protein – (1) Prion
(2) Kuru