

Peptides and Proteins:

Interesting Peptide in Biological Systems:

1. Glutathione

- Tripeptide of glutamate, cysteine, glycine
- Regulates oxidation/reduction reactions in cells
- Destroys destructive free radicals by scavenging oxidizing agents

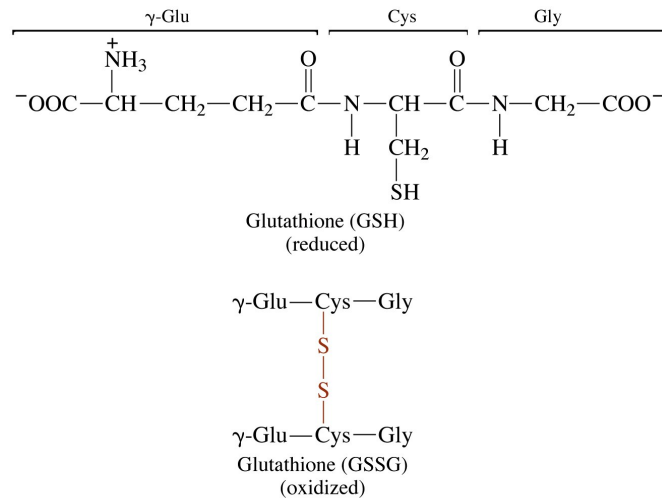


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2. Oxytocin and Vasopressin

- Pituitary gland peptide hormones
- Nonapeptides cyclized by disulfide bond
- Oxytocin stimulates uterine contractions during childbirth – induces labor
- Vasopressin stimulates water resorption by kidneys and increases blood pressure (anti-diuretic hormone)

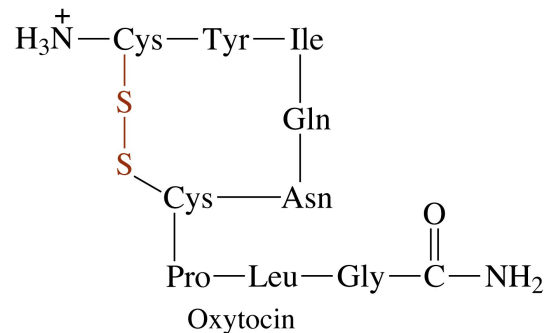


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3. Enkephalins and Endorphins

- Brain and nervous system peptides
- Important in control of pain and emotional states

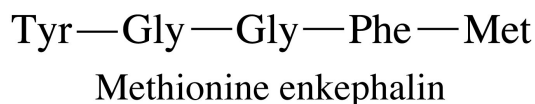
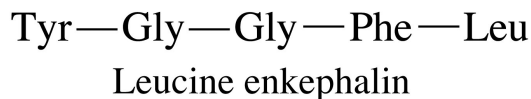


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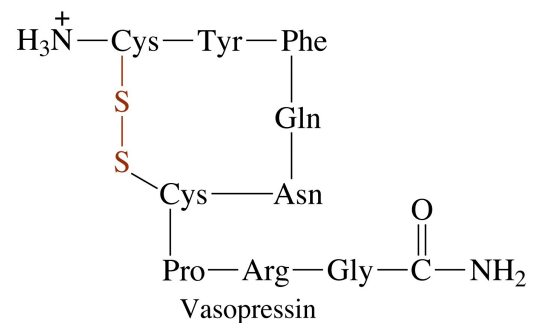


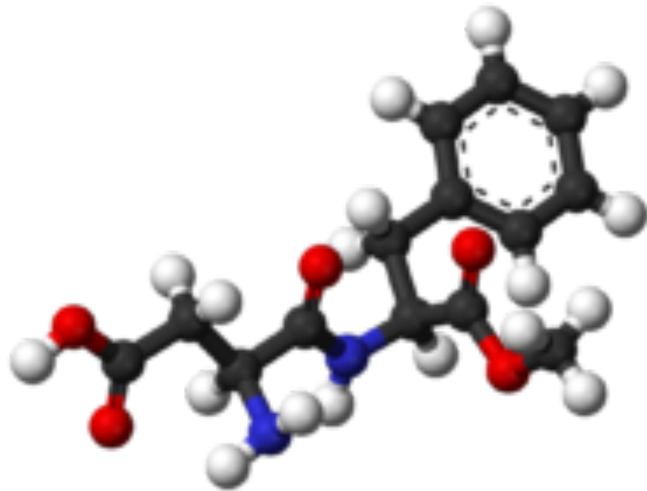
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Bovine Insulin

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4. **Insulin** – Peptide hormone that regulates carbohydrate metabolism. Acts as signal for “fed” state. Functions to cap glucose levels in blood. Stimulates storage of glucose as glycogen among other effects.



5. Synthetic Peptide: Nutrasweet or Aspartame

a. L-aspartyl-L-phenylalanine methyl ester

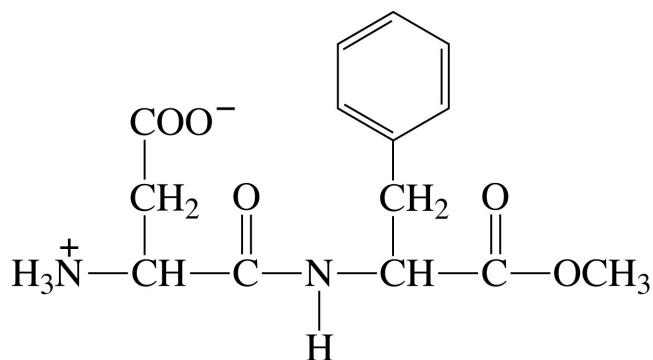


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L-Aspartyl-L-phenylalanine methyl ester
(aspartame)

b. Dipeptide – 200X
sweeter than sucrose and only 1
calorie/teaspoon vs. sucrose that has 16
calories/teaspoon

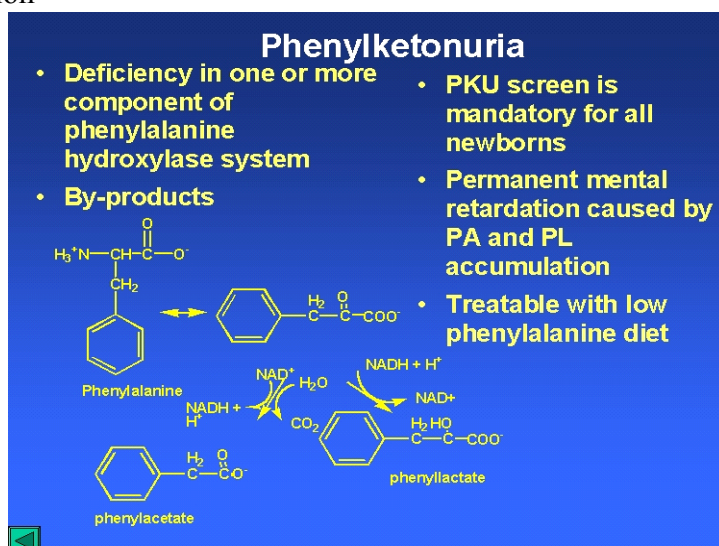
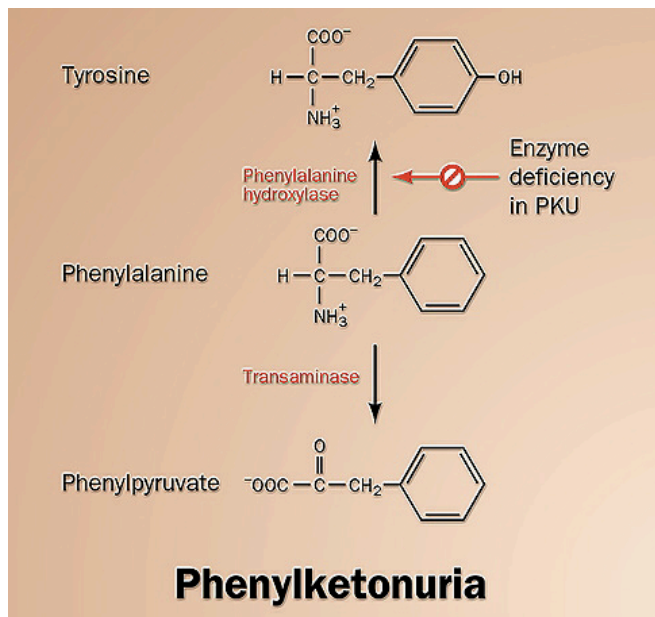
c. Used in diet and low calorie foods and drinks

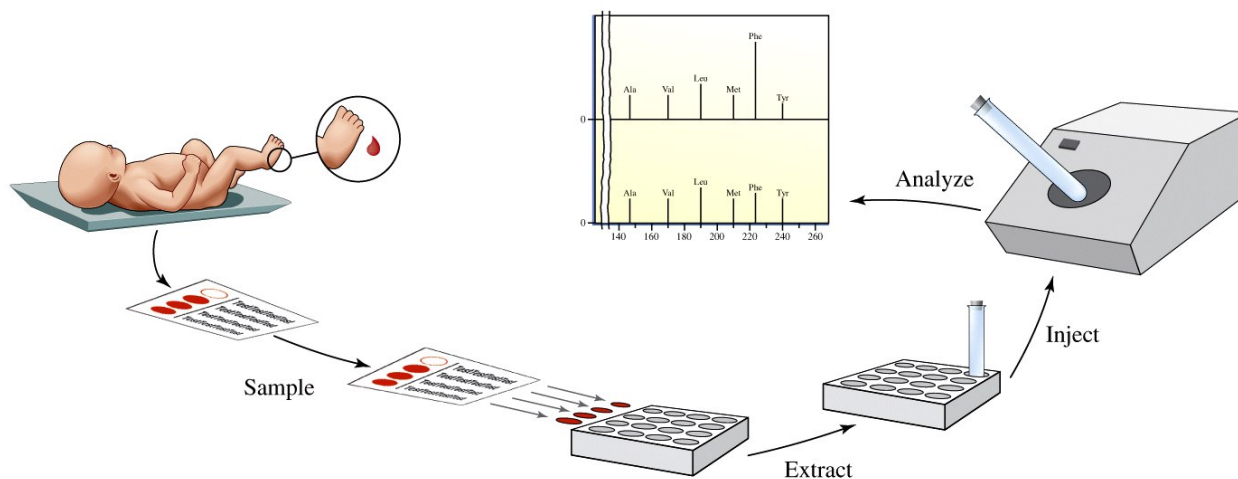
d. Highly profitable

e. If amino acids are in the “D” configuration, the peptide is bitter not sweet.

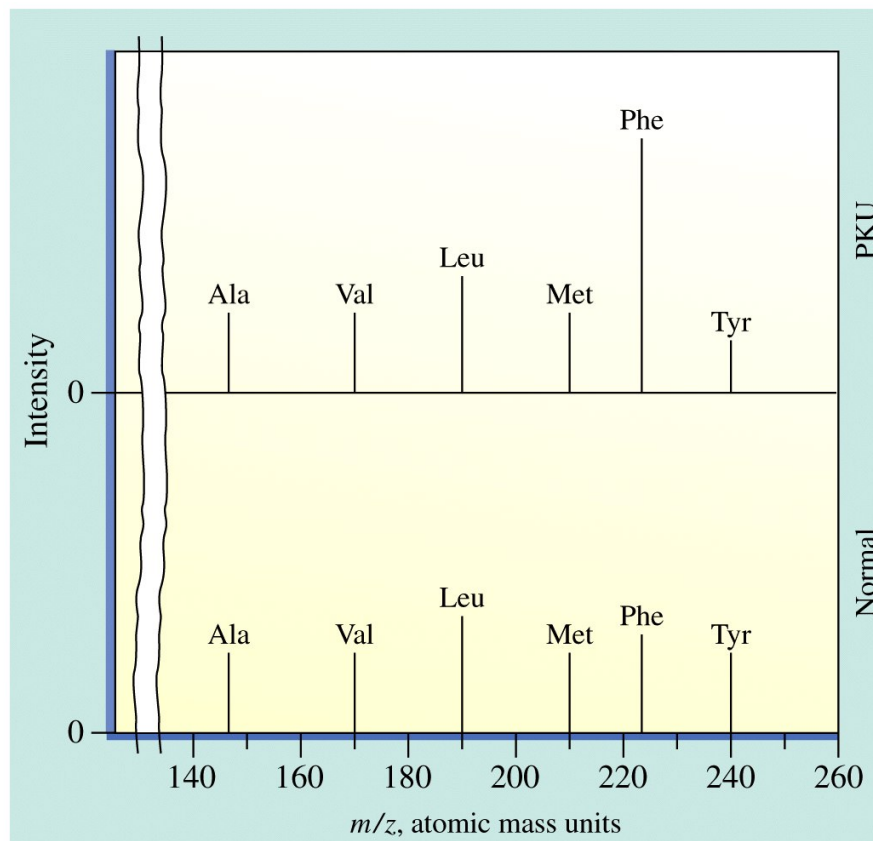
Phenylketonuria:

- Genetic deficiency in **phenylalanine hydroxylase**, the enzyme that converts **Phe → Tyr** (autosomal recessive)
- Incidence: PKU appears in about 1 in 10,000 births in Caucasian and East Asians. Some are higher: Turks are 1 in 2600, Irish are 1 in 4500, and some are lower - Japanese 1 in 143,000. Exceedingly rare in Africans.
- In phenylketonurics, tyrosine is essential – called conditionally essential
- Accumulation of phenylalanine and its derivatives (e.g. phenylpyruvate is found in high levels in urine)
- If left untreated, severe mental retardation occurs after birth due to accumulation of Phe in brain – poisons neurons
- Testing of all infants in US and most of Europe began in mid 1960's
- Testing occur about 48 to 72 hours after birth
- **Treatment:** Low Phe diet and blood monitoring
- In phenylketonurics, Tyr is an essential amino acid
- Reason for warning label on foods containing NutraSweet
- One of the most thoroughly tested and studied food additives the FDA has ever approved – considered safe for the general population
- Aspartame ingestion does produce methanol, formaldehyde and formate, substances that could be considered toxic, but the levels produced are low.
- No “credible evidence” that there is a link between Aspartame and multiple sclerosis, systemic lupus, Alzheimer's disease or vision problems.
- Beware what you read on the internet! Not always factual or credible!



TESTING OF INFANTS FOR PKU:

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Unnumbered figure pg444b Concepts in Biochemistry, 3/e
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PROTEIN STRUCTURE I

Each protein has a characteristic shape, size and function:

Classification of Proteins on the Basis of Biological Role:

1. **Structural Proteins**
 - a. Provide mechanical support to cells and organisms
 - b. Give strength to bones, skin and tendons: collagen, elastin
2. **Enzymes**
 - a. Proteins that serve as *biological catalysts* for chemical reactions in cells
3. **Transport and Storage**
 - a. Carriers for small biomolecules to cellular destinations for use in metabolism or in construction of cell components
 - b. Examples: oxygen, ferritin (iron in liver), lipoproteins that transport cholesterol
4. **Muscle Contraction and Mobility**
 - a. Actin and myosin are components of skeletal muscle
5. **Immune Proteins and other Protective Proteins**
 - a. Proteins used for defensive purposes
 - i. Example: Antibodies are proteins that bind and destroy foreign substances like viruses and bacteria
6. **Regulatory and Receptor Proteins**
 - a. Proteins that regulate cellular and physiological activity
 - i. Hormones
 - ii. DNA Binding Proteins – assist in regulation of protein synthesis
 - b. Receptors
 - i. Proteins that mediate hormone signals and transmit the signal to the inside of the cell
 1. e.g. G-proteins and brain receptors
 2. Aspartame with taste receptor

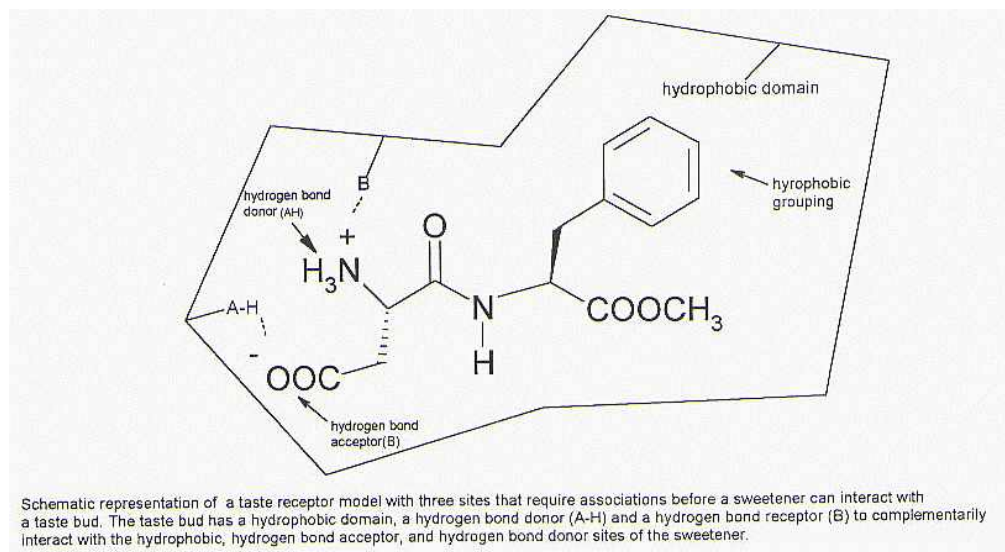


Table 3.4

Classes of proteins based on their biological functions

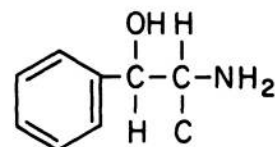
Protein	Biological Function
Enzymes	
Phosphofructokinase	An enzyme in carbohydrate metabolism that catalyzes phosphate group transfer from ATP to fructose-6-phosphate
Trypsin	A digestive enzyme in vertebrates that catalyzes protein hydrolysis
Adenylate cyclase	An enzyme that catalyzes the formation of the second messenger cyclic AMP
RNA polymerase	An enzyme present in all organisms that catalyzes DNA-directed RNA synthesis
Reverse transcriptase	An enzyme found in HIV (the virus that causes AIDS) that catalyzes RNA-directed DNA synthesis
Structural Proteins	
Collagens	Fibrous proteins found in all animals; form cable networks that serve as scaffolding for support of tissues and organs
Elastins	Fibrous proteins found in connective tissue of the lungs and in large blood vessels such as the aorta, which have rubberlike properties that allow them to stretch to several times their normal length
Keratins	Mechanically durable fibrous proteins present in vertebrates as major components of the outer epidermal layer and its appendages such as hair, nails, and feathers
Defense (Immune) Proteins	
Antibodies	Globular proteins produced by the immune system of higher animals that participate in the destruction of biological invaders
Interferons	Proteins, produced by higher animals, that interfere with viral replication
Transport and Storage Proteins	
Hemoglobin	Globular heme-containing protein that carries oxygen from the lungs to other tissues of vertebrates
Apolipoproteins	Components of lipoproteins such as low density lipoprotein (LDL) that participate in triacylglycerol and cholesterol transport
Casein	Protein found in milk that stores amino acids
Ferritin	Widely distributed protein that stores iron
Myoglobin	A heme-containing protein found in vertebrates that binds oxygen
Glucose permease	Carries glucose into erythrocytes
Regulatory and Receptor Proteins	
Lac repressor	Genetic switch that turns off bacterial genes involved in lactose catabolism
Insulin	A protein synthesized in the pancreas that acts as a signal for the fed state in higher animals
Insulin receptor	A membrane protein that binds insulin and sends a message inside the cell to regulate carbohydrate metabolism
Muscle Contraction and Mobility Proteins	
Actin	Component of skeletal muscle
Myosin	Component of skeletal muscle
Dynein	Protein that causes movement of sperm and protozoa by their flagella and cilia

Table 3-4 Concepts in Biochemistry, 3/e

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PPA – Phenylpropanolamine:

- Nasal decongestant and appetite suppressant
- Old formulations of Alka-Seltzer Cold, Tavist-D and Dexatrim
- PPA is a **pressor amine** – substance that is capable of raising blood pressure
- Similar to amphetamines (“systemic upper”)
- Interact with **α -adrenergic receptors** to elicit stimulatory effects in the brain and other tissues
- Produces vasoconstriction
- Raises blood pressure
- Found to increase the risk of **hemorrhagic strokes** due to increase in blood pressure – blood vessels rupture
- Banned by FDA
- Increased risk more prevalent in **women** – women are more likely to take diet pills/appetite suppressants
- Higher concentration in diet pills than cold medicine



phenylpropanolamine

COMMON THEME: RECOGNITION!!

****All dependent on the fact that proteins have three-dimensional shapes!!**

- Proteins interact **selectively** with other proteins or molecules through **NON-covalent** interactions in order to function.
- Reactant with enzyme
- Transported molecule with transporter
- Protein-protein interactions
- Protein-DNA interactions
- **Non-covalent interactions:**
 - Electrostatic interactions
 - Sterics
 - Van der Waals interactions
 - Hydrogen bonds

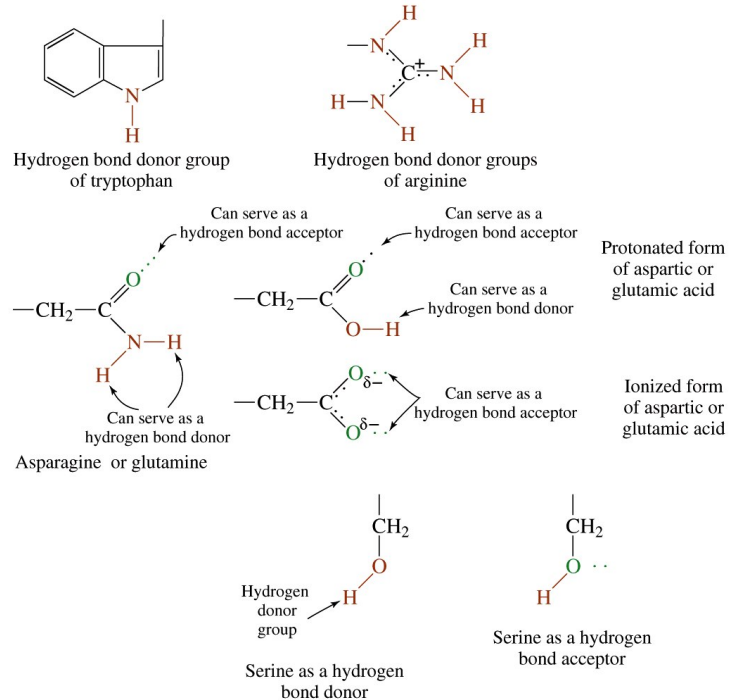
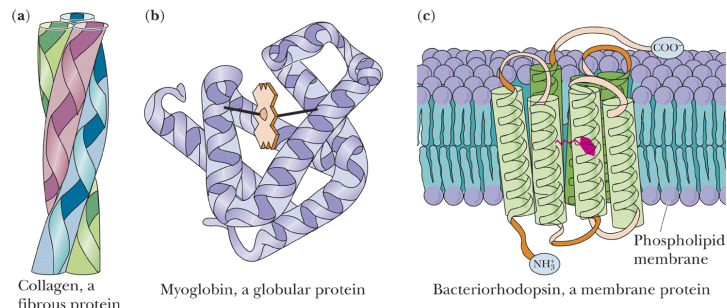


Figure 4-2 Concepts in Biochemistry, 3/e
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Garrett/Grisham, Biochemistry with a Human Focus
Figure 5.1

PROTEIN STRUCTURE:

- Can be **globular**
 - Spherical or near-spherical
 - Soluble in water – lots of charged groups
 - Dynamic and flexible
- Can be **fibrous**
 - Elongated and threadlike
 - Not soluble in water – lots of hydrophobic, non-polar R groups
 - Tough
 - Examples: hair, nails, skin
- Can be **membrane proteins**
- Can be **monomers** – single polypeptide chain
- Can be **oligomers** – multiple polypeptide chains
 - Held together by non-covalent interactions
 - Each polypeptide chain = **subunit** if part of a complex



R

Table 3.6
Examples of globular and fibrous proteins

Type of Protein	Function
Globular Proteins	
Hemoglobin	Transport (oxygen transport)
Myoglobin	Storage (oxygen storage)
Ribonuclease	Enzyme (RNA hydrolysis)
Lysozyme	Enzyme (bacterial wall hydrolysis)
Cytochrome <i>c</i>	Electron transport
Immunoglobulin	Defense (antibody)
Actin	Movement (muscle protein)
Fibrous Proteins	
Collagen	Structural protein
Keratin	Structural protein
Myosin	Movement (muscle protein)
Elastin	Elasticity

Table 3-6 Concepts in Biochemistry, 3/e
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- Size expressed in terms of mass: units of Daltons or kilodaltons
- One Dalton = one atomic mass unit
- o Estimate size = # amino acids x average molecular weight aa
- **110 g/mole per amino acid**

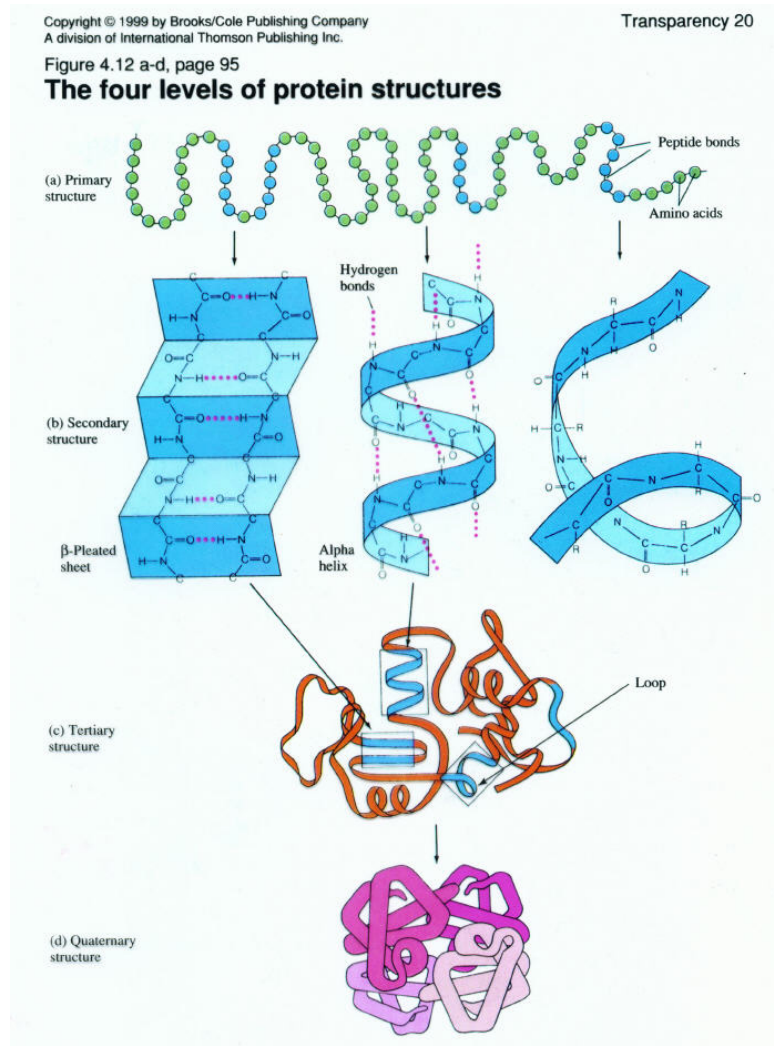
Table 3.5**Molecular properties of some proteins**

Protein	Molecular Mass (Daltons)	Number of Amino Acid Residues	Number of Subunits ^a
Insulin (bovine)	5,733	51	2
Cytochrome <i>c</i> (human)	13,000	104	1
Ribonuclease A (bovine pancreas)	13,700	124	1
Lysozyme (egg white)	13,930	129	1
Myoglobin (equine heart)	16,890	153	1
Chymotrypsin (bovine pancreas)	26,500	241	3
Hemoglobin (human)	64,500	574	4
Serum albumin (human)	68,500	550	1
Immunoglobulin G (human)	145,000	1320	4
RNA polymerase (<i>E. coli</i>)	450,000	4100	5
Ferritin (equine spleen)	450,000	4100	24
Glutamate dehydrogenase (bovine liver)	1,000,000	8300	40

^aThe number of subunits refers to the quaternary structure.Table 3-5 Concepts in Biochemistry, 3/e
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FOUR LEVELS OF PROTEIN STRUCTURE:

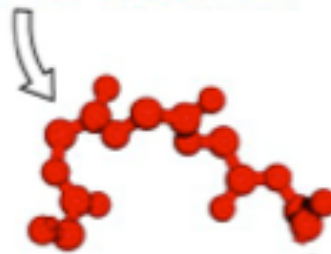
- **Primary (1°)**
 - o Linear sequence of amino acids in a protein
- **Secondary (2°)**
 - o Local 3-dimensional structure of the **PEPTIDE BACKBONE**
 - Ignores the conformation of the side chains
- **Tertiary (3°)**
 - o Global arrangement of secondary structure, side chains (R groups), and other prosthetic groups (e.g. metals)
- **Quaternary (4°)**
 - o Arrangement of multiple proteins into **complexes**



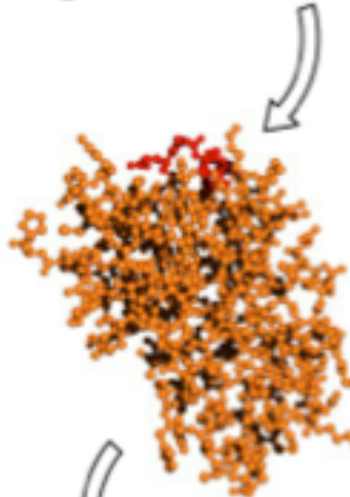
Primary structure
The sequence of
amino acid residues

-Glu-Ser-Phe-Gly-Asp-

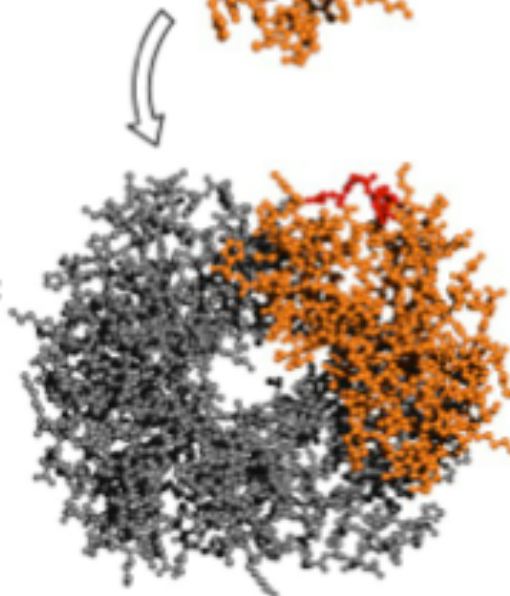
Secondary structure
The localized
conformation of
the polypeptide backbone



Tertiary structure
The three-dimensional
structure of an entire
polypeptide, including
all its side chains



Quaternary structure
The spatial arrangement
of polypeptide chains
in a protein with
multiple subunits



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