Chapter 1:

Functional Organization of the Human Body and Control of the “Internal Environment”

- *Human Physiology* attempt to explain the specific characteristics and mechanisms of the human body that make it a living being.

- *Anatomy* attempt to explain the structure of the body.

- Each type of life, from the simple virus to the largest tree or the complicated human being, has its own functional characteristics.

- The goal of physiology is to explain the physical and chemical factors that are responsible for the origin, development, and progression of life.

- Therefore, the vast field of physiology can be divided into:

  - ❑ *viral physiology*
  - ❑ *bacterial physiology*
  - ❑ *cellular physiology*
  - ❑ *plant physiology*
  - ❑ *human physiology*
  - ❑ .....

The Human Body - A Complex Society of Differentiated Cells

- Cells: the basic structural and functional unit (~ 100 trillion)

- Each type of cell is specially adapted to perform one or a few particular functions.

  - For instance, the red blood cells, numbering 25 trillion in each human being, transport oxygen from the lungs to the tissues. 75 trillion additional cells of other types that perform functions different from those of the red cell.

- Although the many cells of the body often differ markedly from one another, all of them have certain basic characteristics that are alike.

  - For instance, in all cells, oxygen reacts with carbohydrate, fat, and protein to release the energy required for cell function. Further, the general chemical mechanisms for changing nutrients into energy are basically the same in all cells, and all cells deliver end products of their chemical reactions into the surrounding fluids.

- all cells also have the ability to reproduce additional cells of their own kind.

Extracellular Fluid—The “Internal Environment”

- About 60 per cent of the adult human body is fluid, mainly a water solution of ions and other substances.

- Most of this fluid is inside the cells and is called intracellular fluid, about one third is in the spaces outside the cells and is called extracellular fluid.

- Extracellular fluid is transported rapidly in the circulating blood and then mixed between the blood and the tissue fluids by diffusion through the capillary walls.

- The ions and nutrients that are in the extracellular fluid needed by the cells to maintain cell life. Thus, all cells live in essentially the same environment—the extracellular fluid. For this reason, the extracellular fluid is also called the internal environment of the body

- Cells are capable of living, growing, and performing their special functions as long as the proper concentrations of oxygen, glucose, different ions, amino acids, fatty substances, and other constituents are available in this internal environment.

Differences Between Extracellular and Intracellular Fluids.

- The extracellular fluid contains large amounts of sodium, chloride, and bicarbonate ions plus nutrients for the cells, such as oxygen, glucose, fatty acids, and amino acids. It also contains carbon dioxide that is being transported from the cells to the lungs to be excreted, plus other cellular waste products that are being transported to the kidneys for excretion.

- The intracellular fluid differs significantly from the extracellular fluid; specifically, it contains large amounts of potassium, magnesium, and phosphate ions instead of the sodium and chloride ions found in the extracellular fluid. Special mechanisms for transporting ions through the cell membranes maintain the ion concentration differences between the extracellular and intracellular fluids.

“Homeostatic” Mechanisms of the Major Functional Systems

- **Homeostasis**

- The term *homeostasis* is used by physiologists to mean *maintenance of nearly constant conditions in the internal environment.*

- Essentially all organs and tissues of the body perform functions that help maintain these constant conditions.

  - For instance, the lungs provide oxygen to the extracellular fluid to replenish the oxygen used by the cells, the kidneys maintain constant ion concentrations, and the gastrointestinal system provides nutrients.

▪ Different functional systems of the body and their contributions to homeostasis (briefly):

▪ Extracellular Fluid Transport and Mixing System—The Blood Circulatory System

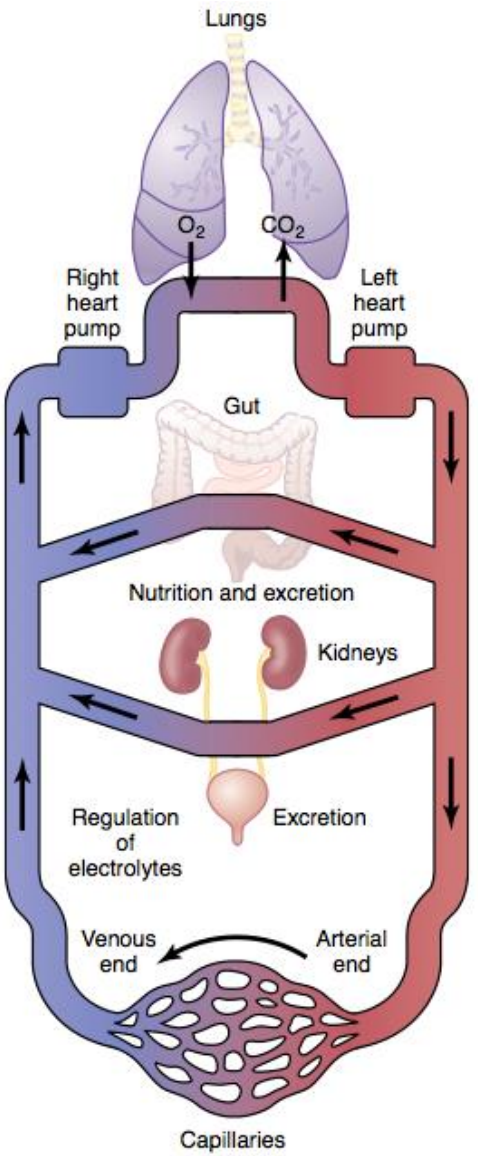


Figure 1–1

General organization of the circulatory system.

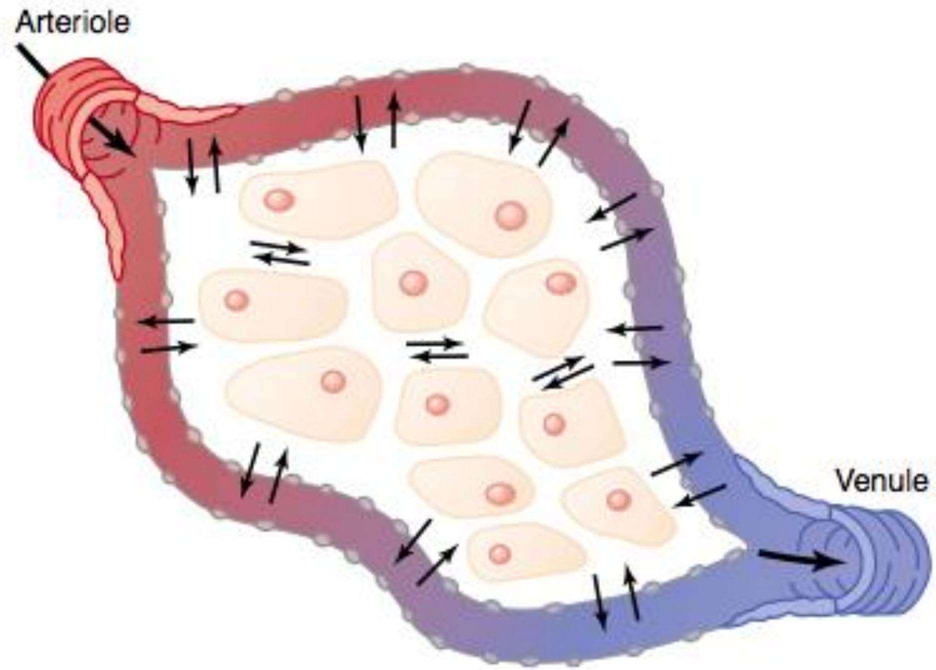


Figure 1–2

Diffusion of fluid and dissolved constituents through the capillary walls and through the interstitial spaces.

The walls of the capillaries are permeable to most molecules in the plasma of the blood, with the exception of the large plasma protein molecules. Therefore, large amounts of fluid and its dissolved constituents diffuse back and forth between the blood and the tissue spaces, as shown by the arrows. This process of diffusion is caused by kinetic motion of the molecules in both the plasma and the **interstitial** fluid.

- **Origin of Nutrients in the Extracellular Fluid**

- Respiratory System acquires the oxygen needed by the cells

- Gastrointestinal Tract absorbs different dissolved nutrients, including carbohydrates, fatty acids, and amino acids from the ingested food into the extracellular fluid of the blood

- Liver and Other Organs That Perform Primarily Metabolic Functions: Not all substances absorbed from the gastrointestinal tract can be used in their absorbed form by the cells. The liver changes the chemical compositions of many of these substances to more usable forms, and other tissues of the body—fat cells, gastrointestinal mucosa, kidneys, and endocrine glands—help modify the absorbed substances or store them until they are needed.

- Musculoskeletal System provides motility for protection against adverse surroundings, without which the entire body, along with its homeostatic mechanisms, could be destroyed instantaneously.

- **Removal of Metabolic End Products**

- Removal of Carbon Dioxide by the Lungs: At the same time that blood picks up oxygen in the lungs, carbon dioxide is released from the blood into the lung alveoli; the respiratory movement of air into and out of the lungs carries the carbon dioxide to the atmosphere.

- Kidneys: Passage of the blood through the kidneys removes from the plasma most of the other substances besides carbon dioxide that are not needed by the cells. These substances include different end products of cellular metabolism, such as urea and uric acid; they also include excesses of ions and water from the food that might have accumulated in the extracellular fluid.

- **Regulation of Body Functions**
- **Nervous System:** The nervous system is composed of three major parts:

① sensory input portion: Sensory receptors detect the state of the body or the state of the surroundings
② central nervous system (or integrative portion): The central nervous system is composed of the brain and spinal cord. The brain can store information, generate thoughts, create ambition, and determine reactions that the body performs in response to the sensations.
③ motor output portion. Appropriate signals are then transmitted through the motor output portion of the nervous system to carry out one's desires.

- **Hormonal System of Regulation.** Located in the body are eight major *endocrine glands* that secrete chemical substances called hormones. Hormones help regulate cellular function.
  - For instance, thyroid hormone increases the rates of most chemical reactions in all cells, thus helping to set the tempo of bodily activity. Insulin controls glucose metabolism; adreno-cortical hormones control sodium ion, potassium ion, and protein metabolism; and parathyroid hormone controls bone calcium and phosphate.

- the hormones are a system of regulation that complements the nervous system. The nervous system regulates mainly muscular and secretory activities of the body, whereas the hormonal system regulates many metabolic functions.
- **Reproduction**
- It helps maintain homeostasis by generating new beings to take the place of those that are dying.

Control Systems of the Body

- The human body has thousands of control systems in it. The most intricate of these are the genetic control systems that operate in all cells to help control intracellular function as well as extracellular function.

- Many other control systems operate within the organs to control functions of the individual parts of the organs; others operate throughout the entire body to control the interrelations between the organs.

Examples of Control Mechanisms

- Regulation of Oxygen and Carbon Dioxide Concentrations in the Extracellular Fluid

    - *oxygen-buffering function of hemoglobin*.
    - Excitation of the respiratory center → causing a person to breathe rapidly and deeply.

- Regulation of Arterial Blood Pressure.
    - baroreceptor system → When the arterial pressure rises too high, the baroreceptors send barrages of nerve impulses to the medulla of the brain

Characteristics of Control Systems

- **Negative Feedback Nature of Most Control Systems**

- if some factor becomes excessive or deficient, a control system initiates negative feedback, which consists of a series of changes that return the factor toward a certain mean value, thus maintaining homeostasis.

  - For instance; In the arterial pressure–regulating mechanisms, a high pressure causes a series of reactions that promote a lowered pressure, or a low pressure causes a series of reactions that promote an elevated pressure. In both instances, these effects are negative with respect to the initiating stimulus.

Example: Negative Feedback Control of Arterial Pressure Promotes Stability

↓ **Art. Pressure** → ↑ **Sympathetic Activity**

↑ **Heart Rate Vasoconstriction**

⊖

- Negative feedback: promotes stability

▪ Positive Feedback Can Sometimes Cause Vicious Cycles and Death

• Positive feedback: promotes a change in one direction, often leading to instability, disease, and sometimes death.

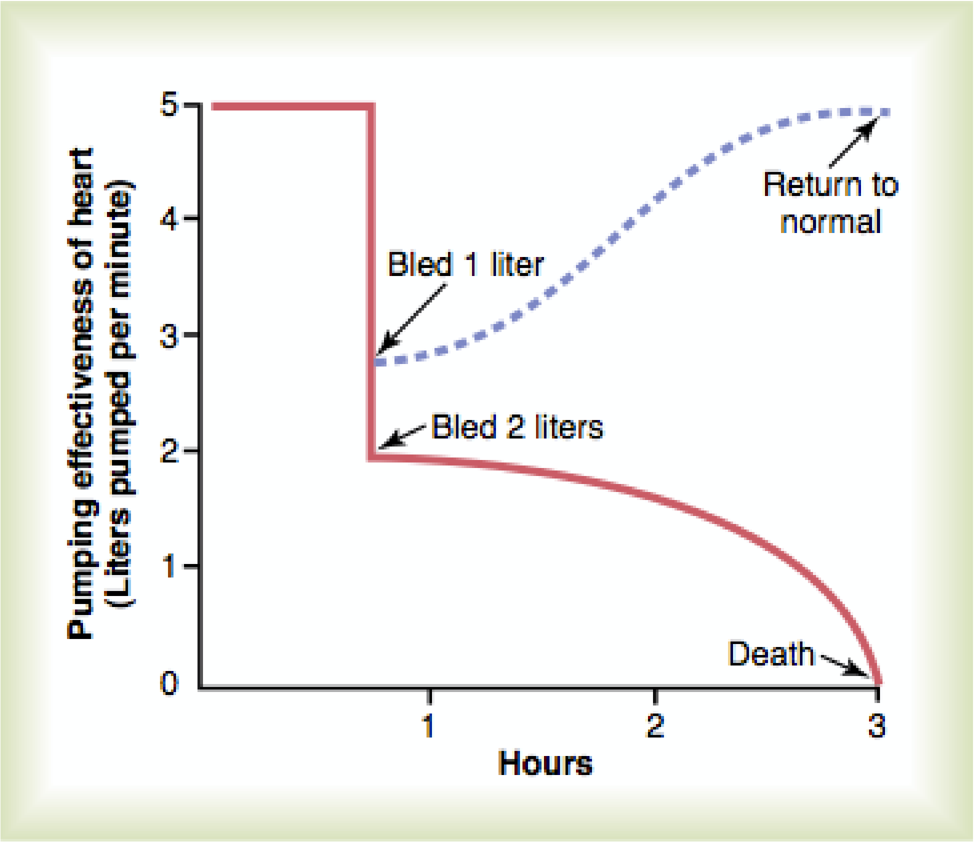
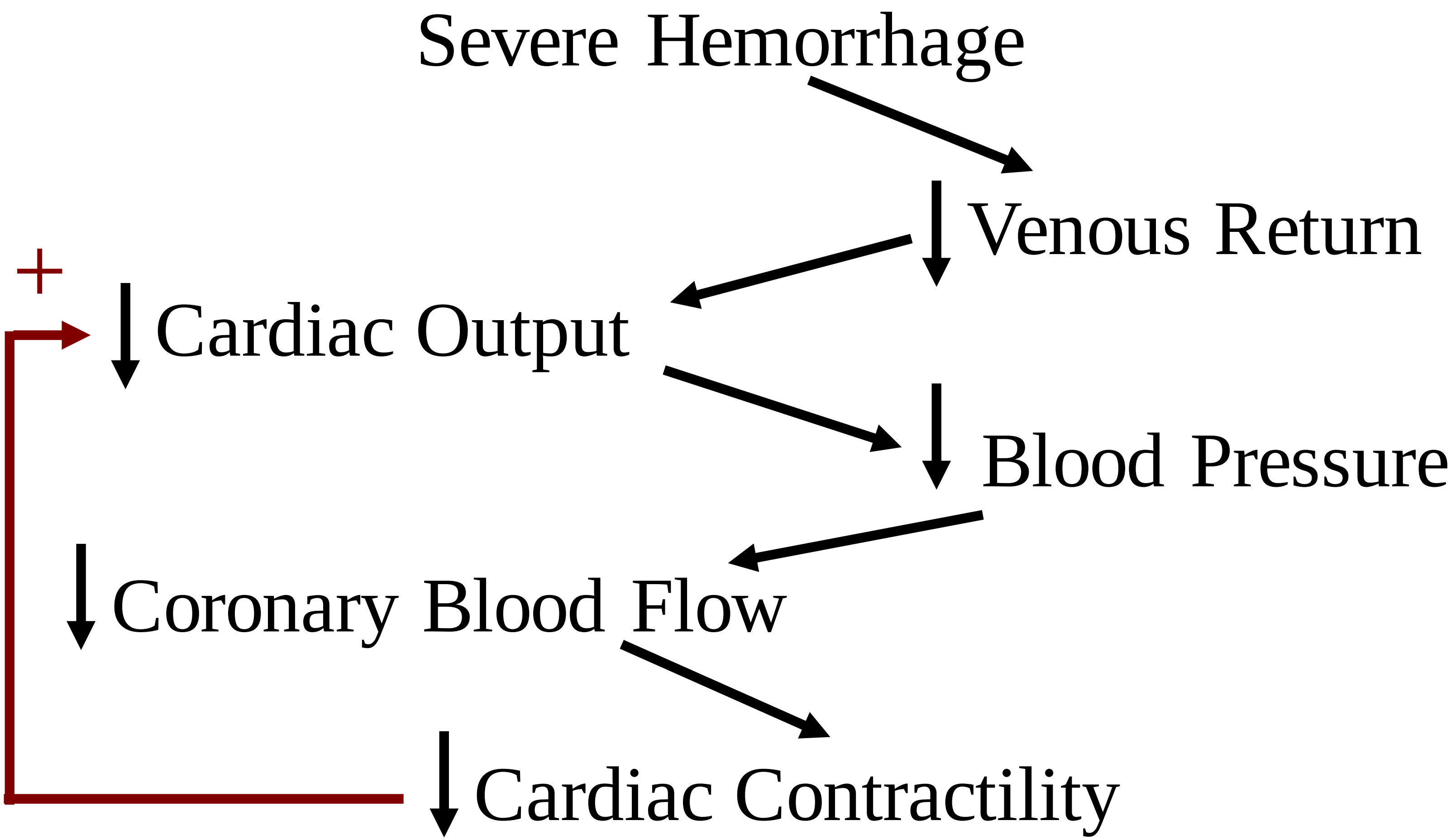


Figure 1–3

Recovery of heart pumping caused by *negative feedback* after 1 liter of blood is removed from the circulation. Death is caused by *positive feedback* when 2 liters of blood are removed.

- Positive feedback is better known as a "vicious cycle," but a mild degree of positive feedback can be overcome by the negative feedback control mechanisms of the body, and the vicious cycle fails to develop.

Example: Hemorrhagic Shock: Positive Feedback



Chapter 2:

The Cell and its Functions

Organization of the Cell

Cell composition:

- Water-----70-85% of cell mass
  - Many cellular chemicals are dissolved in the water and chemical reactions take place among the dissolved chemicals or at the surfaces of the suspended particles or membranes.
- Ions-----potassium, magnesium, phosphate, sulfate, bicarbonate, and smaller quantities of sodium, chloride, and calcium. (do not contribute significantly to cell mass
  - The ions provide inorganic chemicals for cellular reactions. Also, they are necessary for operation of some of the cellular control mechanisms.
- Proteins-----10-20%
  - two types: structural proteins (microtubules→ cytoskeleton) and functional proteins (enzymes).

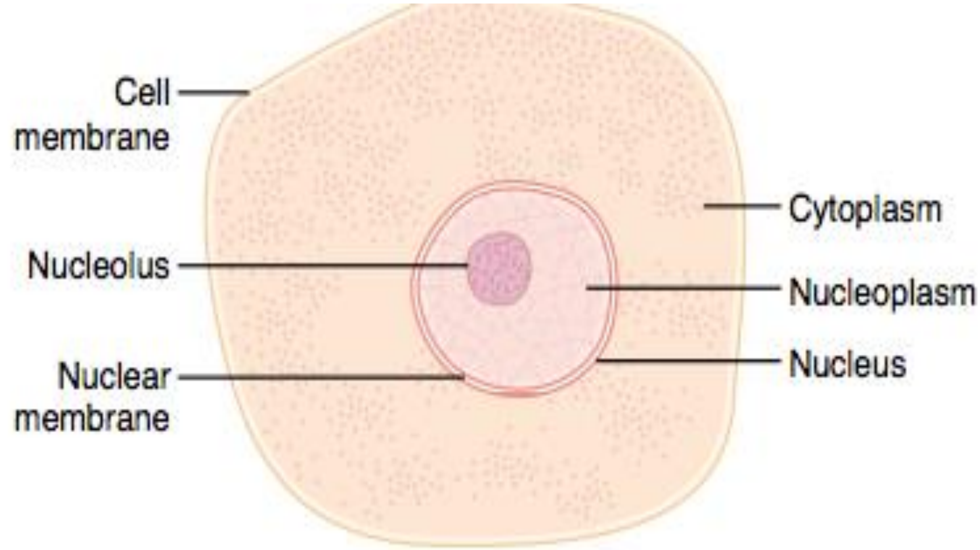


Figure 2–1

Structure of the cell as seen with the light microscope.

- Lipids-----2-95%
  - important lipids are phospholipids and cholesterol. they are mainly insoluble in water and, therefore, are used to form the cell membrane and intracellular membrane barriers that separate the different cell compartments.
- Carbohydrates-----1-6%
  - to supply the cells’ energy needs.

Physical Structure of the Cell

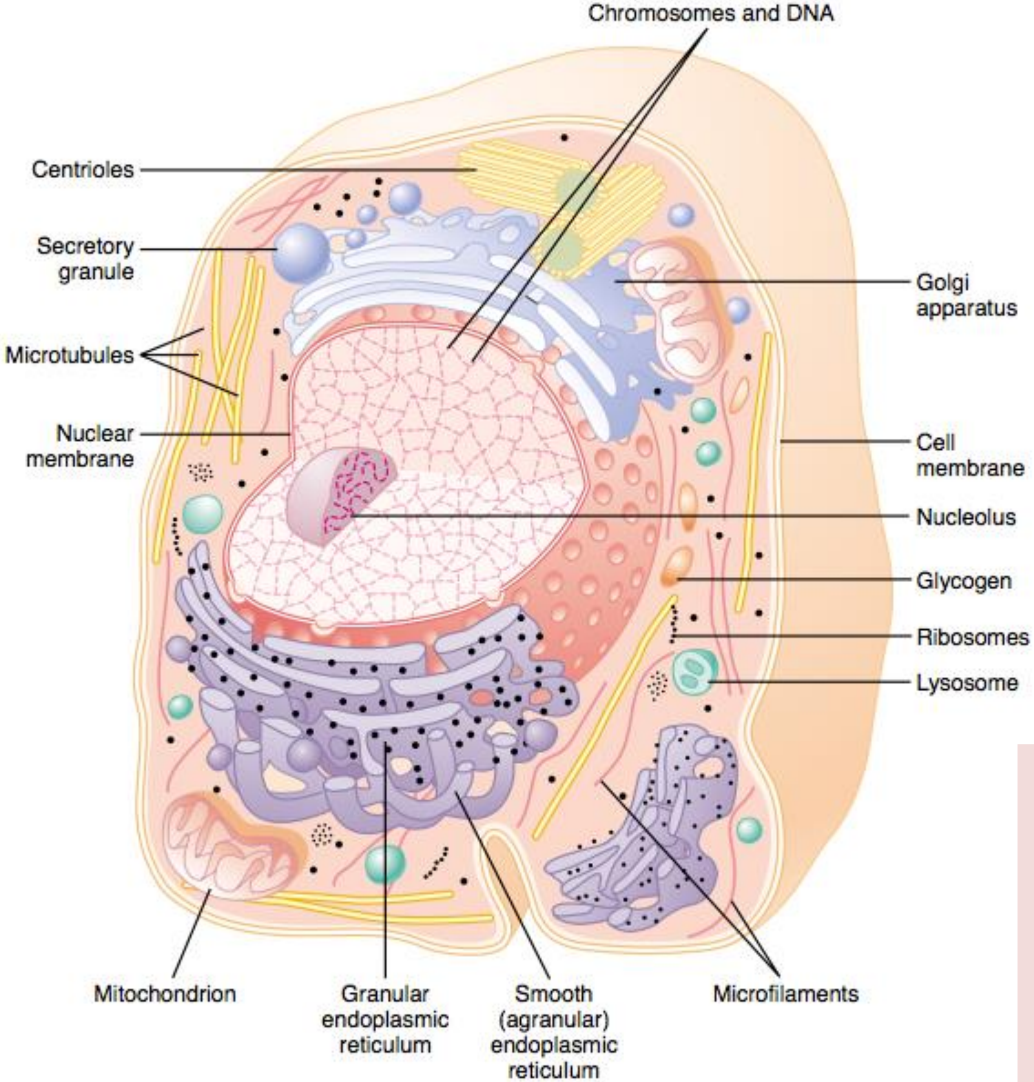


Figure 2–2

Reconstruction of a typical cell, showing the internal organelles in the cytoplasm and in the nucleus.

The cell is not merely a bag of fluid, enzymes, and chemicals; it also contains highly organized physical structures, called intracellular organelles.

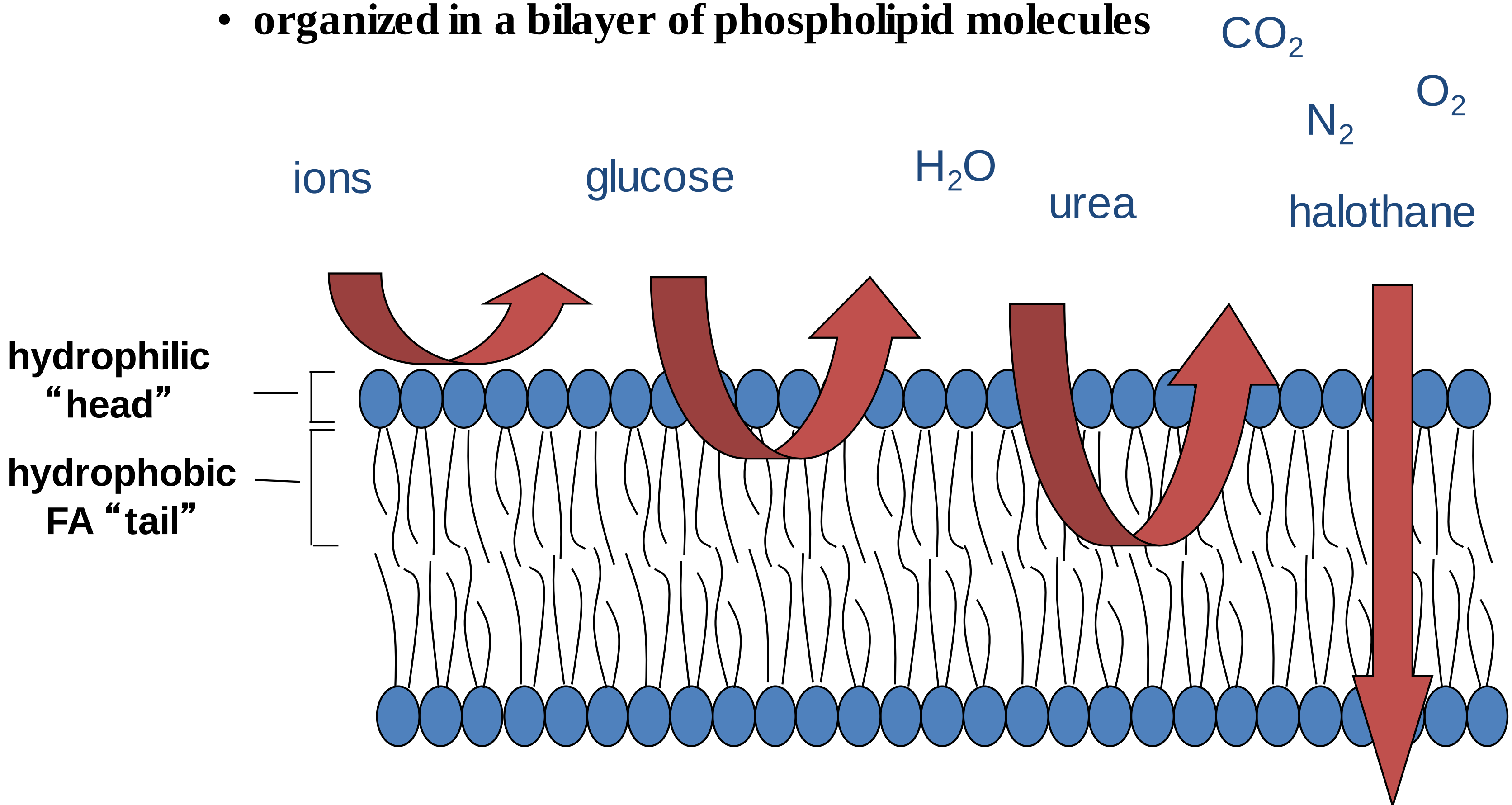
▪ Membranous Structures of the Cell

- Most organelles of the cell are covered by membranes composed primarily of lipids and proteins. These membranes include *the cell membrane, nuclear membrane, membrane of the endoplasmic reticulum, and membranes of the mitochondria, lysosomes, and Golgi apparatus.*

Membrane Components:

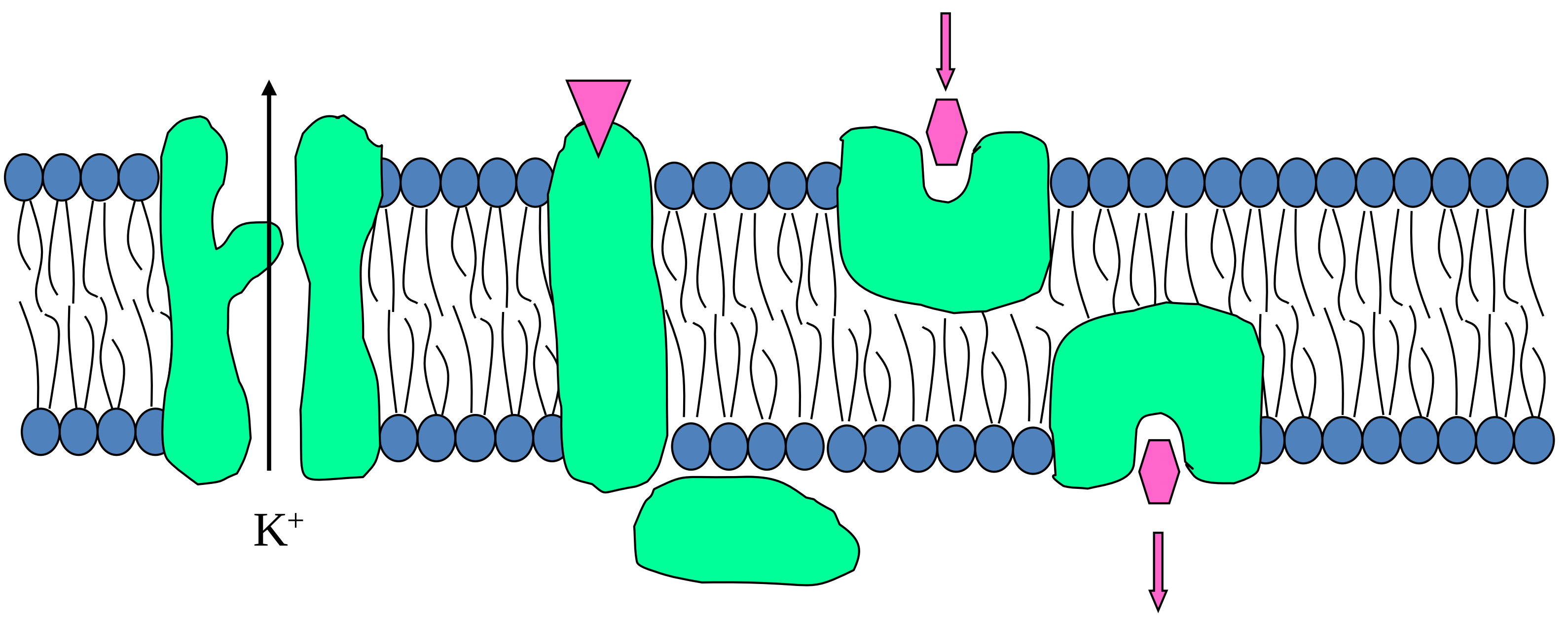
Lipids:

- ~42% of membrane
- barrier to water and water-soluble substances
- organized in a bilayer of phospholipid molecules



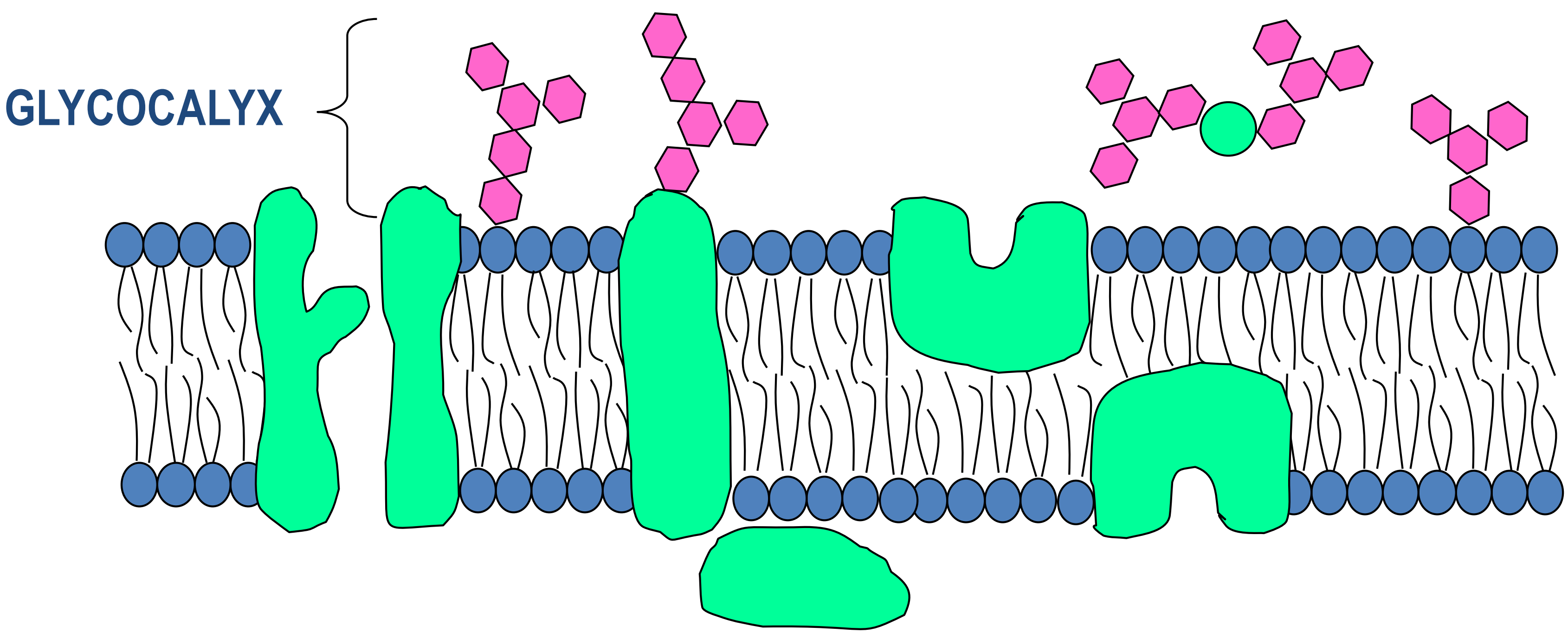
Proteins:

- ~55% of membrane
- provide "specificity" to a membrane
- defined by mode of association with the lipid bilayer
  - <u>integral</u>: protrude all the way through the membrane (channels, pores, carriers, enzymes, etc.)
  - <u>peripheral</u>: attached only to one surface of the membrane and do not penetrate all the way through (enzymes, intracellular signal mediators)



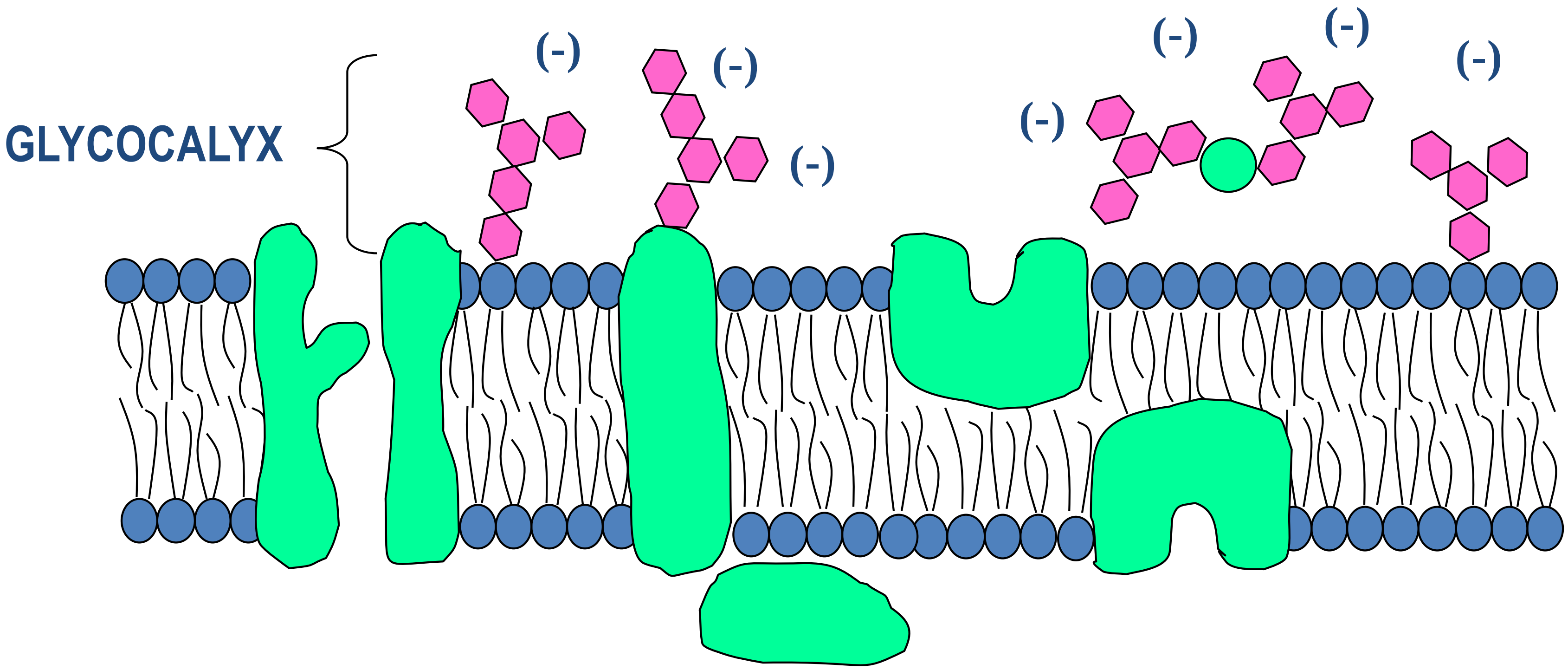
Carbohydrates:

- ~3% of membrane
- glycolipids (approx. 10% of membrane lipids)
- glycoproteins (majority of integral proteins)
- proteoglycans: mainly carbohydrate substances are loosely attached to the outer surface of the cell, and the entire outside surface of the cell often has a loose carbohydrate coat called the ***glycocalyx***.



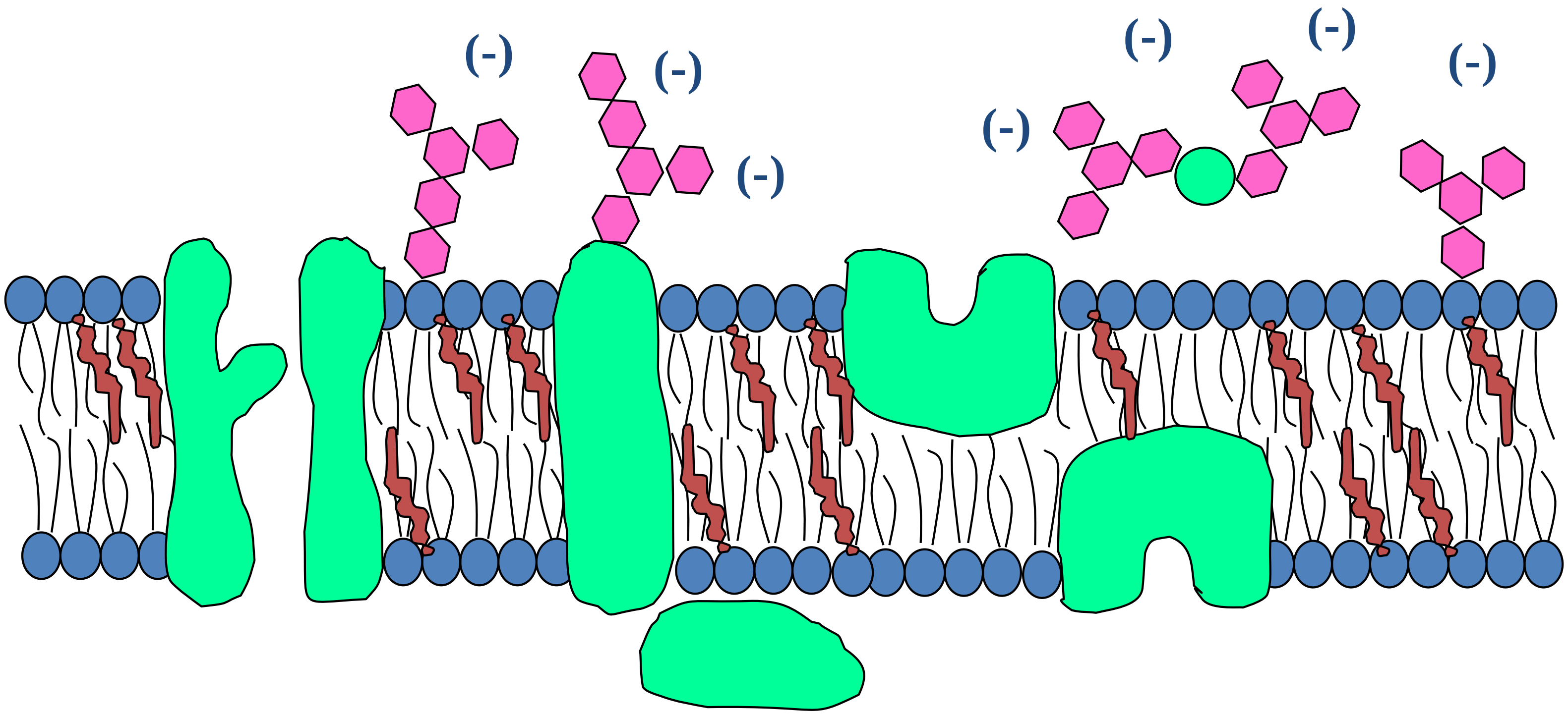
Carbohydrates (Cont.):

- negative charge of the carbo chains repels other negative charges
- The glycocalyx of some cells attaches to the glycocalyx of other cells, thus attaching cells to one another.
- act as receptor substances for binding hormones, such as insulin
- play a role in immune reactions



Cholesterol:

- present in membranes in varying amounts
- generally decreases membrane FLUIDITY and PERMEABILITY
- increases membrane FLEXIBILITY and STABILITY



▪ Cytoplasm and Its Organelles

➢ Endoplasmic Reticulum

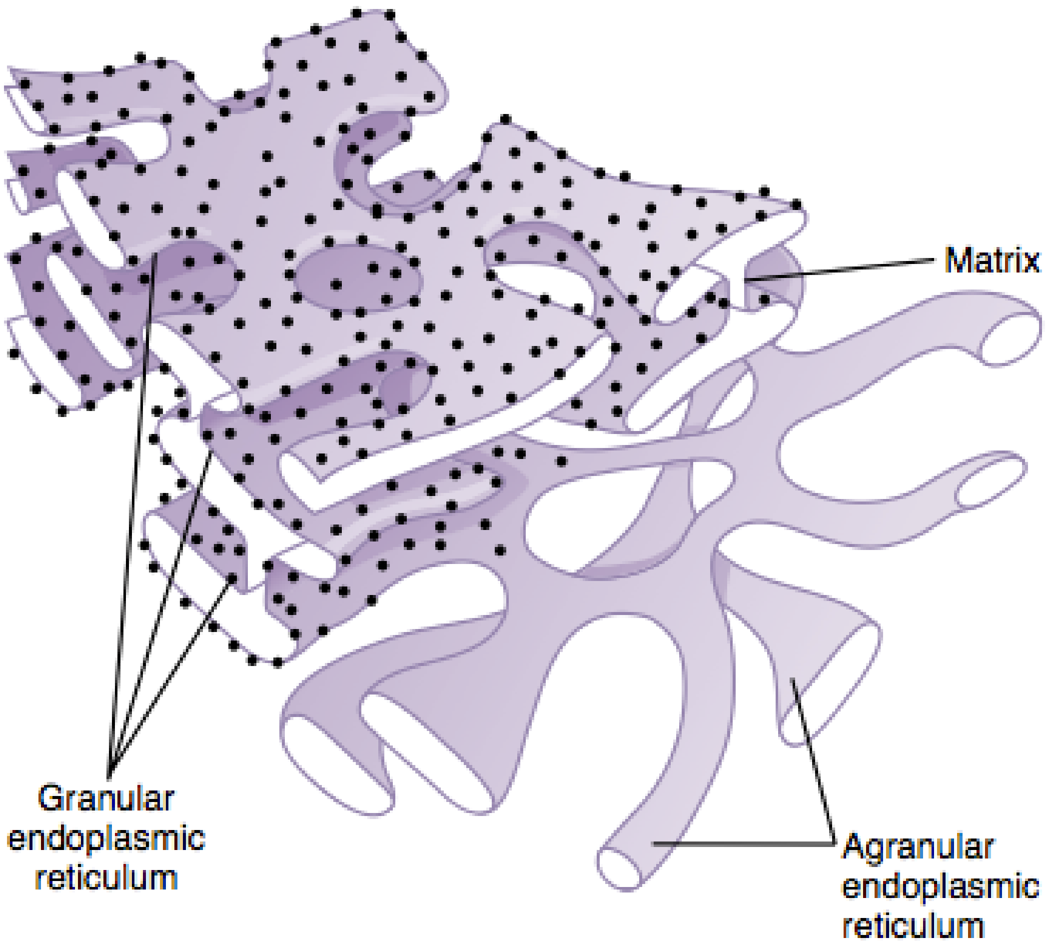
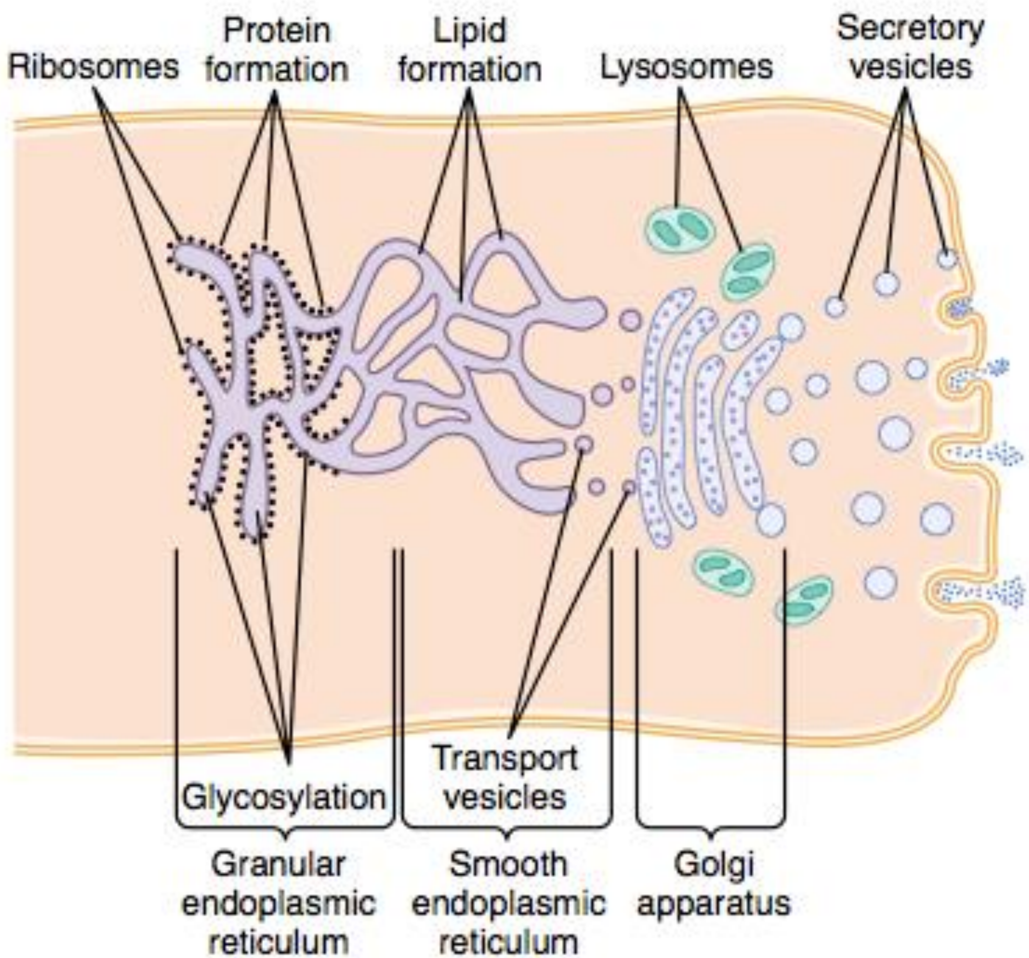


Figure 2–4

Structure of the endoplasmic reticulum. (Modified from DeRobertis EDP, Saez FA, DeRobertis EMF: Cell Biology, 6th ed. Philadelphia: WB Saunders, 1975.)

- Network of tubular and flat vesicular structures
- Space inside the tubules is called the endoplasmic matrix

➢ Ribosomes and the Granular Endoplasmic Reticulum.



- If outer surfaces of many parts of the endoplasmic is covered with ribosomes, the reticulum is called the granular endoplasmic reticulum.
- The *ribosomes* are composed of a mixture of RNA and proteins, and they function to synthesize new protein molecules in the cell.
- If the part of the endoplasmic reticulum has no attached ribosomes, this part is called the agranular, or smooth, endoplasmic reticulum.
- The agranular reticulum functions for the synthesis of lipid substances

➢ Golgi Apparatus

- Membrane composition similar to that of the smooth ER and plasma membrane
- Composed of 4 or more stacked layers of flat vesicular structures

- Receives transport vesicles from smooth ER
- Substances formed in the ER are "processed"
  - phosphorylated
  - glycosylated

- substances are concentrated, sorted and packaged for secretion.

➢ **secretory vesicles** containing proteins synthesized in the RER bud from the Golgi apparatus

- fuse with plasma membrane to release contents
  - constitutive secretion - happens randomly
  - stimulated secretion - requires trigger

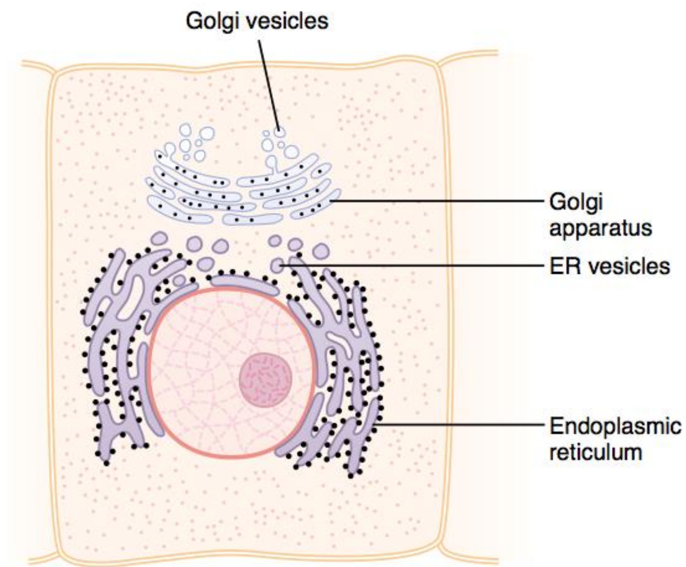
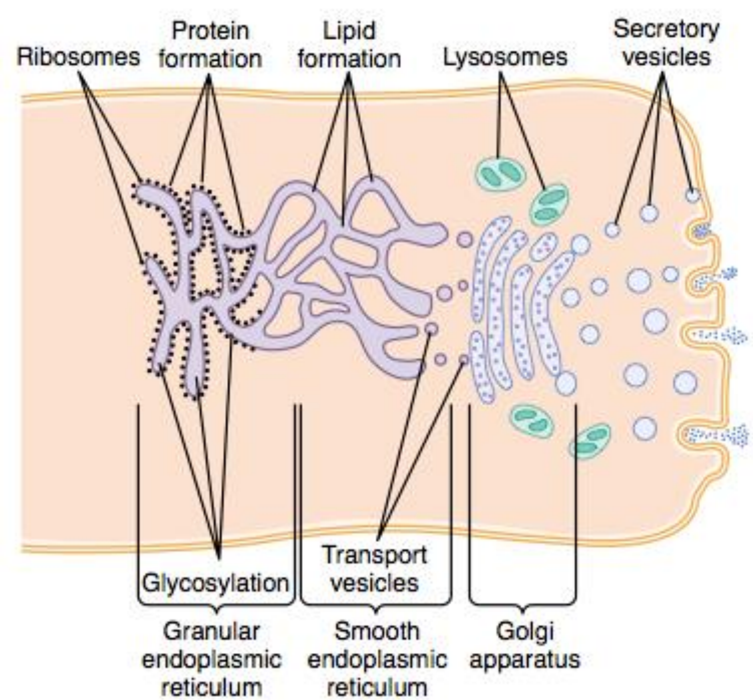


Figure 2–5

A typical Golgi apparatus and its relationship to the endoplasmic reticulum (ER) and the nucleus.



➢ Lysosomes

- vesicular organelle formed from budding Golgi

- contain hydrolytic enzymes (acid hydrolases)
  - phosphatases
  - nucleases
  - proteases
  - lipid-degrading enzymes
  - lysozymes digest bacteria

- fuse with pinocytotic or phagocytotic vesicles to form digestive vesicles

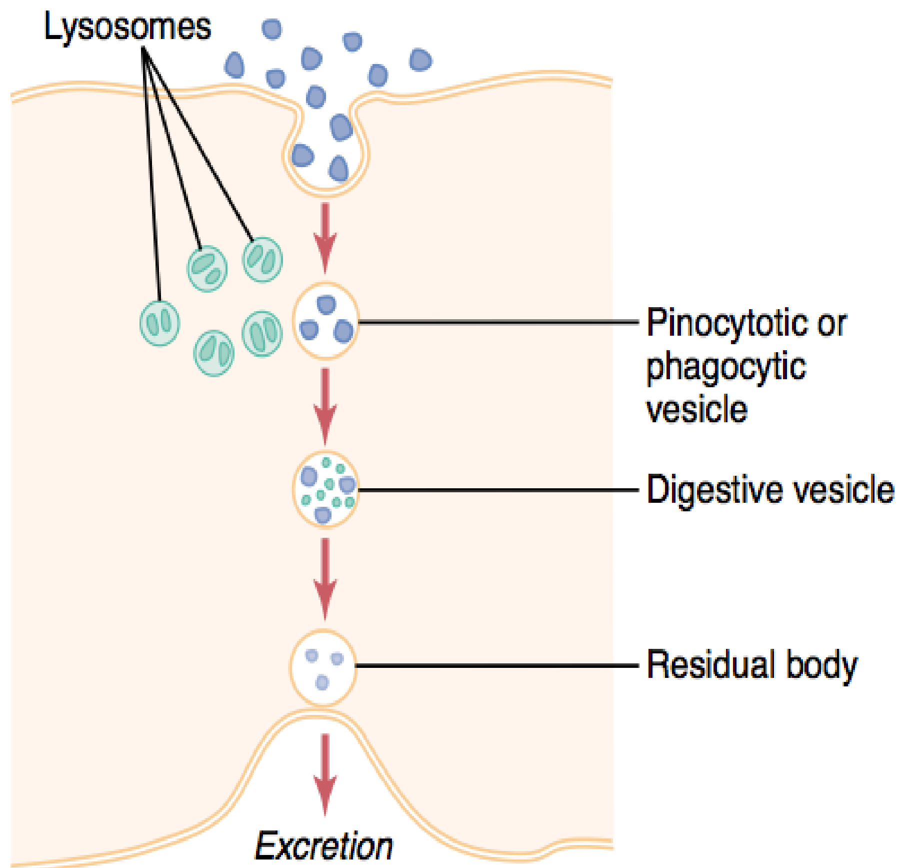


Figure 2–12

Digestion of substances in pinocytotic or phagocytic vesicles by enzymes derived from lysosomes.

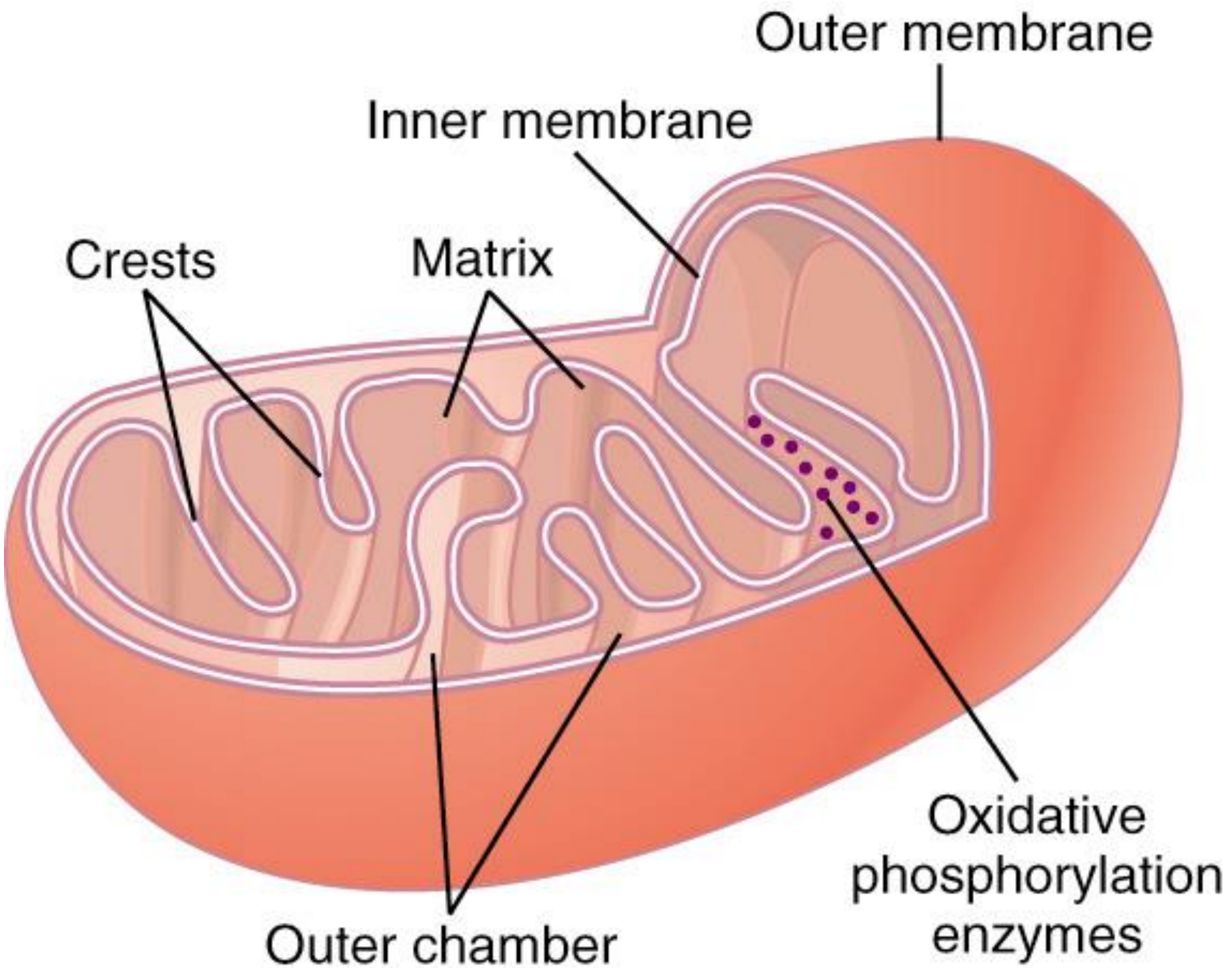
➢ Peroxisomes

- similar physically to lysosomes
- most commonly found in eukaryotic cells.
- two major differences:
  - formed by self-replication
  - they contain oxidases

Function: oxidize substances (e.g. alcohol) that may be otherwise poisonous

➢ Mitochondria

<u>**Primary function**</u>**: extraction of energy from nutrients**



ATP production

Step 1.

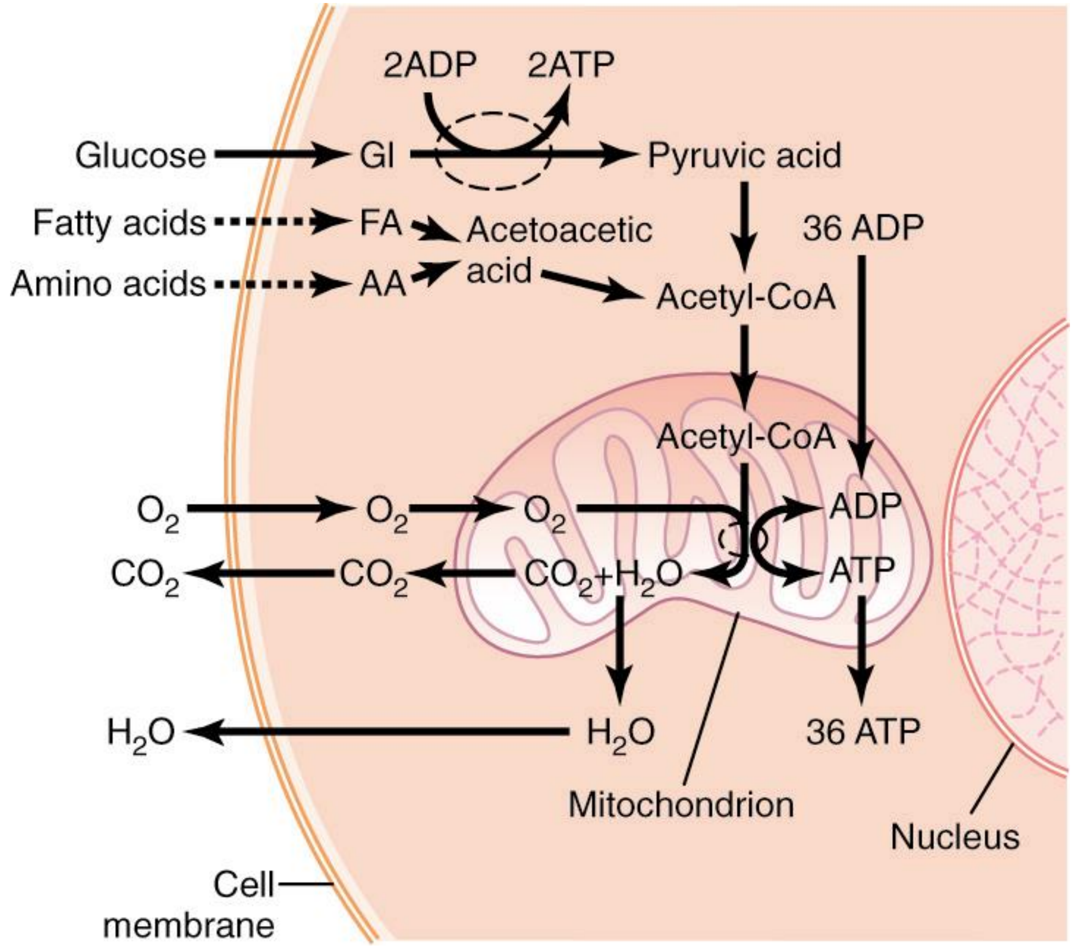
- **Carbohydrates are converted into glucose**
- **Proteins are converted into amino acids**
- **Fats are converted into fatty acids**

Step 2.

- **Glucose, AA, and FA are processed into AcetylCoA**

Step 3.

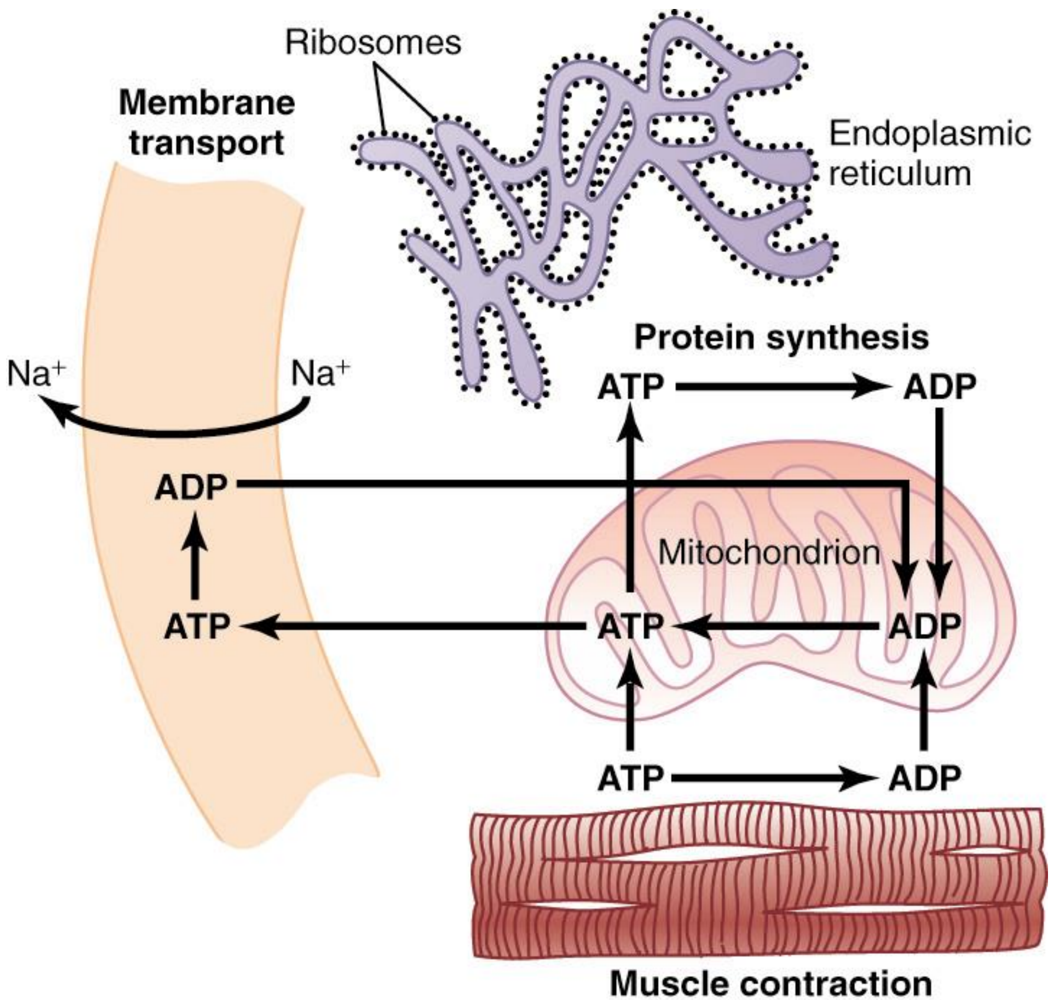
- **AcetylCoA reacts with O_2 to produce ATP**



A maximum of 38 molecules of ATP are formed per molecule of glucose degraded.

The Use of ATP for Cellular Function

1. Membrane transport
2. Synthesis of chemical compounds
3. Mechanical work



- # Nucleus

- The nucleus is the control center of the cell. Briefly, the nucleus contains large quantities of DNA, which are the genes. The genes determine the characteristics of the cell's proteins, including the structural proteins, as well as the intracellular enzymes that control cytoplasmic and nuclear activities.

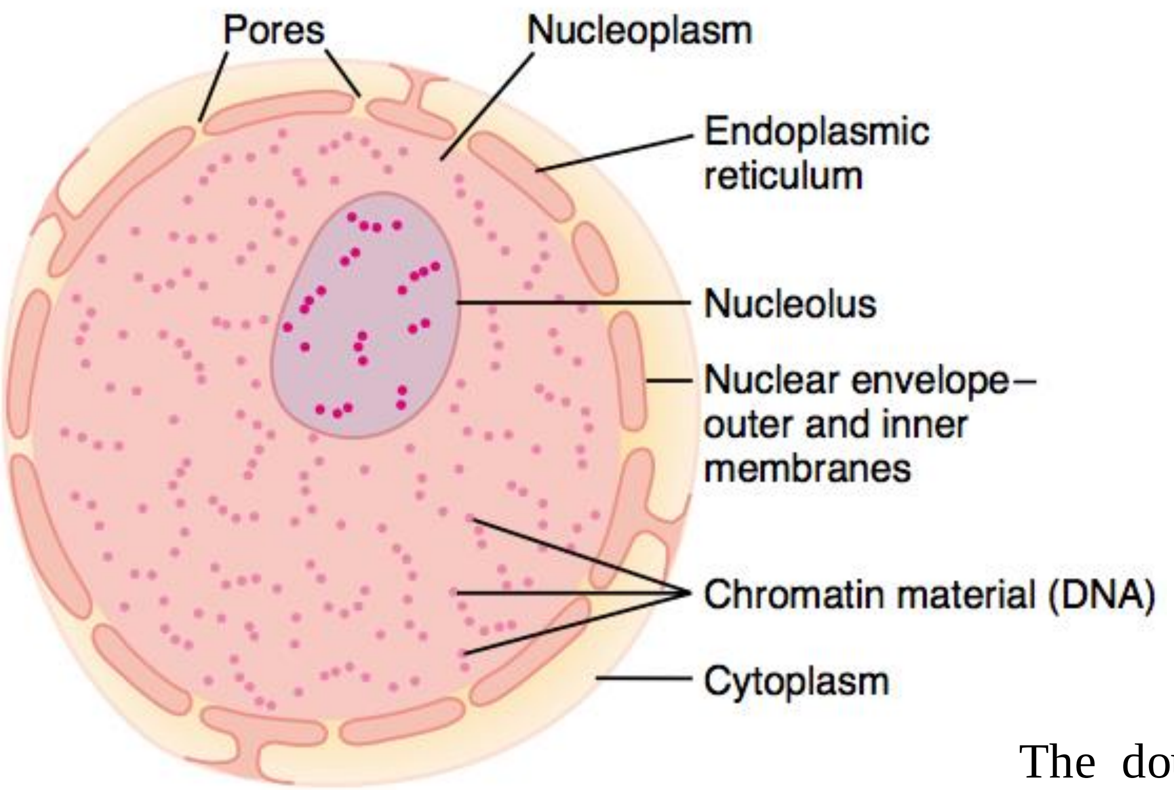


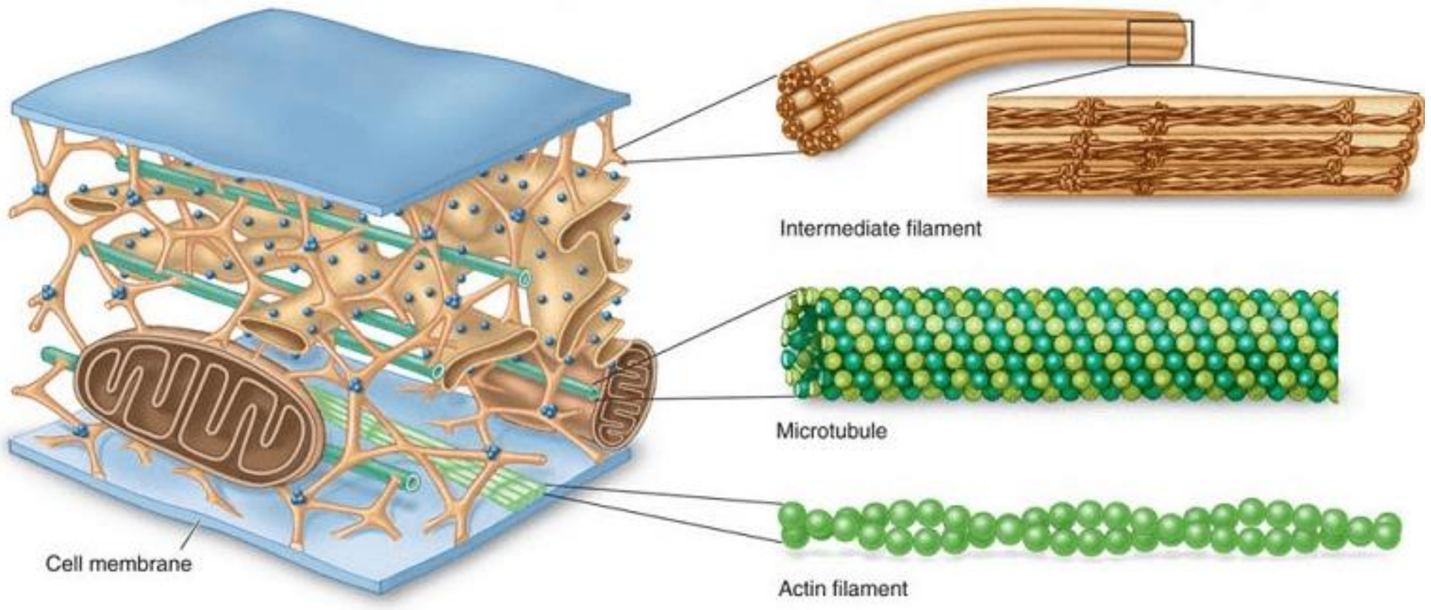
Figure 2–9

Structure of the nucleus.

The double **nuclear membrane** and matrix are contiguous with the endoplasmic reticulum

The Cytoskeleton

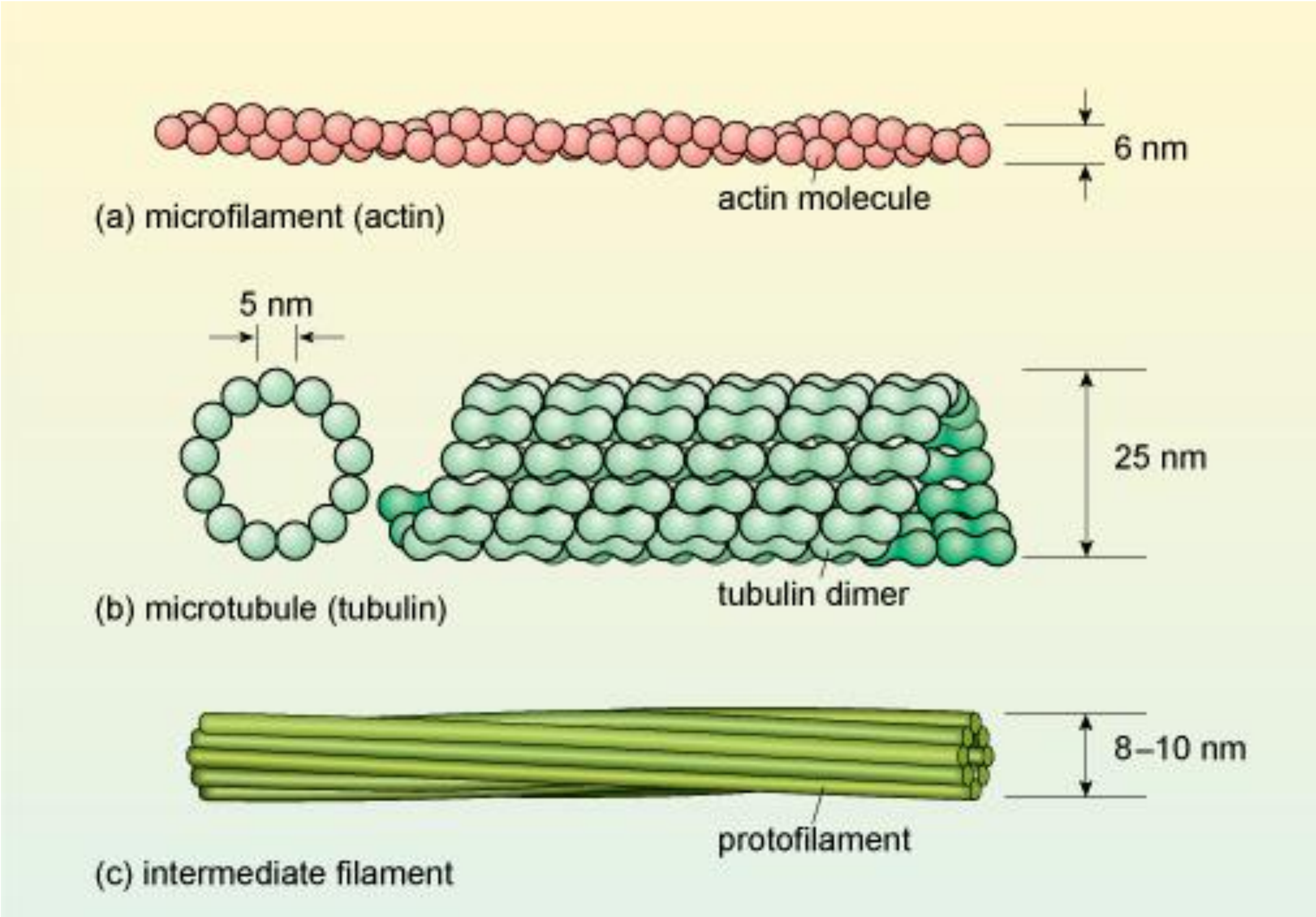
Cytoskeleton, a system of filaments or fibers that is present in the cytoplasm of eukaryotic cells.



Intermediate Filaments

Microtubules

Microfilaments


6 nm
actin molecule
(a) microfilament (actin)
5 nm
25 nm
tubulin dimer
(b) microtubule (tubulin)
8–10 nm
protofilament
(c) intermediate filament

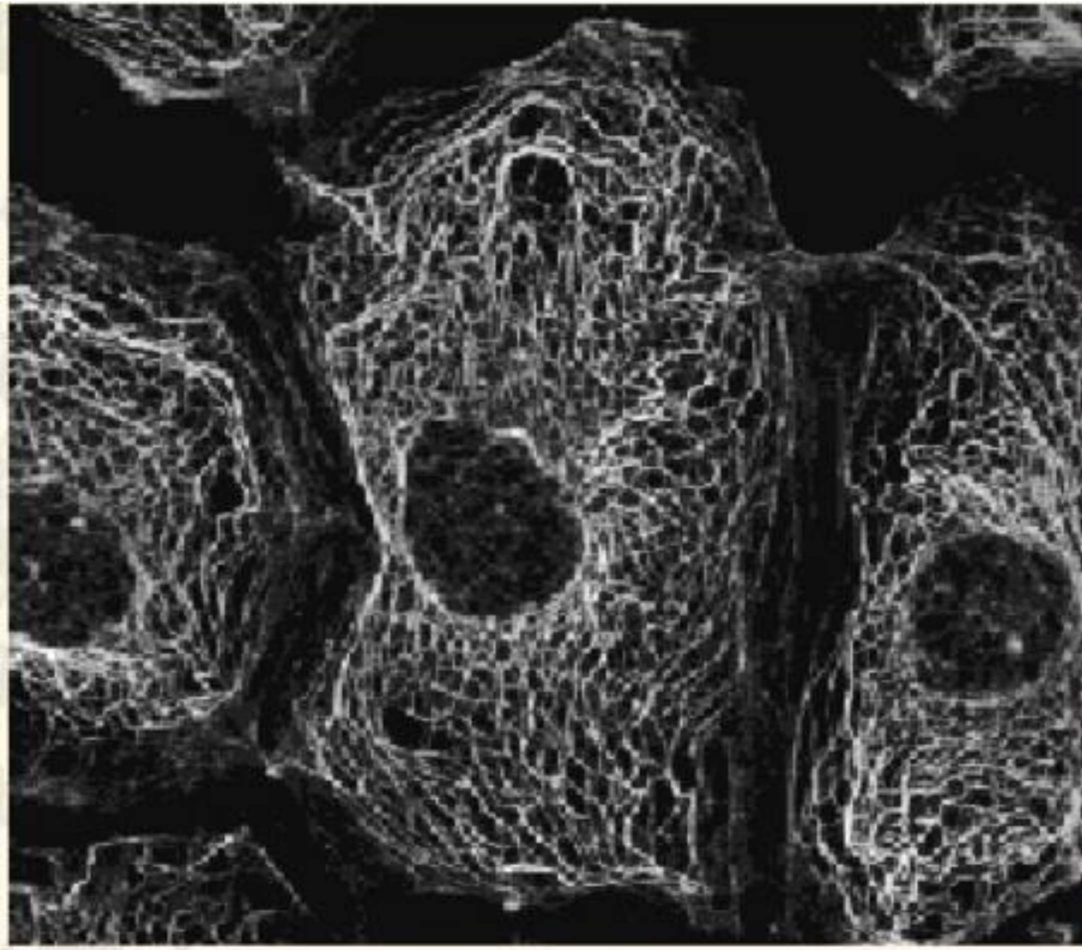
- **Microflaments**

Important in cell contraction and cell movement.

Actin fibres in a cell stained with a fluorescent strain specific for actin

- **Intermediate Filaments**

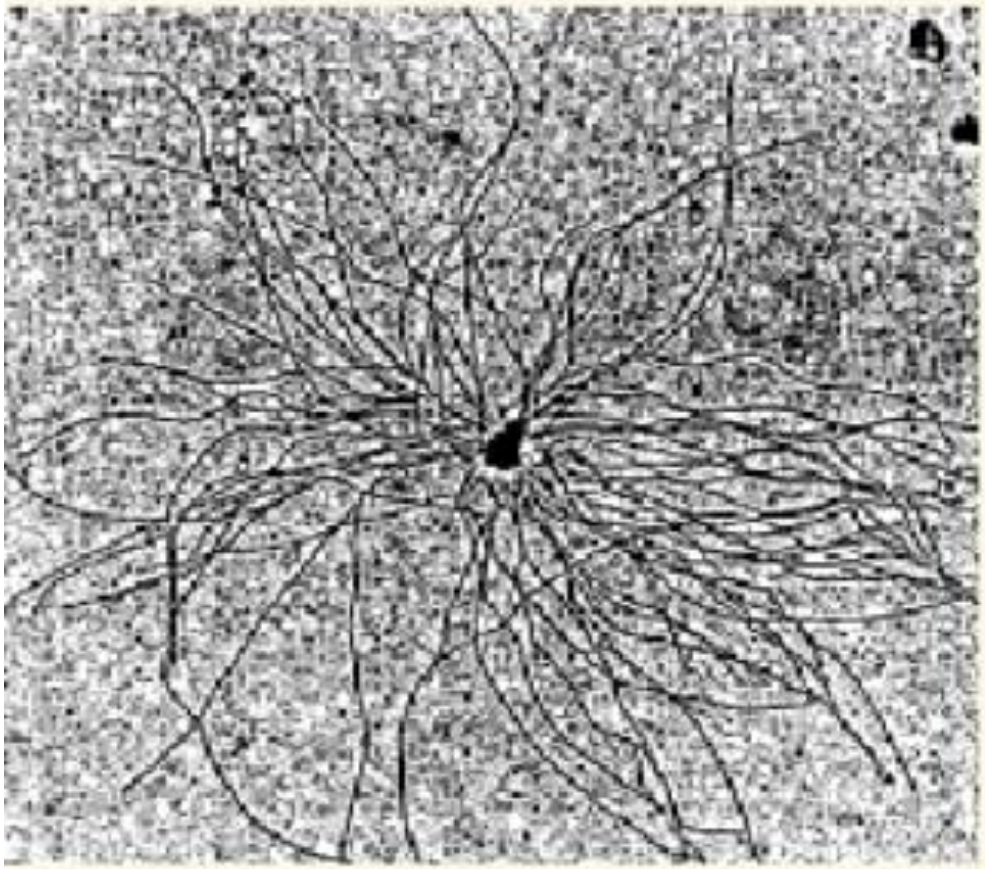
Provide mechanical strenght to cells



The nucleus in epithelial cells is held within the cell by a basketlike network of intermediate filaments made of keratins which have been stained here using a fluorescent stain

- **Microtubules**

▪ Microtubules only form around a centrosome (organising centre)
▪ The centrosome provides a "nucleus" from which the microtubule form. These are important in cell division as part of the spindle fibre network and can move components with the cell

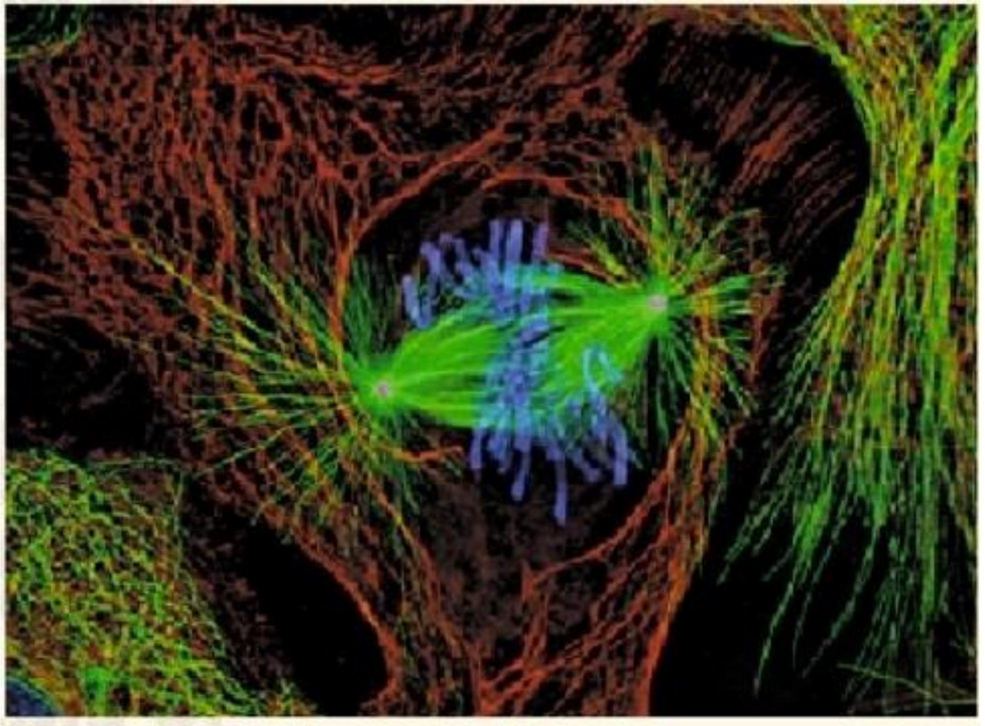


Microtubules growing in vitro from an isolated centrosome

- **Functions**

- All these components give mechanical support and shape to the cell.

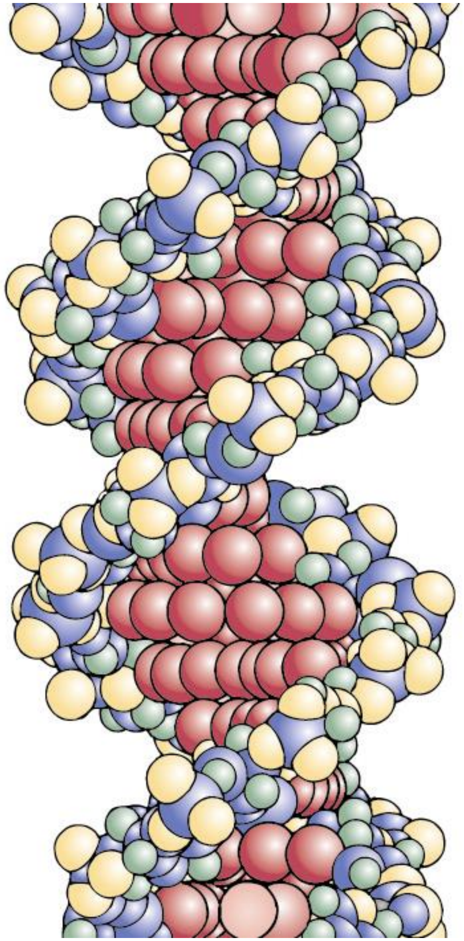
- Primary importance of the cytoskeleton is in cell mobility. Cytoskeleton extends throughout the cytoplasm and determines the internal movement of cell organelles as well as cell locomotion and muscle fiber contraction.



Chapter 3:

Genetic Control of Protein Synthesis, Cell Function, and Cell Reproduction

Central Dogma of Molecular Biology



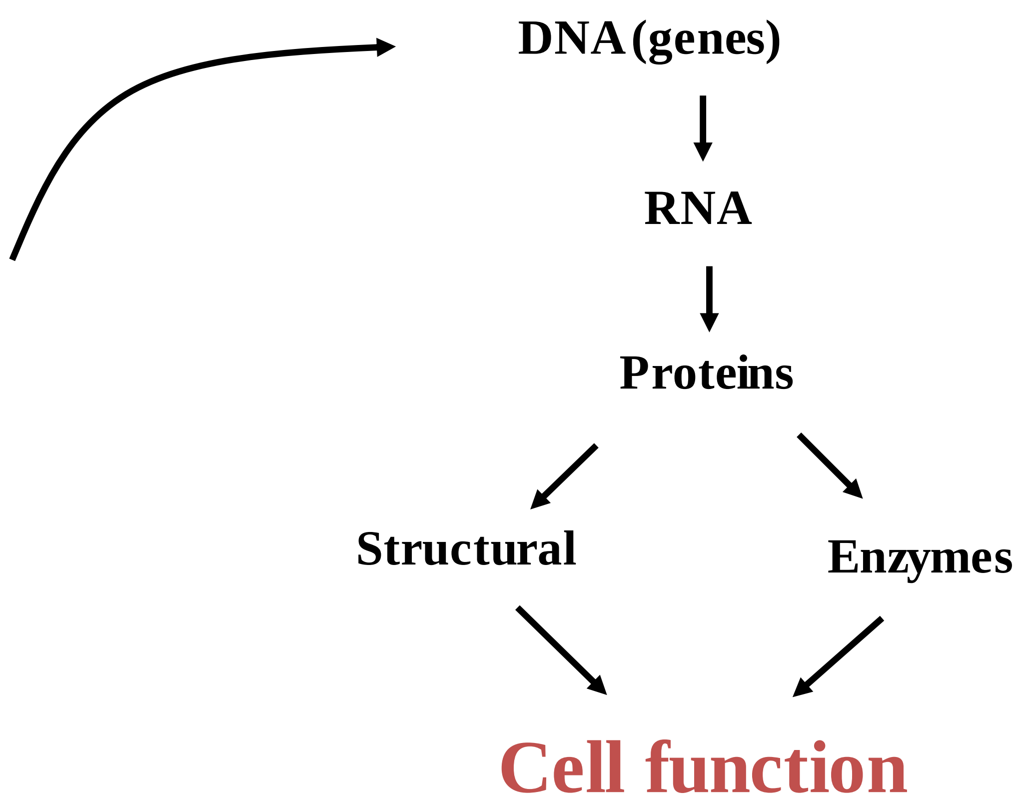


Figure 3-2 The helical, double-stranded structure of the gene. The outside strands are composed of phosphoric acid and the sugar deoxyribose. The internal molecules connecting the two strands of the helix are purine and pyrimidine bases; these determine the "code" of the gene.

➢ Transcription:

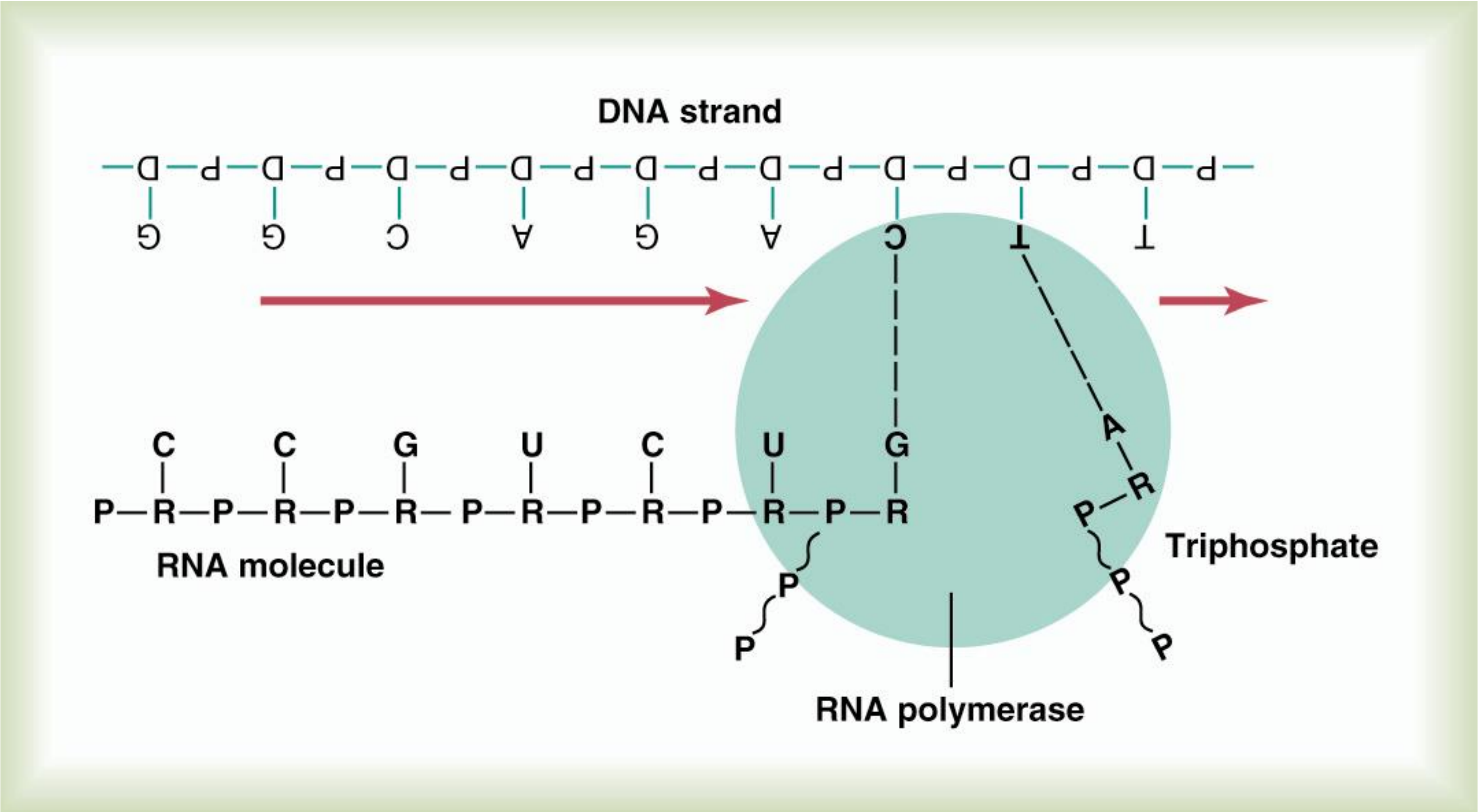


Figure 3-7 Combination of ribose nucleotides with a strand of DNA to form a molecule of RNA that carries the genetic code from the gene to the cytoplasm. The RNA polymerase enzyme moves along the DNA strand and builds the RNA molecule.

Overview

① RNA polymerase binds to the promoter sequence.

② The RNA polymerase temporarily "unwinds" the DNA double helix.

③ The polymerase "reads" the DNA strand and adds complementary RNA molecules to the DNA template.

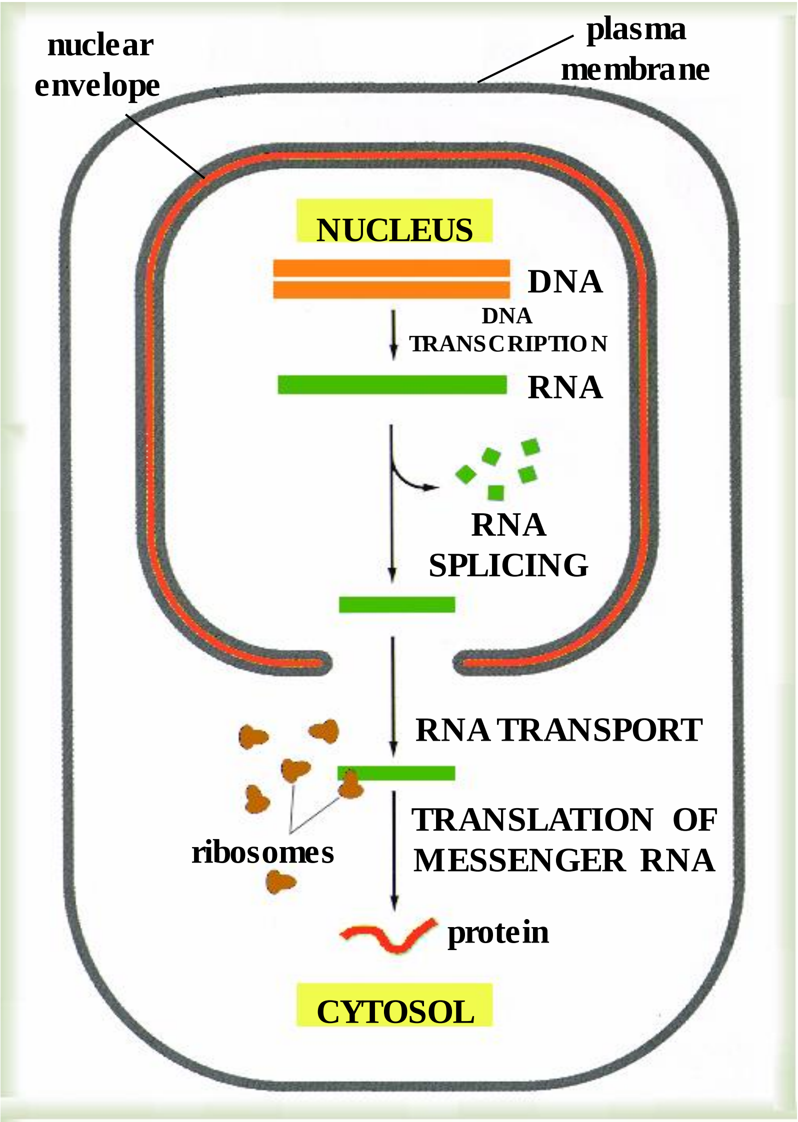
④ "Activated" RNA molecules react with the growing end of the RNA strand and are added (3' end).

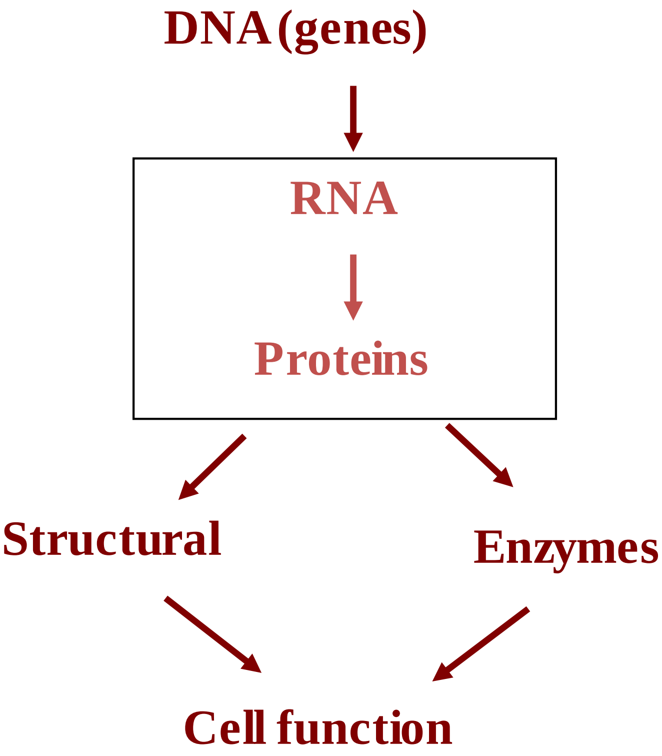
⑤ Transcription ends when the RNA polymerase reaches a chain terminating sequence, releasing both the polymerase and the RNA strand.

Messenger RNA:

- complementary in sequence to the DNA coding strand
- 100's to 1000's of nucleotides per strand
- organized in codons - triplet bases
    - each codon "codes" for one amino acid (AA)
    - each AA - except met- is coded for by multiple codons
    - start codon: AUG (specific for met)
    - stop codons: UAA, UAG, UGA

➢ The Process of Translation





Transfer RNA

- acts as a carrier molecule during protein synthesis
- each transfer RNA (tRNA) combines with one AA
- each tRNA recognizes a specific codon by way of a complementary anticodon on the tRNA molecule

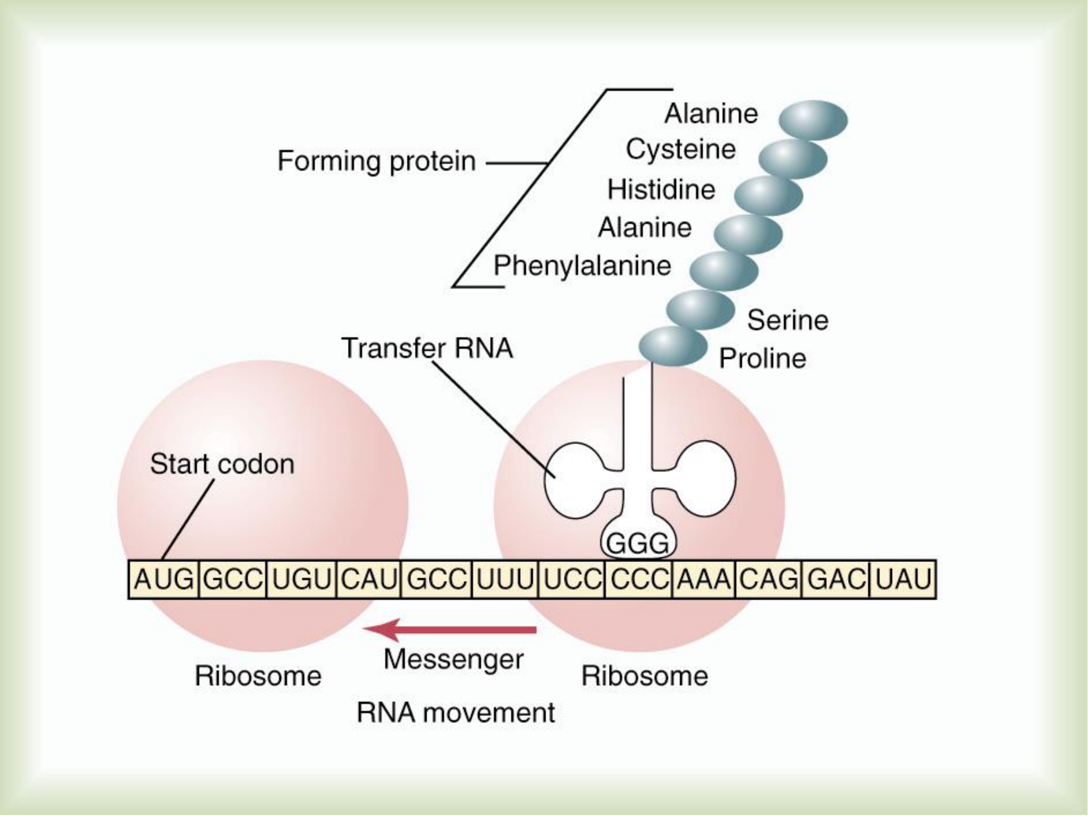


Figure 3-9 A messenger RNA strand is moving through two ribosomes. As each "codon" passes through, an amino acid is added to the growing protein chain, which is shown in the right-hand ribosome. The transfer RNA molecule transports each specific amino acid to the newly forming protein.

Ribosomes

Polyribosomes: multiple ribosomes can simultaneously translate a single mRNA

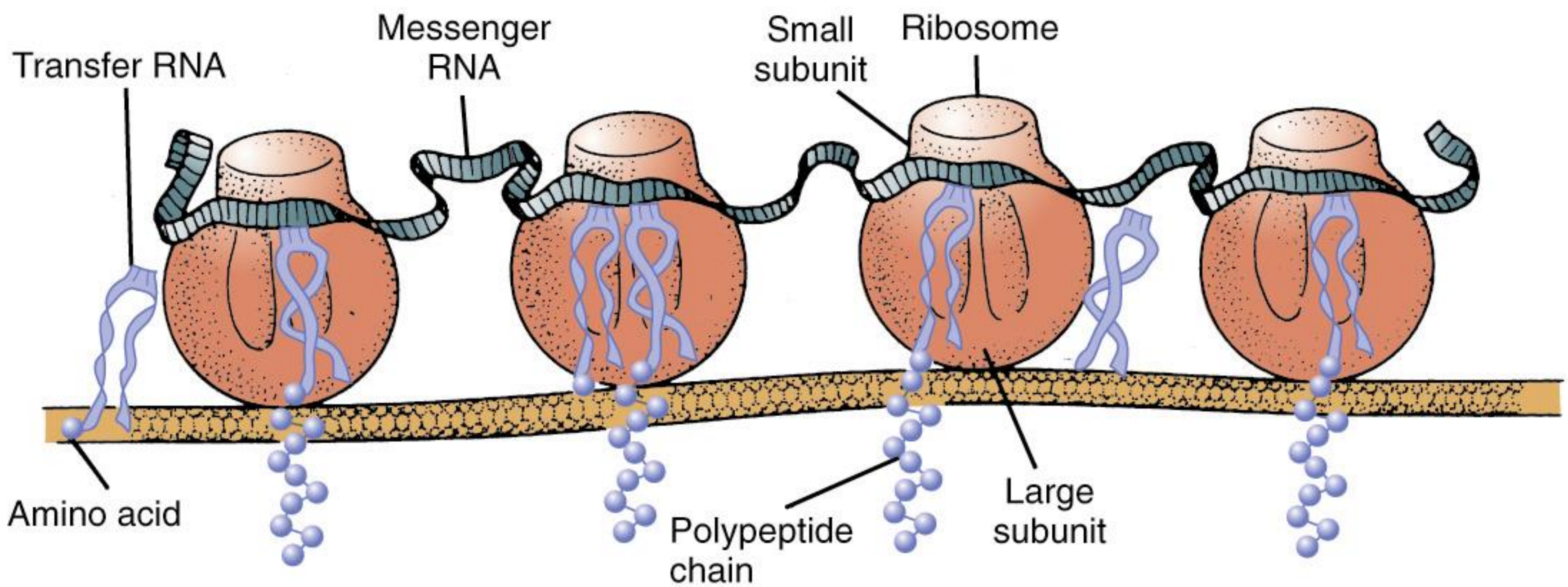


Figure 3-10 Physical structure of the ribosomes, as well as their functional relation to messenger RNA, transfer RNA, and the endoplasmic reticulum during the formation of protein molecules. (Courtesy of Dr. Don W. Fawcett, Montana.)

Overview :Protein Formation

Phase 1: Initiation

- small ribosomal subunit and initiator tRNA (Met) complex binds to 5’ end of an mRNA chain

- this complex moves along mRNA molecule until it encounters a start codon (AUG)

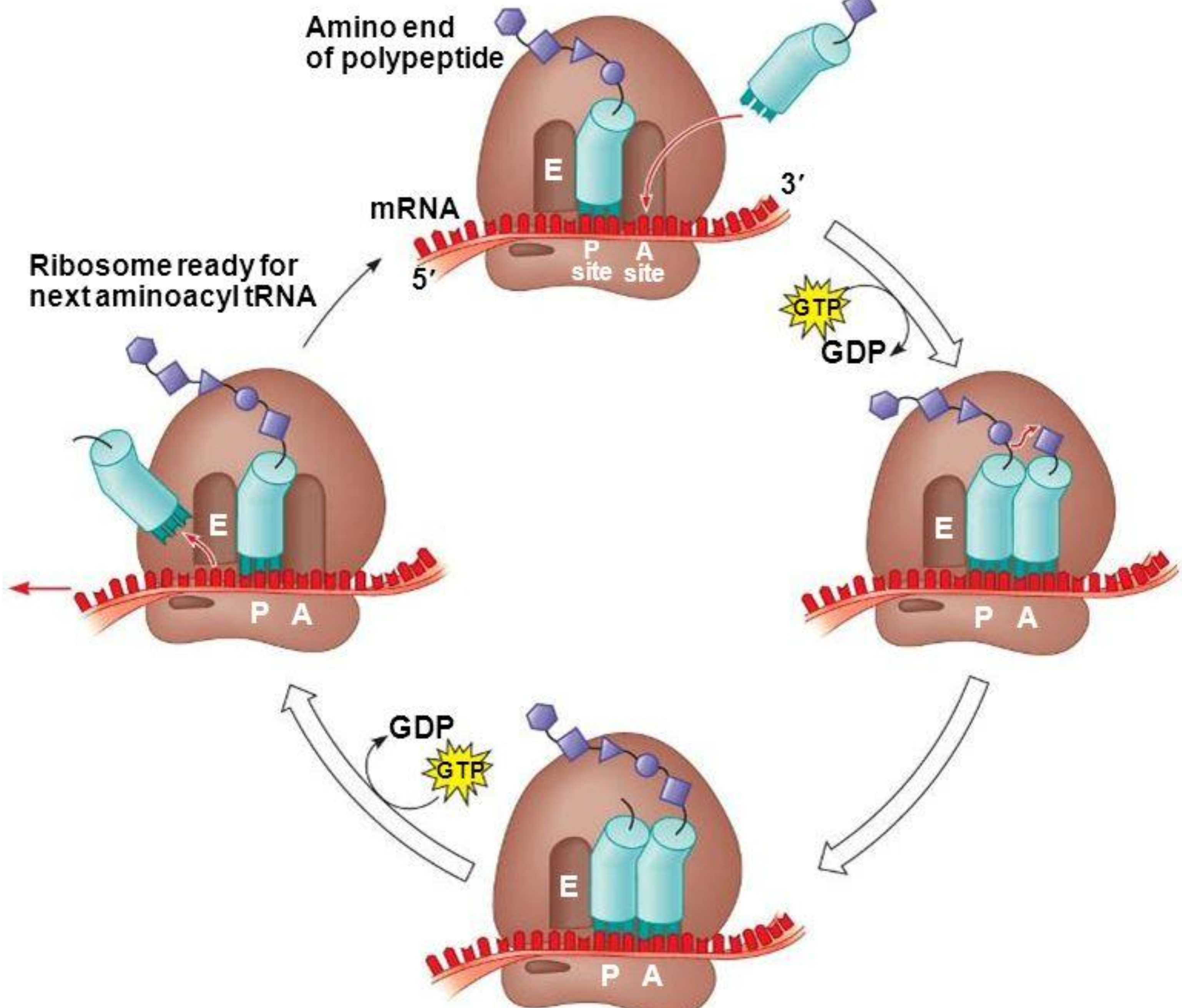
- initiation factors dissociate and large ribosomal subunit binds

Overview :Protein Formation

Phase 2: Elongation

- AA-tRNA binds to the ribosomal A-site
- peptidyl transferase joins the tRNA at the P-site to the AA linked to the tRNA at the A-site with a peptide bond
- the new peptidyl-tRNA is translocated from the A-site to the P-site

Fig. 17-18-4



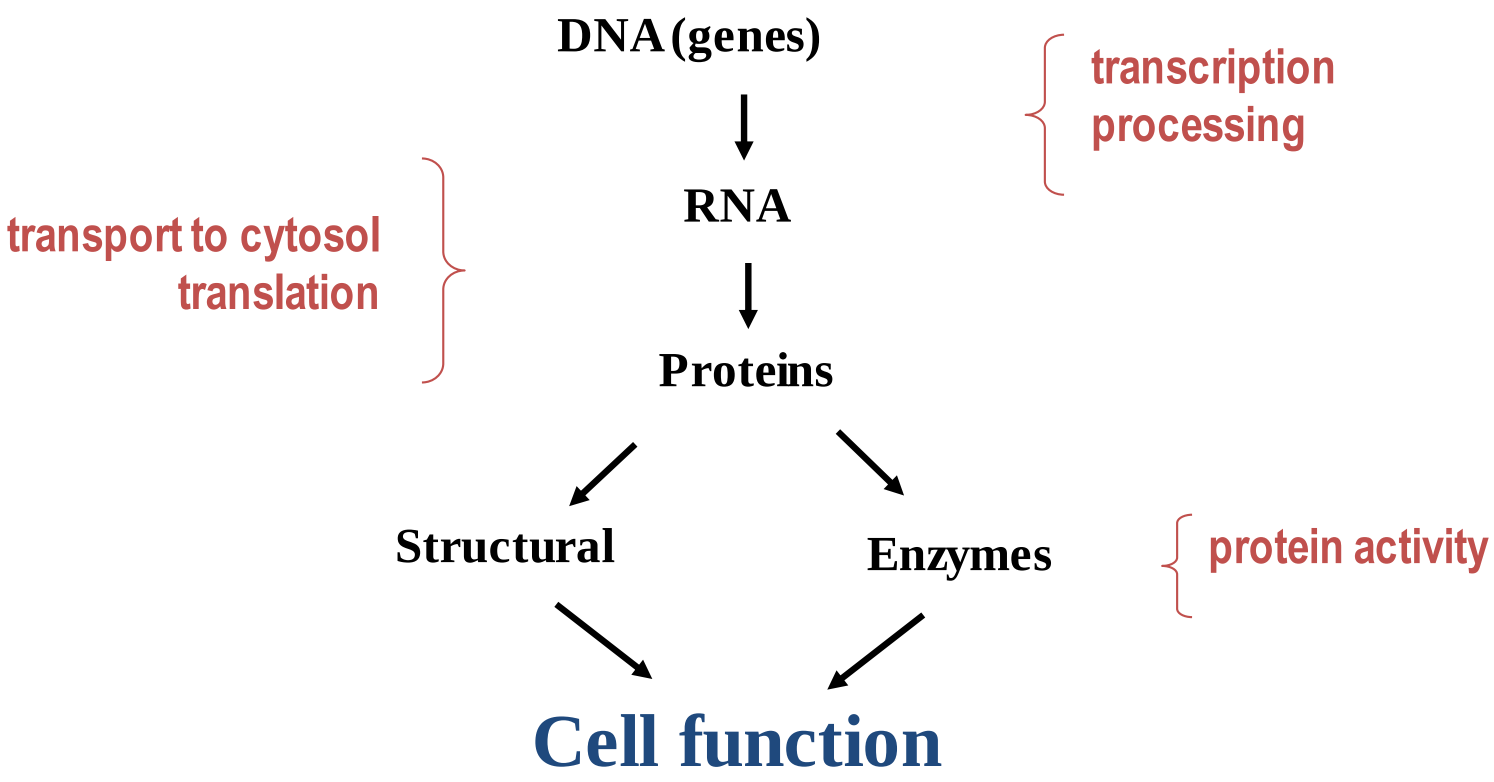
Amino end
of polypeptide
mRNA
3′
5′
E
P
site
A
site
GTP
GDP
E
P
A
E
P
A
GDP
GTP
Ribosome ready for
next aminoacyl tRNA
E
P
A

Overview :Protein Formation

Phase 3: Termination

- Release factor binds to the stop codon.
- Completed polypeptide is released.
- Ribosome dissociates into its 2 subunits.

Control of Genetic Function and Biochemical Activity



➢ Transcriptional Control:

The Operon: a prokaryote model

- series of genes and their shared regulatory elements

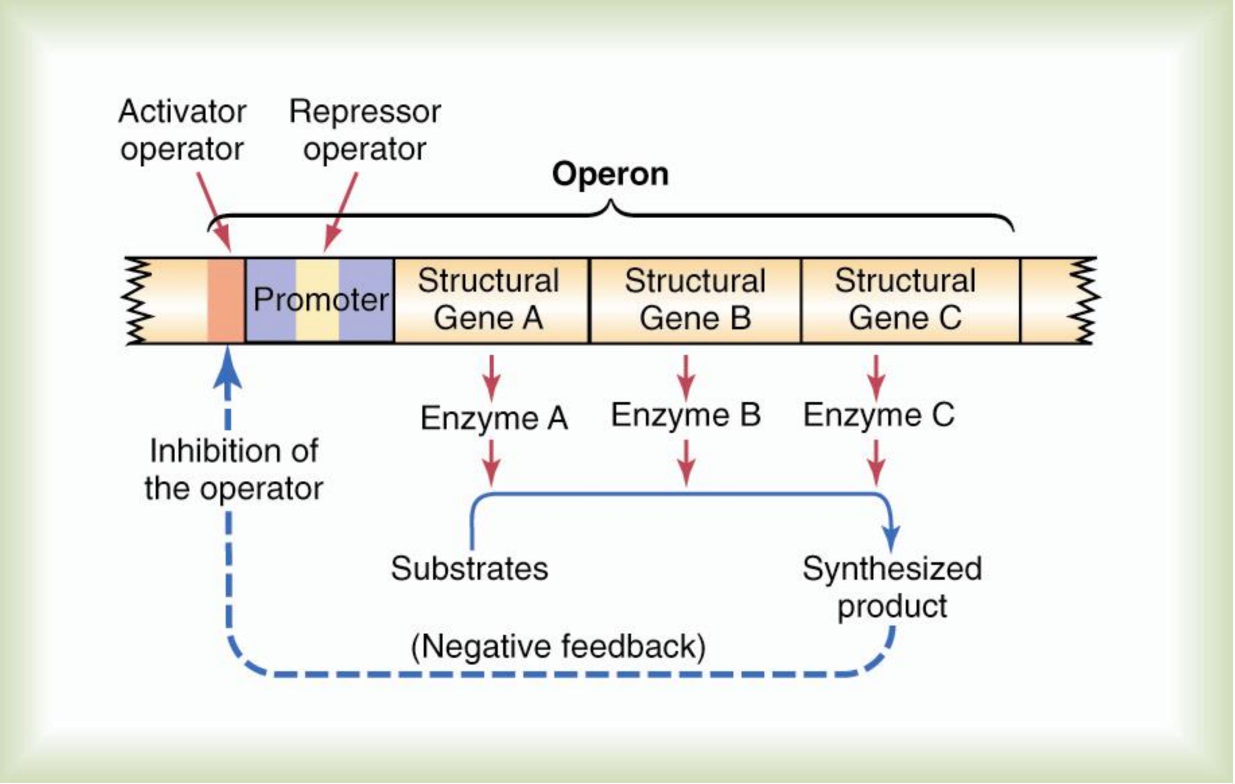


Figure 3-12 Function of an operon to control synthesis of a non protein intracellular product, such as an intracellular metabolic chemical. Note that the synthesized product exerts negative feedback to inhibit the function of the operon, in this way automatically controlling the concentration of the product itself.

Negative Regulation

- sequences called “repressor operators” bind repressor proteins

- binding interferes with the ability of the RNA polymerase to bind to the promoter

NO TRANSCRIPTION

Positive Regulation

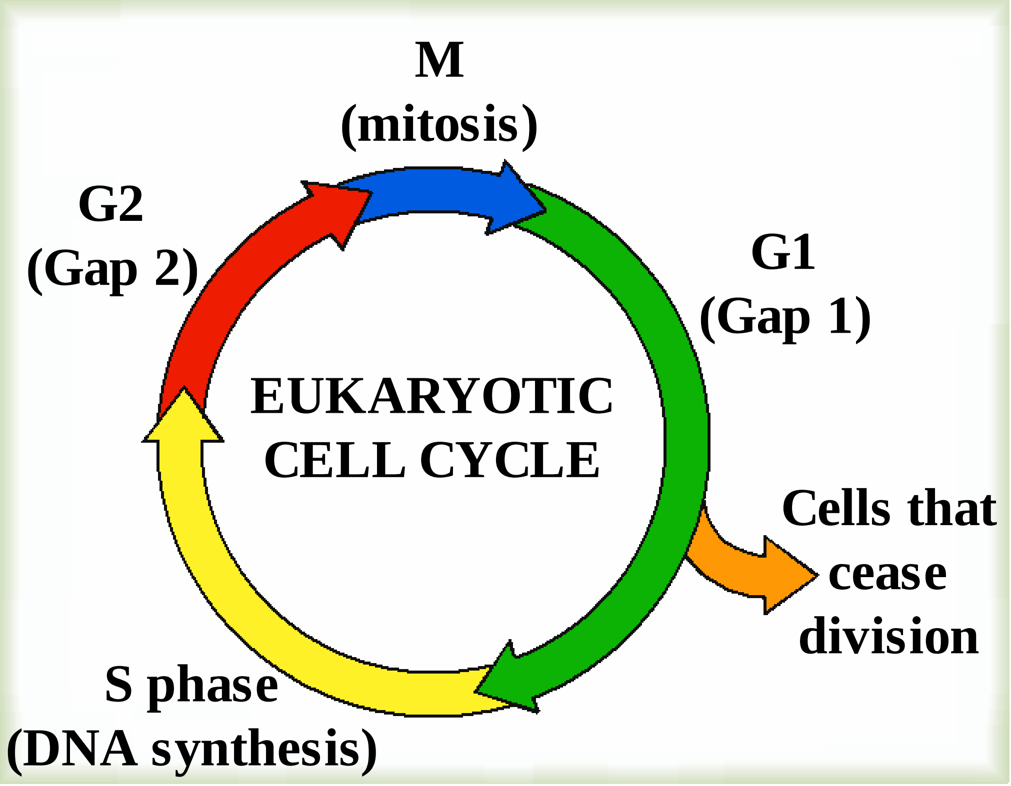
- so-called "activator operators" bind activator proteins

- binding facilitates the association of the RNA polymerase with the promoter

ENHANCED TRANSCRIPTION

Genetic Control of Cell Reproduction

Life Cycle of the Cell:



M phase:

- cytokinesis

Interphase (>95%):

- G_1 phase (Growth)
- S phase (DNA synthesis)
- G_2 phase (Growth and preperation for mitosis)

DNA Repair, “Proofreading,” and “Mutations”

- Following replication and prior to mitosis, DNA polymerase “proofreads” the “new” DNA, and cuts out mismatches
- DNA ligase replaces the mismatches with complementary nucleotides
- A “mistake” during transcription results in a mutation causing the formation of an abnormal protein
- Approximately 10 DNA mutations are passed to the next generation, however two copies of each chromosome almost always ensures the presence of a functional gene