Interesting Peptide in Biological Systems:

1. **Glutathione**
   a. Tripeptide of glutamate, cysteine, glycine
   b. Regulates oxidation/reduction reactions in cells
   c. Destroys destructive free radicals by scavenging oxidizing agents

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

3. **Enkephalins and Endorphins**
   a. Brain and nervous system peptides
   b. Important in control of pain and emotional states

- Tyrr—Gly—Gly—Phe—Leu
  - Leucine enkephalin

- Tyrr—Gly—Gly—Phe—Met
  - Methionine enkephalin
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

   ![Aspartame Structure](image)

   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:

Unnumbered figure pg444a Concepts in Biochemistry, 3/e
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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

[Diagram of a protein structure with labels for hydrophobic domain, hydrogen bond donor, and acceptor sites.]

Schematic representation of a taste receptor molecule with three sites that require associations before a sweetener can interact with it. The bitter site has a hydrophobic domain, a hydrogen bond donor (A-H) and a hydrogen bond acceptor (B) to complementarily interact with the hydrophobic, hydrogen bond acceptor, and hydrogen bond donor sites of the sweetener.
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
**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

**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

**Table 3.6 Examples of globular and fibrous proteins**

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

Garrett/Grisham, Biochemistry with a Human Focus
Figure 5.1

Table 3-6 Concepts in Biochemistry, 3/e © 2006 John Wiley & Sons
- Size expressed in terms of mass: units of Daltons or kilodaltons
- One Dalton = one atomic mass unit
  - Estimate size = # amino acids x average molecular weight aa
  - **110 g/mole per amino acid**

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

*The number of subunits refers to the quaternary structure.

**FOUR LEVELS OF PROTEIN STRUCTURE:**

- **Primary (1°)**
  - Linear sequence of amino acids in a protein

- **Secondary (2°)**
  - Local 3-dimensional structure of the **PEPTIDE BACKBONE**
  - Ignores the conformation of the side chains

- **Tertiary (3°)**
  - Global arrangement of secondary structure, side chains (R groups), and other prosthetic groups (e.g. metals)

- **Quaternary (4°)**
  - Arrangement of multiple proteins into **complexes**
Primary structure
The sequence of amino acid residues

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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