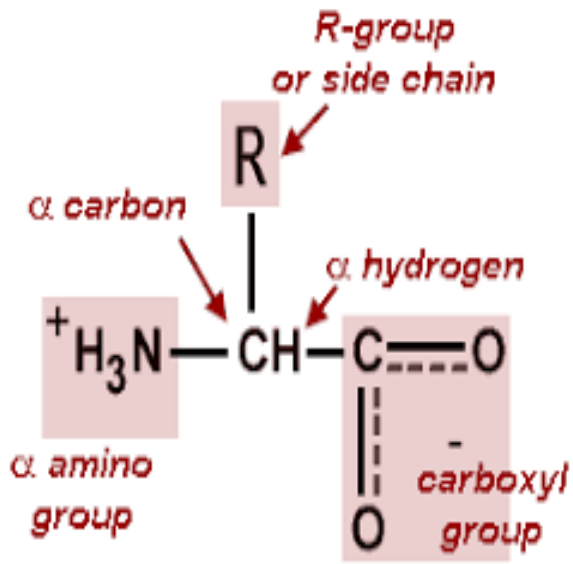
Proteins

- The building blocks of proteins are twenty naturally occurring amino acids, small molecules that contain a free amino group (NH2) and a free carboxyl group (COOH).
- Both of these groups are linked to a central carbon (Cα), which is attached to a hydrogen and a side chain group (R).
- Amino acids differ only by the side chain R group. The chemical reactivities of the R groups determine the specific properties of the amino acids.



- Amino acids can be grouped into several categories based on the chemical andphysical properties of the side chains, such as size and affinity for water. According tothese properties, the side chain groups can be divided into small, large, hydrophobic,and hydrophilic categories.
- Glycine, the smallest amino acid, has a hydrogen atom as the R group. It can therefore adopt more flexible conformations that are not possible for other amino acids.
- Proline is on the other extreme of flexibility. Its side chain forms a bond with its own backbone amino group, causing it to be cyclic. The cyclic conformation makes it very rigid, unable to occupy many of the main chain conformations adopted by other amino acids.
- Certain amino acids are subject to modifications aftera protein is translated in a cell. This is called posttranslational modification.
- The peptide formation involves two amino acids covalently joined together between the carboxyl group of one amino acid and the amino group of another.
- This reaction is a condensation reaction involving removal of elements of water from the two molecules. The resulting product is called a dipeptide.

- The newly formed covalent bond connecting the two amino acids is called a peptide bond. Once an amino acid is incorporated into a peptide, it becomes an amino acid residue.
- Multiple amino acids can be joined together to form a longer chain of amino acid polymer.

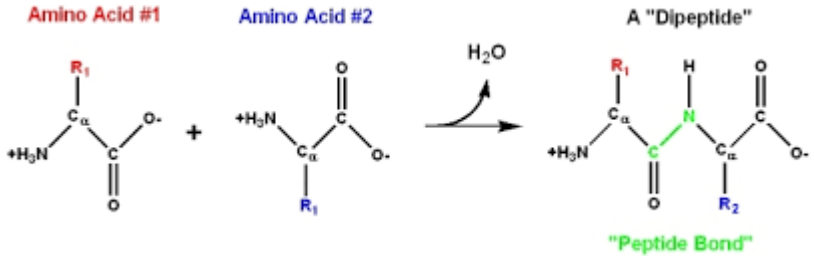


TABLE 12.1. Twenty Standard Amino Acids Grouped by Their Common Side-Chain Features

Amino Acid Group	Amino Acid Name	Three- and One-Letter Code	Main Functional Features
Small and nonpolar	Glycine Alanine Proline	Gly, G Ala, A Pro, P	Nonreactive in chemical reactions; Pro and Gly disrupt regular secondary structures
Small and polar	Cysteine Serine Threonine	Cys, C Ser, S Thr, T	Serving as posttranslational modification sites and participating in active sites of enzymes or binding metal
Large and polar	Glutamine Asparagine	Gln, Q Asn, N	Participating in hydrogen bonding or in enzyme active sites
Large and polar (basic)	Arginine Lysine Histidine	Arg, R Lys, K His, H	Found in the surface of globular proteins providing salt bridges; His participates in enzyme catalysis or metal binding
Large and polar (acidic)	Glutamate Aspartate	Glu, E Asp, D	Found in the surface of globular proteins providing salt bridges
Large and nonpolar (aliphatic)	Isoleucine Leucine Methionine Valine	Ile, I Leu, L Met, M Val, V	Nonreactive in chemical reactions; participating in hydrophobic interactions
Large and nonpolar (aromatic)	Phenylalanine Tyrosine Tryptophan	Phe, F Tyr, Y Trp, W	Providing sites for aromatic packing interactions; Tyr and Trp are weakly polar and can serve as sites for phosphorylation and hydrogen bonding

Note: Each amino acid is listed with its full name, three- and one-letter abbreviations, and main functional roles when serving as amino acid residues in a protein. Properties of some amino acid groups overlap.

- A linear polymer of more than fifty amino acid residues is referred to as a polypeptide. A polypeptide, also called a protein, has a well-defined three-dimensional arrangement.

- A polymer with fewer than fifty residues is usually called a peptide without a well-defined three-dimensional structure.
- The residues in a peptide or polypeptide are numbered beginning with the residue containing the amino group, referred to as the N-terminus, and ending with the residue containing the carboxyl group, known as the C-terminus.
- The actual sequence of amino acid residues in a polypeptide determines its ultimate structure and function.
- The atoms involved in forming the peptide bond are referred to as the backbone atoms. They are the nitrogen of the amino group, the α carbon to which the side chain is attached and carbon of the carbonyl group.
- A peptide bond is actually a partial double bond owing to shared electrons between O=C–N atoms.
- The rigid double bond structure forces atoms associated with the peptide bond to lie in the same plane, called the peptide plane.
- Because of the planar nature of the peptide bond and the size of the R groups, there are considerable restrictions on the rotational freedom by the two bonded pairs of atoms around the peptide bond.
- The angle of rotation about the bond is referred to as the dihedral angle or tortional angle.
- For a peptide unit, the atoms linked to the peptide bond can be moved to a certain extent by the rotation of two bonds flanking the peptide bond. This is measured by two dihedral angles.
- One is the dihedral angle along the N–Cα bond, which is defined as *phi* (φ); and the other is the angle along the Cα–C bond, which is called *psi* (ψ). Various combinations of φ and ψ angles allow the proteins to fold in many different ways.
- Because of the planar nature of the peptide bond and the steric hindrance from the side chain R group, rotation of φ and ψ is limited. Therefore, only a limited range of peptide conformation.
- When φ and ψ angles of amino acids of a particular protein are plotted against each other, the resulting diagram is called a Ramachandran plot. This plot maps the entire conformational space of a peptide and shows sterically allowed and disallowed regions. It can be very useful in evaluating the quality of protein models.

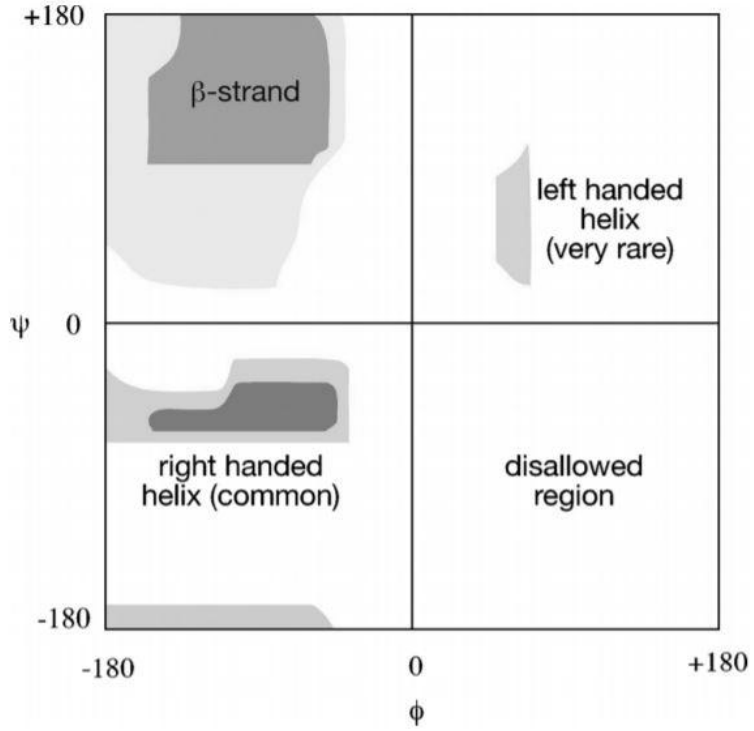


Figure 12.4: A Ramachandran plot with allowed values of ϕ and ψ in shaded areas. Regions favored by α-helices and β-strands (to be explained) are indicated.