HBC 109

BIOMOLECULES

LECTURE 5: The molecular structure, properties and functions of amino acids.

LECTURE 6: The molecular structure, properties and functions of Proteins.

March 10 - 17 2022

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Course Outline

WK	DATE	TOPIC
1	10/02	The occurrence of biomolecules in prokaryotic and eukaryotic cells.
1	10/02	The hierarchy of biomolecular organization.
2	17/02	The molecular structure, properties and functions of monosaccharides.
3	24/03	The molecular structure, properties and functions of disaccharides and polysaccharides.
5	10/03	The molecular structure, properties and functions of amino acids.
6	17/03	The molecular structure, properties and functions of polypeptides
7	21/03	**MONDAY 10AM – 11AM (CAT 1)**

AMINO ACIDS

Proteins are the indispensable agents of biological function, and **amino acids are** the building blocks of proteins. The stunning diversity of the thousands of proteins found in nature arises from the intrinsic properties of only 20 commonly occurring amino acids.

These features include:

- the capacity to polymerize,
- varied structure and chemical functionality in the AA side chains, and
- chirality.

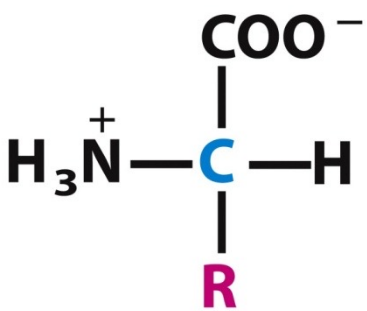
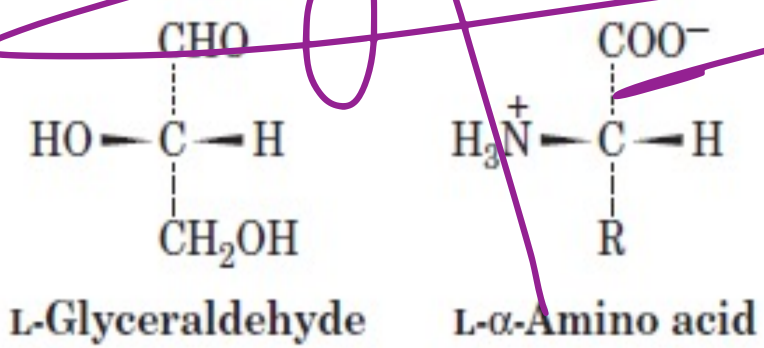


Figure 3-2 Lehninger Principles of Biochemistry, Fifth Edition © 2008 W.H. Freeman and Company



Only L-amino acids are found in proteins.

Genetic code

The code defines how sequences of these nucleotide triplets, called *codons*, specify which amino acid will be added during protein synthesis

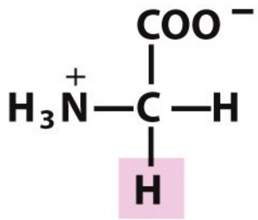
Second Letter

1st letter	U		C		A		G		3rd letter
U	UUU UUC UUA UUG	Phe Leu	UCU UCC UCA UCG	Ser	UAU UAC UAA UAG	Tyr Stop Stop	UGU UGC UGA UGG	Cys Stop Trp	U C A G
C	CUU CUC CUA CUG	Leu	CCU CCC CCA CCG	Pro	CAU CAC CAA CAG	His Gln	CGU CGC CGA CGG	Arg	U C A G
A	AUU AUC AUA AUG	Ile Met	ACU ACC ACA ACG	Thr	AAU AAC AAA AAG	Asn Lys	AGU AGC AGA AGG	Ser Arg	U C A G
G	GUU GUC GUA GUG	Val	GCU GCC GCA GCG	Ala	GAU GAC GAA GAG	Asp Glu	GGU GGC GGA GGG	Gly	U C A G

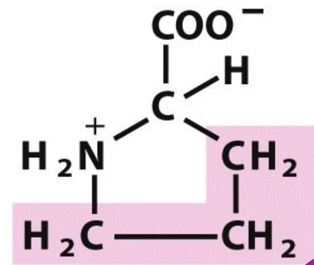
- The start codon is AUG. Methionine is the only amino acid specified by just one codon, AUG. The stop codons are UAA, UAG, and UGA. They encode no amino acid.
- The stretch of codons between AUG and a stop codon is called an open reading frame.

Properties of AA

All the amino acids except proline have both free -amino and free -carboxyl groups.



Glycine



Proline

There are several ways to classify the common amino acids. The most useful of these classifications is based on the polarity of the side chains:

(1) **nonpolar** or hydrophobic amino acids,
(2) neutral (uncharged) but **polar** amino acids,
(3) **acidic** amino acids (which have a net negative charge at neutral pH), and
(4) **basic** amino acids (which have a net positive charge at neutral pH).
(5) **Aromatic** amino acids

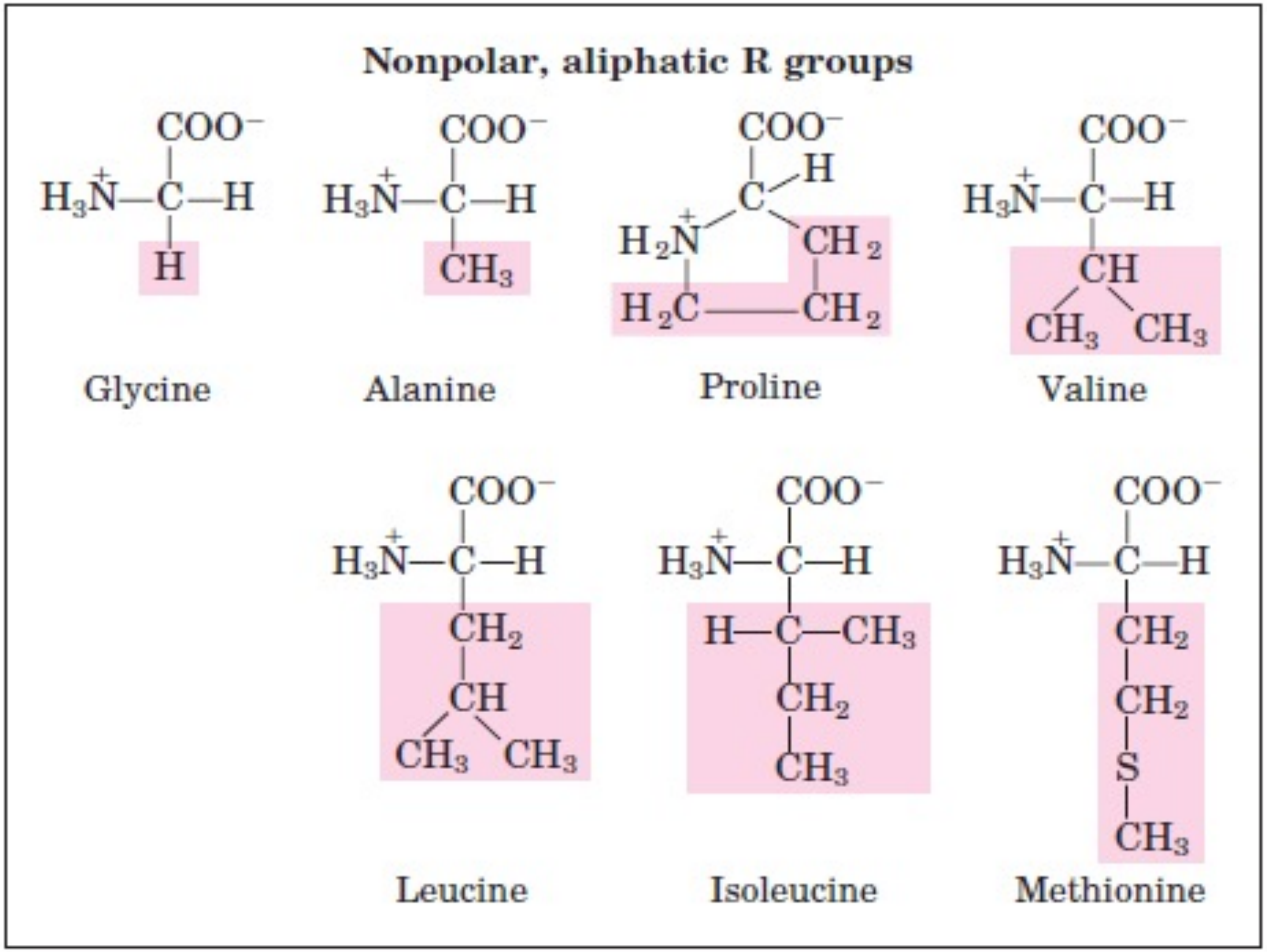
Essential Amino Acids

- There are 10 amino acids that are essential amino acids because they cannot be synthesized in the human body and must be obtained in the diet.
- The 10 essential amino acids are: valine, leucine, isoleucine, phenylalanine, methionine, tryptophan, threonine, histidine, lysine, and arginine.
- Two of these amino acids, arginine and histidine, are essential in children, but not adults.
- Proteins that contain all the essential amino acids are called ***complete proteins***.
- Soybeans and most proteins found in animal products are complete proteins.
- Some plant proteins are incomplete proteins because they lack one or more essential amino acid.

classification of AA

- Common amino acids can be placed in five basic groups depending on their R substituents:

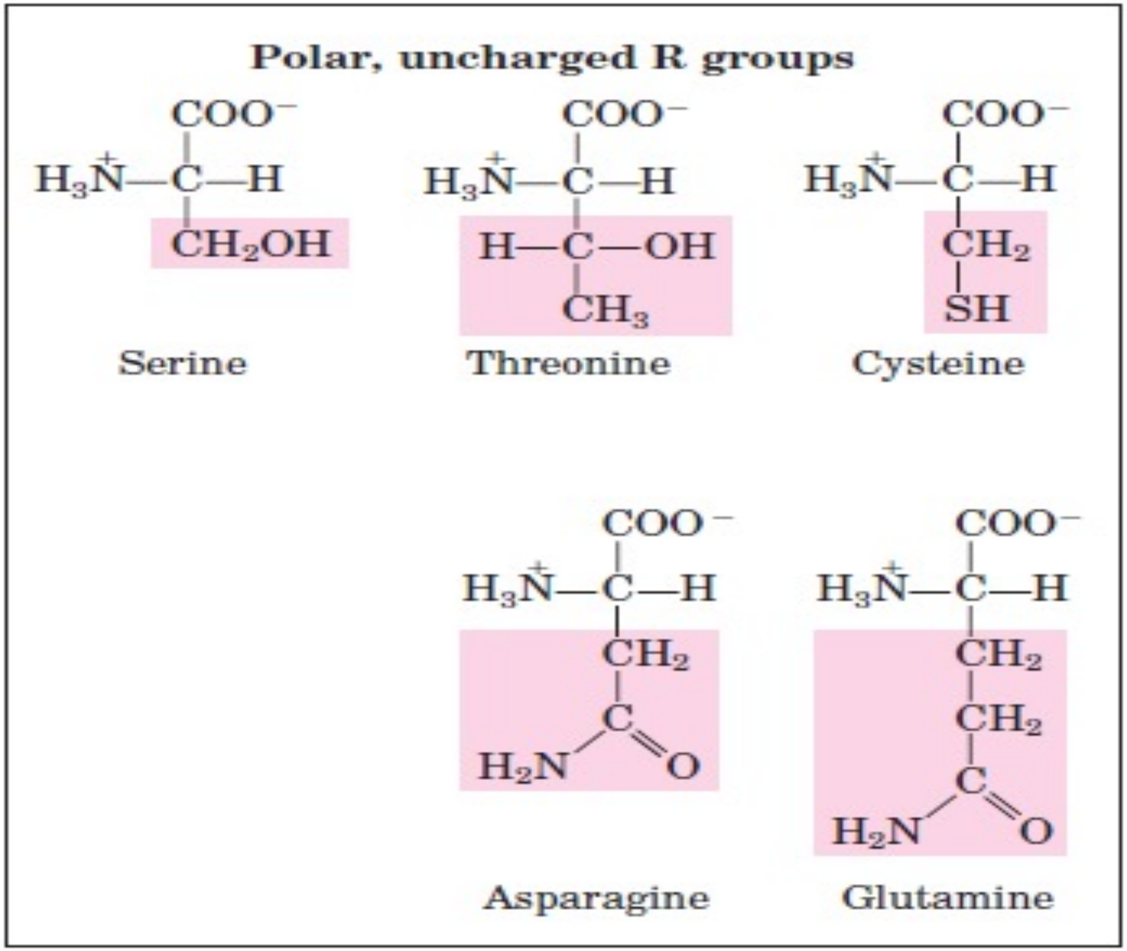
- Nonpolar, aliphatic (7)
- Aromatic (3)
- Polar, uncharged (5)
- Positively charged (3)
- Negatively charged (2)



❖ The R groups in this class of amino acids are **nonpolar and hydrophobic**. The sidechains of **glycine, alanine, valine, leucine, and isoleucine** tend to cluster together within proteins, stabilizing protein structure by means of hydrophobic interactions.

❖ **Methionine,** one of the two sulfur-containing amino acids, has a nonpolar thioether group in its side chain.

❖ **Proline** has an aliphatic side chain with a distinctive cyclic structure. The secondary amino (imino) group of proline residues is held in a rigid conformation that reduces the structural flexibility of polypeptide regions containing proline.



❖ The R groups of these amino acids are more soluble in water, or more hydrophilic, than those of the nonpolar amino acids, because they contain functional groups that form hydrogen bonds with water.

❖ Includes **serine, threonine, cysteine, asparagine, and glutamine.**

❖ The polarity of serine and threonine is contributed by their -OH groups;

❖ The polarity of cysteine is contributed by its –SH group;

❖ The polarity of Asparagine and glutamine by their amide (H_2N) groups.

❖ Cysteine is readily oxidized to form a covalently linked dimeric amino acid called **cystine,** in which two cysteine molecules or residues are joined by a disulfide bond.

disulfide bond formed by cysteine

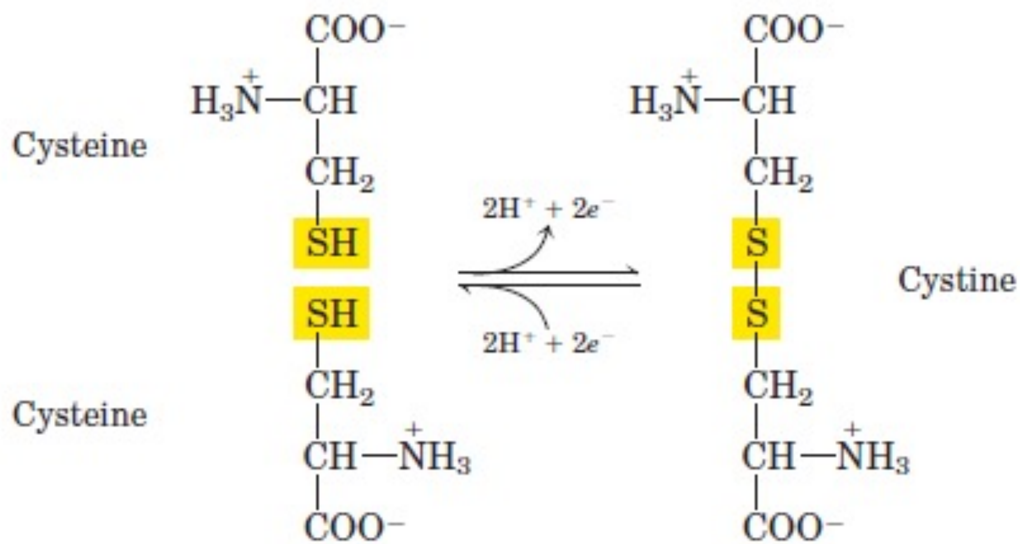
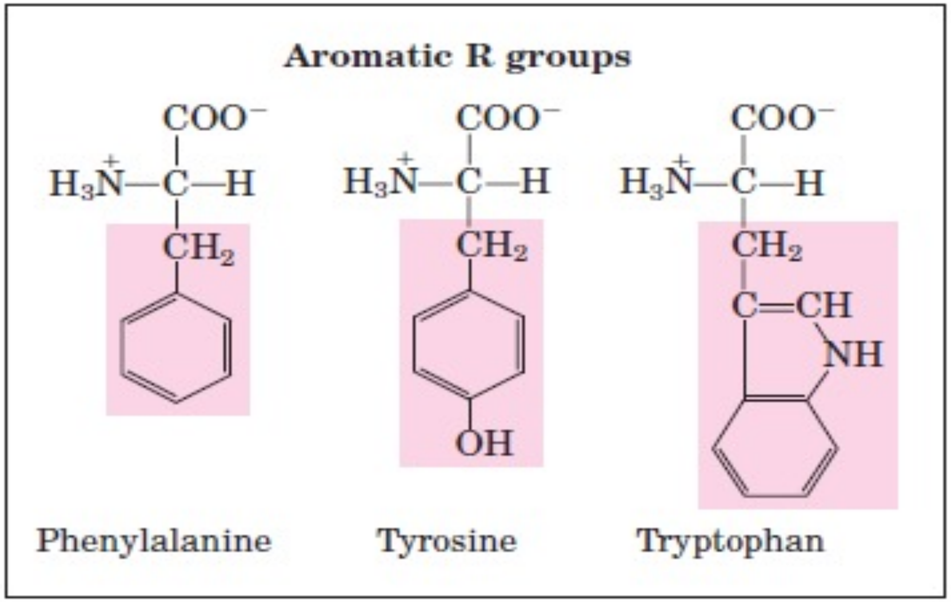


FIGURE 3–7 Reversible formation of a disulfide bond by the oxidation of two molecules of cysteine. Disulfide bonds between Cys residues stabilize the structures of many proteins.

Disulfide bonds play a special role in the structures of many proteins by forming covalent links between parts of a protein molecule or between two different polypeptide chains.

Aromatic R groups



- ***Phenylalanine, tyrosine, and tryptophan,*** with their aromatic side chains, are relatively nonpolar (hydrophobic).
- The -OH group of tyrosine can form hydrogen bonds, and it is an important functional group in some enzymes.
- Tyrosine and tryptophan are significantly more polar than phenylalanine, because of the tyrosine -OH group and the nitrogen of the tryptophan indole ring.

UV absoption spectra of aromatic AA

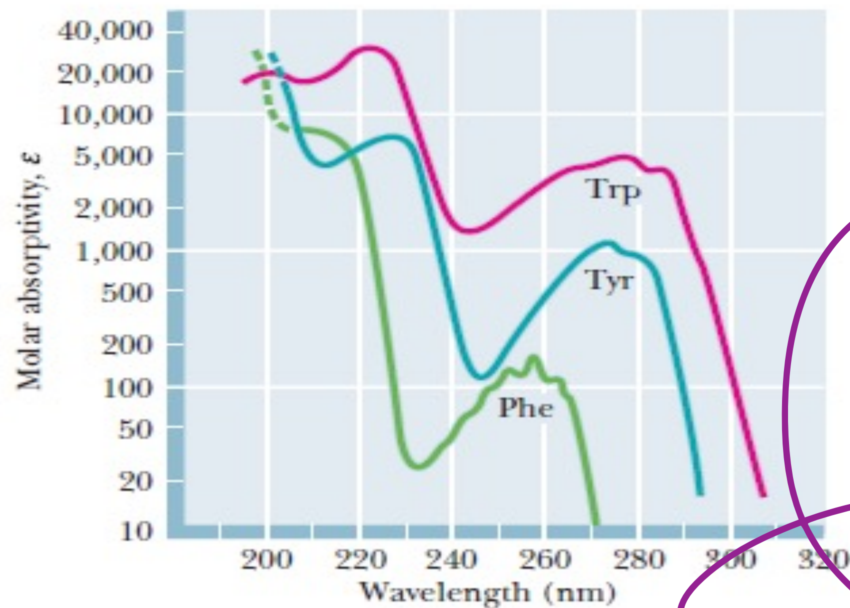


FIGURE 4.10 The ultraviolet absorption spectra of the aromatic amino acids at pH 6. (From Wetlaufer, D.B., 1962. Ultraviolet spectra of proteins and amino acids. *Advances in Protein Chemistry* **17**:303–390.)

- Tryptophan and tyrosine, and to a much lesser extent phenylalanine, absorb ultraviolet light.
- This accounts for the characteristic strong absorbance of light by most proteins at a wavelength of 280 nm, a property exploited by researchers in the characterization of proteins.
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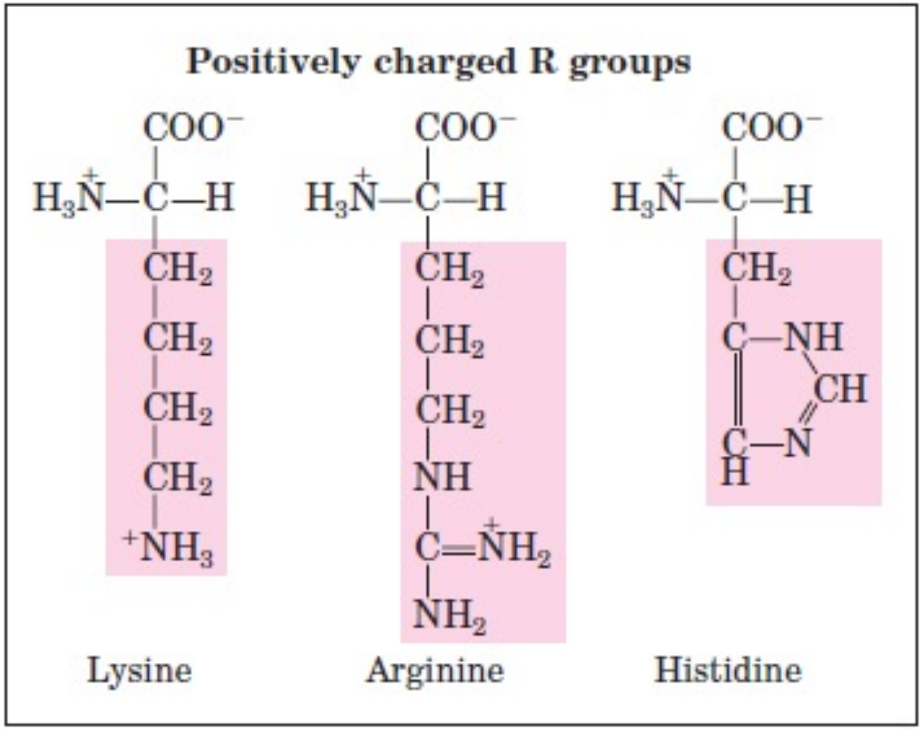
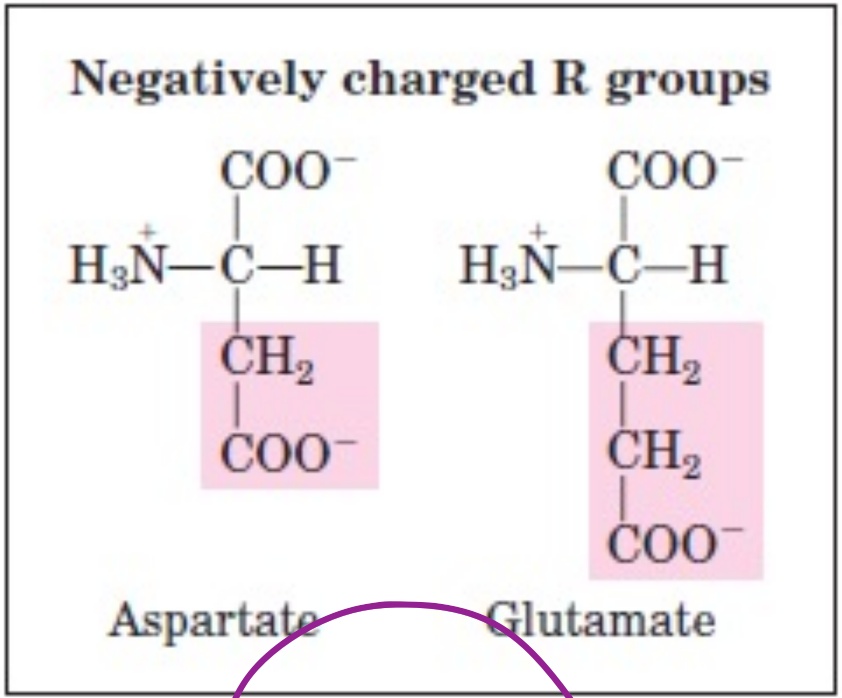
Positively charged R groups



- The R groups have significant positive charge at pH 7.0
  - **lysine:** has amino group at the *position* on its aliphatic chain;
  - **arginine:** which has a **positively** charged guanidino group;
  - **histidine,** which has an imidazole group.

Negatively charged R groups



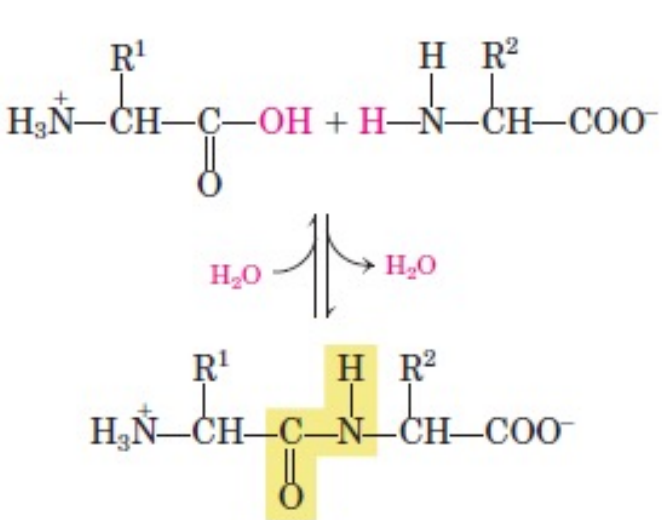
The two amino acids having R groups with a net negative charge at pH 7.0 are **aspartate** and **glutamate,** each of which has a second carboxyl group.

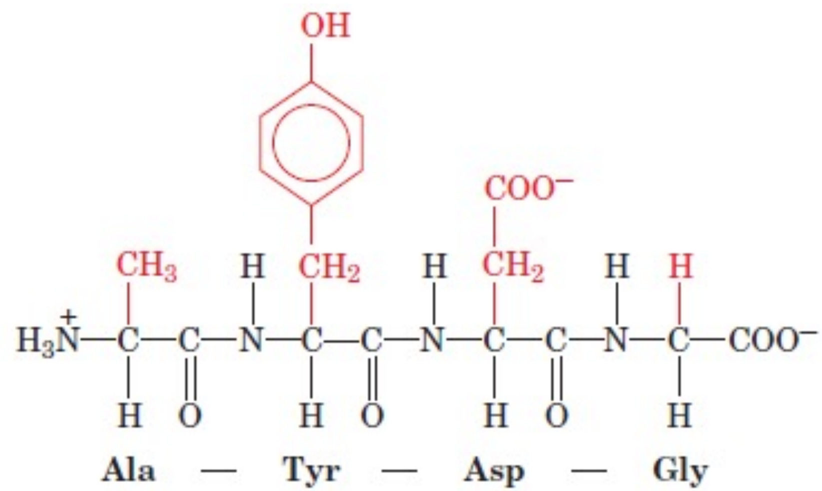
Aspartate and glutamate are formed from oxidation of asparagine and glutamine respectively

Peptide bond

Chemically, proteins are unbranched polymers of amino acids linked head to tail, from carboxyl group to amino group, through formation of covalent **peptide bonds,** a type of amide linkage

** Note that the carbonyl oxygen and the amide hydrogen are *trans to each other.*





This conformation is favored energetically because it results in less steric hindrance between nonbonded atoms in neighboring amino acids. Because the carbon atom of the amino acid is a chiral center (in all amino acids except glycine), the polypeptide chain is inherently asymmetric.

Function of Amino acids

Main functions

- building blocks of proteins
- Energy metabolites
- Source of essential nutrients, amino acids and their derivatives have many biologically important functions.

Function of Amino acids

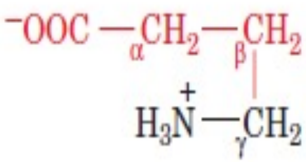
Specialized functions (by amino acid derivatives)

- Amino acids and their derivatives often function as **chemical messengers** in the communications between cells.
  - ✓ **γ-aminobutyric acid (GABA;** glutamate decarboxylation product),
  - ✓ **dopamine** (tyrosine derivative), and
  - ✓ **serotonin** (tyrosine derivative) all all are neurotransmitters (substances released by nerve cells to alter the behavior of their neighbours.
  - ✓ **Histamine (the decarboxylation product of histidine) is a** potent local mediator of allergic reactions;

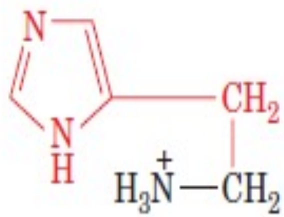
- AA derivatives function as **hormones:**
  - ✓ **Thyroxine** (a tyrosine derivative) is an iodine-containing thyroid hormone that generally stimulates vertebrate metabolism.
  - ✓ **Epinephrine** (also known as **adrenaline), derived from tyrosine,** is an important hormone.

- Certain AA derivatives are important intermediates in various metabolic processes.
  - ✓ **citrulline** and **ornithine,** intermediates in urea biosynthesis;
  - ✓ **homocysteine,** an intermediate in amino acid metabolism.

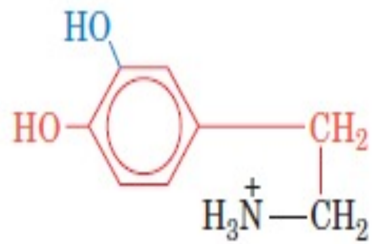
AA derivatives with special functions



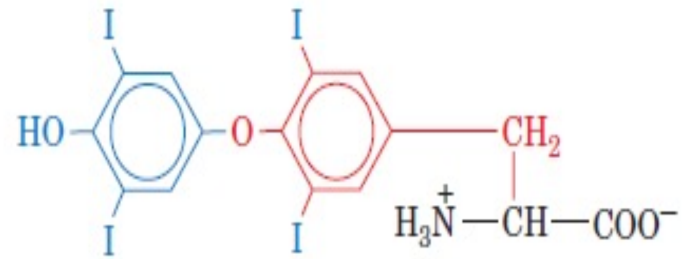
γ-Aminobutyric acid (GABA)



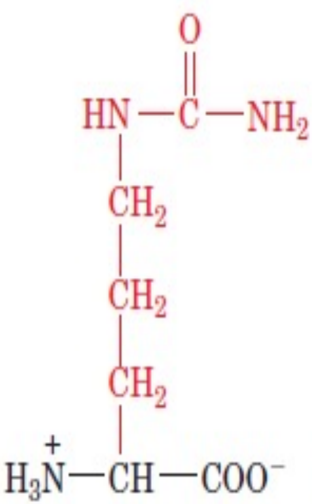
Histamine



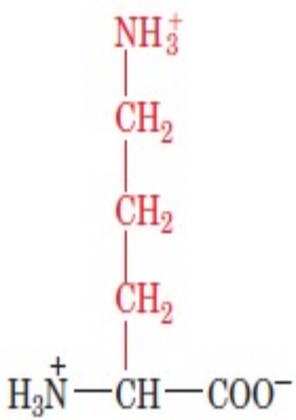
Dopamine



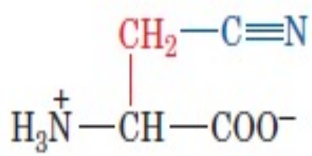
Thyroxine



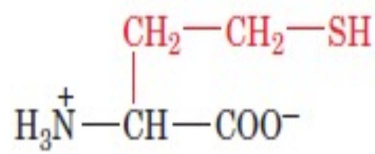
Citrulline



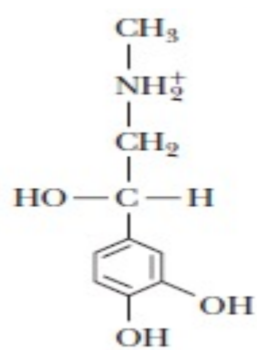
Ornithine



β-Cyanoalanine



Homocysteine



Epinephrine

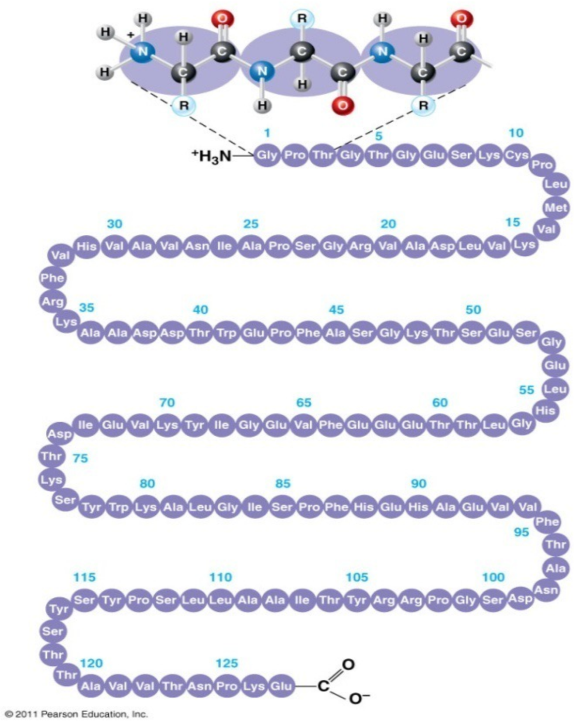
Structure of proteins

The following are the four levels of protein structure:

1. ***Primary (1^o)*** refers to amino acid sequence.
2. ***Secondary (2^o)*** consists of an alpha helix and a beta-pleated sheet.
3. ***Tertiary (3^o)*** refers to the folding of the 2^o structure.
4. ***Quaternary (4^o)*** involves the interaction of two or more polypeptides to form a biologically active protein.

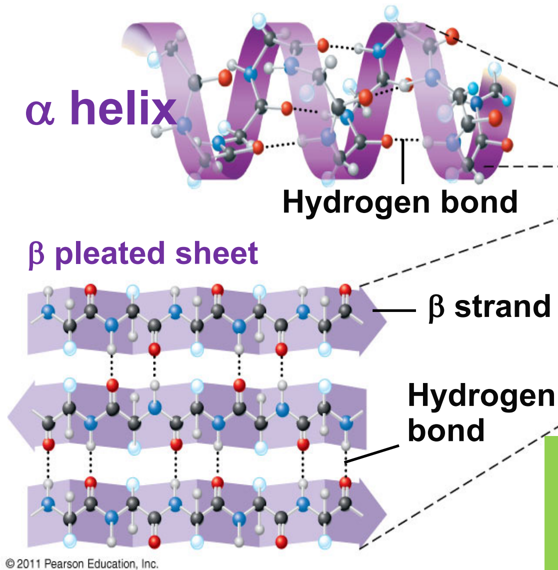
Levels of protein structure

Primary structure



<u>Primary Structure</u>: a protein's unique, linear <u>sequence of amino acids</u> which is determined by genetic information

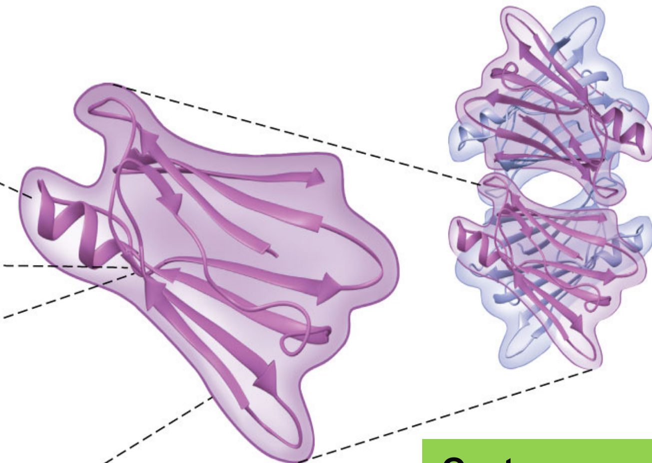
Secondary structure



<u>Secondary Structure:</u> the <u>result of H-bonding</u> between partially negative oxygen & nitrogen of the polypeptide backbone and hydrogen on the backbone (α helix and β sheets)

Tertiary structure

Quaternary structure



<u>Tertiary structure:</u> the overall shape of the polypeptide <u>resulting from interactions between R-groups of amino acids</u>.

<u>Quaternary structure:</u> <u>forms when two or more polypeptide chains aggregate to make one molecule</u>

Classification of proteins

(1) Based on shape

- **Globular protein**—able to dissolve and crystallize
- **Fibrous protein**--generally water-insoluble

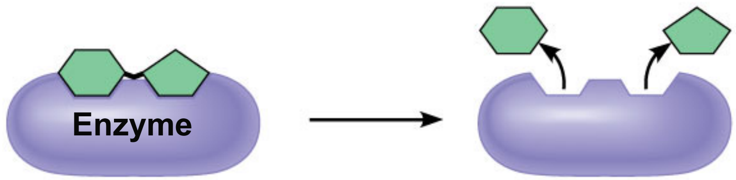
(2) Based on chemical composition

- **Simple protein** –e.g.lysozyme
- **Conjugated protein** –e.g.hemoglobin
  - Glycoproteins, lipoproteins, metalloproteins

Based on function

Enzymatic proteins

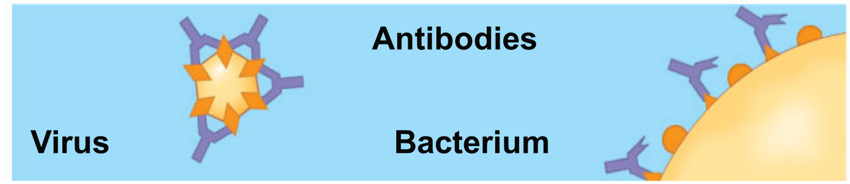
Example: Digestive enzymes catalyze the hydrolysis of bonds in food molecules.



Defensive proteins

Function: Protection against disease

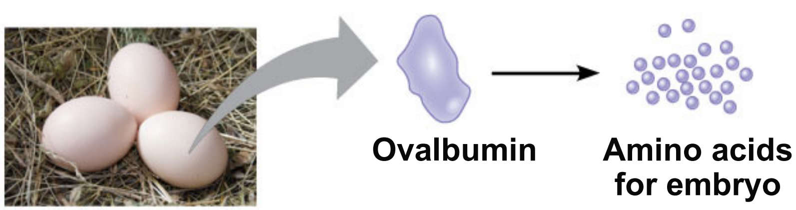
Example: Antibodies inactivate and help destroy viruses and bacteria.



Storage proteins

Function: Storage of amino acids

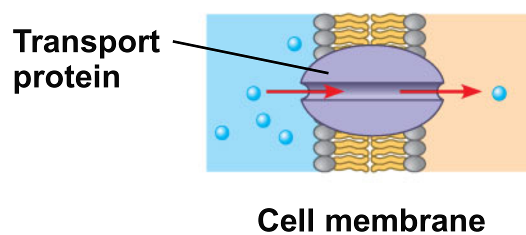
Examples: Casein, the protein of milk, is the major source of amino acids for baby mammals. Plants have storage proteins in their seeds. Ovalbumin is the protein of egg white, used as an amino acid source for the developing embryo.



Transport proteins

Function: Transport of substances

Examples: Hemoglobin, the iron-containing protein of vertebrate blood, transports oxygen from the lungs to other parts of the body. Other proteins transport molecules across cell membranes.

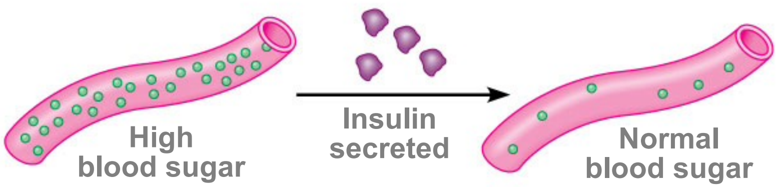


Function of Proteins…continued

Hormonal proteins

Function: Coordination of an organism's activities

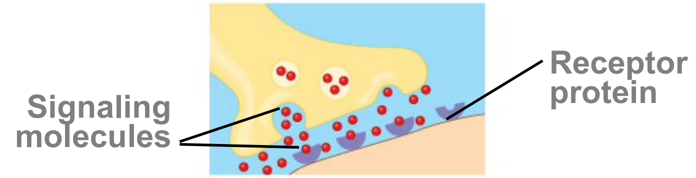
Example: Insulin, a hormone secreted by the pancreas, causes other tissues to take up glucose, thus regulating blood sugar concentration



Receptor proteins

Function: Response of cell to chemical stimuli

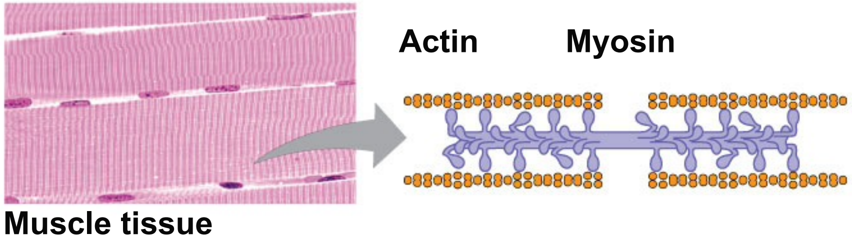
Example: Receptors built into the membrane of a nerve cell detect signaling molecules released by other nerve cells.



Contractile and motor proteins

Function: Movement

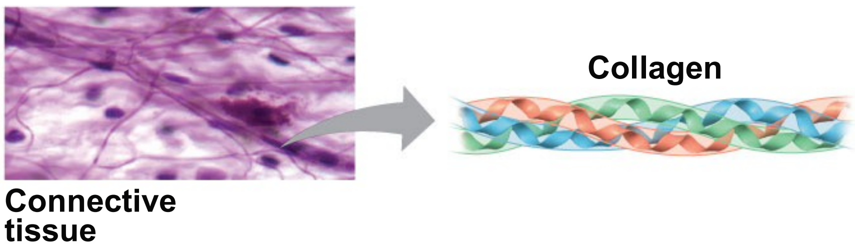
Examples: Motor proteins are responsible for the undulations of cilia and flagella. Actin and myosin proteins are responsible for the contraction of muscles.



Structural proteins

Function: Support

Examples: Keratin is the protein of hair, horns, feathers, and other skin appendages. Insects and spiders use silk fibers to make their cocoons and webs, respectively. Collagen and elastin proteins provide a fibrous framework in animal connective tissues.



Glycoproteins

- **Glycoproteins are proteins that contain oligosaccharide** (glycan) chains covalently attached to their polypeptide backbones.
- The process of attaching the glycans is known as glycosylation.

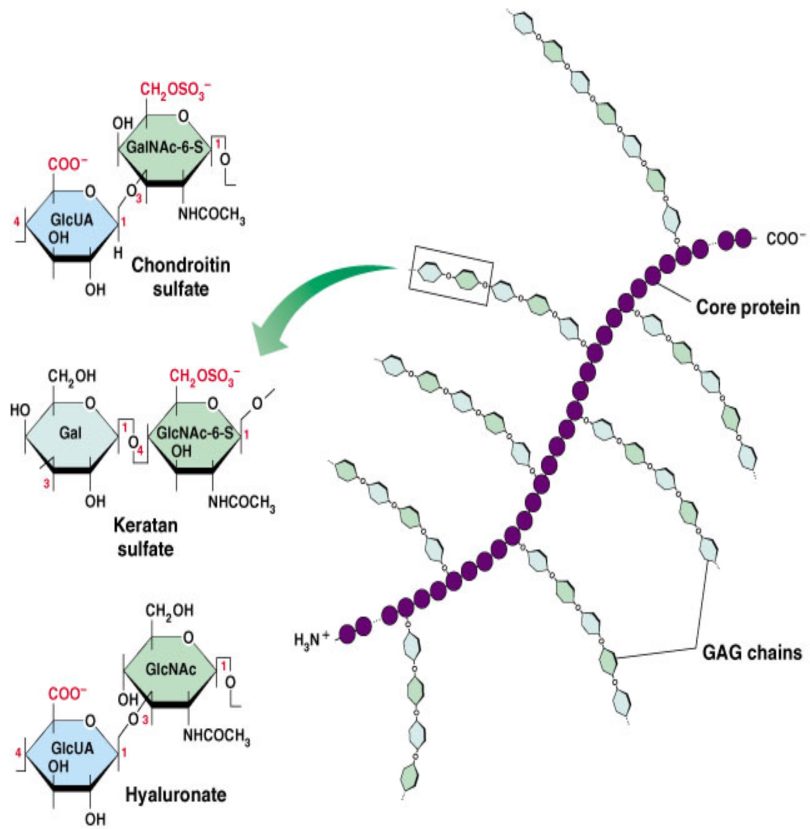
Eight Sugars in Glycoproteins

Sugar	Abbreviation
β-D-Glucose	Glc
β-D-Galactose	Gal
β-D-Mannose	Man
α-L-Fucose	Fuc
N-Acetylgalactosamine	GalNAc
N-Acetylglucosamine	GlcNAc
N-Acetylneuraminic acid	NeuNAc
Xylose	Xyl

Proteoglycans

Proteoglycans are **glycosaminoglycans** that are covalently linked to serine residues of specific **core proteins**.

The glycosaminoglycan chain is synthesized by sequential addition of sugar residues to the core protein in the golgi apparatus

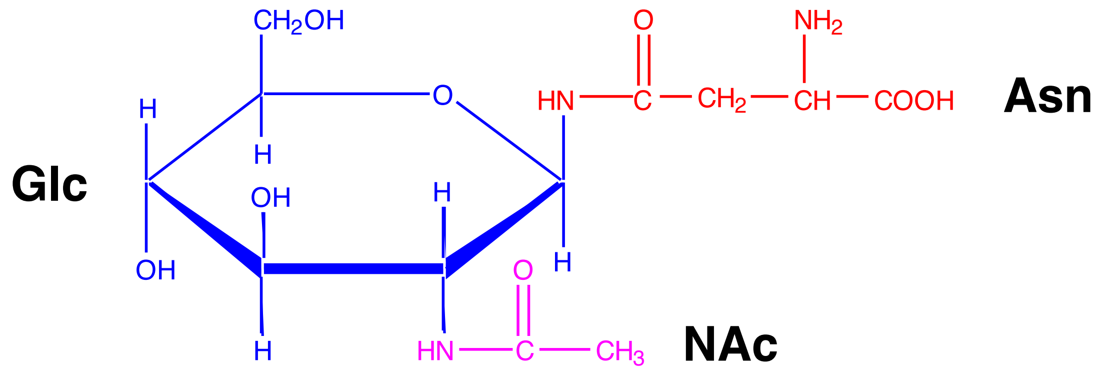


(a) Repeating units of several common GAGs **(b)** Structure of a proteoglycan

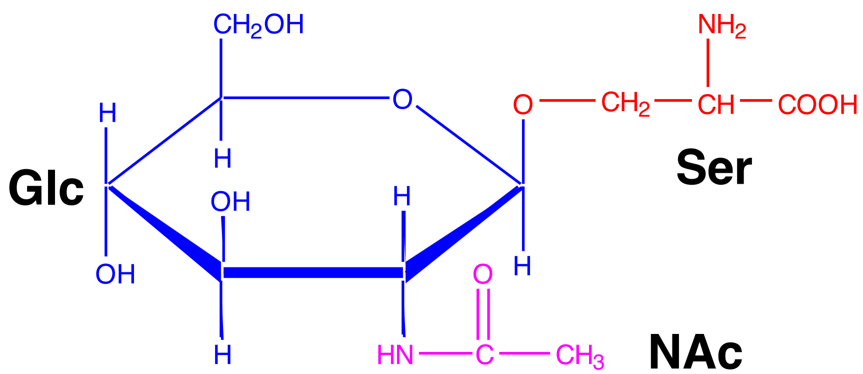
Differences

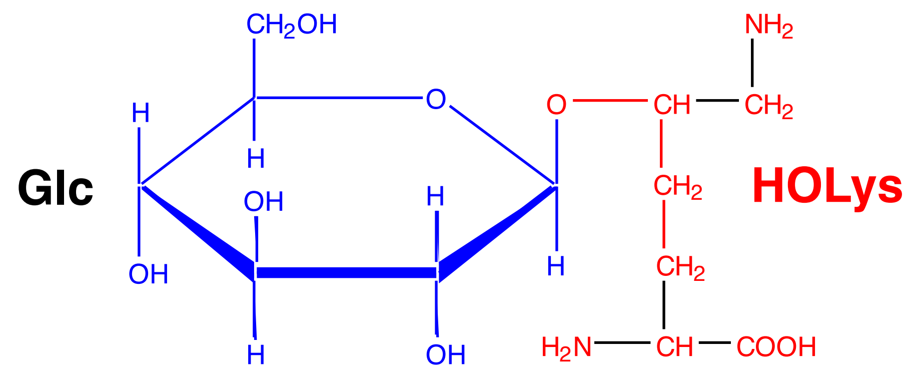
Glycoproteins	-Proteins conjugated to saccharides -lacking a serial repeat unit	Protein >> carbohydrate
Proteoglycans	Proteins conjugated to polysaccharides with serial repeat units	Carbohydrate >> protein
	Glycosaminoglycans/ Mucopolysaccharides	Repeat unit HexN and HexUA

Glycopeptide bonds



Type I *N*-Glycosyl linkage to Asn





Type II *O*-Glycosyl linkage to Ser (Thr)   Type III *O*-Glycosyl linkage to 5-HOLys

Function of Glycoproteins

1. **Structural:** Glycoproteins are found throughout matrices. They act as receptors on cell surfaces that bring other cells and proteins (collagen) together giving strength and support to a matrix. Proteoglycan-linking glycoproteins cross links proteoglycan molecules and is involved in the formation of the ordered structure within cartilage tissue.

2. **Protection:** High molecular weight polymers called mucins are found on internal epithelial surfaces. They form a highly viscous gel that protects epithelium form chemical, physical, and microbial disturbances. Examples of mucin sites are the human digestive tract, urinary tract, and respiratory tracts.

3. **Reproduction:** Glycoproteins found on the surface of spermatozoa appear to increase a sperm cell's attraction for the egg by altering the electrophoretic mobility of the plasma membrane.

Function of Glycoproteins...continued

4. **Adhesion:** Glycoproteins serve to adhere cells to cells and cells to substratum. Cell-cell adhesion is the basis for the development of functional tissues in the body. The interactions between cells is mediated by the glycoproteins on those cell's surfaces. For example, nerve cells recognize and bind to one another via the glycoprotein N-CAM (nerve cell adhesion molecule).
5. **Hormones:** There are many glycoproteins that function as hormones such as human chorionic gonadotropin (HCG), erythropoietin etc
6. **Enzymes:** Glycoprotein enzymes are of three types. These are oxidoreductases, transferases, and hydrolases.
7. **Carriers:** Glycoproteins can bind to certain molecules and serve as vehicles of transport. They can bind to vitamins, hormones, cations, and other substances.
8. **Immunological:** The interaction of blood group substances with antibodies is determined by the glycoproteins on erythrocytes. Adding or removing just one monosaccharide from a blood group structure, the antigenicity and therefore a person's blood type can be altered. Many immunoglobulins are actually glycoproteins.

Structure of Glycoproteins

- May be N-linked or O-linked
- N-linked saccharides are attached via the amide nitrogens of asparagine residues
- O-linked saccharides are attached to hydroxyl groups of serine, threonine or hydroxylysine

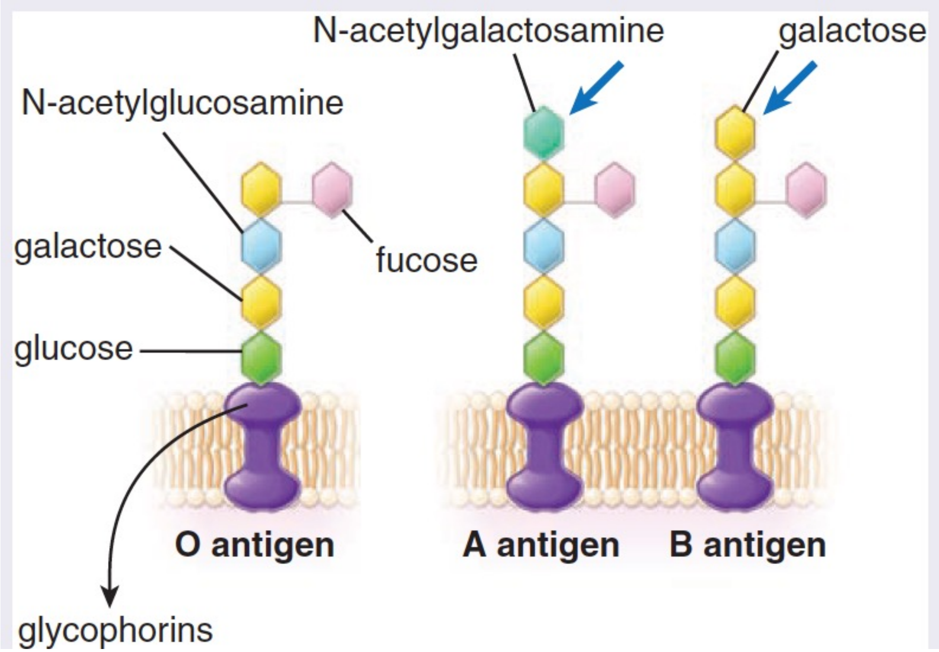
O-linked glycoproteins

- Function in many cases is to adopt an extended conformation
- These extended conformations resemble "bristle brushes"
- Bristle brush structure extends functional domains up from membrane surface

N-linked glycoproteins

- Oligosaccharides can stabilize protein conformations and/or protect against proteolysis
- Involved in targeting proteins to specific subcellular compartments

Blood ABO Antigens



ABO blood group system

An important factor in blood transfusion is the **ABO blood group system**, which essentially involves three antigens called *A*, *B*, and *O* (Table F10.1.1). These antigens are glycoproteins and glycolipids and differ only slightly in their composition. They are present on the surface of erythrocytes and are attached to the extracellular domains of integral membrane proteins called **glycophorins**. The presence of A, B, or O antigens determines the four primary **blood groups: A, B, AB**, and **O**. All humans have enzymes that catalyze the synthesis of the O antigen. Individuals with A blood group have an additional enzyme **(N-acetylgalactosamine transferase** or A-glycosyltransferase) that adds N-acetylgalactosamine to the O antigen. Individuals with B blood group have an enzyme (**galactose transferase** or B-glycosyltransferase) that adds galactose to the O antigen (Fig. F10.1.1). Individuals with the AB blood group express both enzymes, whereas individuals with type O blood group lack both enzymes. In humans, **ABO genes** consist of at least seven exons, and they are located on chromosome 9. The O allele is recessive, whereas A and B alleles are codominant.

TABLE F10.1.1 ABO Blood Group System

Blood Type	Erythrocyte Surface Antigen	Serum Antibody	Can Give Blood to	Can Receive Blood From
A	A antigen	Anti-B	A and AB	A and O
B	B antigen	Anti-A	B and AB	B and O
AB	A and B antigens	No antibodies	Only AB	A, B, AB, and O (universal blood recipient)
O	O antigen (no A or B antigens)	Anti-A and anti-B	A, B, AB, and O (universal blood donor)	Only O

TABLE 6.5	Multiadhesive Glycoproteins			
Name	**Molecular Weight (kDa)**	**Molecular Composition**	**Localization**	**Function**
Fibronectin	250–280	Dimer molecule formed from two similar peptides linked by a disulfide bond	Present in the ECM of many tissues	Responsible for cell adhesion and mediate migration; possesses binding sites for integrins, type IV collagen, heparin, and fibrin
Laminin	140–400	Cross-shaped molecule formed from three polypeptides (α chain and two β chains)	Present in basal laminae of all epithelial cells and external laminae of muscle cells, adipocytes, and Schwann cells	Anchors cell surfaces to the basal lamina. It possesses binding sites for collagen type IV, heparan sulfate, heparin, entactin, laminin, and integrin receptors on the cell surface
Tenascin	1,680	Giant protein formed from six chains connected by disulfide bonds	Embryonic mesenchyme, perichondrium, periosteum, musculotendinous junctions, wounds, tumors	Modulates cell attachments to the ECM; possesses binding sites for fibronectin, heparin, EGF-like growth factors, integrins, and CAMs
Osteopontin	44	Single-chain glycosylated polypeptide	Bone	Binds to osteoclasts; possesses binding sites for calcium, hydroxyapatite, and integrin receptor on the osteoclast membrane
Entactin/ Nidogen	150	Single-chain rodlike sulfated glycoprotein	Basal lamina–specific protein	Links laminin and type IV collagen; has binding sites for perlecan and fibronectin

CAM, cell adhesion molecule; *ECM*, extracellular matrix; *EGF*, epithelial growth factor; *kDa*, kilodaltons.

Ends