

Protein structure and folding

BIOS 1006

20 June 2025

Objectives

- Know all definitions.
- Describe the reactions involving amino acids.
- Describe properties of the bonds in the polypeptide backbone.
- Describe and identify the different classes of protein structure: primary, secondary, tertiary and quaternary.
- Describe the importance of primary structure in protein folding and the relationships between proteins.
- Describe the properties of features, such as secondary structure elements and motifs, that are found in proteins.
- Describe the forces that stabilize tertiary and quaternary structures of proteins.
- Describe the properties of different protein types, classifications and architectures.
- Understand the role of free energy, dynamics, the forces involved and the factors that influence, aid or impede protein folding, shape and function.

Protein structure

Peptide/amide bonds

Dehydration synthesis or condensation reaction

Nitrogen with a lone pair attacks the carbonyl carbon of another amino acid, forming a covalent bond and releasing water. This requires energy and a **ribozyme** (enzyme made out of nucleotides, RNA) called a **ribosome** to catalyze the reaction.

Resonance structures

Electrons (usually in double or triple bonds, or lone pairs) can move around and be "shared" or "delocalized" over two or more atoms. This is called **resonance**.

Resonance hybrids result in the...

- C–N bond having **partial double bond character**.
- peptide bond being shorter and essentially planar. (sp^2 hybridized, trigonal planar)

Resonance structures have characteristics of both arrangements.

Resonance structures of the peptide bond

C_α on opposite sides of the amide bond = **trans** conformation (preferred form in proteins)

C_α on the same side of the amide bond = **cis** conformation (less common, leads to steric clashes)

Dihedral angles

- ϕ (**phi**) **angle**: nitrogen - α carbon, C–N– C_α –C
- ψ (**psi**) **angle**: α carbon - carbonyl carbon N– C_α –C–N
- ω (**omega**) **angle**: carbonyl carbon - nitrogen C_α –C–N– C_α
- Both rotatable

Key terms for peptides

residue an amino acid within a peptide

peptide molecule containing amino acids linked together

oligopeptide molecule containing less than 10 amino acids

polypeptide molecule containing more than 10 amino acids

proteins functional molecules consisting of one or more polypeptides

Levels of protein structure

Primary structure

The unique sequence of amino acids that defines a peptide or polypeptide; shows all covalent bonds.

Secondary structure

α -helices (cylinders/arrows) and β -sheets (arrows, N- to C-terminus) are connected by random coils

The α helix Looks like a spiral staircase, stabilized by hydrogen bonds between amide groups in the protein backbone. The hydrogen bonding pattern unique to alpha helix is that it requires hydrogen bonds between i and $i + 4$ (where i is the amino acid of interest) and are stronger than the hydrogen bond between a regular amine and carboxyl group.

- 3.6 residues per turn
- Pitch (distance between 2 identical points on adjacent turns): 5.4 Å (0.1 nm)
- Rise (distance between 2 identical points on adjacent residues, pitch/residues per turn): 1.5 Å (0.15 nm)
- Torsion angles: $\phi = -60^\circ$, $\psi = -45^\circ$

The β sheet