Name _____

Proteins: Workshop I
Amino Acids - The Building Blocks of Proteins

Chem 306

Overview - Proteins are large biological molecules that perform many different functions. (Table I). Proteins are made of molecular building blocks called amino acids. We will investigate the structure of amino acids and how they affect the structure of a protein. We will also investigate the affect of structure on the function of a protein.

Why learn about proteins? Of the three classes of biomolecules - lipids, carbohydrates, and proteins – proteins have some of the most varied structure and function. For example, even a single amino acid can have a function in the body – the amino acid glutamate is the most abundant excitatory neurotransmitter in the mammalian nervous system. Scaling up things a bit consider the hormone insulin contains over 700 atoms, 51 amino acids, and has a molecular mass of 5700 amu. Some virus proteins are still larger, having molecular weights of over 40 million amu! Many disease processes and clues about disease in the body relates to proteins and protein structure.

Table I – Types of Proteins and Their Functions

Type	Function	Examples
Structure	Shape / Support	Collagen – provides structure to tendons & cartilage
Enzymes	Catalysis	Enzymes aid in biochemical reactions (Amylase begins digestion of carbohydrates by hydrolysis.)
Hormones	Regulate body functions by carrying messages to receptors	Insulin – facilitates use of glucose for energy generation
Storage	Make essential substances available when needed	Myoglobin – stores oxygen in muscles
Contraction	Do mechanical work	Actin & myosin – govern muscle movement
Protection (Immunity)	Defend body against foreign matter	Immunoglobulin – aids destruction of invading bacteria
Transport	Carry substances through body	Hemoglobin - transports O_2 in blood Membrane proteins - perform active transport

Part I – Amino Acids

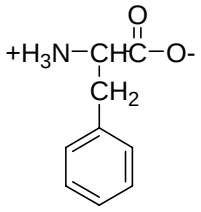
A. General Structure

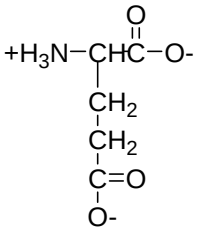
The building blocks of proteins are **α-amino acids**, small molecules that contain a carboxylic acid and an amino group. The amino group is connected to the carbon next to the carboxyl group, the α carbon.

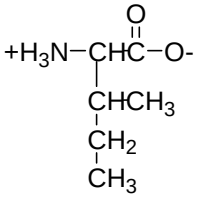
There structure of most amino acids differ only in the side chain (R group). Table II contains the structures of all the 20 amino acides required by the human body to make proteins. The R group for valine is a methyl group, $-CH_3$. Circle the R groups for six amino acids on Table II.

Nine of the 20 amino acids in Table II are "**essential amino acids**" and cannot be made by the body. These "essential amino acids" (His, Leu, Isl, Lys, Met, Phe, Thr , Try, Val) must be obtained in the diet.

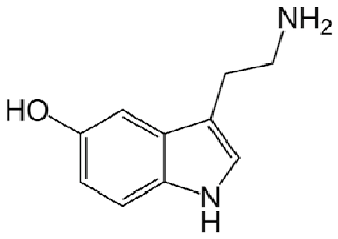
a. Circle the R group in the amino acids below. Name each amino acid and write the three-letter abbreviation for each.





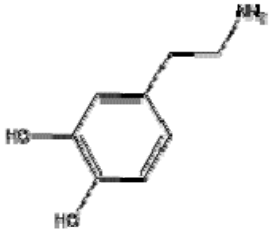


b. Serotonin is a neurotransmitter made from an amino acid. The sites of serotonin synthesis in the body are the central nervous system and the gastrointestinal tract. Serotinin is believed to play an important role in a variety of functions including the modulation of anger, aggression, body temperature, mood, sleep, sexuality, and appetite. Which amino acid is most likely the starting material for the synthesis of serotonin? Is it an essential amino acid?



serotonin

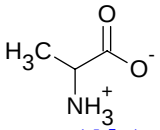
c. Dopamine, a neurotransmitter and hormone, has many functions in the brain including the reward pathway. It is commonly associated with the pleasure system of the brain, providing feelings of enjoyment and reinforcement to motivate a person proactively to perform certain activities. Dopamine, like serotonin, is synthesized from a single amino acid. Which essential amino acid is most likely the starting material for the synthesis of dopamine?

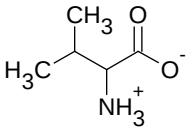


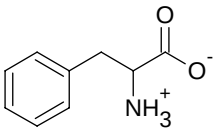
Dopamine

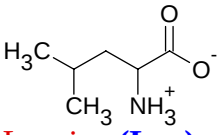
Table II – Structures & abbreviations of the 20 standard amino acids in zwiterionic form. (The pI's are shown in the parentheses.)

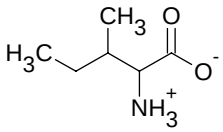
Non-polar side chains

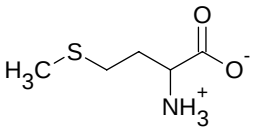

Alanine **(Ala)** (6.0)

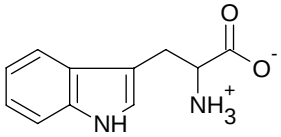

Valine **(Val)** (6.0)

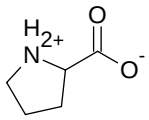

Phenylalanine **(Phe)**

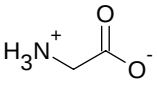

Leucine **(Leu)** (6.0)


Isoleucine **(Ile)** (6.0)

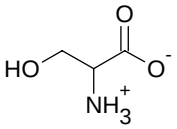

Methionine **(Met)** (5.7)

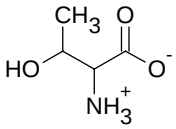

Tryptophan **(Trp)** (5.9)

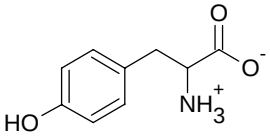

Proline **(Pro)** (6.3)

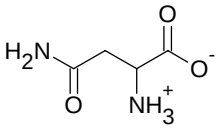

Glycine **(Gly)** (6.0)

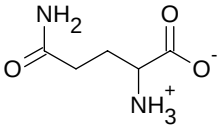
Polar side chains – neutral

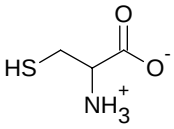

Serine **(Ser)** (5.7)


Threonine **(Thr)** (5.6)

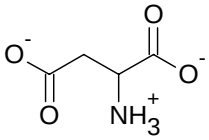

Tyrosine **(Tyr)** (5.7)

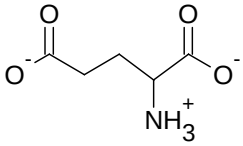

Asparagine **(Asn)** (5.4)


Glutamine **(Gln)** (5.7)

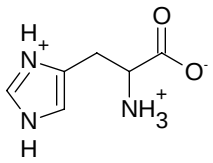

Cysteine **(Cys)** (5.0)

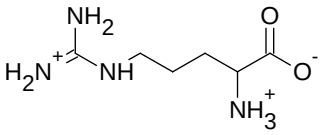
Polar side chains – acidic

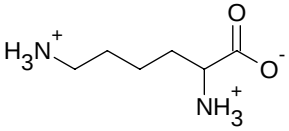

Aspartic Acid **(Asp)** (3.0)


Glutamic Acid **(Glu)** (3.2)

Polar side chains – basic


Histidine **(His)** (7.6)


Arginine **(Arg)** (10.8)


Lysine **(Lys)** (9.7)

d. Draw the generic structure of an α-amino acid. (Note the omission of α when we refer to amino acids. Everyone is "supposed to know"☺)

e. What do you notice about the α carbon?

f. Which amino acid is the only amino acid where the R group is bonded to the α amino group?

B. Classification of Amino Acids

Amino acids are classified according to the characteristics of their side chains – polar, acidic, basic, neutral, etc.

a. Which of the 4 classes of amino acids have R groups that would be hydrophilic (attracted to water)? Explain.

b. Draw an H-bond between the R group of serine and water. Clearly indicate the H-bond. Include partial charges in your structures.

c. Intermolecular forces are an important aspect of the interaction between a pharmaceutical and its receptor site. Experimental evidence indicates that drugs interact with receptor sites which have protein-like properties. Hydrophobic bonds (London dispersion forces) are formed between non-polar hydrocarbon groups on the drug and those in the receptor site. These bonds are not very specific but the interactions do occur to exclude water molecules. Which of the following amino acids would most likely be found at the region of the receptor site involved in hydrophobic interactions?

Val Ser Leu Phe Cys Trp

d. Proteins can be classified in several ways – by structure, function, etc. One classification method divides proteins into **globular** and **fibrous** categories. Globular proteins, such as enzymes and hormones, are water soluble. Fibrous proteins, such as the structural proteins found in skin and hair, and blood vessels, are water insoluble.

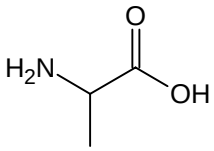
Which of the following amino acids would most likely be found on the external surface of a globular protein? Which would be found in the internal regions of a globular protein? Explain your answer.

Asp Phe Ser Leu Arg

C. Ionic/Acid-Base Properties

Amino acids contain both a carboxylic acid and a basic amino group. The acidic group, -COOH, can donate a proton to the basic group, $-NH_2$ to form a dipolar ion known as a **zwitterion**.

a. The un-ionized structure for alanine is shown below. Draw the zwitterion for alanine. What is the overall charge of the zwitterion form of alanine?



b. Zwitterions have many physical properties that we associate with inorganic salts. Circle the property that best describes a pure amino acid.

Appearance	*Crystalline*	*Powder*
Melting Point	*High*	*Low*
Solubility in Water	*High*	*Low*

Amino acids are always partially ionized. The charge depends on the side chain (-R group) and the environment (pH of the solution).

In acidic solution (low pH) zwitterions accept H+ ions on their carboxylate groups, -COO-. Draw the structure of alanine in acidic solution. What is the overall charge of alanine in acid?

Alanine at Low pH (Overall Charge =)

In basic solution (high pH), amino acid zwitterions lose H+ from their amine groups, $-NH_3^+$. Draw the structure of alanine in basic solution. What is the charge on alanine in base?

Alanine at High pH (Overall Charge =)

The pH at which the net positive and negative charges in a sample of an amino acid are evenly balanced is the amino acid/s **isoelectric point** or **pI**.

Alanine at Its pI (Overall Charge =)

c. Draw the structure for valine under the following conditions:

Low pH pI high pH

d. At a pH below the pI of an amino acid, the overall charge of that amino acid is _____. At a pH above the pI for an amino acid, the overall charge of that amino acid is _____.

Amino acids with acidic or basic side chains have substantially lower or higher pI values than amino acids with neutral side chains. For example, the two amino acids with acidic side chains, aspartic acid and glutamic acid have pI values close to 3. A higher concentration of H+ is required to obtain the overall charge of zero for a sample of these amino acids.

e. Draw the structure of glutamic acid" at pH 7.4. Why are aspartic acid and glutamic acid usually referred to as aspartate and glutamate at physiological pH (7.4)?

f. Draw the structure of the given amino acid as it would commonly exist under each of the following conditions. State whether the given pH is above or below the amino acid pI.

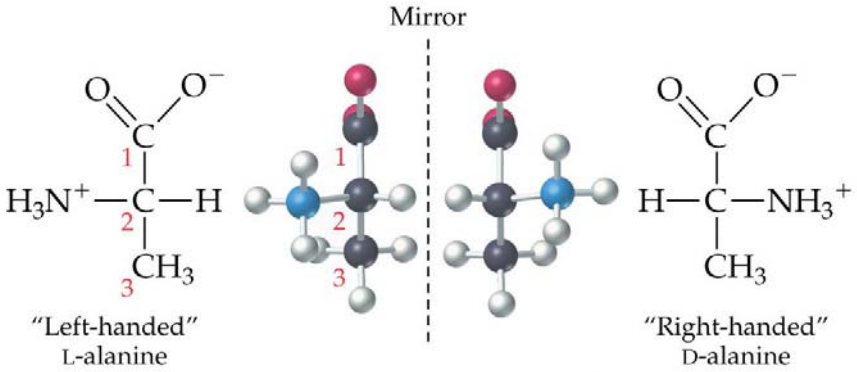
Valine in the small intestine at pH 8.

Tyrosine in the stomach at pH 1.5

Lysine in blood plasma at pH 7.4

D. Chirality of Amino Acids

Amino acids are classified as D or L based on the position of the amino group as shown below.



All living organisms appear to use only L – amino acids to assemble proteins and many organisms are not genetically programmed to synthesize or utilize their D enantiomers. Some bacteria produce enzymes that catalyze the interconversion of D and L enantiomers. The newly formed D enantiomer is used to construct bacterial cell walls.

a. Determine the R/S configuration of the above enantiomers.

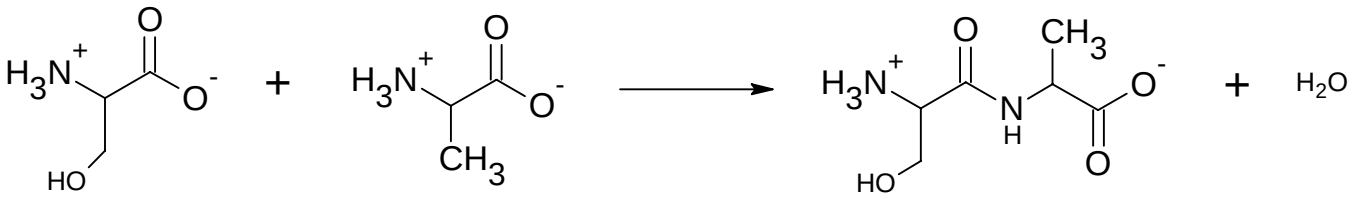
b. Name the only achiral amino acid found in Table II.

c. Draw the Fischer projection of L – phenylalanine.

E. Connecting Amino Acids: Peptide Bond Formation

The amino group of one amino acid and the acid group of another can undergo a condensation reaction to form an amide bond (**peptide bond**).The new molecule is called a dipeptide. More condensations can lead to tripeptides, tetrapeptides, etc. and finally polypeptides.

The condensation reaction of serine and alanine to make a dipeptide:

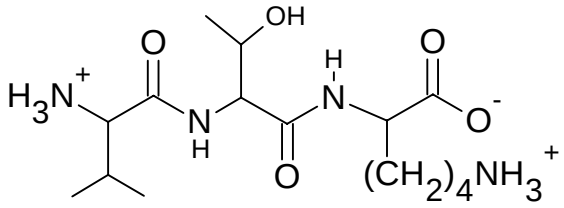


a. Circle and label the part of the dipeptide serylalanine that originated from serine.
b. Circle and lable the part of the dipeptide serylalanine that originated from alanine.
c. Draw an arrow to the peptide bond connecting serine to alanine.

d. Would the dipeptide Ala-Ser be the same molecule as Ser-Ala?
Explain.

e. Explain why peptide bonds may also be called amide bonds.

f. Circle the 3 side chains (R groups) in the following tripeptide. Label the amino acids with their 3 letter abbreviations. Write the peptide sequence using the 3 letter abbreviations for the amino acids.



g. Show the tripeptide formed from glycine, serine, and phenylalanine. Remember to draw the N-terminal on the left. (Hint: Try drawing the backbone only, then fill in the needed atoms and side chains.)