Semester II

Microbiology Core (MBIO CC203)

UNIT - 4

Peptide bond and order of protein Structure

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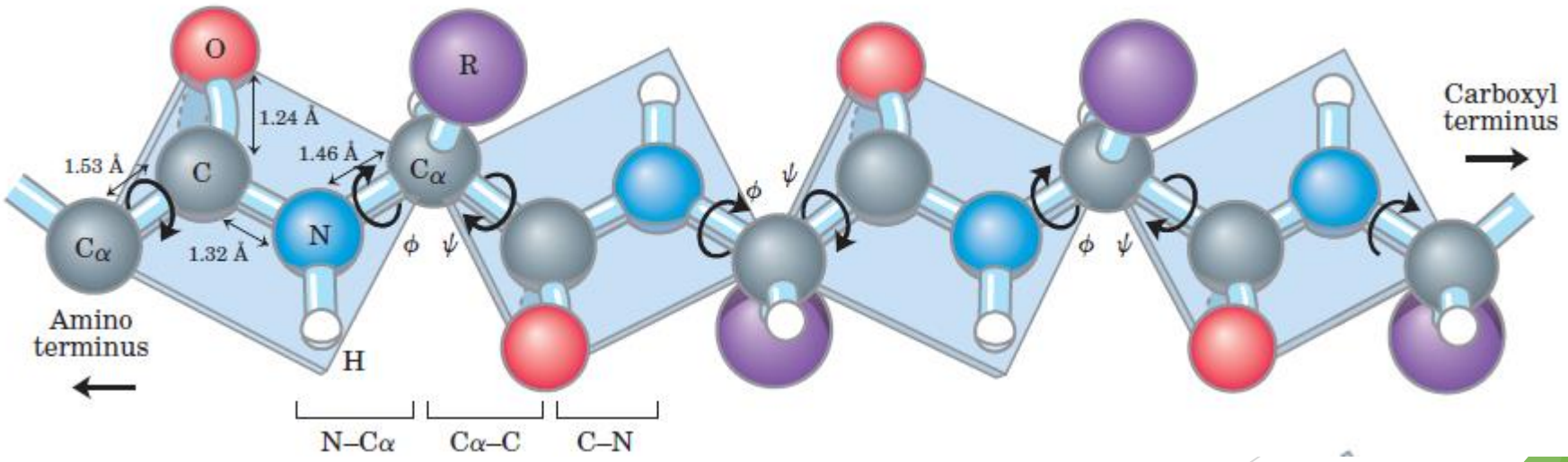
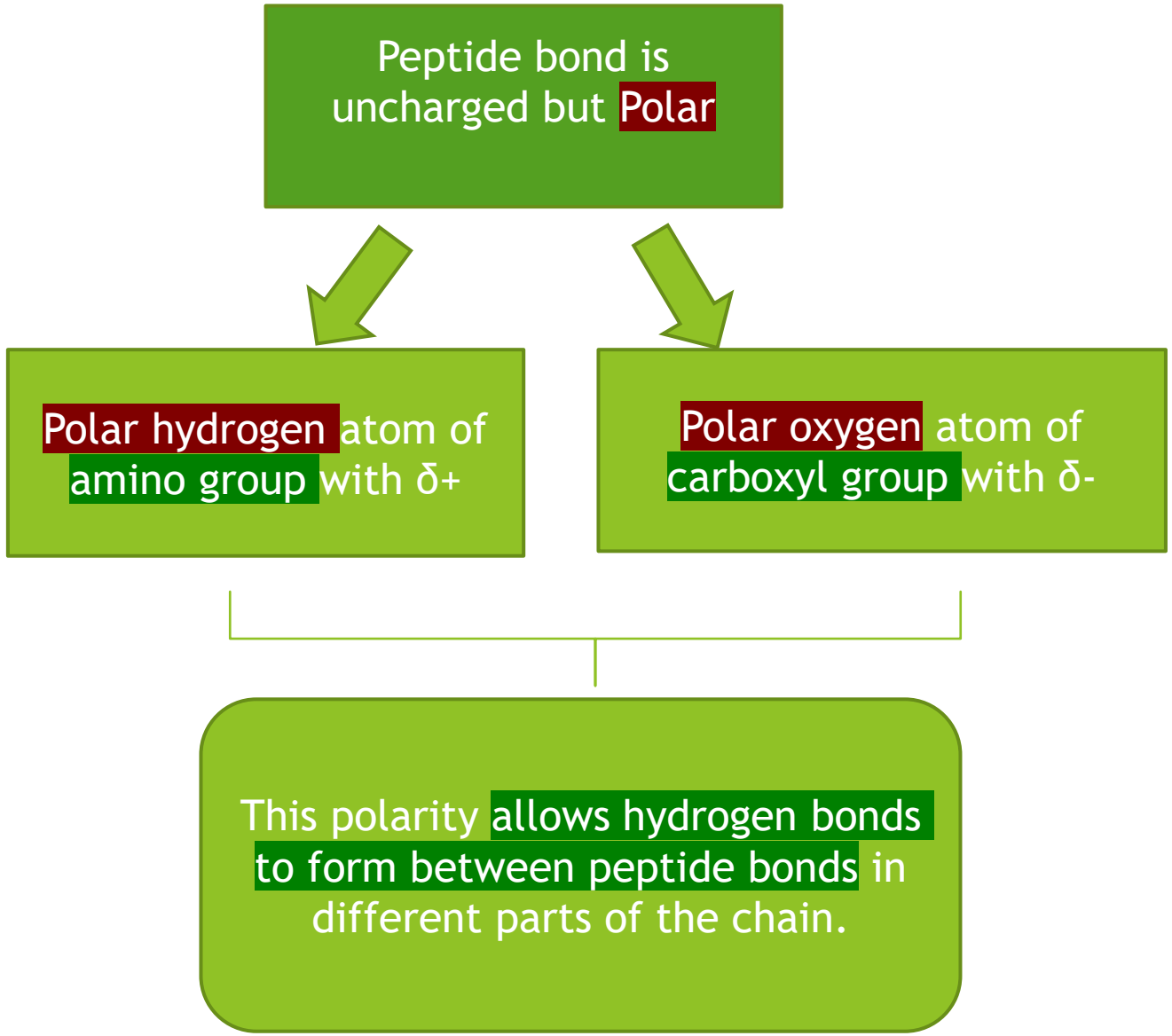
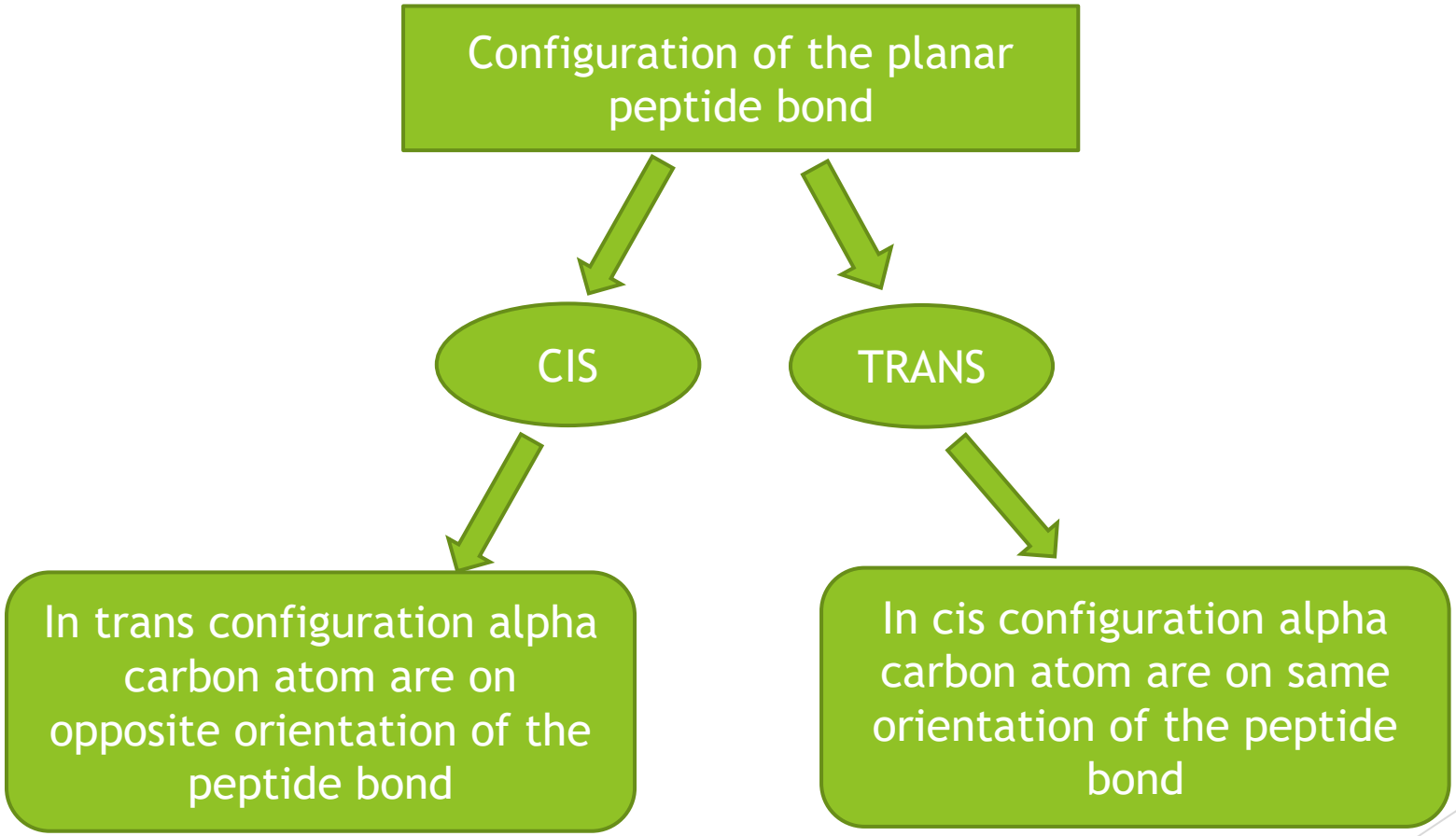
Characteristic features

- The carbons of adjacent amino acid residues are separated by three covalent bonds, arranged as
- Cα- C- N- Cα
- Six atoms lies in a one single plane with oxygen atom of the carbonyl group and the hydrogen atom of the amide nitrogen trans to each other.




Peptide bond is uncharged but Polar
Polar hydrogen atom of amino group with δ+
Polar oxygen atom of carboxyl group with δ-
This polarity allows hydrogen bonds to form between peptide bonds in different parts of the chain.

Peptide bonds are in trans configuration



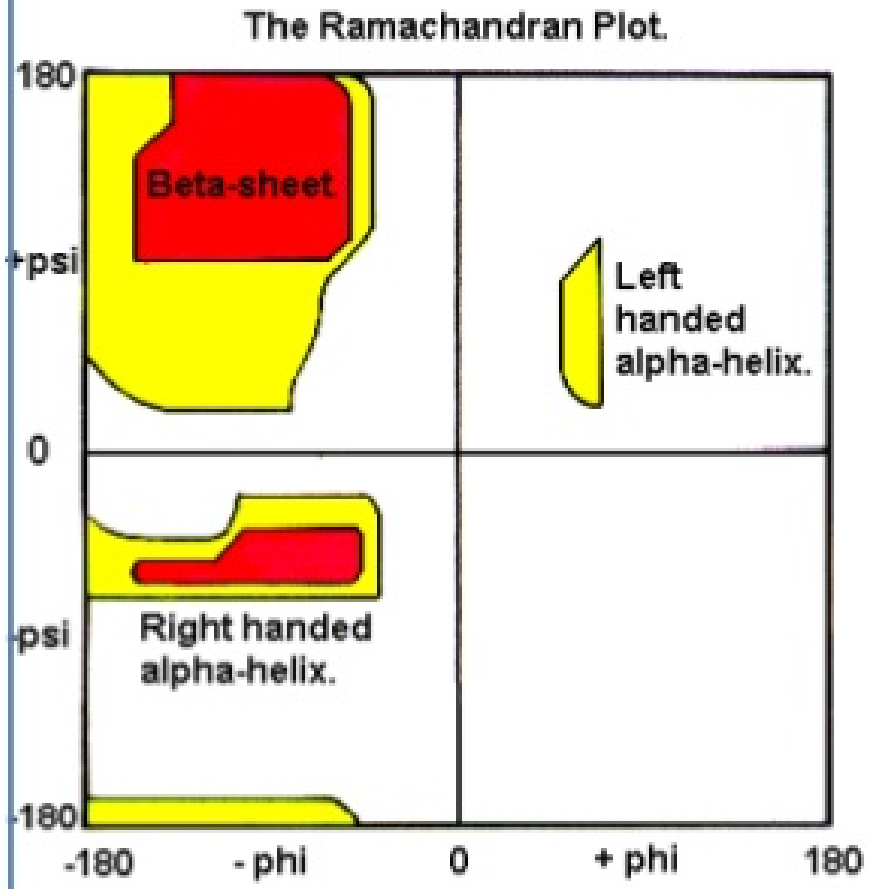
- C-N bonds are unable to rotate freely because of their partial double-bond character.
- The peptide C-N bond is somewhat shorter than the C-N bond in a simple amine and that the atoms associated with the peptide bond are coplanar. This indicated a resonance or partial sharing of two pairs of electrons between the carbonyl oxygen and the amide nitrogen.
- C-N single bond (1.49 Angstrom)
- C=N Double bond (1.27 angstrom)
- C-N distance in a dipeptide (1.27 Angstrom)
- The rotation is permitted about N-Cα (Φ) and Cα-C bonds (ψ).

Torsion angles (Φandψ)

- The conformation of the backbone can be described by the torsion angles (also called as dihedral angles or rotation angles.)
- http://employees.csbsju.edu/hjakubowski/classes/ch331/protstructure/pp0to180.gif

RAMACHANDRAN PLOT

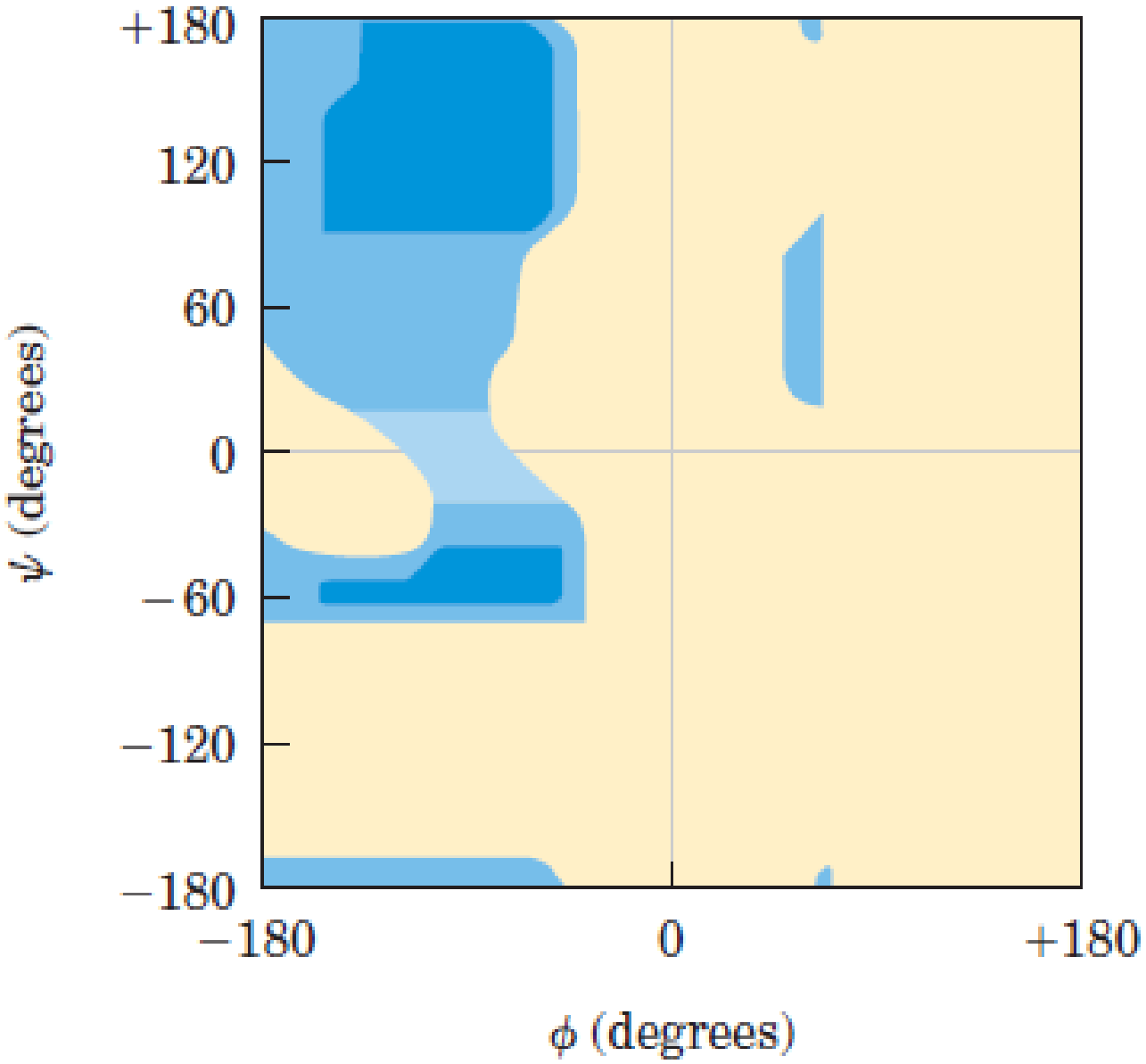
A **Ramachandran plot** (also known as a **Ramachandran diagram** or a **[φ,ψ] plot**), originally developed in 1963 by G. N. Ramachandran.



White regions : Sterically disallowed for all amino acids except glycine.

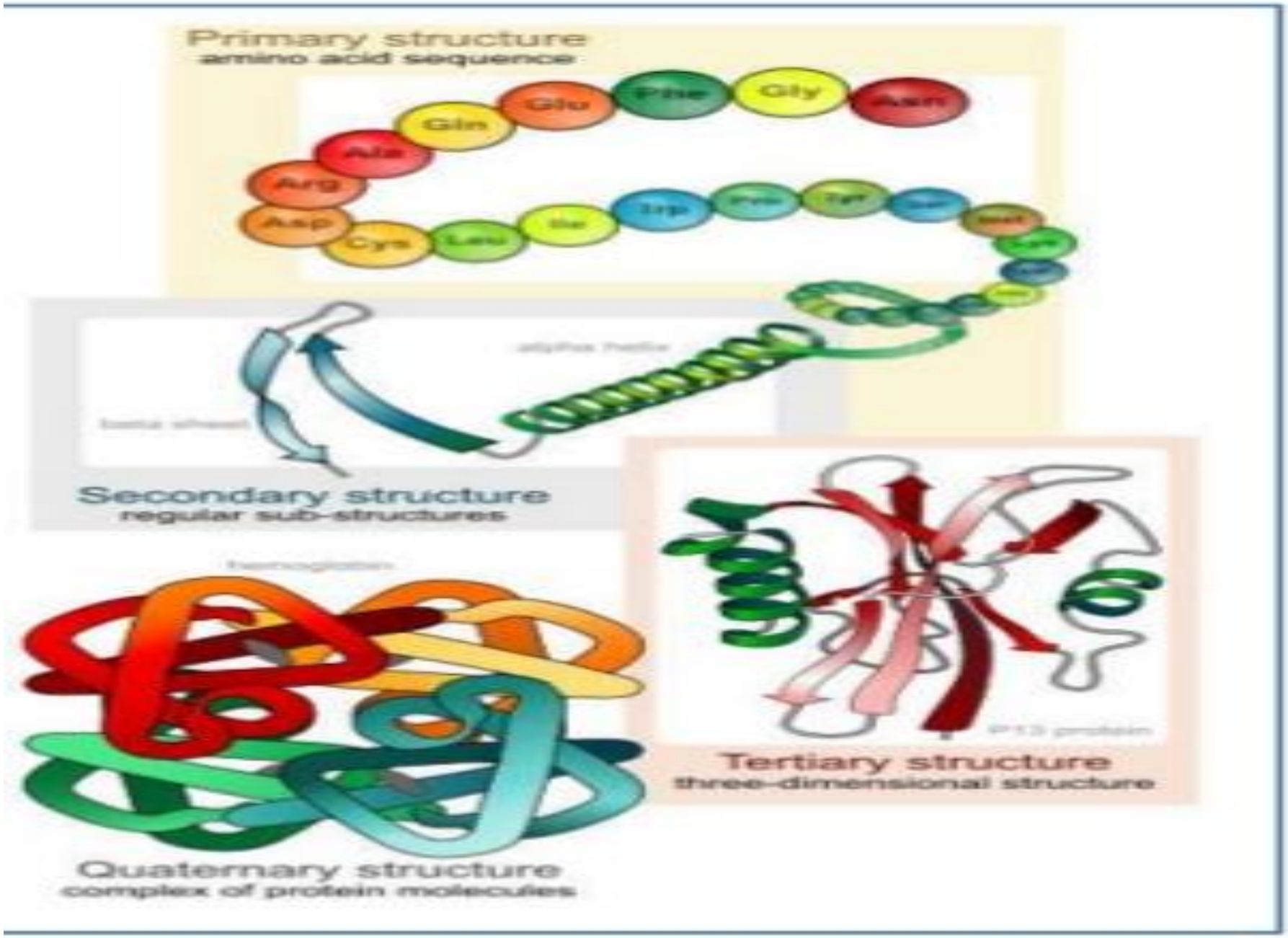
Red regions : allowed regions namely the a-helical and b-sheet conformations.

Yellow areas : outer limit



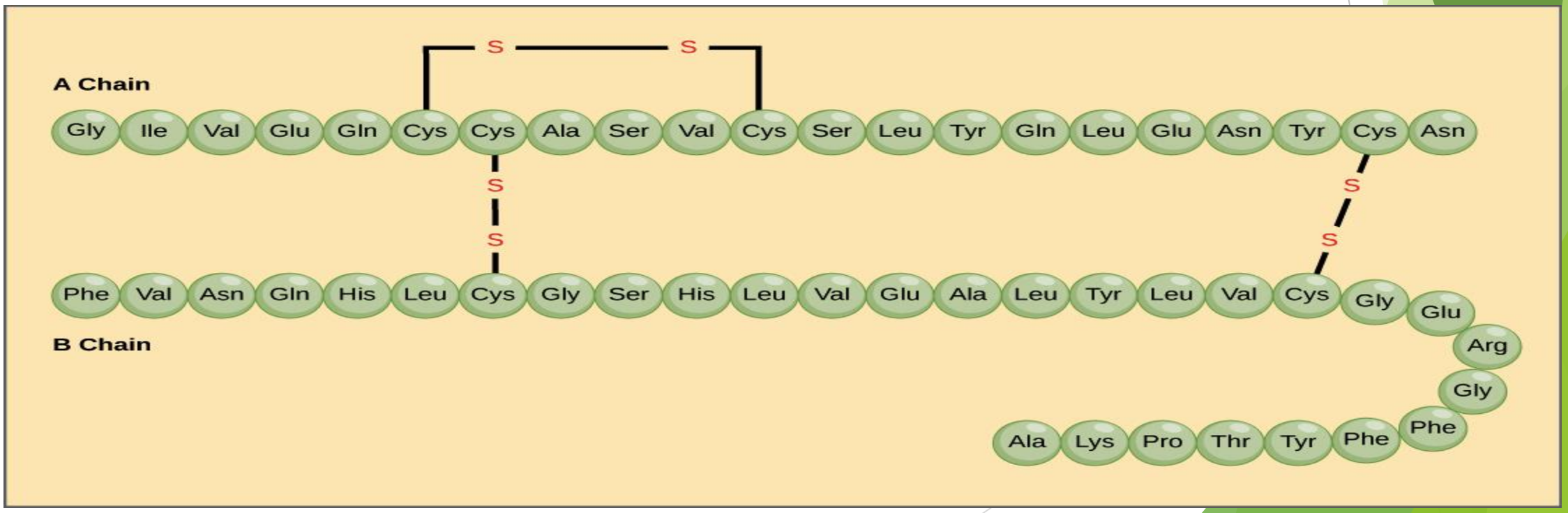
Ramachandran plot for L-Ala residues

- The conformations of peptides are defined by the values of Φ and ψ.
- Conformations deemed possible are those that involve little or no steric interference, based on calculations using known van der Waals radii and bond angles.
- The areas shaded dark blue reflect conformations that involve no steric overlap and thus are fully allowed; medium blue indicates conformations allowed at the extreme limits for unfavorable atomic contacts; the lightest blue area reflects conformations that are permissible if a little flexibility is allowed in the bond angles.


Primary structure
amino acid sequence
Secondary structure
regular sub-structures
Tertiary structure
three-dimensional structure
Quaternary structure
complex of protein molecules

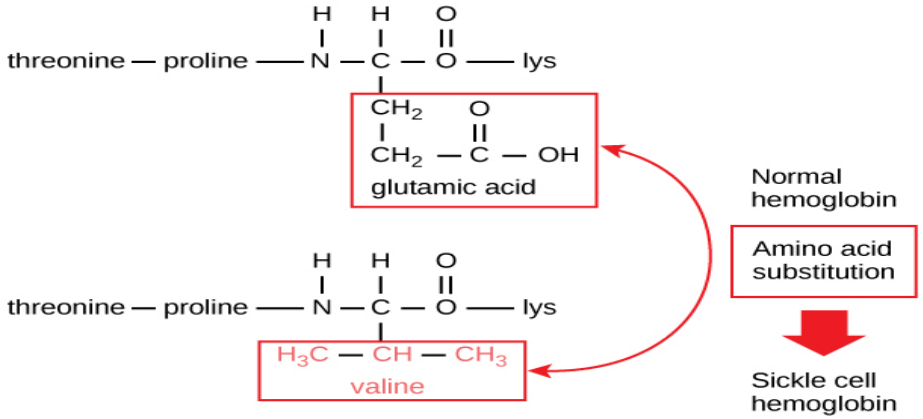
Primary structure

- The simplest level of protein structure is the primary structure
- It is simple the sequence of amino acids in a polypeptide chain.
- The position of covalent disulfide bonds between cysteine residues is also included in the primary structure.
- For eg- insulin has two polypeptide chains- chain A and chain B



Importance of primary structure

- To predict secondary and tertiary structures from sequence homologies with related protein (homology modelling, structure prediction)
- Many genetic diseases results from abnormal amino acid sequence. Eg sickle cell anaemia.



- To trace evolutionary path (lateral gene transfer study).

Secondary structures

- Secondary structures refers to local folded structures that form within a polypeptide due to interactions between atoms of the backbone. (The backbone just refers to the polypeptide chain apart from the R groups – so all we mean here is that secondary structure does not involve R group atoms.)
- The most common types of secondary structures are the α helix and the ß pleated sheet.
- Both structures are held in shape by hydrogen bonds, which form between the carbonyl O of one amino acid and the amino H of another.

SECONDARY STRUCTURE

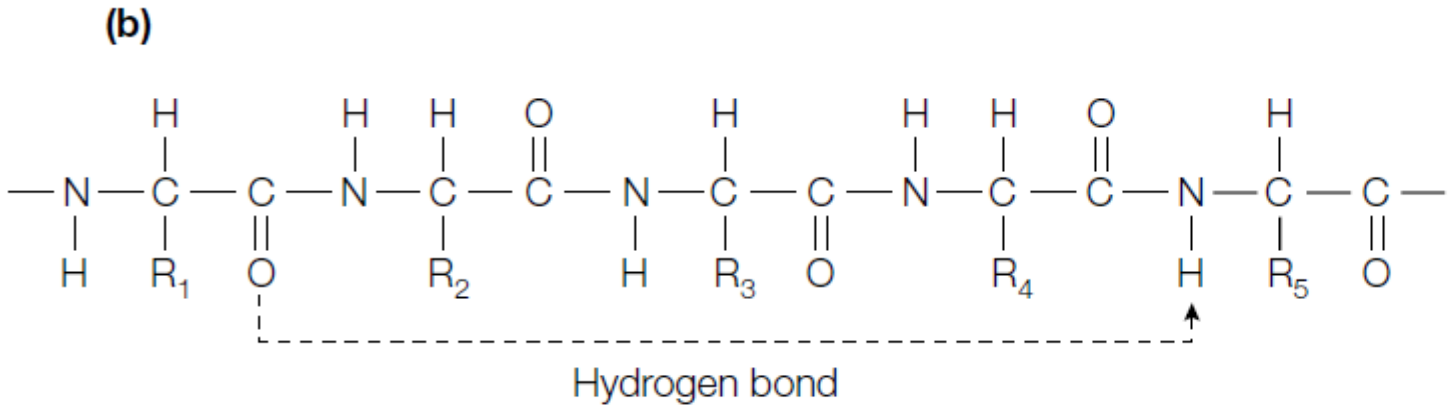
- Localized arrangement of adjacent amino acids formed as the polypeptide chain folds.

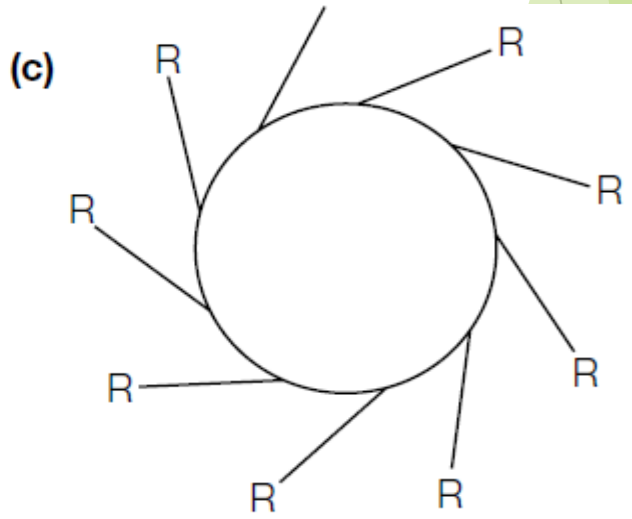
- It consists of
  - α-helix
  - β-pleated sheet
  - β-bends
  - Non repetitive structures
  - Super secondary structures

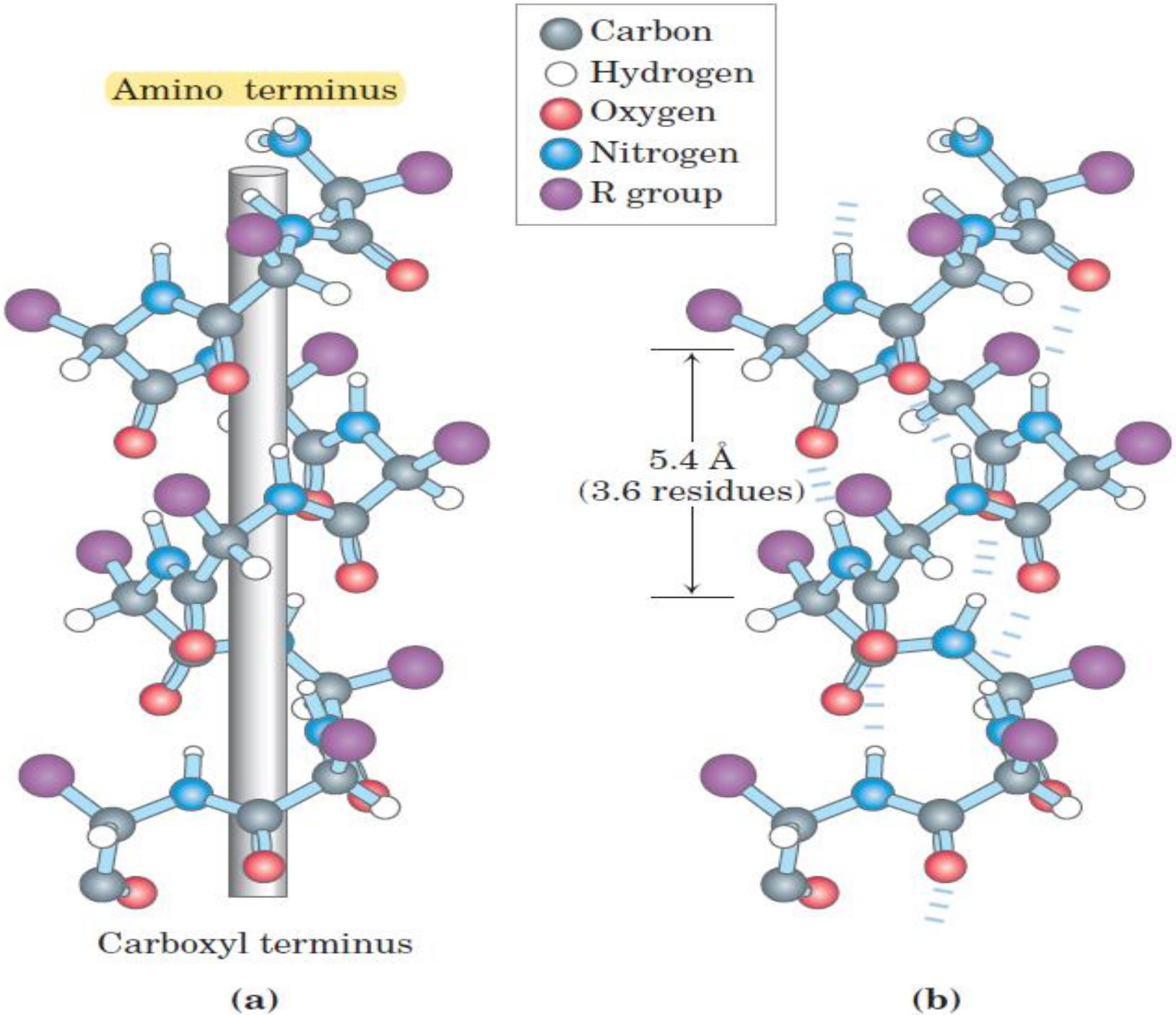
Alpha Helix

- The simplest arrangement the polypeptide chain could assume with its rigid peptide bonds (but other single bonds free to rotate) is a helical structure, which Pauling and Corey called the **helix**.
- In this structure the polypeptide backbone is tightly wound around an imaginary axis drawn longitudinally through the middle of the helix, and the R groups of the amino acid residues protrude outward from the helical backbone.
- In an -helix there are 3.6 amino acids per turn of the helix covering a distance of 0.54 nm, and each amino acid residue represents an advance of 0.15 nm along the axis of the helix.
- The amino acid residues in an helix have conformations with ψ= -45 °to -50° and Φ = -60.
- The helical twist of the helix found in all proteins is right-handed. The *alpha* helix proved to be the predominant structure in -keratins.

- The carbonyl oxygen of each peptide bond is **hydrogen bonded** to the hydrogen on the amino group of the fourth amino acid away, with the hydrogen bonds running nearly parallel to the axis of the helix.
- Within the helix, every peptide bond(except those close to each end of the helix) participates in such hydrogen bonding. Each successive turnof the helix is held to adjacent turns by three to four hydrogen bonds. All the hydrogen bonds combined give the entire helical structure considerable stability.

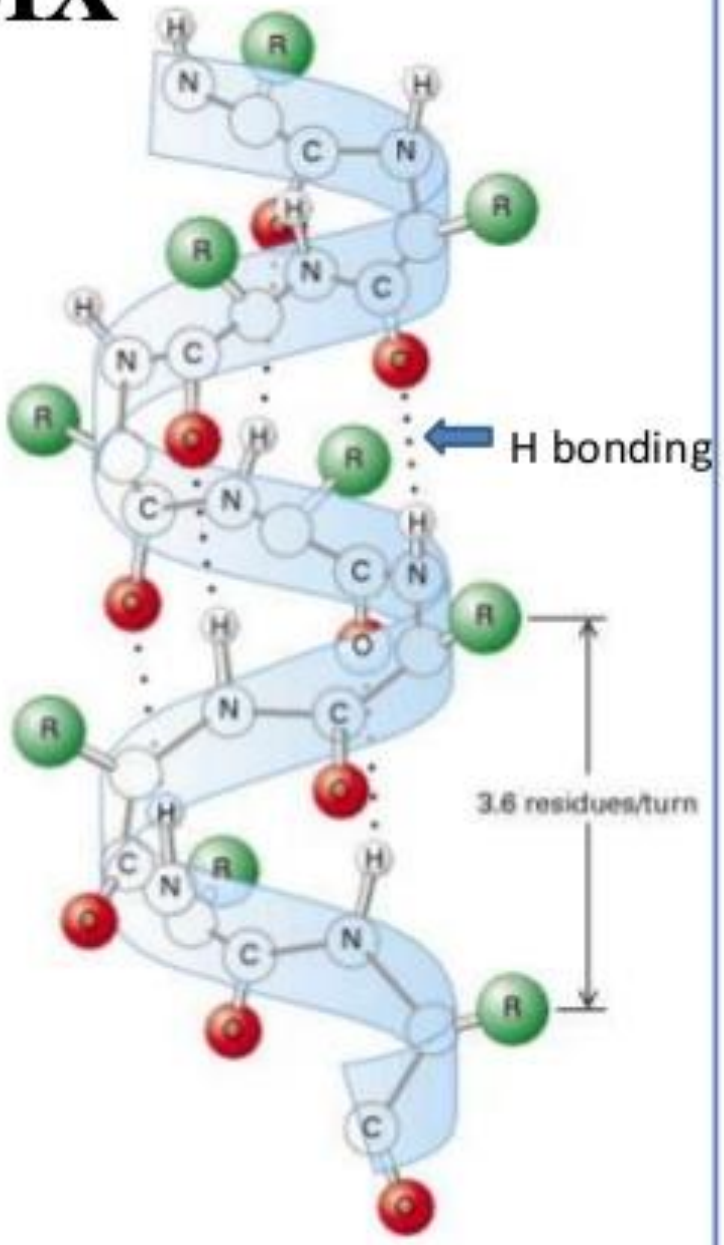





Carbon
Hydrogen
Oxygen
Nitrogen
R group
Amino terminus
Carboxyl terminus
5.4 Å
(3.6 residues)
(a)
(b)

ALPHA HELIX

- Spiral structure
- Tightly packed, coiled polypeptide backbone core.
- Side chain extend outwards
- Stabilized by H bonding b/w carbonyl oxygen and amide hydrogen.
- Amino acids per turn – 3.6
- Pitch is 5.4 A
- Alpha helical segments are found in many globular proteins like myoglobins, troponin- C etc.



Constraints of alpha helix

- five different kinds obeta sheetf constraints affect thestability of an helix:
- the electrostatic repulsion (or attraction) between successive amino acid residues with charged R groups (Glu, Lys/ Arg)
- the bulkiness of adjacent R groups (Asp, Ser, Thr and Cys)
- the interactions between R groups spaced three (or four) residues apart,
- the occurrence of Pro and Gly residues, and
- the interaction between amino acid residues at the ends of the helical segment and the electric dipole inherent to the helix.

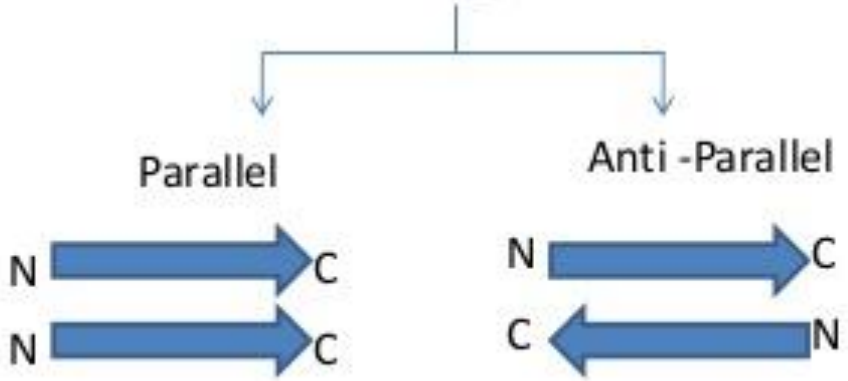
Beeta pleated sheets

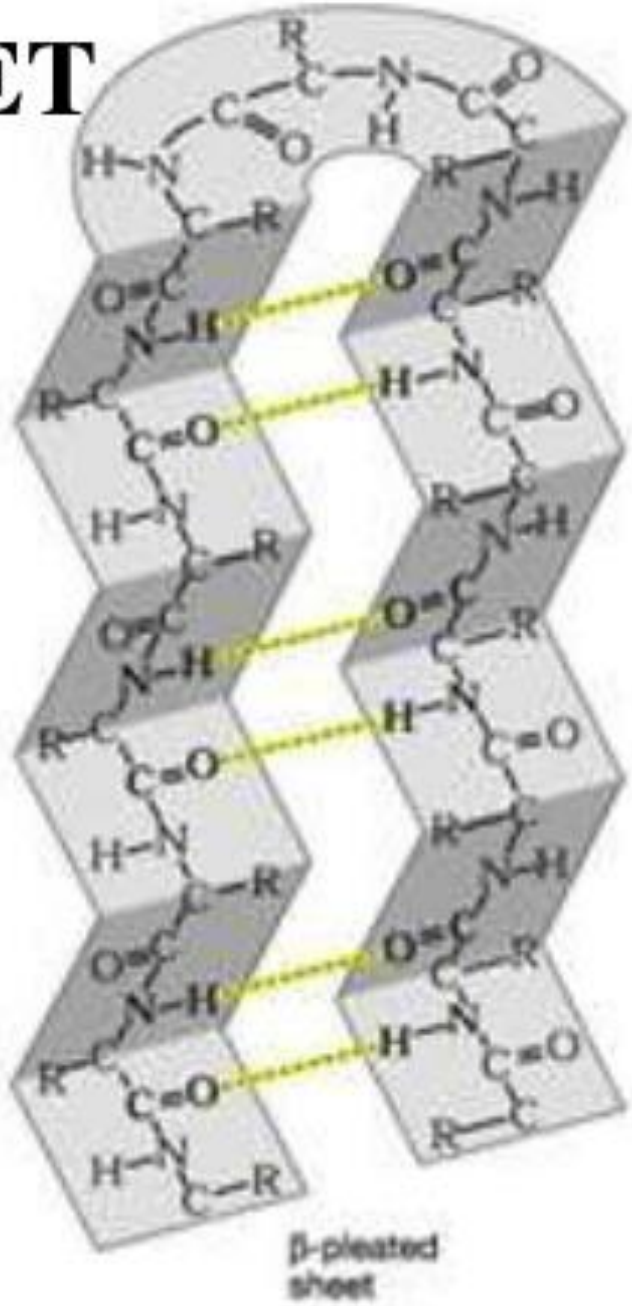
- In the conformation, the backbone of the polypeptide chain is extended into a zigzag
- The zigzag polypeptide chains can be arranged side by side to form a structure resembling a series of pleats. In this arrangement, called a **sheet. That is Beeta sheets.**
- hydrogen bonds are formed between adjacent segments of polypeptide chain. The individual segments that form a sheet are usually nearby on the polypeptide chain, but can also be quite distant from each other in the linear sequence of the polypeptide
- they may even be segments in different polypeptide chains. The R groups of adjacent amino acids protrude from the zigzag structure in opposite directions, creating the alternating pattern

BETA PLEATED SHEET

- Formed when 2 or more polypeptides line up side by side.
- Individual polypeptide - β strand
- Each β strand is fully extended.
- They are stabilized by H bond b/w N-H and carbonyl grps of adjacent chains.

2 types





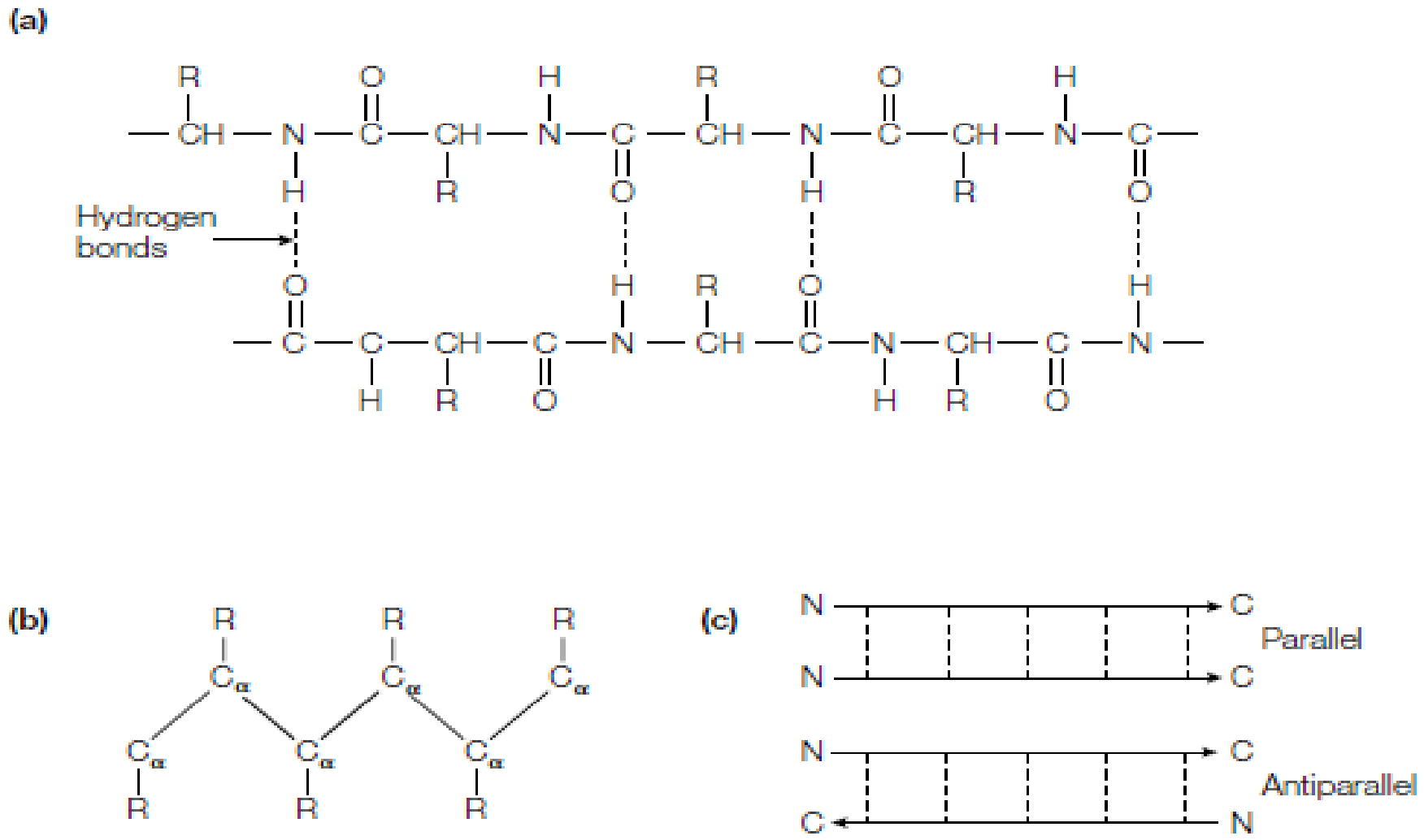
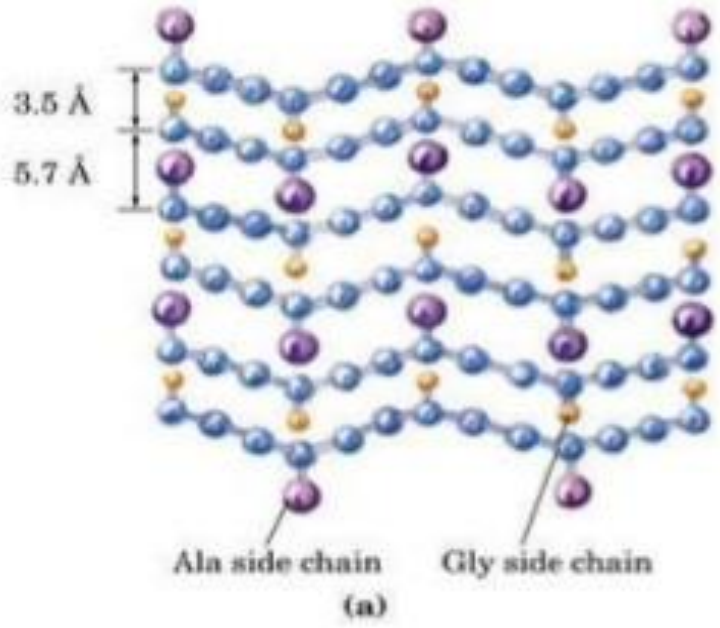


Fig. 6. The folding of the polypeptide chain in a β-pleated sheet. (a) Hydrogen bonding between two sections of a polypeptide chain forming a β-pleated sheet; (b) a side-view of one of the polypeptide chains in a β-pleated sheet showing the side-chains (R groups) attached to the C_α atoms protruding above and below the sheet; (c) because the polypeptide chain has polarity, either parallel or antiparallel β-pleated sheets can form.

EXAMPLES

The collagen triple helix.



Silk fibroin beta sheet.

❑Beeta Keratins such as silk fibroin and the fibroin of spider webs have a very high content of Gly and Ala residues, the two amino acids with the smallest R groups. Indeed, in silk fibroin Gly and Ala alternate over large parts of the sequence.

Beeta Turn

In order to fold tightly into the compact shape of a globular protein, the polypeptide chain often reverses direction, making a hairpin or **β-turn**. In these β-turns the carbonyl oxygen of one amino acid is hydrogen bonded to the hydrogen on the amino group of the fourth amino acid along (*Fig.* 7). β-Turns are often found connecting the ends of antiparallel β-pleated sheets. Regions of the polypeptide chain that are not in a regular secondary structure are said to have a **coil** or **loop conformation**. About half the polypeptide chain of a typical globular protein will be in such a conformation.

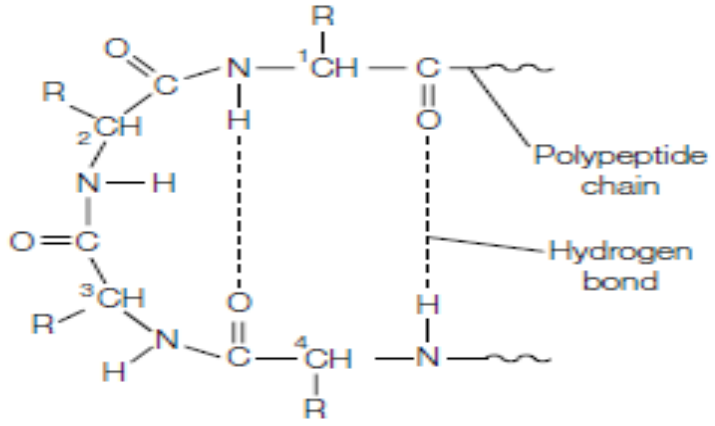


Fig. 7. The folding of the polypeptide chain in a β-turn.

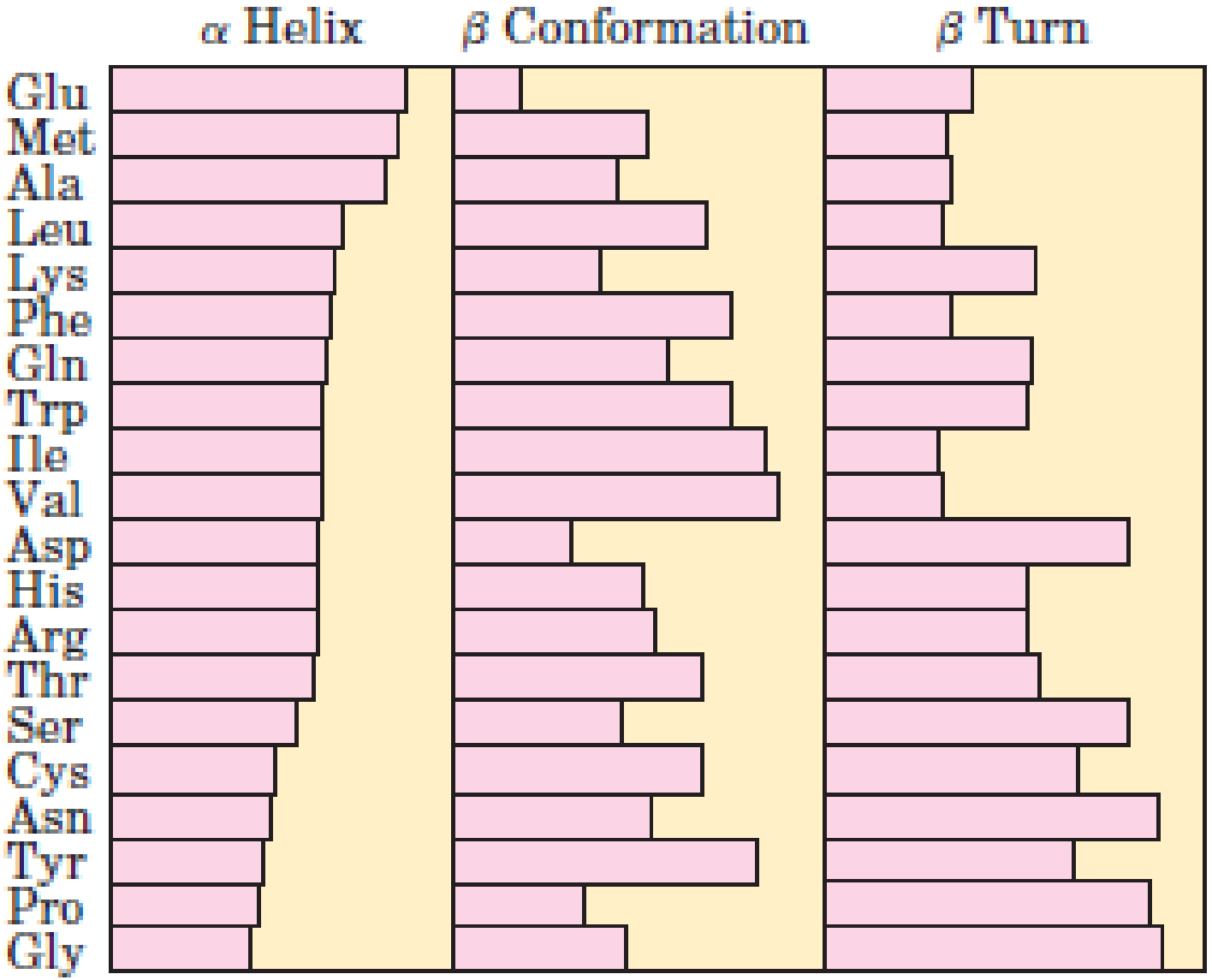


FIGURE 4–10 Relative probabilities that a given amino acid will occur in the three common types of secondary structure.