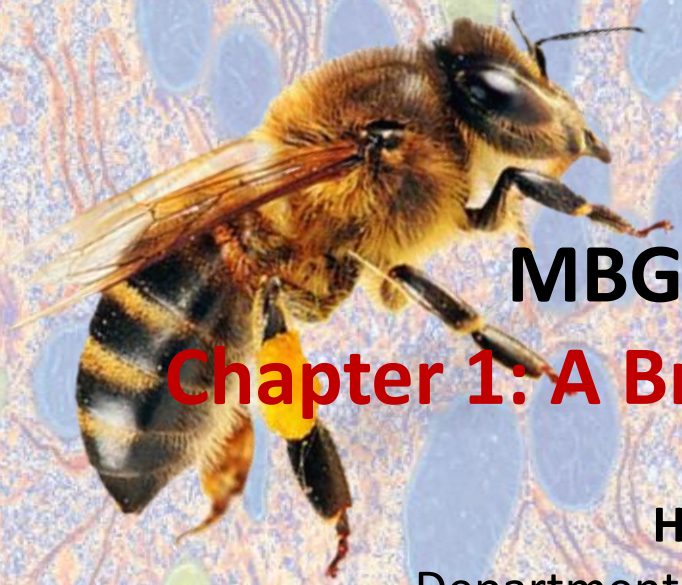


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MBG303 Biochemistry I (Lecture PPTs)

Chapter 1- A Brief History of Biochemistry
Chapter 2- Water
Chapter 3- Acid-Base Chemistry
Chapter 4- Biomolecules
Chapter 5- Carbohydrates
Chapter 6- Lipids
Chapter 7- Amino acids and Proteins
Chapter 8- Nucleic Acids
Chapter 9- Cell



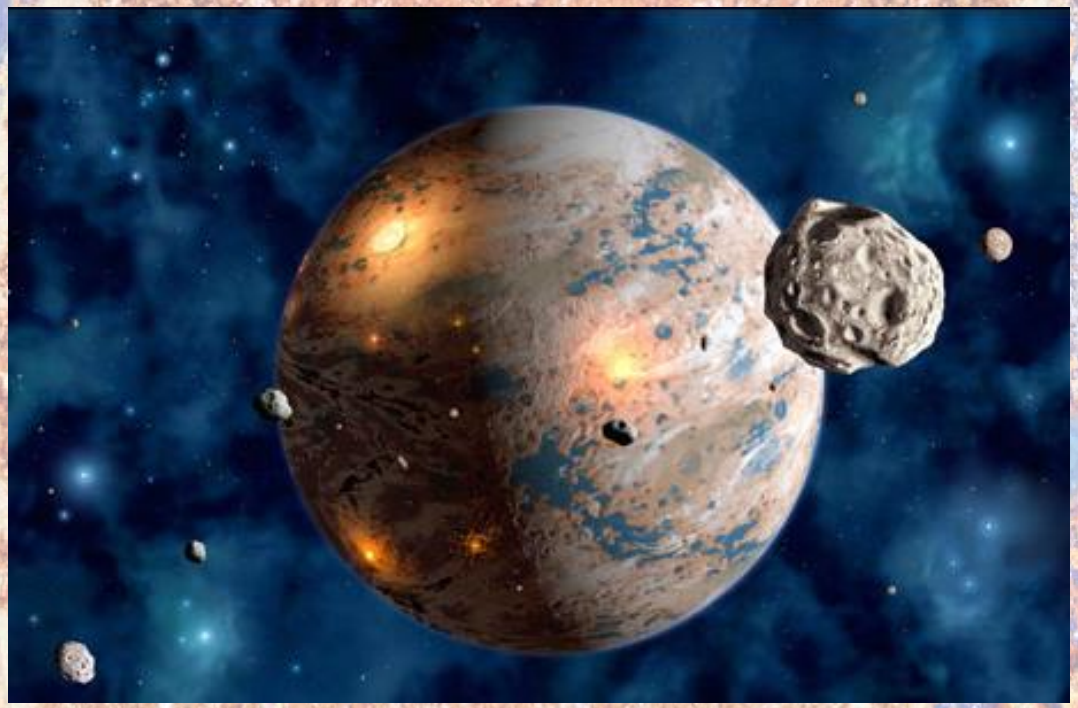
MBG303 Biochemistry

Chapter 1: A Brief History of Biochemistry

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A Brief History of Earth & Life

- Earth was formed about 5 billion years ago, when our solar system (formed 15 billion yeras ago) took shape around the sun.



A current model for the origin of life on earth: The Bubble Hypothesis

- The origin of life is still a mystery, but there are some theories that speculate how inorganic matter was transformed into the organic matter that created life.

- In 1992 it was proposed that bubbles in the sea were the key to helping create complex organic matter that eventually became life.

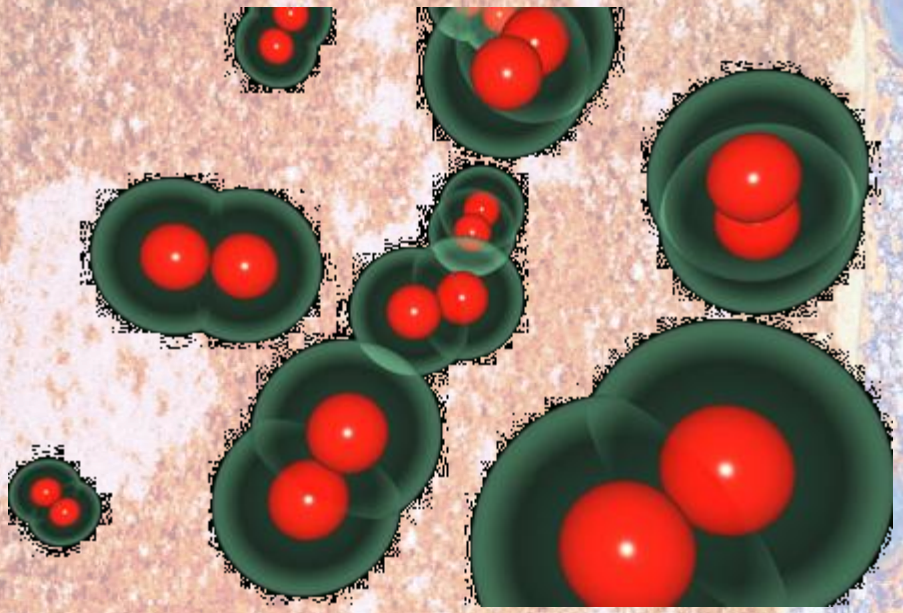
- The first cells are thought to have arisen from aggregations of molecules that were more stable and, therefore, persisted longer.

- It has been suggested that RNA may have arisen before cells and subsequently became packaged within a membrane (RNA world).

- Bacteria were the only life-forms on earth for about 1 billion years. First methane utilizers, then anaerobic photosynthesizers, and eventually O_2-forming photosynthesizers.

- Oxygen levels rise about 2.5 billion years ago, which is thought to have been created by photosynthesis by cyanobacteria living in the sea.

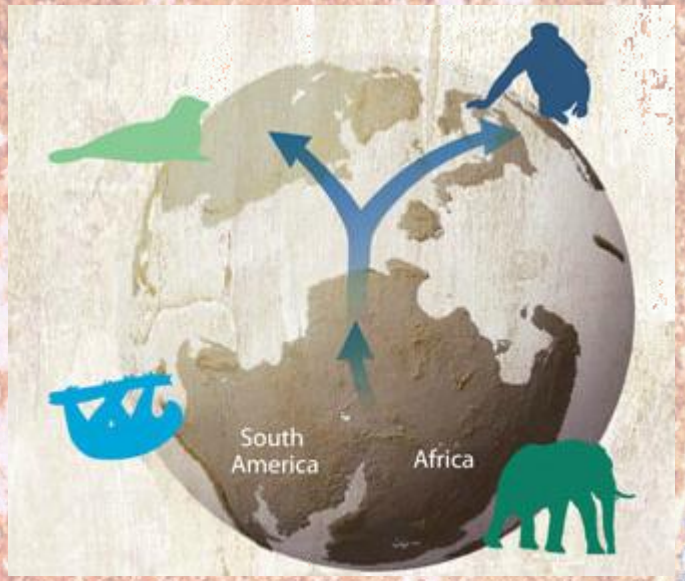
- The oxygen-rich ozone layer was also established, shielding the Earth's surface from harmful solar radiation.



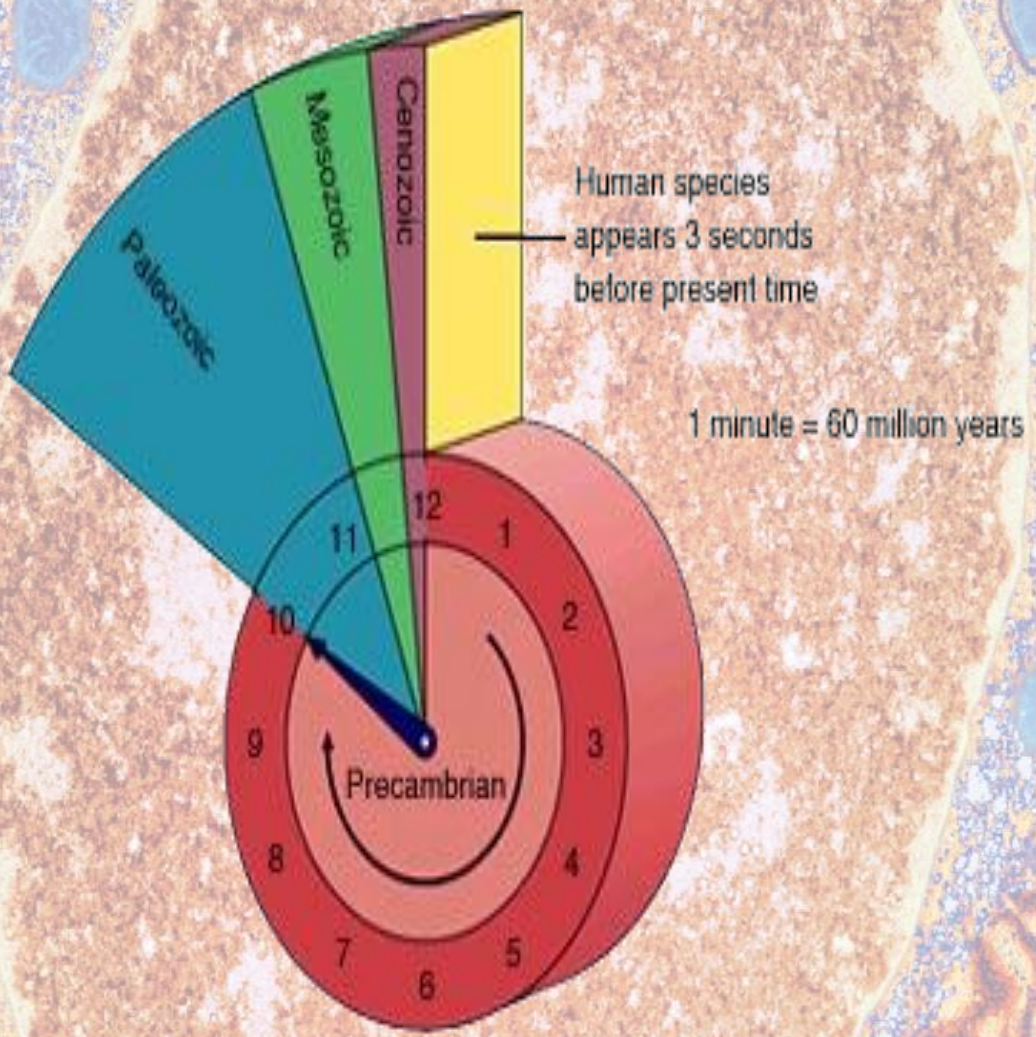
- This further provided our planet for appearence of and inhabitation by other organisms including us.

- Fossils indicate our own species, Homo sapiens, arose in eastern Africa some 190,000 years ago.

- First venturing beyond Africa about 70,000 years ago.

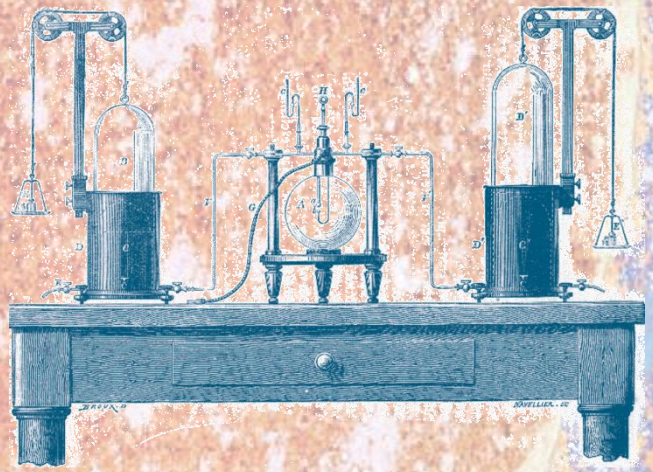


- The first eukaryotes can be seen in the fossil record about 1.5 billion years ago. All organisms other than bacteria are their descendants.



A Brief History of Biochemistry

- 1780s Antoine Lavoisier proposed that the combustion of a candle is similar to the respiration of animals, as both need O_2.

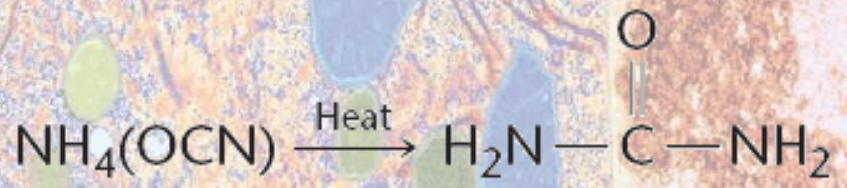


- For the first time a physiological process was explained with reference to a nonliving mechanism.

- Until the early 1800s “vitalism” was a common belief: the compounds found in living organisms (i.e., organic molecules) can only be produced by living organisms and could not be produced in the laboratory.

- Now an obsolete scientific doctrine, vitalists argued that it was the presence of a “vital force” (life force or spirit) that distinguished the living organic world from the inanimate inorganic world.

- Friedrich Wöhler disproved this belief (i.e., vitalism) in 1828 by synthesizing **urea**, an organic molecule and a waste product of animal metabolism, from ammonium cyanate, an inorganic molecule obtained from mineral (i.e., nonliving) sources.



- Many science historians this in vitro synthesis of urea by Wöhler as the starting point of Biochemistry.



▲ **Friedrich Wöhler (1800–1882).** Wöhler was one of the founders of biochemistry. By synthesizing urea, Wöhler showed that compounds found in living organisms could be made in the laboratory from inorganic substances.

- However, many consider Eduard Buchner's first demonstration of alcoholic **fermentation** in 1893 in cell-free yeast extracts as the starting point for the birth of biochemistry.

- This was another blow to the vitalistic thinking, showing that the presence of living yeast cells were not needed for fermentation. Previously, scientists believed that only living cells could catalyze such complex biological reactions.

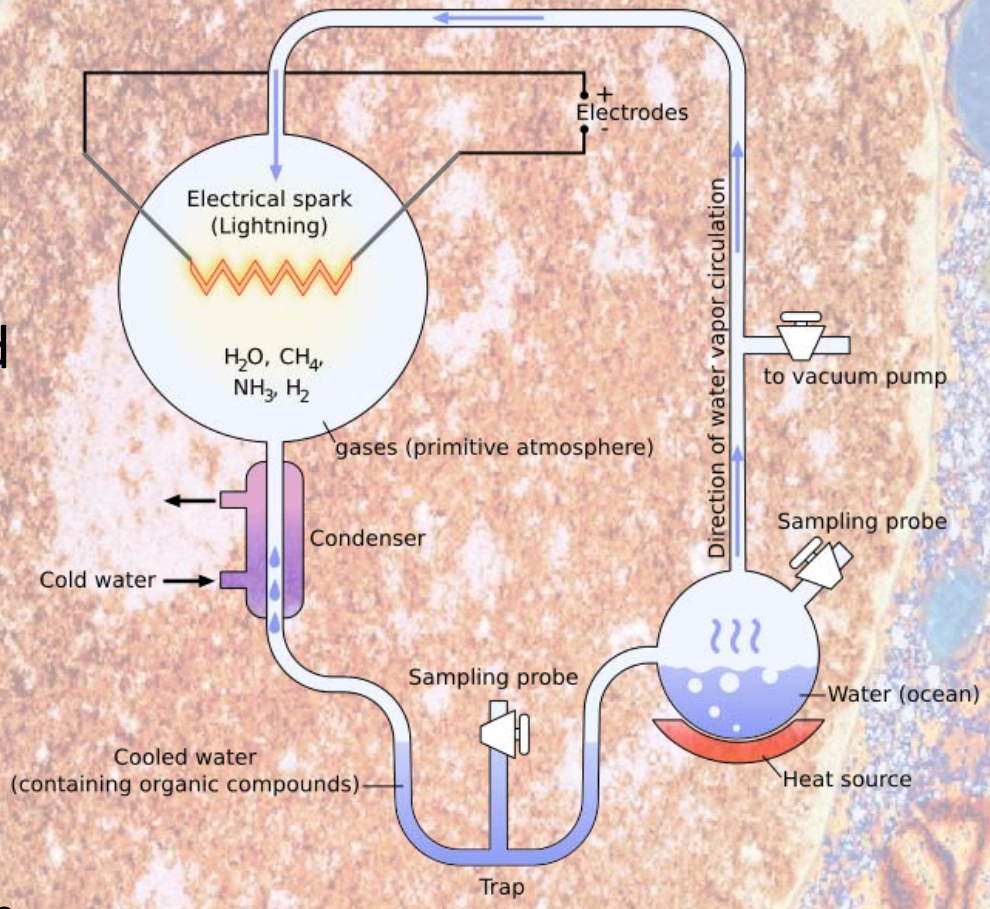


▲ **Eduard Buchner (1860–1917).** Buchner was awarded the Nobel Prize in Chemistry in 1907 "for his biochemical researches and his discovery of cell-free fermentation."

Miller-Urey Experiment

- Experiments recreating the atmosphere of primitive earth, with the energy sources and temperatures have led to the spontaneous formation of amino acids and other biologically significant molecules.

- The Miller-Urey experiment showed that a variety of organic molecules, including the amino acids could form in an early, reducing atmosphere.



Thus,

- Living things obey the standard laws of physics and chemistry.

- And, no “vitalistic” force is required to explain life at the molecular level.

- 1810s-1830s: A major substance from animals and plants was identified, composed of C, H, O, and N. The term “Protein”, meaning the most important thing, was first used in 1838.

- 1850s-1890s: Carbohydrates, lipids, and nucleic acids were recognized.

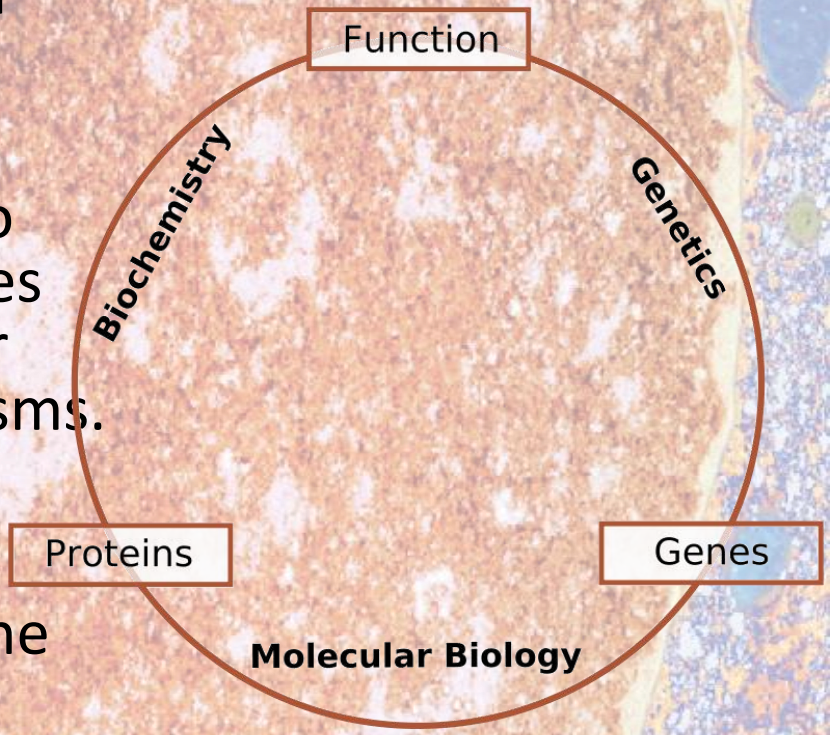
- The term “biochemistry” was coined in the 1870s. (the term Biology in 1800)

What is Biochemistry?

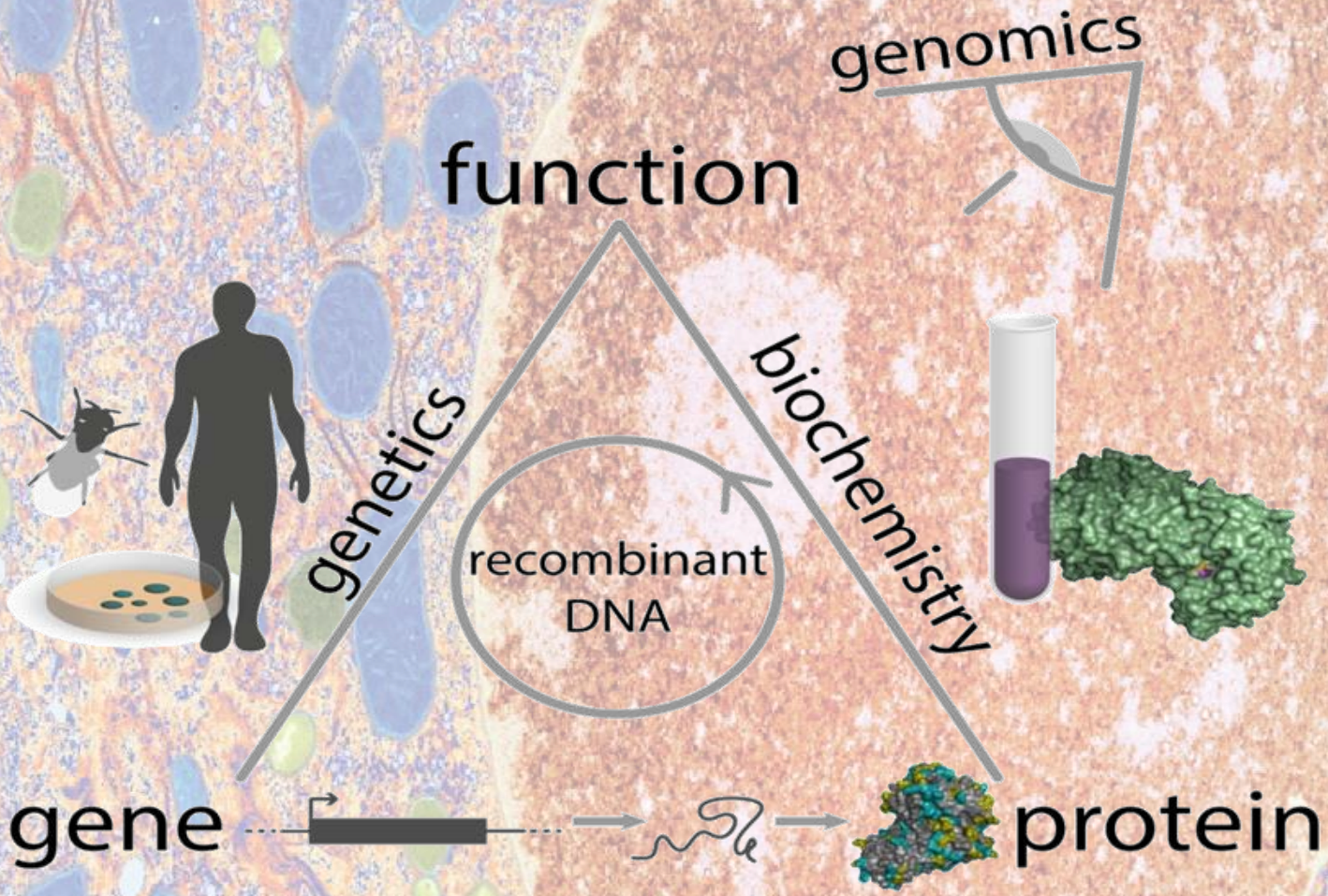
- The study of the molecular basis of life or understanding life phenomena in chemical terms

- The main focus of biochemistry is to understand how biological molecules give rise to the processes that occur within living cells and whole organisms.

- Biochemistry is closely related to molecular biology, the study of the molecular mechanisms by which genetic information encoded in DNA is able to result in the processes of life.



How Biochemistry relates to others



The Chemical Basis of "Life"

- We now know that, "life itself" is constructed from non-living matter (i.e., atoms and elements)

- Living organisms have about 20 elements (compared to 94 elements occuring naturally)

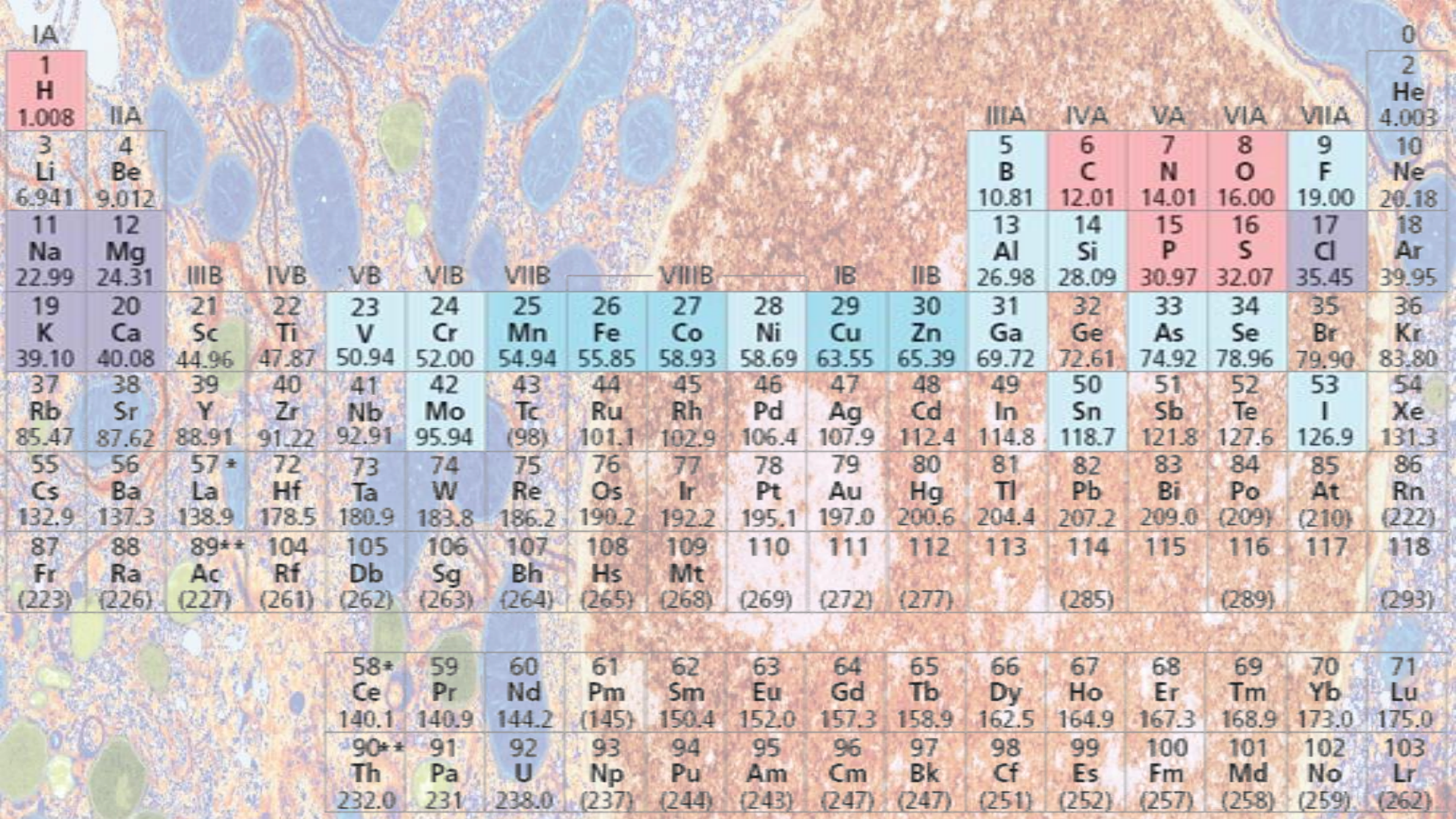
- Carbon, hydrogen, oxygen, nitrogen, phosphorus, and sulfur (CHONPS) account for more than 97% of the weight of most organisms

- The relative amounts (and sometime species) of these elements may vary among organisms.

- Water is a major component of cells and accounts for the high percentage (by weight) of oxygen.

- Carbon is much more abundant in living organisms than in the rest of the universe.

- Some elements, such as silicon, aluminum, and iron, are very common in the Earth's crust but are present only in trace amounts in cells.



The important elements found in living cells are shown in color. The red elements (CHNOPS) are the six abundant elements. The five essential ions are purple. The trace elements are shown in dark blue (more common) and light blue (less common).

Paradox !

- Living organisms and cells are made from non living elements.
- Only cells can produce cells (Cell Theory).
- How the first cell came into being?
- This is on of the greatest scientific questions yet to be answered to explain *the origin of life.*

"Remarkable chemical unity under the biological diversity"

- Remarkable uniformity of organisms of at the molecular and cellular level.
- The common use of DNA and the genetic code by all organisms
- Construction of all organisms from similar molecular components (nucleotides, amino acids, other building blocks and larger molecules)
- Same or similar bosynthetic pathways
- *This uniformity reveals that all organisms on Earth have arisen from a common ancestor*.

Two major breakthroughs in the history of biochemistry are especially notable

1. ***The discovery of the roles of enzymes as catalysts***

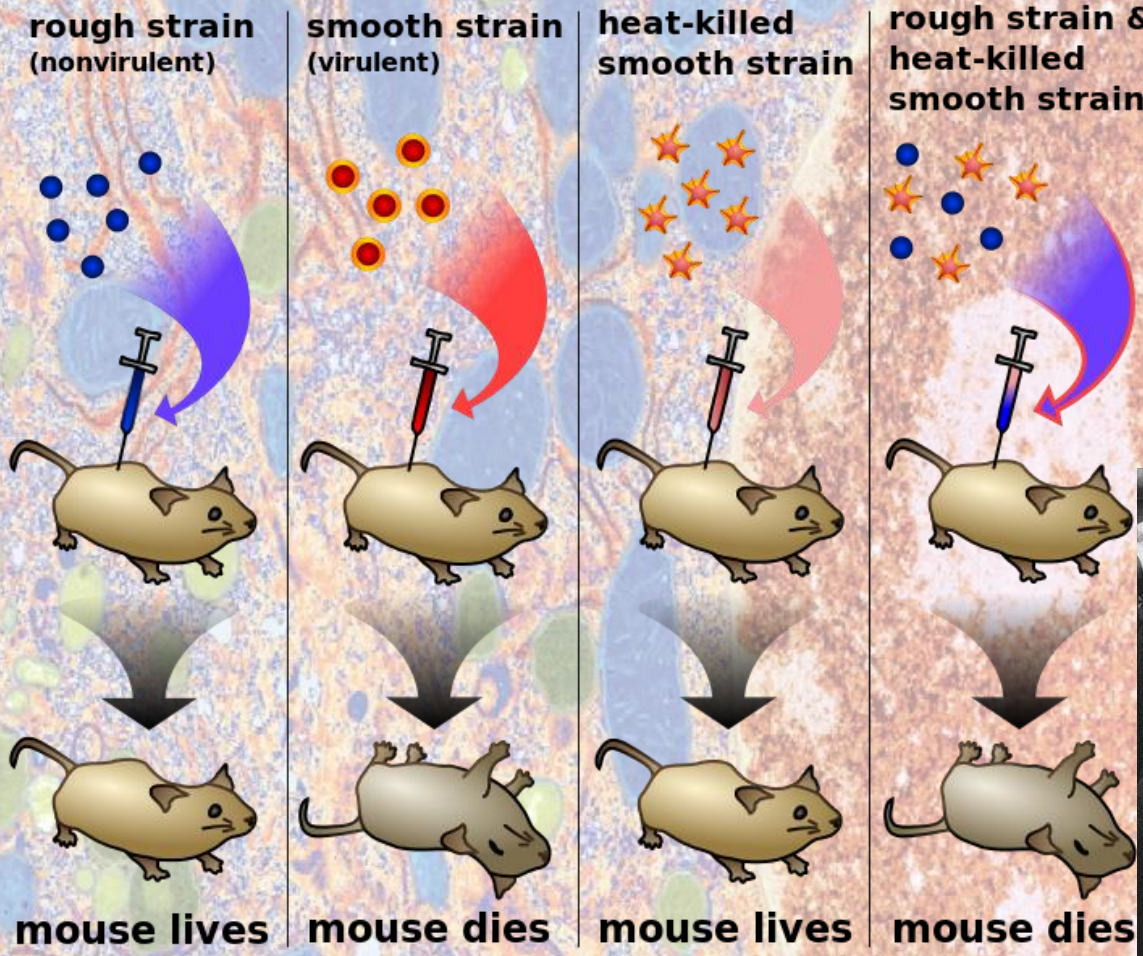
   - The experiments of Buchner showing that extracts of yeast cells could catalyze the fermentation of the sugar glucose to alcohol and carbon dioxide.

   - James Sumner showed that Enzymes are proteins (1920s-1930s).

2. The role of nucleic acids as information-carrying molecules

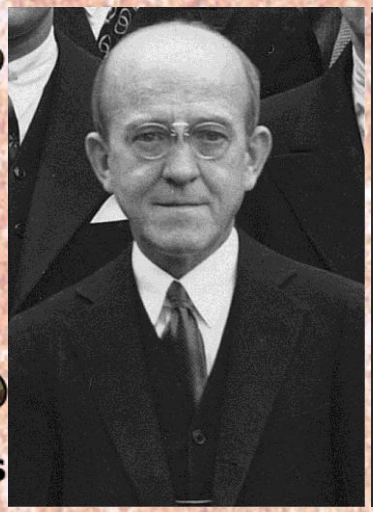
- DNA is the genetic material (1940s)
- Three-dimensional structure of DNA (i.e., DNA double-helix) (1950s)
- Genetic code (1960s)
- Biological infromation flow (i.e., Central Dogma of molecular biology) (1970s)
- Manipulation of DNA (i.e., Genetic Engineering) (1970s)
- Catalytic activity RNA (Ribozyme) (1980s)
- Causes of cancer (1990s)
- Genomic Era (2000s)
- Brain research (2010s)

1940s-1950s: Frederick Griffith's transformation experiment and DNA carries the genetic information

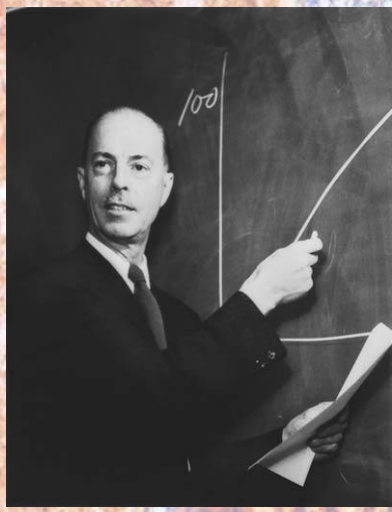




Frederick Griffith

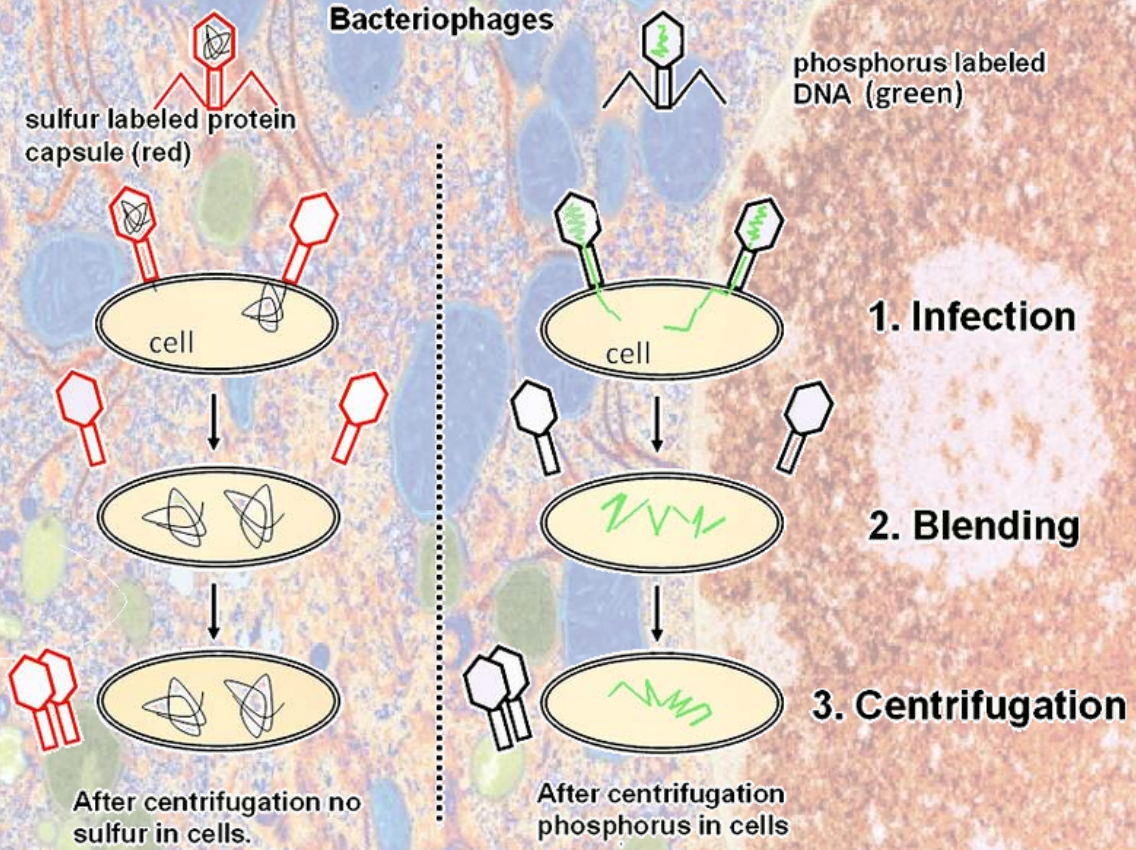


Oswald Avery

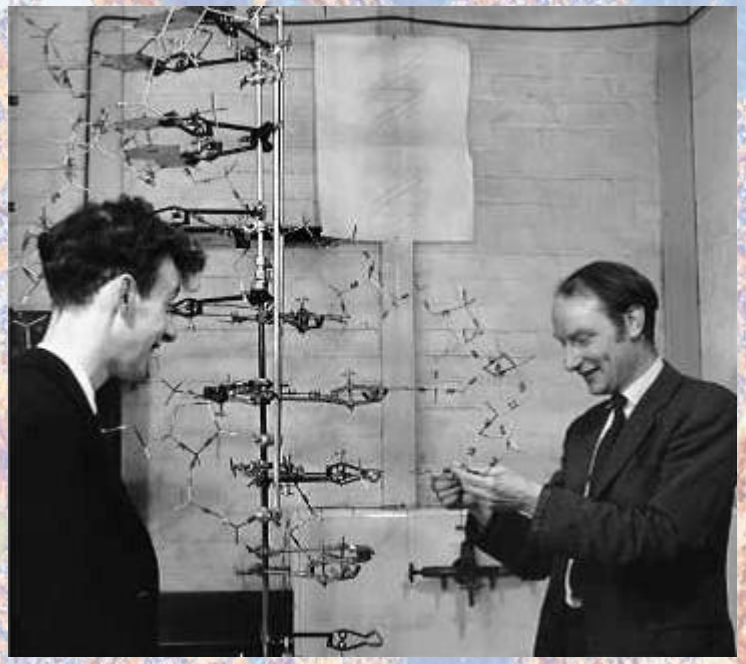


Colin MacLeod

Martha Chase and Alfred Hershey's blender experiment

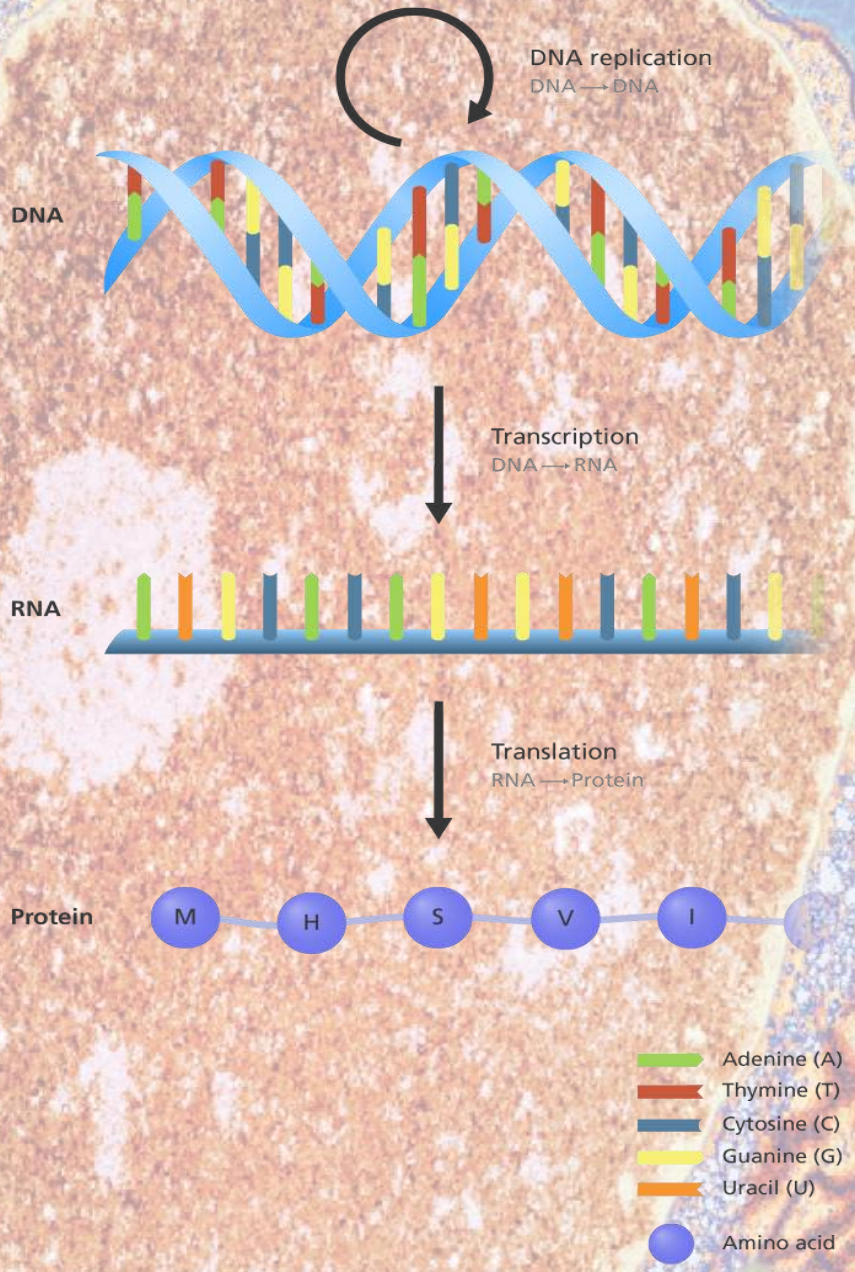




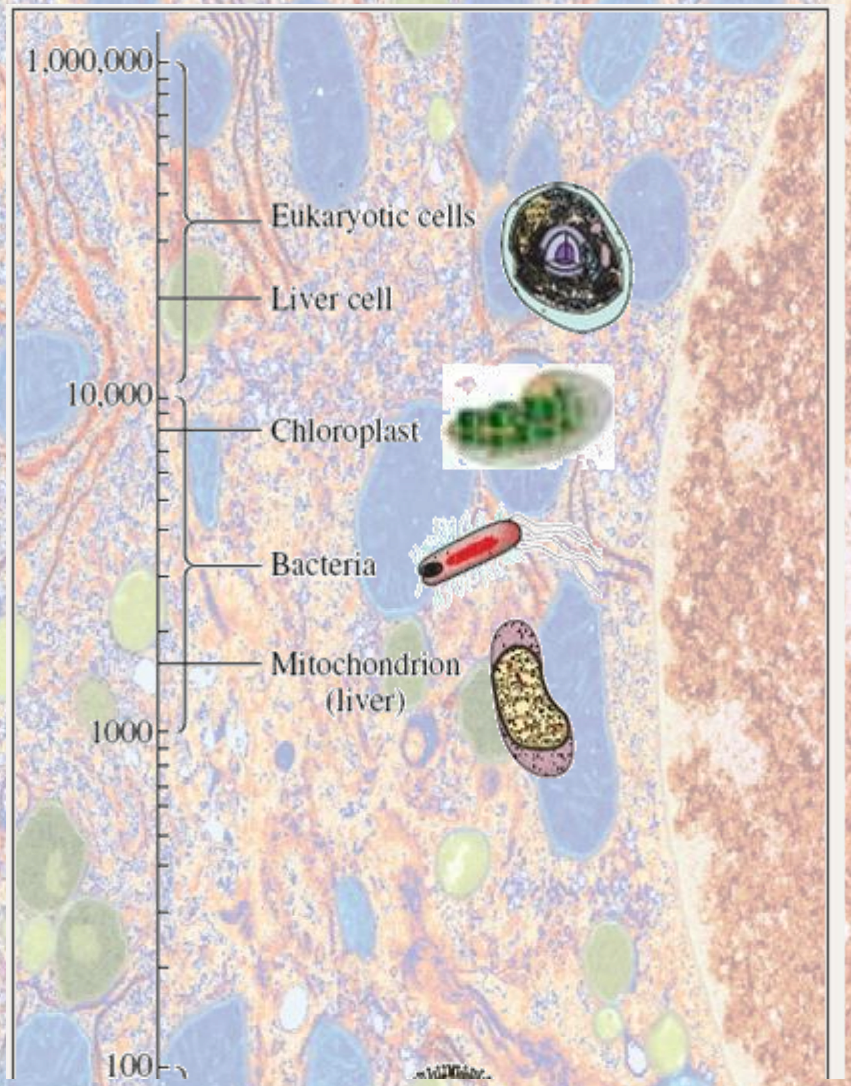


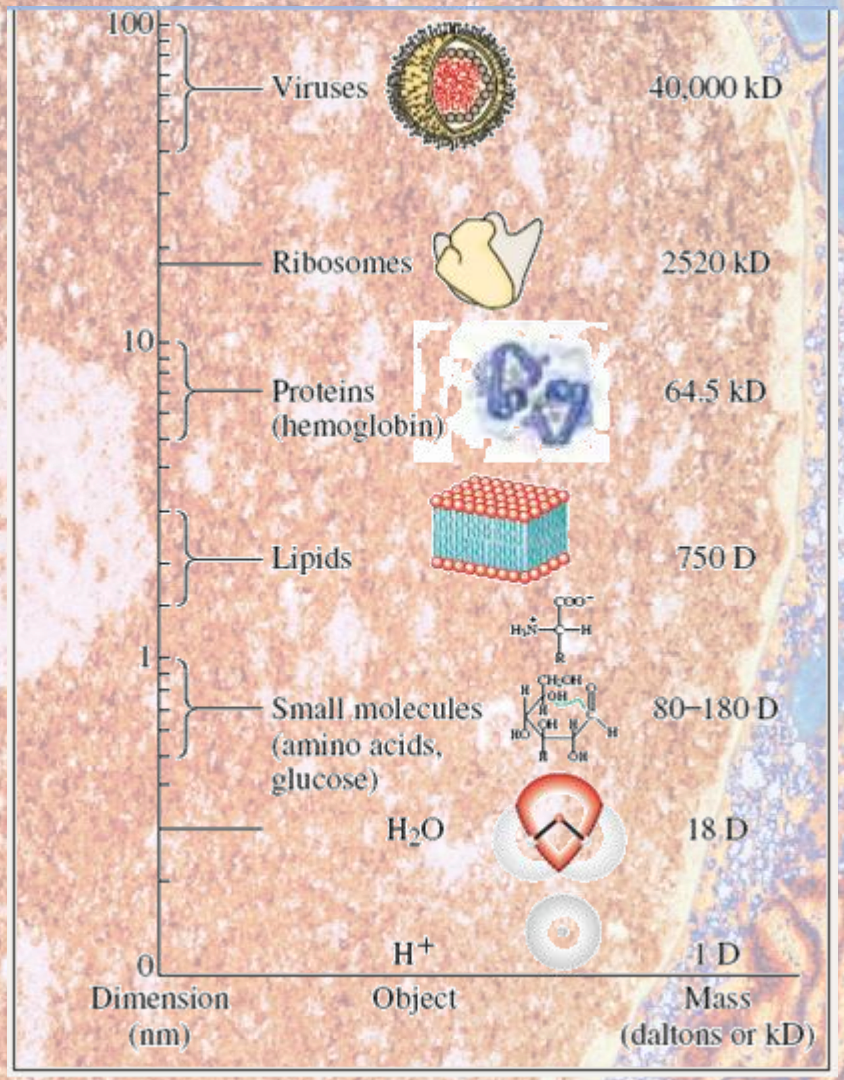
James Watson and Francis Crick with their DNA model





Scale of things in Biochemistry





What does bioochemistry study?

- Biochemistry studies all the processes within a living cell.

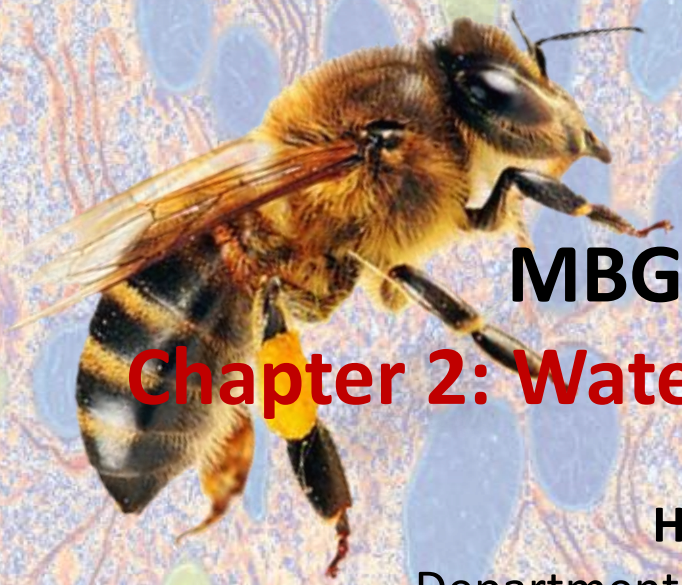
- With their all molecular compounds and contents, understanding how all these processes contribute to health and disease of living cells or organisms are major focus of Biochemistry.

- Throughout the course, you will learn the structure and function of
  - large (carbohydrates, lipids, proteins, and nucleic acids)
  - and small (building blocks, vitamins) molecules

- And how these molecules are metabolized (biosynthesis and breakdown) and their regulation play vital role in the well-being of a cell and organism.

References

- Principles of Biochemistry by Moran et.
- Lehninger Principles of Biochemistry
- Wikipedia



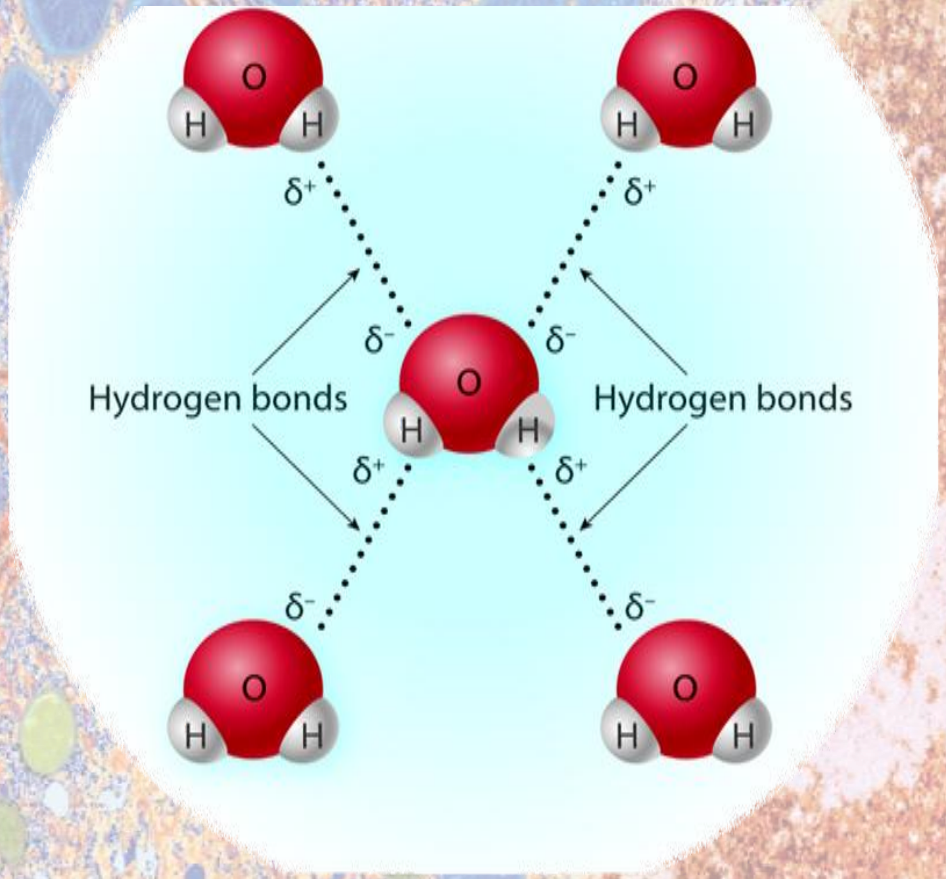
MBG303 Biochemistry

Chapter 2: Water, the unique solvent for life

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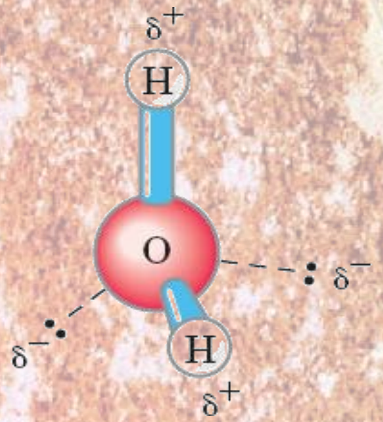
WATER: THE MEDIUM OF LIFE

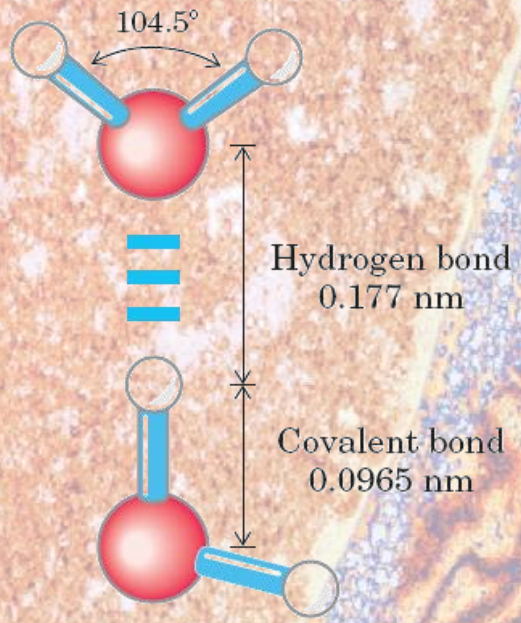
- Water is a polar molecule.
  - Water molecules have polar covalent bonds, characterized by an uneven distribution of electrons.
  - A molecule like water that has regions of positive and negative charge is called a polar molecule
  - Water molecule is made of “covalent” bonds, while water molecules bind each other with “hydrogen” bonds.



Water molecules form hydrogen bonds.
Water molecules possess polar covalent bonds because of a large electronegativity difference between the oxygen atom (highly electronegative) and the hydrogen atoms (less electronegative). Because the shared electrons spend more time on the oxygen atoms, the oxygen attains a partial negative charge, and both hydrogens attain a partial positive charge. Hydrogen bonds form between the mutual attraction of the partially negative oxygen atom on one water molecule and the partially positive hydrogen atom on another water molecule. Each water molecule has hydrogen bonds to four other water molecules in a tetrahedral bonding pattern.

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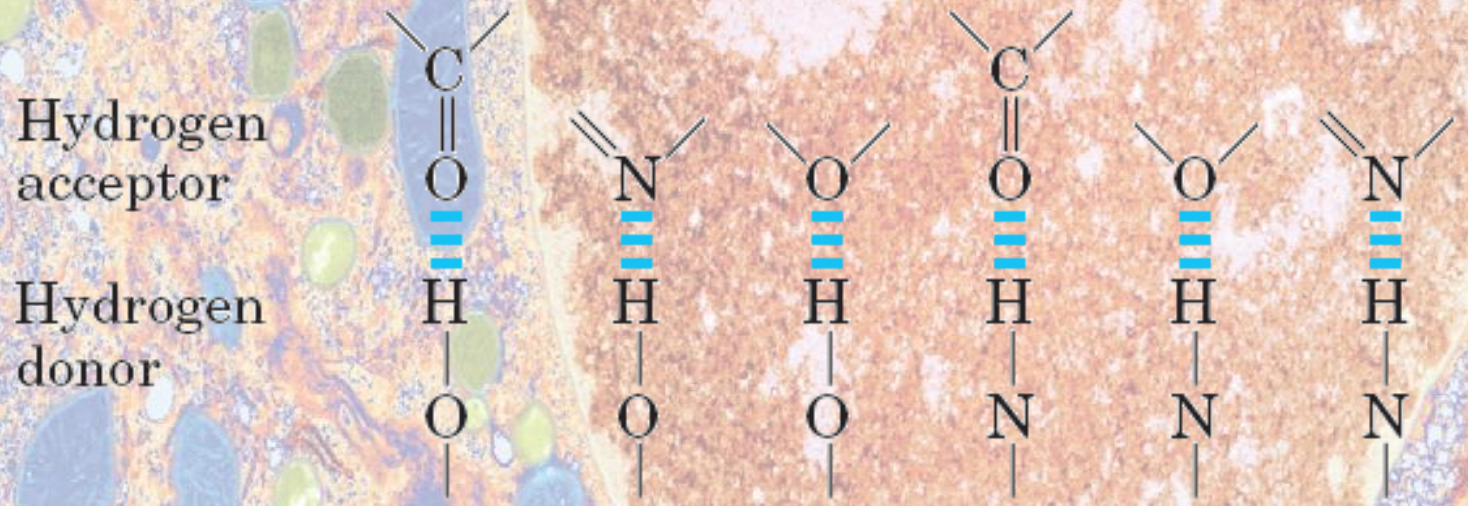




– Molecules, or even different regions of the same molecule, fall into two general classes, depending on how they interact with water:
  - hydrophilic ("water loving")
  - hydrophobic ("water fearing")

– Water Forms Hydrogen Bonds with Polar Solutes

Hydrogen bonds readily form between an electronegative atom (usually O and N) and a hydrogen atom covalently bonded to another electronegative atom.



- Given the similar electronegativity of hydrogen and carbon, H atoms covalently bonded to carbon atoms (i.e., C-H, almost non-polar) do not participate in hydrogen bonding.

- This is why butanol ($CH_3(CH_2)_2CH_2OH$) has a relatively high boiling point of 117 ^oC, whereas butane ($CH_3(CH_2)_2CH_3$) has a boiling point of only 0.5 ^oC.

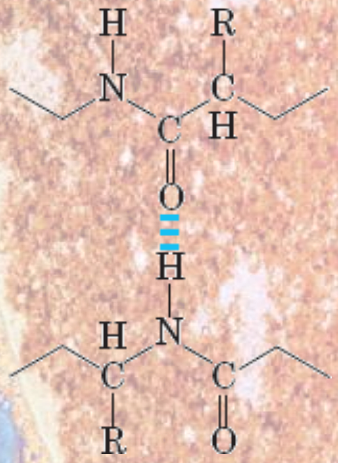
- Butanol has a polar hydroxyl group and thus can form intermolecular hydrogen bonds.

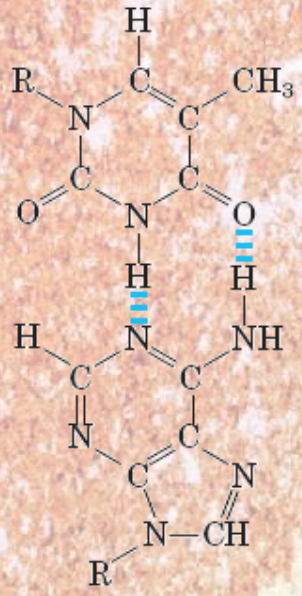
- Uncharged but polar biomolecules (e.g., sugars) dissolve readily in water because of the stabilizing effect of hydrogen bonds between the hydroxyl groups or carbonyl oxygen of the sugar and the polar water molecules.

- Alcohols, aldehydes, ketones, and compounds containing N-H bonds all form hydrogen bonds with water molecules and tend to be soluble in water.









Thymine

Adenine

Unusual Properties of Water

1. A universal solvent
2. The highest heat capacity, conduction of heat, and heat of vaporization
3. The highest surface tension of all liquids
4. The only substance occurring naturally in all three phases: *solid*, *liquid*, and *gas*
5. Water is the medium for bioactivity

1. Water is a universal solvent

- Water is an excellent solvent
- It dissolves more substances than any other liquid.
- This is due to polarity of each water molecule.
- This helps water dissociate ionic compounds into their positive and negative ions.

2. Water has the highest heat capacity, conduction of heat, and heat of vaporization

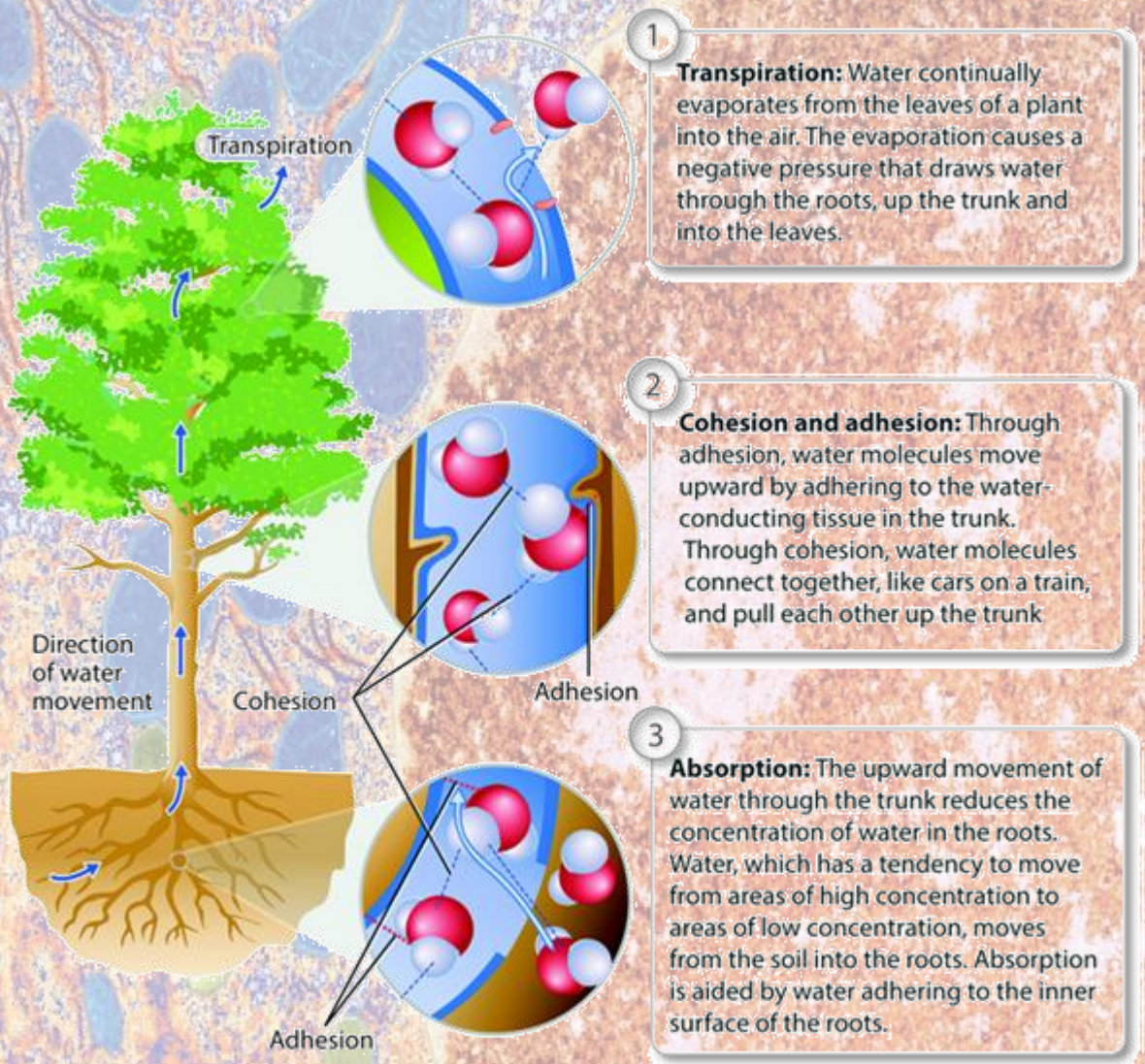
- Temperature is a measure of the motion (kinetic energy) of molecules.
- As the motion increases, energy is higher and thus temperature is higher.
- Water absorbs a great deal of energy before its temperature rises.
- The hydrogen bonds in water allow it to absorb and release heat energy more slowly than many other substances.
- Despite its small molecular weight, water has an incredibly big boiling point. This is because water requires more energy to break its hydrogen bonds before it can then begin to boil. The same concept applies to freezing point.
- It is this function of water that why organisms moderate a relatively stable body temperature when the temperature in the environment rises and falls.

3. Water has the highest surface tension of all liquids

- Water molecules are very **cohesive** (attracting each other) because of the molecule's polarity. This is why you can fill a glass of water just barely above the rim without it spilling or a drop of water can flow over a glass window without breaking.

- The cohesive forces are also related to the water's property of **adhesion**, or the attraction between water molecules and other molecules.

- Cohesive and adhesive forces are important for sustaining life. For example, because of these forces, water can flow up from the roots to the tops of plants to feed the plant.



1 **Transpiration:** Water continually evaporates from the leaves of a plant into the air. The evaporation causes a negative pressure that draws water through the roots, up the trunk and into the leaves.

2 **Cohesion and adhesion:** Through adhesion, water molecules move upward by adhering to the water-conducting tissue in the trunk. Through cohesion, water molecules connect together, like cars on a train, and pull each other up the trunk

3 **Absorption:** The upward movement of water through the trunk reduces the concentration of water in the roots. Water, which has a tendency to move from areas of high concentration to areas of low concentration, moves from the soil into the roots. Absorption is aided by water adhering to the inner surface of the roots.

Water transport in plants.
The processes of transpiration, adhesion, and cohesion pull water from the soil, through a tree's transport vessels, and into its leaves.

- Cohesion gives rise to **surface tension,** the capacity of a substance to withstand rupture when placed under tension or stress. Besides mercury, water has the highest surface tension for all liquids. Thus, even ships made of iron or steel can float in water.



Rounded water droplets resulting from surface tension.
Water drops occur as a result of water's high surface tension. The water molecules pull together into a spherical shape that minimizes contact with air and maximizes the number of hydrogen bonds. In addition, the sticking of these beads to the leaf surface demonstrates water's property of adhesion. *Dr. Keith Wheeler/Science Source.*

Surface Tension

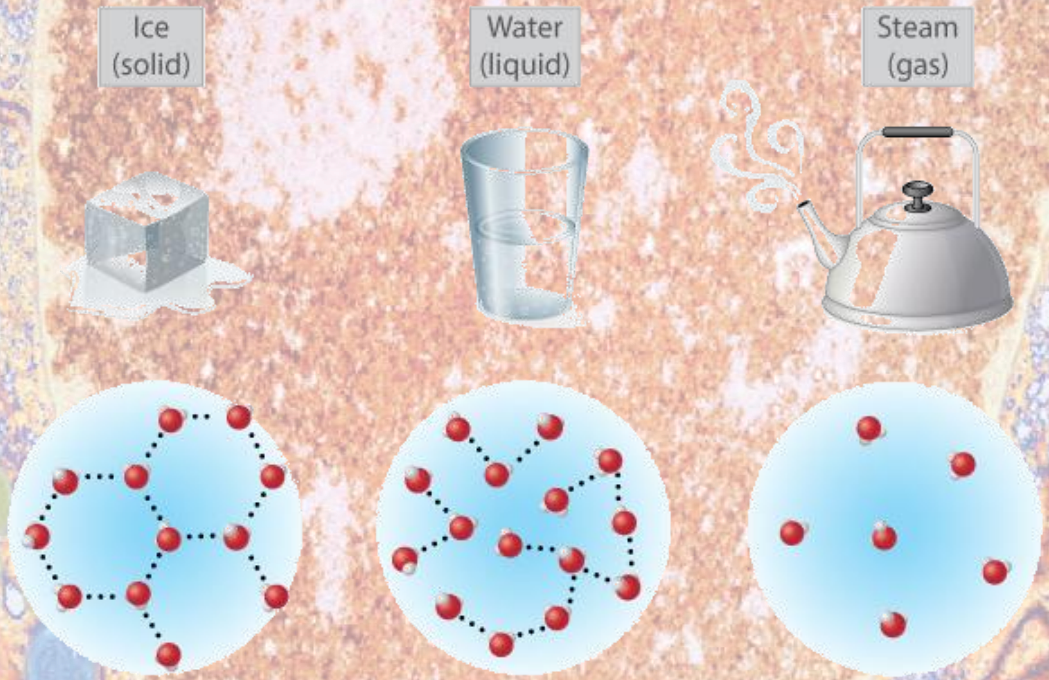


The tension at the surface of water is strong enough to support some animals, such as this water strider. This insect's legs don't quite break the surface.

4. Water is the only substance occurring naturally in all three phases: *solid*, *liquid*, and *gas*

- Water is the only substance which in solid phase (i.e., ice) is less dense than in liquid phase. Water has a maximum density at around 4°C.

- Thus, ice floats over liquid water (this allows fish to survive even the top is frozen in rivers, lakes and oceans).



A comparision …

Melting Point, Boiling Point, and Heat of Vaporization of Some Common Solvents

	Melting point (°C)	*Boiling point (°C)*	*Heat of vaporization (J/g)**
Water	0	100	2,260
Methanol (CH_3OH)	−98	65	1,100
Ethanol (CH_3CH_2OH)	−117	78	854
Propanol ($CH_3CH_2CH_2OH$)	−127	97	687
Butanol ($CH_3(CH_2)_2CH_2OH$)	−90	117	590
Acetone (CH_3COCH_3)	−95	56	523
Hexane ($CH_3(CH_2)_4CH_3$)	−98	69	423
Benzene (C_6H_6)	6	80	394
Butane ($CH_3(CH_2)_2CH_3$)	−135	−0.5	381
Chloroform ($CHCl_3$)	−63	61	247

5. Water is the medium for bioactivity

- Organisms are mostly water (humans 70%)
- Ifluences the shape of and function of biomolecules
- The medium of most biochemical reactions
- Important for transport of nutrients and waste
- Itself may be a participant in chemical reactions

The Acid-Base Chemistry of Water

- The chemistry of aqueous solutions is dominated by the equilibrium between neutral water molecules and the ions they form

$$2H_2O(l) \rightleftharpoons H_3O^+(aq) + OH^-(aq)$$

$$K'_w = \frac{[H_3O^+]\,[OH^-]}{[H_2O]}$$

- Water concentration (moles of water in 1 liter of water):

  $[H_2O]$ = (density of water, g/L) × (molar mass of water, mol/g) = (∼1000 g/L) × (1 mol/18 g) = 55.5 mol/L = 55.5 M

- Comparing this concentration with the concentrations of H_3O^+ and OH^- (i.e., each 1×10^{-7} M) shows how few water molecules actually dissociate:

  $K_w = [H_3O^+][OH^-]$

  $= (1 \times 10^{-7}\ M) \times (1 \times 10^{-7}\ M)$

  $= 1 \times 10^{-14}\ M^2$ at 25 °C

- The value of K_w is used to define whether a solution is acidic, neutral, or basic.

- Any solution can have H_3O^+ and OH^- at equal concentrations, not just water. A solution that has $[H_3O^+] = [OH^-]$ is defined as **neutral**.

- In contrast, some solutions can have unequal proportions of H_3O^+ and OH^- molecules.

- Solutions are defined as **acidic** when $[H_3O^+] > [OH^-]$ and **basic** when $[H_3O^+] < [OH^-]$.

- In other words:

  Acidic: $[H_3O^+] > 1 \times 10^{-7}$ M; $[OH^-] < 1 \times 10^{-7}$ M
  Neutral: $[H_3O^+] = 1 \times 10^{-7}$ M = $[OH^-]$
  Basic: $[H_3O^+] < 1 \times 10^{-7}$ M; $[OH^-] > 1 \times 10^{-7}$ M

- pH term is utilized to express these very small numbers in scientific notation in real (manageable) numbers.

- The scale is logarithmic. So the "p" in pH denotes that it's *the power of 10* or *the power of hydrogen*:

  $pH = -\log[H_3O^+]$ or $[H_3O^+] = 10^{-pH}$

- Thus, an acidic solution with 1×10^{-4} M H_3O^+ will have a pH of 4.

- A basic solution with 1×10^{-10} M H_3O^+ will have a pH of 10.

- Notice that the exponents in the examples above are the pH values.

- However, to calculate the pH value for $n \times 10^{-4}$ where n is any number other than 1, you should have a calculator (e.g., 2.6×10^{-4} M H_3O^+ will have a pH of 3.59).

Where there is water, there is life

- Water is widely regarded as the '*matrix of life*' which is not just a passive scaffold but also has many active roles in molecular biology.

- Despite the apparent simplicity of the water molecule, water is probably the most mysterious substance in our world.

Water and biomolecules

- The oxygen atom of water carries a partial negative charge and thus water could act as a nucleophile (i.e., donates an electron pair to an electrophile) in hydrolysis reactions.

- Water is central to the assembly and three-dimensional shape of proteins and nucleic acids.

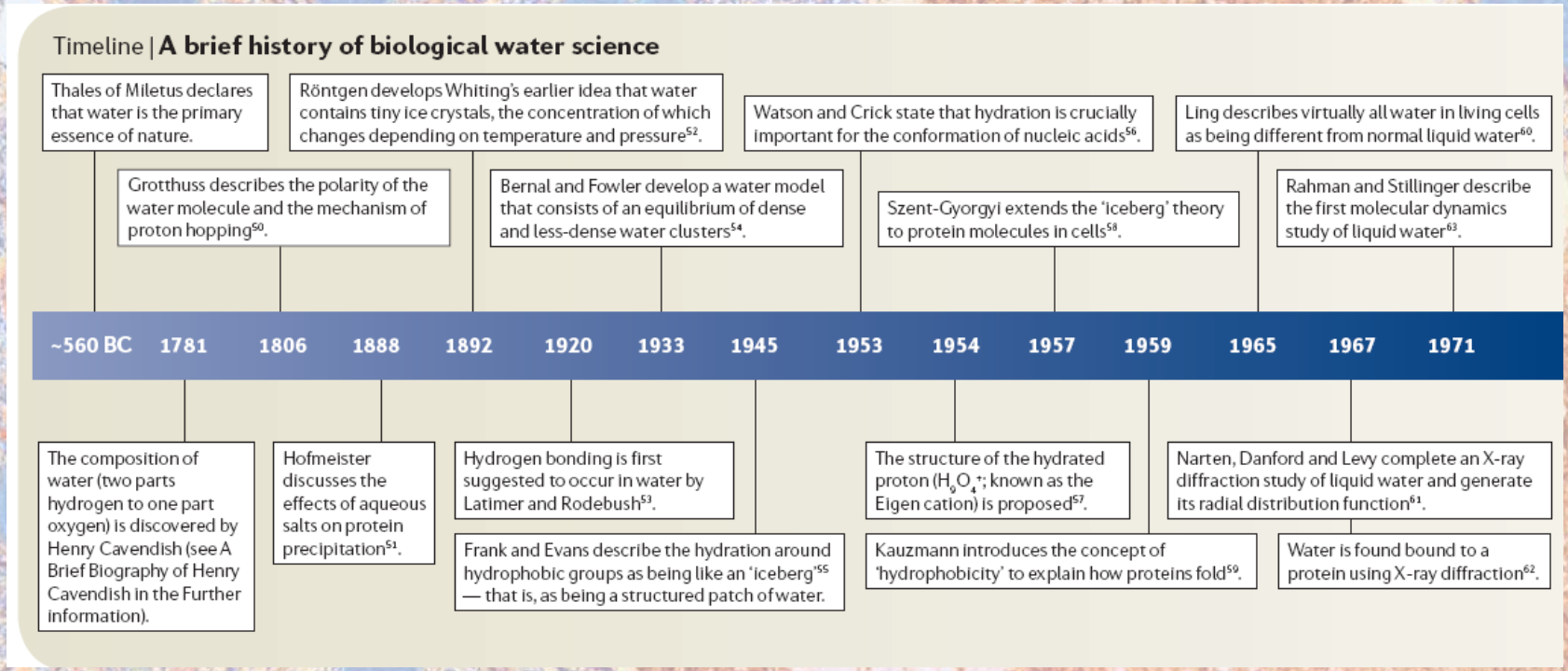
- As well as providing a medium in which enzyme structure and activity is maintained, water is a reactant in many reactions.

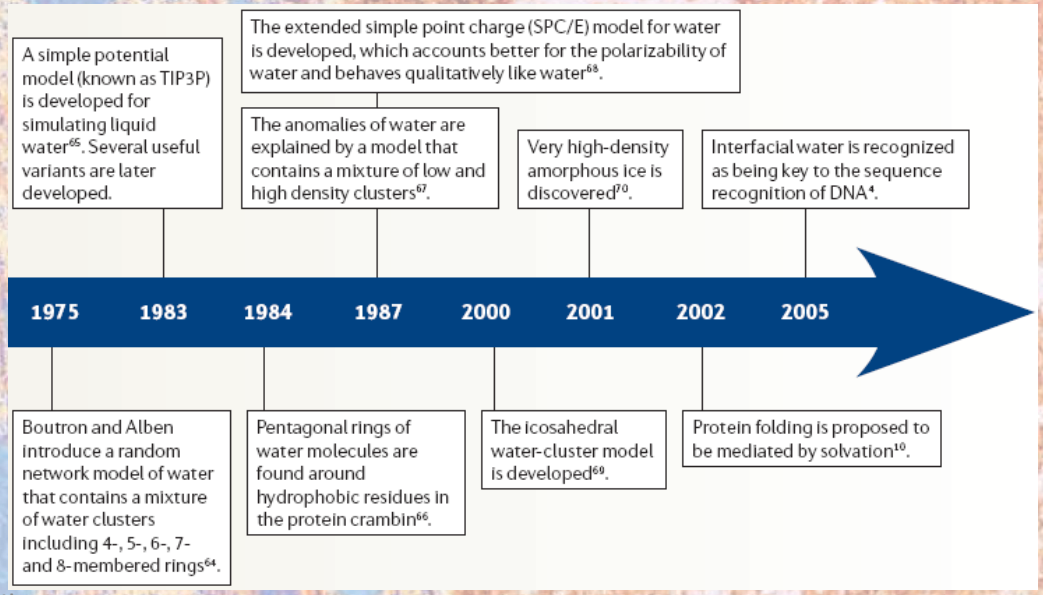
- Nearly 35% of all identified enzymes (namely the hydrolases and some of the lyases involve water as a substrate or product.

- Water molecules ‘locked up’ in the active site can modulate interactions with substrates and contribute to catalysis.

- The DNA helix expanding and contracting depends on its hydration status. Water hydrates DNA by forming links with the polar atoms at the edges of base pairs.

- Most X-ray crystal structures of proteins show water molecules in fixed positions around the exterior of the protein molecules, forming hydrogen-bonding networks that include hydrophilic groups in the protein main and side chains.


Timeline | A brief history of biological water science
Thales of Miletus declares that water is the primary essence of nature.
Röntgen develops Whiting's earlier idea that water contains tiny ice crystals, the concentration of which changes depending on temperature and pressure[52].
Watson and Crick state that hydration is crucially important for the conformation of nucleic acids[56].
Ling describes virtually all water in living cells as being different from normal liquid water[60].
Grotthuss describes the polarity of the water molecule and the mechanism of proton hopping[50].
Bernal and Fowler develop a water model that consists of an equilibrium of dense and less-dense water clusters[54].
Szent-Gyorgyi extends the 'iceberg' theory to protein molecules in cells[58].
Rahman and Stillinger describe the first molecular dynamics study of liquid water[63].
~560 BC
1781
1806
1888
1892
1920
1933
1945
1953
1954
1957
1959
1965
1967
1971
The composition of water (two parts hydrogen to one part oxygen) is discovered by Henry Cavendish (see A Brief Biography of Henry Cavendish in the Further information).
Hofmeister discusses the effects of aqueous salts on protein precipitation[51].
Hydrogen bonding is first suggested to occur in water by Latimer and Rodebush[53].
Frank and Evans describe the hydration around hydrophobic groups as being like an 'iceberg'[55] — that is, as being a structured patch of water.
The structure of the hydrated proton ($H_9O_4^+$; known as the Eigen cation) is proposed[57].
Kauzmann introduces the concept of 'hydrophobicity' to explain how proteins fold[59].
Narten, Danford and Levy complete an X-ray diffraction study of liquid water and generate its radial distribution function[61].
Water is found bound to a protein using X-ray diffraction[62].


A simple potential model (known as TIP3P) is developed for simulating liquid water[65]. Several useful variants are later developed.
The extended simple point charge (SPC/E) model for water is developed, which accounts better for the polarizability of water and behaves qualitatively like water[68].
The anomalies of water are explained by a model that contains a mixture of low and high density clusters[67].
Very high-density amorphous ice is discovered[70].
Interfacial water is recognized as being key to the sequence recognition of DNA[4].
1975
1983
1984
1987
2000
2001
2002
2005
Boutron and Alben introduce a random network model of water that contains a mixture of water clusters including 4-, 5-, 6-, 7- and 8-membered rings[64].
Pentagonal rings of water molecules are found around hydrophobic residues in the protein crambin[66].
The icosahedral water-cluster model is developed[69].
Protein folding is proposed to be mediated by solvation[10].

More amazing facts about water

- Cancer cells contain more free water than normal cells, and the degree of malignancy increases with the degree of cell hydration.

- Thus, intracellular hydration might be a primary factor in carcinogenesis.

- This could be because increased hydration facilitates the acceleration of intracellular processes, including respiration, which enhances the competitive edge of a cancer cell for using nutrients.

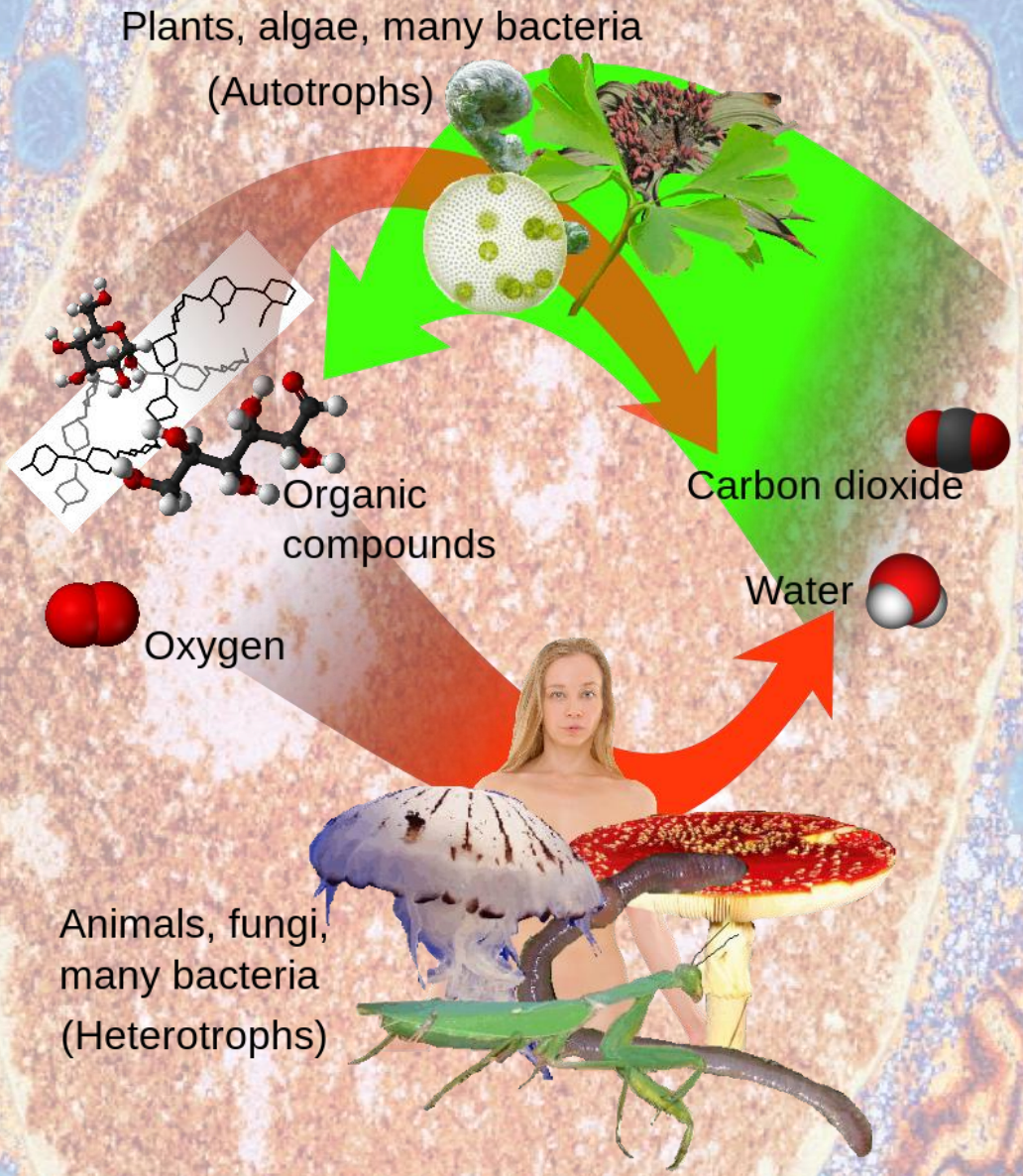
- The invention of the "***water splitting***" by photosynthetic organisms (i.e., plants) about 2.5 billion years ago can be considered as the 'Big Bang of Biology and Evolution'.

- It provided biology with an unlimited supply of hydrogen equivalents destined to reduce carbon dioxide to organic molecules.

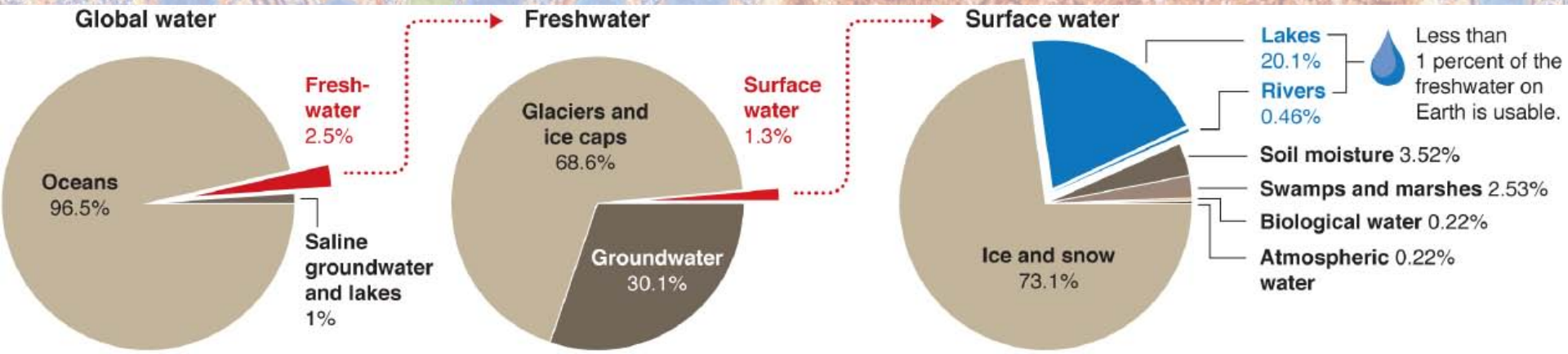
- The byproduct of the reaction is molecular dioxygen (i.e., O_2), which is the oxygen we (and certainly almost all organisms on earth) breath.

- This byproduct has given us an oxygenic atmosphere and allowed aerobic biology to prosper.

- If we had an industry based on splitting water just like the plants do, we would solve all "*energy and global warming problems*" our world faces today.

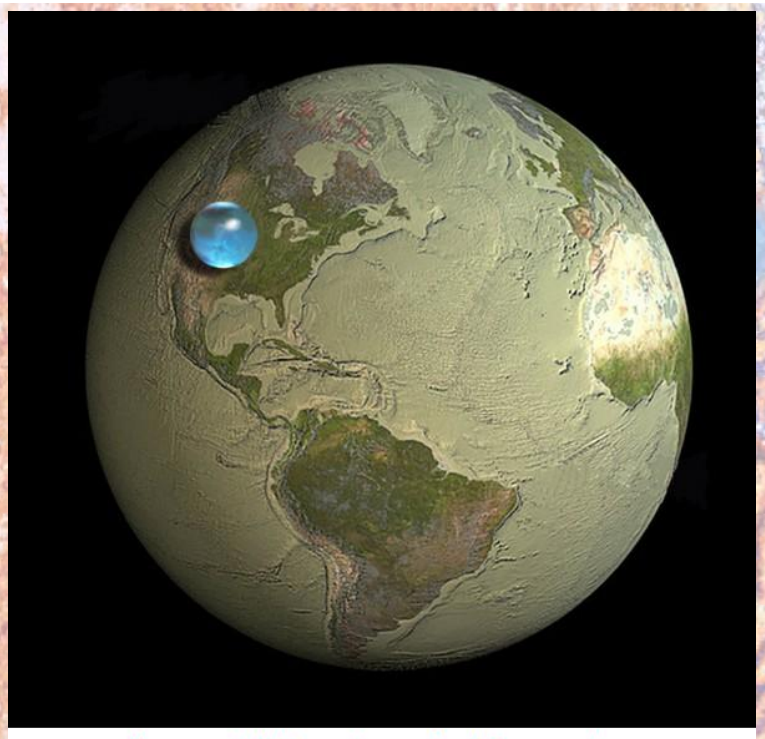


Water scarcity?



- Although 2/3 of earth is covered with water, freshwater accounts for only 2.5% of the total.
  - "*Water, water, everywhere, And all the boards did shrink; Water, water, everywhere, Nor any drop to drink*"

    Samuel Taylor Coleridge



If you put all the water on Earth in one place

Next lecture…

Chapter 3: Acid-Base Chemistry



MBG303 Biochemistry

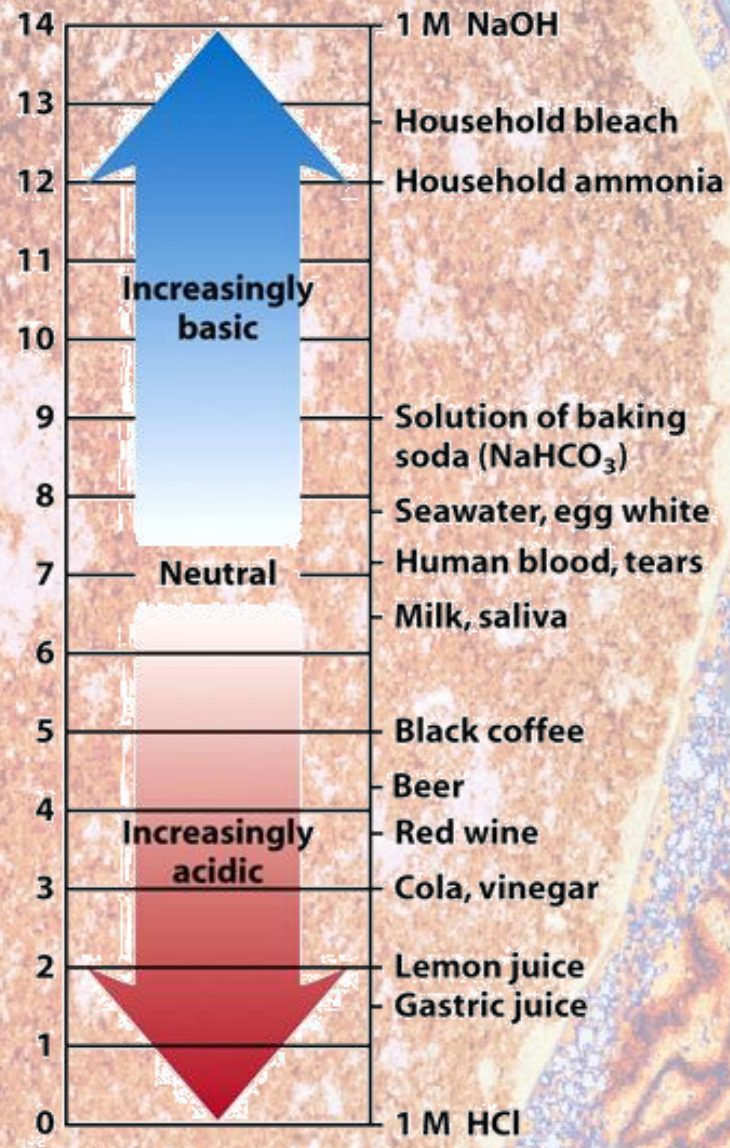
Chapter 3: Acid-Base Chemistry

Hikmet Geçkil, Professor
Department of Molecular Biology and Genetics
Inonu University

pH, pK_a, pI, Acids & Bases

TABLE	The pH Scale		
$[H^+]$ (M)	pH	$[OH^-]$ (M)	pOH*
10^0 (1)	0	10^{-14}	14
10^{-1}	1	10^{-13}	13
10^{-2}	2	10^{-12}	12
10^{-3}	3	10^{-11}	11
10^{-4}	4	10^{-10}	10
10^{-5}	5	10^{-9}	9
10^{-6}	6	10^{-8}	8
10^{-7}	7	10^{-7}	7
10^{-8}	8	10^{-6}	6
10^{-9}	9	10^{-5}	5
10^{-10}	10	10^{-4}	4
10^{-11}	11	10^{-3}	3
10^{-12}	12	10^{-2}	2
10^{-13}	13	10^{-1}	1
10^{-14}	14	10^0 (1)	0

*The expression pOH is sometimes used to describe the basicity, or OH^- concentration, of a solution; pOH is defined by the expression $pOH = -\log [OH^-]$, which is analogous to the expression for pH. Note that in all cases, $pH + pOH = 14$. *Lehninger Principles of Biochemistry, Fifth Edition*



- Measurement of pH is one of the most important and frequently used procedures in biochemistry.

- The pH affects the structure and activity of biological macromolecules;
  - For example, the catalytic activity of enzymes is strongly dependent on pH
  - Measurements of the pH of blood and urine are commonly used in medical diagnoses.

- **pH** term was introduced in 1909 by Sorensen.

- pH is defined as the negative log of the hydrogen ion concentration (i.e., $[H^+]$).

$$pH = -\log [H^+]$$

- The pH scale is logarithmic and is a convenient way of showing $[H^+]$. e.g., for 0.0000001 M $[H^+]$ is simply equal to 7.0 in pH scale.

- Remember! 1 pH unit difference corresponds to 10 fold difference in $[H^+]$, while 2 and 3 pH unit difference correspond to 100 and 1000 times difference in $[H^+]$, respectively.

- Thus, pH 4 is ten times more acidic than pH 5 and 100 times more acidic than pH 6.

Strong acids and bases

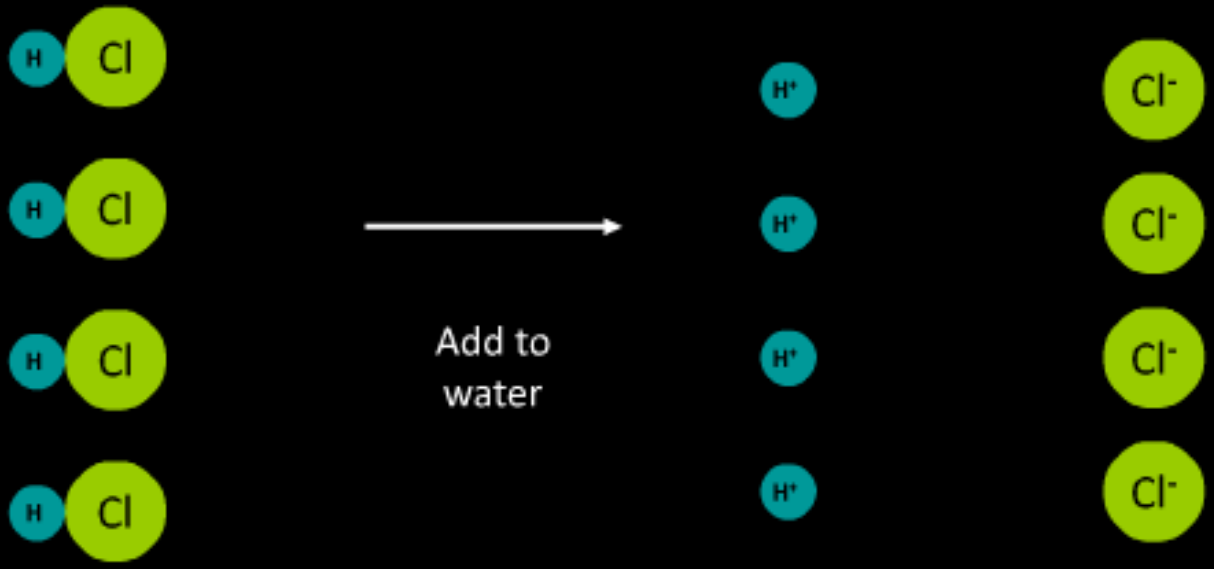
Strong acids and bases dissociate ***completely*** into their component ions in aqueous solution.

Example.

$HCl\ (aq) \longrightarrow H^+\ (aq) + Cl^-\ (aq)$

strong acid

This means if we are given 4 molecules of HCl, once we add these molecules to water, they will separate into 4 H^+ ions and 4 Cl^- ions:



Strong acids and bases

Example. What is the pH of a 0.45 M solution of HCl?

$$HCl\ (aq) \longrightarrow H^+\ (aq) + Cl^-\ (aq)$$

strong acid

We learned on the previous slide that strong acids completely dissociate in water. If we have 4 molecules of HCl, they will break apart into 4 H^+ and 4 Cl^-. If we have 0.45 M HCl, what is the concentration of H^+ and Cl^- in solution?

$$HCl\ (aq) \longrightarrow H^+\ (aq) + Cl^-\ (aq)$$

0.45 M → 0.45 M + 0.45 M

The concentration of H^+ in solution is also 0.45 M because there is a 1:1 ratio between H^+ and HCl in our equation. *pH is defined as the –log of the concentration of H^+*, therefore:

$$-\log [H^+] = -\log (0.45\ M) = \mathbf{0.35}$$

The pH of this solution is 0.35.

Strong acids and bases

Example. What is the pH of a 0.45 M solution of NaOH?

$$NaOH\ (aq) \longrightarrow Na^+\ (aq) + OH^-\ (aq)$$

strong base

Strong bases, like strong acids, completely dissociate in aqueous solution. If we have 4 molecules of NaOH, they will break apart into 4 Na^+ ions and 4 OH^- ions. If we have 0.45 M NaOH, what is the concentration of Na^+ and OH^- in solution?

$$NaOH\ (aq) \longrightarrow Na^+\ (aq) + OH^-\ (aq)$$

0.45 M → 0.45 M + 0.45 M

The concentration of OH^- in solution is 0.45 M because there is a 1:1 ratio between OH^- and NaOH in our equation. *pOH is defined as the –log of the concentration of OH^-*, therefore:

$$-\log [OH^-] = -\log (0.45\ M) = \mathbf{0.35}$$

The pOH of this solution is 0.35.

Strong acids and bases

Example. What is the pH of a 0.45 M solution of NaOH?

$$NaOH\ (aq) \longrightarrow Na^+\ (aq) + OH^-\ (aq)$$

strong base

We have determined that the pOH of 0.45 M NaOH solution is 0.35, but the question asks f
the pH. What is the relationship between pH and pOH? Recall that:

$$pH + pOH = 14$$

*For a detailed explanation, see p. 662, Zumdahl, 9th ed.

In this case:

$$pH + pOH = 14$$

$$pH + 0.35 = 14$$

$$pH = 13.7$$

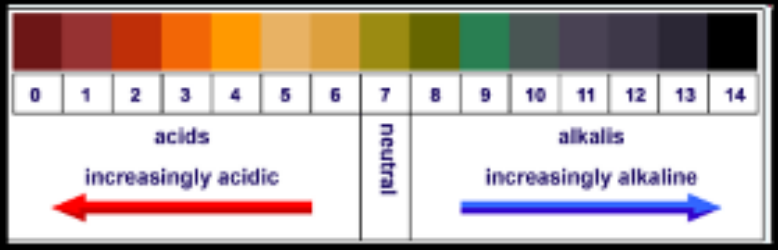
The pH of our strong base solution is 13.7!

Strong acids and bases

Common strong acids and bases are listed below:

Strong acids	
HCl	Hydrochloric acid
HNO_3	Nitric acid
H_2SO_4	Sulfuric acid
$HClO_4$	Perchloric acid
HI	Hydroiodic acid
HBr	Hydrobromic acid

Strong bases	
NaOH	Sodium hydroxide
KOH	Potassium hydroxide
LiOH	Lithium hydroxide
RbOH	Rubidium hydroxide
CsOH	Cesium hydroxide
$Ca(OH)_2$	Calcium hydroxide



Click to advance

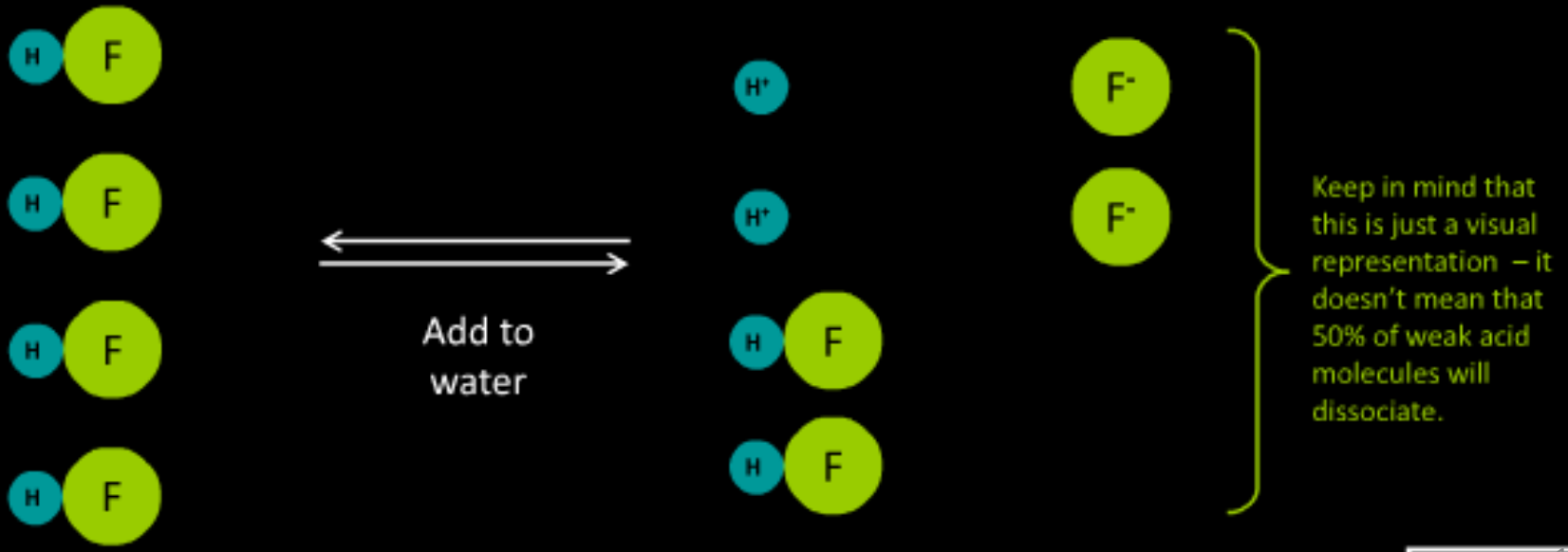
Weak acids and bases

Weak acids and bases do ***NOT*** dissociate completely into their component ions in aqueous solution.

Example.

$$\underset{\text{weak acid}}{HF\ (aq)} \rightleftharpoons H^+\ (aq) + F^-\ (aq)$$

This means if we are given 4 molecules of HF, once we add these molecules to water, only some will separate – the rest will stay together:



Click to advance

Weak acids

Example. What is the pH of a 0.45 M solution of HF? The K_a of HF is 7.2×10^{-4}.

$$HF\ (aq) \rightleftharpoons H^+\ (aq) + F^-\ (aq)$$

weak acid

We learned on the previous slide that weak acids do ***NOT*** completely dissociate. If we have 4 molecules of HF, only a few will break apart into H^+ and F^-. How can we determine the concentration of H^+ and F^- in a 0.45 M solution of HF?

$$HF\ (aq) \rightleftharpoons H^+\ (aq) + F^-\ (aq)$$

0.45 M ? M ? M

In this case, we need to use our knowledge of chemical equilibria and construct a K_a expression for this reaction:

$$K_a = \frac{[products]}{[reactants]} = \frac{[H^+]\,[F^-]}{[HF]}$$

This K is calculated like any other equilibrium constant:

Concentration of products divided by concentration of reactants

We know that this is a K_a because of the H^+ in the expression.

Click to advance

Weak acids

Example. What is the pH of a 0.45 M solution of HF? The K_a of HF is 7.2×10^{-4}.

Step 1. Prepare an ICE table to calculate the equilibrium concentration of H^+.

$$HF\ (aq) \rightleftharpoons H^+\ (aq) + F^-\ (aq)$$

weak acid

I	0.45		0	0
C	- *x*		+ *x*	+ *x*
E	0.45 - *x*		+ *x*	+ *x*

The equilibrium row is simply the sum of the initial and change rows.

Step 2. As we saw on the previous slide, K_a is [products]/[reactants]. Let's substitute in the values from our ICE table.

$$K_a = \frac{[H^+]\,[F^-]}{[HF]} = \frac{[x]\,[x]}{[0.45]} = 7.2 \times 10^{-4}$$

Click to advance

Weak acids

Example. What is the pH of a 0.45 M solution of HF? The K_a of HF is 7.2×10^{-4}.

Step 2. Solving for x.

$$K_a = \frac{[H^+]\,[F^-]}{[HF]} = \frac{[x]\,[x]}{[0.45]} = 7.2 \times 10^{-4}$$

Cross-multiplying by 0.45 to isolate x^2: $x^2 = 3.24 \times 10^{-4}$

Taking the square root of both sides: $x = 0.018\ M$

Step 3. Looking at our ICE table, x is equal to $[H^+]$. If we take the –log of x, we have found pH!

$$pH = -\log(0.018) = \mathbf{1.7}$$

The pH of our weak acid solution is 1.7, a higher pH than the strong acid solution.

Click to advance

Percent dissociation

Example. What percent of our 0.45 M HF solution exists in the ionized state?

Step 1. *Of the original 0.45 M HF, we have calculated that 0.018 M exists in the H^+ form at equilibrium. What percentage of 0.45 is 0.018?*

$$\frac{0.018\ \text{M}}{0.45\ \text{M}} \times 100\% = 4.0\%$$

← 4.0% of this acid exists in the dissociated form

Step 2. *In what other ways can we use this % dissociation number? Say we have a 0.5 M HF solution that is 2.5% ionized. What is the pH of this solution?*

$$\text{Percent dissociation} = \frac{\text{Amount dissociated (mol/L)}}{\text{Initial concentration (mol/L)}} \times 100\%$$

$$2.5\% = \frac{x\ \text{M}}{0.5\ \text{M}} \times 100\%$$

$$x\ \text{M} = 0.0125\ \text{M}$$

$$\text{pH} = -\log(0.0125) = 1.9$$

Click to advance

Weak bases

Weak bases do ***NOT*** dissociate completely into their component ions in aqueous solution, and can accept a proton from H_2O. The reaction between a weak base and water looks like this:

Example. What is the pH of a 0.90 M solution of NH_3? The K_b of NH_3 is 1.8×10^{-5}.

$NH_3\ (aq) + H_2O\ (l) \rightleftharpoons NH_4^+\ (aq) + OH^-\ (aq)$

weak base

Again, we need to use an ICE table to determine the equilibrium concentration of OH^-, which (as a strong base) will determine the pH of solution.

$NH_3\ (aq) + H_2O\ (l) \rightleftharpoons NH_4^+\ (aq) + OH^-\ (aq)$

I	0.90	—		0	0
C	- *x*	—		+ *x*	+ *x*
E	0.90 - *x*	—		+ *x*	+ *x*

The equilibrium row is simply the sum of the initial and change rows. Remember, H_2O is not included because it is a pure substance.

Click to advance

Weak bases

Example. What is the pH of a 0.90 M solution of NH_3? The K_b of NH_3 is 1.8×10^{-5}.

Step 2. Set up a K_b expression using the ICE table and solve for x.

$$K_b = \frac{[\text{products}]}{[\text{reactants}]} = \frac{[NH_4^+]\,[OH^-]}{[NH_3]}$$

$$1.8 \times 10^{-5} = \frac{[x]\,[x]}{[0.90]}$$

Substituting in our values from the ICE table. We ignore x in the denominator (5% rule) to make the math easier.

$$1.62 \times 10^{-5} = x^2$$

Multiplying by 0.90 to isolate x^2

$$0.0040\ M = x$$

Taking the square root of both sides

Step 3. According to the ICE table, x is equal to $[OH^-]$, so we can calculate pOH:

$$pOH = -\log [OH^-] = -\log (0.0040\ M) = 2.40$$

$$pH = 11.6$$

We know our answer is reasonable because the pH of our weak base is 11.6 – lower than the pH of the strong base solution (13.7).

Click to advance

Weak acids and bases

Some common weak acids and bases are listed below:

Weak acids	
HCOOH	Formic acid
CH_3COOH	Acetic acid
HF	Hydrofluoric acid
HCN	Hydrocyanic acid
H_2S	Hydrogen sulfide
H_2O	water

Weak bases	
NH_3	Ammonia
C_5H_5N	Pyridine
NH_4OH	Ammonium hydroxide
N_2H_4	Hydrazine
$C_6H_5NH_2$	Aniline
H_2O	water

Click to advance

Summary

Important points to remember:

- p stands for –log. Therefore, pH = $-\log [H^+]$.
- pH + pOH = 14
- Strong acids and bases dissociate 100%. In the case of strong acids, the concentration of H^+ is equal to the concentration of the acid.
- Weak acids and bases do NOT dissociate 100%. We must use an ICE table to determine the equilibrium concentration of H^+ or OH^-, and then determine pH or pOH.



Click to advance

- **pKa** is the negative log of the dissociation constant, which is a measure of strength of an acid or base .

- When pKa = pH, there is equal concentration of acid and its conjugate base (e.g., acetic acid= acetate).

- pKa of an acid group is defined as the pH at which the protonated and unprotonated species are present in equal concentrations.

- pKa of amino acid side chains play an important role in defining the pH-dependent characteristics of a protein.
  - e.g. The pH-dependent activity of enzymes and the pH-dependence of protein stability are determined by the pKa values of amino acid side chain .

- Most drugs are either weak acids or weak bases.
  - Aspirin is a weak acid with a pK 3.5. Thus, this drug will be protonated (COOH) and uncharged in the stomach which has a pH around 2.0. Uncharged drugs easily cross the cell membranes and shows their effects (e.g., in the case of aspirin, acetylating target proteins and enzymes).

- If pH values < pKa, the compound is protonated
- If pH values > pKa, the compound is deprotonated
- Let's give acetic acid (CH_3COOH) which has pKa 4.76 as the examle:
- At pH<4.76, it is mostly found in CH_3COOH form (i.e., acetic acid)
- At pH> 4.76, it is mostly found in CH_3COO^- form (i.e., acetate)
- At pH= 4.76, the concentration of CH_3COOH is equal to CH_3COO^- (Buffer)

Buffers

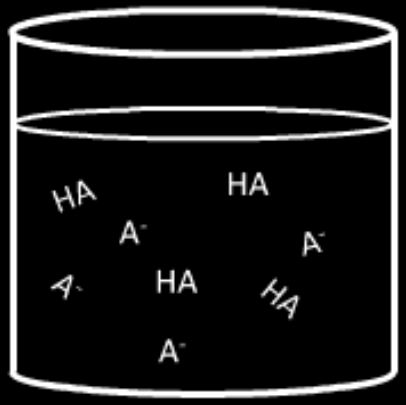
A ***buffer*** is a solution that resists changes in pH when small amounts of acid or base are added to it. How does it do this?

Buffers contain **BOTH** a weak acid *AND* its conjugate base (OR a weak base *AND* its conjugate acid).

Recall that conjugate acid/base pairs differ by only one H^+!

In a solution containing a conjugate acid/base PAIR, one or the other can absorb any strong acid or base that we add, like so:

If we add a small amount of strong acid to this solution, it will react to completion with A^- to form a small amount more of HA.



HA represents a generic weak acid & A^- represents its conjugate base

$$H^+ + A^- \longrightarrow HA$$

This reaction goes 100% because H+ is a strong acid!

Click to advance

A ***buffer*** is a solution that resists changes in pH when small amounts of acid or base are added to it. How does it do this?

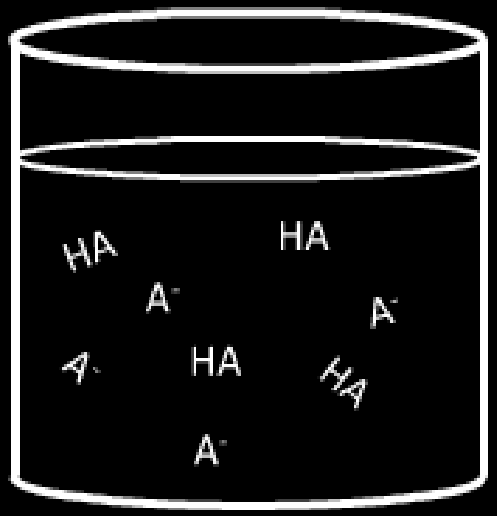
Buffers contain **BOTH** a weak acid *AND* its conjugate base (OR a weak base *AND* its conjugate acid).

Recall that conjugate acid/base pairs differ by only one H^+!

In a solution containing a conjugate acid/base PAIR, one or the other can absorb any strong acid or base that we add, like so:

$$OH^- + HA \longrightarrow A^- + H_2O$$

This reaction goes 100% because OH^- is a strong base!



HA represents a generic weak acid & A^- represents its conjugate base

If we add a small amount of strong base to this solution, it will react to completion with HA to form a small amount more of A^-.

Either way, we have not significantly changed the composition of our solution through the addition of strong acid or strong base.

Click to advance

- The quantitative relationship between the pH of the solution and the concentration of a weak acid and its conjugate base is described by :

Henderson -Hasselbalch equation

$$pH = pKa + \log \frac{(A^-)}{(HA)}$$

Henderson-Hasselbalch Equation

$$pH = pK_a + \log \frac{[base]}{[acid]}$$

This equation allows us to calculate the pH of our buffer, provided we know the concentration of our acid and base components

---

Calculate the pH of a solution containing 0.40 M HF ($K_a = 7.2 \times 10^{-4}$) and 0.20 M NaF:

1. Identify which species is your base, and which is your acid.

HF is our acid, because it can donate a proton

$$HF \rightleftharpoons H^+ + F^-$$

F^- is our base, because it can accept a proton

2. Now, let's fill in the Henderson-Hasselbalch equation with the information that we have:

$$pH = -\log (7.2 \times 10^{-4}) + \log \left(\frac{[0.20\ M]}{[0.40\ M]} \right)$$

$$pH = 3.14 - 0.30 = 2.84$$

Click to advance

Henderson-Hasselbalch Equation

The dissociation constant for a weak acid is:

$$K_a = \frac{[H^+][A^-]}{[HA]} = [H^+]\ \frac{[A^-]}{[HA]}$$

Take the log of each of the terms of this equation.

$$\log K_a = \log[H^+] + \log \frac{[A^-]}{[HA]}$$

Rearrange as follows (remember to change signs):

$$-\log[H^+] = -\log K_a + \log \frac{[A^-]}{[HA]}$$

Substitute pH for $-\log[H^+]$ and pK_a for $-\log K_a$.

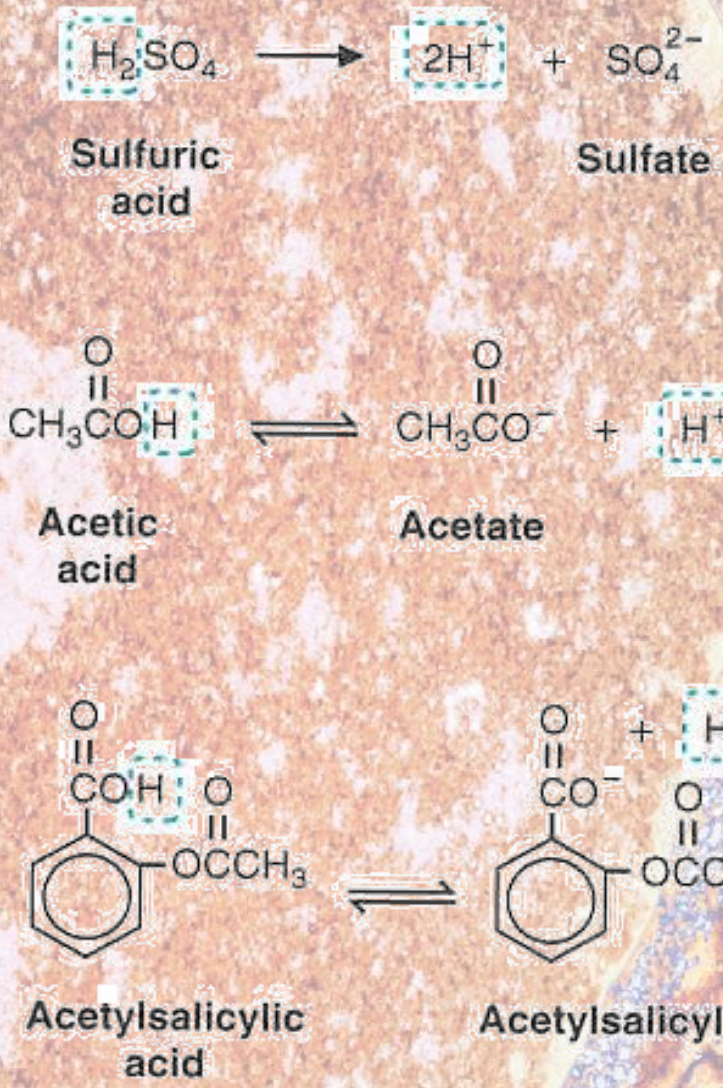
$$pH = pK_a + \log \frac{[A^-]}{[HA]}$$

$$K_a = \frac{[H^+]\ [A^-]}{[HA]}$$

Dissociation constant (K_a) for a weak acid. HA = the undissociated acid; A^- = the conjugate base.

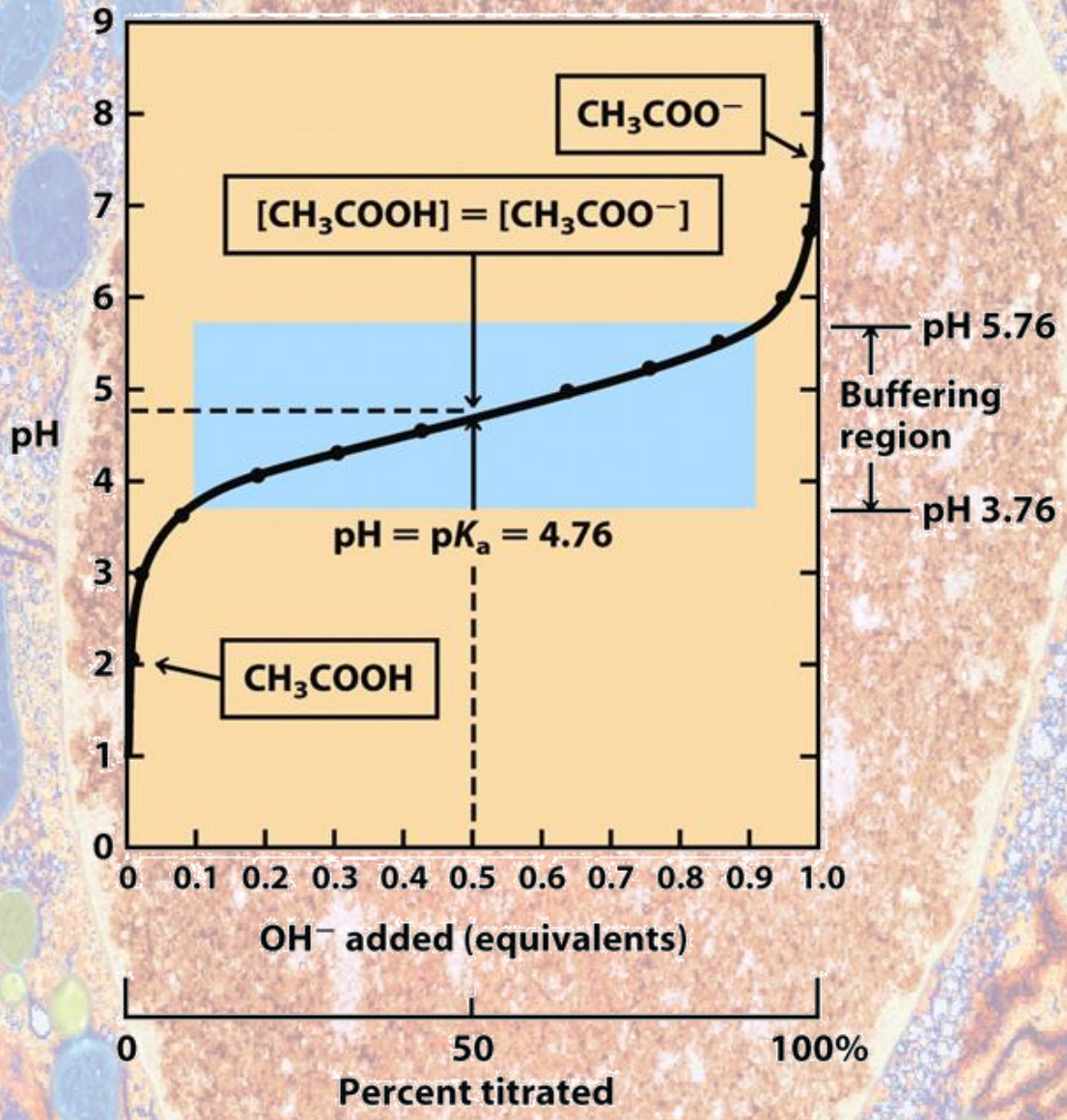
$$pH = pK_a + \log \frac{[A^-]}{[HA]}$$

Henderson-Hasselbalch equation. pK_a, analogous to pH, is the negative log of the dissociation constant, K_a. Note that when the concentrations of HA and A^- are equal, pH = pK_a.



Buffers stabilize pH

Buffers (pKa± 1pH)



- A reaction between CO_2 and H_2O forms carbonic acid, a weak acid that dissociates into carbonate and bicarbonate ions:

$$CO_2 + H_2O = H_2CO_3 = H^+ + HCO_3^- = 2H^+ + CO_3^{2-}$$

- If H+ is added to a carbonic acid (H_2CO_3) solution, it reacts with bicarbonate (CO_3^{2-}) and carbonate (HCO_3^-), which drives the reaction to the left.

- If OH^- is added, it removes H^+ from solution, which pulls the reaction to the right.

- Because carbonic acid is able to remove both excess H^+ and excess OH^- from aqueous solution, it is a **buffer**, or a substance that minimizes changes in pH.

- Weak acids and weak bases act as buffers in aqueous solution.

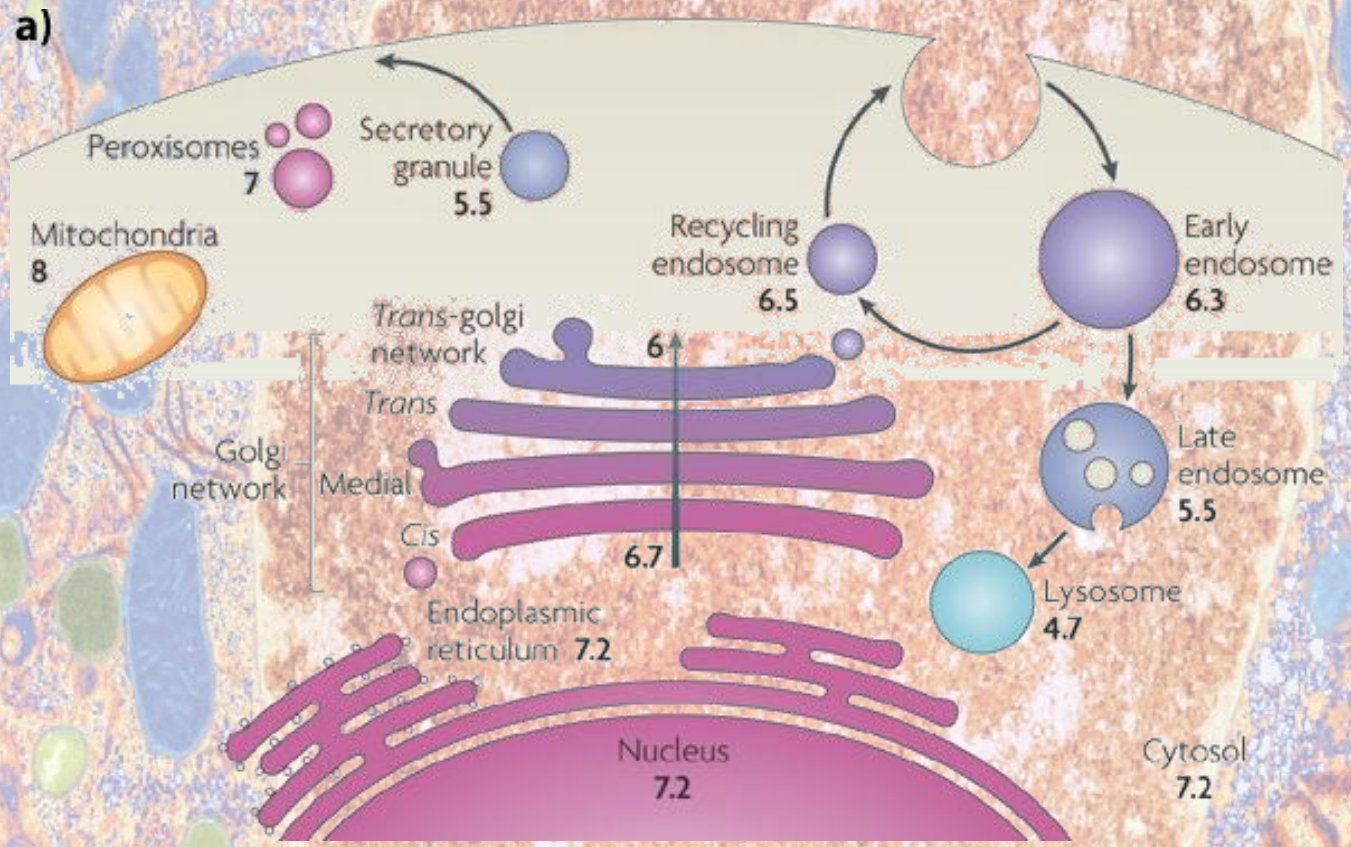
pH buffering in organisms

- Many enzymes are exquisitely sensitive to pH, and pH gradients across intracellular compartments are necessary for various cellular functions.

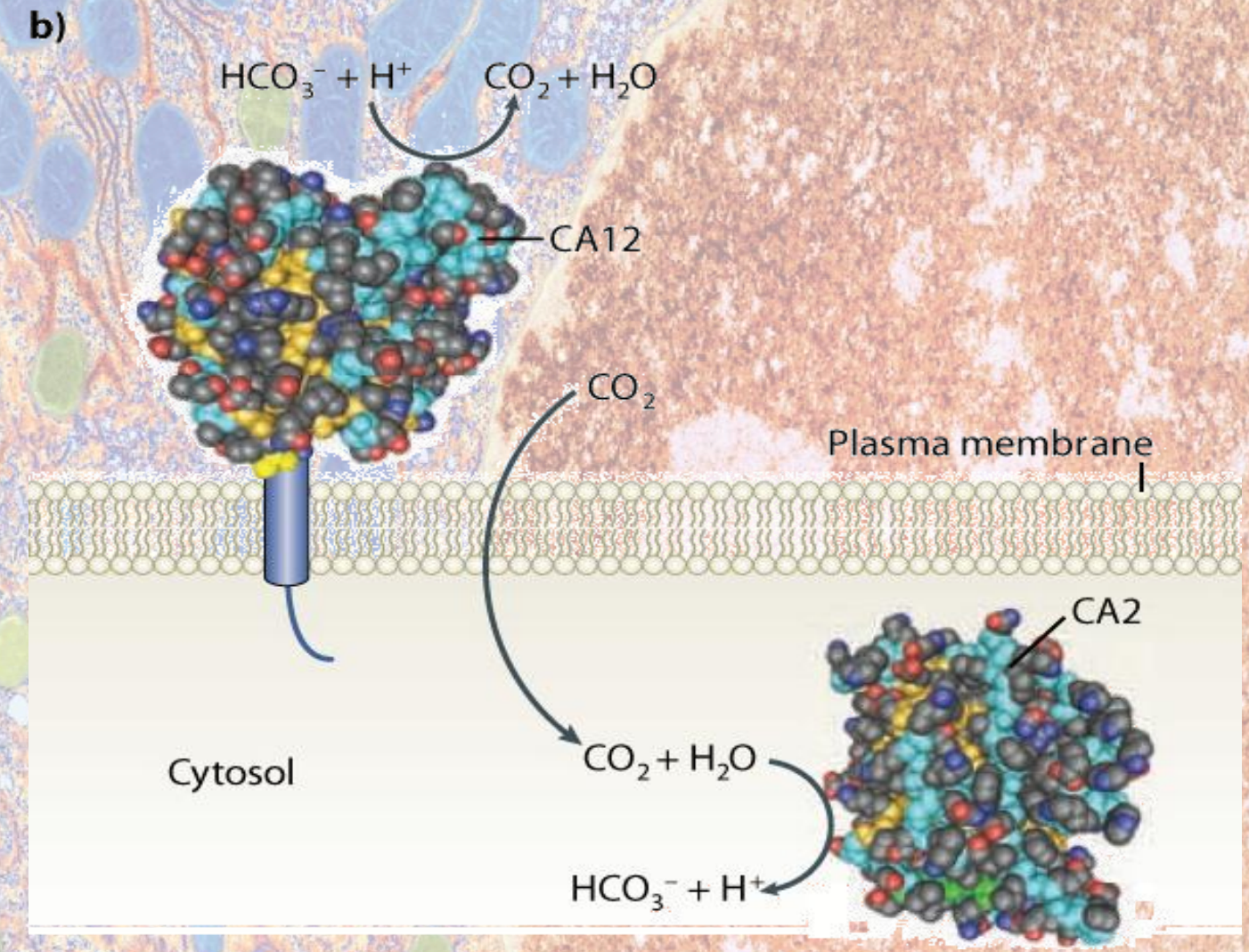
- Thus, intracellular pH is carefully regulated.

pH buffering in organisms

- Many enzymes are exquisitely sensitive to pH, and pH gradients across intracellular compartments are necessary for various cellular functions.
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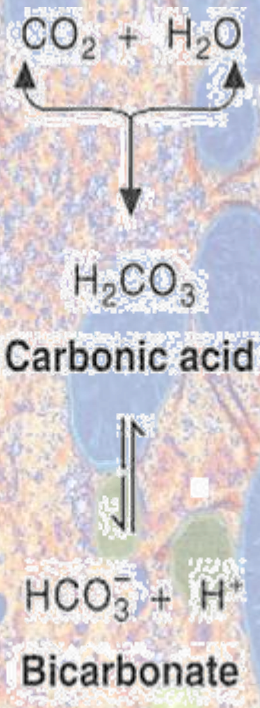


The cytosol and each intracellular compartment in a eukaryotic cell have a characteristic pH.



Carbonic anhydrase increases the speed of buffering by increasing the rate of conversion between carbon dioxide and carbonic acid. Two different forms of carbonic anhydrase (abbreviated CA) are shown: CA2 and CA12.

Physiological Buffers



Conversion of carbon dioxide to bicarbonate.

$$NH_4^+ \underset{}{\overset{pK_a = 9.25}{\rightleftharpoons}} NH_3 + H^+$$

Ammonium ion — Ammonia

Ammonium ions are acids, while ammonia (NH_3) is a base because it can accept a proton to form the acid, NH_4^+. Note that the pK_a for this dissociation is 9.25. Therefore, the acid form (NH_4^+) predominates at physiological pH.

PHOSPHATE BUFFER SYSTEM

$$H_3PO_4 \xrightarrow[pK = 2.0]{-H^+} H_2PO_4^- \xrightarrow[pK = 6.7]{-H^+} HPO_4^{2-} \xrightarrow[pK = 12]{-H^+} PO_4^{3-}$$

- Since protonation-deprotonation are responsible for the charges on biomacromolecules which maintain their solubility in water, their solubility is often lowest at their **isoelectric point pI,** the pH value at which the molecule has no net charge.

- Separation of plasma proteins by charge is done in this manner.

- When pH is kept higher then the isoelectric pH (pI), the proteins will have negative charge and so the proteins will move towards the positive electrode.

- Vice versa, the proteins will move towards the negative electrode.

What if we were to add 0.300 mol of NaOH to 2.0 L of the buffer on the previous page? How would we calculate the change in pH?

1. Identify which component of your buffer the NaOH will react with.

   NaOH is a ***STRONG BASE***, and therefore will react with our ***WEAK ACID***.

	OH^-	+ HF	⟶	F^-	+ H_2O
Before rxn	0.300 mol	2.0 L x 0.400 M = 0.800 mol		0.00 mol	
After rxn	0.300 mol – 0.300 mol = 0.000 mol	0.800 mol – 0.300 mol = 0.500 mol		0.300 mol	

After the reaction takes place, we have completely consumed the strong base (our limiting reactant), and produced an equal amount of F^-.

Our reaction has consumed 0.300 mol of HF, leaving us with 0.500 mol HF. We have produced 0.300 mol of F^-, which we must add to the F^- already in solution. How many total moles of F^- are in our buffer solution?

2.0 L x 0.200 M = 0.400 mol (originally in solution) + 0.300 mol (what we produced through reaction of HF with OH^-) = 0.700 mol F^- total

Click to advance

2. Now we can use the Henderson-Hasselbalch equation to solve for our new pH:

$$pH = pK_a + \log \frac{[base]}{[acid]}$$

$$pH = -\log (7.2 \times 10^{-4}) + \log \left(\frac{\frac{0.700 \text{ mol}}{\cancel{2.8 \text{ L}}}}{\frac{0.500 \text{ mol}}{\cancel{2.8 \text{ L}}}} \right)$$

$$= 3.29$$

Here we can see that it is the molar ratio between amount of acid and base in solution that matters, not necessarily the concentration, because the volume actually cancels out!

We can use the number of moles of acid and base ***instead*** of molarity in the H-H equation, as long as we are consistent.

It makes sense that our pH is increasing (from 2.84 to 3.29) because we are adding a strong base to our solution.

*Remember: There are **two** steps to solving a buffer problem when we add a strong base to a buffer.*

1. *The reaction of the STRONG base with the WEAK acid component of the buffer to produce a certain amount of the conjugate base. Add the amount of conjugate base produced in this reaction to the original amount of conjugate base in solution.*
2. *Use these values in the H-H equation to find the NEW pH.*

Click to advance

Buffer preparation

We know that a buffer *MUST* contain a conjugate acid/base pair. What other chemical features should we look for when we select a pair to use when preparing a buffer?

1. Buffers work best when the desired pH is as close to the pK_a of the weak acid component of the buffer as possible.

When pH = pK_a, the concentration of conjugate acid and base must be equal according to the H-H equation!

$$pH = pK_a + \log \frac{[base]}{[acid]}$$

log of one is equal to zero, therefore pH equals pK_a!

For a discussion of why this is true, please see p. 724 in Zumdahl, 9th ed!

2. The concentration of the buffer components should be large compared to the amount of acid or base that you are adding to the solution.

If the concentration of the buffer components is large, it can absorb more strong acid or base before we see an appreciable change in the solution pH!

Click to advance

Buffer preparation

Say that we would like to prepare a buffer with a pH of 4.85. Which of the following chemical components should we use?

Name	Formula	K_a value
Hydrofluoric acid	HF	7.2×10^{-4}
Nitrous acid	HNO_2	4.0×10^{-4}
Propanoic acid	$HC_3H_5O_2$	1.3×10^{-5}
Hypochlorous acid	HOCl	3.5×10^{-8}
Hydrocyanic acid	HCN	6.2×10^{-10}

Step 1. Calculate the pK_a of the possible weak acids from the K_a values in the table.

→ $pK_a = 3.14$

→ $pK_a = 3.40$

→ $pK_a = 4.89$

→ $pK_a = 7.46$

→ $pK_a = 9.21$

*There are **two** qualities that we are looking for when we prepare a buffer:*

1. *The pH of our solution should be as close to the pK_a of the weak acid as possible: recall that "p" stands for "–log", so pK_a means $-\log(K_a)$.*
2. *More concentrated solutions to absorb greater amounts of strong acid and base without changing the pH radically.*

Click to advance

Buffer preparation

Say that we would like to prepare a buffer with a pH of 4.85. Which of the following chemical components should we use?

Name	Formula	K_a value
Hydrofluoric acid	HF	7.2×10^{-4}
Nitrous acid	HNO_2	4.0×10^{-4}
Propanoic acid	$HC_3H_5O_2$	1.3×10^{-5}
Hypochlorous acid	HOCl	3.5×10^{-8}
Hydrocyanic acid	HCN	6.2×10^{-10}

Step 1. Calculate the pK_a of the possible weak acids from the K_a values in the table.

→ $pK_a = 3.14$

→ $pK_a = 3.40$

→ $pK_a = 4.89$

→ $pK_a = 7.46$

→ $pK_a = 9.21$

Which weak acid should we start with, according to our calculated pK_a values?

Our desired pH, 4.85, is closest to propanoic acid, with a pK_a of 4.89.

Click to advance

Buffer preparation

Now we know we need propanoic acid, $HC_3H_5O_2$, but this is only half of our buffer. Every buffer contains *TWO* components. What is the other component that we need?

H^+ NaCl $NaC_3H_5O_2$

H_2O OH^- HNO_2

Recall that $NaC_3H_5O_2$ is a salt, and therefore will dissociate completely in water, producing Na^+ and $C_3H_5O_2^-$.

Conjugate base of propanoic acid

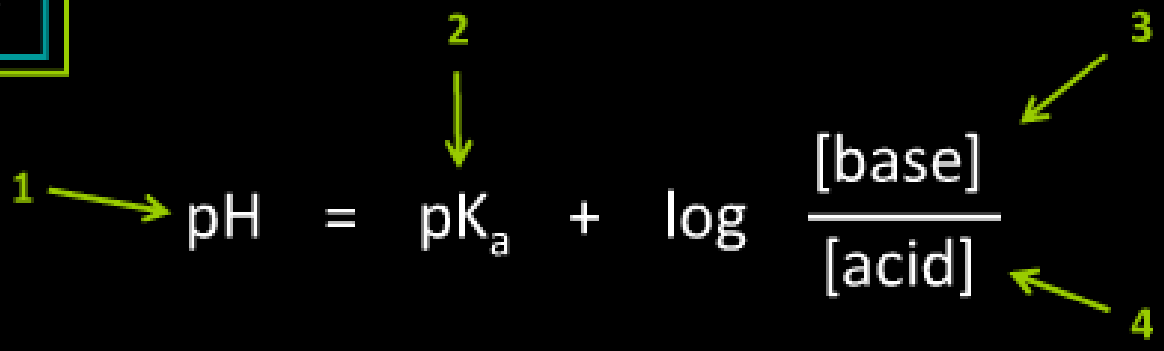
Conjugate acid of a strong base, therefore no acidic or basic properties

Now we have our weak acid/base conjugate pair, $HC_3H_5O_2$ and $C_3H_5O_2^-$. Which solution would act as a better buffer, a solution with 1 M of each or a solution containing 0.3 M each?

A solution containing 1 M $HC_3H_5O_2$ and $C_3H_5O_2^-$ will be able to absorb more strong acid or base before we see a significant change in pH.

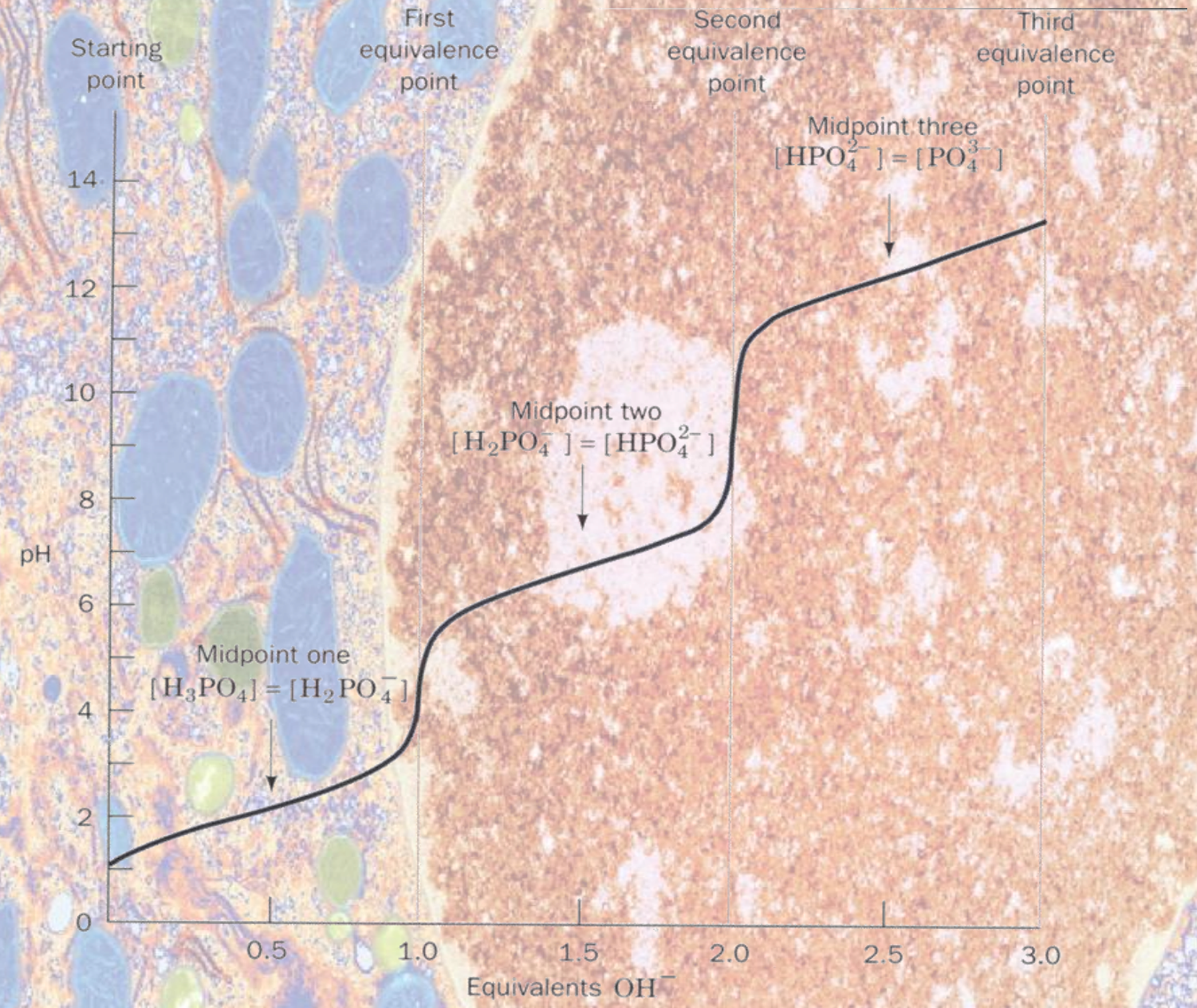
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Summary



1. Buffers are solutions that consist of a weak acid and its conjugate base (or a weak base and its conjugate acid), and can resist changes in pH.
2. There are four possible values to solve for, if you are given information required to find the other three, in the Henderson-Hasselbalch equation.
   - *For example*: Given the desired pH, the K_a and the acid concentration, we can find the necessary base concentration.
3. If we add a small amount of base or acid to a buffered solution, there are two steps to finding the new pH:
   - Determine how much conjugate base (or acid) is produced through reaction of the buffer components with the strong acid or base. Add this to the amount already in solution.
   - Use these new values in the Henderson-Hasselbalch equation to determine the new pH.

Titration curves

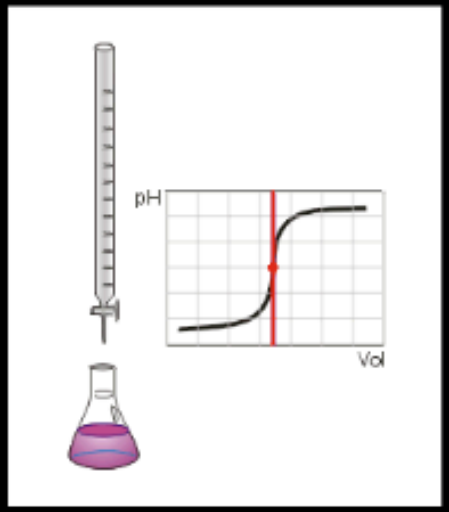


Titrations- Strong Acids and Strong Bases

Acid/base titration is a method by which we can determine the ***unknown*** concentration of an acid or base by neutralization with a base or acid of ***known*** concentration.

Any titration problem can be reduced to a series of acid/base problems. The most important part is understanding which species exist in solution at each step in the titration.

What does a titration look like in the laboratory?



The solution with the unknown concentration (*analyte*) is placed in a flask, while the solution with a known concentration (*titrant*) is placed in a buret. The titrant is slowly added to the flask. You may also add an *indicator* to the flask, which is a chemical compound that changes color near the endpoint of the titration as a visual cue that the titration is complete.

When dealing with strong acids and strong bases, it is important to keep in mind that these compounds dissociate *completely* in solution.

Click to advance

The net ionic reaction for a strong acid / strong base titration is:

$$H^+ (aq) + OH^- (aq) \longrightarrow H_2O (l)$$

To calculate the concentration of H^+ at each step in the titration, we need two values:

1) The number of moles of H^+ (mol) in solution
2) The total volume of the solution (L)

} Recall that pH is defined as −log of $[H^+]$

Example. Let's titrate 50.0 mL of 0.300 M HCl with 0.200 M NaOH, and observe the change in pH.

Step 1. No NaOH has been added.

HCl is a strong acid, and completely dissociates in water. The solution contains the following major species:

H^+ Cl^- H_2O

Before we add any NaOH, we only need to calculate the pH of a strong acid. Since a 0.300 M HCl solution contains 0.300 M H^+:

$[H^+] = 0.300$ M ⟶ pH = −log (0.300) ⟶ **pH = 0.523**

Click to advance

Example. Let's titrate 50.0 mL of 0.300 M HCl with 0.200 M NaOH.

Step 2. 20.0 mL of 0.200 M NaOH has been added.

Which of these ions will react with each other?

Before any reaction occurs, the major species present are: H^+ Cl^- H_2O Na^+ OH^-

	H^+ *(aq)* + OH^- *(aq)*		$\longrightarrow$ H_2O *(l)*
Before rxn	0.050 L x 0.300 M = 0.015 mol	0.020 L x 0.200 M = 0.004 mol	
After rxn	0.015 mol – 0.004 mol = 0.011 mol	0.004 mol – 0.004 mol = 0.00 mol	

After the reaction occurs, the major species present are: H^+ Cl^- H_2O Na^+

All of the OH^- has been consumed in the reaction with H^+!!

$$[H^+] = \frac{\text{number of moles of } H^+ \text{ remaining}}{\text{total volume of solution (L)}} = \frac{0.011 \text{ mol}}{(0.050 \text{ L} + 0.020 \text{ L})} = 0.157 \text{ M}$$

$pH = -\log(0.157) \longrightarrow pH = 0.804$

Click to advance

Example. Let's titrate 50.0 mL of 0.300 M HCl with 0.200 M NaOH.

Step 3. 40.0 mL of 0.200 M NaOH has been added.

Which of these ions will react with each other?

Before any reaction occurs, the major species present are: H^+ Cl^- H_2O Na^+ OH^-

	$H^+(aq)$ +	$OH^-(aq)$ ⟶	$H_2O(l)$
Before rxn	0.050 L x 0.300 M = 0.015 mol	0.040 L x 0.200 M = 0.008 mol	
After rxn	0.015 mol – 0.008 mol = 0.007 mol	0.008 mol – 0.008 mol = 0.00 mol	

After the reaction occurs, the major species present are: H^+ Cl^- H_2O Na^+

All of the OH^- has been consumed in the reaction with H^+!!

$$[H^+] = \frac{\text{number of moles of } H^+ \text{ remaining}}{\text{total volume of solution (L)}} = \frac{0.007 \text{ mol}}{(0.050 \text{ L} + 0.040 \text{ L})} = 0.0778 \text{ M}$$

$pH = -\log(0.0778) \longrightarrow pH = 1.11$

Click to advance

Example. Let's titrate 50.0 mL of 0.300 M HCl with 0.200 M NaOH.

Step 3. 40.0 mL of 0.200 M NaOH has been added.

Which of these ions will react with each other?

Before any reaction occurs, the major species present are: H^+ Cl^- H_2O Na^+ OH^-

	$H^+(aq)$ +	$OH^-(aq)$ ⟶	$H_2O(l)$	
Before rxn	0.050 L x 0.300 M = 0.015 mol	0.040 L x 0.200 M = 0.008 mol		
After rxn	0.015 mol – 0.008 mol = 0.007 mol	0.008 mol – 0.008 mol = 0.00 mol		

After the reaction occurs, the major species present are: H^+ Cl^- H_2O Na^+

All of the OH^- has been consumed in the reaction with H^+!!

$$[H^+] = \frac{\text{number of moles of } H^+ \text{ remaining}}{\text{total volume of solution (L)}} = \frac{0.007 \text{ mol}}{(0.050 \text{ L} + 0.040 \text{ L})} = 0.0778 \text{ M}$$

$pH = -\log(0.0778) \longrightarrow pH = 1.11$

Click to advance

Example. Let's titrate 50.0 mL of 0.300 M HCl with 0.200 M NaOH.

Step 4. 75.0 mL of 0.200 M NaOH has been added.

Which of these ions will react with each other?

Before any reaction occurs, the major species present are: H^+ Cl^- H_2O Na^+ OH^-

	$H^+(aq)$ +	$OH^-(aq)$ →	$H_2O(l)$
Before rxn	0.050 L x 0.300 M = 0.015 mol	0.075 L x 0.200 M = 0.015 mol	
After rxn	0.015 mol – 0.015 mol = 0.00 mol	0.015 mol – 0.015 mol = 0.00 mol	

After the reaction occurs, the major species present are: Cl^- H_2O Na^+

Since Na^+ has no acidic or basic properties, and Cl^- is the conjugate base of a strong acid, neither one affects pH. The pH is determined by water, and the solution is neutral!

pH = 7.00

*This is a special point in the titration! We have added **exactly** enough OH^- to react with the H^+ that we started with.*

This is called the stoichiometric point or equivalence point.

Click to advance

Example. Let's titrate 50.0 mL of 0.300 M HCl with 0.200 M NaOH.

Step 5. 100.0 mL of 0.200 M NaOH has been added.

Which of these ions will react with each other?

Before any reaction occurs, the major species present are: H^+ Cl^- H_2O Na^+ OH^-

	$H^+(aq)$ +	$OH^-(aq)$ ⟶	$H_2O(l)$
Before rxn	0.050 L x 0.300 M = 0.015 mol	0.100 L x 0.200 M = 0.020 mol	
After rxn	0.015 mol – 0.008mol = 0.00 mol	0.020 mol – 0.015 mol = 0.005 mol	

After the reaction occurs, the major species present are: Cl^- H_2O Na^+ OH^-

Now we have added ***more*** than enough OH^- to completely react with the H^+ that we began with!!

$$[OH^-] = \frac{\text{number of moles of excess } OH^-}{\text{total volume of solution (L)}} = \frac{0.005 \text{ mol}}{(0.050 \text{ L} + 0.040 \text{ L})} = 0.033 \text{ M}$$

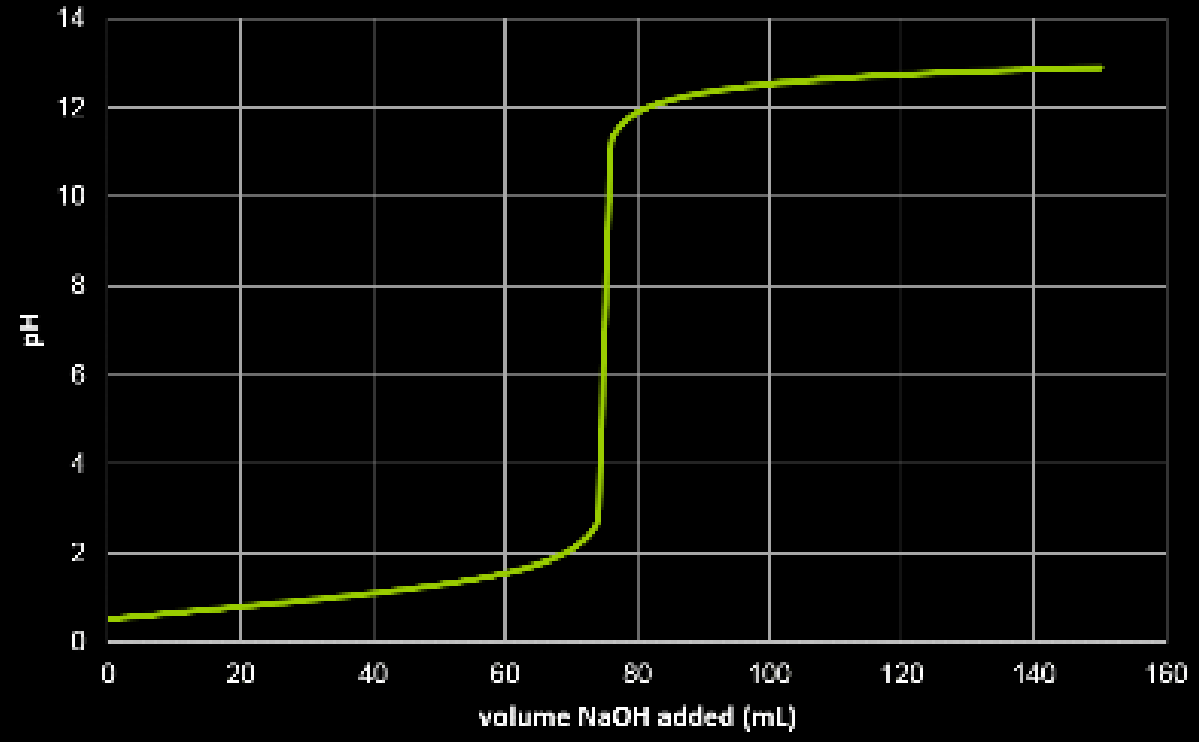
$pOH = -\log(0.033) \longrightarrow pOH = 1.48 \longrightarrow$ **pH = 12.52**

Click to advance

At each step in this titration, we did two things:

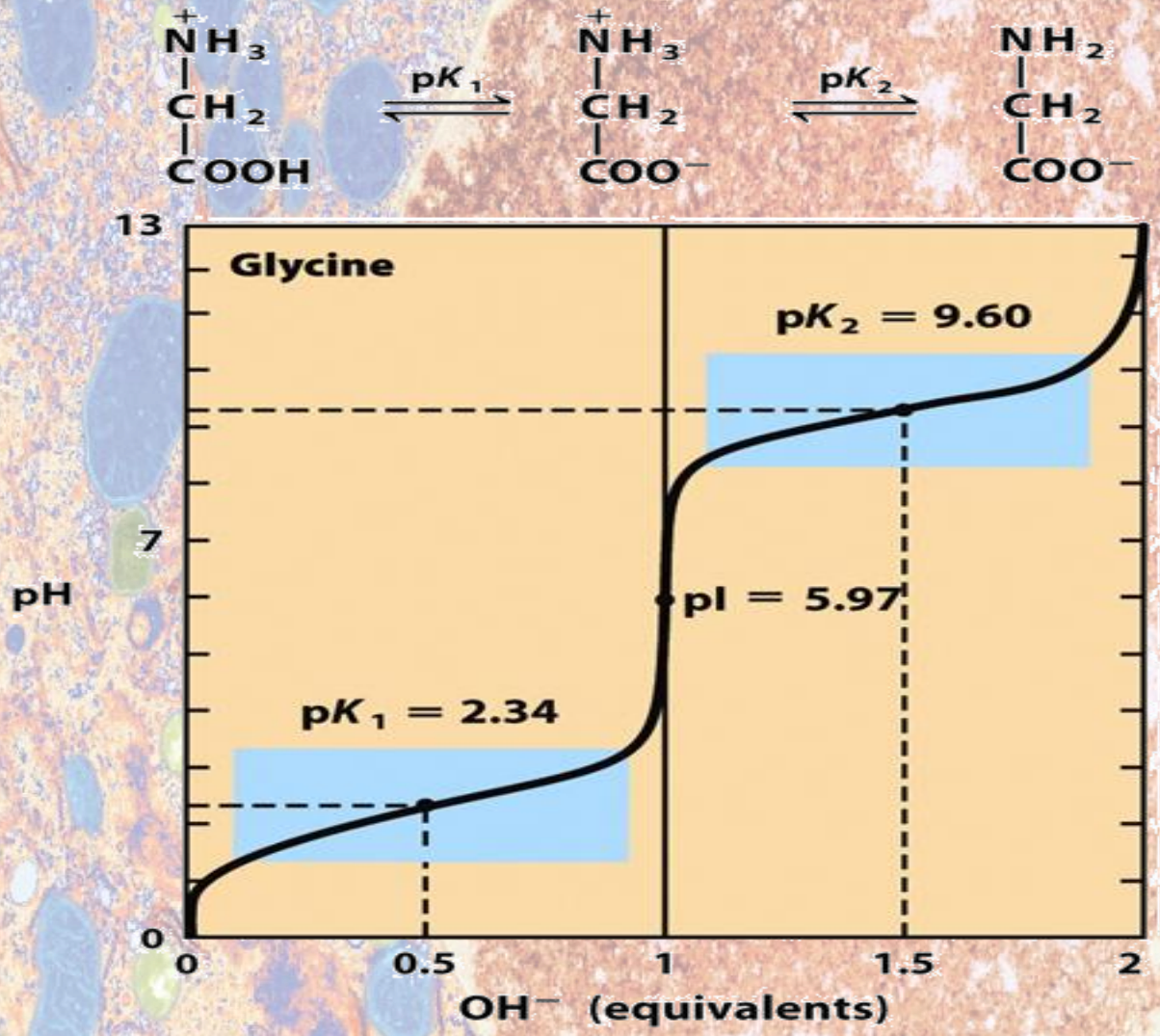
1) Used stoichiometry to determine how many moles of H^+ reacted with OH^-.
2) Added the volume of OH^- to the original volume to find the new total volume of solution. With these two values, we calculated the new $[H^+]$.

We can graph these data points, with pH on the *y*-axis and amount of NaOH added on the *x*-axis, to get a ***titration curve***. The shape of the titration curve can give us information about whether we are titrating strong or weak acids with strong or weak bases, and how many acidic protons the acids have, etc. Using the data from this titration:



Volume NaOH (mL)	pH
0.00	0.523
20.0	0.804
40.0	1.11
75.0	7.00
100.0	12.5

Titrations- Weak Acids and Strong Bases



Weak acid / strong base titrations

The net ionic reaction for a weak acid / strong base titration is:

$$HA\,(aq) + OH^-\,(aq) \rightleftharpoons A^-\,(aq) + H_2O\,(l)$$

There are two steps to finding the new pH of a weak acid solution after we have added OH^-:

1) A stoichiometry problem – the rxn of OH^- with the weak acid goes to completion to form the conjugate base plus some amount of remaining weak acid
2) An equilibrium problem – the position of the weak acid equilibrium must be determined to calculate pH

Example. Let's titrate 50.0 mL of 0.200 M HClO with 0.100 M NaOH.

Step 1. No NaOH has been added.

Since HClO is a weak acid, it is partially dissociated, and the solution contains the following major species:

H^+ ClO^- $HClO$ H_2O

Before we have added OH^-, this is just a weak acid problem.

Click to advance

Weak acid / strong base titrations

Example. Let's titrate 50.0 mL of 0.200 M HClO with 0.100 M NaOH.

Prepare an ICE table to calculate the equilibrium concentration of H^+. The K_a of HClO is 3.0×10^{-8}.

$$HClO\ (aq) \rightleftharpoons H^+\ (aq) + ClO^-\ (aq)$$

HClO (aq): weak acid

	HClO (aq)		H^+ (aq)	ClO^- (aq)
I	0.200		0	0
C	- x		+ x	+ x
E	0.200 - x		+ x	+ x

$$K_a = \frac{[H^+]\,[ClO^-]}{[HClO]} = \frac{[x]\,[x]}{[0.200]} = 3.0 \times 10^{-8}$$

Multiplying by 0.200 to isolate x^2: $x^2 = 6.0 \times 10^{-9}$

Taking the square root of both sides: $x = 7.75 \times 10^{-5}$ M

$x = [H^+]$

$pH = 4.11$

Click to advance

Weak acid / strong base titrations

Step 2. *Continuing with the weak acid calculations from the previous slide.*

Prepare an ICE table to calculate the equilibrium concentration of H^+. The K_a of HClO is 3.0×10^{-8}.

$$HClO\ (aq) \rightleftharpoons H^+\ (aq) + ClO^-\ (aq)$$

weak acid

I	$\frac{0.009\ mol}{(0.050\ L + 0.010\ L)}$	~0	$\frac{0.001\ mol}{(0.050\ L + 0.010\ L)}$
C	$-x$	$+x$	$+x$
E	$\frac{0.009\ mol}{0.060\ L} - x$	$+x$	$\frac{0.001\ mol}{0.060\ L} + x$

$$K_a = \frac{[H^+]\,[ClO^-]}{[HClO]} = \frac{(x)\left(\frac{0.001\ mol}{0.060\ L} + x\right)}{\left(\frac{0.009\ mol}{0.060\ L} - x\right)} = 3.0 \times 10^{-8}$$

Cancel common terms in the numerator and denominator.

Multiplying both sides by 0.009 / 0.001 to isolate x: $x = 2.7 \times 10^{-7}\ M$

$x = [H^+]$

$pH = -\log(2.7 \times 10^{-7}) = 6.57$

Click to advance

Weak acid / strong base titrations

Example. Let's titrate 50.0 mL of 0.200 M HClO with 0.100 M NaOH.

Step 2. 10.0 mL of 0.100 M NaOH has been added.

Which of these ions will react with each other?

Before any reaction occurs, the major species present are: HClO, H_2O, Na^+, OH^-

	$HClO\ (aq)$ +	$OH^-\ (aq)$ ⟶		$ClO^-\ (aq)$ +	$H_2O\ (l)$
Before rxn	0.050 L x 0.200 M = 0.010 mol	0.010 L x 0.100 M = 0.001 mol		0.00 mol	
After rxn	0.010 mol – 0.001 mol = 0.009 mol	0.001 mol – 0.001 mol = 0.00 mol		0.001 mol	

After the reaction occurs, the major species present are: HClO, ClO^-, ~~H_2O~~, ~~Na^+~~

All of the OH^- has been consumed in the reaction with H^+!!

$$HClO\ (aq) \rightleftharpoons H^+\ (aq) + ClO^-\ (aq)$$

Now we must write an equation for the chemical equilibrium that exists among the remaining ions that will determine the pH of the solution.

$$K_a = \frac{[H^+]\,[ClO^-]}{[HClO]}$$

This is just a buffer problem – we have a weak acid, and we have generated its conjugate base through the reaction of the weak acid with a strong base.

Click to advance

Weak acid / strong base titrations

Example. Let's titrate 50.0 mL of 0.200 M HClO with 0.100 M NaOH.

Step 3. 50.0 mL of 0.100 M NaOH has been added.

Which of these ions will react with each other?

Before any reaction occurs, the major species present are: HClO, H_2O, Na^+, OH^-

	$HClO\ (aq)$ +	$OH^-\ (aq)$ ⟶		$ClO^-\ (aq)$ +	$H_2O\ (l)$
Before rxn	0.050 L x 0.200 M = 0.010 mol	0.050 L x 0.100 M = 0.005 mol		0.00 mol	
After rxn	0.010 mol – 0.005 mol = 0.005 mol	0.005 mol – 0.005 mol = 0.00 mol		0.005 mol	

After the reaction occurs, the major species present are: HClO, ClO^-, ~~H_2O~~, ~~Na^+~~

All of the OH^- has been consumed in the reaction with H^+!!

$$HClO\ (aq) \rightleftharpoons H^+\ (aq) + ClO^-\ (aq)$$

Now we must write an equation for the chemical equilibrium that exists among the remaining ions that will determine the pH of the solution.

$$K_a = \frac{[H^+]\,[ClO^-]}{[HClO]}$$

This is called the **HALFWAY POINT**. We have added exactly enough base to consume half of the original amount of acid.

Click to advance

Weak acid / strong base titrations

Step 3. *Continuing with the halfway point calculations from the previous slide.*

Prepare an ICE table to calculate the equilibrium concentration of H^+. The K_a of HClO is 3.0×10^{-8}.

$$HClO\ (aq) \rightleftharpoons H^+\ (aq) + ClO^-\ (aq)$$

weak acid

	$HClO\ (aq)$		$H^+\ (aq)$	$ClO^-\ (aq)$
I	$\frac{0.005\ mol}{(0.050\ L + 0.050\ L)}$		~0	$\frac{0.005\ mol}{(0.050\ L + 0.050\ L)}$
C	$-x$		$+x$	$+x$
E	$\frac{0.005\ mol}{0.100\ L} - x$		$+x$	$\frac{0.005\ mol}{0.100\ L} + x$

$$K_a = \frac{[H^+]\,[ClO^-]}{[HClO]} = \frac{(x)\left(\frac{\cancel{0.005\ mol}}{\cancel{0.100\ L}} + x\right)}{\left(\frac{\cancel{0.005\ mol}}{\cancel{0.100\ L}} - x\right)} = 3.0 \times 10^{-8}$$

Cancel common terms in the numerator and denominator.

In this case, x is equal to K_a, and ***pH is equal to pK_a!***

$x = 3.0 \times 10^{-8}$ M

$$pH = -\log(3.0 \times 10^{-8}) = 7.52$$

At the halfway point, the moles of base added equals ½ of the original number of moles acid present.

Click to advance

Weak acid / strong base titrations

Example. Let's titrate 50.0 mL of 0.200 M HClO with 0.100 M NaOH.

Step 4. 100.0 mL of 0.100 M NaOH has been added.

Which of these ions will react with each other?

Before any reaction occurs, the major species present are: HClO H_2O Na^+ OH^-

	$HClO\ (aq)$	+ $OH^-\ (aq)$	⟶	$ClO^-\ (aq)$	+ $H_2O\ (l)$
Before rxn	0.050 L x 0.200 M = 0.010 mol	0.100 L x 0.100 M = 0.010 mol		0.00 mol	
After rxn	0.010 mol – 0.010 mol = 0.00 mol of H^+	0.010 mol – 0.010 mol = 0.00 mol		0.010 mol of ClO^-	

There are still 0.010 mol of ClO^- left: OH^- reacts ***ONLY*** with H^+, leaving ClO^- behind!!

After the reaction occurs, the major species present are: ClO^- H_2O Na^+

All of the H^+ and OH^- have reacted to form H_2O!!

Click to advance

Weak acid / strong base titrations

Example. Let's titrate 50.0 mL of 0.200 M HClO with 0.100 M NaOH.

Step 4. 100.0 mL of 0.100 M NaOH has been added.

Which of these ions will react with each other?

Before any reaction occurs, the major species present are: HClO, H_2O, Na^+, OH^-

	$HClO\ (aq)$	+ $OH^-\ (aq)$	⟶	$ClO^-\ (aq)$	+ $H_2O\ (l)$
Before rxn	0.050 L x 0.200 M = 0.010 mol	0.100 L x 0.100 M = 0.010 mol		0.00 mol	
After rxn	0.010 mol – 0.010 mol = 0.00 mol of H^+	0.010 mol – 0.010 mol = 0.00 mol		0.010 mol of ClO^-	

There are still 0.010 mol of ClO^- left: OH^- reacts *ONLY* with H^+, leaving ClO^- behind!!

After the reaction occurs, the major species present are: ClO^-, ~~H_2O~~, ~~Na^+~~

All of the H^+ and OH^- have reacted to form H_2O!!

$$ClO^-\ (aq) + H_2O\ (l) \rightleftharpoons HClO\ (aq) + OH^-\ (aq)$$

The pH of the solution is now determined by the conjugate base of the weak acid.

$$K_b = \frac{[HClO]\,[OH^-]}{[ClO^-]}$$

This is called the **EQUIVALENCE POINT**. We have added exactly enough base to react with the original amount of acid.

Click to advance

Weak acid / strong base titrations

Step 4. *Continuing with the equivalence point calculations from the previous slide.*

Prepare an ICE table to calculate the equilibrium concentration of OH^-. The K_a of HClO is 3.0×10^{-8}.

$$ClO^-\,(aq) + H_2O\,(l) \rightleftharpoons HClO\,(aq) + OH^-\,(aq)$$

I	$\frac{0.010\ mol}{(0.050\ L + 0.100\ L)}$			~0	~0
C	- x			+ x	+ x
E	$\frac{0.010\ mol}{0.150\ L}$ - x			+ x	+ x

$$K_b = \frac{[HClO]\,[OH^-]}{[ClO^-]} = \frac{K_w}{K_a} = \frac{1 \times 10^{-14}}{3.0 \times 10^{-8}} = 3.3 \times 10^{-7}$$

$$K_b = \frac{[HClO]\,[OH^-]}{[ClO^-]} = \frac{[x]\,[x]}{0.0667 - x} = 3.3 \times 10^{-7}$$

$$pH = 10.17$$

Multiplying by 0.0667 to isolate x^2: $x^2 = 2.2 \times 10^{-8}$

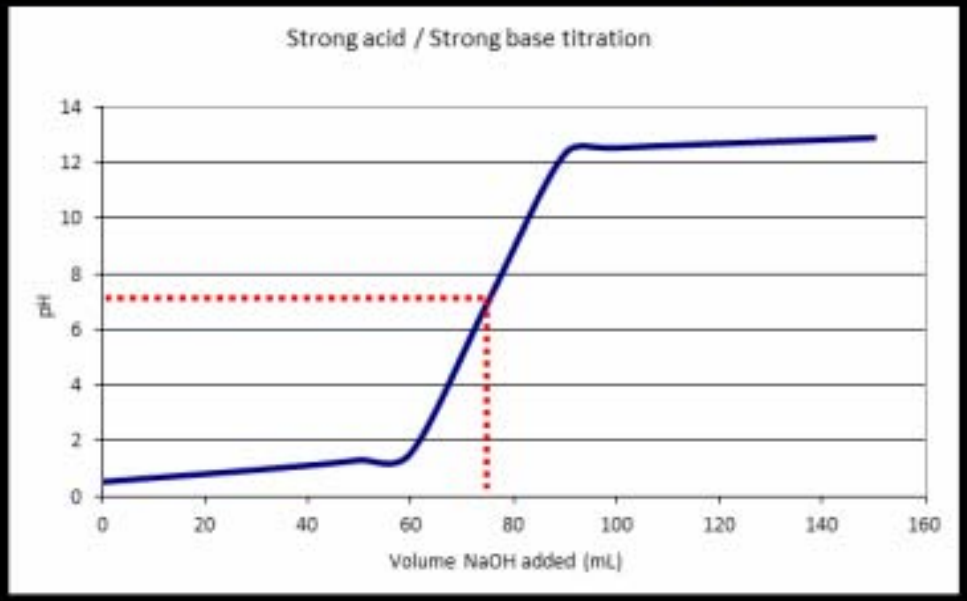
Taking the square root of both sides: $x = 1.48 \times 10^{-4}\ M$

$x = [OH^-]$

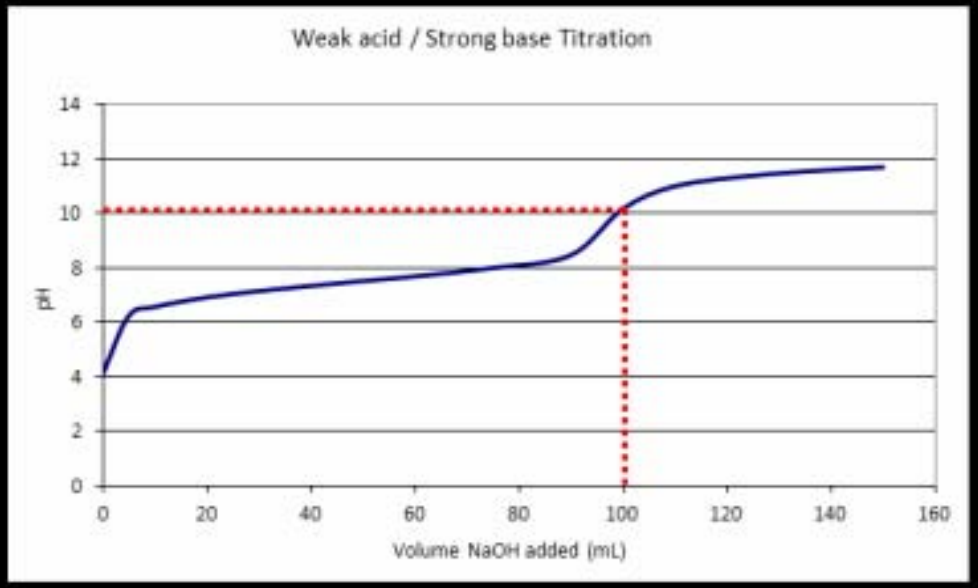
$$pOH = 3.83$$

Click to advance

Weak acid / strong base titrations



We can graph these points, with pH on the y-axis and amount of NaOH added on the x-axis, to get a titration curve. We can see that the shape of the curve has changed drastically from the strong acid / strong base titration that we performed in an earlier CLC tutorial.



For the weak acid / strong base titration, we begin at a higher pH, and our equivalence point is greater than 7.

Click to advance

Henderson-Hasselbalch equation

Finally, it is important to point out that the Henderson-Hasselbalch equation can be used at any point in the titration where we have both the weak acid and its conjugate base in solution – the definition of a buffer!

$$pH = pK_a + \log\left(\frac{[base]}{[acid]}\right)$$

concentration of the conjugate base

concentration of the weak acid

Let's think about which steps in the titration the H-H equation could be applicable to. . .

Step 1. No NaOH has been added. — $HClO$

Step 2. 10.0 mL of 0.100 M NaOH has been added. — $HClO$ ClO^-

Step 3. 50.0 mL of 0.100 M NaOH has been added. — $HClO$ ClO^-

Step 4. 100.0 mL of 0.100 M NaOH has been added. — ClO^-

These two steps are where we have both the weak acid and we have generated some of its conjugate base through reaction with a strong base

Click to advance

Henderson-Hasselbalch equation

$$pH = pK_a + \log\left(\frac{[base]}{[acid]}\right)$$

concentration of the conjugate base

concentration of the weak acid

For example, in step 2, 10.0 mL of 0.100 M NaOH has been added. We have created 0.001 mol of ClO^-, which means that we have 0.009 mol of HClO remaining. Recall that the K_a of HClO is 3.0×10^{-8}.

$$pH = -\log(3.0 \times 10^{-8}) + \log\left(\frac{\frac{0.001\ \text{mol}}{(0.050\ \text{L} + 0.010\ \text{L})}}{\frac{0.009\ \text{mol}}{(0.050\ \text{L} + 0.010\ \text{L})}}\right)$$

Cancel common terms in the numerator and denominator.

$$pH = 6.57$$

the same pH that we arrived at using our ICE table method earlier!

Click to advance

Some pH problems

1. Calculate the ratio of $HPO_4^{2-}/H_2PO_4^-$ ($pK = 6.7$) at pH 5.7, 6.7, and 8.7.

   Solution:

   $$pH = pK + \log [HPO_4^{2-}]/[H_2PO_4^-]$$

   $$5.7 = 6.7 + \log \text{ of ratio; rearranging}$$

   $$5.7 - 6.7 = -1 = \log \text{ of ratio}$$

   The antilog of $-1 = 0.1$ or $1/10$. Thus, $HPO_4^{2-}/H_2PO_4^- = 1/10$ at pH 5.7. Using the same procedure, the ratio at pH 6.7 = 1/1 and at pH 8.7 = 100/1.

2. If the pH of blood is 7.1 and the HCO_3^- concentration is 8 mM, what is the concentration of CO_2 in blood (pK' for $HCO_3^-/CO_2 = 6.1$)?

   Solution:

   $$pK = pK + \log [HCO_3^-]/[CO_2]$$

   $$7.1 = 6.1 + \log 8 \text{ mM}/[CO_2]; \text{ rearranging}$$

   $$7.1 - 6.1 = 1 = \log 8 \text{ mM}/[CO_2].$$

   The antilog of $1 = 10$. Thus, $10 = 8 \text{ mM}/[CO_2]$, or $[CO_2] = 8 \text{ mM}/10 = 0.8 \text{ mM}$.

3. At a normal blood pH of 7.4, the sum of $[HCO_3^-] + [CO_2] = 25.2$ mM. What is the concentration of HCO_3^- and CO_2 (pK' for $HCO_3^-/CO_2 = 6.1$)?

Solution:

$$pH = pK + \log [HCO_3^-]/[CO_2]$$

$$7.4 = 6.1 + \log [HCO_3^-]/[CO_2]; \text{ rearranging}$$

$$7.4 = -\ 6.1 = 1.3 = \log [HCO_3^-]/[CO_2].$$

The antilog of 1.3 is 20. Thus, $[HCO_3^-]/[CO_2] = 20$. Given, $[HCO_3^-] + [CO_2] = 25.2$, solve these two equations for $[CO_2]$ by rearranging the first equation:

$$[HCO_3^-] = 20\ [CO_2]$$

Substituting in the second equation,

$$20\ [CO_2] + [CO_2] = 25.2$$

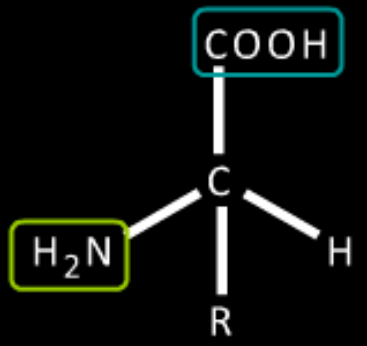
or

$$CO_2 = 1.2 \text{ mM}$$

Then substituting for CO_2, $1.2 + [HCO_3^-] = 25.2$, and solving, $[HCO_3^-] = 24$ mM.

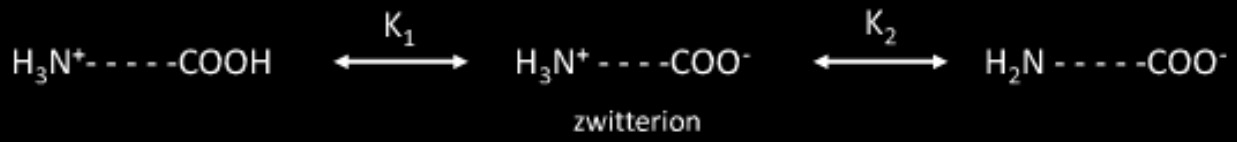
Amino acid titrations

Amino acids serve as a basic building block for molecules that are important in biochemistry such as peptides or enzymes.



This is the general formula for amino acids, where the R-group is any one of twenty known side chains.

Notice that amino acids possess both a basic amino group, NH_2, and an acidic carboxylic acid group, COOH.



zwitterion

In this pH range, the amino acid carries both a positive and a negative charge, resulting in an overall charge of zero. Molecules such as these are called *zwitterions*.

Click to advance

If we were to titrate an amino acid with strong base, what would our titration curve look like?

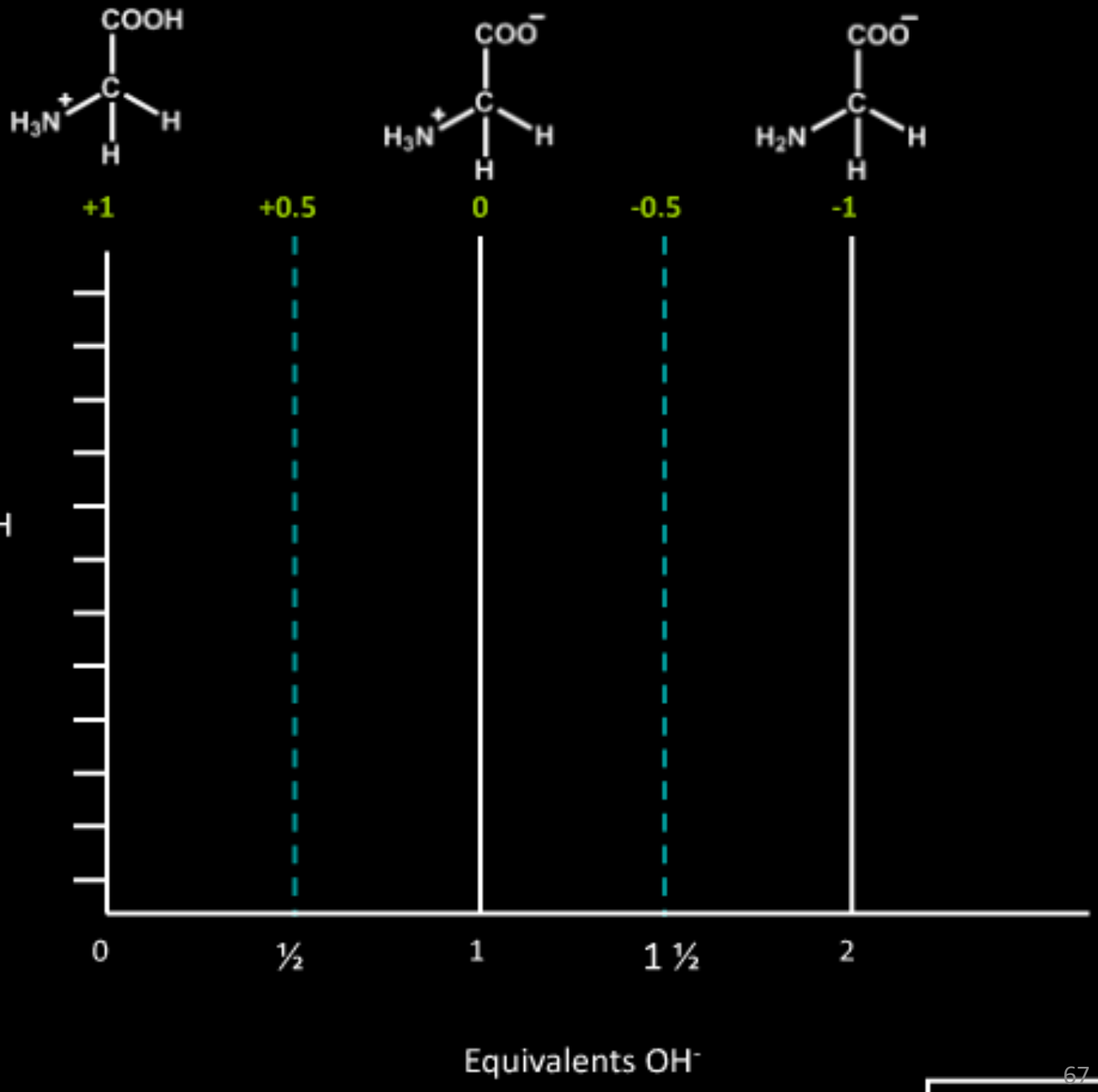
Let's start with glycine:



pK_{COOH} = 2.34

$pK_{NH_3^+}$ = 9.60

For glycine, the R-group is a hydrogen atom. Now we must go through and fill in the chart to the right by calculating the pH at key points in the titration. We begin the titration at a pH below 2.0, to ensure that all possible sites are protonated.



Click to advance

At the first halfway point, we know that *pH is equal to pK_{a1}*:

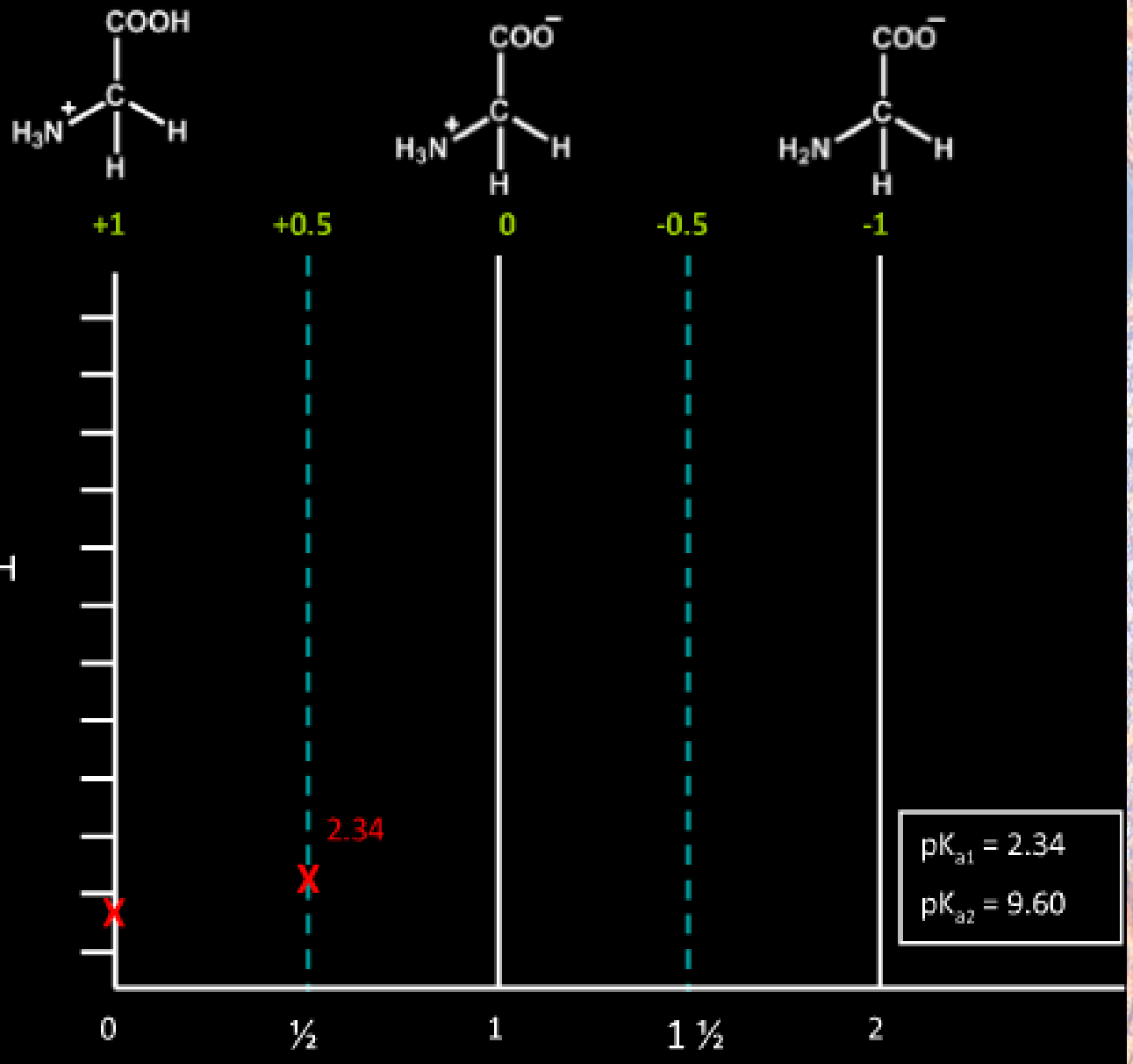
$$pH = pK_a + \log \frac{[base]}{[acid]}$$

We have added enough strong base to react with exactly one half of the strongest acid (-COOH). At this point, the concentrations of our first conjugate acid/base pair are the same:

$$pH = pK_{a1} + \log \frac{\cancel{[base]}}{\cancel{[acid]}}$$

log of one is equal to zero, therefore pH equals pK_{a1}!

$$pH = \boxed{2.34}$$



Click to advance

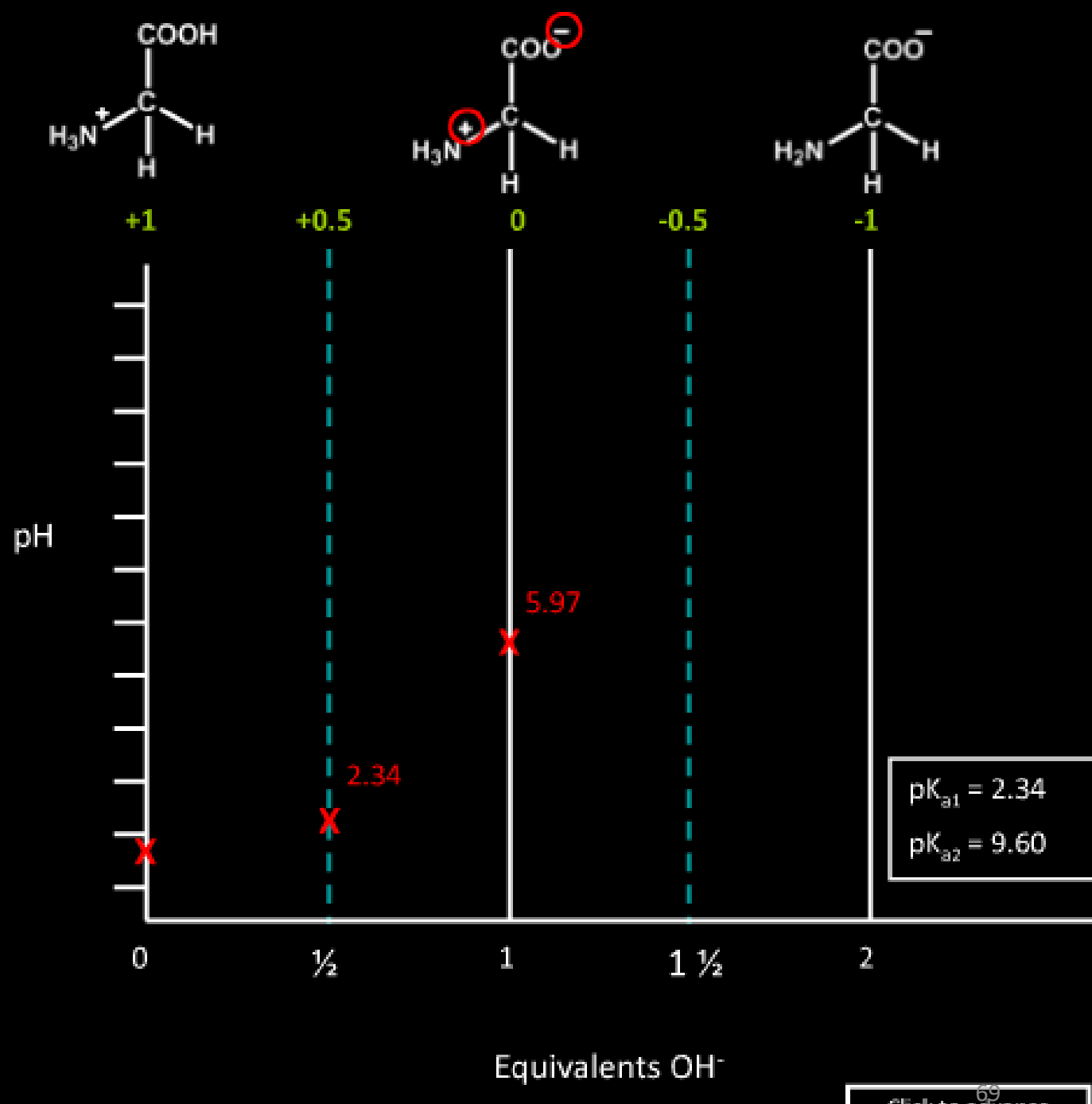
At our first equivalence point, the H^+ has completely dissociated from the COO^- group, and glycine exists as a *zwitterion*. At this point, pH is equal to:

$$pH = \frac{pK_{a1} + pK_{a2}}{2}$$

$$pH = \frac{2.34 + 9.60}{2}$$

$$pH = \boxed{5.97}$$

This is also called the *isoelectric point*, where the total charge on the amino acid is zero.



Click to advance

At our second halfway point, we know that *pH is equal to pK_{a2}*:

$$pH = pK_a + \log \frac{[base]}{[acid]}$$

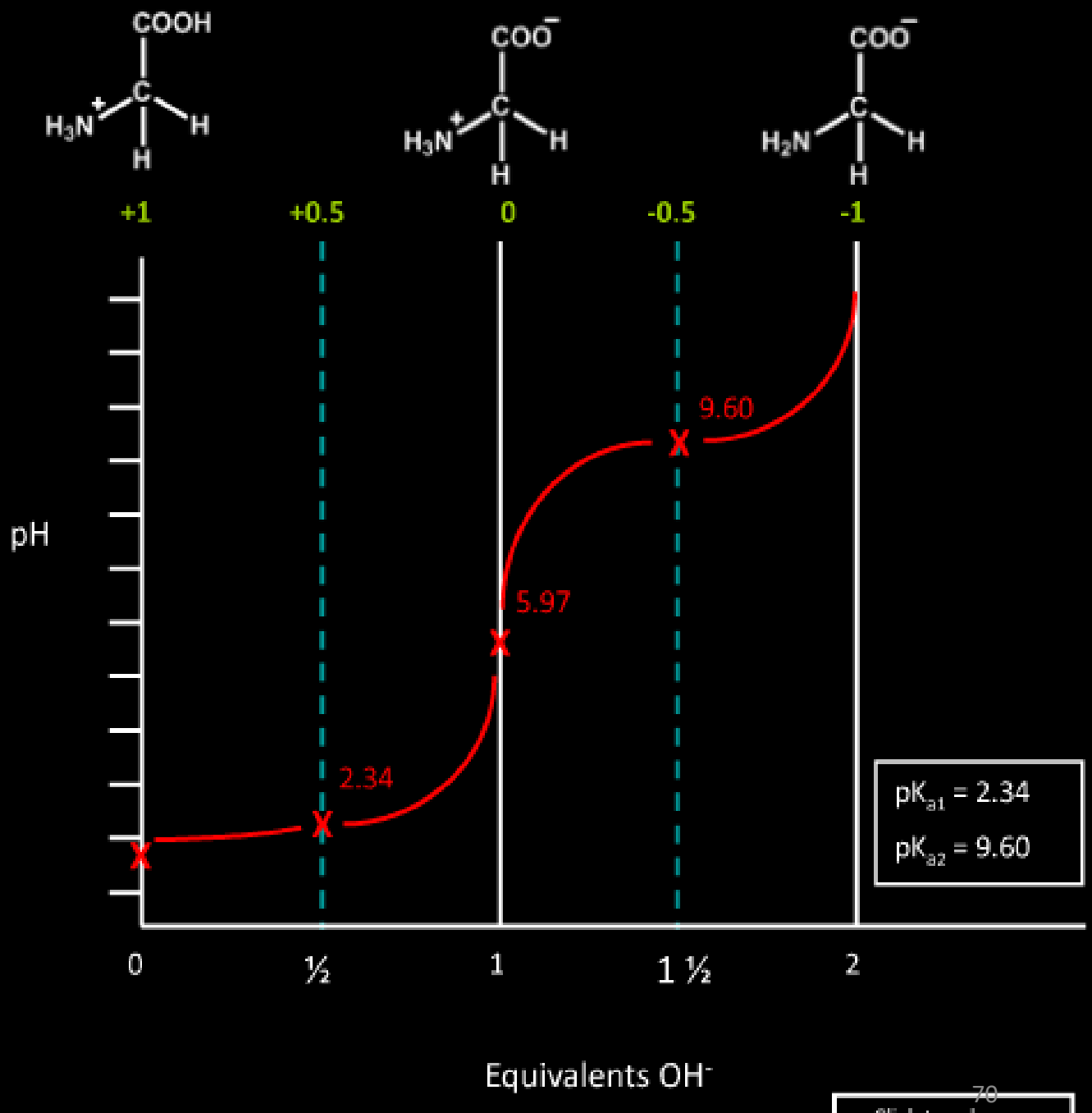
We have added enough strong base to react with exactly one half of the next strongest acid ($-NH_3^+$).

At this point, the concentrations of the 2nd conjugate acid/base pair are the same:

$$pH = pK_{a2} + \log \frac{\cancel{[base]}}{\cancel{[acid]}}$$

log of one is equal to zero, therefore pH equals pK_{a2}!

$$pH = \boxed{9.60}$$

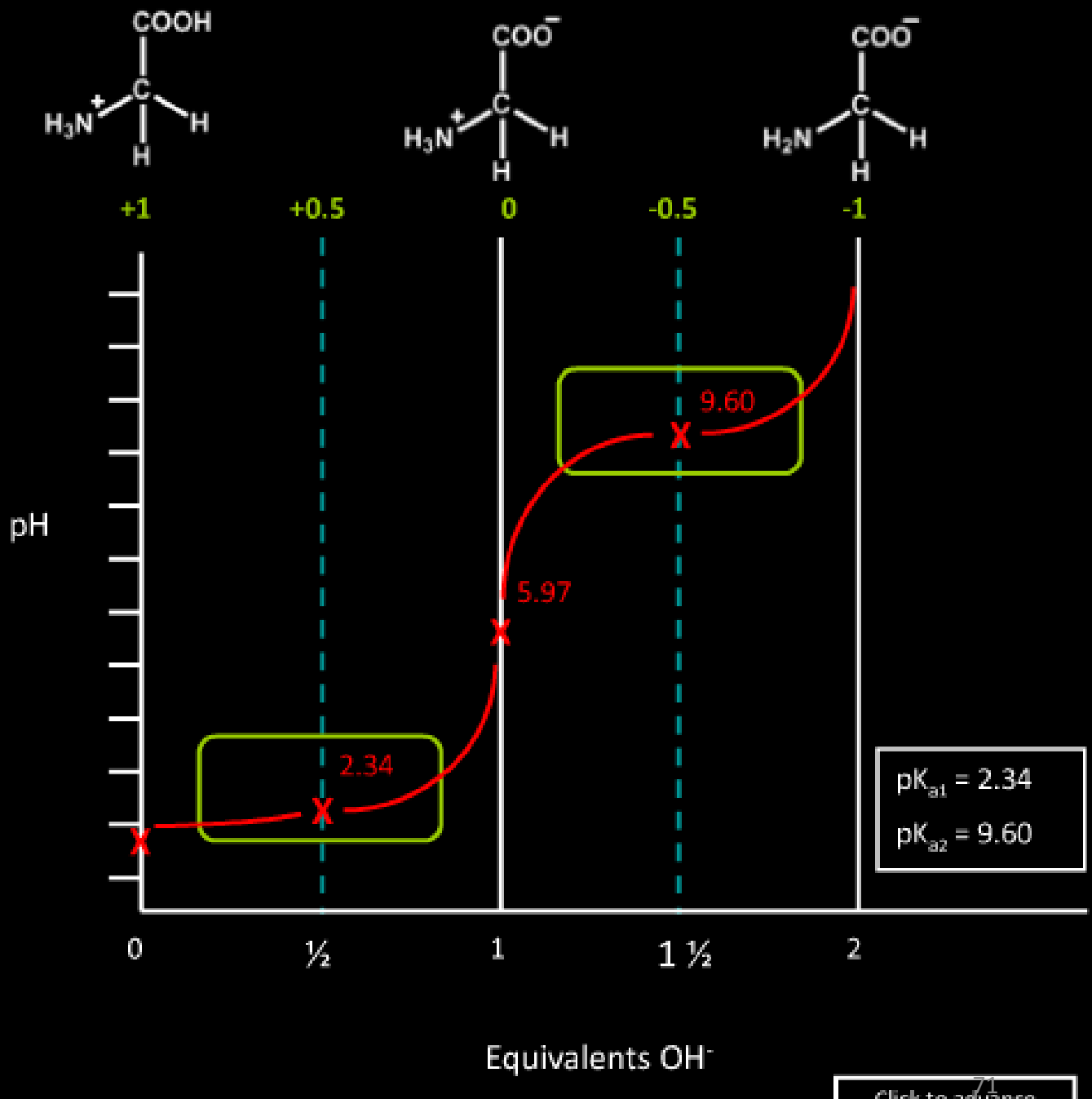


Click to advance

Now, let's locate the buffer regions in this titration curve.

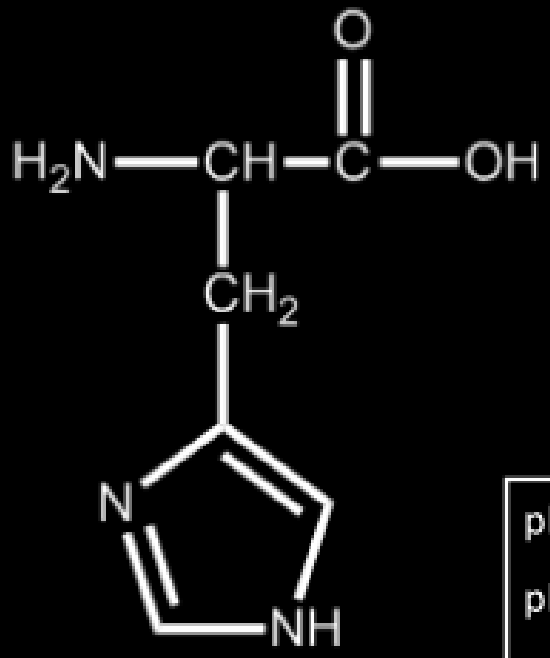
Buffer regions occur when the titration curve is nearly flat. This indicates that the pH does not change very much in response to the strong base that we are adding.

In this case, we have two buffer regions:



Click to advance

Say that we are given *histidine*, an amino acid whose R-group can accept a proton. How does this change our titration curve?



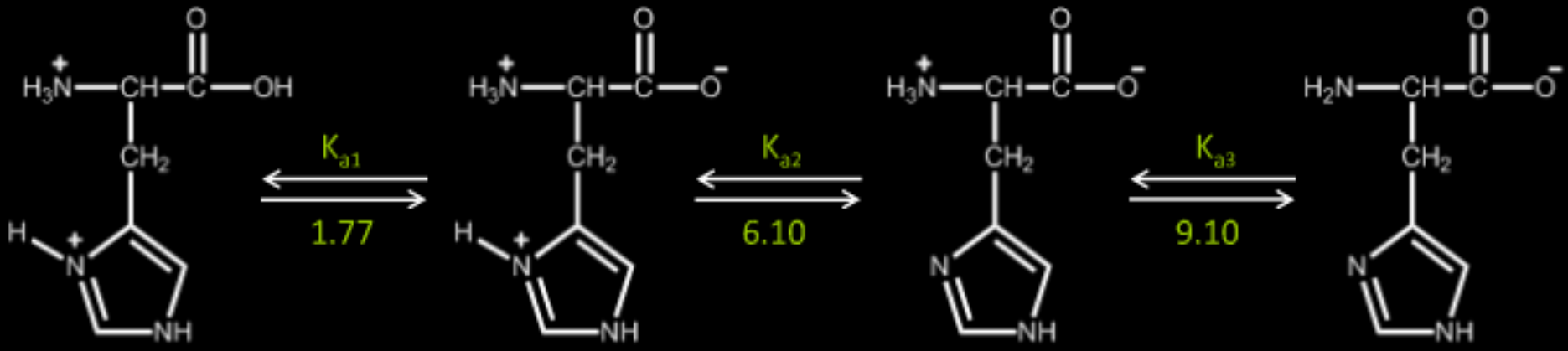
$pK_{COOH} = 1.77$

$pK_{NH_3^+} = 9.10$

$pK_{R\text{-}Group} = 6.10$

Click to advance

Let's think for a moment about the overall charge on histidine, beginning at a very low pH and increasing pH:



At our lowest pH, all three possible sites are protonated

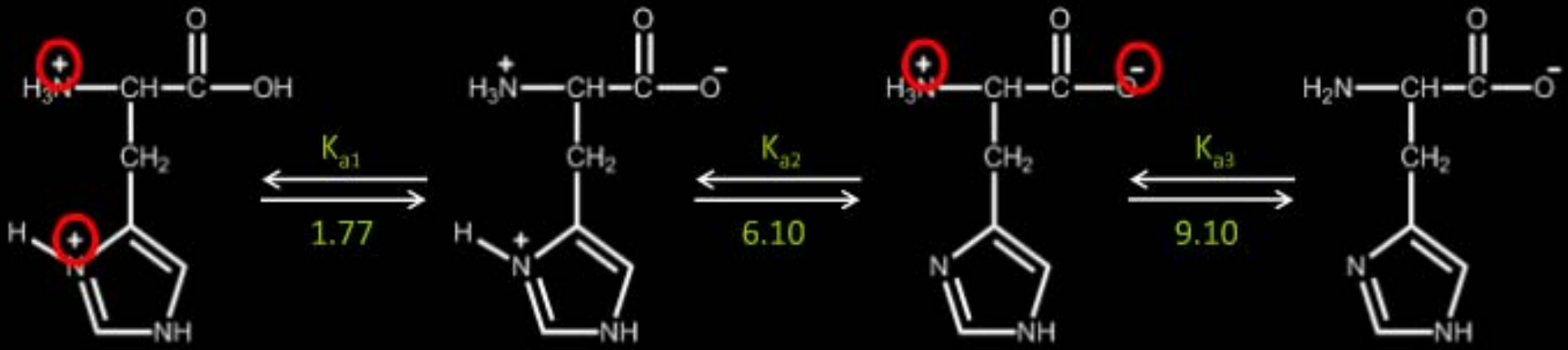
The first group to lose its proton (according to the list of pK_as we were given) will be COOH.

Next, we have added enough OH^- to remove both the carboxylic acid proton AND the proton on the R-group

Finally, all three groups are deprotonated.

Click to advance

Let's think for a moment about the overall charge on histidine, beginning at a very low pH and increasing pH:



What is the total charge on His at a pH lower than pK_{a1}?

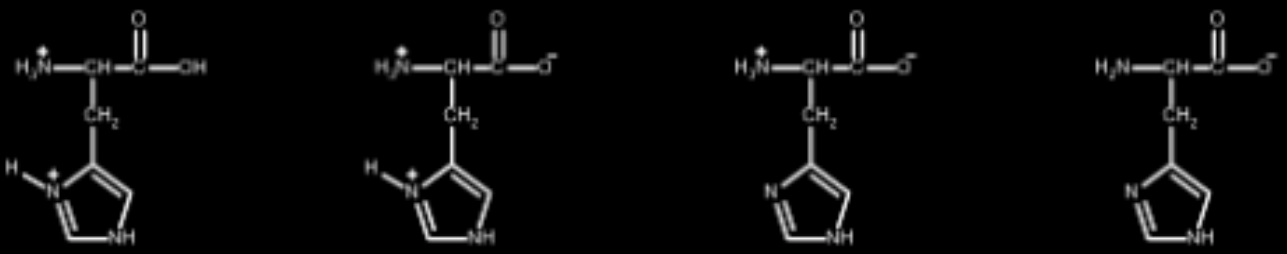
When all three groups are protonated, the total charge on the amino acid is +2.

What is the total charge on His at a pH between pK_{a2} and pK_{a3}?

When the amino group is the only protonated group, the total charge on the amino acid is 0.

Click to advance

With this knowledge, let's take a moment to fill in the titration curve that we expect to see from histidine.



+2 +1.5 +1 +0.5 0 -0.5 -1.0

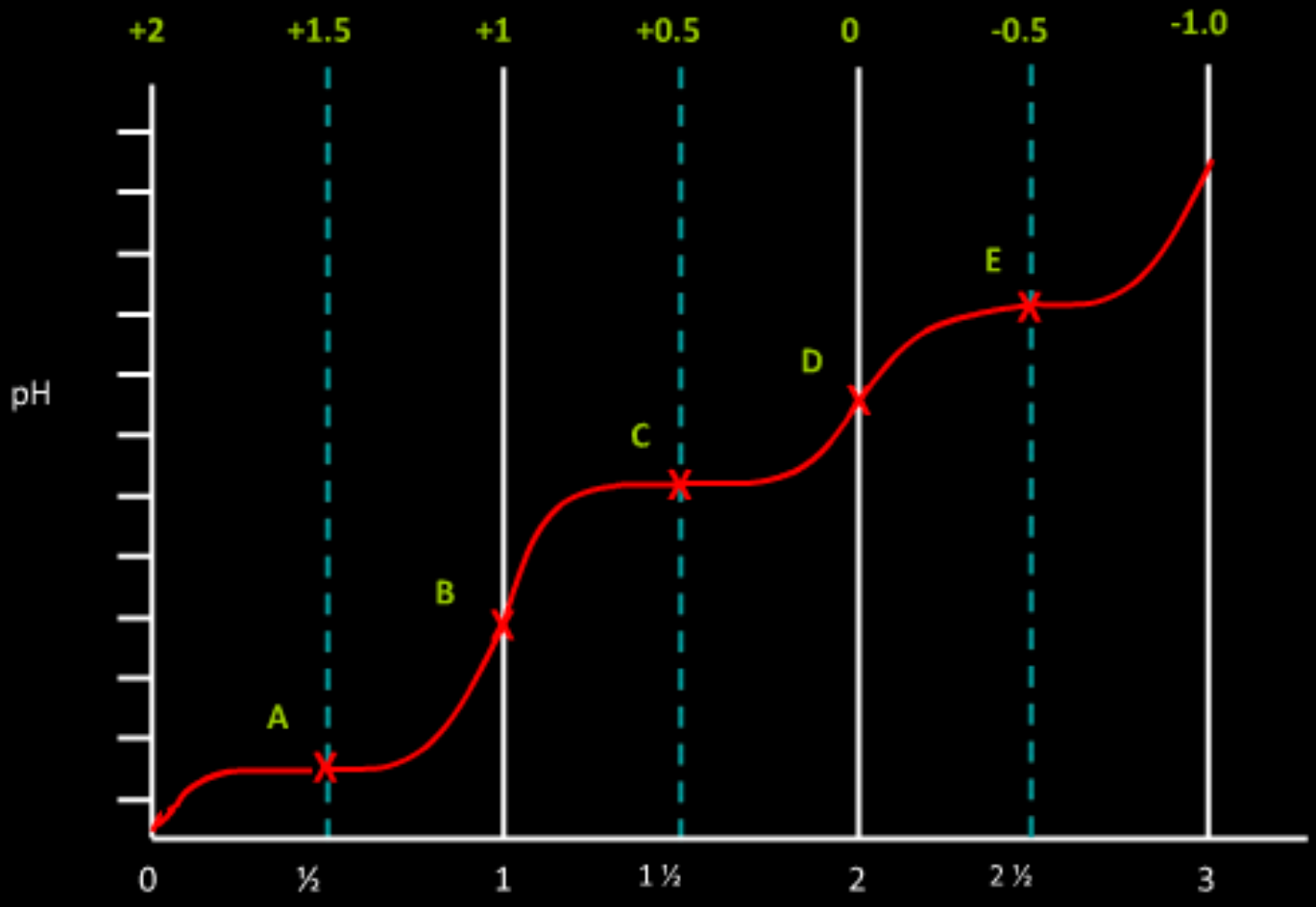
A = pK_{a1}

B = $\frac{pK_{a1} + pK_{a2}}{2}$

C = pK_{a2}

D = $\frac{pK_{a2} + pK_{a3}}{2}$

E = pK_{a3}



Click to advance

Summary

- *Amino acids* are molecules containing both a carboxylic acid functional group, -COOH, an amino group, $-NH_2$, and a side chain that varies between different amino acids.

- Titrations of amino acids are very similar to titrations of polyprotic acids – *multiple* sites on the amino acid can be protonated, and we can utilize the pK_a values for each site to determine which one will be deprotonated first as we add a strong base.

  - If you do not remember acid/base chemistry or weak acid titrations, please see the appropriate CLC tutorials.

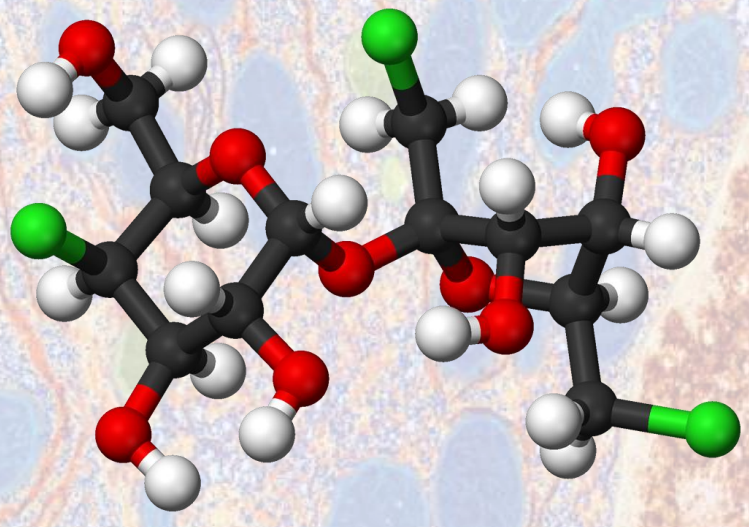
- The *isoelectric point* is when the total charge on the amino acid is equal to *zero*. Remember that the identity of the side chain can influence the point at which this happens in the titration!

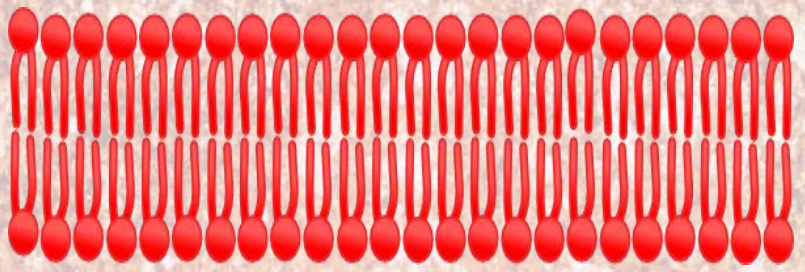


MBG303 Biochemistry

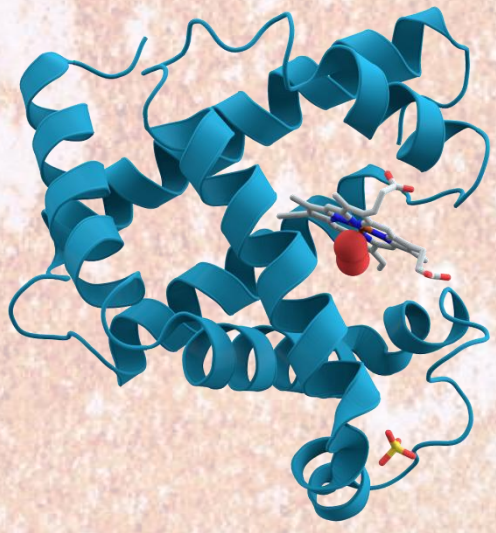
Chapter 4: Biomolecules

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Department of Molecular Biology and Genetics
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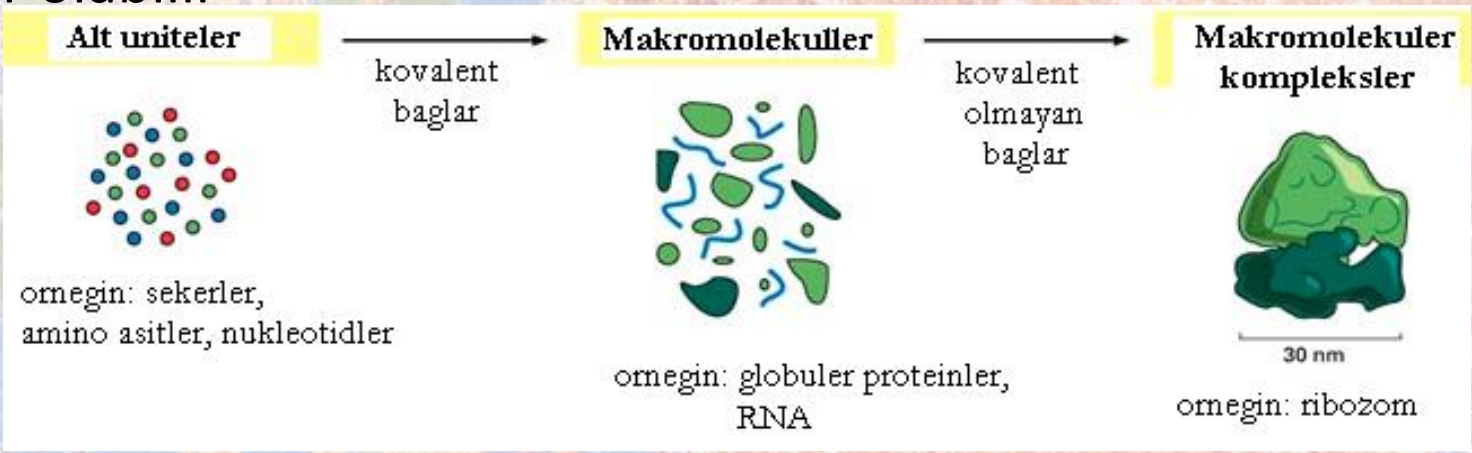


BİYOMOLEKÜLLER

Bilim adamları hücreyi ve dolayısı ile tüm canlıyı yapan molekülleri, makromolekülleri ve makromoleküler kompleksleri belli gruplar altında sınıflayarak analiz etmeye çalışırlar.

Molekül, belli spesifik atomların elektron paylaşımı ile (kovalent bağ) bir arada tutulduğu yapılardır.

Canlıda moleküller, oksijen molekülü (O=O) gibi küçük yapılardan, amino asitler, nükleotidler ve hatta protein, nükleik asit gibi çok daha büyük yapılar olabilir



Canlıların yapısına giren elementler

Canlıların yapısına giren elementlerin cansız dünyadakinden daha az sayıda oldukları bir asırdan beri bilinmektedir.

Canlı yapının % 99'undan fazlasını karbon, azot, oksijen, hidrojen ve fosfor oluşturur ve doğal sayısı 90'dan fazla olan elementten sadece 10-15 tanesi organizmalar için belli bir önem teşkil eder.

Diğer bir deyimle, herhangi bir organizma (bitki, hayvan, mikroorganizma)' nin kimyasal analizi yapıldığında, periyodik cetveldeki elementlerden çok azının bu canlıların temel yapısına girdikleri gözlenir.

Bu 10-15 elementin çoğu düşük molekül ağırlığa (< 80) sahiptir.

Canlı sistemde yüzde miktar olarak en çok bulunan dört element hidrojen, oksijen, azot ve karbon olup sırası ile bir, iki, uç ve dört bağ oluşturabilirler.

Canlıların yapısına giren elementler

Diğer ilginç bir durum ise, bu elementlerin bütün canlıların yapısında hemen hemen aynı yüzde oranlarda bulunmalarıdır;

Element	İnsan	Bitki	Bakteri
O	63	78	74
C	19	11	12
H	9	9	10
N	5	1	3
P	1	1	1
S	1	0.1	0.1

Her ne kadar yukarıdaki 6 element birbirlerine çok çeşitli şekillerde bağlanabilirlerse de, kimyasal analizler göstermiştir ki, nispeten az sayıda temel bilesen vardır.

Bu dersimizde üzerinde duracağımız gibi, su bir çok canlının ağırlığının yaklaşık % 70'in oluşturmaktadır.

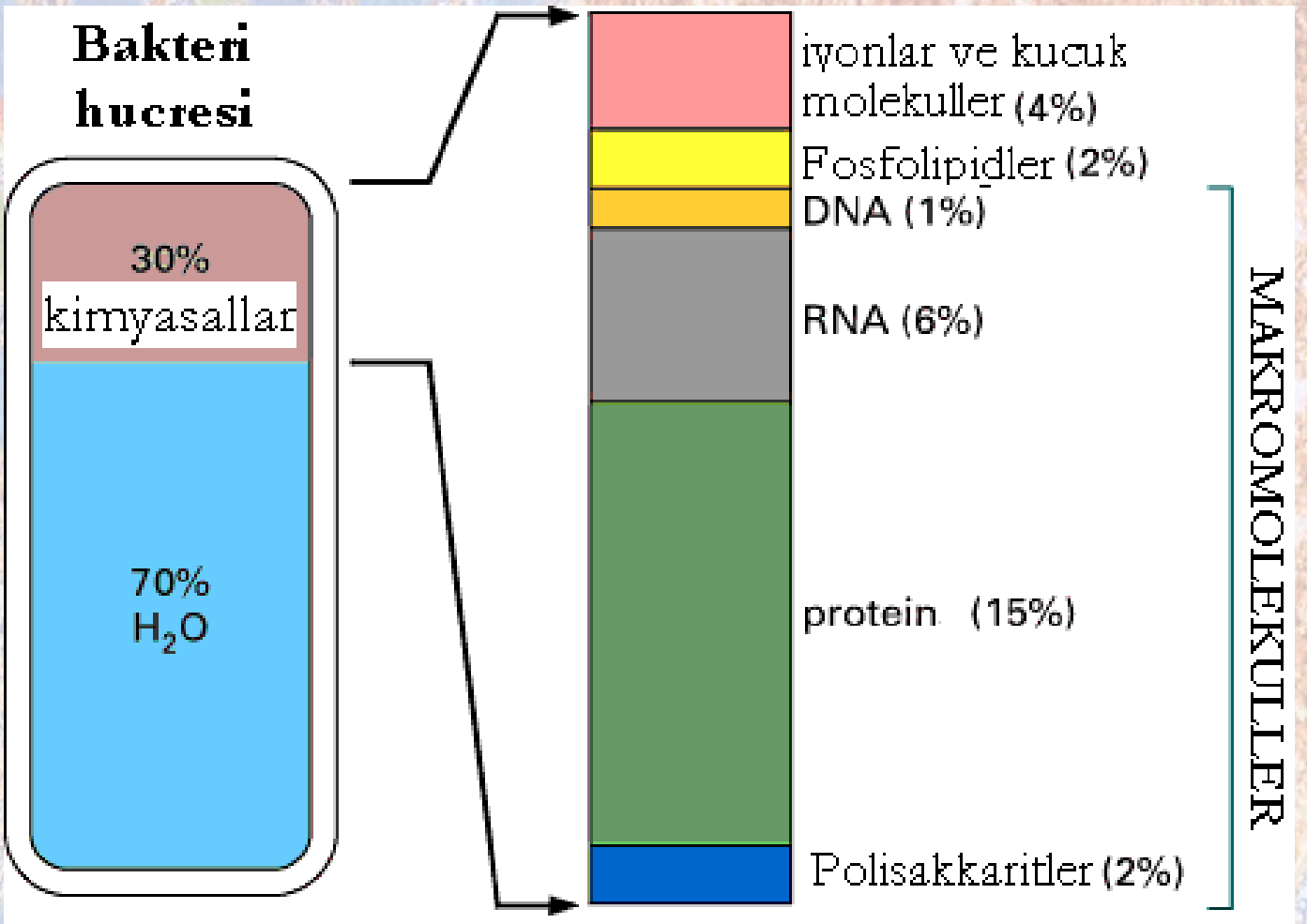
Yapıya giren diğer elemanlar

Geriye kalan temel bileşikler ise karbonhidratlar, yağlar, proteinler ve nükleik asitler (DNA, RNA)'dir.

Organik kimyada milyonlarca bileşik olduğu halde, biyokimyacılar nispeten az sayıda organik madde ile ilgilenirler.

Bunlar daha çok organizmada veya hücrede bulunan organik bileşiklerdir.

Tipik bir bakterinin kimyasal kompozisyonu



Organik? İnorganik?

Karbon dioksit ve karbon monoksit hariç yapısında karbon atomu bulunduran her turlu madde **organik madde**'dir (örneğin, glukoz, amino asitler, etanol, asetik asit vb.)

Yapısında karbon atomu bulunmayan (CO_2 ve CO hariç) her türlü madde **inorganik madde** olarak adlandırılır (örneğin, CO_2, CO, H_2O, O_2, NaCl, bütün elementler, vb.).

Makromoleküller

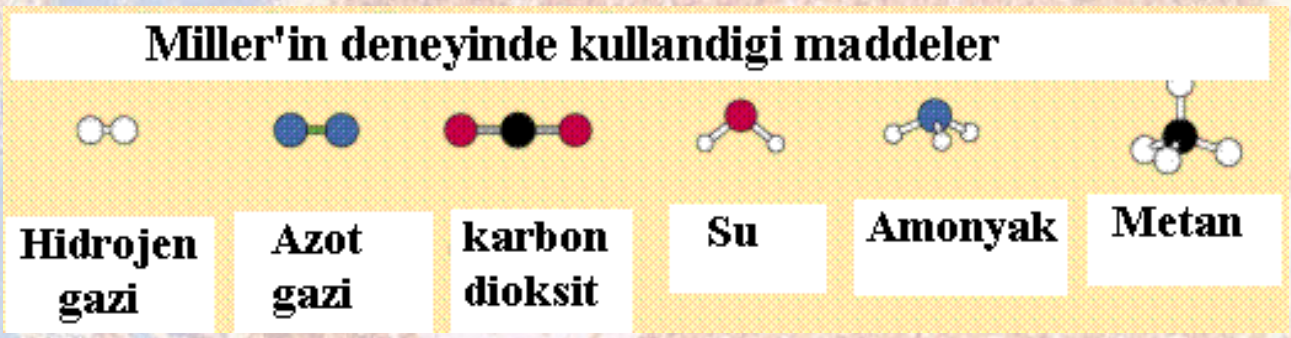
Hücrenin organik materyalinin hemen hemen hepsi yukarıdaki dört çeşit makromolekülden (proteinler, nükleik asitler, lipidler ve polisakkaritler) oluşmuştur.

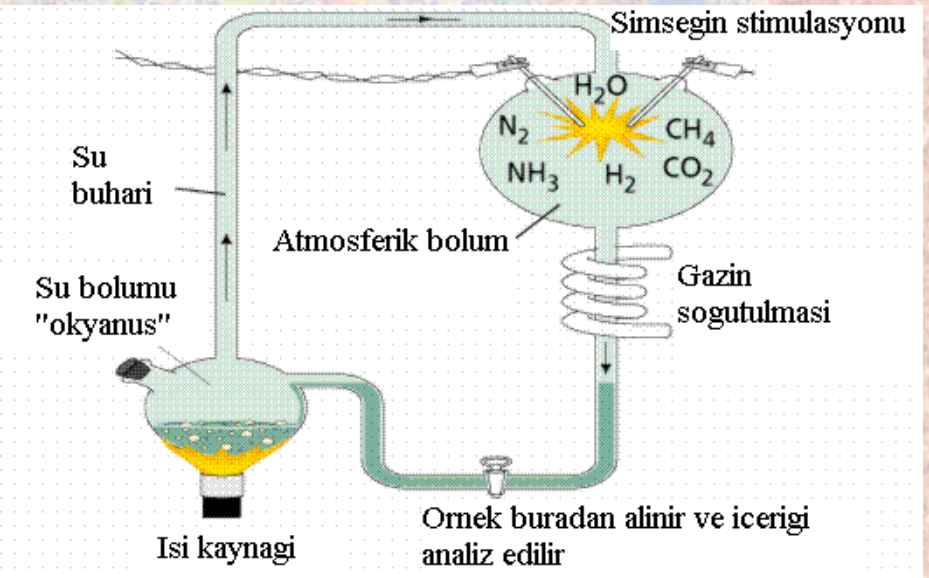
Başlangıçta organik maddelerin sadece canlılar tarafından sentezlenebileceği düşünülmüştü.

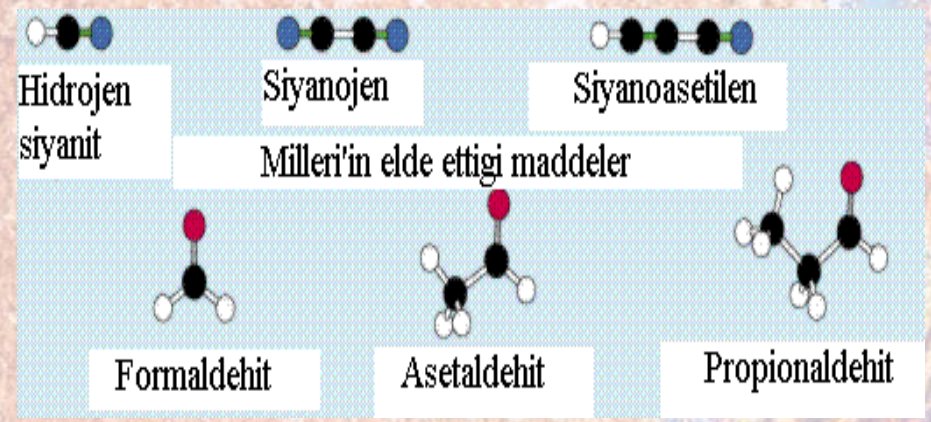
Ancak, günümüzde sayıları milyonlarla ifade edilen organik moleküllerin büyük çoğunluğu laboratuar şartlarında sentezlenmektedir.

Organik sentez

Organik moleküllerin çoğu H, O ve N'un C atomu ile bağ yapabilme özelliğinden yararlanılarak elde edilmişlerdir.







Organik sentez

Miller su bölümünde toplanan maddeleri incelediğinde oluşan organik asitlerin (örneğin, amino asitlerin bazıları, HCN, aldehitler ve siyano bileşikleri) karbonlarının % 10'dan fazlasının metandan geldiğini belirlemiştir.

Su hariç, moleküllerin çoğu hücre içinde makromolekül olarak bulunurlar.

Biyomoleküller ve elementler

Biyomoleküller karbon bileşikleridir.

Hücre kuru ağırlığının 1/3'u bu elementtir.

Metan (CH_4) da dört çift elektron dört hidrojen atomu ile birer bağ kurar.

Karbon aynı zamanda oksijen ve azotla da bir ve iki bağ kurabilir. Ancak, en önemlisi bir karbon atomu başka bir karbon atomu ile, iki, uç ve dört bağ kurabilir.

Kimyasal bağlar

Kovalent bağlanmış karbon bağları lineer, dallanmış veya halkasal yapılar oluşturabilirler.

Karbon-karbon bağları iki-uç adet olabilir.

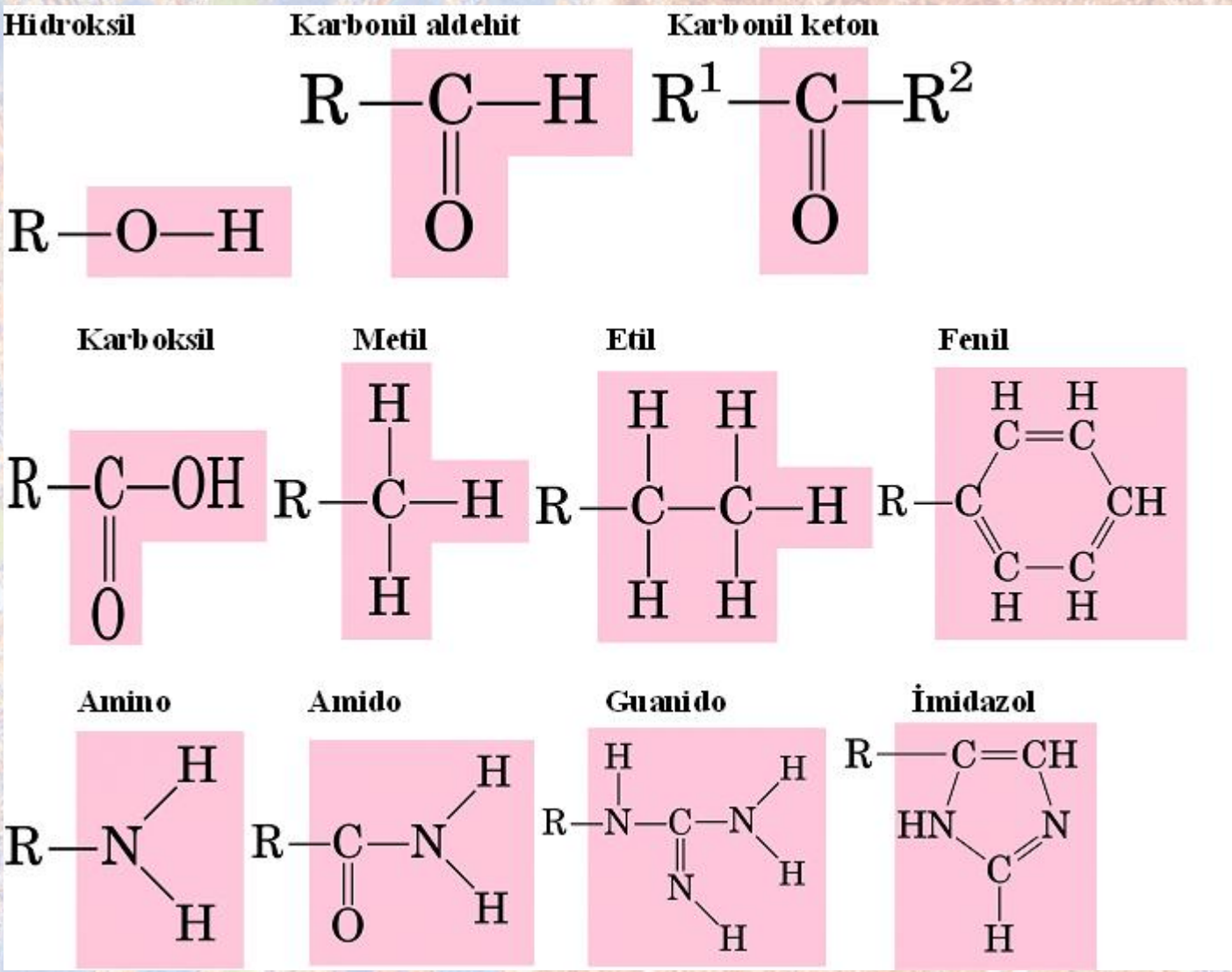
Üçlü bağlar biyomoleküllerde az rastlanan bir durumdur.

Bu şekilde oluşmuş karbon iskeletlerine daha sonra diğer atomlar ve fonksiyonel gruplar eklenmiş olur ki bunlar sayesinde her makromoleküle özel bir özellik kazandırılmış olur.

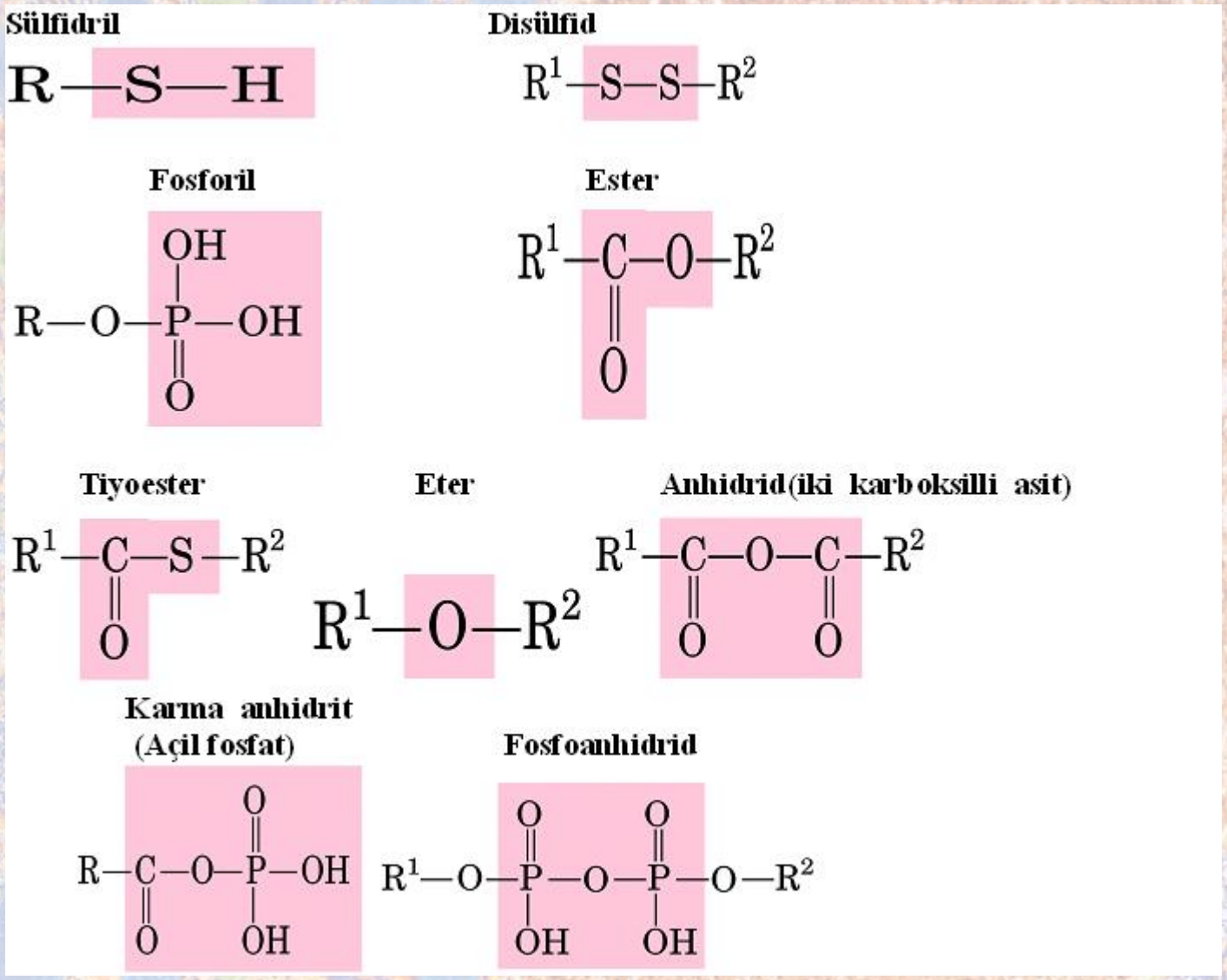
Fonksiyonel gruplar

- Fonksiyonel gruplar kimyasal özelliklerin ortaya çıkmasında rol alırlar. En önemlileri,

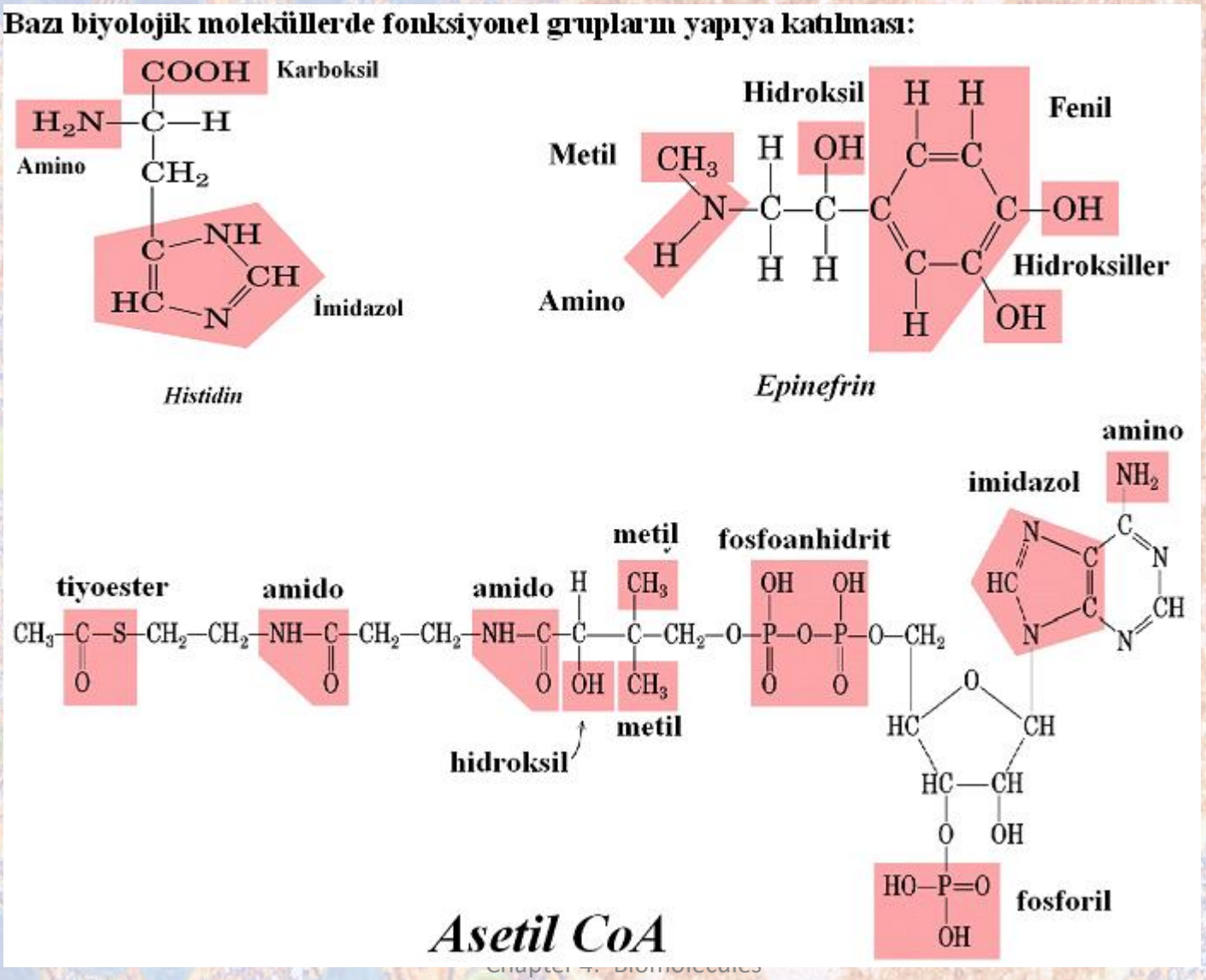
Fonksiyonel gruplar



Fonksiyonel gruplar



Fonksiyonel gruplar



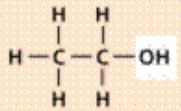
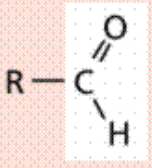
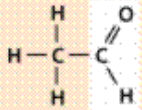
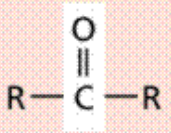
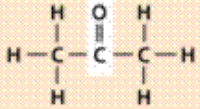
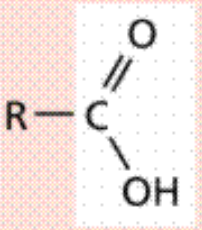
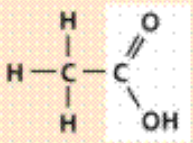
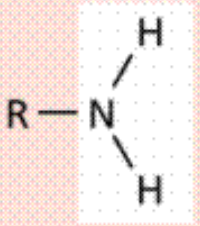
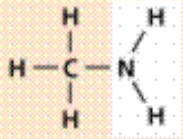
Fonksiyonel gruplar

- Biyomoleküllerin çoğuna hidrokarbon (C-H omurgalı yapılar) türevleri olarak bakılabilir.

- Bu omurga oldukça kararlı bir yapıdır.

- Hidrojen atomları bir çok fonksiyonel grupla değiştirilebilirler ve bu değişim sonucu çeşitli organik moleküller ortaya çıkar.

Fonksiyonel gruplar

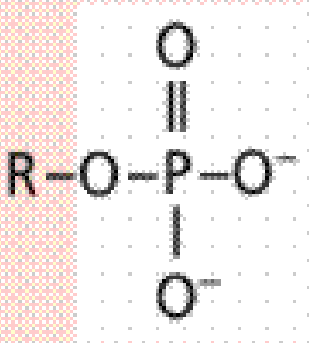
Fonksiyonel grup	Bilesikler	Yapisal formul	Ornek
Hidroksil –OH	Alkoller	R—OH	 Etanol
Karbonil –CHO	Aldehitler		 Asetaldehit
Karbonil \CO/	Ketonlar		 Aseton
Karboksil –COOH	Karboksilik asitler		 Asetik asit
Amino –NH2	Aminler		 Metilamin

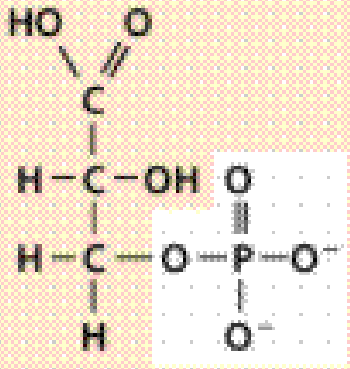
Fonksiyonel gruplar

Fosfat

$-OPO_3^{2-}$

Organik fosfatlar





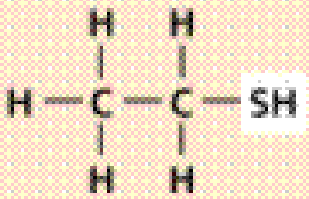
3-fosfogliserik asit

Sulfidril

$-SH$

Tioller





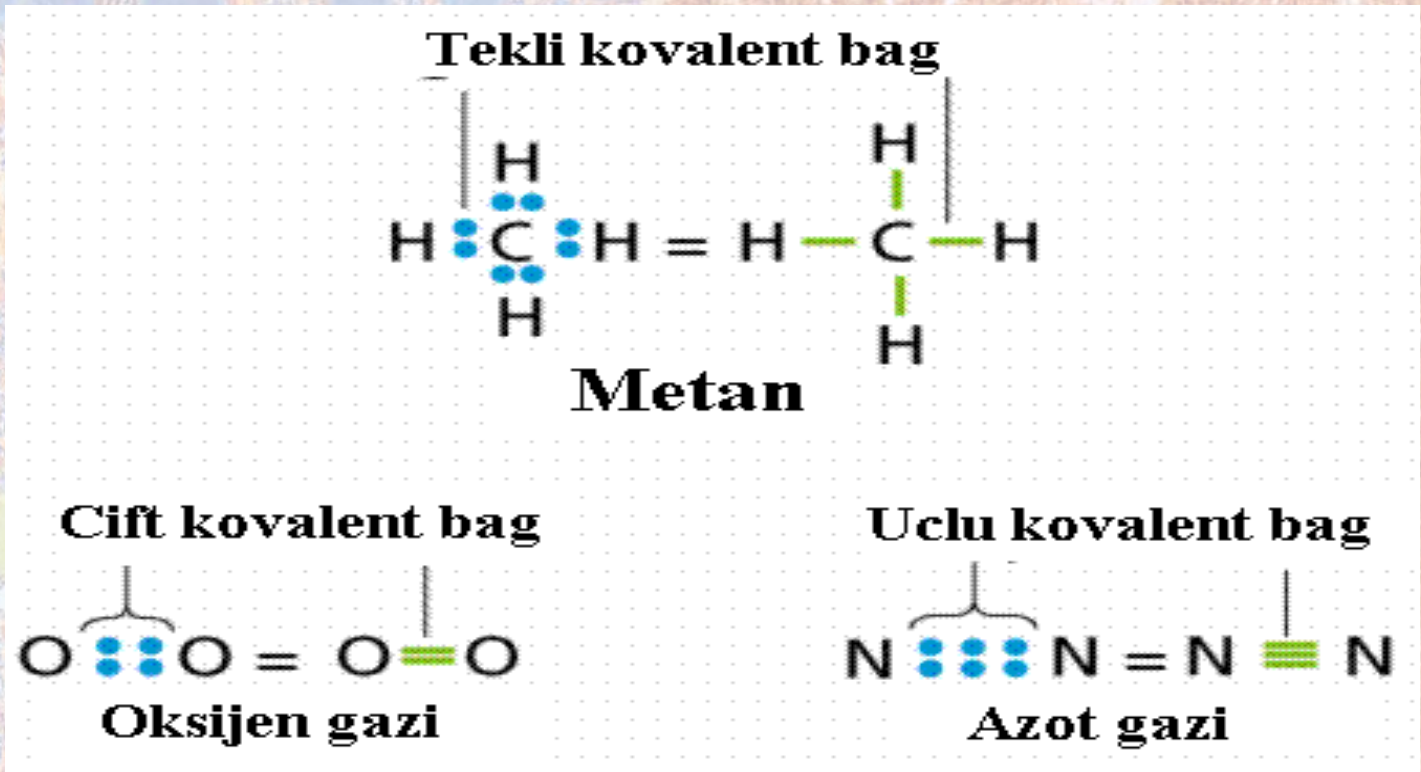
Merkaptoetanol

Kovalent bağlar

- Atomları bir birine özel bir şekilde tutturan kovalent bağlar (C-C, C=C, C-H, H-H, N≡N gibi bağlar kuvvetli kovalent bağlardır) sayesinde kararlı organik maddeler oluşurlar.

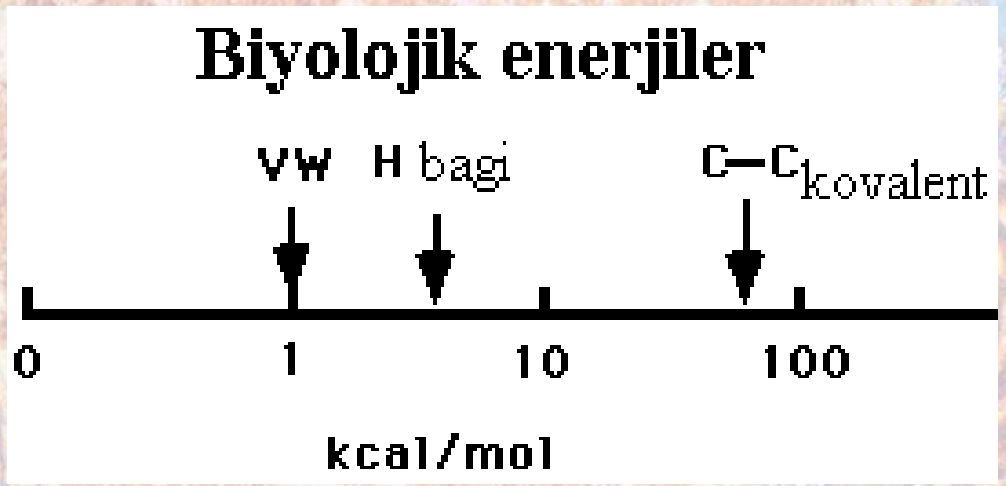
- Nükleotidleri, amino asitleri, şekerleri yapan bu tur bağlardır. Ayrıca, nükleotidler arasındaki fosfodiester, amino asitler arasındaki peptid, ve monosakkaritler arasındaki glikozidik bağlar da kovalent yapıdadırlar.

Kovalent bağlar



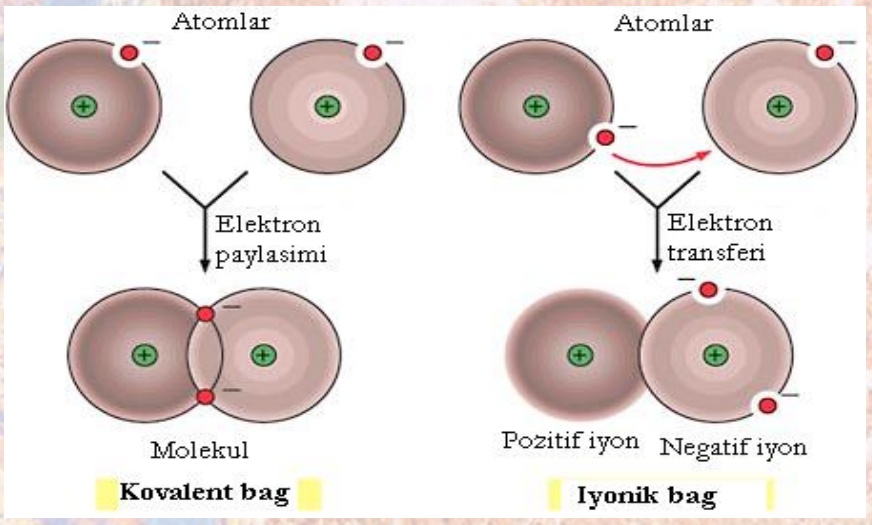
Kovalent olmayan bağlar

Kovalent olmayan bağlar (iyonik bağ, hidrojen bağı, hidrofobik bağ, Van der Waals kuvvetleri) kovalent olan bağlara göre 10-100 kat daha zayıf olsalar da bu bağlar, biyolojik makromoleküllerin ikincil ve üçüncül yapılarının kazanılmasında en önemli rolleri alırlar.



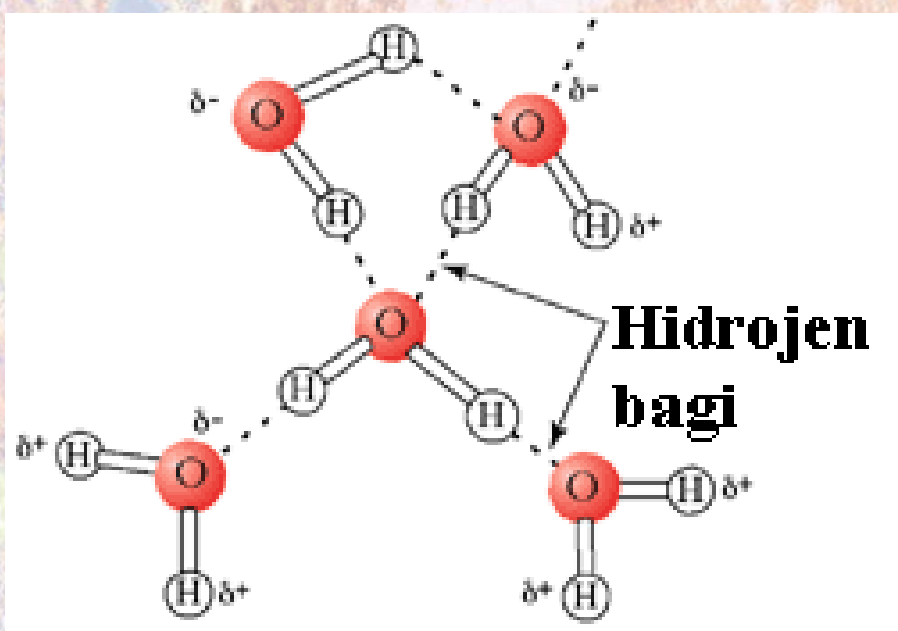
Kovalent olmayan bağlar

- Bu yapılara kovalent bağlar girmez. Kovalent olamayan bağların en kuvvetlisi iyonik bağdır. Bu bağ pozitif ve negatif yüklü iyonlar arasında kurularak bir iyon cifti oluşması sağlanır (ör, NaCl):



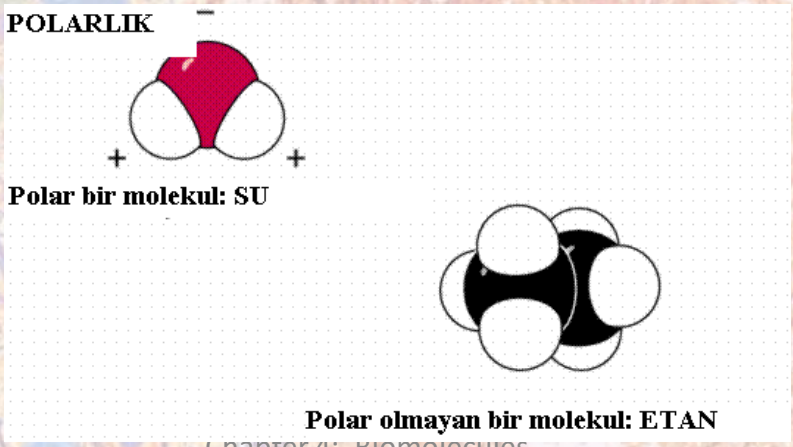
Kovalent olmayan bağlar

- Hidrojen bağı sadece iki su molekülü arasında bulunmaz. İki DNA zinciri arasında kurulan tüm bağlar, proteinlerde alfa-heliks ve beta-tabakalarını oluşturan bağlar hepsi genelde hidrojen bağlarıdır.



Kovalent olmayan bağlar

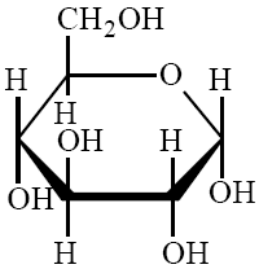
- Hidrojen bağları genellikle bir moleküle bağlı hidrojen atomu ile diğer molekülün daha elektronegatif olan azot veya oksijeni arasında kurulurlar. Polar ve polar olmayan sıvılar aynı ortama konduklarında biri birine karışmazlar (suyu ve yağı düşününüz).



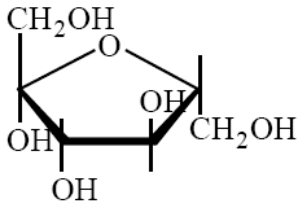
Kovalent olmayan bağlar

- Suda erimeyen bir tabiatta olan polar olmayan maddeler hidrofobik etkileşim veya bağlanmalarla bir araya toplanma eğilimi gösterirler. Hücre membranının ve proteinlerin uç boyutlu yapılarının kazanılmasında önemlidirler. Van der Waals kuvvetleri bütün moleküllerde bulunur. Burada, bir atomun elektronlarının diğer atomun çekirdeğine olan ilgisi söz konusudur. Atomlar biri birine yaklaştıkça bu ilgi (kuvvet) artarken, tersi durumda azalır. Ancak, iki atom biri birlerine dış yörünge elektronları çakışacak kadar yaklaşırlarsa, bu defa da iki atom biri birini iter.

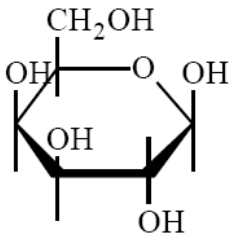
Monosaccharides:



α-Glucose

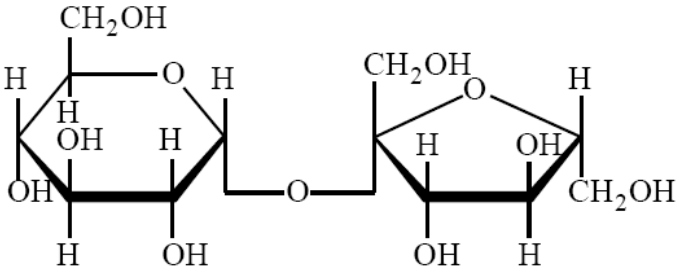


Fructose

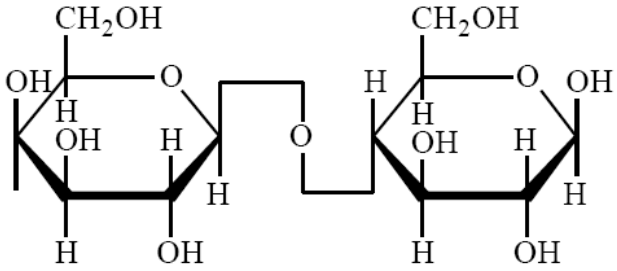


β-Galactose

Disaccharides:

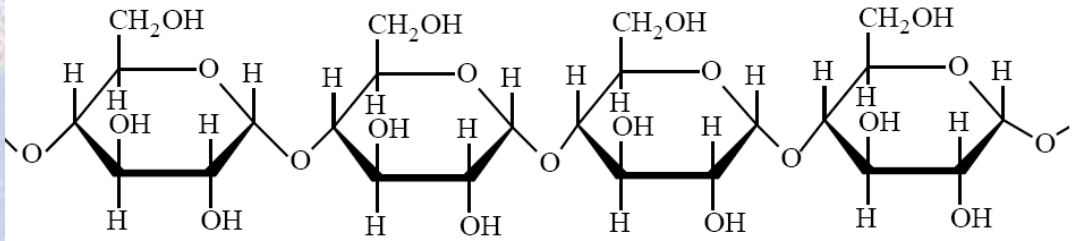


Sucrose

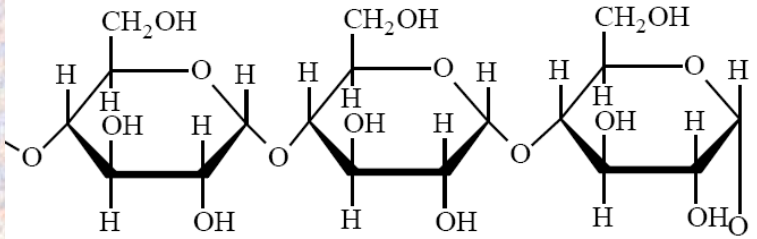


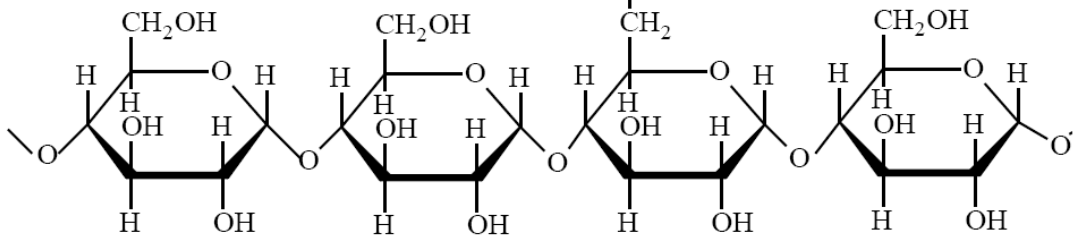
Lactose

Polysaccharides:

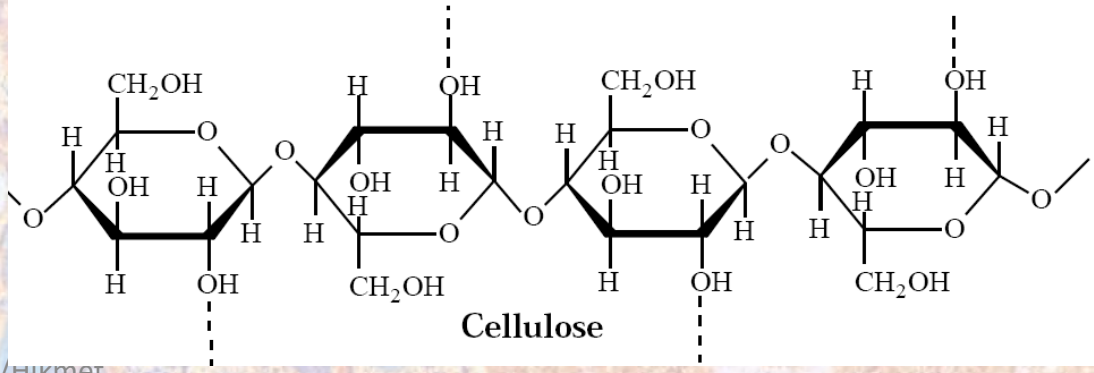


Starch

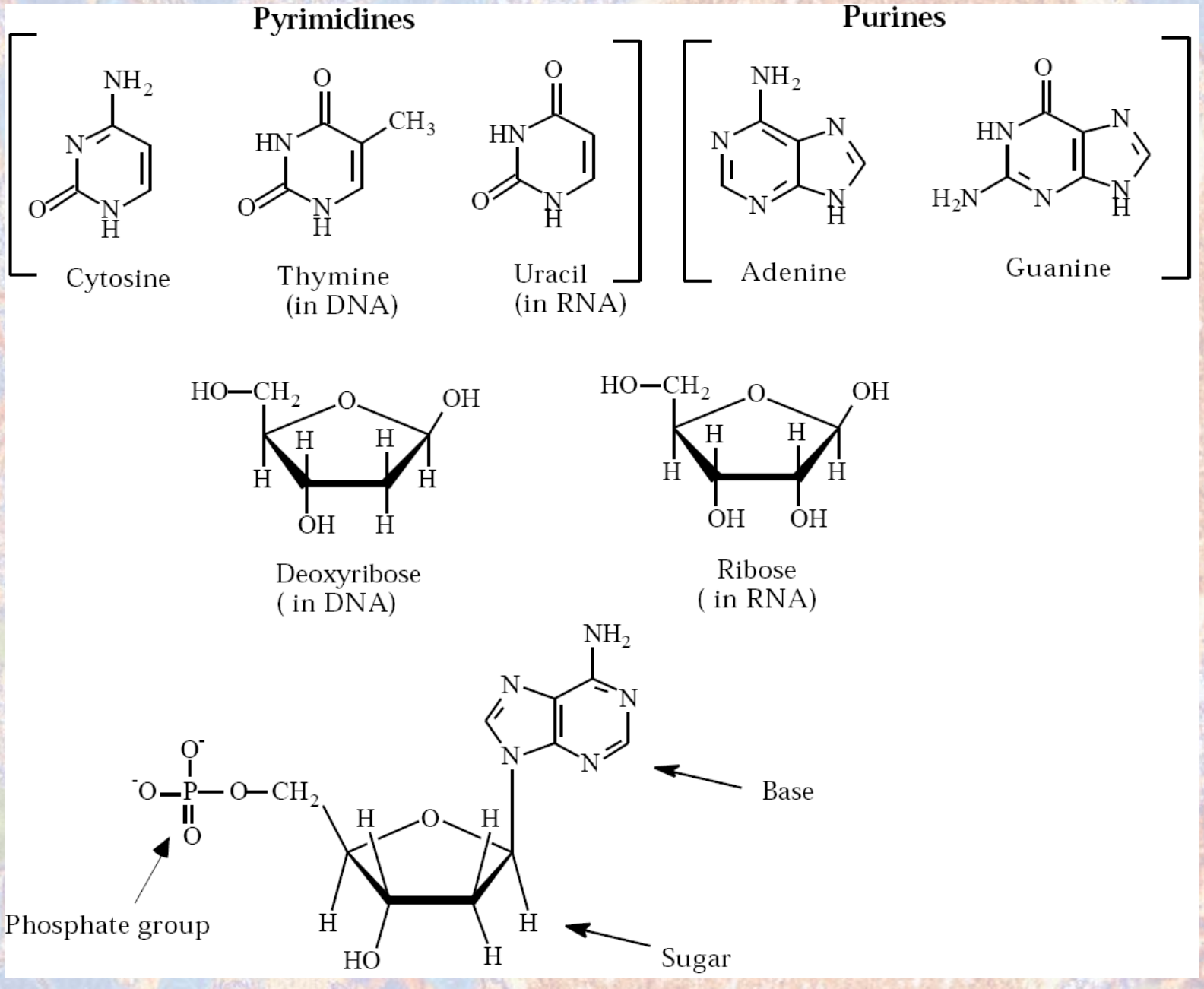




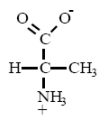
Glycogen



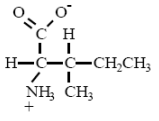
Cellulose


Pyrimidines
Purines
Cytosine
Thymine
(in DNA)
Uracil
(in RNA)
Adenine
Guanine
Deoxyribose
(in DNA)
Ribose
(in RNA)
Base
Phosphate group
Sugar

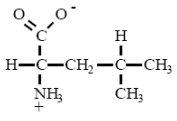
Non-Polar



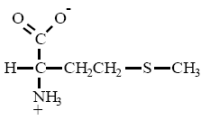
ALANINE
(ala)



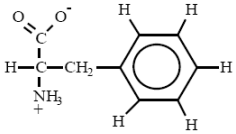
ISOLEUCINE
(ile)



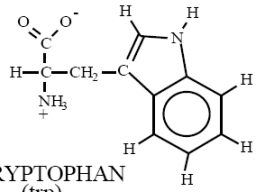
LEUCINE
(leu)



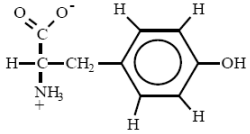
METHIONINE
(met)



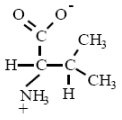
PHENYLALANINE
(phe)



TRYPTOPHAN
(trp)

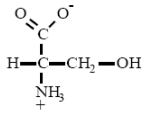


TYROSINE
(tyr)

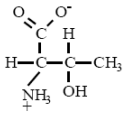


VALINE
(val)

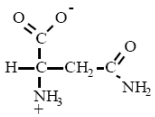
Polar



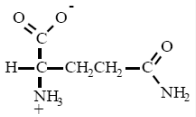
SERINE
(ser)



THREONINE
(thr)

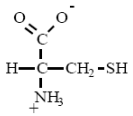


ASPARAGINE
(asn)

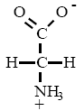


GLUTAMINE
(gln)

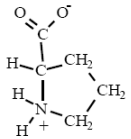
Special Cases:



CYSTEINE
(cys)



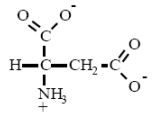
GLYCINE
(gly)



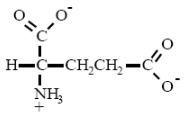
PROLINE
(pro)

Charged

Acidic

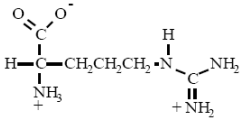


ASPARTIC ACID
(asp)

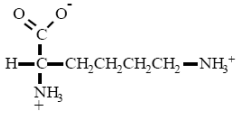


GLUTAMIC ACID
(glu)

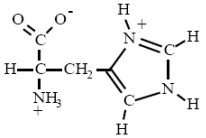
Basic



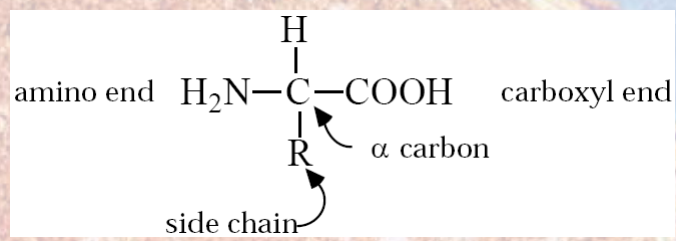
ARGININE
(arg)

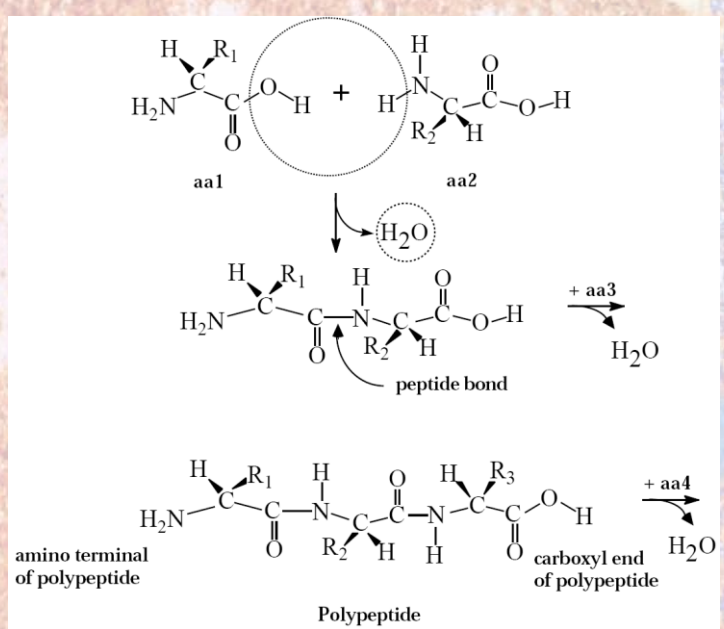


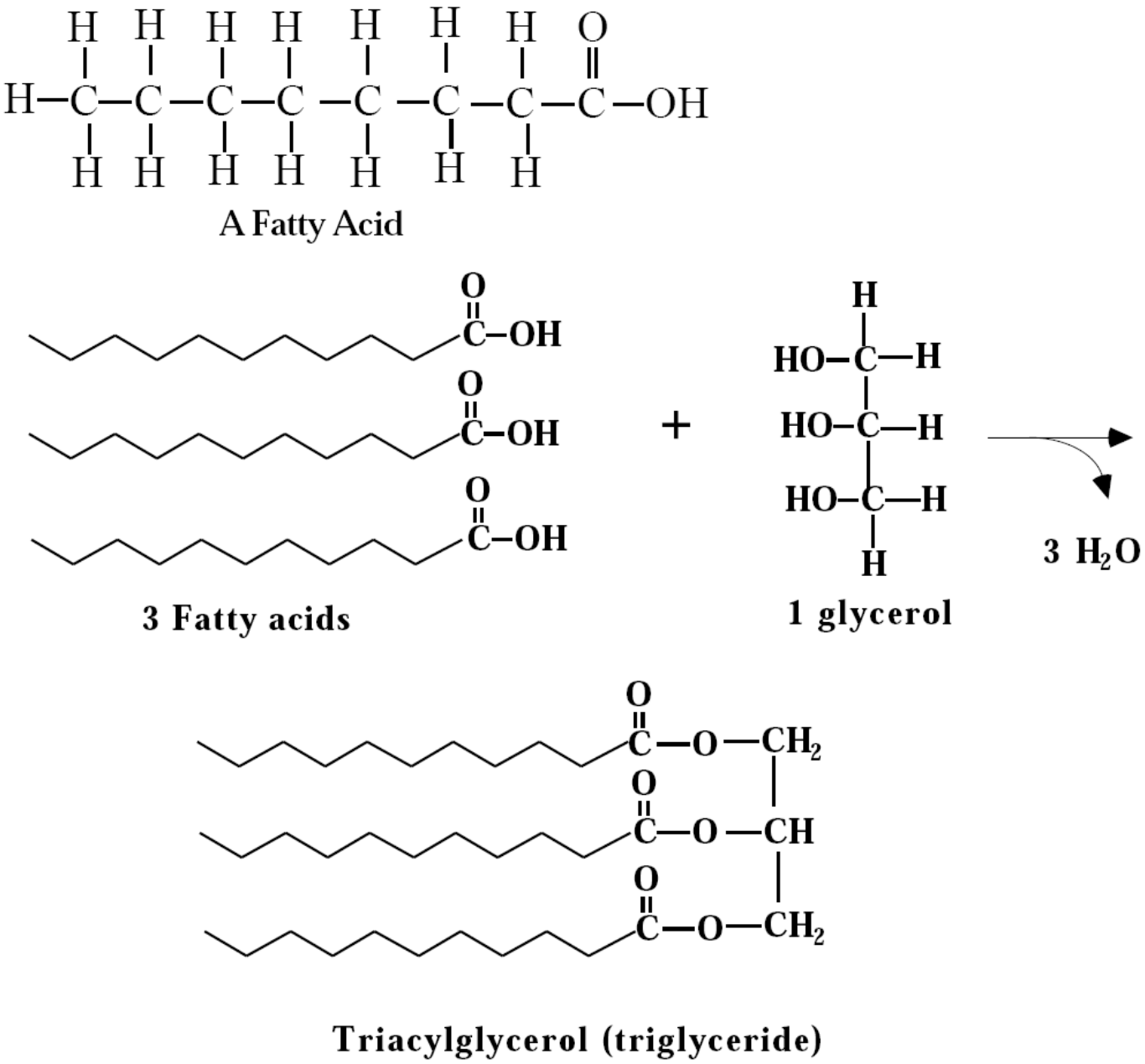
LYSINE
(lys)

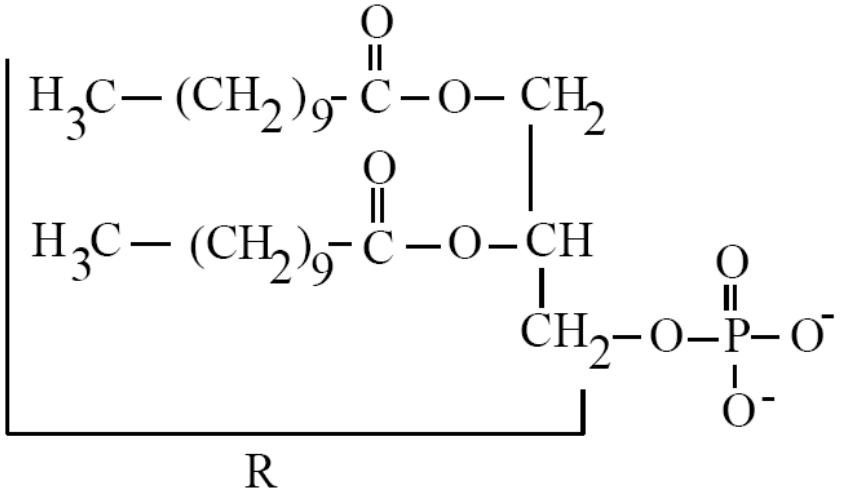


HISTIDINE
(his)

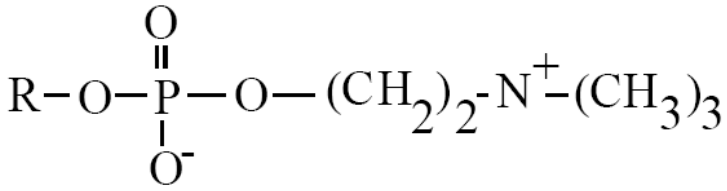




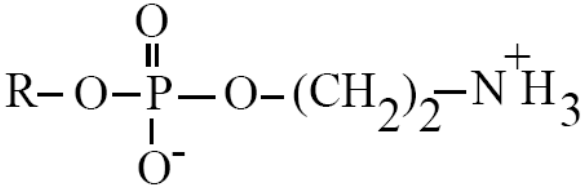

A Fatty Acid
3 Fatty acids
1 glycerol
3 H_2O
Triacylglycerol (triglyceride)



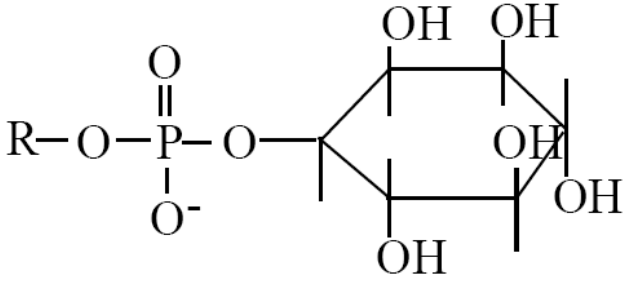
Phosphatidyl choline:



Phosphatidyl ethanolamine:



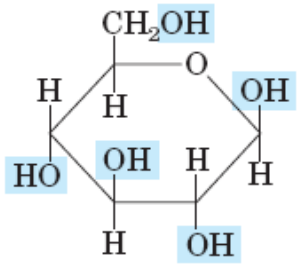
Phosphatidyl inositol:



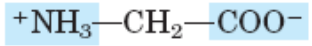
Some Examples of Polar, Nonpolar, and Amphipathic Biomolecules (Shown as Ionic Forms at pH 7)

Polar

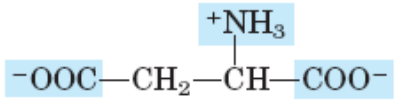
Glucose



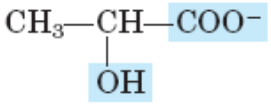
Glycine



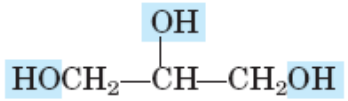
Aspartate



Lactate

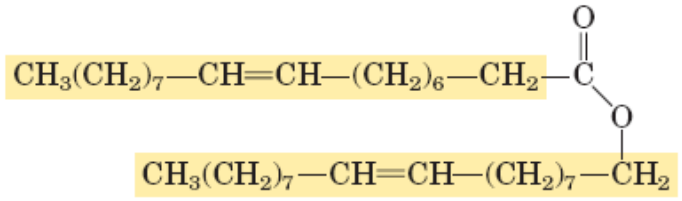


Glycerol



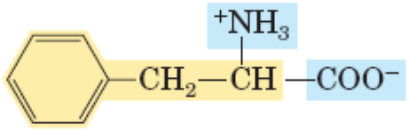
Nonpolar

Typical wax

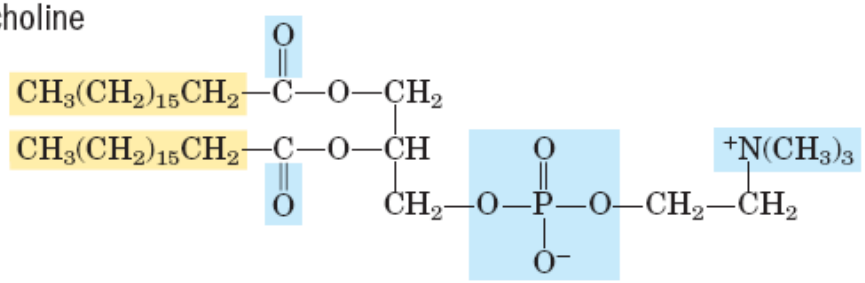


Amphipathic

Phenylalanine



Phosphatidylcholine



Polar groups Nonpolar groups



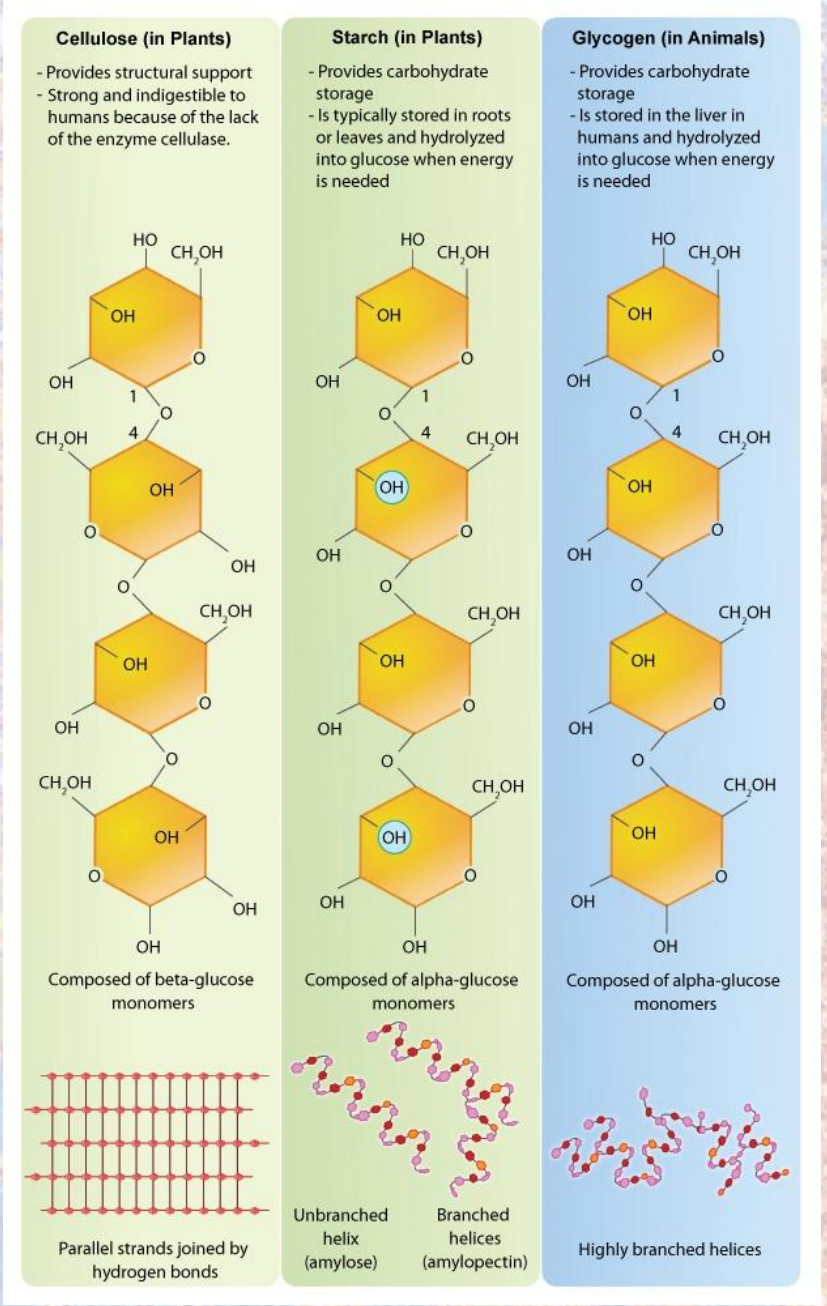
MBG303 Biochemistry

Chapter 5- Carbohydrates

Hikmet Geçkil, Professor
Department of Molecular Biology and Genetics
Inonu University

Carbohydrates





important polysaccharides

- **Cellulose**: β-glucose monomers connected into polymers by β-glycosidic linkages. Each polymer chain of cellulose is unbranched.
- **Starch**: α-glucose monomers that are either branched or unbranched. The α-glycosidic linkages in starch result in an orientation of the hydroxyl groups that differs from the alignment in cellulose.
- **Glycogen**: strands of α-glucose monomers that are also branched. Glycogen is structurally similar to amylopectin, but glycogen contains more branches.

Karbohidratlar

- Doğada yaygın olarak dağılmış ve en büyük kütlesel miktarlarda bulunan biyomoleküllerdir. **Sakkarit** olarak da bilinirler. Kimyasal olarak hem amino asitlerden ve hem de nükleotidlerden daha basit moleküllerdir. Element olarak sadece karbon, hidrojen ve oksijen içerirler. Aynı zamanda güneş enerjisinin "fotosentez" olayında kullanılması ile inorganik karbon (CO_2), hidrojen-oksijen (H_2O)'den meydana gelen ilk organik moleküller karbonhidratlardır. Bundan dolayı canlıların temel enerji kaynağıdırlar.

Karbohidratlar

Karbohidratlar

C, H ve O içeren bileşiklerdir

Genel formül: $C_x(H_2O)_y$

Hepsi C=O ve –OH fonksiyonel gruplarına sahiptir

Sınıflandırılmaları

- Temel karbon zincirine göre
- Şeker (monomer) sayısına göre
- C=O grubunun pozisyonuna göre
- Stereokimyasal olarak

Karbohidrat çeşitleri

Zinzirdeki monomer sayısına göre

Monosakkaritler - Tek monomerli şeker

Disakkaritler - İki monomerli

Oligosakkaritler -2-10 monomer

Polisakkaritler ->10 monomer

Karbohidratlar

- Her ne kadar $C_nH_{2n}O_n$ genel formülü ile tanımlanırlarsa da, bu çoğu zaman yanlış anlaşılmalara neden olur. Çünkü, bazı moleküller bu tanımlamaya uydukları halde (örneğin formaldehit CH_2O, laktik asit $C_3H_6O_3$, gibi) karbonhidrat değildirler. Aynı zamanda karbonhidratlar modifiye olmuşlarsa (örneğin, deoksiriboz $C_5H_{10}O_4$) yukarıdaki tanımlamaya uymazlar.
- Karbonhidratlar en uygun olarak "**polihidroksi aldehit**" veya "**polihidroksi keton**" olarak adlandırılabilirler. Bu nedenle karbonhidratları başka özelliklerini de belirterek tanımlamamız gerekir. **Karbonhidratlar aktif aldehid veya keton grubuna sahip polialkollerin oluşturduğu maddelerdir.** Aldehitlerde karbonil oksijen (-CHO) uçtaki karbon atomu ile birleşmişken, ketonlarda karbonil oksijen iç kısımdaki bir karbon atomuna bağlıdır (-C=O). Doğada karbonhidratlar monosakkarit, oligosakkarit (2-10 monosakkarit) ve polisakkarit halinde bulunurlar.

Karbohidratlar

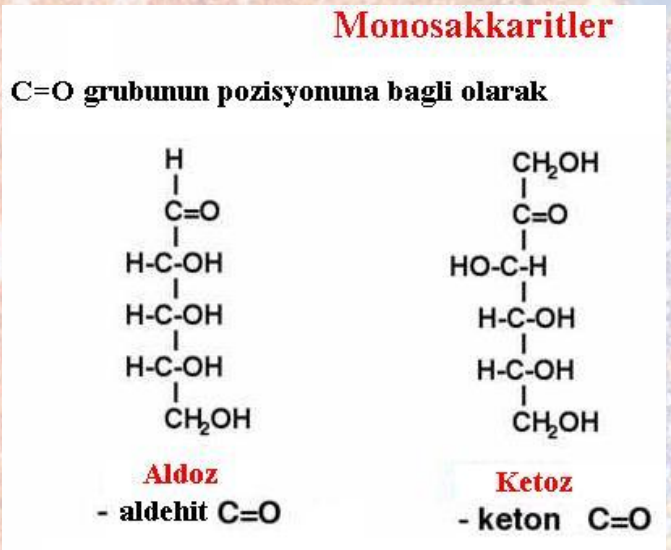
- Monosakkaritler, basit şekerler olarak bilinirler. Yapılarında aldehid veya keton grubu taşımalarına göre aldo şekerler (aldoz) ve keto şekerler (ketoz) olmak üzere 2 gruba ayrılırlar.
- Ayrıca her bir grupta karbon sayısı 3 ila 7 arasında değişen şekerler bulunur.
- Glukoz, monosakkaridleri temsil eden en önemli şekerdir.
- Metabolik olaylarda karbonhidratlar glukoza çevrilmek suretiyle kullanılır.
- Bu nedenle anlattıklarımız glukoz üzerine odaklanacak ve yeri geldikçe diğer bileşiklerle ilişki kurulacaktır. Keto grubu içeren monosakkaridin isminin sonuna “üloz” eki eklenir. Bu bilgiler ışığında aşağıdaki düzenleme yapılabilir.

Karbohidratlar

Karbon sayısı	Formülü	Aldoz	Ketoz
Trioz	$C_3H_6O_3$	Gliseraldehid	Dihidroksi aseton
Tetroz	$C_4H_8O_4$	Eritroz	Eritrüloz
Pentoz	$C_5H_{10}O_5$	Riboz	Ribüloz
		Ksiloz	Ksilüloz
Heksoz	$C_6H_{12}O_6$	Glukoz	Früktoz
Heptoz	$C_7H_{14}O_7$		Sedoheptüloz

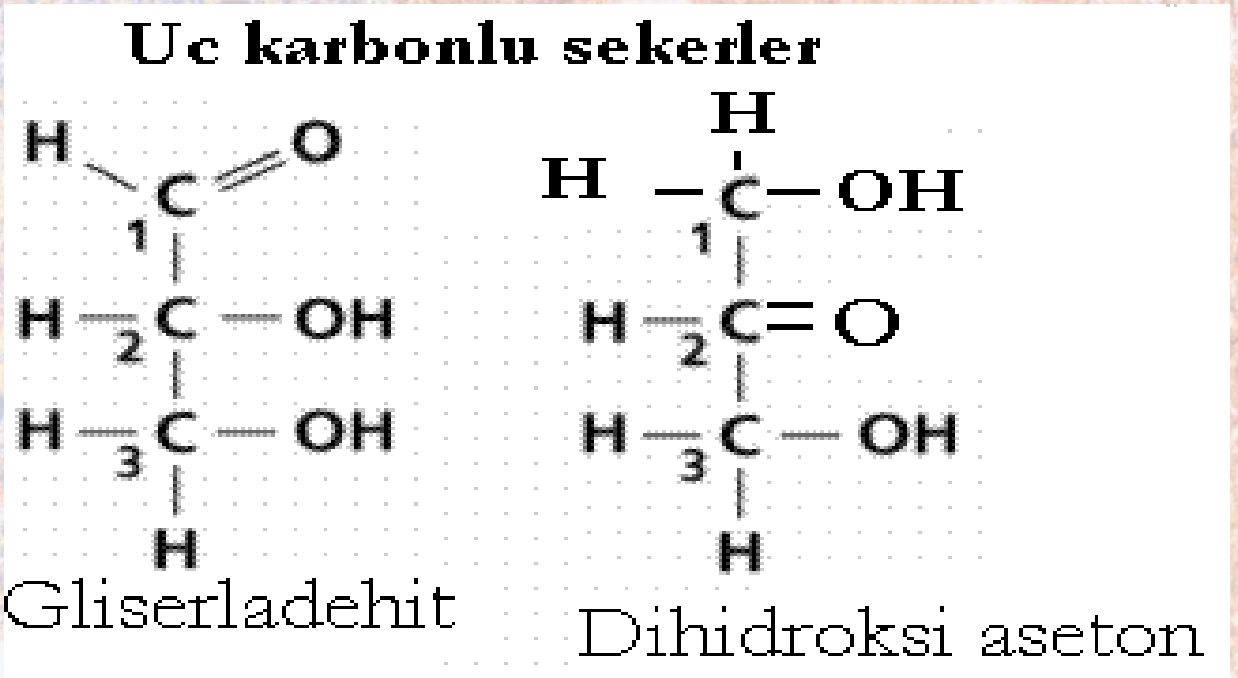
Karbohidratlar

- Bir monosakkarit yapısındaki karbon atomu sayısı ve fonksiyonel karbonil grubu (aldoz veya ketoz)'una göre belirlenir.
- Monosakkaritlerin omurgası dallanmamış bir karbon zincirinden oluşmuştur ki, karbon atomlarından biri bir oksijen atomuna çift bag yapmıştır. Bu gruba **karbonil grubu** denir.
- Geriye kalan karbon atomlarının herbirine bir hidroksil grubu ve hidrojen bağlıdır.
- Canlılarda karbonhidratların D-formu (örneğin D-glikoz) bulunur (amino asitlerin canlıda L-formunda olduklarını hatırlayınız).
- Bu yapı, karbonil karbon atomuna en uzak alfa-karbon atomunun yapısına göre belirlenir. Yani karbonil grubunun bir aldehit olması halinde monosakkarit **aldoz**, karbonil grubunun keton olması halinde ise o monosakkarit **ketoz** olarak adlandırılır:



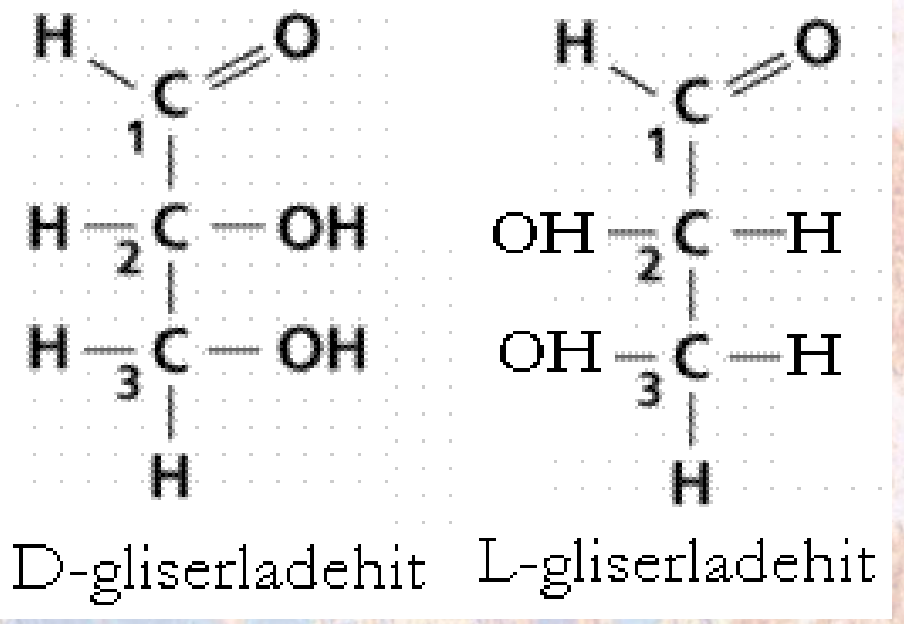
Karbohidratlar

- En basit yapılı monosakkaritler olan 3 karbonlu **gliseraldehit** bir aldoz iken, **dihidroksi aseton** bir ketozdur:



Karbohidratlar

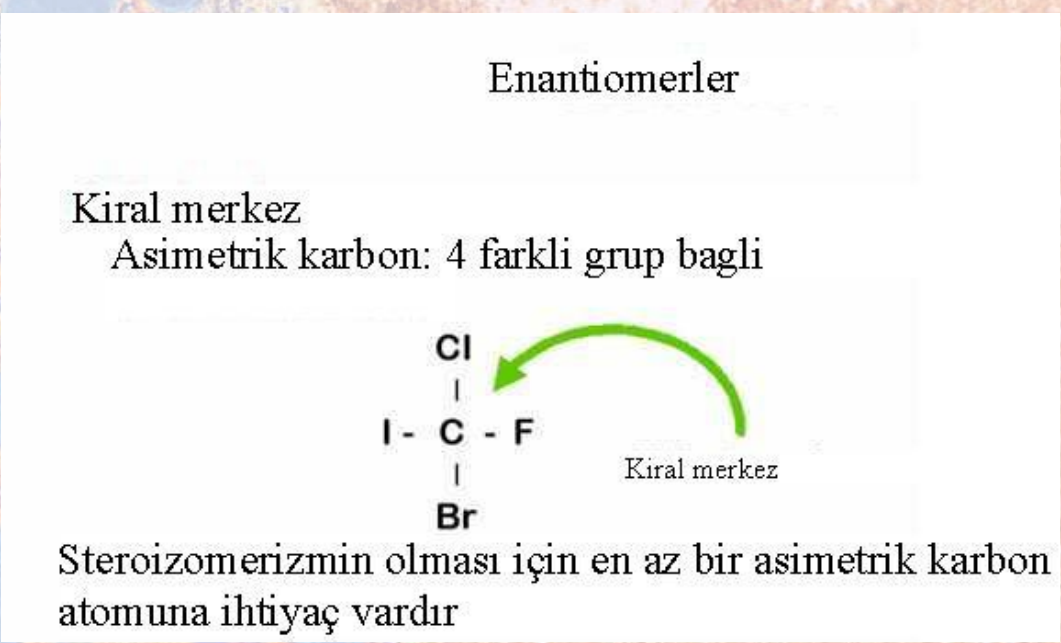
- Dihidroksi aseton hariç monosakkaritler asimetrik alfa karbon atomlarına sahiptirler. Yukarıda da görüldüğü gibi gliseraldehit ortadaki karbon atomundan dolayı iki farklı optik izomere sahiptir. Bunlara **enantiyomerler** denir:





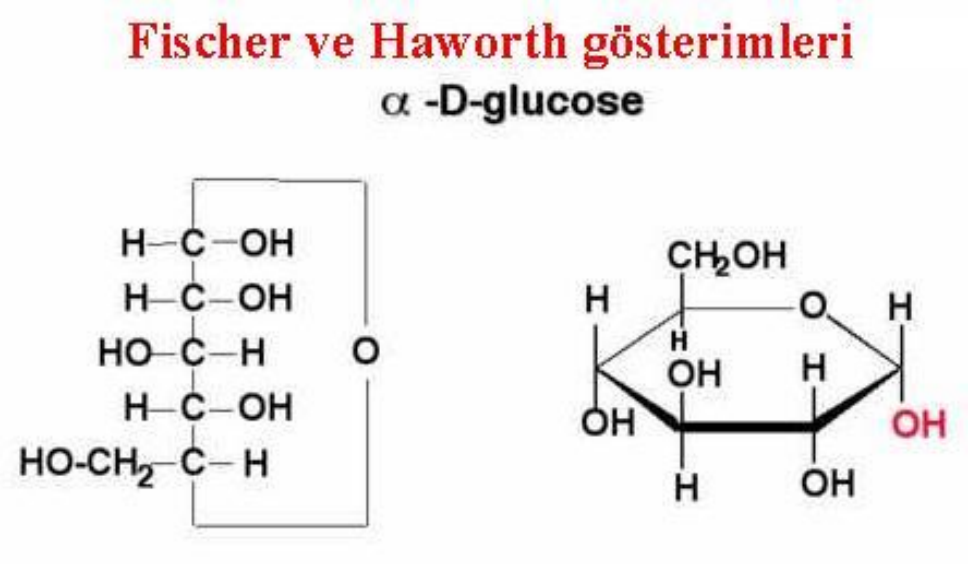
Karbohidratlar

- Genellikle n sayıda asimetrik karbon atomu içeren bir monosakkaritin stereoizomer sayısı 2n olarak ifade edilir. Buna göre, glikoz 4 adet asimetrik karbon atomuna sahip olduğundan, bu şekerin izomer sayısı 16'dir.



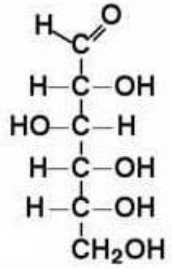
Karbohidratlar

- Glikozun diğer generik ismi '**dekstroz**' olup, doğada en yaygın bulunan organik moleküldür. Yukarıda da tanımladığımız gibi 6 karbondan meydana geldiğinden ve bir aldehit şeker olduğundan "**aldoheksoz**" olarak da tanımlanabilir:



D-glükoz

- Bir aldoheksoz şekerdir
- Avrıca dekstroz, üzüm şekeri ve kan şekeri olarak da bilinir
- Beslenmemizdeki en önemli şekerdir
- Doğada en çok bulunan organik maddedir
- Kandaki seviyesi % 0.1 kadar yüksek olabilir



Karbohidratlar

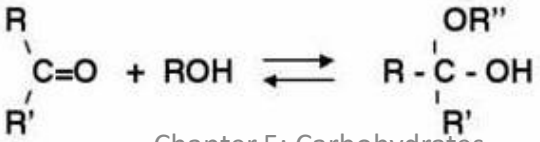
- Solüsyonda glukoz yukarıdaki gibi bir **piran** halkası şeklinde bulunur ve bu yapıya **piranoz** denir (1. pozisyondaki karbonil karbonla 5. pozisyondaki karbon atomu arasında bağ kurulur). Piranoz halkası aldehit ve alkol grubu arasındaki bir reaksiyon sonucu **hemiasetal** denen yapılar ortaya çıkar. Bildiğiniz gibi aldehit ve ketonlar alkollerle reversibl olarak reaksiyona girerek sırası ile hemiasetal ve **hemiketalleri** verir:

Karbohidratlar halkasal yapı oluşturabilirler

Bir çok şeker için yaygın yapı halkasal yapıdır

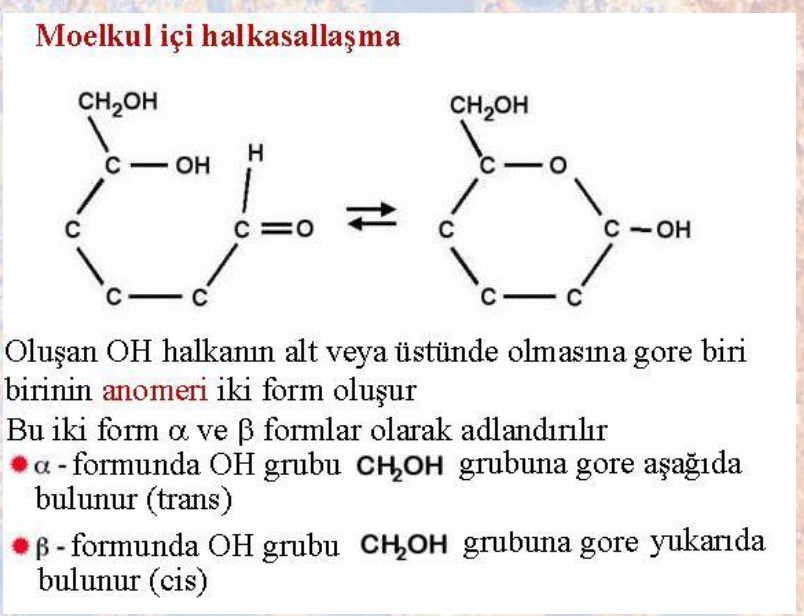
Hemiasetal- Alkol ve aldhitlerden oluşurlar

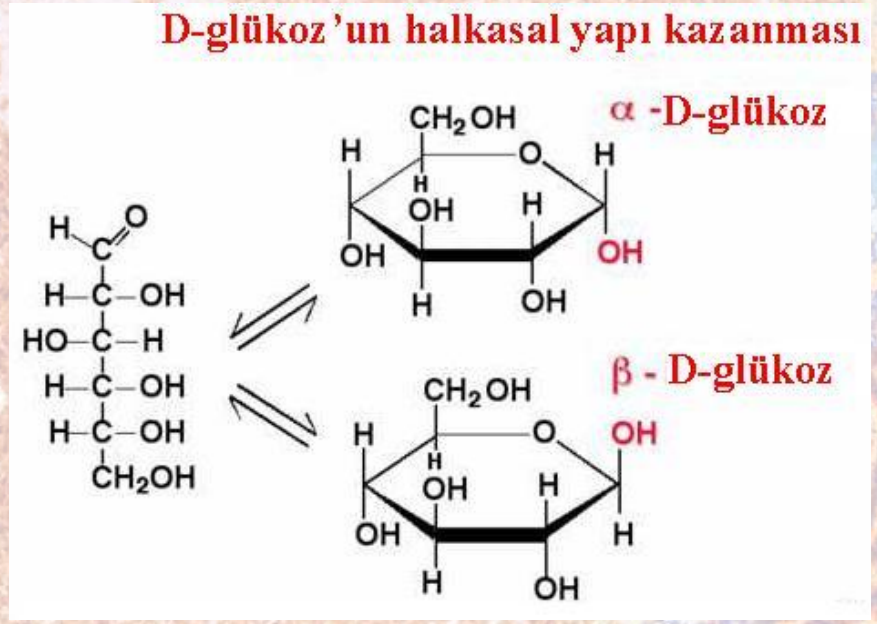
Hemiketal-Alkol ve ketonlardan oluşurlar



Karbohidratlar

- Monosakkaritlerde aynı molekül üzerinde hem OH (alkol grubu) ve hem de C=O bulunduğundan, sulu ortamda ayrı uçlarda bulunan bu iki grup arasında oluşan reaksiyon sonucu, molekül halkasal bir forma dönüşür:





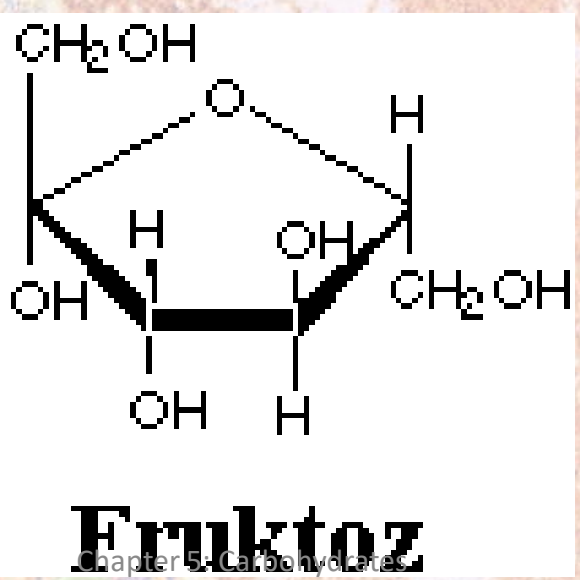
Karbohidratlar

- **Galaktoz** ve **mannoz** da iki yaygın aldoheksoz olup glikozun **izomer**leridir. Bu iki şeker aynı zamanda glikozun birer **epimeridir**ler. Çünkü, her ikisi de glikozdan *sadece bir karbon atomuna bağlı grupların konfigürasyonu ile farklıdır*:



Karbohidratlar

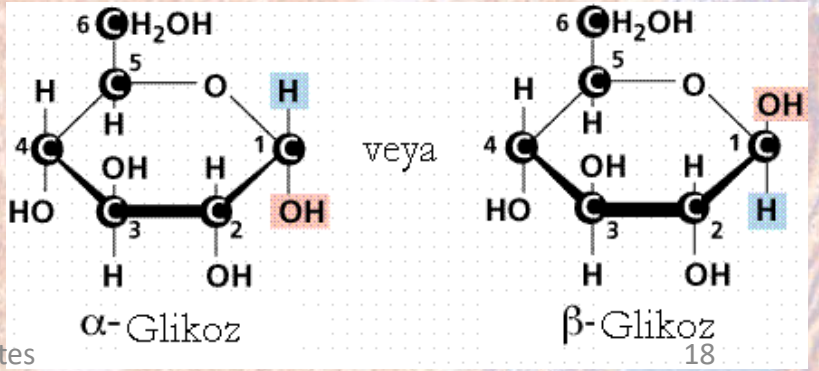
- Ancak, galaktoz ve mannoz birbirlerinin epimeri değildirler. Çünkü her ikisi biri birine iki karbon atomuna bağlı grupları konfigürasyonu bakımından farklılık gösterir.
- Bazen **levuloz** olarak da bilinen **fruktoz** yine en yaygın şekerlerden biridir. Ancak, fruktoz bir **ketoheksoz**dur:



Fruktoz

Karbohidratlar

- Solüsyonda yukarıdaki gibi bir **furan** halkası şeklinde bulunur ve bu yapıya **furanoz** denir. şekerlerin bu yapısal (halkasal) formları termodinamik olarak oluşmaya daha elverişli olduğundan, şekerlerin lineer formları solüsyonda hemen hiç bulunmaz. Konuldukları sıvı ortama bağlı olarak monosakkaritler α veya β formunda bulunabilirler ve bir form diğerine **mutarotasyon** denen bir olayla dönüşebilir:



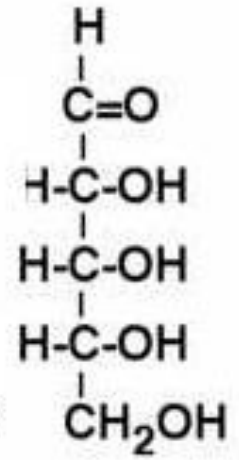
Karbohidratlar

- Biyolojik olarak önemli iki karbonhidrat bildiğiniz gibi DNA ve RNA'nın yapısına giren **deoksiriboz** ve **riboz**dur. Nükleik asitler konusunda bu şekerlere daha detaylı değineceğiz.

D-riboz

Genetik matreyalin yapısına giren önemli bir şeker

- Bu şeker enerji kaynağı olarak kullanılmaz; RNA'nın omurgasını oluşturur
- C-2i'deki OH grubu çıkarıldığında DNA'nın yapısına giren D-deoksiriboz oluşur

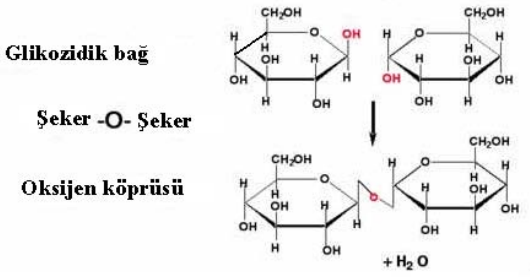


Glükoz ve diğer monosakkaritlerin verdiği reksiyonlar

- Oksidasyon-redüksiyon, Bu şekerlerin metabolik olarak tamamen yıkımı için gerekli reaksiyonlar
- Esterifikasyon, Fosfat esterlerin yapımı
- Amino türevleri, Yapısal malzeme ve glükoprotein yapımı
- Glikozid oluşumu, Monosakkaritlerin biribirine bağlanarak polisakkaritleri oluşturmaları

Glikozid oluşumu

Halkasal monosakkaritlerin α ve β OH grubu başka bir monosakkarit üzerindeki OH grubu ile bağ oluşturabilir

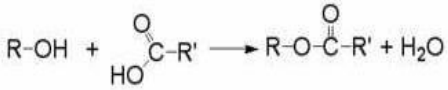


Amino şekerlerin kullanımları

- Bakteri hücre duvarının yapısal malzemesi
- Böcek ve kabuklu hayvanların dış koruma tabakası (kitin polimeri) yapısına girer
- Kondroitin sulfat (bir kartilaj maddesi)' in esas yapısal malzemesi
- Glikoprotein ve glikolipidlerin yapısına girerler

Esterifikasyon

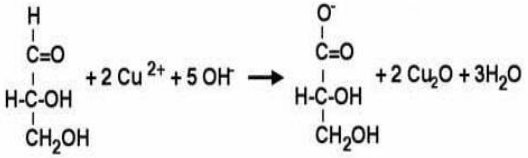
Esterler hidroksil gruplarının (örneğin alkollerin) asitlerle reaksiyonları sonucu oluşurlar



Karbohidratların hidroksil grupları alkollerinkine benzer reaksiyon verirler

Oksidasyon-redüksiyon

Aldehit şekerler (redüklenen) şekerler kolayca oksidize olurlar ve Benedict'in sısvısı ile reaksiyona girerler



Kırmızı bir presipitatın oluşması şekerin varlığını gösterir (özellikle idrarda şeker tayininde)

Diğer önemli testler: Tollen ve Fehling solüsyonları

Glikozidik bağın tipi C-1 OH grubunun pozisyonuna bağlıdır

α glikozidik bağ

C-1 α OH ile C-4 OH arasında

β glikozidik bağ

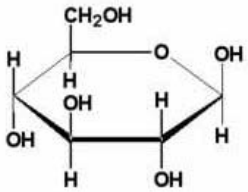
C-1 β OH ile C-4 OH arasında



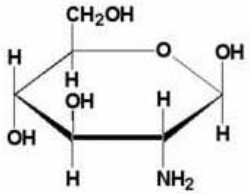
C-4 ucundaki OH grubu, monosakkaritin oryentasyonuna göre yukarıda veya aşağıda olabilir

Amino türevleri

Karbohidrattaki bir hidroksil grubu yerine bir amino grubu girmesi ile oluşurlar

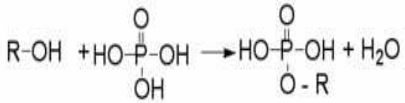


β-D-glükoz



β-D-2-aminoglükoz (glükozamin)

Biyolojide en önemli karbohidrat esterleri fosfat esterleridir



Örnek: ATP'den fosforil grubu bir kinaz (hekzokinaz) enzimi yardımı ile D-glükozla bir ester oluşturur



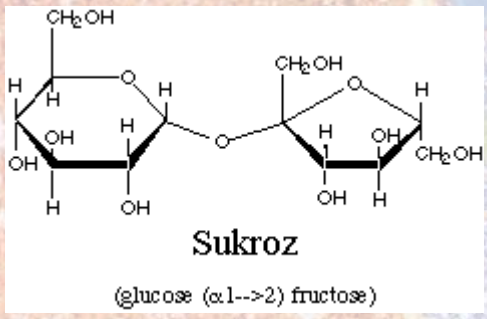
Karbohidratlar

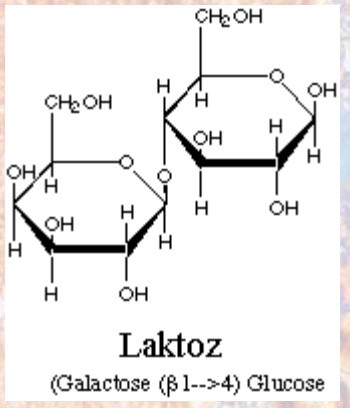
- Modifiye olmuş monosakkaritlere diğer örnek olarak aminoşekerleri verebiliriz. Örneğin, glikozaminlerde bir hidroksil grubu (OH) yerine bir amino grubu (NH2) grubu gelmiştir. Bu çeşit şekerler daha çok kabuklu hayvanların kabuğundaki (böcekler, vb) **kitin** tabakasında bulunurlar.
- Canlı sistemlerde aynı zamanda asidik (oksidize olmuş) ve alkolik (redüklenmiş) şekerler de vardır. Örneğin, üronik asitler mukopolisakkaritlerin yapısına girerler. Mukopolisakkaritler kemik, kartilaj ve deride büyük miktarlarda bulunurlar. Mannitol indirgenmiş bir şeker olup polihidrik bir alkol yapısına sahiptir. Bu şeker 1. karbon atomundaki alkol grubu ile mannozdan farklıdır.

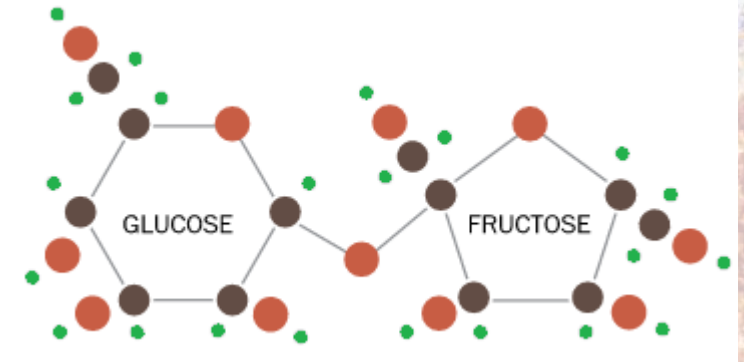
Karbohidratlar

DİSAKKARİTLER ve OLİGOSAKKARİTLER

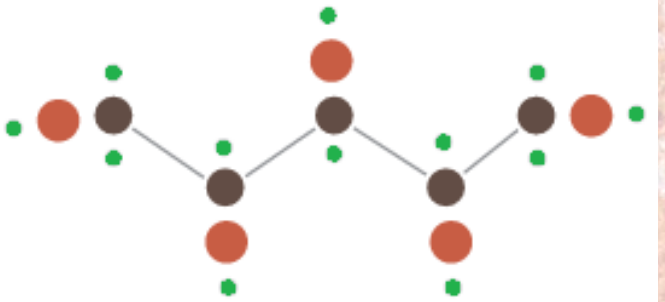
- Doğada en çok bulunan disakkaritler **sükroz** ve **laktoz**dur. Sukroz (çay şekeri) bitkiler tarafından glikoz ve fruktozdan yapılır. Bu iki şeker birbirlerine glikozidik bir bağ ile (α-1,2) bağlanırlar (iki monosakkarit arasındaki OH gruplarından bir su molekülü ayrılması ile):







***Sucrose**, or table sugar, is a disaccharide sugar in which glucose is bonded to fructose. Our bodies produce an enzyme that breaks that bond. High-fructose corn syrup is a liquid solution of unbonded glucose and fructose, with a higher percentage of the latter.*
***Glucose** supplies energy for brain and muscle cells.**Fructose** is converted by the liver into fat.*



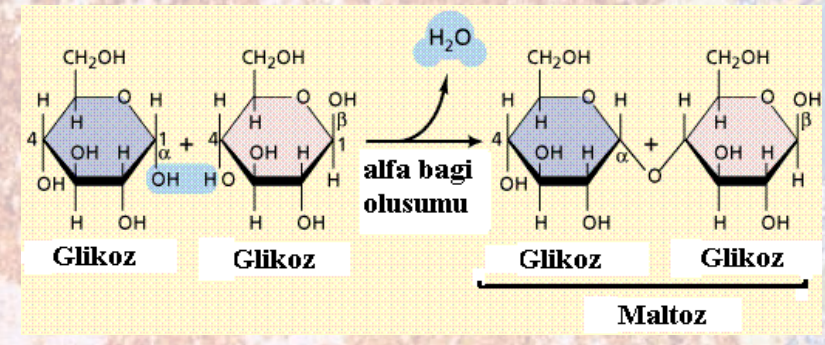
***Xylitol**, synthesized from corncobs and birch trees, can help remineralize tooth enamel.* Even in small amounts, xylitol, which is often found in chewing gum and candy, is poisonous to dogs.

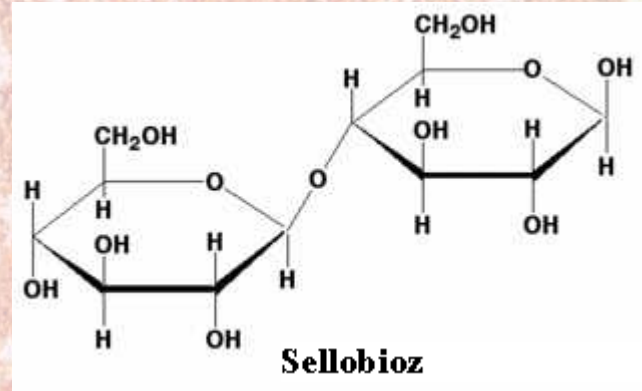
Karbohidratlar

- Şeker kamışının ve şeker pancarının kütlesinin % 20'ye kadarı sükroz olabilir. Sütte bol miktarda bulunan laktoz glikoz ve galaktozdan meydana gelmiştir. Her iki karbonhidrat birbirine β-1,4 glikozidik bağı ile bağlanmışlardır:

Karbohidratlar

- **Maltoz** (glukoz(α,1-4)glukoz) ve **sellobioz** (glukoz(β,1-4)glukoz) diğer iki disakkarit olup (çimlenen tohumlar hariç) doğal olarak oluşmazlar. Bu şekerler ancak ticari olarak nişasta ve sellulozdan elde edilirler. Maltoz α-1,4, sellobioz ise β-1,4 bağları ile bağlı iki glikoz molekülünden meydana gelmişlerdir.





Karbohidratlar

- Bu bağlardan dolayıdır ki glikozun α-1,4 bagları ile bağlanmasından oluşan polimeriler (örneğin, glikojen, nişasta) hayvan ve bitkiler için hazır enerji rezervleri iken, glikozun β-1,4 bagları ile bağlanması ile meydana gelen polimeriler (örneğin selluloz) daha çok yapısal görevlere yönelik olup bir çok canlı tarafından yıkılamazlar. Geviş getiren hayvanların sellulozu yıkmaları onların midesindeki bakterilerin bu bağları parçalayabilen enzimler salgılamasındandır (karıncalar bile odundaki bu sellulozu parçalayacak bakteriler sayesinde bu sindirimi gerçekleştirirler). Selluloz bu şekilde parçalanmasaydı, ölü vejetasyon önemli çevresel ve ekonomik problemlere neden olacaktır.

Karbohidratlar

- Monosakkarit ve disakkaritlerin çoğu etkili redükleyici maddelerdir. Disakkaritlerde en az bir redükleyici aldehit veya keton grubu glikozidik bağın yapısında rol almaz. Ancak, sukrozda her iki grup da bu bağın yapısına girdiğinden bu disakkarit redükleyici bir disakkarit değildir. Monosakkaritler demir (Fe+3+) ve bakır (Cu+2) gibi zayıf oksitleyici maddelerle oksitlenebilirler. Burada karbonil karbon karboksilik aside oksidize olur. şeker tarafından indirgenen demir veya bakırın miktarı şekerin miktarı ile ilişkilendirilerek solüsyondaki (veya kandaki) şeker miktarı bulunur (**Fehling'in reaksiyonu** bu temele dayanır). Ancak son yıllarda kan şekerinin ölçümü daha pratik ve hassas olan enzimatik (glikoz oksidaz) bir reaksiyonla tayin edilmektedir:

D-glikoz + O2 ------ D-glikonat + H2O2

- Reaksiyonunda da görüldüğü gibi açığa çıkan hidrojen peroksit miktarı spektrofotometrik olarak belirlenip dolaylı olarak glikozun miktarı belirlenir.

Karbohidratlar

- Genellikle sadece şekerlerin tatlı bir özelliğe sahip oldukları sanılır. bazı maddeler vardır ki karbonhidrat olmadıkları halde tatlıdırlar. Örneğin, iki amino asitten (aspartik asit ve fenilalanin) oluşan ve ticari olarak **aspartam** adı altında pazarlanan madde sükrozdan 200 kat daha tatlıdır. Yapıya giren amino asitlerin her ikisi de L-amino asittir (proteinlerin yapısına gire amino asitler gibi). L-amino asitlerle D-amino asitlerin karışımından veya tamamen D-amino asitlerden oluşan peptidler acıdır. **Sakkarin** de şeker olmayan diğer bir tatlı madde olup sükrozdan yaklaşık 500 kat daha tatlıdır.

Karbohidratlar

- Bu çeşit maddeler çoğu zaman metabolize olmadıklarından sadece tatlandırıcı olarak kullanılırlar. Dolayısı ile besinsel değerleri fazla değildir.

Ne kadar tatlı!

Şeker	Sükroza göre tatlılık
laktoz	0.16
galaktoz	0.32
maltoz	0.33
sükroz	1.00
früktoz	1.73
aspartam	180
sakkarin	450

Karbohidratlar

Polisakkaritler

- **Depo polisakkaritleri**

  Enerji depolama; glikojen ve nişasta

- **Yapısal polisakkaritler**

  Hücreyi koruyucu duvar ve motor yağının sürtünmeye karşı fonksiyona benzer fonksiyon (eklemlerde); seluloz ve mukopolisakkaritler

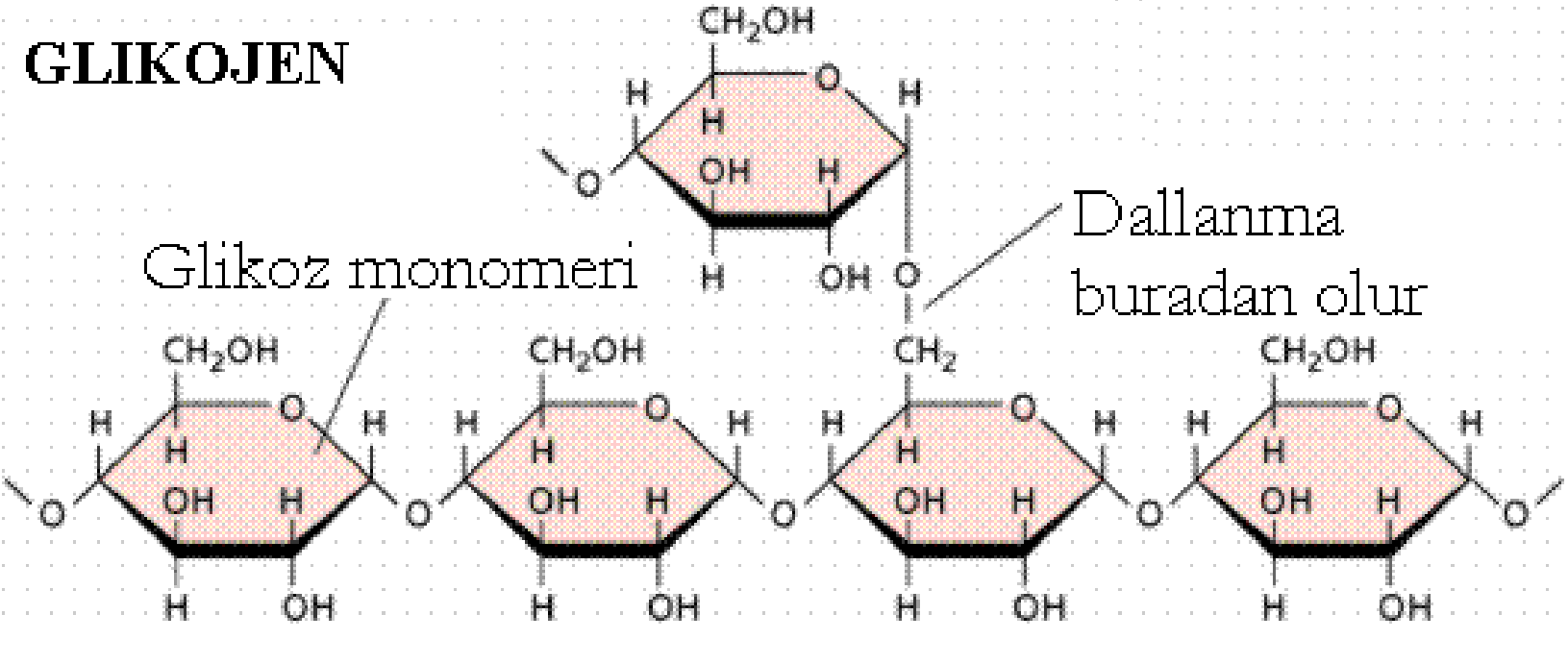
- **Yapısal peptidoglikanlar**

  Bakteri hücre duvarı

Karbohidratlar

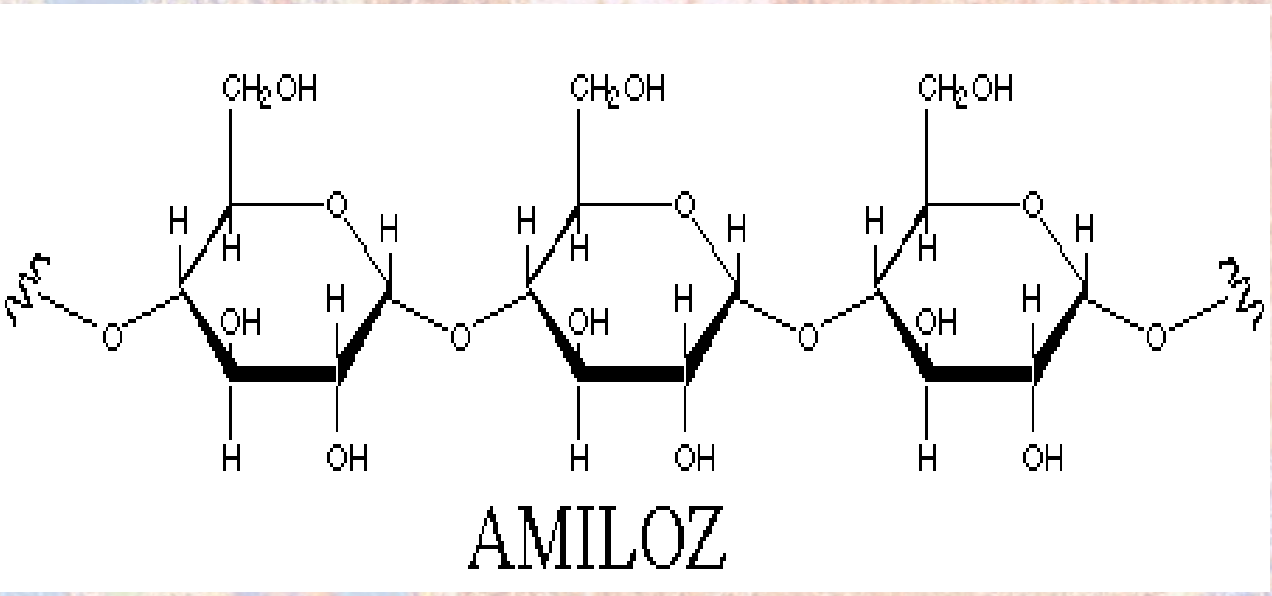
- En iyi bilinen polisakkaritler D-glikozun polimerleridir. Bunlar enerji rezervleri olarak (örneğin, hayvanlarda **glikojen**, bitkilerde **nişasta**) kullanılırlar. Glikojen α-1,4 glikoz alt ünitelerinden ve α-1,6 dallanmalarından oluşur. Bu dallanmalar her 8-12 glikoz alt ünitesinde bir tekrarlanır.

Karbohidratlar



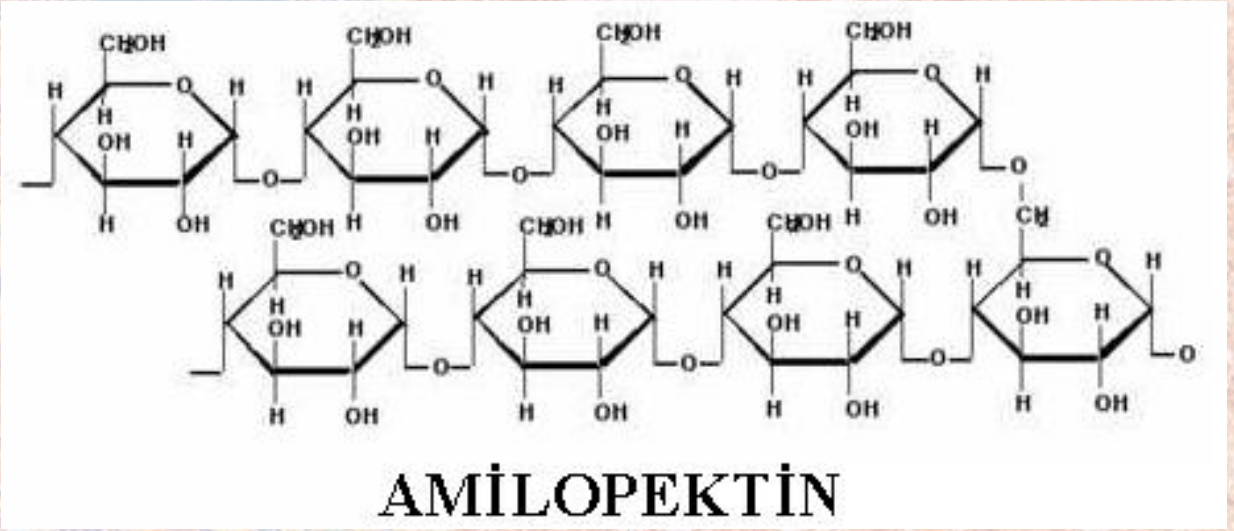
Karbohidratlar

- Nişasta **amiloz** ve **amilopektin** polimerlerinin bir karışımıdır (4000 kadar glukoz monomeri olabilir). Her iki polimer de salt glikoz ünitelerinden meydana gelir. Maltoz (glikoz + glikoz) amilozun yapısal ünitesidir.



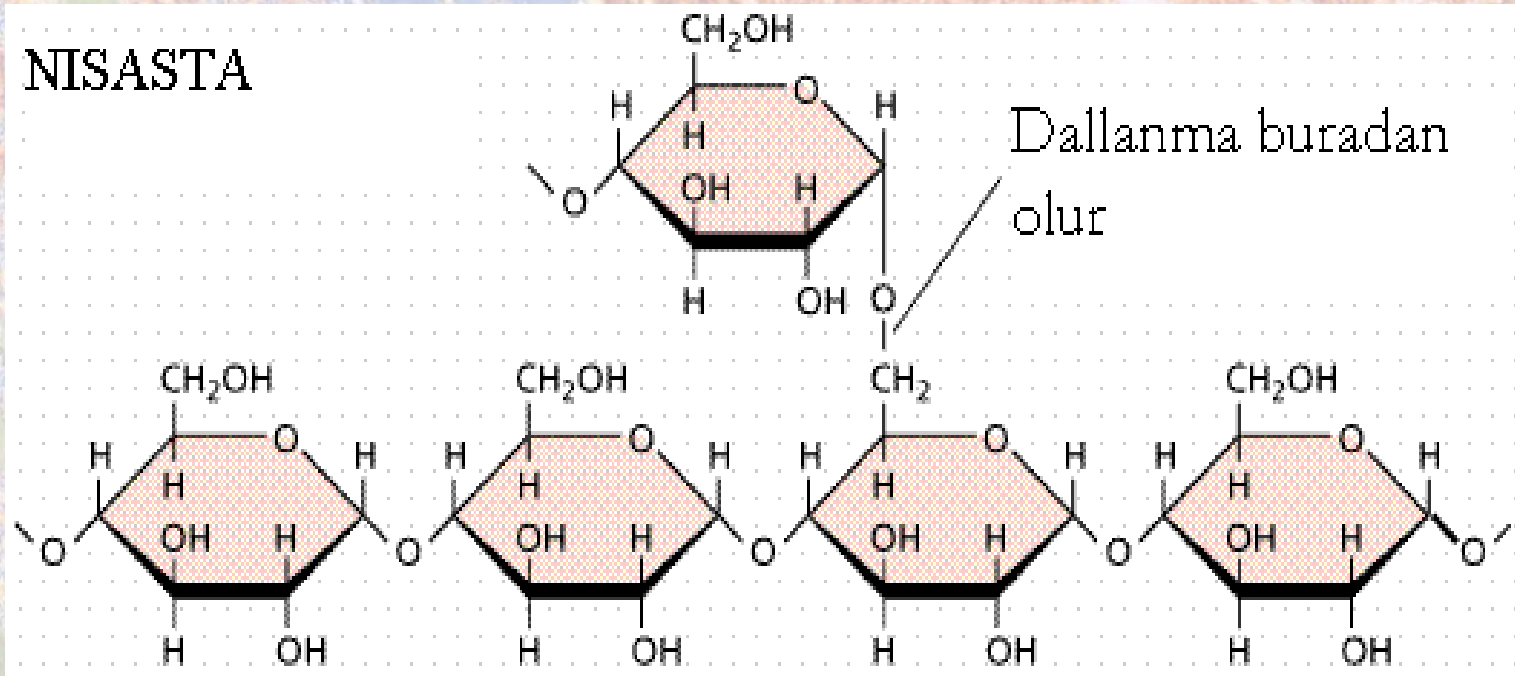
Karbohidratlar

- Amilopektin ise amilozun dallanmış formudur ve glikojene benzerlik gösterir. Ancak amilopektin glikojene göre daha az yoğun bir paketlenme gösterir.



AMİLOPEKTİN

Karbohidratlar

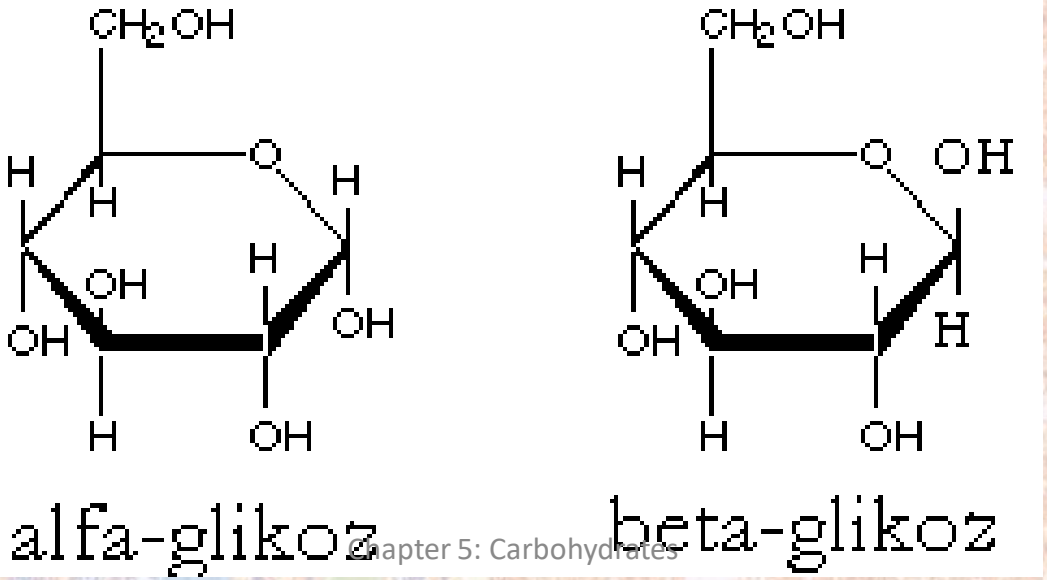


Karbohidratlar

- Hayvanlarda glikojen amilopektine benzer. Farklı olarak, glikojen daha büyük ve dallanmış bir polimerdir. İnsanlarda glikojen kişinin beslenme durumuna bağlı olarak kas ve karaciğerde değişik miktarlarda bulunur. Glikojeninin sentezi için glikozun aktif hale gelmesi gerekir. Bunun için glikozun uridin difosfata (UDP) bağlanması gerekir. UDP burada ATP'ye benzer bir fonksiyon yapar. Glikojen ve nişastanın enerji molekülleri olarak kullanımını metabolizma konusunda isleyeceğiz.

Karbohidratlar

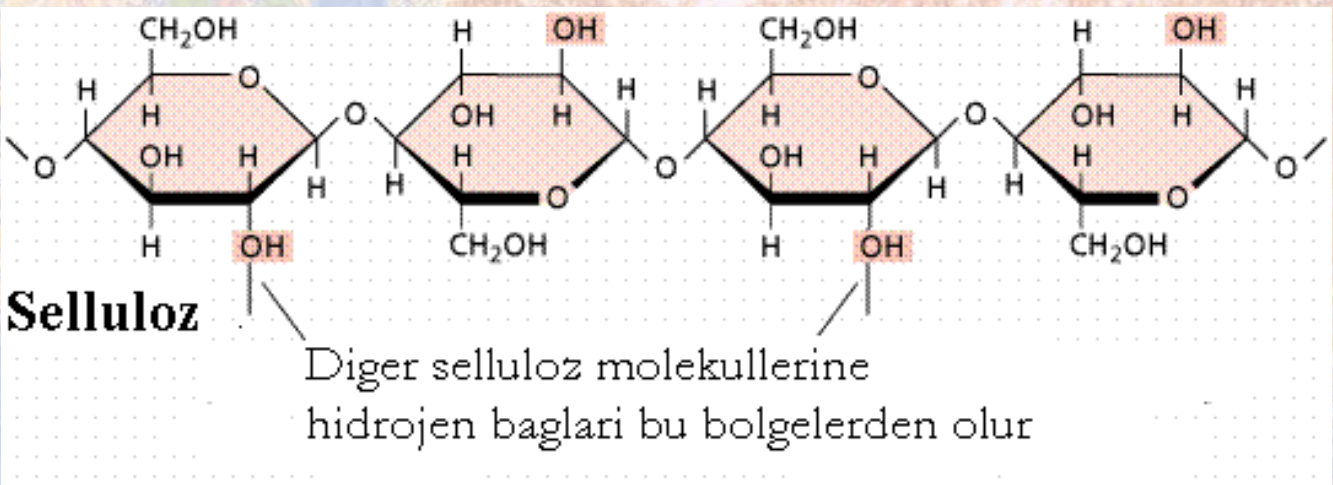
- Polisakkaritler yapısal malzeme (örneğin, bitki hücre duvarını oluşturan **selluloz**) olarak da kullanılırlar. Selluloz tekrarlanan sellobioz ünitelerinden meydana gelmiş olup doğada en fazla bulunan makromoleküldür. Selluloz bitki hücre duvarının yapısal malzemesi olmasının yanında, gövde, dal, yaprak ve tüm odunsu kısımlarda bulunur. Odunumsu her malzemenin büyük kısmı bu makromolekülden oluşmuştur. Pamuk ise hemen hemen tamamen sellulozdur. Glikojen ve nişastanın tersine selluloz molekülleri dallanma göstermezler ancak diğer selluloz molekülerine kovalent olmayan hidrojen bagları ile bağlanabilirler. Sellulozun yapısını veren glikoz molekülleri (10,000-15,000 adet glikoz) β yapıdadır:



Karbohidratlar

- Dolayısı ile sellulozda polimer yapı glikoz monomerlerinin birbirine β-1,4 bagları ile bağlanması ile oluşur:

- Bu fark selluloza kolay sindirilemeyen ve daha farklı bir üç boyutlu yapı kazandırır.



Karbohidratlar

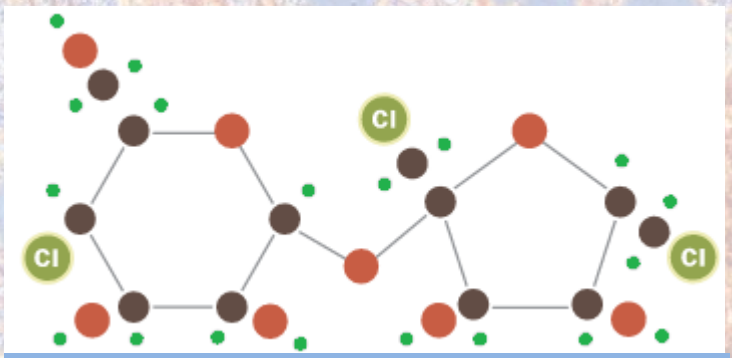
- Glikojen ve nişastanın tersine selluloz suda erimez özellik taşır. Glikojen ve nişastanın suda kolay eriyebilmelerinin nedeni, sellulozun tersine bir çok hidroksil grubunun (OH) açıkta serbest halde bulunmasıdır. Bu gruplar dolayısı ile su ile hidrojen bağları kurarak bu makromoleküllerin erir olmasını sağlarlar.
- Yine yiyeceklerle alınan glikojen ve nişasta **α-amilaz** enzimleri (bu enzimler tükürük ve ince bağırsakta bulunurlar) sayesinde hidrolize edilirler (α-1,4 ve dallanma bölgelerindeki α-1,6 bagları parçalanır). Sellulozda bu tur bağlar bulunmadığından (sellulozda β-1,4 bağları glikoz monomerleri arasına kurulmuştur) selluloz bu enzimler tarafından parçalanamaz. Bu baglar yukarıda da bahsettiğimiz gibi anacak geviş getiren hayvanların midesinde bulunan bakterilerin salgıladığı **sellulaz** enzimi tarafından yıkılabilir.

Karbohidratlar

- Suda erimeyen özelligi olan selluloza benzer diğer bir molekül **kitin**dir. Yine β-1,4 bağlarından oluşan bu makromolekül hayvanlar tarafından sindirilemez. Sellulozdan tek farkı glikozun ikinci karbon atomunda OH grubu yerine asetillenmiş bir amino grubunun (-NH-CO-CH3) girmesidir. Sellulozdan sonra doğada en çok bulunan polimerdir. Böcek ve kabuklu deniz hayvanlarının dış iskeletinin temel yapı maddesi kitindir.

Karbohidratlar

- Bakteri hücre duvarını oluşturan sert yapı yine karbonhidrat bileşimleri olan ve bir birlerine β-1,4 bagları ile bağlanan N-**asetilglikozamin** ve N-**asetilmuramik asit**'den meydana gelmiştir. Bu yapıya **peptidoglikan tabakası** denir. Bu bağlar ancak **lizozim** enzimi ile parçalanabilirler. Hayvansal dokularda hücreler arası matriks jöle şeklinde bir madde ile doludur. Bu maddenin elementleri polisakkarit ve fibröz proteinlerdir. Bu bölgede en çok bulunan üç karbonhidrat birer monosakkarit olan N-asetilglikozamin, ve **glukorinik asit** ve her ikisinin birleşmesinden meydana gelen bir polimer olan **hiyaluronik asit**tir. Bu polimer yapışkan bir formda olup eklemlerin hareketinde motor yağına benzer fonksiyon yapar.



Sucralose *is made by removing three oxygen atoms from sucrose and substituting three chlorine atoms.*

Heteropolisakkaridler

- Bu moleküllerde tekrarlayan üniteler, birden fazla ve farklı yapıda monosakkarid içerirler. Örneğin A,B harfleri birbirinden farklı monosakkaridleri temsil ediyorsa, bir heteropolisakkarid aşağıdaki şekilde şematize edilebilir: Heteropolisakkaridler canlılarda hücrelere dışarıdan destek sağlarlar. Bir başka deyişle hücreler arası boşluğu doldururlar. Heteropolisakkaridlerde tekrarlıyan birimlerde amino şekerler bulunduğu için bunlara **glikozaminoglikan** denir. Nisbeten eskimiş tıp literatüründe bu bileşiklere **mukopolisakkarid**ler denmekte idi. Glikozaminoglikanlarda yapıya, ek olarak sülfat iyonu katılmıştır

Karbohidratlar

- Gerek bu gruplar ve gerekse dissosiye olan uronik asitler bu moleküle aşırı negatif bir yük kazandırır. Bu nedenle glikozaminoglikanlar polianyonik birleşiklerdir. Bu nedenle yapıya katyon olarak sodyum ve su bağlanması gerçekleşir ve ortaya koyu kıvamlı kaygan bir madde çıkar.
  Glikozaminoglikanlar dokularda **çekirdek protein** (kor protein) denilen proteinlere bağlanmış olarak bulunur ve böylece çoğunluğu karbonhidrat, azınlığı proteinden meydana gelen büyük bir yapı oluşur ki buna da **proteoglikan** denir.

Karbohidratlar

- Proteoglikanlarda karbonhidrat-protein bağlanması kovalan olup; O-glikozidik (ksiloz-serin/treonin, N-Asetilglukozamin-serin/treonin) veya N-glikozidik(N-Asetilglukozamin-asparagin amino asidinin amido grubu) tarzda gerçekleşir. Şimdi önemli glikozaminoglikanları yapı ve çeşitli özelliklerini gözden geçirelim.

Karbohidratlar

- **1. Hyalüronik asit**:β-glukuronik asit ve N-Asetil-glukozaminden oluşur. Hyalüronik asit hayvanlar dünyasında hücre dışı ortamın en önemli kısmını oluşturur Hücreleri bir arada tutar, oksijen ve diğer besleyici maddelerin geçişine olanak verir. Tendon ve kıkırdak dokusunda bulunur ve onlara esneklik ve dayanıklılık kazandırır. Eklem boşluklarını doldurarak kayganlık sağlar. Gözdeki vitreus sıvısı da hyalüronik asittir. **Hyalüronidaz**, hyalüronik asitteki glikozidik bağları koparan bir enzimdir. Bu nedenle hyalüronidaz salgılayan bakteriler, karşılarındaki doku engelini kolayca aşarak yayılma olanağı bulurlar. Aynı enzime sahip **spermatosit**ler de benzer tarzda **ovum**a ulaşırlar. Hyalüronik asidin bir proteinle bağlantısı tespit edilememiştir.

Karbohidratlar

- **2. Kondroitin sülfat**: Tekrarlayan ünite β-glukuronik asit ve N-Asetilgalaktozamin dir. Sülfat kökü 4. veya 6. karbonlarına bağlandığı için kondroitin-4-sülfat ve kondroitin-6-sülfat olmak üzere iki tipi vardır. Kondroitin sülfat kıkırdak dokusunun en önemli ara maddesidir. Burada ortalama 40 kadar kondroitin sülfat birimi tek bir çekirdek proteinine bağlanır ve böylece oluşan proteoglikan yapıları bağlama proteinleri aracılığı ile omurga konumundaki yalüronik asit ile ilişki kurarak gayet büyük bir proteoglikan kümesi oluştururlar.

Karbohidratlar

- **3. Keratan Sülfat**: Tekrarlayan N-Asetilglukozamin ve galaktoz üniteleridir ve kondroitin sülfatla birlikte bağ dokusunda bulunur.

Karbohidratlar

- **4. Heparin**: Sülfatlı glukozamin ve sülfatlı idüronik asit ikilisinin oluşturduğu bir heteropolisakkarittir. Mast hücreleri tarafından sentezlenen ve kan pıhtılaşmasını engelleyen bir maddedir.

Karbohidratlar

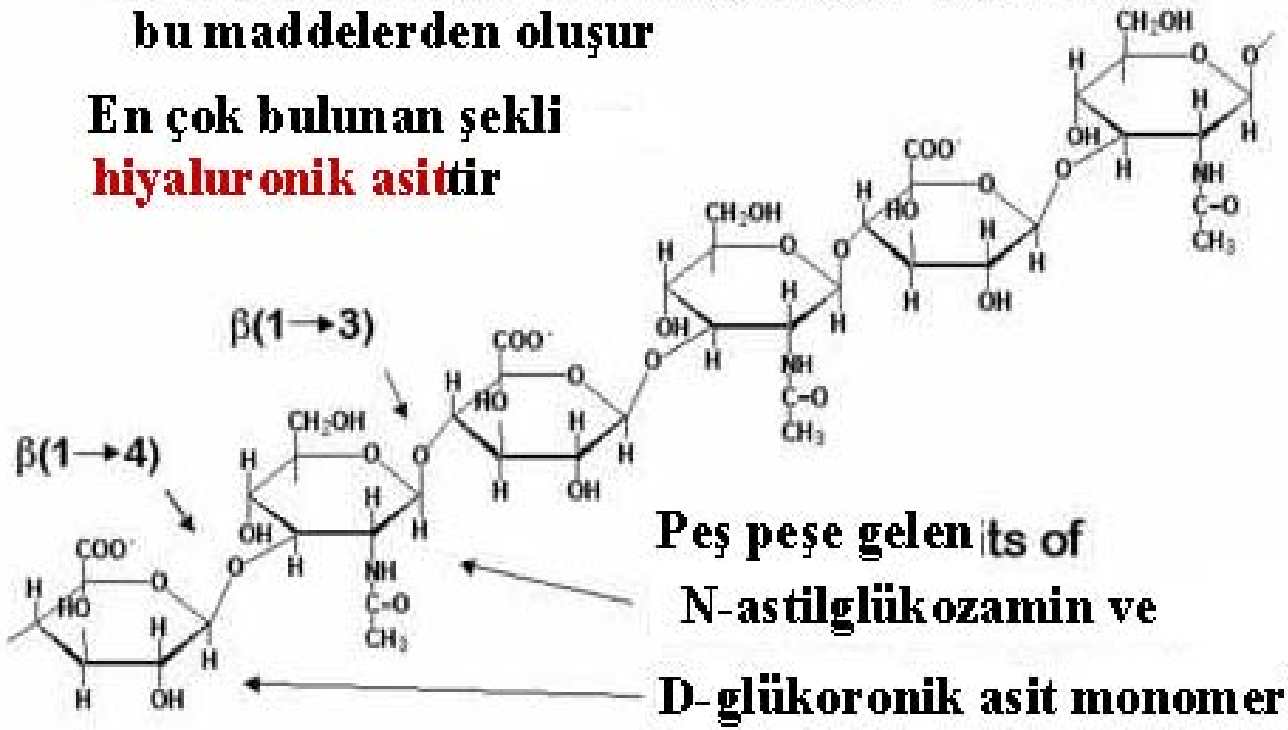
- **5. Heparan sülfat**: Sülfatlı glukozamin ve glukuronik asitten meydana gelir. Bu glikozaminoglikan proteoglikan haline geçtikten sonra hücre membranına yerleşir ve bu yapısıyla bir reseptör gibi görev yapar.

Karbohidratlar

Mukopolisakkaritler

Hücrelerin dışındaki ince, jöle gibi viskoz kılıf bu maddelerden oluşur

En çok bulunan şekli hiyaluronik asittir



Peş peşe gelen ts of

N-astilglükozamin ve

D-glükoronik asit monomerleri

Karbohidratlar

- Karbonhidratlar kovalent olarak diğer biyomoleküllere bağlı olarak da bulunabilirler örneğin, glikolipidler, glikoproteinler de olduğu gibi:

GLİKOPROTEİNLER

- Canlı organizmalarda bulunan bir başka protein-karbonhidrat kombinasyonu, karbonhidratların azınlıkta, proteinlerin çoğunlukta olduğu yapılardır. Bu yapılara **glikoprotein** denir. Glikoproteinler, proteinlerin en büyük bölümünü oluşturur Konumuz gereği, biz bu karışık yapının karbonhidrat zinciri ile ile ilgileneceğiz Glikoproteinlerin karbonhidrat kısmında 7 çeşit monosakkarid bulunur. Bu monosakkaridler o kadar değişik sıralama ve farklı bağ yapıları ile bir araya gelirler ki sonuçta çok sayıda karbonhidrat zinciri yapısı ortaya çıkar. Glikoprotenlerde yer alan monosakkaridler aşağıda gösterilmiştir. Glikoproteinlerde karbonhidrat-protein bağlantısı O-glikozidik veya N-glikozidik bağ tipinde olur.

Karbohidratlar

- Sialik asit birçok yapıda zincirin en başında yer alır ve bu konumuyla bazı glikoproteinlerin karaciğer tarafından yakalanıp parçalanmasını engeller. Bazı glikoproteinlerde ise karbonhidrat zincirinin en başını işgal eden mannoz-6-fosfat bu proteinin lizozoma doğru yönlendirilmesini sağlar.

Karbohidratlar

Glikoproteinler

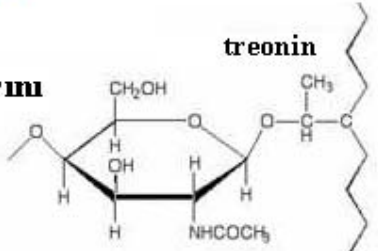
Kovalent olarak karbohidrat bağlı proteinlerdir

Birçok biyolojik fonksiyona sahiptirler

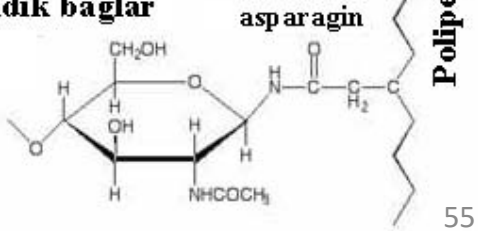
- **İmmün koruma**
- **Hücre-hücre tanımı**
- **Kanın pıhtılaşması**
- **Konakçı-patojen ilişkisi (bağlanma)**

Glikoproteinlerin yapısı

Serin ve treoninin OH gruplarını kullanarak oluşan O-glikozidik bağlar



Asparaginin yan zincir amid azotunu kullanarak oluşan N-glikozidik bağlar



Karbohidratlar

- Polisakkaritler ticari veya tıbbi (laboratuar) bir çok amaçla kullanılabilirler. Bunlardan en önemli ikisi yine glikoz polimerleri olan **dekstrin** ve **dekstran**lardır. Dekstrin (nişasta sakızı) nişastanın kısmi parçalanması ile elde edilen çeşitli ürünlere verilen addır. Bir çok farklı büyüklük ve dallanmaya sahip dekstrinler tekstilde (boyaların yoğunlaştırılmasında) yapışkan madde olarak, tıbbi olarak da dekstrinler hap kaplamasından, su geçirmeyen bandajların yapılmasına kadar bir çok alanda kullanılırlar.

Karbohidratlar

- Dekstranlar bazı bakteriler tarafından yapılırlar. Bir çok farklı tipi vardır. Dekstranların şeker sanayisinde, boya endüstrisinde (cila) kullanımları vardır. Laboratuarda kolon kromatografisi materyali olarak en çok kullanılan matrikslerdendir. tıbbi olarak da şok geçiren hastalarda plazma hacim genişletici olarak kullanılırlar. Kırmızı kan hücrelerinin oluşması veya hücrelerdeki hemoglobin miktarını arttırmak için dekstran-demir bileşikleri kullanılır.

Karbohidratlar

GLİKOLİPİDLER

- Karbonhidratlar lipidlerle birleşerek glikolipidleri oluştururlar. Bunun organizmamızdaki en güzel örneği kan grubu antijenleridir. Glukoz, galaktoz, N-asetil-galaktozamin ve fükozdan oluşan karbonhidrat yapısı, eritrosit membranlarında sfingolipidlere bağlanarak kan grubu antijenlerini meydana getirir (aynı tip karbonhidratlar sekresyon materyelinde proteinlere bağlanır).

Karbohidratlar

- Eritrositlerdeki temel kan grubu antijeni O grubu antijenidir. Bu antijenin karbonhidrat kısmı glukoz-galaktoz- N- asetilgalaktozamin-galaktoz ve fükoz dan oluşur. Lipid kısmında ise sfingozin(amino-alkol) ve yağ asidi bulunur. O grubu antijenine N-asetilgalaktozamin eklenmesiyle A grubu antijeni, galaktoz eklenmesiyle B grubu antijeni meydana gelir.



MBG303 Biochemistry

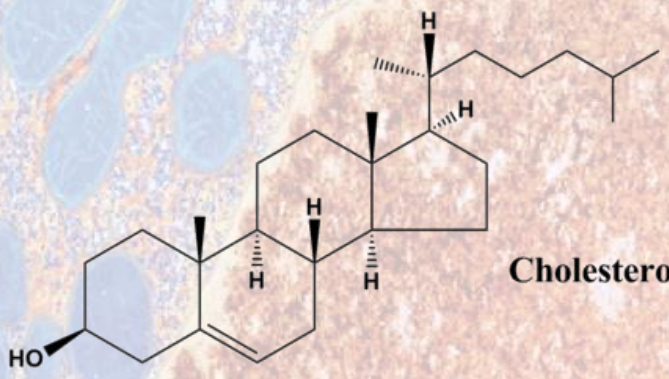
Chapter 6: Lipids

Hikmet Geçkil, Professor
Department of Molecular Biology and Genetics
Inonu University

Lipids

- Lipids include a diverse group of compounds that are largely nonpolar in nature.
- This is because they are hydrocarbons that include mostly nonpolar carbon–carbon or carbon–hydrogen bonds.
- Lipids perform many different functions in a cell.
  - Storage of energy
  - Insulation from the environment
  - Building blocks of many hormones
  - Constituent of all cellular membranes
  - Signaling
- Lipids include fats, oils, waxes, phospholipids, and steroids.

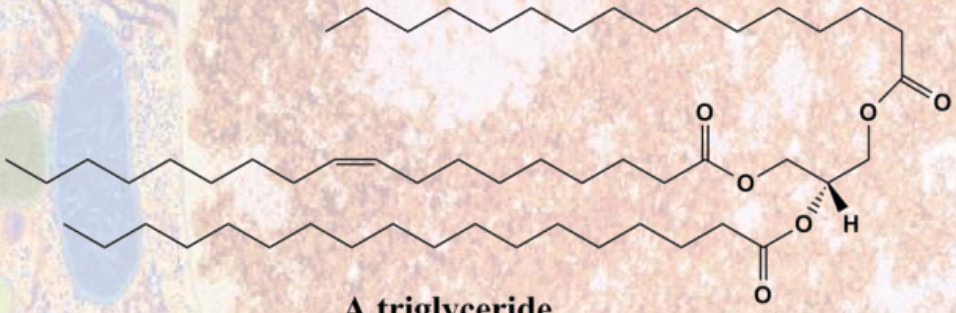




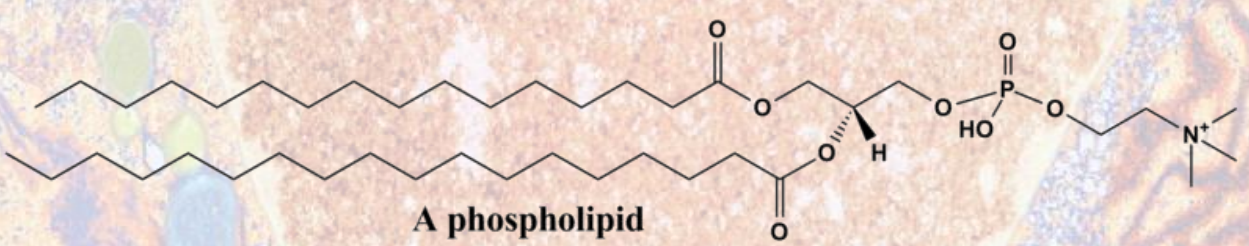
Cholesterol



A free fatty acid



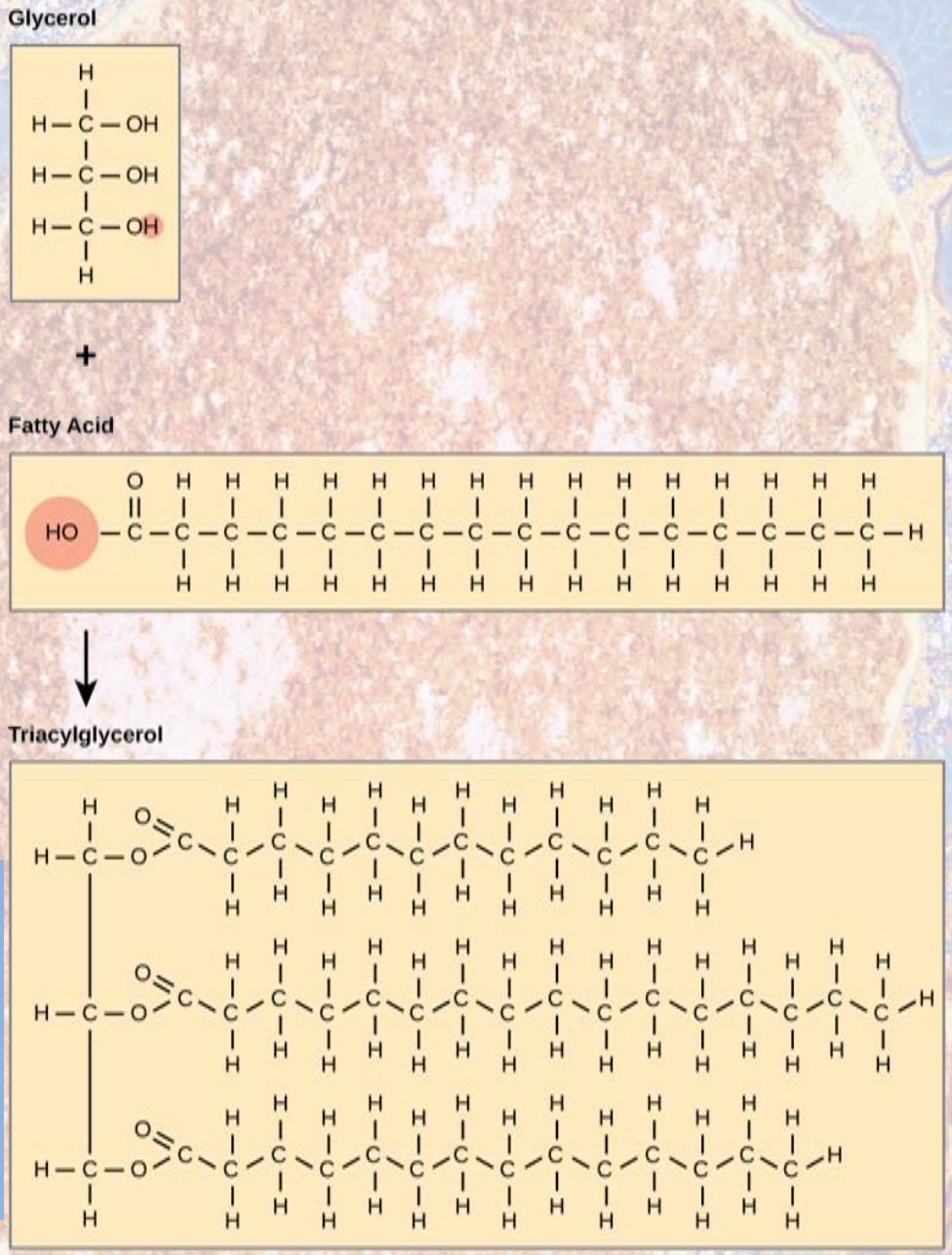
A triglyceride



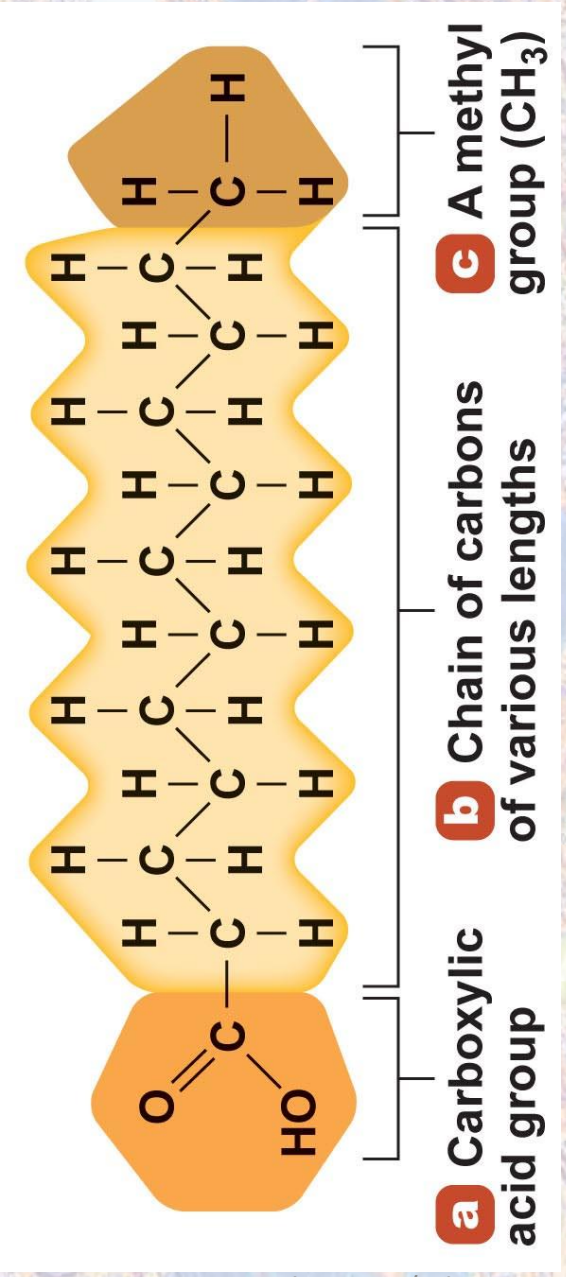
A phospholipid

Fats and Oils

- A fat molecule consists of two main components
  - Glycerol
  - Fatty acids.

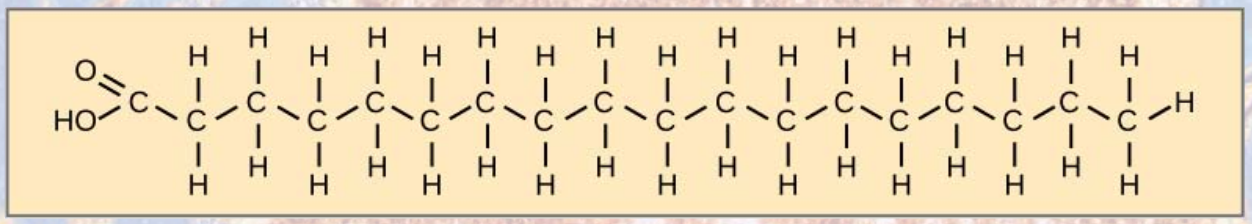


Triacylglycerol is formed by the joining of three fatty acids with an ester bond through an oxygen atom to a glycerol backbone in a dehydration reaction. Three molecules of water are released in the process.



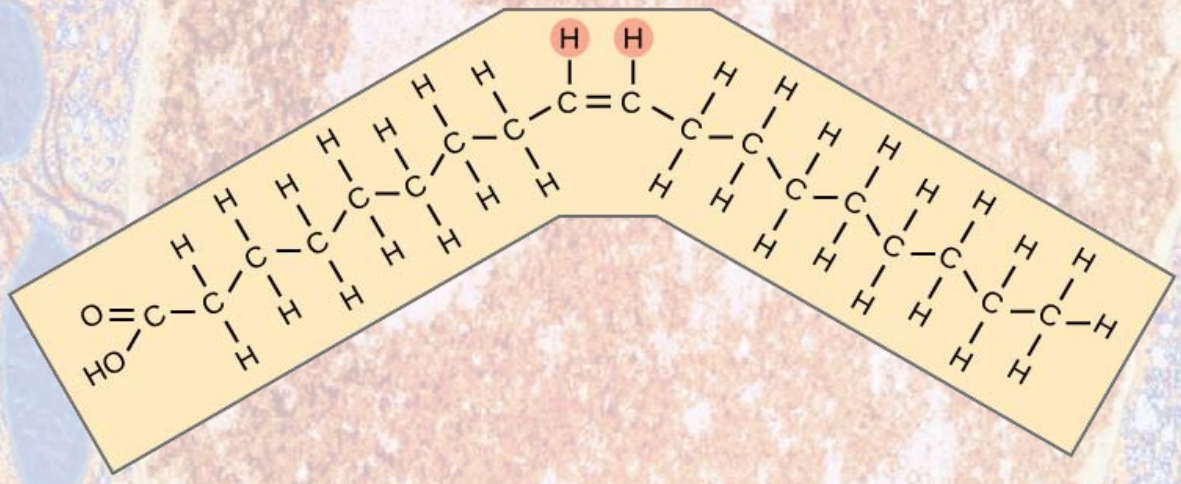
Saturated fatty acid

Stearic acid

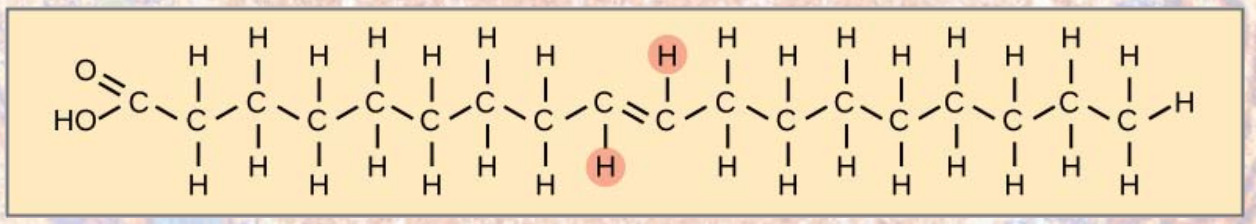


Unsaturated fatty acids

Cis oleic acid

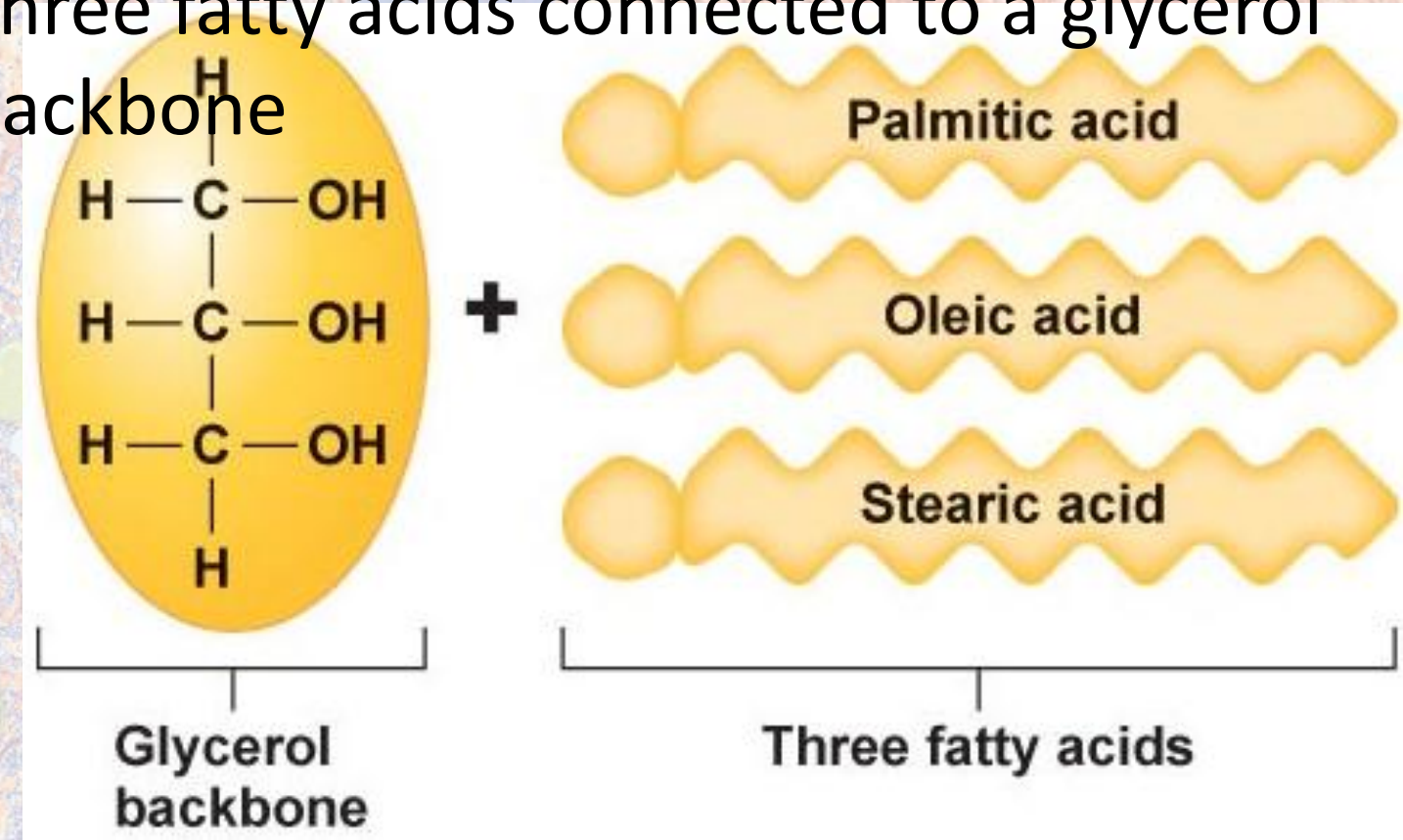


Trans oleic acid



Triglycerides

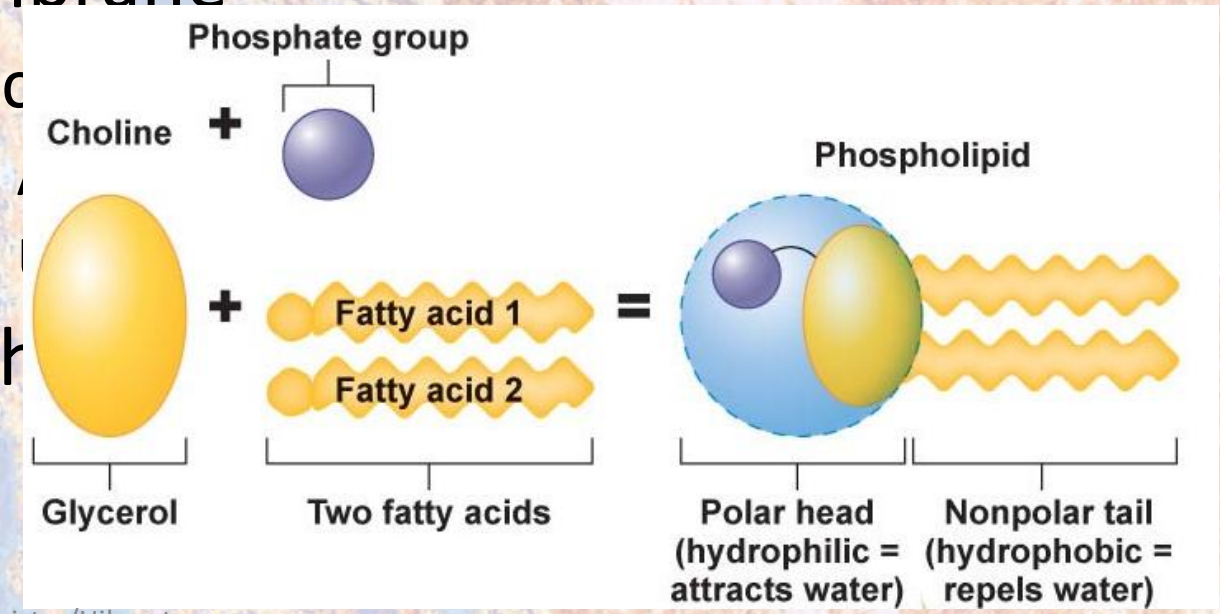
- Three fatty acids connected to a glycerol backbone



Portion of Figure 5.7

Phospholipids

- Hydrophilic on one end; hydrophobic on the other
- Make up the phospholipid bilayer in the cell membrane
  - Lec
    - A
    - I
- Synth



Portion of Figure 5.8

Fatty Acids Vary in Shape

- Unsaturated fatty acids form two different shapes

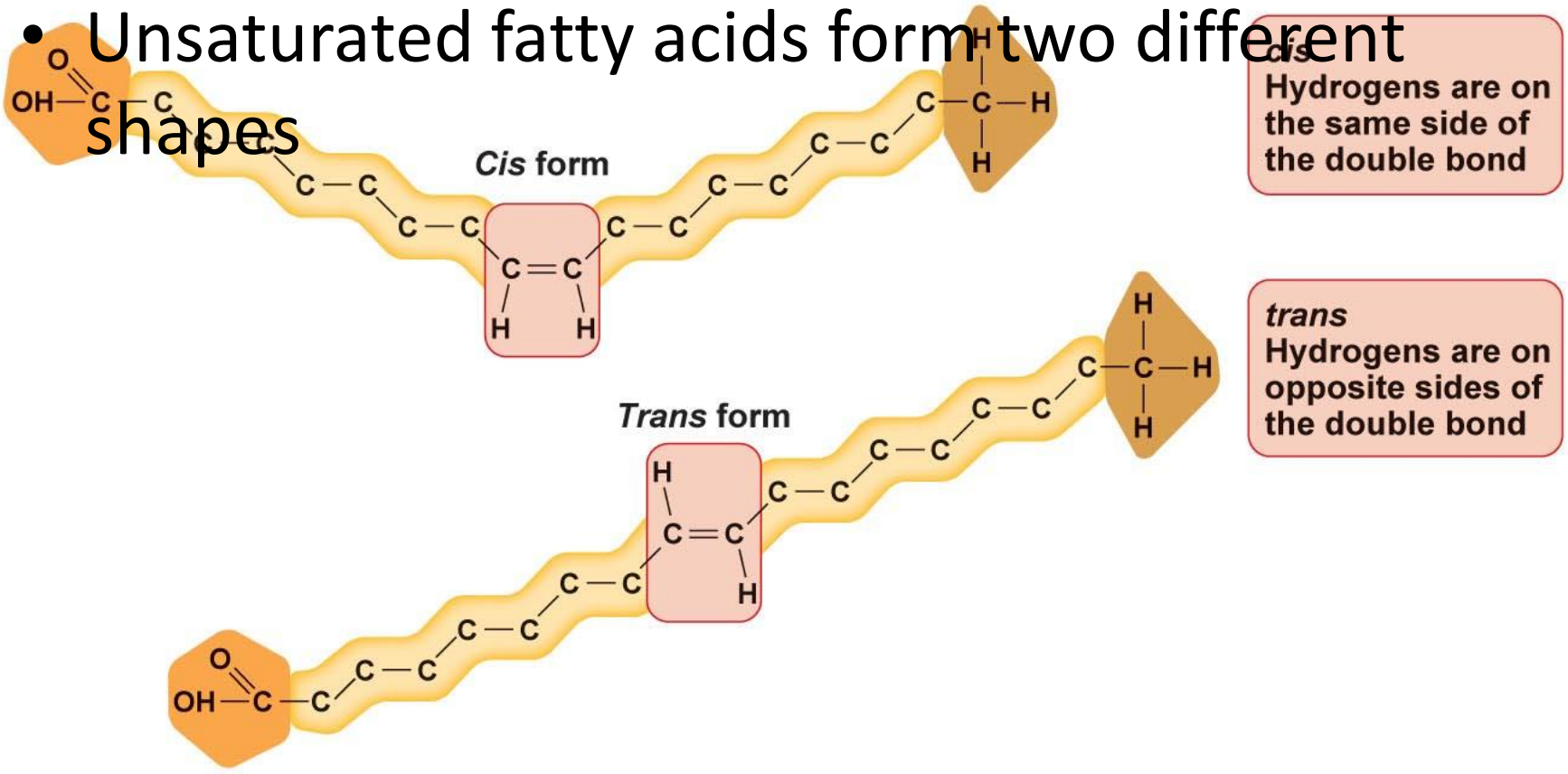
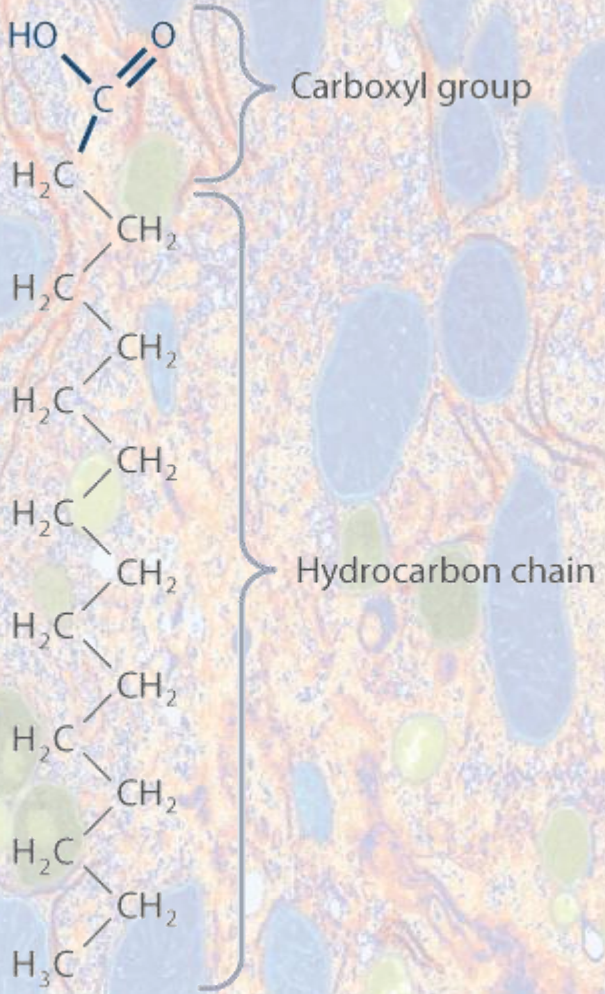


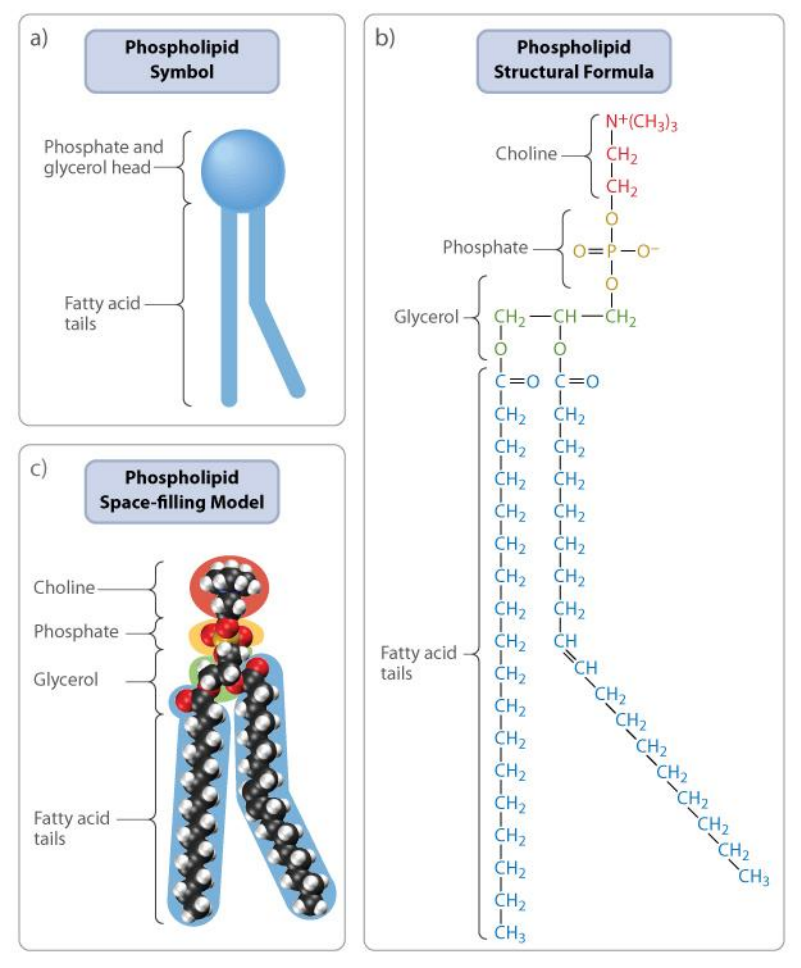
Figure 5.5

Structure of a fatty acid



- A fatty acid molecule is composed of a carboxyl group and a hydrocarbon chain.

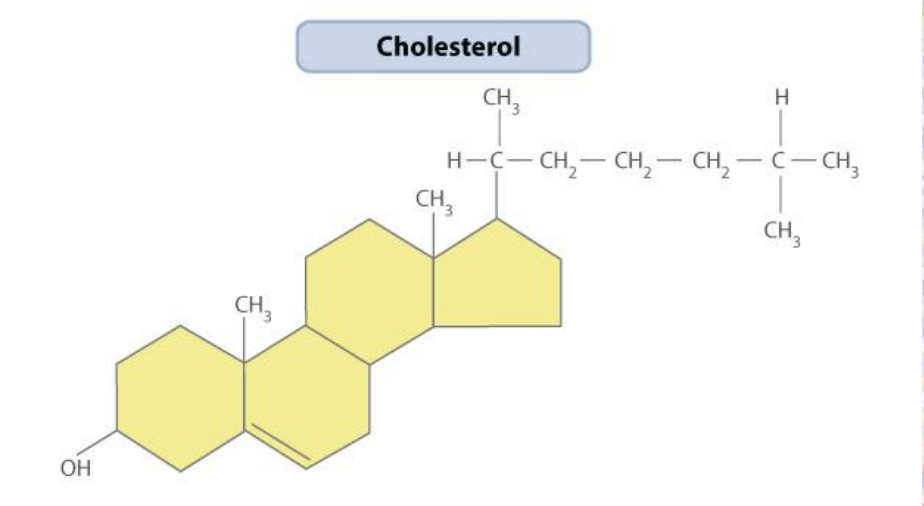
Chemical structure of a phospholipid



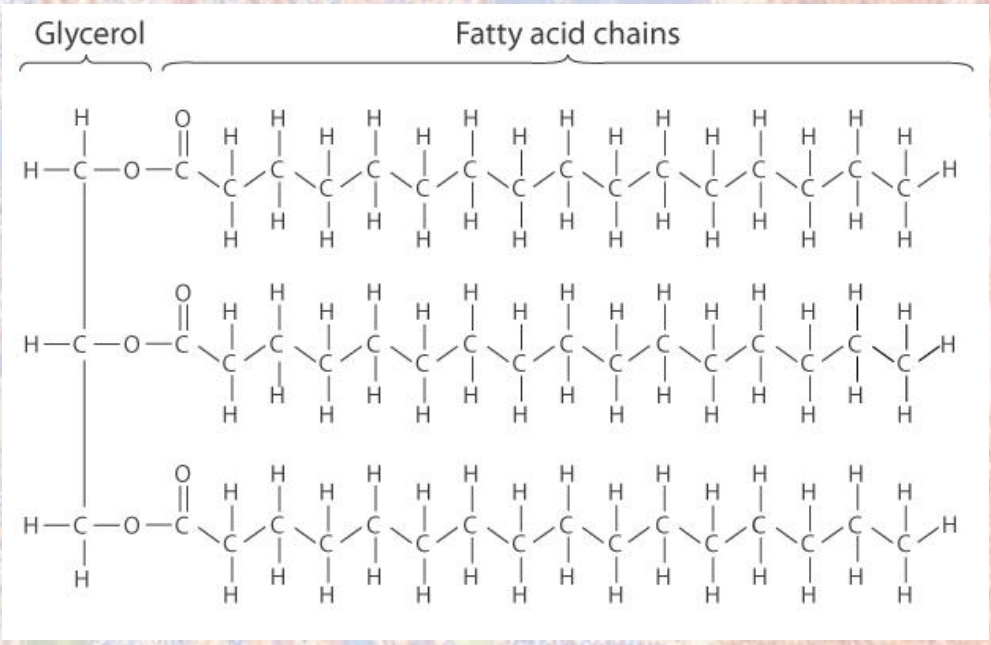
- a) Often, phospholipids are drawn symbolically with a polar head group and two hydrophobic tails. In the phospholipid shown, one tail is bent due to the presence of a double bond. b) The structural formula of phospholipids reveals that the choline and phosphate regions contain a positive and a negative charge, respectively. These charges are attracted to the polar water molecules, and together the glycerol, choline and phosphate regions make up the hydrophilic head. The fatty acid tails, which have no net charges and are nonpolar, have no affinity for water and are described as the hydrophobic tails. c) The space-filling model shows the three-dimensional arrangement of atoms on a typical phospholipid.

Cholesterol structure

- The cholesterol molecule, like all steroids, consists of four fused carbon rings with other groups attached. Cholesterol is an important precursor to other steroids and a component of the cell membrane.

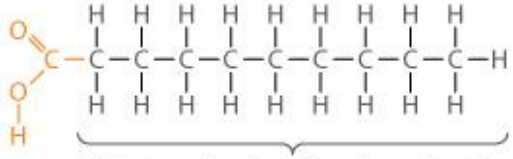


Structure of a triacylglycerol molecule



- A fat, or triacylglycerol molecule, is composed of one glycerol molecule and three fatty acid molecules.

Saturated fatty acid tail



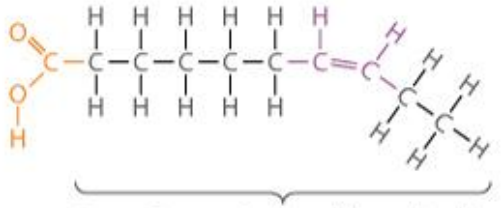
All C atoms in the tail are bound to the maximum number of H atoms

Properties of saturated fatty acids:

- No double bonds between C atoms in the tail
- C fully "saturated" with H atoms
- Often solid at room temperature

Some common saturated fatty acids:	Examples:
Butyric acid	Butter
Lauric acid	Coconut oil
Myristic acid	Dairy
Palmitic acid	Palm oil, meats
Stearic acid	Cocoa butter, meat

Unsaturated fatty acid tail



Some C atoms in the tail have double bond with other C atoms, rather than with an H atom

Properties of unsaturated fatty acids:

- Some double bonds between C atoms in the tail
- C atoms are "unsaturated" with H atoms
- Often liquid at room temperature

Some common unsaturated fatty acids:	Examples:
Palmitoleic acid	Macadamia oil
Oleic acid	Olive oil
Myristoleic acid	Nutmeg oil
Linoleic acid	Grape seed oil
Arachidonic acid	Eggs

Saturated fats

Triacylglycerol molecules with the maximum number of hydrogen atoms. They pack tightly together and to remain as solids at relatively higher temperatures (i.e., room temperature).

Unsaturated fats

These have some carbon atoms that are not fully bonded to hydrogen atoms. They pack together less tightly than they would if saturated, with the result that unsaturated fatty acids tend to be liquids at relatively higher temperatures (i.e., room temperature).

- **Trans fat** is an unsaturated fat with a trans double bond. A *trans* double bond does not produce a kink. Therefore, a *trans* bond allows for a more dense arrangement of triacylglycerol molecules, and trans unsaturated fats, or just "trans fats," remain solid at room temperature.

- Humans do not produce trans fats but can consume them in their diet. About 2–9 percent of the fat from sheep and cow's milk is trans fat. Trans fats can also be produced in factories: the food industry sometimes treats vegetable oils through a process called hydrogenation. Hydrogenation reduces the number of double bonds in vegetable oil, but this process can also introduce *trans* double bonds. Hydrogenation is used to make the fat semi-solid at room temperature and to increase its shelf life. Unfortunately, consumption of trans fats leads to negative health effects. Trans fats have been shown to raise LDL levels and lower HDL levels, and these fats may be linked to increased risk of heart disease.

- There are two types of fatty acid required for human health that the human body cannot synthesize. The two essential fatty acids in humans, omega-3 and omega-6, must be consumed. They are necessary to produce other molecules essential for life processes. Omega-3 and omega-6 occur in foods like fish, pumpkin, sunflower seeds, and leafy vegetables. The names of these omega molecules derive from the double bonds between the specific carbon atoms in their carbon skeletons; for omega-3 fatty acids, it is the double bond between the third and fourth carbons, and for omega-6 fatty acids, it is the double bond between the sixth and seventh carbons.
- Plants store energy in polysaccharide molecules. The exception to this is plants' storage of oils as a long-term food source in seeds. Animals rely on fats as an energy reserve. Fat compounds hold twice as much energy as polysaccharides such as starch. A polysaccharide is a relatively bulky molecule that is adequate for plants because plants do not move around. Animals require a more compact energy source. Fats are stored in adipose cells that swell and shrink as the reserves are stored and used. In addition to serving as an energy source, fats provide insulation.
- Triacylglycerols, or fats, circulate in human blood in two different types of lipoproteins, chylomicrons and very low-density lipoproteins. When the body needs energy, the triacylglycerols are broken down, releasing fatty acids. If more calories are consumed than needed, the triacylglycerols are stored in adipose tissue.

White, brown, beige

- The predominant form of fat in mammals, including in humans, is known as white fat. White fat cells are found throughout the body, primarily under the skin, as well as in larger deposits in the abdomen. They are highly specialized for energy storage, hoarding calories in the form of lipid droplets.

- The white cells are complemented by brown fat cells, which specialize in converting chemical energy from glucose and lipids into heat, generally when an animal is exposed to the cold. This burning of carbohydrates and fat also helps counteract obesity and metabolic disorders.

- When functioning appropriately, white fat cells will limit metabolic disease.

- Healthy white fat protects the body by providing a 'safe home' for lipids, which can be toxic to other tissues such as muscle or the liver. So these fat cells hold on to the lipids until the energy they are storing is needed, when they release them into the blood.

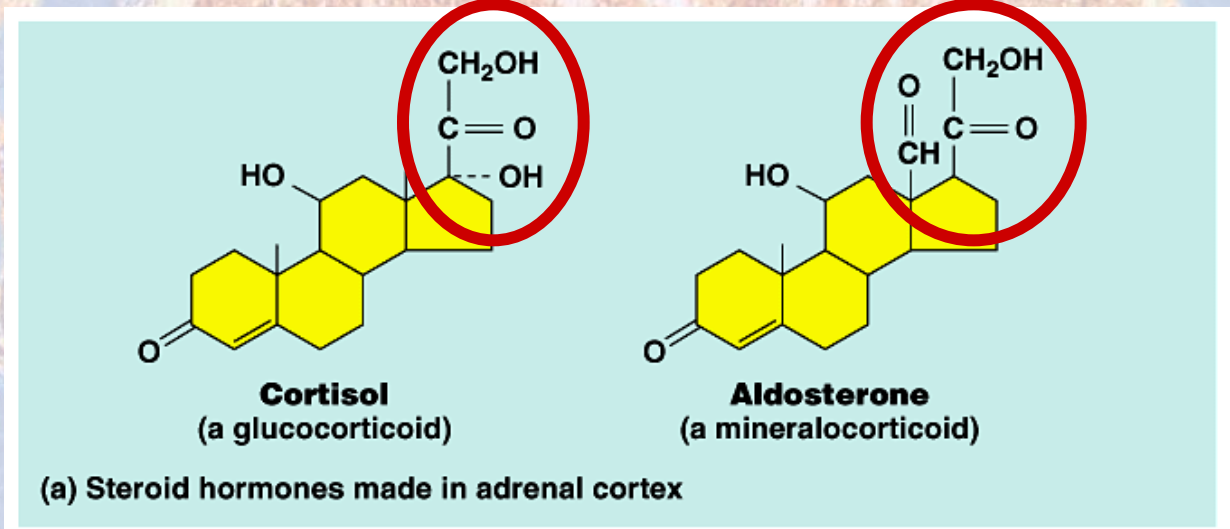
From Cholesterol → Sex Hormones

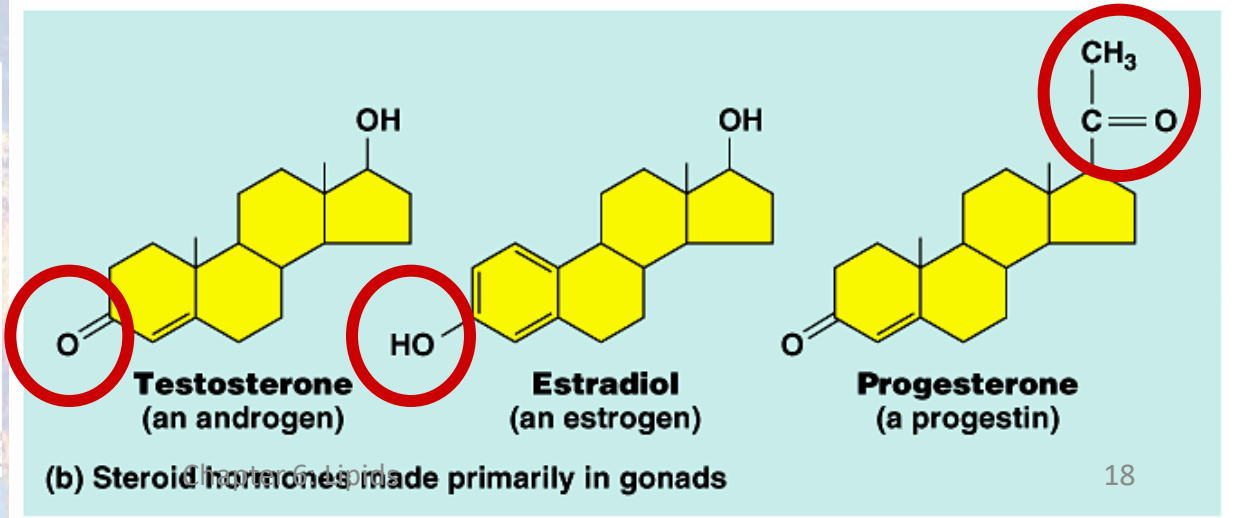
- What a big difference a few atoms can make!





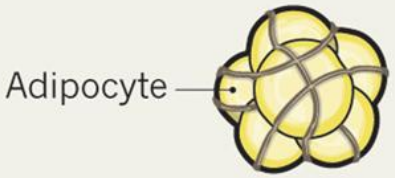




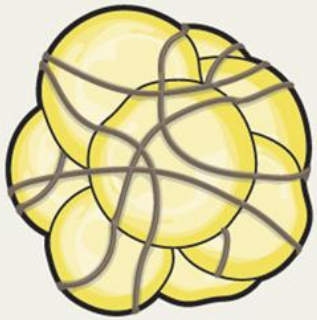


TISSUE TURNS BAD

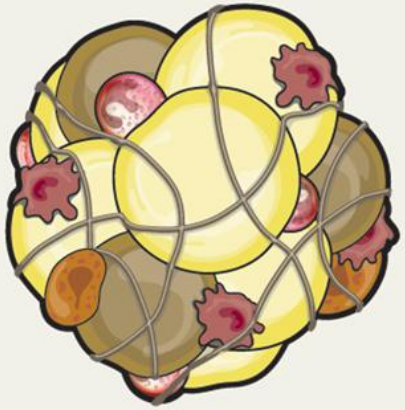
Cells overloaded with lipids rapidly outgrow oxygen supply, leading to cell death and inflammation.



Normal fat tissue



Hypertrophy



Obese

Low-grade inflammation, insulin resistance and, ultimately, metabolic disease.



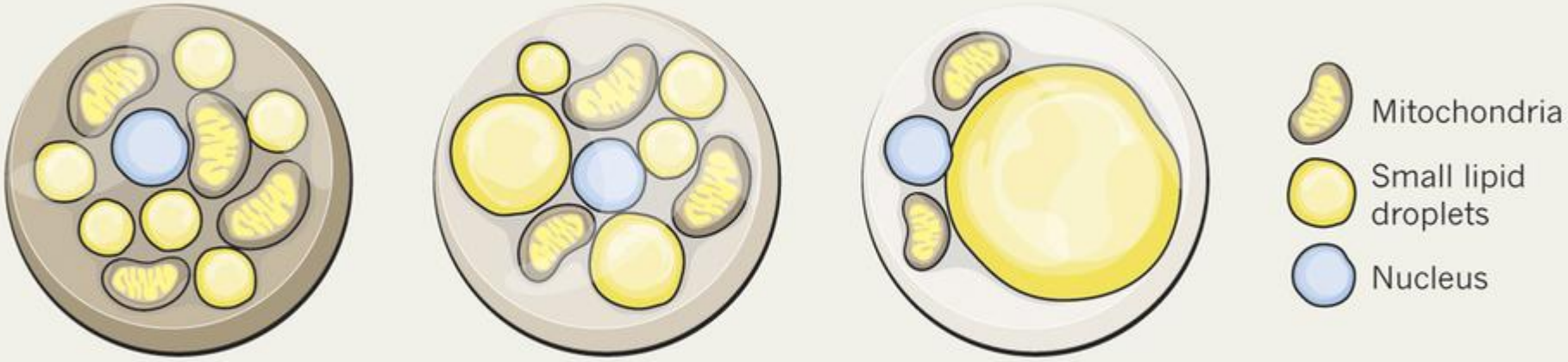
Macrophages, lymphocytes, neutrophils and other immune cells.



The different functions of white, brown and beige fat might yield new targets in the fight against obesity and metabolic disease
Researchers are attempting to harness the ability of brown cells to burn fat.

SHADES OF A CELL

Three distinct types of fat cell have been identified to date, are there more to follow?



Brown fat cell

Converts chemical energy to heat to protect against cold weather.

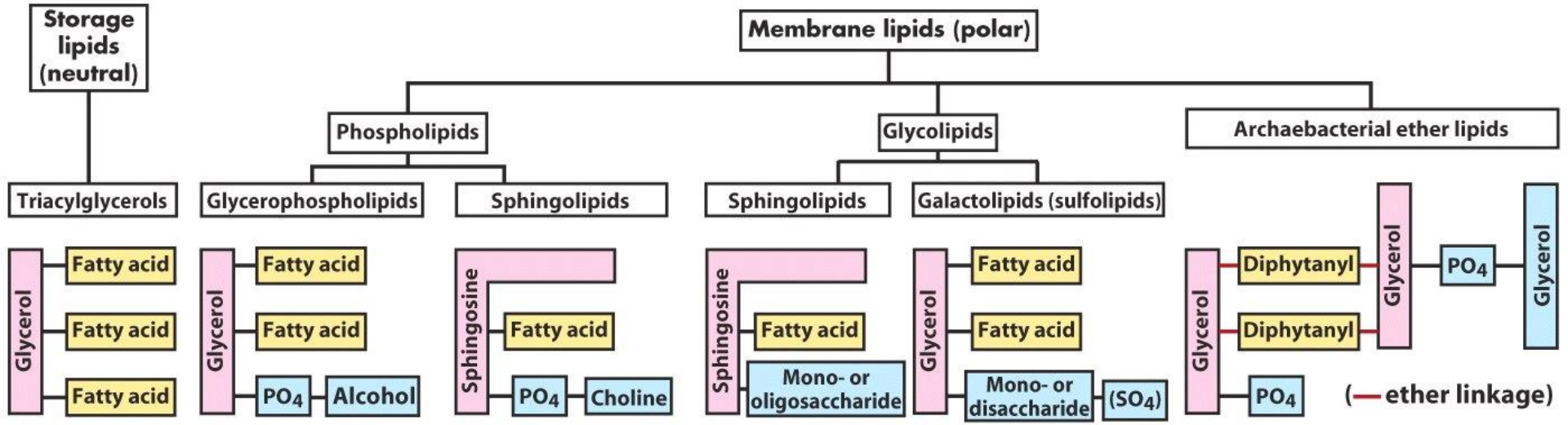
Beige fat cell

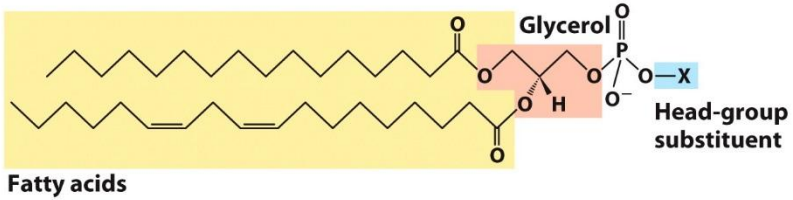
Immature cell in white fat tissue matures to burn fat.

White fat cell

Most common fat cell, used to store fat and found beneath the skin and abdomen.

Major Types of Lipids





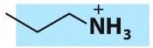
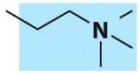
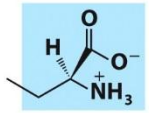
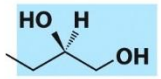
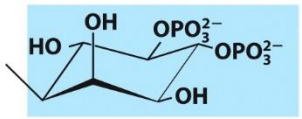
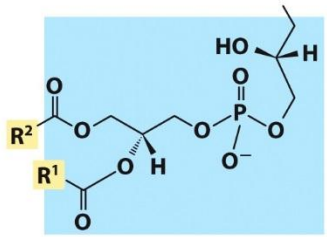
Name of glycerophospholipid	Name of X—O	Formula of X	Net charge (at pH 7)
Phosphatidic acid	—	—H	−2
Phosphatidylethanolamine	Ethanolamine		0
Phosphatidylcholine	Choline		0
Phosphatidylserine	Serine		−1
Phosphatidylglycerol	Glycerol		−1
Phosphatidylinositol 4,5-bisphosphate	*myo*-Inositol 4,5-bisphosphate		−4*
Cardiolipin	Phosphatidyl-glycerol		−2

Figure 10-9
Lehninger Principles of Biochemistry, Sixth Edition
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Phosphatidylcholine

- Phosphatidylcholine is the major component of most eukaryotic cell membranes
- Many prokaryotes, including *E. coli,* cannot synthesize this lipid; their membranes do not contain phosphatidylcholine

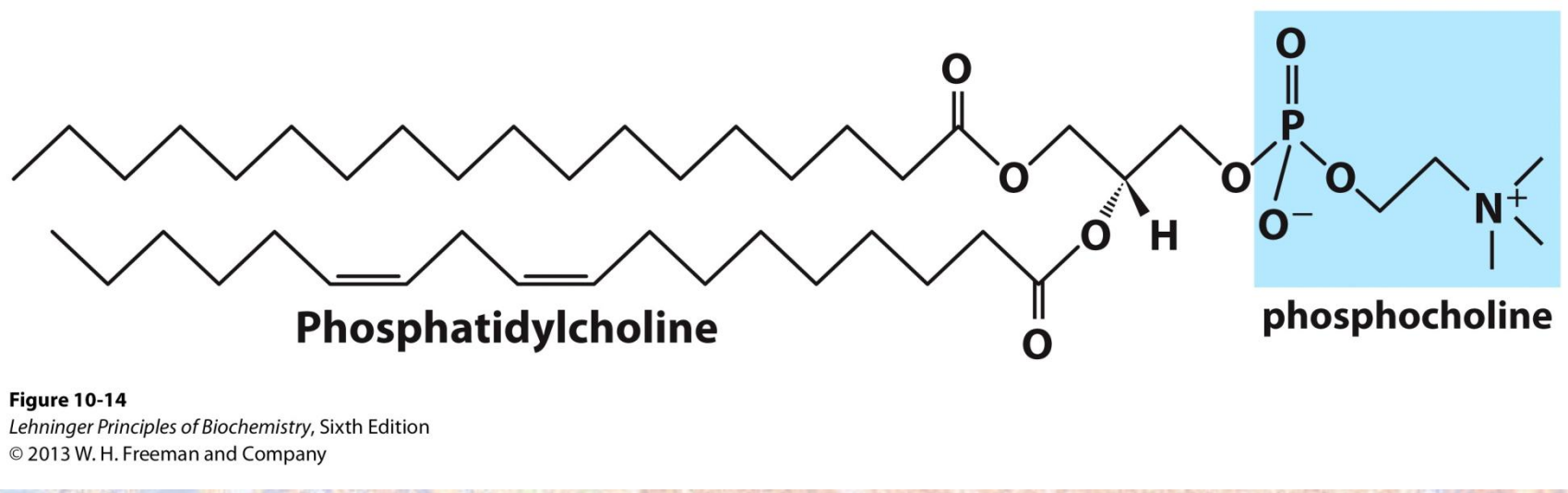
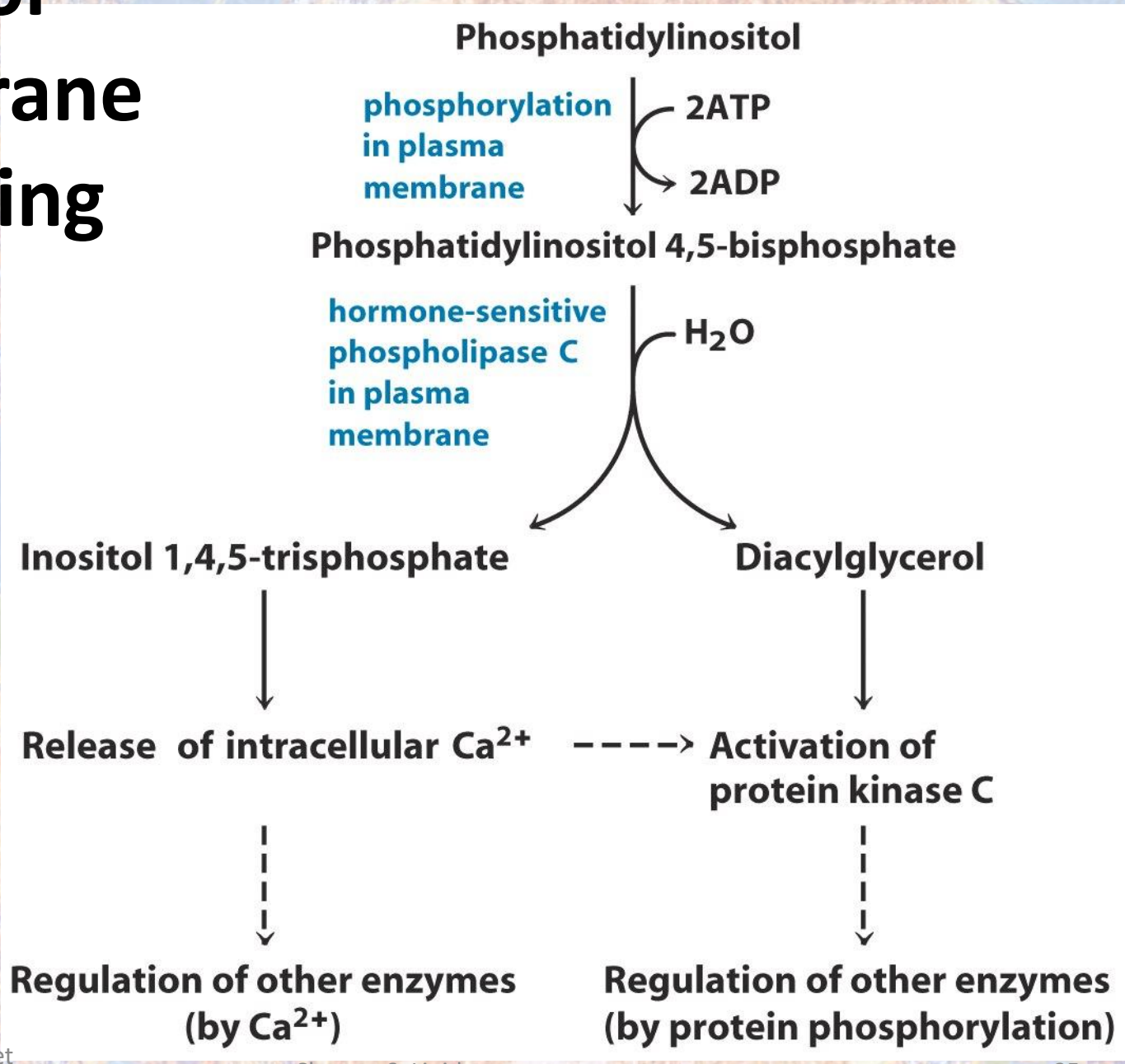
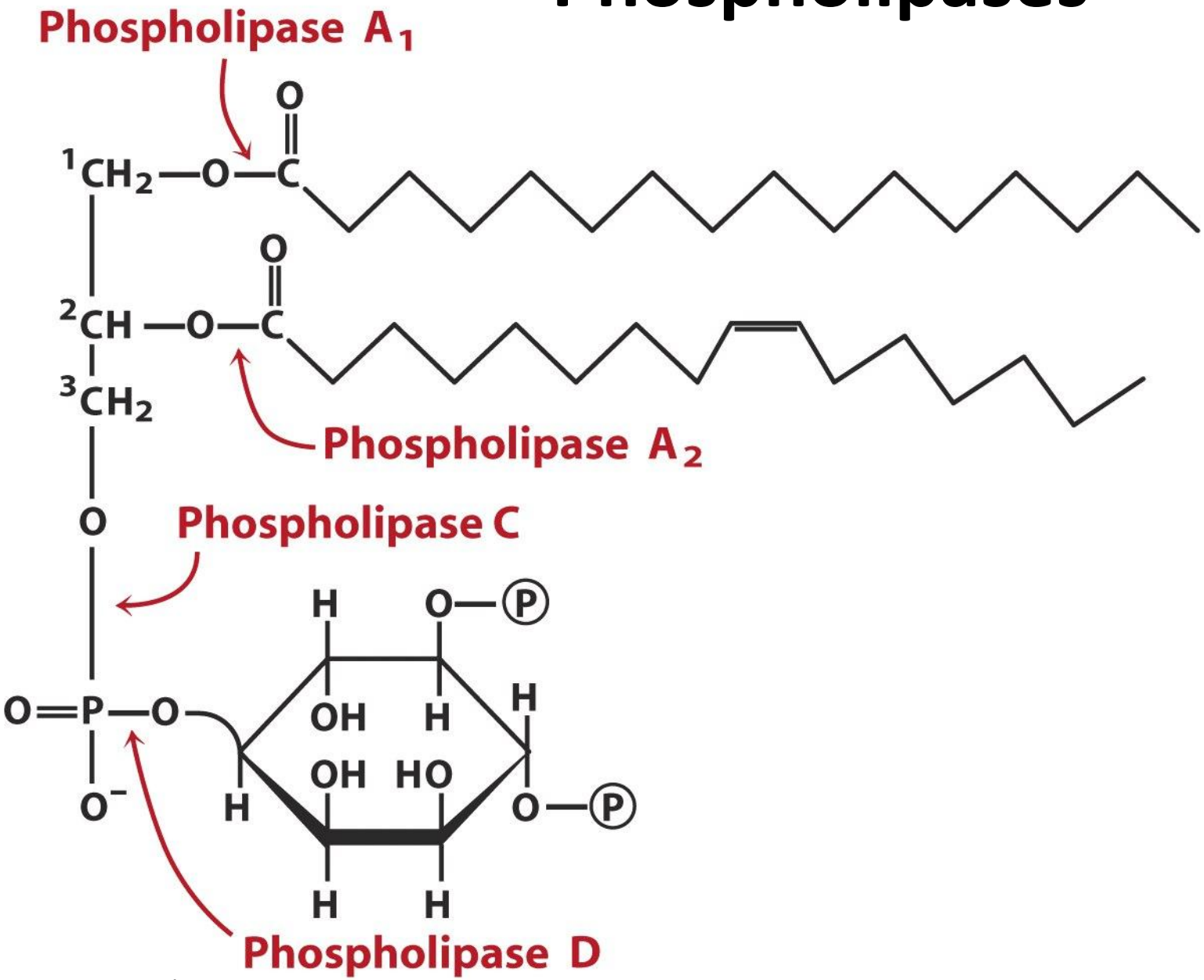


Figure 10-14
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Inositol – Membrane Signaling



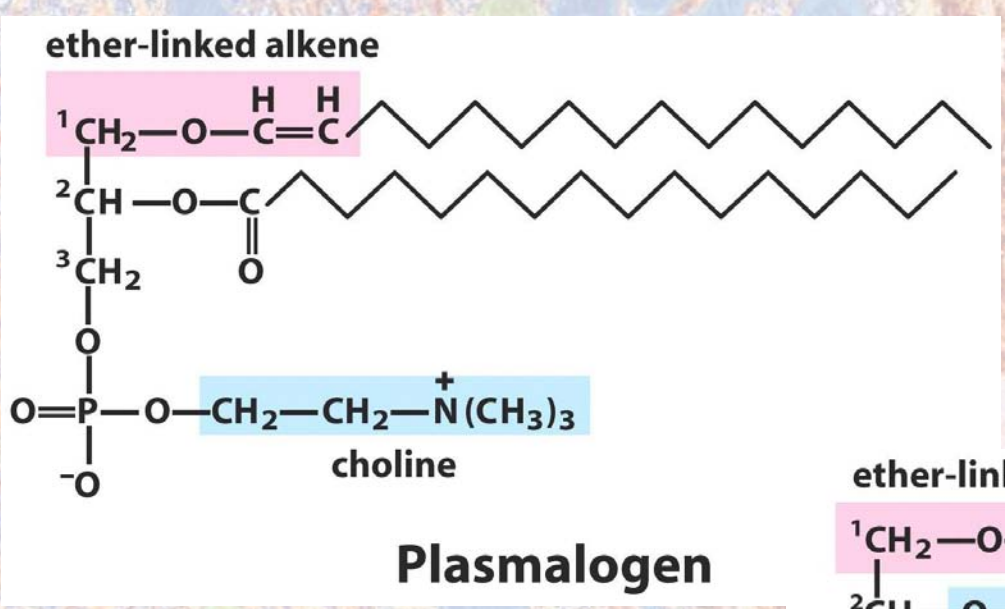
Phospholipases



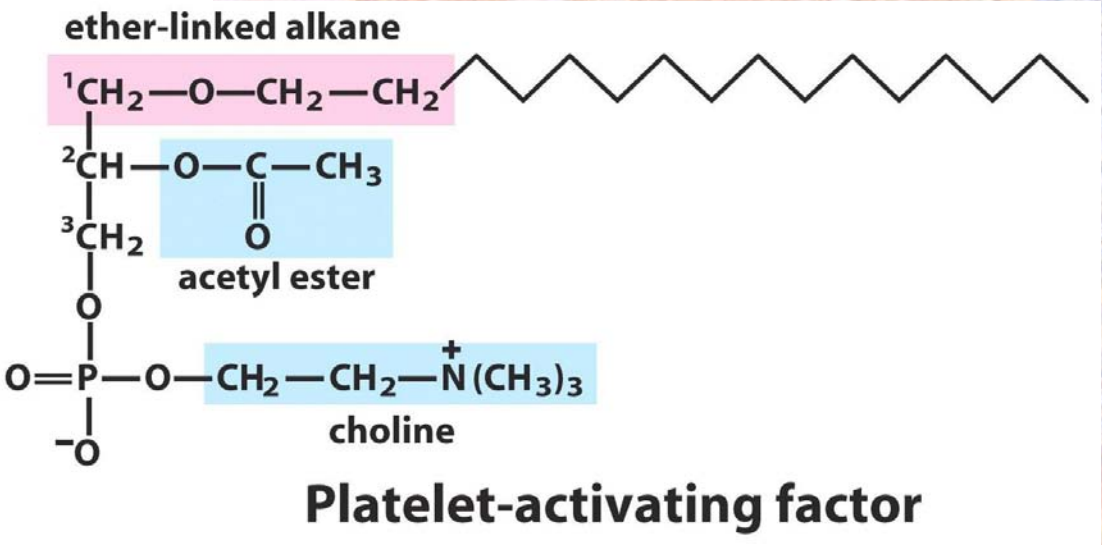
Ether Lipids: Plasmalogen

- Vinyl ether analog of phosphatidylethanolamine
- Common in vertebrate heart tissue
- Also found in some protozoa and anaerobic bacteria
- Function is not well understood
  - Resistant to cleavage by common lipases but cleaved by few specific lipases
  - Increase membrane rigidity?
  - Sources of signaling lipids?
  - May be antioxidants?

Two Ether Linked aliphatic groups

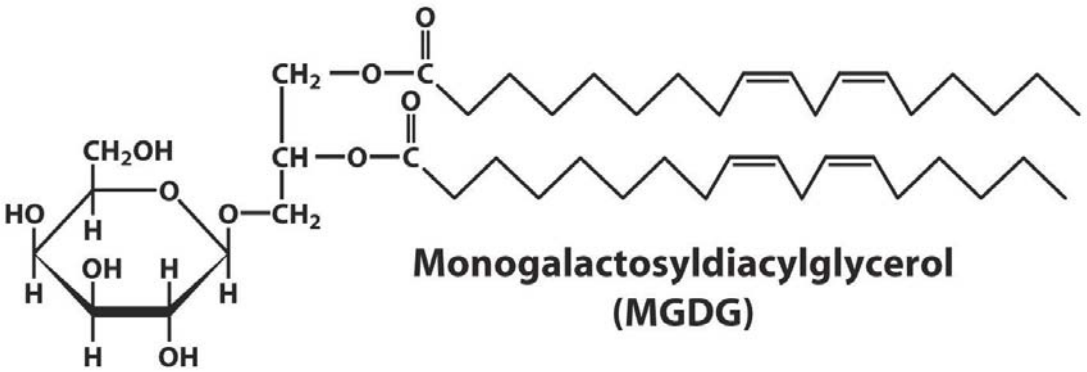


High concentration in Heart Lipids



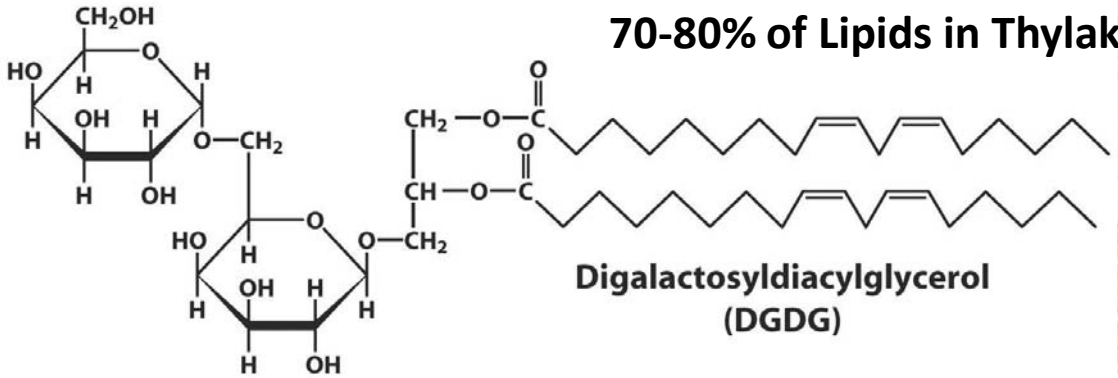
Active at 10^{-9} M … Part of many things including Inflammation

Galactolipids – in Chloroplasts

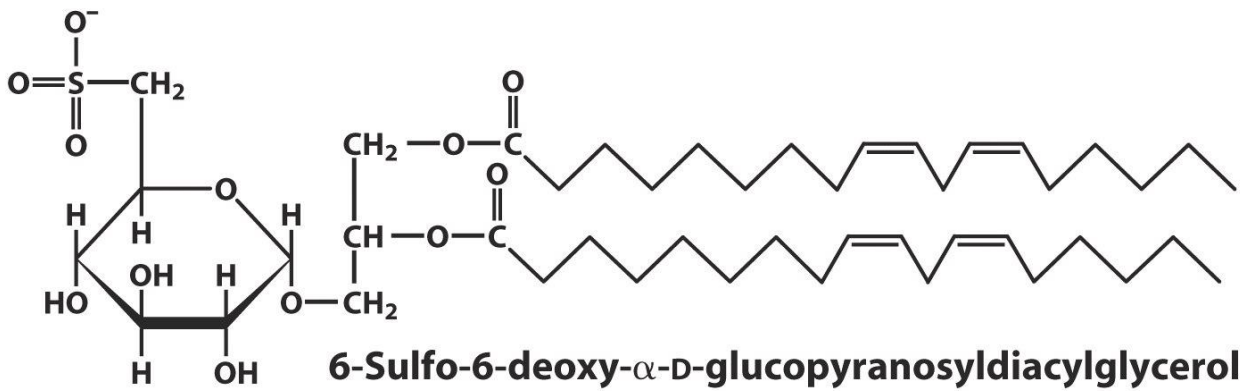


Monogalactosyldiacylglycerol
(MGDG)

70-80% of Lipids in Thylakoid Membranes

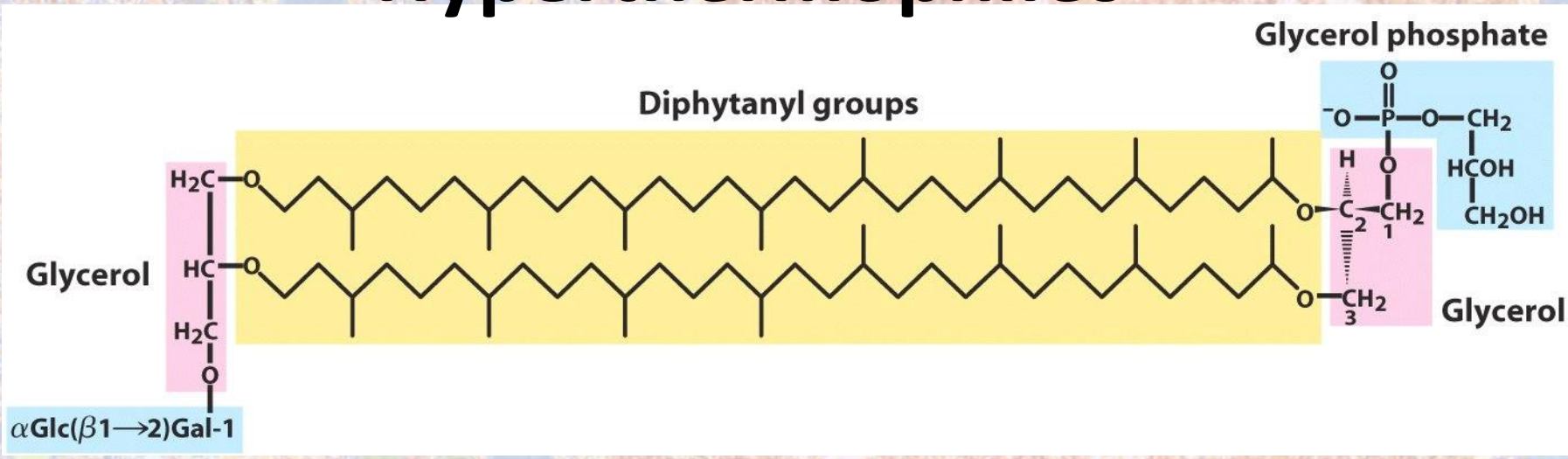


Digalactosyldiacylglycerol
(DGDG)



6-Sulfo-6-deoxy-α-D-glucopyranosyldiacylglycerol
(a sulfolipid)

One Type of Achaea Membrane Lipid in Hyperthermophiles



Sphingolipids

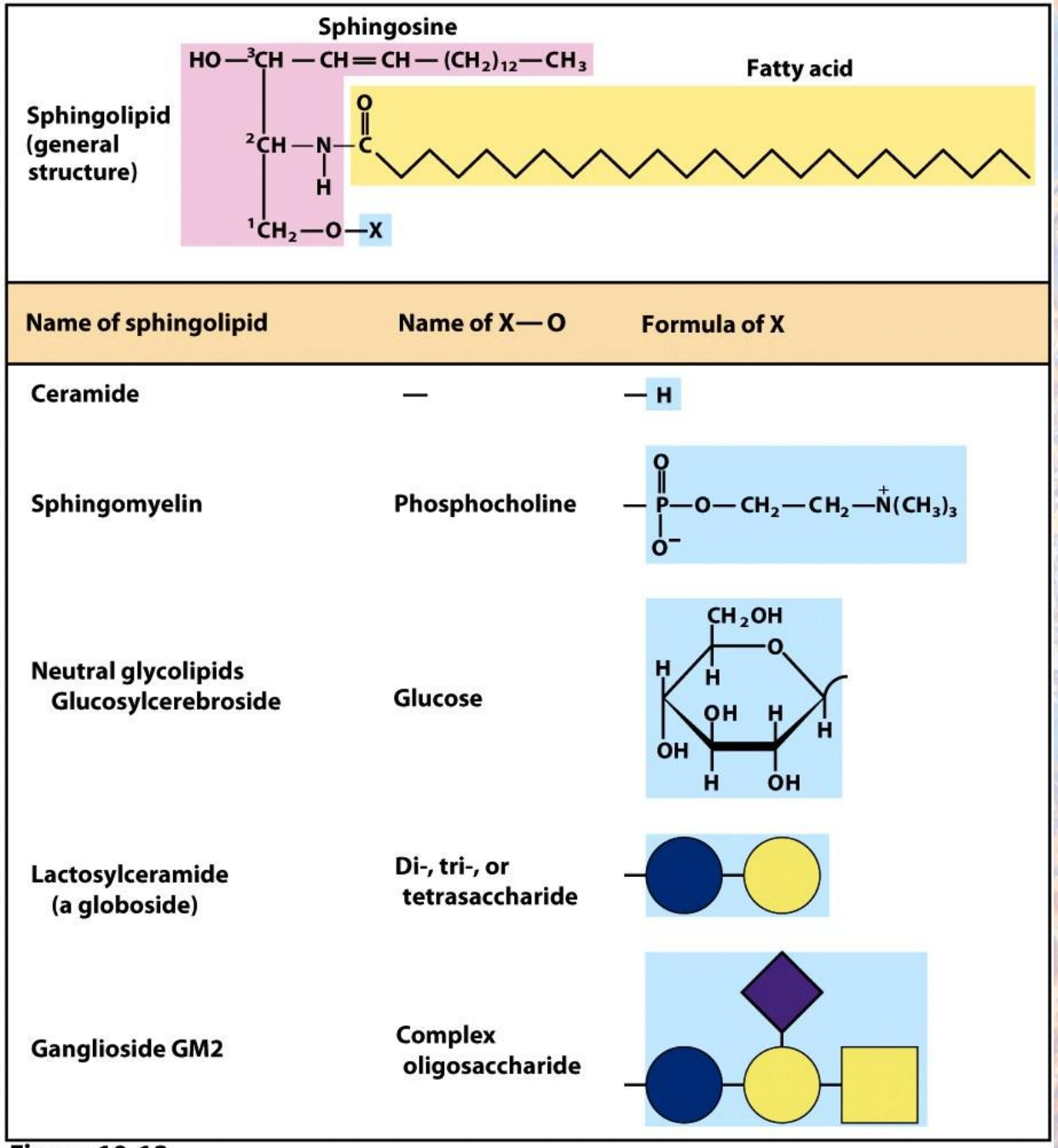


Figure 10-13
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ABO Blood Groups

Glc-Gal-GalNAc-Gal

Fuc

I

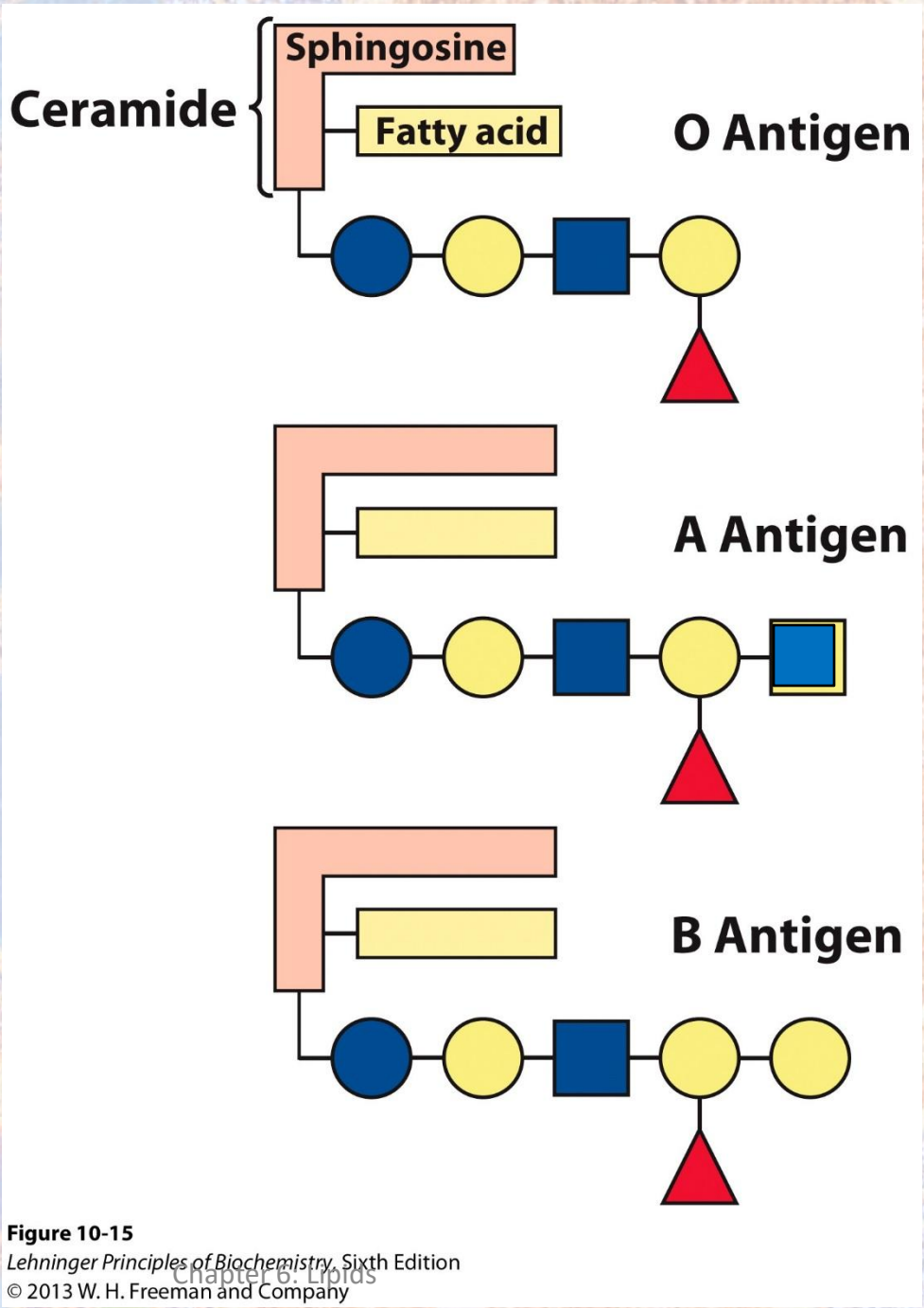
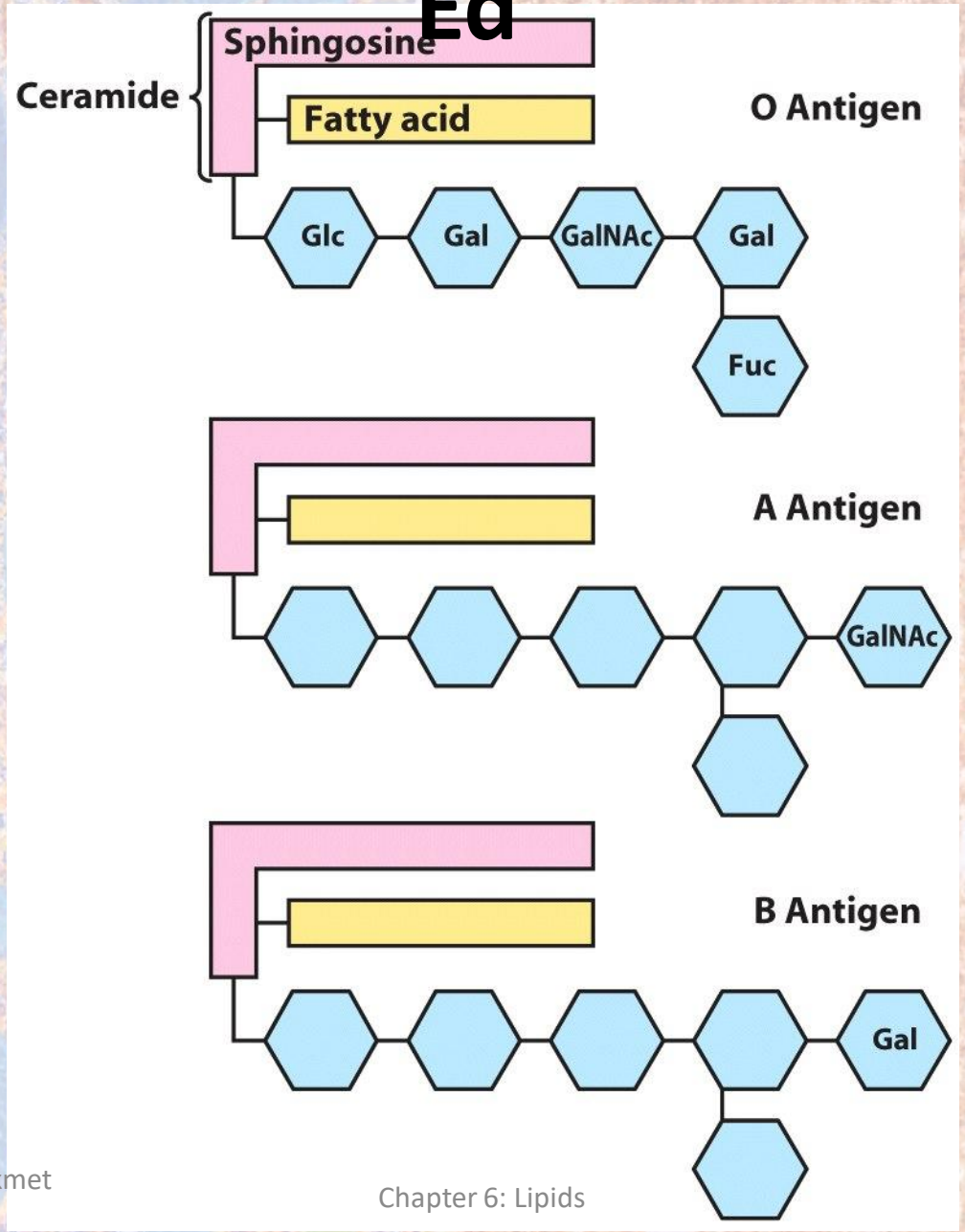


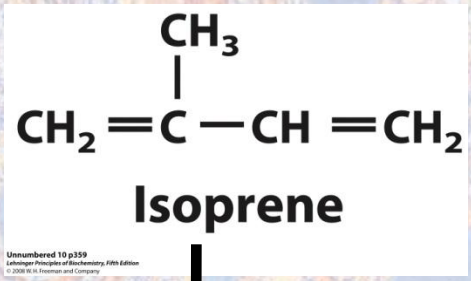
Figure 10-15
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ABO Blood Group Substances, 5th Ed



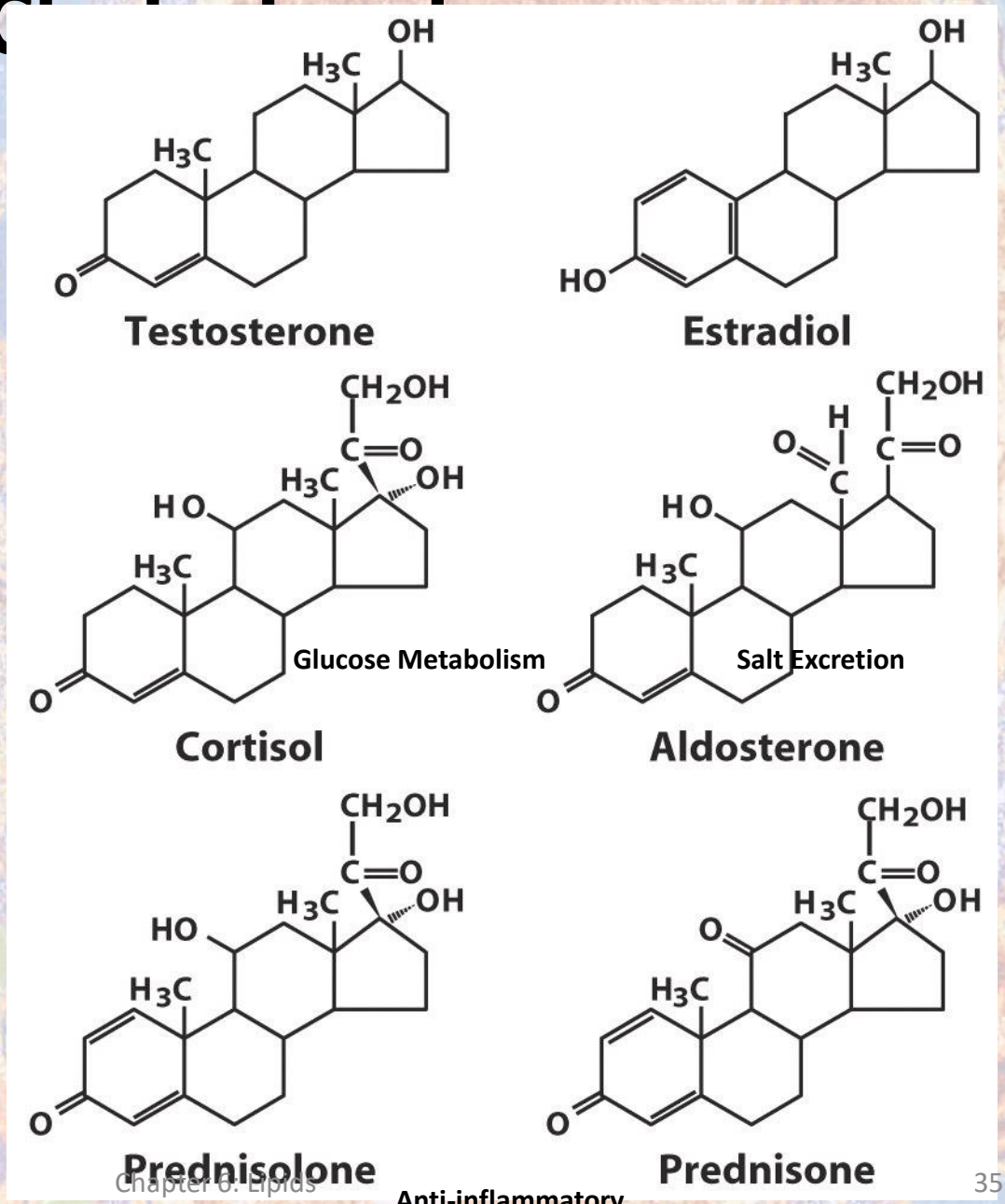
Cholesterol – Steroid (= 4 fused rings)

Steroid Hormones Made from Cholesterol

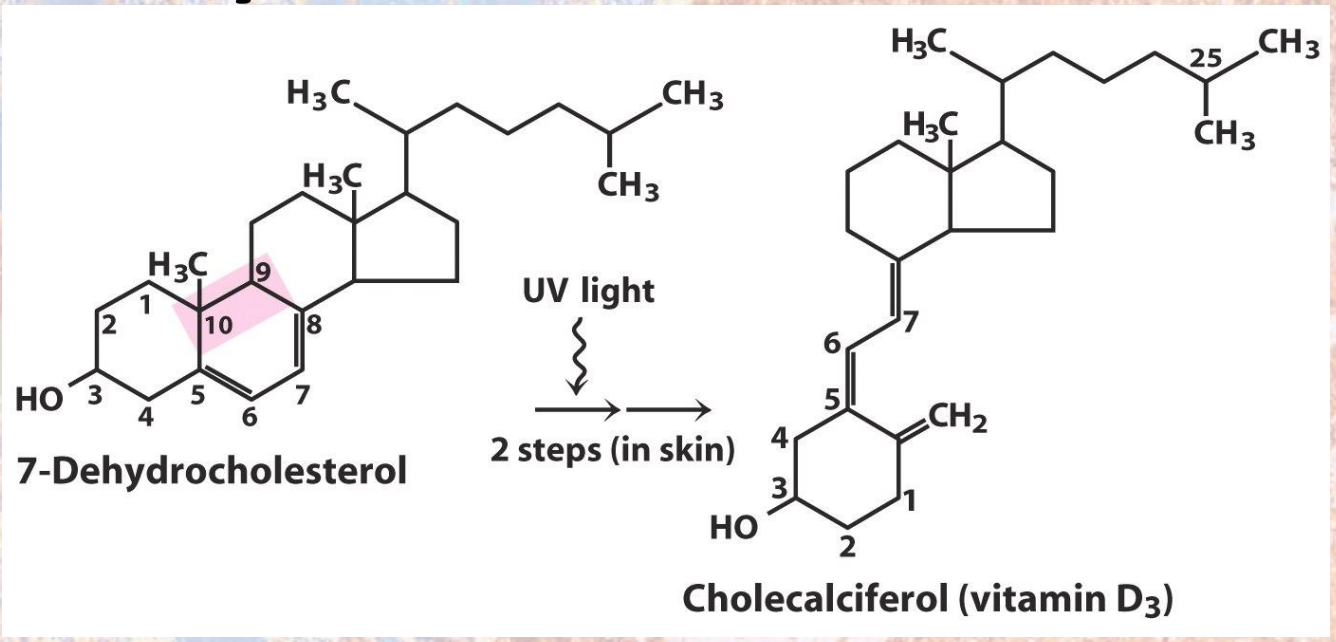


Multistep

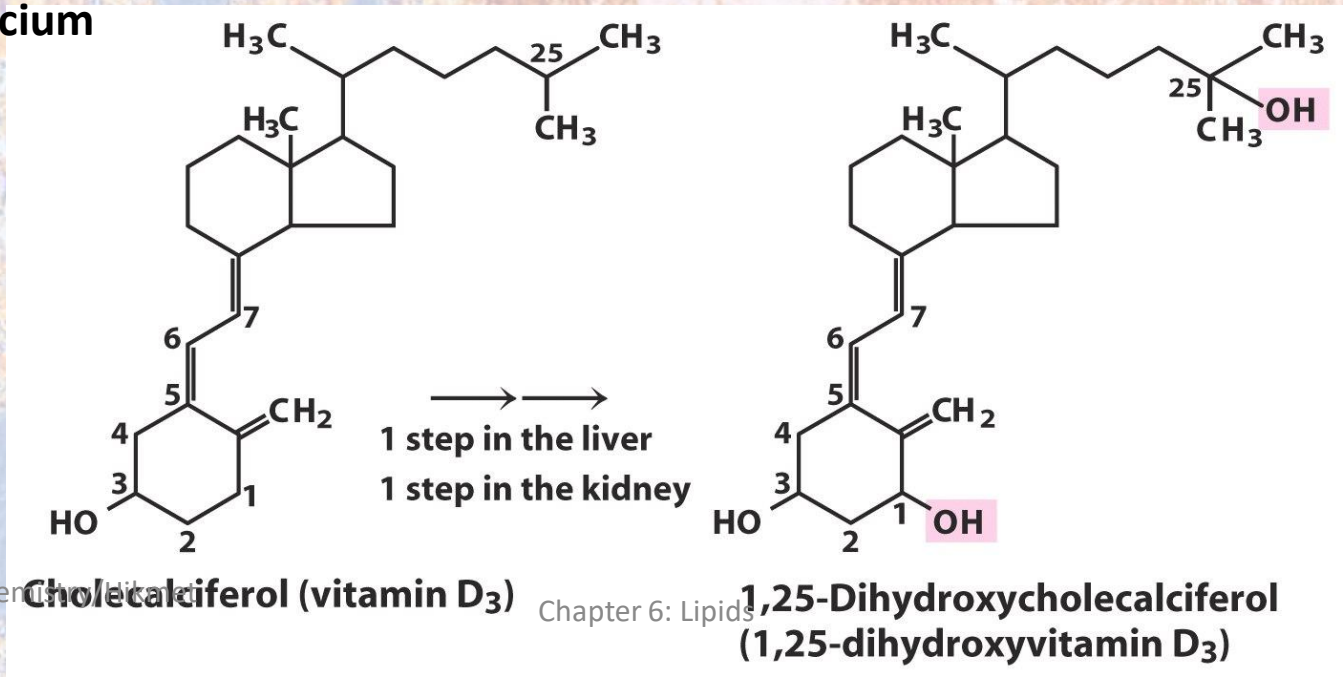
Cholesterol



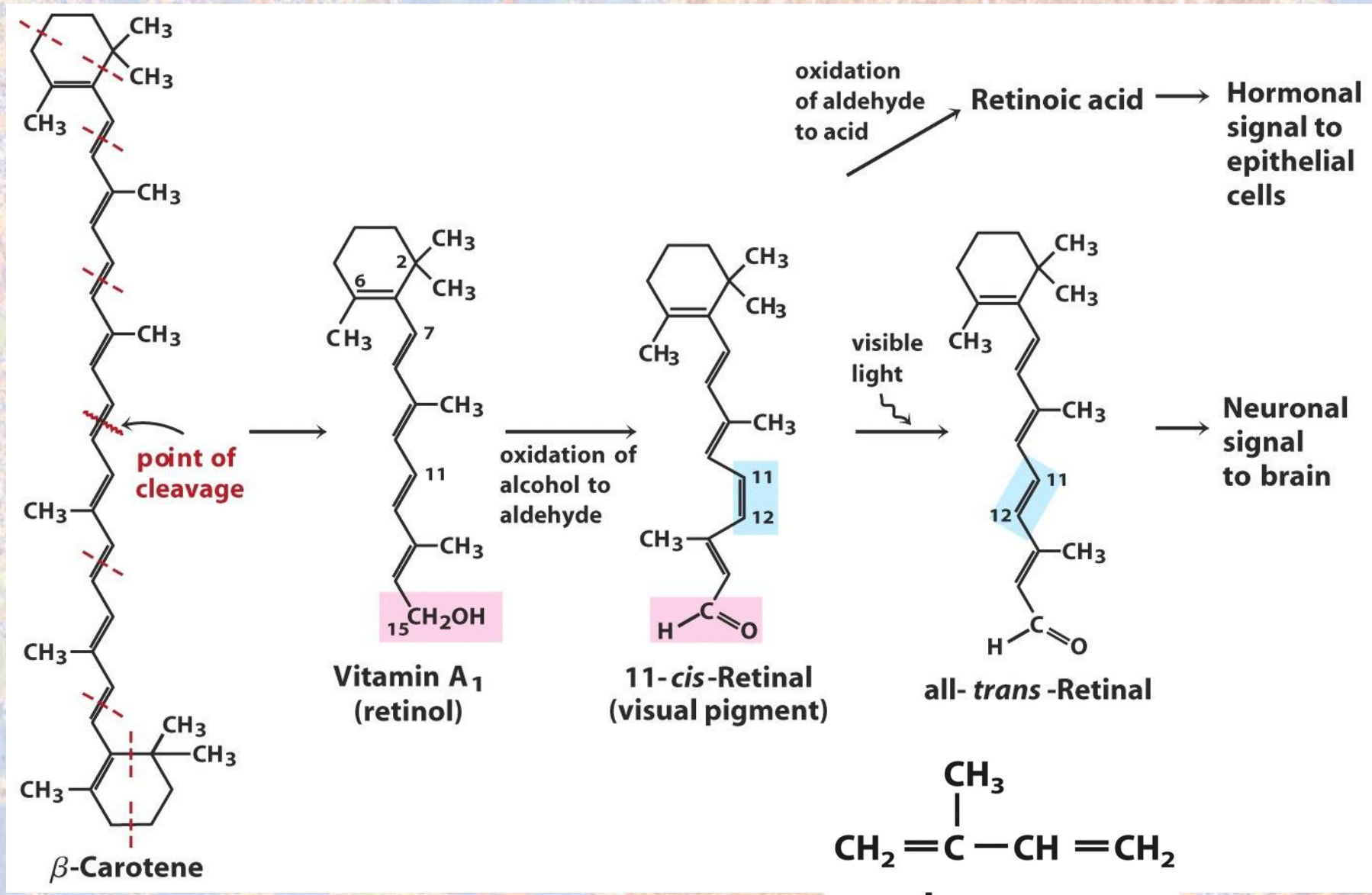
Synthesis of Vitamin-D



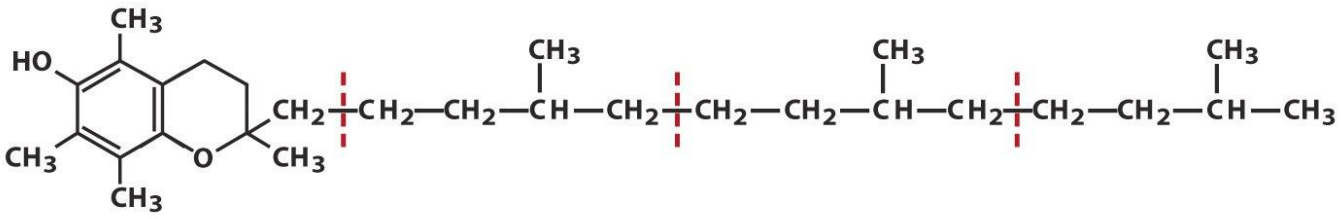
Regulate Calcium Metabolism



Retinal Comes from Carotene

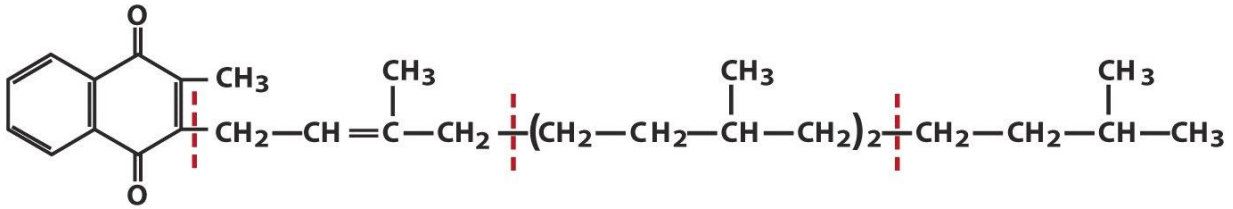


Isoprene Vitamins



(a)

Vitamin E: an antioxidant

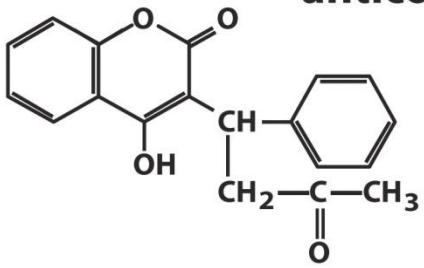


(b)

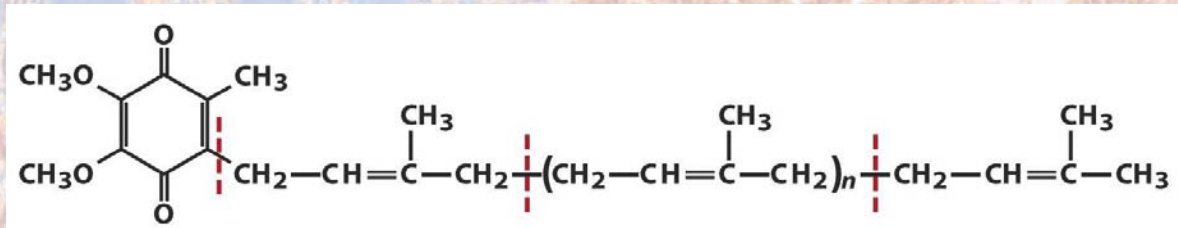
Vitamin K_1: a blood-clotting cofactor (phylloquinone)

(c)

Warfarin: a blood anticoagulant

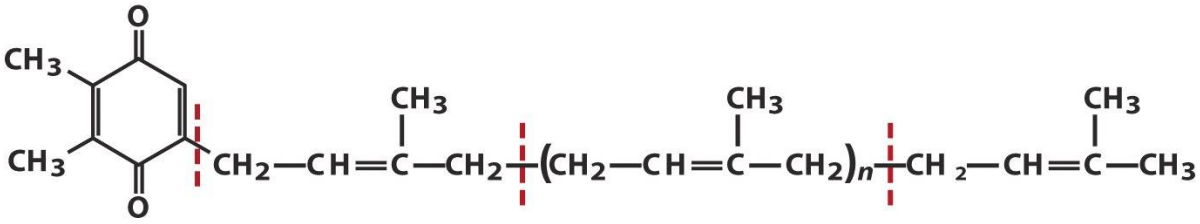


Mitochondrial and Chloroplast Membrane Electron Carriers



(d)

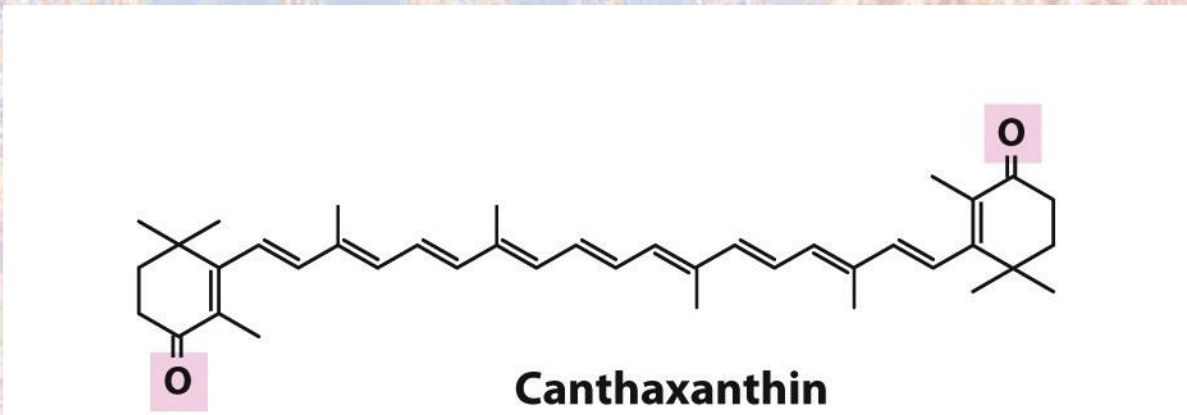
Ubiquinone: a mitochondrial electron carrier (coenzyme Q) ($n = 4$ to 8)



(e)

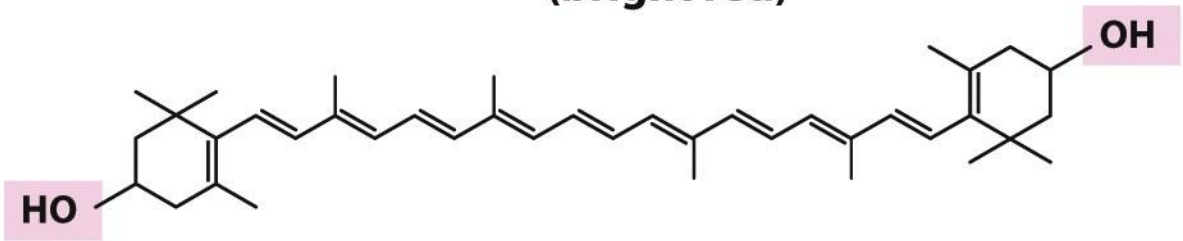
Plastoquinone: a chloroplast electron carrier ($n = 4$ to 8)

Carotenoids



Canthaxanthin
(bright red)

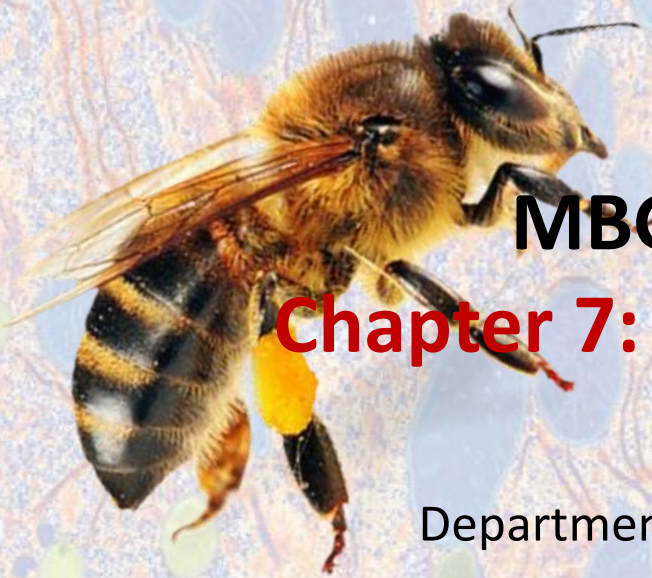




Zeaxanthin
(bright yellow)



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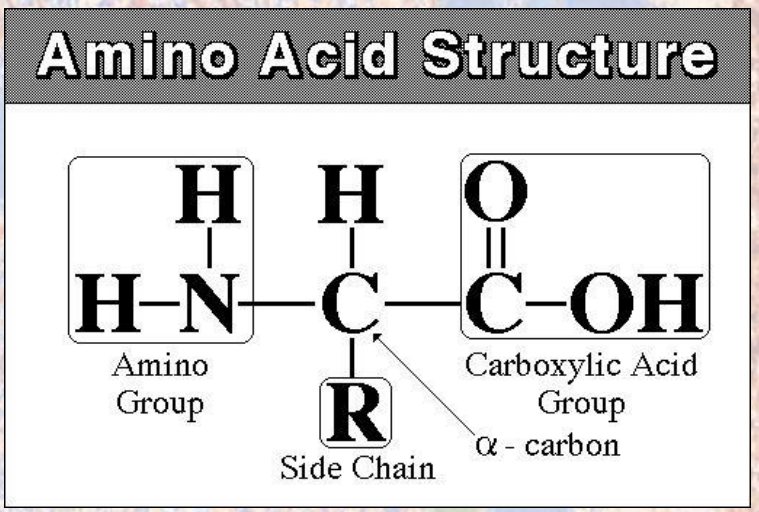


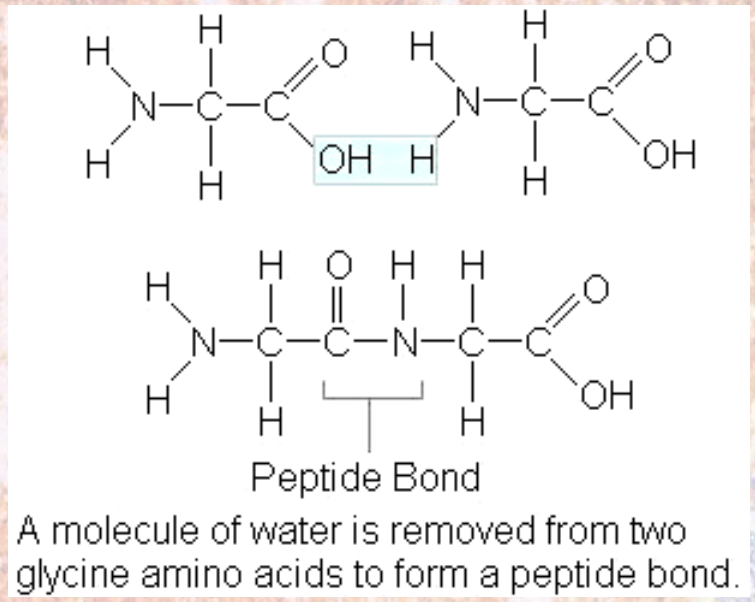
MBG303 Biochemistry

Chapter 7: Amino acids and Proteins

Hikmet Geçkil, Professor
Department of Molecular Biology and Genetics
Inonu University

Fundamental Structure of Amino Acids

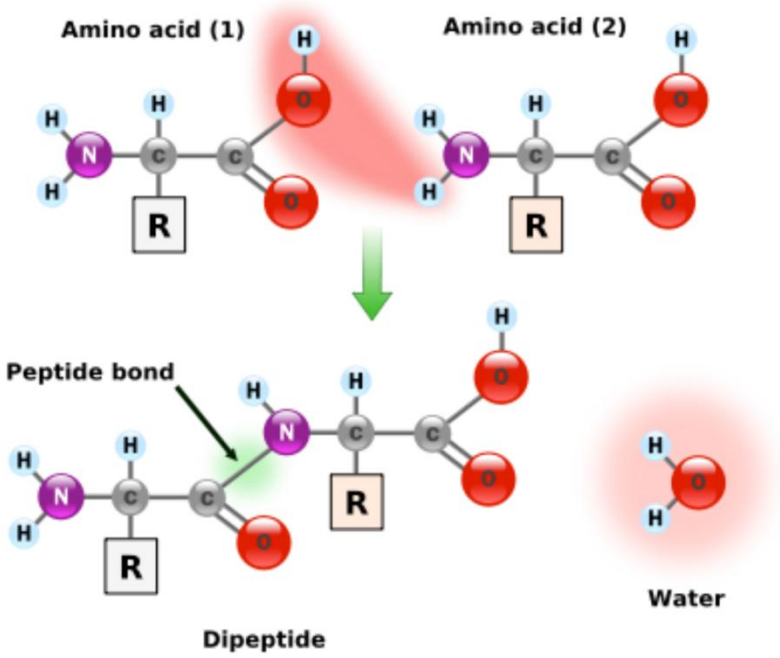




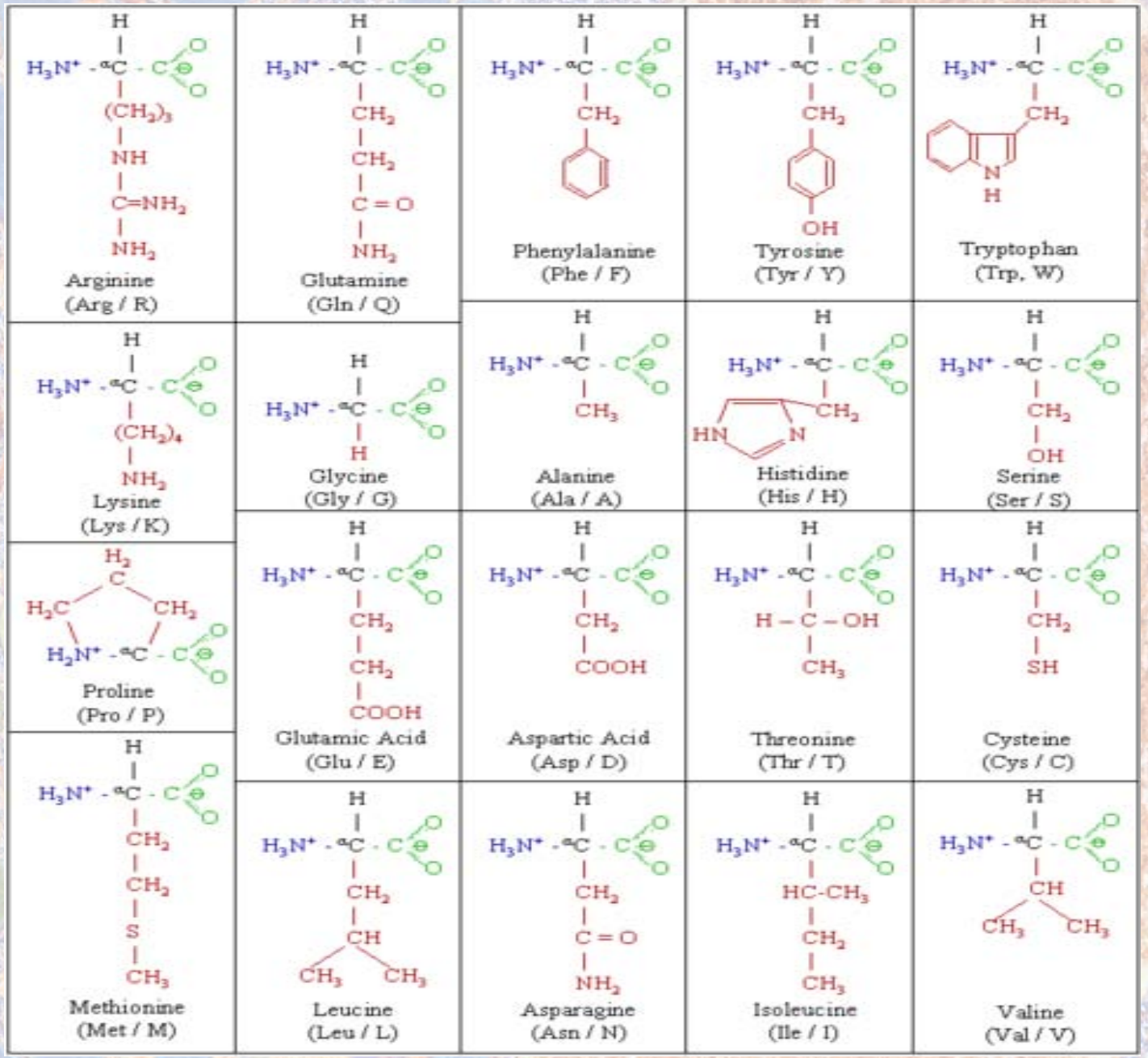
A molecule of water is removed from two glycine amino acids to form a peptide bond.

Amino acids are most logically grouped according to the physical properties of their side chains.

Figure 1.47 Polypeptide chains form through the formation of peptide bonds

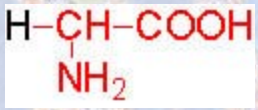


The carboxyl group of one amino acid is linked to the amino group of another amino acid through a dehydration reaction. The peptide bonds start at the amino end (N terminus) and are added one by one. The backbone of a polypeptide is repetitive, the attached amino acid side chains are the cause of diversity in the polypeptide.

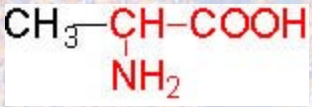

Arginine (Arg / R)
Glutamine (Gln / Q)
Phenylalanine (Phe / F)
Tyrosine (Tyr / Y)
Tryptophan (Trp, W)
Lysine (Lys / K)
Glycine (Gly / G)
Alanine (Ala / A)
Histidine (His / H)
Serine (Ser / S)
Proline (Pro / P)
Glutamic Acid (Glu / E)
Aspartic Acid (Asp / D)
Threonine (Thr / T)
Cysteine (Cys / C)
Methionine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

Nonpolar (Hydrophobic) R Groups

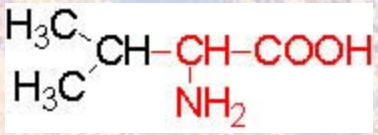
Glycine (Gly)



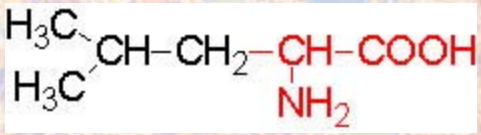
Alanine (Ala)



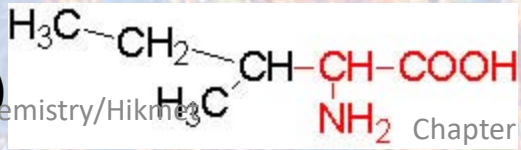
Valine (Val)



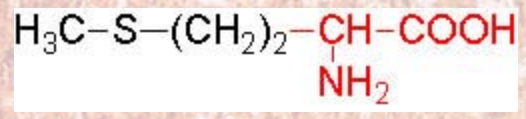
Leucine (Leu)



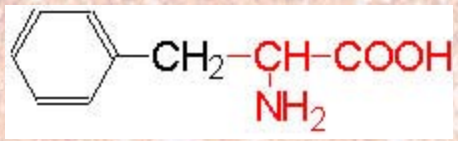
Isoleucine (Ile)



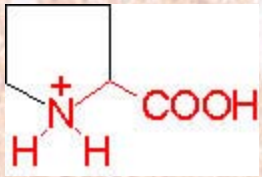
Methionine (Met)



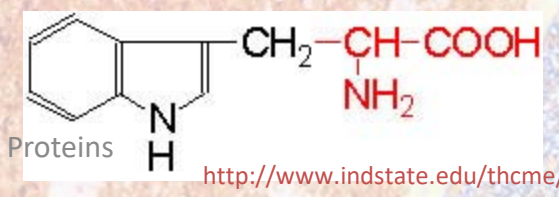
Phenylalanine (Phe)



Proline (Pro)



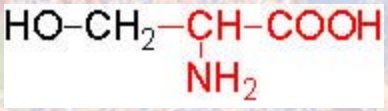
Tryptophan (Trp)



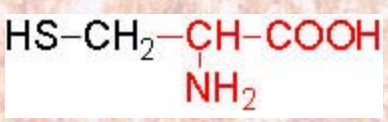
http://www.indstate.edu/thcme/mwking/amino-acids.htm

Polar (Hydrophilic) R Groups

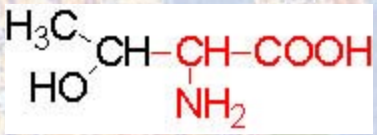
Serine (Ser)



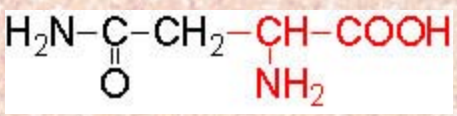
Cysteine (cys)



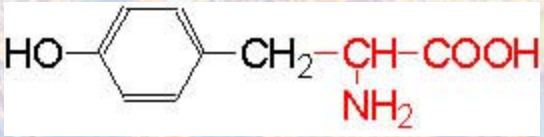
Threonine (Thr)



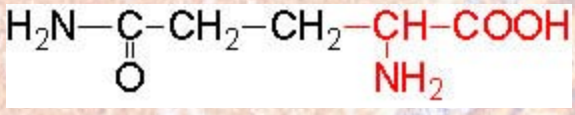
Asparagine (Asn)



Tyrosine (Tyr)



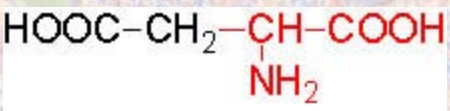
Glutamine (Gln)



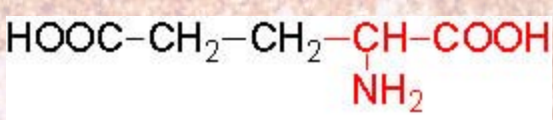
http://www.indstate.edu/thcme/mwking/amino-acids.html

Negatively (Nonpolar) Charged R Groups

Aspartic acid (Asp)



Glutamic acid (Glu)

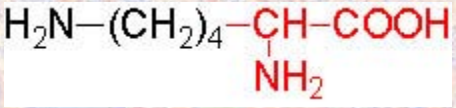


Two amino acids with negatively charged (i.e. acidic) side chains - Aspartate (Aspartic acid) and Glutamate (Glutamic acid).

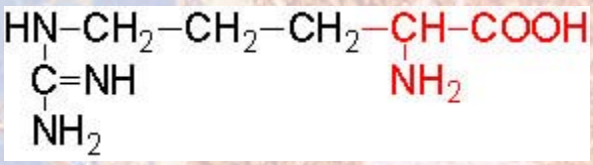
These amino acids confer a negative charge on the proteins of which they are part.

Positively Charged R Groups

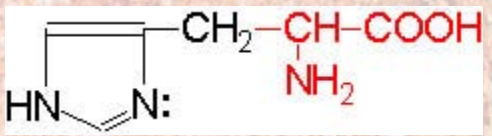
Lysine (Lys)



Arginine (Arg)



Histidine (His)



- Lysine and Arginine both have pKs around 10.0 and are therefore always positively charged at neutral pH.

- With a pK of 6.5, Histidine can be uncharged or positively charged depending upon its local environment.
- Histidine has an important role in the catalytic mechanism of enzymes and explains why it is often found in the active site.

Classification Based on Chemical Constitution

Small amino acids – Glycine, Alanine

Branched amino acids – Valine, Leucine, Isoleucine

Hydroxy amino acids (-OH group) – Serine, Threonine

Sulfur amino acids – Cysteine, Methionine

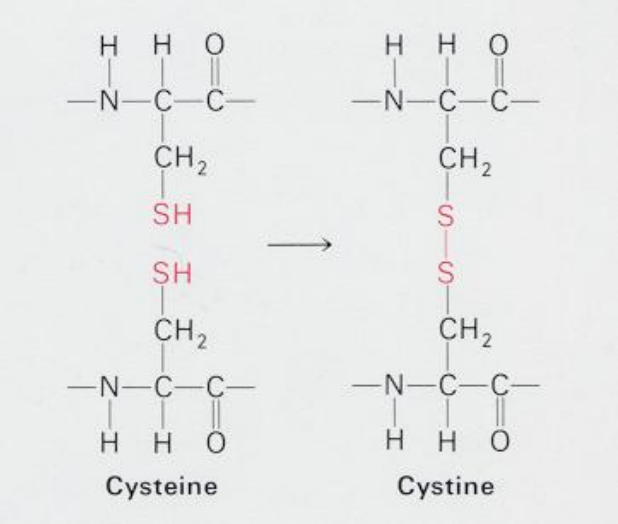
Aromatic amino acids – Phenylalanine, Tyrosine, Tryptophan

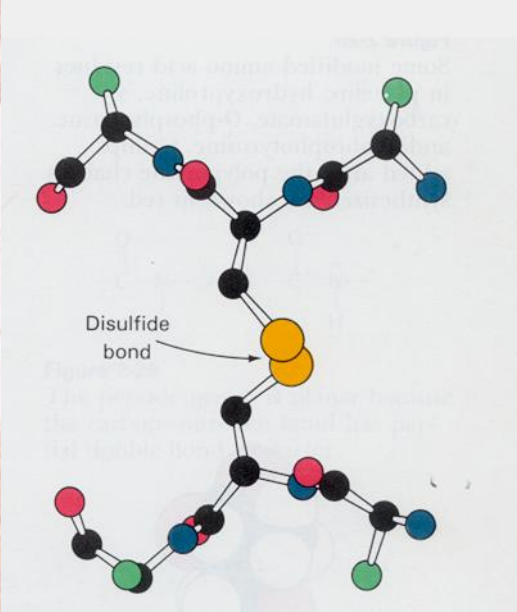
Acidic amino acids and their derivatives – Aspartate, Asparagine, Glutamate, Glutamine

Basic amino acids – Lysine, Arginine, Histidine

Imino acid - Proline

Disulfide Bond Formation



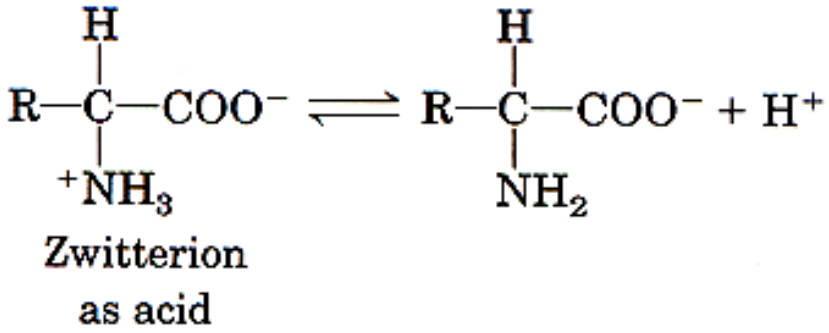


Nonionic and zwitterion forms of amino acids

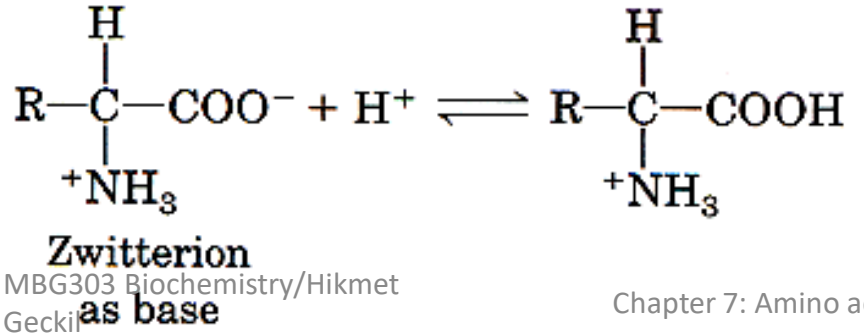
The zwitterion predominates at neutral pH



Zwitterion = in German for „hybrid ion“

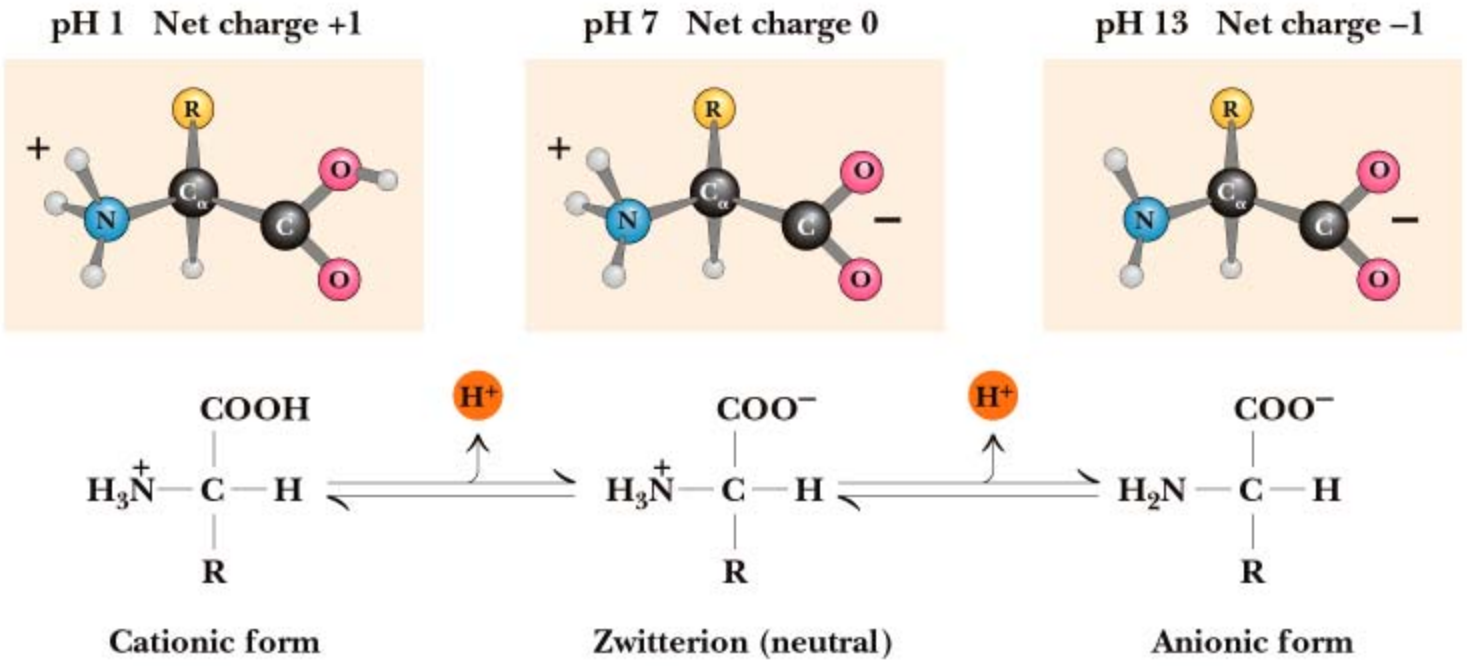


Week acid



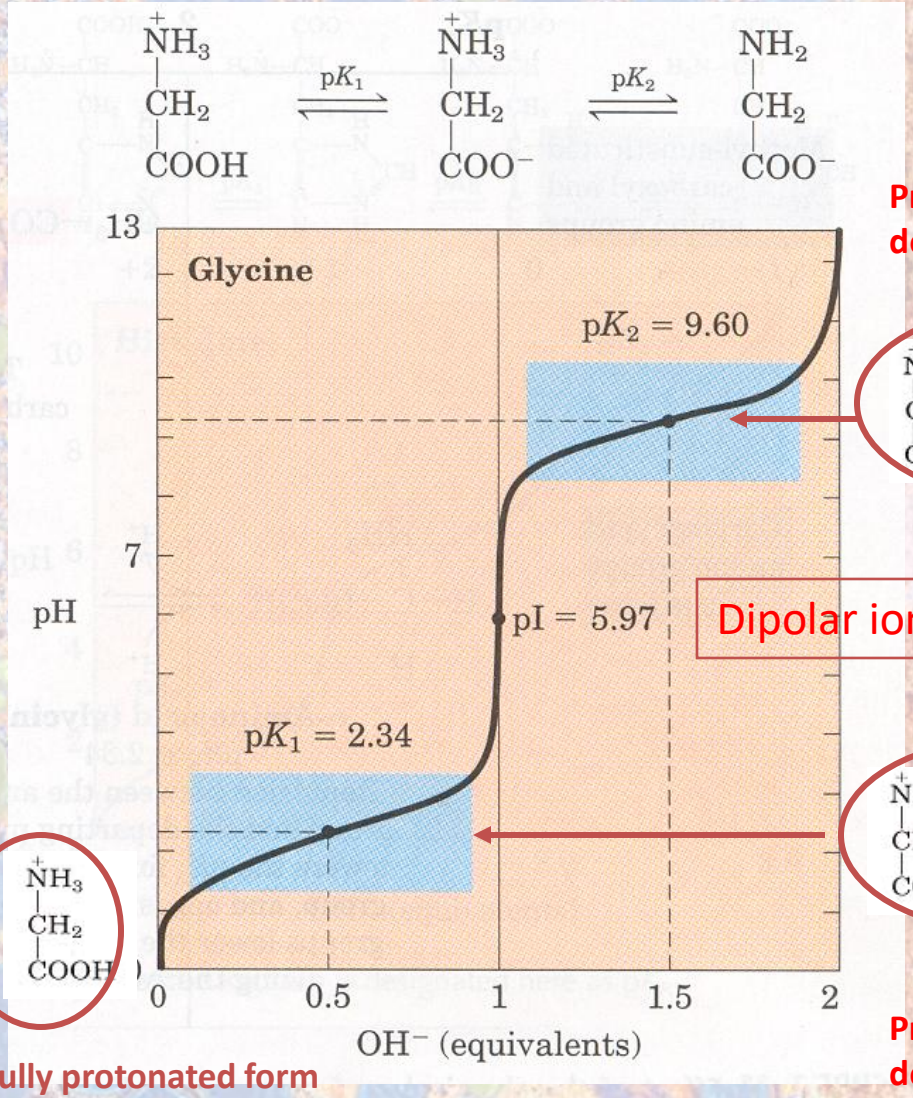
Week base

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Figure 4.6



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Amino acids have characteristic titration curves



Proton donor

Proton acceptor

At the midpoint – pK=9.60 there is equimolar concentration of proton donor and proton acceptor.

Izoelectric point

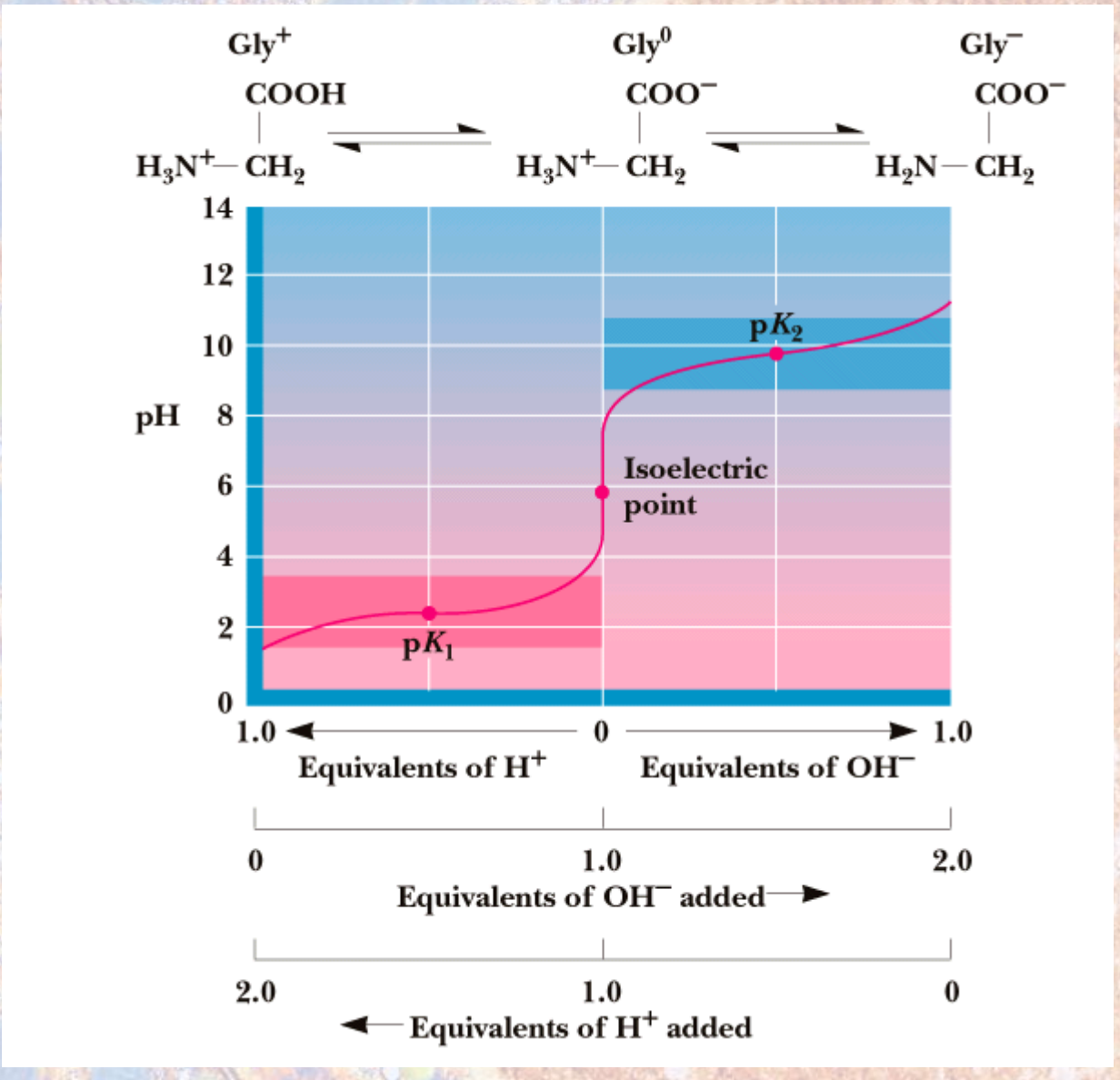
Dipolar ion

At the midpoint – pK1=2.34 there is equimolar concentration of proton donor and proton acceptor.

Proton donor

Proton acceptor

Fully protonated form at wery low pH


Gly+
COOH
H3N+— CH2
Gly0
COO−
H3N+— CH2
Gly−
COO−
H2N — CH2
14
12
10
8
6
4
2
0
pH
pK2
Isoelectric point
pK1
1.0
0
1.0
Equivalents of H+
Equivalents of OH−
0
1.0
2.0
Equivalents of OH− added
2.0
1.0
0
Equivalents of H+ added

Henderson/Hasselbach equation and pK_a

Protonated form Unprotonated form (conjugate base)

$$HA \rightleftharpoons H^+ + A^-$$

$$K_a = \frac{[H^+]\ [A^-]}{[HA]}$$

$$[H^+] = K_a \times \frac{[HA]}{[A^-]}$$

$$-\log\ [H^+] = -\log\ K_a - \log \frac{[HA]}{[A^-]}$$

$$pH = pK_a + \log \frac{[A^-]}{[HA]}$$

Essential Amino Acids in Humans

- Required in diet
- Humans incapable of forming requisite carbon skeleton

Arginine*	Lysine
Histidine*	Methionine
Isoleucine	Threonine
Leucine	Phenylalanine
Valine	Tryptophan

* Essential in children, not in adults

Non-Essential Amino Acids in Humans

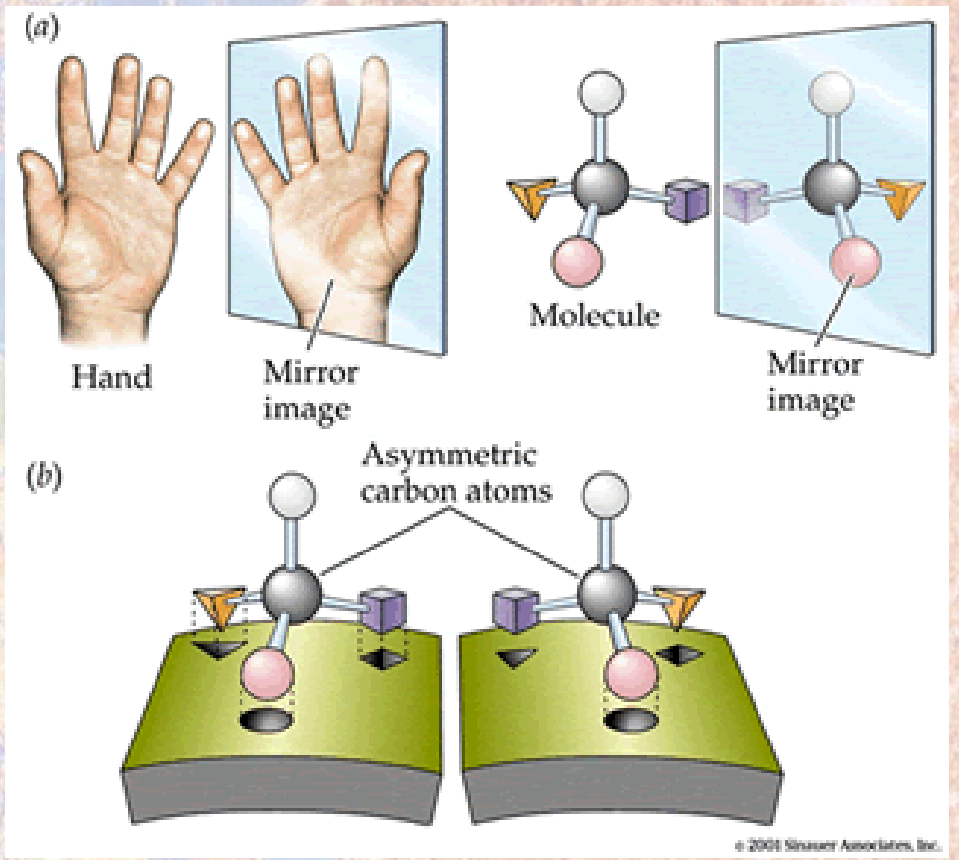
- Not required in diet
- Can be formed from a-keto acids by transamination and subsequent reactions

Alanine	Glycine
Asparagine	Proline
Aspartate	Serine
Glutamate	Cysteine (from Met*)
Glutamine	Tyrosine (from Phe*)

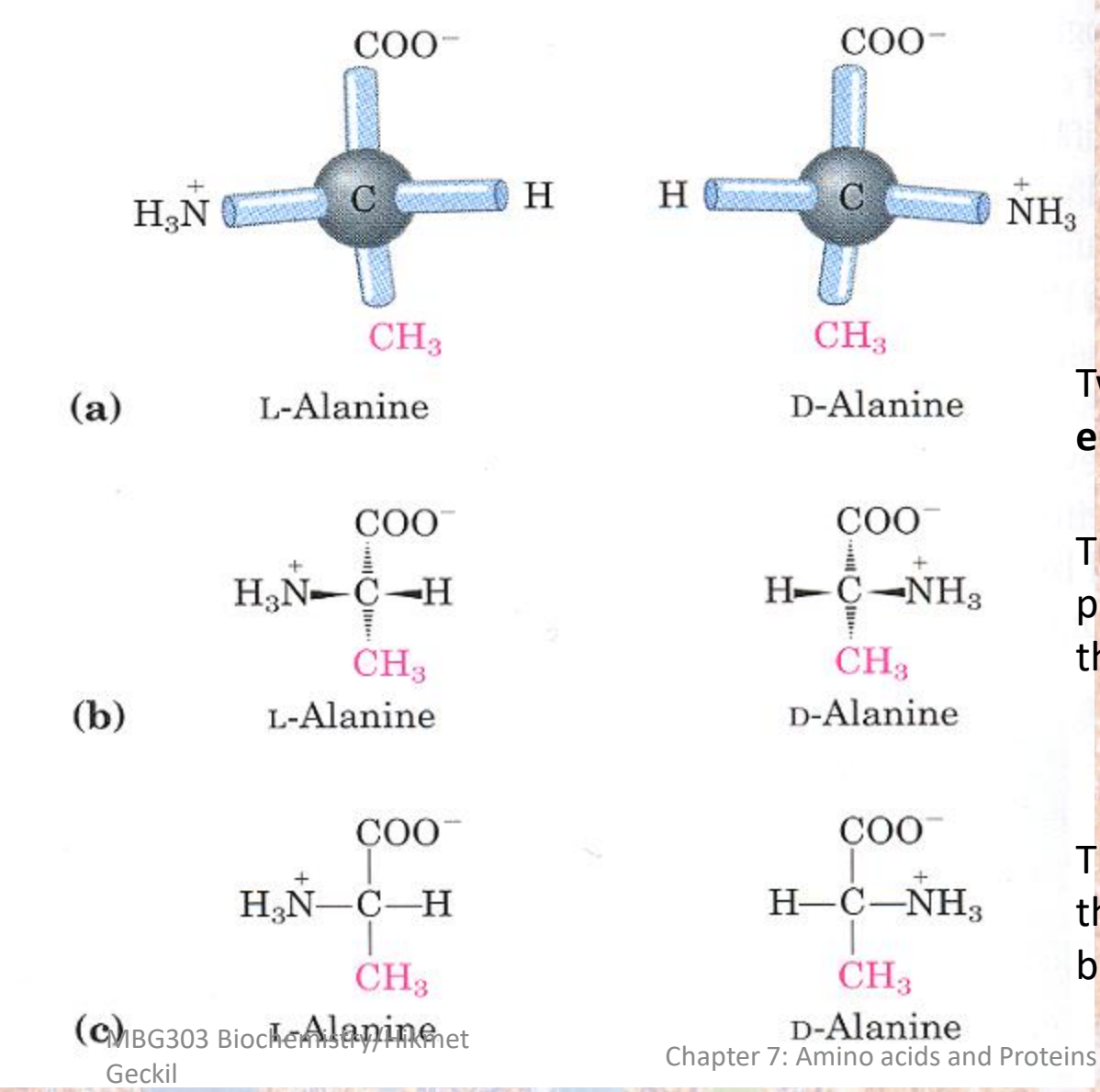
* Essential amino acids

The Stereochemistry of Amino Acids

Chiral molecules existing in two forms



The two stereoisomers of alanine



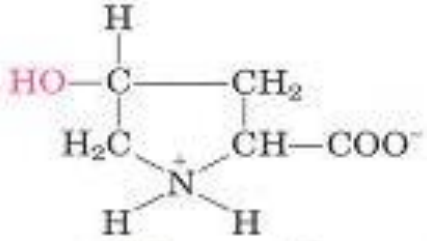
α–carbon is a **chiral center**

Two stereoisomers are called **enantiomers.**

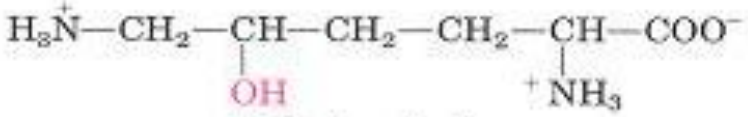
The solid wedge-shaped bonds project out of the plane of paper, the dashed bonds behind it.

The horizontal bonds project out of the plane of paper, the vertical bonds behind.

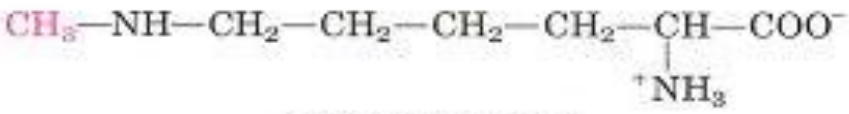
Uncommon amino acids found in proteins



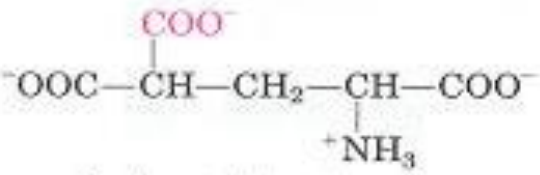
4-Hydroxyproline



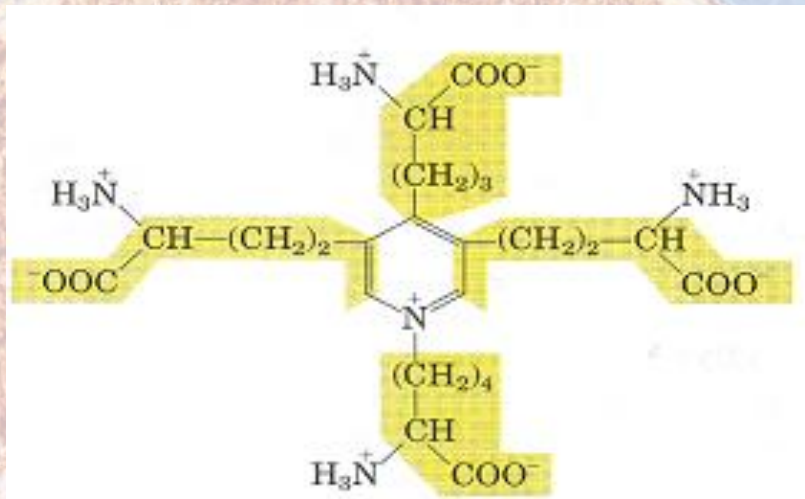
5-Hydroxylysine



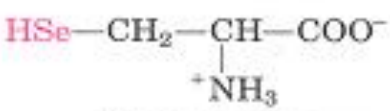
6-*N*-Methyllysine



γ-Carboxyglutamate

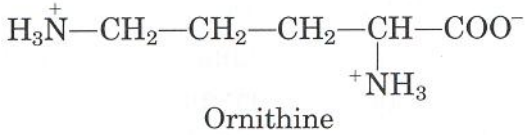


Desmosine

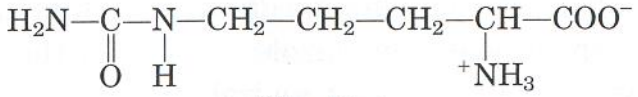


Selenocysteine

Intermediates of biosynthesis of arginin and in urea cycle

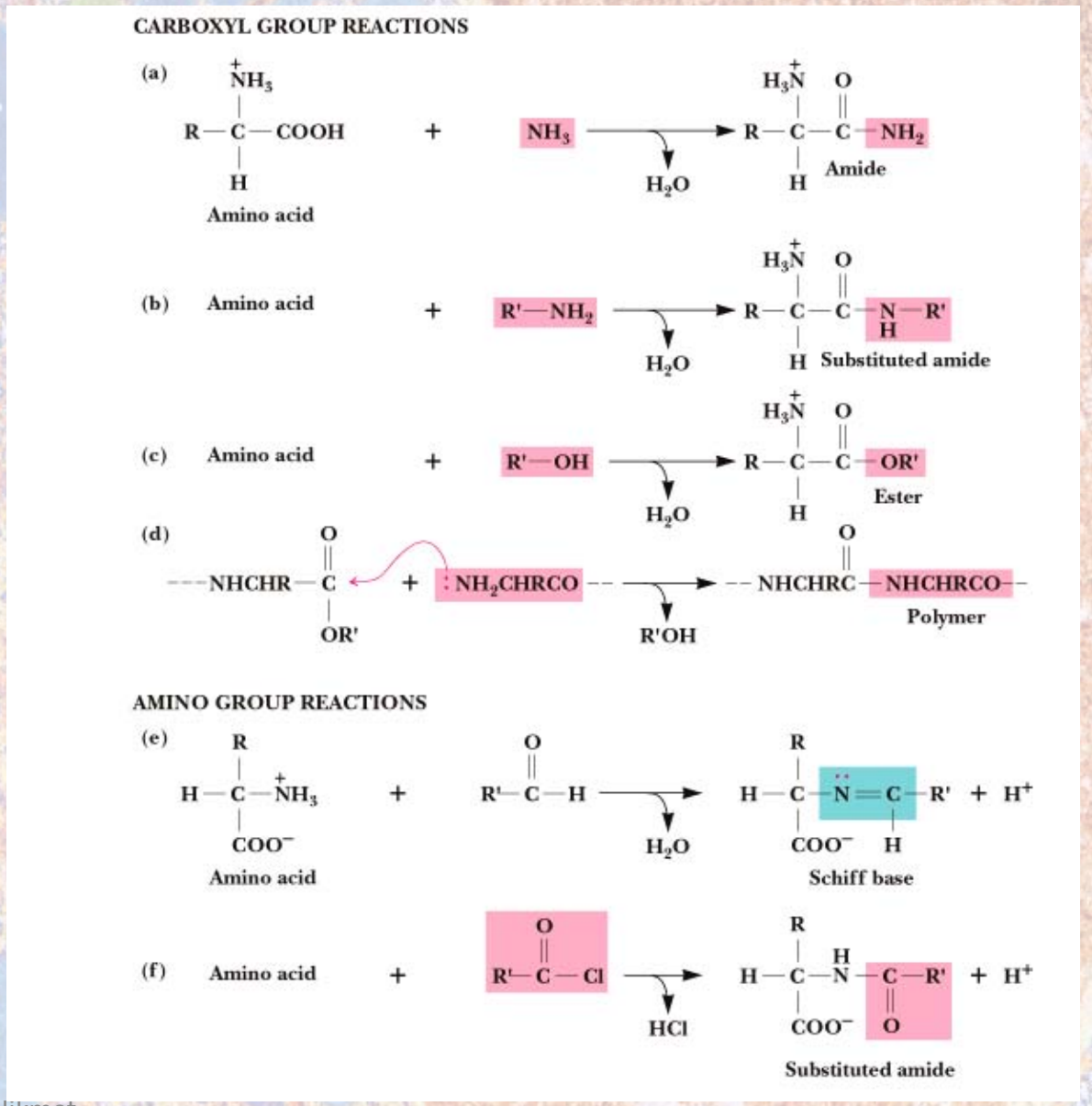


Ornithine

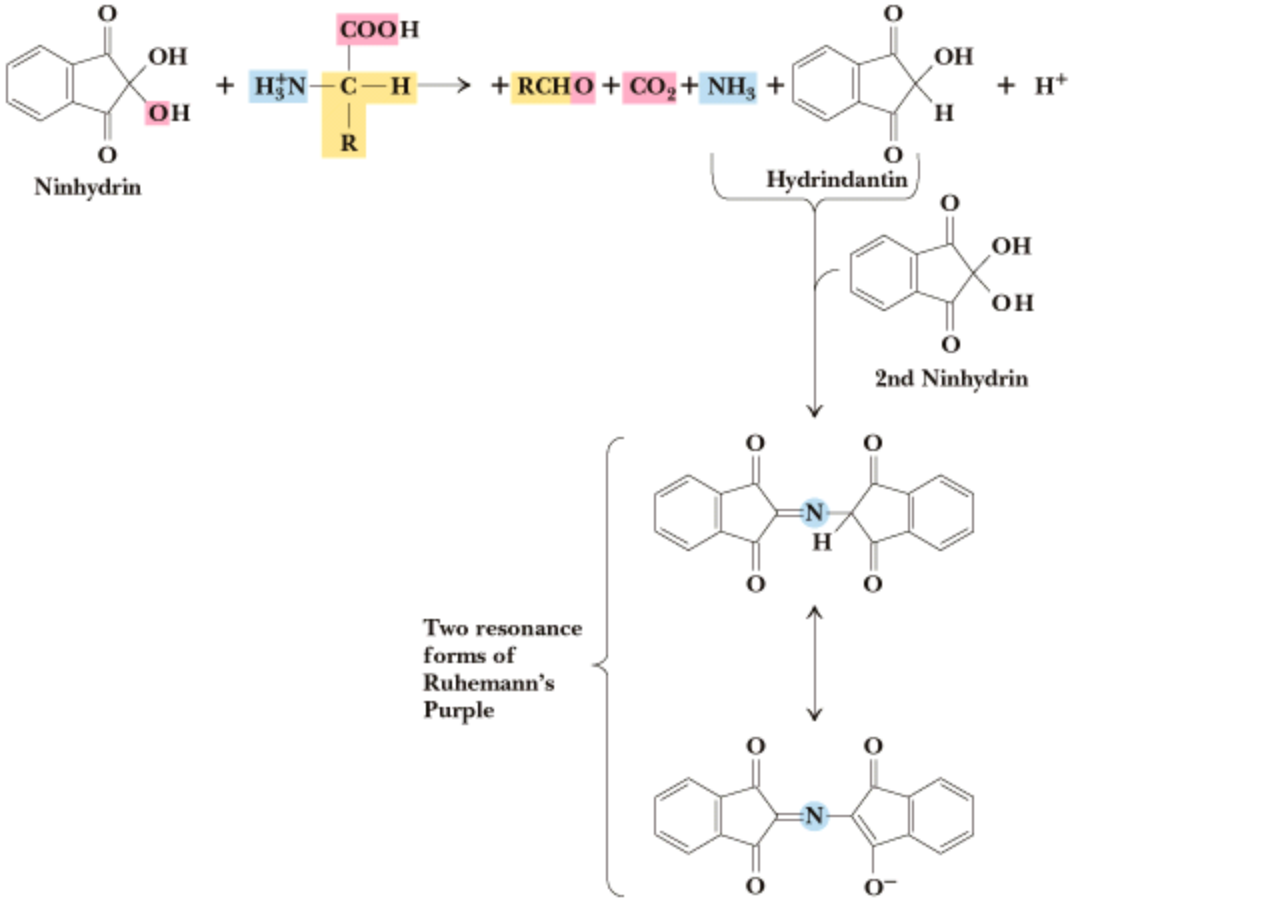


Citrulline

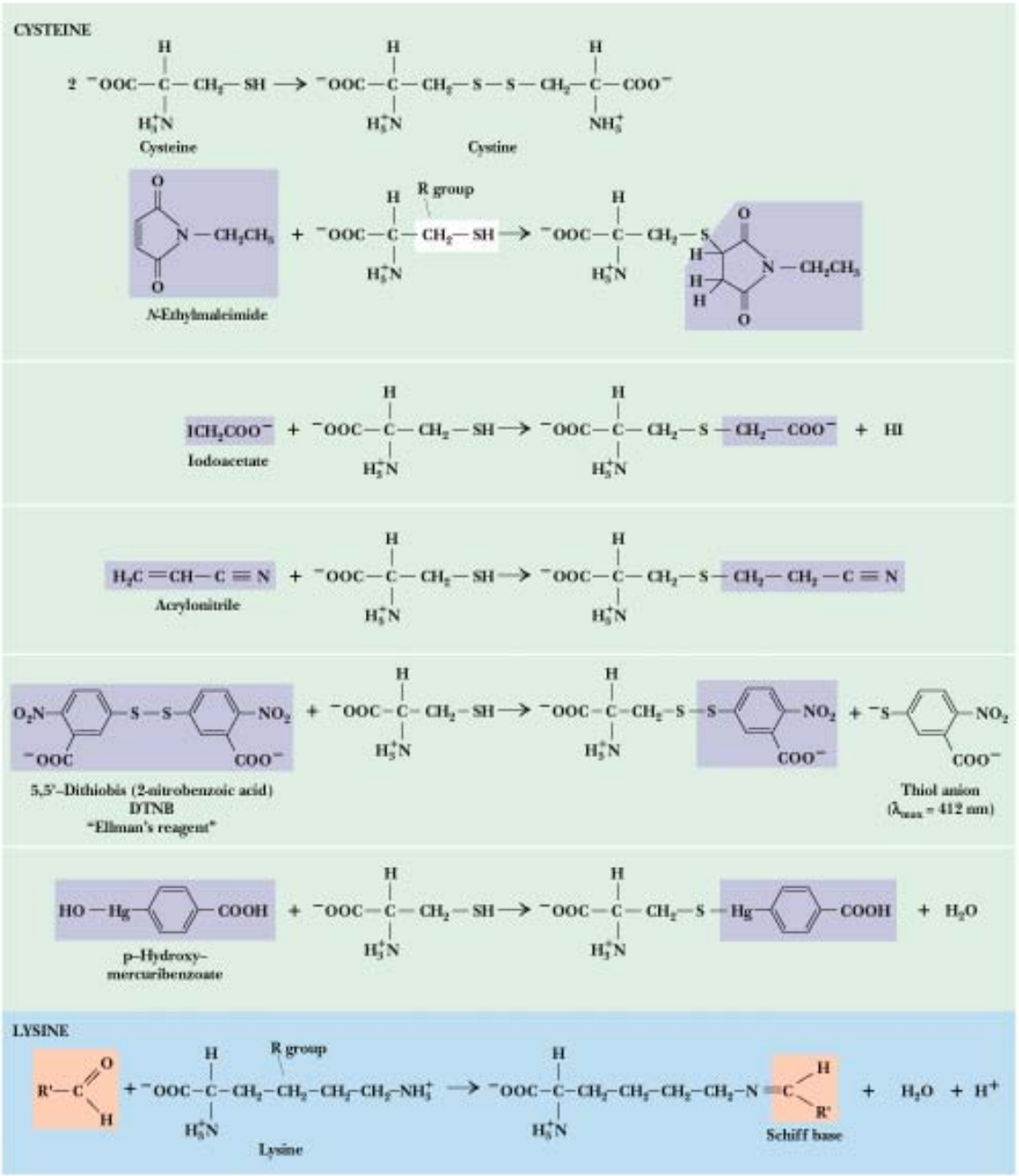
Reactions of Amino Acids



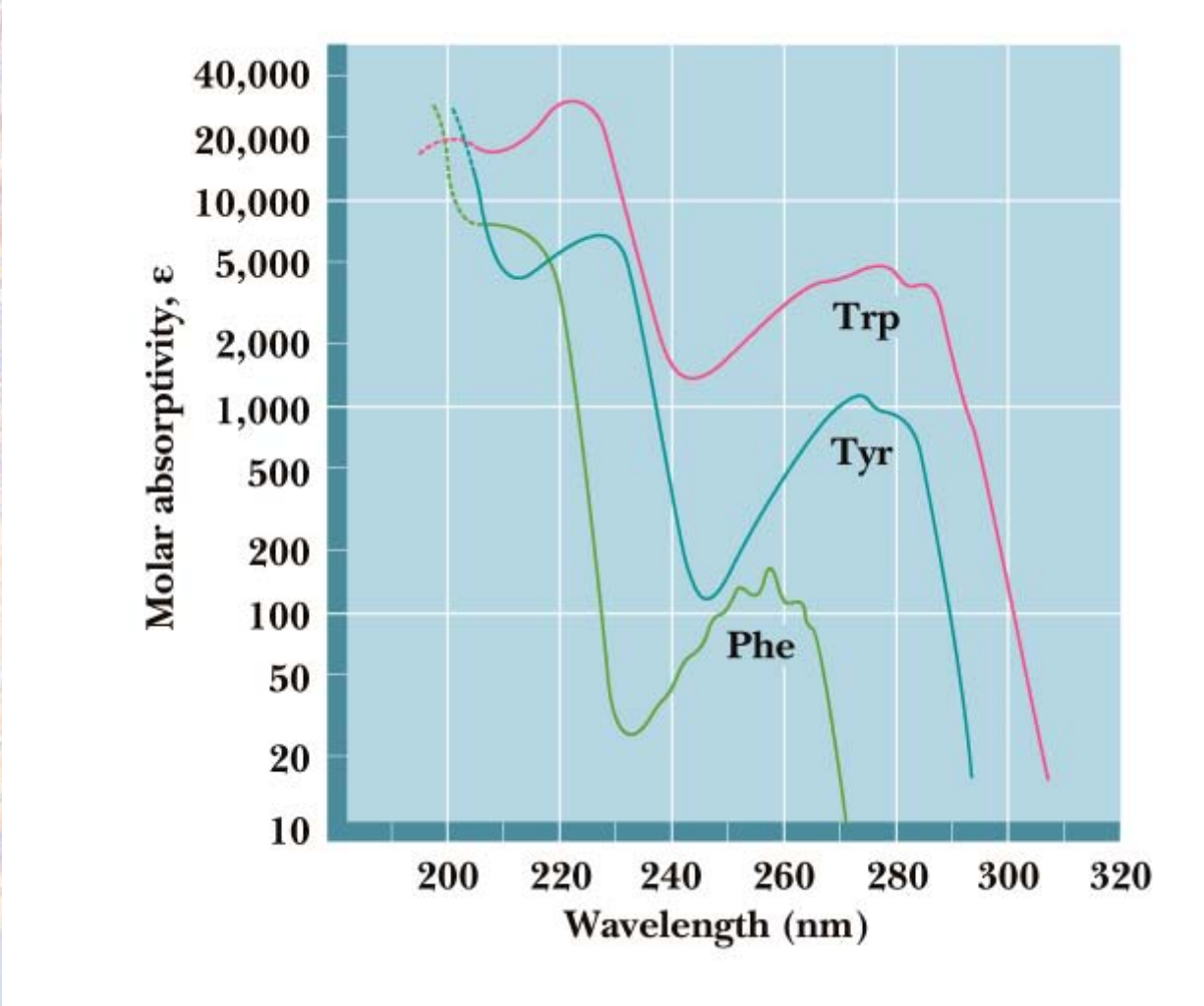
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Figure 4.10



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CYSTEINE
Cysteine
Cystine
R group
N-Ethylmaleimide
Iodoacetate
Acrylonitrile
5,5'-Dithiobis (2-nitrobenzoic acid)
DTNB
"Ellman's reagent"
Thiol anion
(λmax = 412 nm)
p-Hydroxy-
mercuribenzoate
LYSINE
Lysine
Schiff base

Spectroscopic Properties



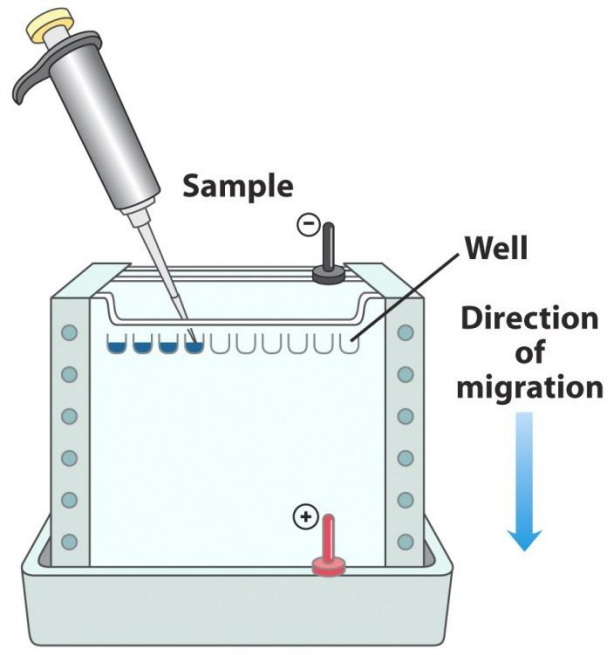
Separation of Amino Acids

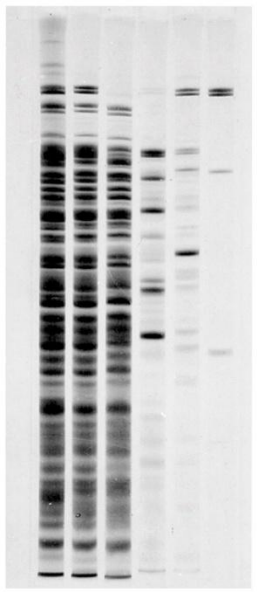
- Many chromatographic methods exist for separation of amino acid mixtures
  - Ion exchange chromatography
  - High-performance liquid chromatography

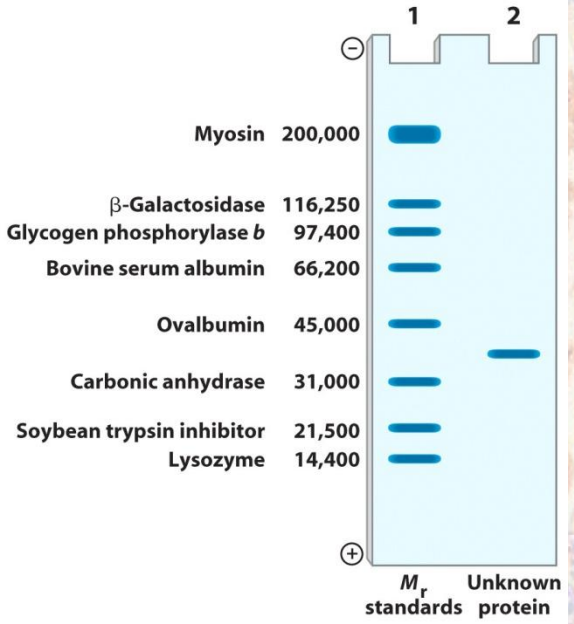
Spectroscopic Properties

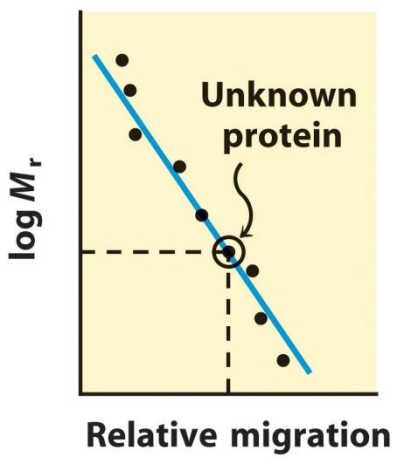
- All amino acids absorb in infrared region
- Only Phe, Tyr, and Trp absorb UV
- Absorbance at 280 nm is a good diagnostic device for amino acids
- NMR spectra are characteristic of each residue in a protein, and high resolution NMR measurements can be used to elucidate three-dimensional structures of proteins

Gel Electrophoresis



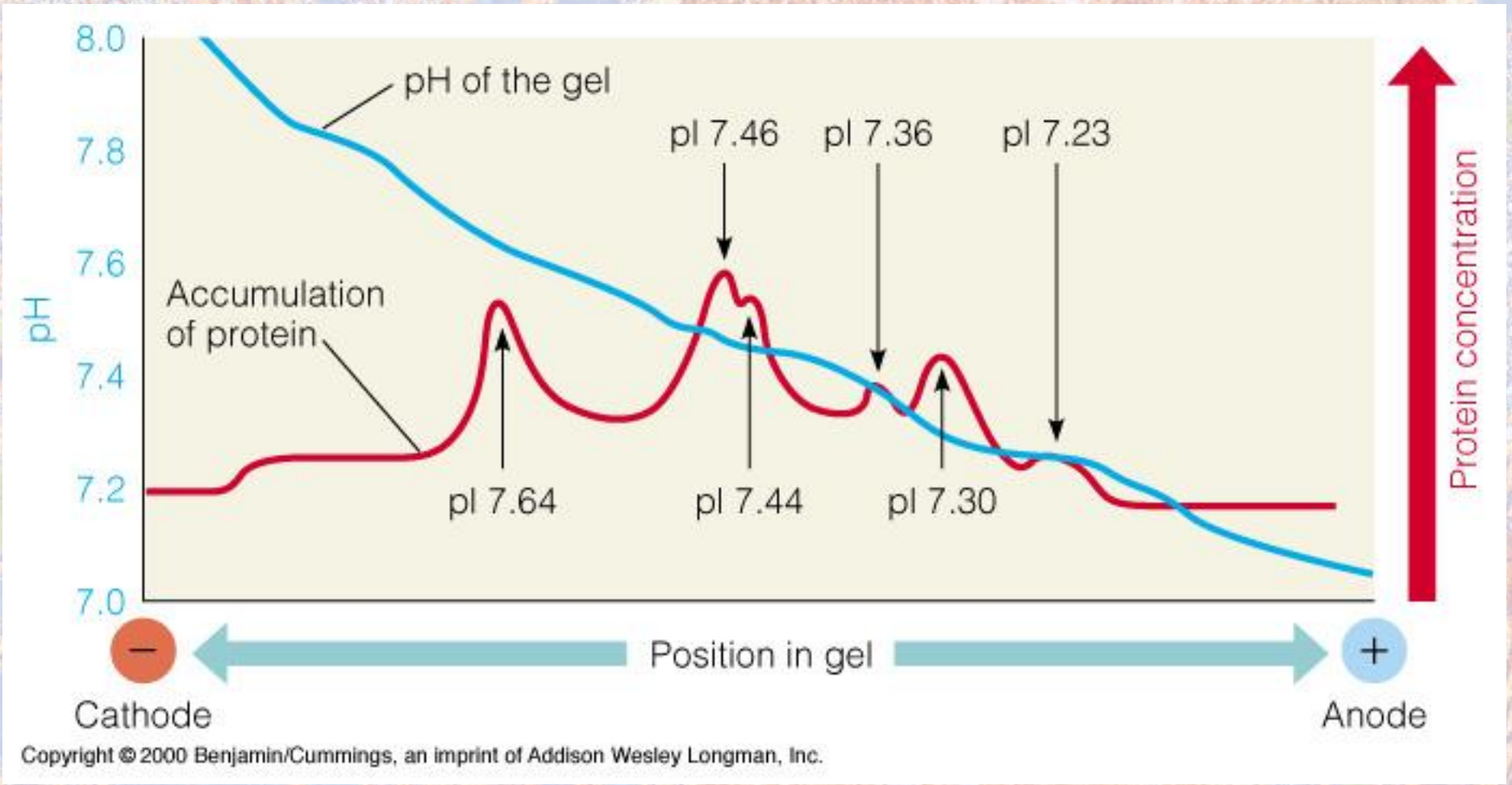






Isoelectric Focusing

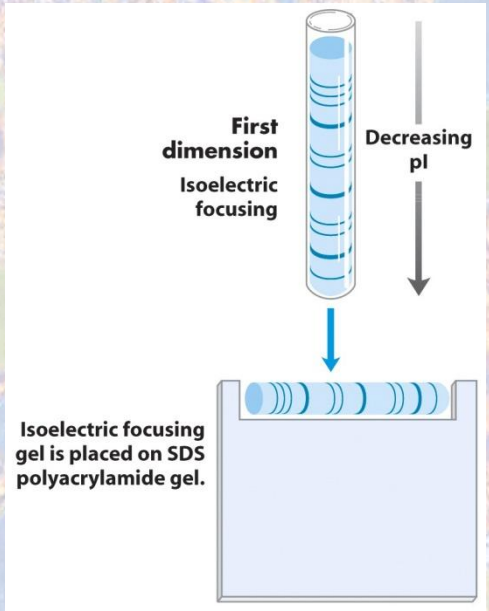
Electrophoresis through polyacrylamide gel in which there is a pH gradient.

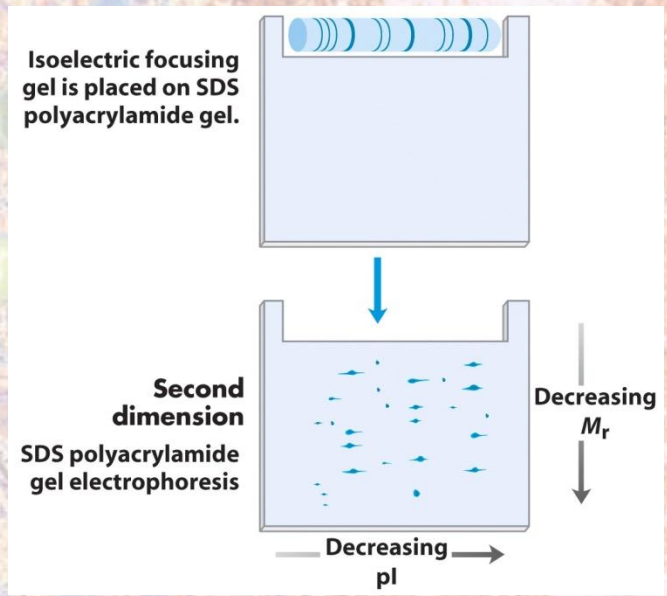


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Two-Dimensional Gel Electrophoresis

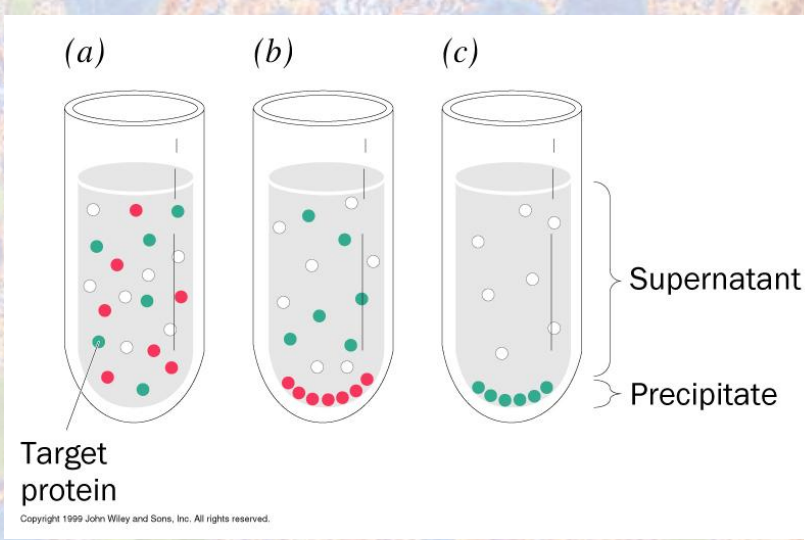
- Separate proteins based on isolectric point in 1st dimension
- Separate proteins based on molecular weight in 2nd dimension



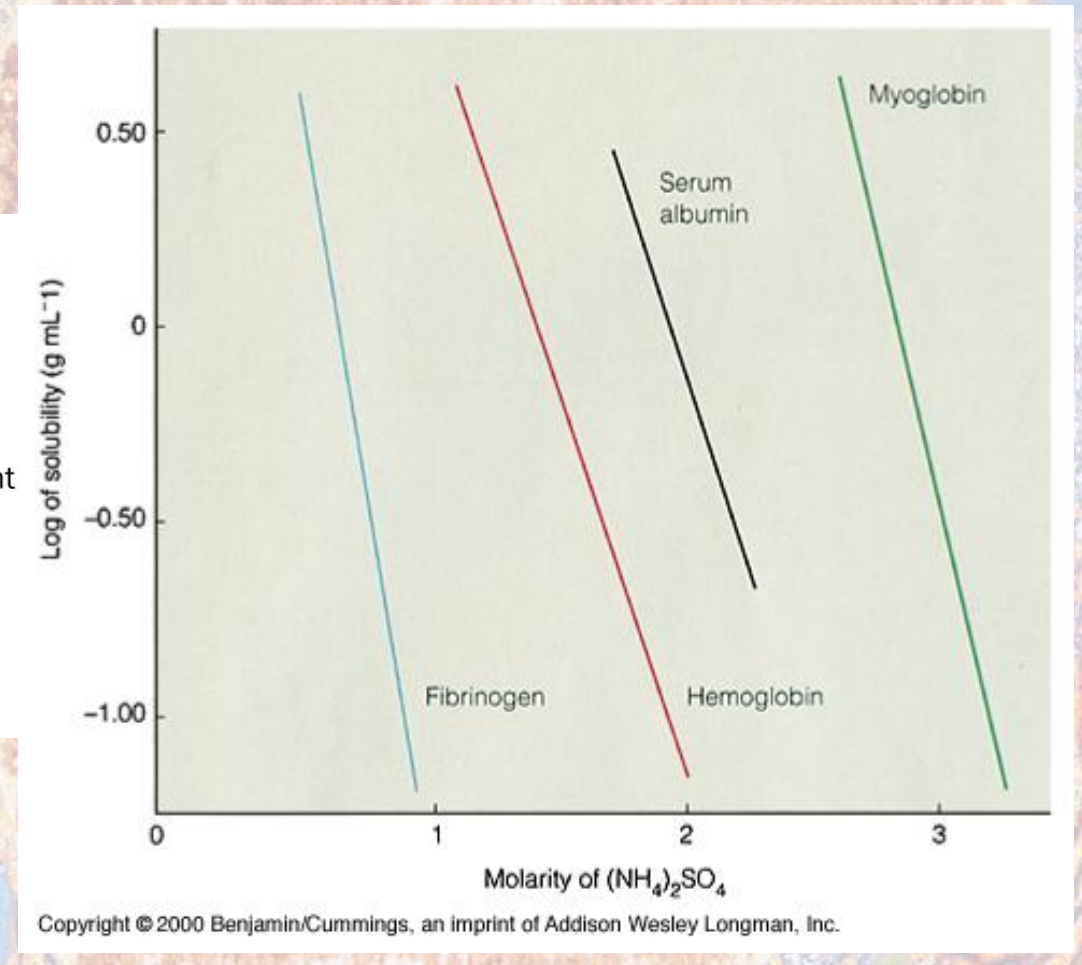




“Salting Out”: Ammonium Sulfate Precipitation in Protein Fractionation

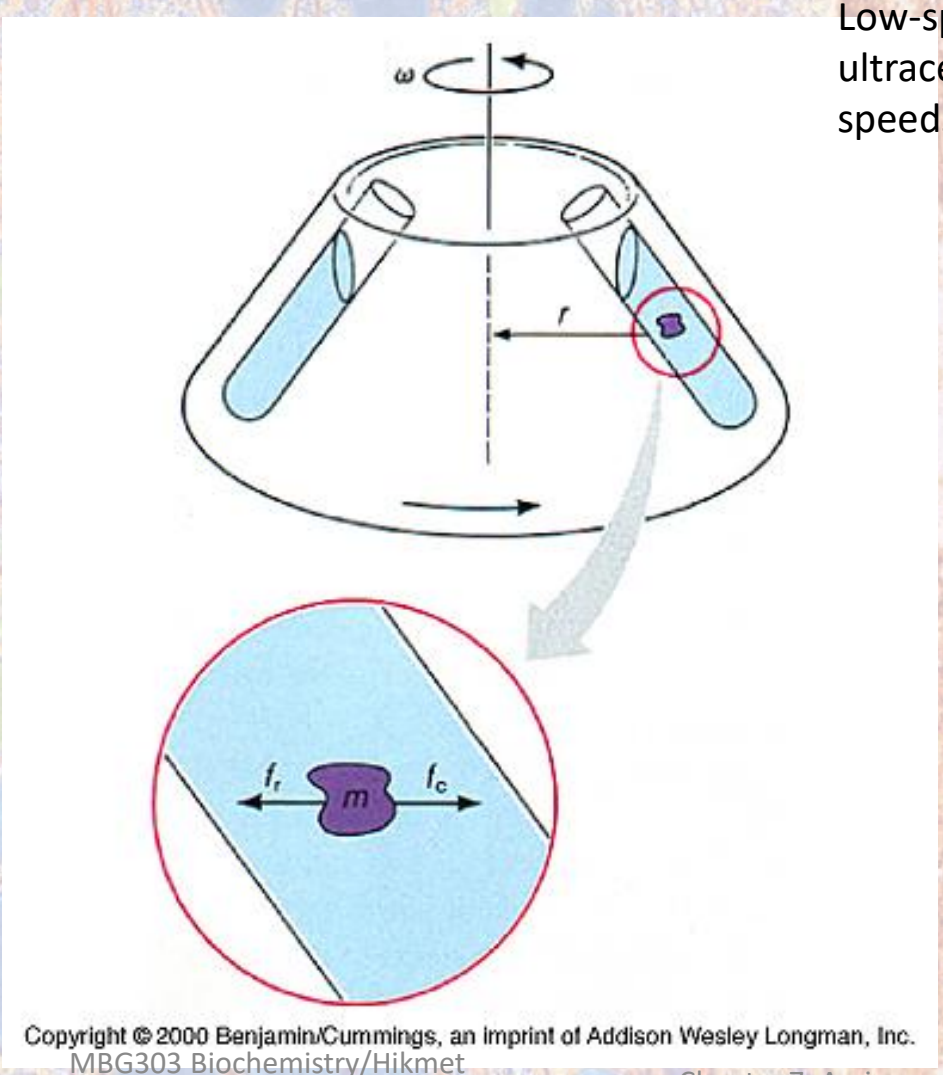


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Centrifugation



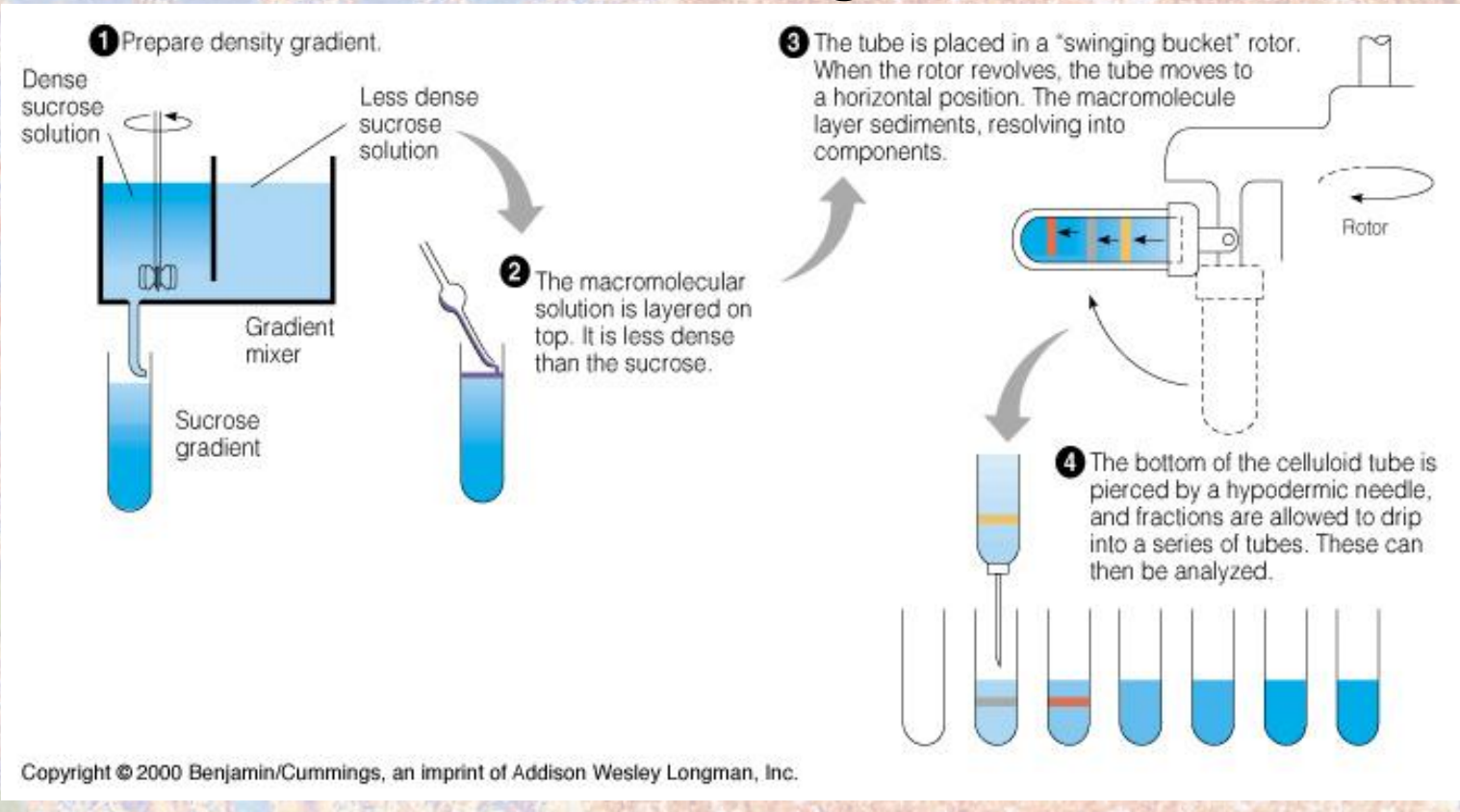
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Low-speed, high-speed, or ultracentrifugation: different spin speeds and *g* forces

Centrifugation Methods

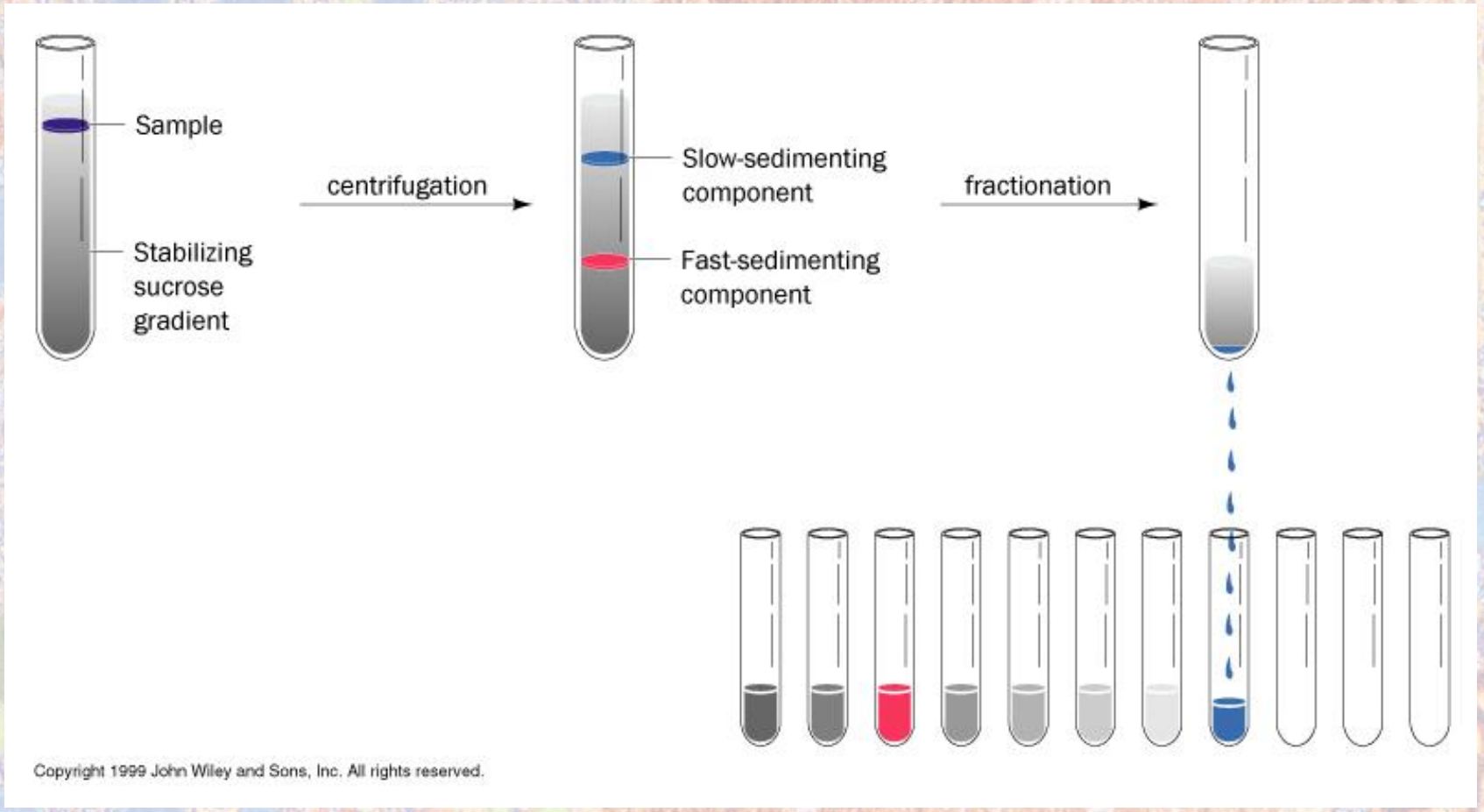
- Differential (Pelletting) – simple method for pelleting large particles using fixed-angle rotor (pellet at bottom of tube vs. supernatant solution above)
- Zonal ultracentrifugation (*e.g.*, sucrose-gradient) – swinging-bucket rotor
- Equilibrium-density gradient ultracentrifugation (*e.g.*, CsCl) – swinging-bucket or fixed-angle rotor

Zonal Centrifugation: Sucrose-Gradient Preparative Ultracentrifugation



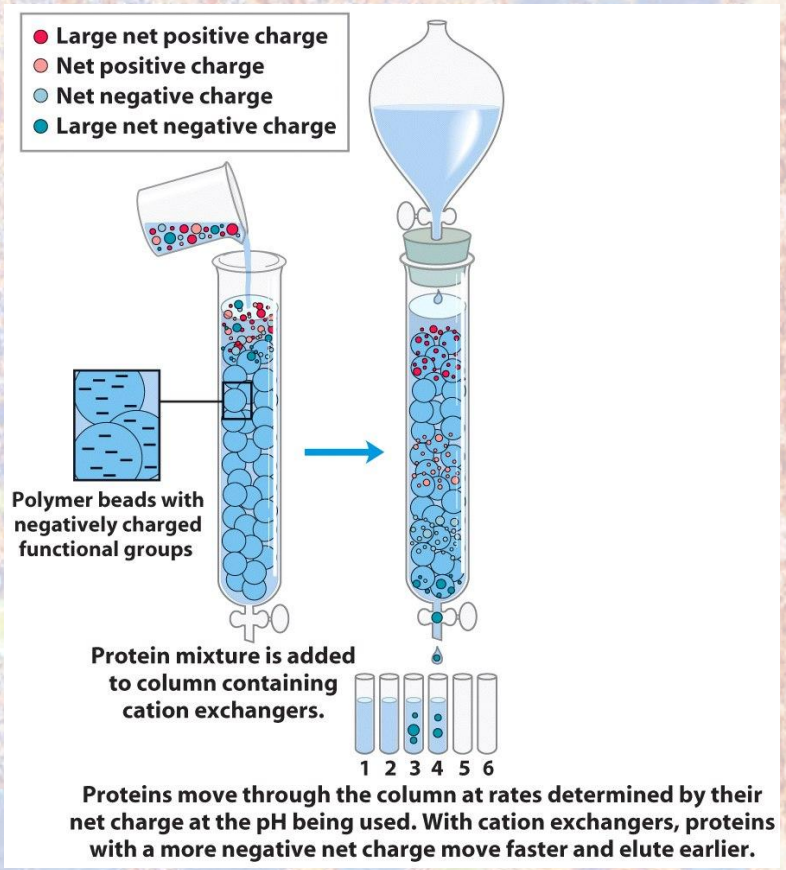
Separates by sedimentation coefficient (determined by size and shape of solutes)

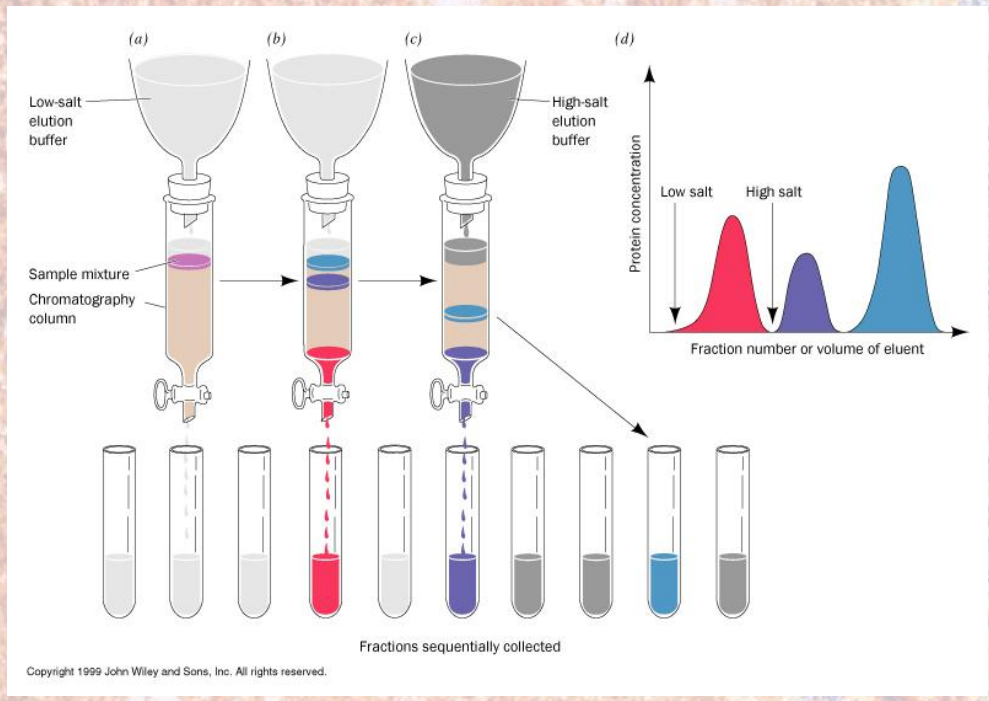
Sucrose-Gradient Preparative Ultracentrifugation



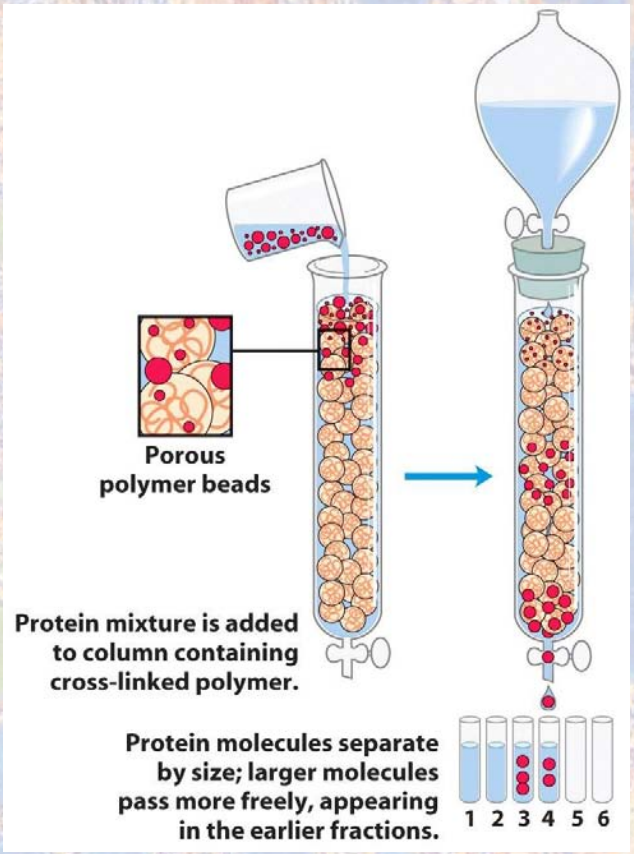
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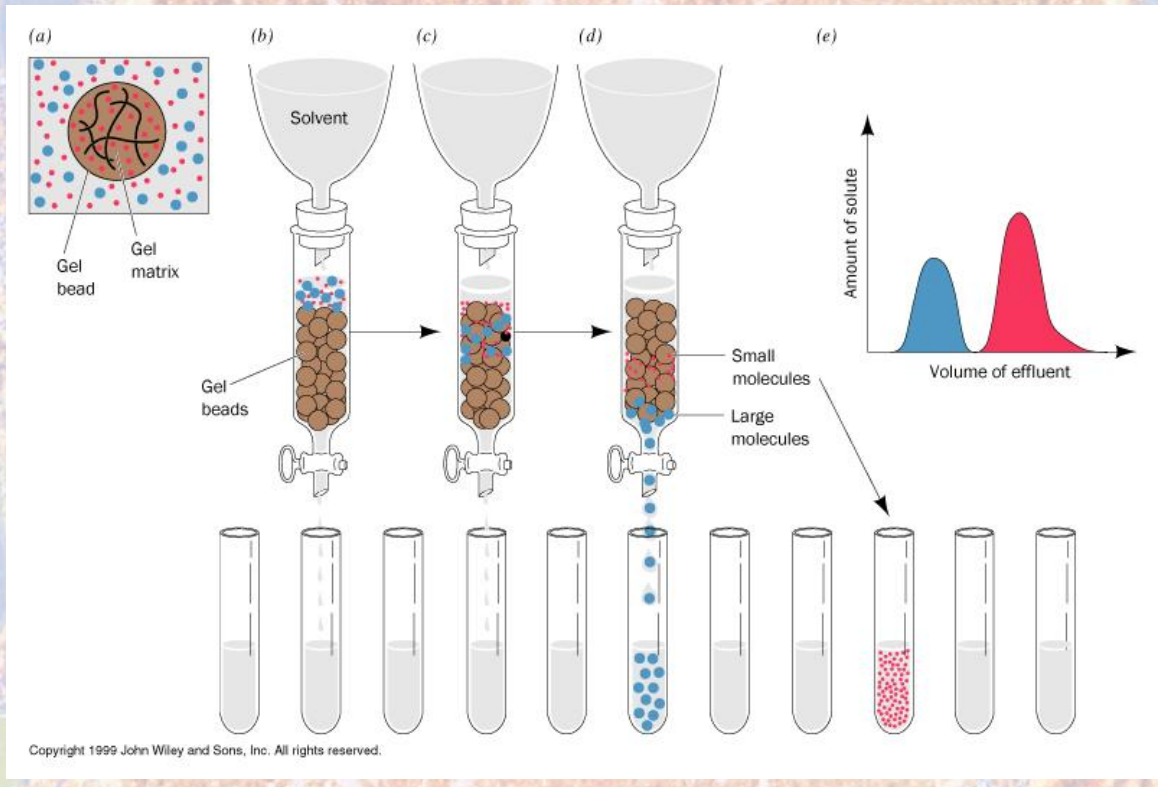
Ion-Exchange Chromatography



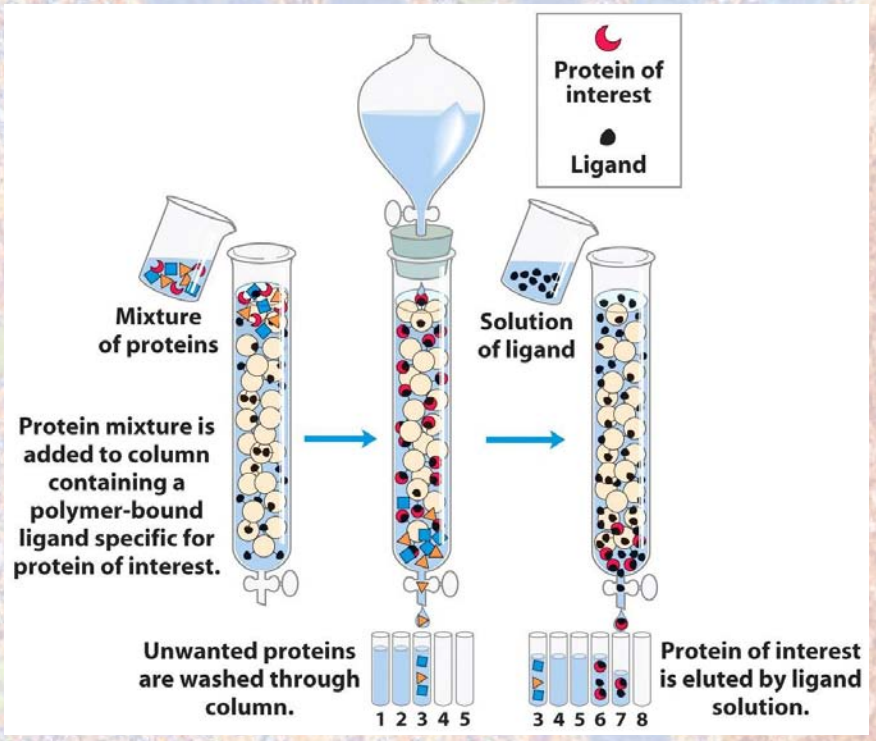


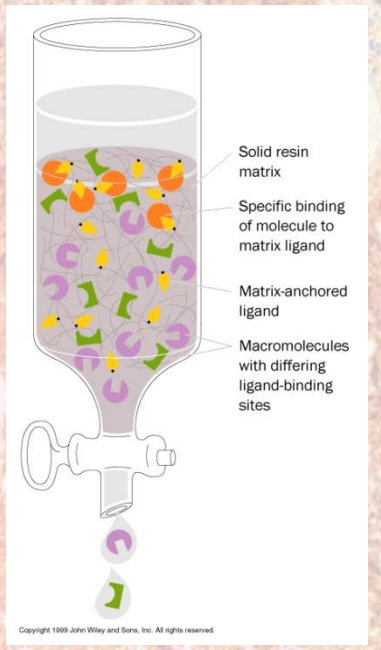
Gel Filtration Chromatography

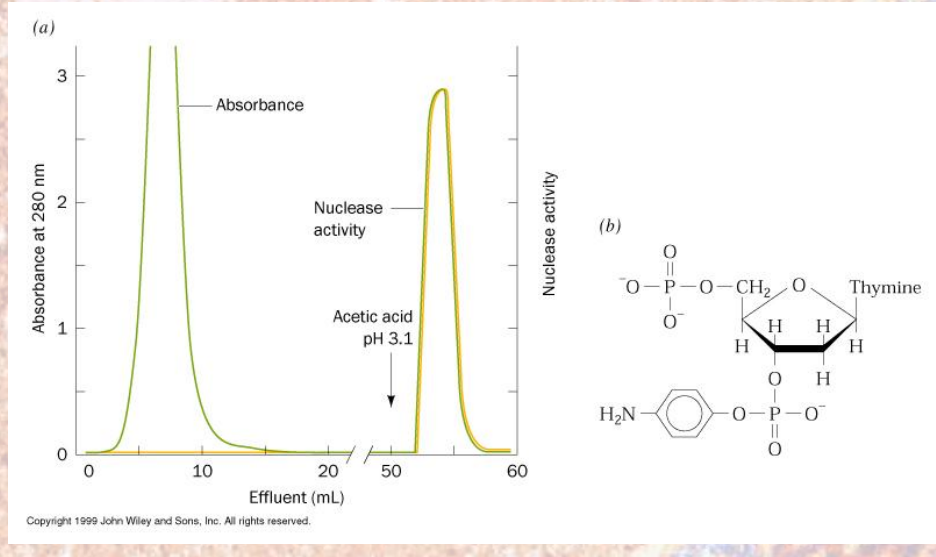




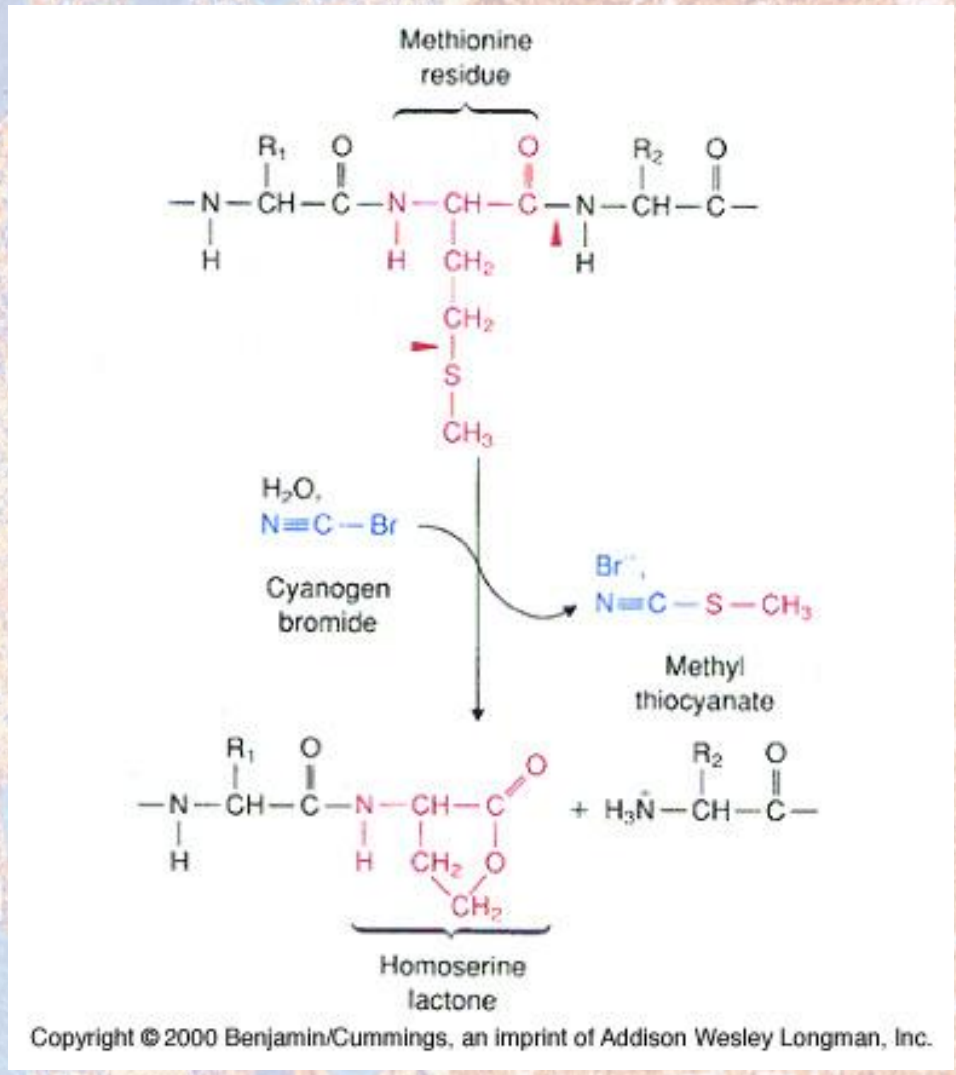
Affinity Chromatography





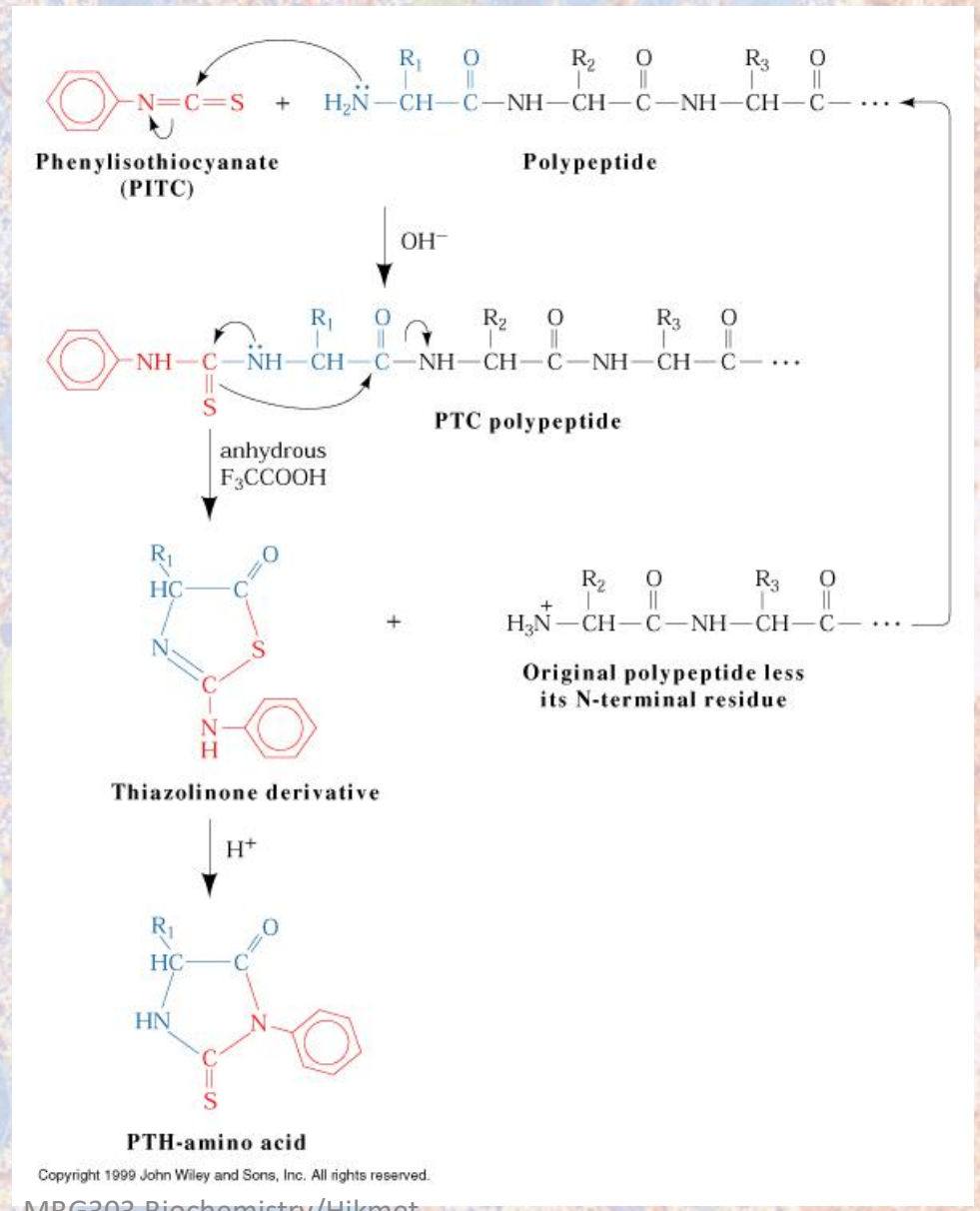


Cyanogen Bromide Cleavage at Methionine Residues



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Protein Sequencing: Edman Degradation

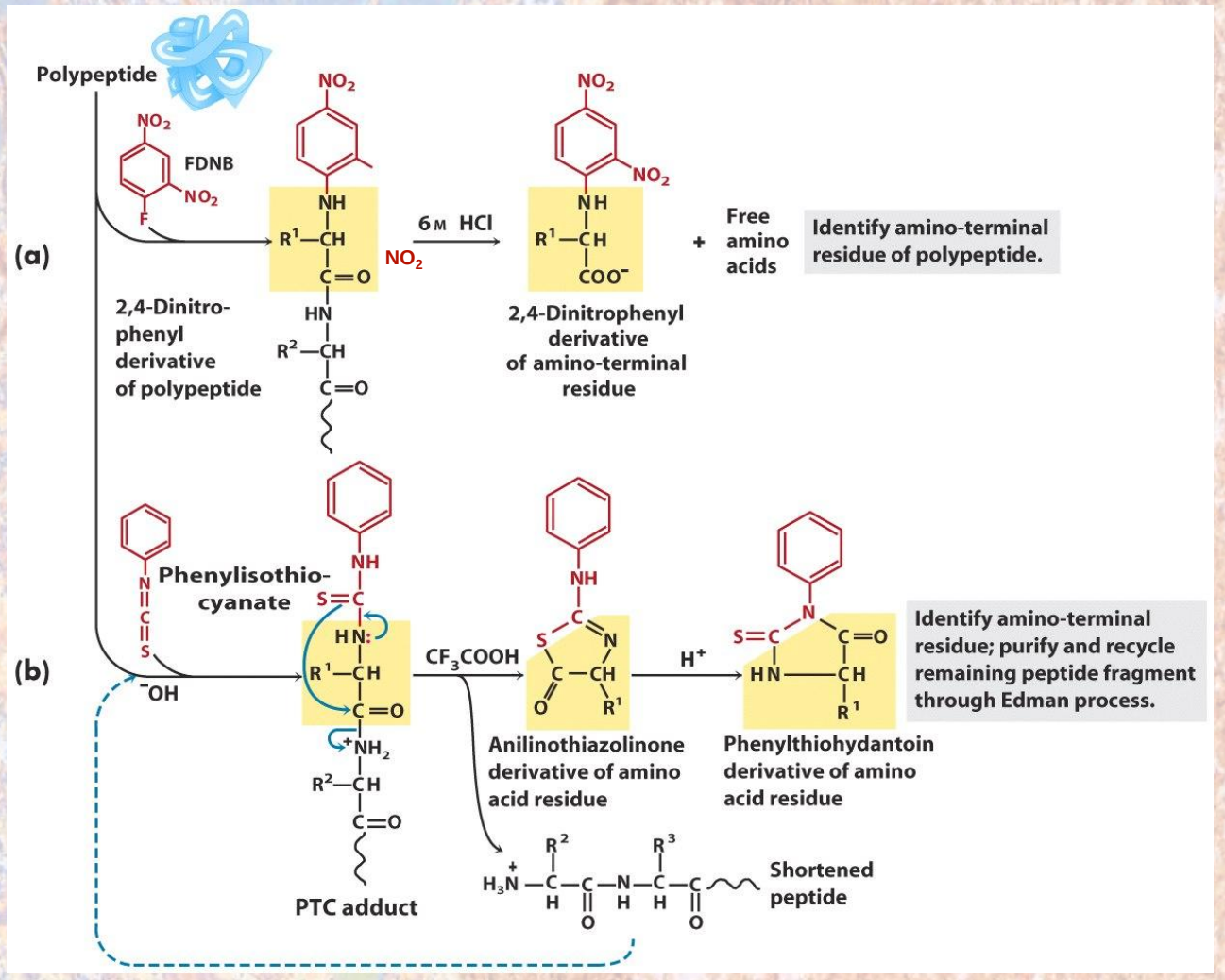


PTC = phenylthiocarbamyl

F_3CCOOH = trifluoroacetic acid

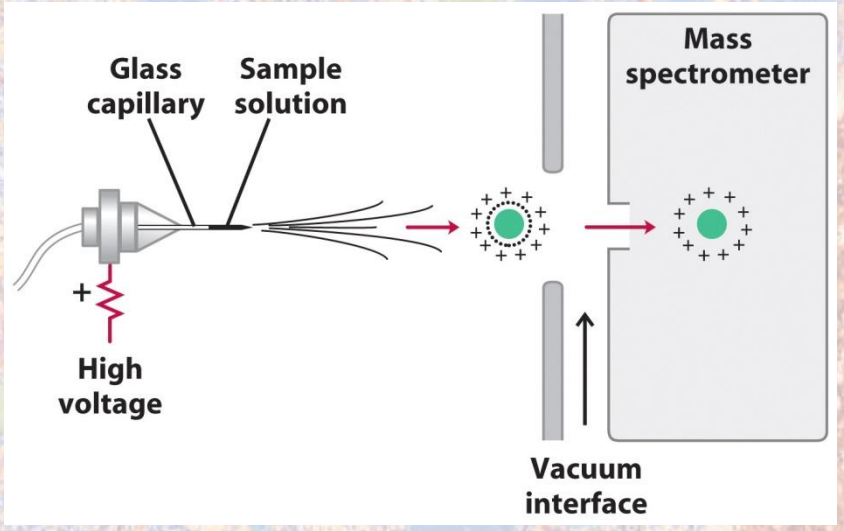
PTH = phenylthiohydantion

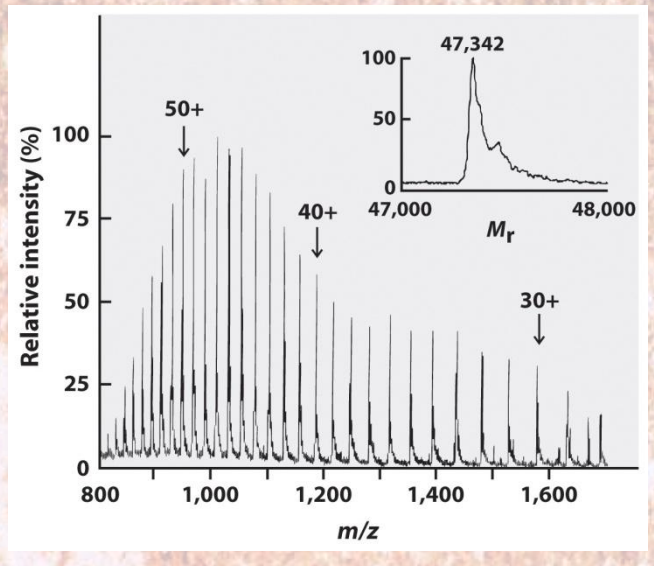
Identification of N-Terminal Residue

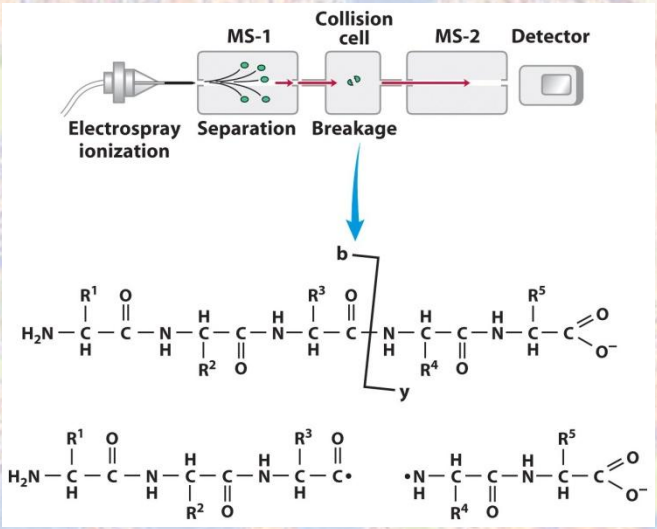


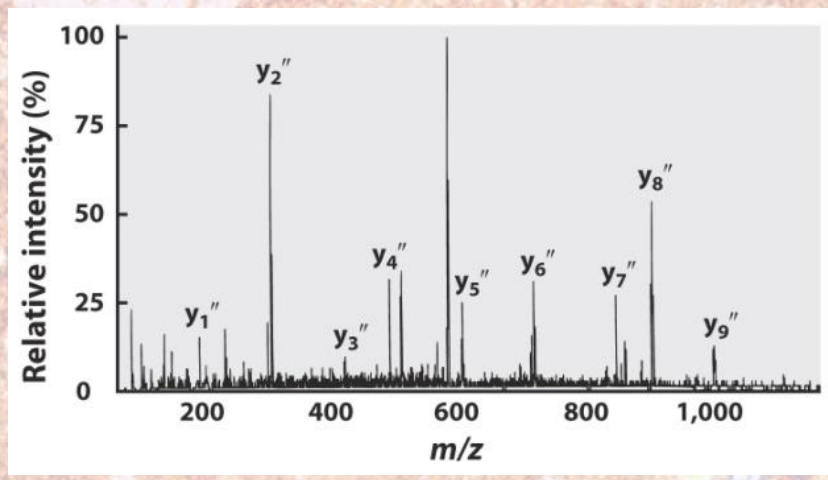
Note: Identification of C-terminal residue done by hydrazinolysis (reaction with anhydrous hydrazine in presence of mildly acidic ion exchange resin) or with a C-terminus-specific exopeptidase (carboxypeptidase).

Protein Identification by Mass Spectrometry









Denaturing a Protein

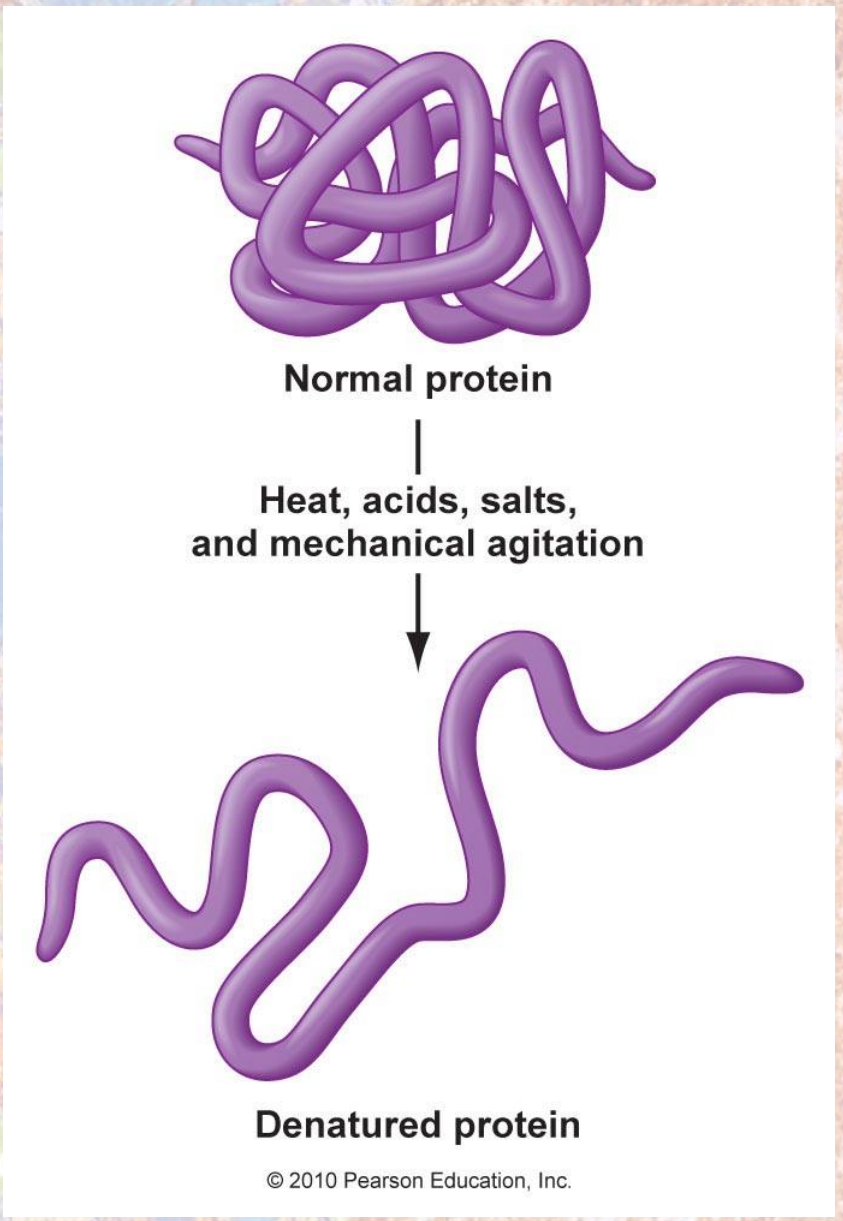
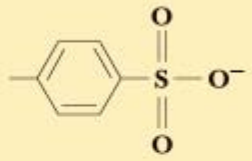
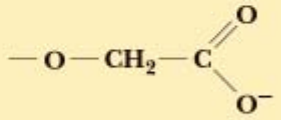
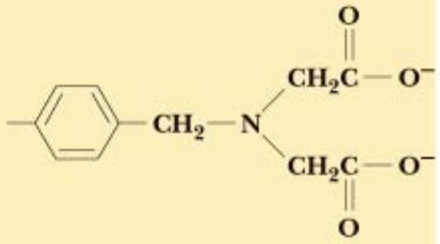
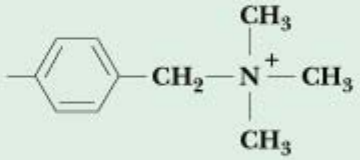
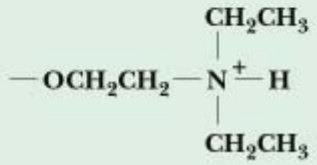
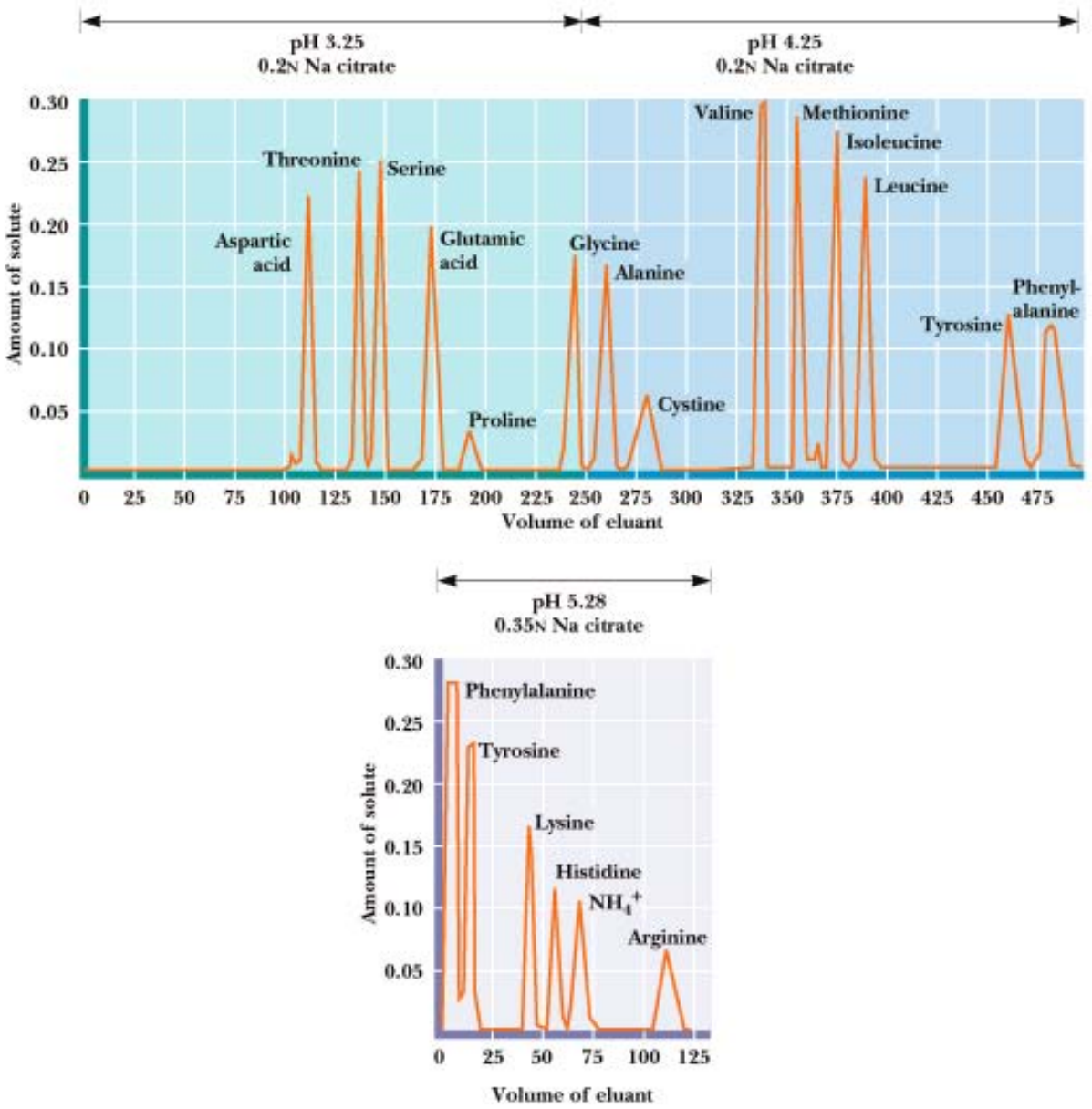


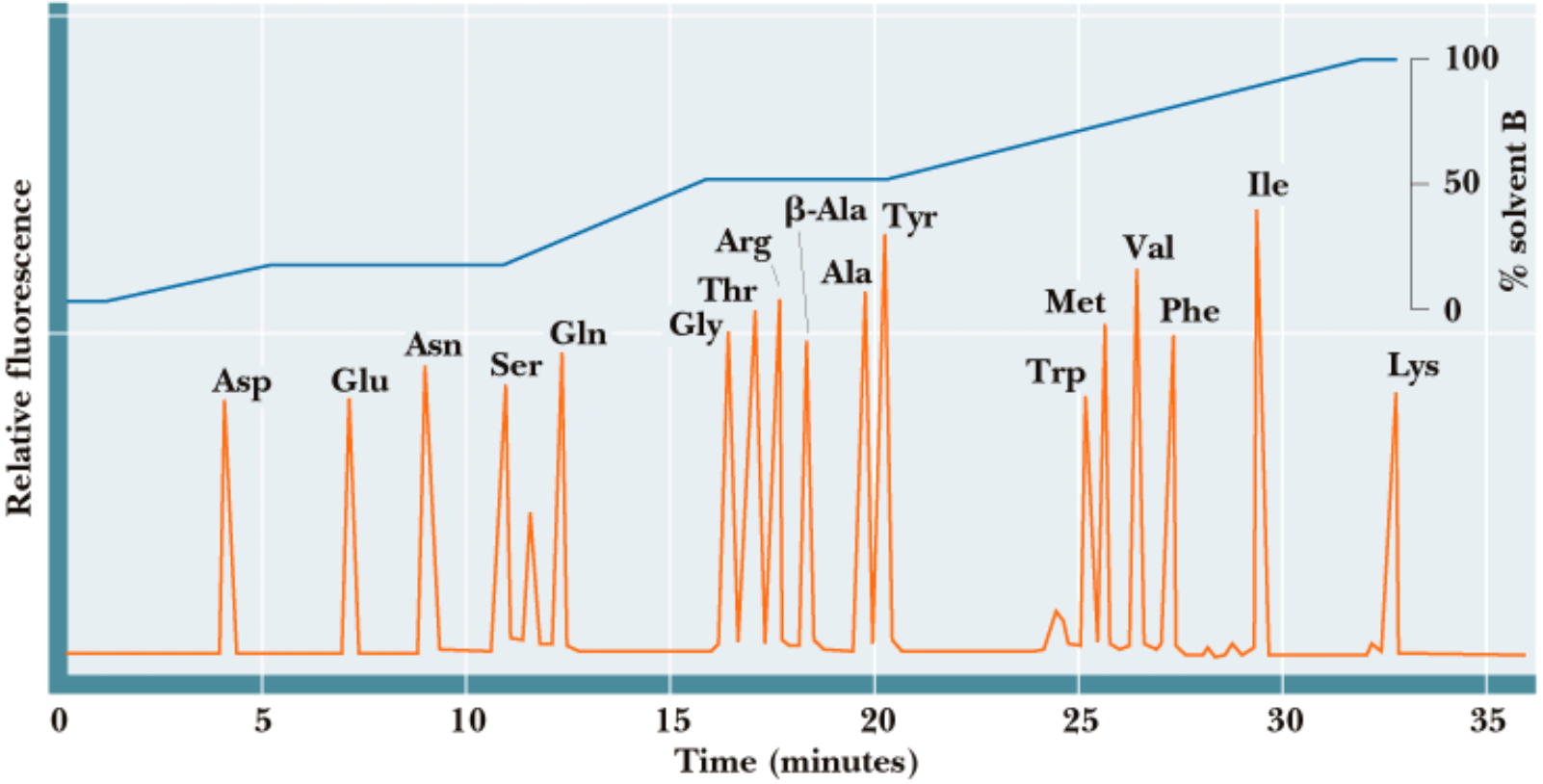
Figure 6.5

(a) Cation Exchange Media	Structure
Strongly acidic, polystyrene resin (Dowex–50)	
Weakly acidic, carboxymethyl (CM) cellulose	
Weakly acidic, chelating, polystyrene resin (Chelex–100)	

(b) Anion Exchange Media	Structure
Strongly basic, polystyrene resin (Dowex–1)	
Weakly basic, diethylaminoethyl (DEAE) cellulose	

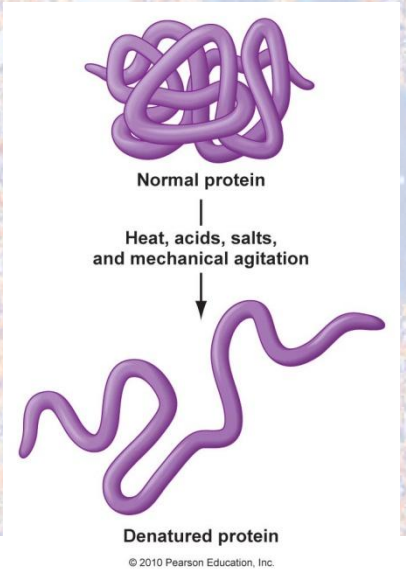

pH 3.25
0.2N Na citrate
pH 4.25
0.2N Na citrate
Amount of solute
0.30
0.25
0.20
0.15
0.10
0.05
Aspartic acid
Threonine
Serine
Glutamic acid
Proline
Glycine
Alanine
Cystine
Valine
Methionine
Isoleucine
Leucine
Tyrosine
Phenyl-alanine
0 25 50 75 100 125 150 175 200 225 250 275 300 325 350 375 400 425 450 475
Volume of eluant
pH 5.28
0.35N Na citrate
Amount of solute
0.30
0.25
0.20
0.15
0.10
0.05
Phenylalanine
Tyrosine
Lysine
Histidine
NH_4^+
Arginine
0 25 50 75 100 125
Volume of eluant

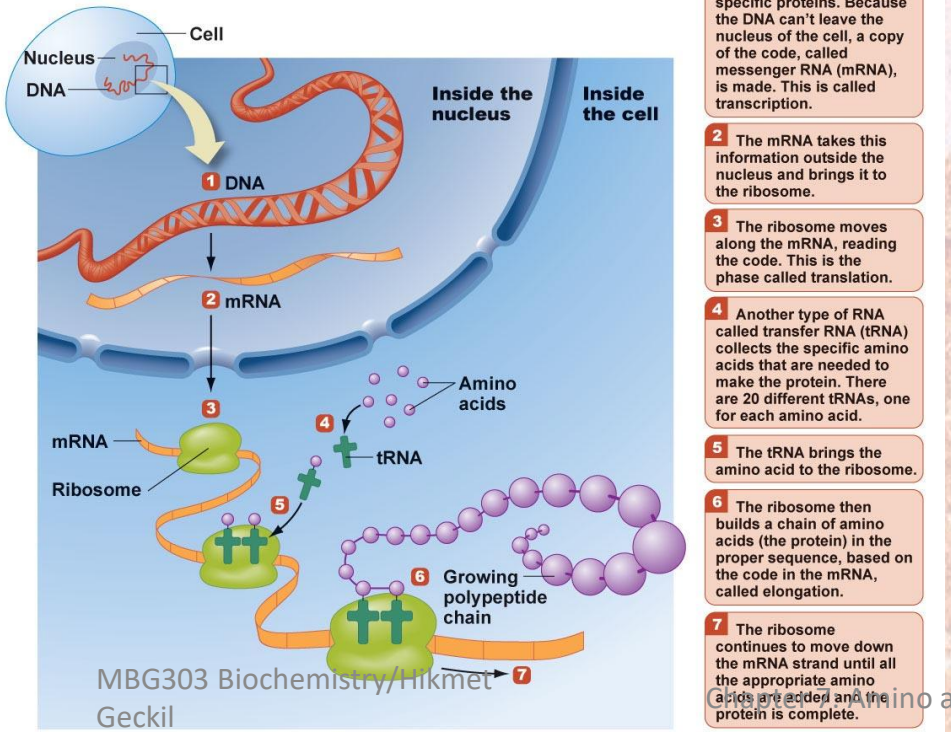
Garrett & Grisham: Biochemistry, 2/e
Figure 4.22

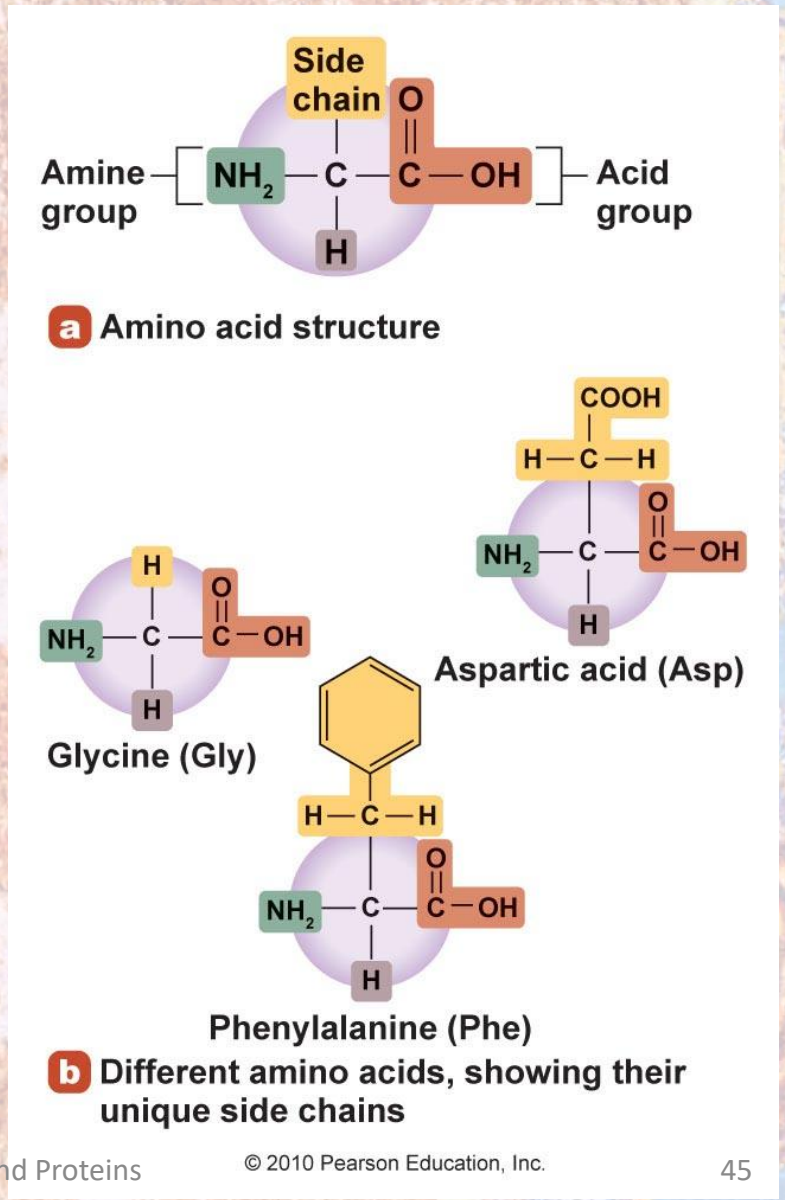


Saunders College Publishing

Proteins and Amino Acids





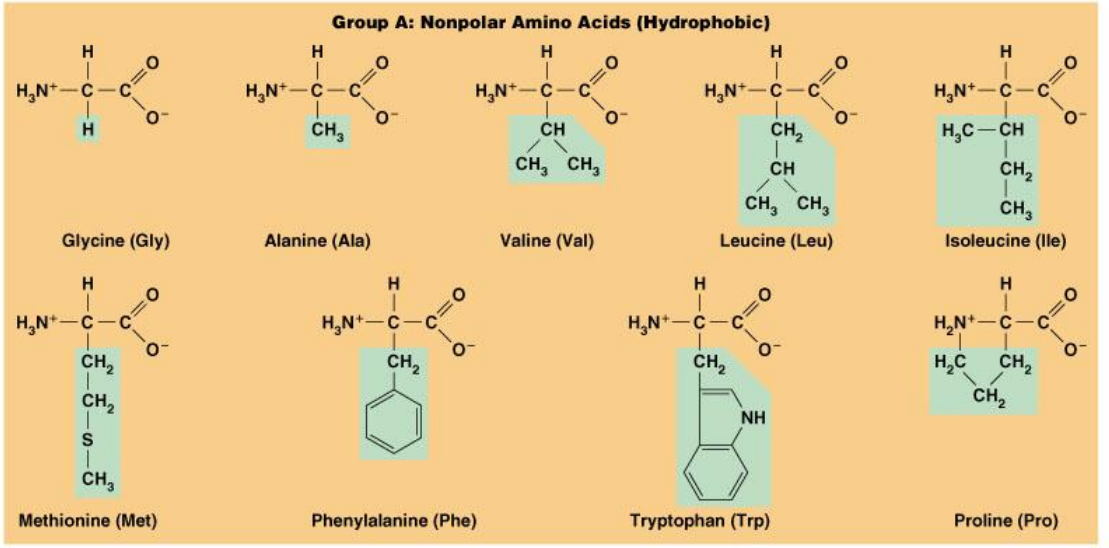


The structures of the 20 amino acids found in proteins

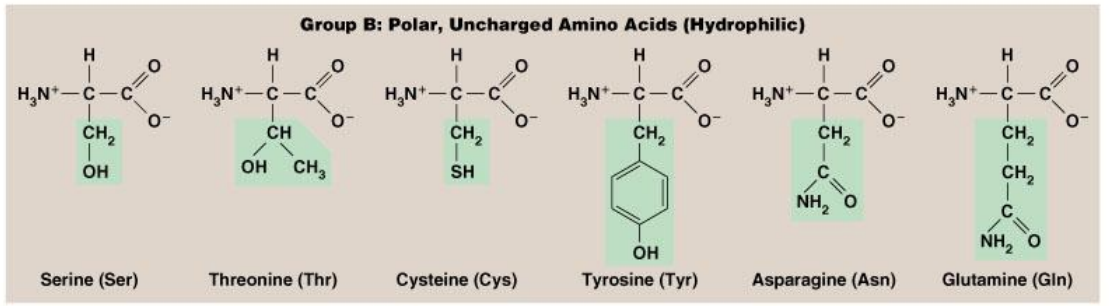
Table 3-2 Abbreviations for Amino Acids

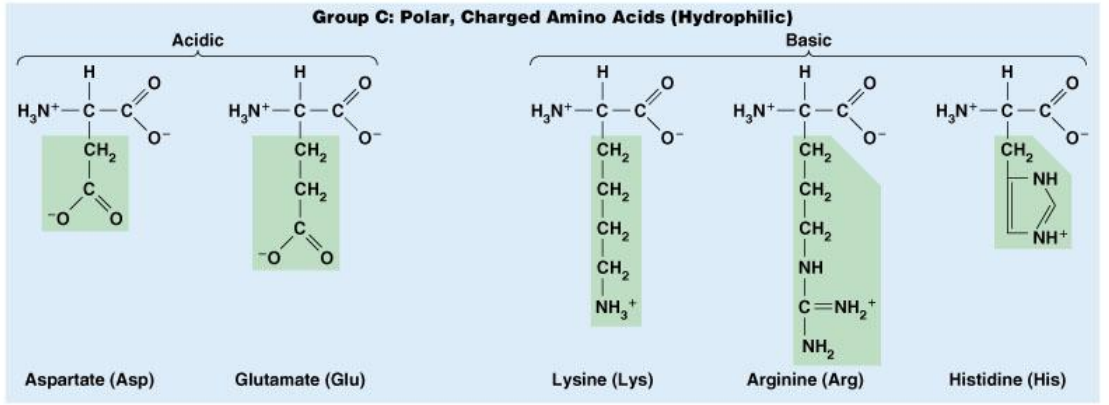
Amino Acid	Three-Letter Abbreviation	One-Letter Abbreviation
Alanine	Ala	A
Arginine	Arg	R
Asparagine	Asn	N
Aspartate	Asp	D
Cysteine	Cys	C
Glutamate	Glu	E
Glutamine	Gln	Q
Glycine	Gly	G
Histidine	His	H
Isoleucine	Ile	I
Leucine	Leu	L
Lysine	Lys	K
Methionine	Met	M
Phenylalanine	Phe	F
Proline	Pro	P
Serine	Ser	S
Threonine	Thr	T
Tryptophan	Trp	W
Tyrosine	Tyr	Y
Valine	Val	V

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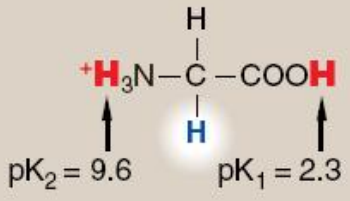
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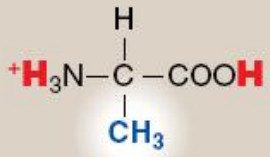


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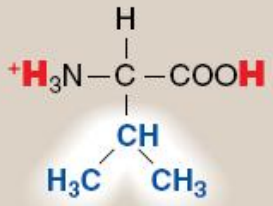
NONPOLAR SIDE CHAINS



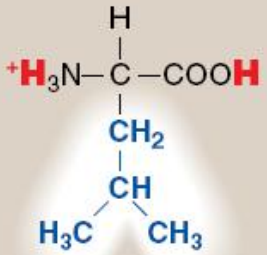
Glycine



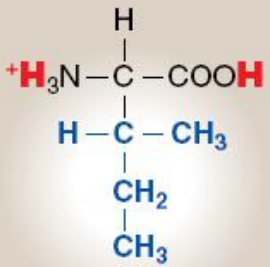
Alanine



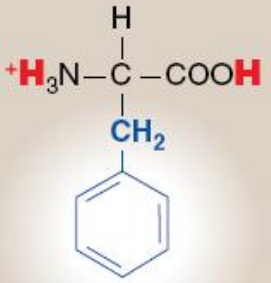
Valine



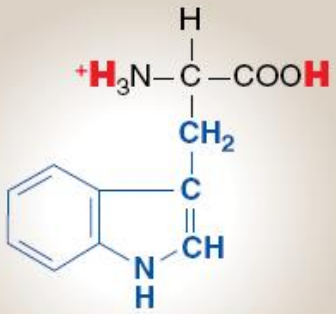
Leucine



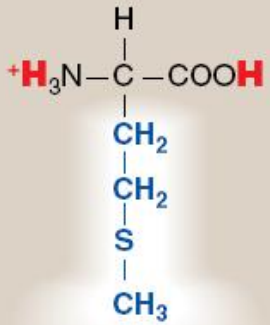
Isoleucine



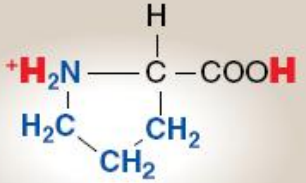
Phenylalanine



Tryptophan



Methionine



Proline

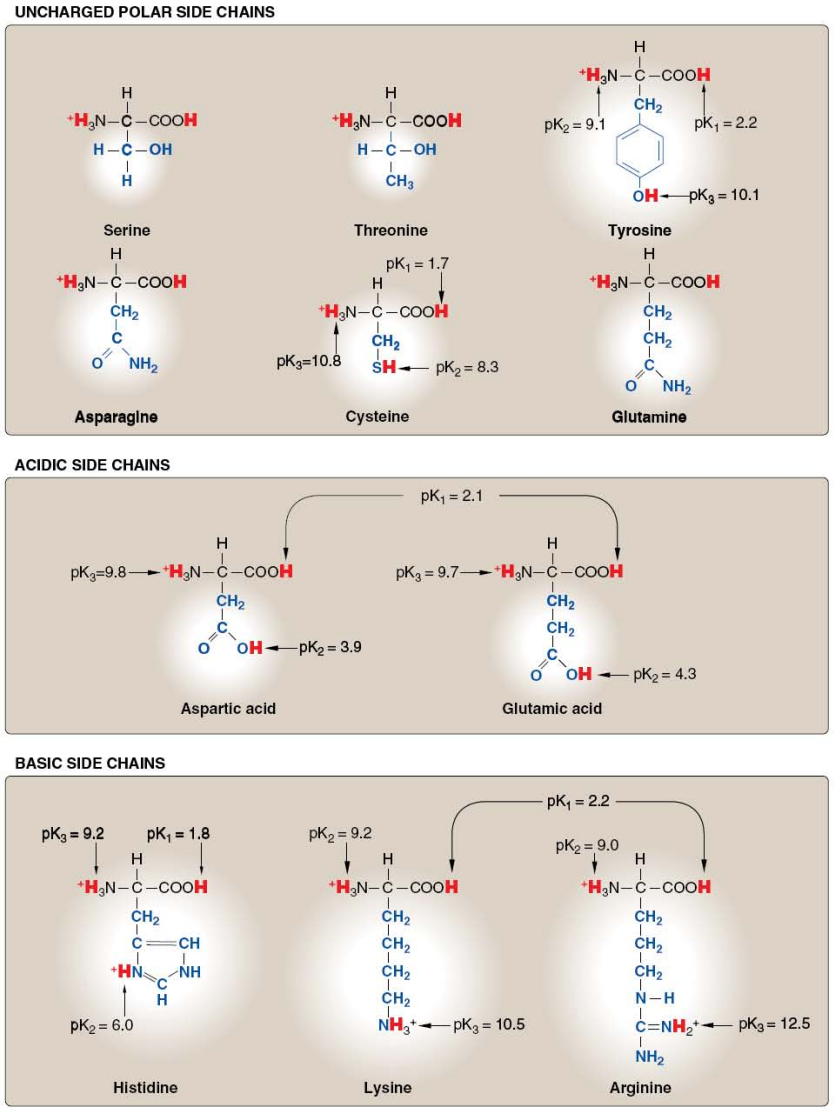
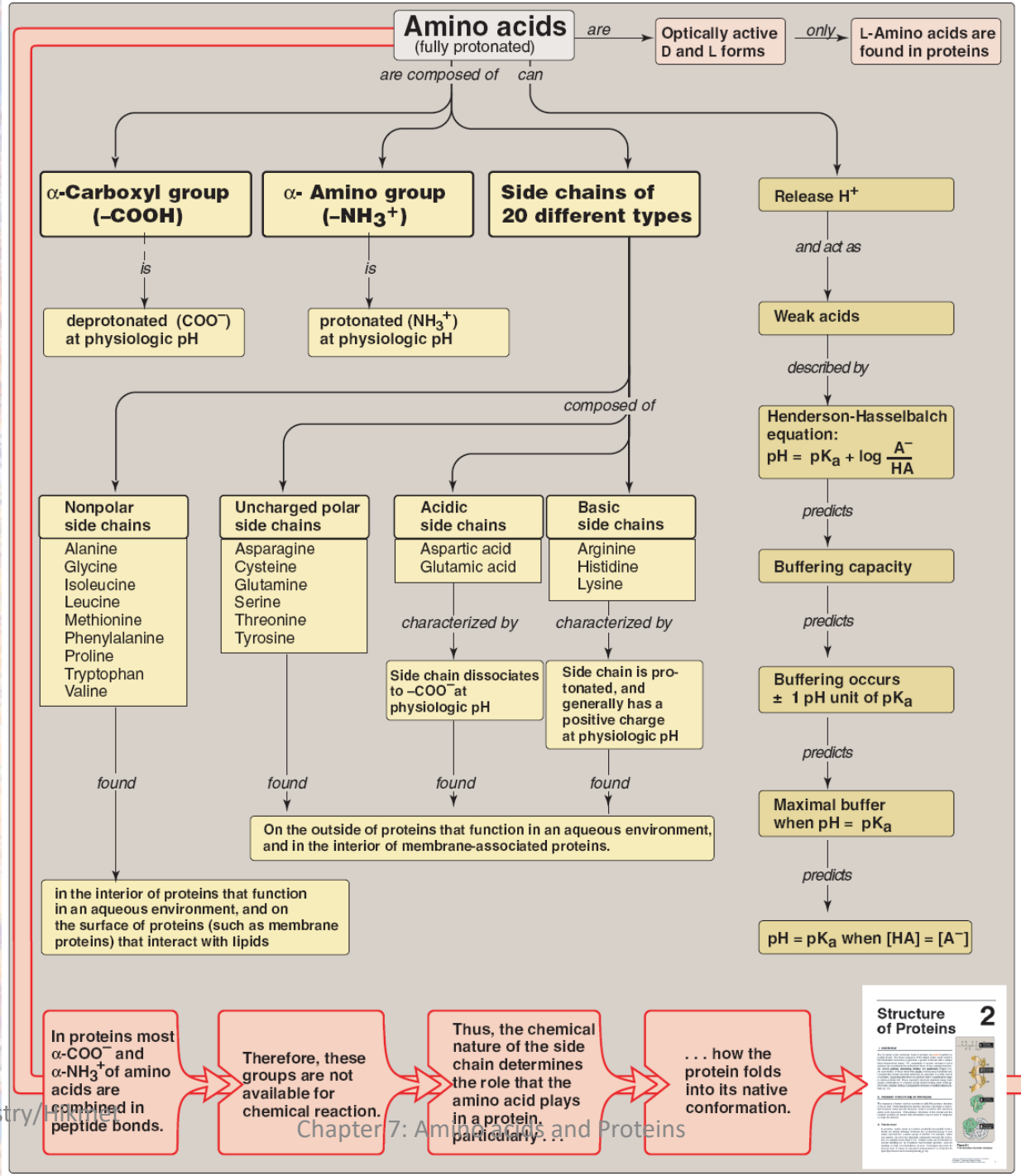
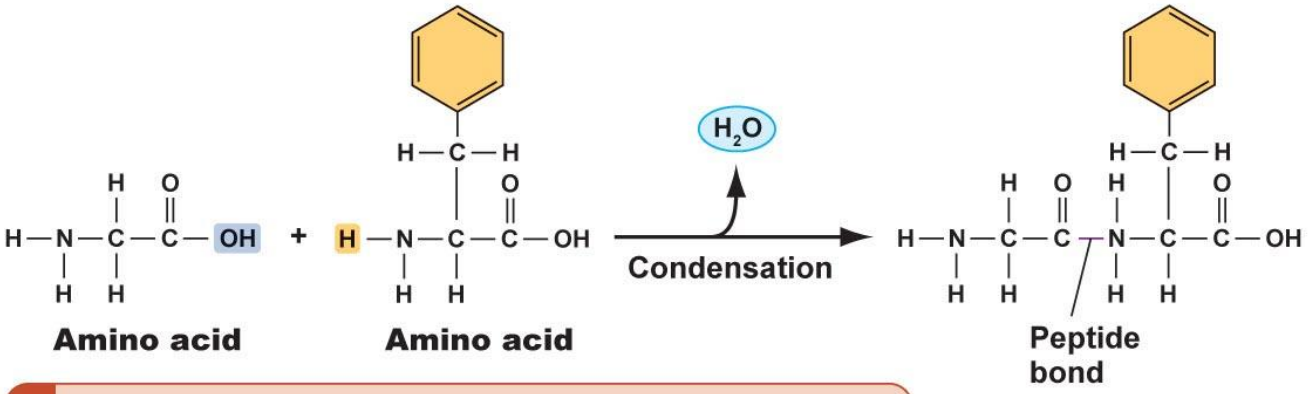


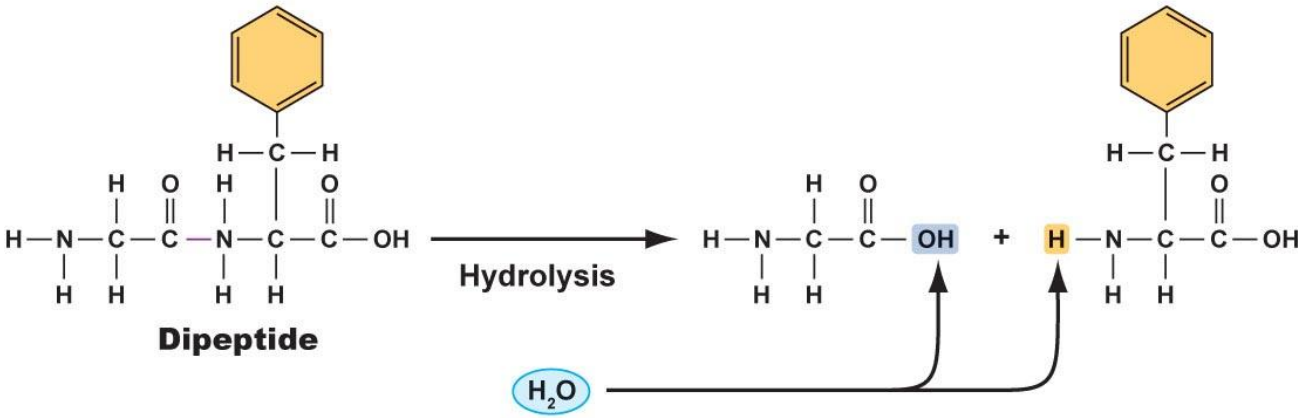
Figure 1.3
Classification of the twenty amino acids found in proteins according to the charge and polarity of their side chains (continued from Figure 1.2).


Amino acids
(fully protonated)
are
Optically active
D and L forms
only
L-Amino acids are
found in proteins
are composed of
can
α-Carboxyl group
(–COOH)
α- Amino group
(–NH3+)
Side chains of
20 different types
Release H+
and act as
Weak acids
described by
Henderson-Hasselbalch
equation:
pH = pKa + log A−/HA
predicts
Buffering capacity
predicts
Buffering occurs
± 1 pH unit of pKa
predicts
Maximal buffer
when pH = pKa
predicts
pH = pKa when [HA] = [A−]
is
deprotonated (COO−)
at physiologic pH
is
protonated (NH3+)
at physiologic pH
composed of
Nonpolar
side chains
Alanine
Glycine
Isoleucine
Leucine
Methionine
Phenylalanine
Proline
Tryptophan
Valine
Uncharged polar
side chains
Asparagine
Cysteine
Glutamine
Serine
Threonine
Tyrosine
Acidic
side chains
Aspartic acid
Glutamic acid
Basic
side chains
Arginine
Histidine
Lysine
characterized by
Side chain dissociates
to –COO− at
physiologic pH
characterized by
Side chain is pro-
tonated, and
generally has a
positive charge
at physiologic pH
found
found
found
found
On the outside of proteins that function in an aqueous environment,
and in the interior of membrane-associated proteins.
in the interior of proteins that function
in an aqueous environment, and on
the surface of proteins (such as membrane
proteins) that interact with lipids
In proteins most
α-COO− and
α-NH3+ of amino
acids are
combined in
peptide bonds.
Therefore, these
groups are not
available for
chemical reaction.
Thus, the chemical
nature of the side
chain determines
the role that the
amino acid plays
in a protein,
particularly . . .
. . . how the
protein folds
into its native
conformation.
Structure
of Proteins
2

Condensation and Hydrolytic Reactions



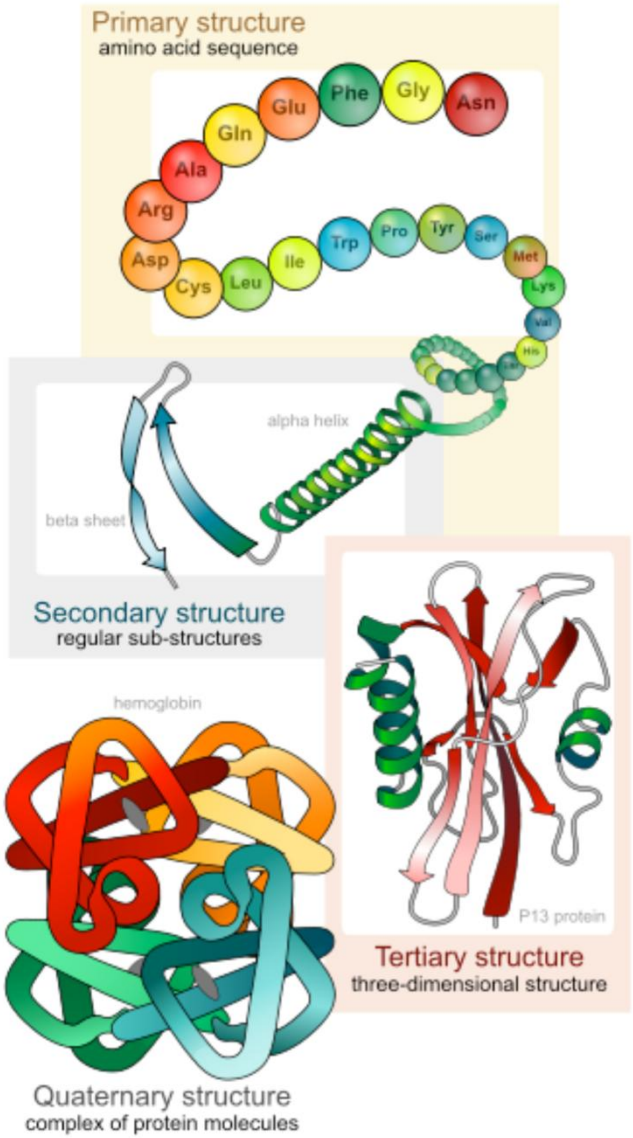
a A peptide bond forms by condensation when the acid group (COOH) and amine group of two different amino acids join and release a molecule of water.



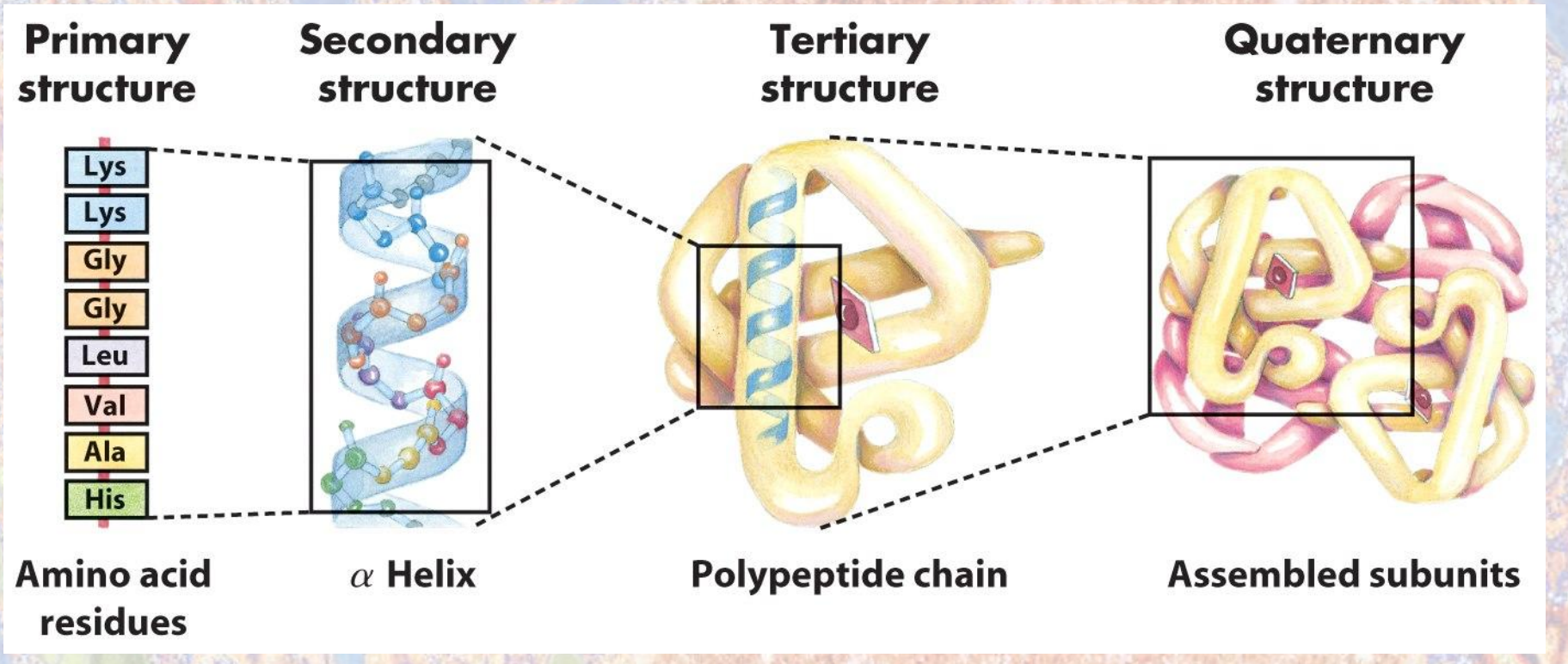
b When peptide bonds are broken by hydrolysis, the hydroxyl group (OH) and hydrogen (H) from water are added.

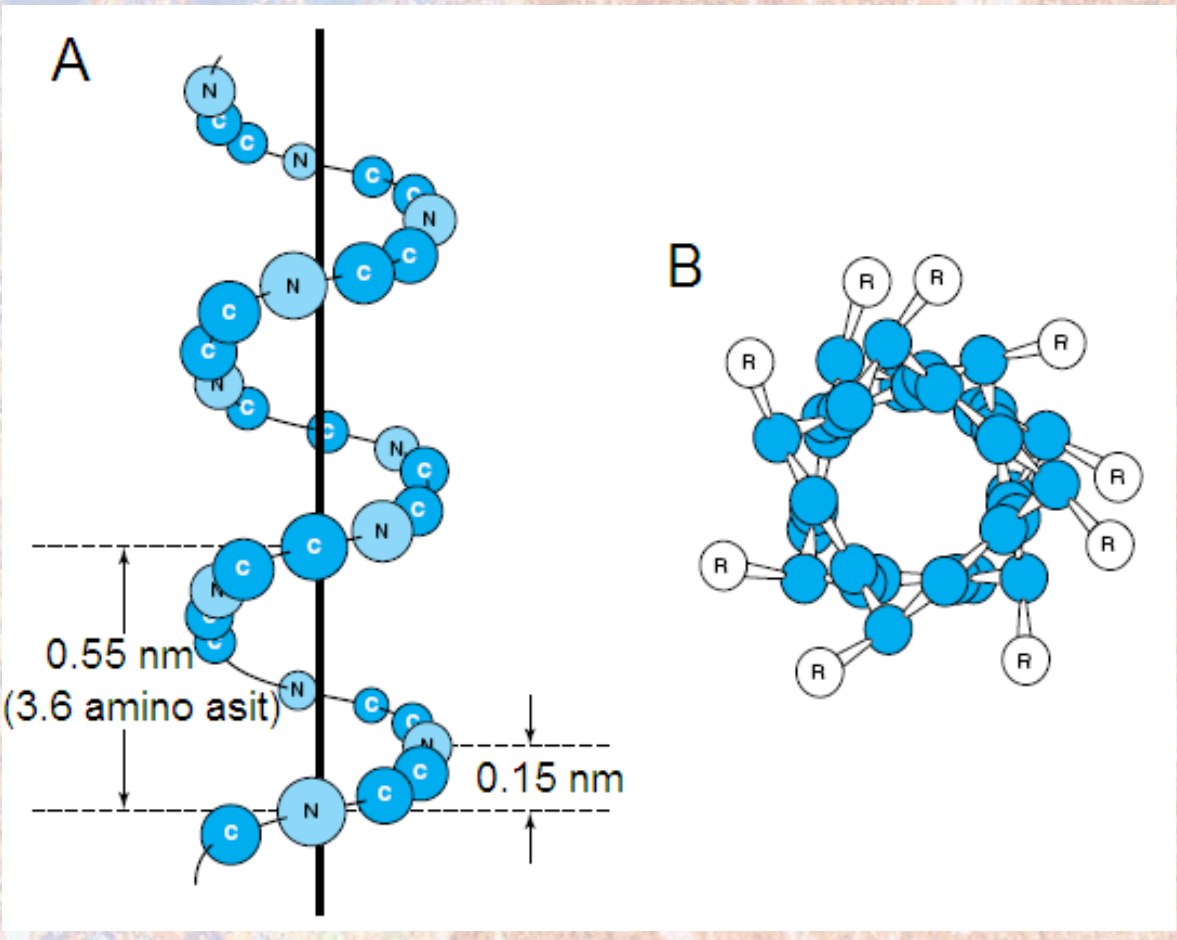
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Figure 1.52 Protein Structure



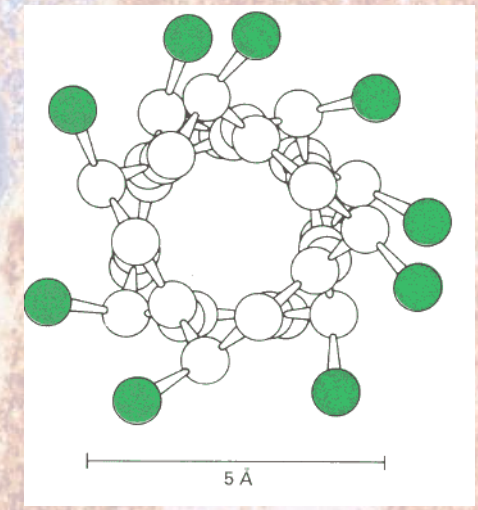
The primary structure of a protein is the linear chain of amino acids. The primary structure gives rise to the secondary structure, which then associates via side-chain interactions to create the tertiary and finally the quaternary structure of the protein.

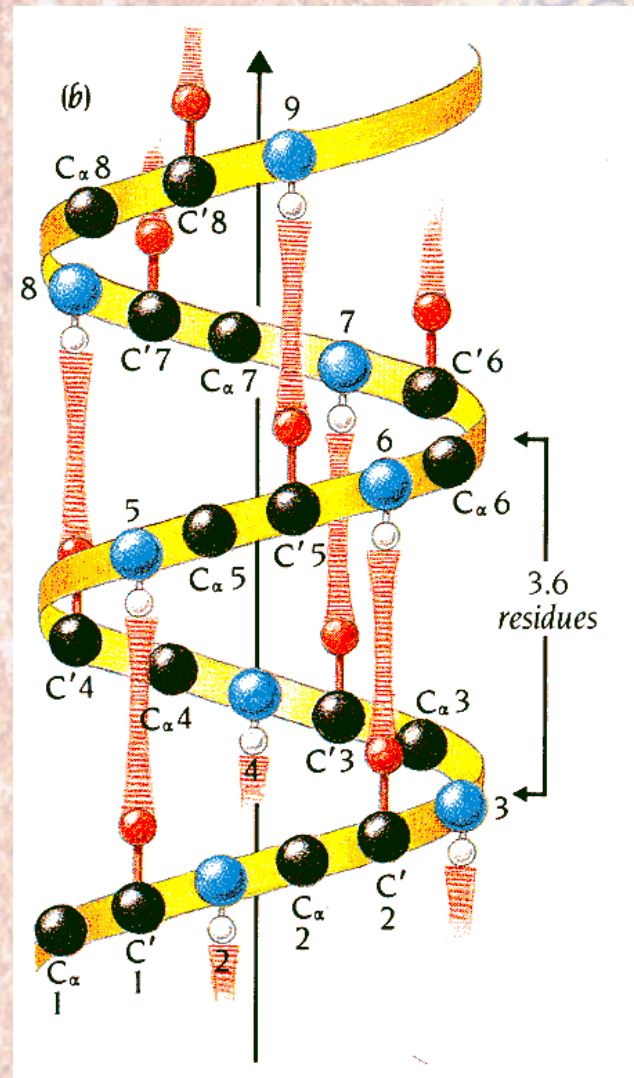

Primary structure
Secondary structure
Tertiary structure
Quaternary structure
Lys
Lys
Gly
Gly
Leu
Val
Ala
His
Amino acid residues
α Helix
Polypeptide chain
Assembled subunits


A
B
0.55 nm
(3.6 amino asit)
0.15 nm

Properties of the alpha helix

- <u>Hydrogen bonds</u> between C=O of residue *n*, and NH of residue *n*+4
- 3.6 residues/turn
- 1.5 Å/residue rise

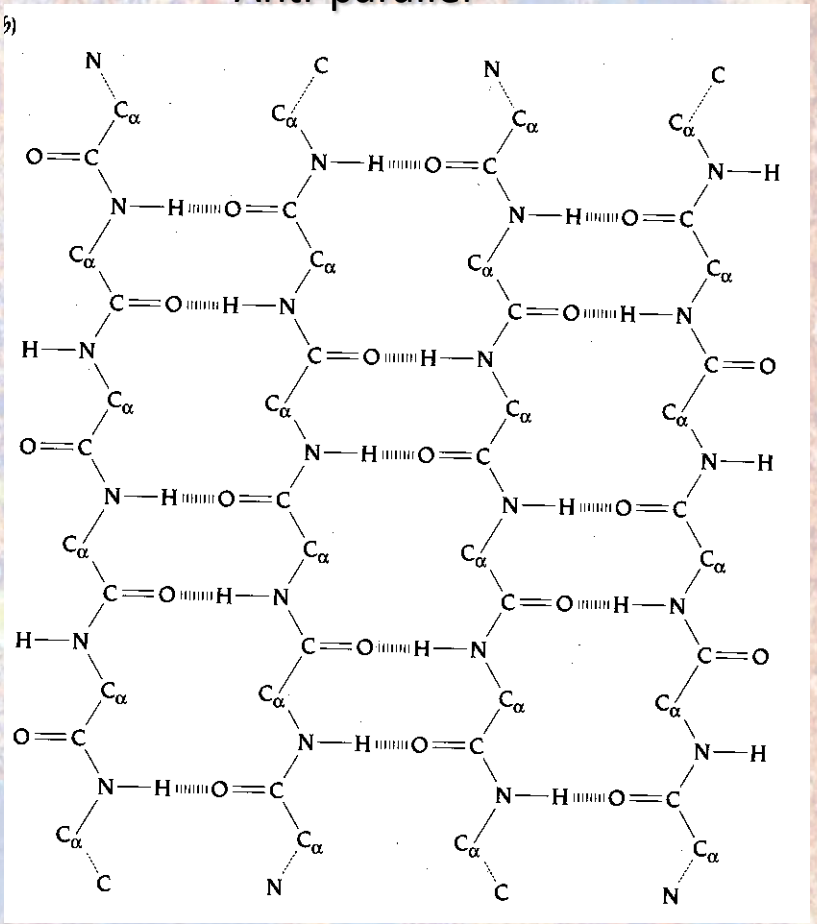




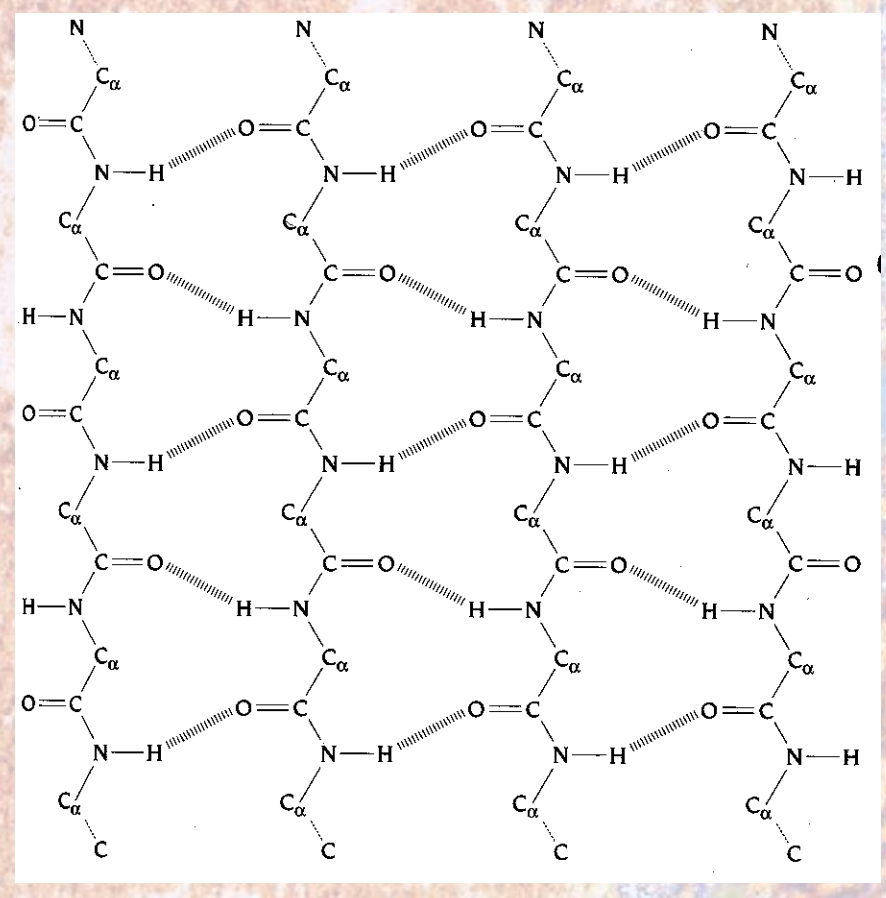
Parallel and anti-parallel β-sheets

- Anti-parallel is slightly energetically favored

Anti-parallel

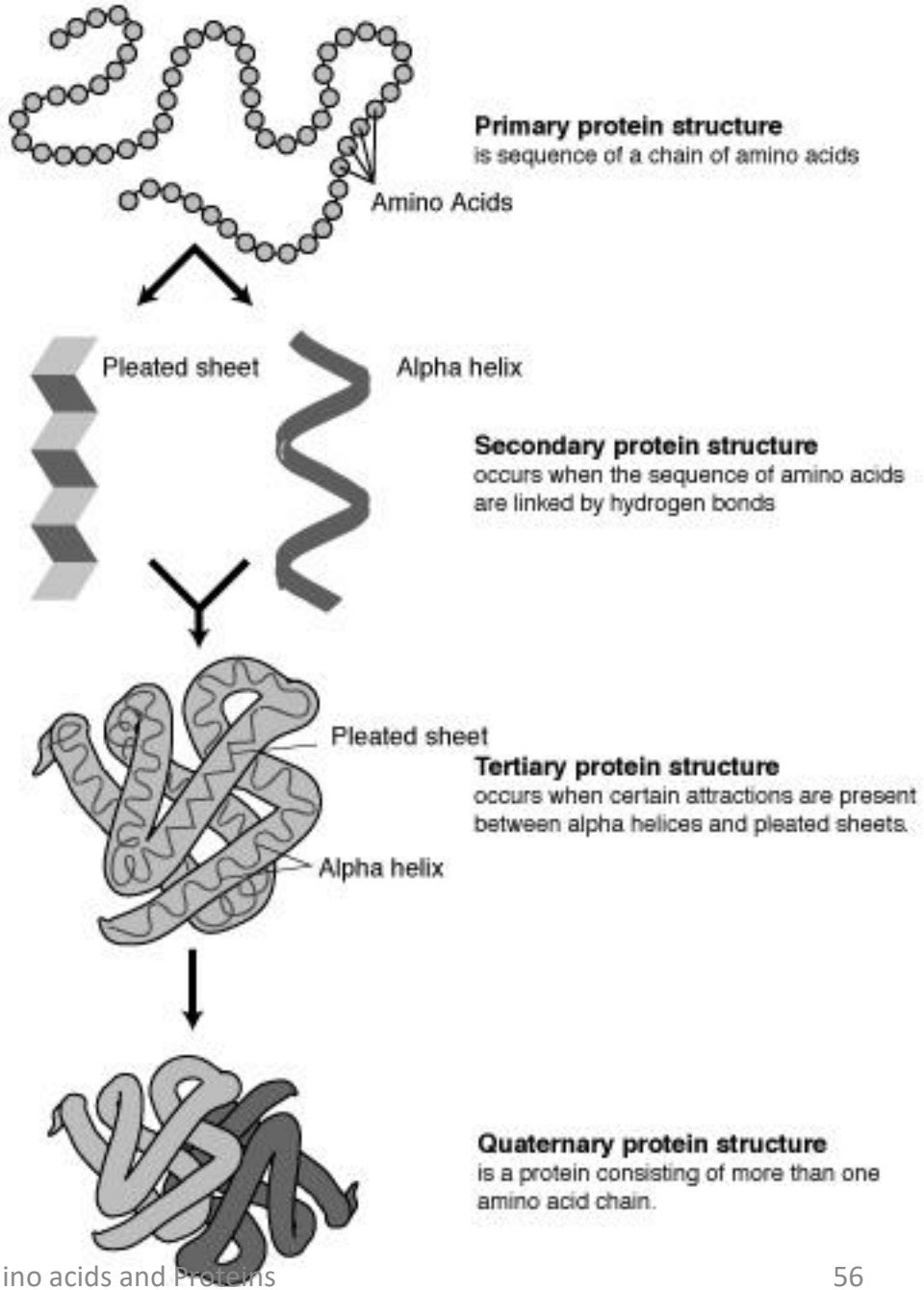


Parallel

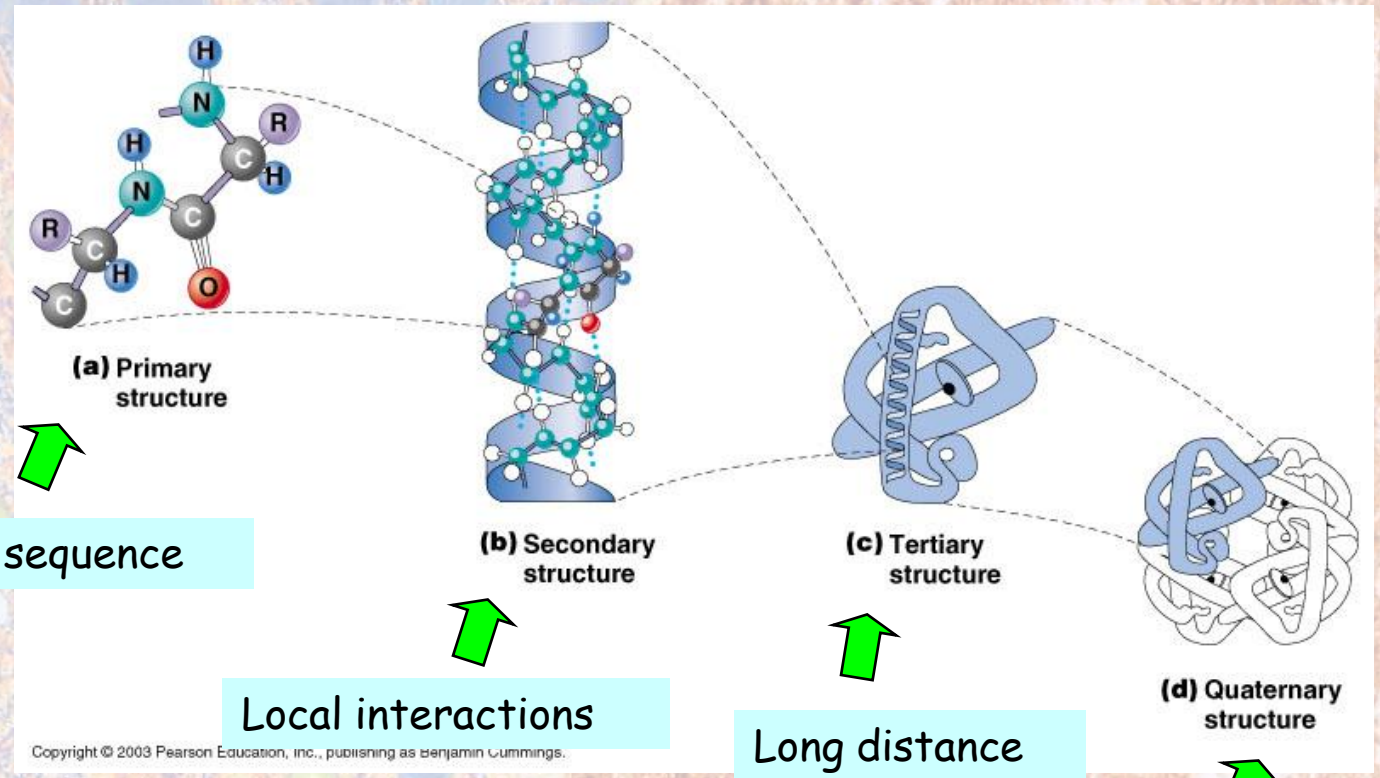


Levels of Protein Structure

- Secondary structure elements combine to form tertiary structure
- Quaternary structure occurs in multienzyme complexes
  - Many proteins are active only as homodimers, homotetramers, etc.



Protein structure depends on amino acid sequence and interactions

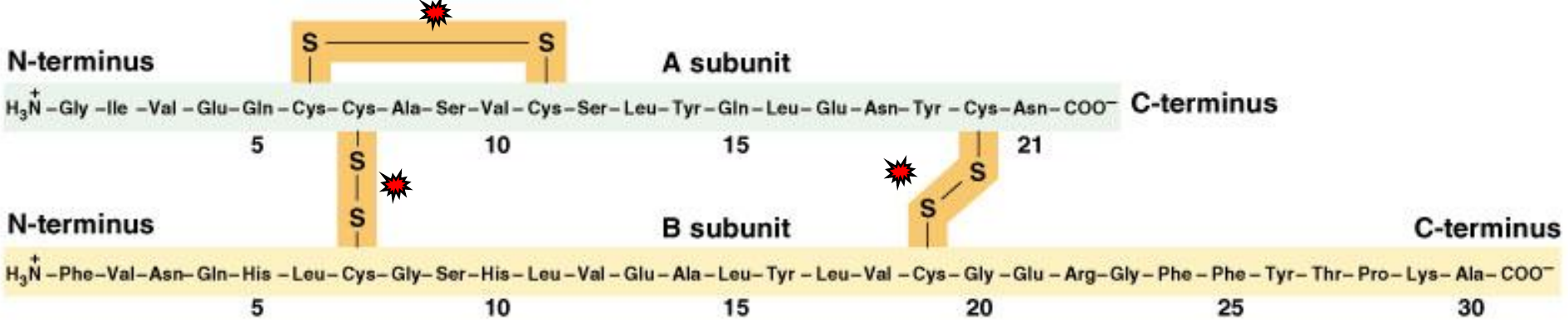


Amino acid sequence

Local interactions

Long distance interactions

Interactions between subunits



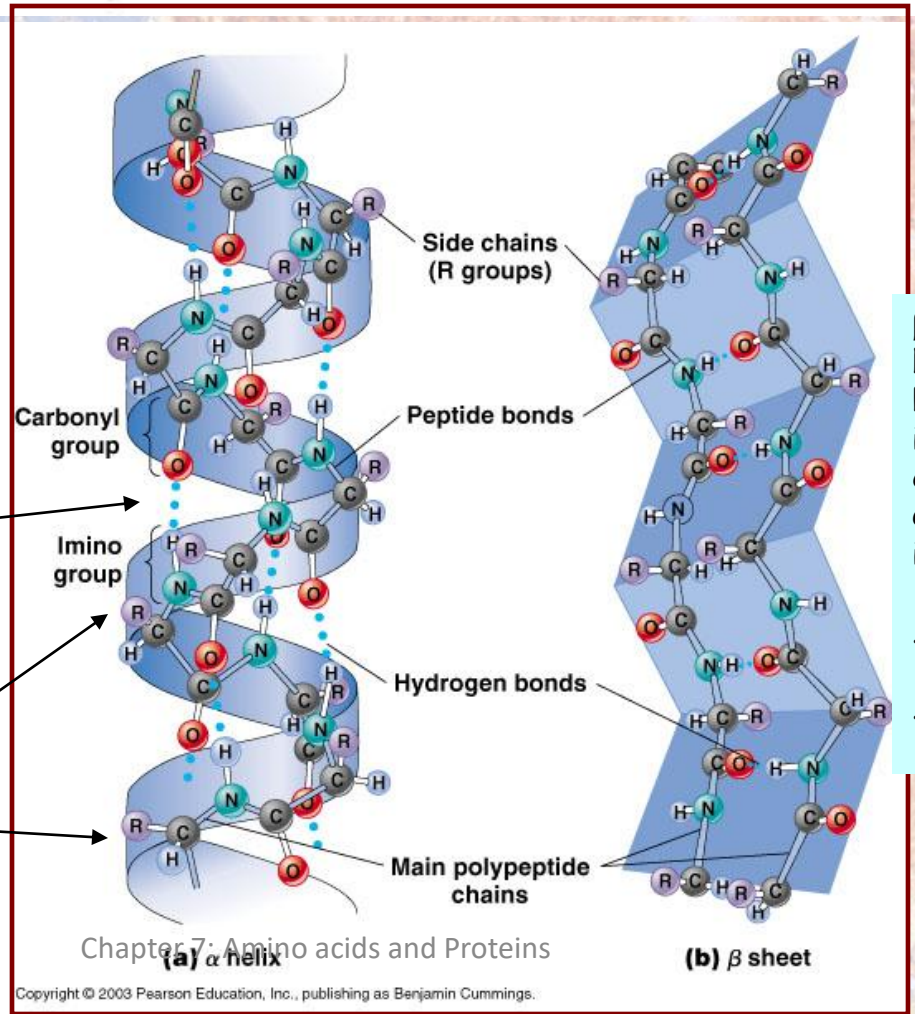
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The primary structure (a.a. sequence determines all higher level structures)

The secondary structure: repetitive patterns of local structure.

αhelix: 3.6 a.a., every peptide is hydrogen bonded between imino group (-NH-) of the 1sr a.a. and the carbonyl (-CO) group of the 4th a.a.

R groups jutting out from the backbone



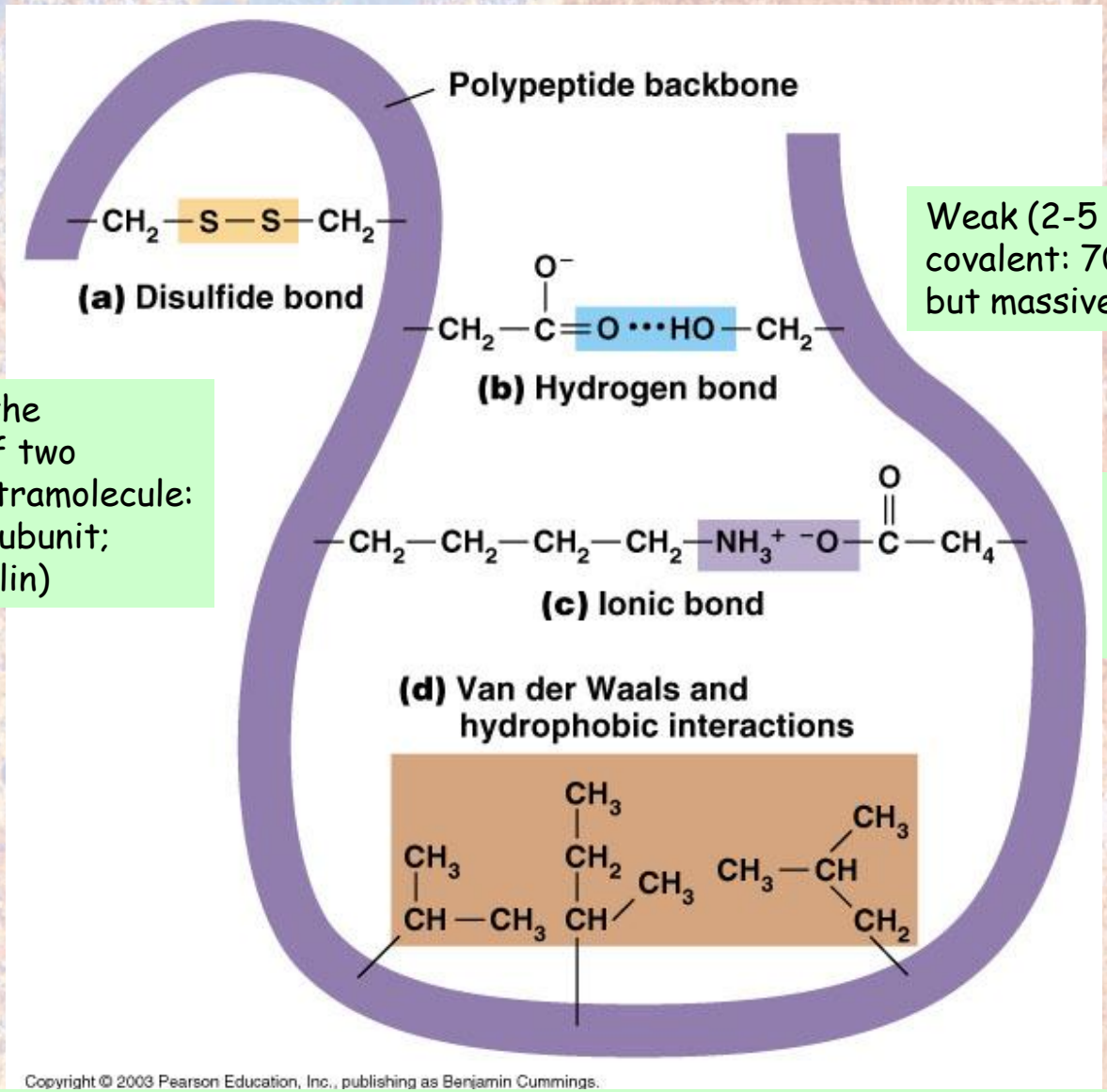
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β sheet: again form by hydrogen bonds between neighboring imino group and carbonyl group; can be either intra- or intermolecular.

. Parallel β sheet

. Anti-parallel β sheet

Important bonds for protein folding and stability



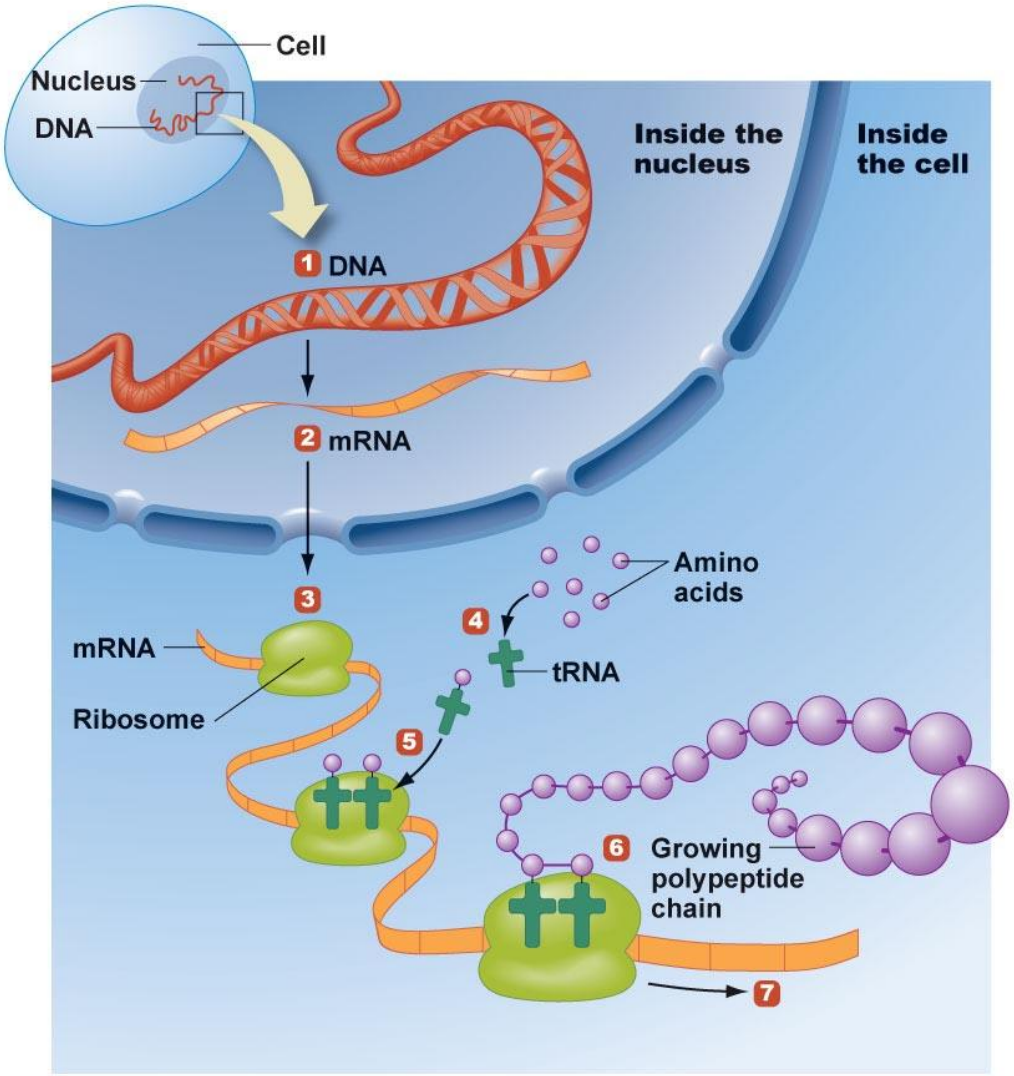
Weak (2-5 kcal/mol vs. covalent: 70-100 kcal/mol), but massive

The oxidization of the sulfhydryl groups of two cystein residues (intramolecule: ribonuclease; intersubunit; dimeric protein insulin)

Weak (3 kcal/mol), affected by pH value

Dipole molecules attract each other by van der Waals force (transient and weak: 0.1-0.2 kcal/mol)
Hydrophobic interaction, a tendency of hydrophobic groups or molecules being excluded from interact with hydrophilic environment

Protein Synthesis



1 Each strand of DNA holds the code to create specific proteins. Because the DNA can't leave the nucleus of the cell, a copy of the code, called messenger RNA (mRNA), is made. This is called transcription.

2 The mRNA takes this information outside the nucleus and brings it to the ribosome.

3 The ribosome moves along the mRNA, reading the code. This is the phase called translation.

4 Another type of RNA called transfer RNA (tRNA) collects the specific amino acids that are needed to make the protein. There are 20 different tRNAs, one for each amino acid.

5 The tRNA brings the amino acid to the ribosome.

6 The ribosome then builds a chain of amino acids (the protein) in the proper sequence, based on the code in the mRNA, called elongation.

7 The ribosome continues to move down the mRNA strand until all the appropriate amino acids are added and the protein is complete.

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Figure 6.8

Metabolic Fate of Amino Acids

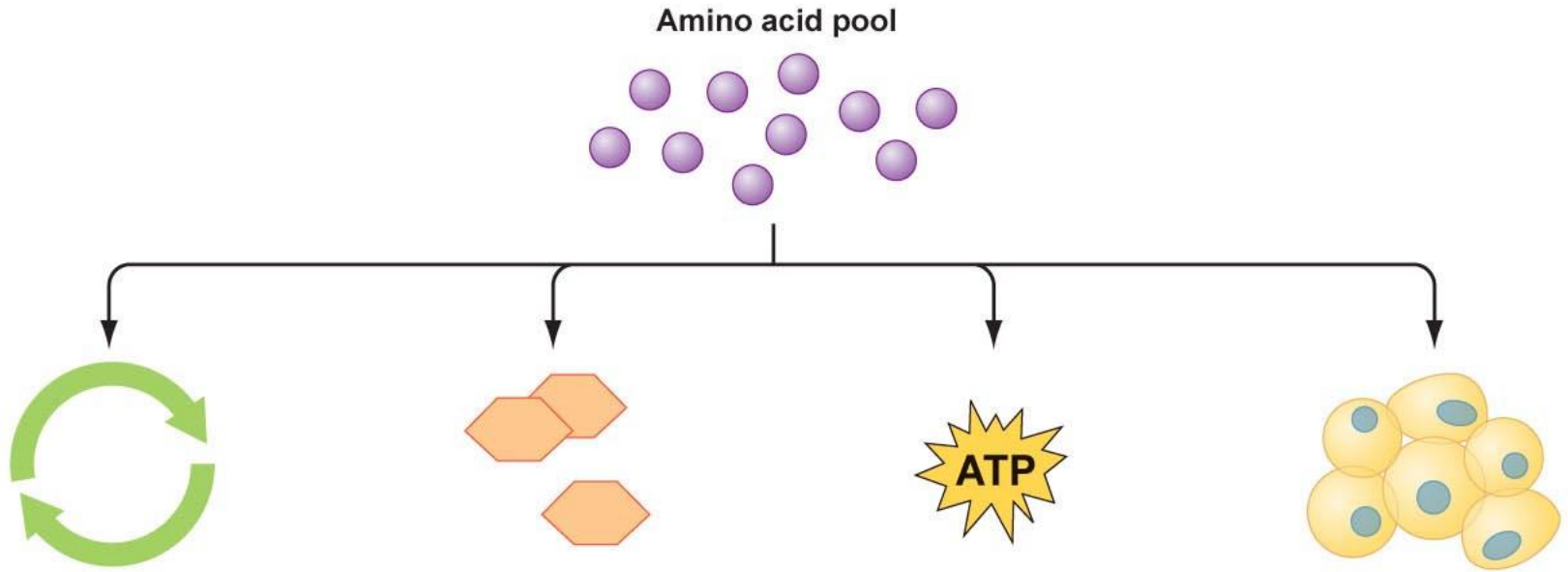


Figure 6.7



MBG303 Biochemistry

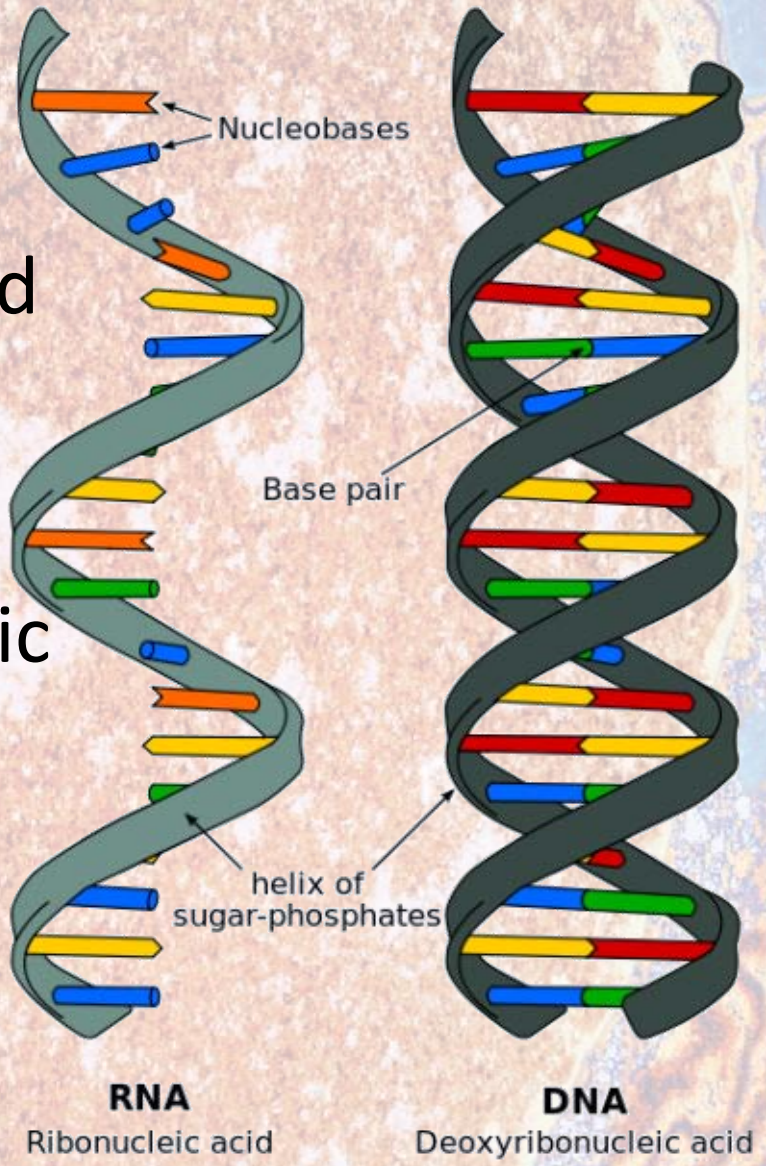
Chapter 8: Nucleic Acids

Hikmet Geçkil, Professor
Department of Molecular Biology and Genetics
Inonu University

Nucleic acids

- Nucleic acids are large biomolecules (indeed the largest)

- Two general type of nucleic acids:
  1. DNA(deoxyribonucleic acid)
  2. RNA (ribonucleic acid)

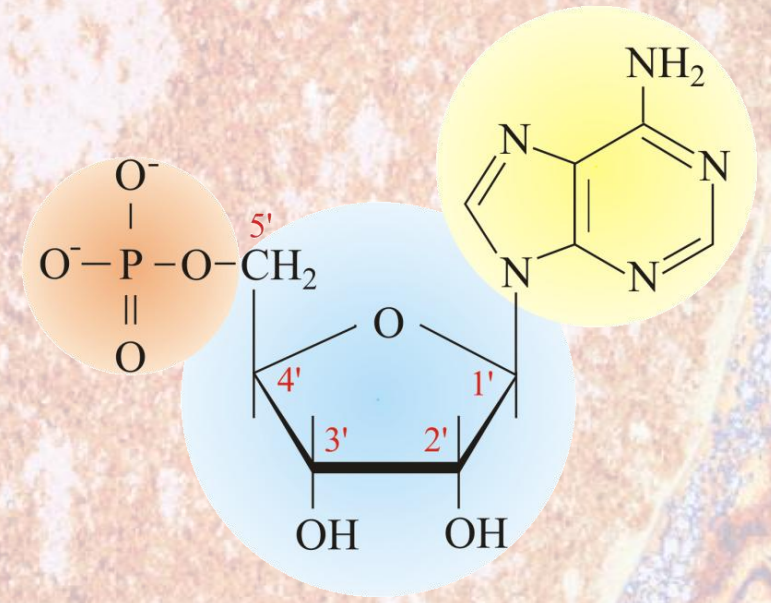


Nucleotides: The Building Blocks of Nucleic Acids

- Nucleic acids are biopolymers made from nucleotide monomers.

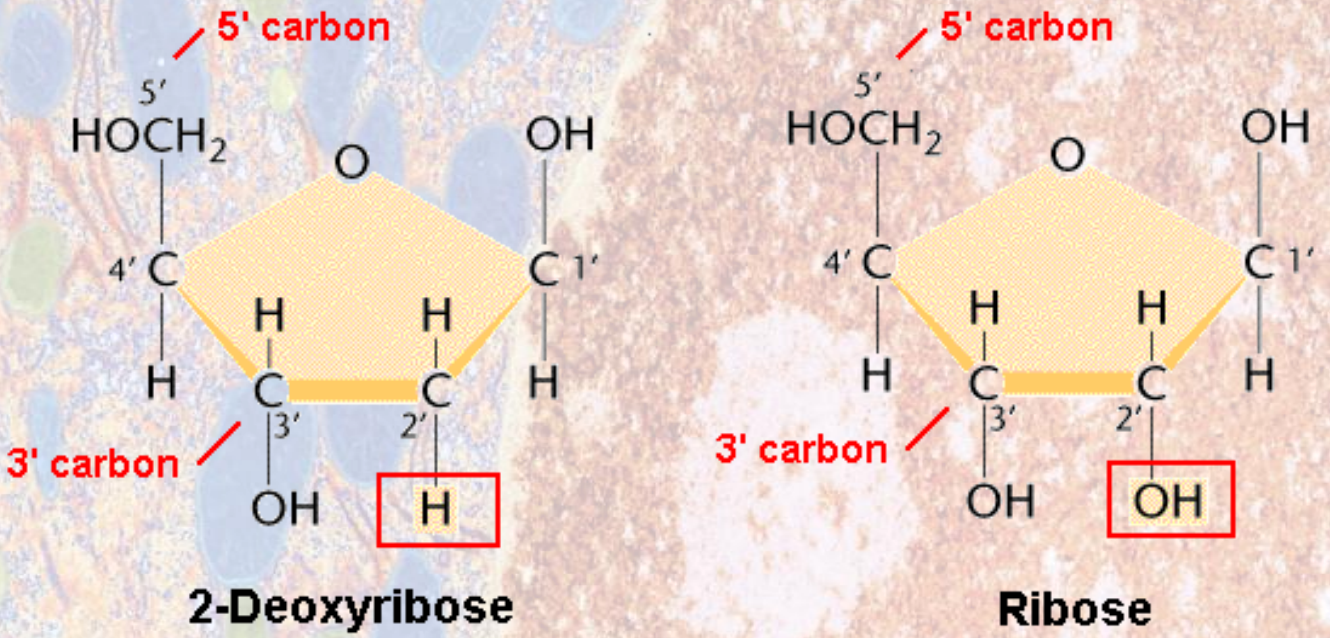
- Each nucleotide has three components:
  1. a 5-carbon sugar
  2. a phosphate group
  3. a nitrogenous base

     (Amine bases)



e.g., AMP (Adenosine monophosphate)

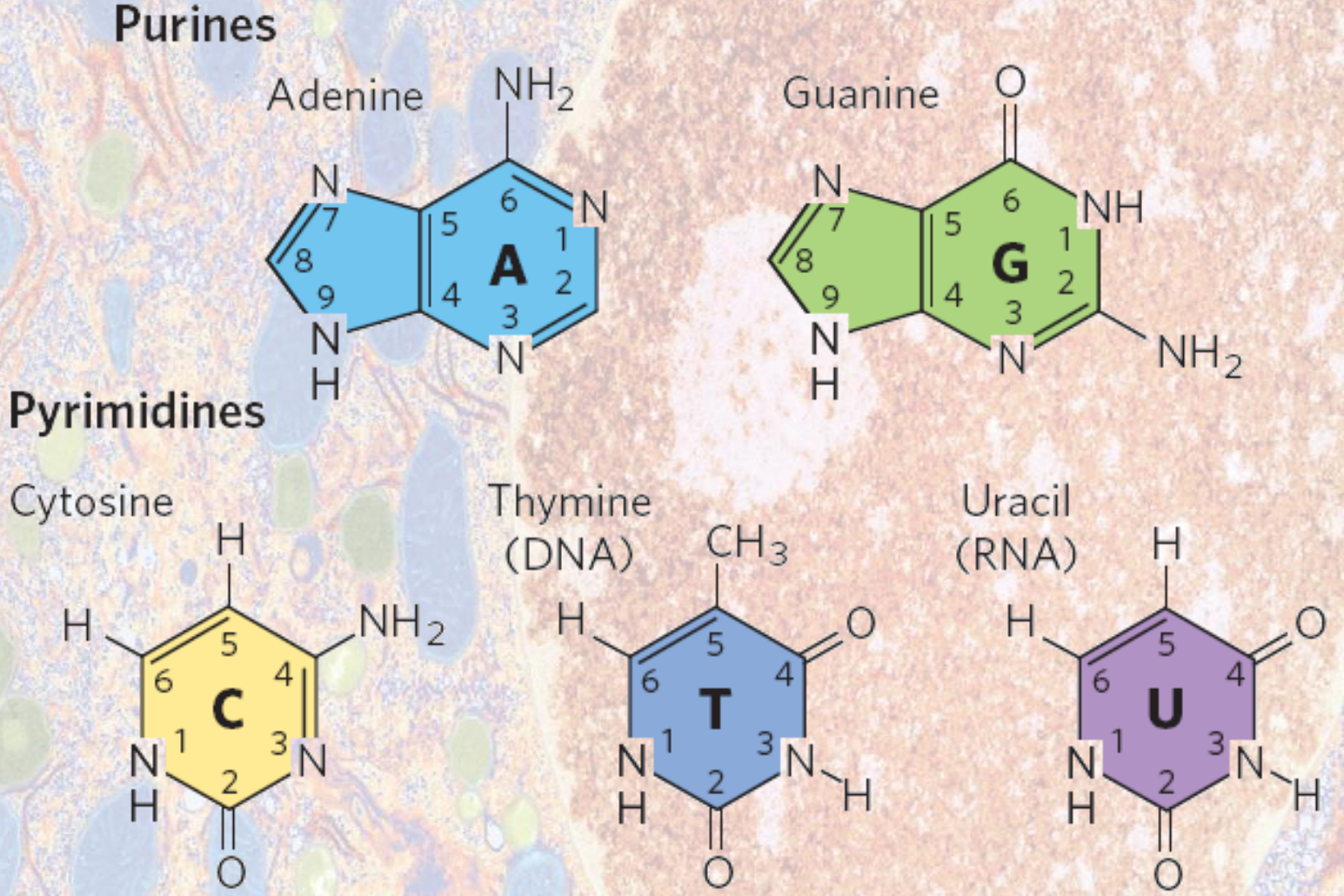
A 5-Carbon Sugar

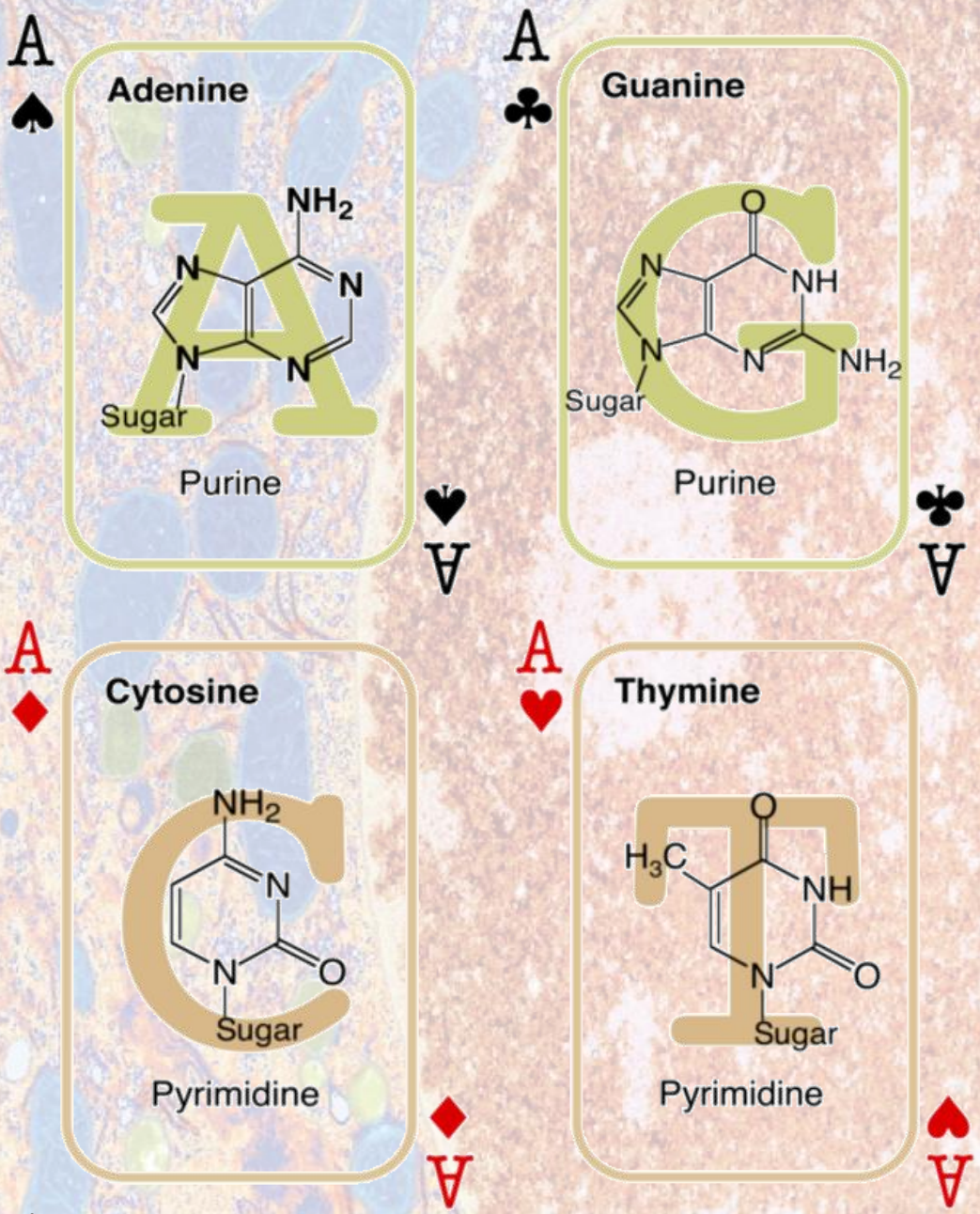


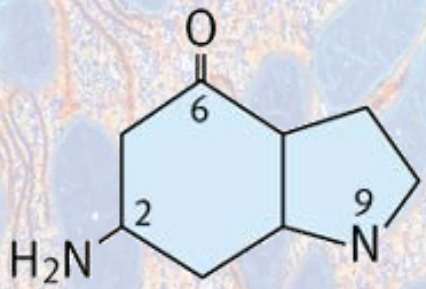
- Ribose in RNA, deoxyribose in DNA

Nitrogenous Bases

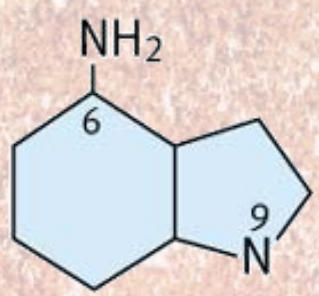
The nitrogenous bases are planar, aromatic, heterocyclic molecules which are derivatives of either **purine** or **pyrimidine.**



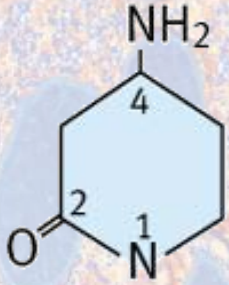

A
Adenine
NH2
N
N
N
N
Sugar
Purine
A
A
Guanine
O
NH
N
N
N
NH2
Sugar
Purine
A
A
Cytosine
NH2
N
N
O
Sugar
Pyrimidine
A
A
Thymine
O
H3C
NH
N
O
Sugar
Pyrimidine
A



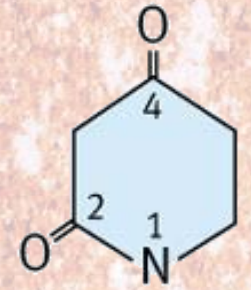
Guanine; 2-amino-6-oxypurine



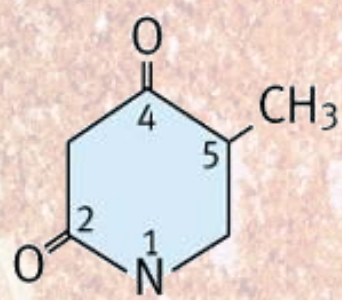
Adenine; 6-aminopurine



Cytosine; 2-oxy-4-aminopyrimidine

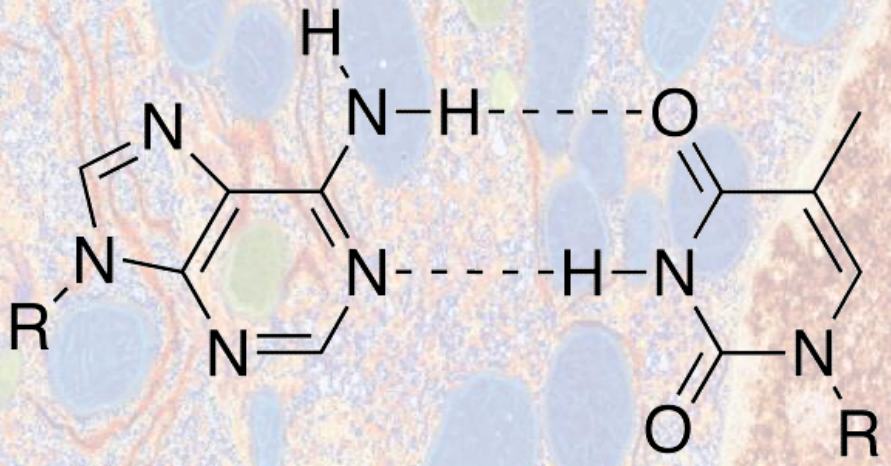


Uracil; 2,4-dioxypyrimidine

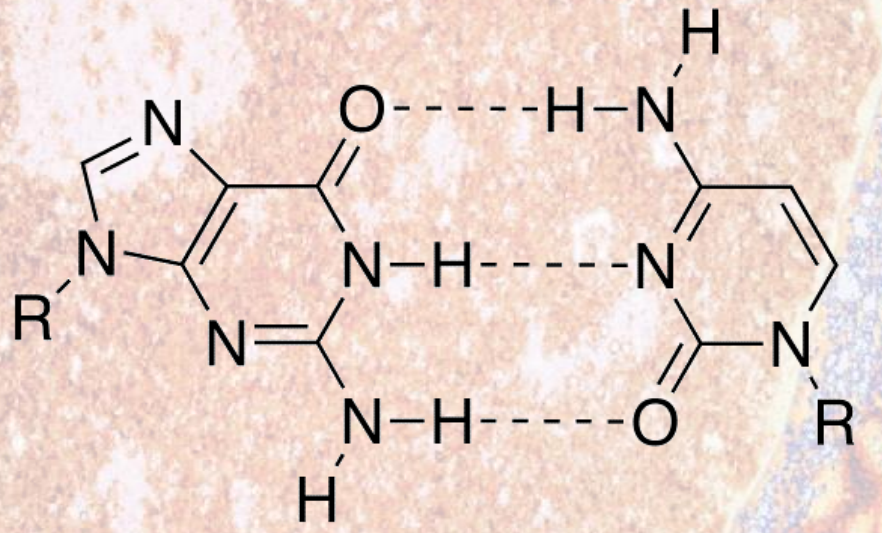


Thymine; 2,4-dioxy-5-methylpyrimidine

Base pairing with H-bonds



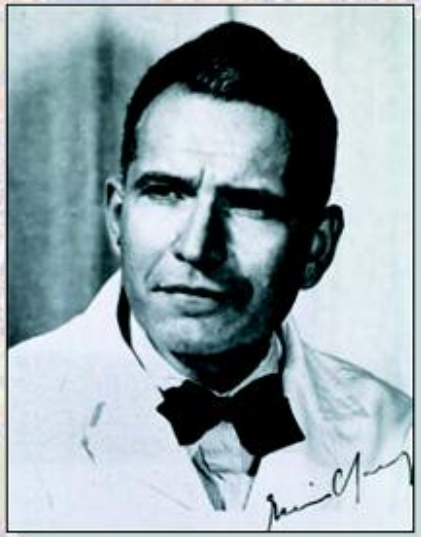
Adenine Thymine



Guanine Cytosine

Erwin Chargaff's Work Provided a Clue to Base Pairing

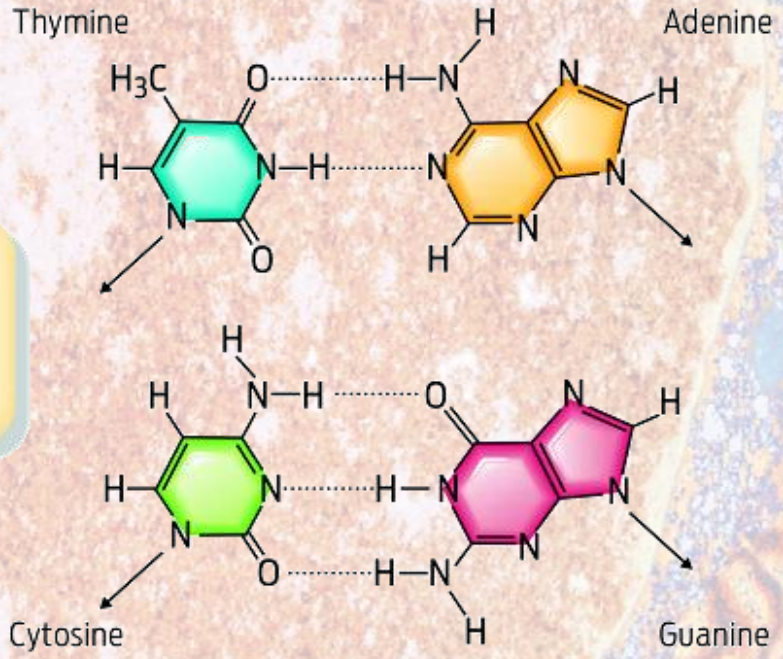
Erwin Chargaff studied the nitrogenous bases of DNA. He found that no matter which DNA molecule he analyzed, it always contained equal amounts of adenine and thymine bases and equal amounts of cytosine and guanine bases. These data suggested that adenine must pair with thymine and that cytosine must pair with guanine. This base pairing further supported the idea of a double-stranded DNA structure.



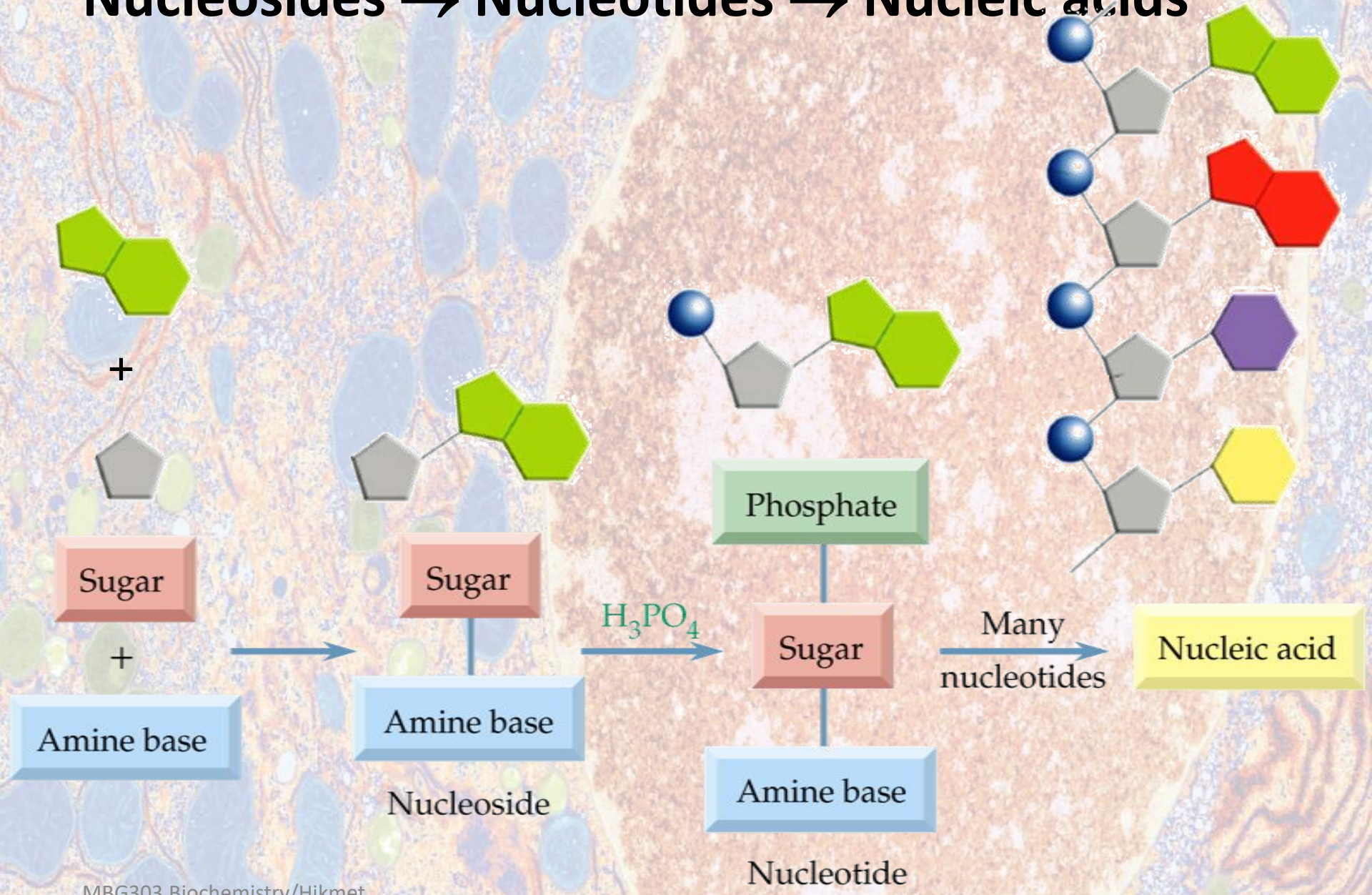
Erwin Chargaff
August 11, 1905–June 20, 2002

Within any DNA molecule:
% adenine = % thymine
% cytosine = % guanine

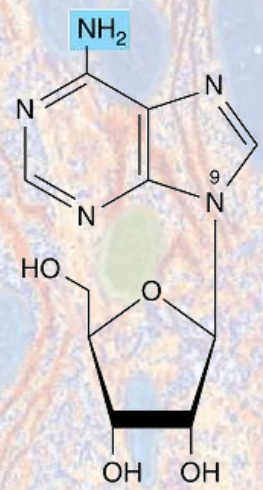
Chargaff's Rule of Base Pairing



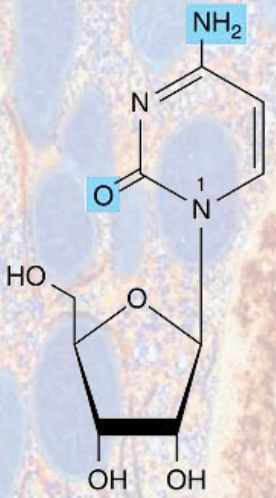
Nucleosides → Nucleotides → Nucleic acids



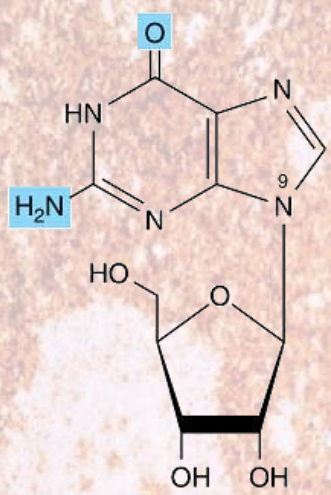
Ribonucleosides and Deoxyribonucleosides



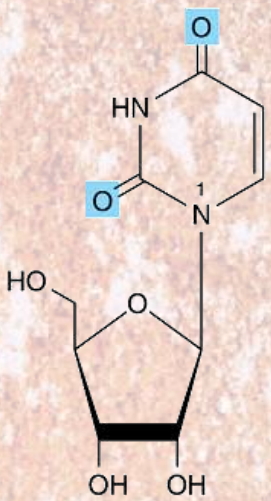
Adenosine



Cytidine

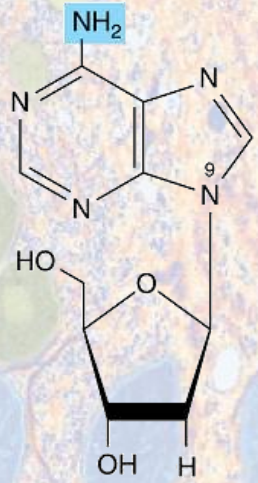


Guanosine

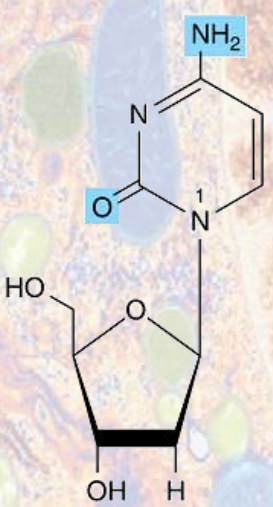


Uridine

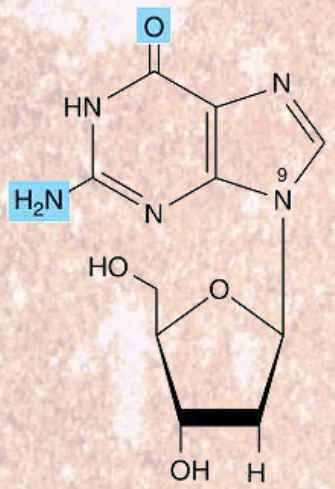
RNA



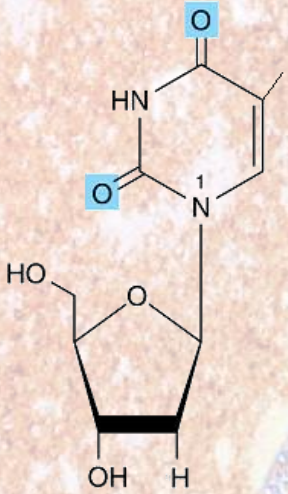
Deoxy-Adenosine



Deoxy-Cytidine



Deoxy-Guanosine

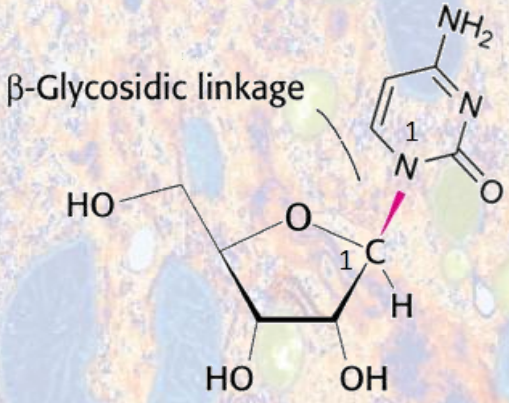


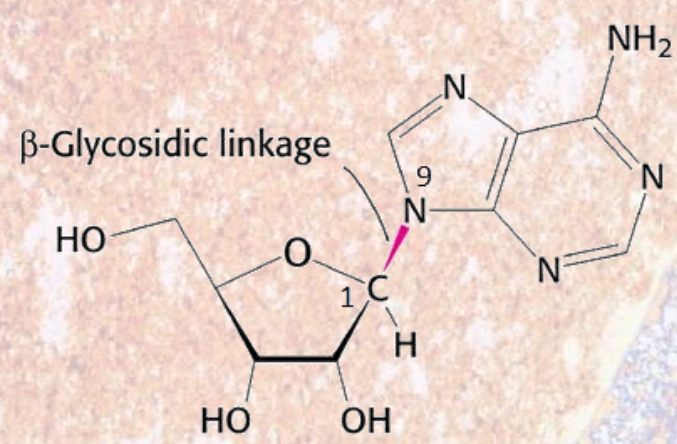
Deoxy-Tymidine

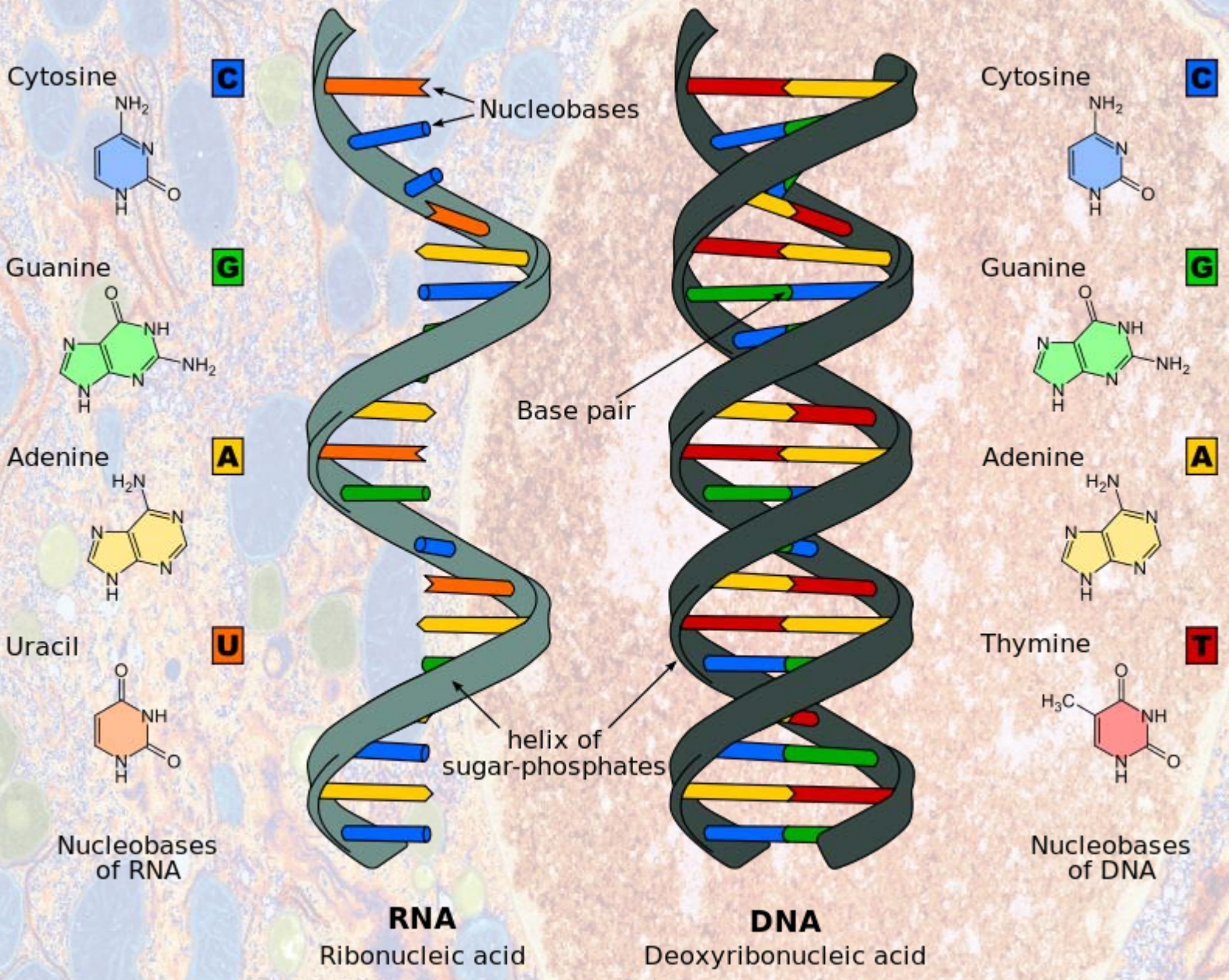
DNA

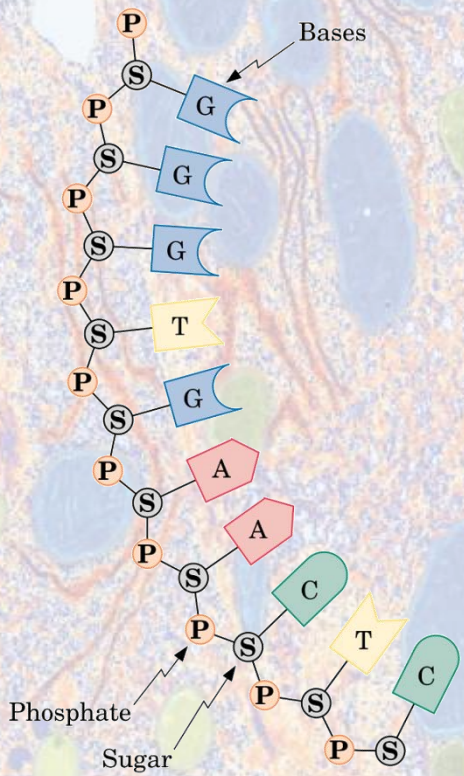
β–*N*-Glycosidic Bond

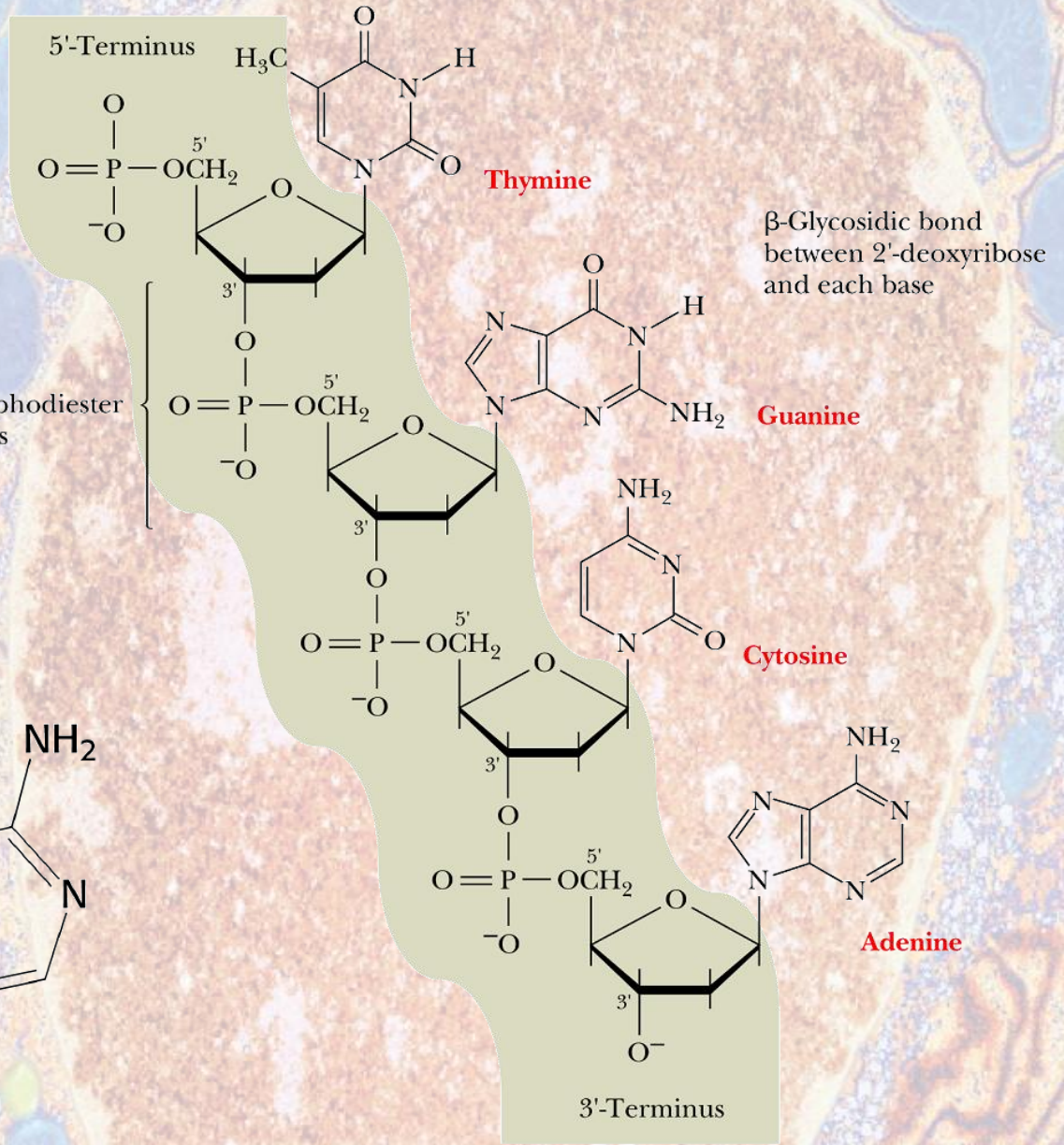
- In nucleotides the pentose ring is attached to the nucleobase via *N*-glycosidic bond
- The bond is formed C1 of ribose (or deoxyribose attached to:
  - position N1 in pyrimidines
  - position N9 in purines

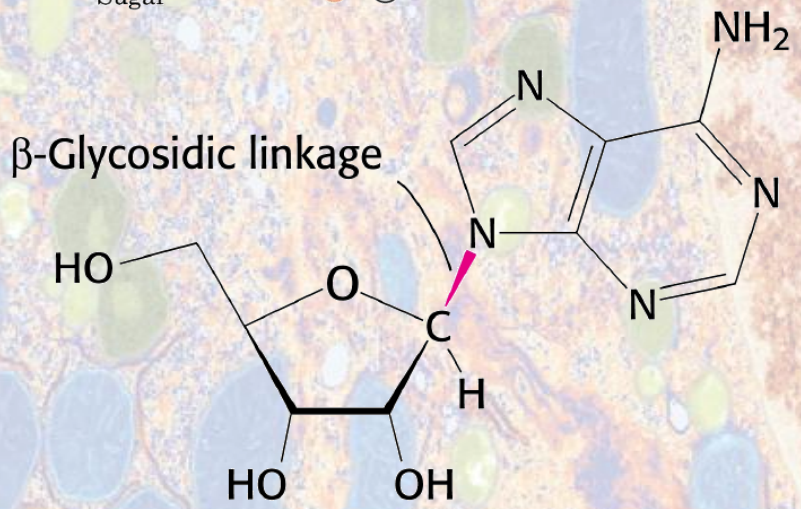




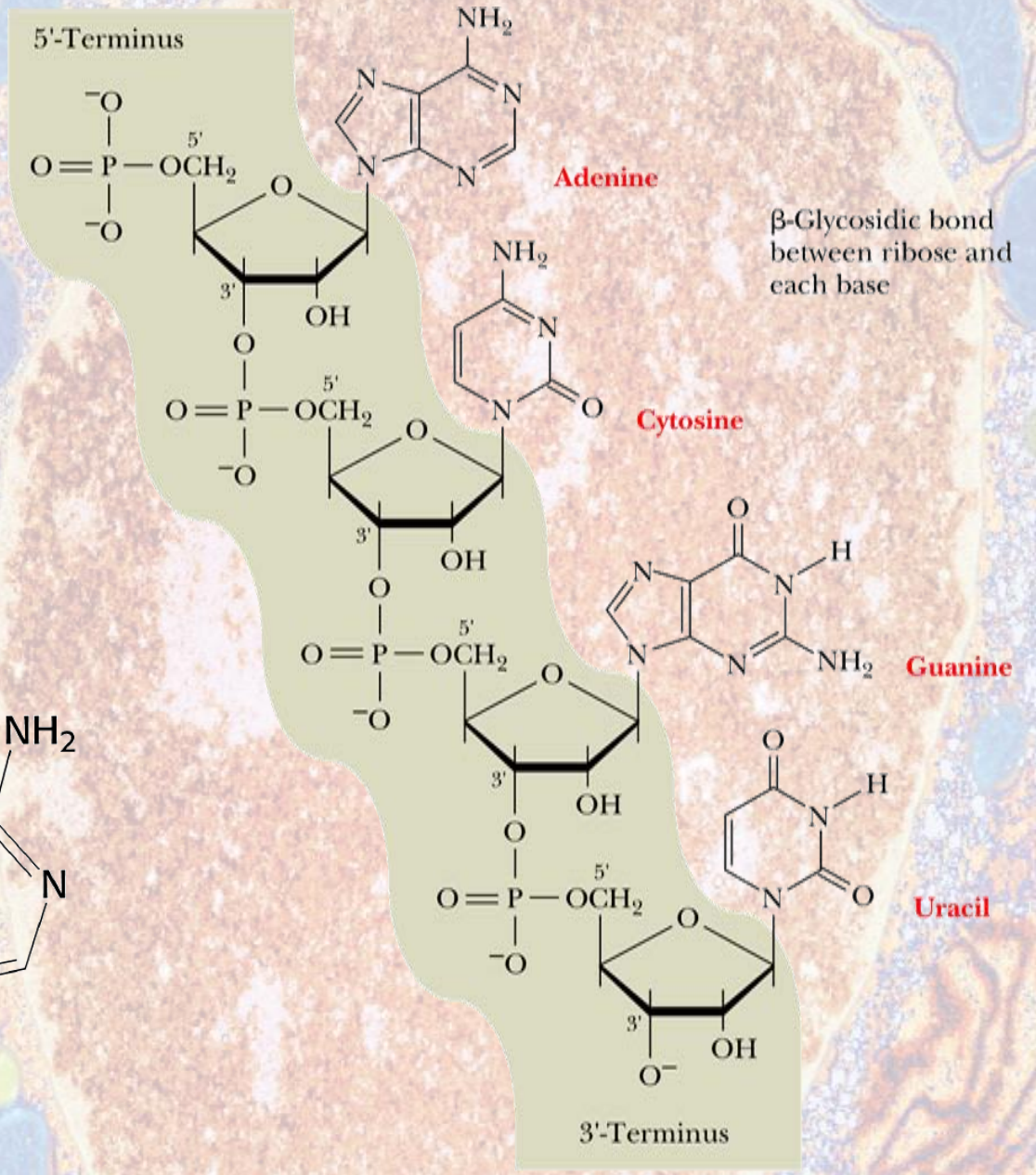

Cytosine
C
Guanine
G
Adenine
A
Uracil
U
Nucleobases of RNA
Nucleobases
Base pair
helix of sugar-phosphates
RNA
Ribonucleic acid
DNA
Deoxyribonucleic acid
Cytosine
C
Guanine
G
Adenine
A
Thymine
T
Nucleobases of DNA


Bases
Phosphate
Sugar

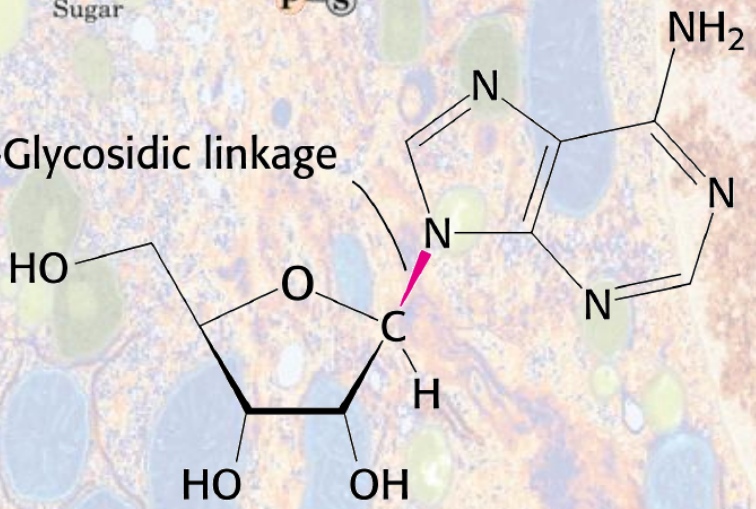

5'-Terminus
Thymine
β-Glycosidic bond between 2'-deoxyribose and each base
3'-5'-Phosphodiester bonds
Guanine
Cytosine
Adenine
3'-Terminus

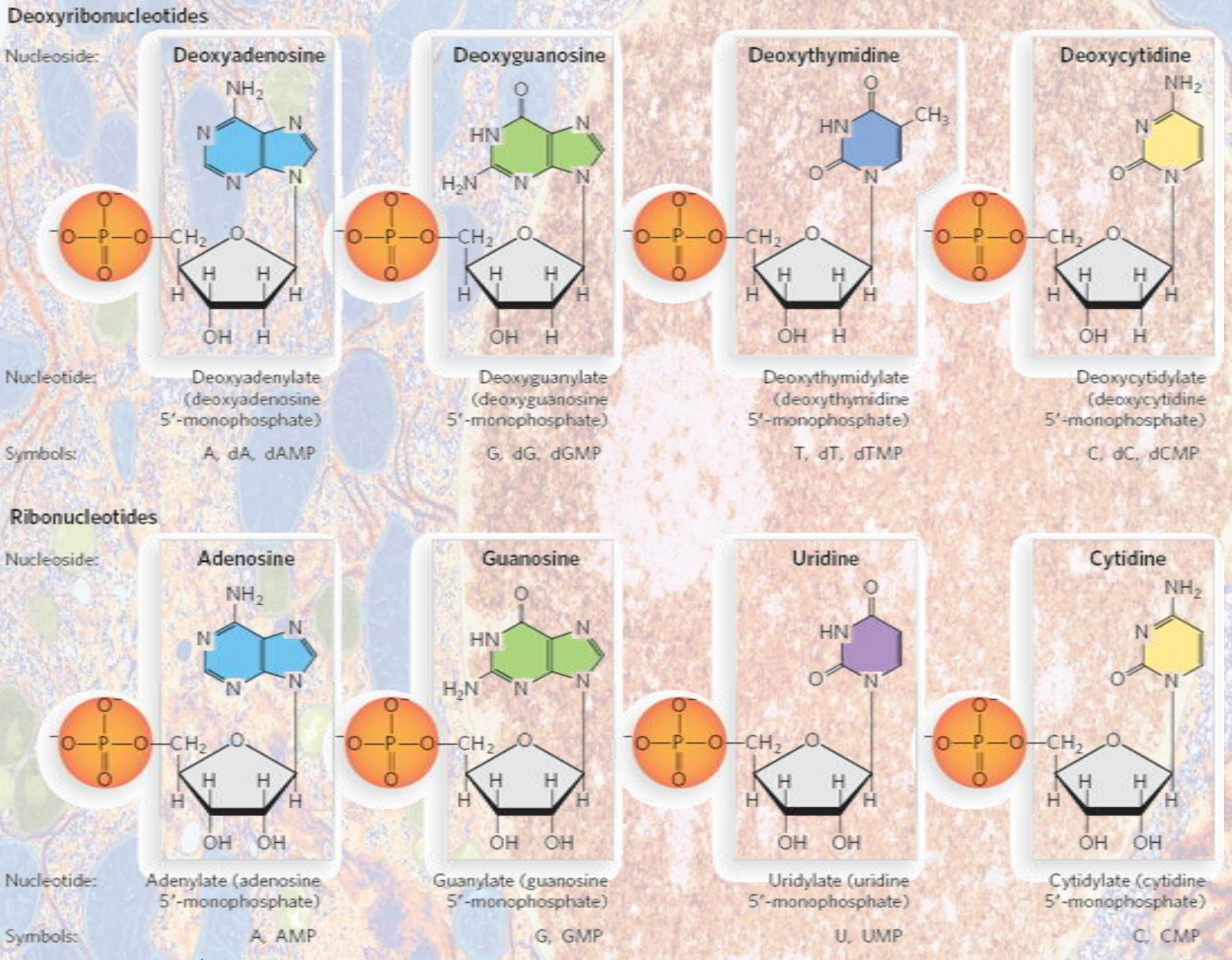

β-Glycosidic linkage



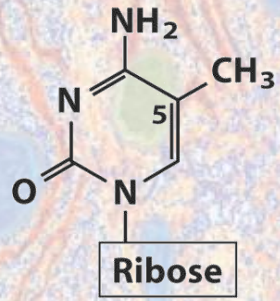


β-Glycosidic linkage

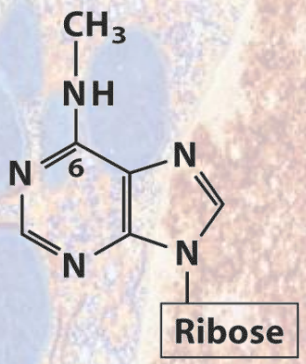



Deoxyribonucleotides
Nucleoside:
Deoxyadenosine
Deoxyguanosine
Deoxythymidine
Deoxycytidine
Nucleotide:
Deoxyadenylate (deoxyadenosine 5′-monophosphate)
Deoxyguanylate (deoxyguanosine 5′-monophosphate)
Deoxythymidylate (deoxythymidine 5′-monophosphate)
Deoxycytidylate (deoxycytidine 5′-monophosphate)
Symbols:
A, dA, dAMP
G, dG, dGMP
T, dT, dTMP
C, dC, dCMP
Ribonucleotides
Nucleoside:
Adenosine
Guanosine
Uridine
Cytidine
Nucleotide:
Adenylate (adenosine 5′-monophosphate)
Guanylate (guanosine 5′-monophosphate)
Uridylate (uridine 5′-monophosphate)
Cytidylate (cytidine 5′-monophosphate)
Symbols:
A, AMP
G, GMP
U, UMP
C, CMP

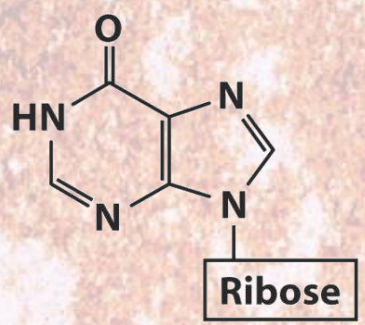
Some minor purine and pyrimidine bases



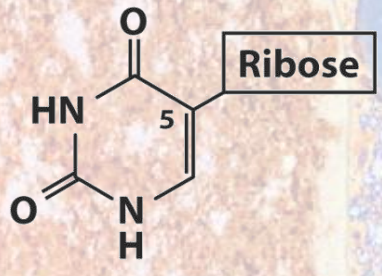
5-Methylcytidine



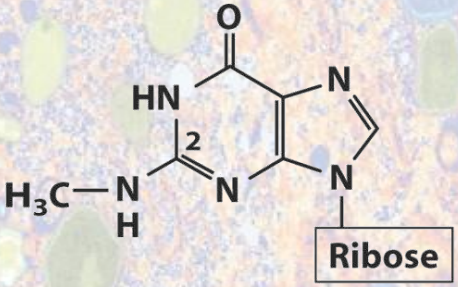
N^6-Methyladenosine



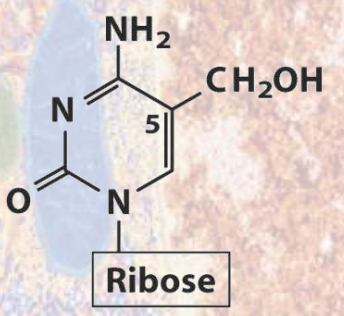
Inosine



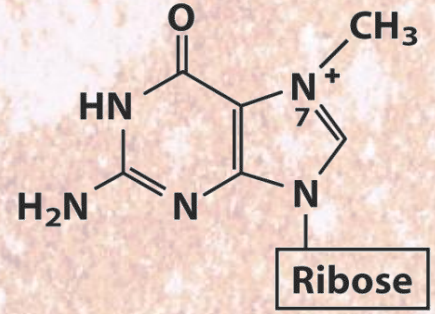
Pseudouridine



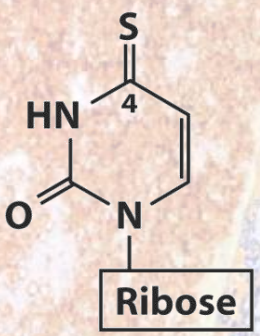
N^2-Methylguanosine



5-Hydroxymethylcytidine



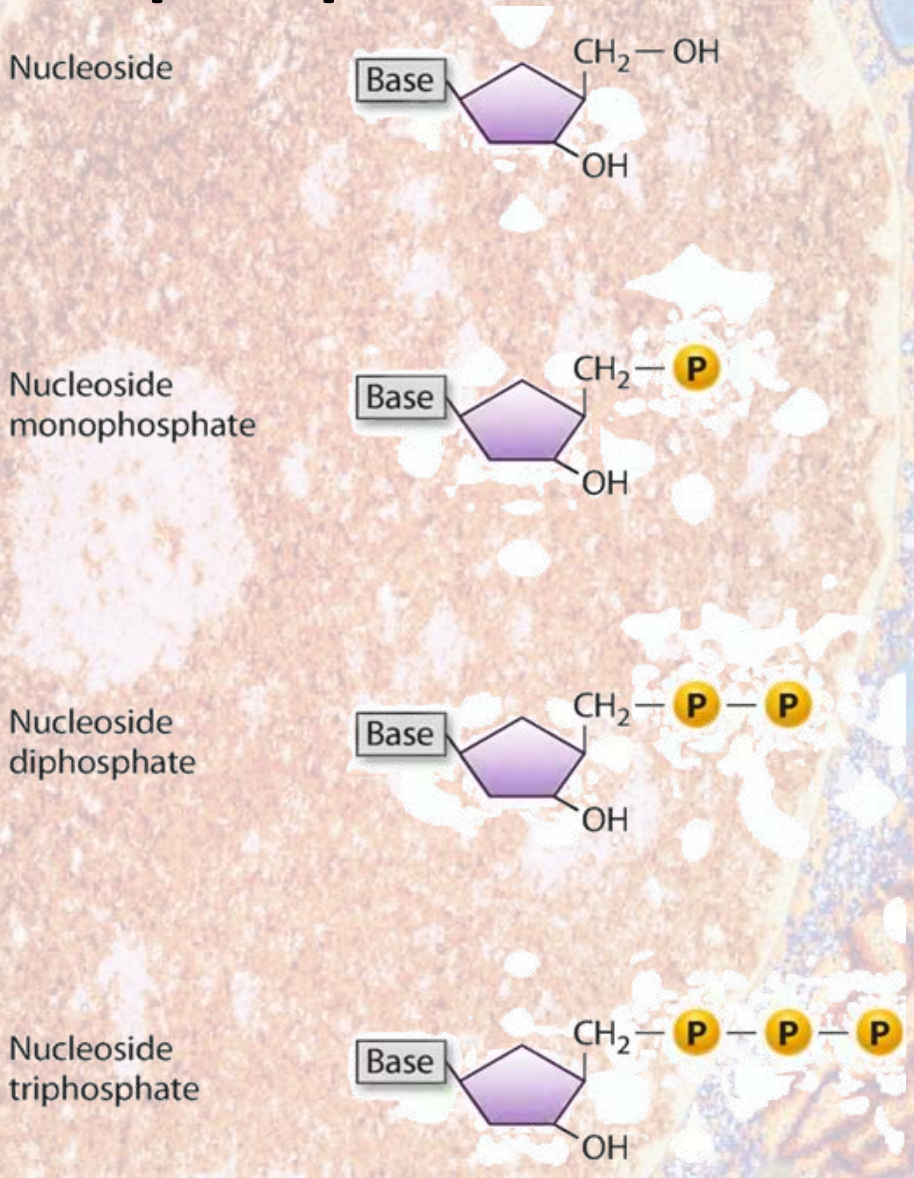
7-Methylguanosine

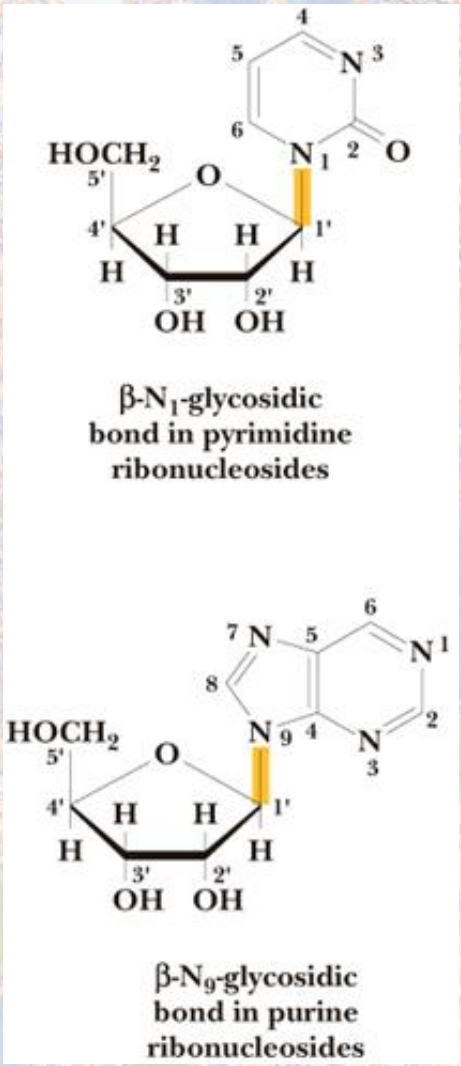


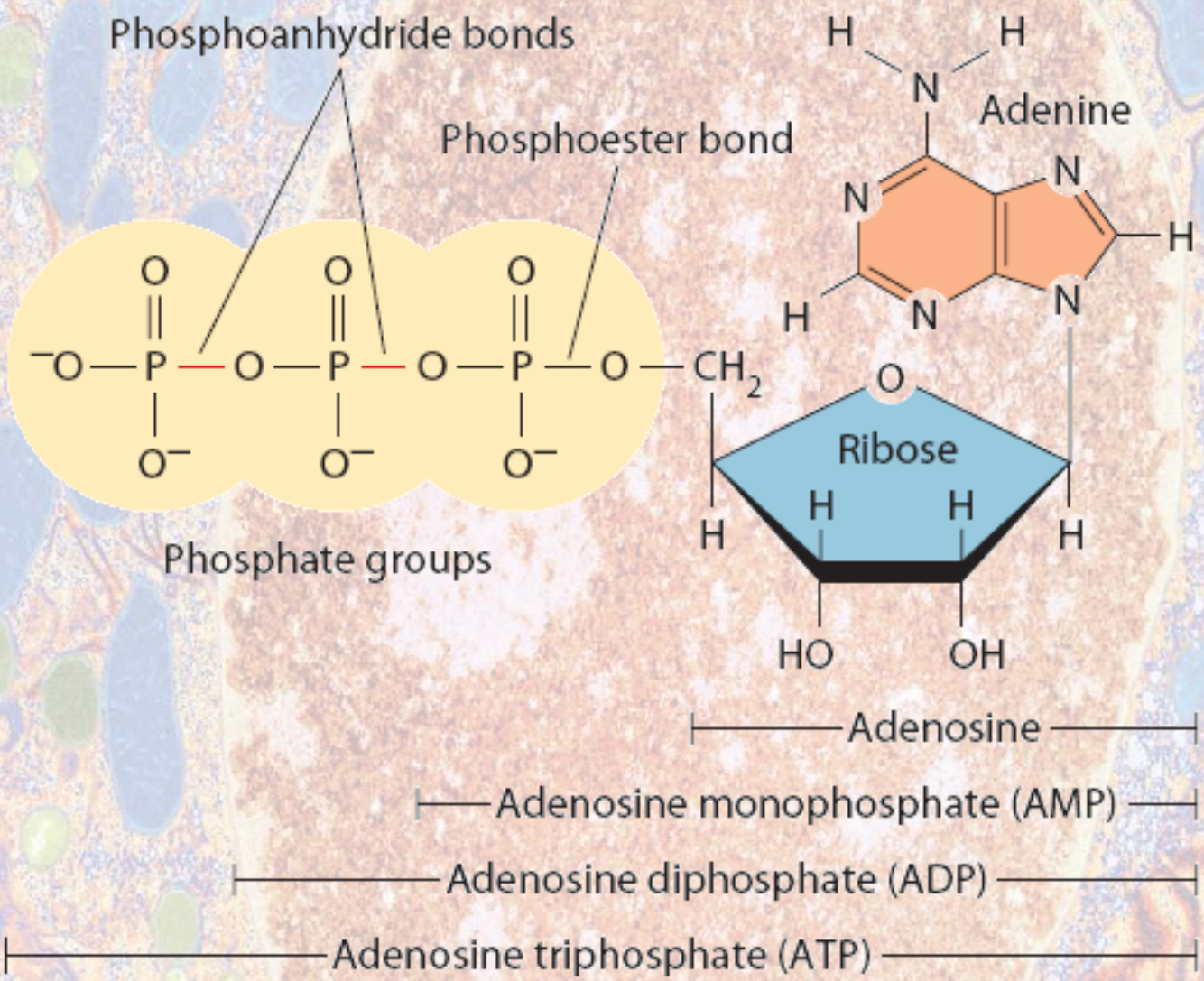
4-Thiouridine

Nucleoside and nucleoside phosphates.

- A nucleoside is a sugar attached to a base
- Nucleotides are nucleosides with one, two, or three phosphate groups



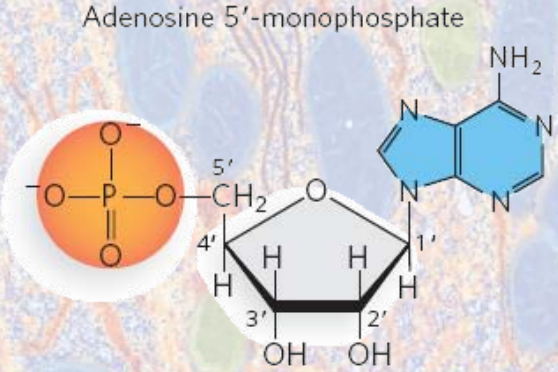

β-N1-glycosidic bond in pyrimidine ribonucleosides
β-N9-glycosidic bond in purine ribonucleosides

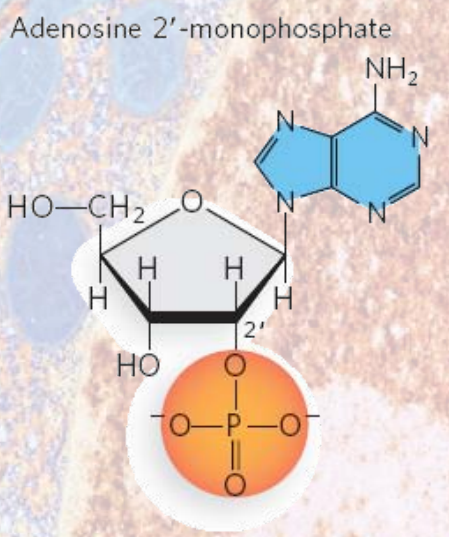

Phosphoanhydride bonds
Phosphoester bond
Adenine
Phosphate groups
Ribose
Adenosine
Adenosine monophosphate (AMP)
Adenosine diphosphate (ADP)
Adenosine triphosphate (ATP)

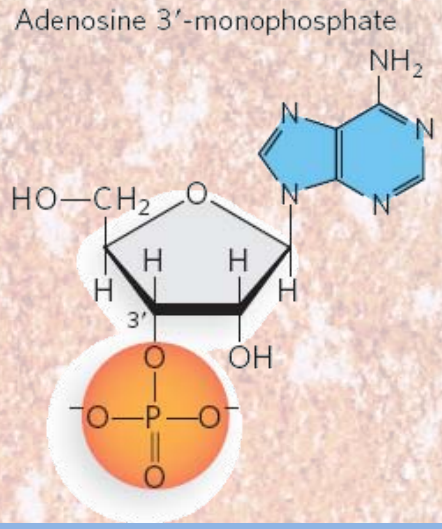
- **Nucleoside triphosphates** (e.g., ATP and GTP), are the "energy-rich" end products of the majority of energy-releasing pathways

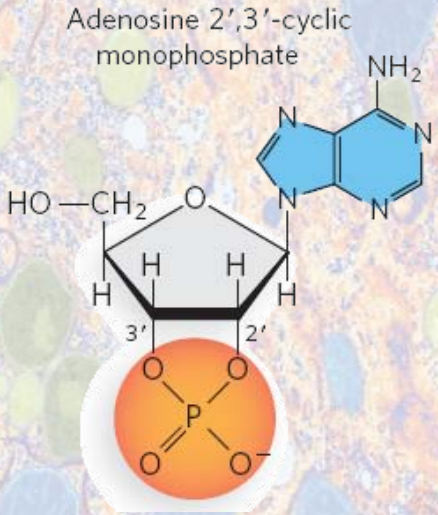
- Their utilization drives most energy-requiring (i.e., endergonic) processes.

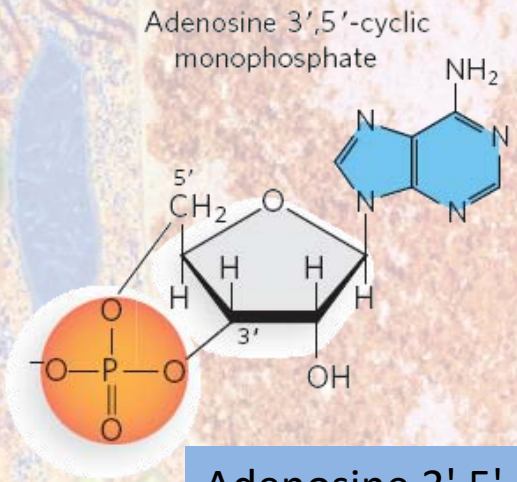
Examples of adenosine monophosphates









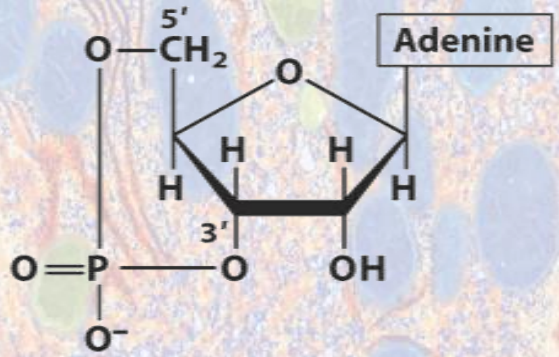


Adenosine 5'-monophosphate, the most common one.

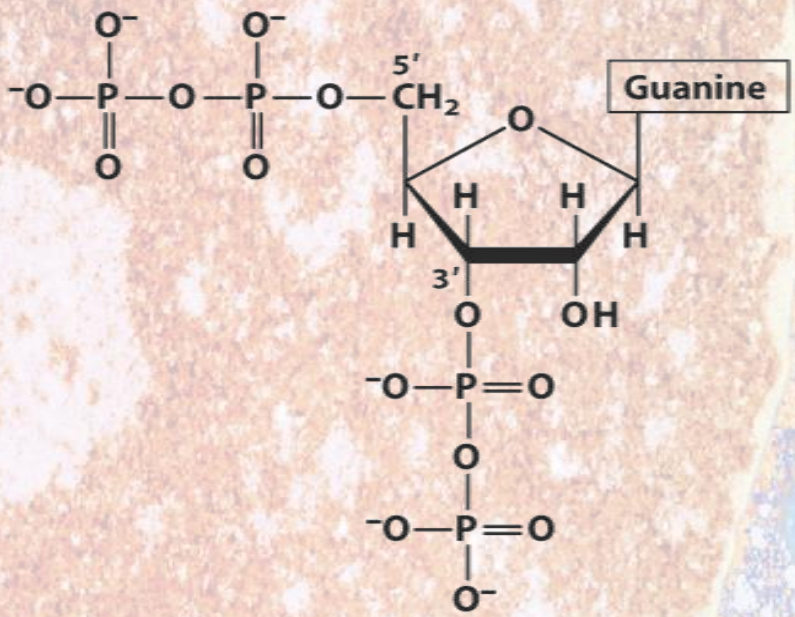
Adenosine 2'-monophosphate, adenosine 3'-monophosphate, and adenosine 2',3'-cyclic monophosphate are formed during enzymatic or alkaline hydrolysis of RNA.

Adenosine 3',5'-cyclic monophosphate (cAMP) is a signaling molecule that accumulates when the cell has a limited supply of nutrients (e.g., glucose).

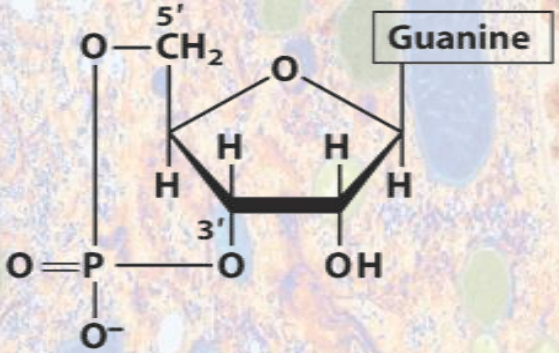
Regulatory nucleotides



Adenosine 3′,5′-cyclic monophosphate
(cyclic AMP; cAMP)



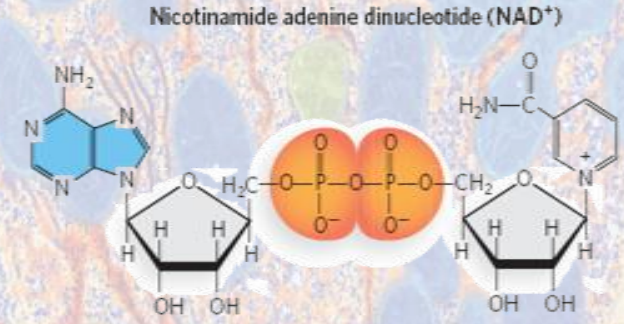
Guanosine 5′-diphosphate, 3′-diphosphate
(guanosine tetraphosphate)
(ppGpp)

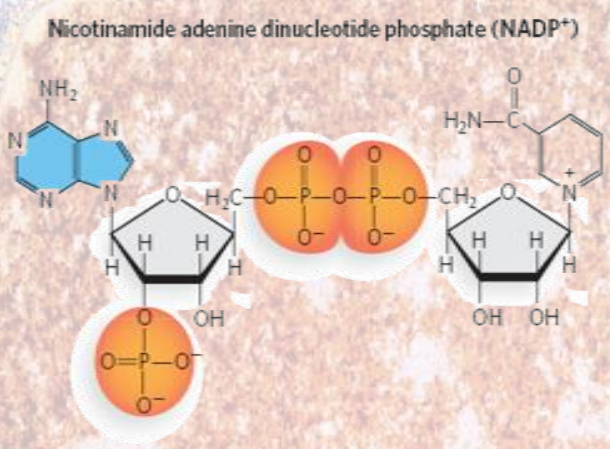


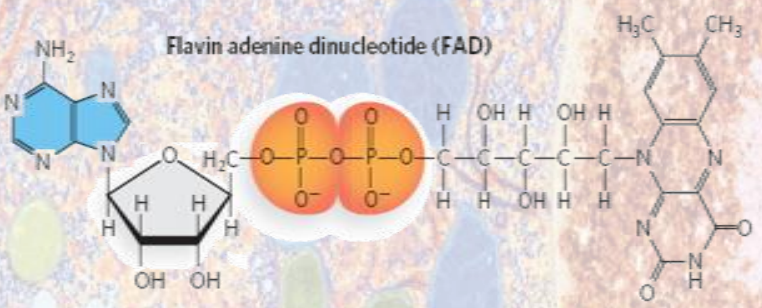
Guanosine 3′,5′-cyclic monophosphate
(cyclic GMP; cGMP)

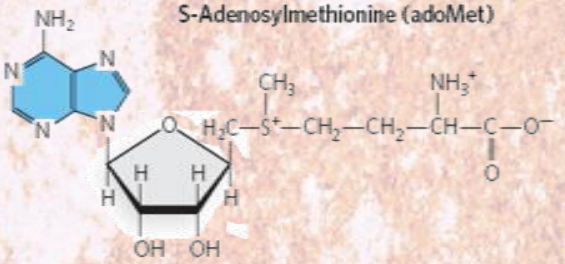
Coenzymes (organic cofactors)

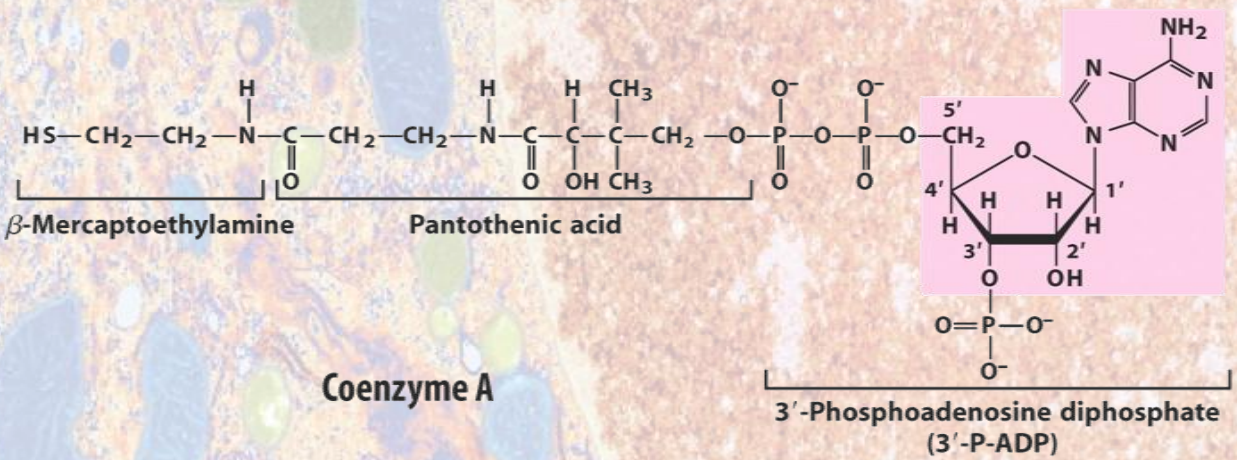
- Many coenzymes are derived from **vitamins** (especially B vitamins)
- Vitamin B2 (aka. riboflavin) is the component of FAD, vitamin B3 (aka. niacin or nicotinic acid) is the component of NAD, vitamin B5 (aka. pantothenic acid) is the component of CoA
- Coenzymes also contain the nucleotide adenosine monophosphate (AMP) as part of their structures
- They are participants in many enzymatic reactions for energy (ATP) production.


Nicotinamide adenine dinucleotide (NAD+)


Nicotinamide adenine dinucleotide phosphate (NADP+)


Flavin adenine dinucleotide (FAD)

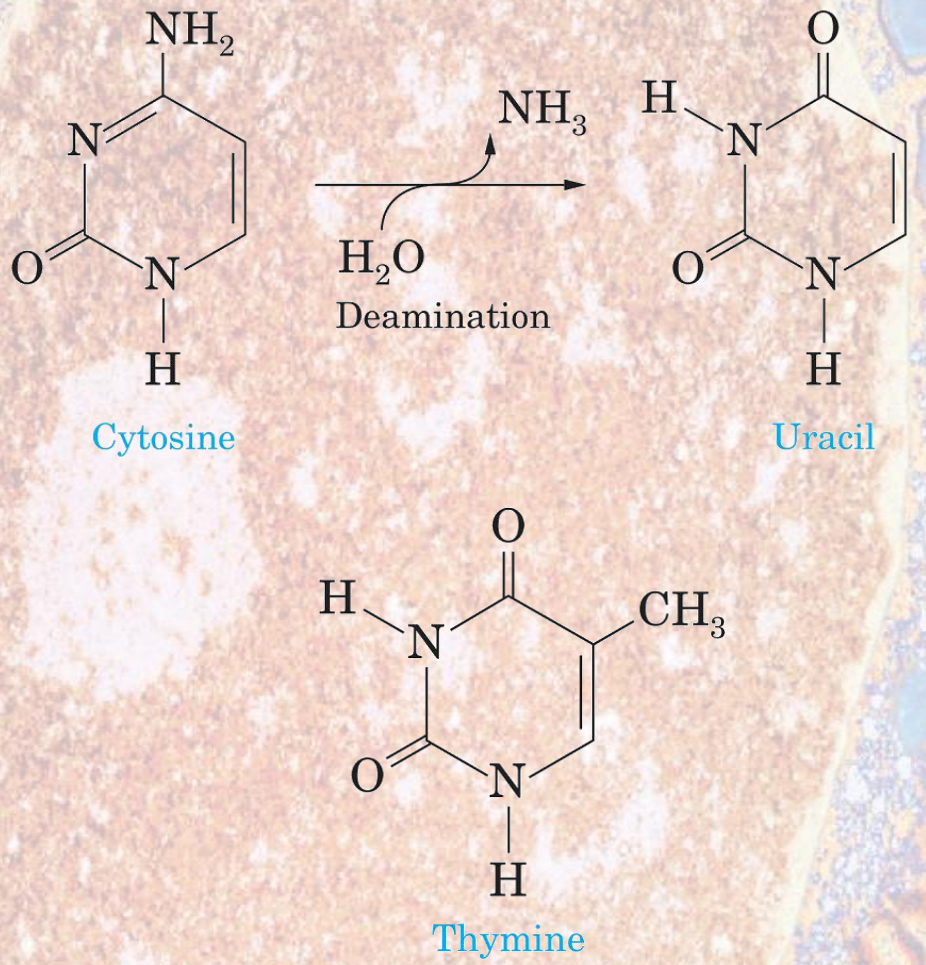

S-Adenosylmethionine (adoMet)


β-Mercaptoethylamine
Pantothenic acid
3′-Phosphoadenosine diphosphate
(3′-P-ADP)

Coenzyme A

Why Does DNA Contain Thymine and Not Uracil?

- Both uracil and thymine base-pair with adenine
- So, why does RNA contain uracil and DNA contain thymine?
- It is believe that RNA was the original hereditary molecule, and that DNA developed later.
- Thymine has a methyl group at C-5, not involved in base pairing. Thus, thymine does the same thing as uracil but requires more energy to produce.



- Thymine helps guarantee replication fidelity. One of the most common spontaneous mutations of bases is the natural deamination of cytosine.

- At any moment, a small but finite number of cytosines lose their amino groups to become uracil.
- During replication C–G base pair separates. If at that moment the C deaminates to U, it would tend to base-pair to A instead of to G.
- If U were a natural base in DNA, the DNA polymerases would just line up an adenine across from the uracil, and there would be no way to know that the uracil was a mistake.
- This would lead to a much higher level of mutation during replication. Because uracil is an unnatural base in DNA, DNA polymerases can recognize it as a mistake and can replace it.
- Thus, the incorporation of thymine into DNA, though energetically more costly, helps ensure that the DNA is replicated faithfully.

- There is a methyl group is on thymine. When thymine is demethylated it turns to uracil.

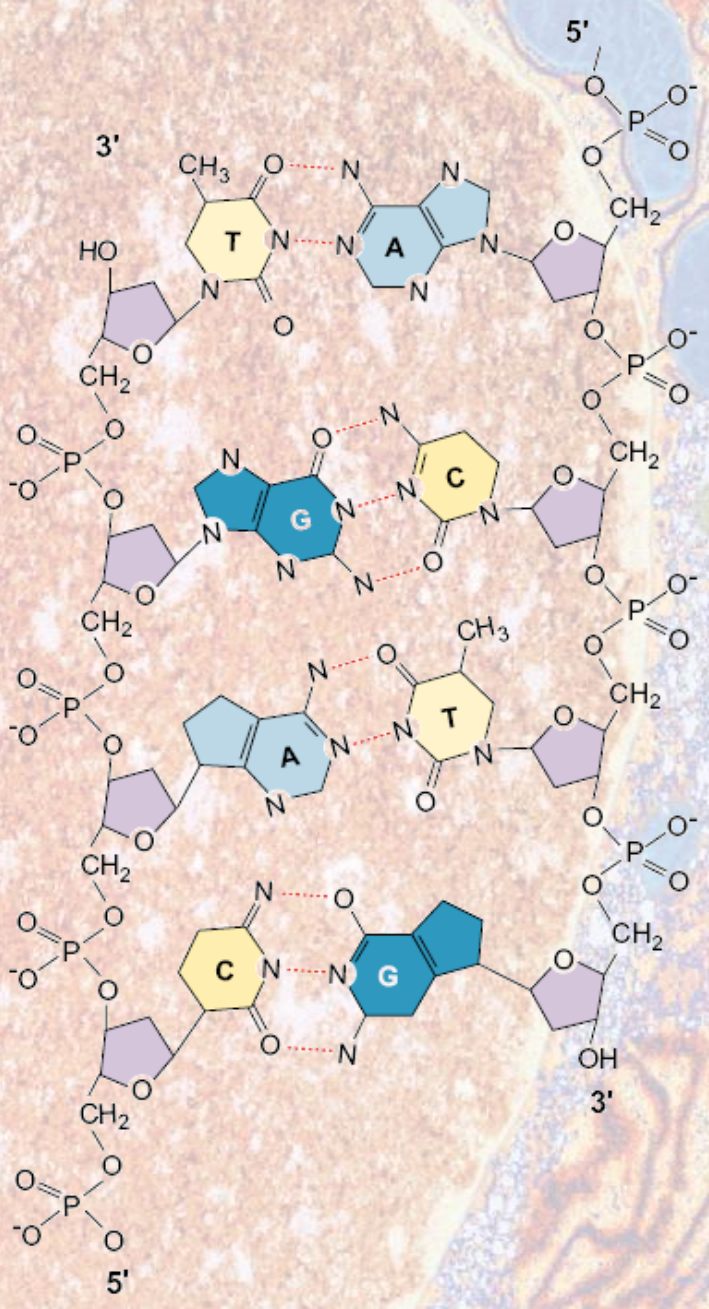
- The enzyme ***uracil DNA glycosylase*** excises uracil bases from double-stranded DNA.

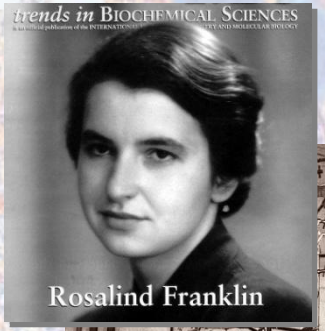
- The inability to repair such damage doesn't matter for RNA as the mRNA is comparatively short-lived and any potential errors don't lead to any lasting damage.

- It matters a lot for DNA as the errors are continued through every replication. Now, this explains why there is an advantage to using thymine in DNA, it doesn't explain why RNA uses uracil.

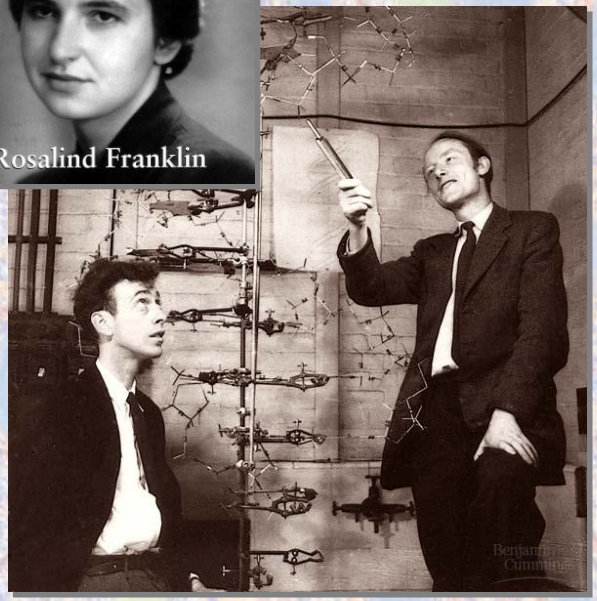
Detailed Structure of DNA

- Base pairing between purines (in blue) and pyrimidines (in yellow), and the phosphodiester linkages of the backbone.
- Opposite purines-pyrimidines pairs held together by H-bonds
- All other bonds (including the phosphodiester linkages) are covalent
- Two strands are anti-parallel and run (synthesized) in 5’→ 3’ diretion.

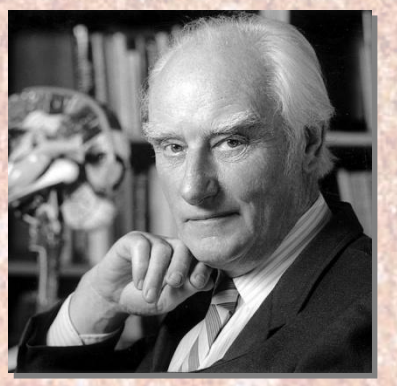




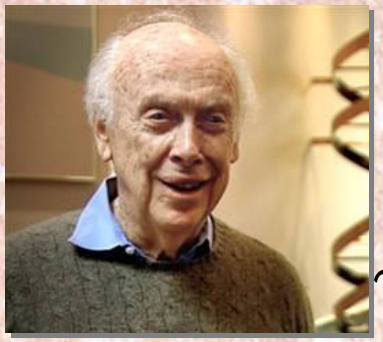
Rosalind Franklin
1920-1958



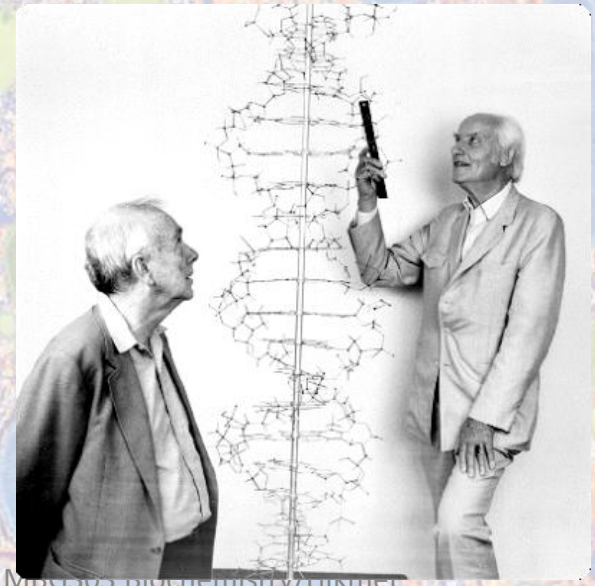
Watson (left) and Crick at their famous DNA helix model in 1953



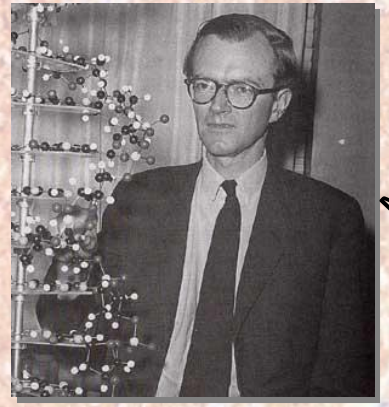
Francis Crick
1916-2004



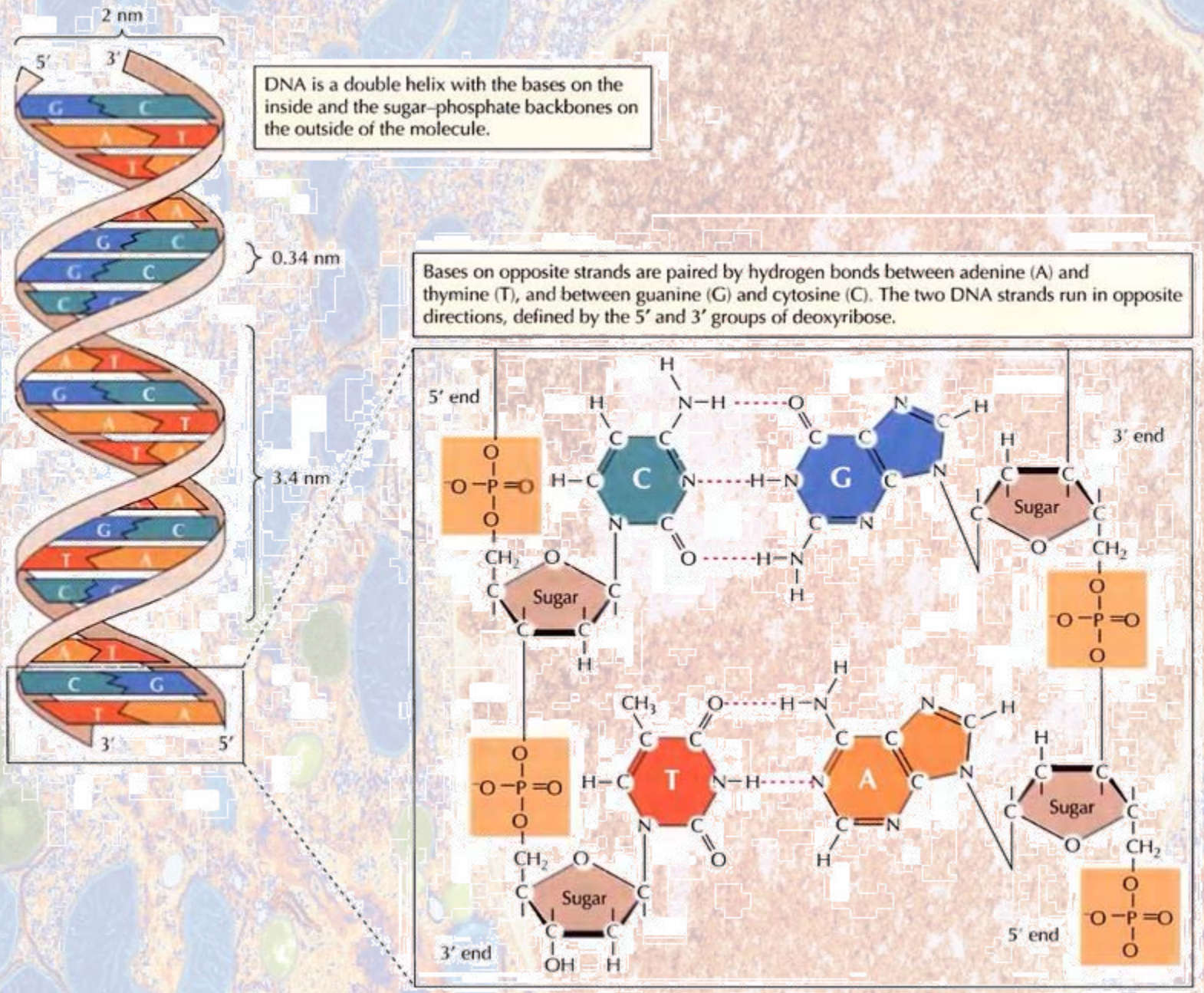
James Watson
2015, 87 years old



Watson and Crick recreate their demonstration of the double helix model for DNA in 1990.

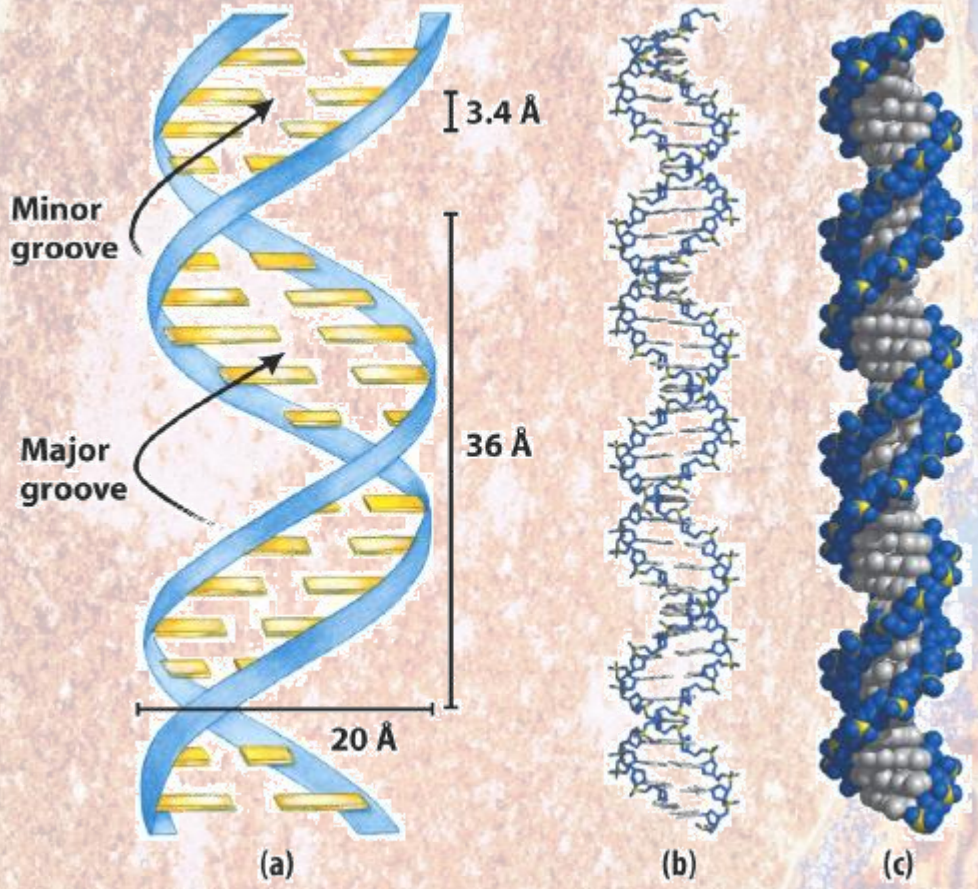


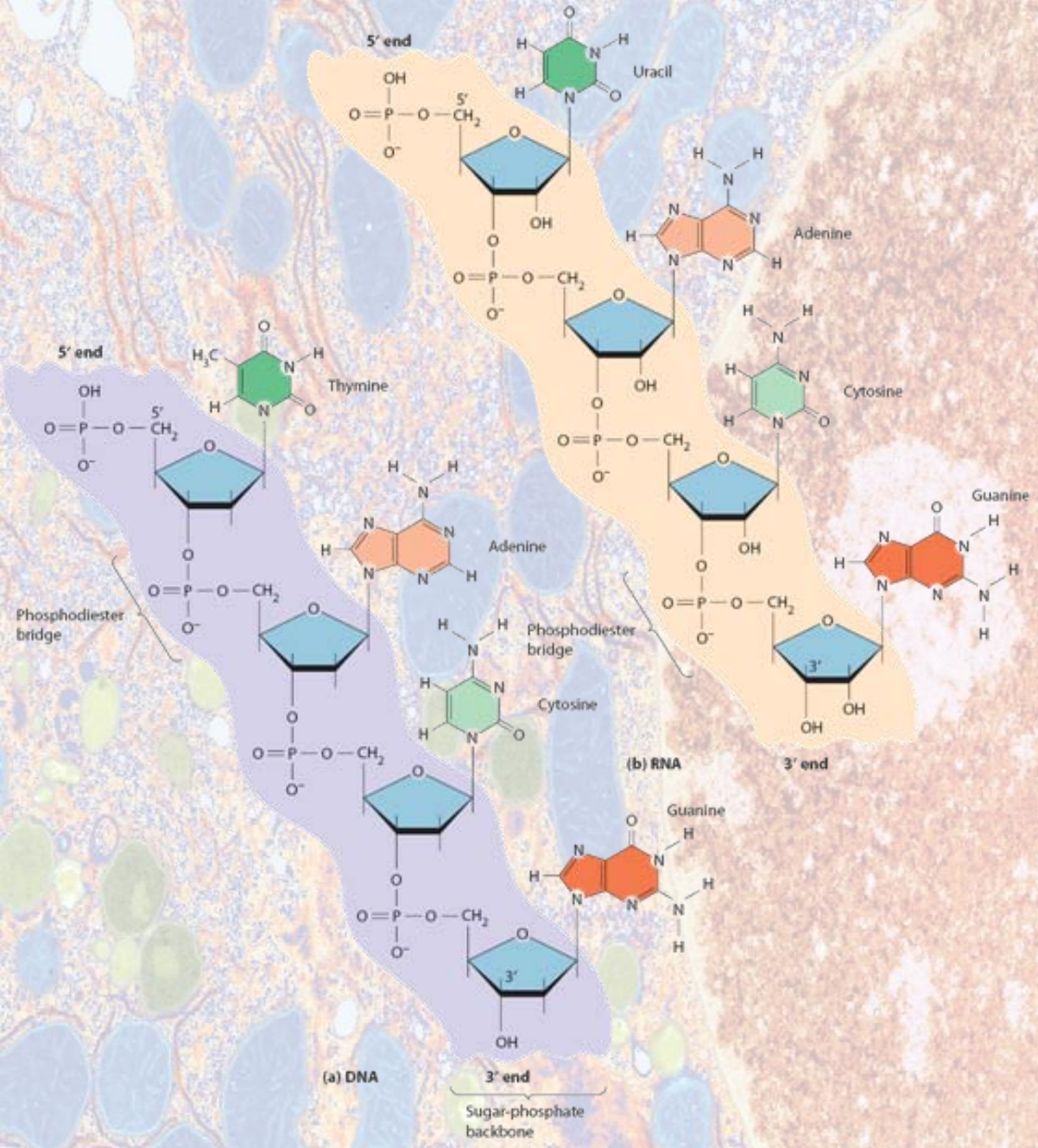
Maurice Wilkins
1916-2004


2 nm
5′
3′
0.34 nm
3.4 nm
3′
5′
DNA is a double helix with the bases on the inside and the sugar–phosphate backbones on the outside of the molecule.
Bases on opposite strands are paired by hydrogen bonds between adenine (A) and thymine (T), and between guanine (G) and cytosine (C). The two DNA strands run in opposite directions, defined by the 5′ and 3′ groups of deoxyribose.
5′ end
3′ end
Sugar
C
G
T
A
OH

The Structure of Nucleic Acids

- DNA consists of two helical chains wound around the same axis in a right-handed fashion aligned in an antiparallelfashion.
- There are 10.5 base pairs, or 36 Å, per turn of the helix.
- Alternating deoxyriboseand phosphate groups on the backbone form the outside of the helix.
- The planar purineand pyrimidinebases of both strands are stacked inside the helix.

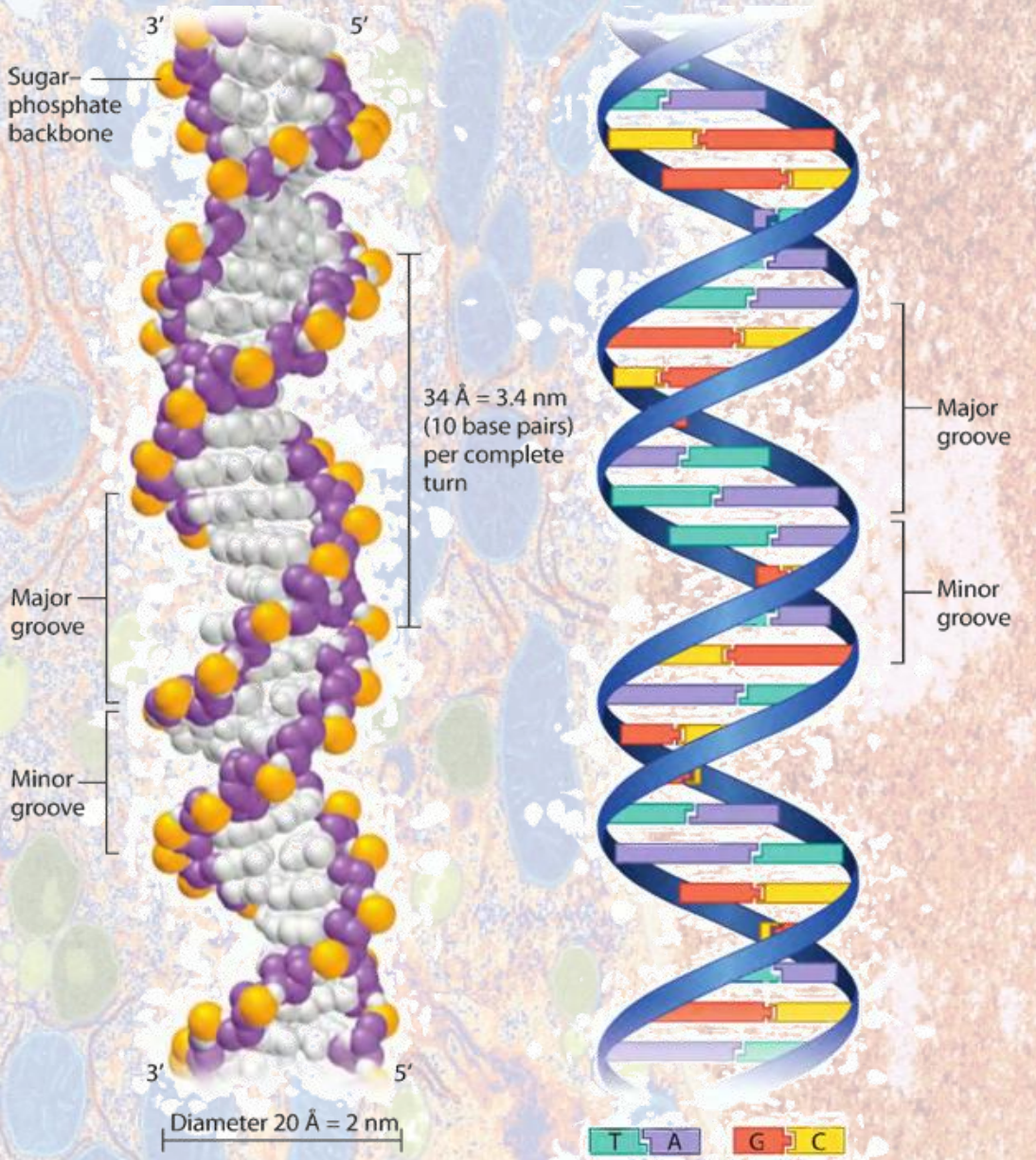


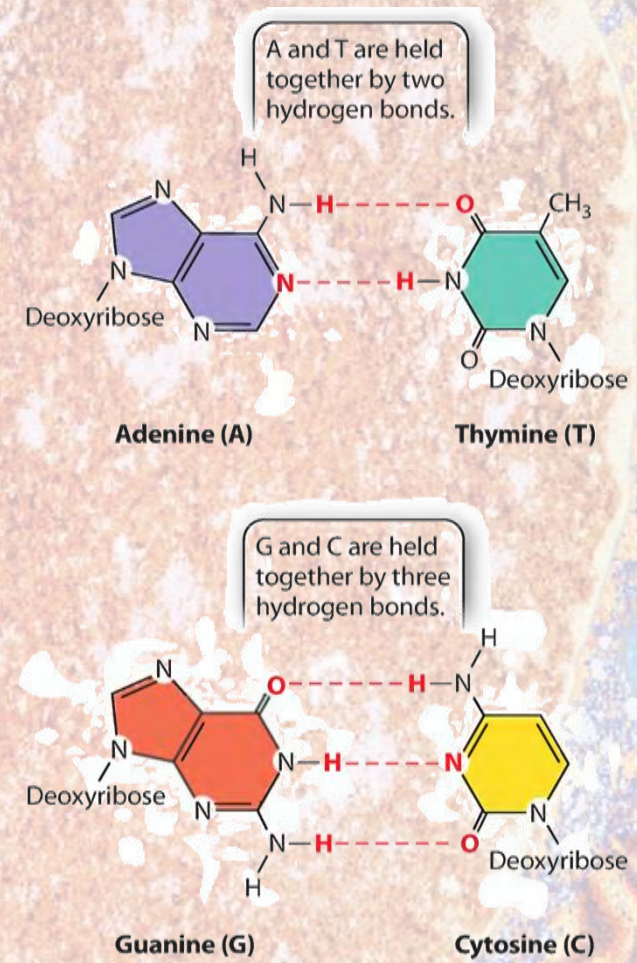


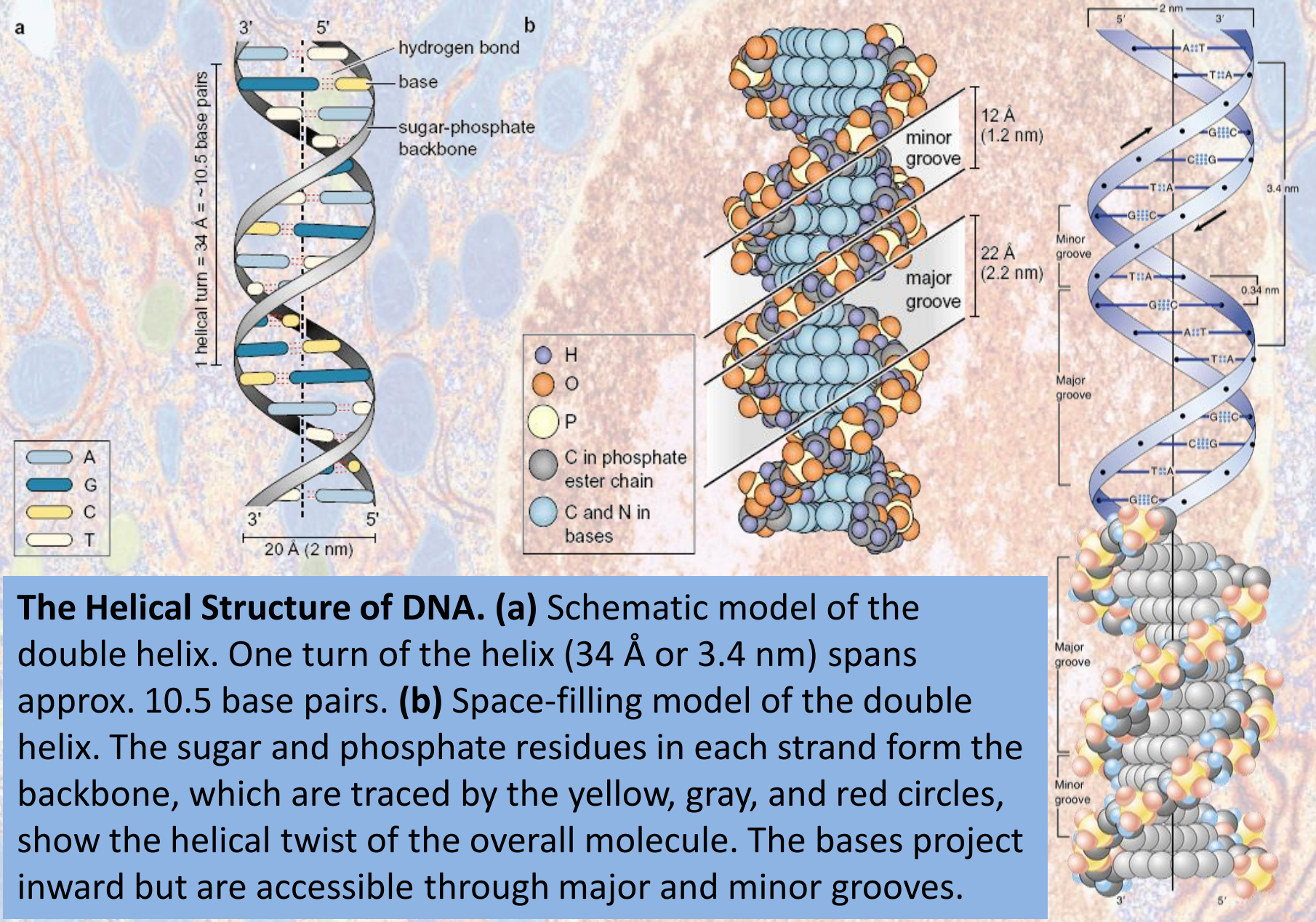
The Structure of Nucleic Acids

Nucleic acids consist of linear chains of nucleotides, each containing a sugar, a phosphate, and a base. The sugar is **(a)** deoxyribose in DNA and **(b)** ribose in RNA. Successive nucleotides in the chain are joined together by 3′, 5′ phosphodiester bridges. The resulting polynucleotide has an intrinsic directionality, with a 5′ end and a 3′ end. For both DNA and RNA, the backbone of the chain is an alternating sugar-phosphate sequence, from which the bases jut out.

Ref: Becker's World of the Cell

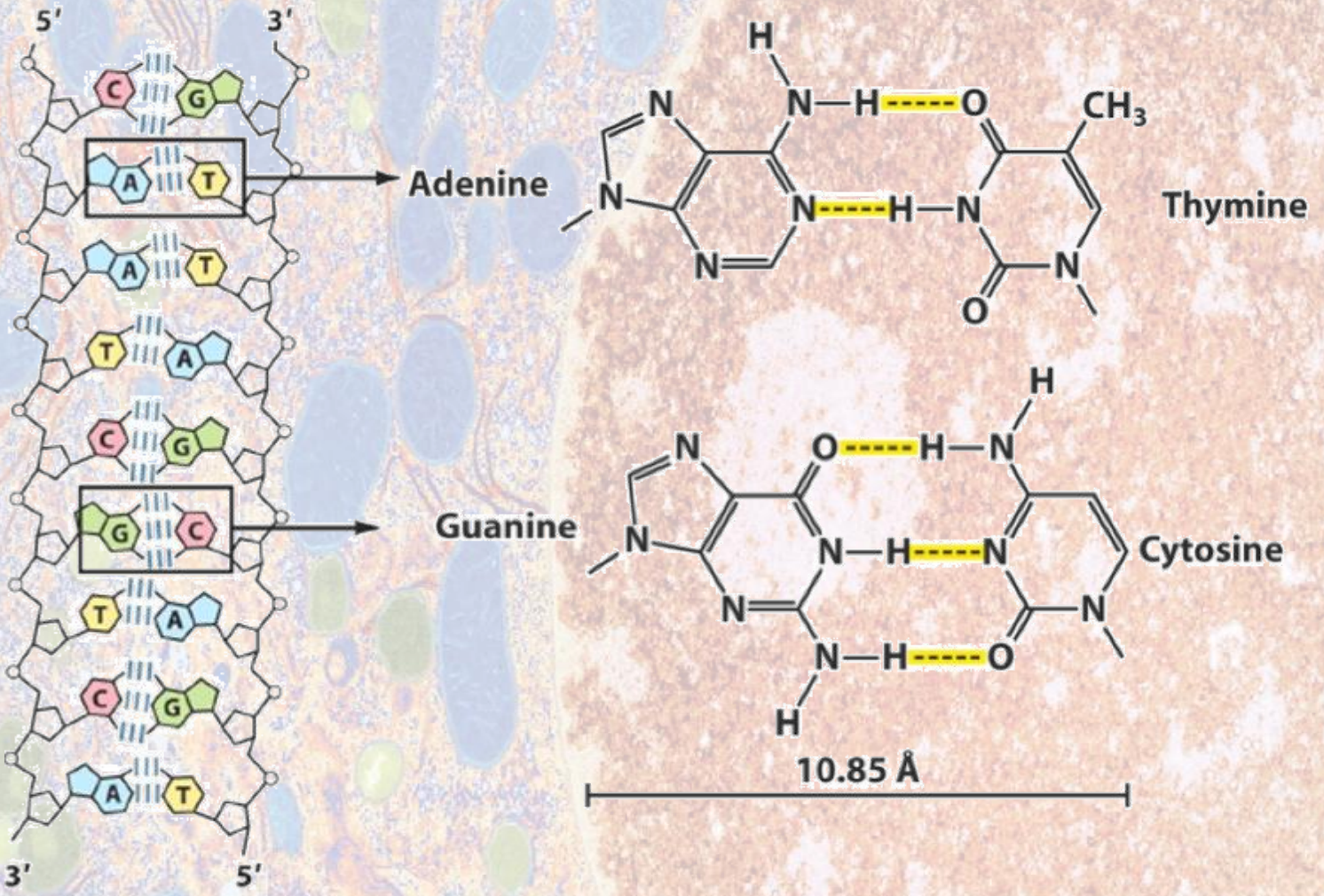

3′
5′
Sugar–phosphate backbone
34 Å = 3.4 nm (10 base pairs) per complete turn
Major groove
Minor groove
3′
5′
Diameter 20 Å = 2 nm
Major groove
Minor groove
T
A
G
C


A and T are held together by two hydrogen bonds.
Deoxyribose
Deoxyribose
Adenine (A)
Thymine (T)
G and C are held together by three hydrogen bonds.
Deoxyribose
Deoxyribose
Guanine (G)
Cytosine (C)



The Helical Structure of DNA. (a) Schematic model of the double helix. One turn of the helix (34 Å or 3.4 nm) spans approx. 10.5 base pairs. **(b)** Space-filling model of the double helix. The sugar and phosphate residues in each strand form the backbone, which are traced by the yellow, gray, and red circles, show the helical twist of the overall molecule. The bases project inward but are accessible through major and minor grooves.

Watson-Crick base pairing in DNA

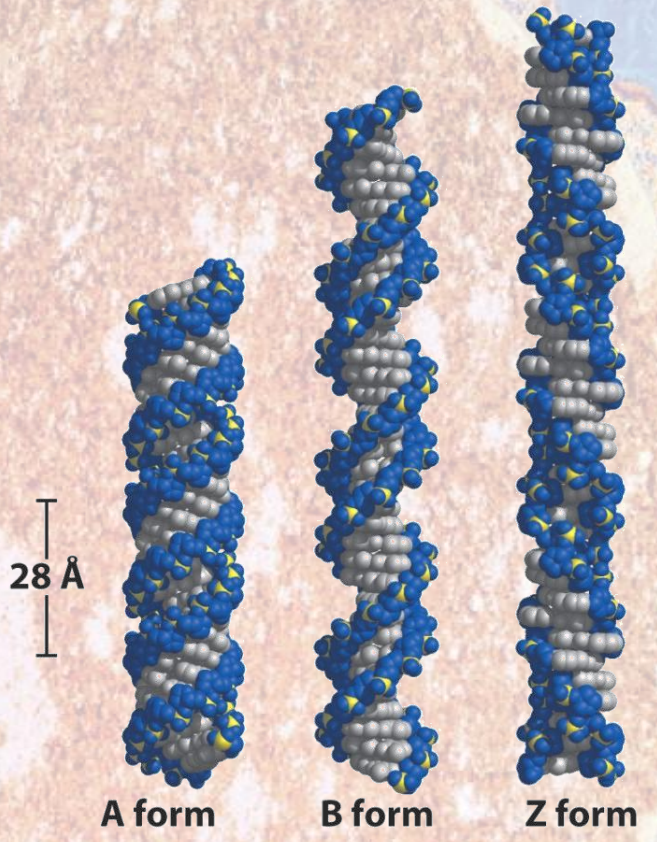


Base pairing is through hydrogen bonds.

The most common form, present in most DNA at neutral pH and physiological salt concentrations, is **B-form**.

A- form is thicker right-handed duplex with a shorter distance between the base pairs present mostly in RNA-DNA duplexes and RNA-RNA duplexes.

Z-form is left-handed helical structure formed by stretches of alternating purines and pyrimidines, e.g. GCGCGC.



Feature	B-DNA	A-DNA	Z-DNA
Type of helix	Right-handed	Right-handed	Left-handed
Helical diameter (nm)	2.37	2.55	1.84
Rise per base pair (nm)	0.34	0.29	0.37
Distance per complete turn (pitch) (nm)	3.4	3.2	4.5
Number of base pairs per complete turn	10	11	12
Topology of major groove	Wide, deep	Narrow, deep	Flat
Topology of minor groove	Narrow, shallow	Broad, shallow	Narrow, deep

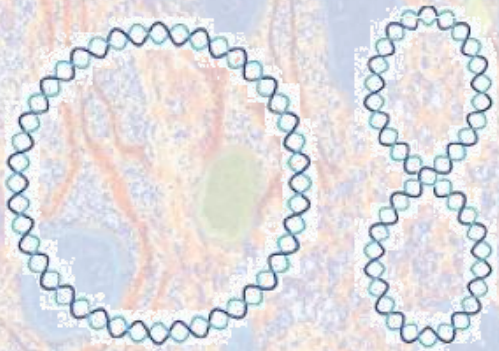
Types of RNA

- mRNA (messenger RNA)
  - Template for protein synthesis (translation)
- tRNA(transfer RNA)
  - Carries activated amino acids to ribosome for protein synthesis
  - At least one kind of tRNAfor each of the 20 amino acids
- rRNA(ribosomal RNA)
  - Major component of ribosomes

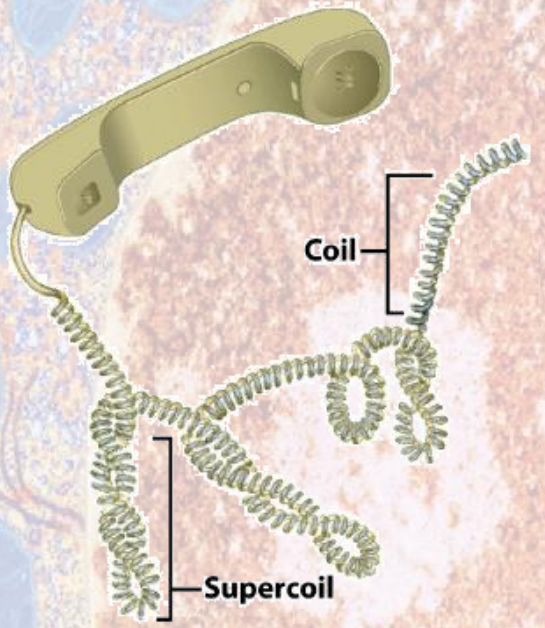
Regulatory RNAs

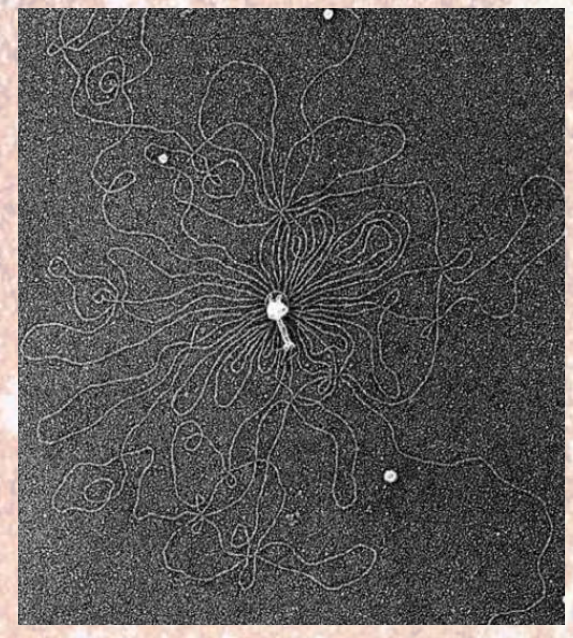
- **MicroRNAs (miRNAs)**
  - diverse roles in biological processes, including development, proliferation and differentiation such as RNA silencing and post-transcriptional regulation of gene expression
- **Small interfering RNAs (siRNAs)**
  - interfering with the expression of specific genes with complementary nucleotide sequences.
- **Long noncoding RNAs**
  - Regulation of gene transcription, epigenetic regulation
- **CRISPR RNA**
  - Found in bacteria, resistance to viruses (as if immunity)
- **Ribozymes (aka. catalytic RNAs)**
  - RNA molecules that are capable of catalyzing specific biochemical reactions, similar to the action of protein enzymes.
- **Small nuclear RNAs (aka. U-RNAs)**
  - Found within the splicosomes and Cajal bodies of the cell nucleus in eukaryotic cells.
- **Telomerase RNA**
  - Used to extend telomeres

DNA: So TALL, yet so SMALL

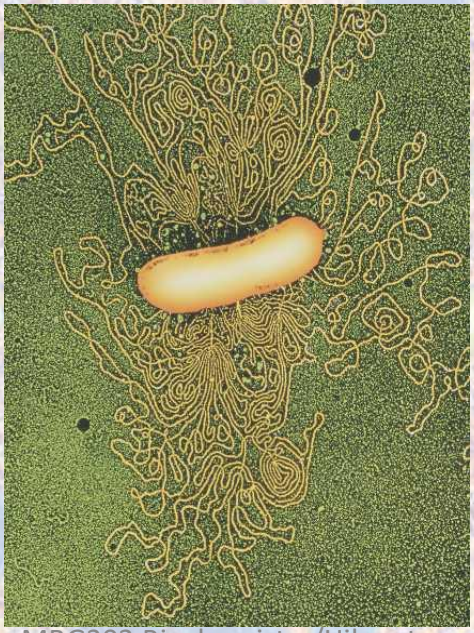


circular DNA DNA supercoil





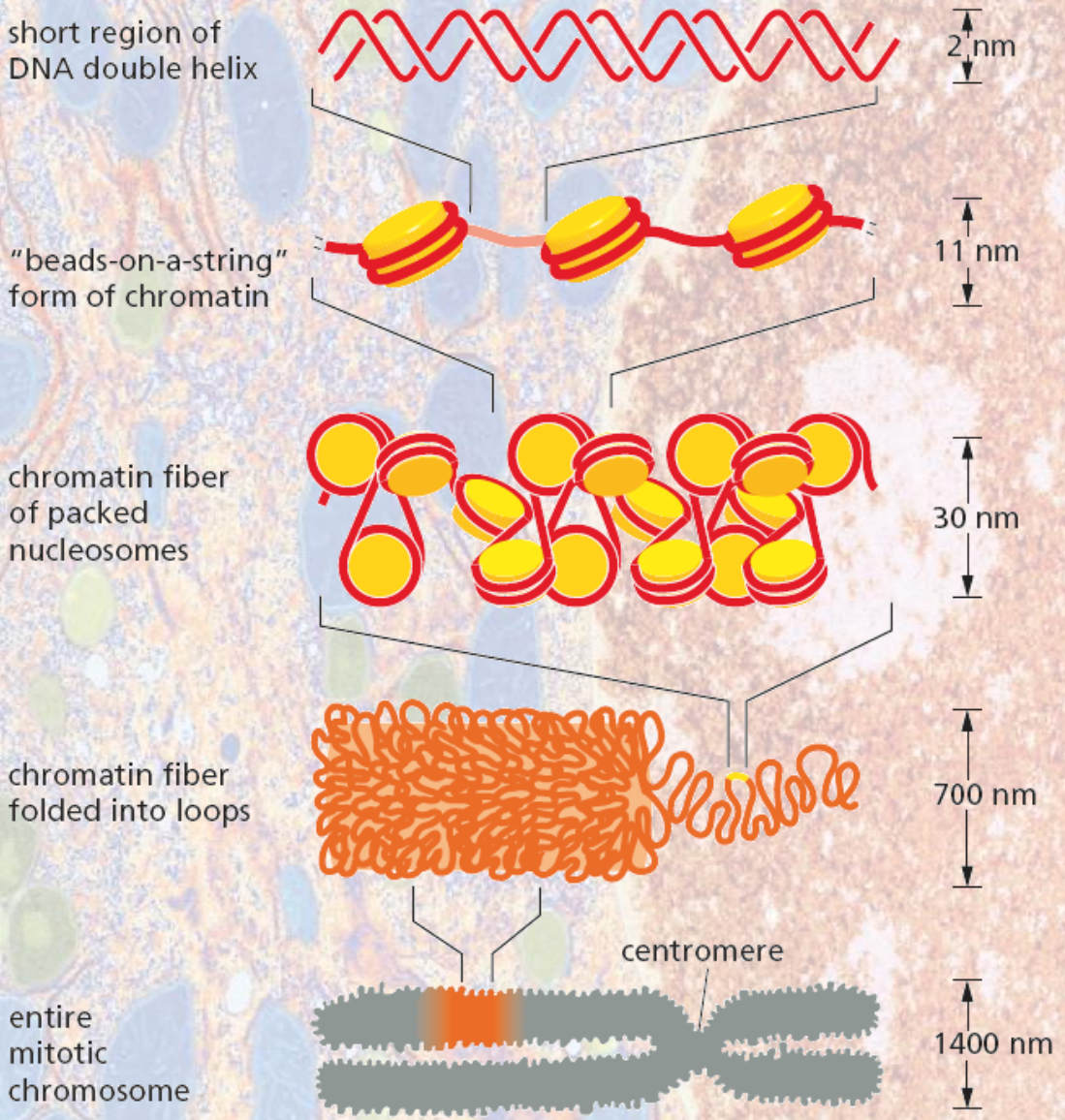
(a)



(b)

Electron micrograph of a bacteriophage (a), bacterium (b), and their DNA

DNA packaging: DNA to Chromosome



Assuming that the histone octamer forms a cylinder 9 nm in diameter and 5 nm in height and that the human genome forms 32 million nucleosomes.

- What volume of the nucleus (6 µm in diameter) is occupied by histone octamers? (Volume of a cylinder is $\pi r2h$; *volume* of a sphere is $4/3\ \pi r3$.)
- *What fraction* of the total volume of the nucleus do the histone octamers occupy?
- How does this compare with the volume of the nucleus occupied by human DNA?

Amazing DNA facts!

- Each cell contains roughly 2 metres of DNA
- DNA is 2 nm in width
- You could fit 25,000 strands of DNA side by side to make it the width of a single hair (50 micronmeter).
- There are approximately 3 billion (3,000,000,000) base pairs in a diploid human cell (2n= 46 chromosomes)
- The four letters in the DNA alphabet (A, C, G and T) are used to carry the instructions for making all organisms (compare this with 26 letters in English and 29 letters in Turkish alphabet).
- Of these four, every 3 letters make a “word” (i.e., amino acids)
- Using 20 amino acids, you can make innumerable “sentences” (i.e., proteins)

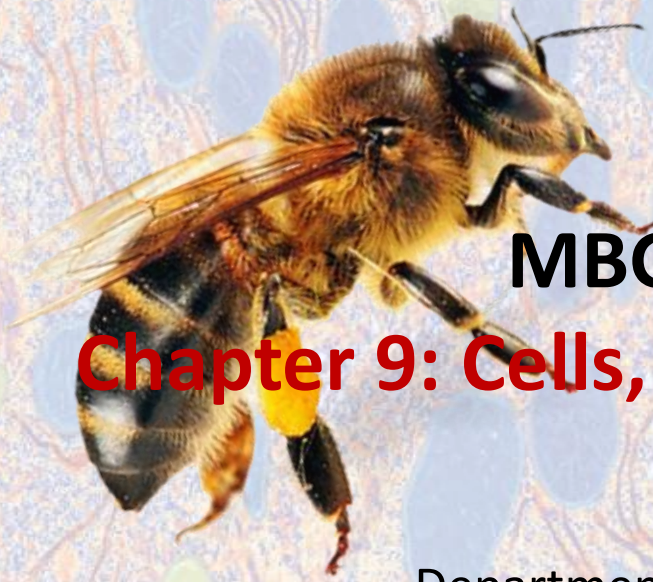
- DNA is the largest molecule in any cell.
- Each chromosome is made of a single DNA molecule (the largest being the one in chromosome # 1, the smalest in chromosome # 22 and Y chromosome).
- Even DNA in chromosme Y is larger than any molecule in the cell (remember! A single molecule DNA in any chromosome encodes 100s if not 1000s of proteins which are themselves among the largest molecules in the cell)

- All the DNA in a single human cell when tied end-to-end makes about 2 m in length (which still can pack in a several micronmeters size nucleus) (Q: How?)

- All the DNA from our 200 trillion or so cells can span the earth around for about 10 million times or extend to sun 2666 times. (Q: Justify!) (Earth from equator 40,000 km, distance to sun 150 million km)

- Still all the DNA in our body weighs around one kilogram (Q: Calculate)

- Everyday we produce about 60 billion new cells, replicationg over 100 billion meters of DNA which is a distance to Mars and back (mars is about 50 million km from Earth).



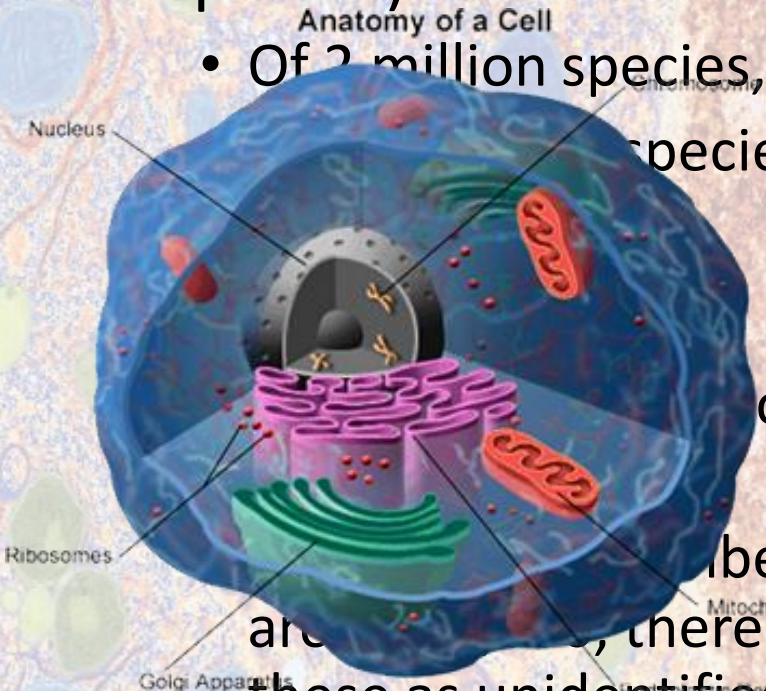
MBG303 Biochemistry

Chapter 9: Cells, The Fundamental Units of Life

Hikmet Geçkil, Professor
Department of Molecular Biology and Genetics
Inonu University

Unity and Diversity of Cells

– there may be up to 100 million distinct species of living things on our planet (2 million known species).



- Of 2 million species, are about 1 million insects

  species

one of the smallest groups, with

ber of knownbacteria species is

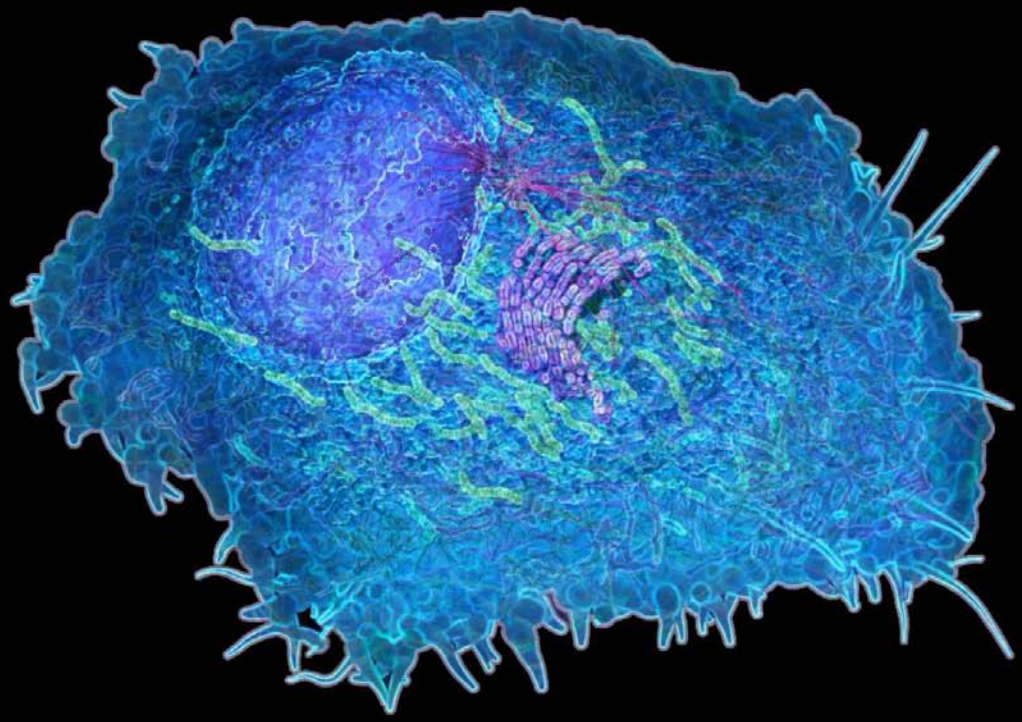
are , there may be 100 and 1000 times of of these as unidentified bacteria

Cells Vary Enormously in Appearance and Function

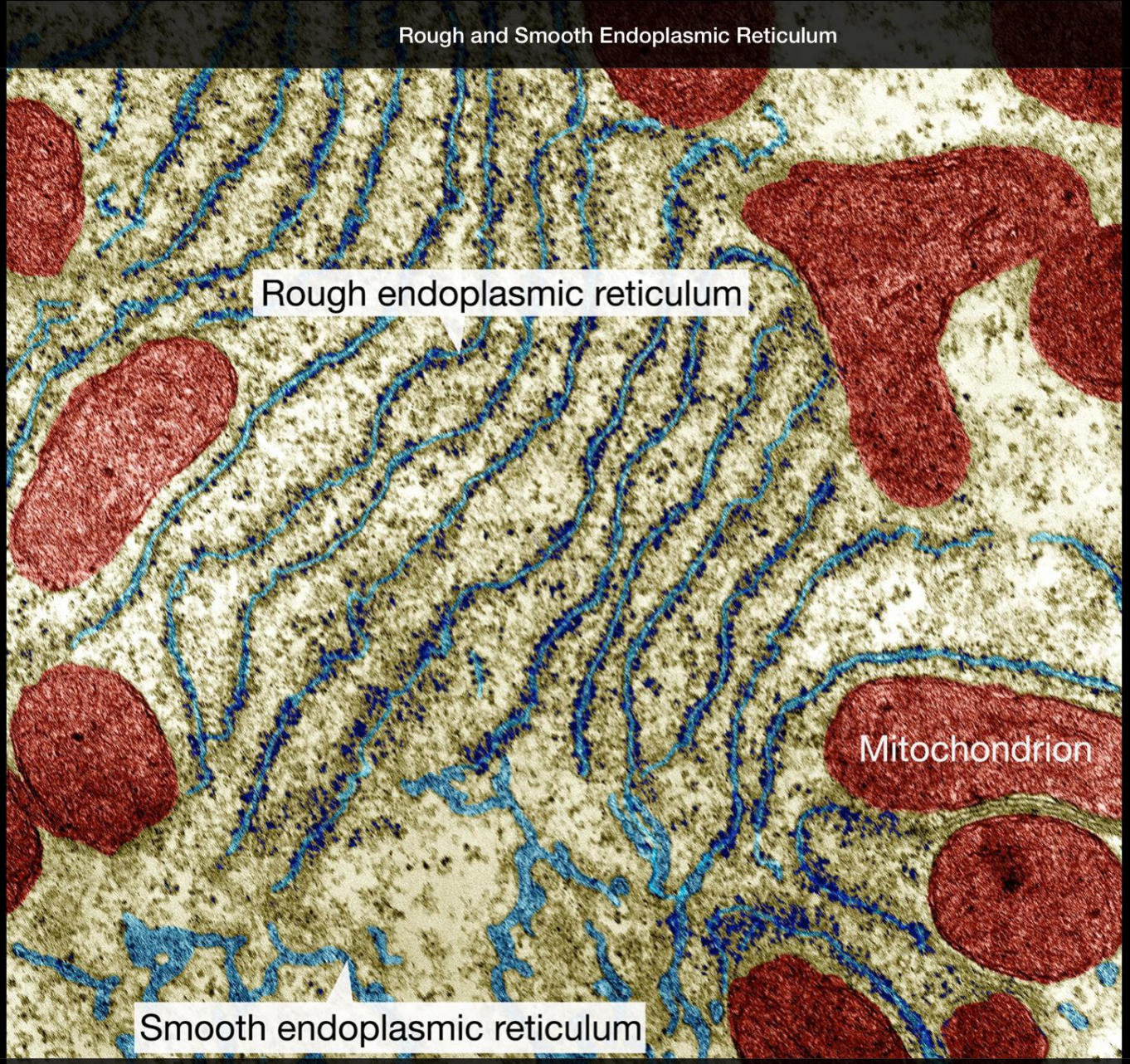
- A bacterial is a few micrometers, or µm, in length. That's about 25 times smaller than the width of a human hair.
- A frog egg is also a single cell and has a diameter of about 1 millimeter.
- If we scaled them up to make the *a bacterium the size of a person, the frog egg would be 800 meter* high

Structures of the Cell

Cell Membrane | Ribosomes | Endoplasmic Reticulum | Golgi Apparatus | Mitochondria | Cytoskeleton | Nucleus



Rough and Smooth Endoplasmic Reticulum

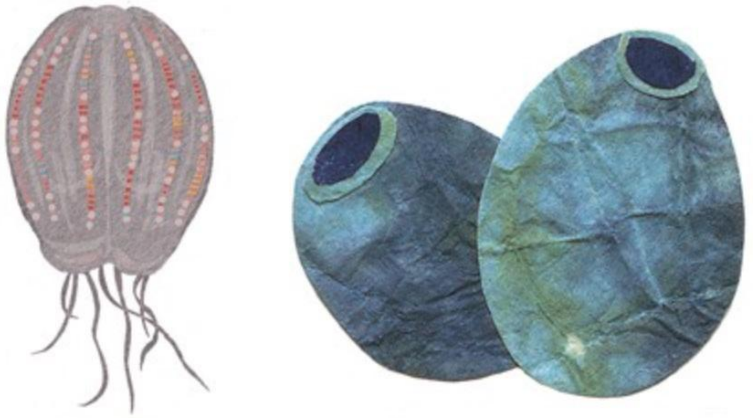


This colorized electron micrograph shows rough and smooth endoplasmic reticulum (blue) and nearby mitochondria (red). The black dots studding the surface of the rough endoplasmic reticulum are ribosomes, the protein-synthesizing machines of the cell. Ribosomes that are making proteins destined to remain embedded in cellular membranes become attached to the endoplasmic reticulum and extrude the new proteins into the membrane surface. Smooth endoplasmic reticulum is the site of lipid synthesis for the creation of new membrane for these and other organelles.

A brief history of life

1¼ billion years ago
The first multicellular lifeforms—primitive algae—appear in the ocean.





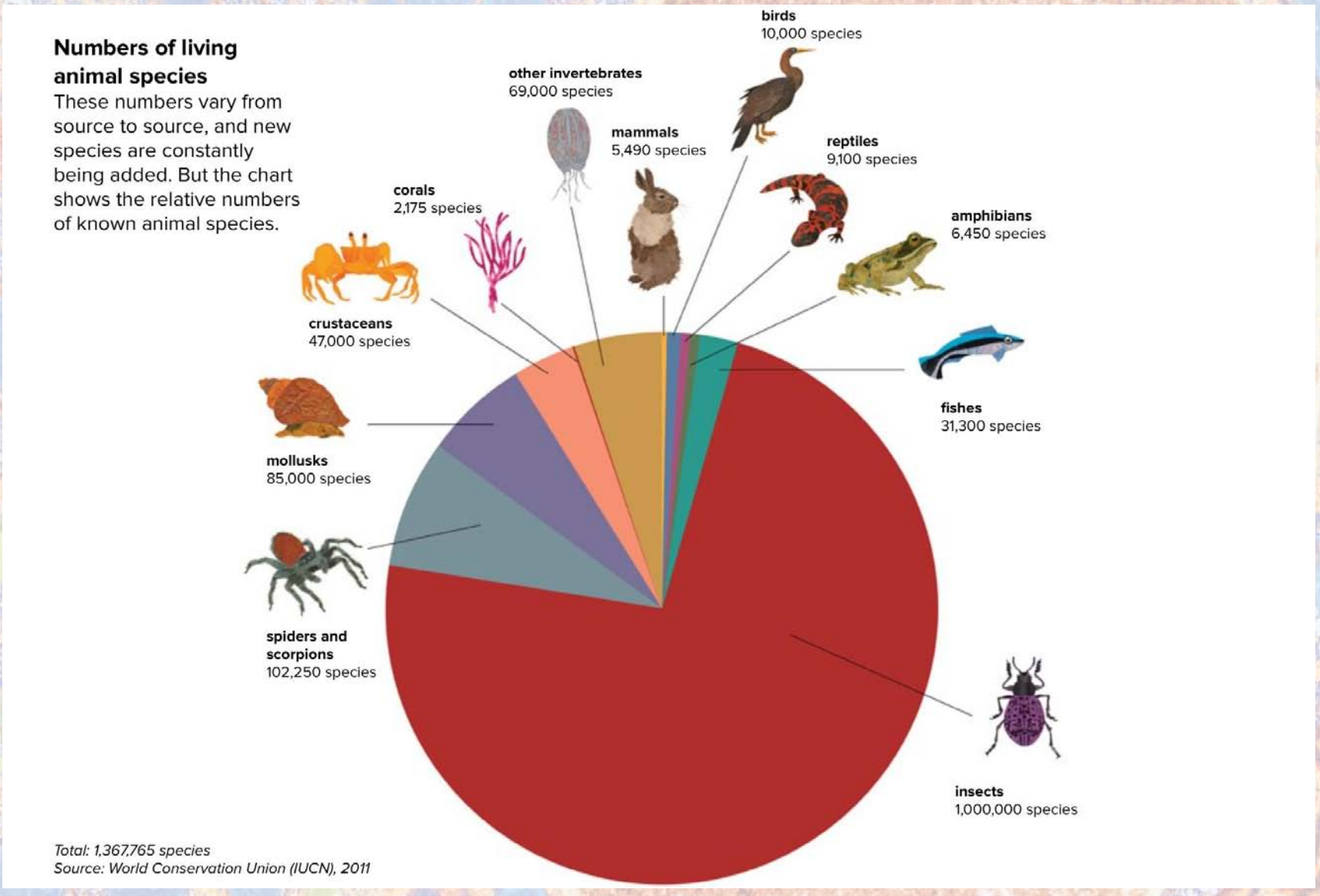
3½ billion years ago
The first single-celled organisms appear.

650 million years ago
The first animals—comb jellies, jellyfishes, and sponges—are living in the seas.

Millions and millions

Based on the way animals look and behave—skeleton or no skeleton, hair or scales, swimmers or flyers—they are sorted into different groups. A species is the basic group used by biologists to categorize the animal world. Members of the same species usually look alike, act alike, and can mate and produce offspring. So far, almost 1½ million species of animals have been named. Another 17,000 or so are added every year. The total number of living animal species could be 10 million or more.

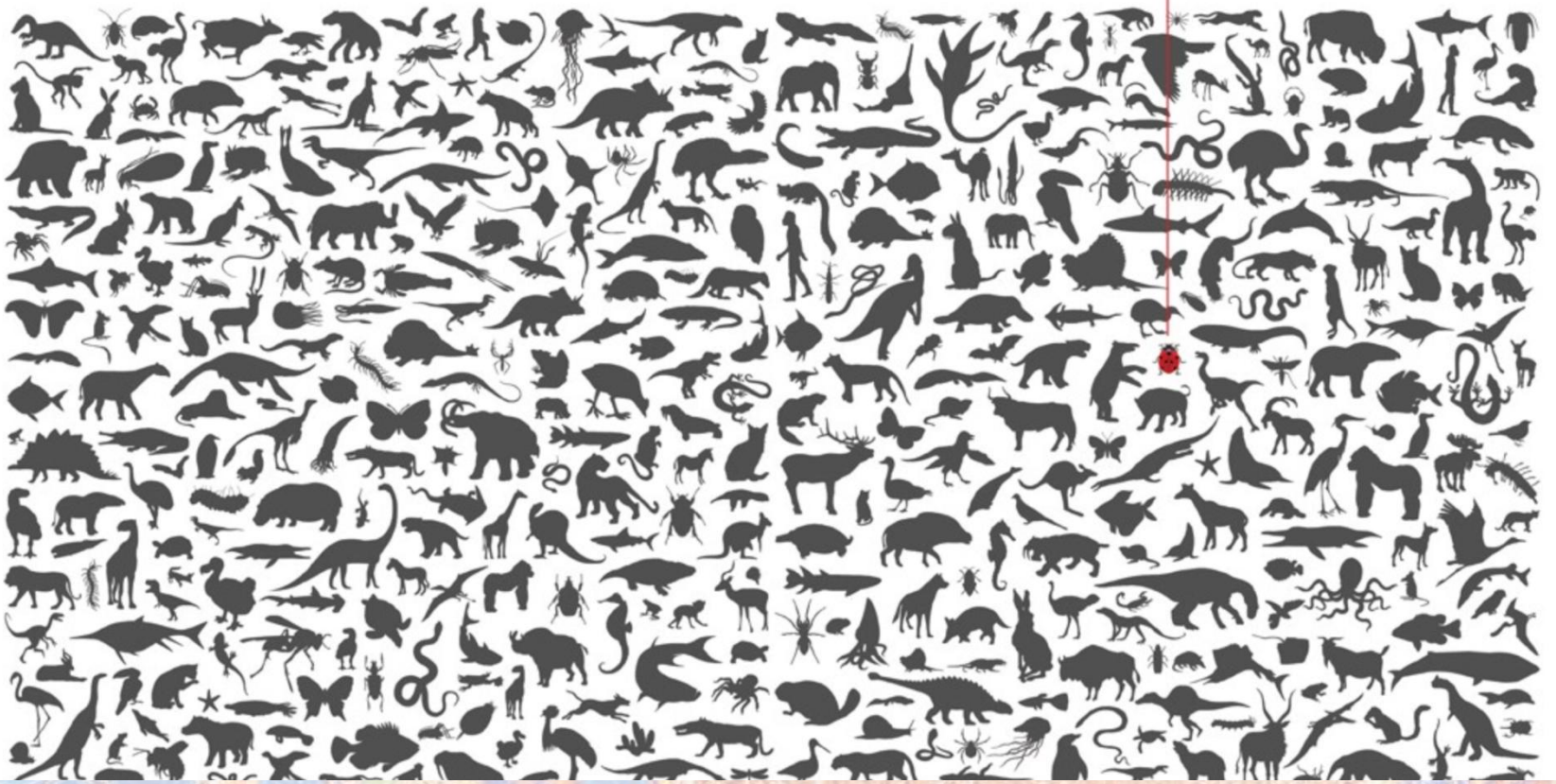


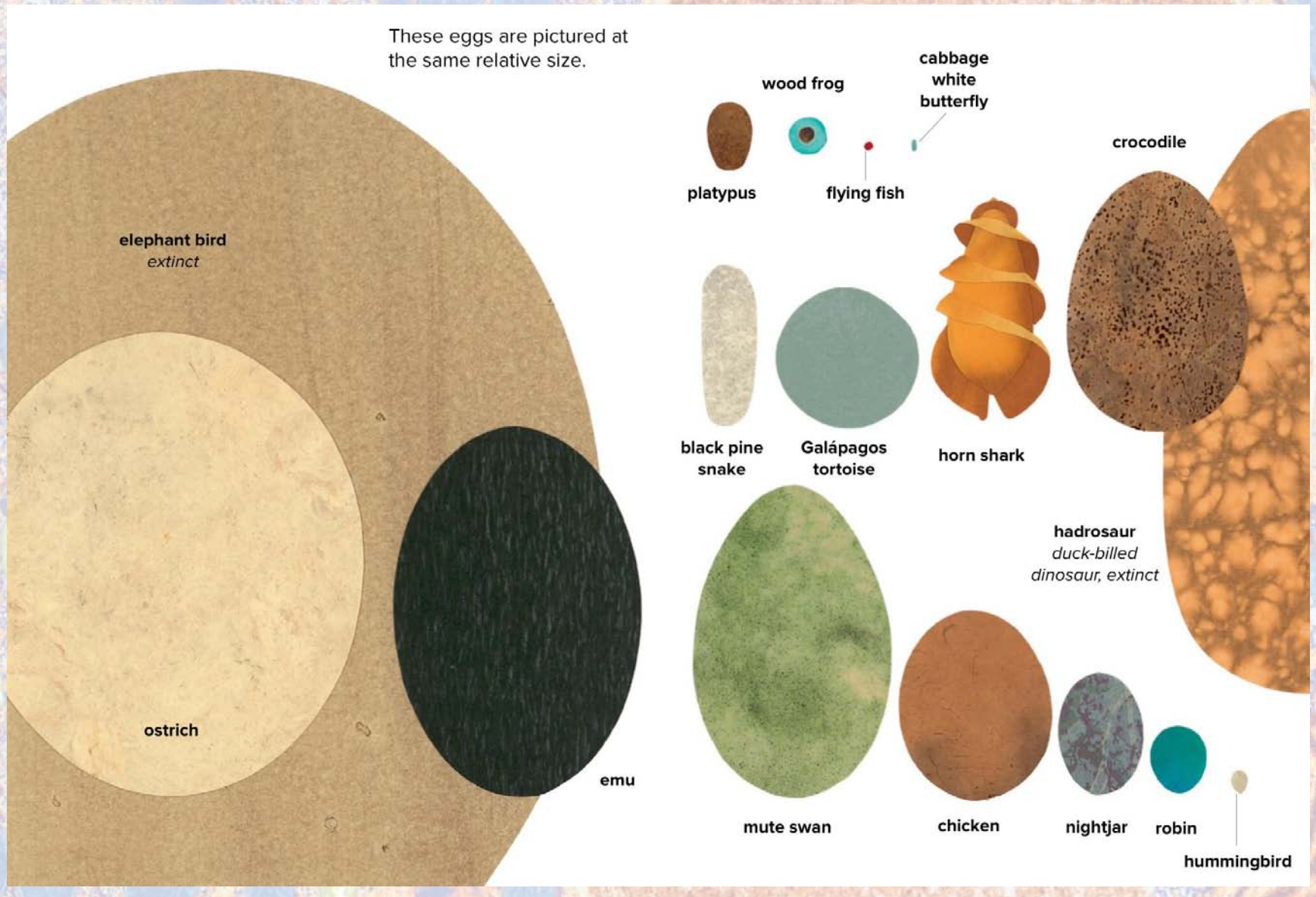

Numbers of living animal species
These numbers vary from source to source, and new species are constantly being added. But the chart shows the relative numbers of known animal species.
birds
10,000 species
other invertebrates
69,000 species
mammals
5,490 species
reptiles
9,100 species
corals
2,175 species
amphibians
6,450 species
crustaceans
47,000 species
fishes
31,300 species
mollusks
85,000 species
spiders and scorpions
102,250 species
insects
1,000,000 species
Total: 1,367,765 species
Source: World Conservation Union (IUCN), 2011

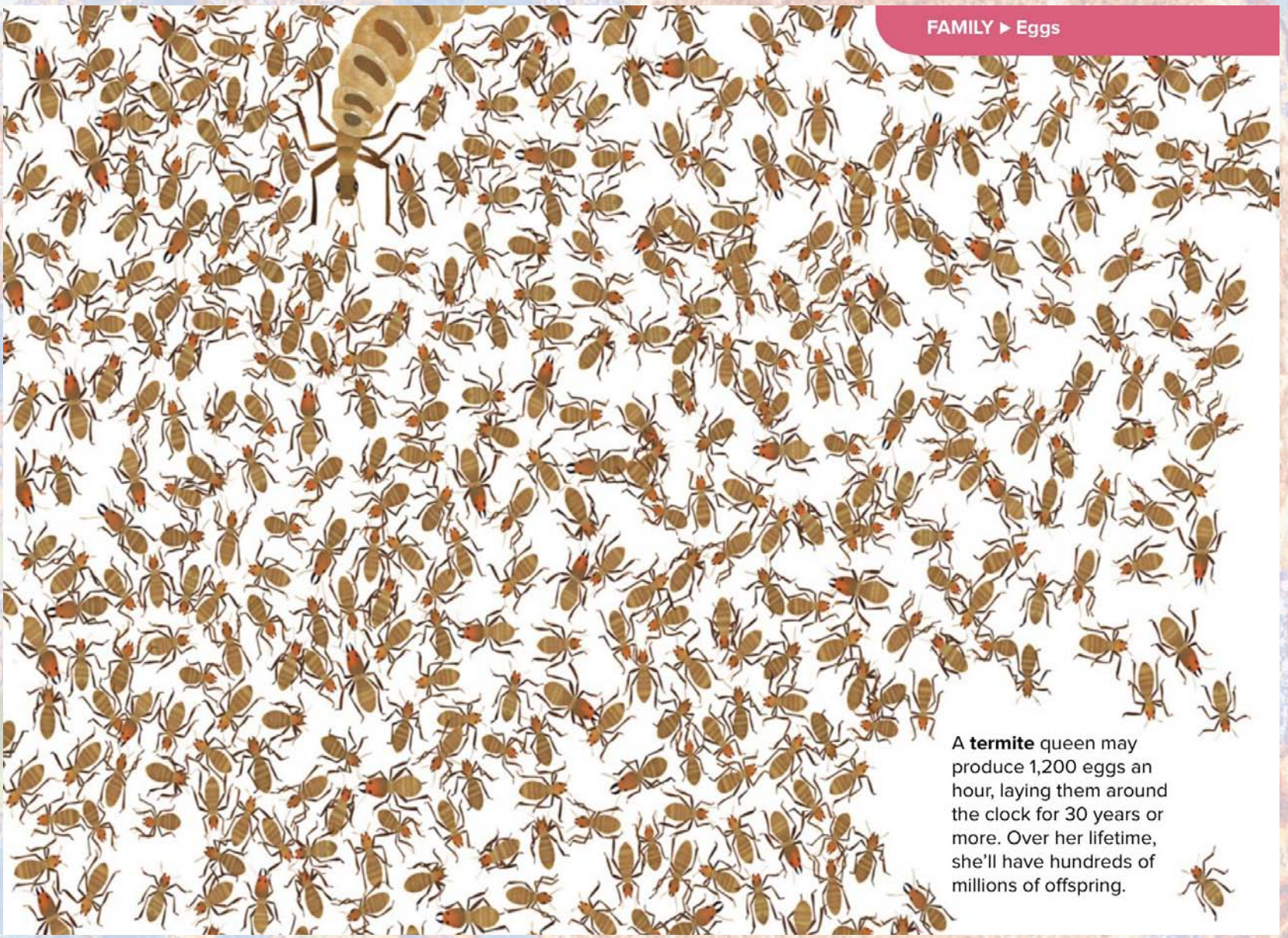
More animals are extinct.

The bad news: on average, an animal species becomes extinct after about 10 million years. The good news: modern humans have existed for only about 200,000 years.

For every species alive today, there are probably 1,000 that have died out, or gone extinct.



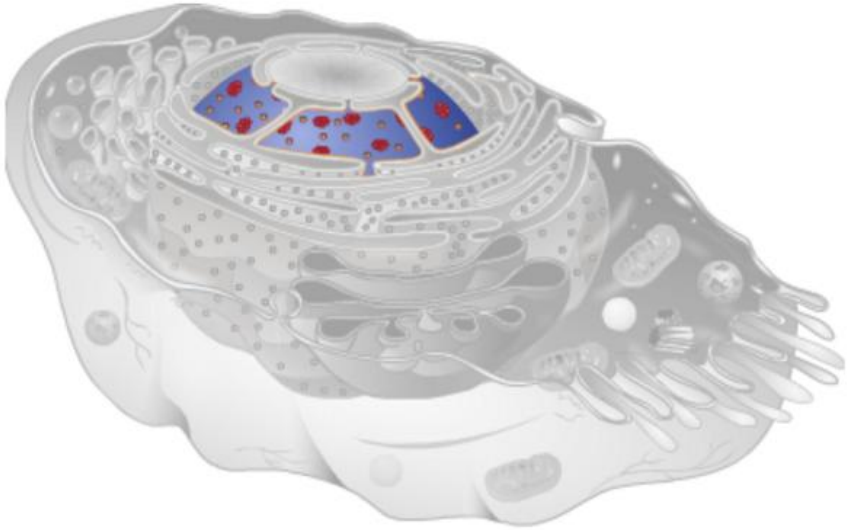

These eggs are pictured at the same relative size.
elephant bird
extinct
ostrich
emu
wood frog
cabbage white butterfly
platypus
flying fish
crocodile
black pine snake
Galápagos tortoise
horn shark
hadrosaur
duck-billed dinosaur, extinct
mute swan
chicken
nightjar
robin
hummingbird


FAMILY ▸ Eggs
A **termite** queen may produce 1,200 eggs an hour, laying them around the clock for 30 years or more. Over her lifetime, she'll have hundreds of millions of offspring.

A typical animal cell.

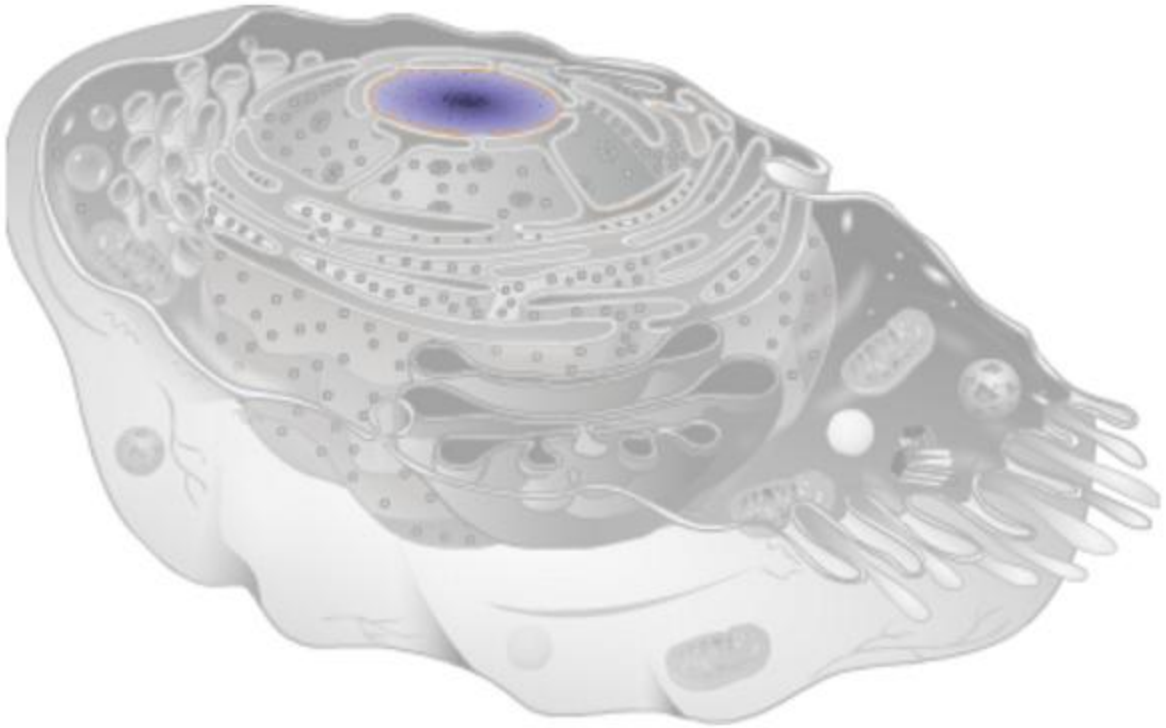
A view inside an animal cell. Notice the structures that are not present in plant cells: the centrosome, centrioles, and lysosomes. Remember that cells are dynamic. The position and shape of many cell structures change from one moment to the next.

- Nucleus
- Nucleolus
- Rough endoplasmic reticulum
- Smooth endoplasmic reticulum
- Mitochondria
- Ribosome
- Plasma membrane
- Golgi apparatus
- Peroxisome
- Food Vacuole
- Lysosome
- Centrosome
- Centriole



The nucleus is the control center of the cell, processing inputs from the cytoplasm, storing and retrieving information, and carrying out instructions contained within the genetic material in the nucleus. It is bound by a double-membrane called the nuclear envelope.

- Nucleus
- Nucleolus
- Rough endoplasmic reticulum
- Smooth endoplasmic reticulum
- Mitochondria
- Ribosome
- Plasma membrane
- Golgi apparatus
- Peroxisome
- Food Vacuole
- Lysosome
- Centrosome
- Centriole



The dense center of the nucleus is the nucleolus, which synthesizes ribosomal RNA.

X

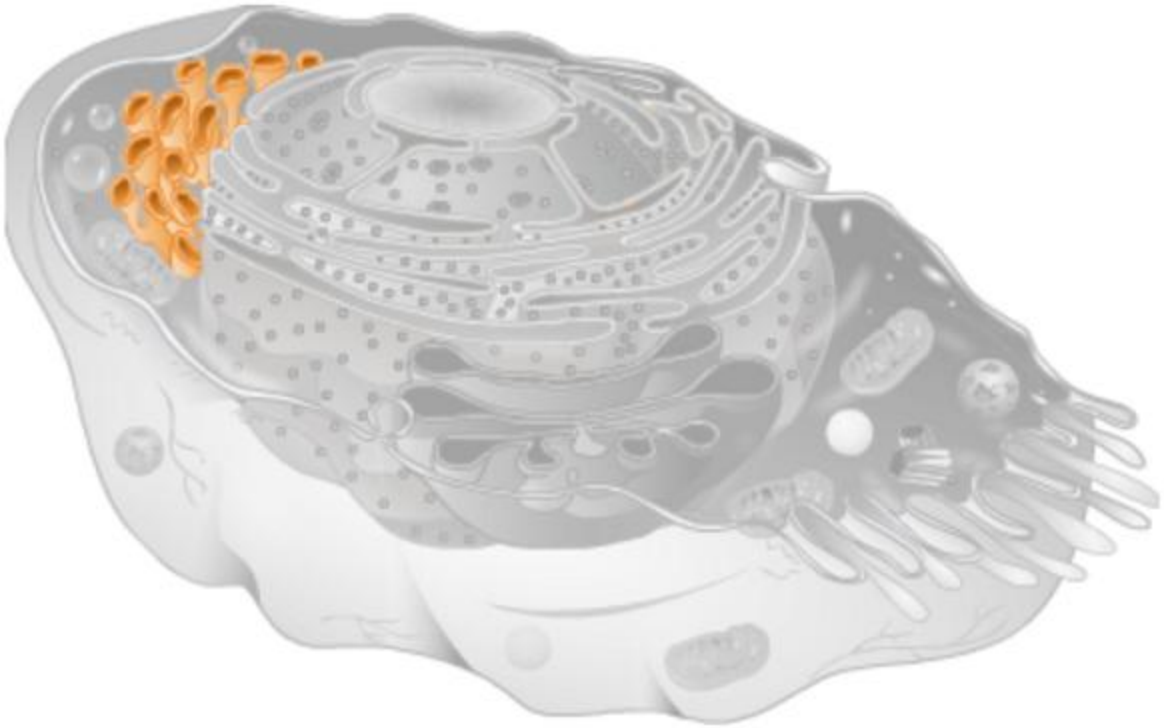
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- Peroxisome
- Food Vacuole
- Lysosome
- Centrosome
- Centriole



The endoplasmic reticulum (ER) is an extensive network of membrane-enclosed compartments that connect directly to the nuclear envelope. Rough endoplasmic reticulum (RER) appears rough because it is studded with ribosomes. The rough ER is the site of secretory protein synthesis, and is also a source of membrane phospholipids.

X

- Nucleus
- Nucleolus
- Rough endoplasmic reticulum
- Smooth endoplasmic reticulum
- Mitochondria
- Ribosome
- Plasma membrane
- Golgi apparatus
- Peroxisome
- Food Vacuole
- Lysosome
- Centrosome
- Centriole



The endoplasmic reticulum (ER) is an extensive network of membrane-enclosed compartments that connect directly to the nuclear envelope. Smooth endoplasmic reticulum does not contain ribosomes. It is primarily involved in lipid synthesis, modification of carbohydrates, calcium ion storage, and in breaking down some toxic substances.

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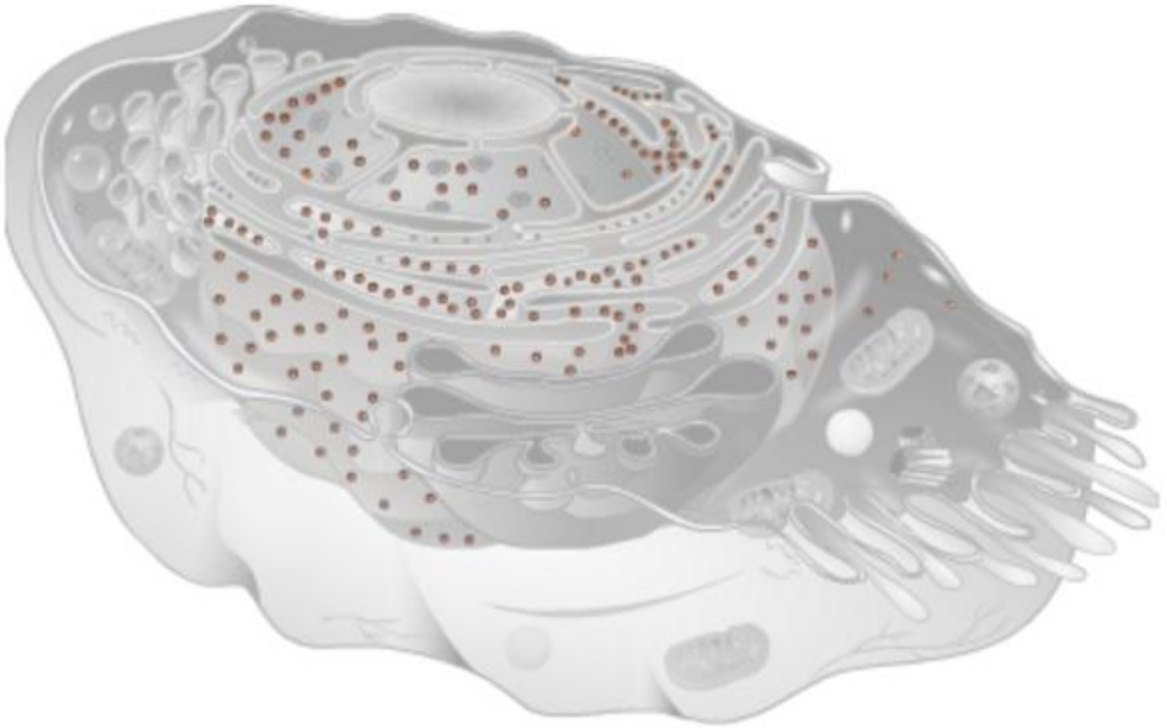
- Nucleus
- Nucleolus
- Rough endoplasmic reticulum
- Smooth endoplasmic reticulum
- Mitochondria
- Ribosome
- Plasma membrane
- Golgi apparatus
- Peroxisome
- Food Vacuole
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Mitochondria are the energy powerhouses of the cell. These organelles synthesize ATP, the cell's main energy source, through cellular respiration.

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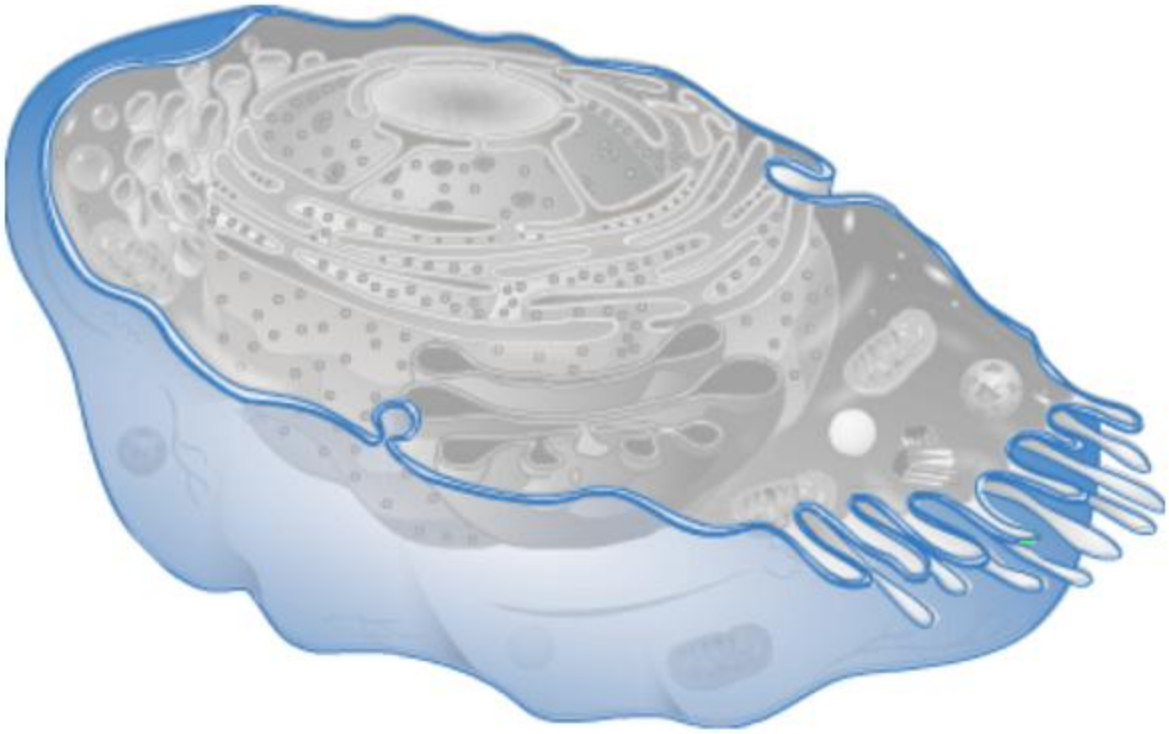
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Ribosomes are the protein-producing factories of the cell. They are located in the cytoplasm or attached to the rough endoplasmic reticulum.

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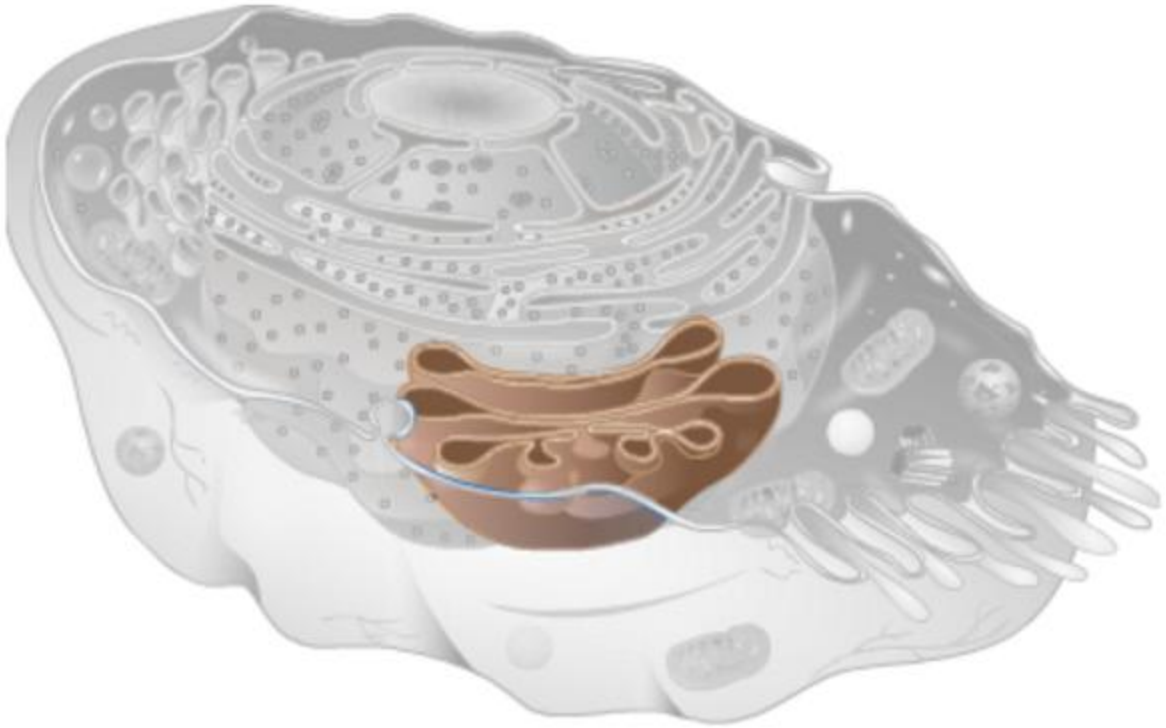
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The plasma membrane is the outer barrier of the cell and is composed of a phospholipid bilayer that contains proteins and cholesterol. It regulates what can enter and exit the cell.

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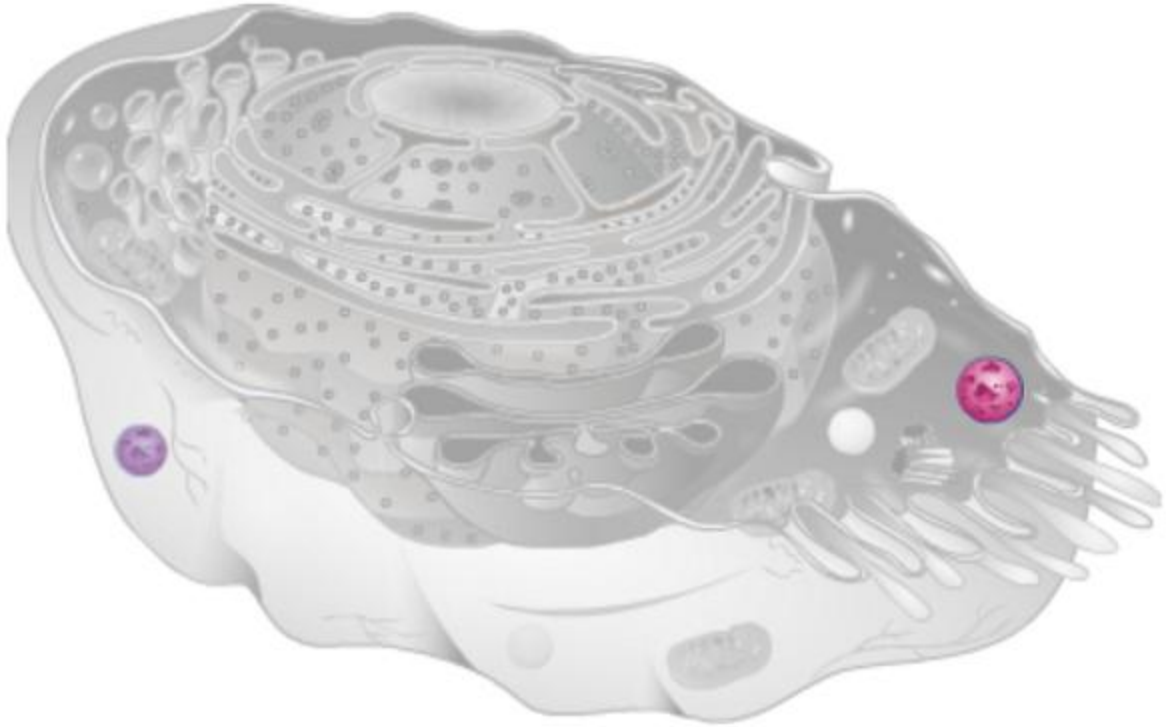
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The Golgi apparatus is the "shipping and receiving" center of the cell's endomembrane system. This organelle modifies, stores, and exports substances from the cell.

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Peroxisomes contain enzymes that break down molecules by removing hydrogen and transferring the hydrogen to oxygen molecules to create hydrogen peroxide. This reaction can serve many purposes including detoxifying substances such as metabolic waste or ingested toxins including alcohol and drugs.

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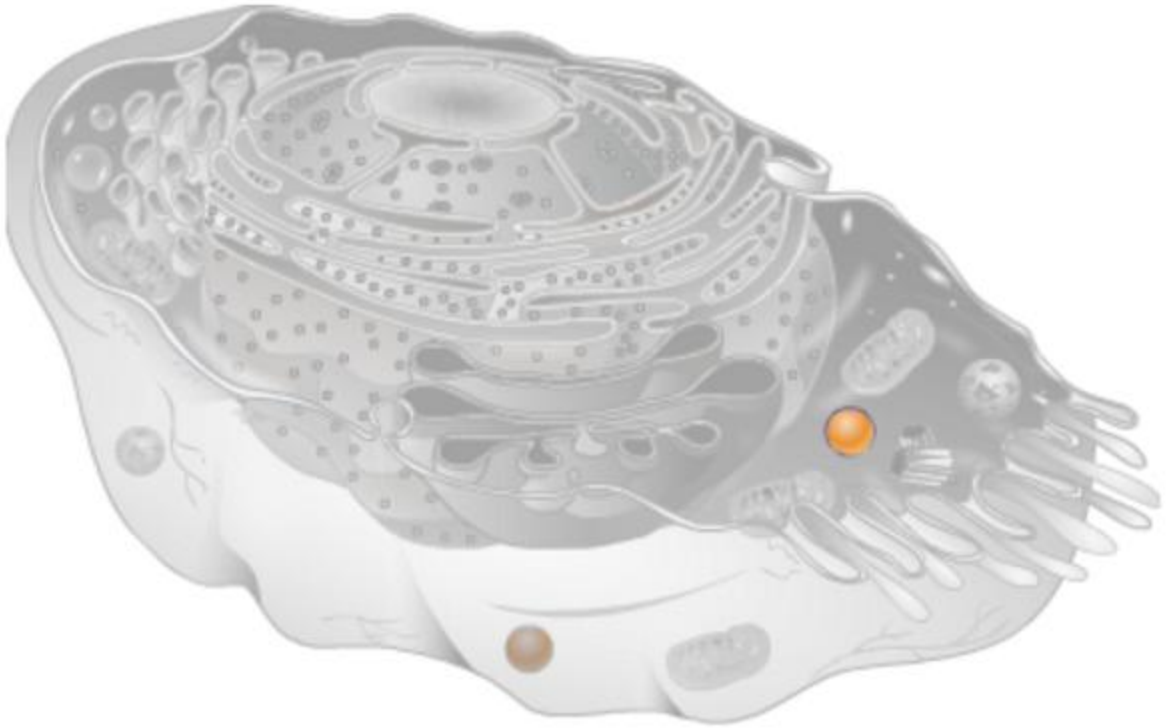
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A food vacuole is a vesicle inside the cytoplasm of the cell which contains an engulfed food item. It will bind with the lysosome to be digested.

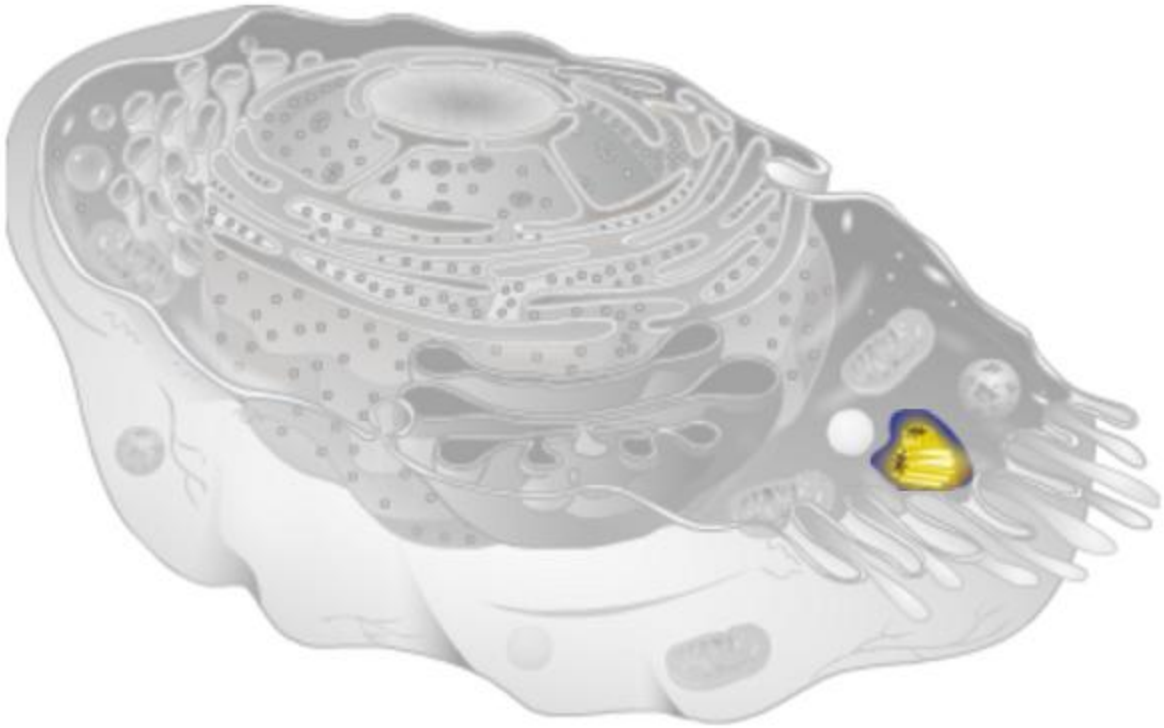
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Lysosomes are vesicles containing powerful enzymes that digest food items engulfed by the cell. X

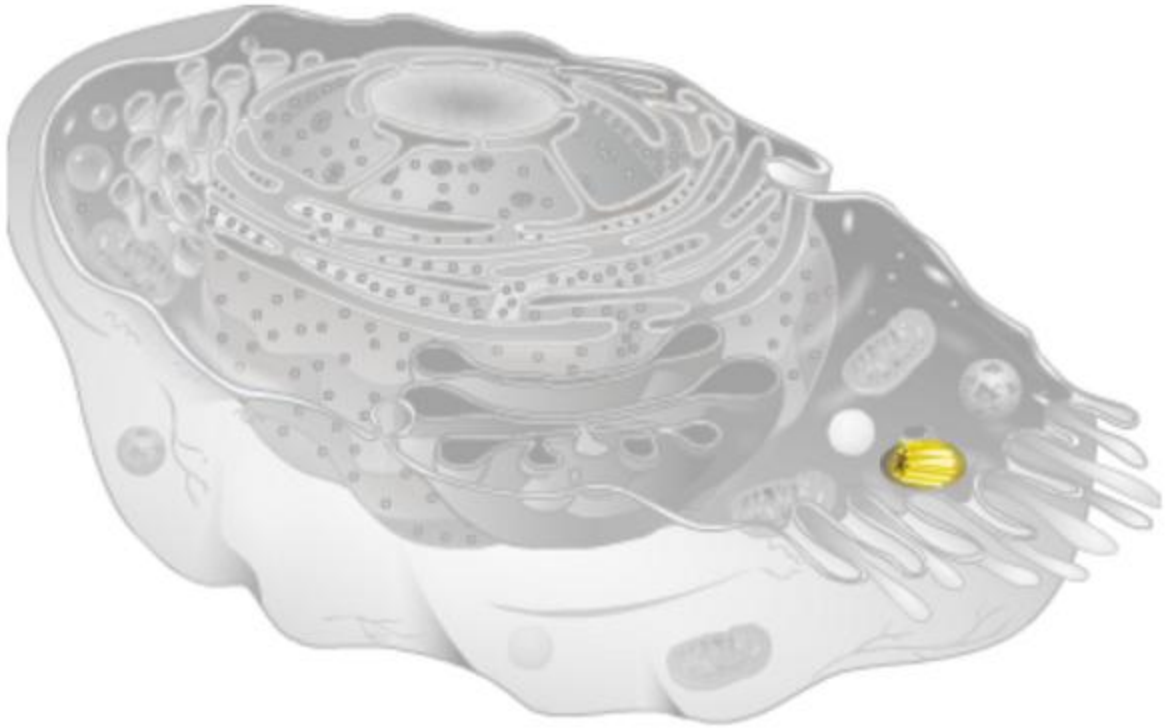
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The centrosome is the microtubule organizing center of the cell and functions primarily in animal cell division.

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Centrioles are within the centrosome. They help organize the mitotic spindle and function in cytokinesis in some animals.

X