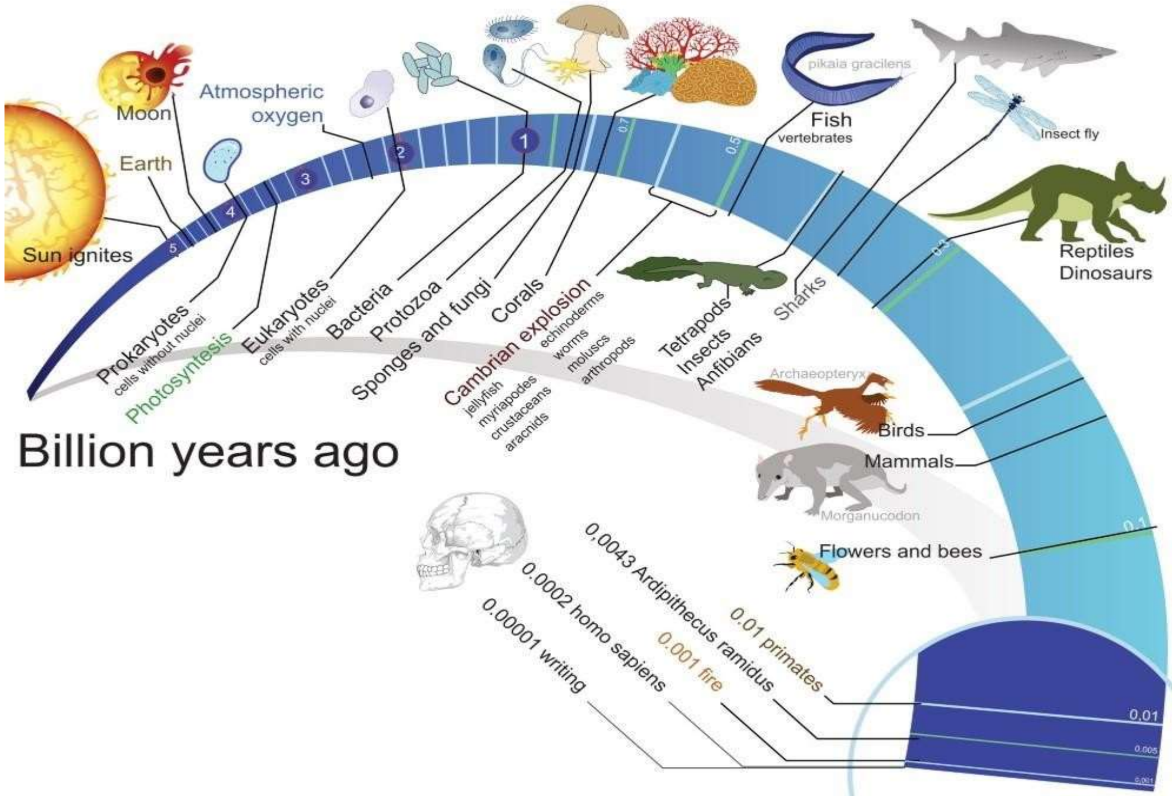
What is Science?

- Study of the **physical** and **natural world** using theoretical models and data from experiments or observations.

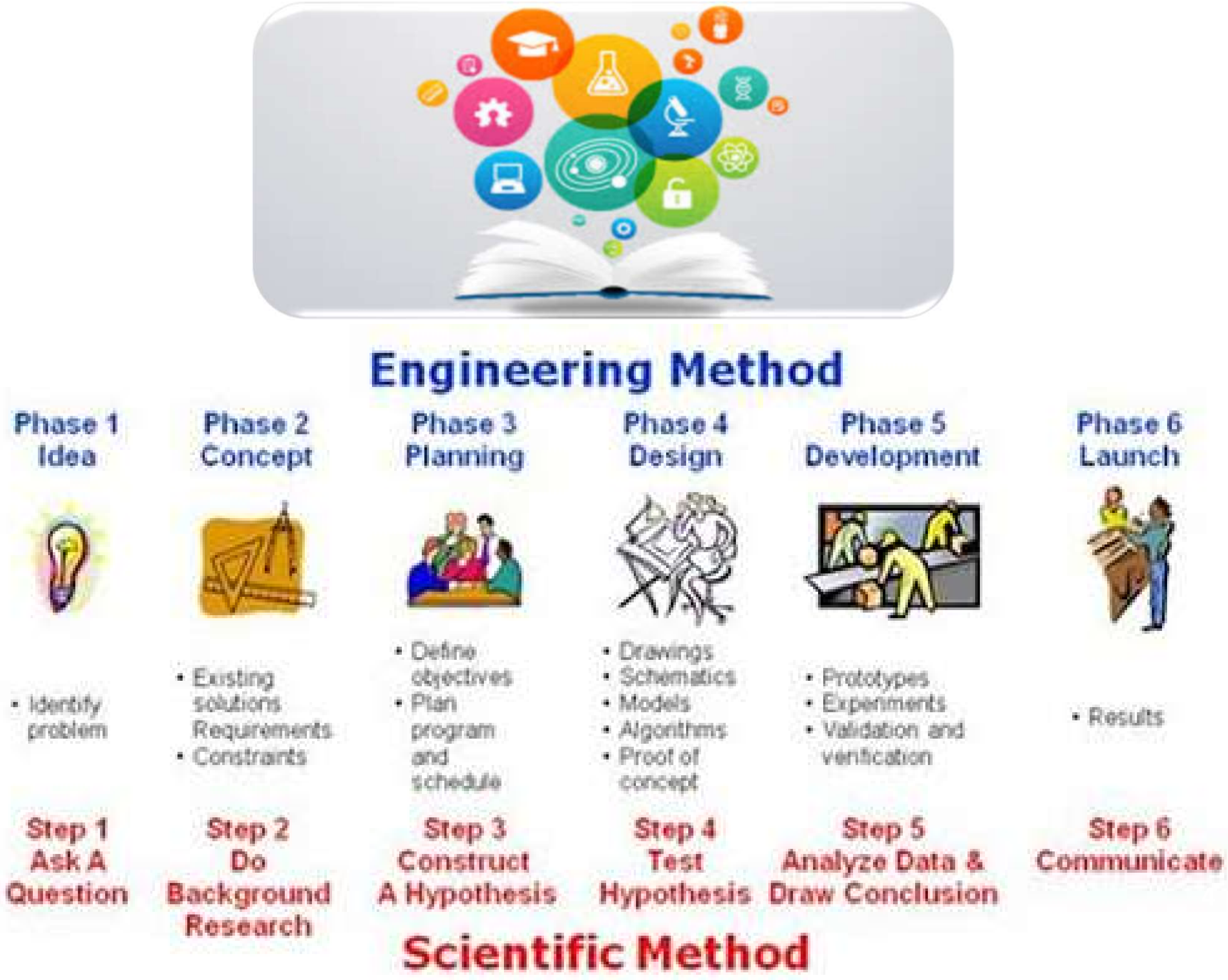
Why do you do Science?

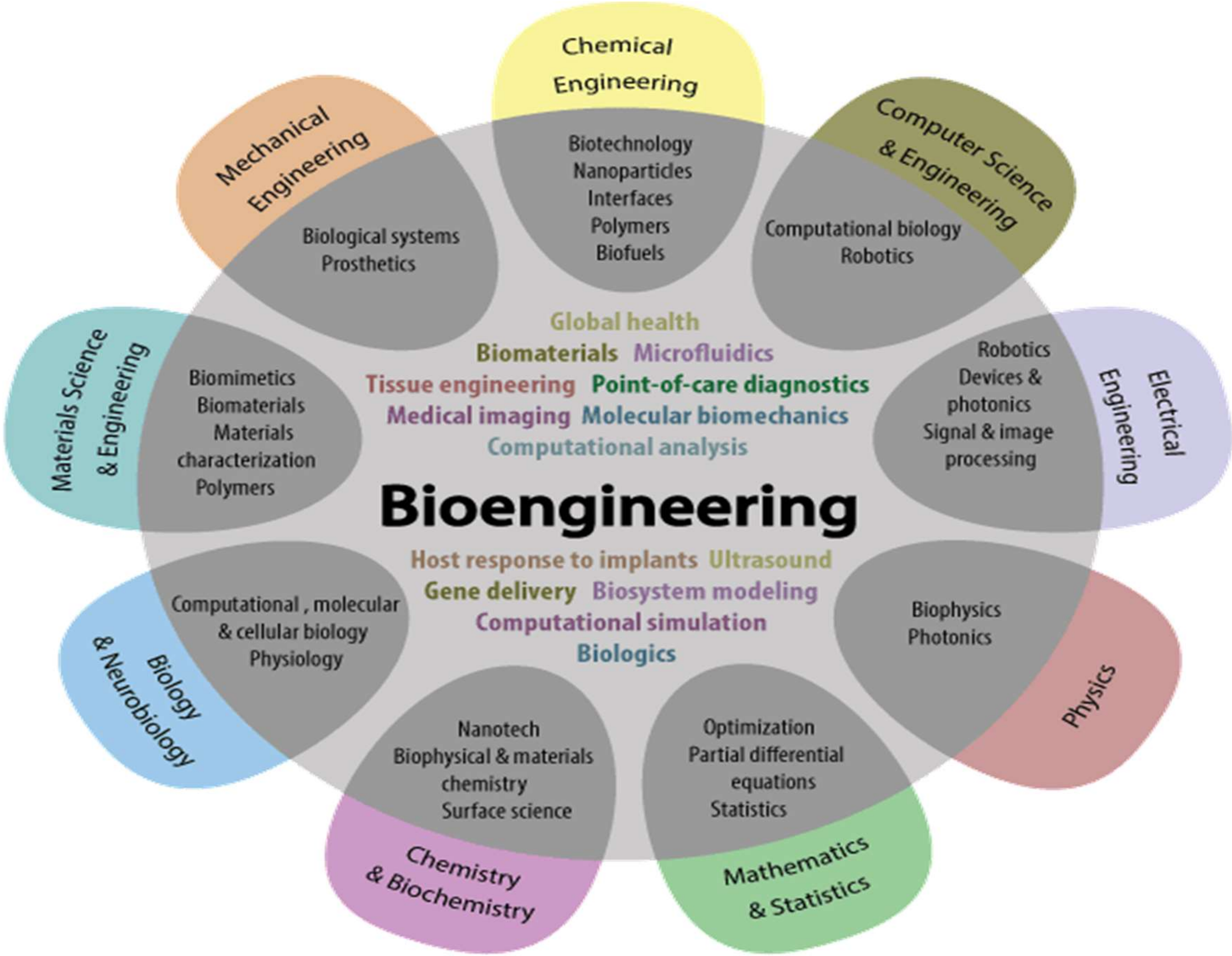
To understand the world better!



- The five **components** of the **scientific** method are:

  - ✓ Observations
  - ✓ Questions
  - ✓ Hypothesis
  - ✓ Methods
  - ✓ Results


Engineering Method
Phase 1
Idea
Phase 2
Concept
Phase 3
Planning
Phase 4
Design
Phase 5
Development
Phase 6
Launch
• Identify problem
• Existing solutions Requirements
• Constraints
• Define objectives
• Plan program and schedule
• Drawings
• Schematics
• Models
• Algorithms
• Proof of concept
• Prototypes
• Experiments
• Validation and verification
• Results
Step 1
Ask A Question
Step 2
Do Background Research
Step 3
Construct A Hypothesis
Step 4
Test Hypothesis
Step 5
Analyze Data & Draw Conclusion
Step 6
Communicate
Scientific Method


Bioengineering
Chemical Engineering
Biotechnology
Nanoparticles
Interfaces
Polymers
Biofuels
Mechanical Engineering
Biological systems
Prosthetics
Computer Science & Engineering
Computational biology
Robotics
Global health
Biomaterials
Microfluidics
Tissue engineering
Point-of-care diagnostics
Medical imaging
Molecular biomechanics
Computational analysis
Materials Science & Engineering
Biomimetics
Biomaterials
Materials characterization
Polymers
Electrical Engineering
Robotics
Devices & photonics
Signal & image processing
Host response to implants
Ultrasound
Gene delivery
Biosystem modeling
Computational simulation
Biologics
Biology & Neurobiology
Computational , molecular & cellular biology
Physiology
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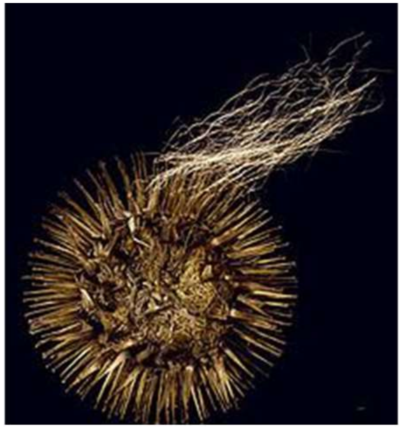
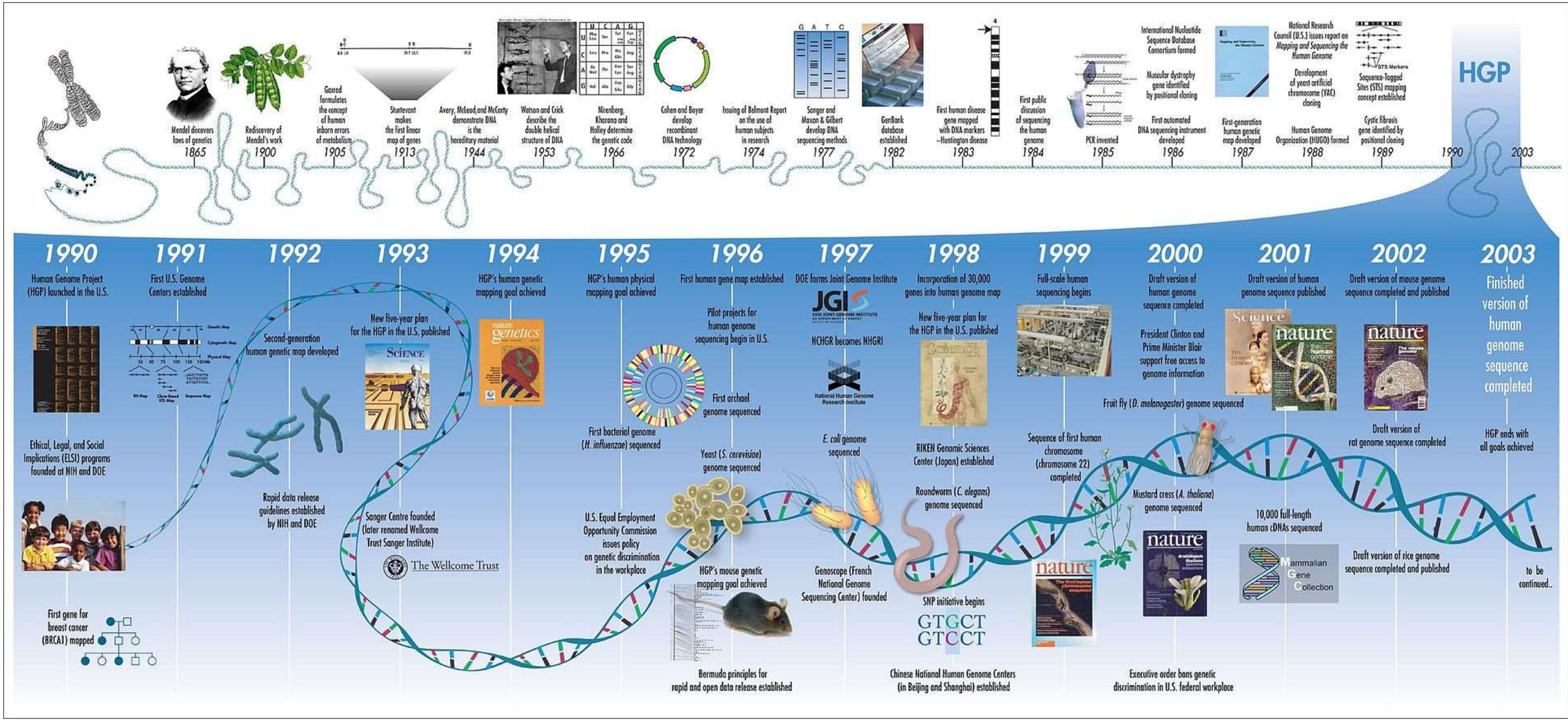
Biophysics
Photonics
Chemistry & Biochemistry
Nanotech
Biophysical & materials chemistry
Surface science
Mathematics & Statistics
Optimization
Partial differential equations
Statistics

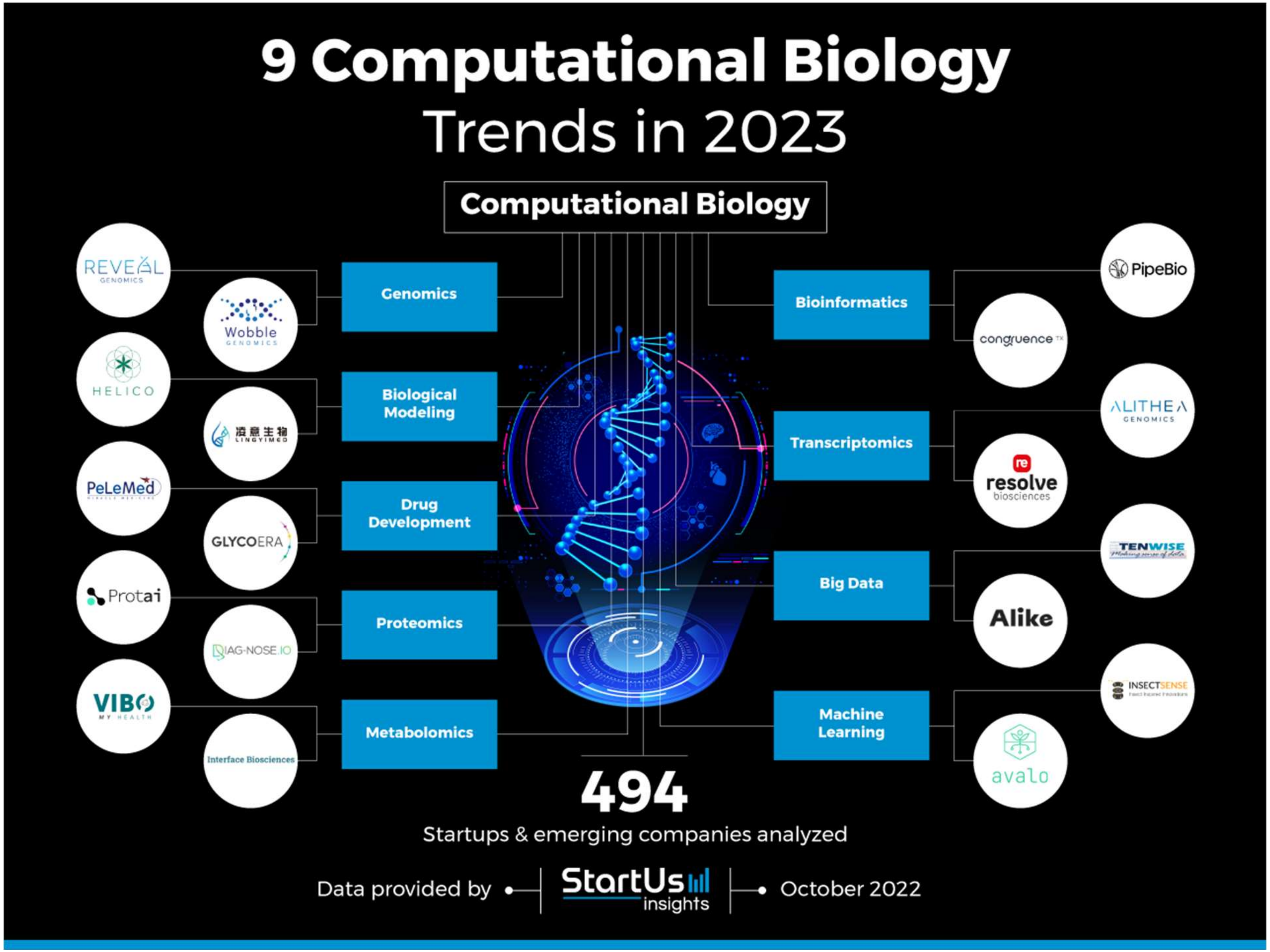


Velcro

Velcro fastening was invented in 1941 by Swiss engineer George de Mestral, who took the idea from the burrs that stuck to his dog's hair. Under the microscope he noted the tiny hooks on the end of the burr's spines that caught anything with a loop - such as clothing, hair or animal fur. The 2-part Velcro fastener system uses strips or patches of a hooked material opposite strips or patches of a loose-looped weave of nylon that holds the hooks.

HUMAN GENOME PROJECT





9 Computational Biology
Trends in 2023
Computational Biology
Genomics
Biological Modeling
Drug Development
Proteomics
Metabolomics
Bioinformatics
Transcriptomics
Big Data
Machine Learning
REVEAL GENOMICS
Wobble GENOMICS
HELICO
凌意生物 LINGYIMED
PeLeMed
GLYCOERA
Protai
DIAG-NOSE.IO
VIBO MY HEALTH
Interface Biosciences
PipeBio
congruence
ALITHEA GENOMICS
resolve biosciences
TENWISE
Alike
INSECTSENSE
avalo
494
Startups & emerging companies analyzed
Data provided by
StartUs insights
October 2022

Computational biology

Anne Carpenter, a computational biologist and senior director of the Imaging Platform of the Broad Institute of MIT and Harvard. She developed **CellProfiler**, a widely used open-source software for measuring phenotypes (sets of observable traits) from cell images. It has been cited in more than 12,000 publications since its release in 2005.

https://www.youtube.com/watch?v=KDQFUmDJ3nY

https://www.youtube.com/watch?v=gFuEo2ccTPA – Introduction to cells

https://www.youtube.com/watch?v=URUJD5NEXC8 - Biology of cell structure

1 metre = 100 cm

1 cm = 10 mm

1mm = 1000 micrometers (μm)

1 μm = 1000 nanometers (nm)

1 nanometer = 1000 picometers (pm)

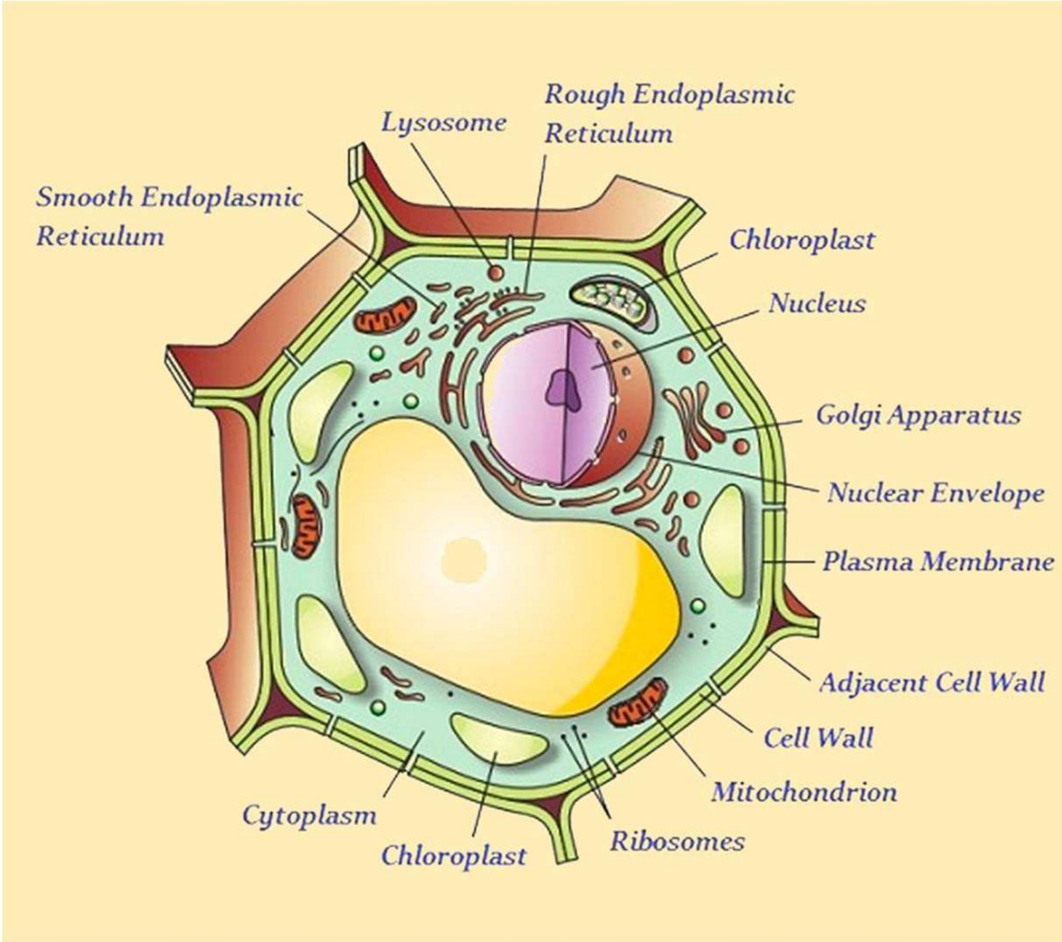
1 picometer = 1000 femtometers (fm)

UNIT - 1

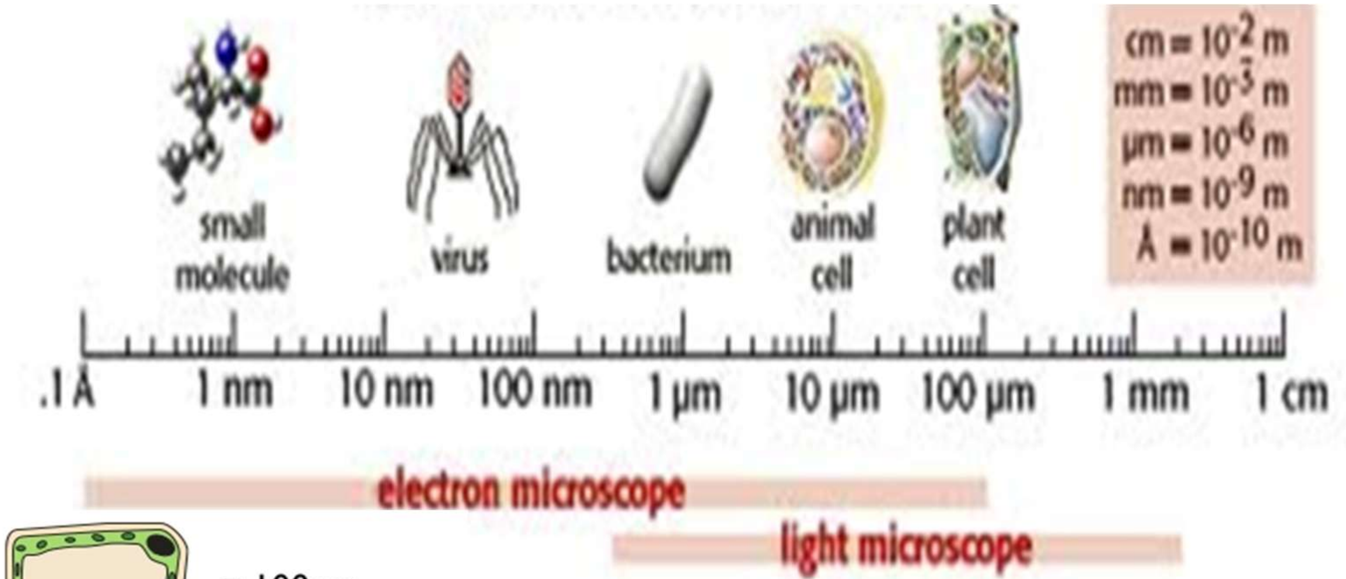
THE FACTS OF LIFE

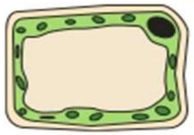
Cell : The Unit of Life

- The smallest functional unit of life is cell, discovered by Robert Hooke in 1665.
- A cell can independently perform all necessary activities to sustain life. Hence cell is the basic unit of life.
- There are two types of cells → plant cell and animal cell.
- Cells have different organelles, each one with a distinct function.
- Size of cells vary greatly
- Generally small and seen only with microscope



Relative sizes of the cells



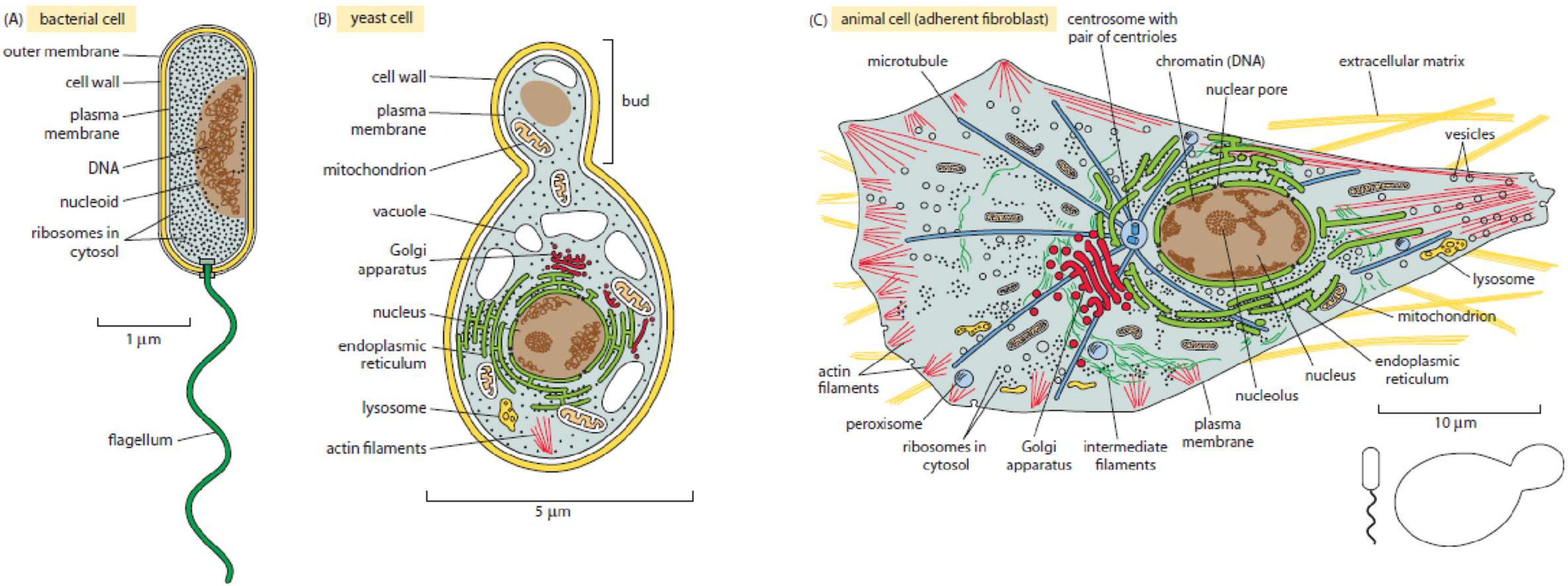
Plant Cell  = 100µm

Animal Cell  = 10µm

Bacteria  = 1µm

Virus  = 50 - 100nm

Size and Geometry of cells

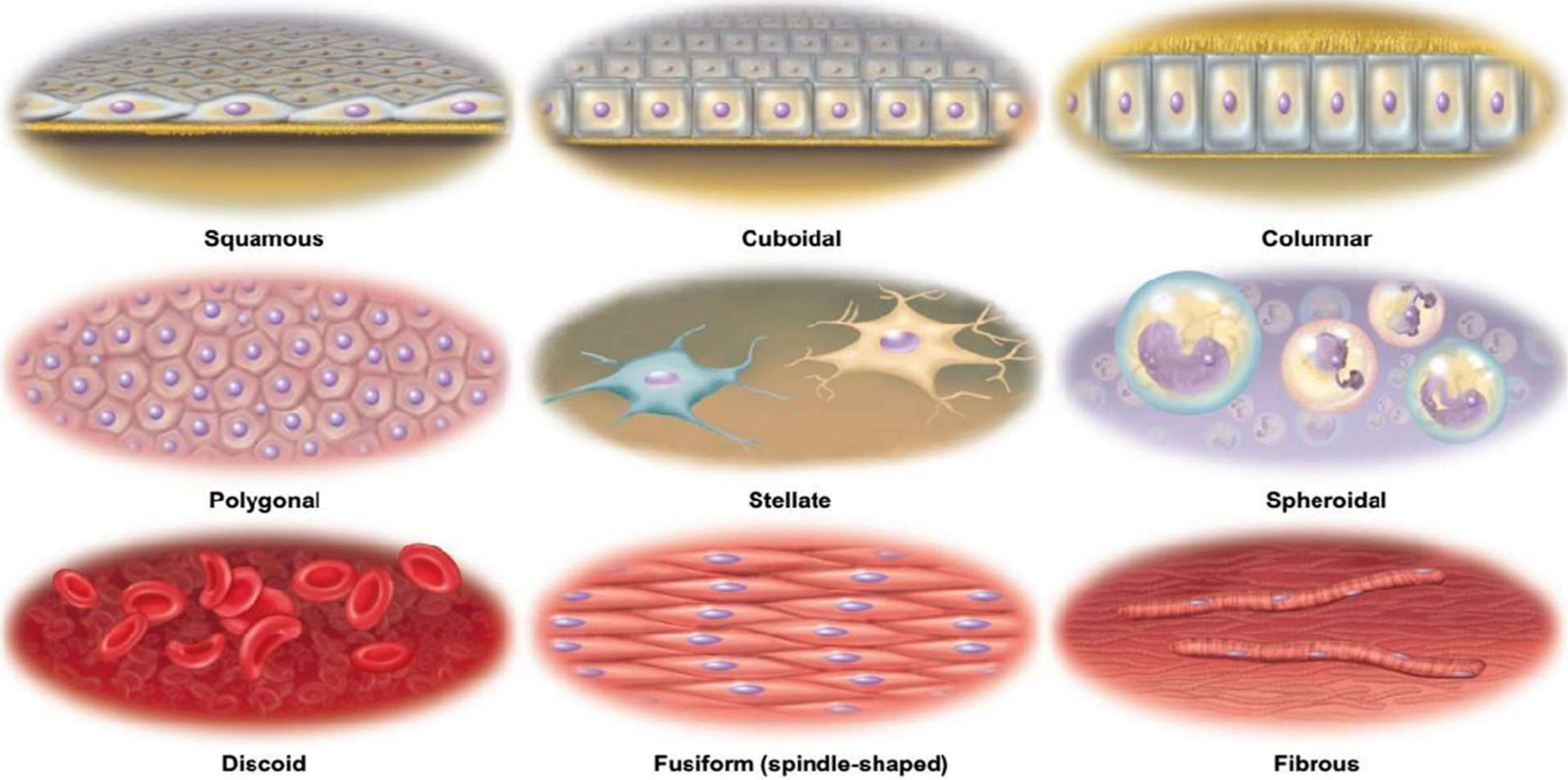


The standard cells. (A) A schematic bacterium revealing the characteristic size and components of *E. coli*. (B) A budding yeast cell showing its characteristic size, its organelles, and various classes of molecules present within it. (C) An adherent human cell. (adapted from Alberts B, Johnson A, Lewis J et al. [2015] Molecular Biology of the Cell, 6th ed. Garland Science.)

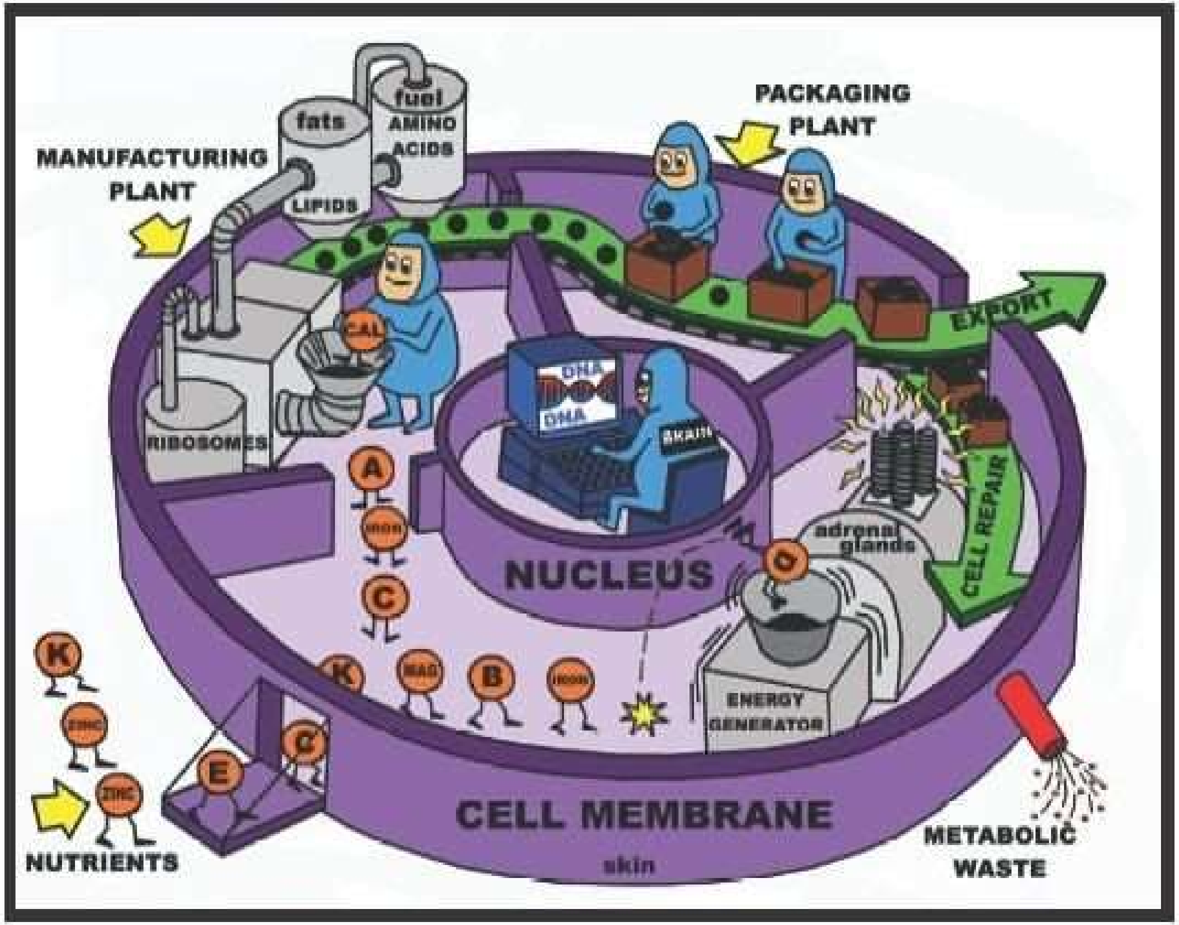
Both plant and animal cells show diverse shapes such as –

Cell	Shape	Function
Human Red Blood Carpuscles	circular and biconcave	to pass through narrow capillaries and transport oxygen.
White Blood Carpuscles	amoeboid with pseudopodia so that it can change shape.	to engulf the foreign microorganisms that enter in the body.
Nerve cells	long and elongated	to conduct impulse from distant parts of the body to the brain and vice-versa.
Muscle cells	long, spindle shape, contractile	to pull or squeeze the parts.
Guard cells (Stomata)	bean shaped	to open or close the pores.

Cell Shapes and Sizes



Cells as Chemical Factories



media-cache-ec0.pinimg.com

Cells get raw materials — including water, oxygen, minerals and other nutrients — from the foods. Nutrients are transported through the cell membrane: the thin, elastic structure that forms the border of each cell.

● Nucleus - it controls cell function. It contains DNA (deoxyribonucleic acid), the master organizer for how cells work.

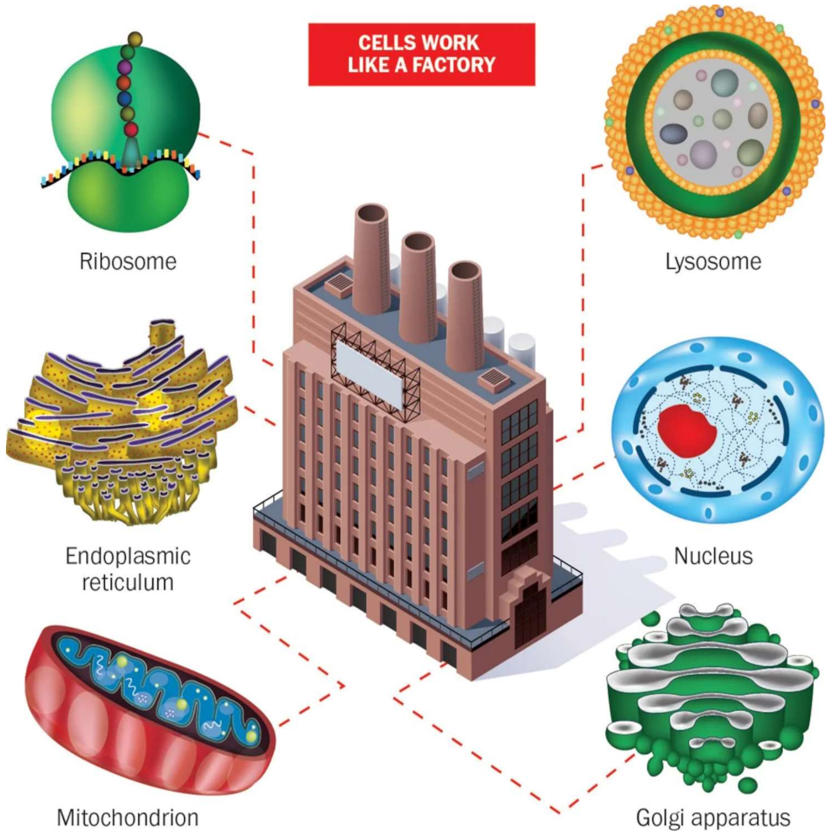
● Mitochondria are the "batteries" in your cells. Chemical reactions within the mitochondria create the energy that powers cell functions.

● Lysosomes are fluid-filled vesicles, or sacs, that act as a waste-disposal system for cells.

● Ribosomes are the cell's molecule makers. They assemble proteins from amino acids.

● The endoplasmic reticulum is a system of tubelike structures that's essential for the production of proteins and lipids (fats).

● The Golgi apparatus is like a conveyor belt that "wraps" proteins inside vesicles so they can be "shipped" out of the cell.



(iStock images/The Washington Post illustration)

Cell Organelles/Compartments -

Plasma membrane – Boundary, Protection and transport

Nucleus - hereditary data essential for multiplication and cell development.

Endoplasmic Reticulum & Golgi apparatus- Protein processing and Lipid biosynthesis

Mitochondria - Energy factories of cells

Lysosomes - digest undesirable materials present in the cell

Chloroplast (only Plant cells) – Photosynthesis

Ribosomes – Protein synthesis

Cell Theory

Cells were discovered in 1665 by Robert Hooke.

Early studies of cells were conducted by

- Mathias Schleiden (1838)
- Theodor Schwann (1839)

Schleiden and Schwann proposed the Cell Theory.

Cell Theory

Cell Theory

1. All organisms are composed of cells.
2. Cells are the smallest living things.
3. Cells arise only from pre-existing cells.

All cells today represent a continuous line of descent from the first living cells.

Cell Theory

Microscopes are required to visualize cells.

Cell size is limited.

-As cell size increases, it takes longer for material to diffuse from the cell membrane to the interior of the cell.

Light microscopes can resolve structures that are 200nm apart.

Electron microscopes can resolve structures that are 0.2nm apart.

Cell Theory

All cells have certain structures in common.

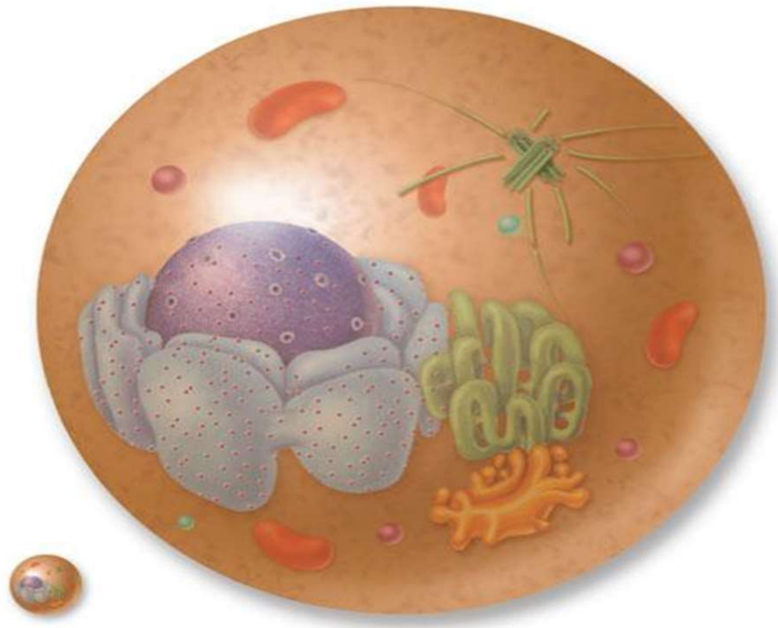
1. genetic material – in a nucleoid or nucleus
2. cytoplasm – a semifluid matrix
3. plasma membrane – a phospholipid bilayer

Why are cells so small?

- Cells need to produce chemical energy (via metabolism) to survive and this requires the exchange of materials with the environment
- The *rate of metabolism* of a cell is a function of its <u>mass / volume</u> (larger cells need more energy to sustain essential functions)
- The *rate of material exchange* is a function of its <u>surface area</u> (large membrane surface equates to more material movement)

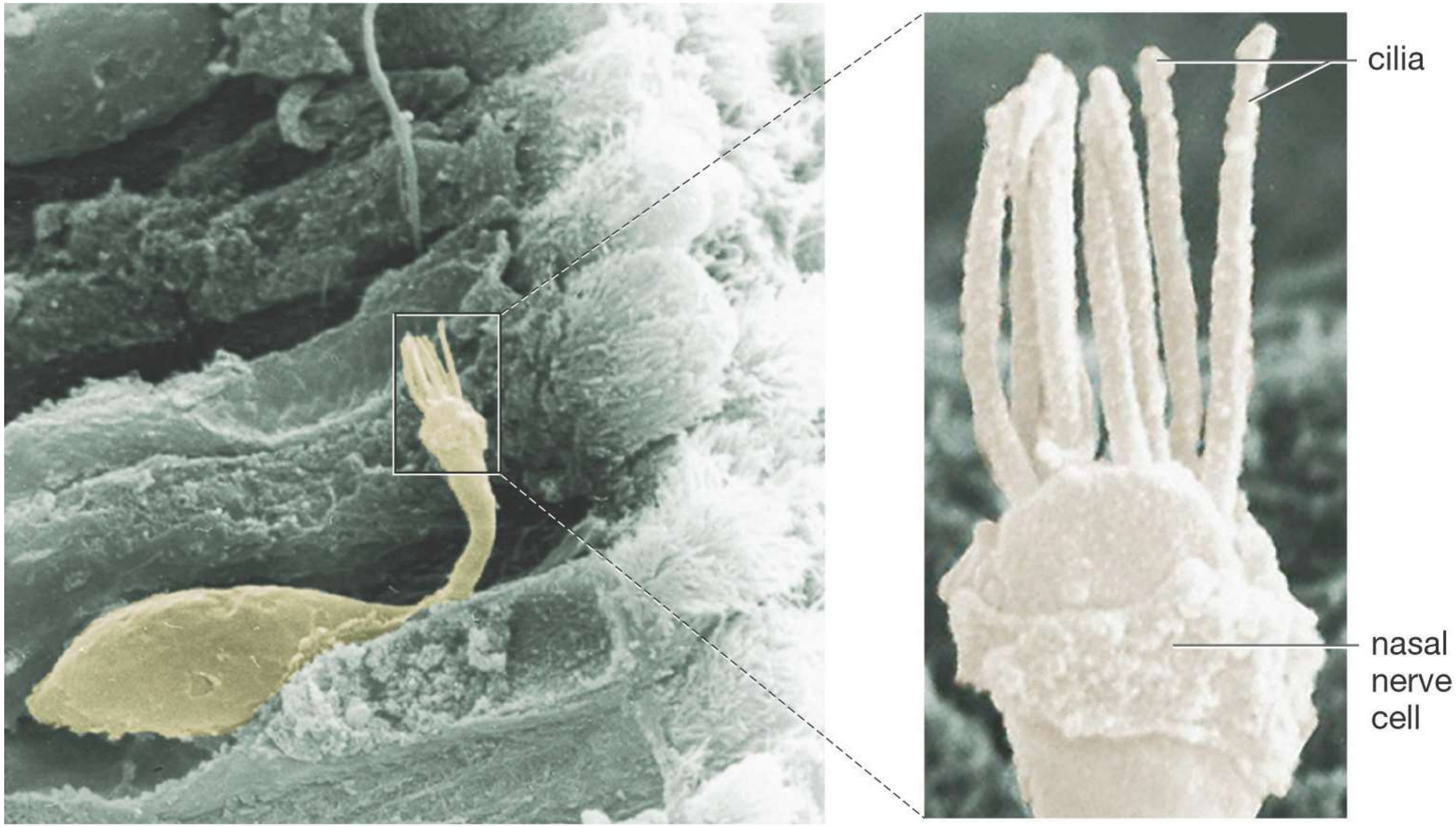
- As a cell grows, volume ($units^3$) increases faster than surface area ($units^2$), leading to a decreased SA:Vol ratio
- If metabolic rate exceeds the rate of exchange of vital materials and wastes (low SA:Vol ratio), the cell will eventually die
- Hence growing cells tend to divide and remain small in order to maintain a high SA:Vol ratio suitable for survival

Cell Theory



Cell radius (r)	1 unit	10 unit
Surface area ($4\pi r^2$)	12.57 $unit^2$	1257 $unit^2$
Volume ($\frac{4}{3}\pi r^3$)	4.189 $unit^3$	4189 $unit^3$
Surface Area / Volume	3	0.3

Cells are Us

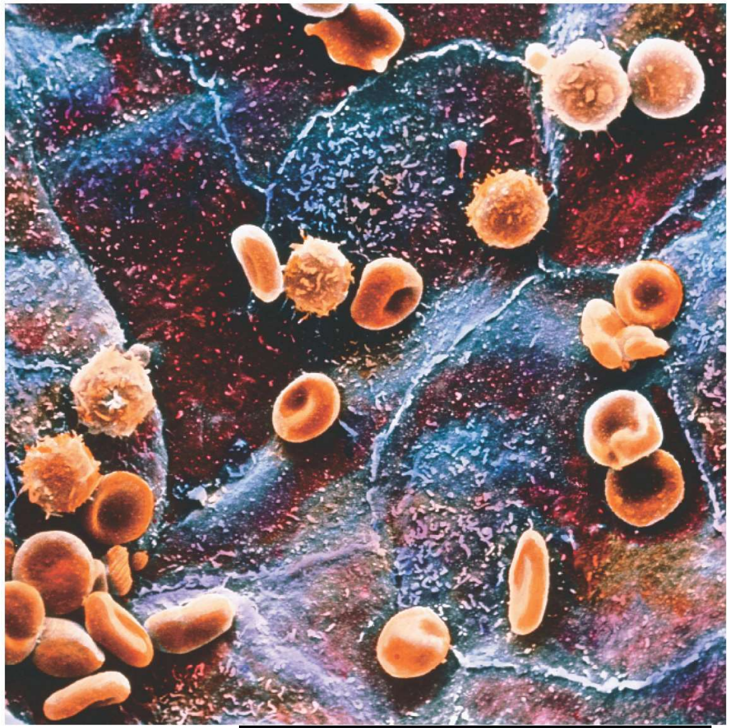


Cells are Us

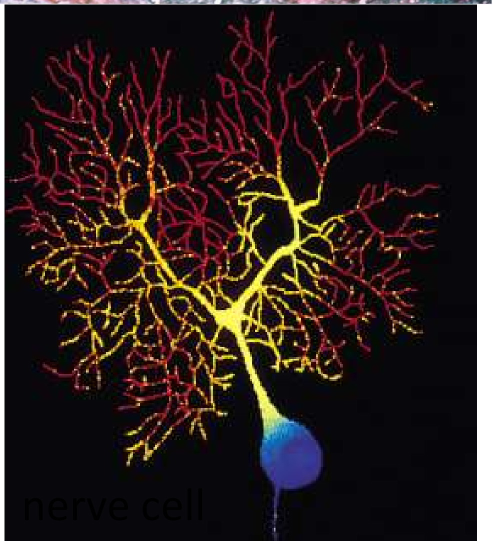
A person contains about 100 trillion cells. That's 100,000,000,000,000 or 1 x 10^{14} cells.

There are about 200 different cell types in mammals (one of us).

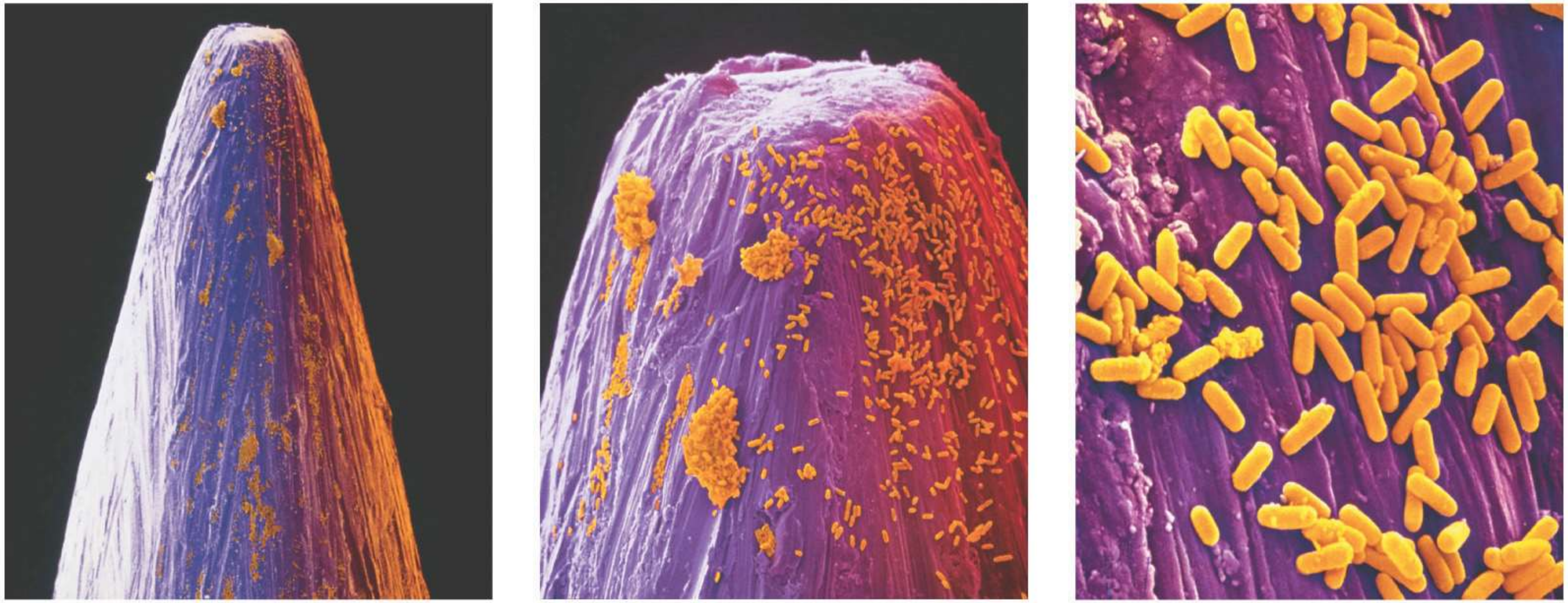
Cells are tiny, measuring on average about 0.002 cm (20 um) across. That's about 1250 cells, "shoulder-to-shoulder" per inch.



Red and white blood cells above vessel-forming cells.



A Sense of Scale and Abundance – Bacteria on the Head of a Pin



(a) Bacteria on a pin, magnified x 85 **(b)** Magnified x 425 **(c)** Magnified x 2100

Prokaryotic Cells

Prokaryotic cells lack a membrane-bound nucleus.

-genetic material is present in the **nucleoid**

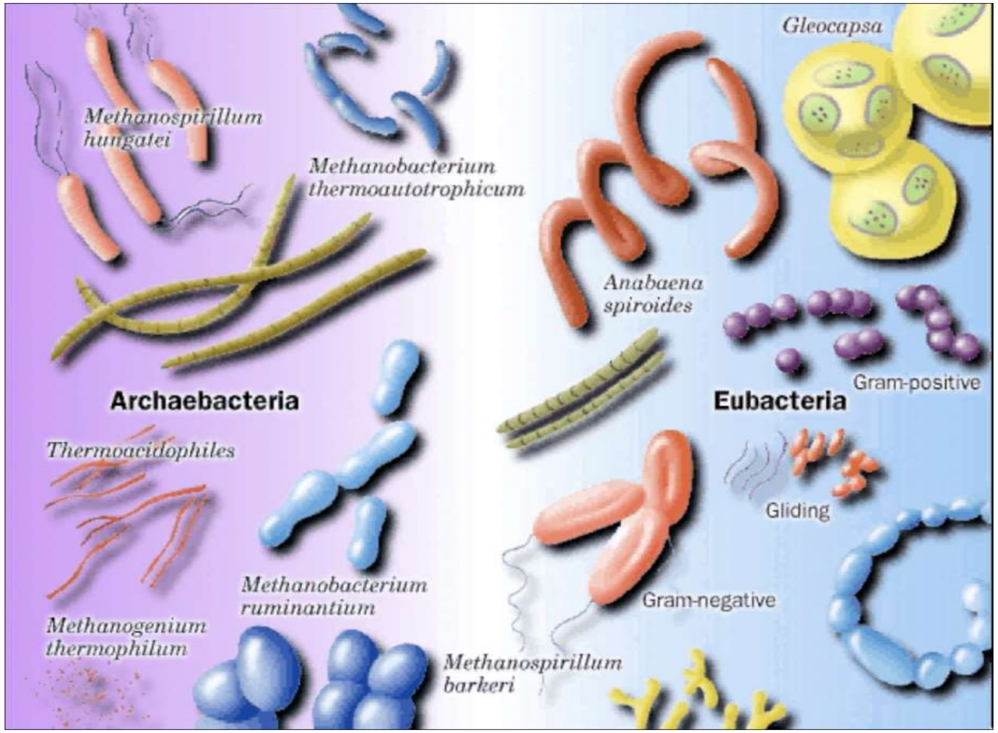
Two types of prokaryotes:

-archaea

-bacteria

Prokaryotic Cells: Bacteria

- Either classified as eubacteria or archaea.
  - Eubacteria: commonly found
  - Archaea: Live in extreme environments



Prokaryotic Cells

Prokaryotic cells possess

-genetic material in the nucleoid

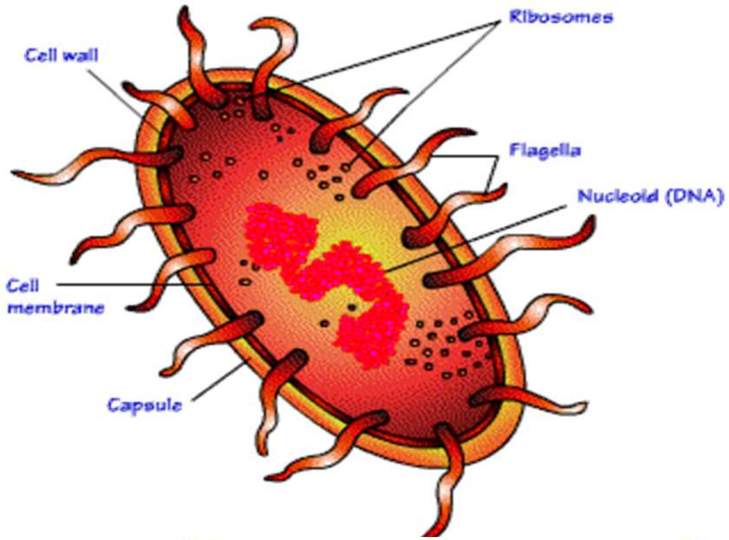
-cytoplasm

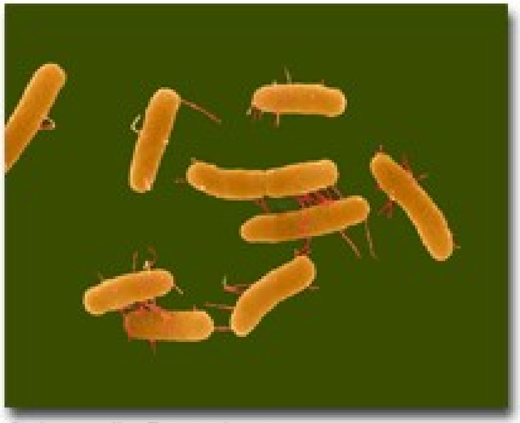
-plasma membrane

-cell wall

-ribosomes

-no membrane-bound organelles

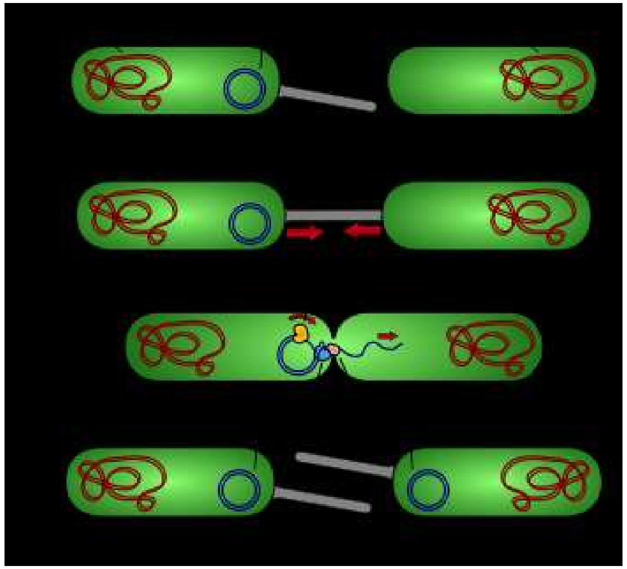


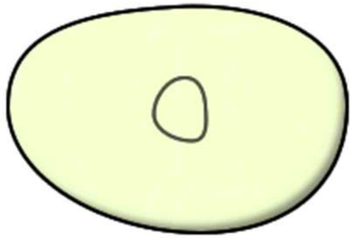


Salmonella Bacterium

Prokaryotic Cells: Bacteria

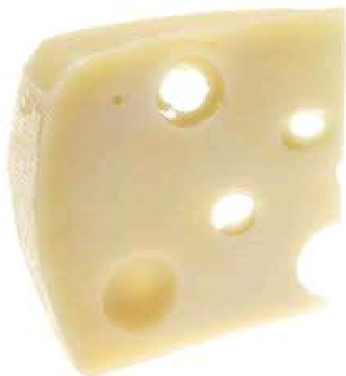
- Reproduction: Usually Asexual
  - Binary Fission: an organism duplicates its DNA and then divides into two parts, with each new organism receiving one copy of DNA.
  - Conjugation: Exchange of DNA between bacteria (not Asexual)





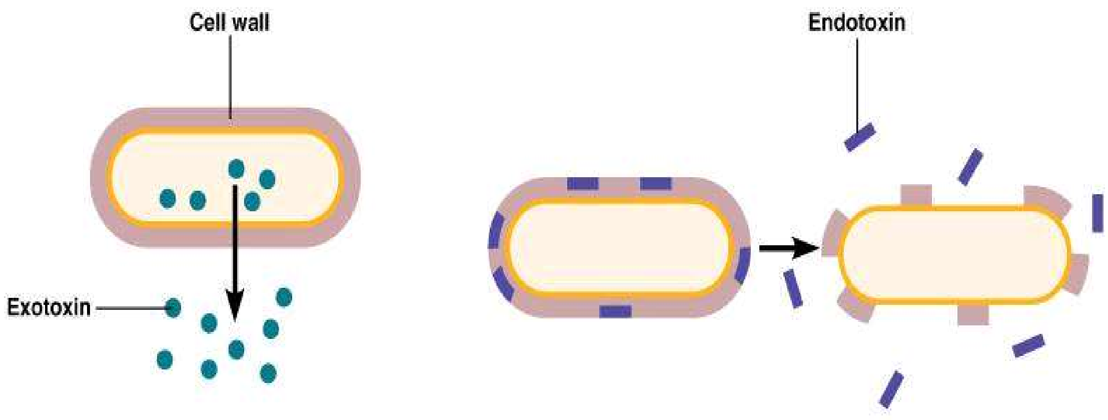
Prokaryotic Cells: Bacteria“The Good”

- Bioremediation: organisms are added to water to convert toxic pollutants, such as oil, into harmless substances.
- Food Production: Butter, Cheese, Yogurt, Sauerkraut, Beer, Pickles, Olives, Chocolate, Coffee, Soy sauce, meats, etc.
- Decompose dead organisms
- Digesting food
- Fix Nitrogen for Plants



Prokaryotic Cells: Bacteria“The Bad”

- Food Spoilage
- Can cause disease in plants and animals
- Produce Toxins

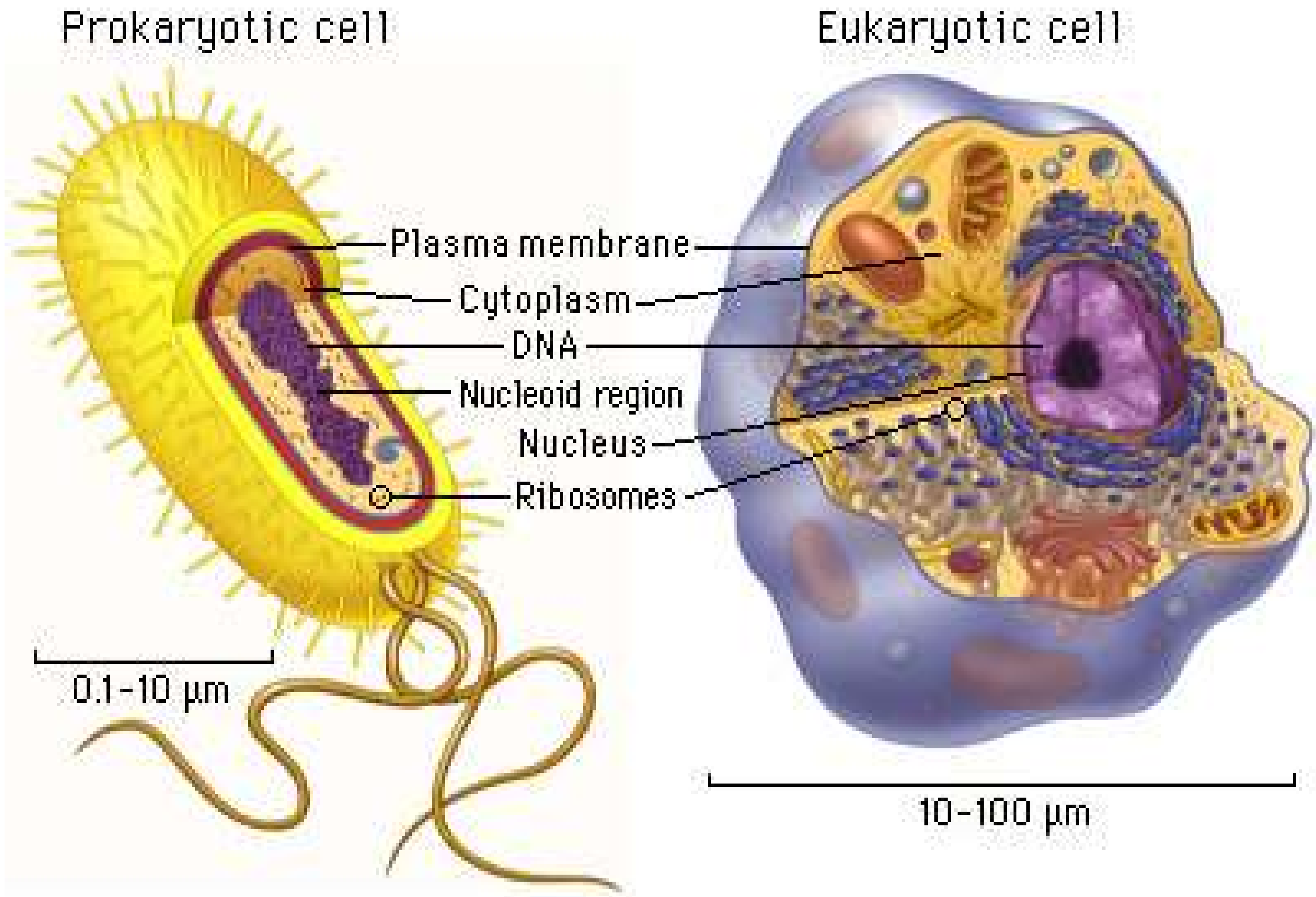


(a) Exotoxins are produced inside mostly gram-positive bacteria as part of their growth and metabolism. They are then secreted or released following lysis into the surrounding medium.

(b) Endotoxins are part of the outer portion of the cell wall (lipid A; see Figure 4.12c) of gram-negative bacteria. They are liberated when the bacteria die and the cell wall breaks apart.

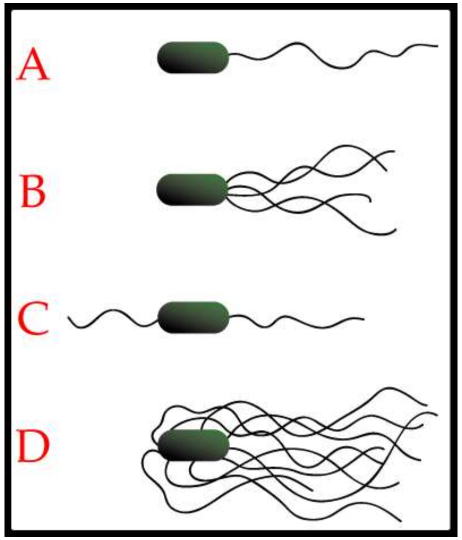
Prokaryotic Cells: Bacteria"The Ugly"

- Must be dealt with every day.
- People die each year from infections.
- Bubonic Plague:
  - Killed 2 out of 3 patients in 2-6 days without treatment
  - *Yersina pestis*
- Anthrax

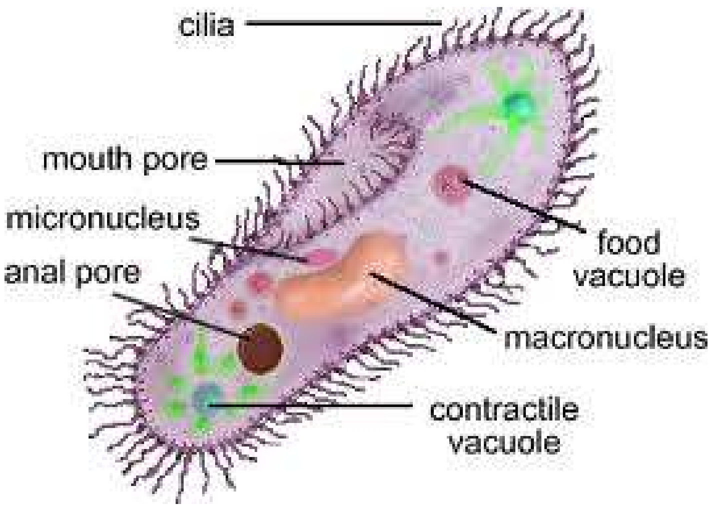


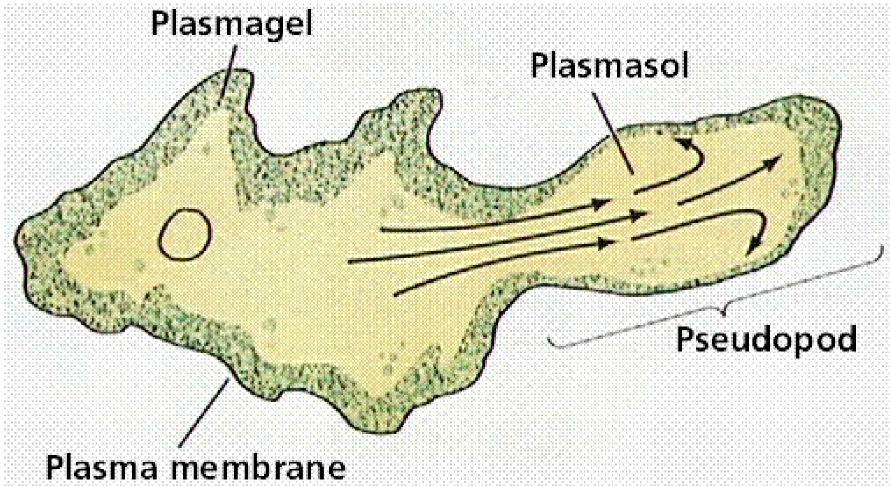
Prokaryotic cell
Eukaryotic cell
Plasma membrane
Cytoplasm
DNA
Nucleoid region
Nucleus
Ribosomes
0.1-10 µm
10-100 µm

Cell Movement



- Flagella: tail-like projections – prokaryotes and eukaryotes
- Pseudopodia: false-foot in eukaryotes
- Cilia: finger-like projections (some non-motile) in eukaryotes





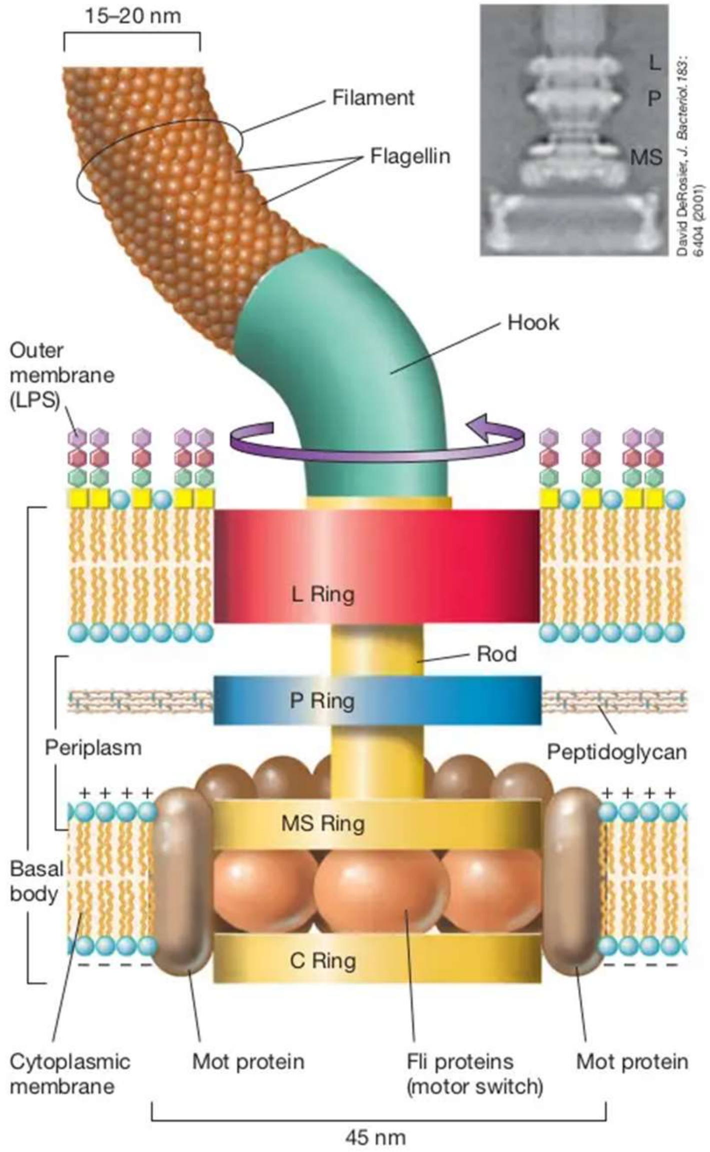
Prokaryotic Cells

Flagella

-present in some prokaryotic cells

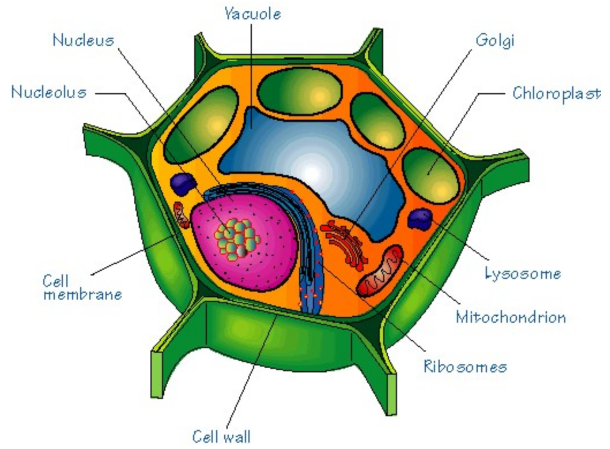
-used for locomotion

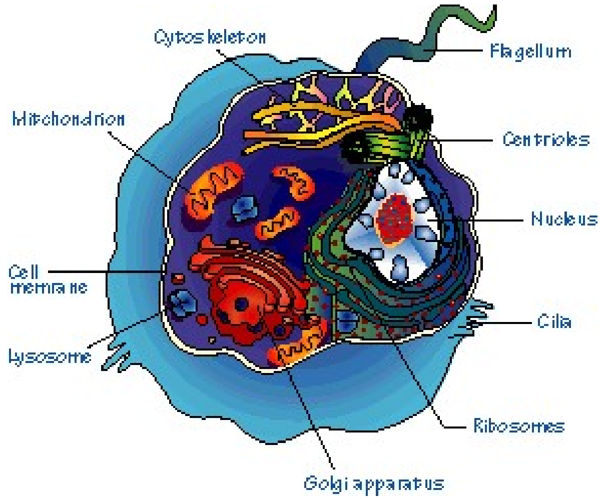
-rotary motion propels the cell



Main Types of Cells

- Eukaryotic (YOU!)
  - More complex & larger than prokaryotes
  - Have membrane bound organelles
  - Has a nucleus
  - Has more DNA than prokaryotes
  - DNA is linear
  - Animal, plant, fungi
  - NOT BACTERIA





Eukaryotic Cells

Eukaryotic cells

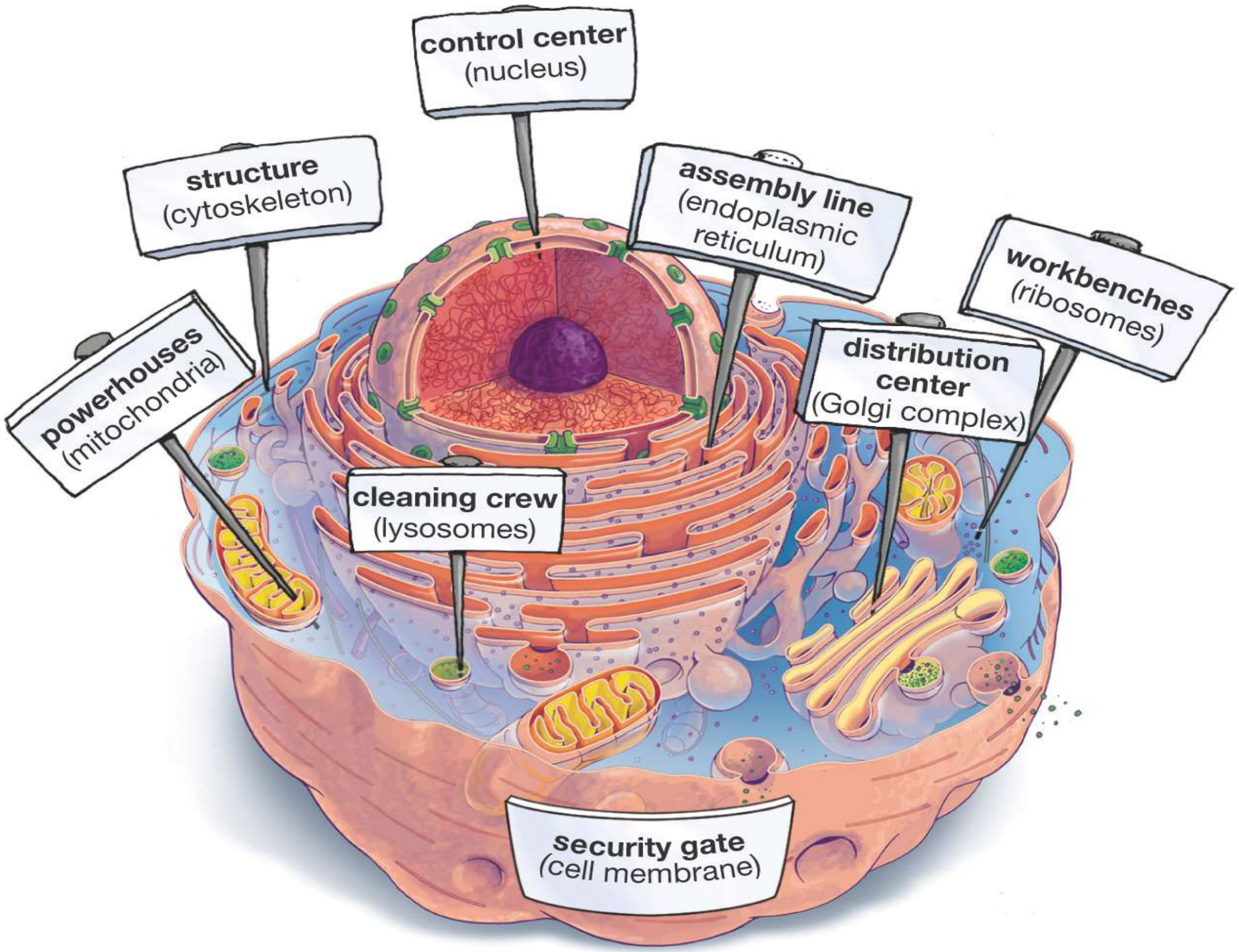
-possess a membrane-bound nucleus

-are more complex than prokaryotic cells

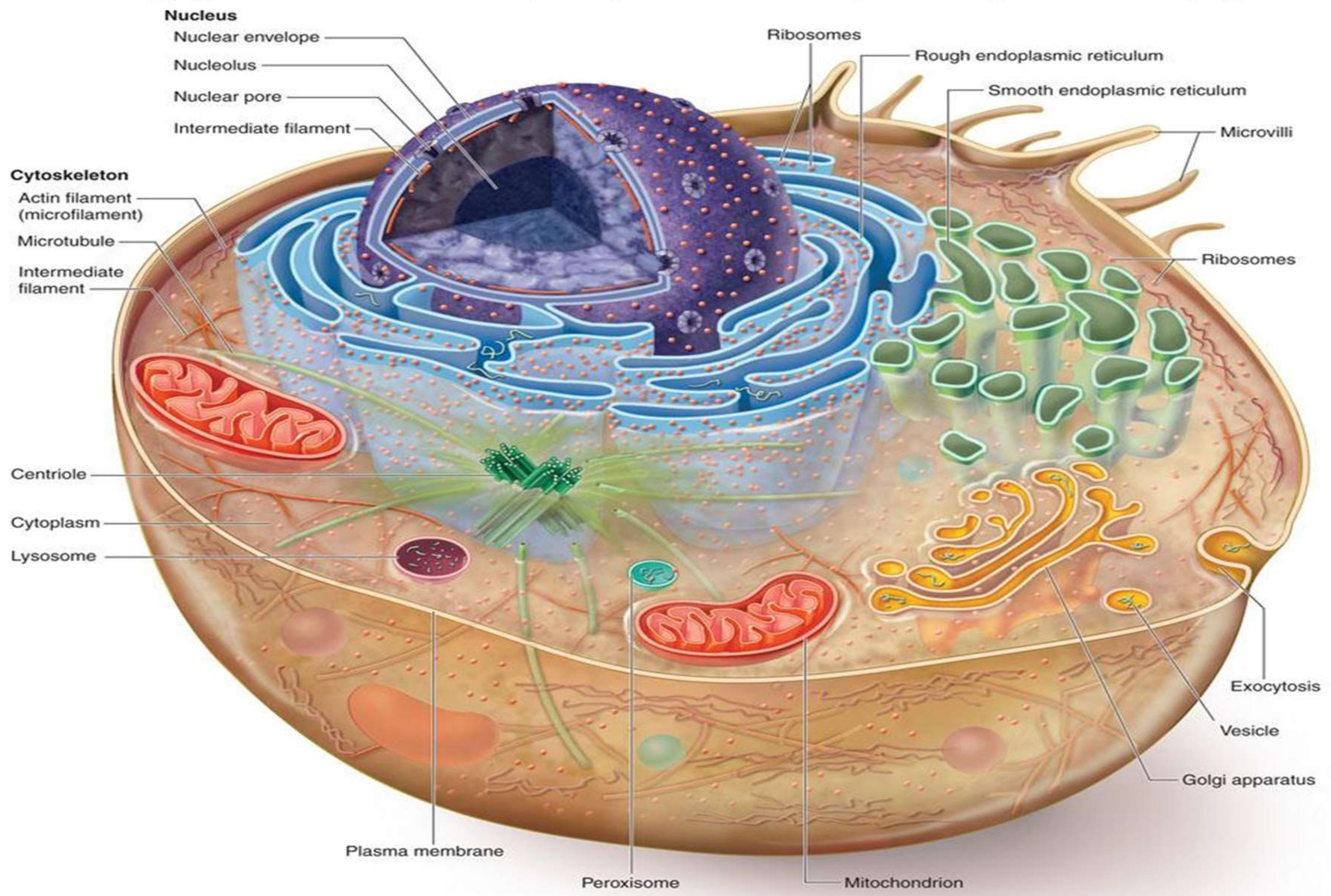
-compartmentalize many cellular functions within **organelles** and the **endomembrane system**

-possess a **cytoskeleton** for support and to maintain cellular structure

Cellular Anatomy

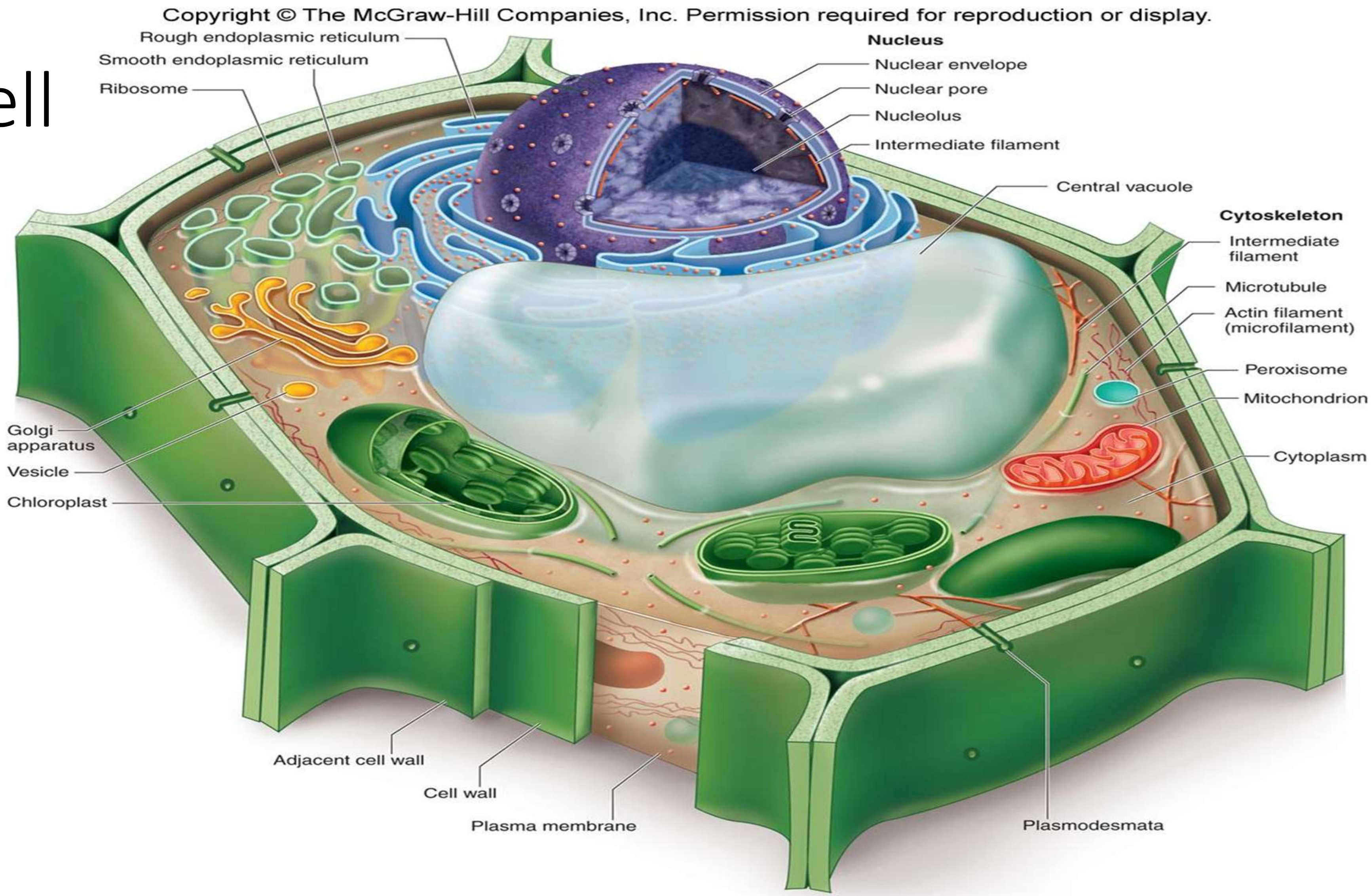


Animal Cell



Nucleus
Nuclear envelope
Nucleolus
Nuclear pore
Intermediate filament
Cytoskeleton
Actin filament (microfilament)
Microtubule
Intermediate filament
Centriole
Cytoplasm
Lysosome
Plasma membrane
Peroxisome
Mitochondrion
Ribosomes
Rough endoplasmic reticulum
Smooth endoplasmic reticulum
Microvilli
Ribosomes
Exocytosis
Vesicle
Golgi apparatus

Plant cell



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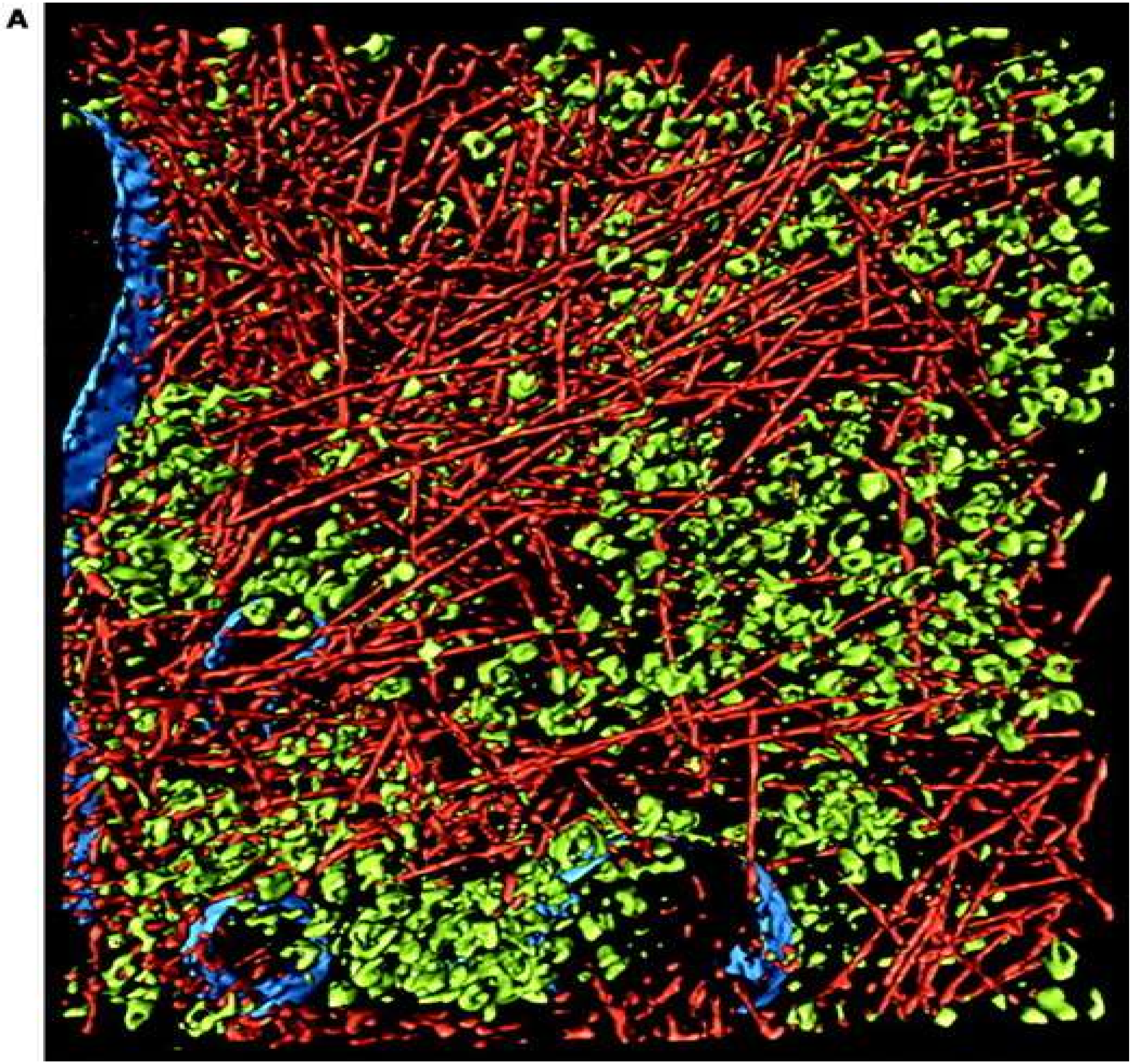
Rough endoplasmic reticulum
Smooth endoplasmic reticulum
Ribosome
Nucleus
Nuclear envelope
Nuclear pore
Nucleolus
Intermediate filament
Central vacuole
Cytoskeleton
Intermediate filament
Microtubule
Actin filament (microfilament)
Peroxisome
Mitochondrion
Cytoplasm
Golgi apparatus
Vesicle
Chloroplast
Adjacent cell wall
Cell wall
Plasma membrane
Plasmodesmata

It’s Crowded In There



A micrograph showing cytoskeleton (red), ribosomes (green), and membrane (blue)

Eukaryotic Cells

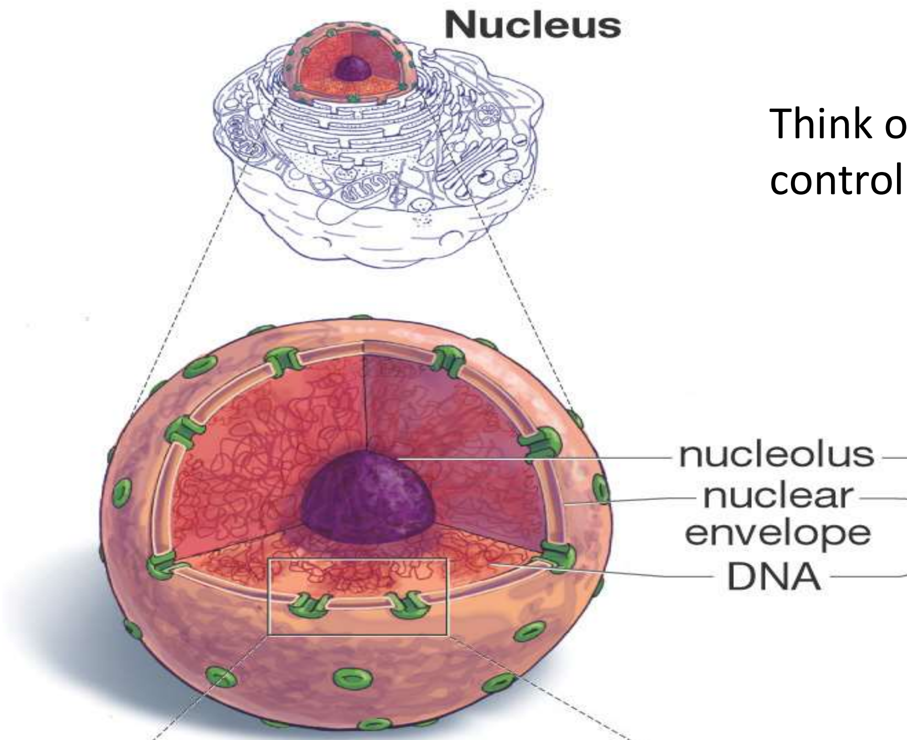
Nucleus

-stores the genetic material of the cell in the form of multiple, linear chromosomes

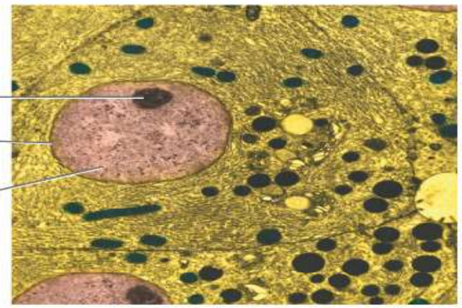
-surrounded by a **nuclear envelope** composed of 2 phospholipid bilayers

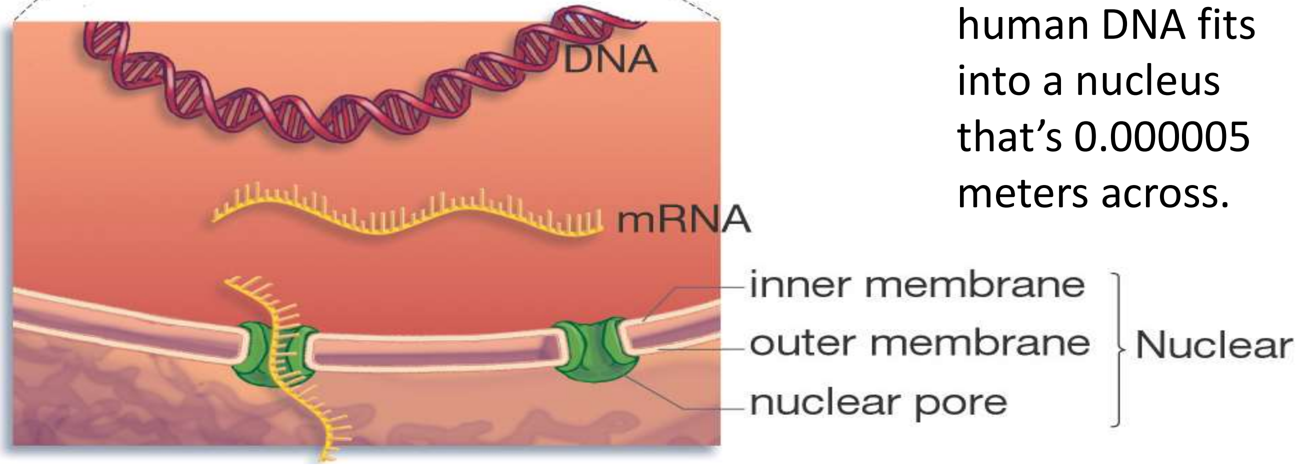
-in chromosomes – DNA is organized with proteins to form **chromatin**

The Nucleus



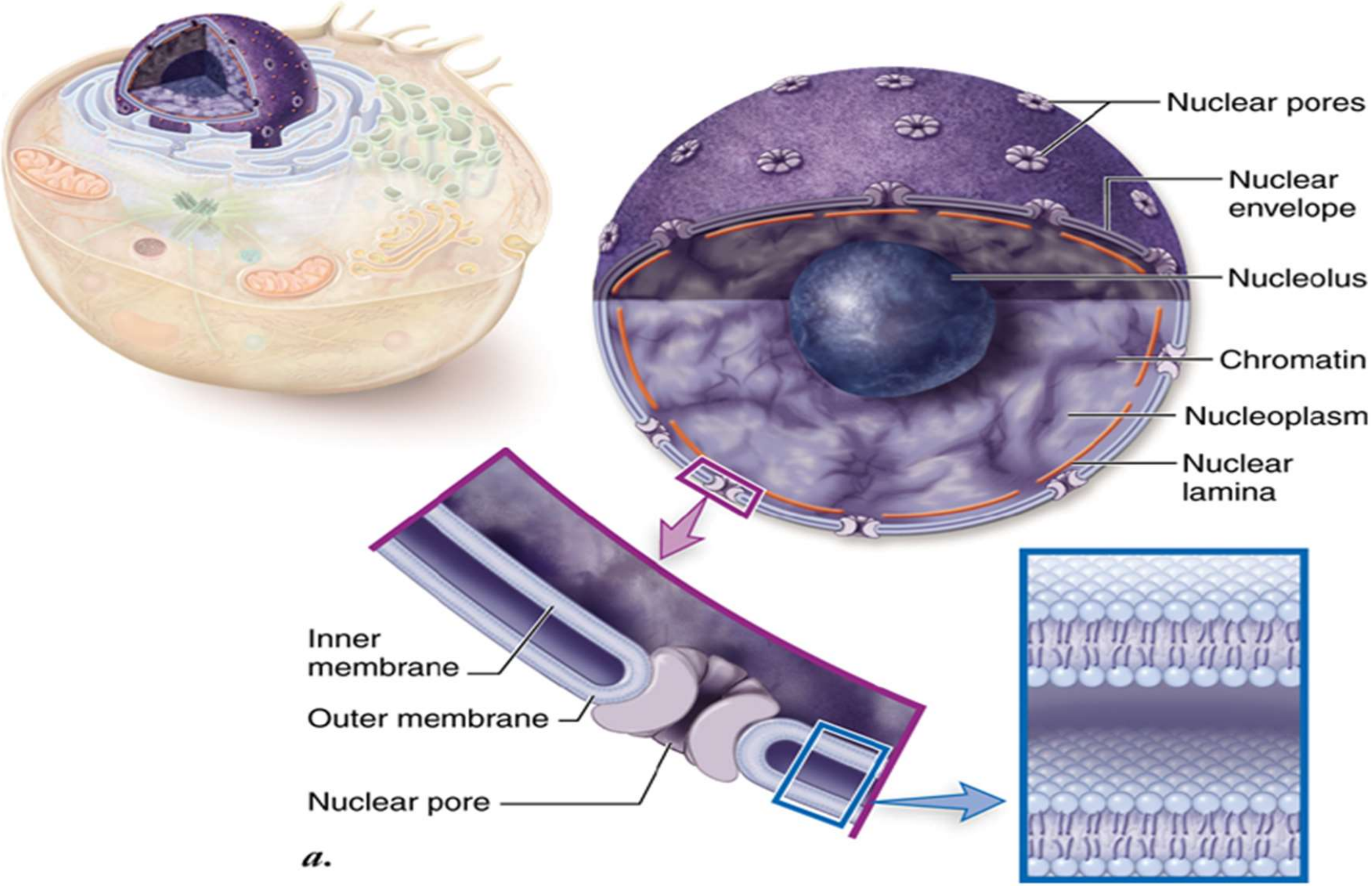
Think of the nucleus as the cell’s control center.





Two meters of human DNA fits into a nucleus that’s 0.000005 meters across.

Eukaryotic Cells



Eukaryotic Cells

Ribosomes

-the site of protein synthesis in the cell

-composed of **ribosomal RNA** and proteins

-found within the cytosol of the cytoplasm and attached to internal membranes

Endomembrane System

Endomembrane system

-a series of membranes throughout the cytoplasm

-divides cell into compartments where different cellular functions occur

1. endoplasmic reticulum
2. Golgi apparatus
3. lysosomes

Endomembrane System

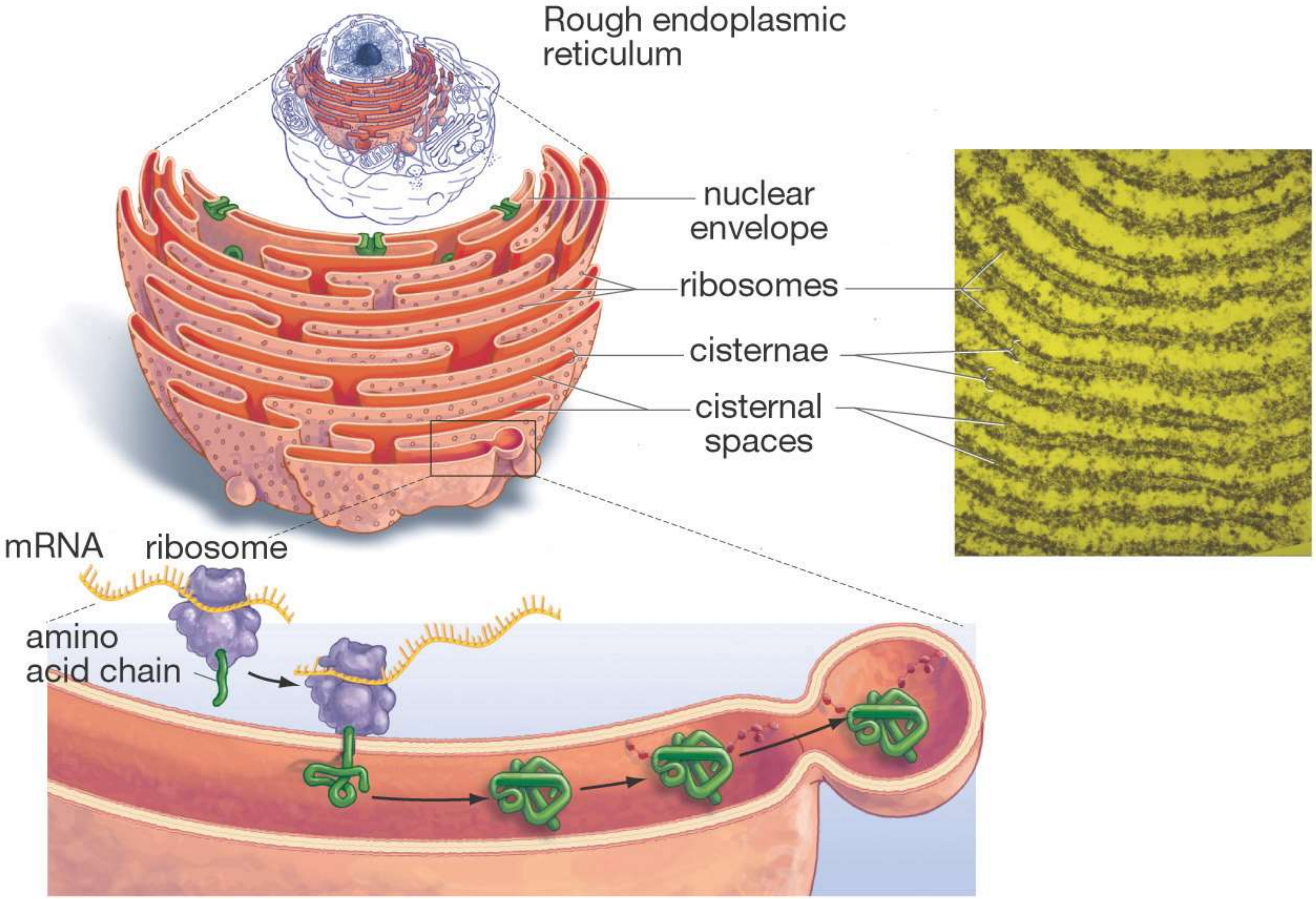
Rough endoplasmic reticulum (RER)

-membranes that create a network of channels throughout the cytoplasm

-attachment of ribosomes to the membrane gives a rough appearance

-synthesis of proteins to be secreted, sent to lysosomes or plasma membrane

Ribosomes and the Endoplasmic Reticulum



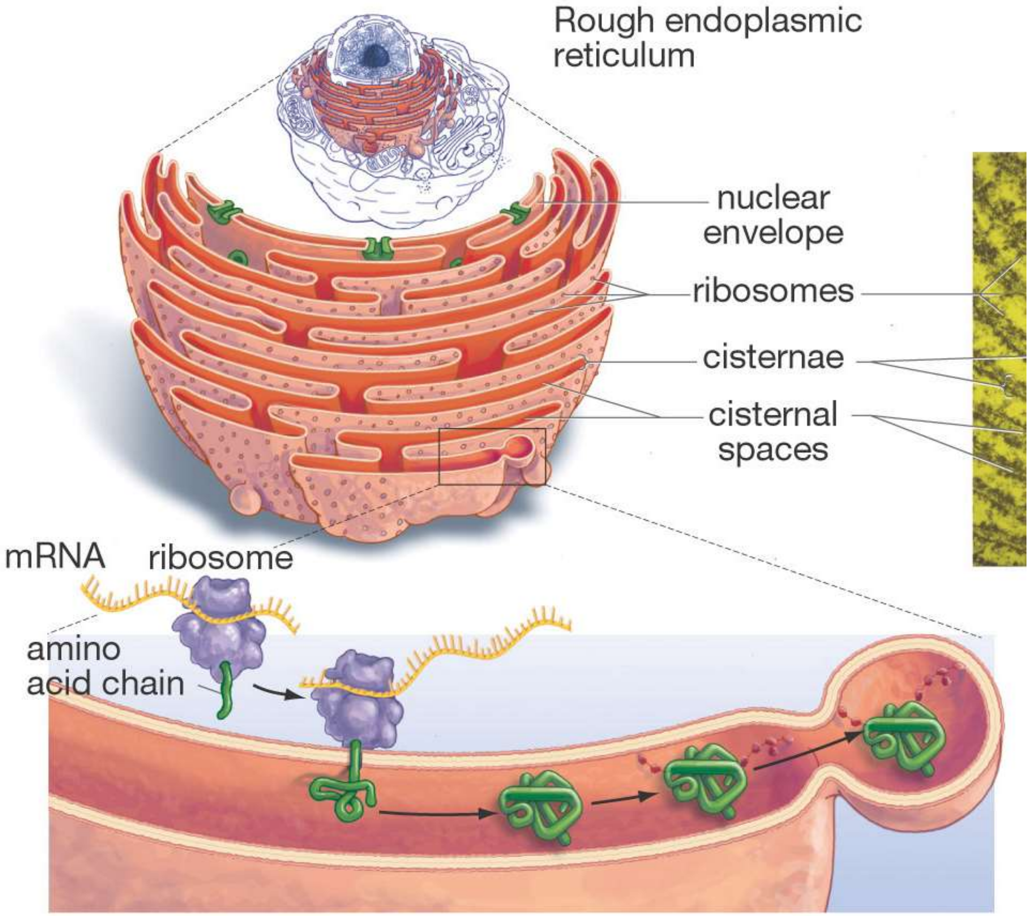
The Rough Endoplasmic Reticulum

Functions:

Protein synthesis (about half the cell's proteins are made here).

Protein movement (trafficking)

Protein "proofreading"



Endomembrane System

Smooth endoplasmic reticulum (SER)

-relatively few ribosomes attached

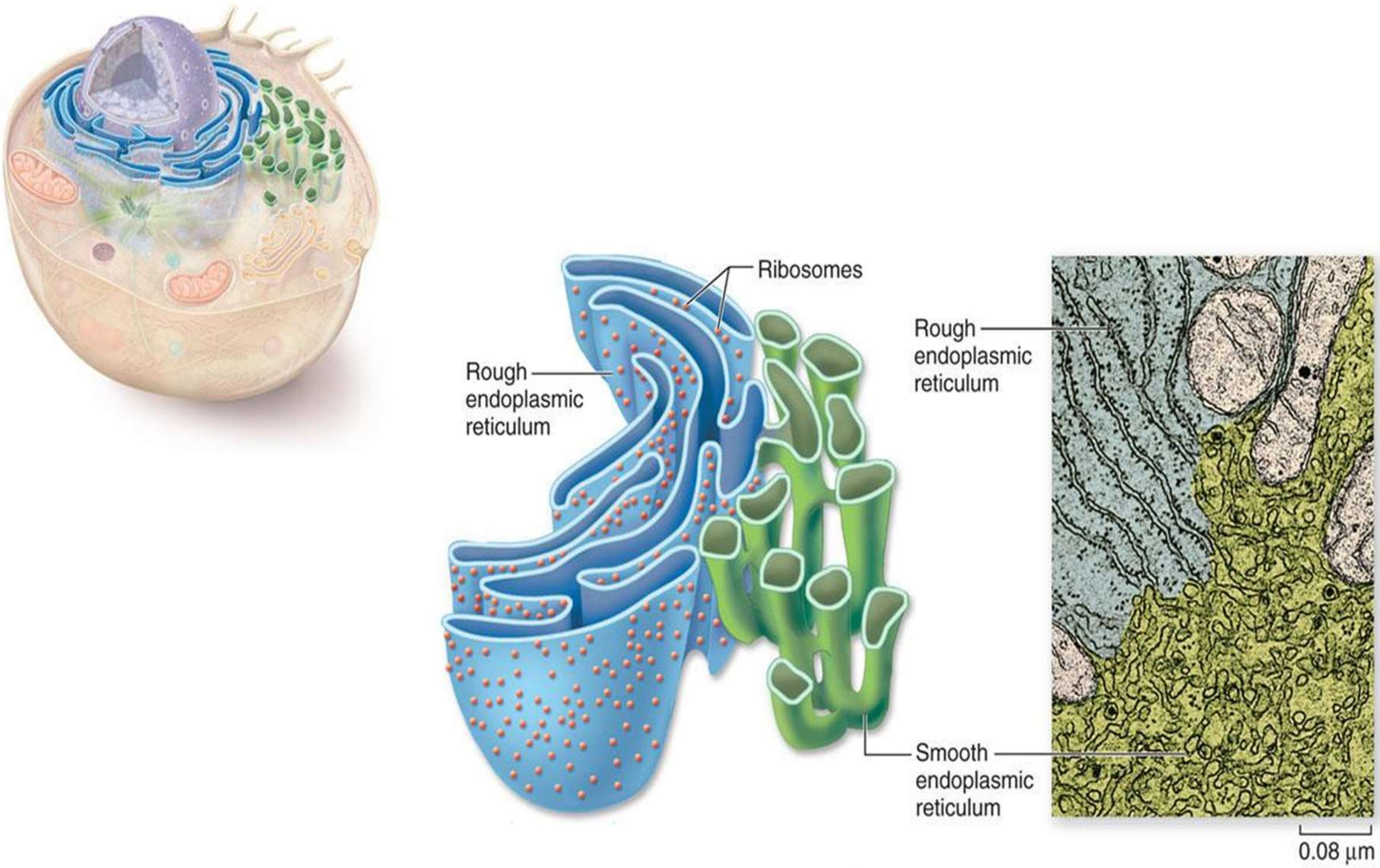
-functions:

-synthesis of membrane lipids

-calcium storage

-detoxification of foreign substances

Endomembrane System



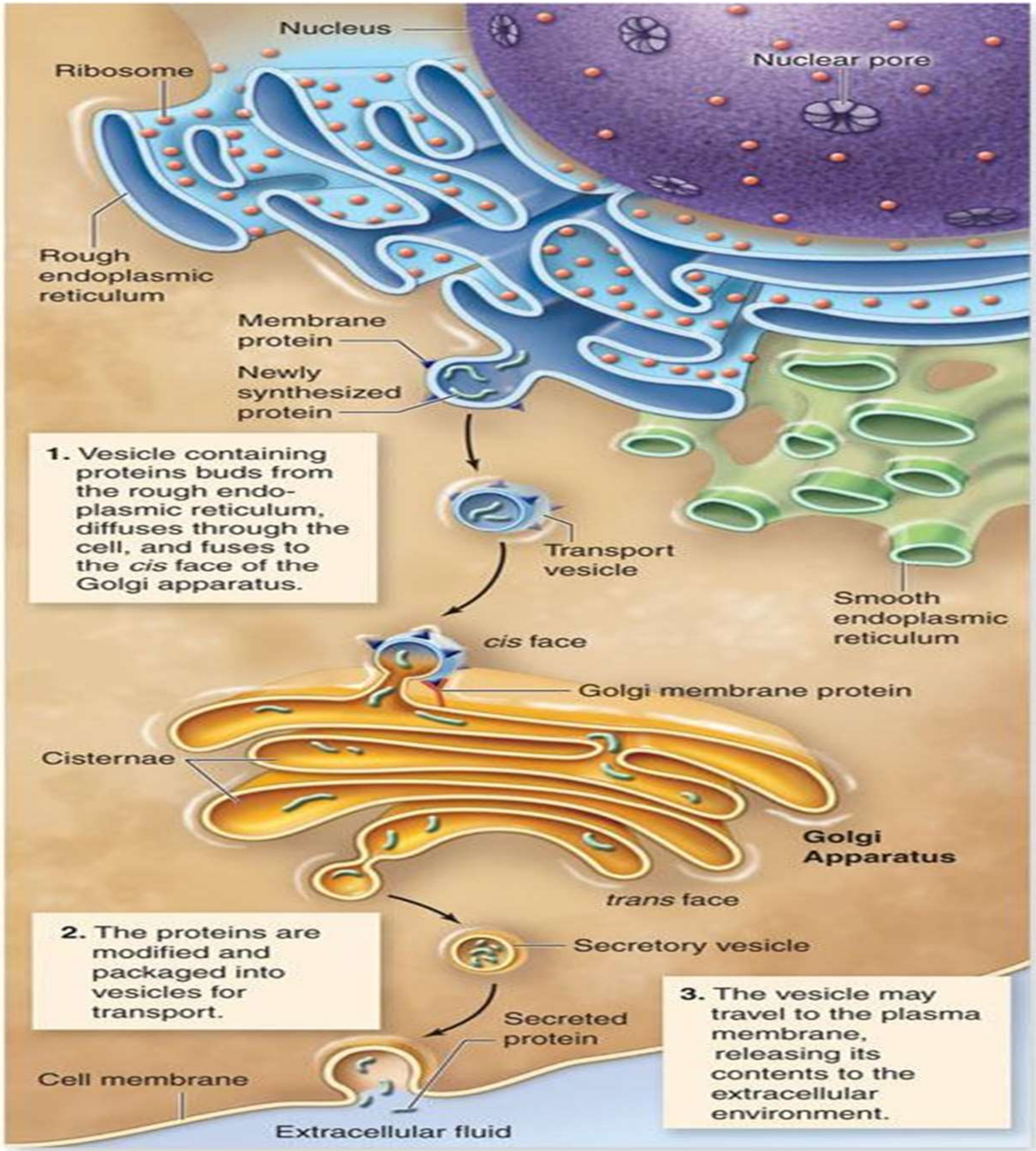
Endomembrane System

Golgi apparatus

-flattened stacks of interconnected membranes

-packaging and distribution of materials to different parts of the cell

-synthesis of cell wall components


Nucleus
Ribosome
Nuclear pore
Rough endoplasmic reticulum
Membrane protein
Newly synthesized protein
1. Vesicle containing proteins buds from the rough endo-plasmic reticulum, diffuses through the cell, and fuses to the *cis* face of the Golgi apparatus.
Transport vesicle
Smooth endoplasmic reticulum
cis face
Golgi membrane protein
Cisternae
Golgi Apparatus
trans face
2. The proteins are modified and packaged into vesicles for transport.
Secretory vesicle
Secreted protein
3. The vesicle may travel to the plasma membrane, releasing its contents to the extracellular environment.
Cell membrane
Extracellular fluid

Endomembrane System

Lysosomes

-membrane bound vesicles containing digestive enzymes to break down macromolecules

-destroy cells or foreign matter that the cell has engulfed by phagocytosis

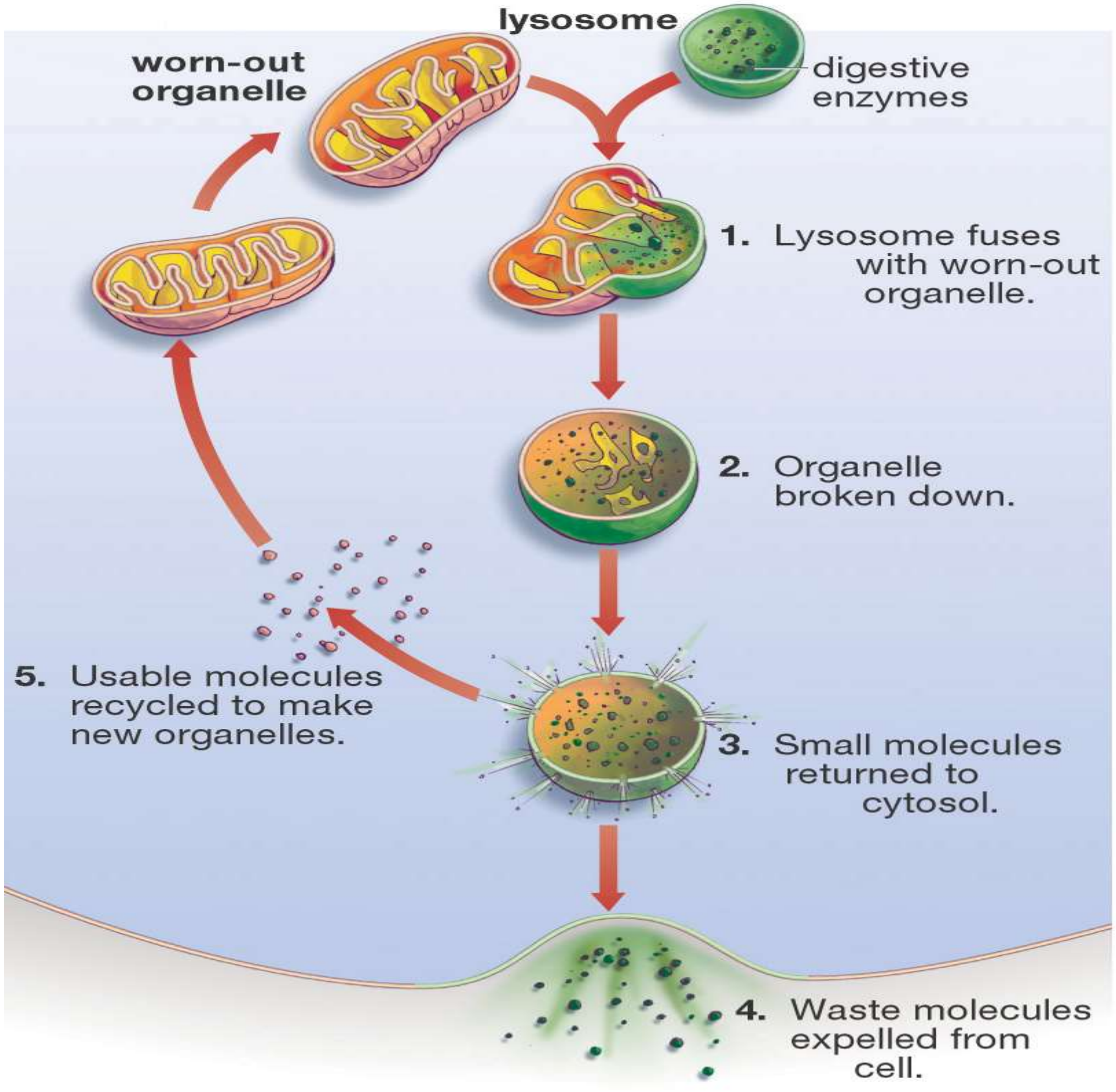
The Lysosome

Functions:

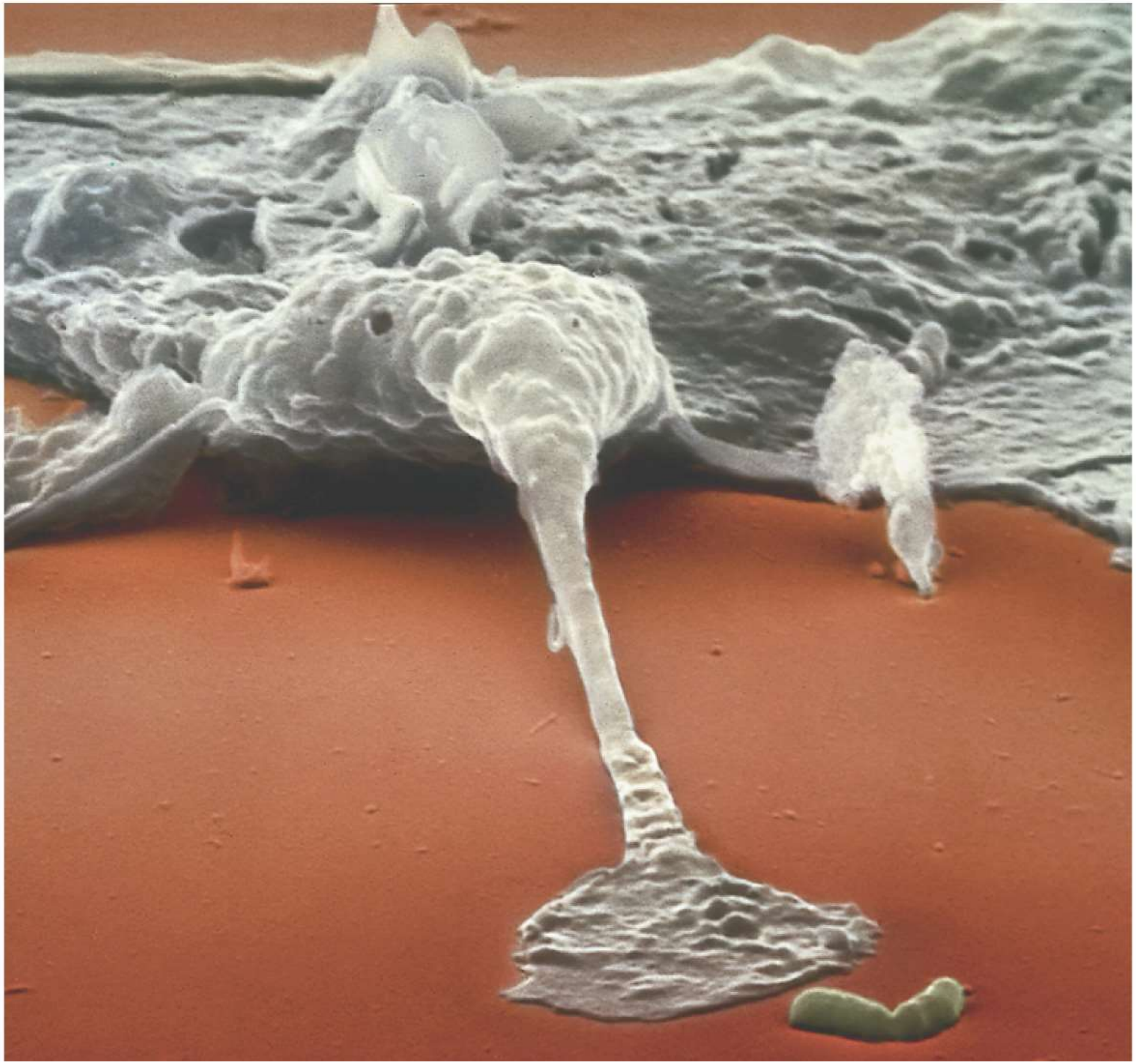
Digesting food or cellular invaders

Recycling cellular components

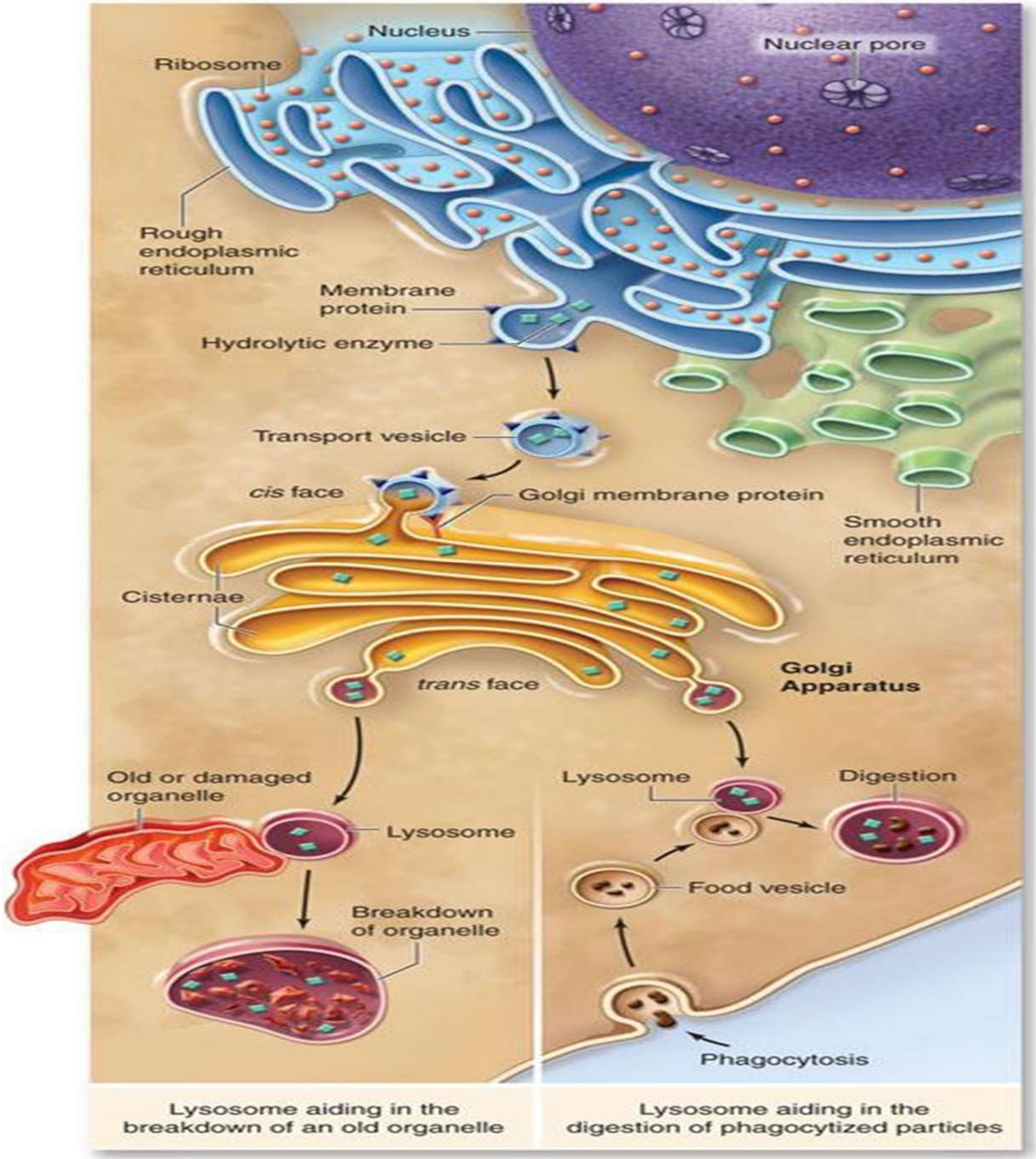
Cell suicide (suicide is bad for cells, but good for us!)



The Lysosome



This bacterium about to be eaten by an immune system cell will spend the last minutes of its existence within a lysosome.


Nucleus
Nuclear pore
Ribosome
Rough endoplasmic reticulum
Membrane protein
Hydrolytic enzyme
Transport vesicle
cis face
Golgi membrane protein
Smooth endoplasmic reticulum
Cisternae
trans face
Golgi Apparatus
Old or damaged organelle
Lysosome
Breakdown of organelle
Lysosome
Digestion
Food vesicle
Phagocytosis
Lysosome aiding in the breakdown of an old organelle
Lysosome aiding in the digestion of phagocytized particles

Endomembrane System

Microbodies

-membrane bound vesicles

-contain enzymes

-not part of the endomembrane system

-**glyoxysomes** in plants contain enzymes for converting fats to carbohydrates

-**peroxisomes** contain oxidative enzymes and catalase – detoxification of reactive oxygen species, metabolism (fatty acid oxidation),cell signalling, bile acid synthesis.

Endomembrane System

Vacuoles

-membrane-bound structures with various functions depending on the cell type

There are different types of vacuoles:

-**central vacuole** in plant cells

-contractile vacuole of some protists

-vacuoles for storage

Mitochondria

Mitochondria

-organelles present in all types of eukaryotic cells

-contain oxidative metabolism enzymes for transferring the energy within macromolecules to ATP

-found in all types of eukaryotic cells

-surrounded by 2 membranes

 -smooth outer membrane

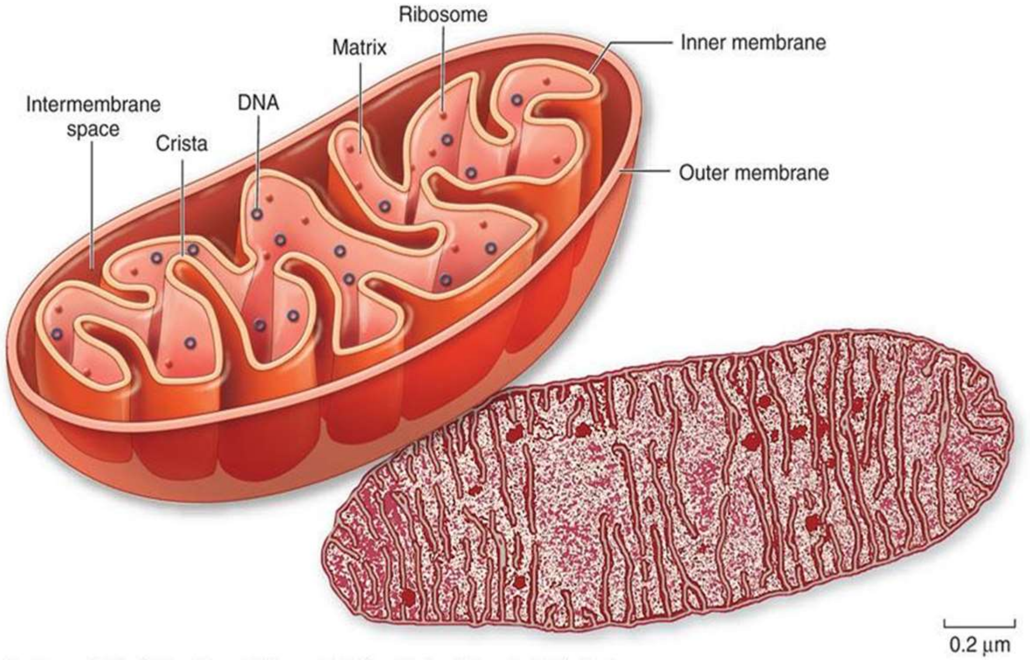
 -folded inner membrane with layers called **cristae**

-**matrix** is within the inner membrane

-**intermembrane space** is located between the two membranes

-contain their own DNA

Mitochondria



The Mitochondrion

- A class of diseases that causes muscle weakness and neurological disorders (Alziehmers, Huntington's, Parkinson's) are due to malfunctioning mitochondria.
- Worn out mitochondria may be an important factor in aging.

	Prokaryotes	Eukaryotes	Mitochondria of Eukaryotic cells	Chloroplasts of Photosynthetic eukaryotes
DNA	1 single, circular chromosome	Multiple linear chromosomes compartmentalized in a nucleus	1 single, circular chromosome	1 single, circular chromosome
Replication	Binary Fission	Mitosis	Binary Fission	Binary Fission
Ribosomes	"70 S"	"80 S"	"70 S"	"70 S"
Electron Transport Chain	Found in the plasma membrane around cell	Not found in the plasma membrane around cell	Found in the plasma membrane around mitochondrion	Found in the plasma membrane around chloroplast
Size (approximate)	~1-10 microns	~50 - 500 microns	~1-10 microns	~1-10 microns
Appearance on Earth	Anaerobic bacteria: ~3.8 Billion years Photosynt.bacteria: ~3.2 Billion years Aerobic bacteria: ~2.5 Billion years	~1.5 billion years ago	~1.5 billion years ago	~1.5 billion years ago

Mitochondria & Chloroplasts

Much evidence supports this endosymbiosis theory.

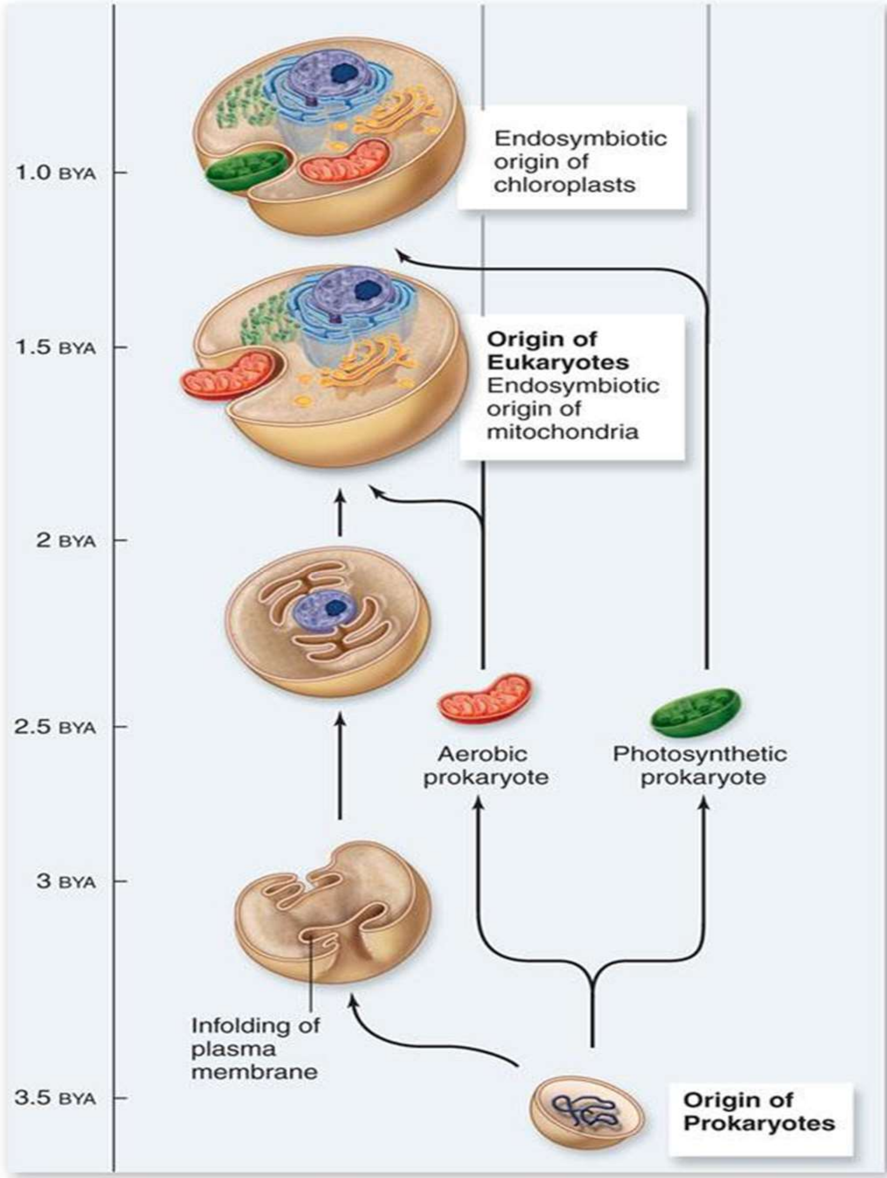
Mitochondria and chloroplasts:

-have 2 membranes

-possess DNA and ribosomes

-are about the size of a prokaryotic cell

-divide by a process similar to bacteria



Mitochondria & Chloroplasts

Endosymbiosis

-proposal that eukaryotic organelles evolved through a symbiotic relationship

-one cell engulfed a second cell and a symbiotic relationship developed

-mitochondria and chloroplasts are thought to have evolved this way

Chloroplasts

Chloroplasts

-organelles present in cells of plants and some other eukaryotes

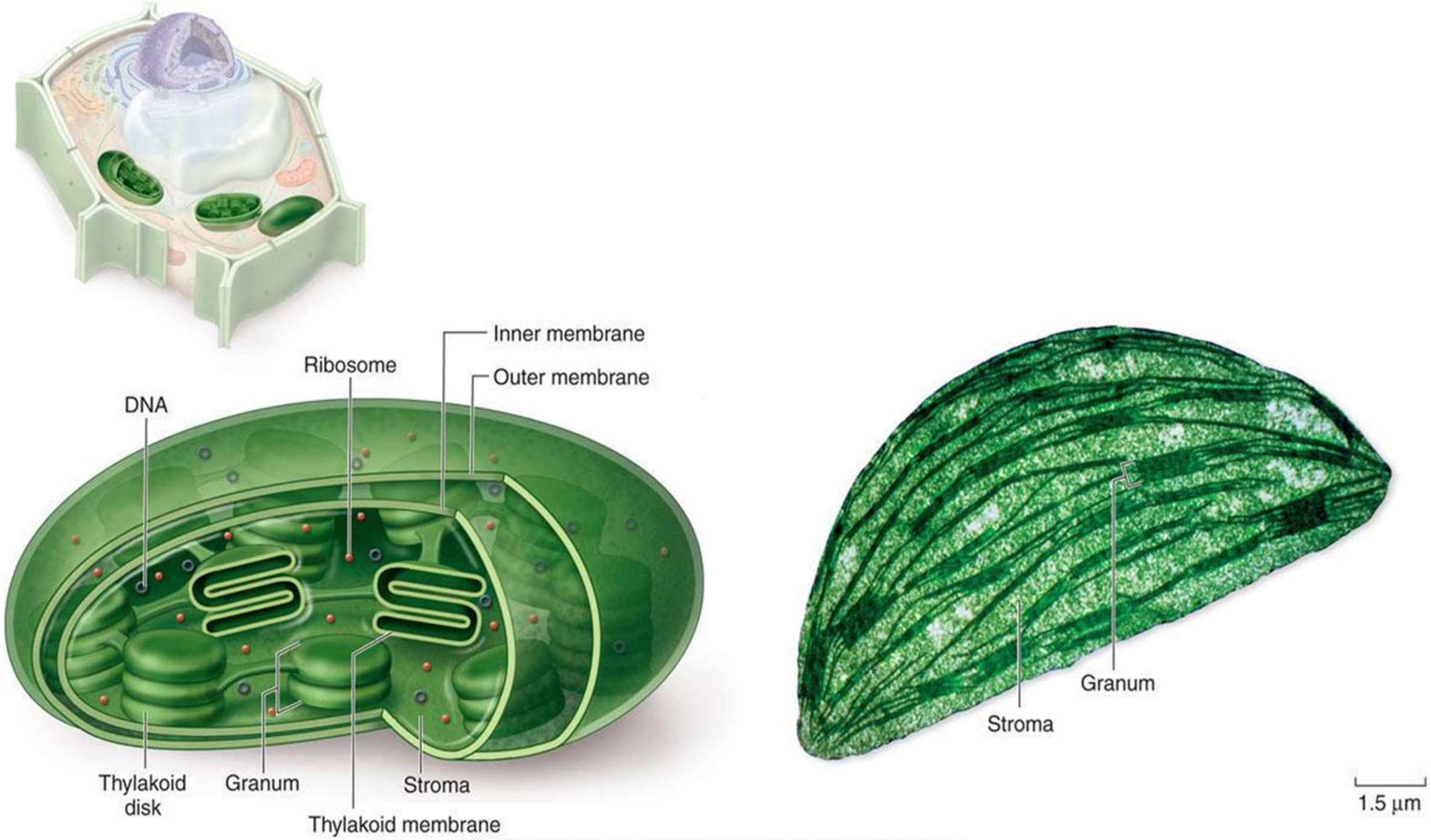
-contain chlorophyll for photosynthesis

-surrounded by 2 membranes

-**thylakoids** are membranous sacs within the inner membrane

-**grana** are stacks of thylakoids

Chloroplasts



Cytoskeleton

Cytoskeleton

-network of protein fibers found in all eukaryotic cells

-supports the shape of the cell

-keeps organelles in fixed locations

-helps move materials within the cell

Cytoskeleton

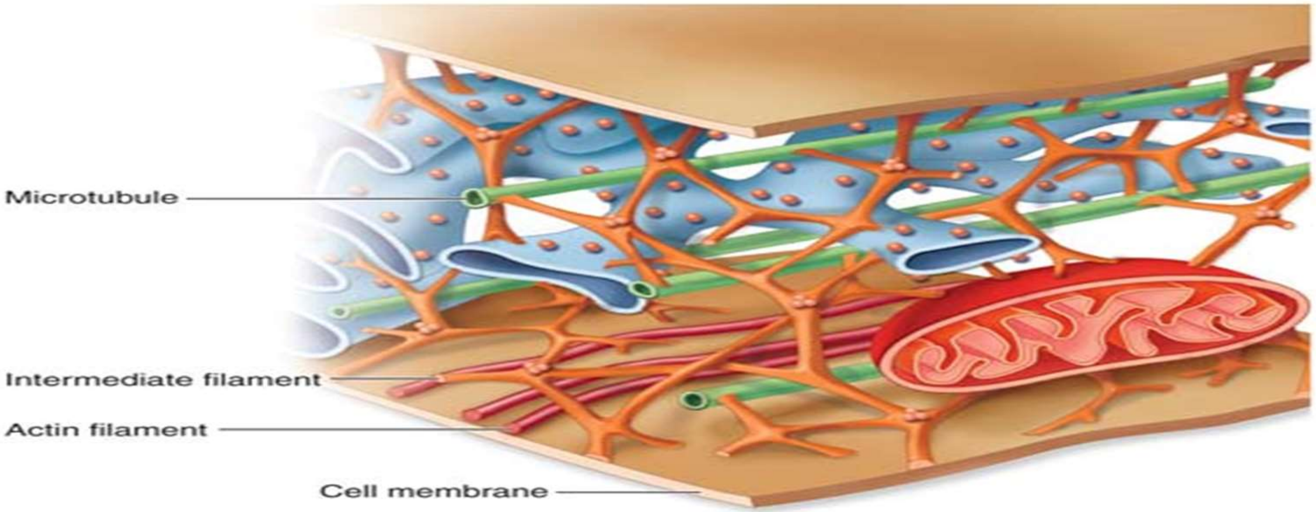
Cytoskeleton fibers include

-actin filaments – responsible for cellular contractions, crawling, “pinching”

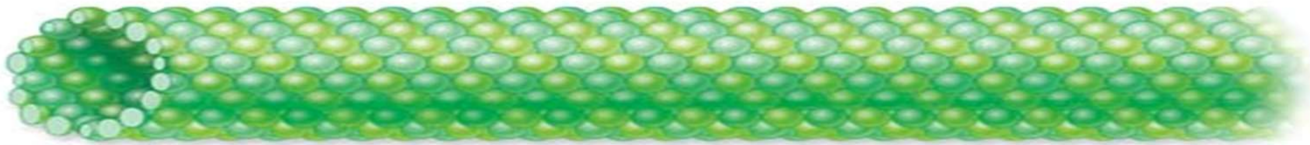
-microtubules – provide organization to the cell and move materials within the cell

-intermediate filaments – provide structural stability

Cytoskeleton



a. Actin filaments

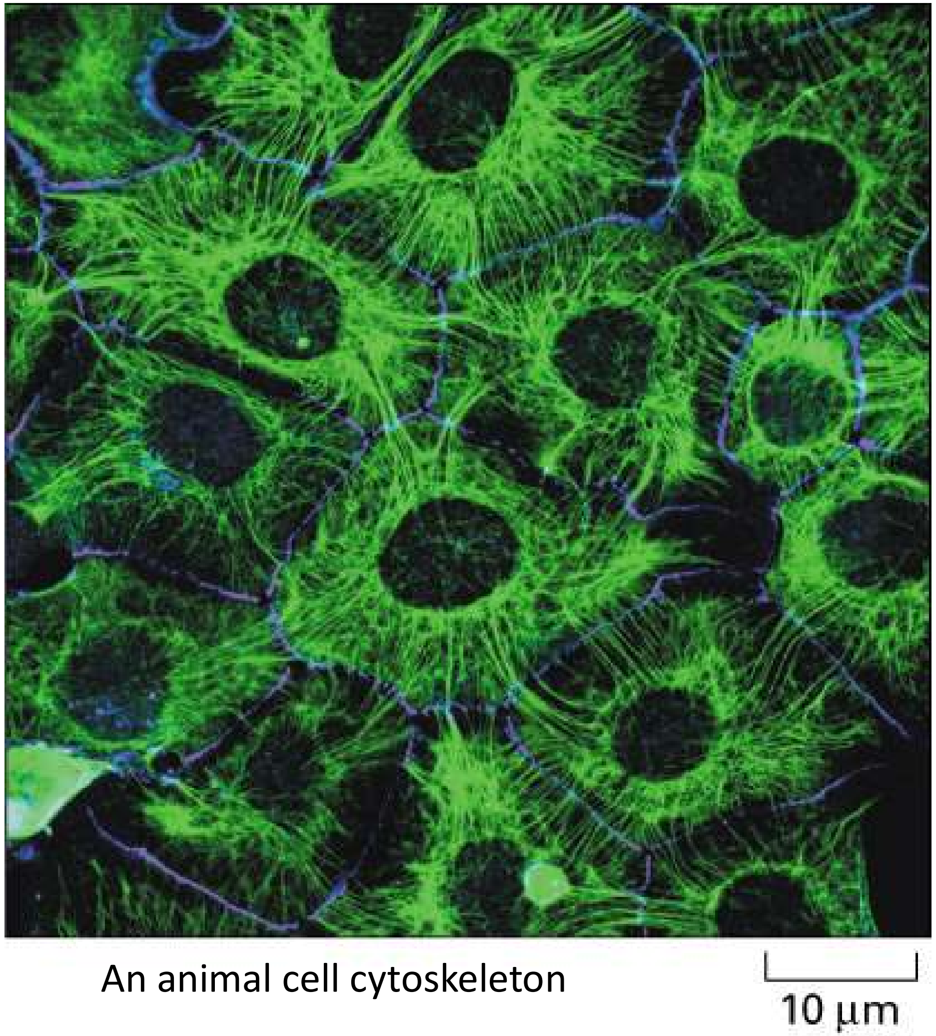


b. Microtubules

c. Intermediate filament

The Cytoskeleton

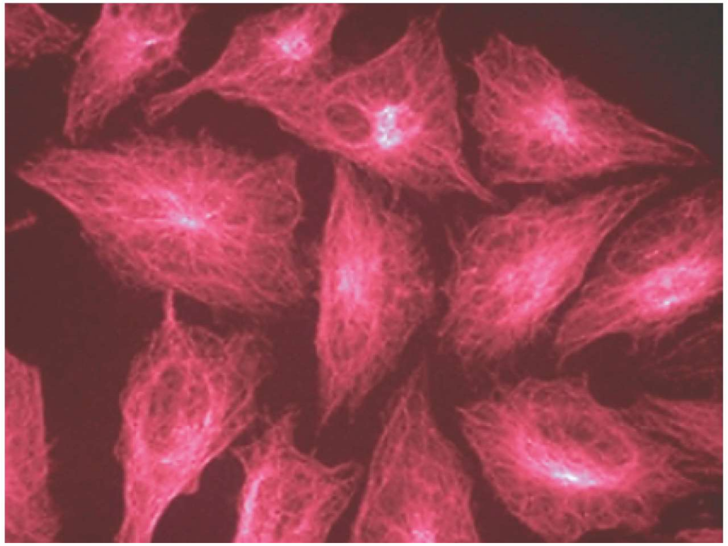
The name is misleading. The cytoskeleton <u>is</u> the skeleton of the cell, but it's also like the muscular system, able to change the shape of cells in a flash.

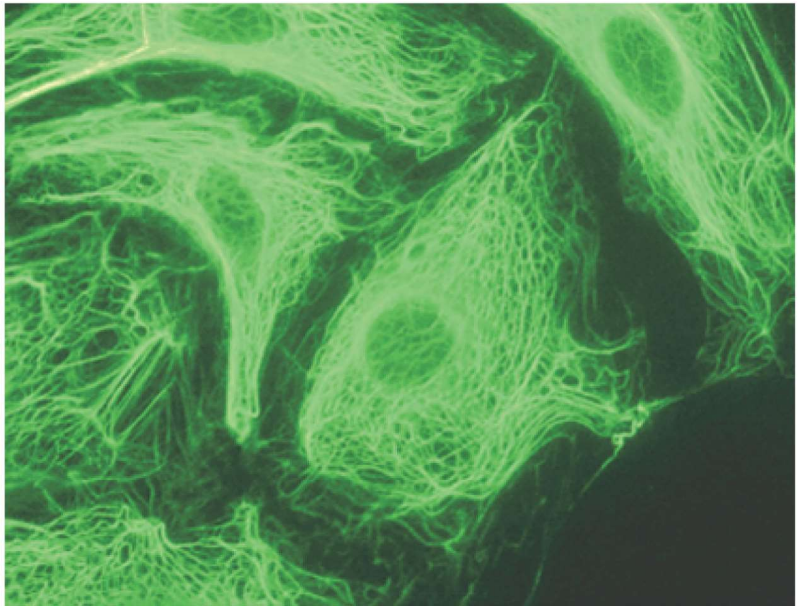


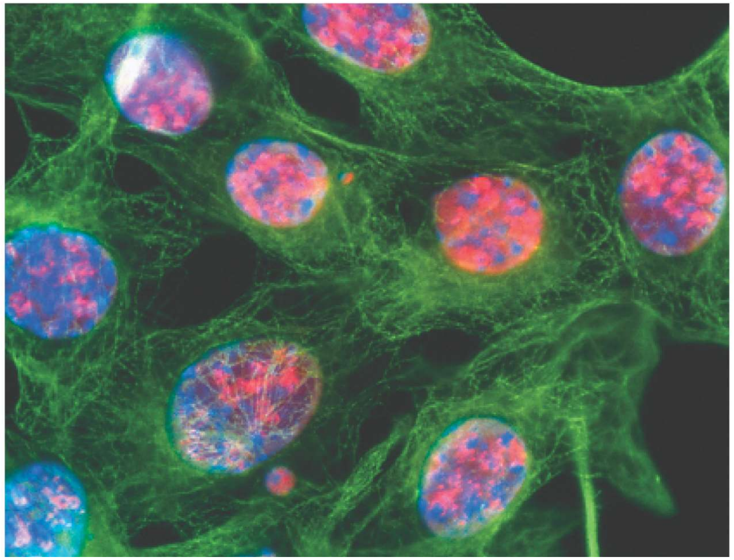
An animal cell cytoskeleton

Figure 16–18. Molecular Biology of the Cell, 4th Edition.

A Cytoskeleton Gallery







Cell Movement

Cell movement takes different forms.

-Crawling is accomplished via actin filaments and the protein **myosin**.

-**Flagella** undulate to move a cell.

-**Cilia** can be arranged in rows on the surface of a eukaryotic cell to propel a cell forward.

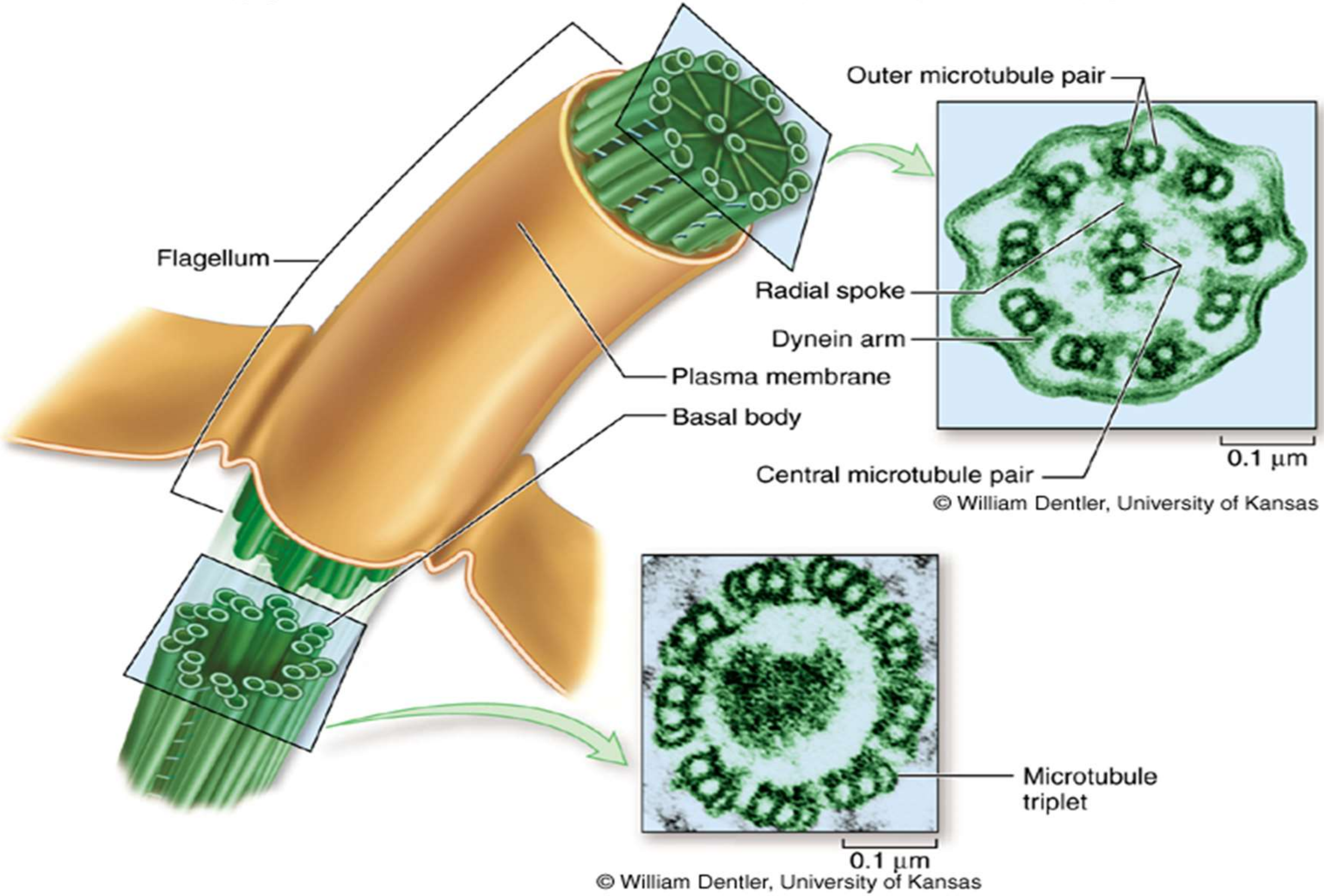
Cell Movement

The cilia and flagella of eukaryotic cells have a similar structure:

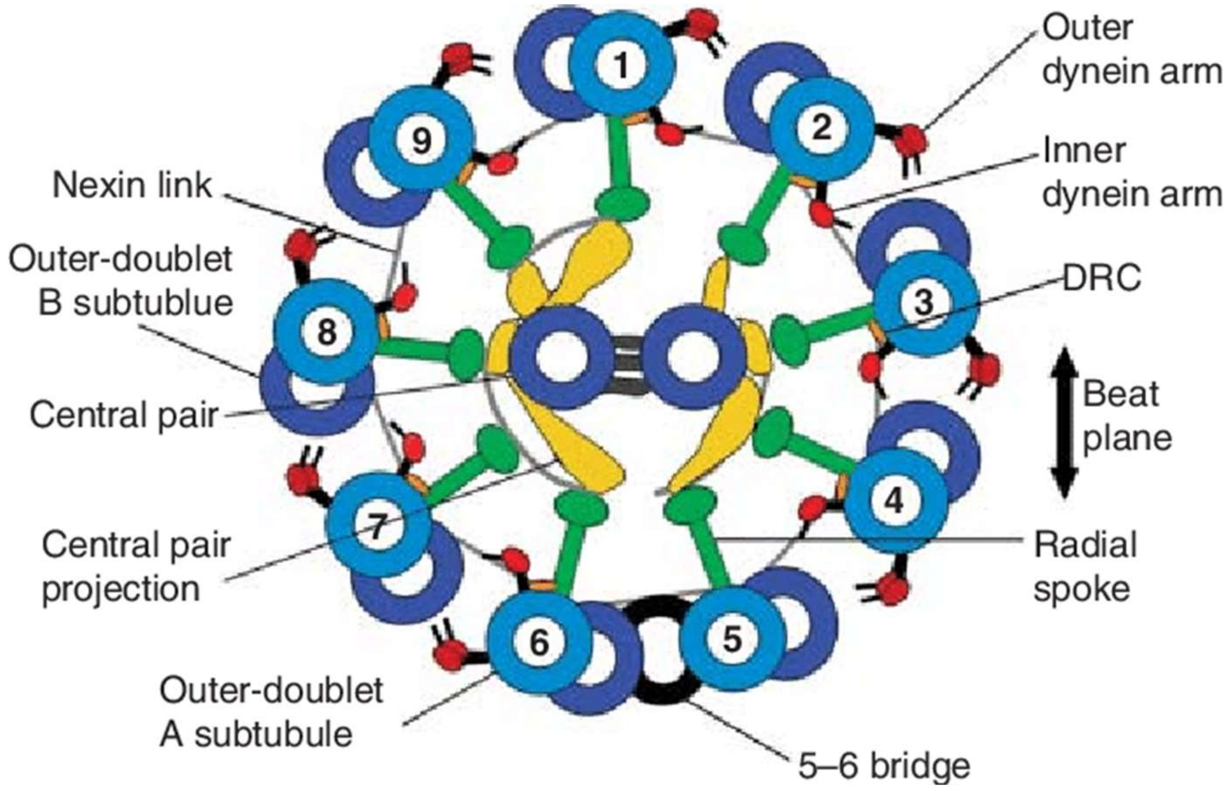
9+2 structure: 9 pairs of microtubules surrounded by a 2 central microtubules

Cilia are usually more numerous than flagella on a cell.

Cell Movement



Detailed structure of eukaryotic cilia/flagellum



A schematic diagram of the axoneme of a eukaryotic cilium or flagellum as viewed in cross-section. The component parts are labeled for the convenience of the reader. Reproduced with permission from Lindemann, CB & Lesich KA 2010. Flagellar and ciliary beating: the proven and the possible. Journal of Cell Science 123 519–528. (doi:10.1242/jcs.051326) q Company of Biologists.

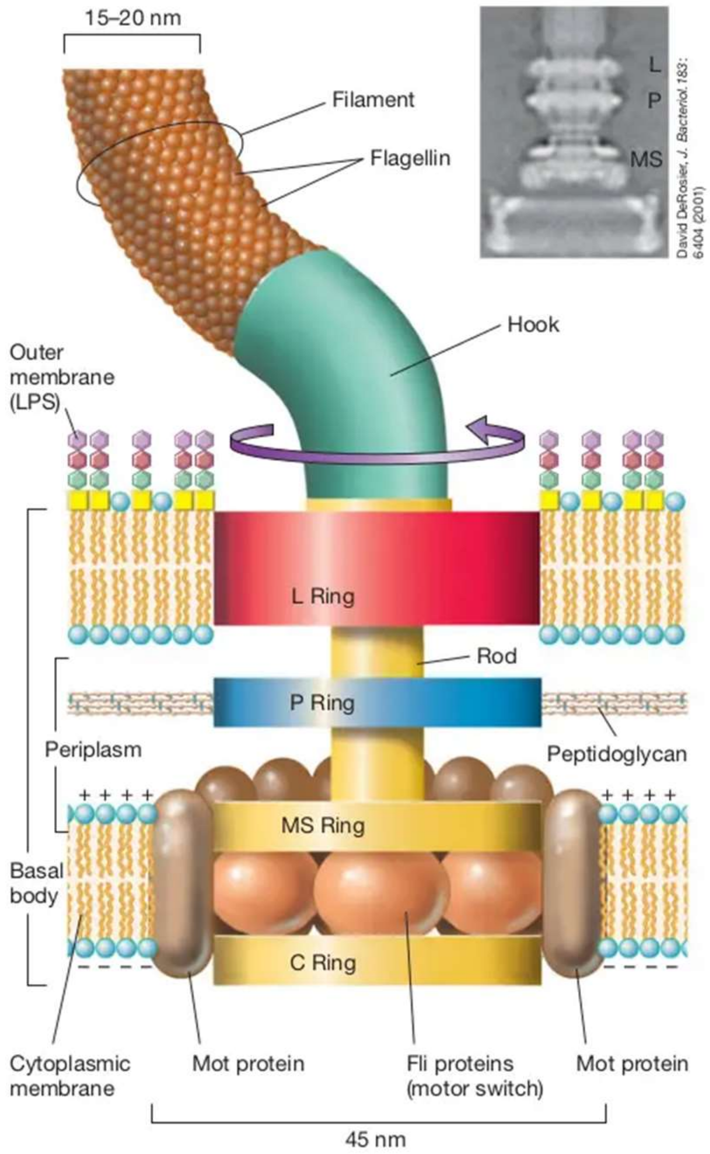
Bacterial Flagella

Flagella

-present in some prokaryotic cells

-used for locomotion

-rotary motion propels the cell



Extracellular Structures

Extracellular matrix (ECM)

-surrounds animal cells

-composed of glycoproteins and fibrous proteins such as collagen

-may be connected to the cytoplasm via **integrin** proteins present in the plasma membrane

Extracellular Structures

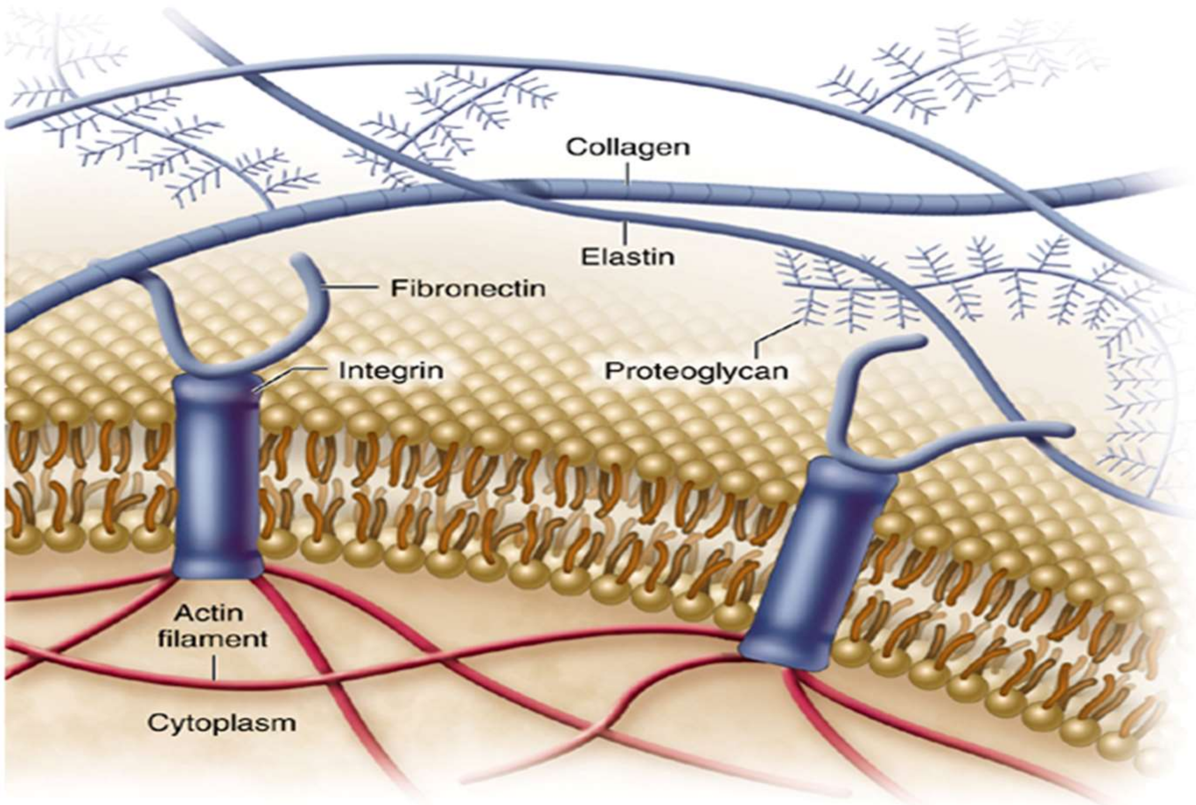


TABLE 4.3 A Comparison of Prokaryotic, Animal, and Plant Cells

	Prokaryote	Animal	Plant
EXTERIOR STRUCTURES			
Cell wall	Present (protein-polysaccharide)	Absent	Present (cellulose)
Cell membrane	Present	Present	Present
Flagella/cilia	Flagella may be present	May be present (9 + 2 structure)	Absent except in sperm of a few species (9 + 2 structure)
INTERIOR STRUCTURES			
ER	Absent	Usually present	Usually present
Ribosomes	Present	Present	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 DNA	Multiple; DNA–protein complex	Multiple; DNA–protein complex
Lysosomes	Absent	Usually present	Present
Vacuoles	Absent	Absent or small	Usually a large single vacuole

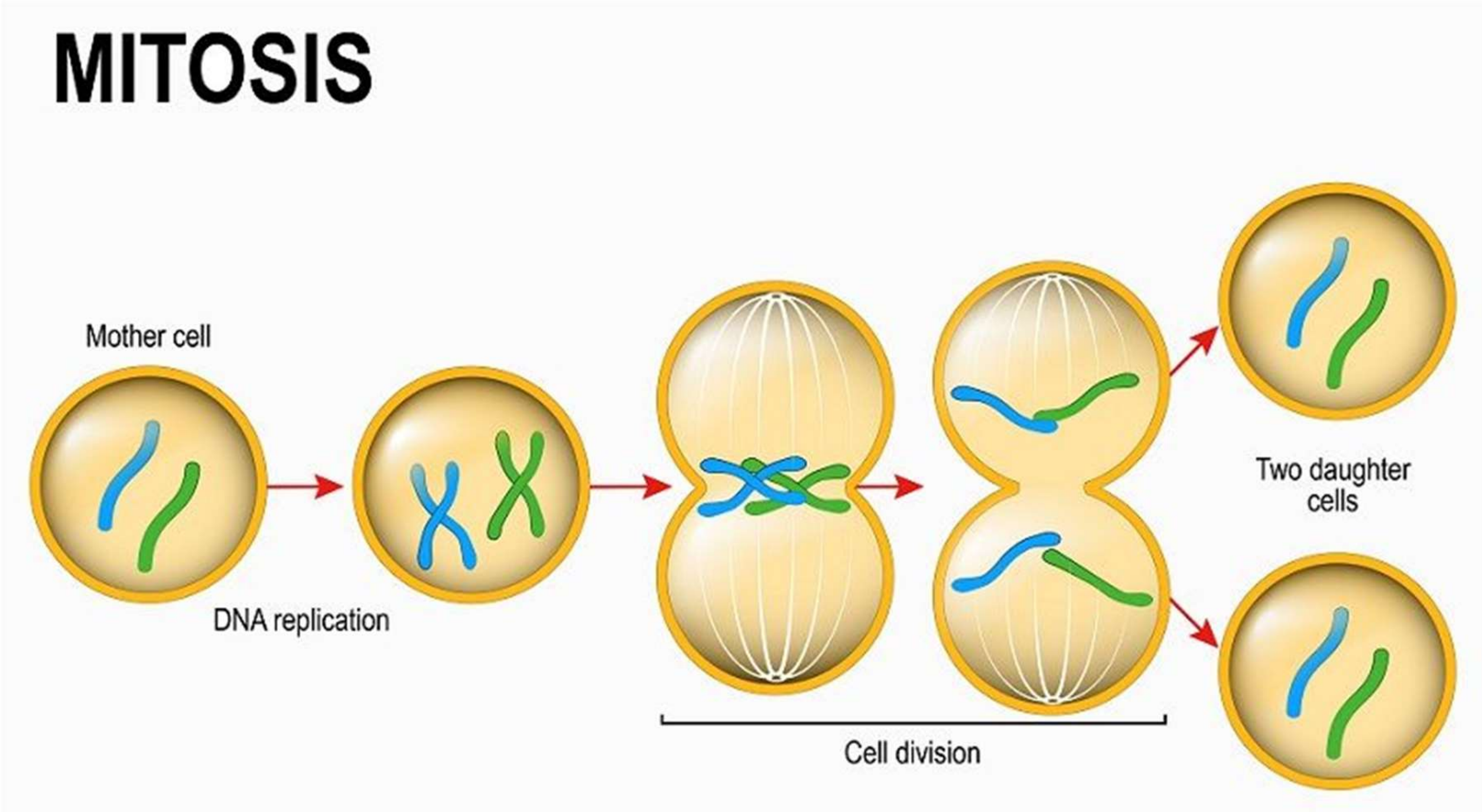
How cells are constructed?

- New cells are created from existing cells through a process referred to as the cell cycle. One cell can make a copy of itself and form two new daughter cells.

- There are two major tasks that have to happen every cell cycle. First, cells have to make an exact copy of their DNA. DNA is like the instruction manual for a cell. It encodes genes for characteristics and dictates things like eye color and blood type.

- The second major task of every cell cycle is for the replicated chromosomes to be organized and separated into opposite sides of the cell. This happens during mitosis, or M phase of the cell cycle.

- The cell then grows longer, further separating those masses of chromosomes. The middle of the cell then pinches off in a process known as cytokinesis, splitting the cell into two cells. A new cell has been created and that completes the cell cycle.


MITOSIS
Mother cell
DNA replication
Cell division
Two daughter cells

Mitosis

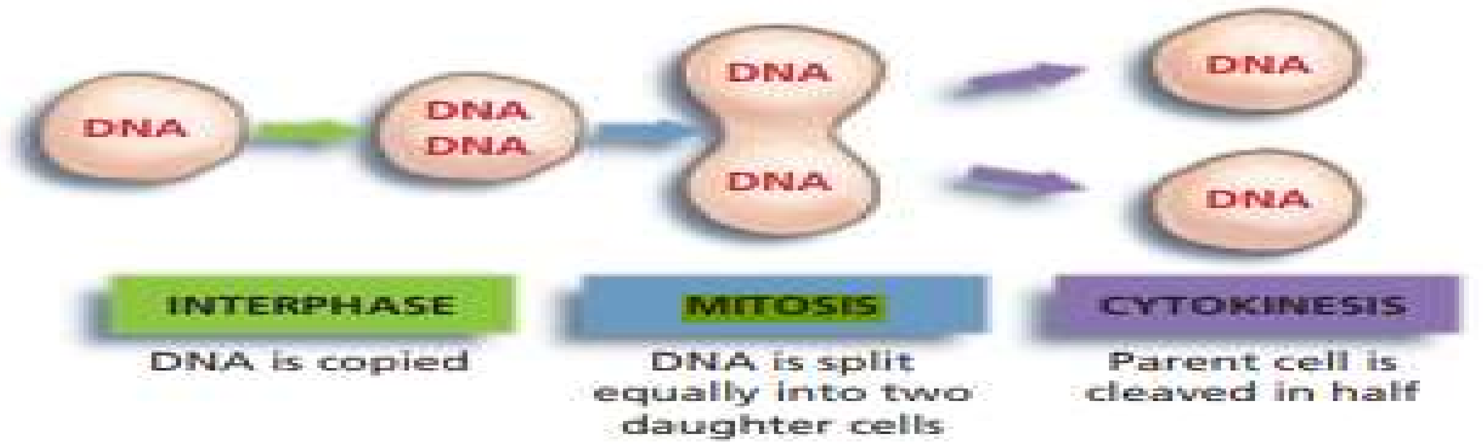
Mitosis is a process of cell division in which each of two identical daughter cells receives a diploid complements of chromosomes same as the diploid complement of the parent cell. It is usually followed by cytokinesis in which the cell itself divides to yield two identical daughter cells.

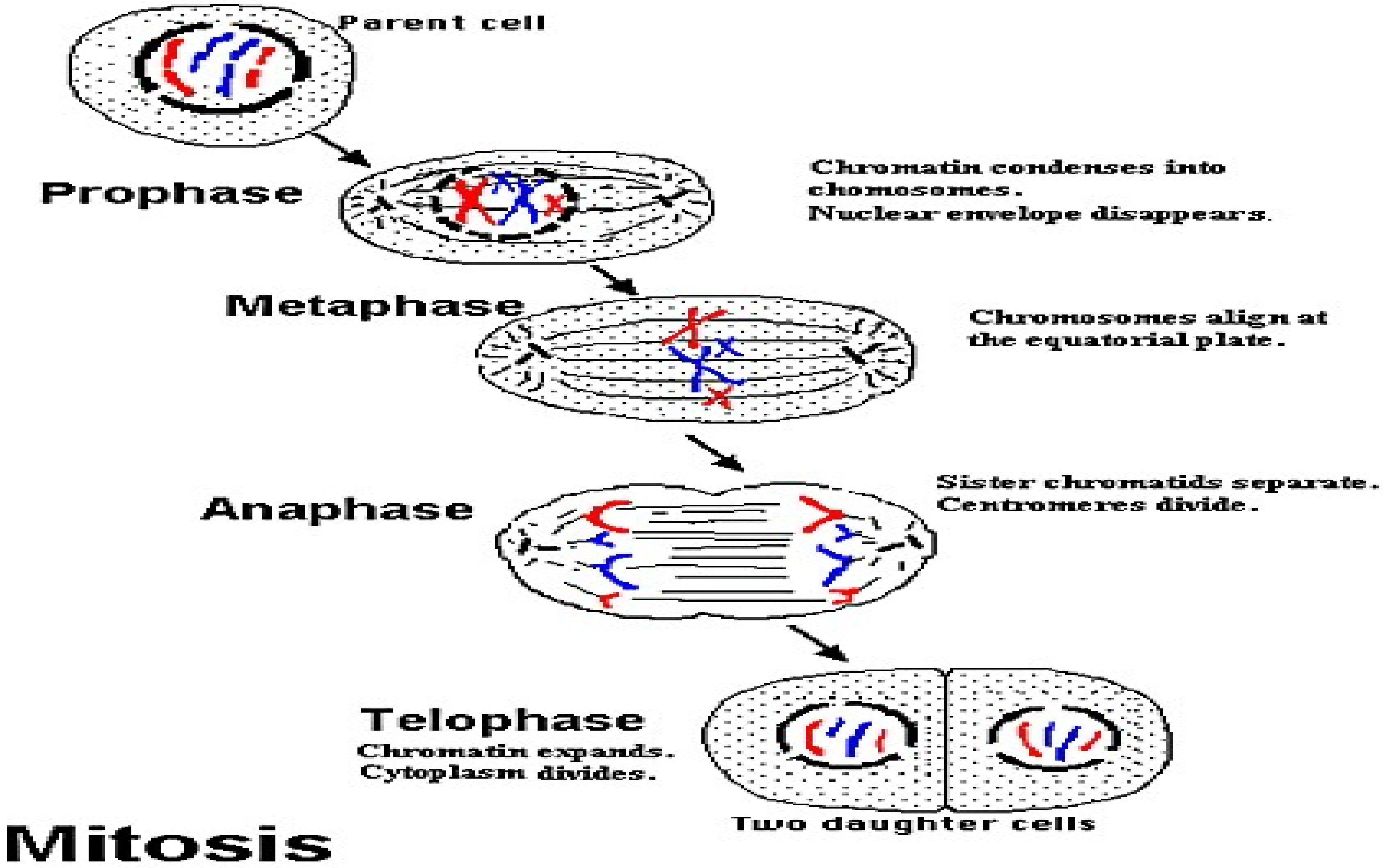
The basics in mitosis include:

1. Each chromosome is present as a duplicated structure at the beginning of nuclear division (2n).

2. Each chromosome divides longitudinally into identical halves and become separated from each other.

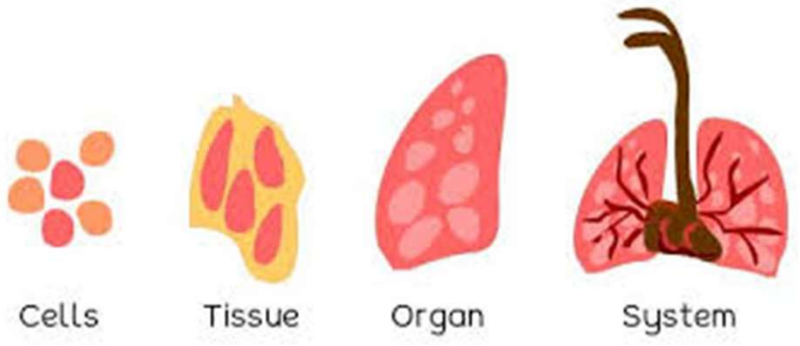
3. The separated chromosome halves move in opposite directions, and each becomes included in one of the two daughter nuclei that are formed.

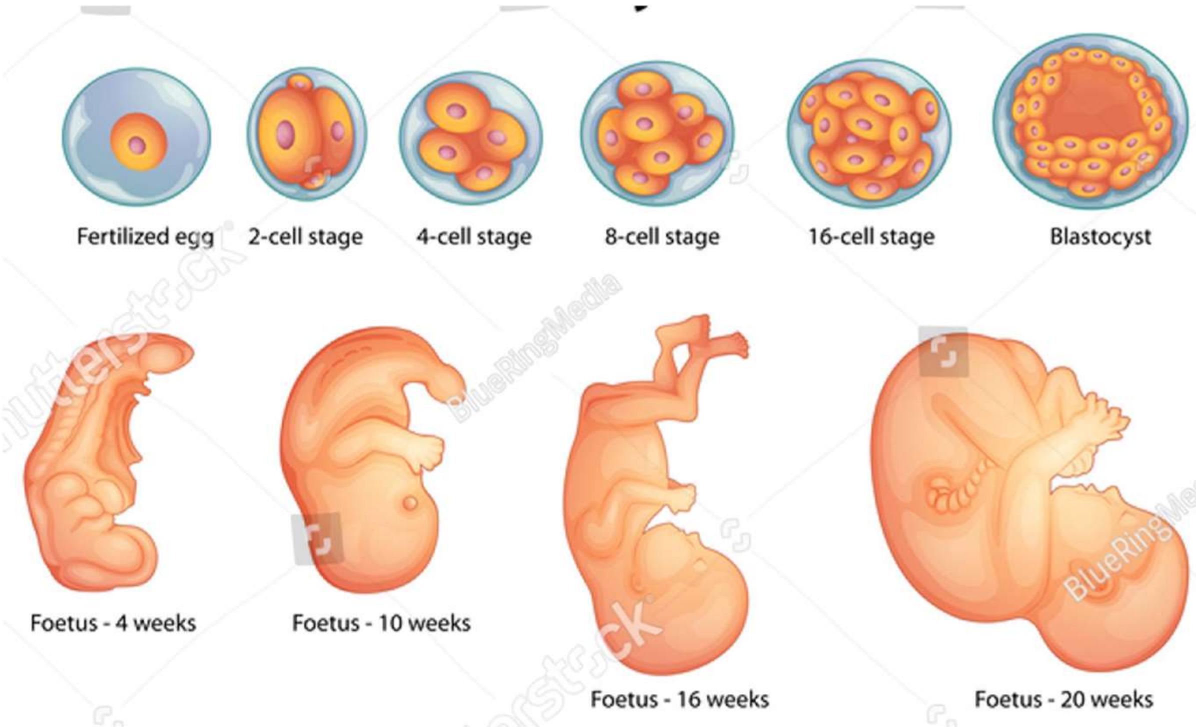



Parent cell
Prophase
Chromatin condenses into chomosomes.
Nuclear envelope disappears.
Metaphase
Chromosomes align at the equatorial plate.
Anaphase
Sister chromatids separate.
Centromeres divide.
Telophase
Chromatin expands.
Cytoplasm divides.
Two daughter cells
Mitosis

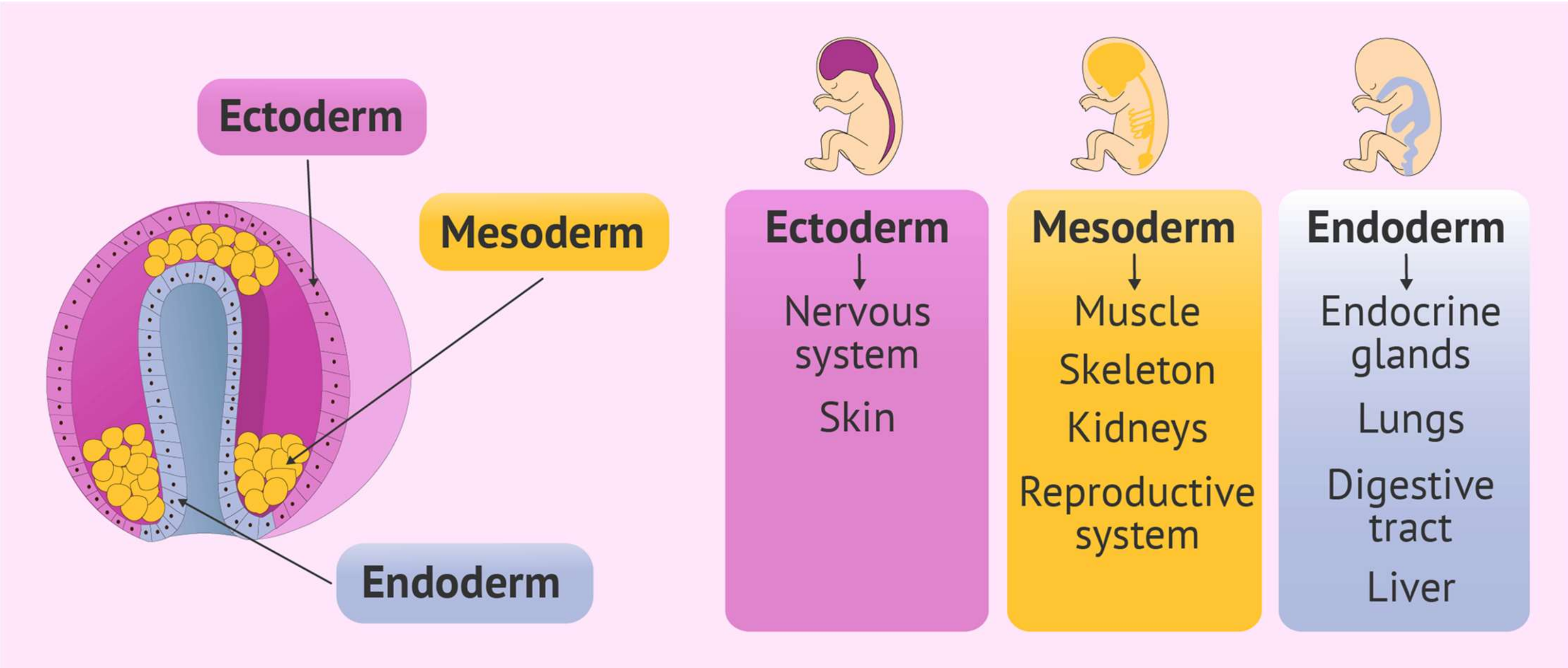
How cells build Organisms ?

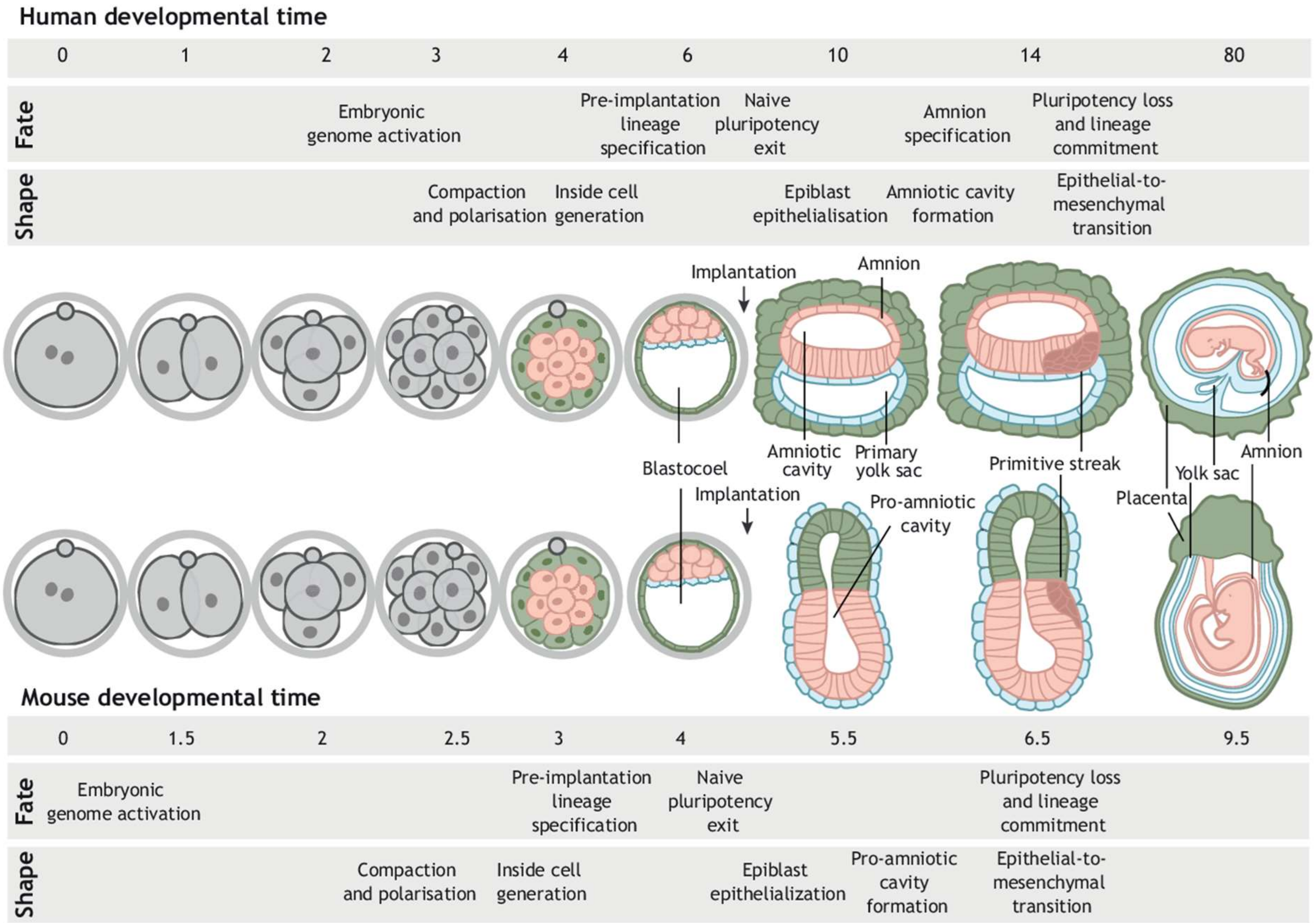
Organizational control mechanism allows cells to form tissues and anatomical structures in the developing embryo



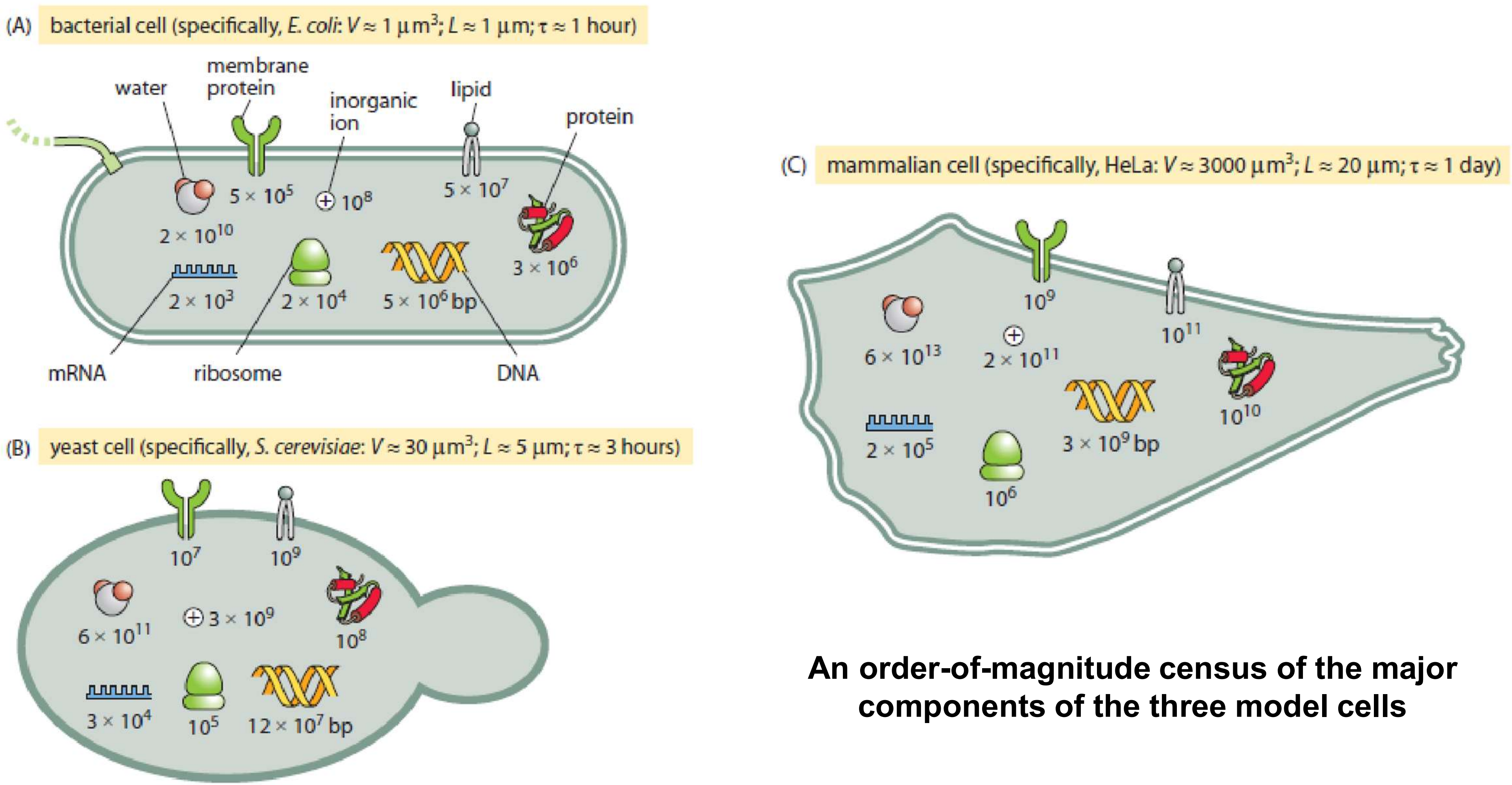


Spatial and Temporal organization




Human developmental time
0
1
2
3
4
6
10
14
80
Fate
Embryonic genome activation
Pre-implantation lineage specification
Naive pluripotency exit
Amnion specification
Pluripotency loss and lineage commitment
Shape
Compaction and polarisation
Inside cell generation
Epiblast epithelialisation
Amniotic cavity formation
Epithelial-to-mesenchymal transition
Implantation
Amnion
Blastocoel
Amniotic cavity
Primary yolk sac
Primitive streak
Yolk sac
Amnion
Placenta
Implantation
Pro-amniotic cavity
Mouse developmental time
0
1.5
2
2.5
3
4
5.5
6.5
9.5
Fate
Embryonic genome activation
Pre-implantation lineage specification
Naive pluripotency exit
Pluripotency loss and lineage commitment
Shape
Compaction and polarisation
Inside cell generation
Epiblast epithelialization
Pro-amniotic cavity formation
Epithelial-to-mesenchymal transition

Cell Census



An order-of-magnitude census of the major components of the three model cells

property	*E. coli*	budding yeast	mammalian (HeLa line)
cell volume	0.3–3 μm^3	30–100 μm^3	1000–10,000 μm^3
proteins per μm^3 cell volume	2–4 × 10^6		
mRNA per cell	10^3–10^4	10^4–10^5	10^5–10^6
proteins per cell	~10^6	~10^8	~10^{10}
mean diameter of protein	4–5 nm		
genome size	4.6 Mbp	12 Mbp	3.2 Gbp
number protein coding genes	4300	6600	21,000
regulator binding site length	10–20 bp	5–10 bp	
promoter length	~100 bp	~1000 bp	~10^4–10^5 bp
gene length	~1000 bp	~1000 bp	~10^4–10^6 bp (with introns)
concentration of one protein per cell	~1 nM	~10 pM	~0.1–1 pM
diffusion time of protein across cell ($D \approx 10$ μm^2/s)	~0.01 s	~0.2 s	~1–10 s
diffusion time of small molecule across cell ($D \approx 100$ μm^2/s)	~0.001 s	~0.03 s	~0.1–1 s
time to transcribe a gene	<1 min (80 nts/s)	~1 min	~30 min (incl. mRNA processing)
time to translate a protein	<1 min (20 aa/s)	~1 min	~30 min (incl. mRNA export)
typical mRNA lifetime	3 min	30 min	10 h
typical protein lifetime	1 h	0.3–3 h	10–100 h
minimal doubling time	20 min	1 h	20 h
ribosomes/cell	~10^4	~10^5	~10^6
transitions between protein states (active/inactive)	1–100 μs		
time scale for equilibrium binding of small molecule to protein (diffusion limited)	1–1000 ms (1 μM–1 nM affinity)		
time scale of transcription factor binding to DNA site	~1 s		
mutation rate	10^{-8}–10^{-10}/bp/replication		

Importance of cell census

- Realistic physical picture of any biological phenomenon demands a precise, quantitative understanding of the individual molecules involved and the distance between them
- You will find the cell interior is extremely crowded in contrast to the dilute and homogeneous environment of the biochemical test tube.
- We will see that the mean spacing between protein molecules within a typical cell is less than 10 nm.
- This is extremely useful to estimate the rates of macromolecular synthesis during the cell cycle.

E Coli: a model organism which has led to astounding discoveries

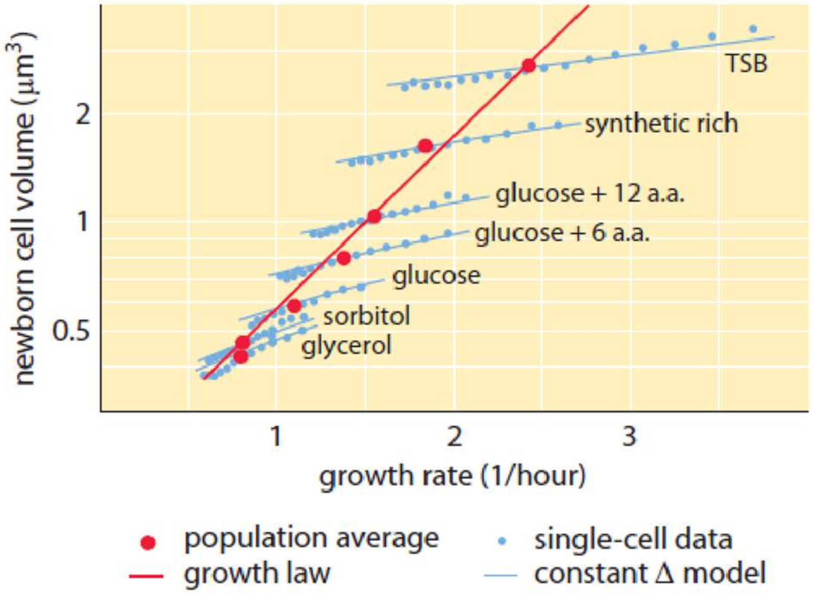
- Is easy to isolate present in human fecal matter
- E. coli is able to grow well in the presence of oxygen
- Easy to culture in lab, has high growth rate
- Genome has been sequenced 1997
- It carries plasmids extra-chromosomal DNA which can be manipulated easily by molecular biology techniques.
- Molecular biology techniques are easy to apply for creation of mutants
- Often, we will have recourse to *E. coli* because of particular experiments that have been performed on this organism.
- Further, even when we speak of experiments on other cells or organisms, often E. coli will be behind the scenes coloring our thinking.

Size of an *E. coli* cells and molecular composition

- E. coli. are made up of an array of different macromolecules as well as small molecules and ions. To estimate the number of proteins in an E. coli cell
- We begin by noting that with its 1 fL volume, the mass of such a cell is roughly 1 pg, where we have assumed that the density of the cell is that of water which is 1 g/mL.
- Measurements reveal that the dry weight of the cell is roughly 30 percent of its total and half of that mass is protein.
- As a result, the total protein mass within the cell is roughly 0.15 pg
- We can also estimate the number of carbon atoms in a bacterium on the grounds that roughly half the dry mass comes from the carbon content of these cells, a figure that implies 1010 carbon atoms per cell
- Revealing the extent of crowding within a bacterium, we can estimate the number of proteins by assuming a mean protein of 300 amino acids with each amino acid having a characteristic mass of 100 Da.
- Using these rules of thumb, we find that the mean protein has a mass of 30,000 Da.
- Using the conversion factor that 1 Da 1.6 × 10^{-24} g, we have that our typical protein has a mass of 5 × 10^{-20} g.

How big is an *E. coli* cell ?

- The size of a typical bacterium such as *E. coli* serves as a convenient standard ruler for characterizing length scales in molecular and cell biology
- Diameter ≈1μm, a length of ≈2μm, and a volume of ≈1μm3
- The shape can be approximated as a spherocylinder—that is, a cylinder with hemispherical caps.
- Inferences can vary with cell types under various conditions.



Relation between cell volume and growth rate. Using microscopy and microfluidic devices, cell volume can be measured at the single-cell level under various conditions, confirming that the average cell volume grows exponentially with growth rate.

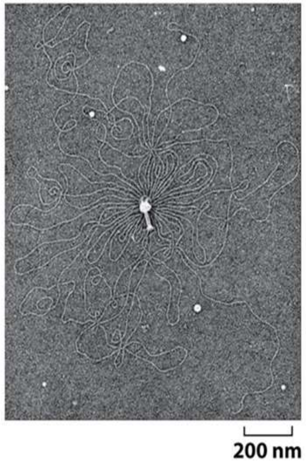


Figure 1.13 Physical Biology of the Cell (© Garland Science 2009)

	Quantity of interest	Symbol	Rule of thumb
E. coli	Cell volume	$V_{E.\ coli}$	$\approx 1\ \mu m^3$
	Cell mass	$m_{E.\ coli}$	≈ 1 pg
	Cell cycle time	$t_{E.\ coli}$	≈ 3000 s
	Cell surface area	$A_{E.\ coli}$	$\approx 6\ \mu m^2$
	Genome length	$N_{bp}^{E.\ coli}$	$\approx 5 \times 10^6$ bp
	Swimming speed	$v_{E.\ coli}$	$\approx 20\ \mu m/s$
Yeast	Volume of cell	V_{yeast}	$\approx 60\ \mu m^3$
	Mass of cell	m_{yeast}	≈ 60 pg
	Diameter of cell	d_{yeast}	$\approx 5\ \mu m$
	Cell cycle time	t_{yeast}	≈ 200 min
	Genome length	N_{bp}^{yeast}	$\approx 10^7$ bp
Organelles	Diameter of nucleus	$d_{nucleus}$	$\approx 5\ \mu m$
	Length of mitochondrion	l_{mito}	$\approx 2\ \mu m$
	Diameter of transport vesicles	$d_{vesicle}$	≈ 50 nm
Water	Volume of molecule	V_{H_2O}	$\approx 10^{-2}\ nm^3$
	Density of water	ρ	$1\ g/cm^3$
	Viscosity of water	η	≈ 1 centipoise (10^{-2} g/(cm s)) $=10^{-3}$ Pa·sec
	Hydrophobic embedding energy	$\approx E_{hydr}$	25 cal/(mol Å^2)
DNA	Length per base pair	l_{bp}	$\approx 1/3$ nm
	Volume per base pair	V_{bp}	$\approx 1\ nm^3$
	Charge density	λ_{DNA}	2 e/0.34 nm
	Persistence length	ξ_P	50 nm =147bp
Amino acids and proteins	Radius of "average" protein	$r_{protein}$	≈ 2 nm
	Volume of "average" protein	$V_{protein}$	$\approx 25\ nm^3$
	Mass of "average" amino acid	M_{aa}	≈ 100 Da
	Mass of "average" protein	$M_{protein}$	$\approx 30{,}000$ Da
	Protein concentration in cytoplasm	$c_{protein}$	≈ 300 mg/mL
	Characteristic force of protein motor	F_{motor}	≈ 5 pN
	Characteristic speed of protein motor	v_{motor}	≈ 200 nm/s
	Diffusion constant of "average" protein	$D_{protein}$	$\approx 100\ \mu m^2/s$
Lipid bilayers	Thickness of lipid bilayer	d	≈ 5 nm
	Area per molecule	A_{lipid}	$\approx \frac{1}{2}\ nm^2$
	Mass of lipid molecule	m_{lipid}	≈ 800 Da

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1 Da = (mass of one carbon-12)/12

$$V_E \approx 1\mu m^3 = 1\ fL$$

$$m_{E.Coli}^{Coli} \approx 1pg$$

$$\rho_{E.Coli} \approx 1g/mL \approx \rho_{water}$$

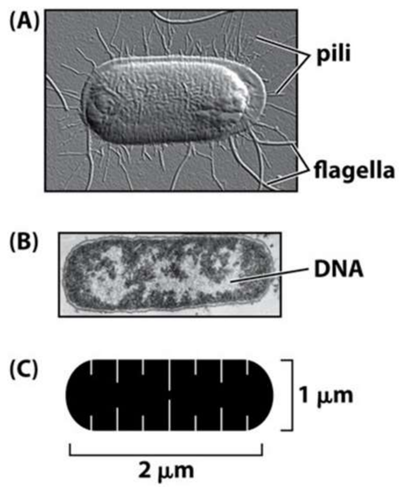


Figure 2.1 Physical Biology of the Cell (© Garland Science 2009)

$$1\ molecule / 1\ fL = \frac{1mol}{6 \times 10^{23} \times 10^{-15} L} \approx 2nM$$

Thermal energy scale (at 300K)

$k_B T = 4.14 \times 10^{-21}\ J = 4.14\ pN \cdot nm$

$\square\ 0.59 kcal/mol$

$$AB \square A + B$$

$$\Delta G = k_B T \log K_d = k_B T \log \frac{[A][B]}{[AB]} \approx k_B T \log 10^{-9} = -2.3 \times 9 k_B T \approx -20 k_B T$$

Typical protein-protein interaction energy

$$\approx 20 k_B T\ (K_d = 1nM)[1 molecule\ cell]$$

$$\approx 14 k_B T\ (K_d = 1\mu M)[10^3 molecules / cell]$$

$$\approx 7 k_B T\ (K_d = 1mM)[10^6 molecules / cell]$$

Water is 70 % of the cell mass $(m_{E.Coli} = 1pg)$

Dry mass of the cell (30% of 1pg) = 0.3 pg

Half of the dry mass (=0.15 pg) = proteins

1 Da = mass of a hydrogen atom = $\frac{1}{6 \times 10^{23}} g = 1.6 \times 10^{-24} g$

1 amino acid = 100 Da

average protein size = 300 a.a. → 30,000 Da

$N_{prot} = \frac{0.15\ pg}{30,000\ Da} = \frac{0.15\ pg}{30,000 \times 1.6 \times 10^{-24}\ g} \approx 3,000,000$

$= \begin{cases} \frac{1}{3} N_{prot} \rightarrow \text{membrane proteins} \\ \frac{2}{3} N_{prot} \rightarrow \boxed{\text{cytoplasmic proteins}} \end{cases}$

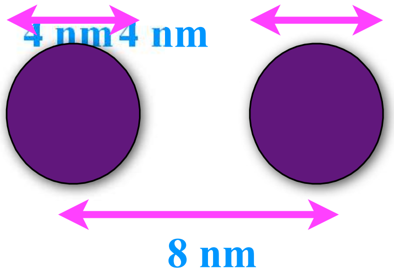
$m_{water} = 0.7\ pg$

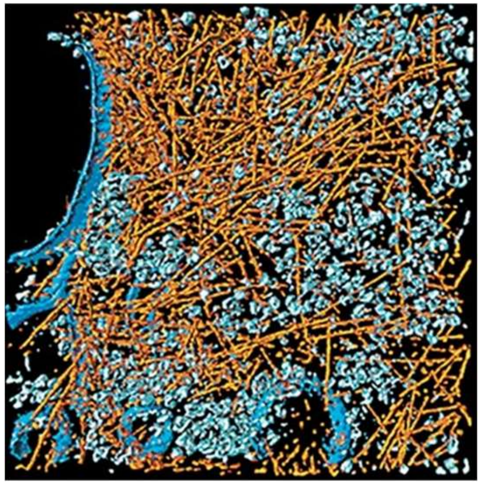
$N_{water} = \frac{0.7\ pg}{18Da \times (1.6 \times 10^{-24} g / Da)} \approx 2 \times 10^{10}$

There are 2×10^6 proteins in cytoplasm

$$c_{prot} = 2 \times 10^6 / 1\mu m^3$$

$$d_{prot-prot} = c^{-1/3} = \left(\frac{(10^3\, nm)^3}{2 \times 10^6} \right)^{1/3} = (500 nm)^{1/3} \approx 8nm$$





Mean spacing between the macromolecules in cell

~

size of macromolecules themselves

Cell is very crowded ...

Membrane

Surface area of *E.Coli*

$$A_{E.Coli} \approx (2\pi R) \times L \approx 6\mu m^2$$

E. coli has double (inner and outer) membranes and each membrane is made of bilayer.

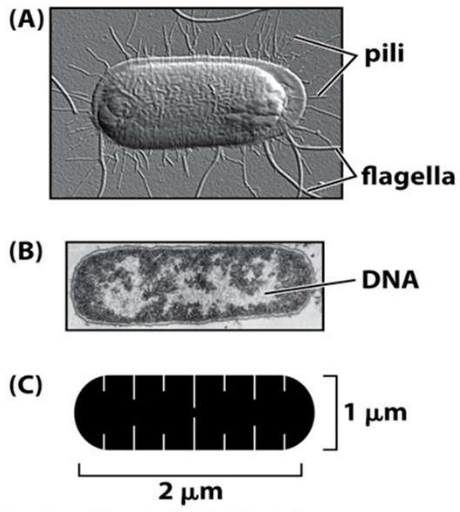


Figure 2.1 Physical Biology of the Cell (© Garland Science 2009)

Half of the surface area is covered with membrane proteins

$$N^{lipid}_{E.Coli} \approx \frac{4 \times 0.5 \times 6\mu m^2}{0.5 nm^2} \approx 2 \times 10^7$$

Taking the molecular census to set criteria for the judgement

Measurement of protein census of *E. Coli* using 2D polyacrylamide gel electrophoresis
Experimental determination of biomolecular content

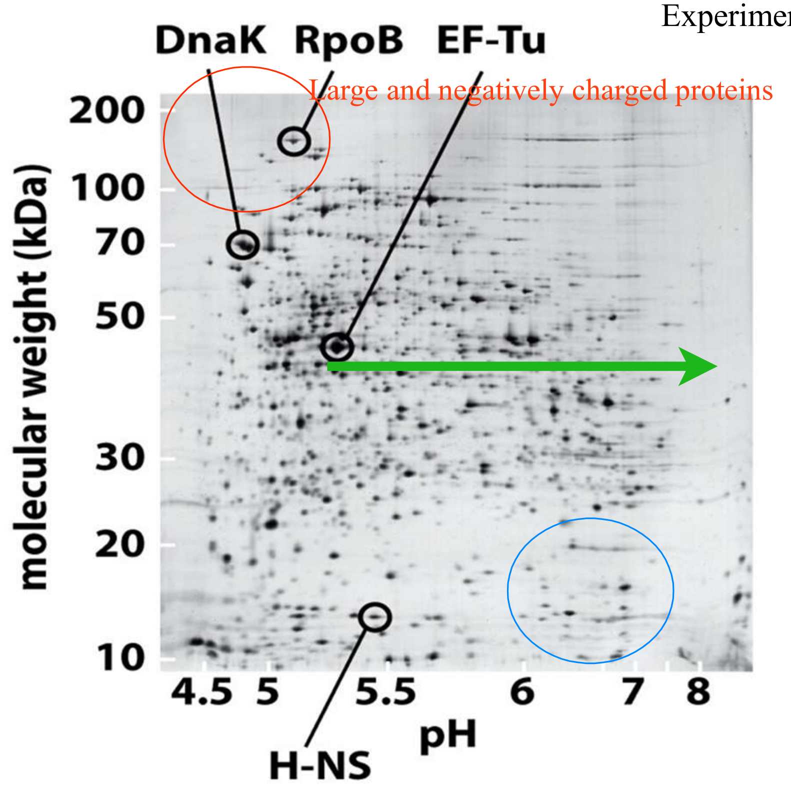


Figure 2.3 Physical Biology of the Cell (© Garland Science 2009)

1.Protein mixture loaded at one end of the gel and an electric field is applied across the gel. ($F=qE=\zeta v$)

2.A charged detergent binding to proteins is added. (charge of detergent ~ protein size; $q \sim R \sim v$)

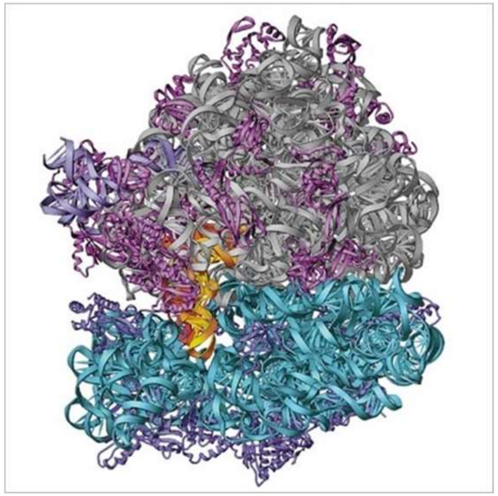
3. Proteins are stained using dye. Conc ~ Intensity of the spot.

4.Cut each spot, elute the proteins and determine the size and amino acid content using mass spectroscopy.

small and positively charged proteins

RIBOSOME

20% of the protein complement of a cell = ribosomal proteins



Ribosome (70S) = Large subunit + small subunit
Large subunit (50S) = 23S r-RNA + r-proteins
Small subunit (30S) = 16S r-RNA + r-proteins

S : Svedberg constant (sedimentation constant)
- A heavier particle sediments faster in the centrifugation, thus have a larger S value.

$$m(1-\rho\bar{v})r\omega^2 = \xi \frac{dr}{dt}$$

$$\frac{M(1-\rho\bar{v})D}{RT} = \frac{d \log r}{\omega^2 dt} \equiv S$$

$$\text{ribosome (2.5MDa)} \begin{cases} r-RNA: \text{ 2/3 of the mass} \\ r-protein: \text{ 1/3 of the mass} \end{cases}$$

$$m_{r-protein} = 830,000Da$$

$$M_{r-protein} = 20\% \times M_{protein}$$

$$\therefore N_{ribosome} = \frac{M_{r-prot}}{m_{r-prot}} = \frac{0.2 \times 0.15\,pg}{830,000Da} = 20,000$$

$$\approx 19,000$$

Substance	% of total dry weight	Number of molecules
Macromolecule		
Protein	55.0	2.4×10^6
RNA	20.4	
23S RNA	10.6	19,000
16S RNA	5.5	19,000
5S RNA	0.4	19,000
Transfer RNA (4S)	2.9	200,000
Messenger RNA	0.8	1,400
Phospholipid	9.1	22×10^6
Lipopolysaccharide	3.4	1.2×10^6
DNA	3.1	2
Murein	2.5	1
Glycogen	2.5	4,360
Total macromolecules	**96.1**	
Small molecules		
Metabolites, building blocks, etc.	2.9	
Inorganic ions	1.0	
Total small molecules	**3.9**	

Table 2.1 Observed macromolecular census of an *E. coli* cell. (Data from F. C. Neidhardt et al., Physiology of the Bacterial Cell, Sunderland, Sinauer Associates Inc., 1990 and M. Schaechter et al., Microbe, Washington DC, ASM Press, 2006.)

Table 2.1 Physical Biology of the Cell (© Garland Science 2009)

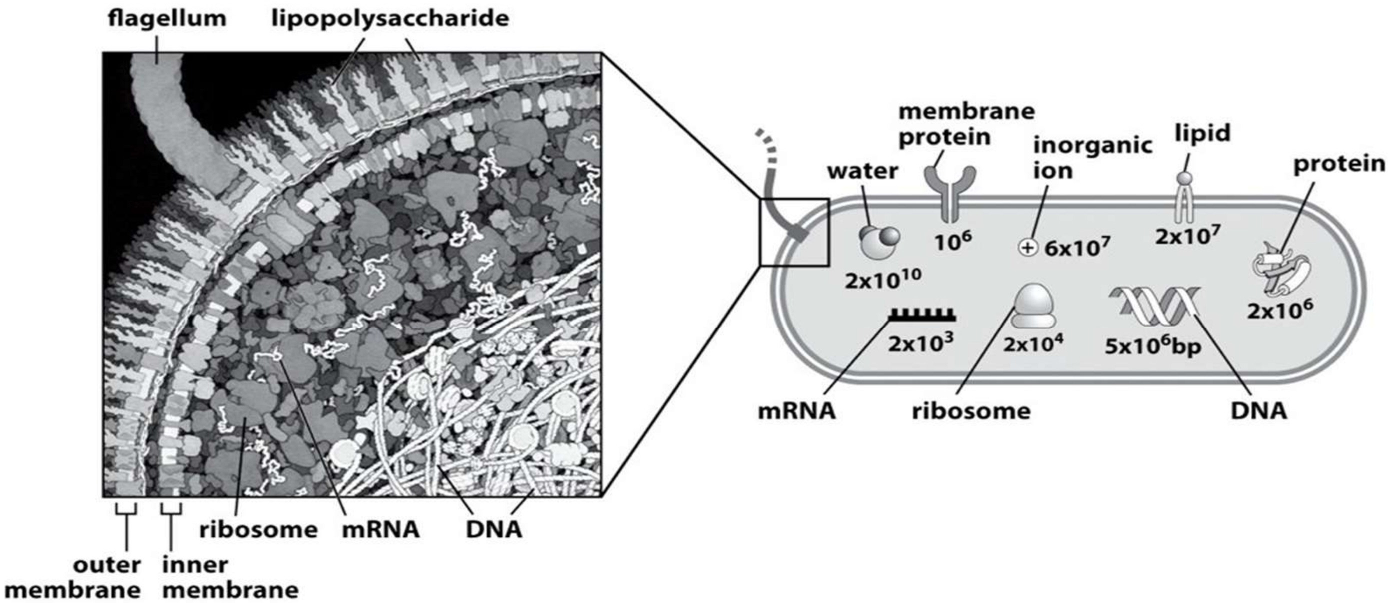


Figure 2.2 Physical Biology of the Cell (© Garland Science 2009)

Conversion : Number ⇨ Concentration ⇨ Average distance

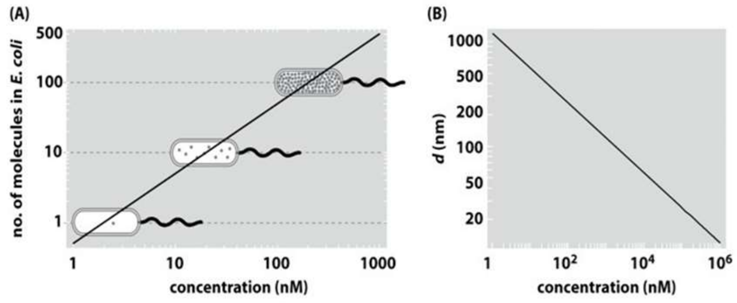
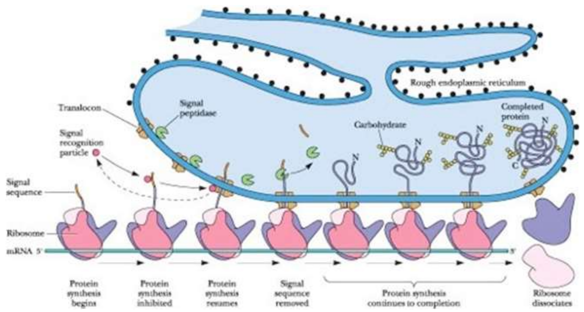


Figure 2.4 Physical Biology of the Cell (© Garland Science 2009)

* 1 molecule in a *bacterium* ~ 2 nM.

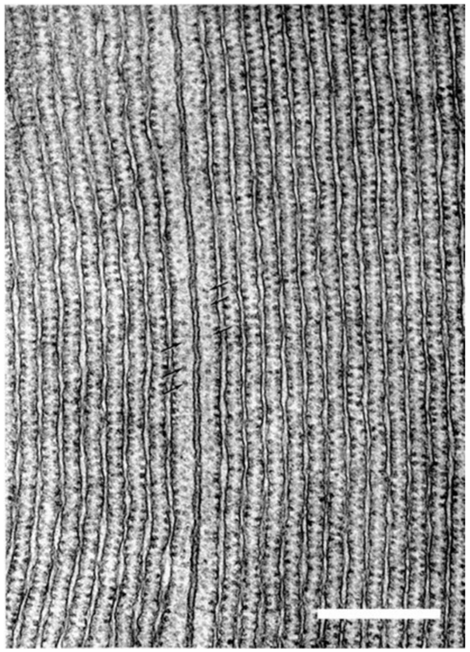


Example : Ribosome $1L = 10^{-3}\, m^3$

no. of ribosome = 19,000 (Table 2.1)

Concentration = 19,000/1fL ~ 32 μM

Average distance ~ 37 nm.



Cellular crowding and its implications

- The Cellular Interior Is Highly Crowded With Mean Spacings Between Molecules That Are Comparable to Molecular Dimensions
- Increase in the effective concentration of macromolecules alters the rates and equilibrium constants of their reactions
- Alters dissociation constants by favoring the association of macromolecules, such as when multiple proteins come together to form protein complexes, or when DNA-binding proteins bind to their targets in the genome
- Crowding may also affect enzyme reactions involving small molecules if the reaction involves a large change in the shape of the enzyme.[10]
- The size of the crowding effect depends on both the molecular mass and shape of the molecule involved,

Cellular crowding and its implications

- the increase in the strength of interactions between proteins and DNA[5] is importance in processes such as transcription and DNA replication
- involved in processes as diverse as the aggregation of hemoglobin in sickle-cell disease, and the responses of cells to changes in their volume.[4]
- the crowding effect can accelerate the folding process,
- crowding can reduce the yield of correctly folded protein by increasing protein aggregation.[
- increase the effectiveness of chaperone proteins such as GroEL in the cell,[17]
- Crystallins fill the interior of the lens. These proteins have to remain stable and in solution for the lens to be transparent; precipitation or aggregation of crystallins causes cataracts
- Crystallins are present in the lens at extremely high concentrations, over 500 mg/ml, and at these levels crowding effects are very strong.

- The large crowding effect adds to the thermal stability of the crystallins, increasing their resistance to denaturation
- This effect may partly explain the extraordinary resistance shown by the lens to damage caused by high temperatures.[22]
- Crowding may also play a role in diseases that involve protein aggregation, such as sickle cell anemia, alzheimer's disease,

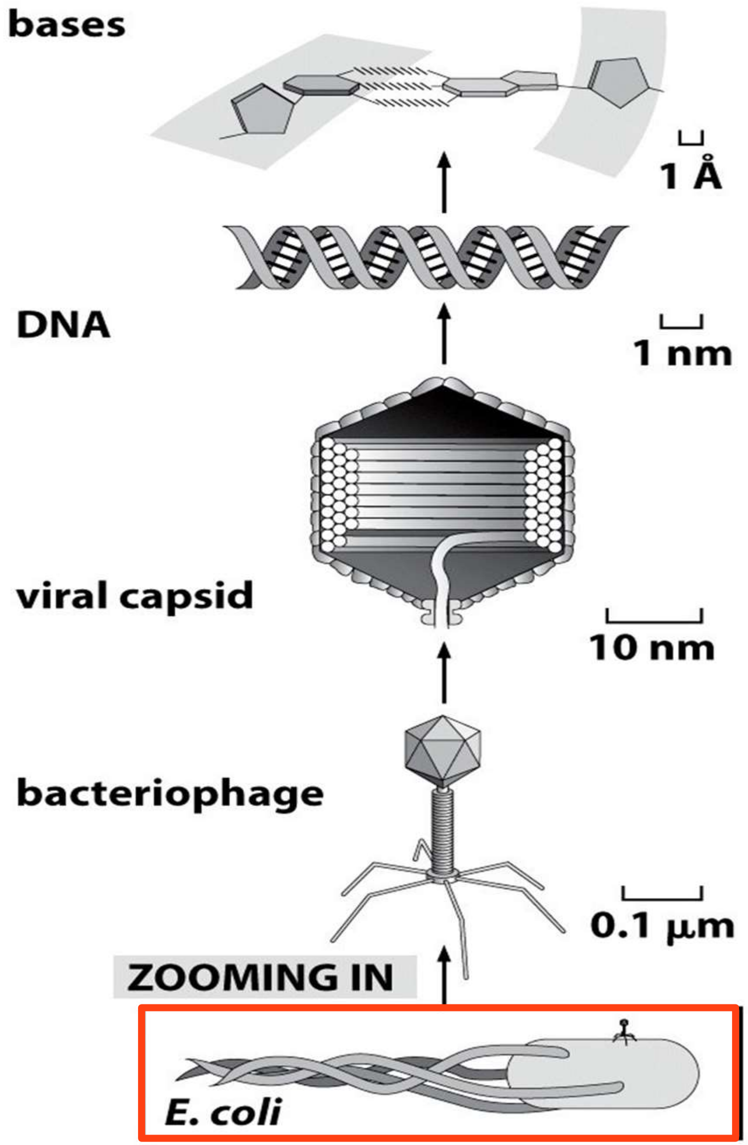


Figure 2.7 (part 1) Physical Biology of the Cell (© Garland Science 2009)

Biological Structures exist over a huge range of scales

Hierarchy of spatial scales

Number of proteins in an E.coli cell

3,000,000

Number of ribosomes in an E.coli cell

20,000

Number of lipids in an E.coli cell

20,000,000

Size of genome in an E.coli cell

5,000,000 bp

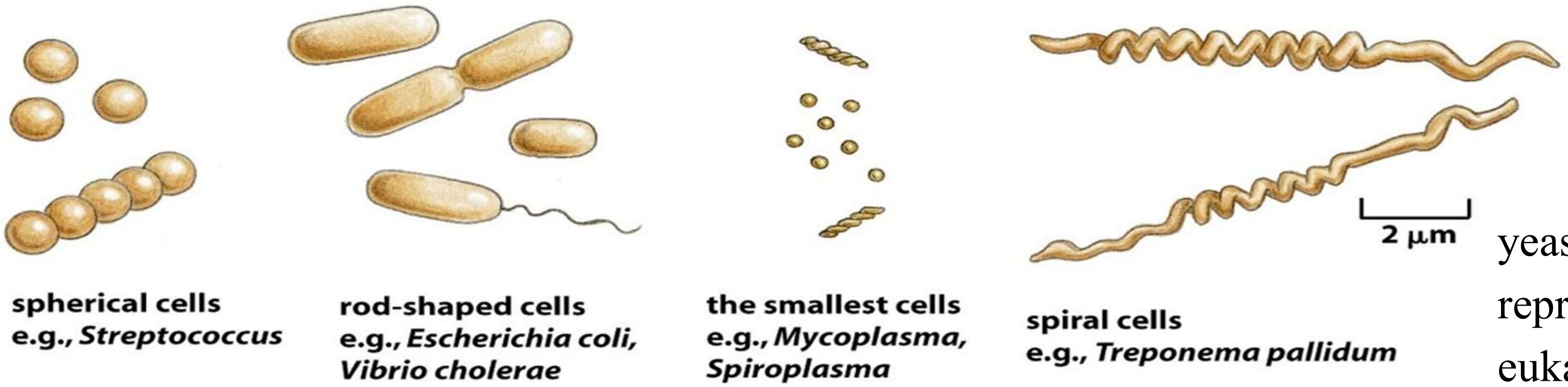


Figure 1-17 Molecular Biology of the Cell 5/e (© Garland Science 2008)

yeast cell : useful representative to study eukaryotes

Tremendous diversity in living cells ...

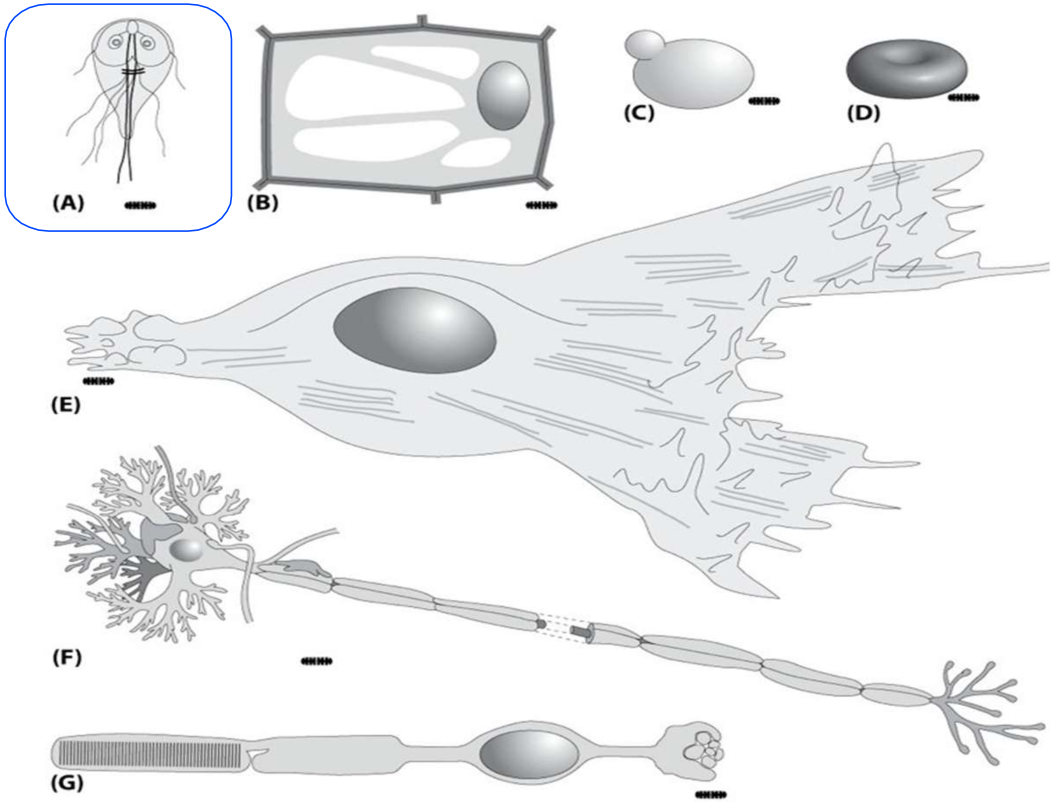


Figure 2.8 Physical Biology of the Cell (© Garland Science 2009)

Figure 20.3 Physical Biology of the Cell (© Garland Science 2009)

Protist

Cells

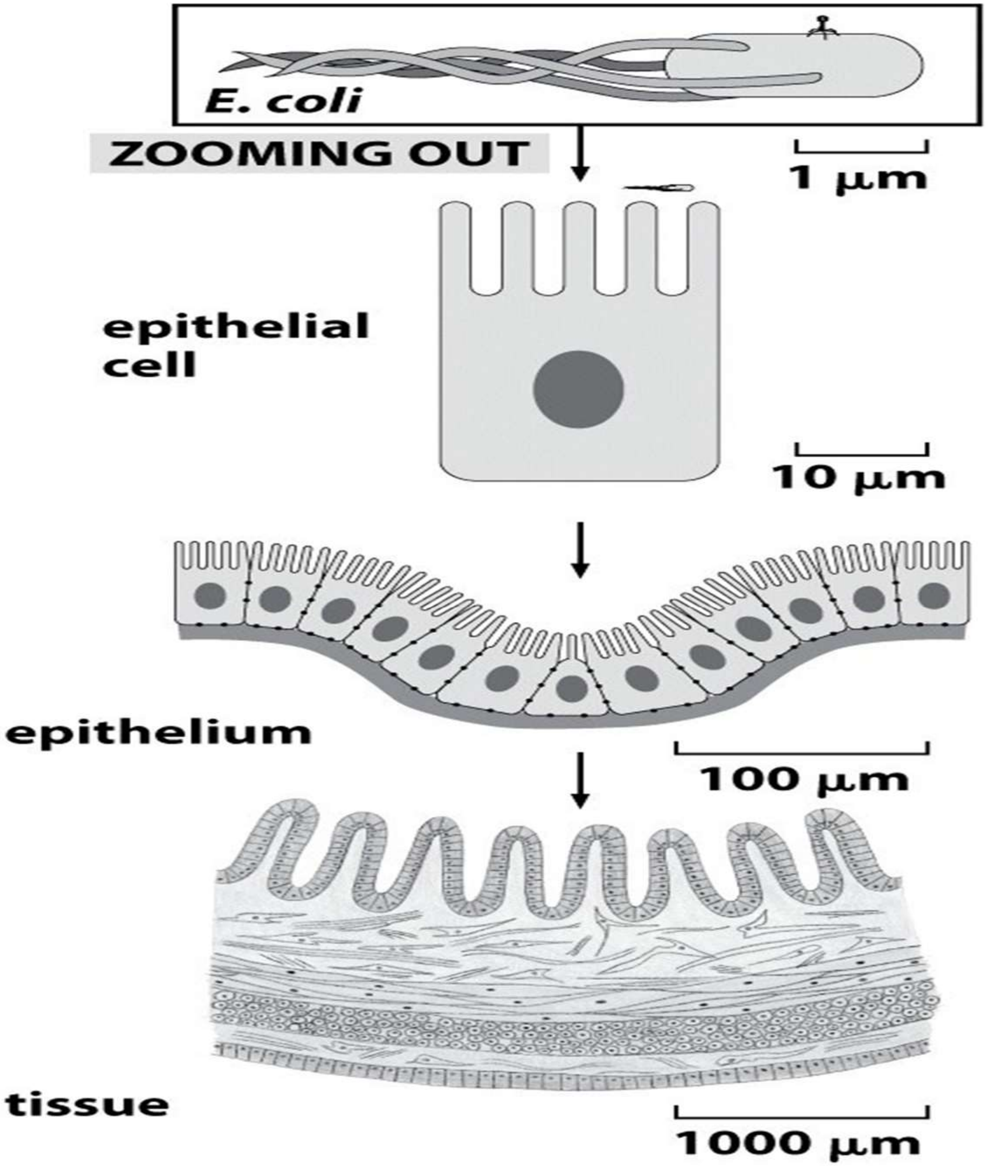


Figure 2.7 (part 2) Physical Biology of the Cell (© Garland Science 2009)

Biological Structures exist over a huge range of scales

Hierarchy of spatial scales

yeast cell : model system to study a single eukaryote cell

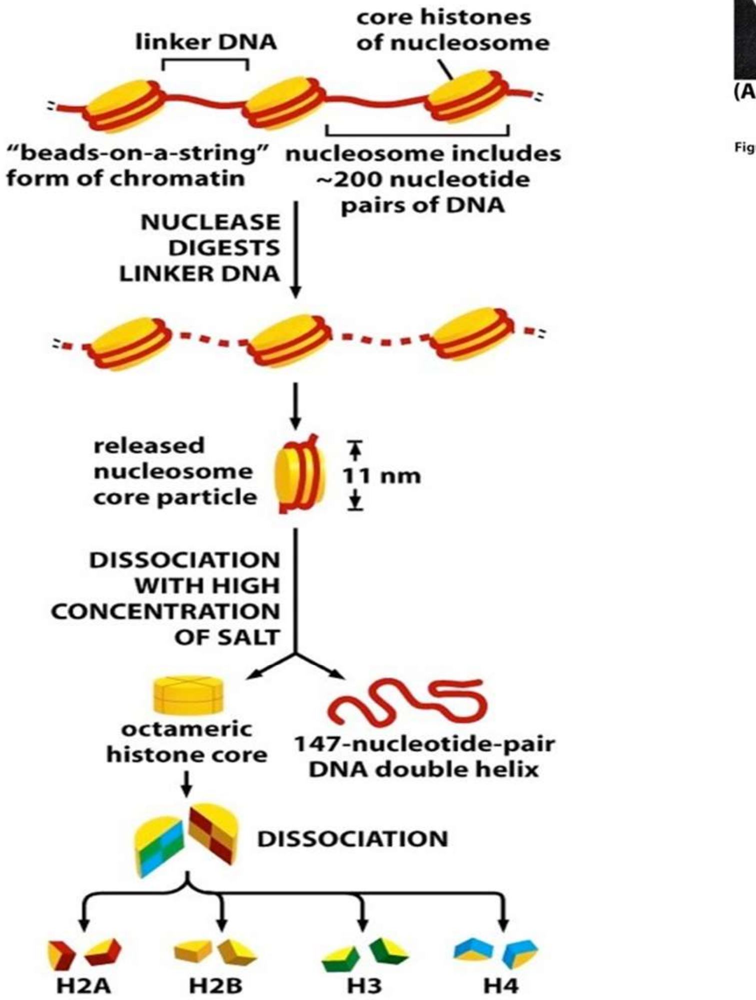


Figure 4-23 Molecular Biology of the Cell 5/e (© Garland Science 2008)

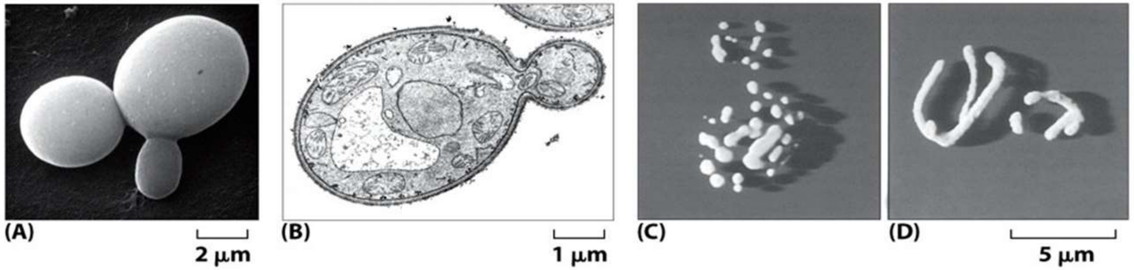


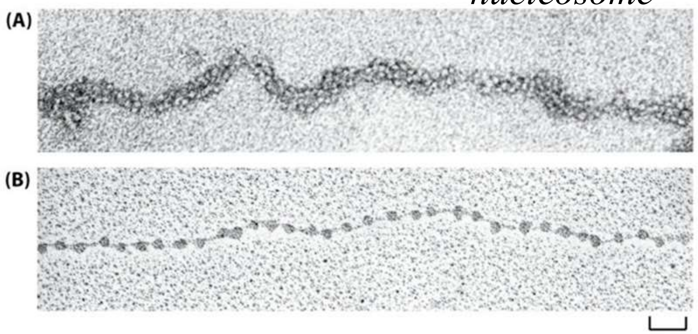
Figure 2.9 Physical Biology of the Cell (© Garland Science 2009)

$$L_{yeast} \approx 5\mu m \qquad V_{yeast} = \frac{4}{3}\pi(2.5\mu m)^3 \approx 60\mu m^3 \approx 60 V_{E.Coli}$$

$$N^{Yeast}_{protein} \approx 60 \times N^{E.Coli}_{protein}$$

$$N^{Yeast}_{lipid} \approx \frac{2 \times 0.5 \times (80\mu m^2)}{0.5 nm^2} \approx 2 \times 10^8$$

$$N_{genome} \sim 1.2 \times 10^7 bp \qquad N_{nucleosome} \approx \frac{1.2 \times 10^7 bp}{200bp / nucleosome} = 60,000$$



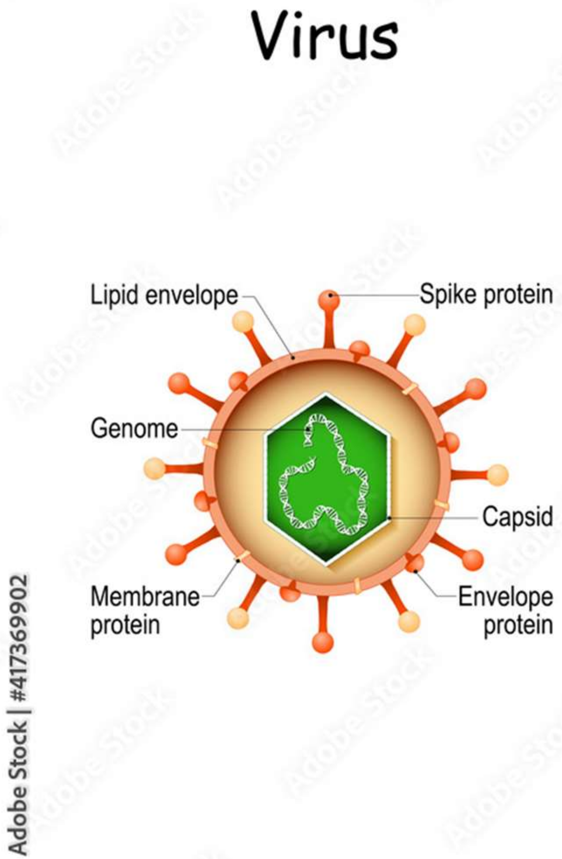
Video resources

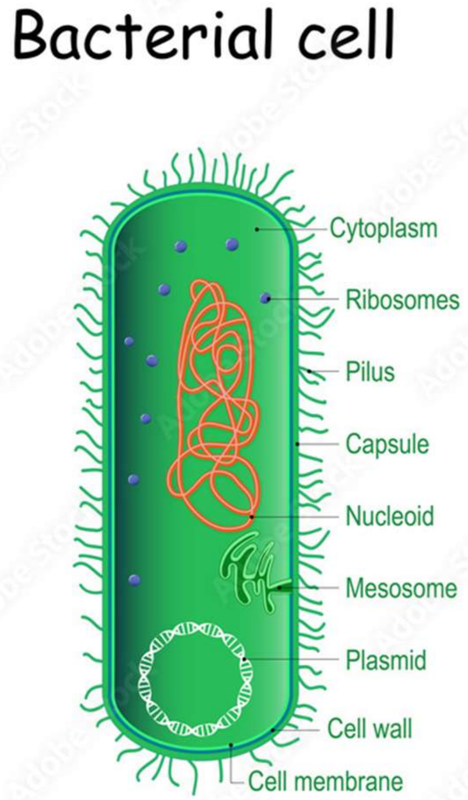
https://www.youtube.com/watch?v=URUJD5NEXC8

https://dnalc.cshl.edu/resources/3d/08-how-dna-is-packaged-advanced.html

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

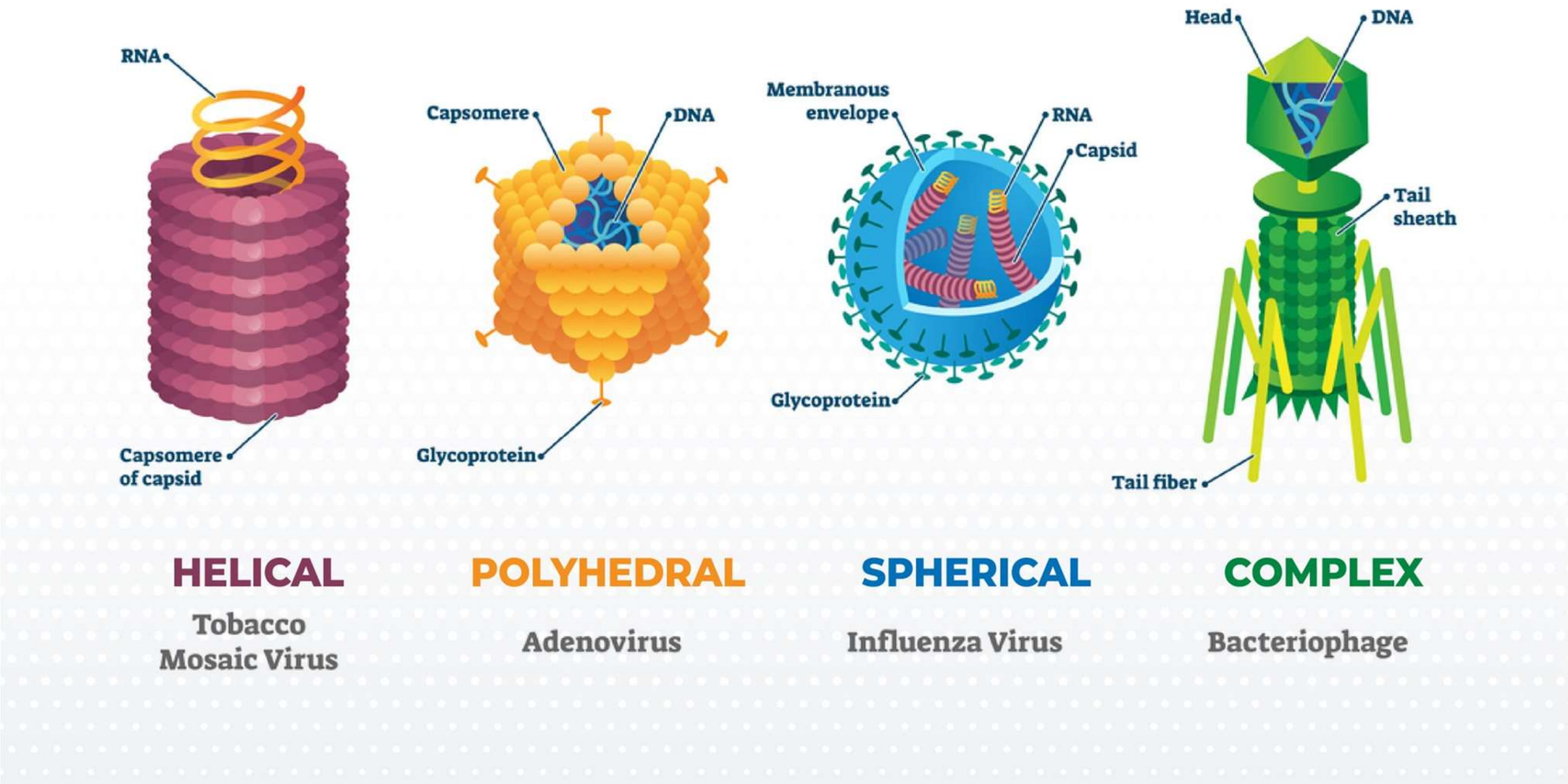
VIRUSES





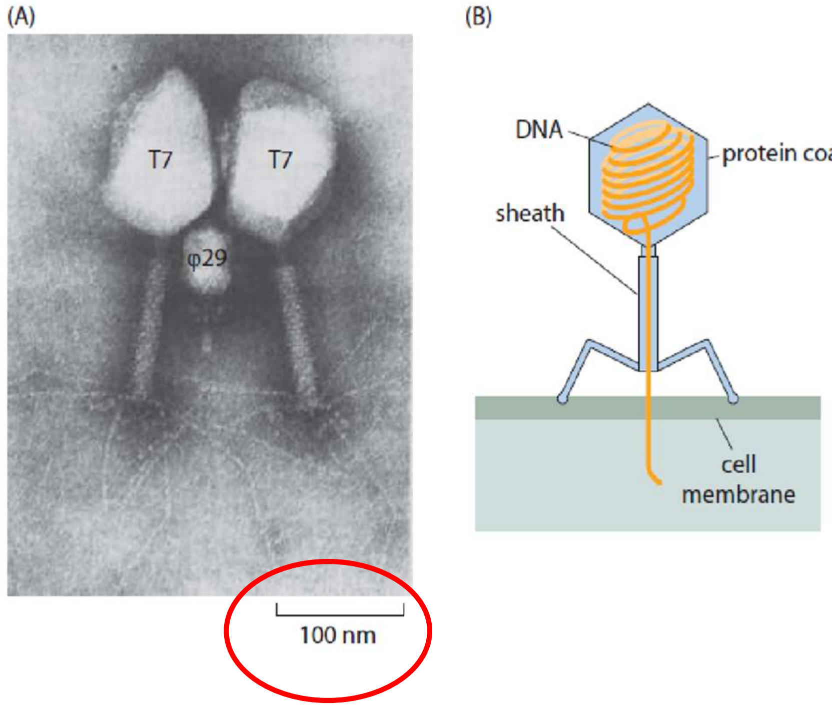
- A virus is an infectious microbe consisting of a segment of nucleic acid (either DNA or RNA) surrounded by a protein coat.
- A virus cannot replicate alone; instead, it must infect cells and use components of the host cell to make copies of itself.
- Often, a virus ends up killing the host cell in the process, causing damage to the host organism.
- Well-known examples of viruses causing human disease include AIDS, COVID-19, measles and smallpox.

TYPES OF VIRUSES



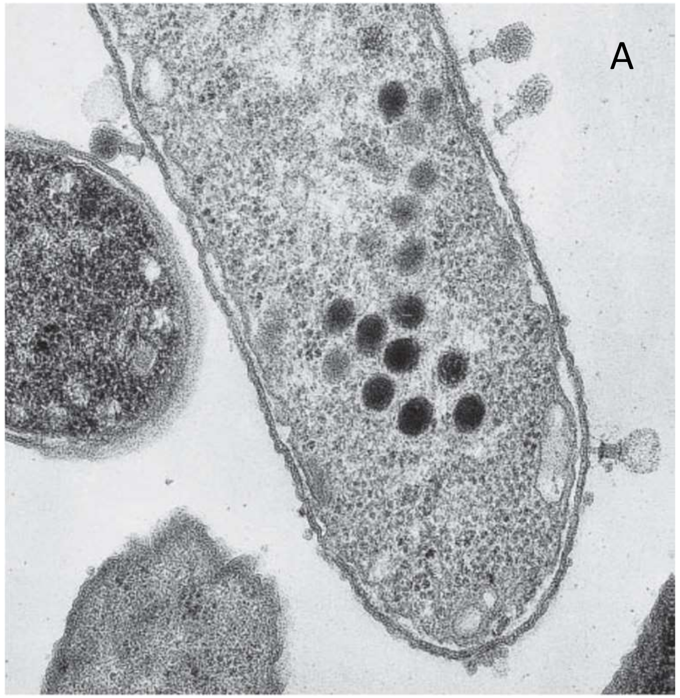
- Viruses are much smaller than the cells they infect.
- They could pass through filters small enough to remove pathogenic bacterial cells.
- These genomes can be DNA or RNA, single-stranded or double-stranded (that is, ssDNA, dsDNA, ssRNA, or dsRNA) with characteristic sizes ranging from 103–106 bases

virus	size (nm)	genome size (nucleotides)	genome type, capsid structure
porcine circovirus (PCV)	17	1760	circular ssDNA, icosahedral
cowpea mosaic virus (CPMV)	28	9400	2 ssRNA molecules, icosahedral
cowpea chlorotic mottle virus (CCMV)	28	7900	3 ssRNA molecules, icosahedral
φX174 (*E. coli* bacteriophage)	32	5400	ssDNA, icosahedral
tobacco mosaic virus (TMV)	40 × 300	6400	ssRNA, rod shaped
polio virus	30	7500	ssRNA, icosahedral
φ29 (*Bacillus* phage)	45 × 54	19,000	dsDNA, icosahedral (T3)



(A) Electron microscopy image of phi29 and T7 bacteriophages as revealed by electron microscopy. (B) Schematic of the structure of a bacteriophage. (A, adapted from Grimes S, Jardine PJ & Anderson D [2002] *Adv Virus Res* 58:255–280.)

Viral infection



A virus infection. (*a*) Micrograph showing a late stage in the infection of a bacterial cell by a bacteriophage. Virus particles are being assembled within the cell, and empty phage coats are still present on the cell surface. (*b*) Micrograph showing HIV particles budding from an infected human lymphocyte.

Cellular building blocks

Chemical Basis of Life

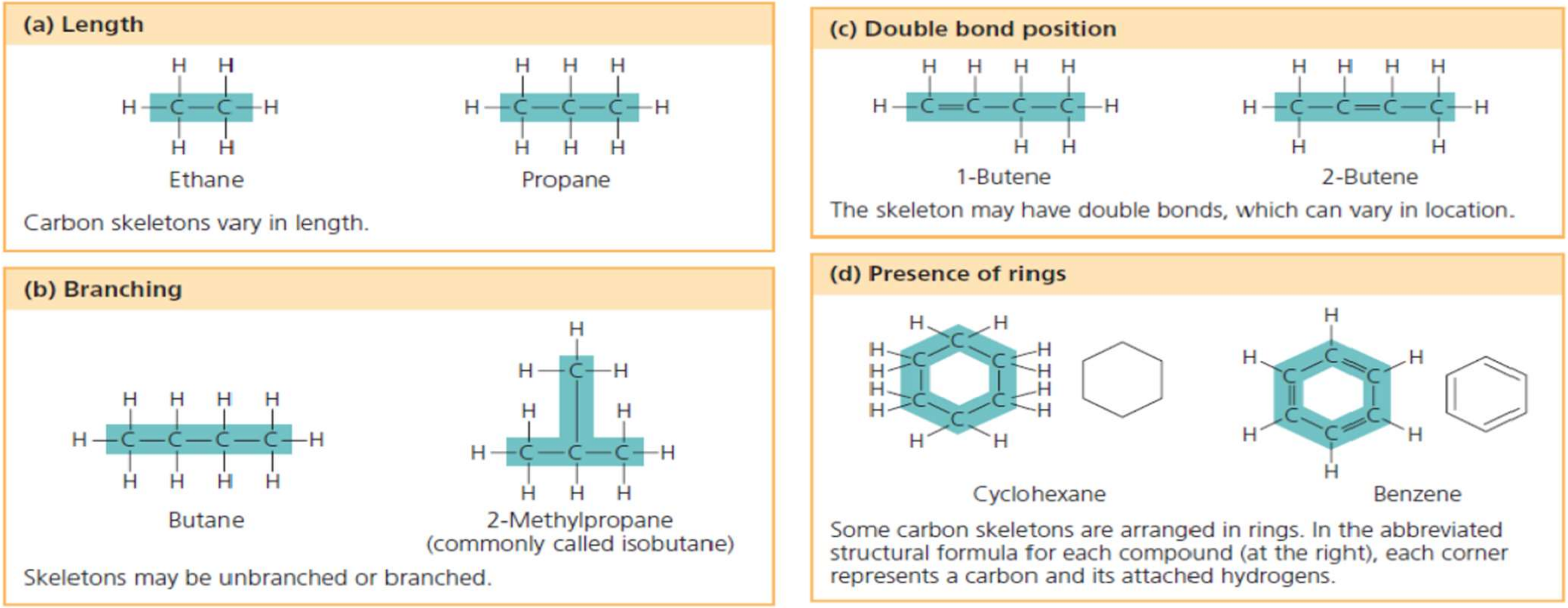
Table 2.1 Elements in the Human Body

Element	Symbol	Percentage of Body Mass (including water)	
Oxygen	O	65.0%	96.3%
Carbon	C	18.5%	
Hydrogen	H	9.5%	
Nitrogen	N	3.3%	
Calcium	Ca	1.5%	3.7%
Phosphorus	P	1.0%	
Potassium	K	0.4%	
Sulfur	S	0.3%	
Sodium	Na	0.2%	
Chlorine	Cl	0.2%	
Magnesium	Mg	0.1%	

Trace elements (less than 0.01% of mass): Boron (B), chromium (Cr), cobalt (Co), copper (Cu), fluorine (F), iodine (I), iron (Fe), manganese (Mn), molybdenum (Mo), selenium (Se), silicon (Si), tin (Sn), vanadium (V), zinc (Zn)

- Essential Elements
- Trace Elements
- CHON makes 96% of living matter
- Some elements are toxic - Arsenic

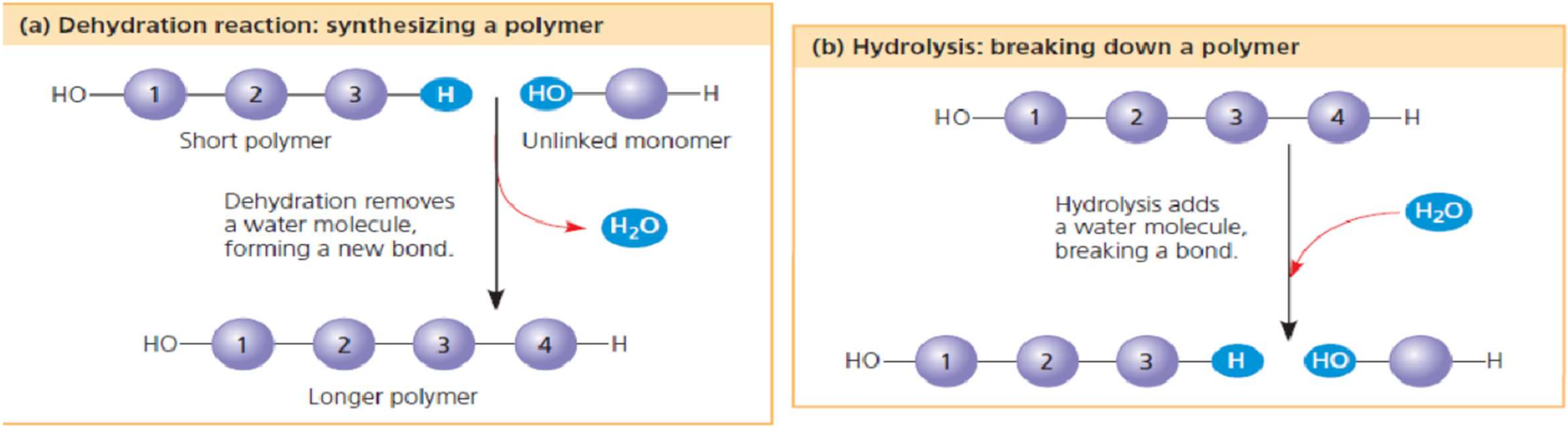
Molecular Diversity Arising from Carbon Skeleton Variation



Hydrocarbons and Isomers

Large Biological Molecules

Macromolecules are polymers, built from monomers



Diversity of Biological Molecules

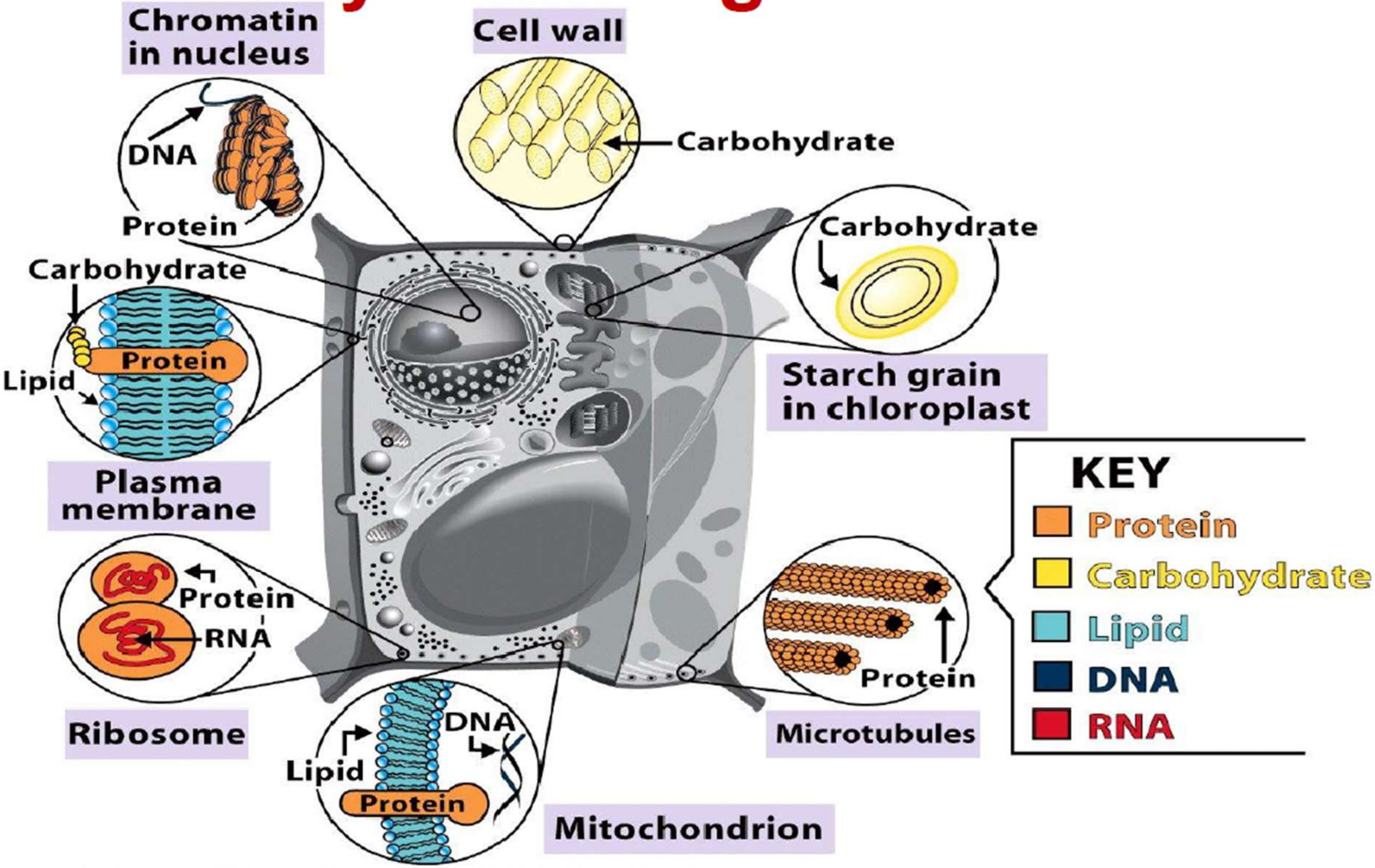
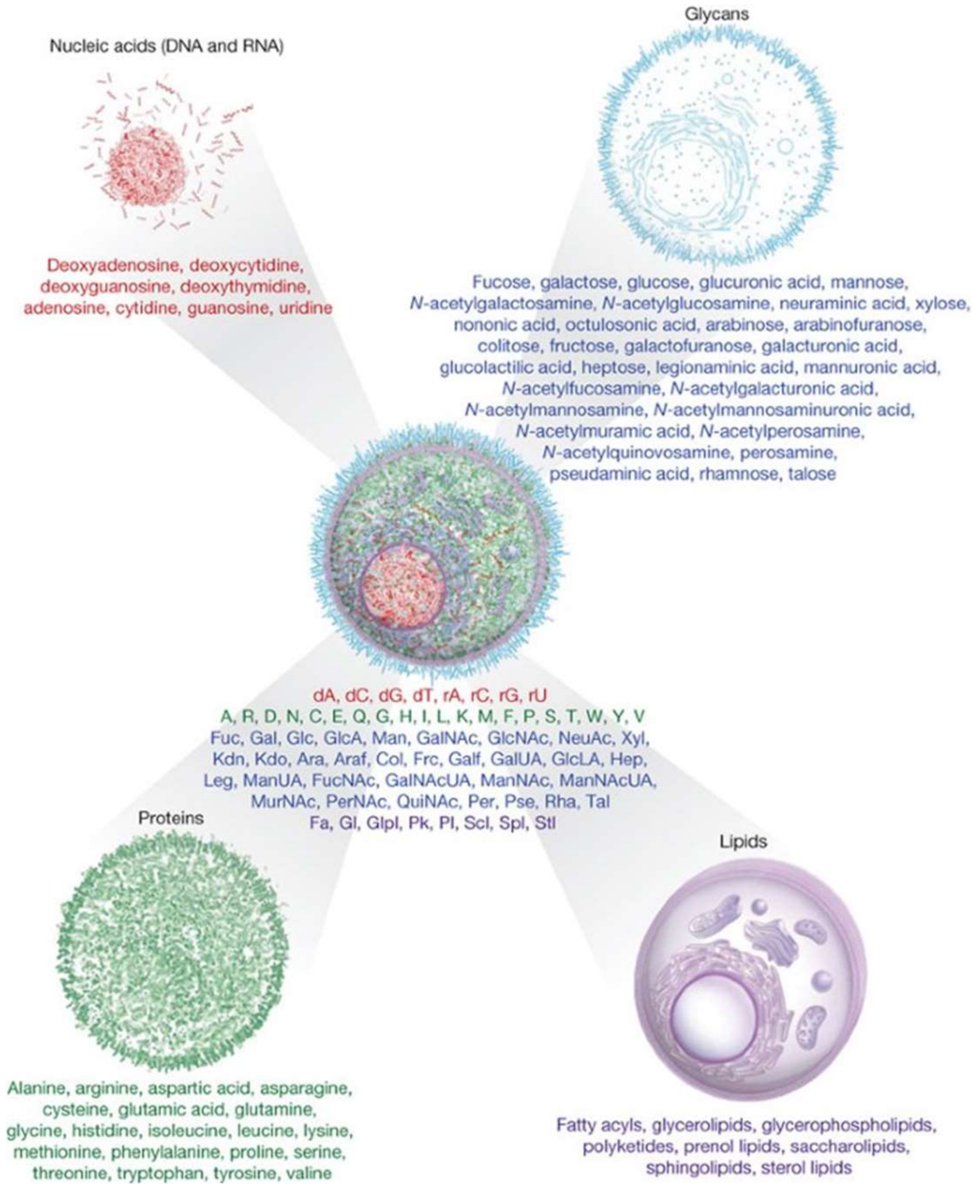


Figure 2-11 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

Basic Functions

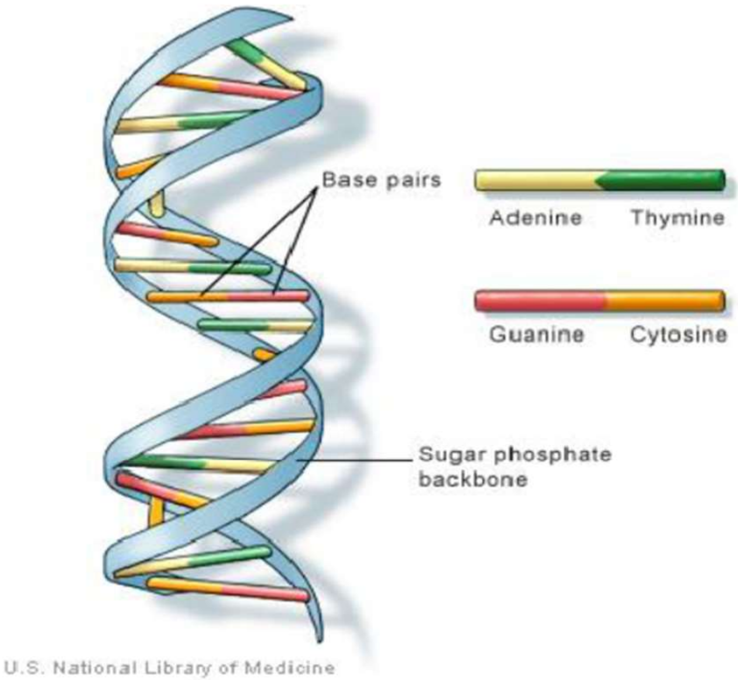
	Carbs	Lipids	Nucleic Acids	Proteins
Functions	• Energy • Storage • Structure	• Long term storage • Insulation • Protection	• Inheritance • Blueprint for metabolism	• Catalysts • Hormones • Structure
Forms	• Starch • Glycogen • Glucose • Sucrose • Cellulose	• Lipid • Fats • Oils • Waxes	• DNA • RNA • ATP	• Proteins • Enzymes



- Cells of all organisms consist of four fundamental macromolecular components: nucleic acids (including DNA and RNA), proteins, lipids and glycans.
- From the construction, modification and interaction of these components, the cell develops and functions.
- DNA and RNA are produced from the 8 nucleosides. Although deoxyribose (d) and ribose (r) are saccharides, they are an integral part of the energetically charged nucleoside building blocks that are used to synthesize DNA and RNA.
- There are 20 natural amino acids used in the synthesis of proteins.
- Glycans derive initially from 32, and possibly more, saccharides used in the enzymatic process of glycosylation and are often attached to proteins and lipids.
- Lipids are represented by 8 recently classified categories and contain a large repertoire of hydrophobic and amphipathic molecules.

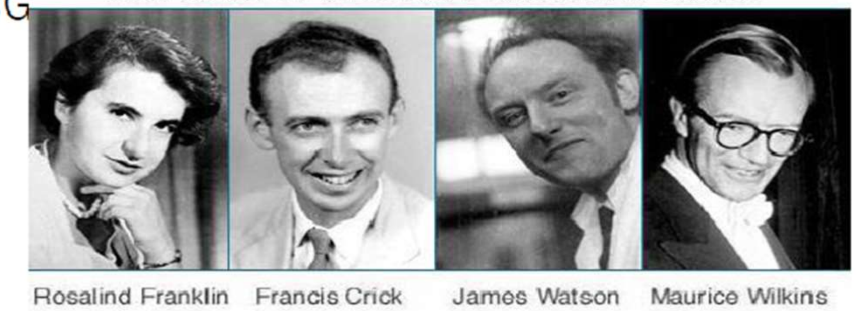
DNA (Deoxyribonucleic acid)

DNA as a CPU of the cell

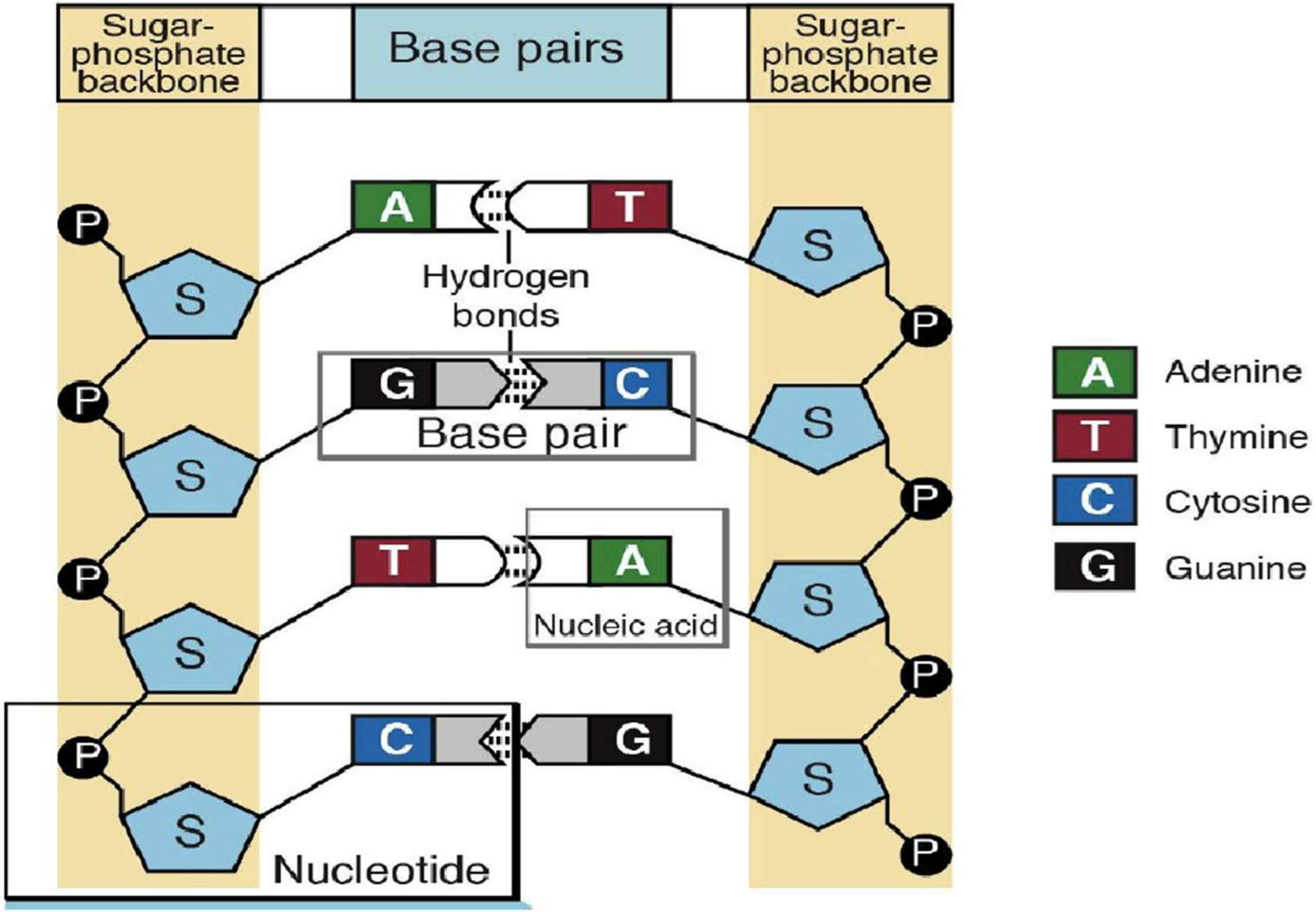


GTACCTTGATTTCGTATTCTGAGAGGCTGCTGCTT
AGCGGTAGCCCCTTGGTTTCCGTGGCAACGGAAA
AGCGCGGGAATTACAGATAAATTAAAACTGCGACT
GCGCGGCGTGAGCTCGCTGAGACTTCCTGGACGG
GGGACAGGCTGTGGGGTTTCTCAGATAACTGGGC
CCCTGCGCTCAGGAGGCCTTCACCCTCTGCTCTG
GGTAAAGGTAGTAGAGTCCCGGGAAAGGGACAGG
GGGCCCAAGTGATGCTCTGGGGTACTGGCGTGGG
AGAGTGGATTTCCGAAGCTGACAGATGGGTATTC
TTTGACGG
GTAAGGCG

Crick, Watson, and Wilkins were awarded the Nobel Prize for Franklin's work.



DNA (Deoxyribonucleic Acid)



DNA (Deoxyribonucleic acid)

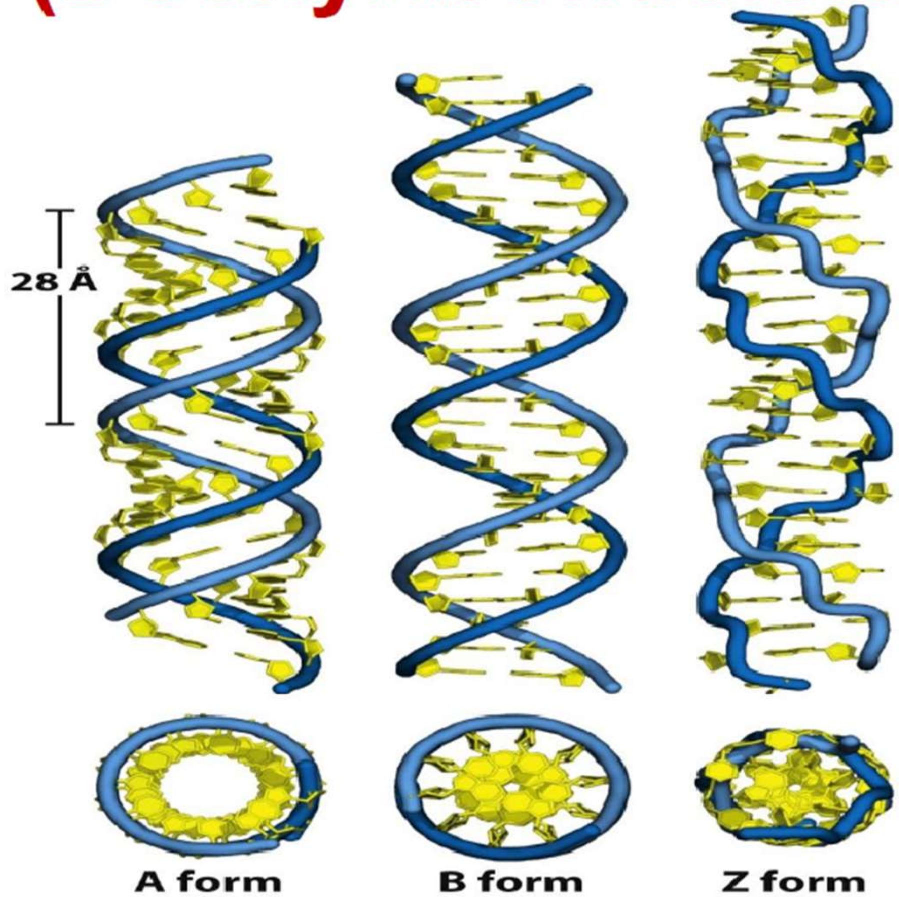


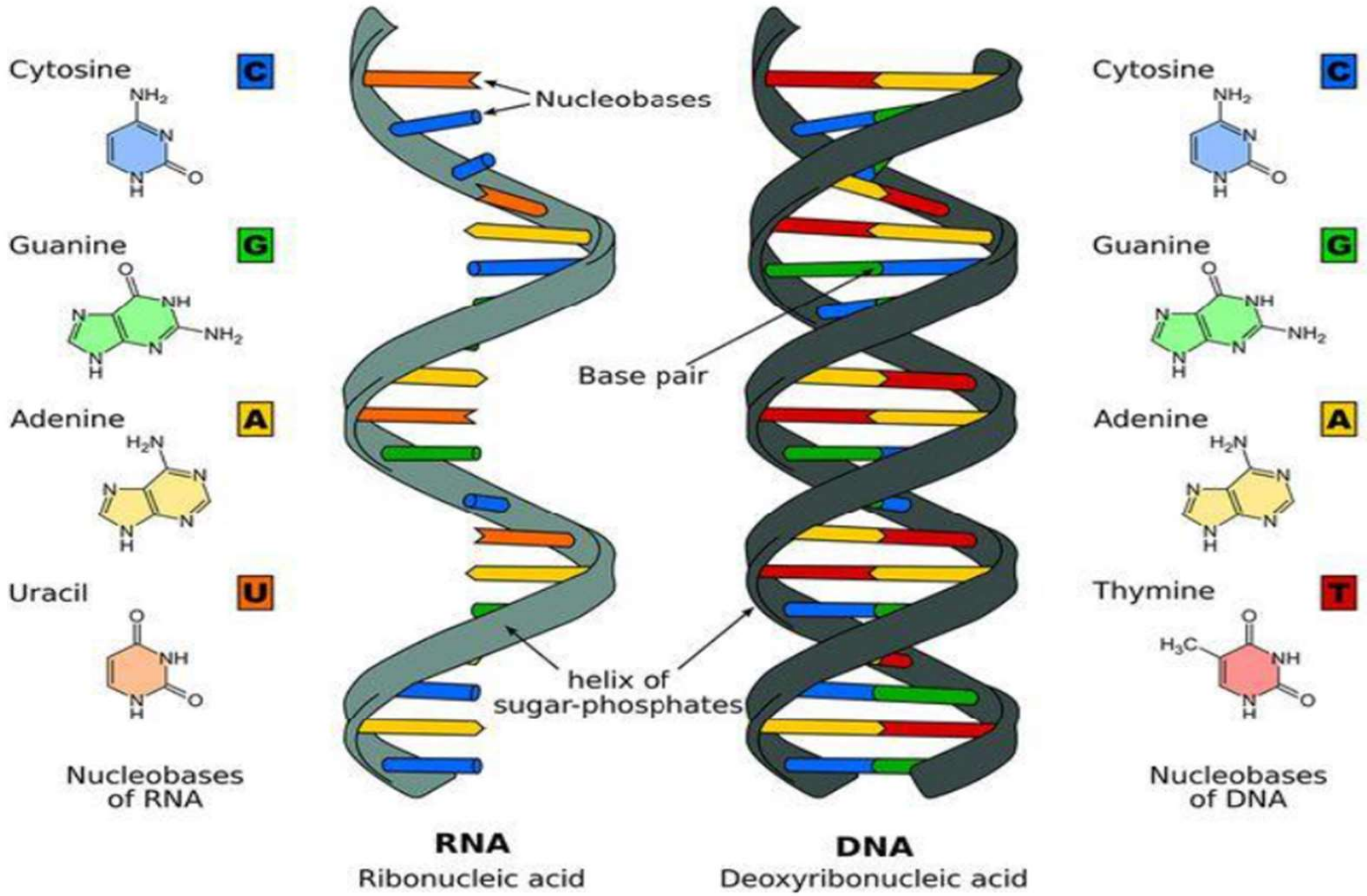
Figure 8-17 part 1
Lehninger Principles of Biochemistry, Sixth Edition

All prokaryotes and eukaryotes have B form of DNA

	A form	B form	Z form
Helical sense	Right handed	Right handed	Left handed
Diameter	~26 Å	~20 Å	~18 Å
Base pairs per helical turn	11	10.5	12
Helix rise per base pair	2.6 Å	3.4 Å	3.7 Å
Base tilt normal to the helix axis	20°	6°	7°
Sugar pucker conformation	C-3′ endo	C-2′ endo	C-2′ endo for pyrimidines; C-3′ endo for purines
Glycosyl bond conformation	Anti	Anti	Anti for pyrimidines; syn for purines

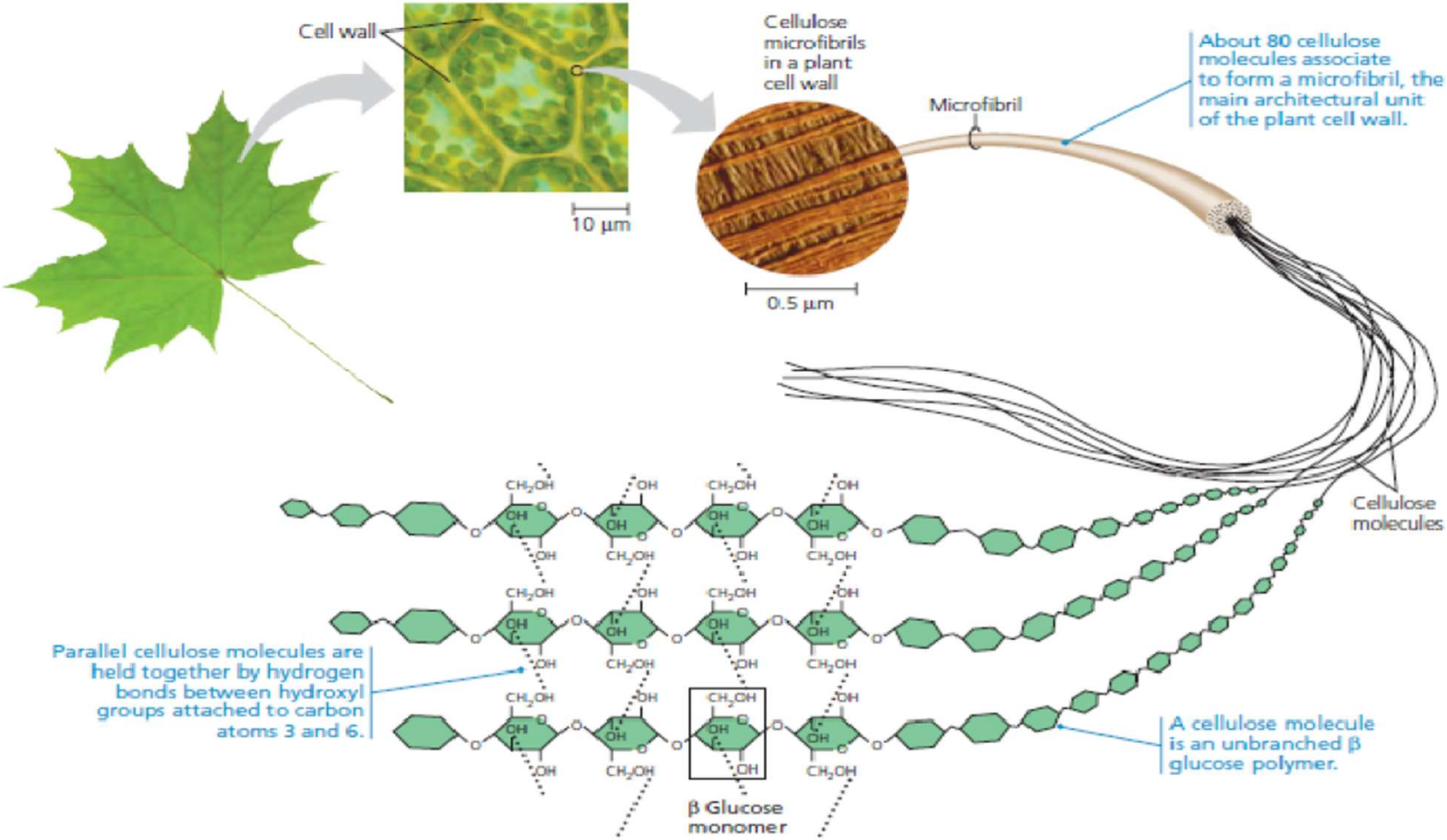
Figure 8-17 part 2
Lehninger Principles of Biochemistry, Sixth Edition

RNA (Ribonucleic Acid)



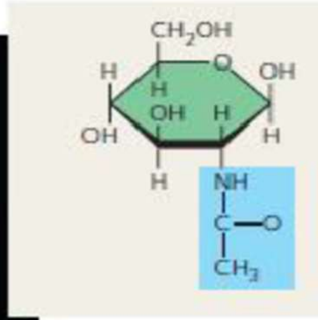
RNA molecules perform a variety of roles in the cell but are mainly involved in the process of **protein synthesis** (**translation**) and its regulation

Carbohydrates



▲ **Figure 5.8 The arrangement of cellulose in plant cell walls.**

Carbohydrates



The structure of the chitin monomer

Chitin forms the exoskeleton of arthropods. This cicada is molting, shedding its old exoskeleton and emerging in adult form.

Chitin is used to make a strong and flexible surgical thread that decomposes after the wound or incision heals.

Figure 5.9 Chitin, a structural polysaccharide.

Several functions

- Cellulose
- Chitin
- Starch

What are Carbohydrates ? :

Carbohydrates are defined as polyhydroxy aldehyde or ketone with empirical formula $(CH_2O)_n$., the simplest being glyceraldehyde or dihydroxy acetone. Carbohydrates include sugars, starches, cellulose and many other compounds found in living organisms.

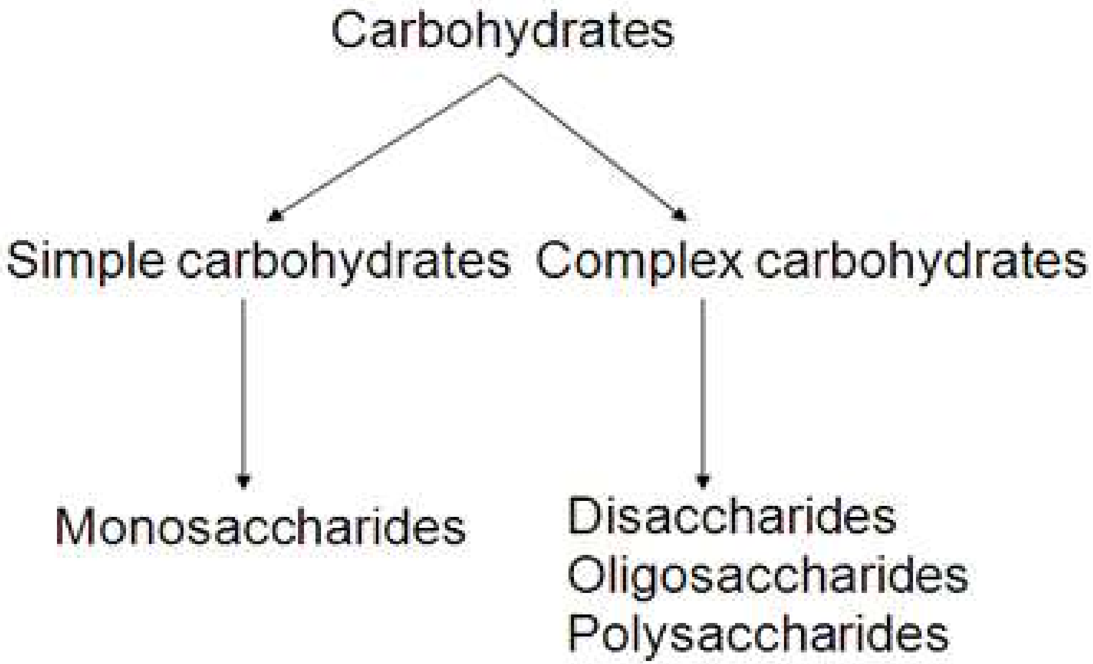
What are saccharides? :

- Saccharide is a term derived from the Latin for sugar (origin = "sweet sand”).The term carbohydrate is most common in biochemistry where it is a synonym of **saccharide**.

- Carbohydrates are often classified according to the number of saccharide units they contain. They are divided into four chemical groupings: monosaccharides, disaccharides, oligosaccharides and ploysaccharides.

- In their basic form, carbohydrates are simple sugars or monosaccharides. These simple sugars can combine with each other to form more complex carbohydrates. The combination of two simple sugars is a disaccharide. Carbohydrates comprising of 2-10 monosaccharide units are called oligosaccharides, and those with a larger number are called polysaccharides.

Classification of carbohydrates :



Simple Carbohydrates :

- These are made up of a single basic sugar. Simple carbohydrates are responsible for the sweet taste in our food. Fruit sugar, table sugar or corn sugar are all simple sugars. On consumption, these sugars are directly absorbed in the blood and generally used for energy requirements of the body.

- Glucose provides instant energy and reaches different parts of the body via blood, by being quickly metabolized.

- Simple sugars are occur in plenty in natural foods like fruits, vegetables, milk and milk products. Additionally, honey, molasses, corn and maple syrup are also rich sources of simple sugars.

Monosaccharides :

- 'Mono' refers to single.

- These are the basic compounds consisting of carbon, hydrogen and oxygen in the ratio 1:2:1 having the emperical formula of $(CH_2O)_n$.

- Monosaccharides are sweet to taste, colourless crystalline solids, freely soluble in water but insoluble in nonpolar solvents.

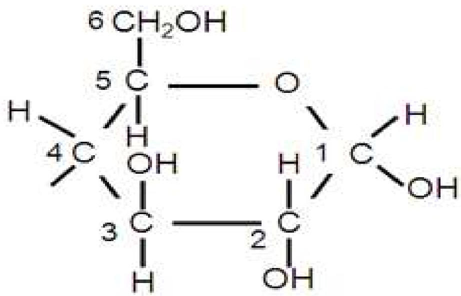
- Glucose, fructose and galactose are types of monosaccharides.

Properties of monosaccharides :

• Simple monosaccharides are reducing agents because of their ability to reduce potential oxidising agents like Cu^{2+} and hydrogen peroxide.They are thus called "reducing sugars".

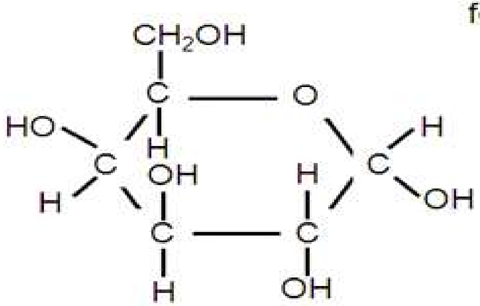
• This reaction forms the basis of Bendict's test for qualitative analysis of simple sugars.

• Glucose, the "blood sugar" and an immediate source of energy for cellular respiration.



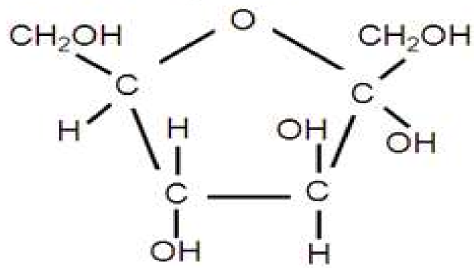
Glucose

Galactose :



Galactose

Fructose, a ketohexose sugar found in honey fruits.



Fructose

Disaccharides :

• When two monosaccharides bond together by a condensation reaction, thereby releasing a molecule of water, a disaccharide is formed. The two monosaccharide units are linked by **glycosidic bond** in α or β anomeric carbon.

• Commonly available disaccahrides are sucrose, maltose and lactose.

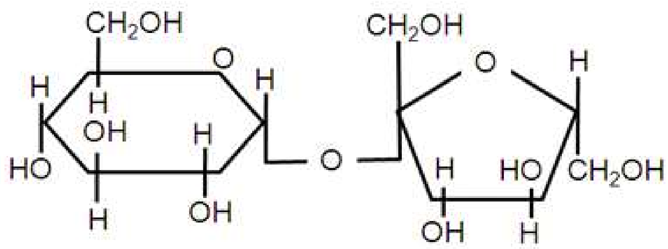
• Disaccharides cannot be absorbed through the wall of the small intestine into the bloodstream. They are therefore hydrolyzed to respective monosaccharides by carbohydares present in small intestine, specifically sucrase or invertase, maltase and lactase (β - galactosidase).

Major Disaccharides :

Sucrose :

• Major carbohydrate present in canesugar, commonly called table sugar.

• Glucose +fructose are linked by α(1 --> 1) glycosidic bonds.



Haworth projection of sucrose

Lactose :

- A major sugar in milk and milk products.
- Glucose + galactose units linked by α(1 --> 4) glycosidic bonds.

Maltose :

- Simplest sugar; present in barley malt and also a product of starch digestion.
- Glucose + glucose linked by α (1 --> 4) glycosidic bonds.

Cellobiose :

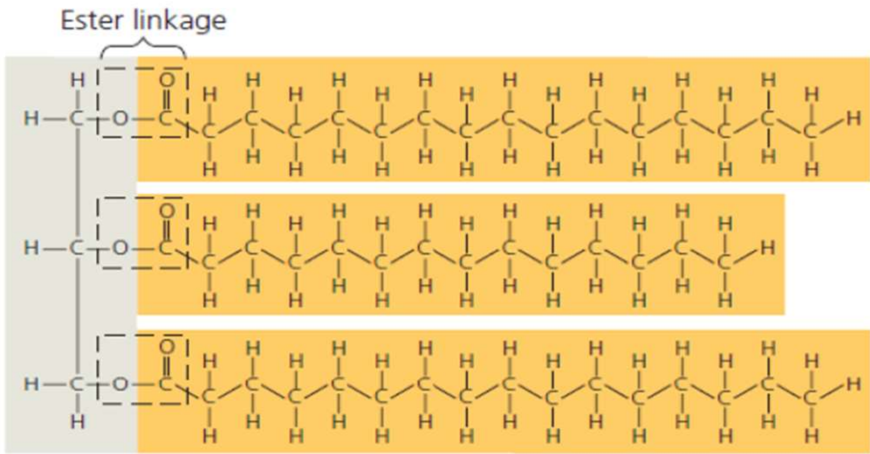
The molecule is derived from the condensation of two glucose molecules linked in a β(1 --> 4) fashion. It can be obtained by enzymatic or acidic hydrolysis of cellulose and cellulose rich materials such as cotton, jute or paper.

Oligosaccharides :

- Carbohydrates having more than two or up to ten monosaccharide units are termed as oligosaccharides. Raffinose and stachyose are two major examples of oligosaccharides which consist of repetitive chains of fructose, galactose and glucose.

Lipids

Fats in Practice



Fat in Theory

Fatty acids, oils, phospholipids, and steroids

Fats and oils

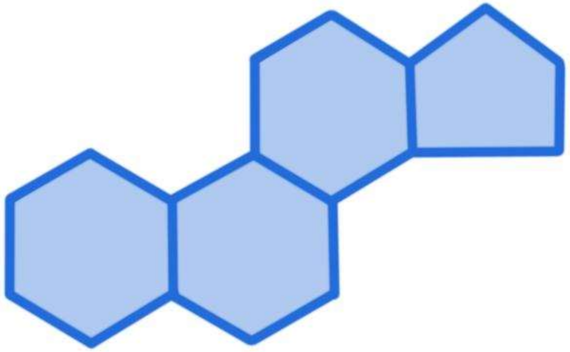
	Fats	Oils
Similarities	Triglycerides made up of one glycerol molecule and three fatty acid molecules	Triglycerides made up of one glycerol molecule and three fatty acid molecules
Differences	Saturated / no C=C bonds	Unsaturated / one or more C=C bonds
	Saturated chains packed closely together	Unsaturated chains packed less closely
	Van der Waal's forces between molecules are stronger	Van der Waal's forces between molecules are weaker

Steroids and waxes

Types of Lipids: Steroids and Waxes

STEROIDS

Steroids are characterized by a 4 ring structure.

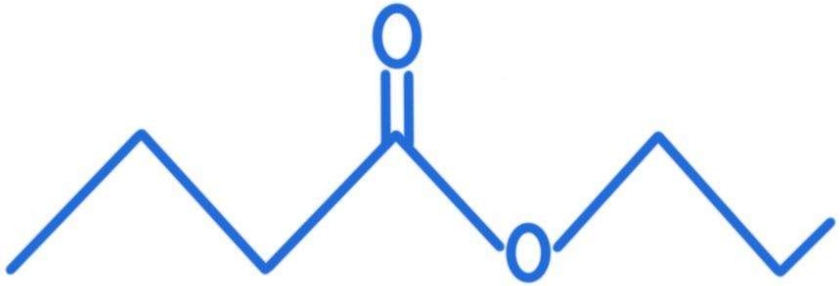


Steroids are found in the cell membrane, where they influence the membrane's fluidity.

They can also act as hormones in the body.

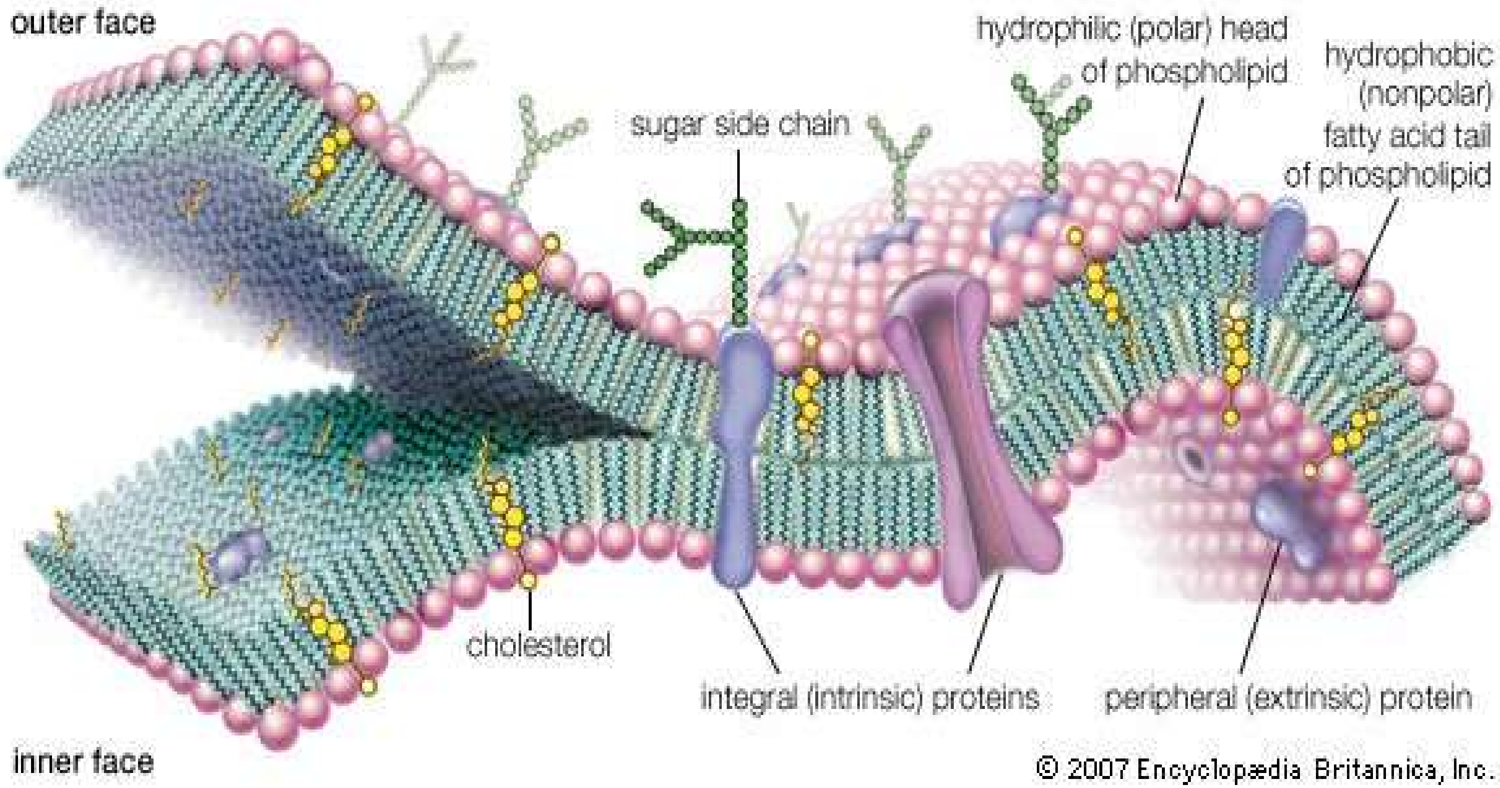
WAXES

Waxes are esters made of an alcohol chain and a fatty acid chain.

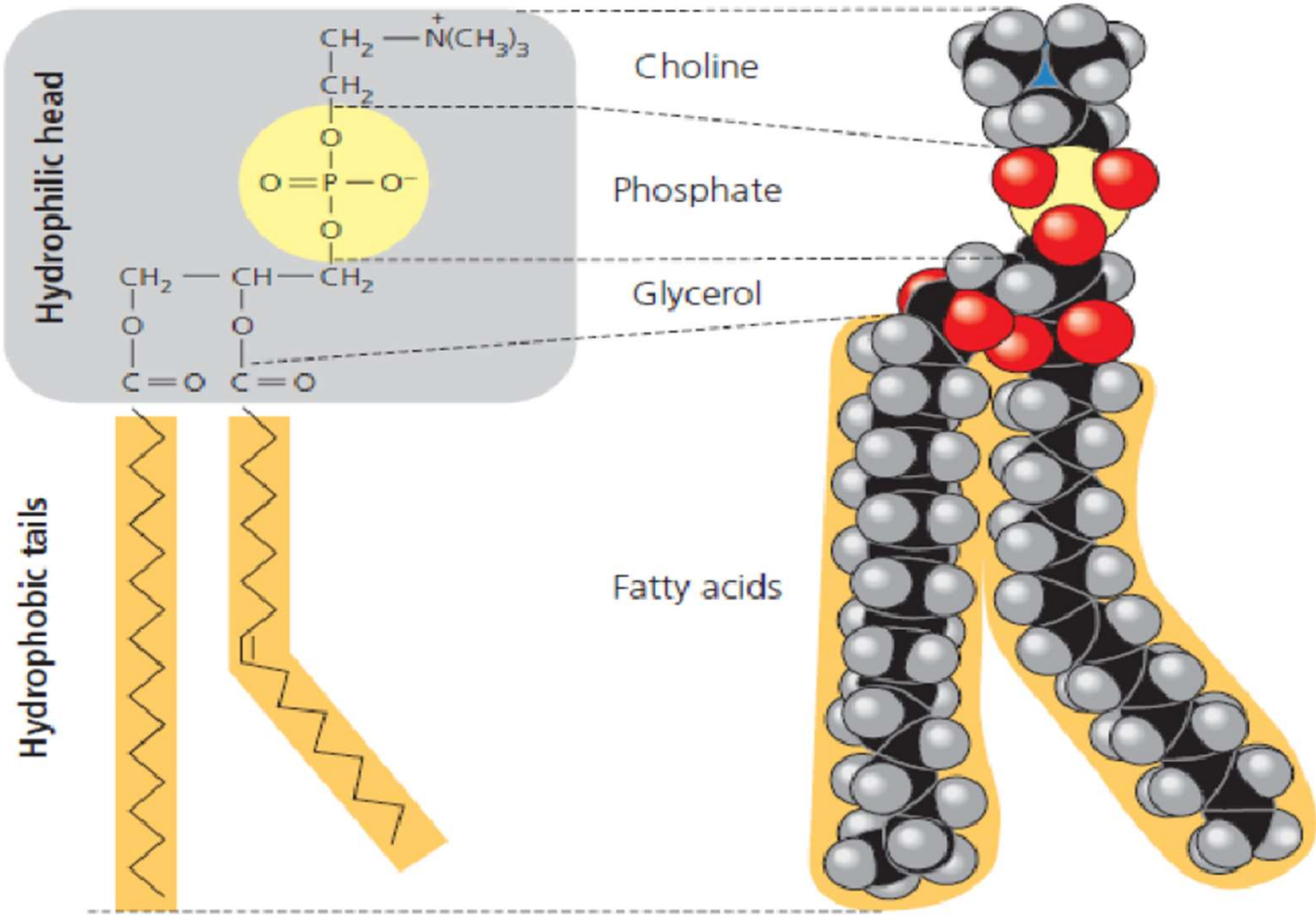


Many plants have wax-covered leaves to prevent water loss.

Structure of Cell membrane



Phospholipids



(a) Structural formula (b) Space-filling model

Phospholipids – Lipid Bilayer

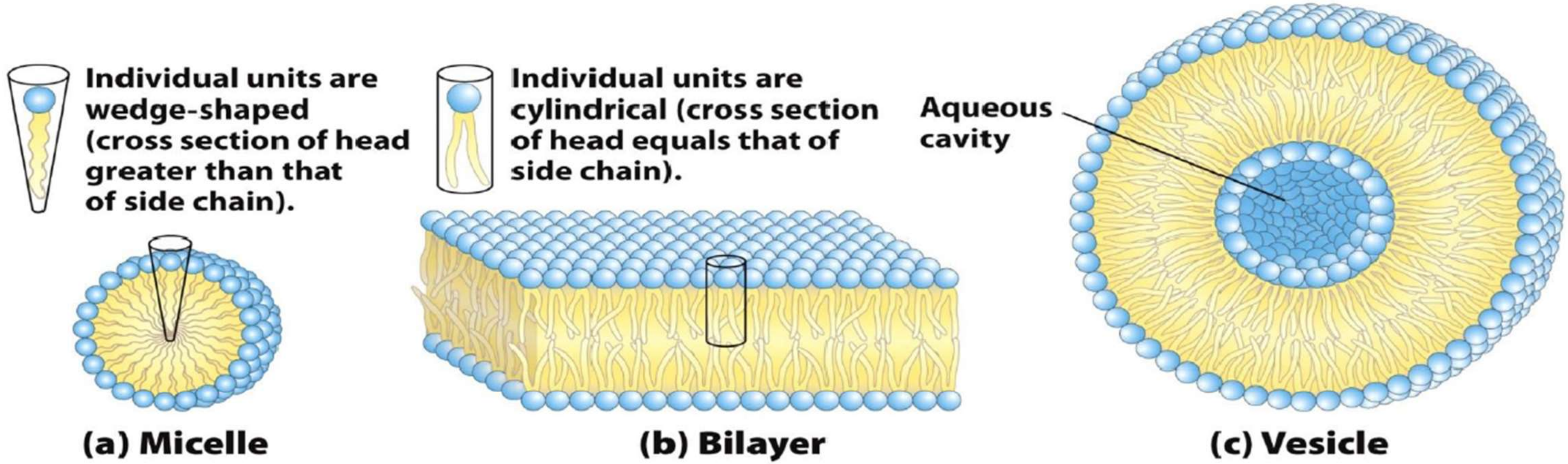


Figure 11-4
Lehninger Principles of Biochemistry, Sixth Edition

What are lipids? :

• Lipids are one among the four major biomolecules of living systems.

• By definition, these are the class of biomolecules which are insoluble or sparingly soluble in aqueous solutions and soluble in organic solvents.

• Fatty acids are major constituents of lipids. Fatty acids are mono carboxylic acid containing short/ long-chain hydrocarbon molecules. Some important fatty acids are enlisted below.

• The numbering of carbons in fatty acids begins with the carbon of the carboxylate group. Fatty acid represented by the total number of carbons e.g, palmitic acid a 16-carbon fatty acid $CH3(CH_2)_{14}COOH$ is designated as C16.

• It is customary to write it as C 16:0 where zero represent that there is no double bond in the fatty acid). If there is one double bond, then it will be written as C:16:1

Representation	Common Name	Structure
4:0	Butyric acid	$CH3(CH_2)_2COOH$
6:0	Caproic acid	$CH3(CH_2)_4COOH$
10:0	Decanoic acid	$CH3(CH_2)_8COOH$
12:0	Lauric acid	$CH3(CH_2)_{10}COOH$
14:0	Myristic acid	$CH3(CH_2)_{12}COOH$
16:0	Palmitic acid	$CH3(CH_2)_{14}COOH$
18:0	Stearic acid	$CH3(CH_2)_{16}COOH$
20:0	Arachidic acid	$CH3(CH_2)_{18}COOH$

Types of fatty acids :

• Saturated fatty acids :

All sets of examples in the previous table were fatty acids that contained no carbon-carbon double bonds. These are called saturated fatty acids. Saturated fatty acids having short carbon chain are liquid at room temperature, whereas long carbon chain fatty acids are solid.

• Unsaturated fatty acids :

These have carbon-carbon double bonds in between, thus leading to unsaturation. The representations for these fatty acids consists of the number of carbon atoms, followed by the number double bond and the place of unsaturation. The place of unsaturation in a fatty acid is indicated by the symbol (Δ) and the number of the first carbon of the double bond in superscript form. Thus oleic acid a 16-carbon fatty acid with one site of unsaturation between carbons 9 and 10, and will be represented by $C16:1\Delta^9$.

Some commonly occurring unsaturated fatty acids are:

$18:1\Delta^{9}$	Oleic acid	$CH_3(CH_2)_7C{=}C(CH_2)_7COOH$
$18:2\ \Delta^{9,12}$	Linoleic acid	$CH_3(CH_2)_4C{=}CCH_2C{=}C(CH_2)_7COOH$
$18:3\ \Delta^{9,12,15}$	Linolenic acid	$CH_3CH_2C{=}CCH_2C{=}CCH_2C{=}C(CH_2)_7COOH$
$20:4\ \Delta^{5,8,11,14}$	Arachidonic acid	$CH_3(CH_2)_3(CH_2C{=}C)_4(CH_2)_3COOH$

The presence of double bonds in unsaturated fatty acids significantly lowers the melting point making them liquid. More the no. of bonds lower the MP.

Biological functions of lipids :

Lipids perform and are involved in variety of important cellular functions. However, following are some of the major physiological functions attributed to lipids :

- Energy source in animals, insects, birds and high lipid seeds e.g. triacyl glycerols.
- Activators of enzymes namely glucose-6-phosphatase, stearoyl CoA desaturase, monooxygenases which are important mitochondrial enzymes.
- Some of the lipids derivatives serve as vitamins and hormones e.g. Prostaglandins.
- Essential components of biological membranes e.g. shingolipids and glycoloipids.
- As lipoproteins in protein modification and recognitions.
- Components of the electron transport system in the inner membrane of mitochondria.

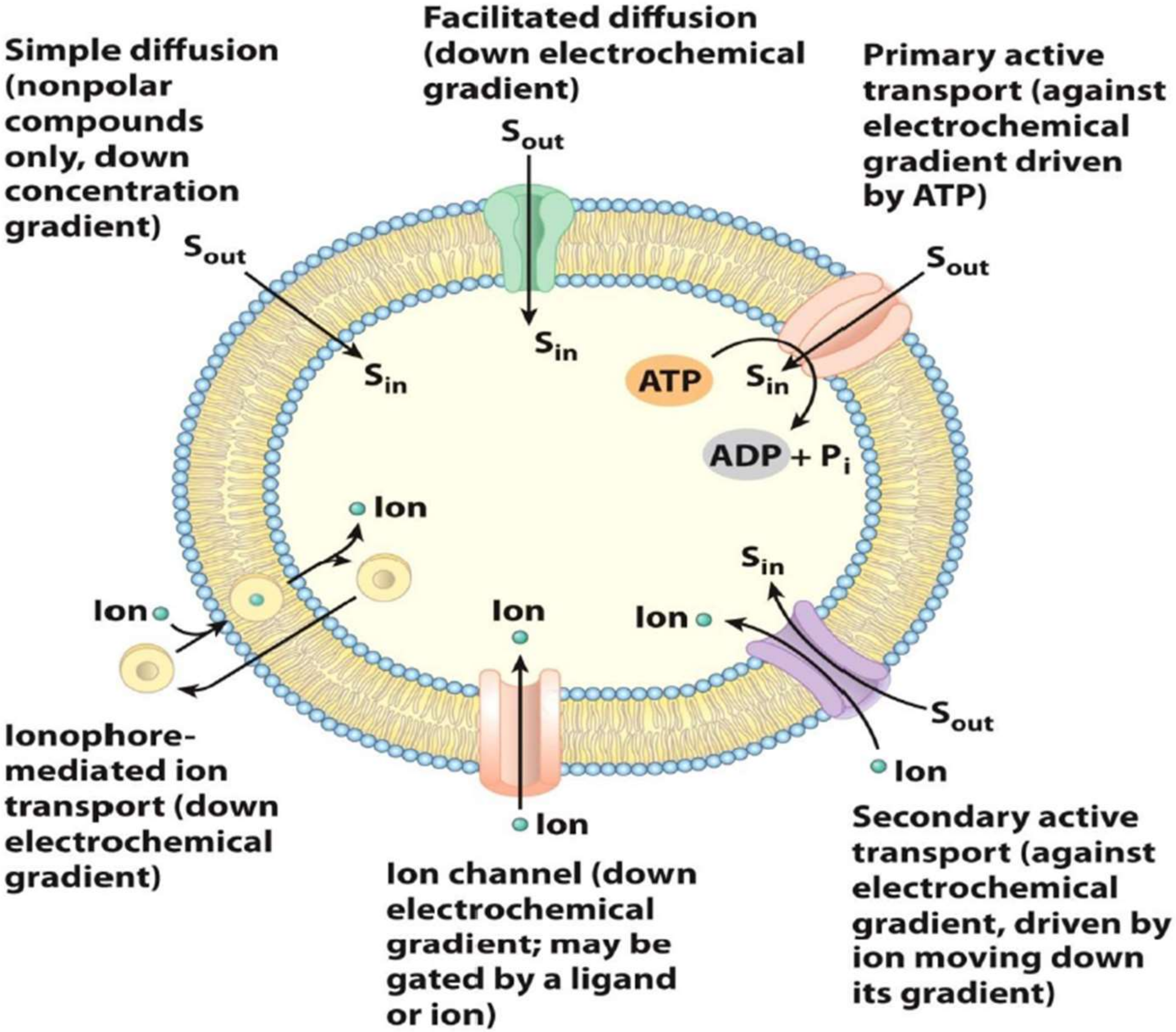


Figure 11-26
Lehninger Principles of Biochemistry, Sixth Edition

Cell Membrane

Proteins

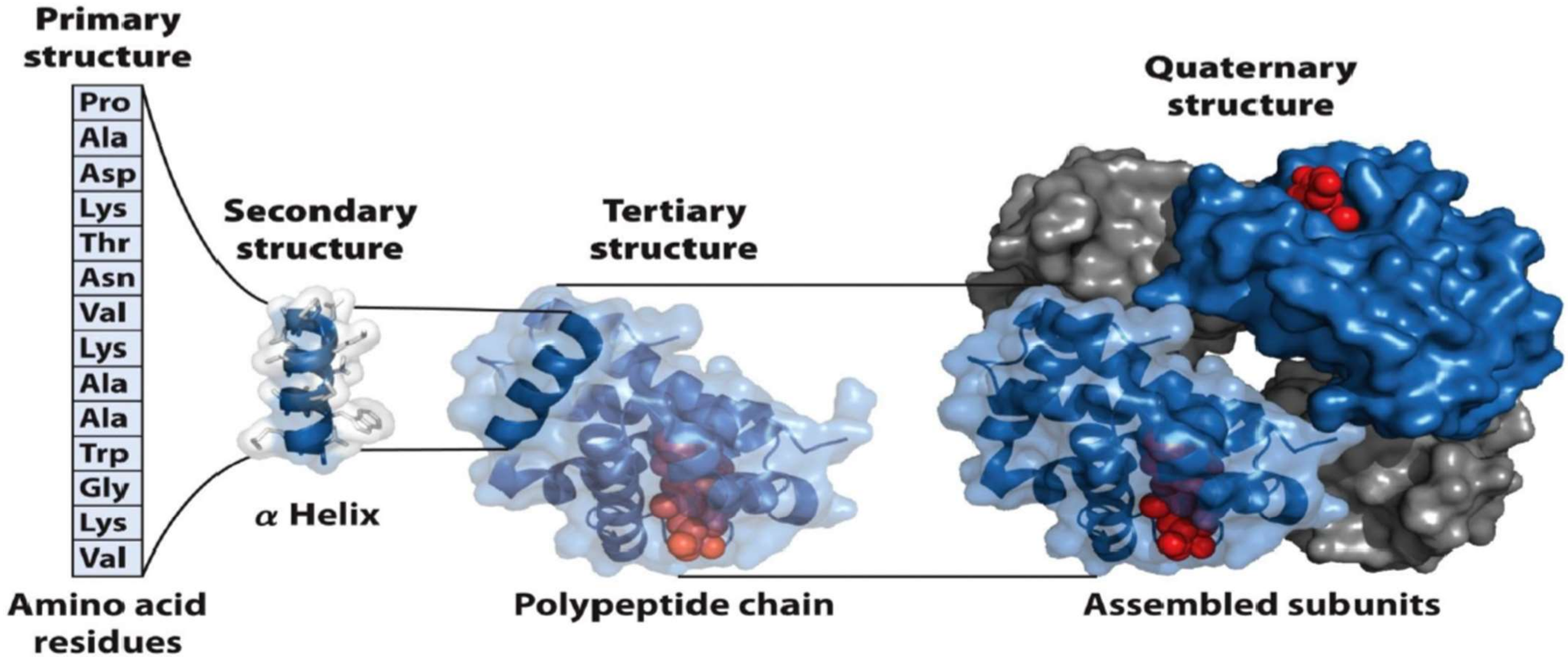
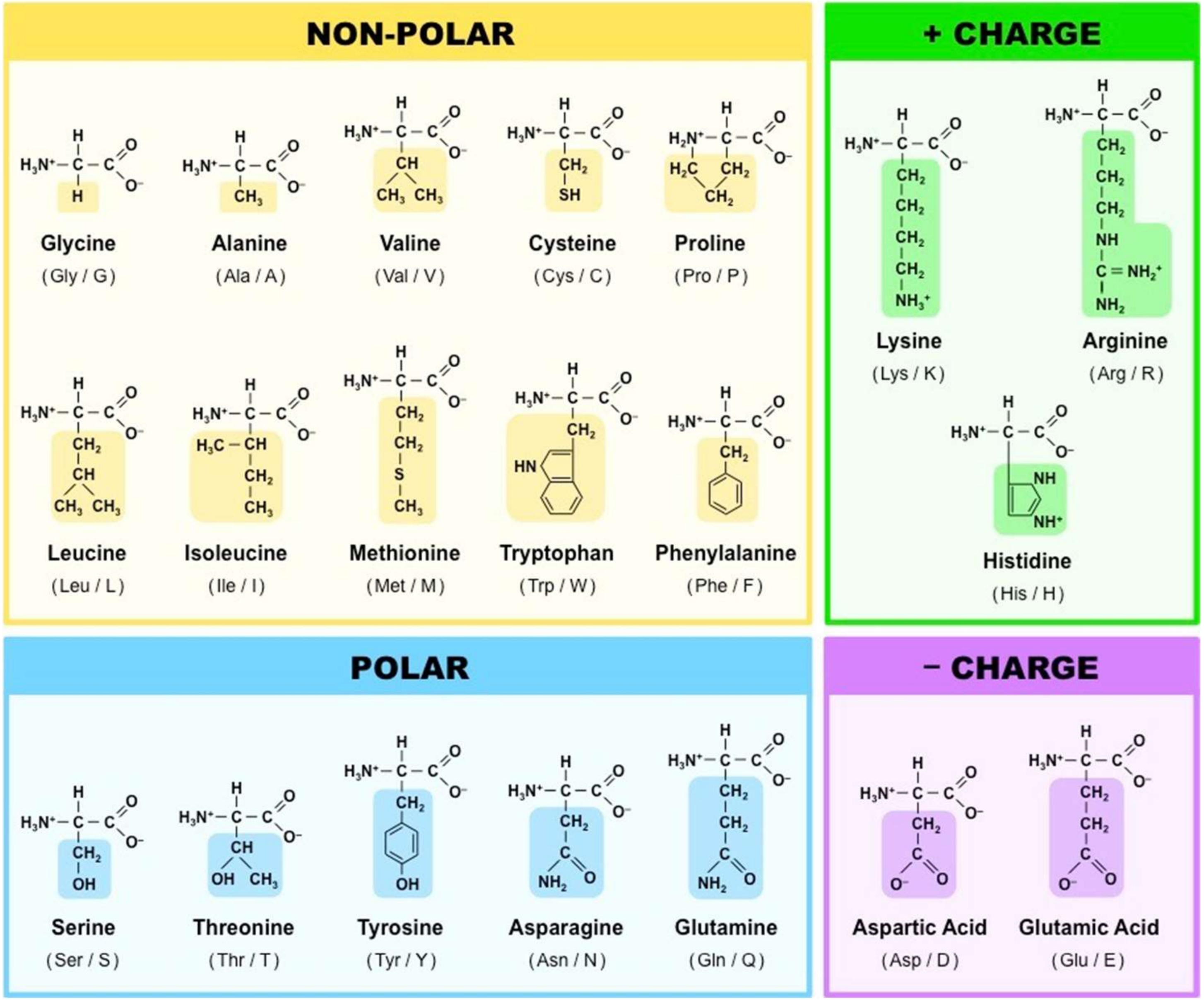


Figure 3-23
Lehninger Principles of Biochemistry, Sixth Edition

Proteins are made up of Amino Acids (building blocks for proteins)


NON-POLAR
Glycine (Gly / G)
Alanine (Ala / A)
Valine (Val / V)
Cysteine (Cys / C)
Proline (Pro / P)
Leucine (Leu / L)
Isoleucine (Ile / I)
Methionine (Met / M)
Tryptophan (Trp / W)
Phenylalanine (Phe / F)
+ CHARGE
Lysine (Lys / K)
Arginine (Arg / R)
Histidine (His / H)
POLAR
Serine (Ser / S)
Threonine (Thr / T)
Tyrosine (Tyr / Y)
Asparagine (Asn / N)
Glutamine (Gln / Q)
− CHARGE
Aspartic Acid (Asp / D)
Glutamic Acid (Glu / E)

Structural Organization of Proteins

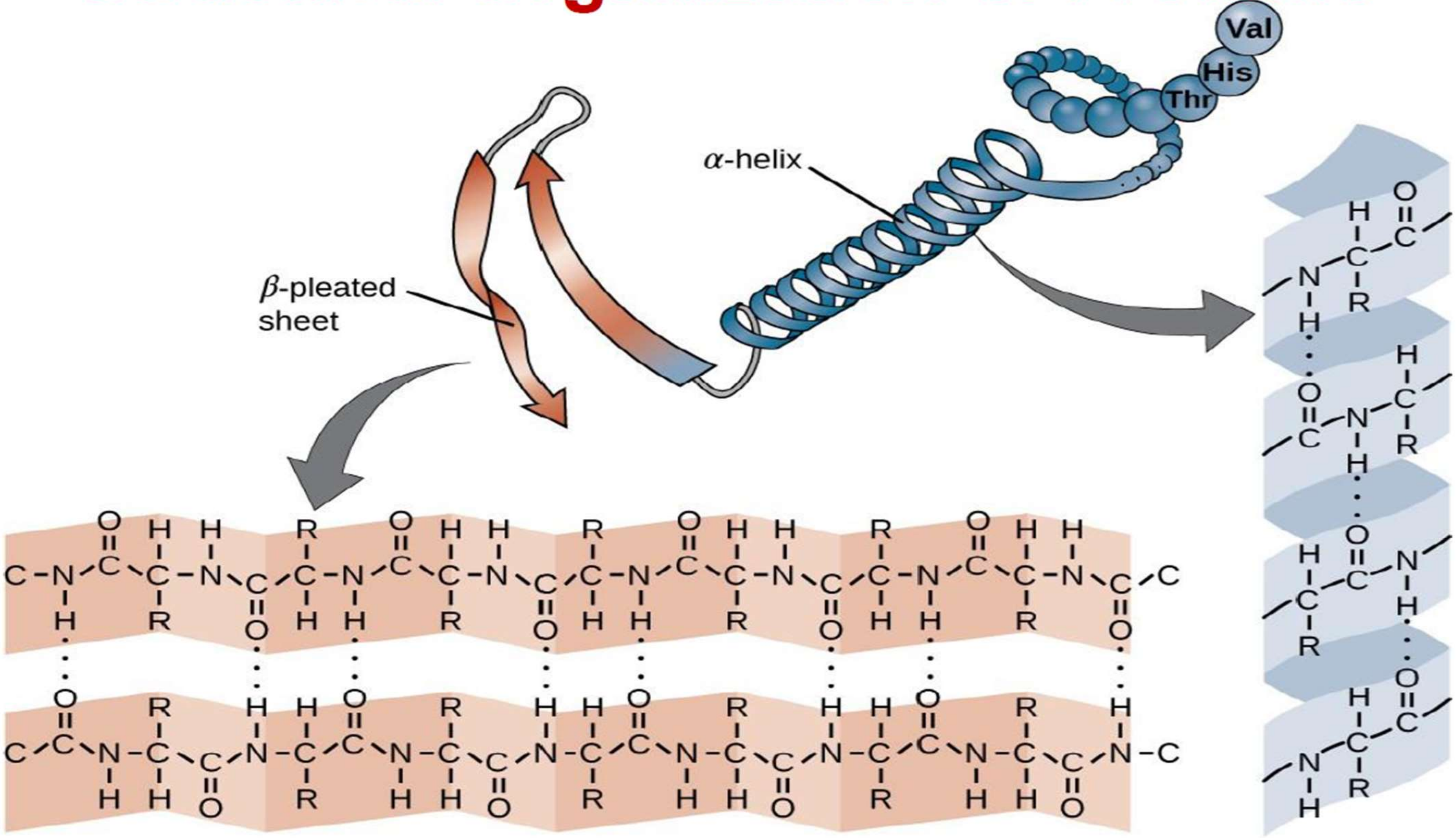
- **Primary Structure**: two dimensional, simple chain of AA with peptide (covalent) bond e.g. Insulin

- **Secondary Structure**: Various functional groups exposed on outer surface interact with hydrogen bonds
  α-helix – e.g. keratin, hair, fur, clans, hooves
  β-pleated – B. keratin of feathers, silk fibroin
  Collagen Helix: 3 α-helices coiled around one another

- **Tertiary Structure**: Additional bonds between functional groups, twisting of secondary structure, weak covalent and high energy disulphide bonds are formed e.g. Myoglobin

- **Quaternary** Structure: Formed as a result of 2-more polypeptide chain and have specific orientation

Structural Organization of Proteins



Different Types of Proteins

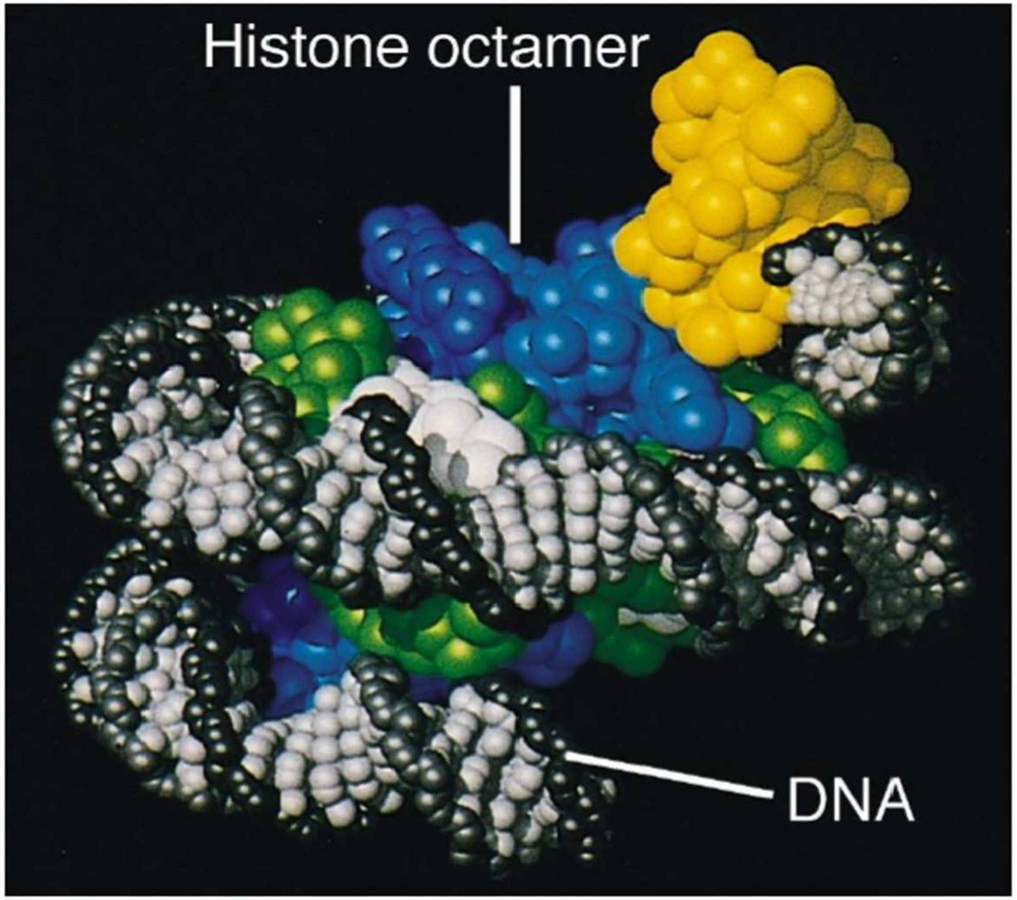
Types of proteins according to structure

1. **Fibrous** – collagen fibres, keratin, elastin, fibrin, fibroin, actin, myosin
2. **Globular** – glutelin, protemine, globulin, albumin, glutenin, orygemin.
3. **Intermediate** – myosin, fibrinogen

Types of proteins according to chemical nature

1. **Simple** – only AA. Albumin, globulin, protanine, fish, prolamine (corn, pl, wheat), histone (corn, wheat), glutelin (glutenin), keratin.
2. **Conjugated** – protein + non protein (prosthetic group) e.g. **Nucleoprotein** (nucleic acid), **chromoprotein** (Hb, cytochrome), **metallo** (with metals Zn, Fe), **lipoprotein**, **glycoprotein** etc

Structural Proteins



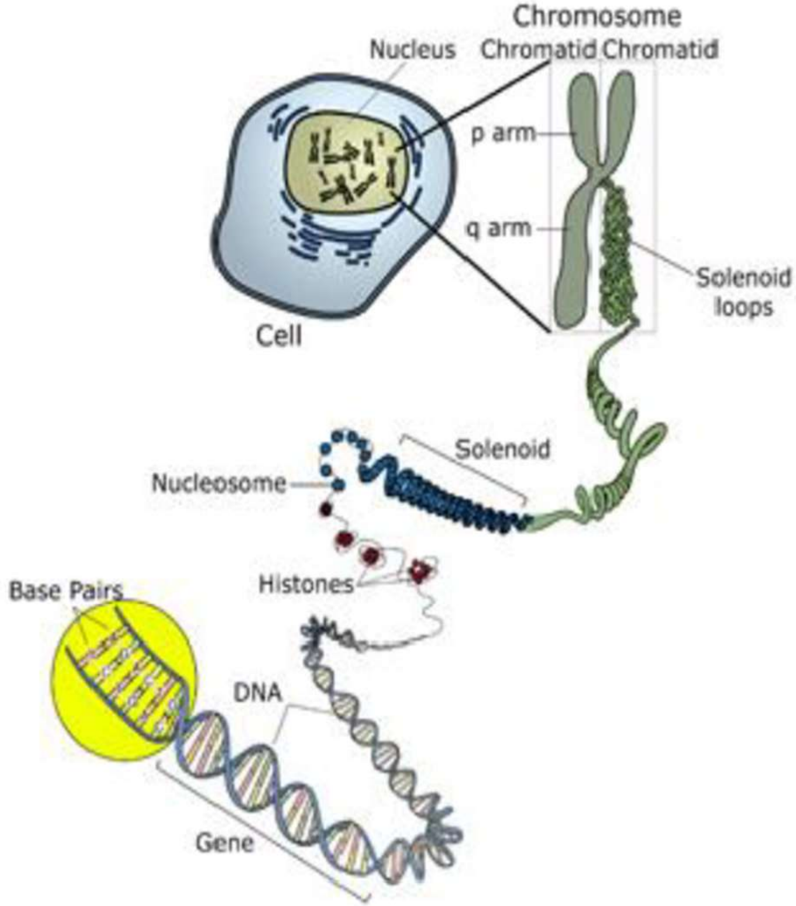
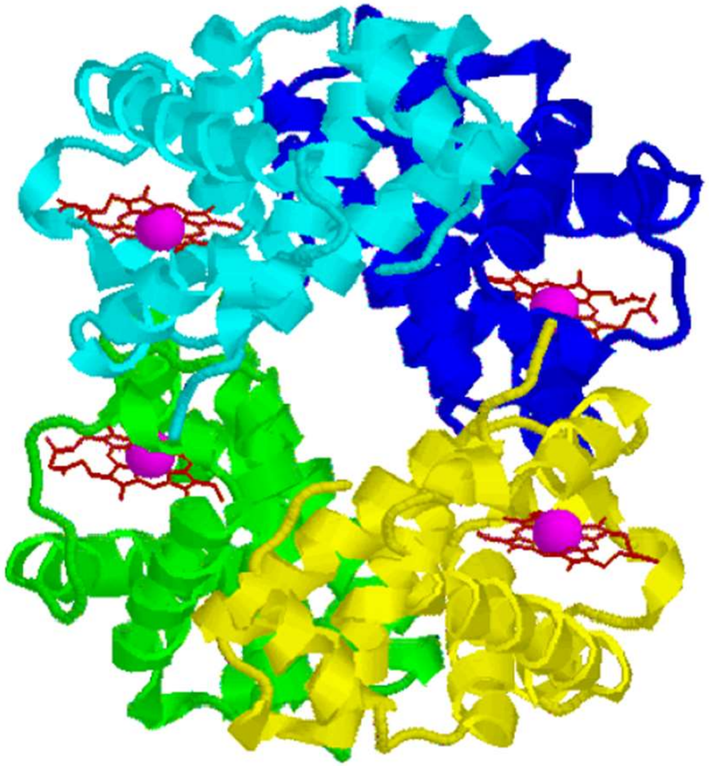
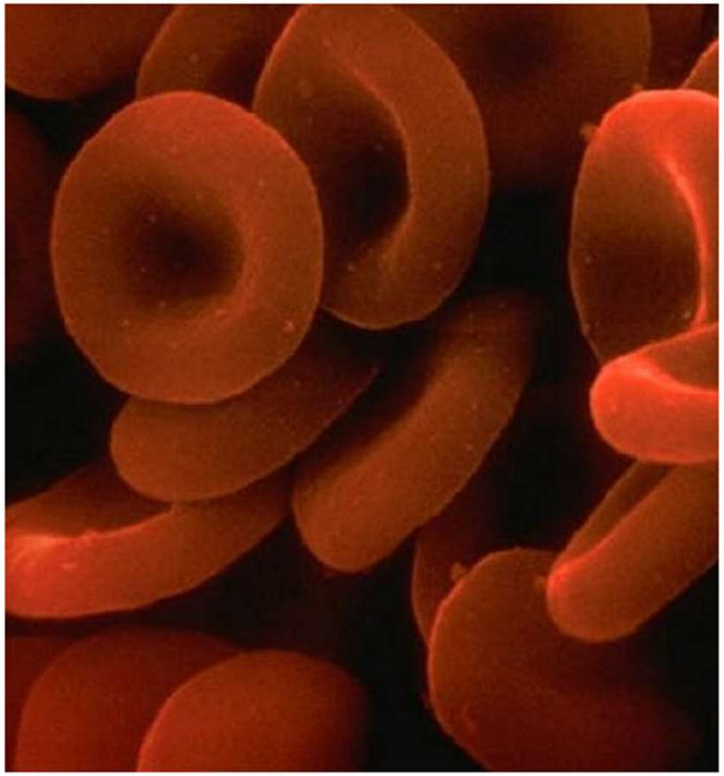


Image adapted from: National Human Genome Research Institute.

Transport Proteins

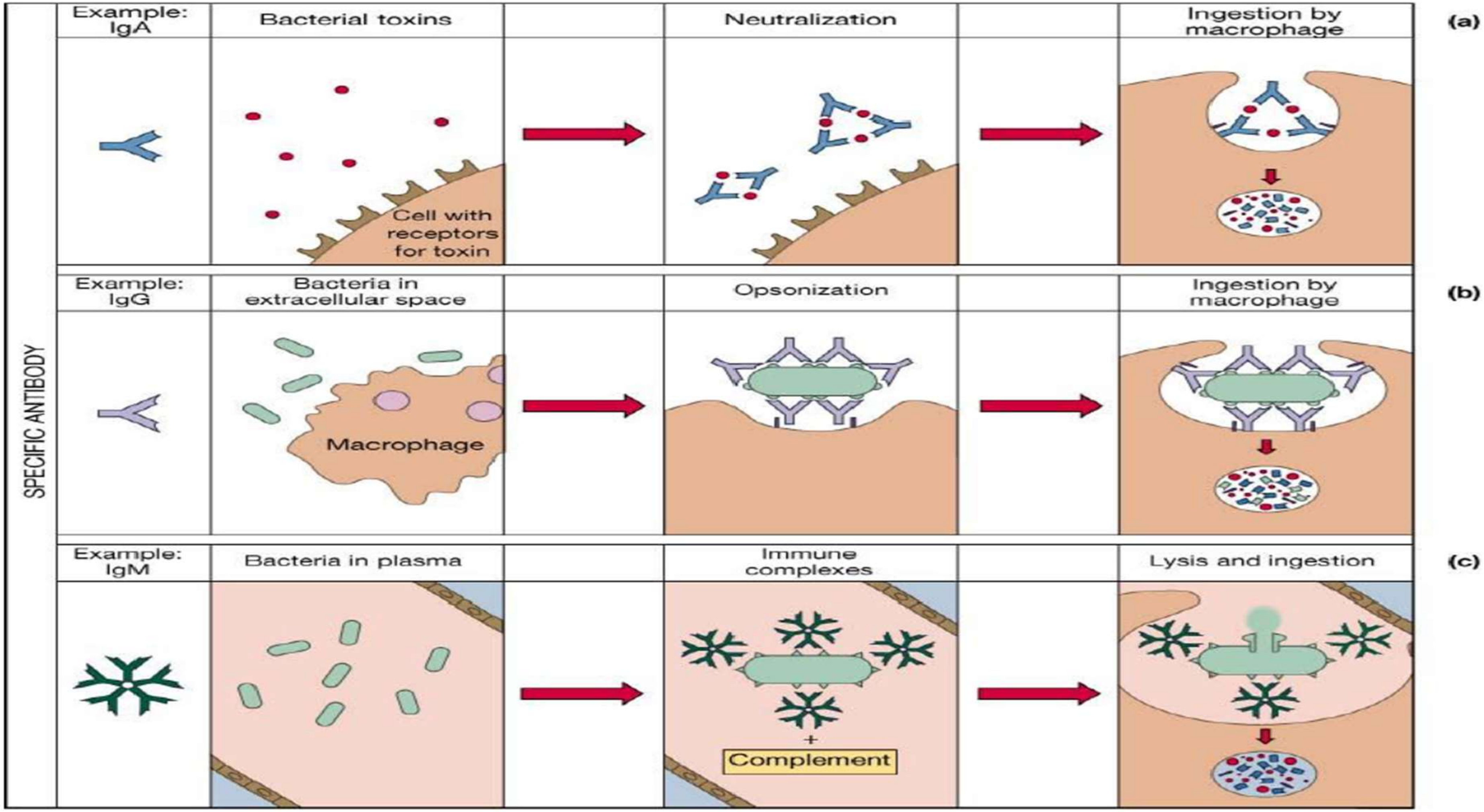


Hemoglobin

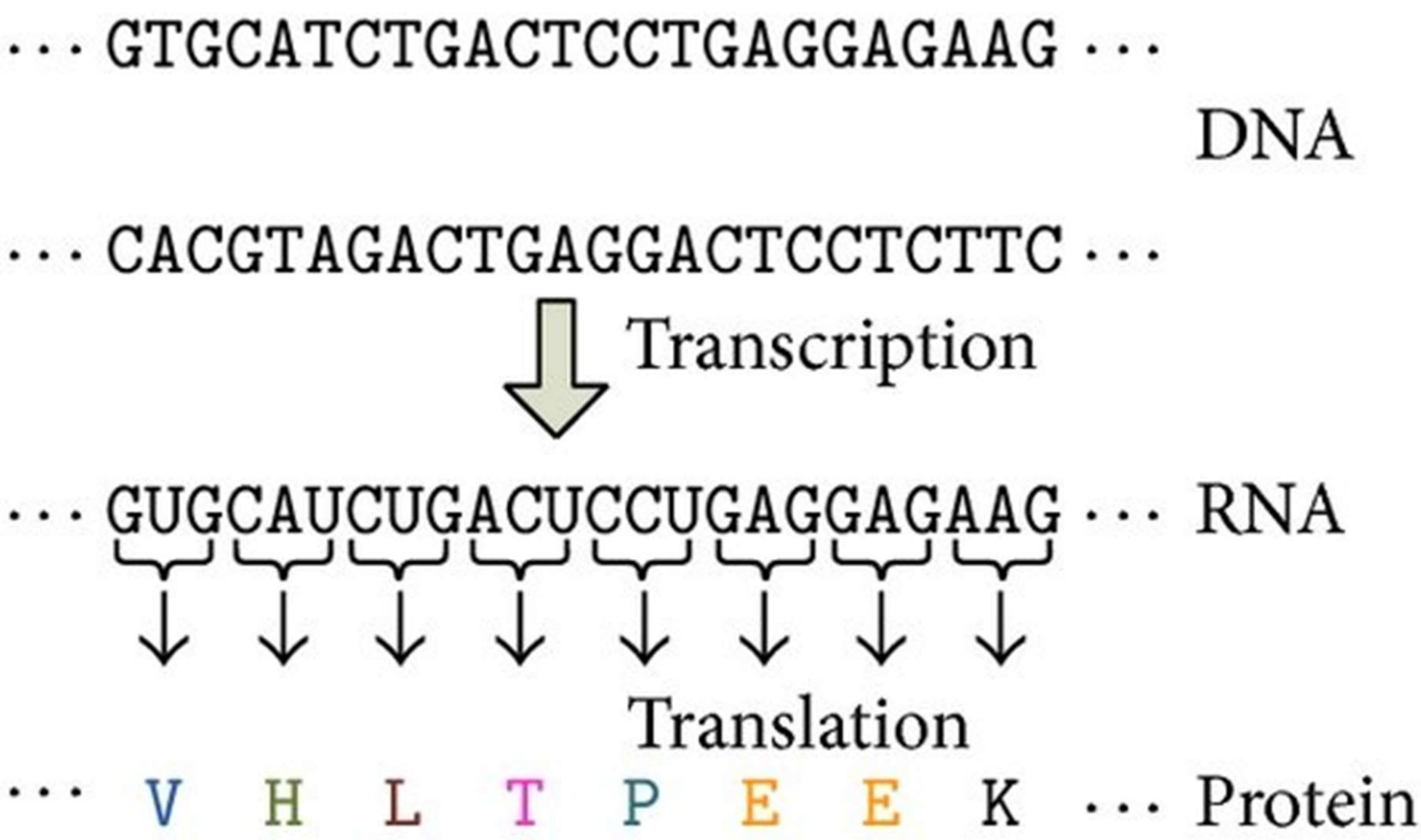


Red Blood Cell

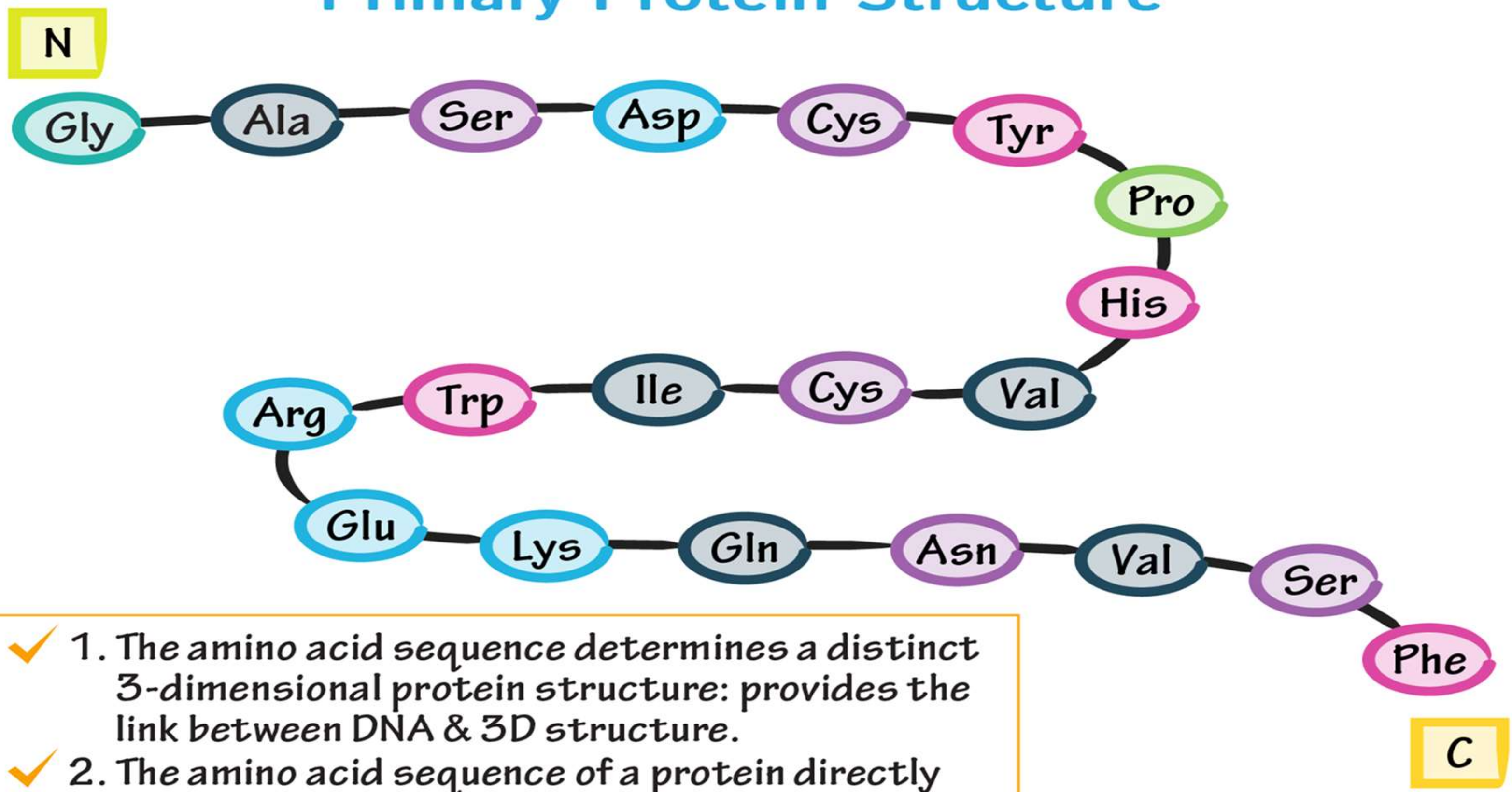
Immunity: Antibodies



The central dogma of Life

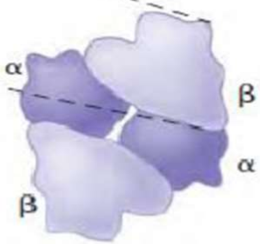
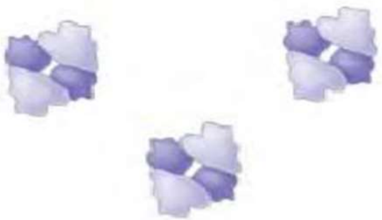
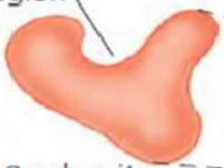
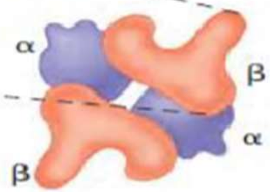
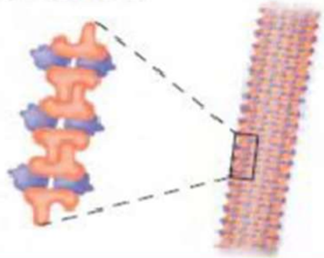


Primary Protein Structure



1. The amino acid sequence determines a distinct 3-dimensional protein structure: provides the link between DNA & 3D structure.
2. The amino acid sequence of a protein directly relates to its mechanism of action.
3. Changes in amino acid sequence (even of a single amino acid) can disrupt normal protein function and result in disease.
4. Protein sequence gives insight into its evolutionary history as proteins with a common ancestor have similar sequences.

Sickle-cell Anemia

	Primary Structure	Secondary and Tertiary Structures	Quaternary Structure	Function	Red Blood Cell Shape
Normal hemoglobin	1 Val 2 His 3 Leu 4 Thr 5 Pro 6 Glu 7 Glu	 β subunit	Normal hemoglobin 	Molecules do not associate with one another; each carries oxygen. 	Normal red blood cells are full of individual hemoglobin molecules, each carrying oxygen.  10 µm
Sickle-cell hemoglobin	1 Val 2 His 3 Leu 4 Thr 5 Pro 6 Val 7 Glu	Exposed hydrophobic region  β subunit	Sickle-cell hemoglobin 	Molecules interact with one another and crystallize into a fiber; capacity to carry oxygen is greatly reduced. 	Fibers of abnormal hemoglobin deform red blood cell into sickle shape.  10 µm

Functions of proteins :

Proteins carry out most diverse and possibly the largest volumes of cellular functions. Some of the key functions are summarized as below :

- Biocatalysis- Almost all the biological reactions are catalyzed by the enzymes. These are substrate specific and carry out reactions at very high rates under mild physiological conditions. Several thousand enzymes have been identified to date.

- Membrane are constitute of lipoprotein and some proteins are integral part of membrane. Receptors found on the membrane are also protein in nature.

- Transport and storage proteins - small molecules are often carried by proteins in the physiological setting e.g. haemoglobin is responsible for the transport of oxygen to tissues.

- Muscle are made up of proteins and their contraction is done by actin and myosin protein.

- Mechanical support - skin and bone are strengthened by the protein collagen.

- Antibodies of immune system are protein structures.

- Many of the hormones and growth factors such as insulin or thyroid stimulating hormone are proteins.

Signals: Key Models, Cells & Organisms

SIGNAL TRANSDUCTION

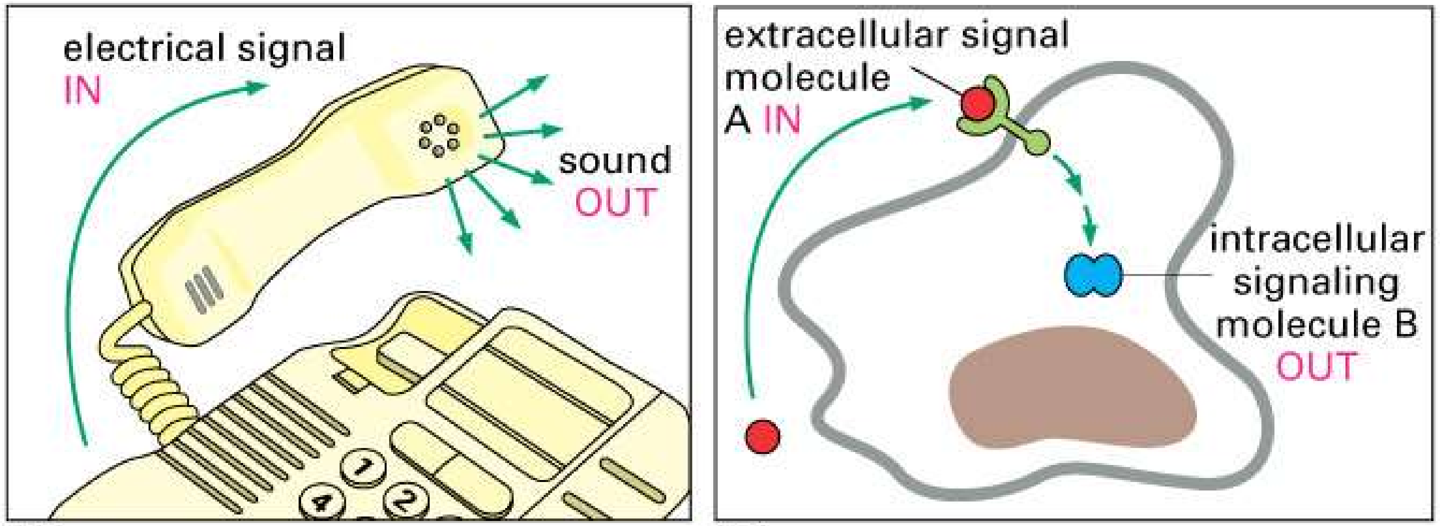
- Cells can exist as single celled organisms or be part of a multi-cellular organism
- How do they know what is happening around them?
- Cells do not have ‘eyes’, ‘noses’, or ‘ears’

SIGNAL TRANSDUCTION

Cells communicate with others and have mechanisms to sense their environments using a variety of methods as we will uncover - whichever method is used it involves a very important principle.

Signal Transduction

The conversion of a signal, of some type, from one physical form to another.



(A) (B)

Electrical impulses are converted to sound waves that we hear

Signal molecules are received by target cells via receptors and converted to other intracellular forms

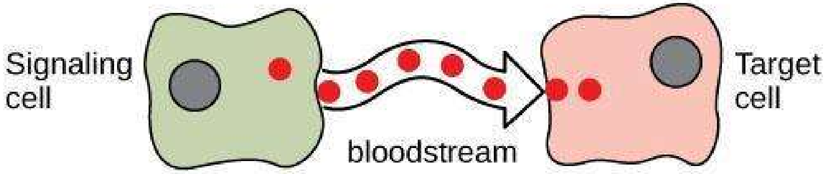
Figure 16-2 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Cell Signaling types

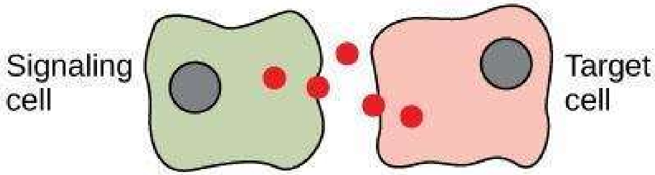
- Endocrine - hormones, long distance
- Paracrine - local vicinity
- Neuronal - very short distances
- Contact-dependent - physical contact
- Autocrine - act on self

**Contact signaling involves communication between cells that are in direct contact with each other. This communication is often mediated by gap junctions in animal cells and plasmodesmata in plant cells. One example of contact-dependent signaling is the Delta-Notch pathway used in embryonic development.

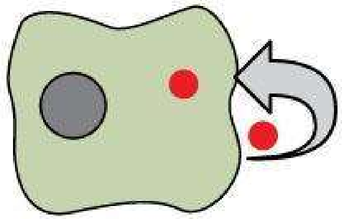
Forms of Chemical Signaling	
Endocrine	A cell targets a distant cell through the bloodstream.



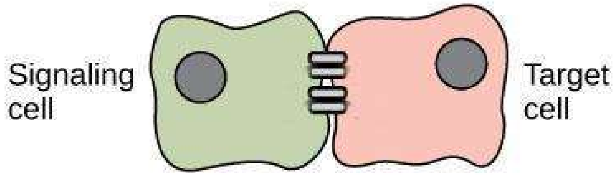
Paracrine	A cell targets a nearby cell.



Autocrine	A cell targets itself.



Contact-Dependent	Cells must physically interact to initiate signaling



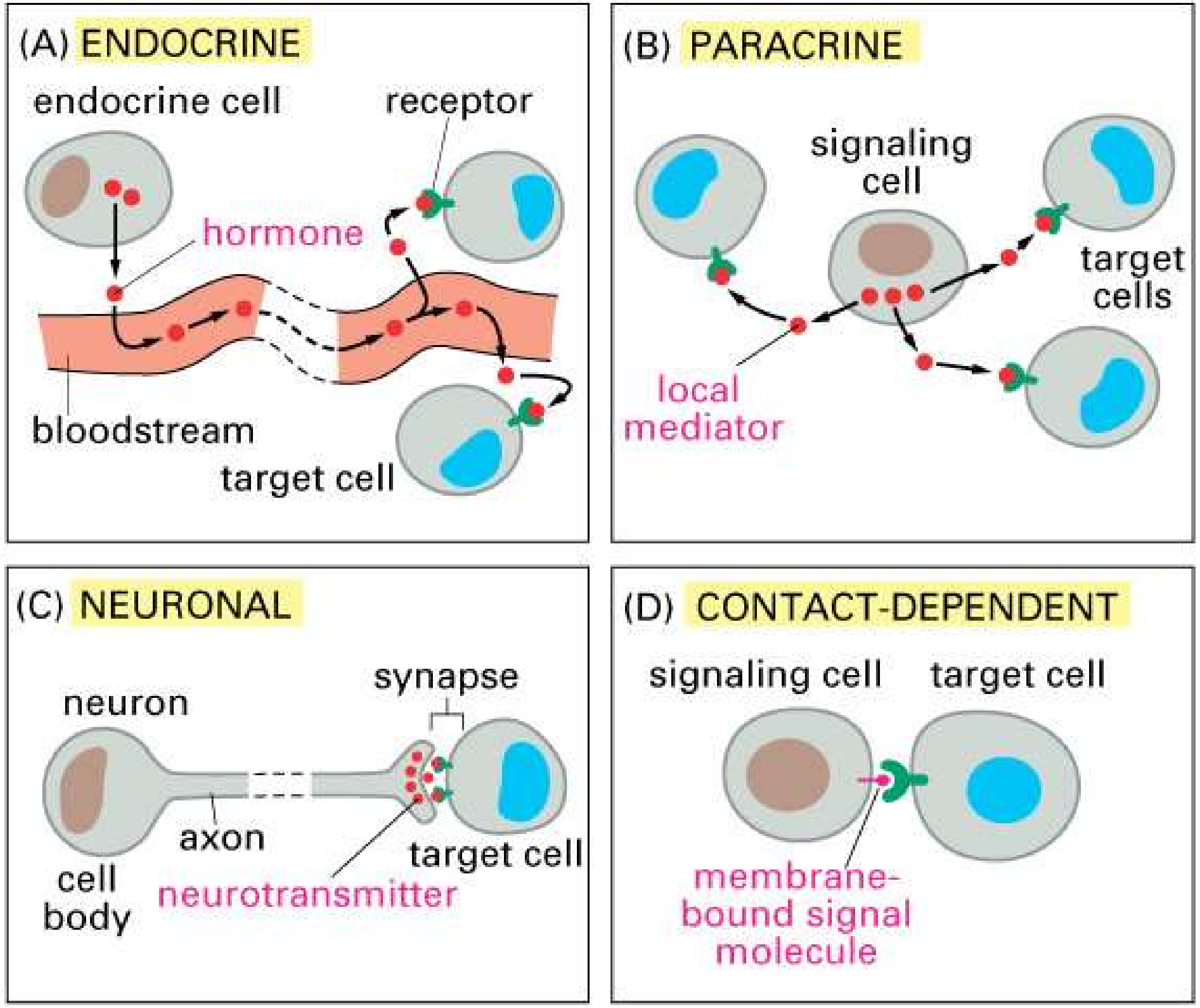
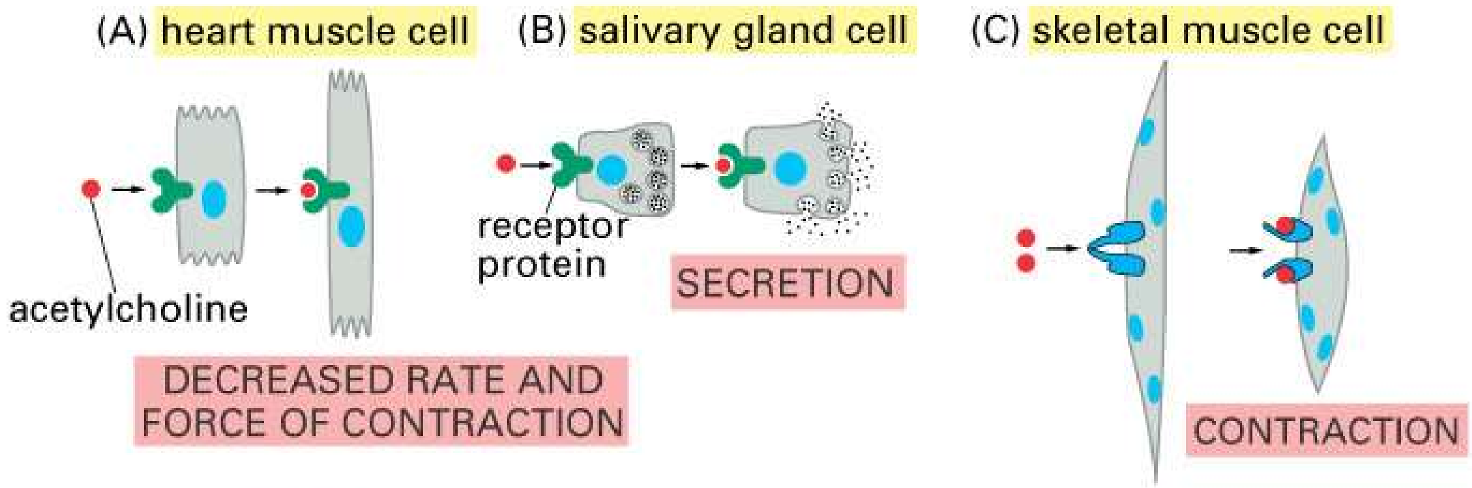
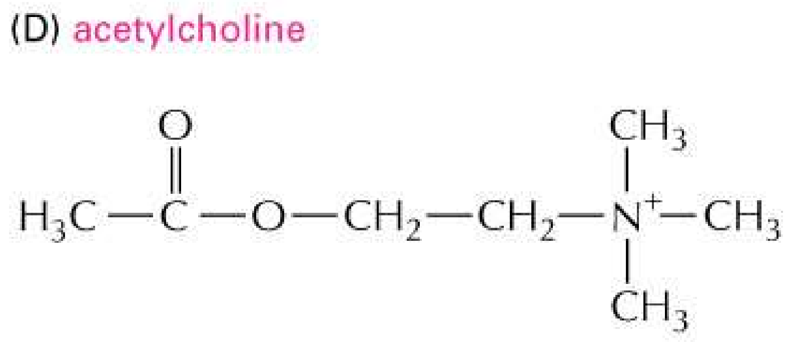


Figure 16-3 Essential Cell Biology, 2/e. (© 2004 Garland Science)

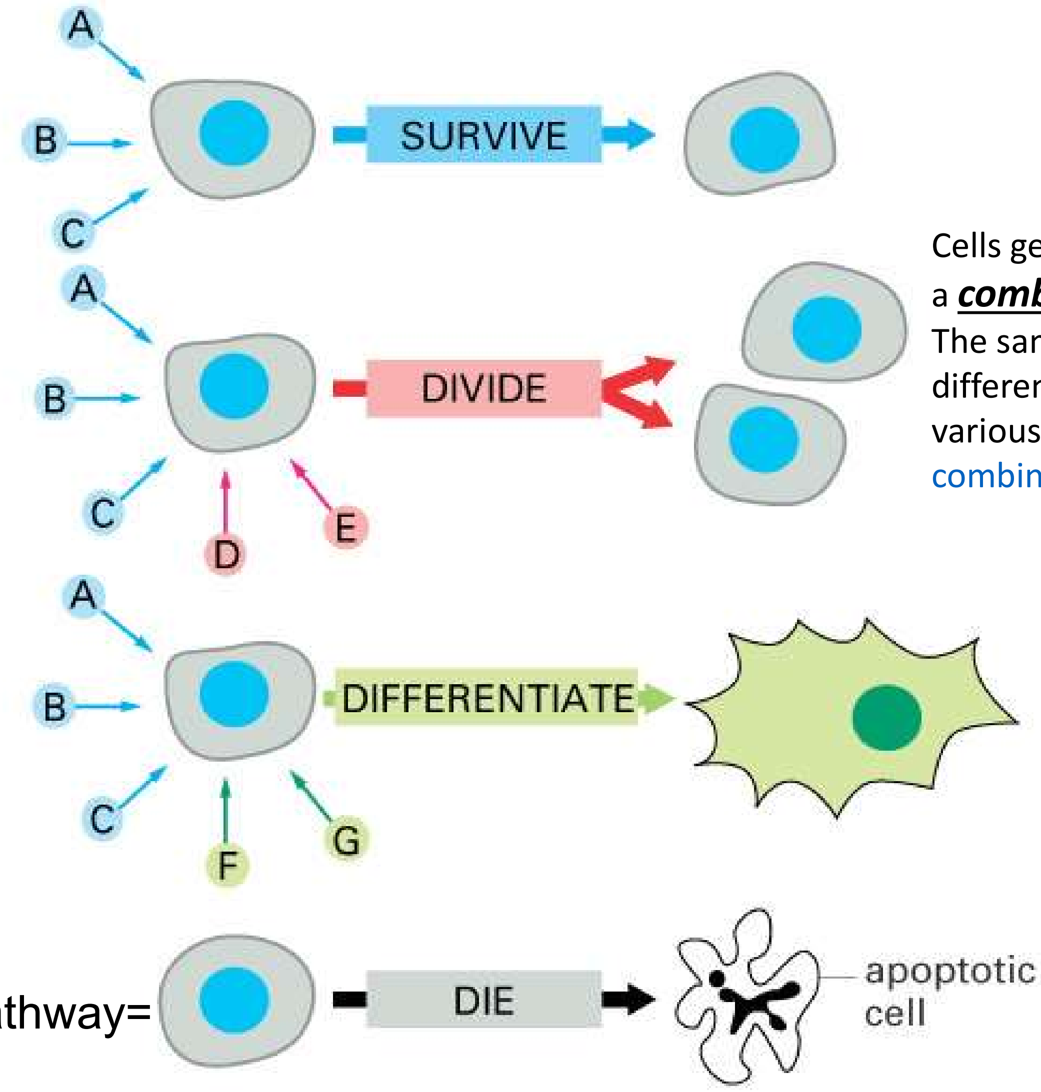
The same signal molecule may interact with different cells with entirely different effects. Here is an example of acetylcholine





Acetylcholine has a role in both branches of your nervous system
It has a half-life of about 2 minutes.

Figure 16-5 Essential Cell Biology, 2/e. (© 2004 Garland Science)



The default pathway=

Figure 16-6 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Cells generally respond to a ***combination*** of signals. The same cell may have different outcomes to various signal combinations

Cells that DO NOT RECEIVE SIGNALS **DIE**

How do these signals work

At which level?

Where?

How many?

General Plan of Action

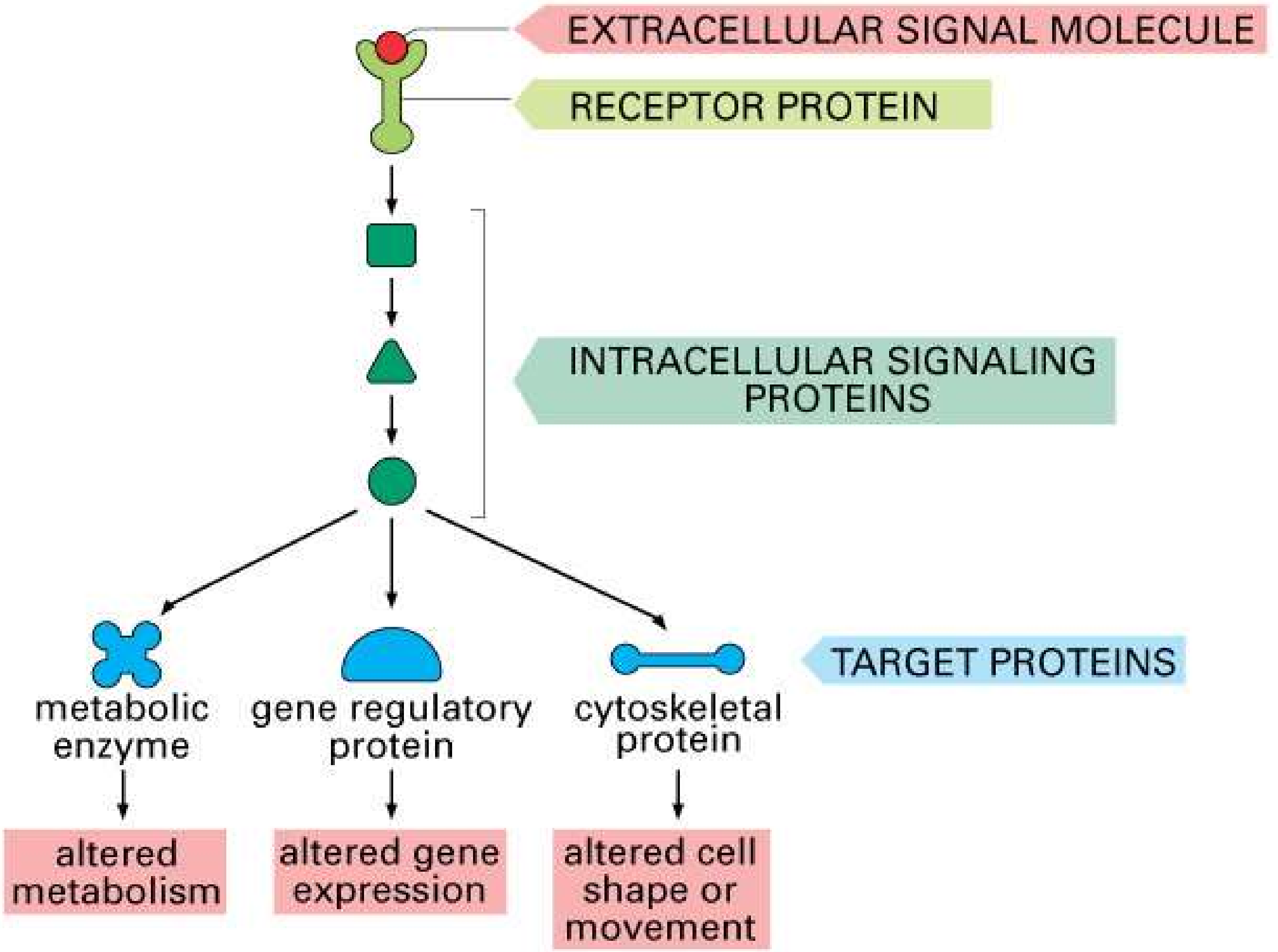


Figure 16-7 Essential Cell Biology, 2/e. (© 2004 Garland Science)

- Each cell responds to a limited set of signals - why?

- These signals change the activity of internal cellular proteins which changes the behavior of the cell

- These signals follow a chain of events known as the signal cascade
    - A system of relaying information from the site of reception to the point of action
    - Normally the signal is amplified too - a small input is quickly converted to a large response

General Overview 2

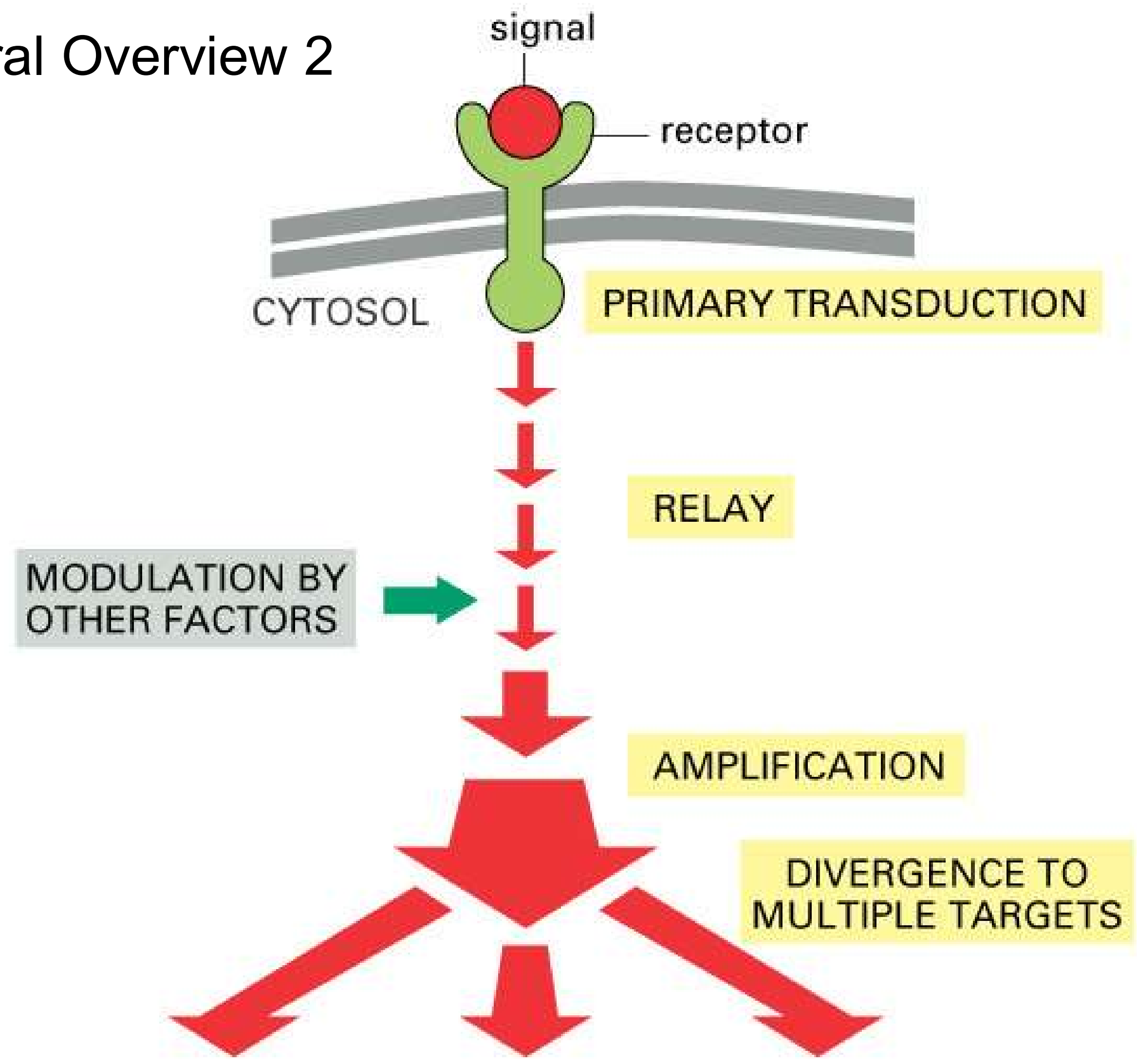
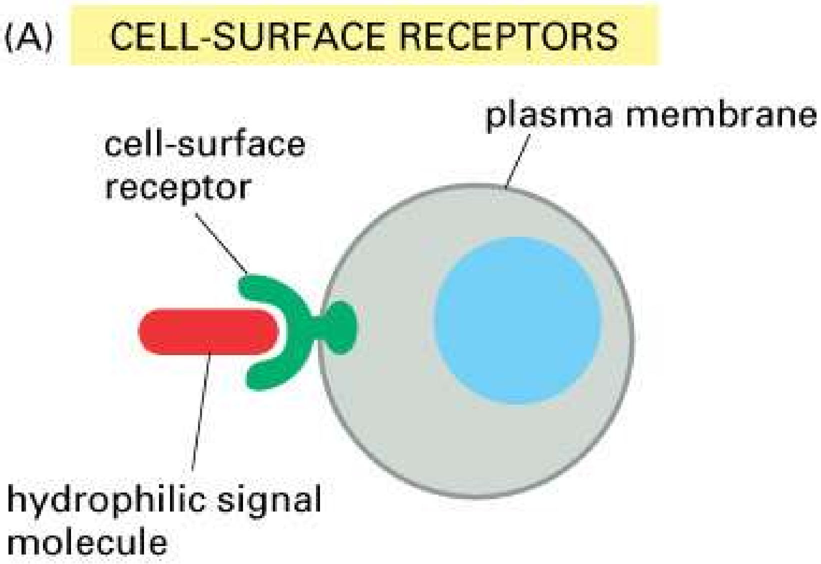
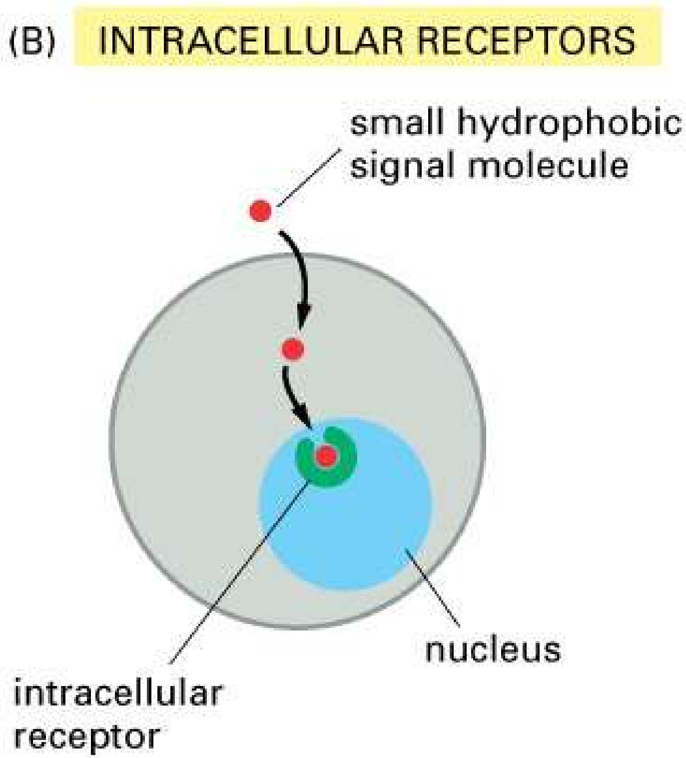


Figure 16-8 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Some signal molecules act at the cell surface whilst others can enter the cell readily and act inside such as steroids.



The red signal molecule has a target receptor to which it binds and that's that. Note that it is usually hydrophilic.



Other receptors enter the cell and they must pass through the membrane.

Figure 16-9 Essential Cell Biology, 2/e. (© 2004 Garland Science)

A simple example of how a steroid works.

-The signal can enter the cell through the membrane and bind to its target protein.

-This is now able to enter through the nuclear pore and control transcription directly of certain target genes

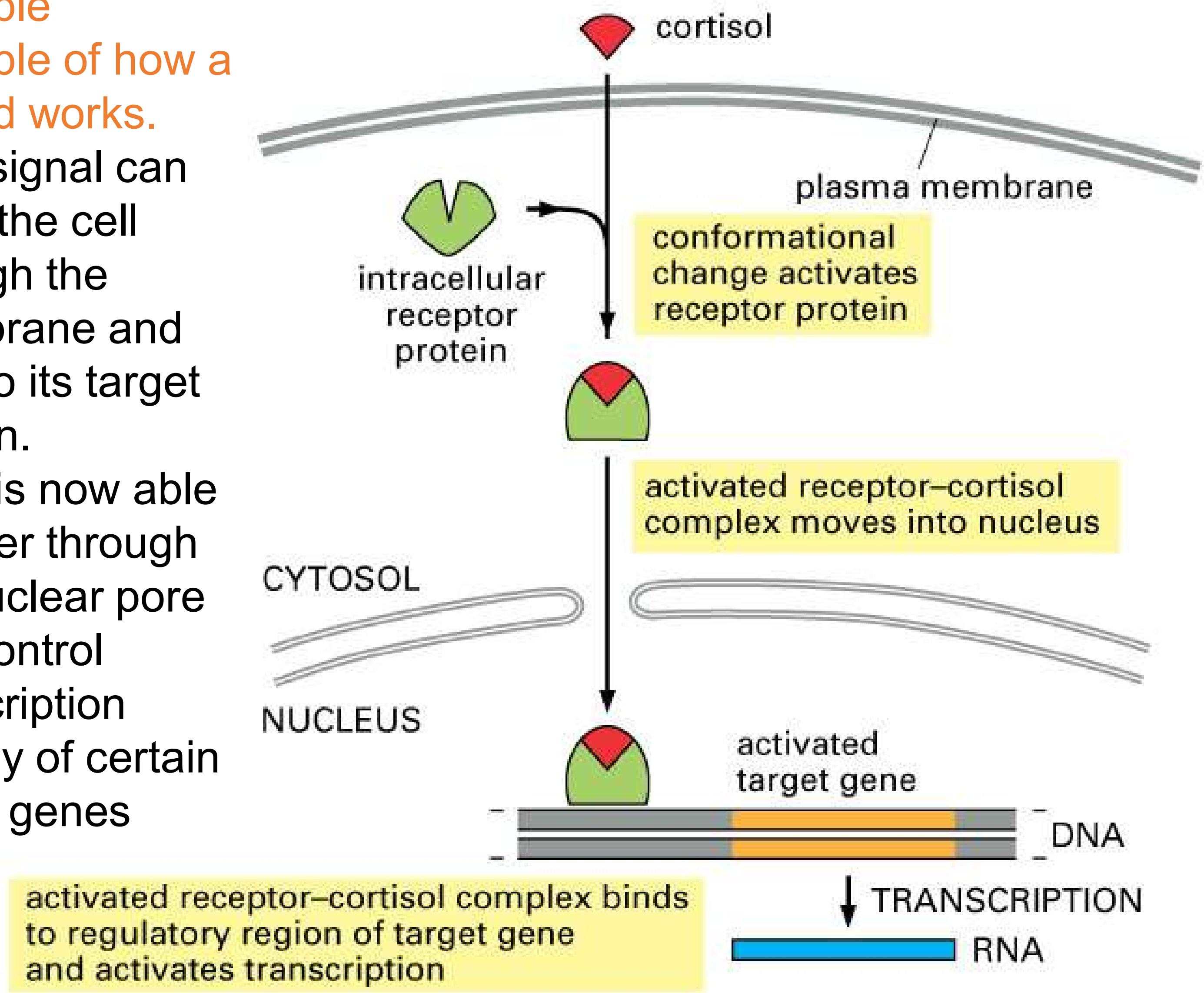


Figure 16-12 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Ion-channel linked receptors

- All nerve impulses are generated via ion-channel linked receptors
  - The release of neurotransmitter causes the ion-channel on the target neuron to allow the passage of ions (which?) into the cell. This action is propagated through the nerve cell along its axon.

Many interactions taking place within the cell act to turn **on** or **off** proteins. These are known as molecular switches.

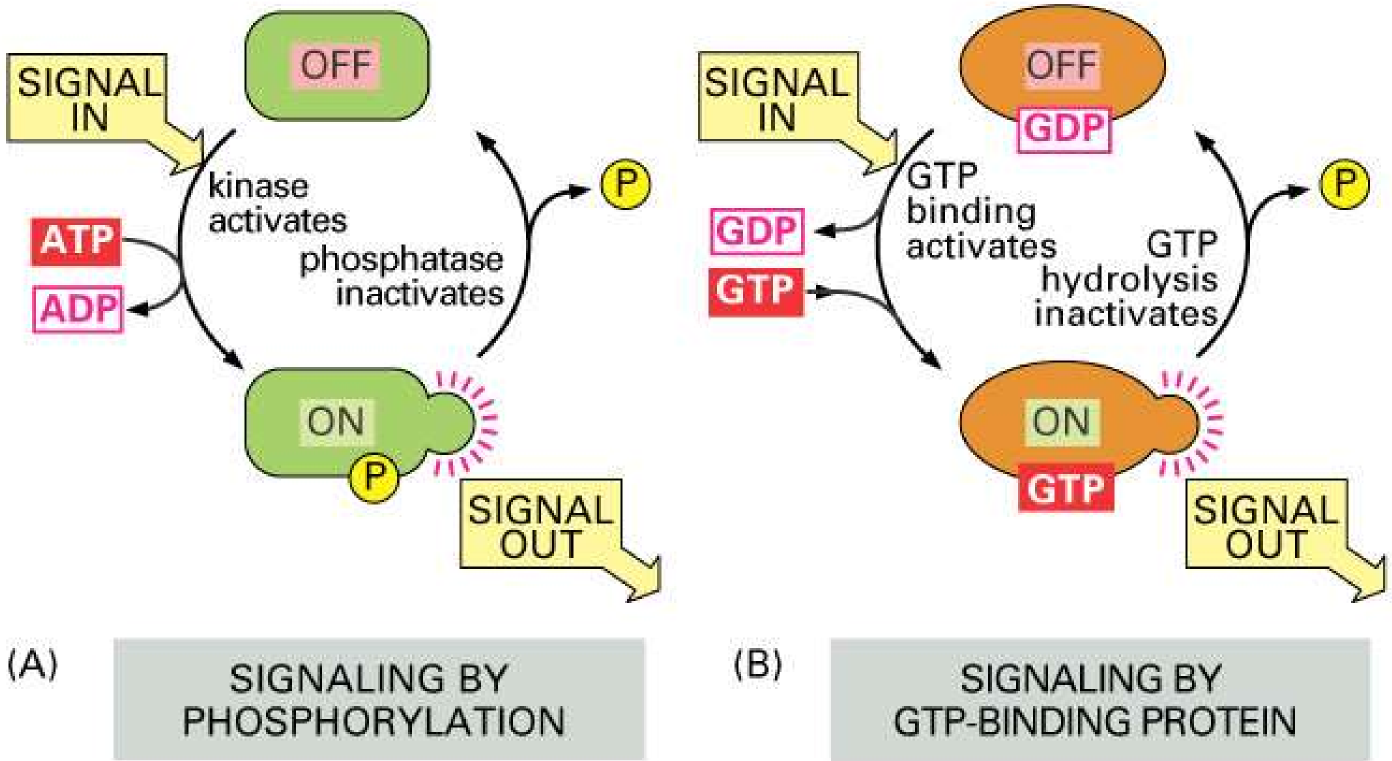


Figure 16-15 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Some cellular responses are quick, whilst others are slow.

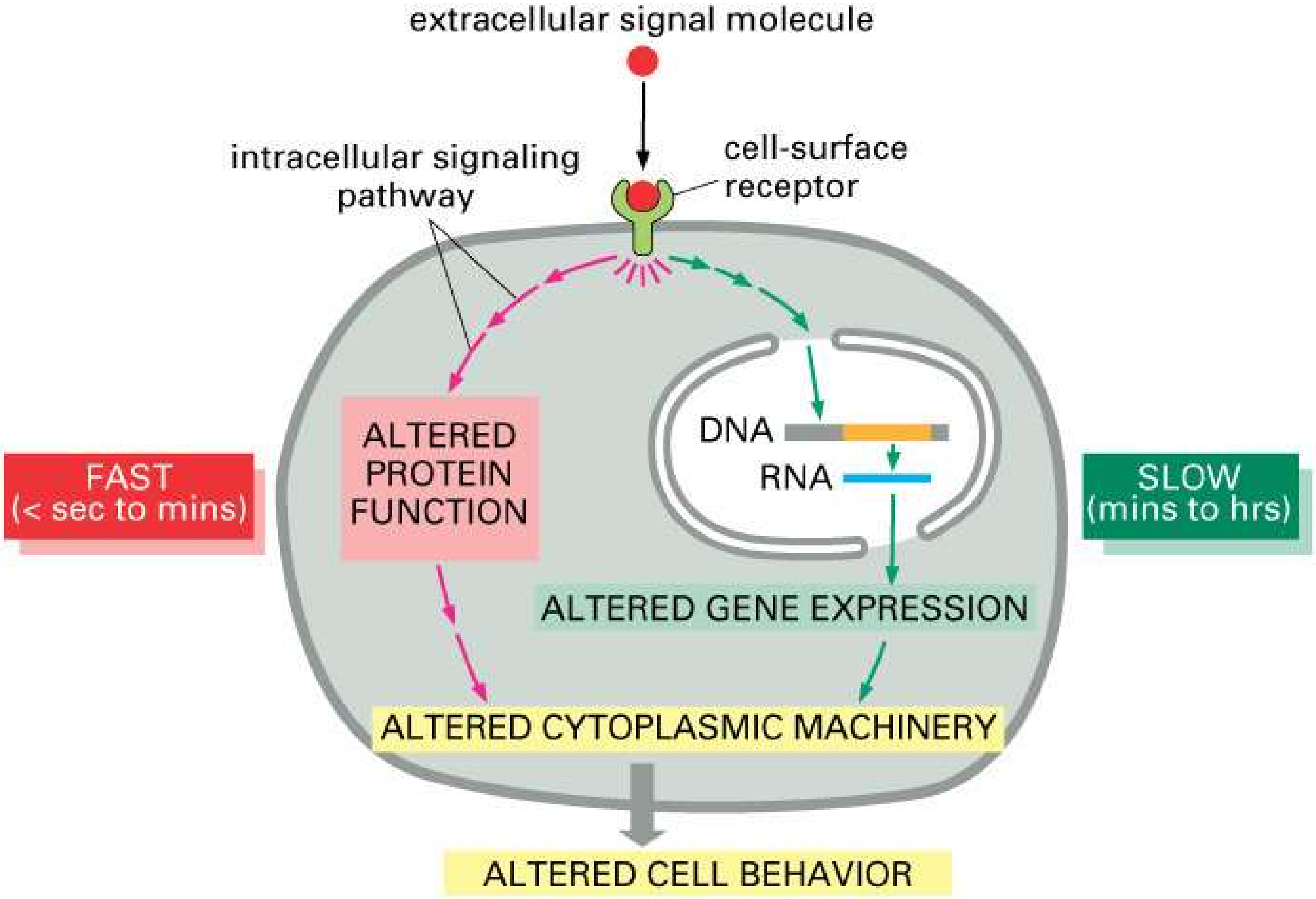
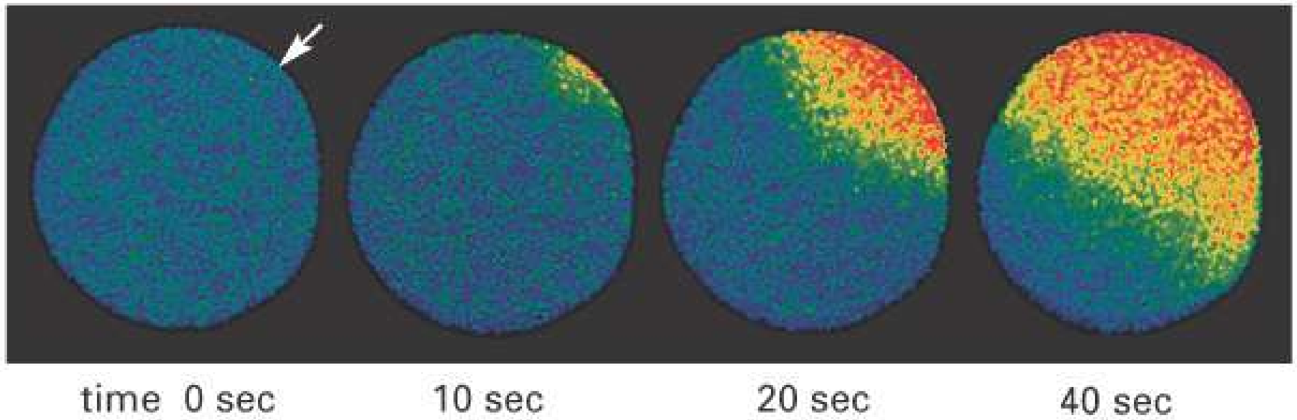


Figure 16-23 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Fertilization

Calcium has a very important role to play as an intercellular messenger.
As we know the concentration of calcium is extremely low in the cytoplasm of a typical cell, compared to the outside and to that of the ER.



In this example fertilization results in the wave of receptors opening up to permit the influx of calcium into the cell. This results in a change in the cell surface which both initiates cell division and prevents other sperm from entering the cell.

Figure 16-26 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Photoreceptor

The speed at which signaling cascades operate is clearly illustrated by the photoreceptors of the eye.

The human eye has two forms of receptors - rods and cones
The cones are further divided depending on the wavelength of light they respond to - red, green, and blue

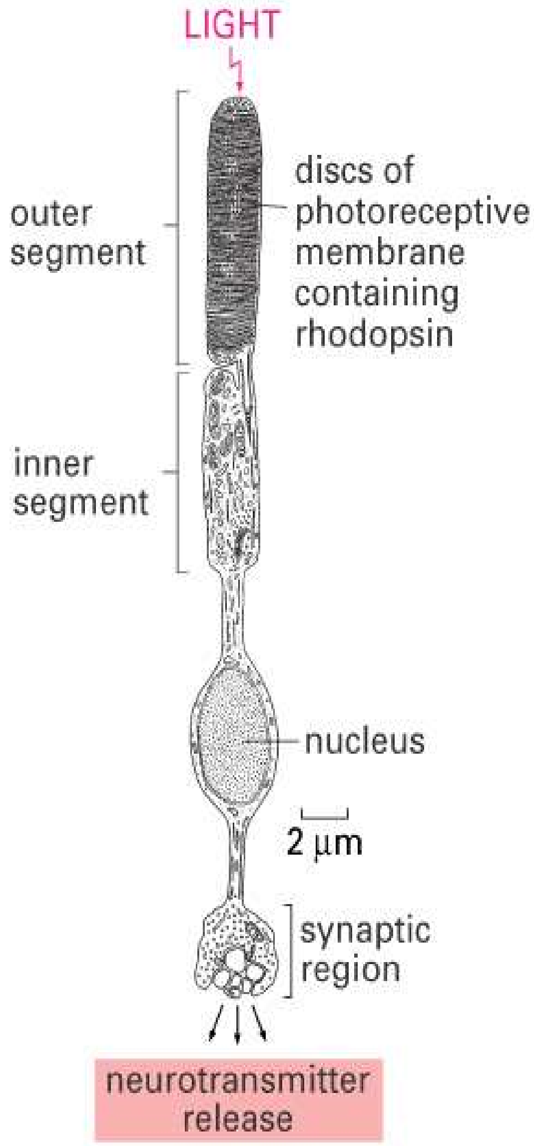


Figure 16-28 Essential Cell Biology, 2/e. (© 2004 Garland Science)

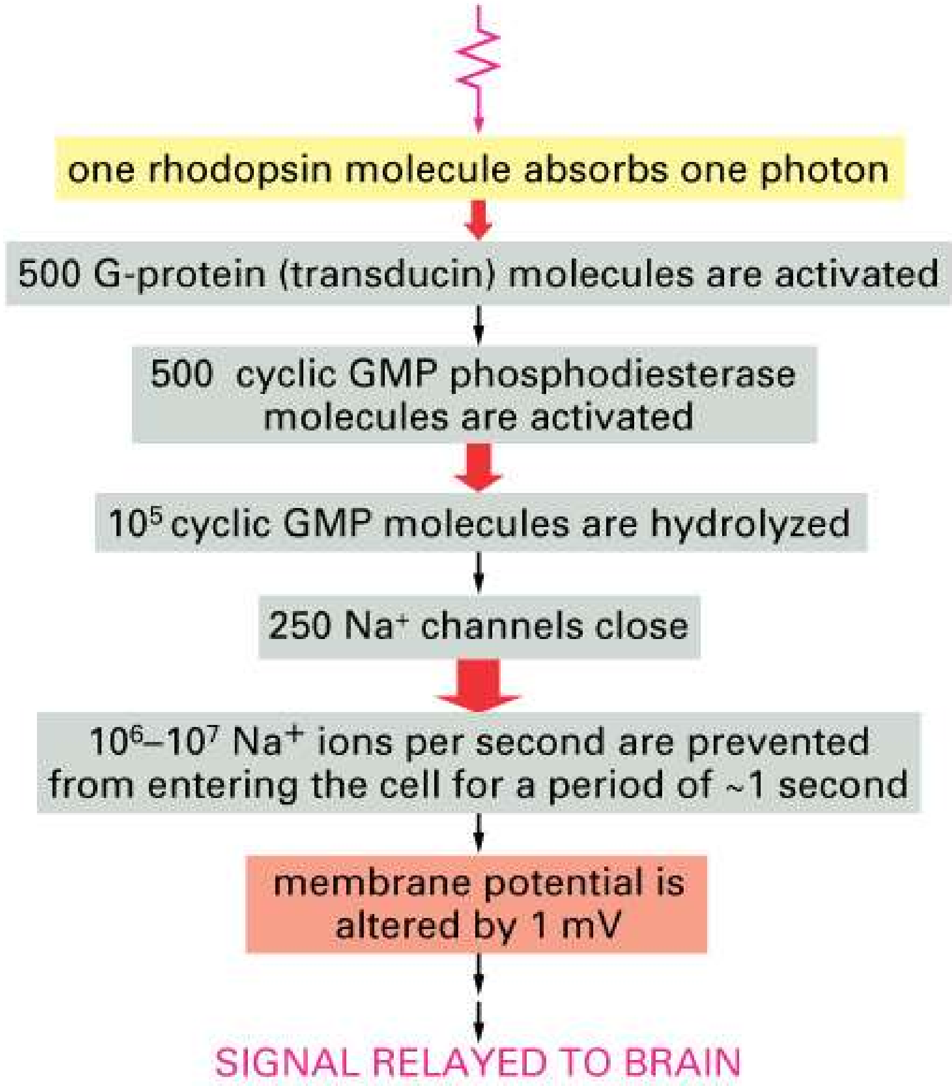


Figure 16-29 Essential Cell Biology, 2/e. (© 2004 Garland Science)