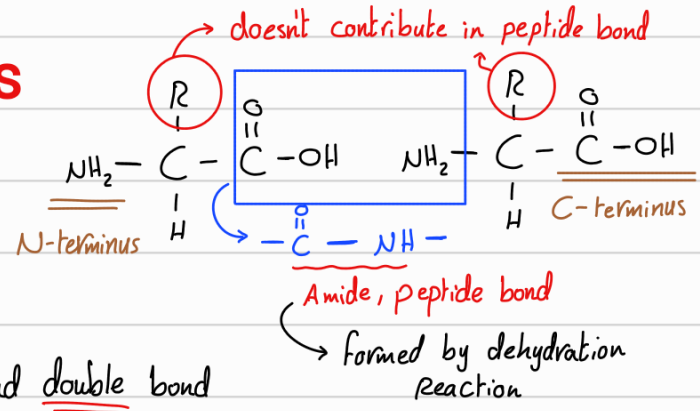
# Peptides




☆ Peptide ⇝ more than one amino acids linked by peptide bond

- Zigzag structure
- Resonance: shifting between single and double bond
  - No rotation ← Rigid

Each amino acid is about 110 dalton

☆ Back bone ⇝ H, α-C, $NH_2$, Carbonyl

☆ Side chain ⇝ R

☆ All amino acids can form H-bonds except proline ⇝ because it is a secondary amine

# Examples on peptides

## 1) Carnosine

- β-alanine + L-Histidine
  - Amino group on β-Carbon
- Protection against ROS and Muscle contraction

## 2) Glutathione

- γ-glutamate + Cystein + Glycine
  - Amino group on γ-Carbon
- Scavenging oxidizing agents by forming disulfide bonds with Cys of other molecule

## 3) Enkephalins

- Tyr + Gly + Gly + Phe + (Met / Leu)
  - C-terminus
- Analgesics (pain killer)
- Similar to opiate (morphine) due to aromatic (Tyr, Phe) residues

## 4) Oxytocin, Vasopressin

- Cyclic, 9 amino acids
  - by disulfide bond between 1-6 A.A
- have amide group on C-terminus to increase its half life and stability

☆ Oxytocin

- 3 ⇝ Ile, 8 ⇝ Leu
- Contraction of uterine

☆ Vasopressin (ADH)

- 3 ⇝ Phe, 8 ⇝ Arg
- Vasoconstriction, Water Retention, ↑BP

## 5) Aspartame

- has a methyl Ester (methanol) on C-terminus
- L-Aspartate + L-Phe
- artificial sweetner
- D-isomer ⇝ Bitter

Must be avoided for PKU patient

Phe hydroxylase defect → phenylpyruvate accumulate → Mental retardation

Alatame ⇝ Aspartate + alanine

Polypeptide ⇝ long chain of amino acids, without 3D structure

Protein ⇝ 1 or more polypeptide chains with a functional 3D structure

Native conformation

## Primary Structure

☆ Sequence of amino acids (polypeptide chain)

☆ determine other levels

☆ Isoforms are proteins have Similar function with a slight difference on primary structure

☆ Changes in the primary structure causes malfunctional Proteins

1) Sickle cell anemia (HbS)
   - β-chain, 6th A.A changed
     Glu → Val
   - defect in RBCs

2) Cystic fibrosis

## Secondary structure

☆ arrangement and rotation of backbone, stabilized by H-bonds

Connect

### Regular

1) α-helix
   helical rod with 3.6 AA per turn and 5.4 A° (pitch)
   ☆ R-group outward
   ☆ linear H-bonds
   ☆ X Glycine
   ☆ X proline
   ☆ X Close similar charges
   ☆ X β-branches (Val, Ile, Thr)

2) β-sheets
   ☆ 2 or more straight straight chains H-bonded side by side
   ☆ Can be parallel or anti-parallel
   ☆ X proline
   ☆ Aromatic + β-branches are common

### Non-Regular

Loops
- long
- No conserved Structure

β-turns
- Short, compacted
- Glycine + Proline are common

## Tertiary structure

- Overall polypetid 3D structure
- Interactions between R groups

☆ Shape determining interactions (Non Covalent)

1) H-bonds 2) Electrostatic
3) Van Der Waals 4) Hydrophobic

The most important

☆ Stabilizing factors

1) disulfide bond between thiol groups of 2 Cys forming Cystine
2) Metals → Iron in myoglobin (covalent)
   - Zinc in Carbonic anhydrase (salt bridges)

## Quaternary structure

Overall structure of protein with many polypeptide chains (subunits)

☆ Subunits are linked by disulfide and non-covalent bonds

☆ Immunoglobulin, Hemoglobin have Quaternary structure

## Super-Secondary structure: a region of the polypeptide with many secondary structures

1) Motif

Repetitive secondary structures
- structural modules
- not related to function

2) Domain

a large regoin which fold and function independently on the rest of the protein

3) Fold ⇝ many domains with a specific function

Fold > Domain > Motif

Denaturation: disruption of the native conformation by breaking non-covalent and disulfide bonds

The protein loses its properties and function, become insoluble (form aggregates)

Denaturing agents:
1) Heat ⇝ break Van Der Waals
2) Extreme pH ⇝ break electrostatic and H-bonds
3) Urea and guanidine hydrochloride ⇝ break hydrophobic and H-bonds
4) Detergents ⇝ Triton X100 (uncharged) ⇝ break hydrophobic
   ↳ SDS (anionic) ⇝ break hydrophobic & H-bonds
5) Reducing agent (β-mercaptoethanol, dithiothreitol) ⇝ break disulfide

all A.A Trans > Cis except proline

Renaturation ⇝ Returning the native conformation
- Chaperon ⇝ help misfolded proteins to refold, so prevent aggregation
- Cis-trans isomerase ⇝ Shifting between Trans and Cis conformations
- Protein disulfide isomerase ⇝ break and reform disulfide bonds

☆ Misfolded when accumulated ⇝ form aggregates, leading to disorders:

1) Prion disease ⇝ transmissible
misfolded prion disease
$PrP^C$ (α-helix) ⇝ $PrP^{SC}$ (β-sheets)
Examples: Creutzfeldt-Jacob disease (human)
Scrapie (sheep), Mad Cow disease

2) Alzeheimer disease
↳ not transmissible
accumulation of tau and amyloid protein due to misfolding in the APP

Apoprotein ⇝ protein contains only amino acids
Holoprotein ⇝ protein + Non protein (prosthetic group)
- ↳ Coenzymes (organic factors)
- ↳ Metals
- ↳ lipids, sugars, Heme, phosphate