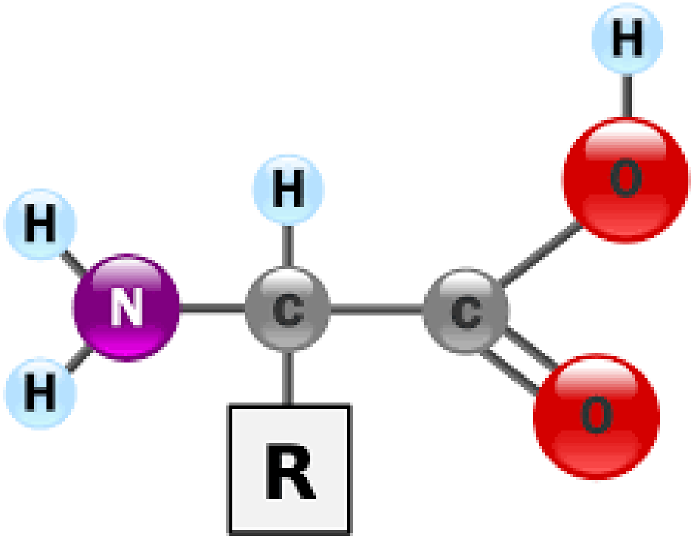
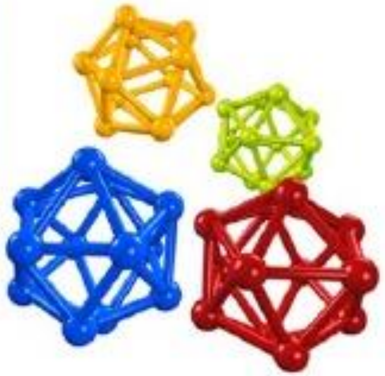
AMINO ACID



SAYANTI KAR

AMINO ACIDS

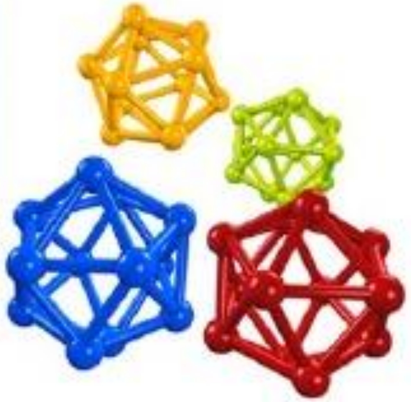


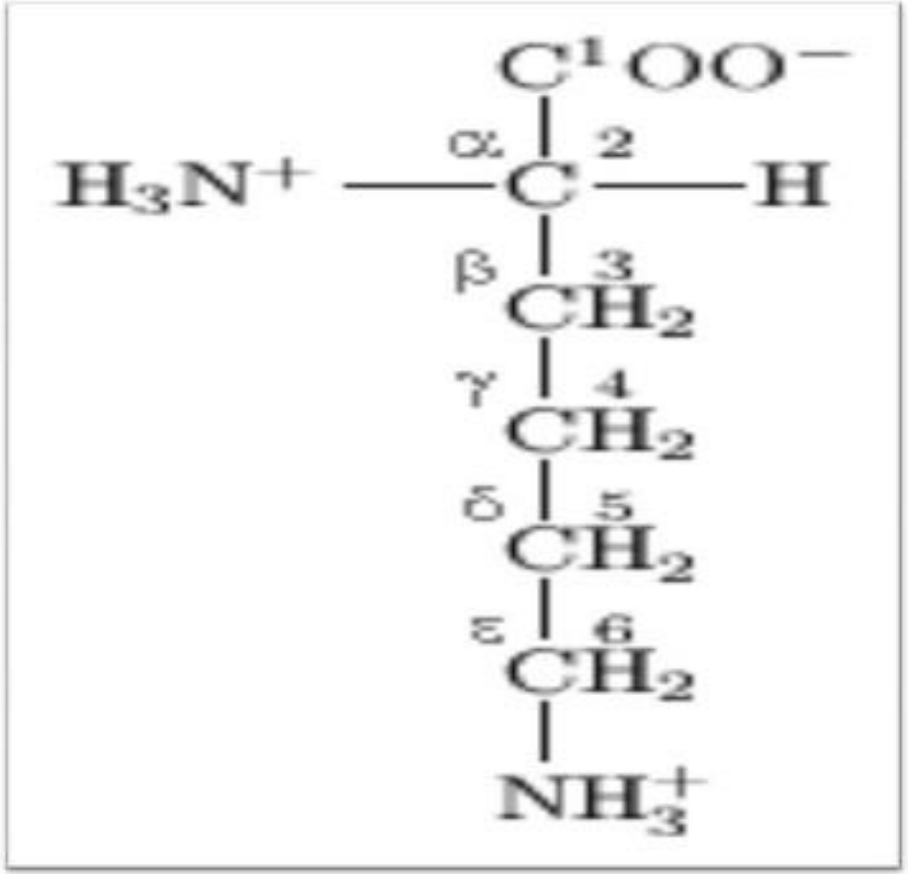
- **They are molecules containing an amine group, a carboxylic acid group, and a side-chain that is specific to each amino acid.**

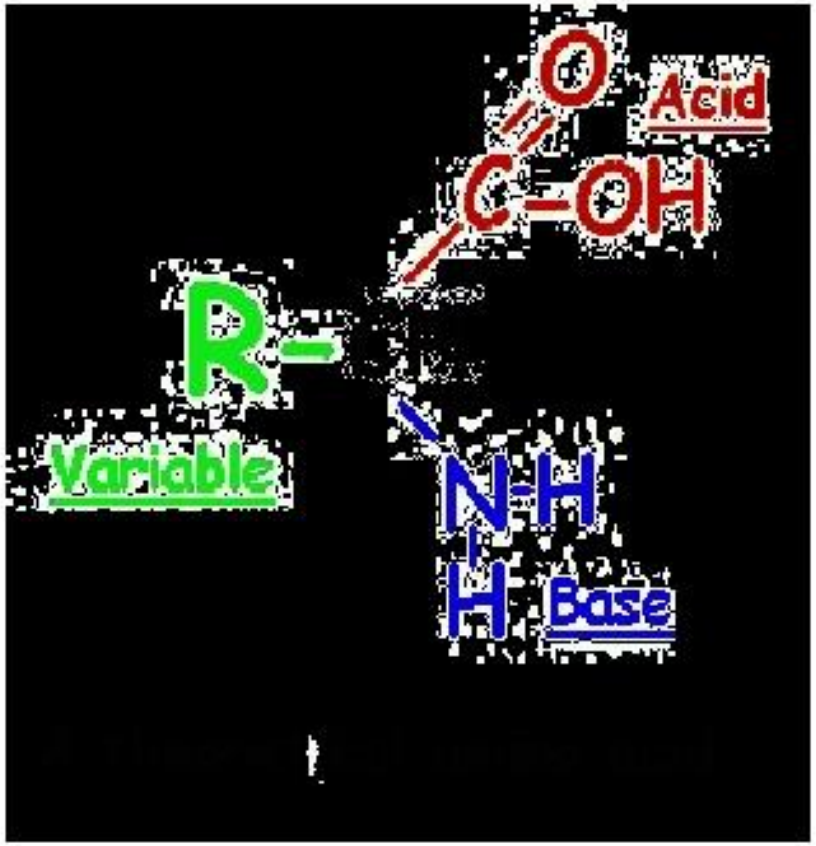
- **The key elements of amino acid are carbon, hydrogen, oxygen, and nitrogen.**

- **Amino acids are the basic structural building units of protein and other biomolecules; they are also utilized as an energy source.**

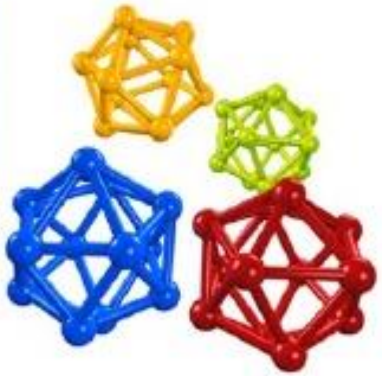
General Structure of Amino acids.





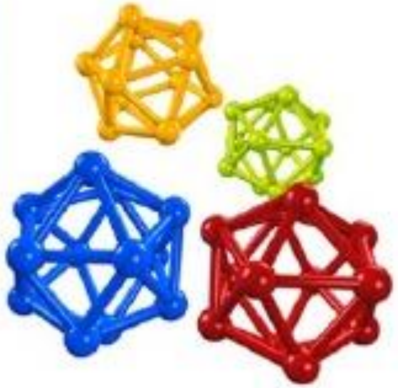


Difference between essential and non-essential amino acids

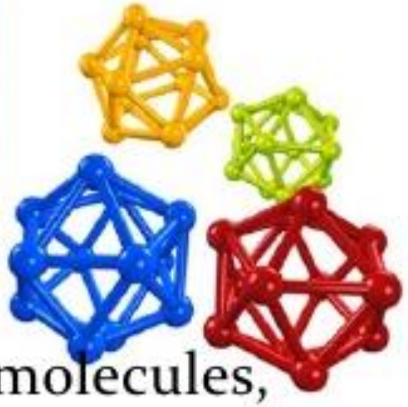


- There are 20 different amino that make up all proteins in the human body.
- These amino acids are needed to replenish tissue, red blood cells, enzymes, and other substances.
- 9 - 12 can be manufactured by the body-nonessential amino acids, not obtained from the diet.
- The remaining 8 to 11 -essential amino acids, must be obtained from the diet.

Essential	Nonessential
Histidine	Alanine
Isoleucine	Arginine*
Leucine	Asparagine
Lysine	Aspartic acid
Methionine	Cysteine*
Phenylalanine	Glutamic acid
Threonine	Glutamine*
Tryptophan	Glycine
Valine	Ornithine*
	Proline*
	Selenocysteine*
	Serine*
	Taurine*
	Tyrosine*



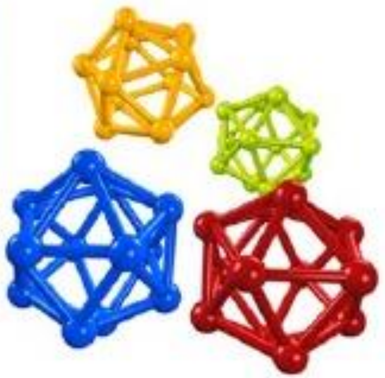
Non-protein functions



Many amino acids are used to synthesize other molecules, for example:

- Tryptophan is a precursor of the neurotransmitter serotonin.
- Tyrosine is a precursor of the neurotransmitter dopamine.
- Glycine is a precursor of porphyrins such as heme.
- Arginine is a precursor of nitric oxide.
- Aspartate, glycine, and glutamine are precursors of nucleotides.

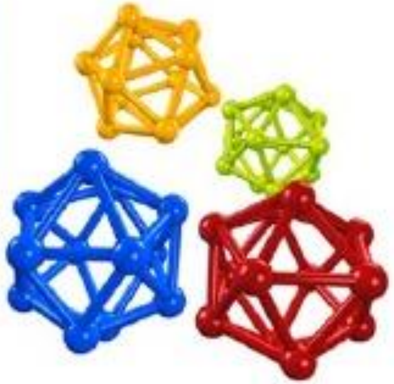
Classification according to functions



- Anabolic/Catabolic Responses and Tissue pH Regulation :-
  - Glutamic Acid
  - Glutamine

  The Urea Cycle and Nitrogen Management
  - Arginine
  - Citrulline
  - Ornithine
  - Aspartic Acid
  - Asparagine

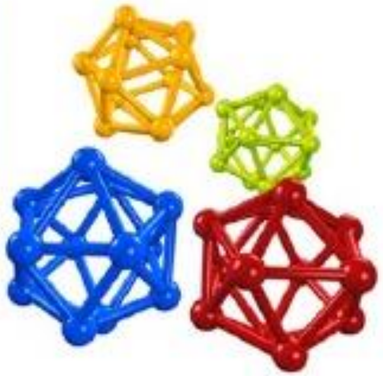
- Essential Amino Acids for Proteins and Energy
  - Isoleucine
  - Leucine
  - Valine
  - Threonine
  - Histidine
  - Lysine
  - Alpha-Aminoadipic Acid



- Sulfur Containing Amino Acids for Methylation and Glutathione
  - Methionine
  - Cystine
  - Homocysteine
  - Cystathionine
  - Taurine

- Neurotransmitters and Precursors
  - Phenylalanine
  - Tyrosine
  - Tryptophan
  - Alpha-Amino-N-Butyric Acid
  - Gamma-Aminobutyric Acid

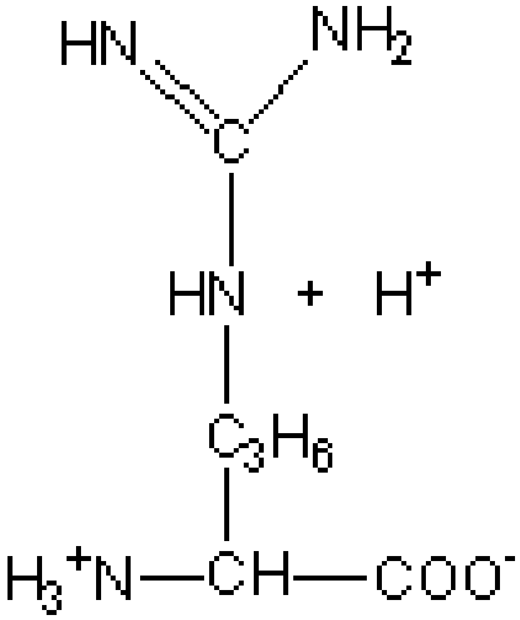
- Methylhistidines
  - 1-methylhistidine
  - 3-methylhistidine



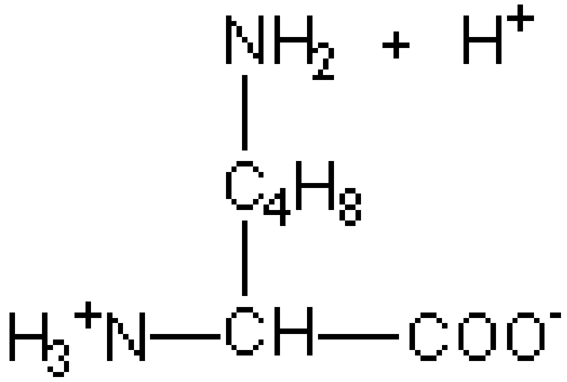
- Precursors to Heme, Nucleotides and Cell Membranes
  - Glycine
  - Serine
  - Sarcosine
  - Alanine
  - Ethanolamine
  - Phospethanolamine
  - Phosphoserine
- Bone Collagen Specific Amino Acids
  - Proline
  - Hydroxyproline
  - Hydroxylysine

Acidic and Basic Amino Acids

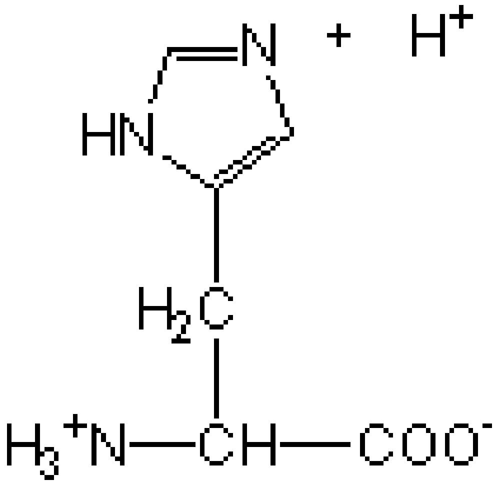
There are three amino acids that have ***basic*** side chains at neutral pH. These are arginine (Arg), lysine (Lys), and histidine (His). Their side chains contain nitrogen and resemble ammonia, which is a base. Their pKa's are high enough that they tend to bind protons, gaining a positive charge in the process.



Arginine



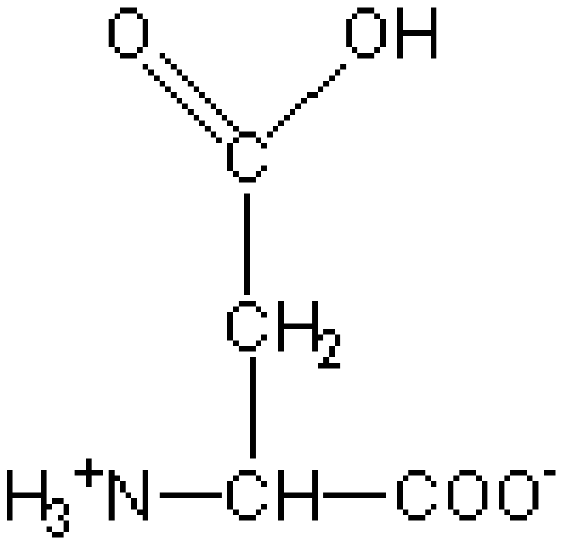
Lysine



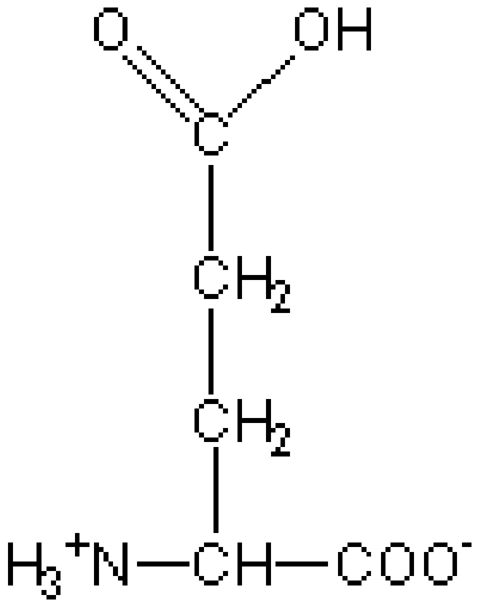
Histidine

Two amino acids have ***acidic*** side chains at neutral pH. These are aspartic acid or aspartate (Asp) and glutamic acid or glutamate (Glu).

Their side chains have carboxylic acid groups whose pKa's are low enough to lose protons, becoming negatively charged in the process.



Aspartate

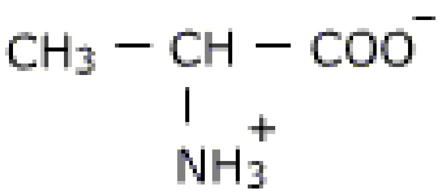


Glutamate

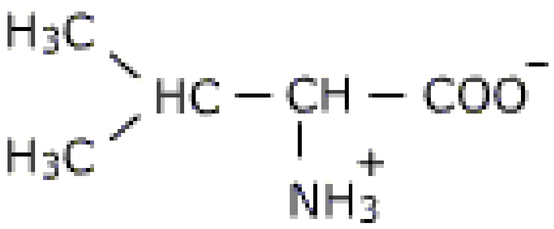
POLAR AND NON POLAR AMIO ACID

- On the basis of polarity, amino acids can be classified as **polar and non-polar amino acids**. **Polar amino acids** can again classify as positively charged and negatively charged amino acids.

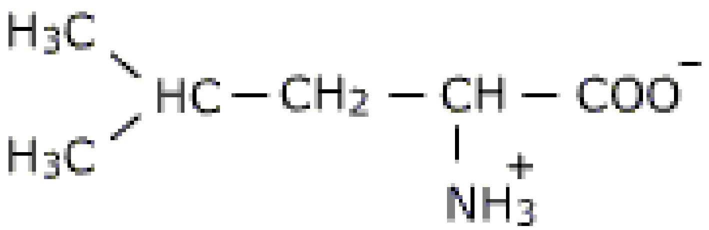
- Non Polar Amino Acids have equal number of amino and carboxyl groups and are neutral. These amino acids are hydrophobic and have no charge on the 'R' group.



Alanine

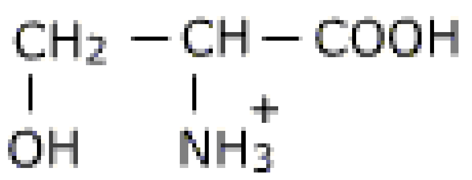


Valine

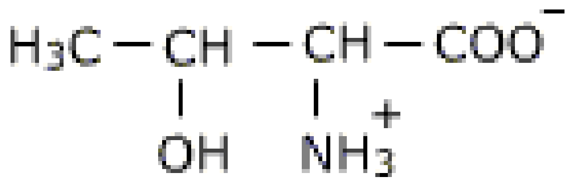


Leucine

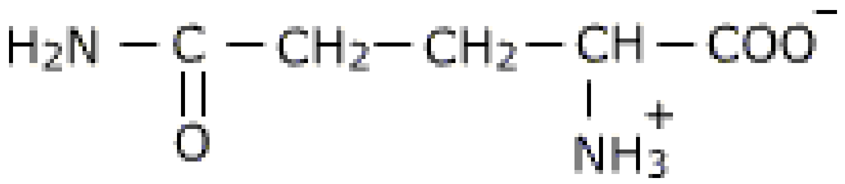
Polar Amino Acids with No Charge



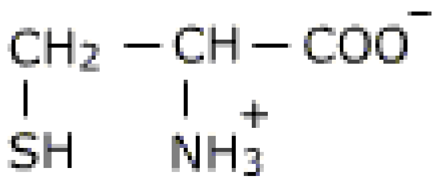
Serine



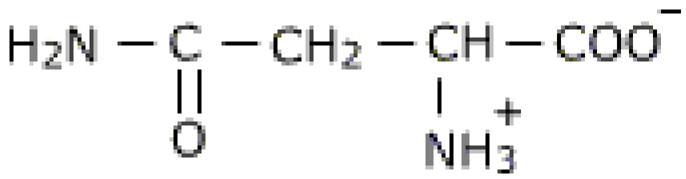
Threonine



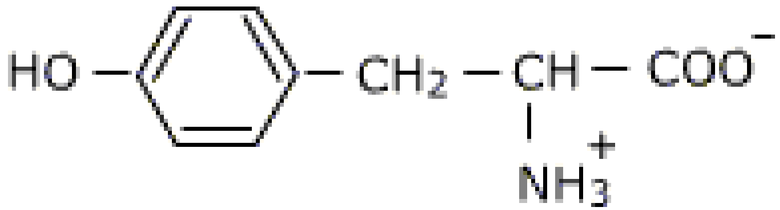
Gultamine



Cysteine



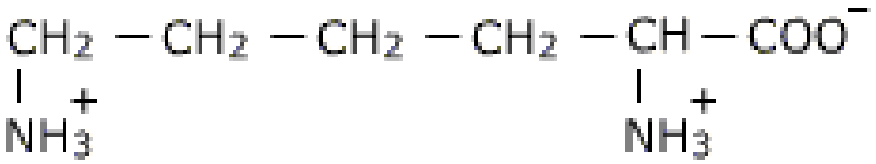
Aspargine



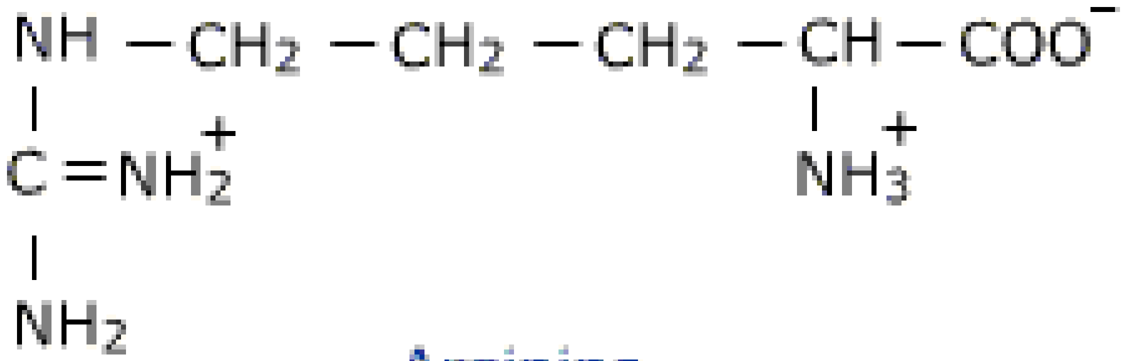
Tyrosine

Polar Amino Acids with Positive Charge

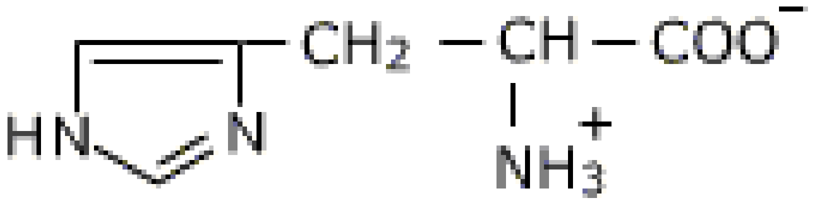
Polar amino acids with positive charge have more amino groups as compared to carboxyl groups making it basic. The amino acids, which have positive charge on the 'R' group are placed in this category. They are **lysine, arginine and histidine**.



Lysine



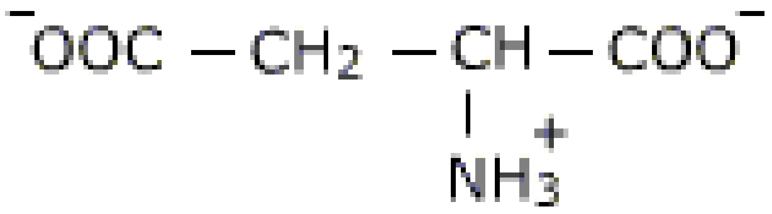
Arginine



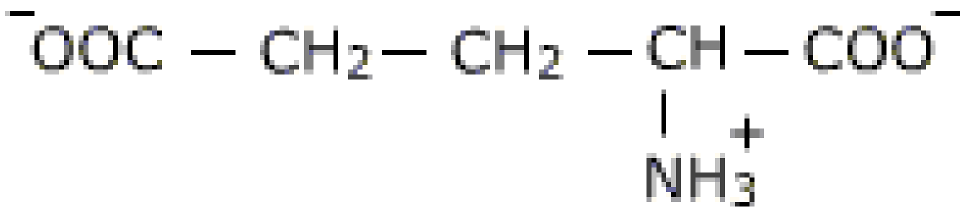
Histidine

Polar Amino Acids with Negative Charge

Polar amino acids with negative charge have more carboxyl groups than amino groups making them acidic. The amino acids, which have negative charge on the 'R' group are placed in this category. They are called as **dicarboxylic mono-amino acids**. They are **aspartic acid and glutamic acid**.

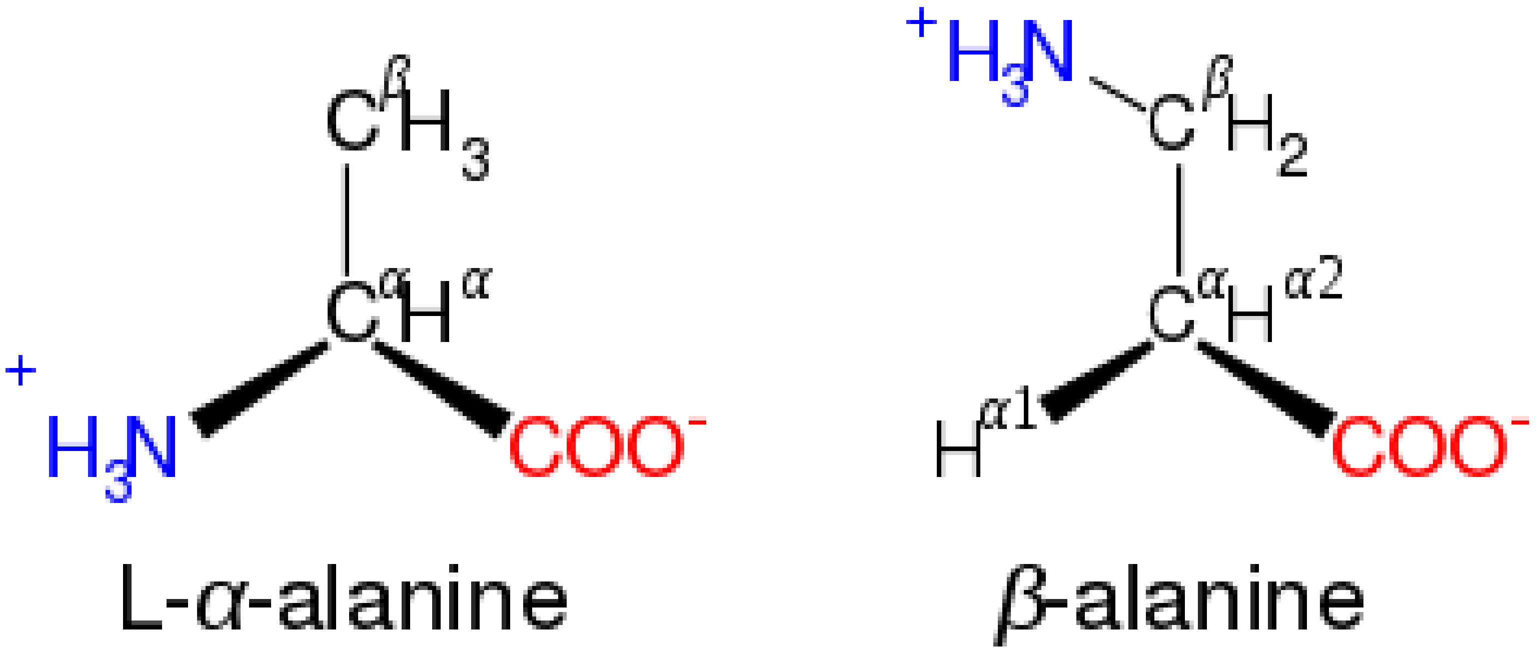


Aspartic acid



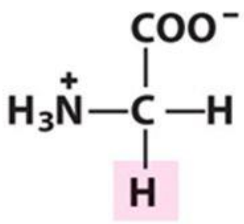
Glutamic acid

The **alpha carbon** (**Cα**) in organic molecules refers to the first carbonatom that attaches to a functional group, such as a carbonyl. The second carbon atom is called the **beta carbon** (**Cβ**)



Zwitterion

- At a particular pH, the amino acid carries no net charge and is called a zwitterion.

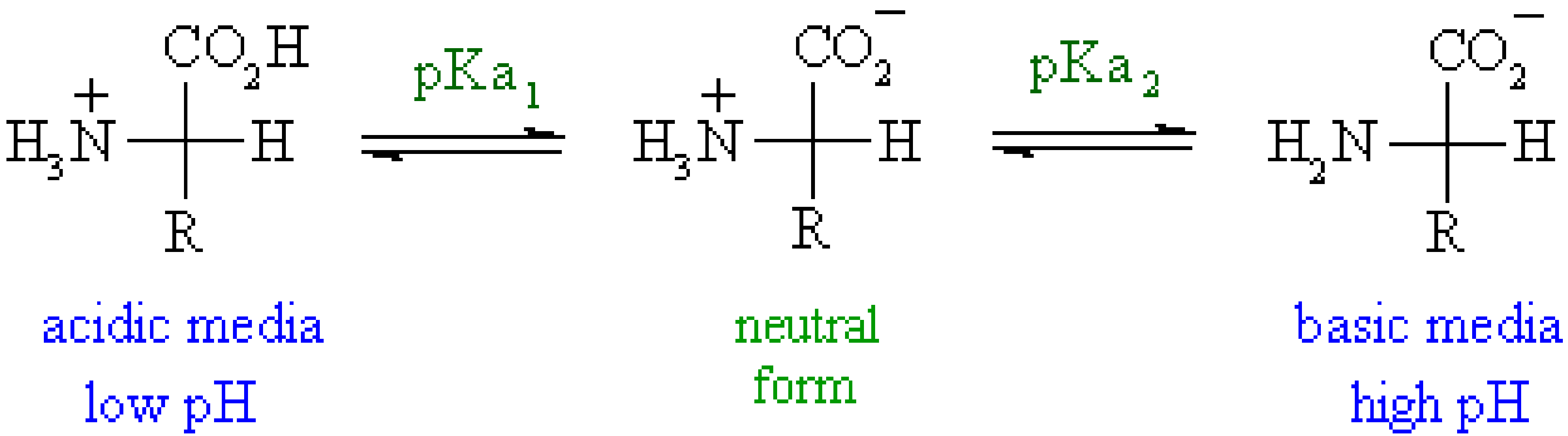


- Zwitterion …. dipolar ion – has 1 positive and 1 negative charge
- Amphoteric (ampholytes)

- pH, at which the amino acid has a net charge of zero is called the isoelectric point (pI),
- At the isoelectric point (pI), the + and – charges are equal.

The **isoelectronic point** or isoionic **point** is the pH at which the **amino acid** does not migrate in an electric field. This means it is the pH at which the **amino acid**is neutral, i.e. the zwitterion form is dominant.

A **zwitterion** is a molecule with functional groups, of which at least one has a positive and one has a negative electrical charge. The net charge of the entire molecule is zero. Amino acids are the best-known examples of **zwitterions**



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

pKa—an association constant. It’s the negative logarithm of the ratio of dissociated acid and conjugated base, over the concentration of the associated chemical.

pI—called the “isoelectric point,” this is the pH at which a molecule has a net neutral charge.

$$K_{COOH} = \frac{[R - COO^-][H^+]}{[R - COOH]} \quad ; \quad K_{NH_3^+} = \frac{[R - NH_2][H^+]}{[R - NH_3^+]}$$

pKa of $-COOH$ [1.8-4.3]

pKa of $-NH_2$ [9.1-12.5]

- For an amino acid with only one amine and one carboxyl group, the pI can be calculated from the mean of the pKa of this molecule:

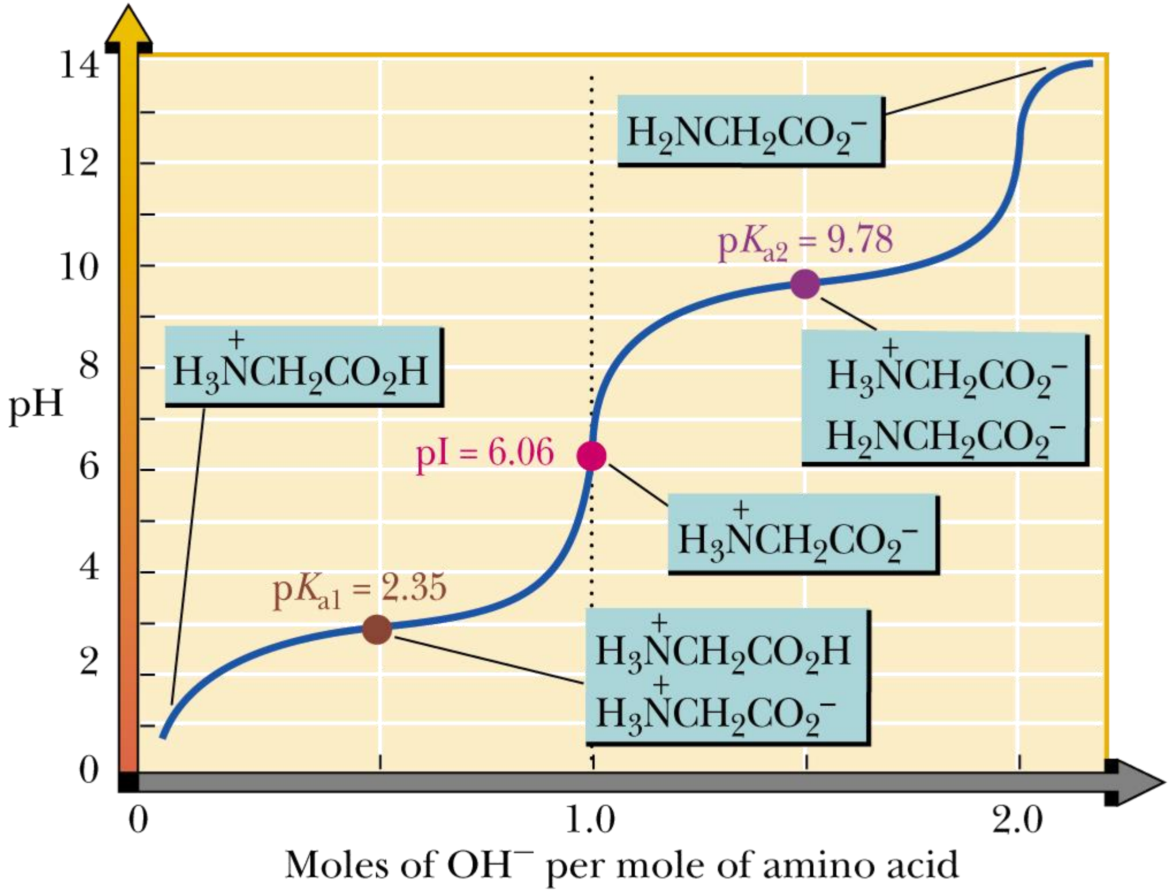
$$\boxed{pI = (pKa1 + pKa2)/2}$$

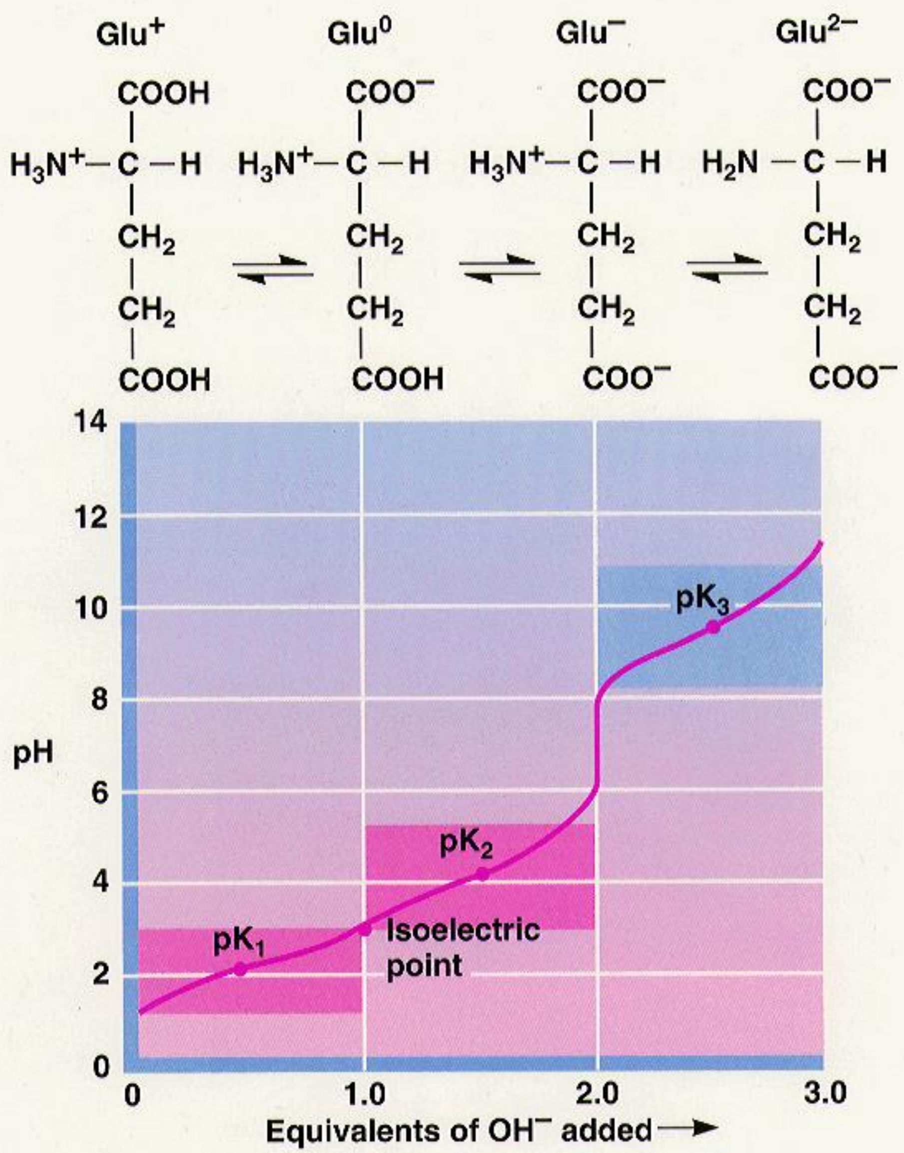
Leucine:

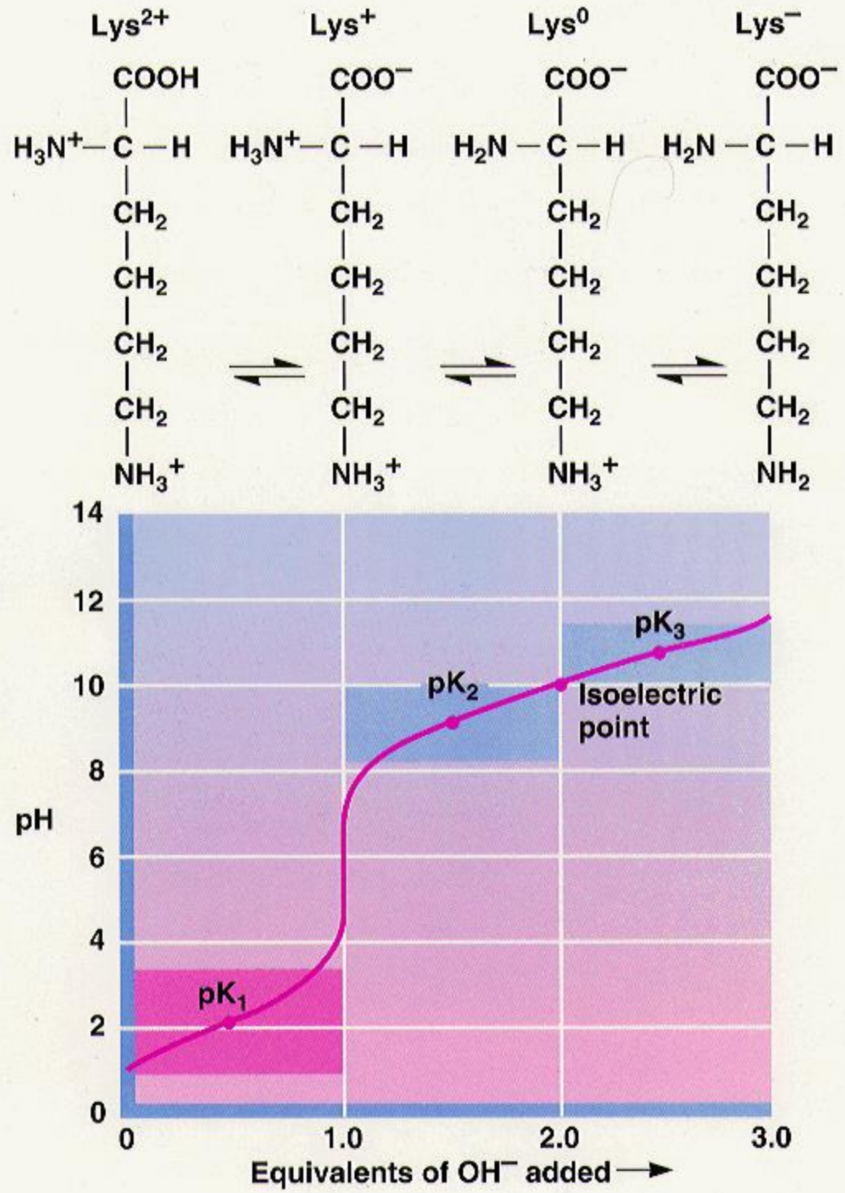
$$pI = \frac{pK_{COOH} + pK_{NH_3^+}}{2} = \frac{2,36 + 9,6}{2} = 5,98$$

Titration of Amino Acids

- Titration of glycine with NaOH




Glu+
Glu0
Glu−
Glu2−
COOH
COO−
H3N+—C—H
H2N—C—H
CH2
COO−
pK1
pK2
pK3
Isoelectric point
pH
14
12
10
8
6
4
2
0
1.0
2.0
3.0
Equivalents of OH− added


Lys2+
Lys+
Lys0
Lys−
COOH
COO−
H3N+—C—H
H2N—C—H
CH2
NH3+
NH2
pK1
pK2
pK3
Isoelectric point
pH
14
12
10
8
6
4
2
0
1.0
2.0
3.0
Equivalents of OH− added

Isoelectric Point (pI)

Nonpolar & polar side chains	pK_a of $\alpha\text{–COOH}$	pK_a of $\alpha\text{–NH}_3^+$	pK_a of Side Chain	pI
alanine	2.35	9.87	----	6.11
asparagine	2.02	8.80	----	5.41
glutamine	2.17	9.13	----	5.65
glycine	2.35	9.78	----	6.06
isoleucine	2.32	9.76	----	6.04
leucine	2.33	9.74	----	6.04
methionine	2.28	9.21	----	5.74
phenylalanine	2.58	9.24	----	5.91
proline	2.00	10.60	----	6.30
serine	2.21	9.15	----	5.68
threonine	2.09	9.10	----	5.60
tryptophan	2.38	9.39	----	5.88
valine	2.29	9.72	----	6.00

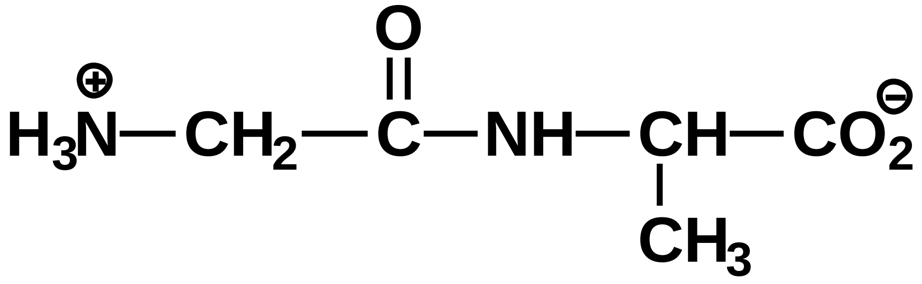
Isoelectric Point (pI)

Acidic Side Chains	pK_a of α–COOH	pK_a of α–NH_3^+	pK_a of Side Chain	pI
aspartic acid	2.10	9.82	3.86	2.98
glutamic acid	2.10	9.47	4.07	3.08
cysteine	2.05	10.25	8.00	5.02
tyrosine	2.20	9.11	10.07	5.63

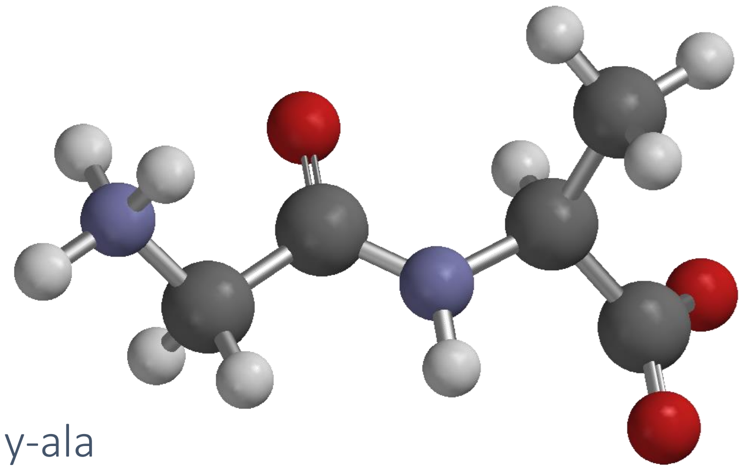
Basic Side Chains	pK_a of α–COOH	pK_a of α–NH_3^+	pK_a of Side Chain	pI
arginine	2.01	9.04	12.48	10.76
histidine	1.77	9.18	6.10	7.64
lysine	2.18	8.95	10.53	9.74

PROTEIND AND PEPTIDES

- Peptides are amino acid polymers containing 2–50 individual units
- Peptides with >50 units are called proteins
- By convention, peptide structures are written with the *N*-terminal amino acid on the left and the *C*-terminal amino acid on the right.



A dipeptide



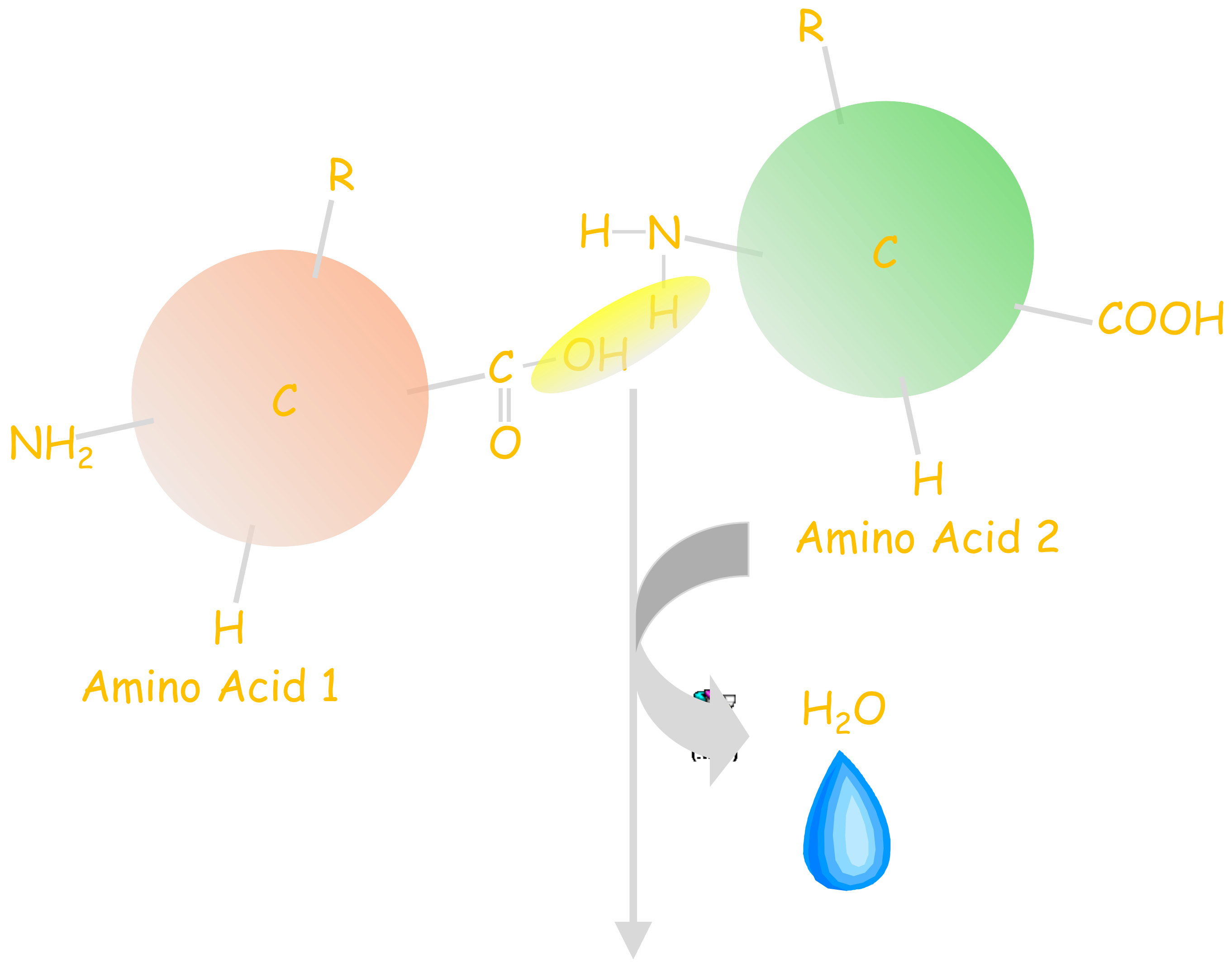
glycylalanine = gly-ala

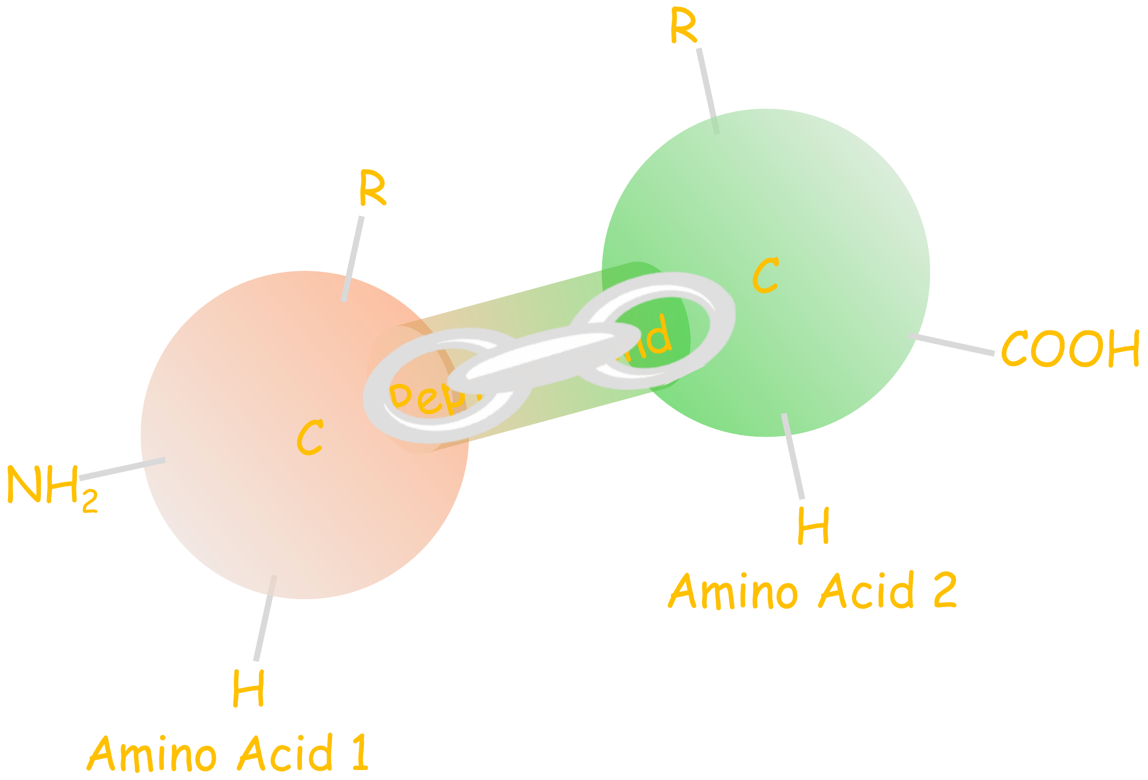
STRUCTURE OF PROTEIN

There are four types:

- **Primary structure-** The amino acid sequence.
- **Secondary structure-** Regularly repeating local structures stabilized by hydrogen bond.
- **Tertiary structure-**Three dimensional structure of polypeptide.
- **Quaternary structure-**The structure formed by several protein molecules (polypeptide chains).

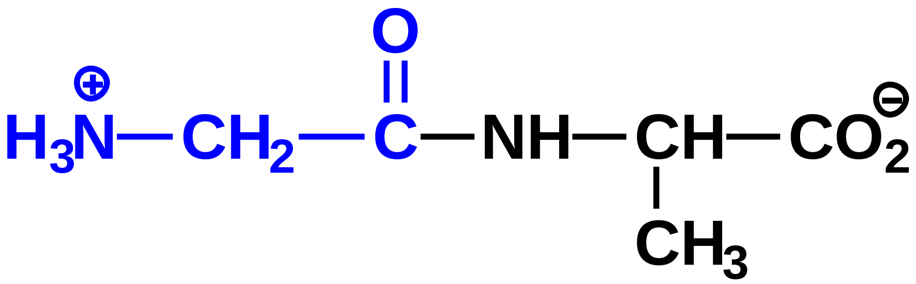
Peptide bonds form by dehydration synthesis




R
C
COOH
H
Amino Acid 2
R
C
NH2
H
Amino Acid 1

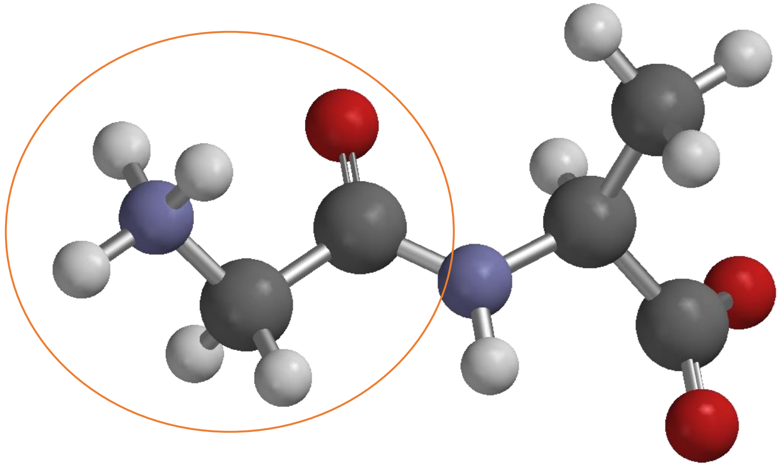
Peptides

glycylalanine = gly-ala



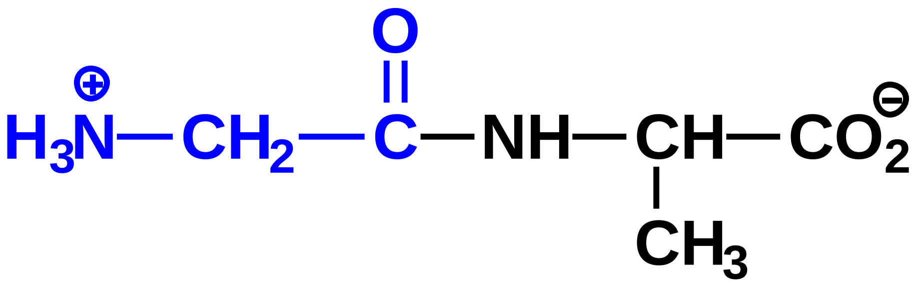
glycine

amino-terminal amino acid



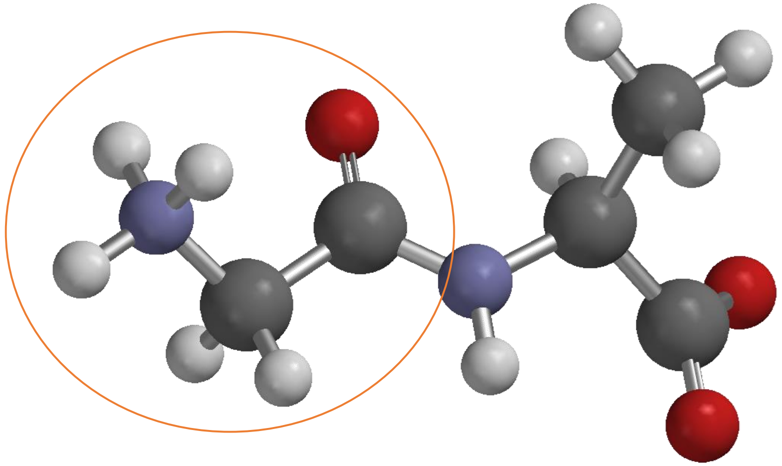
Peptides

glycylalanine = gly-ala



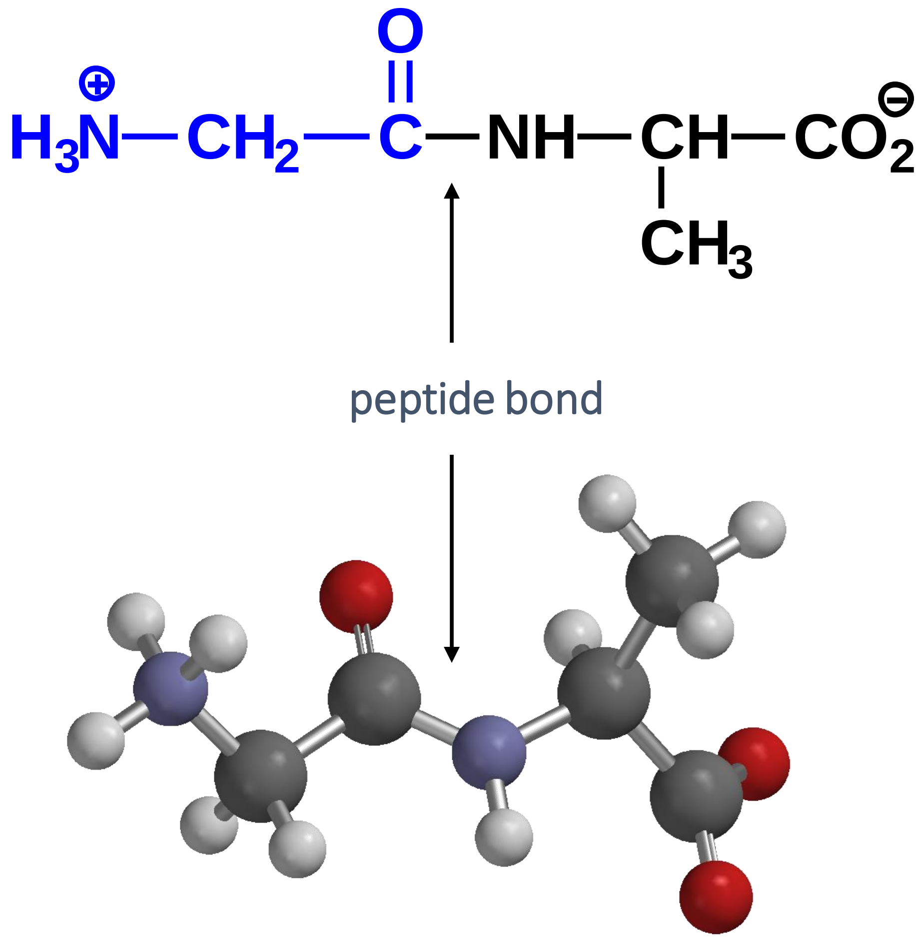
alanine

carboxy-terminal amino acid



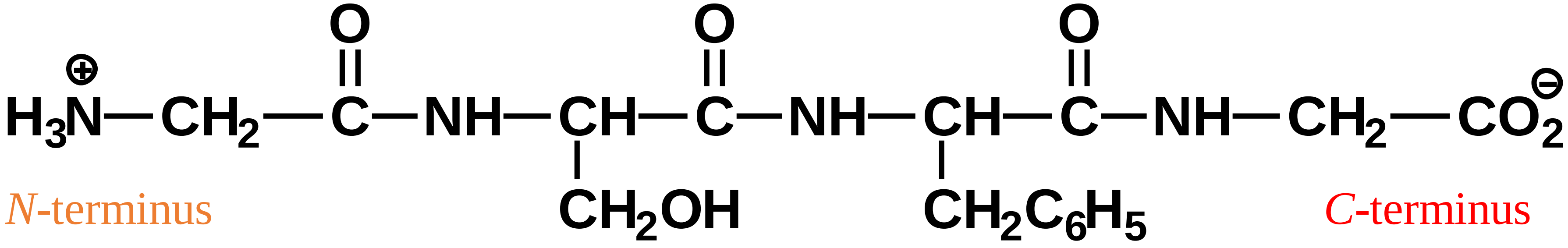
Peptides

glycylalanine = gly-ala



Peptides

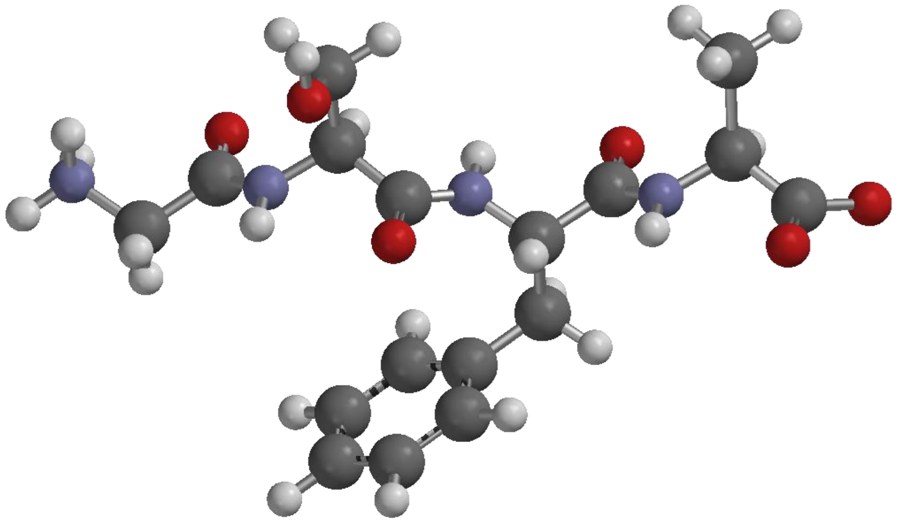
- A tetrapeptide:



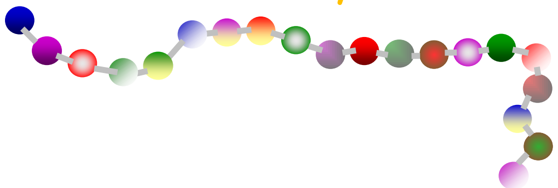
N-terminus

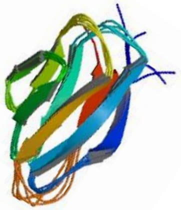
C-terminus

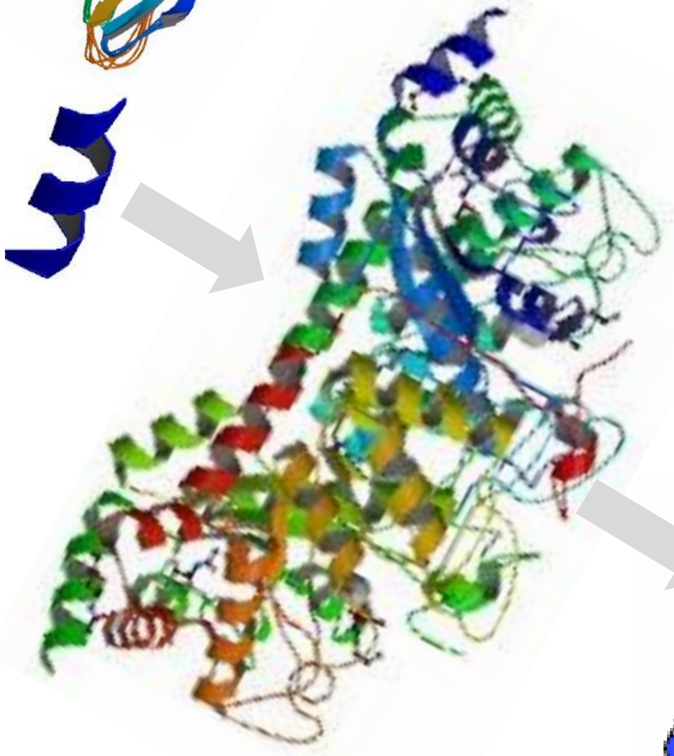
glycylserylphenylalanylglycine gly-ser-phe-gly

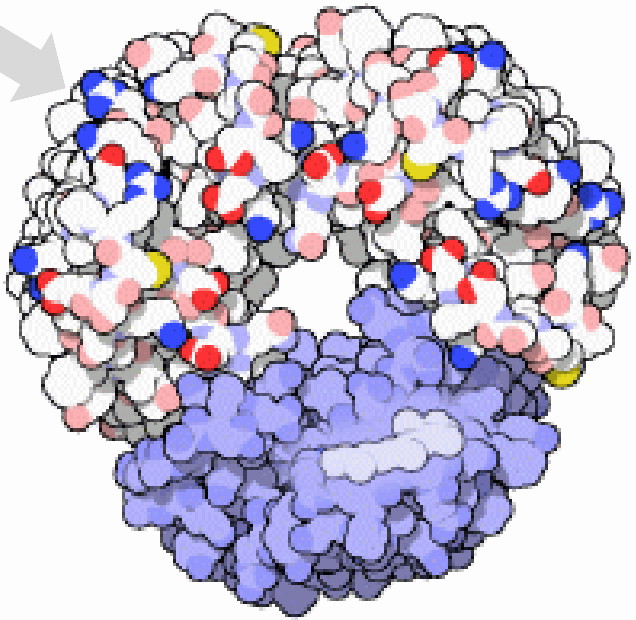


Primary Secondary Tertiar y Quaternary



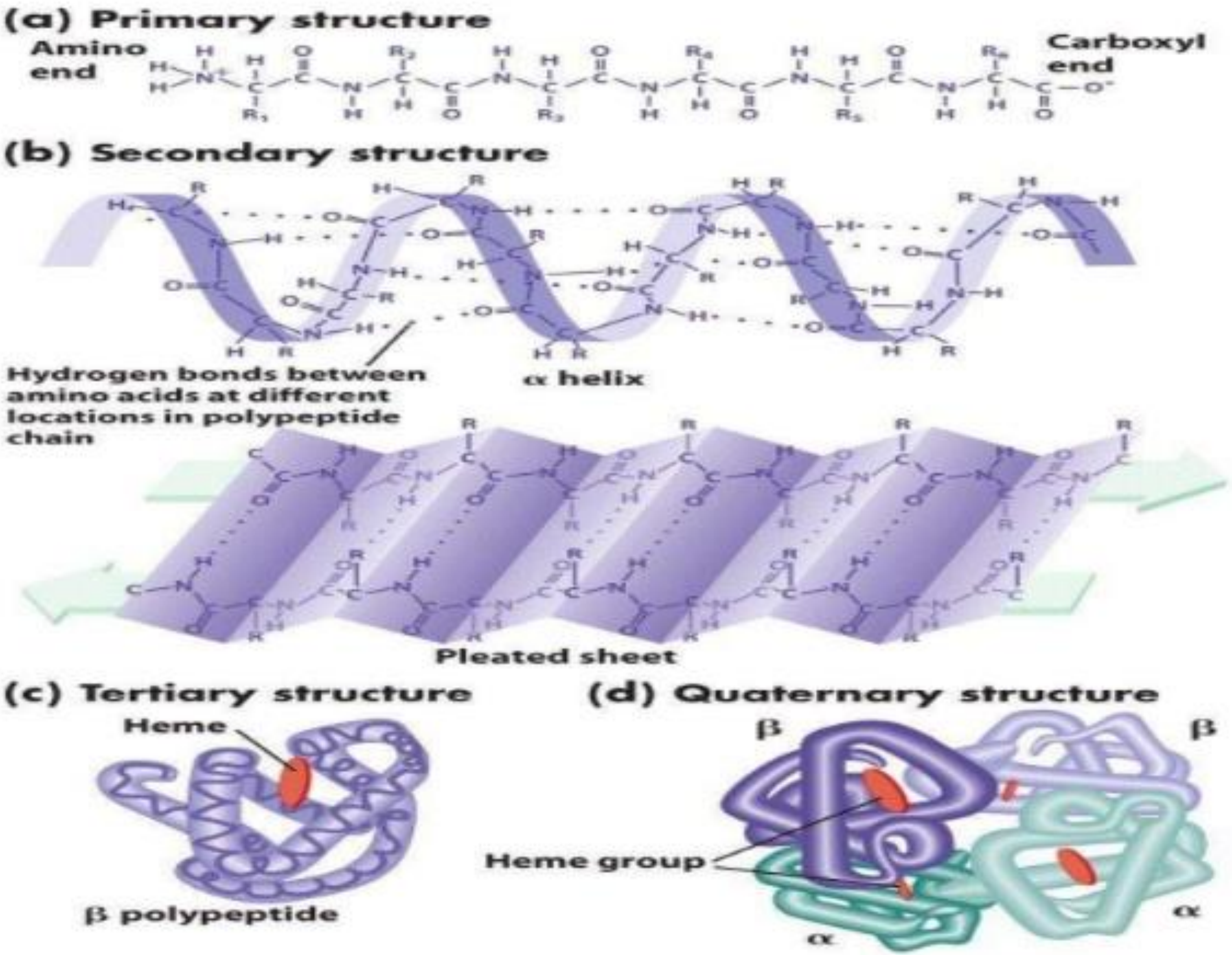


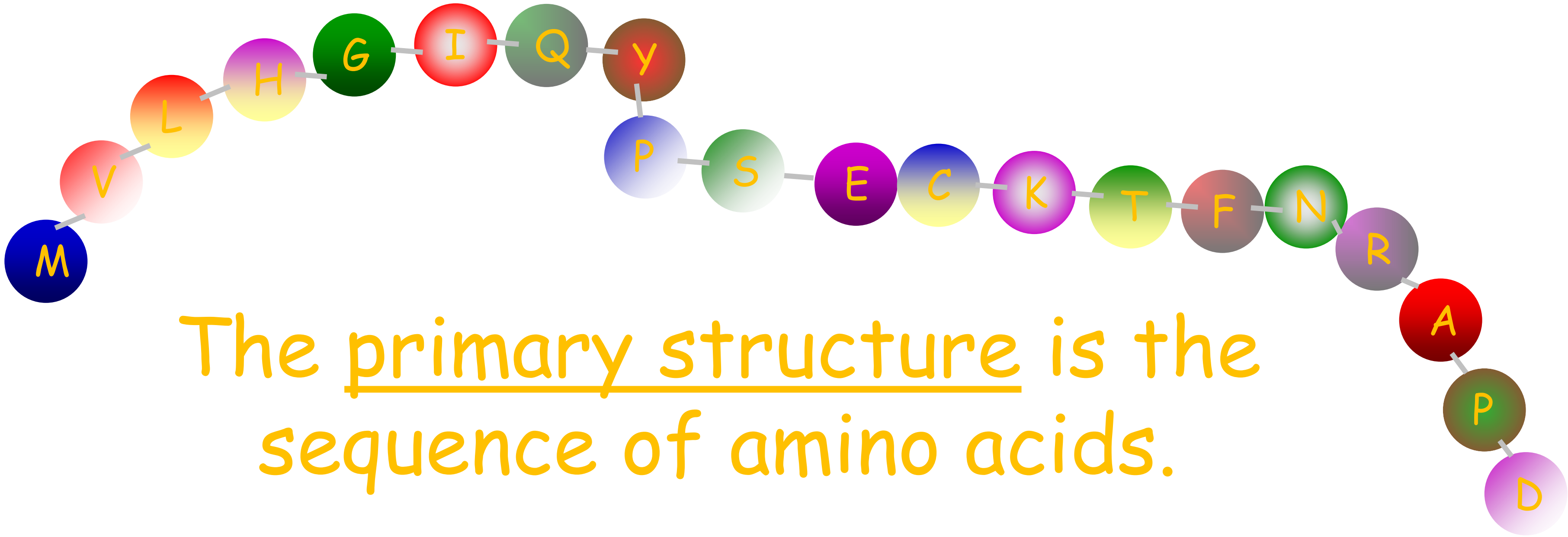




There are 4 basic

Levels of Protein Structure

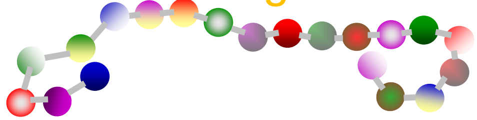

(a) Primary structure
Amino end
Carboxyl end
(b) Secondary structure
Hydrogen bonds between amino acids at different locations in polypeptide chain
α helix
Pleated sheet
(c) Tertiary structure
Heme
β polypeptide
(d) Quaternary structure
β
β
Heme group
α
α



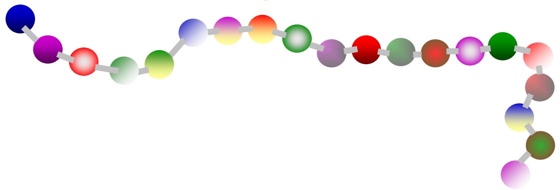
The primary structure is the sequence of amino acids.

The <u>secondary structure</u> is primarily composed of alpha helices and beta-pleated sheets.

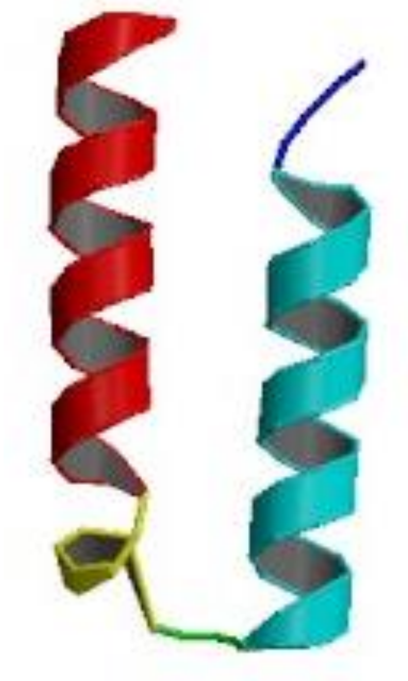
Folding Back and Coiling



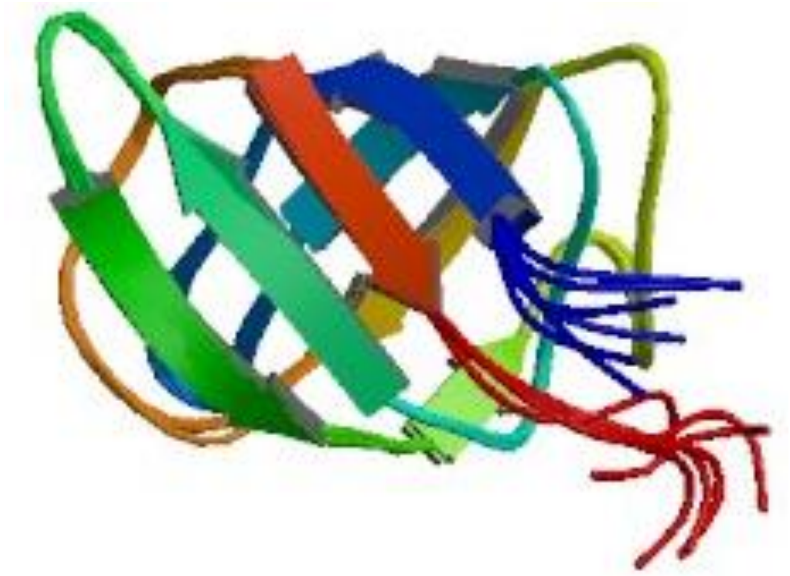
Primary Structure



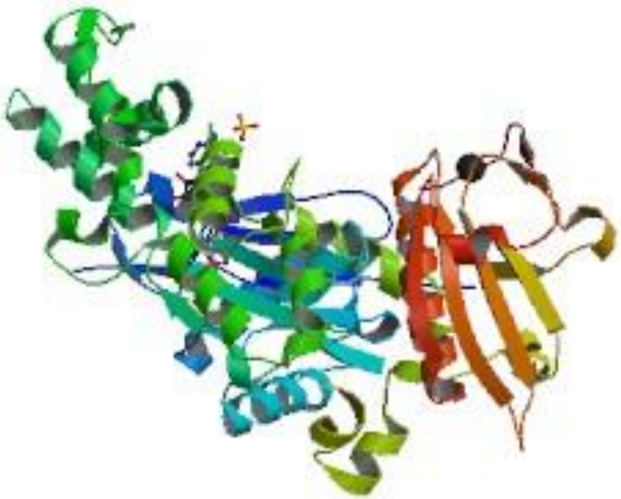
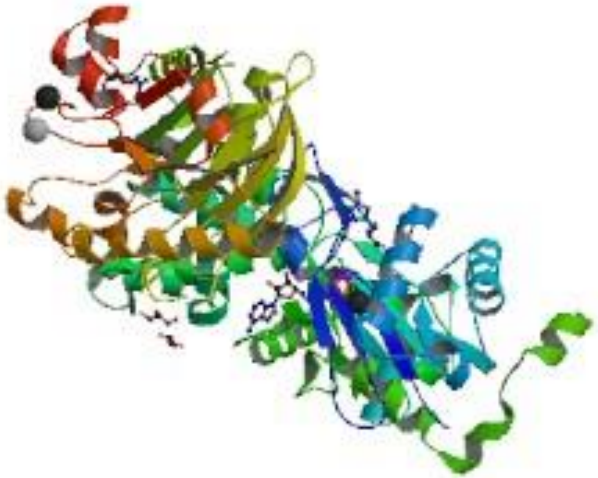
Alpha Helix



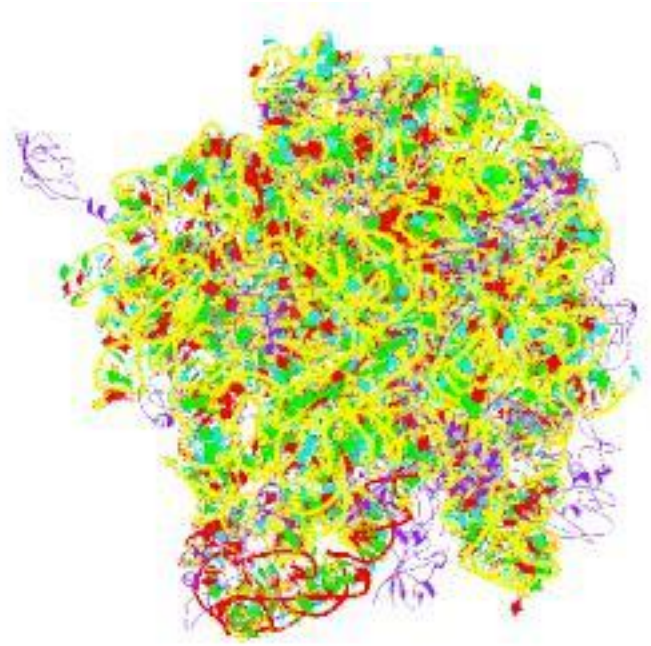
Beta-Pleated Sheet

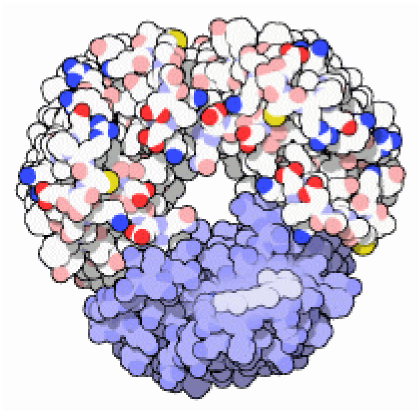


The tertiary structure is the protein's 3D shape.

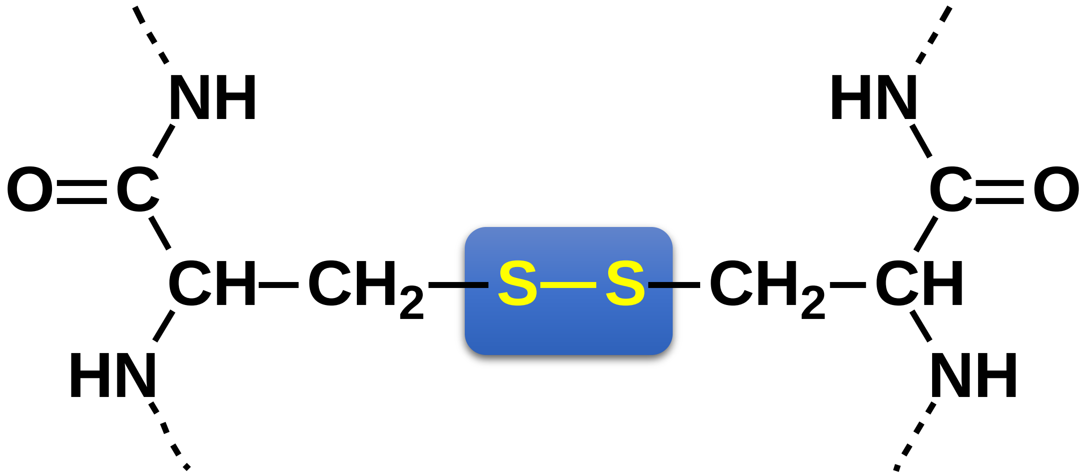

The quaternary structure is the assembly of folded subunits.





Peptides

- The only other type of covalent bond between amino acids in proteins and peptides is the ***disulfide linkage*** between two ***cysteine*** units:



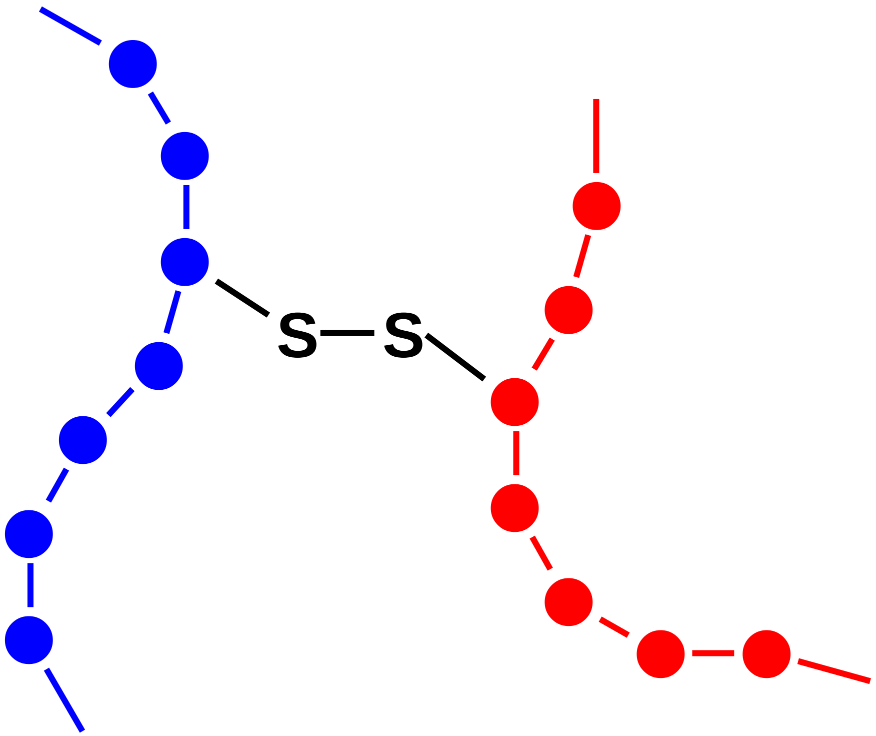
Peptides

- Note:
  - Thiols are readily ***oxidized*** to disulfides.
  - Disulfides are readily ***reduced*** to thiols.

$$\mathrm{R{-}SH} + \mathrm{HS{-}R} \underset{[H]}{\overset{[O]}{\rightleftharpoons}} \mathrm{R{-}S{-}S{-}R}$$

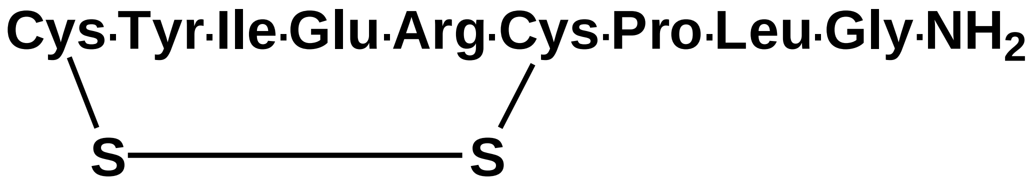
Peptides

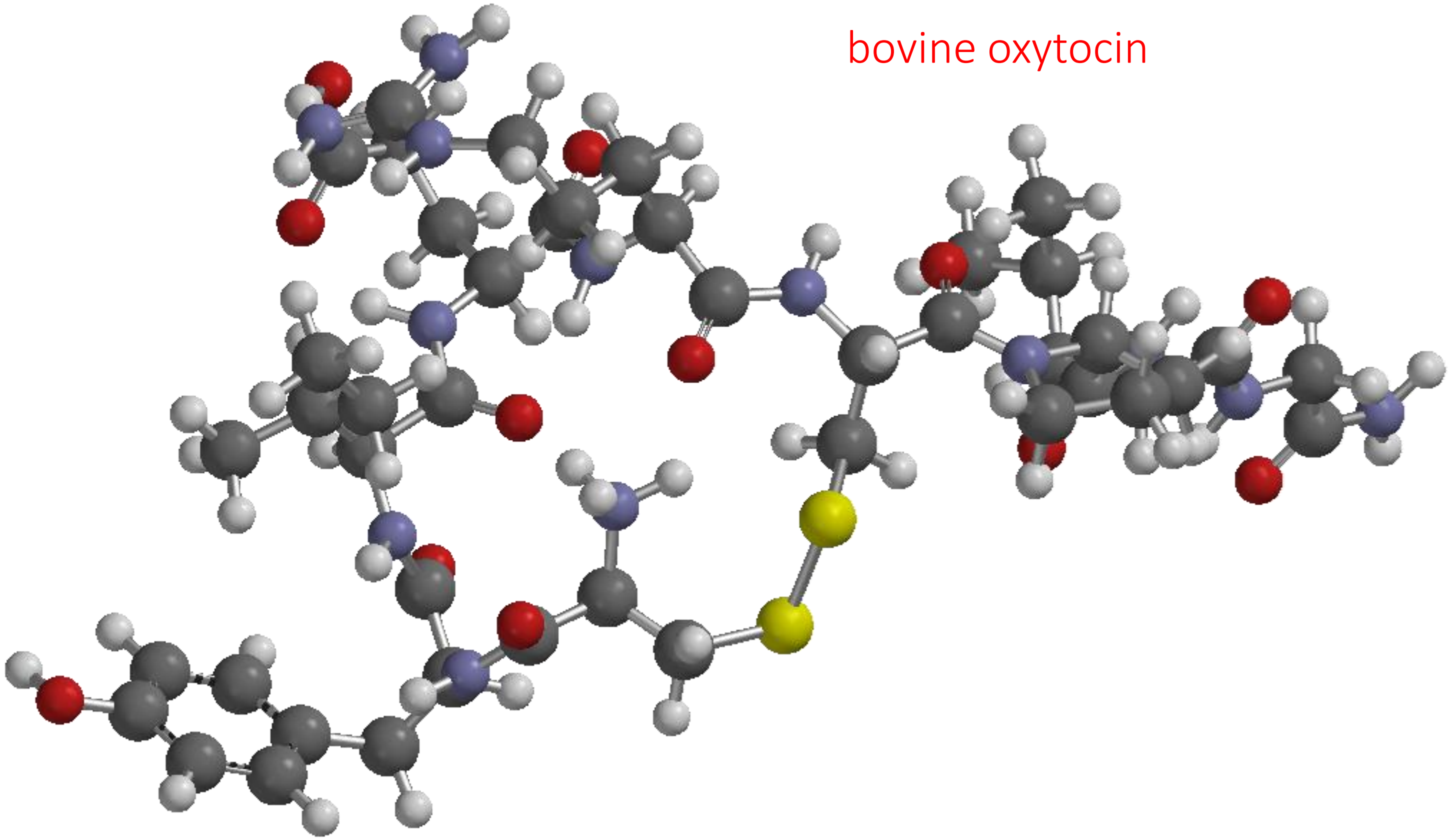
- Disulfide links serve to connect polypeptide chains:



Peptides

- … or can form a macrocycle:





bovine oxytocin

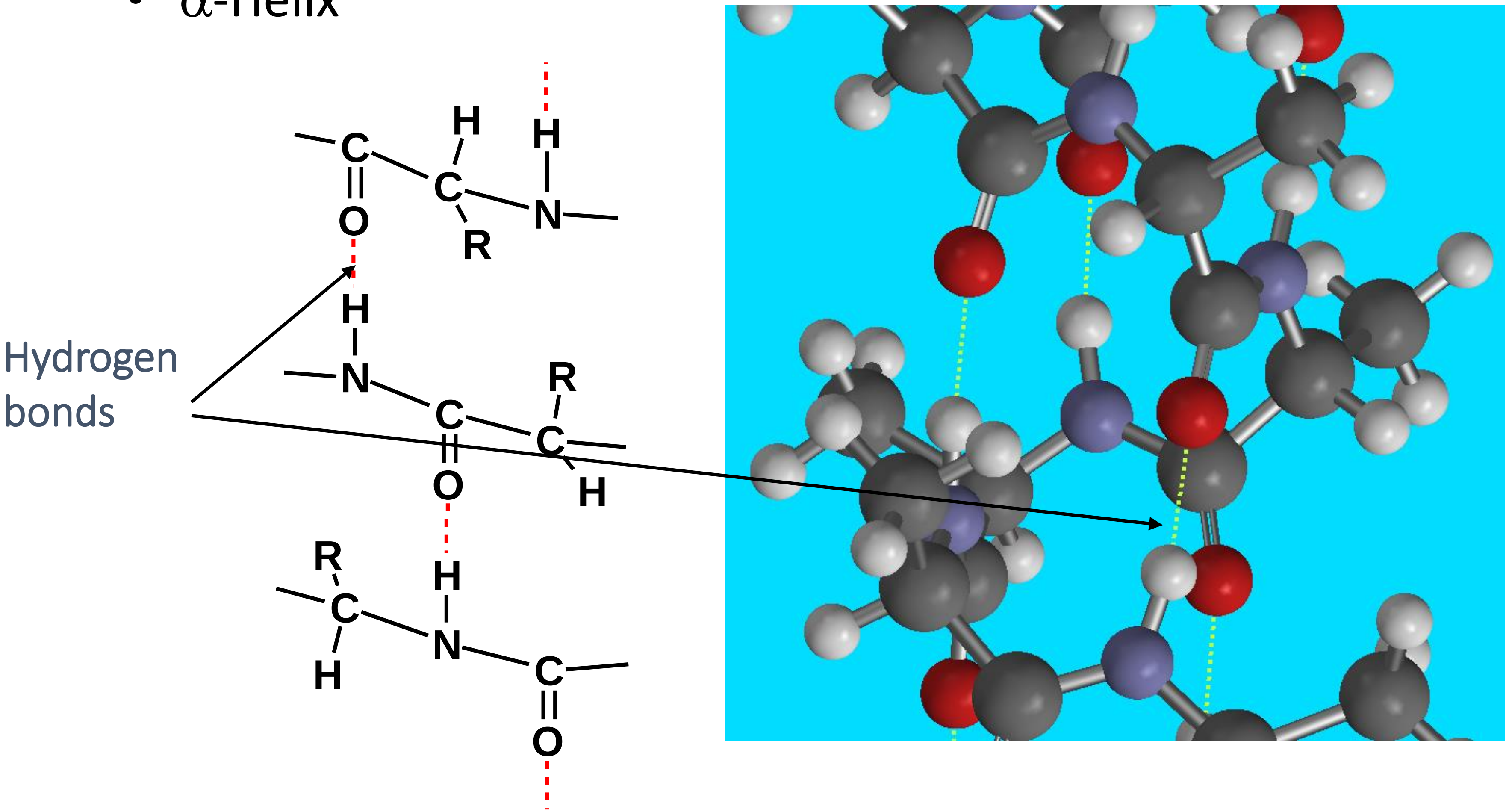
Proteins

- Protein function depends on structure.
    - Depends on various amino acids.

- ***Primary Structure:*** The amino acid sequence.

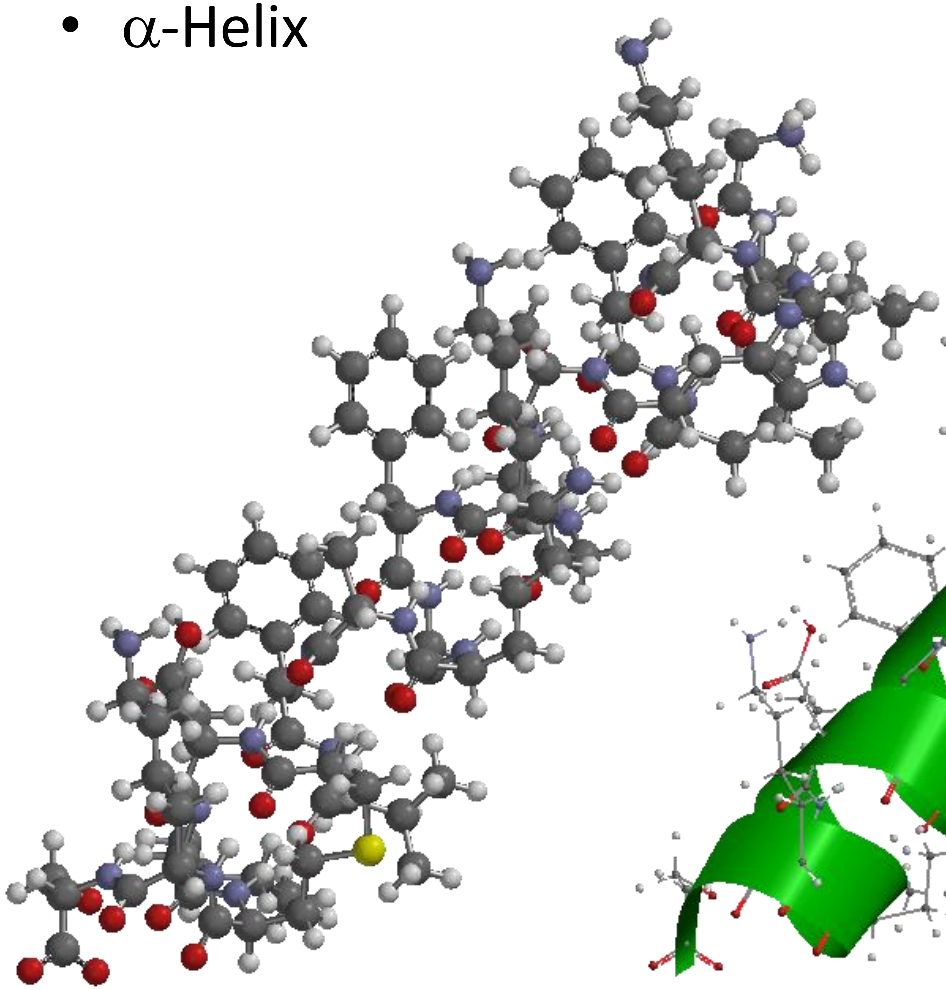
Proteins

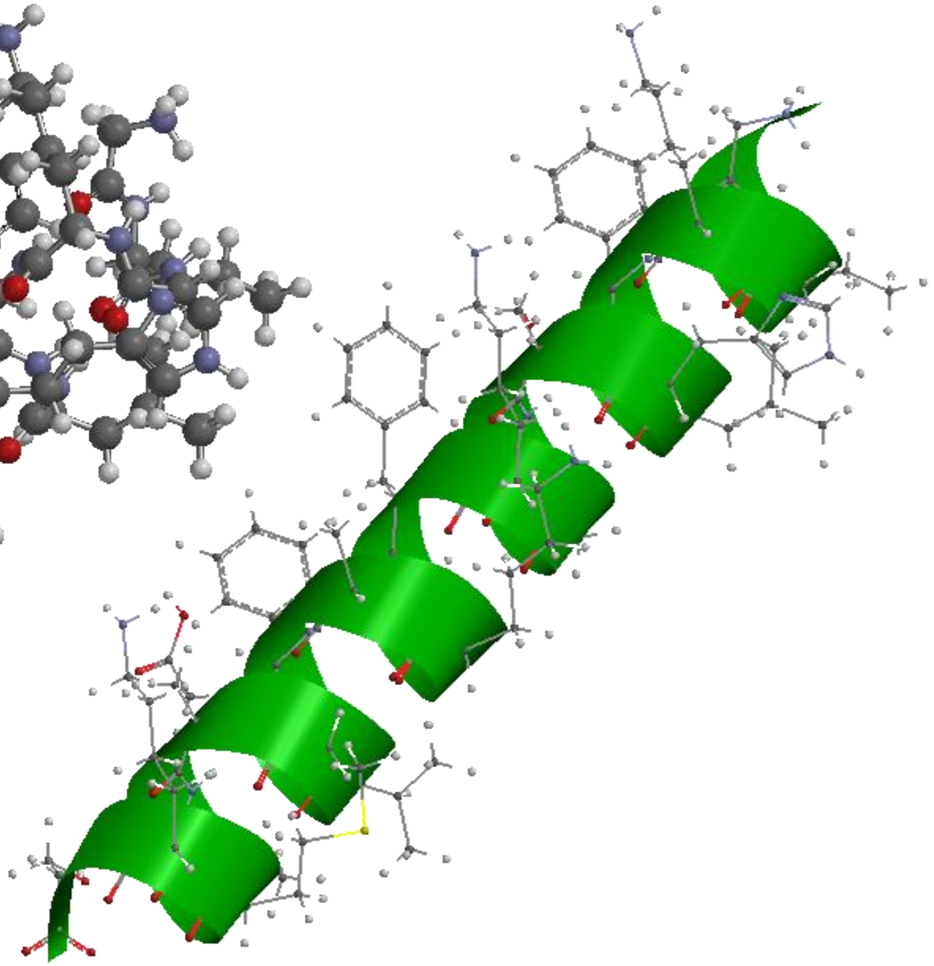
- ***Secondary Structure:*** The "local" hydrogen-bonding scheme.
  - α-Helix



Proteins

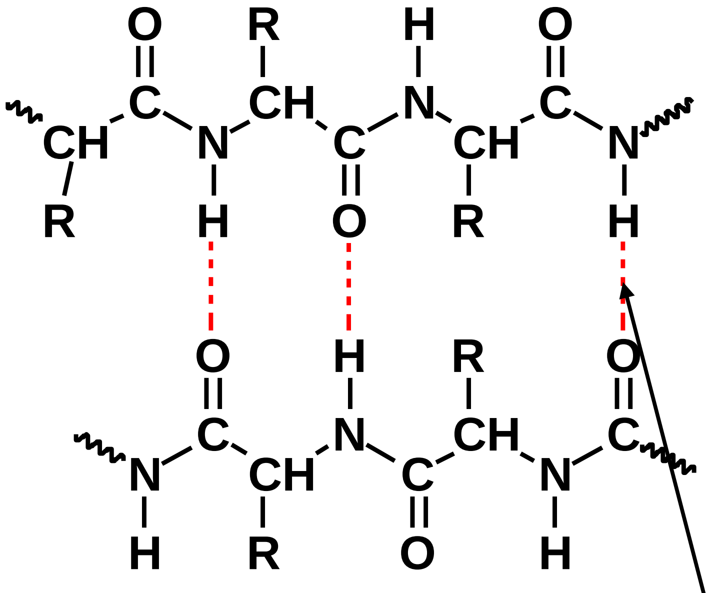
- *Secondary Structure:* The “local” hydrogen-bonding scheme.
  - α-Helix

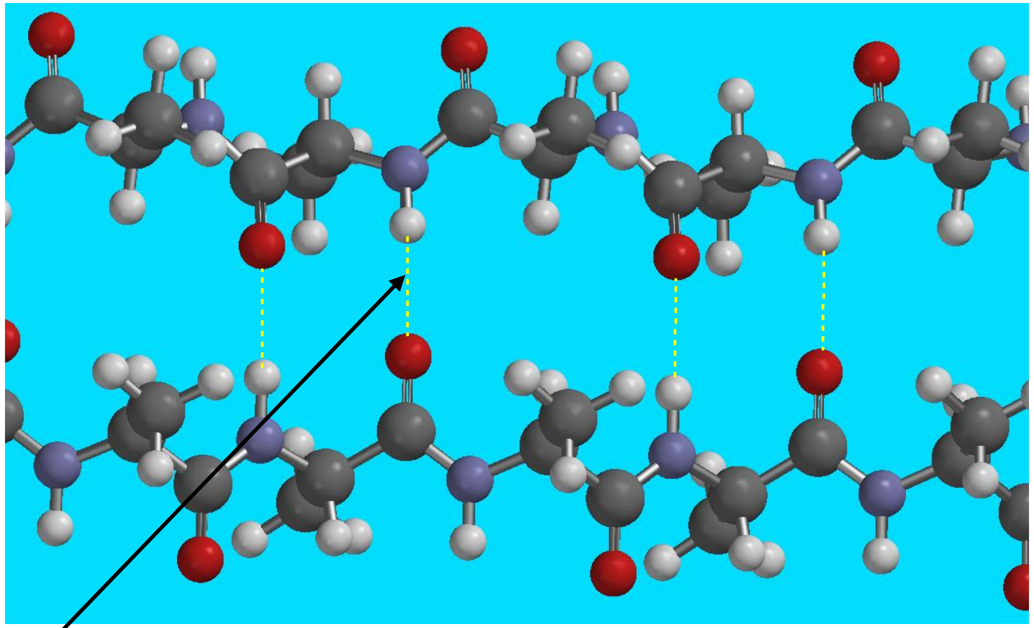




Proteins

- ***Secondary Structure:*** The “local” hydrogen-bonding scheme.
    - β-Sheet





Interchain **hydrogen bonds**

Proteins

- ***Tertiary Structure:*** How the protein, with all of its regions of secondary structure (α-helix, β-sheet) has folded over upon itself

- **Interaction between R-groups is important**

- All intermolecular forces we have studied are at play

Proteins

- ***Tertiary Structure:*** Chemical bonds between cysteines

$$-CH_2-\boxed{SH} + \boxed{HS}-CH_2-$$

$$\downarrow$$

$$-CH_2-\boxed{S-S}-CH_2-$$

Disulfide bonds