

# **Polypeptides and proteins**

## **Lecture 1**

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# Peptide bond

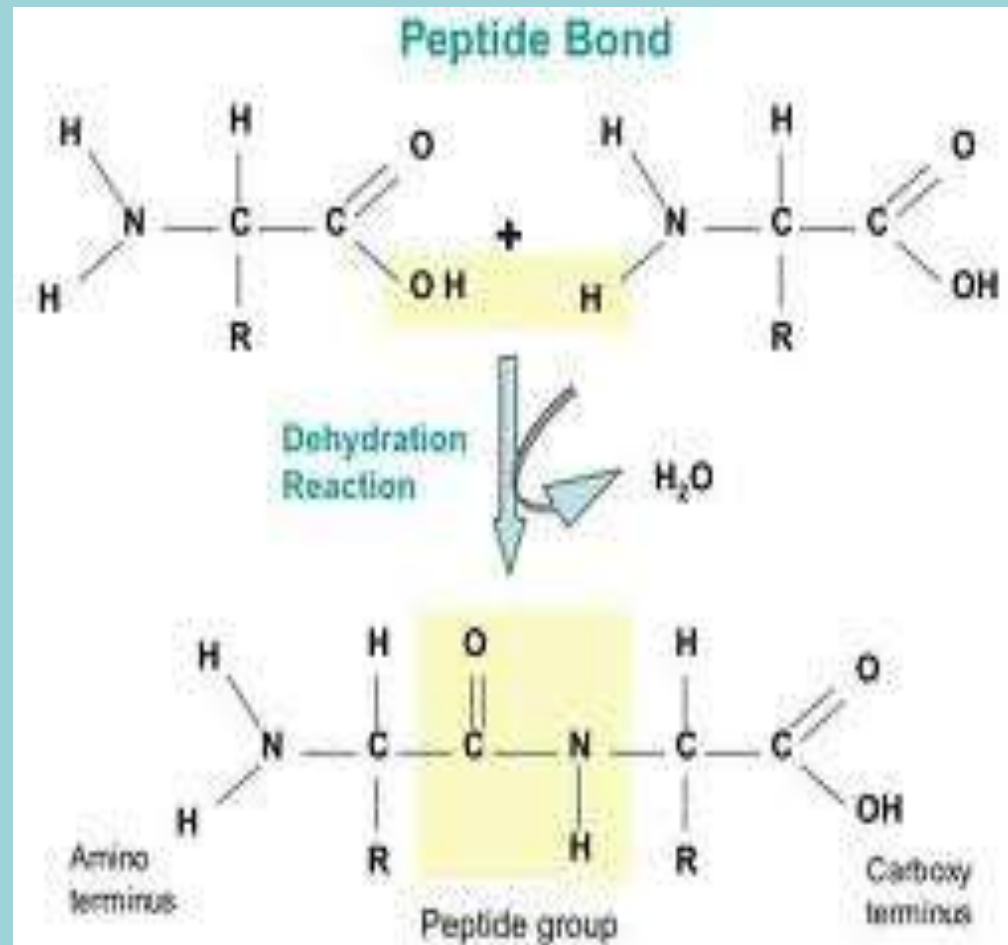
is a chemical bond that is formed between two amino acids when the carboxyl group of one molecule reacts with the amino group of the other molecule, releasing a molecule of water (H<sub>2</sub>O).

**This is a dehydration synthesis reaction (also known as a condensation reaction), and usually occurs between amino acids**

The resulting CO-NH bond is called a peptide bond, and the resulting molecule is an amide.

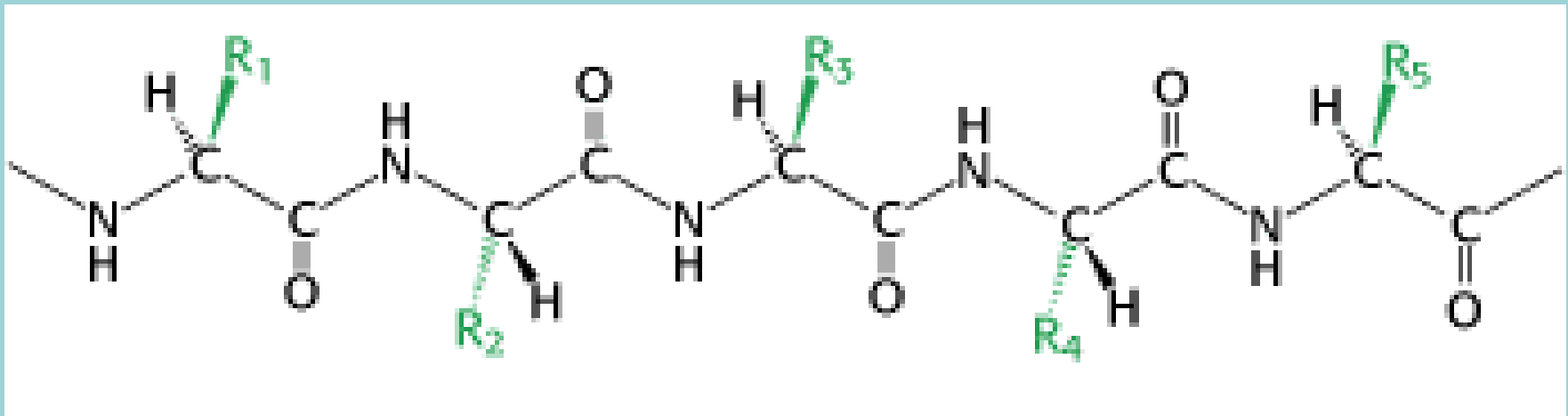
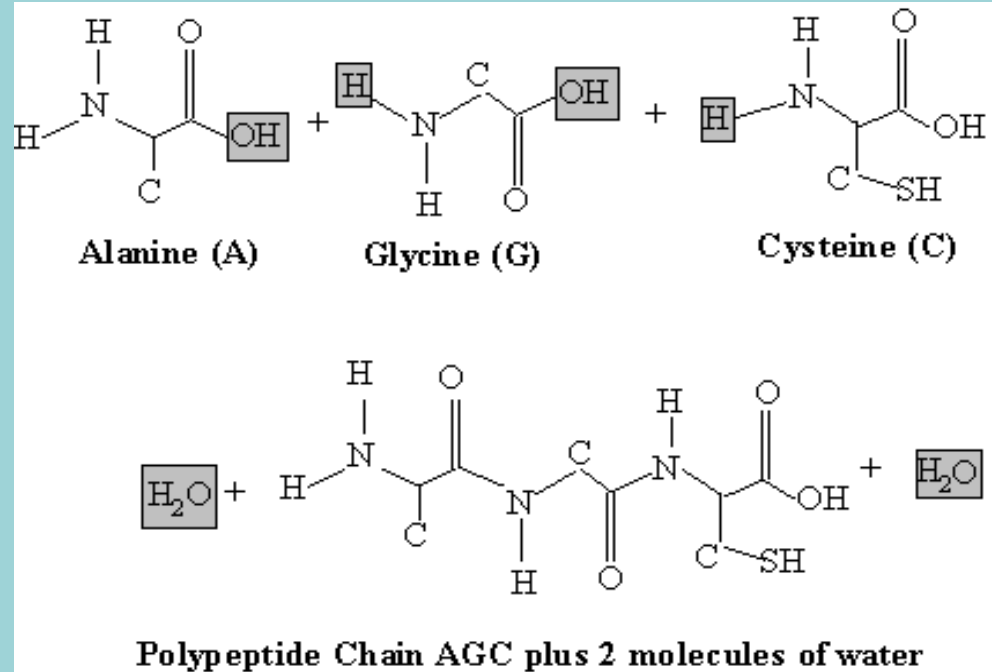
Di-peptides have two amino acids, tri-peptides have three amino acids, and a sequence of amino acids linked by peptide bonds is known as a polypeptide.

**Polypeptides and proteins are chains of amino acids held together by peptide bonds**



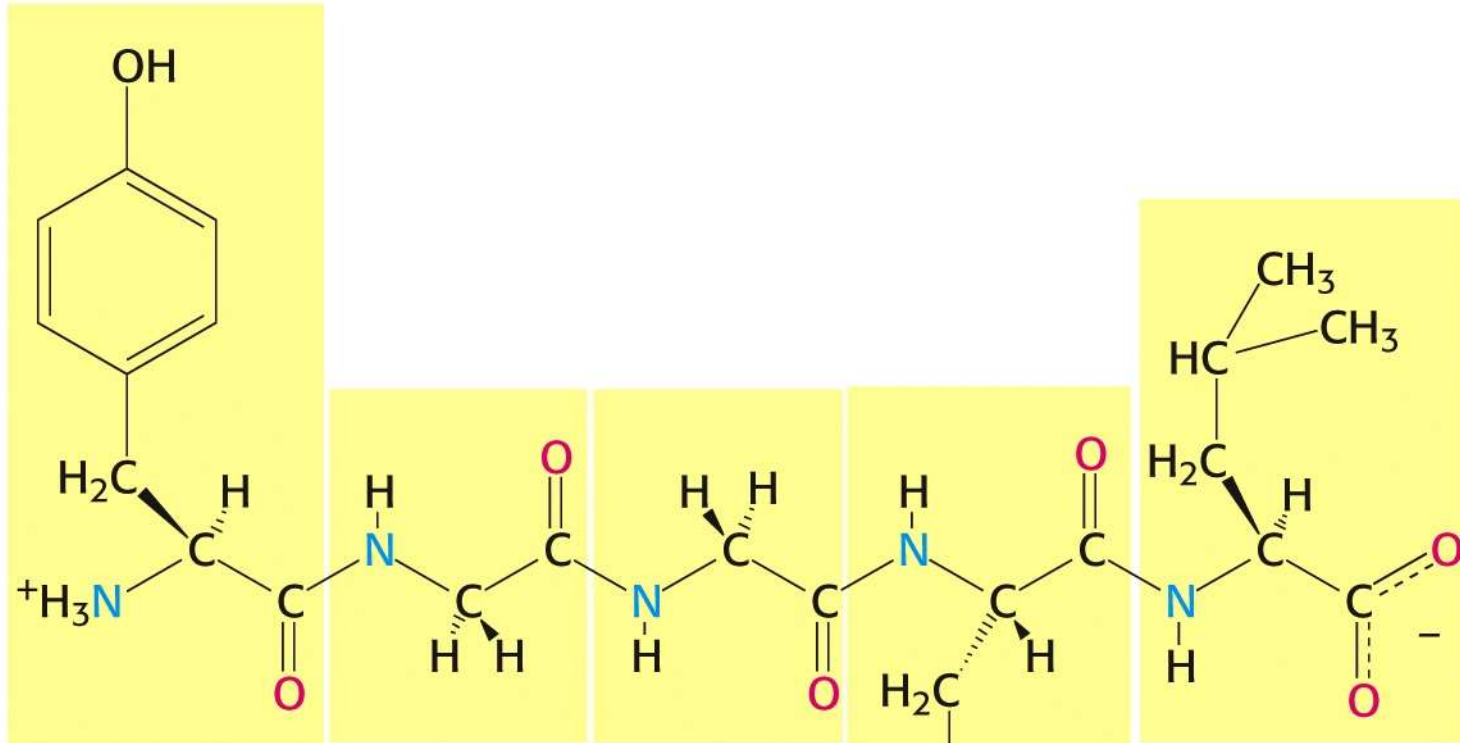
# Direction of Polypeptide chain

Sequences of amino acids in a polypeptide are read from the amino terminal end to the carboxy-terminal end.



A polypeptide chain consists of a constant backbone (black) and variable side chains “R” (green).

# Polypeptide chain has direction



Tyr

Gly

Gly

Phe

Leu

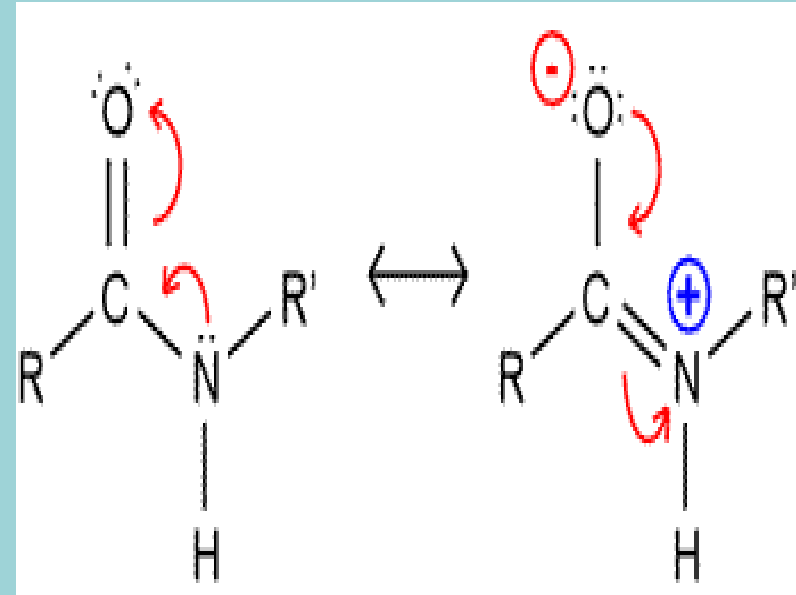
Amino  
terminal residue

Carboxyl  
terminal residue



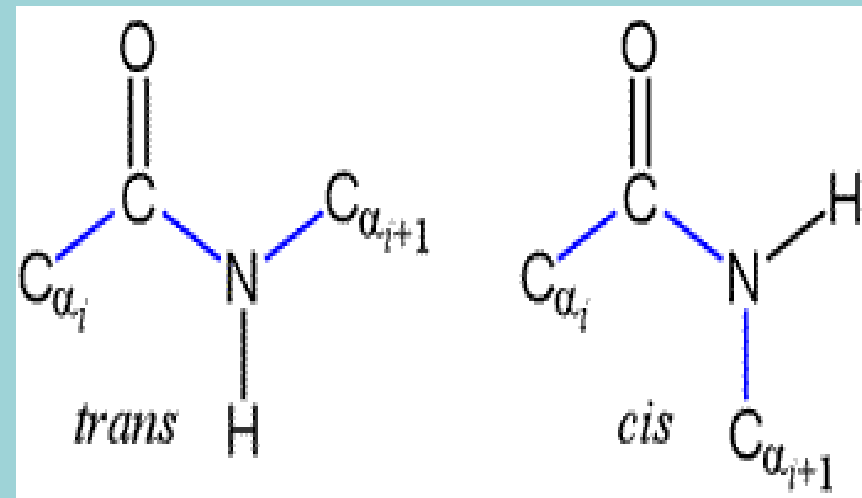
# Characteristics of the peptide bond:

1. It is a covalent bond.
2. Strong bond
3. Peptide bond is uncharged but polar
4. Lack of rotation around the bond: The peptide bond has a partial double-bond character- that is; **it is shorter than a single bond and is therefore rigid and planar.**



5. Trans configuration: The peptide bond is generally a trans bond (instead of cis).

**Trans form is strongly favoured because of steric clashes that occur in the cis form**



# Proteins

Proteins are composed of one or more than one of polypeptide chains containing hundreds of amino acids.

Each protein has its own **unique amino acid sequence** that is specified by the nucleotide sequence of the **gene encoding** this protein.

Protein builds, maintains, and replaces the tissues in your body. Your muscles, your organs, and your immune system are made up mostly of protein.

Your body uses the protein you eat to make lots of specialized protein molecules that have specific jobs. For instance, your body uses protein to make hemoglobin, the part of red blood cells that carries oxygen to every part of your body.

**Proteins are the chief actors within the cell, said to be carrying out the duties specified by the information encoded in genes**

# Proteins Biomedical Importance

- 1- They provide immune protection, antibodies search out foreign invaders.
- 2- They function as catalysts: enzymes catalyse reactions that generate energy, synthesize and degrade biomolecules, replicate and transcribe genes, etc.
- 3- They transport and store other molecules such as Haemoglobin transports oxygen,
- 4- They provide mechanical support, the internal protein network “cytoskeleton”, maintains cellular shape and physical integrity.
- 5- They generate movement, actin and myosin filaments form the contractile machinery of muscle.
- 6- They work as receptors that enable cells to sense and respond to hormones and other environmental cues.

# Structure-function relationship in proteins

1. The function of a protein is directly dependent on its three dimensional structure.
2. Proteins contain **a wide range of functional groups**. These functional groups accounts for the broad spectrum of protein function. For instance, the chemical reactivity associated with these groups is essential to the function of enzymes.
3. Proteins can interact with one another and with other biological macromolecules to form complex assemblies. Example, replication of DNA, the transmission of signals within cells, and many other essential processes.
4. Some proteins are quite rigid, whereas others display limited flexibility. Rigid units can function as structural elements or in connective tissue. Parts of proteins with limited flexibility may act as to assembly proteins with one another and with other molecules into complex units, and to the transmission of information within and between cells.



# Protein structure

Four levels of protein structure:

Primary structure: (Amino acid sequence)



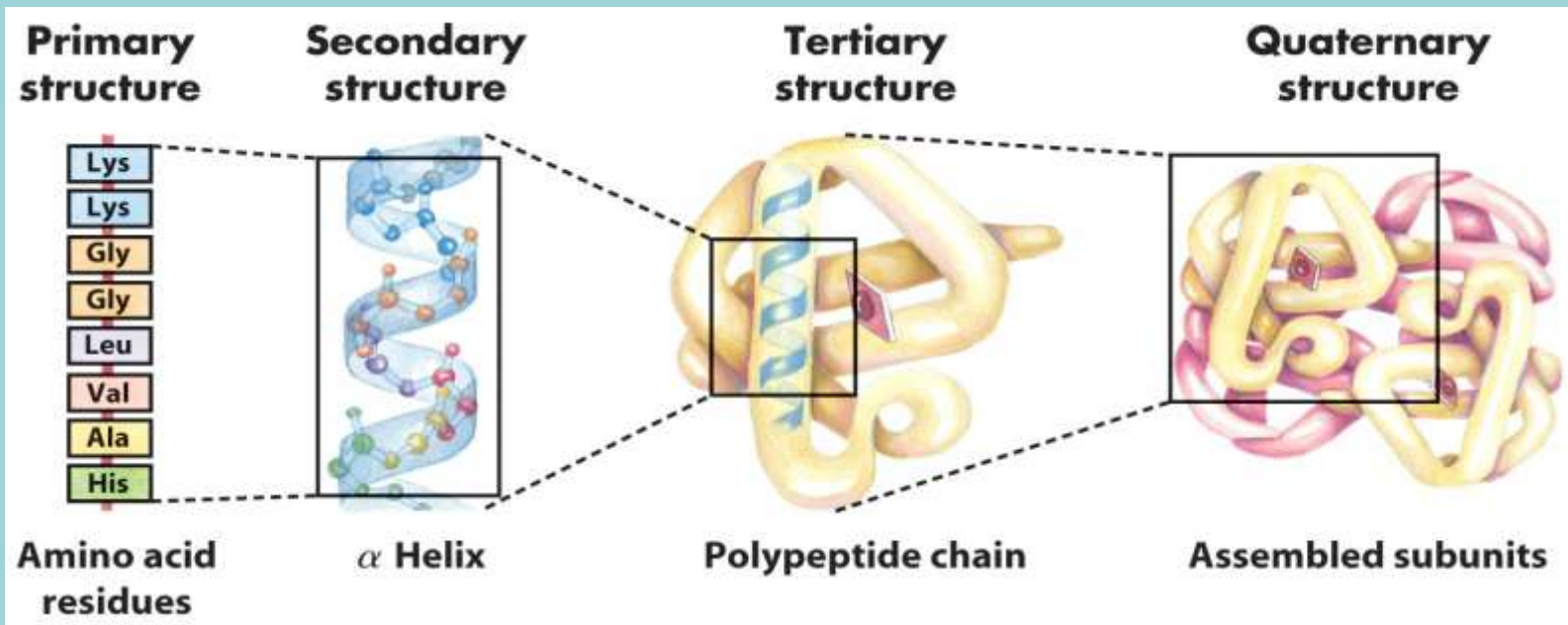
Secondary structure:  $\alpha$ -helix,  $\beta$ -sheet, turns



Tertiary structure: Three-dimensional structure formed by assembly of secondary structures



Quaternary structure: formed by more than one polypeptide chains



# 1- Primary structure of proteins

The primary structure is the sequence of residues (amino acids) in the polypeptide chain.

By convention, the primary structure of a protein is reported starting from the amino-terminal (N) end to the carboxy-terminal (C) end.

The sequence of amino acids in a protein is determined by the genetic code for the protein.

**The genetic code** is the set of rules by which information encoded in genetic material (DNA or mRNA sequences) is translated into proteins (amino acid sequences) by living cells.

transcription → translation

		Second letter				
		U	C	A	G	
First letter	U	UUU UUC	UCU UCC UCA UCG	UAU UAC	UGU UGC	U C
		UUA UUG		UAA UAG	UGA UGG	A G
	C	CUU CUC CUA CUG	CCU CCC CCA CCG	CAU CAC	CGU CGC CGA CGG	U C A G
		AAU AUC AUA AUG		AAA AAG	AGU AGC AGA AGG	U C A G
A	GUU GUC GUA GUG	GCU GCC GCA GCG	GAU GAC	GGU GGC GGA GGG	U C A G	

## 2- Secondary structure of proteins

Secondary structure is a local regularly occurring structure in proteins and **is mainly formed through hydrogen bonds between backbone atoms.**

There are two major types of stable secondary structures:

Alpha helices and beta-sheets. Alpha-helices and beta-sheets are preferably located at the core of the protein, whereas loops prefer to reside in outer regions.

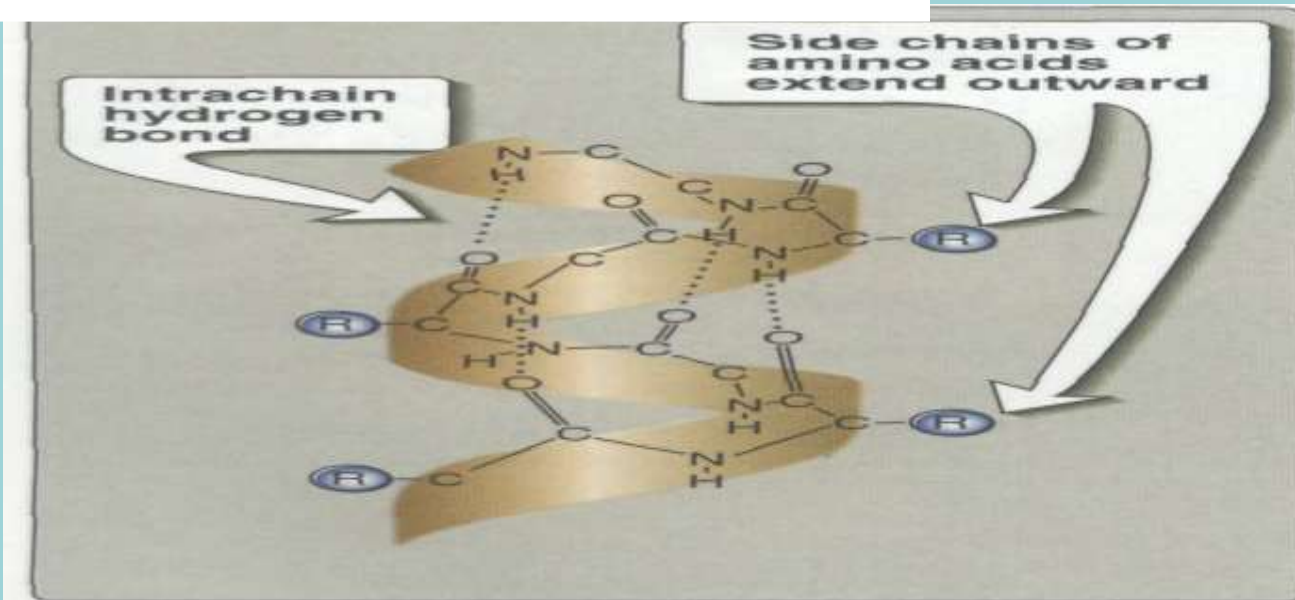
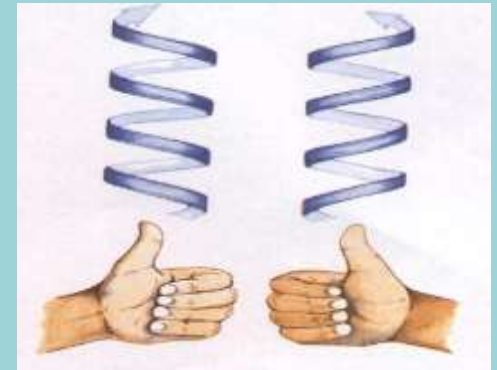
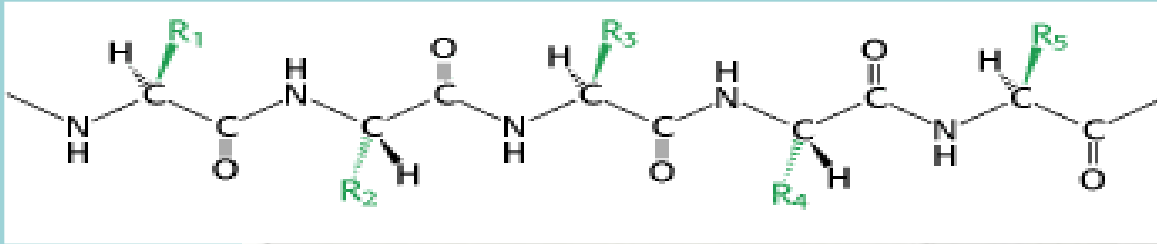
Amino acids vary in their ability to form the various secondary structure elements. **Proline** and **glycine** are sometimes known as "helix breakers" because they disrupt the regularity of the  $\alpha$  helical backbone conformation; however, both have unusual conformational abilities and are commonly found in turns.

By contrast, the large aromatic residues (tryptophan, tyrosine and phenylalanine) prefer to adopt  $\beta$ -strand conformations

# $\alpha$ -helix

The alpha helix ( $\alpha$ -helix) is a right-handed coiled or spiral conformation, in which every backbone **N-H** group donates a **hydrogen bond** to the backbone **C=O** group of the amino acid four residues earlier

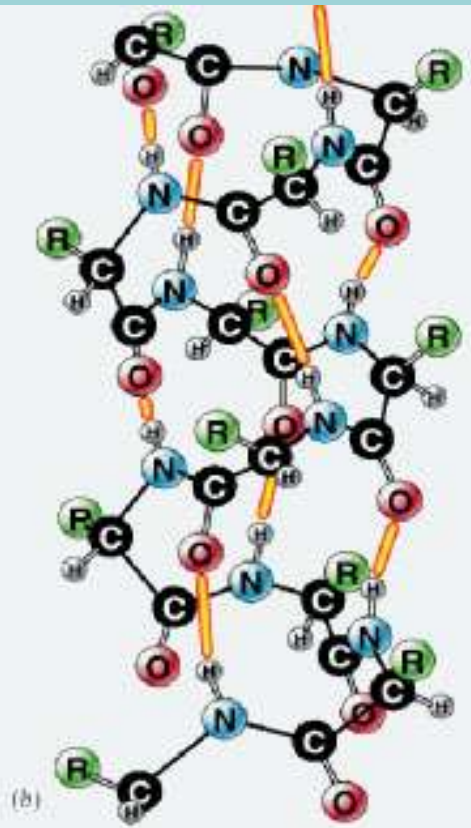
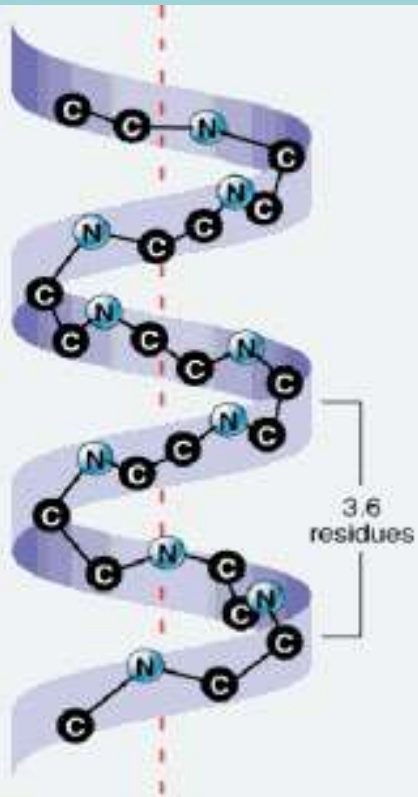
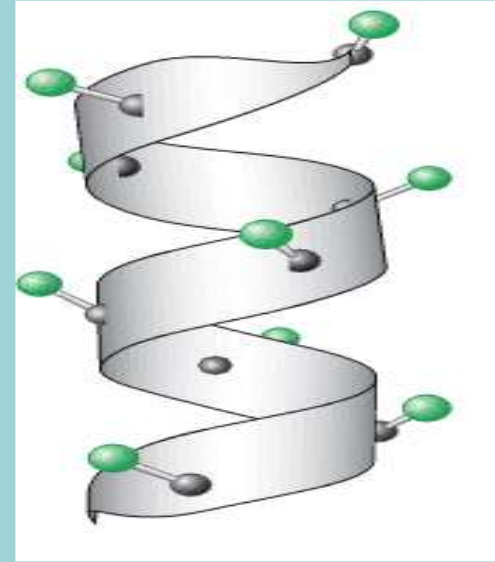
The right-handed  $\alpha$ -helix is one of the most common secondary structures while the left handed  $\alpha$ -helix, is rarely found in nature.



# $\alpha$ -helix

In the alpha helix, the polypeptide chain is coiled tightly in the fashion of a spring.

The "backbone" of the peptide forms the inner part of the coil while the side chains extend outward from the coil.



The helix is stabilized by hydrogen bonds between the N-H of one amino acid and the C=O on the 4th amino acid away from it. One "turn" of the coil requires 3.6 amino acid units.

# Amino-acid propensities

Different amino-acid sequences have different propensities for forming  $\alpha$ -helical structure.

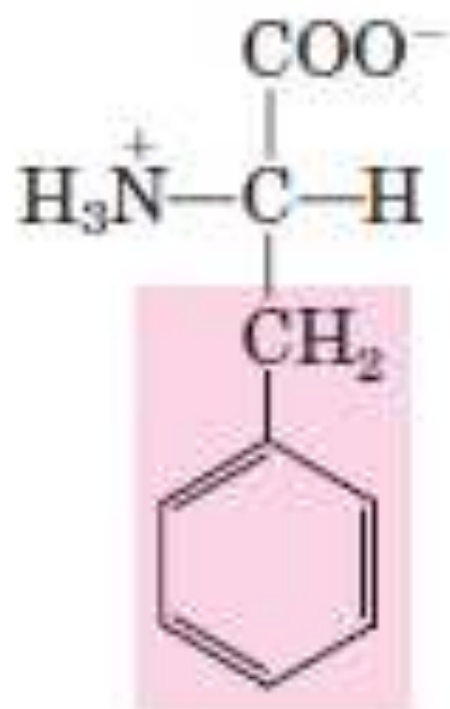
Methionine, alanine, leucine, uncharged glutamate, and lysine all have high helix-forming propensities, whereas proline and glycine have poor helix-forming propensities.

Proline either breaks or kinks a helix, both because it cannot donate an amide-hydrogen bond (having no amide hydrogen), and also because its side chain interferes sterically with the backbone of the preceding turn - inside a helix, this forces a bend of about  $30^\circ$  in the helix axis.

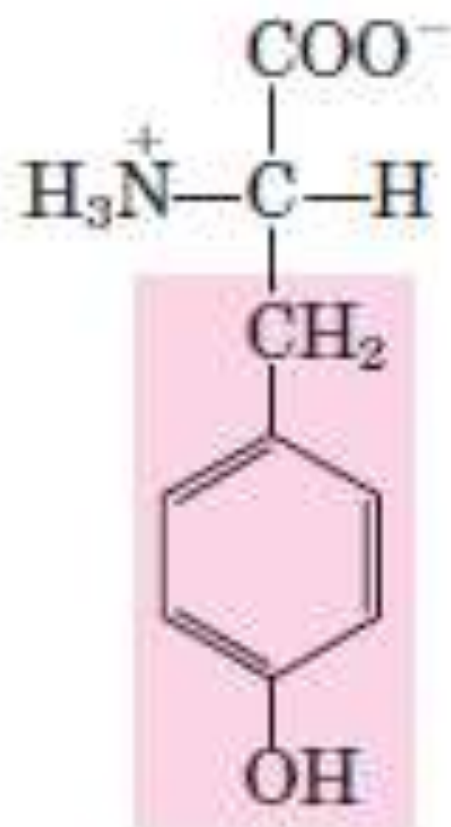
**Large numbers of charged amino acids** (for example, glutamate, aspartate, histidine, lysine, or arginine) also disrupt the helix

amino acids with bulky side chains, such as tryptophan, can interfere with formation of the  $\alpha$ -helix **if they are present in large numbers.**

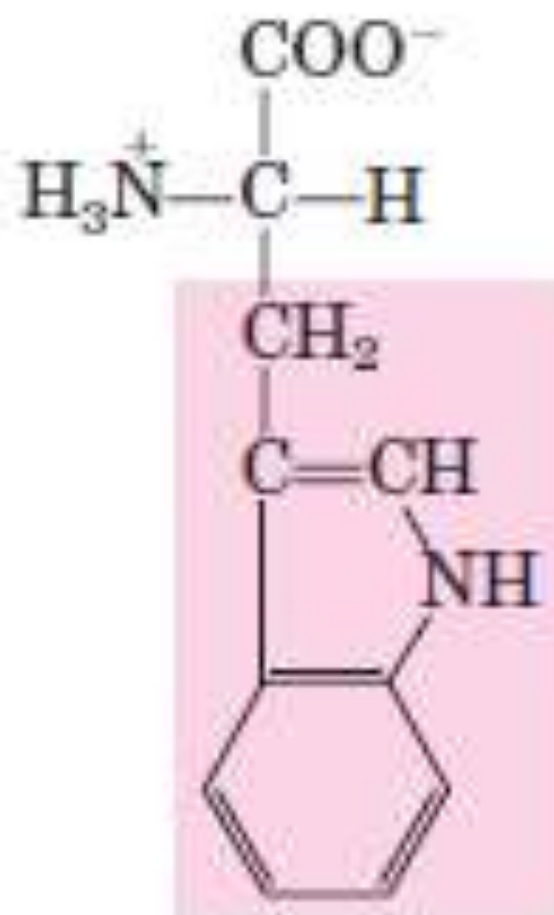
## Aromatic R groups



Phenylalanine



Tyrosine



Tryptophan

# $\beta$ -sheet

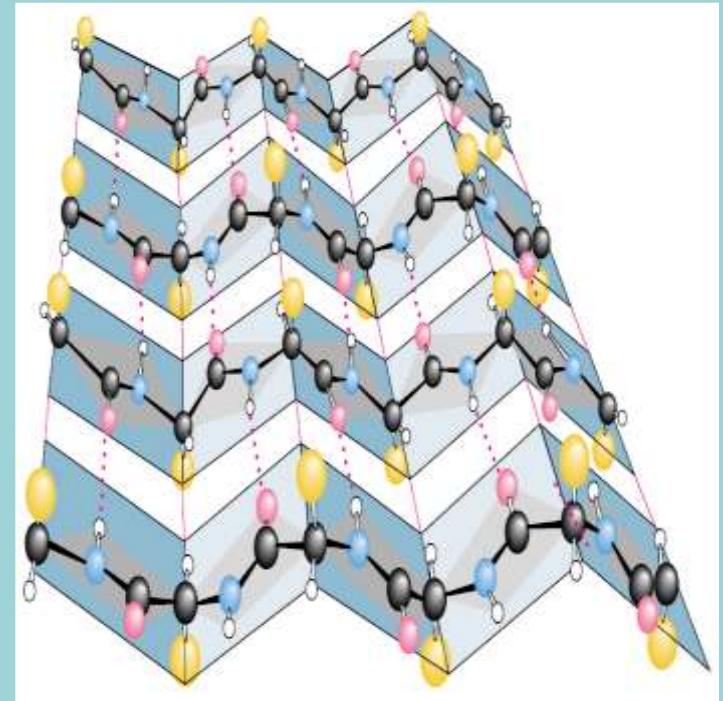
The  $\beta$  sheet (also  $\beta$ -pleated sheet) is less common than the  $\alpha$ -helix.

Beta sheets consist of beta strands connected laterally by at least two or three backbone hydrogen bonds, forming a generally twisted, pleated sheet.

**A beta strand** is a stretch of polypeptide chain typically 3 to 10 amino acids long with backbone in an almost fully extended conformation.

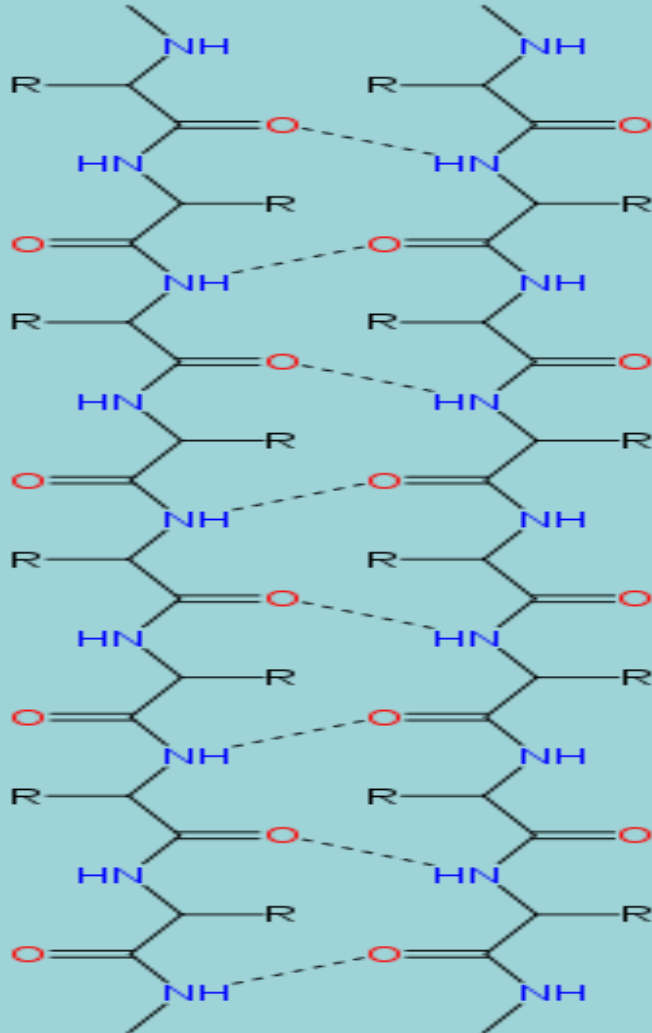
The majority of  $\beta$  strands are arranged adjacent to other strands and form an extensive hydrogen bond network with their neighbors in which the N-H groups in the backbone of one strand establish hydrogen bonds with the C=O groups in the backbone of the adjacent strands.

In the fully extended  $\beta$  strand, successive side chains point straight up, then straight down, then straight up, etc.

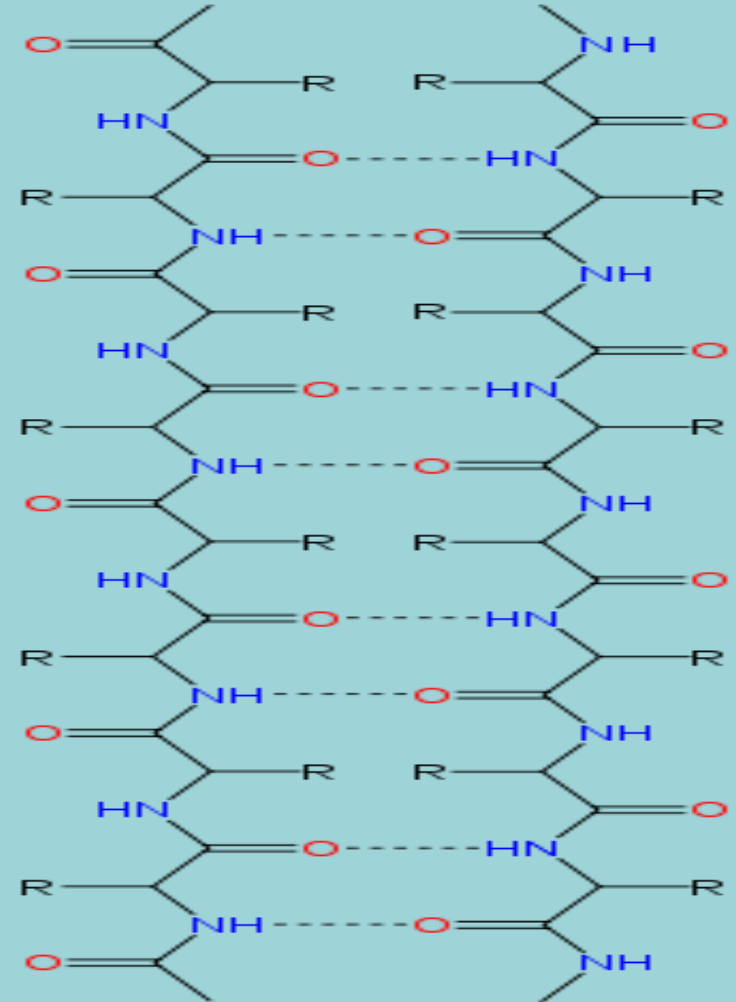




# Parallel and antiparallel $\beta$ -sheets



**Parallel:** Adjacent polypeptide chains running in the same direction



**Antiparallel:** when the adjacent polypeptide chains run in opposite direction

# Turns

A turn is an element of secondary structure in proteins where the polypeptide chain reverses its overall direction

A turn is a structural motif where the C<sup>α</sup> atoms of two residues separated by few (usually 1 to 5) peptide bonds are in close approach (less than 7 Å), while the corresponding residues do not form a regular secondary structure element such as an alpha helix or beta sheet.

## Tight turns

Are classified according to the separation between the two end residues:

A- In an Alpha-turn the end residues are separated by *four* peptide bonds

B- In a Beta-turn or Beta-bend (**the most common form**) by *three* bonds

C- In a Gamma-turn, by *two* bonds

D- In a Delta-turn, by *one* bond

E- In a π-turn, by *five* bonds

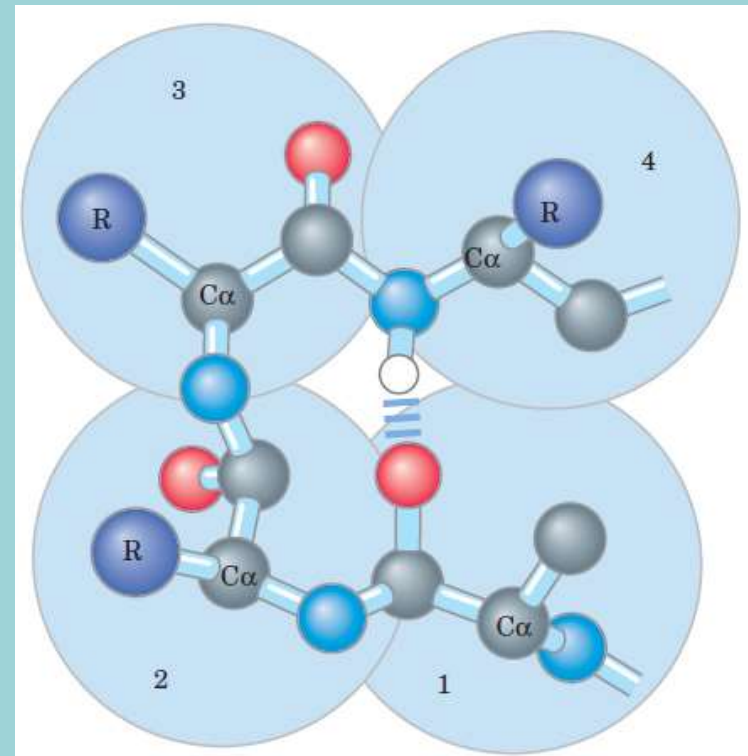
# $\beta$ -Bends

Often found at sites where the peptide chain changes direction.

$\beta$ - Bends are stabilized by the formation of hydrogen bonds and By having a distance of less than  $7\text{\AA}$  between the  $C\alpha$  atoms of residues one and four

$\beta$ -bends are generally composed of four amino acids, one of which may be **proline** that causes a "kink" in the polypeptide chain.

**Glycine**, the amino acid with the smallest R-group, is also frequently found in  $\beta$ -bends.

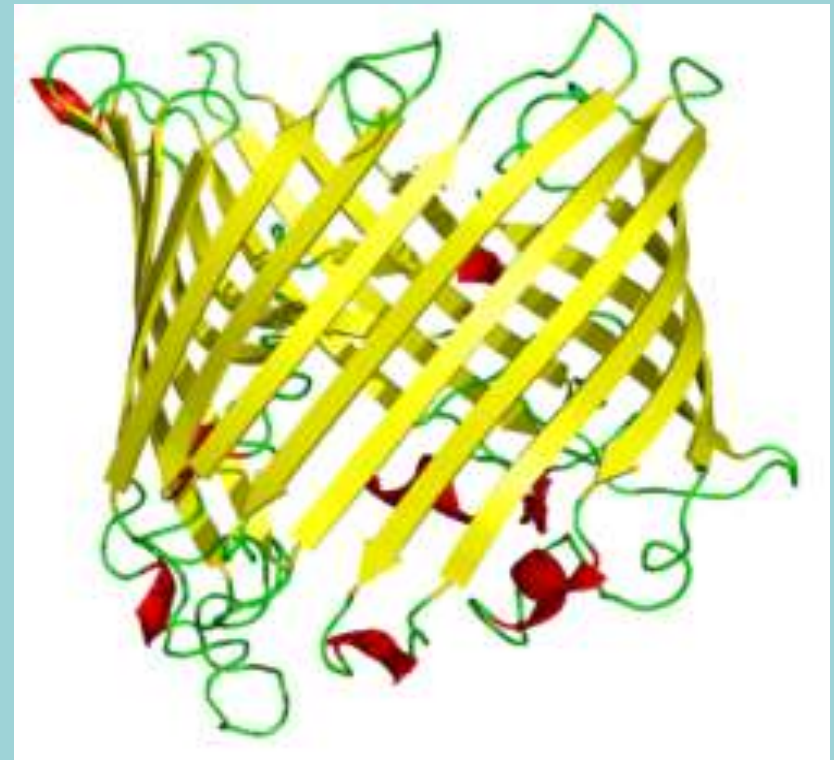


# Super secondary structures (also called motifs)

Super secondary structures are combinations of alpha-helices and beta-structures connected through loops.

These folding patterns are stabilized through the same kind of linkages than the tertiary level. Sometimes the term “motif” is used to describe these super secondary structures.

These structures can be relatively simple, as alpha-alpha (two alpha helices linked by a loop), Beta-Beta (two beta-strands linked by a loop), Beta-alpha-Beta (Beta-strand linked to an alpha helix that is also linked to other beta strand, by loops) or more complex structures, like the beta-barrel.



**Beta-barrel motif**